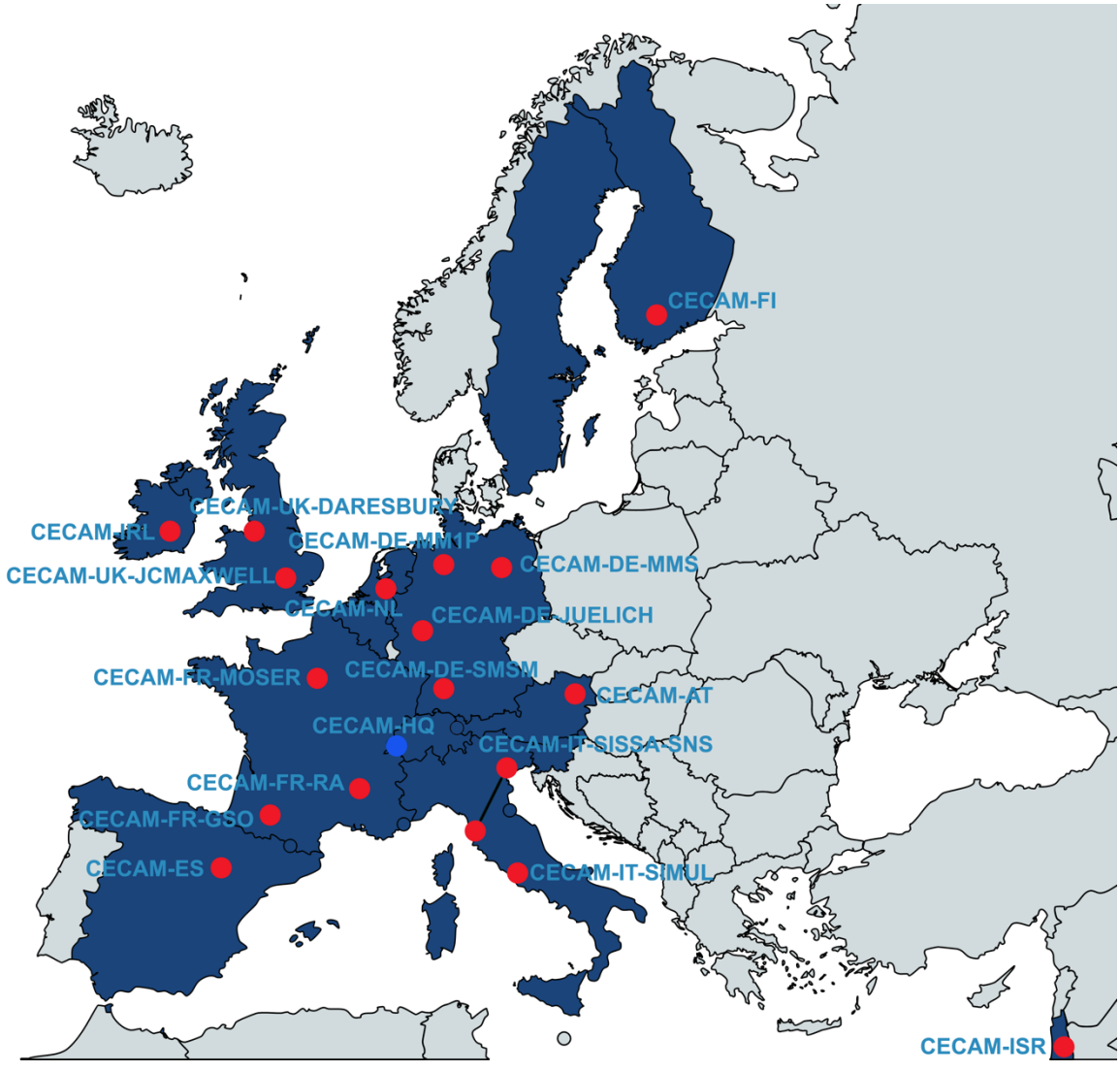
Workshops Scientific Reports

2018



cecam
Centre Européen de Calcul Atomique et Moléculaire

In 2018, the CECAM flagship program sponsored 53 workshops and 19 schools in the area of molecular and materials simulations. 13 workshops and 5 schools took place at the CECAM Headquarters in EPF-Lausanne, with an additional 3 workshops held in Switzerland at USI Lugano. 2988 scientists from 63 different countries were involved in these events. These figures consolidate the growing trend in activities and participation registered in the last few years. The nodes' contribution to the success of the flagship program is substantial and greatly benefits from the diversity and geographical spread of the CECAM network.

This publication presents the main findings of our workshop program as described in the scientific reports submitted to CECAM by the organizers. These reports demonstrate the variety of topics discussed at CECAM events, ranging from the traditional core areas of electronic structure and statistical mechanics to more recent domains including data driven science and genomics.

Reports from the workshop program of the E-CAM project (www.e-cam2020.eu) are also presented here. E-CAM is funded by the Horizon2020 program, coordinated by CECAM HQ and it involves 16 CECAM Nodes. The project implements a complementary set of actions in software development, training and interactions with industry with the medium-long term goal of creating applications and competence to fully exploit high-end HPC capacities in Europe. Post-doctoral and software engineer fellowships are directly funded by the project and, in the first three years of the project 10 fellows and 3 software engineers have been deployed in institutions affiliated with 13 nodes across the network. CECAM contributes to the project, which has considerably enhanced collaborations between nodes and scientists in our community, by funding 4 Extended Software Development, 2 State of the Art, and 2 Scoping (industry oriented) Workshops per year.

This publication documents the excellent health of CECAM, the longest-standing European institution devoted to promoting research in modelling and simulations, as it approaches 50 years of existence. It also provides an engaging and complete description of the state of the art in well-established and new domains of simulation. Scientific excellence, timely selection of topics, a friendly and open environment to foster discussion and promote interactions of leaders in the field and new practitioners among themselves and with each other are at the core of our service. We are committed to continue along the same path, benefitting from the invaluable input and work of the community that recognizes, establishes and sustains CECAM's role as a global key player in our domain.

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E-CAM Workshops 2018

Anharmonicity and Thermal Properties of Solids

Location: CECAM-FR-MOSER
Webpage: https://www.cecam.org/workshop-0-1397.html
Dates: January 10, 2018 to January 12, 2018

1 State of the art

In numerous fields of research, the behavior of materials as a function of temperature is a key quantity for both fundamental and practical or applied purposes. For a long time, the thermal evolution of material properties has been evaluated in the framework of classical simulations. A large number of methods has been proposed and implemented successfully, in order to take temperature/entropy effects into account explicitly. Due to their historically prohibitive computational cost, the works evaluating the temperature dependency of electronic and lattice dynamics from an ab initio point of view have been much scarcer. Apart from some pioneering works, these calculations mainly extrapolated ground state results to non-zero temperature by means of the so called quasi-harmonic approximation (QHA).

In the past ten years, strong efforts have been made to take into account explicit temperature effects and major advances have been obtained. New methods capturing the thermal properties of solids at non-zero temperature are now available and can be applied in ab initio calculations. These approaches combine ideas including finite large displacements, molecular dynamics sampling, self consistent harmonic theories, and different force fitting schemes.

2 Major outcomes

This workshop has been a strong opportunity for many scientists to exchange together. Many scientific questions took place, some of them have been widely discussed along the meeting, other ones were punctually debated:

-The first concerns the reproducibility of experimental results by the various codes developed around the world. A strategy to compare different implementations / approaches has been proposed in order to evaluate differences or convergences between codes. The presence of leading experimentalists has been decisive for this purpose. Some of them have not hesitated to highlight the differences in theoretical results that sometimes exist between codes / approaches.

-The second discussion is rather a debate. This one took place during the presentation of some results showing that the negative thermal expansion of silicon could be explained by the new approaches. Actually, this point had already been solved in the past (30 years ago) using a coarser approach (QHA). This fair discussion made it possible to distinguish what was

the contribution of the new approaches compared to the old ones. If the QHA approach can explain the thermal expansion of silicon, on the other hand this method completely fails to describe the variation of phonon modes. Using recent approaches, these two features are well reproduced.

-The third discussion focused on the distinction between perturbative and self-consistent approaches. Are the first ones still able to account for the phenomenon when the anharmonicity becomes very important? Are the seconds able to extract all the quantities of interest and to describe all the shapes of anharmonicities? The debate was still open at the end of the workshop and no definitive conclusion was provided.

-The fourth discussion was rather a leitmotif of the workshop. How to reduce the computational cost (time and resources) of these simulations? Several interesting approaches have been proposed: to generate the minimal number of configurations using stochastic approaches rather than molecular dynamics, to minimize the useful parameters of the problem, to optimize the calculations by taking even more account of the symmetries ...

All these interesting discussions (to which many participants have taken part) have paced these 3 days of conference.

3 Community needs

To date, we are not aware of the needs of the community in terms of computing resources. It seems that everyone has its own supercomputers / clusters, or at least has sufficient computational resources available where he is.

In the opinion of all, this conference was timely. The main request formulated (in particular to us, as organizers) was that such conference could be repeated regularly (every two years). For three reasons:

- If most of the participants knew each other by name (through published articles or developed methods) very few knew each other in real life. The workshop was therefore a first opportunity to get to know many participants.

- Moreover, if one wishes to progress and advance this field of science (by developing and comparing the codes for example, but also to generate collaborations with experimentalists), it becomes necessary to set meeting points. These will allow to set deadlines, and to federate for this purpose.

-It would be also important for young scientists (PhD or post-docs) to show their results and prensent themselves to the community. Several (around 10) were present at this meeting.

Therefore, a series of CECAM workshops on this subject would be greatly appreciated. As a first step, a second meeting could take place in Paris at the beginning of 2020.

4 Funding

We have benefited from several sources of funding for the organization of this workshop:

- The allocation of CECAM (12 000 euros)
- Funding from Psi-K (5,000 euros)
- A grant from CEA (2,000 euros)

If we have the possibility to organize this workshop again, other sources of funding could be envisaged (GDR, ERC ...), especially if the workshop focuses on a specific application (earth and planetary science, thermal conductivity ...).

To our knowledge, no joint research proposals were discussed during the meeting.

5 Will these developments bring societal benefits?

We didn't think that the theoretical/computational developments discussed during this workshop could "bring societal benefits" (in the short term) concerning sustainability, health... The only benefit that could be expected is economic for the industry.

The third and last day of the conference was devoted to thermal conductivity (low or high). During the morning, many studies were presented. Some of them have shown that an automation of structural research and calculation of thermal conductivity is possible and allows the discovery of new materials with the desired thermal properties.

In particular, two works have investigated thermal conductivity in a high-throughput fashion by:

1/ using machine learning methods

2/ computing interatomic forces as a function of temperature by means of ab initio calculations (which was widely discussed the two first days of the meeting)

3/ solving the Boltzmann transport equation (discussed the third day).

The applications would be numerous in the field of thermoelectric materials, heat sink materials, thermal medical devices...

6 Participant list

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Frontiers in Computational Biophysics: Understanding Conformational Dynamics of Complex Lipid Mixtures Relevant to Biology

Location: CECAM-Lugano, Lugano, Switzerland
Webpage: https://www.cecam.org/workshop-0-1452.html
Dates: January 10, 2018 to January 12, 2018

1 State of the art

Cell membranes are complex assemblies that regulate a wide variety of cell functions. A wealth of knowledge has been produced about the properties and behaviour of simple lipid systems, and even more complex membranes, by the use of biophysical experiments and computer simulations.

Cells contain a large number of lipid species, exceeding at times the number of genes in many organisms. Human health and disease is linked to membrane biology. It is essential to understand the functions of membrane lipids in cell biology and physiology. The regulatory role of the complex lipid composition in cell functions is, however, not well understood, and the potential to enhance the performance of lipid-based materials through the use of complex biological mixtures remains unexploited. Nanobiological engineering at the cellular level has been proposed to be the next great revolution in both medicine and nanotechnology. Fundamental understanding of the relation between cell structure and function is arguably the greatest challenge in developing systems that can mimic biological processes, or that can be engineered into functional bionanomaterials.

From a computational perspective, methods and hardware are at the stage where we can study cell membranes realistically. To this end, a comprehensive understanding of conformational dynamics of complex lipid mixtures relevant to biology is needed, and how to approach this was addressed in the workshop.

Judging from the presentations and discussions, there is currently strong coupling in the field between simulations and experiments. Experimental groups appreciate the ability of simulations to suggest new theories or approaches, whereas computationally-oriented groups rely on experiments for ideas and validation.

2 Major outcomes

The workshop included 30 oral presentations (6 of them by students), each of which was followed by a 10-min discussion, poster presentations including flash oral presentations of the posters during the lunch breaks and two discussion sessions. Major scientific points that were discussed included new directions in computer simulations of lipid membranes, coupling between simulation and experiment, and education.

New directions in simulations of lipid membranes:

For many years, simulations have considered a uniform presentation of lipid membranes, where membranes were modelled as flat bilayers of 1-2 types of common lipids, and sometimes also cholesterol. Developments of tools to build membranes of different compositions, atomistic and coarse-grained force-fields and topologies have in the recent years led to the possibility of modelling more complex systems. Those included membranes of more realistic compositions (with multiple types of lipids as presented in cells), geometries and sizes. In the workshop, the membrane response to the presence of peptide or mechanical forces was discussed. Altogether, the field appears to move towards an era where the complexity of the membrane in different topologies (flat bilayers, organelles, liposomes for drug delivery and bicelles) will be considered.

Coupling between simulation and experiment:

Different views on the coupling between simulation and experience were discussed. Experimental scientists participated in the meeting (over one third of the participants). Some of them have, in recent years, recruited senior scientists that are mainly involved in carrying out simulations as they recognised the limitations of experiments in terms of resolution and timescales. An important outcome of the discussion was that computationally-oriented scientists were encouraged to try and present their work in meetings that were oriented towards experimental biologists. Interestingly, many theoretically-oriented scientists presented some experimental results and vice-versa, showing de facto that the coupling between biochemists and theoretical biophysicists is rather good.

Education:

During discussion the issue of first cycle education (B.Sc in chemistry and biology) came out several times. It became apparent that in some institutes, undergraduate students are exposed to the concepts of molecular simulations and programming early on, and that many student appreciate the opportunity to practice chemistry or biology in the computer. On the other hand, it was clear that aversion towards calculations persists among many students, despite the clear significance of quantitative approach to fields such as systems biology.

3 Community needs

Community needs were discussed in the discussion sessions. Experimetalists and theoreticians alike mentioned the need for some repository of simulation trajectories and input files. Such a repository could be useful for post-analysis of the results, and enable other groups to view the simulations without relying on animation files, focusing on any region of interest.

Many participants mentioned their wish for events similar to this CECAM meeting in the future. It was apparent that the mixture of theoretically-oriented and experimental scientists of various career stages was good. It is also worth mentioning that there was a waiting list and not all the applications received to participate in the workshop could be accepted.

The need for computational infrastructure was discussed following one of the lectures. Systems that contain lipid membranes are typically larger than systems that are used in simulations of soluble proteins or polymers, and the anticipated complexity of systems that will be studied will further increase those requirements. There will be a need for systems that would allow not only running of the simulations but also streamlined storage and analysis.

4 Funding

Most presenters acknowledged funding from national sources and less commonly from the European Union. Collaborative studies were mentioned, but those were usually funded by the respective parts rather than a common source. There is a limitation in the possibility to fund collaborative research in the subject in mainland Europe. EU research funding schemes most often take a top-down approach, i.e., they have very specific aims that do not necessarily align with the needs of the scientific community that deals with bio-molecular simulations. The UK usually awards funding to collaborative research; this has some limitations but may work out for scientists in the field, where experiments and simulations are tightly coupled.

We applied for funding to FEBS (Federation of European Biochemical Societies) to co-sponsor this workshop but the application was not successful because 'the event was an already established CECAM work'. Similar response was received from Biophys.Soc.

5 Will these developments bring societal benefits?

The workshop dealt with biomolecular simulations, the outcome of which could carry clear societal benefits. Work that can lead to better understanding of diseases was discussed in several presentations. Other scientists presented studies related to drug delivery, or to gathering knowledge on diseases of crops. The importance of lipid membranes within all domains of life was clearly demonstrated, and so was the usefulness of simulations in their study. Any genetic or pathogenic alternation of the membrane may lead to severe diseases, and it is not always clear why and how without the use of simulations that yield molecular pictures of the perturbed lipid structures.

Although drug-design was not the main topic, the importance of membrane proteins as drug targets was mentioned and cannot be overstated. Without correctly addressing the membrane, simulations of membrane proteins cannot be realistic.

Last but not least, it became clear that tools developed for theoretical studies of bio-membranes were later used in many other areas, from modelling of sugars and polymers by coarse-grained force-field to the development of new search engines inspired by the wish to study peptide-membrane interactions. This is a clear demonstration for the strength and significance of curiosity-driven basic science.

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CECAM-Lorentz Joint Workshop: Multiscale-Modelling of Nucleosomes and Their Positioning on DNA

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1410.html
Dates: January 15, 2018 to January 19, 2018

1 State of the art

About three quarters of our DNA is wrapped around protein cylinders forming nucleosomes. The location of nucleosome binding is known to be biologically crucial, e.g. to be closely connected to epigenetics via methylation patterns. As the DNA is strongly bent in a nucleosome the affinity of a given stretch of DNA depends on its elasticity and shape as encoded in its letters, i.e. the nucleotide sequence as well as on methylation patterns and other base modifications. In addition, mechanical cues can also be written on top of genes exploiting the fact that the genetic code is degenerate. This suggests that DNA molecules have evolved mechanically to guide their own packaging on nucleosomes which in turn affects the expression of their genes.

To understand the role of sequence-dependent DNA elasticity in gene expression requires the coordinated effort of many different theoretical and simulation groups with expertise ranging from all-atom molecular dynamics simulations of DNA, building of coarse-grained mathematical models of DNA and nucleosomes up to bioinformatics approaches that study properties of whole genomes, as well as of course actual experimentalists. This is the right time to set such a concerted effort in motion as high quality data are pouring in almost daily ranging from single-molecule experiments up to genome-wide nucleosome cartography for many organisms.

2 Major outcomes

The program consisted of 21 full talks (1 hour) and 4 short talks (30 minutes) and about 15 posters. The talks covered a wide range of approaches from analytical work, coarse grained modelling, all-atom simulations, bioinformatics approaches, to experiments. There were lively discussions during and after each talk. The progress in this field over the last 20 years has been tremendous. It became clear that a major step forward was taken 20 years ago when the artificial 601 nucleosome positioning sequence was extracted in the lab of the late Jonathan Widom, as nearly all of the current experiments and many simulations reported at this workshop were based on that sequence.

These are exciting times, as the level of detail that is possible on the experimental side (e.g. through FRET, mechanical micromanipulation, cryo-EM, small angle X-ray diffraction, DNA looping experiments…) has reached a point where a detailed modelling is necessary and, as the result of increasing computer power, possible. For instance, the mechanisms underlying chromatin remodellers was up to recently only understood schematically but progress in cryo-EM allows now to build detailed models, many of which were presented in this workshop. In order to do so DNA mechanics at the base-pair level needs to be accounted for. We learned

at this workshop about the huge progress in various coarse grained descriptions of the DNA double helix. Which model is the “best” model is still under debate and this might also depend on the problem to be studied. Such models are necessary to come to a mechanistic understanding of nucleosome positioning on DNA. Exciting new results show that mechanical signals that position nucleosomes in humans and various other vertebrae are indeed widespread.

Of great interest are also the structures beyond single nucleosomes. Whereas at very large scales there is tremendous progress based on a range of techniques (chromosome conformation capture methods, a subject that the organisers deliberately left out), the conformations of just a dozen neighboring nucleosomes (or even just two of them) remains still unclear. The classical textbook view of the chromatin fiber is currently in a crisis as there is not enough evidence that such fibers exist in living cells. Many fiber models rely on regular spacings between nucleosomes as they can be assembled in vitro using regular arrays of the 601 sequence. These structures show rich properties and can be studied by a variety of methods, as discussed in this workshop by several speakers. But it is unclear how a longer fiber could form inside a living cell, as nucleosomes are to our knowledge not evenly spaced. An exiting highlight of this workshop was a preliminary report of a new technique that allows to pull on a single gene that was extracted from a cell. Remarkably the force response of this gene shares strong similarities with the behavior of regular in vitro chromatin fibers. This demonstrates that chromatin fibers remain a hot topic.

In short, we learned that the strongly interconnected fields of DNA mechanics, nucleosomes and arrays of nucleosomes (“chromatin fibers”) are currently making huge progress by combining clever experimental methods (often using several methods in one setup) and coarse grained modelling of DNA, nucleosomes and chromatin fibers. In addition, progress in all-atom molecular dynamics gives it now predictive power providing important additional insights.

3 Community needs

At this point there is a huge number of open questions. To a large extent this is the case because nucleosomes are complex objects with many degrees of freedom, hard to work with experimentally and hard to model. As this workshop demonstrated, there is a wide range of models used in this field and it is not quite clear which are the best models. Currently we still need to make many choices when building a model, e.g. which DNA model to use and how to account for the interaction of the model DNA to the protein core. Many models use at this point still representations of DNA that cannot account for important effects, e.g. the stiffening of A-tracts which in turn repel nucleosomes from such regions. Important will also be to account for DNA methylation to study its impact on nucleosome positions or the effect of posttranslational mutations of the histone tails and how they influence the interactions between nucleosomes.

The workshop demonstrated that we are still at a stage where we have to accept the presence of many competing models. There might be a good reason to use different models depending on the level of detail one is interested in. E.g. some current models can predict the positions of nucleosomes genome wide, whereas other can provide detailed insight on nucleosome dynamics for a few given sequences.

The progress on the experimental side provides now increasingly detailed data so that models can be ranked according to their prediction successes. What seems to be needed most for this community is to meet regularily and to make new connections between members of this community. This workshop has provided many such new links which we believe will strengthen our community. This is crucial in a field where members have very different backgrounds.

4 Funding

The event was funded by CECAM and the Lorentz Center. We are not aware of external funding sources that could finance an event like ours. Joint research proposals were not discussed at the meeting, at least not on the formal level.

5 Will these developments bring societal benefits?

Unlike in bacteria, the nucleosome, not bare DNA, is the substrate that the machinery of the eucaryotic cell has to deal with. The positions of nucleosomes and their stability profoundly influence a wide range of essential processes, such as gene regulation, transcription, replication, recombination, chromatin breakage, retroviral and transposon integration sites, mutations, DNA repair, and nucleosome retention in sperm cells allowing the transmission of epigenetic information from fathers to offsprings. The recent progress in our understanding of DNA mechanics, nucleosome energetics and dynamics and chromatin fiber geometry and energetics suggests that we might be able to eventually achieve such predictive capabilities that we will be able to understand in depth e.g. how a normal cells turns into a malignant cancer cell, or how it could be turned back to a normal cell. We have still far to go to achieve such a goal but we begin to get a grasp at a quantitative understanding of various key elements.

6 Participant list

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Electronic Structure Library Coding Workshop: ESL Demonstrator

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1425.html
Dates: February 5, 2018 to February 16, 2018

1 State of the art

Electronic structure methods and software still overwhelmingly work on a paradigm of separate complete programs that are self-contained and depend only on the compiler and a few basic libraries. Because of this, most of the large codes independently maintain routines providing overlapping functionalities and make use of non-universal data formats. Furthermore, the complexity of the separate programs keeps on growing, in order to keep up with the theory as well as computer hardware. This makes it increasingly difficult for scientists to contribute new ideas built on top of existing software, without becoming deeply involved with the development of a specific package.

At the moment it is widely recognized in the community that these are important, yet unsolved, problems. There have been and there are a few notable efforts to go beyond the traditional paradigm by producing communal software and libraries that are agnostic to the specific electronic structure code in which they are used. Examples include visualization, symmetry analysis, the computation and use of maximally-localized Wannier functions, libraries for exchange and correlation, and data structures and standards.

In 2014 the Electronic Structure Library was launched in collaboration with CECAM, with the idea of fostering a new paradigm of library-based development for electronic structure, following the promise of the early examples mentioned above. The aim of project, therefore, is to create a common online repository of high-quality software libraries, programming interfaces and data standards in the field of electronic structure, which will facilitate reuse of code, interoperability between different code bases, rapid and efficient evolution to new computer architectures, and development of new methodologies.

2 Major outcomes

The main objective of this coding workshop was to write a simple DFT code from scratch using as many software libraries from the CECAM Electronic Structure Library as possible and without having to implement any complex numerical routines. Such demonstrator code will provide powerful, non-trivial examples of how the ESL libraries can be used by existing electronic structure codes. It will also provide a platform to test the performance and usability of the libraries in an environment as close as possible to real-life situations. With these ideas in mind, and after surveying the software libraries that are currently part of the ESL and the know-how of the participants, it was decided to write a demonstrator code capable of performing calculations using two types of basis sets: plane-waves and atom-centred atomic orbitals. These two types of basis-sets require different numerical methods to solve the Kohn-

Sham equations and pose very diverse challenges. The writing of this demonstrator code was successful and it is accessible through the E-CAM gitlab:

https://gitlab.e-cam2020.eu/esl/esl-demo

A second topic addressed during the workshop was the distribution of the ESL software libraries. Three distribution channels targeting different types of users have been chosen:

1) Packages for the more popular Linux distributions, providing a simple and straightforward way for users who are not experts in compiling complex pieces of software and their dependencies to have a working version of the libraries installed on their personal computers.
2) Specifications to integrate the ESL libraries into the EasyBuild framework (URL), which is a powerful and efficient software manager for HPC systems.
3) The ESL bundle, incorporating all the ESL libraries into a single package and using a unified framework for compilation and installation. This targets users who wish to compile and install the libraries themselves.

Distribution channels 1) and 2) are already at least partially covered, so it was decided to focus our efforts on the ESL bundle. The JHBUILD framework was chosen for compilation and installation and a dedicated project was created on the E-CAM gitlab:

https://gitlab.e-cam2020.eu/esl/esl-bundle

By developing the demonstrator using the versions of the libraries currently included in the bundle, it was possible to ensure their compatibility.

The participants engaged in extensive discussions regarding the future of the CECAM ESL. The writing of the demonstrator code highlighted tasks and topics not covered by the existing ESL libraries, namely tools for k-point generation, preconditioners for the eigenvalue problem, and mixing of density/potentials during SCF.

Presentation of the Molecular Sciences Software Institute showed that there are several areas where the two projects can collaborate, like sharing of experiences and best-practices, but also the establishment of common data-standards and cooperation in software development.

Participants also expressed the wish for better communication of ESL activities and to participate in ongoing discussions. As a result, it was decided to create a mailing list.

Finally, one of the main challenges identified by the participants is the sustainability of the entire project. Although the ESL development started as an initiative of CECAM and has been supported by the E-CAM centre of excellence, it still relies mainly on contributions from volunteers within the electronic structure community.

3 Community needs

Currently most of the needs of the ESL in terms of infrastructure and event organization are well covered: we have been using the existing E-CAM infrastructure and CECAM, E-CAM and Psi-k have contributed towards the organization of a successful series of workshops. We can only wish this support to continue.

On the other hand, one recurrent request since the start of the ESL project has been the availability of people with the time and skills to contribute to the development of the ESL software libraries and their integration within the community codes. Being developed mainly by a group of volunteers, the amount of time they can dedicate to the project is limited, and this has been the main bottleneck in the ESL development.

Concerning the topics covered by the ESL, the participants of the workshop pointed out a few areas not presently covered that would be of interest for the electronic structure community:

- tools to handle and generate k-point grids
- mixing of density/potential during self-consistent cycle procedures
- preconditioners for eigensolvers and mixing
- geometry optimization

4 Funding

Traditionally there have been few funding channels specifically aimed at the development of scientific software. Some calls, like the ones held by PRACE and other Horizon 2020 programs, are meant for optimization and porting to new architectures of existing applications. One obvious funding channel for the ESL is the E-CAM Centre of Excellence, which has already contributed to several ESL activities.

ELSI, one of the ESL components, has been funded by a Software Infrastructure for Sustained Innovation - Scientific Software Integration (SI2-SSI) software infrastructure project from the US National Science Foundation. We will explore the possibility of applying for similar projects.

Another source of funding for ESL activities is Psi-k. Recently there has been a reorganization of Psi-k's working groups and there is now one specifically dedicated to software engineering, where projects like the ESL fit perfectly.

5 Will these developments bring societal benefits?

Scientific software has become an essential tool used by researchers in many domains. In the field of electronic structure theory, a large ecosystem of codes is nowadays routinely used to compute a great variety of properties of solids and molecules, both in academia and in industry. Many of these codes have evolved into complex packages spanning hundreds of thousands of source code lines and are developed by large, multidisciplinary teams. Therefore, anything that improves the development process of these codes can have a tremendous impact in a huge range of applications.

The Electronic Structure library aims at providing layers of functionality within modules which are general, standardized and efficient. In this way, new ideas, and new science, can be coded by scientists without needing to rewrite functionalities that are already well-established, and without needing to know more software engineering than science. In other words, it allows to separate the coding effort for cutting-edge research from the software infrastructure it rests on top of, which needs maintaining and rewriting at every step of the hardware race.

6 Participant list

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3rd NOMAD (Novel Materials Discovery) Industry Workshop

Location: Cumberland Londge, Windsor, Berkshire, SL4 2HP
Webpage: https://www.cecam.org/workshop-0-1572.html
Dates: February 5, 2018 to February 6, 2018

1 State of the art

The objectives of NOMAD Center of Excellence (CoE) include the creation of a materials encyclopaedia, the development of Big-Data analytics and advanced graphics tools for materials science and engineering. These goals are complementary with those of the other two CoEs supported by the European Commission and active in the field of CECAM activities (E-cam and Max). The NOMAD Researchers are currently creating a large, homogenized materials database, as well as the analytical tools and code developments necessary to extract information from it. We are confident that the available HPC infrastructure and the envisaged developments will contribute to the discovery of new scientific phenomena, novel devices, and advances in materials science and engineering. An essential corner stone of the project is the NOMAD Repository which contains the produced data in the form of input and output files of many high-quality calculations performed by fellow researchers working all over the world. The Repository is unique as it is not restricted to a few simulation programs but it accepts entries from all relevant codes. As of early January 2018, it contains results from more than 50 million total energy calculations, corresponding to more than 2 billion CPU-core hours used on high-performance computers all over the planet. Recently, there has been a very significant growth of industrial interest (from large companies as well as SMEs) in computational materials science, motivated by the innovation potential of new materials and improved existing materials. However, the scientific complexity of the topic and the heterogeneous and fragmented nature of the research field make it difficult to translate research leadership into accomplished innovation. Thus, it is particularly important at this point in time to bring materials modelling closer to industrial/societal exploitation in real terms. We think that workshops with industry representatives are indispensable to gather such feedback.

2 Major outcomes

Industry Networking:

NOMAD gathered very useful feedback from industry in its strive to determine how to make NOMAD useful for industry. Based on feedback from industry representatives and industrial advisory committee (IAC) members, several recommendations have been made some of which were already implemented. For example, an on-site usage of the platform has been provided for industrial users during the development. In order to ensure uptake of NOMAD tools and services by industry, the NOMAD team wishes to ensure that there are minimal barriers to use for industry users. Industry representatives have suggested the possibility of facilitating in-house usage of NOMAD to minimize potential intellectual property rights (IPR) issues. Furthermore, several groups within NOMAD are currently involved with developing case studies, some of which were showcased at the CECAM workshop to illustrate practical application of the NOMAD tools.

NOMAD Encyclopaedia:

NOMAD Encyclopaedia is accessible to various types of users (engineers, material scientists, non-experts) and provides general reviews and statistics via a WEB interface. Up until now, over 400,000 materials have been registered. As a result of the suggestions collected during the industry meetings, a series of new features have been introduced. Among others, this includes a newly developed user-friendly GUI, which enables users to perform property-based searches. Upon feedback from the workshop, the NOMAD team will add more specific system types and methodologies to the already existing features.

NOMAD Big-Data Analytics Toolkit:

The objective of the NOMAD Big-Data Analytics Toolkit is to facilitate the design of new materials with desired properties; many of the tools apply machine-learning methods to data originating from computational high-throughput methods.

The structure of the NOMAD Big-Data Analytics Toolkit is a combination of a software framework and notebook representation of the actual analytic task.

Acting upon feedback from the workshop, the NOMAD team will keep extending the breadth of its analytic tools, in terms of both methodology and example cases.

NOMAD Advanced Graphics:

The innovative methods developed within this NOMAD work package allow both for local visualization running on researcher's workstations, as well as remote visualization tools running on HPC clusters. Local visualization tools also cover immersive virtual reality (VR) environments. Local tools are complemented by remote visualization tools, which allow for visualization of datasets too large for ordinary workstations, but with a lesser degree of interactivity. The general feedback gathered at the workshop pointed at establishing a closer integration between the Advanced Graphics and the NOMAD Encyclopaedia. After a previous workshop on the visualization tools took place in September 2017, a specific one for VR tools usage is now being planned (April 2018), open to the participation of industry representatives.

Outreach and connecting academia with Industry:

A special student-oriented tutorial on Machine-learning and VR based on data contained in the NOMAD repository relative to an industry case study was run during the workshop, which turned out to be much appreciated. Feedback was also gathered on the perceived exposure of materials modelling students to the practices and needs of industrial R&D, which turned out to be deemed largely insufficient by over 90% of the attending students and young researchers.

3 Community needs

The two main concerns emerged in discussions with the workshop industry delegates addressed IP and Sustainability issues, while a considerable time was spent addressing issues related to data quality and usability. Furthermore, dissemination measures and how to increase the visibility of NOMAD were also addressed as one in need of attention. In this context, the case studies presented at the workshop to demonstrate NOMAD value have been initiated and are in continuous development, to help internal publicising of the value implied collaborating with the NOMAD team. In more detail, the emerging consensus was that:

IP: A top priority is to protect commercial data, which should be allowed not to leave commercial environments. NOMAD's tool and data should be able to be downloaded and kept behind the industrial firewalls before performing any kind of data analytics on it. The local installation of data analytics tool also raises the issue of managing sensitive data and IP, while the suggestion that part of proprietary data might be volunteered to the public at large was received with mixed enthusiasm among our attending industrial partners.

Data and Usability: The wish for more tutorial services (training material/courses) and a user-friendly GUI interface to reduce the barrier to use the NOMAD tool was meanwhile clearly expressed and iterated. Searches for properties, rather than materials as well the integration of additional data on a wider range of material properties and experimental data etc. are features that, it was felt, greatly improve the usability of NOMAD. One of the main challenges of using NOMAD for industrial R&D remains how to combine in-house data with NOMAD's data for cross-analysis, as for this the in-house proprietary data must be similarly formatted, and must be of a similar quality to NOMAD. Delegates greatly appreciated NOMAD's effort to be visible, to continuously develop case studies, and to guarantee the safeguard of archived data.

4 Funding

The NOMAD initiative originates from a merging of two projects (the NOMAD Laboratory CoE and the NOMAD Repository) and receives funding from the European Union's Horizon 2020 research and innovation programme. On the long-run, applying for a second funding phase beyond the current Horizon 2020 funding is perceived as strategic and is currently at an advanced stage of planning. The Max-Planck Society has already guaranteed to reassurance the lifetime of the NOMAD Repository for 10 years from last data upload. Concerning more short-term related funding topics it was agreed that many activities necessary for reaching out to SMEs (such as, e.g., webinars) will be practically feasible that need a lower level of commitment, and low-costs.

5 Will these developments bring societal benefits?

Considering that one of the main goals of NOMAD is to be useful to the industry and work in close collaboration with them, the project is already successfully delivering several societal benefits:

- It is setting a standard on how to deal with large as well as small-sized datasets (for both quality and consistency).

- It enables efficient searches for a wide range of materials properties thus enabling the selection of the most promising materials for specific applications, as needed in industrial R&D. This involves significant saving time and economic resources, which will be beneficial for the industry. Discovering how to fine-tune NOMAD's tools to respond to industry needs was actually a main scope of the workshop.

- It is promoting a constructive resource- and information-exchanges between industry and research institutions, and to some extent among industry itself.

- It is encouraging and facilitating student placements as well as academic stuff embedding in industry (the workshop was, in the event, a venue where industry-generated job vacancies for young people with a background in data science could be announced and circulated).

- It is contributing to close the gap between academic and industrial research boosting communication and collaborations.

6 Participant list

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Frontiers of Electronic Structure: Correlated Electron Materials

Location: Berlin, DPG/EPS Spring Meeting of the Condensed Matter Section (SKM) together with the EPS Berlin, 11 March - 16 March 2018
Webpage: https://www.cecam.org/workshop-0-1557.html
Dates: March 11, 2018 to March 16, 2018

1 State of the art

Exploring, understanding, and describing materials with strong electronic Coulomb correlations remain among the big challenges of modern condensed matter physics. Correlated materials are characterized by an extreme sensitivity to external probes such as pressure or temperature, and slight changes in composition, constraints during the growth process (e.g. by heterostructuring) or off-stoechiometries can significantly alter their properties. As a result, even a qualitatively reliable theoretical description may depend on quantitative details of the electronic structure, stressing the need for both, an accurate treatment of many-body effects and first principles techniques with predictive capabilities. The task is even harder as, in general, the properties of correlated materials display intrinsic non-trivial temperature dependences (in particular beyond simple Fermi factors) and many of the most intriguing phenomena involve excited states.

Despite of these challenges, the field is rapidly evolving, and progress at the many-body theory and first principles frontiers, as well as at their intersection, is substantial. Moreover, recent developments in machine learning and data science promise to greatly extend the scope of many-body methods and improve our ability to discover new correlated electron physics.

2 Major outcomes

The goal of our symposium was to give an overview of recent developments in the field of correlated electron materials. Various strategies of approaching the problem from a combined first principles many-body perspective were presented, along with applications to recent materials questions.

Invited Speakers and the titles of their talks at the symposium were:

- Ali Alavi (Max Planck Institute for Solid State Research, Stuttgart, Germany) - Recent developments in FCIQMC: real-time propagation and improved convergence with walker number
- Gabriel Kotliar (Rutgers University, USA) - Computational Approach to the Electronic Structure of Strongly Correlated Materials: Towards Theoretical Spectroscopy and Theory Assisted Material Design
- Katarzyna Pernal (Lodz University of Technology, Poland) - Correlating electrons via adiabatic connection approach: a general formalism, approximations, and applications

While the invited lectures had a focus on correlated electron materials, the symposium covered the general field of computational materials and electronic structure theory with more than 70 contributed talks and 15 posters. This was an official symposium at the DPG/EPS Spring Meeting, hosted by the Surface Science Division of the DPG and more than 100 participants of the DPG/EPS meeting joined the symposium.

More information can be found here: https://th.fhi-berlin.mpg.de/meetings/DPGSym2018/

CECAM ENDORSED THIS MEETING, BUT DID NOT PROVIDE ANY FINANCIAL SUPPORT.

3 Community needs

This type of symposium should continue.

4 Funding

5 Will these developments bring societal benefits?

6 Participant list

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Electrostatics in Concentrated Electrolytes

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1423.html
Dates: March 20, 2018 to March 23, 2018

1 State of the art

Concentrated electrolytes are ubiquitous in biology and industry and have been studied since the 19th century. However, a series of recent experimental and computational results suggest that the conventional wisdom requires substantial revision. For example, recent surface force measurements show that the interaction between charged surfaces in a concentrated electrolyte is long-ranged and the screening length increases with ion concentration ("underscreening"), and the oscillation wavelength of the structural force abruptly "switches" as a function of concentration. This is at odds with liquid state theories in the literature. Recent studies have also revealed surprises in the arrangements of ions near electrochemical interfaces: the differential capacitance of ionic liquid-solvent mixtures is experimentally shown to be a non-monotonic function of composition, and a voltage induced phase transition is observed in simulations. A theoretical picture of ions driven far from equilibrium is elusive yet important for understanding physical phenomena such as phoretic effects and the use of electrolytes as lubricants.

Almost parallel to the large body of literature about the "physics" of concentrated electrolytes is the study of the "chemistry" of electrolytes. Water and aqueous electrolytes are a well-known tough nut, but an understanding of the chemistry of polar solvent and organic electrolytes is important (yet equally challenging) as they are often used in batteries and supercapacitors. Room temperature ionic liquids – a widely used class of solvents and electrolytes – are molten salts at room temperature thanks to non-trivial chemical interactions, yet the electronic structure of ion pairs and ion clusters is still an open question.

This workshop bought together a diverse group of leading researchers in electrolyte physics and chemistry. The workshop identified and discussed important gaps in literature, leading to an action plan for the community.

2 Major outcomes

Underscreening

Robert Evans, Roland Kjellander, Ram Adar, Andreas Hartel, Alex Smith and David Limmer discussed recent advances in underscreening. However, the participants converged to the sobering conclusion that no current theory can explain it! The key challenge is to explain the scaling of the screening length as a function of concentration observed in experiments and the sheer magnitude of the screening length. On the bright side, it seems that the oscillation wavelength of the structural force can be explained by a density functional theory model proposed by Andreas Hartel.

Going forward, the discussions identified the fact that all screening length measurements to date were done with the SFB/AFM (Alexander Smith and Michal Borkovec enlightened us on the frontiers of experiments) – the open challenge is developing a “surface free” method to probe correlation lengths in the bulk, e.g. neutron scattering discussed by Elise Duboue-Dijon in the context of fitting force fields. Simulations are uniquely able to fill the gap between theory and experiment. Large scale molecular simulations with a box size larger than the measured screening length is needed. The question of ion pairs popped up frequently in discussions – from activity coefficients (Jean-François Dufrêche) and structure of ionic liquids (Jan Forsman) to the argument that ion pairs acts as effective depletant that causes like-charged colloids to attract (Monica Olvera de la Cruz). An independent way to probe ion pairs is needed in order for it to be a useful theoretical concept.

Dielectric “constant” and the polar medium

The discussions in the workshop problematized the concept of dielectric constant in ionic fluids, and identified the proper treatment of the polar solvent an important research direction.

The dressed ion theory, discussed by Roland Kjellander, highlights the fact that the dielectric function is non-local. Ralph Colby presented experimental dielectric spectroscopy measurements of polyelectrolytes, and a recurring theme in discussions was how to relate it to the dielectric constant that enters into theories. Fyl Pincus’ talk problematized the concept of charge, and proposed that the effective charge of an ion in water might not be the bare charge. Measuring polarization and response near interfaces is a non-trivial in simulations too - Michiel Sprik discussed the recent advances in modeling a finite electric field across electrolyte solutions. Yan Levin discussed a Green's Function method to simulate ions near metallic electrodes.

Reconciling the “chemistry” and “physics” of electrolytes

A key challenge that emerged from the workshop is the need to reconcile the chemistry and physics of electrolytes. For example, Patricia Hunt discussed quantum mechanical modeling of ion pairs and clusters, and Matej Kanduc, Zhujie Li and Elise Duboue-Dijon discussed atomistic force fields for simulating of concentrated electrolytes. It seems that those atomistic insights are not incorporated into liquid state theories, e.g. the solvent in liquid state theory models is still considered as a dielectric continuum. The community needs to bridge the gap between analytical models and atomistic simulations and quantum simulations, specifically elucidating what are the salient physics for the various experimentally relevant questions. Chemistry must be taken seriously!

Electrolytes out of equilibrium

The workshop identified the non-equilibrium physics of electrolytes as the next frontier.

Rene van Roij reminded us that hidden gems abound in “simple” Poisson-Nernst-Planck-Stokes electrokinetics. Using NEMD simulations, Michael Urbakh explained experimentally observed regimes of stick-slip motion for ionic liquids confined between charged surfaces. Celine Merlet discussed coarse-grained models for ion transport in supercapacitors, and dyanmic effects are important in ionic nanophotonics (Alexei Kornyshev) and mechanics (Rui Qiao).

3 Community needs

First, we propose organizing a CECAM workshop on concentrated electrolytes in 2020. The format of CECAM workshops, which emphasizes discussion time, is particularly suited for forming a community. It seems that there is a longstanding gap between the chemistry community focusing on the molecular aspects of concentrated electrolytes and the physics community focusing on analyzing statistical physics models of Coulomb fluids. Bridging the two approaches is crucial to make electrolytes work in industrially relevant contexts.

Second, the community needs to widen its engagement with experimentalists to expand the types of experiments done to probe concentrated electrolytes. The surface force balance and atomic force microscope communities have been central to the screening length debate, but there are many other measurements that would be extremely enlightening, e.g. probing the structure of charged colloid suspensions or double difference neutron scattering. The community should coordinate experimental efforts. Moreover, experiments should be constructed such that it can falsify or verify a theoretical idea. This will require work from the theorists, as there are concepts in the parlance of concentrated electrolytes such as “speciation” and “ion pairing” that are not quantitatively defined.

Third, constant potential molecular dynamics simulations are becoming an important tool in the community. The community should make different implementations open source, as well as set clear benchmarks. There were three different constant potential methods discussed in the workshop, and it is unclear how to compare them. There is a similar problem in force field development. There are many heuristics in developing force fields for molecular electrolytes, e.g. charge scaling and coarse graining were discussed in the workshop, and there is a need for a systematic benchmarking of the different heuristics.

4 Funding

Funding proposals were not specifically discussed in the workshop. Typically, participants are able to attract funding on such fundamental problems only by linking them to practical applications. It is not obvious that currently available national and European funding schemes would support collective initiatives on the transverse underlying scientific issues. This underlines the value of networking activities such as the present workshop to provide a platform for open discussions not related to specific applications, from experimental, theoretical and simulation perspectives.

5 Will these developments bring societal benefits?

Concentrated electrolytes are important for energy storage devices such as supercapacitors and batteries, which are crucial to enable the transition from fossil fuel-based energy generation to renewable energy. A theoretical understanding of electrostatics in concentrated electrolyte is needed to bring about advances in those areas. Moreover, the physics insights gained from cracking the concentrated electrolytes problem, for example an understanding of

dipolar solvation and activity coefficients, can provide opportunities for significant advances in the fields of biophysical chemistry (the interior of a cell or physiological fluids are far from dilute electrolytes), chemical engineering (understanding electrostatic interactions and speciation in concentrated electrolyte solutions is crucial e.g. for separation chemistry and recycling) or engineering (ionic liquids as lubricants to limit energy losses due to friction). As such, the study of concentrated electrolytes is timely and will bring about significant societal benefits.

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Multiscale Modelling in Electrophysiology: From Atoms to Organs

Location: CECAM-Lugano, Lugano, Switzerland
Webpage: https://www.cecam.org/workshop-0-1471.html
Dates: March 26, 2018 to March 28, 2018

1 State of the art

The flow of electric current through cell membranes plays an essential role in life. Electrophysiology, the study of the electrical properties of biological cells and tissues, involves measurements of electric currents on a wide variety of scales from single ion-channel proteins to whole organs like the heart, and in neuroscience, it includes measurements of the electrical activity of neurons. In these excitable cells, the transport of charged particles through the cell membrane is facilitated by membrane proteins; ion channels and transporters are perhaps the most fundamental interface between cells and their surroundings. Our present day understanding and methods of modeling neural excitability have been significantly influenced by the landmark work of Hodgkin and Huxley. After decades, the Hodgkin-Huxley model of excitable cells still stands as an outstanding example of how modelling and experiments can complement each other and contribute to the understanding of biological processes. Perhaps, as a result of this early success in the field, electrophysiology is likely to be one of the areas in the life sciences with ample number of examples where experiments, modelling and simulation are connected and form part of the same process.

With progress in the experimental determination of 3D structures of ion channels together with the relentless development of computational algorithms, the increasing speed and availability of supercomputers and new hardware technologies, it is now possible to investigate an immense range of biological phenomenon using simulation. More importantly in this area, is to connect and model the interfaces between atomistic, cellular and tissue-level models as current computational models are used to analyze events on different time and length scales in physiology starting from the atomic crystal structures up to organs. Crucially, there is a need to bridge the gaps between molecular, cellular and tissue levels of information to build integra

2 Major outcomes

The workshop included i) 30 oral presentations (6 of them by students), each of which was followed by a 10-min discussion, ii) poster presentations including flash oral presentations of the posters during the lunch breaks and iii) two discussion sessions. Major scientific points that were discussed included (a) ways to couple different levels of modelling and enhance interactions between the communities working at each level, (b) provision of right tools to perform multiscale simulations, (c) the advantages and disadvantages of toy models versus more elaborated models featured in each community represented in the workshop, (d) complexity of biological systems and experimental probes versus simplicity of the most elaborated computational systems. In multiscale modelling of electrophysiology, the link

between atomic simulations and ionic currents clearly emerged as the most critical one, while more advanced multiscale modelling is already possible at the cellular and tissue level. Part of the difficulty in including atomic simulations in a multiscale framework was ascribed to the limited time scale accessible by Molecular Dynamics simulations. However, as pointed out in several presentations during the meeting, the limited time scale is not the main issue preventing multiscale modelling of excitable cells any longer. The lengths of the atomic trajectories presented by many of the participants dealing with atomic simulations ranged from tens of microseconds to milliseconds, and in one case, even hundreds of milliseconds. At the same time, experimental data on the dynamics of ion channels in the sub-millisecond time scale were presented during the meeting. Why atomistic simulations cannot reproduce these experimental data quantitatively was a major topic of discussion. One critical aspect that emerged was how well the atomic models reproduce the complexity of the experimental setup. The following effects were proposed as deserving further investigation: (a) the initial structures adopted to define atomic models for simulations, considering that also experimental structures are models of the “real” atomic structures of ion channels in the experimental environment, (b) the composition of the lipid membrane, (c) the boundary conditions of ion concentrations, (d) the presence of auxiliary subunits. The participants agreed that at the current stage, blind multiscale modelling is likely to be unsuccessful. Instead, one way forward is establishing collaborations between experimental and computational research groups to identify simplified model systems that could be used to refine atomic simulations, and to develop a multiscale strategy (e.g. drug binding to well defined channel states, or effects of single residue mutations on transition rates).

3 Community needs

Community needs were considered in the discussion sessions. At present, it is difficult to feedback from one level of theory to another, and reach from atoms (e.g. a lead compound) up to validation in humans. Each computational community working on ion channels is focused in different things, either the functional or the structural aspects, and so their needs are different. In order to facilitate mutual engagement, time is required and exploratory projects that usually lead to limited number of scientific papers, and so in general, people are not willing to invest time on it.

Another important aspect discussed was the lack of development of proper theories due to several limitations (e.g education at university level) which is needed.

Despite the concerns expressed by some researchers, force fields are not an issue and behave overall with some exceptions (e.g. some divalent ions), as simulations on the microsecond timescales presented by DEShaw showed. We have the right tools to perform multiscale modelling but it usually works well when only two scales are linked which is a limitation.

The need for computational infrastructure was discussed following one of the lectures. There is the need for hardware that would allow not only running the simulations but also streamlined storage and analysis. The USA is ahead Europe in this respect thanks to the efforts of DEShaw research.

Overall, although the two communities attending this workshop are distinct, they can work together (feeding themselves sequentially) without the requirement to become a single one. Many participants mentioned their wish for events similar to this CECAM meeting in the future. It was apparent that the mixture of scientists from two distinct communities at various career stages was good. Not all the applications received requesting participation in the workshop could be accepted. The workshop consistent on 40 participants.

4 Funding

Most presenters acknowledged funding from national sources and less commonly from the European Union. Collaborative studies were mentioned, but those were usually funded by the respective parts rather than a common source. There is a limitation in the possibility to fund collaborative research in the subject in mainland Europe. EU research funding schemes most often take a top-down approach, i.e., they have very specific aims that do not

necessarily align with the needs of the scientific community that deals with simulations.

We applied for funding to FEBS (Federation of European Biochemical Societies) to co-sponsor this workshop but the application was not successful because 'the event was an already established CECAM work'. Similar response was received from Biophysical Society.

5 Will these developments bring societal benefits?

The workshop dealt with biomolecular simulations of ion channels, the outcome of which carry clear societal benefits. Work that can lead to better understanding of diseases was discussed in several presentations. Some scientists presented studies related to drug delivery and sensing. The importance of ion channels within all domains of life was clearly demonstrated, and so was the usefulness of simulations in their study. Any genetic or pathogenic alternation of these proteins may lead to severe diseases, and it is not always clear why and how without the use of simulations that yield information at the atomic level. During the workshop, some of the critical issues that still prevents the modelling of excitable cells at the atomic scale were pointed out thanks to fruitful discussions involving scientists working on modelling at different scales and on experimental analyses. Including atomic details in simulations of excitable cells will have a tremendous impact in biology and medicine, as it will allow to investigate complex biological processes (e.g. cardiac rhythm) at an unprecedented level of detail. Although drug-design was not the main topic, the importance of ion channels as drug targets and their involvement in anaesthesia was mentioned and cannot be overstated.

6 Participant list

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Emerging Technologies in Scientific Data Visualisation

Location: Scuola Normale Superiore CECAM-IT-SISSA-SNS Node
Webpage: https://www.cecam.org/workshop-0-1586.html
Dates: April 4, 2018 to April 6, 2018

1 State of the art

Visualisation allows us to tap into high-bandwidth cognitive hierarchies of our brains and allows us to process high densities of information at once. In the field of atomistic and molecular simulations, it is a key element to research: we use ball-and-stick figures to represent the simulation scenarios, graphs to recognize or communicate parametric relationships of equations. The “Big Data” trend gave rise to several projects with vast output of data, many data-driven approaches are being introduced. For instance, a new EU Center of Excellence, "NOMAD", is established to collect, store and regularize data to build a materials encyclopedia.

Visual analytics is also making its way into material simulations beyond traditional ways. Two notable examples are i) a successful crystal structure prediction study using data clustering method supported by visual analytics,[1] ii) a time-aggregated 2D heat-map method that reduces the time to explore inner tunnels of proteins.[2] Nevertheless, visual analytics beyond XY plots or ball-and-stick representations is still an emerging field. Several aspects are yet to be identified and discussed between different communities.

Some of the open questions of the state-of-the-art that the workshop addressed are:

-Data Producers: What are the emerging visualization needs for Big Data; how are they different than scaled-up versions of existing tools?

-Data Analysts: How to enhance current analysis tools or create new ones with visualization? What visual analytics techniques, representations and mapping methods can we borrow from other fields now that the molecular simulations can produce a variety of data other than molecular representations?

-Technologists: How can we better use the developing technologies such as Virtual Reality, haptic feedback mechanisms, graphical artificial neural networks, and computer vision to reveal patterns and relationships that were previously not exposed to visualization at all?

[*1] Stuart Card, J.D.*

2 Major outcomes

Prior to the beginning of the workshop we organizers doubted about the possibility of keeping the interest contributors and attendees from so many different research areas (about half of the participants came from communities outside the CECAM “core business” of atomistic and molecular simulations). As the workshop begun, we realised that the same doubts were also held by many invited speakers.

However, since the first talk these doubts vanished and remained a non issue for all the three days. All the contributions were followed with keen interest by attendees and many questions were raised by the audience after every intervention. This may constitute a point for further consideration as it may imply that such an event tapping both from inside and outside our community may be an opportunity for fruitful contamination of ideas. Obviously, these positive aspects could be outbalanced by a constraint on the scope and depth of their talks but feedbacks collected during the workshop did not highlight this issue and many attendees stated that talks were source of (unexpected) inspiration for their research. Another general point worth mentioning is the basic techniques of visualization discussed particularly in the first day that, for many participants (even experienced ones), constituted material for learning according to their feedback. Perhaps a different event (such as school or part of it) blending visualization and machine learning may be worth of consideration in future CECAM events.

The workshop was an opportunity to discuss on the following topics which were perceived as very important by participants:

1. Data visualization for complex data sets: the importance of selecting the most appropriate metaphor for conveying information to the reader from different sources and with different means and the importance of correctly selecting things such as glyphs and colour maps. The adaption of these choice to different contexts (e. g. research, dissemination) was also stressed. Direct Volume Rendering and switch to different representations with an increasing/decreasing number of represented objects were cited as “must have” features for modern visualization applications.

2. Creation of intelligent workflow systems. Development and testing of scientific software. The large computational infrastructures available in Europe allow to address high performance computing (HPC) -based investigations in material science and soft matter. We strongly need shared resources across Europe (and outside Europe?) and more importantly environments providing a flexible and customisable integration of such resources. Sharing and validation of the of the large amount of data generated are to be really exploited to the fullest extent. The same hold for scientific software development, testing and versioning. Projects such as NOMAD constitute a model for such efforts.

3. Immersive Virtual Reality for science. The potential benefits and disadvantages of IVR in scientific applications were debated. On one hand, some of the participants showed IVR environments with different degrees of maturity showing how with IVR it is possible to integrate very large and complex data sets (especially in molecular medicine and genomics) and even collaborate within these environments. On the other hand some of the attendees argued that IVR may be too dispersive and distracting for users and effort should be focused on scalable 2D applications. Alternatives to IVR (such as multiple display walls) were also presented.

4. Machine Learning and Molecular Dynamics. The accuracy and flexibility of MD Force Fields (FF) trained using Neural Networks has been shown and discussed as one approach that will have a deep impact on Molecular Simulations. Also the central role of Unsupervised Learning methods such Clustering algorithms and dimensionality reduction methods has been demonstrated to be crucial for any large scale simulation study and to develop effective visualization methods

3 Community needs

One need that was highlighted for this type of event was to increase the time allotted for open and informal discussion as compared to the presentaion of talks. The demontrations of IVR were appreciated but perhaps there was an umbalance between the focus given on Virtual

Reality in the demontrations and the talks. Other “hands on” sessions should have considered in the schedule.

From a general point of view, inviting experts to show how to tap into new, emerging technologies has been fruitful and it should be done again in the future even if it is not straightforward how to organize these events without veering too much off the spirit of CECAM workshops. For sure the workshop has highlighted a big gap between what specialists either from the visualization world or from Big Data and Analitycs consider a solid standard that should be used and widespread and what many (young) participants normally use in their studies. This gap may be perhaps overcame by making available more powerful middleware (see point 2 above) but also by organizing more mixed type events such as this one.

4 Funding

Typical channels to organize these future conferences would be CECAM and Psi-K. However, in future events a greater commitment by private firms working in data analytics and/or visualization should be sought, to keep the level of multidisciplinarity of the workshops. We have one sponsorship from hardware vendors but our attempts to other companies failed, not because of interest (e. g. one speaker came from the Unicredit bank research team) but for lack of time: big companies (or public organizations) not already aware of the type of research carried out by the CECAM community may need many bureaucratic steps before agreeing to a sponsorship even if the economic commitment is not very relevant to them (such was precisely the case for Unicredit).

5 Will these developments bring societal benefits?

Computational approaches are becoming central in every scientific discipline; the open research policies set in H2020 [1] push researchers to adopt data intensive approaches to remain competitive. Increasing the awareness of the CECAM community in this type of events to the new possibilities created by the Big Data trend has therefore the potential of increasing the quality and quantity of research from the community and, as a consequence, bring societal benefits in all the areas were atomistic and molecular simulation may have an impact, such as nanomedicine or new materials. It may also constitute a chance for scientists with a different background to get in touch with what is CECAM and what type of research its associates do. The development and deployment of powerful and engaging visualization and virtual reality technologyhas the potential to reach a wider audience highly effective ICT tools for educational purposes and science outreach in molecular sciences, in agreement with the H2020 guidelines on open education.[2]

[1] http://ec.europa.eu/education/policy/strategic-framework/education-technology_en

[2] https://ec.europa.eu/programmes/horizon2020/en/h2020-section/science-education

6 Participant list

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CompAllo: Towards a Unified Approach to the Analysis and Design of Allostery

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1468.html
Dates: April 9, 2018 to April 11, 2018

1 State of the art

Allostery is a regulatory phenomenon underlying many cellular processes. The allosteric coupling between regulatory and functional sites allows proteins to sense environmental cues, for example metabolic substrates, and to fine-tune their biological activity accordingly.

Typically, an allosteric ligand binds to the allosteric site and modulates the activity of the orthosteric site. Allosteric regulation is the most direct and efficient mechanism to sense concentration changes in small molecules and to modulate pathway activity to maintain metabolic homeostasis. This, in part, because allosteric regulation of enzyme activity is considerably faster than expression-level control.

Therefore, allosteric control of protein function is an essential part of protein interaction networks and signalling pathways and it offers opportunities for drug targeting.

Although allostery has been studied for several decades, some fundamental aspects are still not clearly understood; for example, the debate is still active on the relative significance of conformational selection and induced fit in ligand binding. Several studies have shown that allostery can be conveyed through multiple pathways across the protein structure, that conformational selection plays an important role and that we can compute the contributions of individual residues to the allosteric signal transmission. However, the flexibility of proteins, the relatively small energetic changes involved in allosteric transitions and the fact that water plays a role in binding processes alltogether render computational predictions a difficult taks. Additionally, our computational methods generally do not include interfaces for experimental data. Hence, interaction between theoreticians and experimentalists was a main focus of the workshop.

2 Major outcomes

To advance our knowledge effectively, active collaboration between experimentalists and theoreticians was promotedduring the workshop to profit from methodological advances, to integrate expertise and discuss limitations, and finally to set common goals.

Wilfred van Gunsteren presented his experience in interpreting, validating and ‘invalidating’ experimental evidence. It was stressed that experimental evidence was generally obtained as average over various timescales and the interpretation of molecular mechanisms by computational methods needed to disentangle these by addressing the ‘ensemble nature of allostery’ as Vincent Hilser has stated clearly.

The talk of Martin Blackledge naturally followed, discussing his experience in both, collecting and analysing dynamical data on proteins. He stressed the importance of motional averaging and the use of population-weighted averages of chemical shifts. He discussed the concept of conformational funneling between two interacting states in which the interaction is regulated by the intrinsic free- state of the two partners. He also discussed his interesting approach to back- model features from ensemble averages of experimental observables. Paola Picotti presented another interesting and novel approach from the experimentalist community: to study conformational changes and assemblies by limited protein lysis and Mass Spectrometry. She showed the extraction of new markers to highlight conformational transitions in cell extracts. Shuguang Yan discussed the activation mechanism of a GPCR and the role of water in the central channel. Rob Cooke from Heptares Therapeutics discussed the fact that the number of allosteric ligands for this class of molecules is constantly growing, but without us being able to confidently predict novel allosteric binding sites and their ligands. Additionally, the effect of allosteric ligand may depend on the orthosteric ligand.

In regard to allostery in structural biology as conveyed by multiprotein assemblies, Tom Blundell gave an overview of structures in which no evident internal conformational changes were detected, despite very long-ranged allosteric structural changes that were tightly associated with regulatory function.

In computational methods, the use of coevolution has been explored as an integral part of developed approaches, as highlighted by Alessandro Pandini and Alessandra Carbone. The balance between dynamical information from structural simulations and evolutionary information from sequence-based methods has yet not been investigated in full detail and the precise contribution of each in terms of information content has yet to be clarified. There were discussions on specific binding modes and communication between orthosteric and allosteric ligands (Colombo, Fornili and Papaleo) and the design of allosteric inhibitors (Ernst). The presented studies have shown that allostery can be conveyed through multiple pathways across the protein structure, that conformational(selection plays an important role and that we can compute the contributions of individual residues to the allosteric signal transmission. Fast computational methods like normal mode analysis (Guarnera and Berezovsky) and Gaussian networks (Haliloglu), both using a Calpha-only representation, are suitable for the detection of allosteric signal transmission. The coarse-grained representation can be obtained from long (ns to s) Molecular Dynamics (MD) simulations combined with structural alphabets and network analyses (Pandini and Macpherson).

The Free-Energy and Entropy contributions to allosteric communication and regulation were detailed in the presentations of Chris Oostenbrink and Bojan Zagrovic; new models need further exploration of these contributions to better quantify the modulation and selections of ligands.

3 Community needs

The discussion sessions were clearly showing a diverse range of opinions on the subject of community needs.

While some participants favoured a unified approach to software and benchmark data, others were sceptical about the value of such efforts. This diversity stemmed partly from the fact that *allostery* itself has many facettes, leading to a limited overlap between the studied systems and methods applied. One might conclude that the research field is currently evolving in a divergent manner and it would be an enormous effort to channel the wide spectrum of activities towards more unified approaches.

However, the community would unquestionably profit from a clearer definition of *allosteric mechanisms*, for example how they are characterised (enthalpic, entropic, conformational, temporal) and under which boundary conditions they operate.

Interaction between theoreticians and experimentalists appear to be sparse in the field. Again, this might be attributed to the difficulty in finding a system that is suitable for a joined study. Notwithstanding this, project planning should include an option for collaborative work, as it provides an opportunity to strengthen observations and mechanistic models. Theoreticians are encouraged to provide a software module to include experimental data into their models and experimentalists should consider to provide their data in a format that is suitable as input for theoretical models.

4 Funding

Allostery falls into the category of functional 'switch' mechanisms, where the switch (allosteric site) is in the extreme case a fully independent module with respect to the orthosteric site. Currently the largest potential appears to be in pharmaceutical applications, where allosteric sites offer a range of novel opportunities to regulate biomolecular functions.

However, it is not only of interest to study the naturally evolved allosteric mechanisms, but also modified and *de novo* designed switches or modulators. Such designs could serve as nano-sized sensors and biomechanical devices.

Funding channels include therefore the Horizon2020 programme, section 1.3 of the Health initiative "Infectious diseases and improving global health", where allostery plays a role in immune responses of the host and escape mechanisms of bacteria, and the Nanotechologies initiative "Open innovation test beds for bio- based nano-materials and solutions."

5 Will these developments bring societal benefits?

The continuing increase in life expectancy, the rapid spread of microbial resistance to antibiotics and the difficulties in controlling silent epidemic

diseases like diabetes, inflammation and allergy all create increasing pressure on society to develop novel medical treatments. Compared to its potential, allostery is a largely unexplored route to such treatments. Particularly when a better understanding of allosteric mechanisms will allow for a fine-tuned modulation of molecular function, there is promise for interventions that control disease processes better than current medications. The pharmaceutical industry is adopting allosteric regulation as additional (and in few cases sole) strategy, but the methodology to develop allosteric is overall not yet as advanced as the classical drug design pipelines. For example, predicting allosteric pockets and the regulatory interplay between allosteric and orthosteric sites are challenging problems. Nevertheless, we expect to see an increasing number of allosteric dugs on the market within the next decades, possibly in combination with orthosteric drugs.

6 Participant list

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Strongly Correlated Materials: Experiments and Computation

Location: CECAM-ISR
Webpage: https://www.cecam.org/workshop-0-1588.html
Dates: April 9, 2018 to April 12, 2018

1 State of the art

Heavy fermion materials, transition metal oxides, and a variety of rare-earth compounds exhibit strong correlation: electrons in partially filled d and f shells of constituent atoms are delicately balanced between interaction-induced localization and kinetic delocalization, resulting in rich phase diagrams with remarkable and potentially useful switching properties. Most widespread computational approaches to materials, which are based on weak-correlation theories such as Density Functional Theory (DFT), Hartree-Fock and GW, fail to fully capture strong correlations.

Strongly correlated physics is of broad fundamental interest, with recent examples including the elusive theory of topological Kondo insulators, the formation of multipolar orders in actinide oxides and the controversial nature of high temperature superconductivity in plutonium-based materials. Some of the most societally pressing and yet long-standing issues involve the radioactive actinides, and better theoretical methods are critical to addressing nuclear waste remediation.

An emerging, cutting-edge generation of methods has begun addressing the challenge of performing realistic simulations of strongly correlated materials. However, the problem remains extremely difficult, and attacking it requires a large-scale multidisciplinary effort. In this conference, we brought together leading researchers working on separate but synergistic sides of the problem, from both the theoretical and experimental perspectives.

2 Major outcomes

The workshop took place in Tel Aviv University and included 47 participants. Of these, 12 were invited speakers from abroad, 11 were invited speakers from institutes in Israel, and the rest were faculty members, postdocs and students.

In addition to the topics detailed below, the conference included a two-hour poster session and an excursion to Acre, as well as several opportunities for discussion. We are already aware of several collaboration opportunities that arose during the conference.

The topics presented were ordered into six sessions, the vast majority of which resulted in lively discussions. These interactions generated new ideas and collaborative directions, both between theoretical and computational teams and between theory and experiment.

Session 1: "Density Functional Theory in Correlated Systems"

Chair: Eitan Eidelstein

Alexander Shick, "DFT+U+ED approximation for modeling of f-electon nanomaterials"

Amir Natan, "The Structure and Composition Statistics of 6A"

Maytal Caspary Toroker, "Advances in modeling water splitting with iron oxide"

Pavel Jelinek, "Strong correlated molecules on surfaces: SPM, DFT and beyond"

Oswaldo Dieguez, "Handling transition metals in perovskite oxides: DFT+U and hybrid functionals results "

Session 2: "Strong Correlations in Complex Systems"

Chair: Thomas Gouder

Silvie Maskova, "Tuning of electronic properties of metallic systems by H absorption"

Itzhak Halevy, "Structural, electronic, and magnetic characteristics of Np2(Co/Ni) 17 and analogue compounds under pressure"

Eyal Yahel, "Phase Diagrams and a Reversible Liquid-Liquid Transition in Liquid bismuth"

Yoram Dagan, "The phase diagram of (111) SrTiO3/LaAlO3 interfaces."

Session 3: "Theoretical Approaches to Strong Correlations"

Chair: Alexander Schick

Alexander Lichtenstein,"Electronic Structure and Magnetism of Correlated Materials"

Alexey Rubtsov, "Non-local collective fluctuations in correlated materials beyond DMFT"

Hyowon Park, "DFT+DMFT study of magnetic excitations and energetics in strongly correlated materials"

Evgeny Stepanov, "Effective Heisenberg model and quantum spin fluctuations of correlated electrons"

Emanuel Gull (replacement of Dominika Zgid), "Self-energy embedding theory"

Session 4: "Approaches to Oxides"

Chair: Oswaldo Dieguez

Ilya Grinberg, "First-Principles Based Studies of Complex Oxide Materials"

Mark Nikolaevsky, "Electronic Properties of the Spinel and Post Spinel Phases in MgFe2O4 and ZnFe2O4"

Session 5: "Pathways to 4f and 5f Systems"

Chair: Alexander Lichtenstein

Emanuel Gull,"Charge order in the extended Hubbard model"

Brenda Rubenstein, "Ab Initio Finite Temperature Auxiliary Field Quantum Monte Carlo"

Eitan Eidelstein, "Multiorbital Inchworm in the Hybridization Expansion"

Thomas Gouder, "Photoelectron Spectroscopy and BIS Study of the Intermediate Surface Oxide U2O5"

Ladislav Havela, "New findings about old UH3 – a way to room temperature 5f ferromagnetism"

Session 6: "Open Quantum Systems"

Chair: Guy Cohen

Dmitriy Shapiro, "Thermoelectric effect and noise in junctions of Majorana and Dirac channels"

Roi Baer, "Unraveling open-system quantum dynamics of non-interacting Fermions"

Oded Hod, "Electron Dynamics in Open Quantum Systems via The Driven Liouville von Neumann (DLvN) Approach"

3 Community needs

This conference revolved around common ground shared by several theoretical and experimental communities. As these communities are different from each other, so are their needs: for example, some of the participants depend on large national facilities as synchrotrons and supercomputers, while others rely only on their own dedicated resources. Several of the participating experimentalists work on actinides, which can be highly radioactive or poisonous and therefore require specialized facilities.

In terms of code, some participants use open source or commercial codes while others develop their own specialized software. As progress in the field depends on ongoing integration between these very separate pieces of software, collaborations are particularly important. In the future, it may be useful to include tutorial sessions on certain software tools. Furthermore, as disconnects exist between the communities represented here, networking is a strong need. We therefore believe a workshop of this nature every two to three years would be very useful.

4 Funding

This particular workshop was jointly funded by CECAM IL, which provided 45% of the funding; and the PAZY foundation, which provided 45% of the funding. The School of Chemistry at Tel Aviv University accounted for 4.5%, the Faculty of Exact Sciences for 4.5%, and registration fees for 1%.

We expect that future workshops could be similarly funded; other less specific sources in Israel include the Israel Science Foundation and the Institute for Advanced Studies of the Hebrew University. Of course, future conferences on this topic will most likely not be limited to Israel, but will also be conducted in one of several European countries.

5 Will these developments bring societal benefits?

The main theme of this workshop was the development of computational and experimental tools for characterizing strongly correlated materials in conditions which are both scientifically interesting and technologically relevant. Correlated electron materials are important in a variety of technological fields. One example, which was brought up in several sessions, is that transition-metal oxides are widely considered to be a strong contender for eventually replacing semiconductors in the electronics industry. This would allow for manufacturing smaller, faster

and more energy efficient electronic devices, and have a major impact on technological development.

Talks in the workshop also addressed other practical issues having to do with electronic correlations in materials and molecules. Many of the talks focused on actinides, which are important in various energy and metrology applications. Other specific examples of technological issues that were discussed include nanomagnets adsorbed on surfaces, which may be used in next-generation data storage applications; iron-oxides for solar catalysis, which may be used to renewably extract hydrogen for fuel cells; and superconductivity in 2D interfaces, which could revolutionize the design of many devices if it can be stabilized at higher temperatures.

6 Participant list

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Phoretic Effects at the Nanoscale

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1633.html
Dates: April 18, 2018 to April 20, 2018

1 State of the art

Electrophoretic phenomena are relatively well understood but progress in numerical modelling of other phoretic transport is hampered by the lack of a well-defined statistical mechanical formulation. The standard description of transport induced by thermodynamic gradients is based on Onsager's macroscopic thermodynamics of irreversible processes. In the linear response regime, the chemical potential gradients are coupled to the fluxes via Kubo relations. This connection between equilibrium and non-equilibrium situations is exploited in simulations at various levels to determine transport coefficients. However, classical Green-Kubo expressions for the thermal conductivity exist for pairwise additive systems but not for systems with many-body interactions and with coarse-grained and implicit-solvent models it is not easy to properly account for the contribution of the degrees of freedom that have been averaged out to the transport coefficient, as well as for finite size effects.

The microscopic simulation of osmotic pressure and osmotic flows has attracted little attention compared to the high importance of this phenomenon. The osmotic coefficients of solutions can be obtained from direct molecular simulations or within a coarse-graining strategy whereby effective potentials are first determined from molecular simulations. Most of the modelling of thermophoresis and diffusio-osmosis of colloidal suspensions, as well as the interpretation of experiments of osmosis and reverse osmosis through nanopores is based on continuous approaches. Diffusio-osmosis was modelled at this level to account for the effect of hydrodynamic slip. The use of molecular simulation to improve simple models has been much less explored in the context of thermal or osmotic transport. The workshop focused on the thermal and osmotic effects, but also touched other types of thermodynamic gradients relevant and challenging to simulate.

2 Major outcomes

The research on the topic of the workshop has intensified in the recent years – confirming the evaluation of the previous discussion meetings. During the workshop, the discussions clustered around two main themes:

1. Transport in nanopores

(lectures of Lydéric Bocquet, Roland Netz, René van Roij, Elisabeth Charlaix, Ignacio Pagonabarraga, Nikita Kavokine, Laurent Joly, Guillaume Galliero, Jérôme Burelbach, Alberto Parola)

Several open questions have been identified that present key obstacles for understanding and applying transport phenomena in nanoconfinement, e.g. nanopores. We have discussed the effects of flow, electrical charges, adsorption and coupled phenomena (mechanical, electric, chemical…) on the transport. An intriguing observation is the emergence of the so-called space charge zones, whose explanation requires a proper treatment of the nonlinear effects. Another emerging open question is to understand the role of interfaces that become

dominant when the confinement approaches the nanometre scale. A suitable order parameter to measure the relative importance of interface and bulk is the Dukhin number, which was discussed in transport of electrolytes in a solvent and in binary mixtures. The discussions throughout the workshop clearly pointed out that there is a need to unify the approaches to model such phenomena. The concrete open questions that surfaced are:

- What phenomena originate in thermodynamics and what is due to dynamic effects
- Can temperature gradient be modelled as an external field?
- What are nonequilibrium stationary states? How can we formulate these problems in term of them?
- Can we design simple models of complex phenomena at these scales?
- How to bridge the gap between gases and liquids?
- How to address collective effects?

2. (Self-)diffusiophoresis, thermo-phoresis and thermo-osmosis of nanoparticles

(lectures of Tuomas Knowles, Ray Kapral, Marisol Ripoll, Roberto Piazza , Régine Perzynski, Maziar Heidari, Erika Eiser, Aloïs Würger)

The second set of topics revolved around the transport of particles in thermodynamic gradients. It was pointed out that the microscopic origin of motion is not always clear, i.e. if decomposing the response into separate processes, it is not easy to say which one dominates. A promising way to study these questions seems to be by using the light to induce thermal gradients and to investigate the response of the system. We also discussed how we can move from understanding the transport to controlling it in applications. In the experiments on flow of molecules (e.g. proteins) in thermodynamic gradients, it is in principle possible to characterize the molecular properties by analysing their response to the gradients. This could result in a breakthrough in the accuracy of molecular recognition techniques. However, a better understanding is needed of how the phoretic response is related to the microscopic properties.

3 Community needs

Perhaps the strongest community need is the need to unify the approaches to modelling. There are several approaches to model fluid flow, interfaces, electrostatic interactions, temperature gradients etc. Progress along these lines is clearly visible but further discussions in form of CECAM workshop are essential. Moreover, the nature of the problems discussed within the workshop clearly requires a closely orchestrated efforts on the experimental and modelling fronts. There was a good mixture of expertise in the present meeting and it seems that several new collaborative research projects have been initiated. Finally, as mentioned above, there is also a question about how to use our understanding of phoretic effects in experiments and applications to control the transport. In order to discuss this in more detail, it would be good to involve relevant participants from industry. We strongly believe that similar workshops should be organized in the future. Due to the rapid progress that has recently been made, probably another workshop in 2 years would be ideal.

4 Funding

The workshop organizers and some participants are taking part in two European Horizon 2020 projects that are focused on the transport of soft matter at the nanoscale: European Training Network (ETN NANOTRANS) and Future and Emerging Technologies (FET NANOPHLOW). The possibility to apply for new funding has been discussed and the conclusion is that due to the extremely competitive nature of the European funding within Horizon 2020, it would be good to come up with a new proposal within the next one or two years.

5 Will these developments bring societal benefits?

Exploration of equilibrium properties of colloidal suspensions resulted in a rapid development of the field of Soft Matter in the past few decades. Colloids in the micrometre range have been successfully used as model systems to probe fundamental questions in statistical mechanics, material science, biological and atomic physics and numerous applications have emerged, ranging from biomedicine, pharmaceutical and food industry, to novel smart and functional materials. Further progress along these lines largely depends on understanding soft matter systems at smaller scales (i.e. nanoscale) and far from equilibrium. The potential economic impact of phoretic technologies is difficult to over-estimate: nanoscale transport at interfaces and in thermal or chemical gradients determines the efficiency of energy storage, oil recovery from porous matter and production of smart materials – technologies that are responsible for the majority of global human CO2 emissions. We expect that new solutions for providing sustainable sources of energy and water will emerge at the nanoscale where the behaviour of matter departs from the common expectations. Furthermore, new techniques based on phoresis will dramatically enhance the separation power of analytical tools in protein science, which will enable a better way to probe the molecular origins of protein aggregation, a phenomenon that occurs in neurodegenerative disorders such as Alzheimer’s and Parkinson’s diseases.

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Epigenetics and Multiscale Genomics

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1539.html
Dates: May 2, 2018 to May 4, 2018

1 State of the art

The meeting illustrates recent advances in the multi-scale representation of DNA, from the Watson-Crick duplex from the entire chromatin. The talks present a variety of techniques, from classical molecular dynamics simulations (where improvements in force-field and simulation protocols were widely discussed), to coarse grained representations, nucleosome fiber simulation and chromosome and chromatin simulation. In addition, recent front-line applications of the methodologies were shown, showing the power of simulation techniques, especially when coupled to experimental validation.

Talks discussed in detail the impact of epigenetic changes such as DNA methylation in the physical properties of the duplex and the importance of epigenetic marks on the histones in modulating the global chromatin fold and how this impact cellular functioning.

Large discussion was centred on the deconvolution of experimental information obtained from cellular pools and whether the experimental signals are real at the cellular level, or just an “artefact” arising from cellular averaging that are used incorrectly to bias theoretical simulations.

In my opinion all talks, including the short ones, were of high quality showing state of the art results, many of the yet unpublished. I really enjoy the conference, and come home with multiple new ideas.

2 Major outcomes

Major advances have emerged at the different scales:

i) Atomistic simulations: New force-fields both based on pairwise additive schemes and on polarized potentials have been presented, as well as their application in the context of molecular dynamics in different topics regarded DNA functionality

ii) Coarse grained: New coarse-grain approaches have been outlined including methods aimed to reproduce single stranded DNA and nucleic acids under variable pH conditions

iii) Mesoscopic models: Approaches based on the use of helical deformability parameters but scaping from the nearest neighbour’s paradigm have been presented and shown to improve the representation of naked DNA

iv) Chromatin simulation: Methods based on mesoscopic description of linkers and a CG description of the nucleosome have been presented and used to describe long (around 100 nucleosome) fibers.

v) Chromatin simulations: New approaches based on the use of polymer physics, complemented or not with epigenetic signals and eventually HiC maps have been presented. Deep discussions on the cell-specific vs cell-averaging nature of the experimental data and how to introduce them to bias simulations have emerged.

vi) Computer platforms: Different groups have presented integrated platforms to deal with chromatin simulation at the different levels of resolution. These platforms aimed to put together tools and data and facilitate the integration of experimental and simulation methods facilitating their use for non-expert community

vii) Applications: A large number of application of simulation methods (supported or not by experimental measures) have been discussed. As example: i) the mechanism of DNA repairing, ii) the impact of epigenetics in modulating DNA physical properties, iii) the relationship between nucleosome fiber flexibility and enhancer-promoter interactions, iv) the role of chromatin structure on senescence, v) the role of chromatin structure on cell differentiation, vi) the mechanism of threating DNA sequence by effector proteins.

3 Community needs

The community shows large and very diverse needs. Groups working on atomistic or coarse grained simulations are very heavily dependent on HPC. Some of the calculations discussed in the meeting implied systems with more than 40 million atoms, such as those shown by P.Dans, which require large memory and very numerical high throughput. Others like those shown by T.Cheatham were based on millisecond-scale trajectories and were possible only thanks to the use of specific purpose computers. Simulation side is moving towards the GPU-world, but support of Tier-0 PRACE centers is a major requirement in the area. The need to store the trajectories is emerging as a major problem and also as an opportunity to share raw data for further mining of valuable information. First databases, such as Bignasim are created (mmb.irbbarcelona.org/BIGNASim/) generating an increasing need for data storage. In the larger scales the problems are different, access to data, robust and validated software and procedures and interoperability between software is more important than the access to HPC facilities. Initiatives such as MuG (http://www.multiscalegenomics.eu/) are being created to facilitate the interaction between the different levels of resolution in the representation of chromatin and to approach experimentalist and simulation groups.

Interaction with experimentalist is a “must”. A series of CECAM meeting focused at the different levels of resolution, and joining experimental and theoretical groups will be fantastic. I envision one of atomistic simulations bringing together QM. & MD groups with NMR, X-Ray and EM groups. Another on medium sized systems bringing together CG-MD and CG-MC groups with others working in macroscopic methods and single particle experiments. Finally, a third one should bring together mesoscopic and polymer physics groups with those doing nucleosome architectural analysis, HiC and ultra-resolution microscopy.

4 Funding

The topic covered by the meeting fits into the “basic science” paradigm and must be funded by public agencies. Some of the topics covered in the meeting require complex experimental set-ups and research then becomes very expensive. Typically groups at the meeting were funded by NSF and NIH (for American groups) and national agencies and the EU H2020 scheme for groups working in Europe. This is a very active and novel area of research and several of the groups attending the meeting were recipients of grants from the European Research Projects. Possibilities to organize ETN networks and to put together a H2020 grant application were discussed during the meeting.

5 Will these developments bring societal benefits?

The topic covered by the meeting fits into the “basic science” paradigm and benefits will arrive only on the medium to long term. There are however clear indications that the information derived from the calculations commented in the meeting are going to provide extremely valuable information. For example, studies at the atomistic level are providing clues on the mechanisms of repairing DNA and on those involved in epigenetic signaling, which open the possibility to use this type of calculations to direct drug design studies. Coarse-grained is becoming instrumental to direct biotechnological applications of DNA and combined with higher level calculations to define new bioactive nucleic acids (ex. DNAzymes). The chromatin scale simulations are providing information of direct impact in human health as they show that pathologies such as cancer and changes in basal cell activity related to senescence or differentiation are coupled to alterations in the global chromatin structure. We are in a field where, large societal impact is expected not in the short- but in the medium-to-long term.

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Solubility Physiological Role of Ions in The Brain: Towards a Comprehensive View by Molecular Simulation

Location: Scuola Normale Superiore, Pisa, Italy
Webpage: https://www.cecam.org/workshop-0-1619.html
Dates: May 21, 2018 to May 23, 2018

1 State of the art

The physiological role of monovalent and divalent ions such as H+, Na+, K+, Ca2+, Cl- in neurons has been mostly investigated in the context of ion channels and pumps, yet these chemical species play an indirect role in many other respects. Examples include: (i) Their dramatic change in concentration in the neuronal cytoplasm upon ion channel gating. This may affect many signaling processes, yet we know very little about this; (ii) Their presence affects non-coding RNAs interactions with its cellular partners and DNA/protein complexes in processes of relevance for neuroepigenetics; (iii) Their effect as allosteric modulators (e.g. sodium ions in neuronal GPCR's); their impact on enzymatic function. Many of these processes, besides poorly studied, poses unmet challenges to the theoretician. Indeed, the prediction of energetics associated with systems at different concentrations (and often with concentrations depending on time) may challenge the domain of applicability of force fields. In addition, the ions are acting in a crowded, cellular environment, impacting on structure, dynamics and energetics in a non-trivial manner. Finally, solvent and protein-ligand exchange reactions are poorly described at any level of theory that can be realistically implemented in a molecular dynamic or monte-carlo scheme, including standard implementations of density functional theory. This CECAM workshop aims at building up an unprecedented forum discussing these fundamental problems in Chemical Physics, of great impact for future molecular-level modeling of brain processes. Most importantly, it puts together chemical physicists, carrying out rigorous calculations on simple systems with biophysicists, who need to treat large, highly complex systems, necessarily at a lower level of theory.

2 Major outcomes

Several major outcomes within the workshop include (1) classical (non-ab initio) molecular dynamics simulations seem to be the main method to be used in the field in the near future (5 years, maybe more), (2) hence, the community will need to invest in more accurate models or force fields to deal with ions that interact with neurobiological molecules, and (3) studies at the molecular level are crucial to understand ion interactions, transport, allostery and trafficking. This is of particularly importance for the development of new drugs. The EU and pharma industries have spent billions on modelling the brain, yet we lack basic understanding on ion channels in the brain: the talk of B. De Groot (MPI Goettingen), which showed that we do not have even a consensus on the way the K+ channel (the most characterized ion channel), works. Similar, the mechanisms based on which how ions are transferred to and from the brain are still largely to be clarified. Some highlights of our workshop were the interactions between the more physical chemistry oriented participants and the biomolecular

applications sciences, which in addition to very high-level talks also allowed participants to obtain an overview over other fields (receptors, DNA) where ions are of critical importance. Outstanding were given by experimentalists in the field. For instance, Rachel Neuchstai (Hebrew University, Jerusalem) showed how proteins in the mitochondria, containing metal ions, are key targets for neurological diseases.

Altogether, the meeting covered many topics in the field of metal ions in biological simulations. Metal ions present a very important physiological role in the brain and their modeling is obviously of great help to the scientific community but it arises also numerous challenging problems. An outcome of the workshop is that various Hamiltonians are being used at the moment, by the different research groups, each one with its own associated problems and efficacy. There is currently no unique methodology proved to be always successful on treating accurately these systems and this is reflected in the various ways that scientists exploit to tackle different problems. The discussion also pointed out that one of the challenges in molecular simulations still lies on how to model protein oligomerization and aggregation processes. This shows the need to bridge system modeling typically starting at quantum and atomistic level with other coarse-graining approaches. For this purpose, new multi-scale approaches that link different experts and approaches on biological problems such as the understanding of neurodegenerative diseases must be strongly envisaged in the future.

Great attention has been paid to Gender diversity: one of the organizers is female, and 45% of the talks were given by women. The latter constituted 36% of the participants.

3 Community needs

During several discussions and exchanges between the participants, several needs of our Communities have been identified. One clear requirement to push-forward the state-of-the-art and to tackle larger and more challenging biological systems for one will not only require faster and better hardware but mostly more CPU power. At the moment, the computational scientific community can successfully predict certain systems' properties and it would be interesting to try and have experimentalists and computational people speaking the same language on certain themes, such as the present one, i.e. the physiological role of ions in the brain. This would be no easy matter and it would be necessary to be very strict on the different speakers' presentations, to ensure a fruitful workshop. For this reason, we need to support the cross-talking between fields. Our workshop strongly took advantage from the enthusiastic participation of some distinguished experimentalists. Several participants encouraged to continue this also in future to allow focusing further on the needs of both communities (experimental and theoretical ones) and bridge the gap between the fields. The great importance to correlate theoretical studies with experiments and the need to foster the cross-talk between the two communities was evident throughout the event.

4 Funding

Next to the CECAM, typical funding channels to organize these future conferences would be psi-K, a European network in the field of computational electronic structure calculations (http://psi-k.net/) and Bioexcel, a Centre of Excellence for provision of support to academic and industry in the use of high-performance and high-throughput computing in biomolecular research (https://bioexcel.eu/). The latter already contributed financially and scientifically to our workshop and we will also seek such contributions in the future. Specific COST actions on 'structural and functional annotations of bioinorganic systems' can also help in the organization of focused meetings. Funding is available from the NIH and the NSF in the USA. In Europe they are provided by the European Program Horizon2020, In Italy by Telethon, Italian Cancer Research Association (AIRC), Italian Ministry for Education and Research (MIUR), in Germany by the DFG, then Human Brain Project, and in France by the ANR and CNRS.

5 Will these developments bring societal benefits?

One of the obvious benefits of our workshop for society is that, with ions being a part of proteins, problems in ion-transport are directly relevant to diseases. Many of the presented projects displayed highly biomedically relevant topics such as receptors, channels and amyloidogenic proteins interacting with metal ions.Insights into the dynamical and functional behaviour of these systems can thus be anticipated to be beneficial for biomedical and clinical applications. The social benefits are drawn from this kind of scientific meeting because it promotes the exchange of ideas and initiates new collaboration that yield advances in science as n immediate outcomes. The theme of our meeting was particularly timely as it had an immediate link to the pathogenesis of illnesses associated with the brain. Clearly, a deep understanding of the physiological role of metal ions in the brain will finally lead to further understanding of the molecular basis of several neurodegenerative diseases, in particular in the workshop systems related to Alzheimer´s and Parkinson´s diseases were discussed. This type of studies may help lie the molecular foundation for novel drug design.

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Liquid Liquid Phase Separation in Cells

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1520.html
Dates: May 23, 2018 to May 25, 2018

1 State of the art

This workshop brought together 30 scientists in physics, chemistry, applied mathematics, molecular biology, and chemical engineering, who work in the field of liquid-liquid phase separation (LLPS), to discuss the current understanding of how a cell uses LLPS to create membraneless organelles and what are their properties. These questions have been asked for at least 10 years, but the field is changing rapidly, and even the name of the organelles is not yet settled - are they membraneless organelles, intracellular condensates, or droplets?

The formation of droplets in the cytoplasm is an example of liquid-liquid phase separation that leads to regions enriched in some species (e.g., RNA and selected protein types) surrounded by the remaining species-poor cytoplasm. Known droplets include the nucleolus, centrosomes, stress granules, the neuronal post-synaptic density, and RNA particles. They are a powerful mechanism to spatially organize complex biochemical reactions within the cell. Droplets typically contain many molecular species - P granules, P bodies, stress granules, have ~ 40 components but their relative abundance is not known.

It is clear experimentally that the droplets are fluid (they flow and merge, and are often spherical), but they are not a simple fluid. They have a high viscosity (much greater than bulk water), and on aging for several days can transform from a fluid phase into a fibrous, tangled network. The dynamics of their formation and evolution are largely unknown. As this workshop revealed, even identifying a droplet is non-trivial. The most basic question one can ask - why does the cell produce this droplet? - may not be the most important one to ask. Some droplets may not have a cellular function, but be a by-product of other processes. This workshop addressed the question of what properties experimentalists should measure, and what are promising routes for developing a more precise theoretical understanding of droplet dynamics.

2 Major outcomes

The dominant message from the talks was that the field is in its infancy. Experimentally, the number and type of intracellular condensates is increasing, and systematic characterization of droplets is at an early stage. Many distinct protein and RNA combinations are known to form droplets (or amyloids in some cases), and many droplets contain large numbers of components.

We need more chemical biological means of perturbing the droplets in the cell. Fluorescently tagging a single protein and measuring its diffusion in a microscope does not reveal the complexity of a droplet that contains dozens of molecule types; over-expression of proteins to make it easier to follow their dynamics changes the balance of protein to cellular environment.

Some condensates fail to assemble if a single component is knocked out, but others manage to form even if several components are eliminated.

The structure of many droplets requires super-resolution methods to study. A key result from the discussion is that it is desirable, but challenging, to have ~10 nm spatial resolution to study the droplets. We need to experimentally characterise liquid droplets (physical chemical aspects) in a) composition, b) structure/sub-structures, c) dynamics - simple liquid, viscous, visco-elastic. Surface tension could be measured using fluctuations or a force; optogenetics could be used to measure forces, and optical tweezers could be used to move a particle into a cell and measure the viscosity. FRAP is useful to follow the fluidity of multiple components inside a droplet. But it is hard to tag ~5 proteins. Gene editing of protein structure is useful but we need more examples.

From a theoretical perspective, the workshop revealed that existing thermodynamic explanations for the formation of condensates are too simple. In order to improve our theories, higher spatial and temporal resolution are required in microscopy tools, and a greater exchange of information between experiments and theory. Flory-Huggins theory is a good starting point for describing phase separation but does not capture the complete physics. The role of nearby membranes is an example, e.g., in mitochondria. A condensed phase may "wet" a membrane surface and be modified thereby. Such a system is not well-described using Flory-Huggins theory. For large copy number proteins, with well defined droplet size and surface, current models predict that there are far fewer phases than predicted. Improved computational methods of exploring the phase behaviour of multi-component mixtures are needed.

Connecting simulations and theoretical models with in vitro data is crucial but hard. In simulations with crowders, what are the effects of polydisperse crowders? Experimentally, the effects of osmotic pressure due to "inert" crowding molecules are not the same if you use PEG or a large macromolecule. Theory must distinguish between small/large crowders, or globular versus polymer crowders.

Another important outcome is the recognition that other molecular species in the cytosol modulate the formation of condensates. In vitro experiments have shown that the critical point for phase separated liquids can be moved by the addition of inert filler molecules, such as PEG. It is hard to distinguish if ATP powers an enzyme that mechanically changes things or acts as a hydrotope or "glue" to modify interactions between proteins. We need to go beyond equilibrium thermodynamics and consider entropy flow and non-equilibrium processes

Most computational approaches to date have invoked phenomenological coarse-grained continuum models originally developed to investigate phase transitions in inanimate systems. Non-equilibrium processes have been included in these models in an ad-hoc way, and the development of particle-based simulation models for multicomponent systems including non-equilibrium activity would aid the development of better, physics-based models for living systems.

3 Community needs

From a theoretical/computational perspective, it is clear that the construction of theoretical models of intracellular condensates is at an early stage. There are more questions than answers in linking experimental phases to theoretical models. For simple systems like oil and water, there is a well-understood thermodynamic description, recognised phases and natural timescales. But cells are alive, and their active state must be taken into account. Current models of intracellular condensates are based on equilibrium thermodynamics, but if this does

not apply, what do we use? What happens if cytoplasm is not even in steady-state? When is it legitimate to apply tools and techniques from equilibrium thermodynamics (such as Gibbs phase rule)? What is clearly needed is a theory of non-equilibrium self-assembly. The development of such a theory necessarily requires an integrated approach involving molecular models, coarse-graining methods, and development of experimental probes able to provide information about droplet structure and dynamics down to nanometer length scales and microsecond time scales. The workshop laid the groundwork for a more holistic approach towards these goals.

4 Funding

Many participants emphasized the need for more interdisciplinary studies, and better cooperation between theory and experiment: but that such funding is hard to obtain. The EU funding program is good at supporting interdisciplinary fields, as is the Human Frontier Science Project, but there is a need for more programs like that. We are hopeful that the funding from CECAM for the workshop will pay dividends in the long run by helping this relatively new, but rapidly growing community, find synergies and develop larger collaborations.

5 Will these developments bring societal benefits?

The workshop brought together a multidisciplinary group of researchers with expertise in optical characterization of protein-rich droplets in cells, theories and simulations of transport processes and phase transitions in multicomponent systems (both particle-based and coarse-grained continuum ones), and non-equilibrium statistical mechanics. A number of open scientific issues were identified. In particular, the need for experimentalists and theorists to share a common language was emphasized during the discussions. Secondly, characterizing intracellular condensates in vivo is very hard because of their large number of component molecule types, and new experimental techniques that provide information on droplet structure and dynamics down to nanometer length scales and microsecond time scales were identified. Thirdly, these experimental systems will benefit from the insight provided by simulations and theoretical analysis of model systems that predict the structure and dynamics of the condensates. An important direction for these simulations is to extend them to multicomponent systems that include non-equilibrium activity.

More broadly, the workshop highlighted the importance of intracellular condensates in living cells, and attendees agreed that this fundamental research could feed into pharmaceutical research, drug delivery mechanisms, and identify new routes for drugs with an ability to disrupt aberrant phase separation. Currently, research is still at the exploratory stage of identifying droplets, their components, and designing experiments that can unambiguously identify the molecular properties that give rise to them. It is too early to tell if intracellular condensates will be a paradigm shift, but their recognized role in various neurological diseases, ALS, Alzheimer's and Parkinson's disease suggest that the medical needs could indeed be significant.

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Proteins in Realistic Environments: Simulation Meets Experiment

Location: CECAM-DE-SMSM
Webpage: https://www.cecam.org/workshop-0-1598.html
Dates: May 23, 2018 to May 25, 2018

1 State of the art

The rapid increase in accessible high performance computing resources allows for the exploration of time and length scales by simulation, which gradually approach the experimentally relevant domains. If Moore's law still holds, millisecond simulations of protein-solvent systems at atomic resolution will be standard within five years from now. Detailed mechanistic models of proteins in realistic environments are promising tools to design biocatalytic processes, develop medical applications, and understand the properties of proteins in their natural environments.

Proteins in a bioreactor or in a cell are solvated in a complex mixture of highly concentrated components which differs considerably from the dilute solutions of most in vitro studies. Therefore, characterizing the properties of proteins in the context of their environment is of crucial importance for a complete understanding of their function. An approach which combines experimental techniques with modelling methods on different scales is expected to provide mechanistic insights into the complex interactions that mediate biochemical and biophysical properties of proteins in realistic environments.

The kinetics of an enzymatic reaction does not only depend on the chemical structure of the substrate and the enzyme, but is described by a multidimensional parameter space: concentrations of the enzyme and additional proteins, state of the enzyme (monomeric, multimeric, clusters, or immobilized), protein sequence, concentrations of substrate(s) and of co-substrate(s), concentrations of product(s) and side-product(s), components of the solvent (water, organic solvent, additives, salts), temperature, and pressure. It is a major challenge to explore this huge parameter space, and strategies such as high-throughput experimentation, workflow system for parallel modeling, and statistical analysis or deep learning methods to reduce the dimensionality of parameter space, are highly desirable.

2 Major outcomes

During the three-day workshop, the planned times for discussion as well as the poster pitch presentations before the poster session were highly appreciated by the participants and proved to be fruitful to stimulate discussion.

An important aspect of bringing modeling studies closer to reality is the ability to quantitatively describe fundamental thermodynamic properties such as the chemical potential not only in the ideal case of infinite dilution but rather in situations of strong non-ideality such as present under process conditions. The applied force fields require a tradeoff between accuracy, transferability, and computational cost (Chris Oostenbrink). To develop and improve force fields, machine learning approaches are of increasing importance (Jörg Behler). Given the

diversity in the approaches for atomistic simulations, it will become necessary to establish benchmarks for method validation.

Free-energy simulation methods based on atomistic simulations are considered to be the most rigorous route to predict a wide range of thermodynamic properties in various research areas to investigate protein stability, solvent effects, or ligand binding. Equilibrium constants have been estimated from direct MD simulating in the micro- to millisecond timescale (Albert C. Pan). To simulate slow binding or dissociation events, path sampling approaches have been applied to capture rare events (Ron Elber).

For a more detailed insight into the properties of proteins, careful experimentation is combined with extensive simulation to learn about the mechanism of cold adaption of enzymes (Johan Aqvist), the role of protein dynamics in enzymatic reactions (Silvia Osuna), the relevance of water channels for the substrate specificity of enzymes (Benoit David) and the combined effects of crowding, osmolytes, temperature and pressure on the conformational dynamics and reactivity of proteins (Roland Winter). While molecular simulations reliably describe structure, dynamics, and interactions of molecules, the combination of quantum chemical with molecular mechanics methods provide valuable insights into enzymatic reactions (Walter Thiel).

In enzymology, deterministic steady-state models are used in the analysis of enzyme kinetics by evaluating individual binding and dissociation steps of reactants and the catalytic steps from experimentally determined initial rates or from progress curves. However, the identification of macroscopic kinetic parameters from real experimental data is by far not straightforward, but requires appropriate statistics and should be supported by a suitable experimental design (Nicole Radde). Careful kinetic modelling is prerequisite to bioprocess engineering (John Woodley). However, protocols are not standardized (Santiago Schnell), and the subsequent reporting of experimental data is generally incomplete (Peter Halling), which prevents reproducibility of experiments and a systematic comparison of published parameters. This limitation will become most important as novel methods for high-throughput experimentation become available (Florian Hollfelder). Experimentation and modelling are generating a rapidly increasing amount of highly complex, distributed, and incomplete data, calling for strategies to handle this big data.

3 Community needs

In this workshop, we have exchanged and discussed different complementary views to enzymes and their function: quantum chemical modelling, statistical-mechanical modelling, thermodynamic modelling, kinetic modelling, and experimentation. Three major aspects have been addressed and discussed:

1. Bridging the length and time scales in modelling of enzyme function
2. Handling of experimental data, with small hint towards handling of simulation data
3. Rigorous thermodynamic modeling of the complex solvent environment

In order to overcome the current limitations, we see a need to

1. Integrate different modelling techniques such as QM with MM (QM/MM), molecular and kinetic modelling (by direct MD simulation), thermodynamic and kinetic modelling (by using thermodynamic activity rather than concentration) as well as machine learning. Because

the integration of different techniques requires training of researchers in different fields, we see an urgent need for exchange and for interdisciplinary training for example in the form of summer schools.

2. Standardization of experimental data:

LIMS for raw data acquisition and documentation of experiments, BioCatNet for pre-processing and kinetic modelling, STRENDA for publication and long-term storage

3. To put forward the idea of scale-bridging modelling approaches well defined benchmark systems and standardized workflows will be essential.

4 Funding

The workshop was generously supported by the local CECAM node CECAM-DE-SMSM through the Collaborative Research Center 716 “Dynamic simulation of systems with large particle numbers” located at the University of Stuttgart and funded by the German Research Foundation (DFG). Additionally, the Cluster of Excellence in Simulation Technology (SimTech) also located at the University of Stuttgart and funded by the DFG provided financial support. As the workshop was received very well by all participants the organization of a follow-up meeting in about two or three years should be considered.

5 Will these developments bring societal benefits?

The workshop brought together current experts from different albeit complementary fields which allowed obtaining an overview of state-of-the-art methods. The question of how the scientific knowledge from different scales and fields of expertizes can be merged into a holistic view of proteins in realistic environments is an emerging area of research that is yet to ascertain the full extent of its practical applicability. Exemplary applications are in the fields of protein aggregation that are related to disease states. Moreover, better understanding of protein action in high concentration environments might lead to more efficient biocatalytic synthesis processes. To this end, more reliable, rigorous and efficient methods to model proteins in realistic environments on the one side and improved protocols and standards to obtain and report experimental data on the other side will have a strong practical potential for protein engineering, drug design and improvement of biotechnological processes.

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Bio-, Chem-, and Nanoinformatics Approaches to Study Bionano Interface

Location: CECAM-IRL
Webpage: https://www.cecam.org/workshop-0-1646.html
Dates: May 23, 2018 to May 25, 2018

1 State of the art

2 Major outcomes

3 Community needs

4 Funding

5 Will these developments bring societal benefits?

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Les Houches – TSRC Protein Dynamics Workshop

Location: CECAM-FR-RA
Webpage: https://www.cecam.org/workshop-0-1630.html
Dates: May 27, 2018 to June 1, 2018

1 State of the art

Proteins fulfill their functions by dynamically sampling a range of conformations. The different sub-states are involved, for example, in catalytic turnover or binding to ligands or other proteins. Understanding functional processes, therefore relies on the characterization not only of “static” 3D structures, but of the ensemble of inter-converting states, and relate the amplitude and time scales of motions to function. The wide range and diversity of exchanging states represents a major technological challenge for experimental methods. The integration of experimental methods with numerical simulations has been central to the protein dynamics field from the very early days. The study of complex biomolecular dynamics has seen remarkable enhancements in computational algorithms and resources alongside impressive advances in experimental methodologies. Increasingly, the spatial and time domains accessible to state-of-the-art computational models and experiments are commensurate, providing opportunities for previously unprecedented critical comparisons of the predictions of computational models as well as the molecular-level interpretation of experimental data.

The Les Houches/TSRC Protein Dynamics workshop, organized biennially since 2014, brings together a wide range of experts in various experimental methods (X-ray crystallography, NMR spectroscopy, scattering methods, spectroscopies, atomic-force microscopy and electron-microscopy), as well as simulation methods. This exceptional inter-disciplinary setting with a small number of participants (ca. 60 in the 2018 edition) enabled the exchange of ideas, and the participants were enthusiastic about the open-minded atmosphere of the workshop. The workshop comprised primarily junior and senior faculty (ca. 75 %), as well as post-doctoral researchers and PhD students (ca. 25 %).

2 Major outcomes

The conference comprised 28 invited lectures from diverse experimental and simulation techniques. The speakers put particular emphasis on a pedagogical introduction of their area of research at a level understandable for the broad audience, followed by a presentation of their latest research results as well as open questions and limitations of their field. Integral to each of the 45 minutes slots, about 10-15 minutes were dedicated after each talk to discussions. Additionally, four contributed talks were selected from the submitted abstracts, and 21 posters were displayed in two poster sessions. The talks and posters showed various aspects of protein dynamics, including the role of entropy in protein interactions, hydration dynamics, intrinsically disordered proteins, protein folding, ultra-fast dynamic rearrangements in photoswitchable proteins, ligand binding/unbinding, and motions seen by single-molecule spectroscopies. In a majority of the experimental presentations, strong links were established to either MD simulations or numerical modeling of structures and structural ensembles.

The lively discussions after the presentations, during poster sessions and outside the lecture halls were indeed highly stimulating, and contributions from many colleagues from different experimental/simulations perspectives created new views onto questions central to the field. An important part of the discussions was centered around novel ways of enhanced sampling in numerical simulations. New concepts as well as the question which sampling methods are best suited for which types of molecular systems were discussed. Interesting contributions arose in the context of integrating experimental data in molecular dynamics simulations to guide and control enhanced sampling schemes. Furthermore, several presentations discussed the role of water in biological systems, both from a simulations and experimental perspective.

Along the various presentations, it became clear that the set of data typically available to experimentalists are insufficient, and it is interesting to see an ever-increasing integration of experimental and numerical approaches.

3 Community needs

The community includes a number of research groups that utilize state-of-the-art computational modelling techniques to explore protein dynamics on multiple time and length scales with varying resolution. These projects require access to high performance computing infrastructure with a particular focus on support for large numbers of small to medium-sized calculations due to limitations in the scalability of molecular simulations. The requirements are being met sufficiently so far for most groups in the community, either via access to locally operated computing facilities or national supercomputing centers.

A currently more pressing need for many of the computational groups (as expressed to us by several participants of the workshop) is to have a platform that allows for direct and unrestricted exchange of ideas between computational and experimental researchers in the field of protein dynamics. The complexity of biomolecular systems rarely allows for straightforward simulations of theoretical models to answer questions regarding the function, mechanism and dynamical properties of proteins, but instead requires constant feedback between experiments and computational models. Likewise, new experimental techniques require extensive computation, either to process extremely complex experimental data (cryo-EM, X-FEL data) or to relate observations to microscopic events. Such projects can only be realized in close collaboration between multiple groups. The Les Houches workshop on Protein Dynamics has successfully provided a platform, which acts as a catalyst in the formation of such collaborations by bringing together computational end experimental research groups, including several leaders of the field, in a specialized workshop, which strongly encourages the presentation of cutting-edge, unpublished results. We therefore plan to continue to organize this workshop in the future for which we have received unison support from all participants of the past 2018 meeting.

4 Funding

Funding for meetings: Typically, this meeting may be supported by local, national and international research societies. The Les houches Physics school is already kindly supported by the Grenoble university, the French Commissariat à l'énergie atomique et énergies alternatives (CEA), and the Ecole Normale Supérieure. Other funding sources are national (Societé Francaise de Biophysique) and European biophysics societies (EBSA).

Research funding: Along this meeting several collaborations appeared, between different experimentalists as well as between experimentalists and simulation experts. Funding opportunities may include binational funding sources (e.g., German DFG, French ANR, Swiss SNSF). Larger funding opportunities, such as ERC Synergy Grants may eventually arise, but need more structured action than just one workshop, and may arise as a consequence of collaborations initiated during the meeting. Furthermore, as discussed below, the significance of the community work for pharmaceu

5 Will these developments bring societal benefits?

Characterizing the function and dysfunction of proteins lays the basis for understanding living systems at the molecular level. Protein dynamics intervene in all biomolecular events: understanding unfolded proteins, protein folding and misfolding is directly related to human pathologies such as Alzheimer's or Parkinson's disease, which are urgent problems in an ageing society. Several presentations of the Workshop addressed the conformational properties of disordered proteins, and the process of folding, including misfolding of amyloid-beta peptides to fibrils. Understanding these processes and intermediate stages in detail may help design novel drugs that avoid amyloid formation.

Furthermore, great efforts are currently made by pharmaceutical companies to understand the mechanisms of drug binding and unbinding, and our workshop featured a presentation from an industrial research group in this direction. Their work is part of a large consortium ("Kinetics for Drug Discovery", k4dd.eu), which received >20 M€ funding (European Union, FP7; and industrial contributions). As part of our community is very close to such pharmaceutically relevant applications, one may envisage obtaining funding for basic research in this direction.

Taken together, the work of the community, which encompasses simulations and experimental methods and their integration, has societal impact due to its relevance for biomedical research, and socio-economic impact related to the development of new pharmaceuticals.

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Machine Learning at Interfaces

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1516.html
Dates: June 4, 2018 to June 8, 2018

1 State of the art

Machine-learning is all over the news, and has become a very active research area also in chemistry, physics and materials science. This is because it shows great promise to solve some of the most significant problems that affect the field. For instance, it provides a route to sidestep expensive electronic structure calculations, obtaining accurate models of atomic-scale properties interpolating between a small number of reference calculations. Another interesting area involves searching for the most stable - or promising in terms of properties - configurations of complex systems.

Research is focusing on the development of effective representation of atomistic structures, that are then fed to regression algorithms (most often kernel ridge regression and neural networks) that learn correlations between structures and properties for some training configurations, as well as in the determination of what are the most important configurations that have to be included.

Active learning attempts to solve this last problem by incrementing the train set as the simulation progresses, every time a "new" structure is encountered.

Machine learning is also used to identify phase transitions, reduce the dimensionality of the representation of the structure and dynamics of complex systems, and to estimate their free energy landscapes.

2 Major outcomes

Before the workshop started, multiple open questions persisted within the field. They were related to the advantages and disadvantages of the various choices which can be made when generating machine learning models. The entire workshop was dominated by contributions centred around supervised learning problems. Typically, input variables include information about structure or geometry of the system, while output variables are energy, or other relevant properties. Unsupervised learning applications were hardly discussed. While many of the open questions were discussed, they could not be resolved conclusively. However, throughout the various discussion sessions, multiple, rather consensual conclusions were drawn among the participants. We believe that these conclusions are not trivial and fully justify the efforts necessary to make this workshop happen. They included

-Machine Learning is not fitting! The former implies generalization while the latter does not

-Larger reference data sets are needed for training and testing in order to push the field forward

-Improved machine learning models are needed to enable even more accurate predictions requiring even less training data

-The impact of various representations have been presented using learning curves in order to compare different approaches

-It is not clear if the (human-expertise or machine based) optimization of the representation on the training data does not imply overfitting

-Linear kernel ridge regression can achieve competitive performance

-Neural networks are currently hyped and promise exponentially improving account for the complexity of the target function while kernel ridge regression models can only improve polynomially with training set size. The best performing methods in the field, however, are kernel ridge regression based. It is still not clear if either regressor is favourable.

-Recent studies on exploration versus exploitation and active learning based approaches have been successfully applied computational compound design challenges (at interfaces and elsewhere).

3 Community needs

The community is in strong need of substantial high-performance computing infrastructure. In fact, this is an understatement. Within the application of machine learning models to quantum mechanics based reference calculations, the success of the field will be directly proportional to the amount of diverse training data sets. Since materials and chemical compound space is extremely large (in practice as good as infinite for all intents and purposes) the success of the field will be directly proportional to the amount of computing resources given to the community. While this has already been the case for conventional ab initio or force-field based atomistic simulations, the situation only gets worse in the context of machine learning. This need for CPU time can be directly related to the need for larger training data sets. The larger and more diverse the training data the more accurate and transferable, and therefore useful, the resulting machine learning models. As such, the counter-intuitive conclusion can be drawn: While machine learning models are extremely fast to execute once they have been trained, the actual need for CPU time to obtain training data represents a maximum with respect to the needs of all other computational science based communities.

4 Funding

The various principal investigators who attended the conference typically do not complain about problems to secure funding. On the contrary, there is often more funding than qualified doctoral and postdoctoral candidates who could be hired. As such, no joint research proposals were discussed during the meeting. Rather, the meeting focussed on discussions related to the latest scientific results and to the progress made and to the problems observed. The entire group of participants agreed that there is a major need for additional data. As such, lack of CPU time to generate more data is maybe the most pressing issue, rather than lack of funding.

5 Will these developments bring societal benefits?

The benefits of machine learning for society are frequently discussed throughout all intellectual circles, and are well known. These models enable predictions with controlled accuracy and with unprecedented computational speed. Prediction of quantum properties which previously took CPU days, weeks, or even months, can nowadays be done within milli-seconds using a machine learning model (if a representative training set was provided for the training of that model). The solution to many important technical and scientific questions hinge on the computational complexity associated with the corresponding equations of physics, and our inefficient ways of solving these equations according to conventional compute protocols. The statistical surrogate models which constitute machine learning, therefore represent a viable and attractive potential alternative which will speed up progress in science and engineering by multiple orders of magnitude. It seems to us that it is hard to overestimate the societal benefits which will be derived from these developments.

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Open Databases Integration for Materials Design

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1525.html
Dates: June 11, 2018 to June 15, 2018

1 State of the art

In the last few years, there has been a major game change in materials design. Thanks to the exponential growth of computer power and the development of robust first-principles electronic structure codes, it has become possible to perform large sets of calculations automatically. This is the burgeoning area of high-throughput (HT) ab initio computation. The concept though simple is very powerful. HT calculations are used to create large databases (DBs) containing the calculated properties of existing and hypothetical materials. These DBs can then be intelligently interrogated, searching for materials with desired properties and so removing the guesswork from materials design.

In this framework, various open-domain DBs have appeared online (such as AFlow, the Materials Cloud, the Materials Project, NOMAD, ..). In some of those cases, a Representational State Transfer (REST) Application Program Interface (API) is available to interrogate the DB through scripts. But, so far, it is only possible to interrogate one DB at a time and the APIs are very different from one DB to another. The OPTIMADE workshop gathered all the key developers involved in the different efforts, both in Europe and in the US, as well as some of their users with the aim to continue to develop a common API. The advantage of such a solution is twofold. It allows the users to interrogate all the databases using the same query. And, it permits the database developers to develop their user base.

The present workshop has built up on the achievements of a previous meeting held at the Lorentz Center in Leiden, Netherlands from 2016-10-24 to 2016-10-28. That meeting contributed to setting the foundations of the work that has been continued at the CECAM.

2 Major outcomes

Building on the results achieved in our previous workshop at the Lorentz Center in Leiden (24-28 October 2016) and subsequent discussions on the OPTiMaDe mailing list, the present workshop aimed at continuing to work in the direction of making the various DBs interoperational through the development of the OPTiMaDe API and actual implementations of it.

The workshop consisted of both presentations (45 minutes including questions and answers) and discussions with a larger part (between 55% and 60%) dedicated to the latter. Such discussions are really required to achieve a consensus. Groups were created to discuss different topics and then they presented their results in front of the complete audience for further debate and achievement of a consensus. But, presentations are also important, in particular, since some of the participants (some of which are commercial companies) were new in the consortium.

For the "old" members of the consortium, the presentations focused on the different DBs and their ongoing efforts with respect to the implementation of the OPTiMaDe API (problems encountered and proposed solutions). For the "new" members, the presentations were dedicated to their existing APIs. Furthermore, they had been asked to read the specifications to the OPTiMaDe API in order for them to comment about it and on how they could possibly integrate it.

Many very fruitful discussions (involving the validation and the verification of the data, as well as the integration of the user standpoint) took place about the pros and cons of the different solutions (sometimes they would last during the breaks and even the conference dinner). Actually, the discussions were quite in-depth. Many improvements were adopted for the existing OPTiMaDe API. The new specifications will be finalized in the coming months. A precise schedule has been set up with various tasks assigned to the participants through the use of a GitHub repository: https://github.com/Materials-Consortia (structured through the use of labels and a to-do list). A paper should also be published about it. Points that still need to be discussed have been listed and lines for further improvement have been delineated.

The OPTiMaDe workshop can definitely be considered a success since very important improvements were achieved for the common API (removal of different flaws, new possible queries, writing of a schema, development of a parser to be shared among the different DBs if possible, preliminary version of a structure definition). More importantly, tighter connections have been established between the different projects. The participants really appreciated the workshop and indicated that the location had been key to its success.

3 Community needs

As already discussed in the section about the state of the art, materials design could clearly benefit from the common OPTiMaDe API since the latter would make it possible to interrogate all the databases using the same query. The effort that has been started is thus really important and could have really high impact.

It should definitely be continued trying to involve as many important players as possible. For example, at the present CECAM workshop, a particular attention was dedicated to databases which are not open. The commercial companies who were invited (from GrantaDesign, MPDS [Material Phases Data System], NIMS [National Institute for Materials Science]) indicated a high interest in the OPTiMaDe initiative.

It is this really important to continue to maintain this community with a common target (the OPTiMaDe) which will be very beneficial for the community. Furthermore, the links that are created among the different persons can also serve a different purpose. Indeed, there has already been discussion about the possibility to use the same community to define some standards. Indeed, since it gathers an important number of players in the field, this number can be used as leverage to push towards the adoption of a standard.

For all the reasons above, we believe that the OPTiMaDe effort should be continued. And, some help from the CECAM would really be appreciated in order to organize a series of CECAM workshops.

4 Funding

Among the different presentations, we would like to pinpoint the one by Gerhard Goldbeck and Adam Hashibon who presented the European Materials Modeling Council (https://emmc.info). In particular, they indicated a very strong interest about the OPTiMaDe API that is clearly in line with their objectives.

The discussion that followed their presentation largely addressed the possible links with OPTiMaDe and, in particular, the participation of various members of the OPTiMaDe community to some of the boards of the European Materials Modeling Council.

This clearly opens some possible funding schemes in Horizon 2020. Indeed, the Europen Materials Modeling presently benefits from a Coordination and Support Action (CSA) from the EU which started in November 2016. And, there are clearly plans to submit a new proposal when a call appears. OPTiMaDe could clearly join when this happens.

5 Will these developments bring societal benefits?

Materials design has clearly a great impact on society. Many new applications require specific materials with targeted properties. Furthermore, improving the efficiency of existing technologies (e.g. denser batteries, photovoltaics, faster computer, ...) also benefits from the design of materials with better properties.

The development of the OPTiMaDe API can clearly contribute to making materials design easier. Indeed, the users will be able to interrogate many different databases with the same query. This will give them access to many more materials without the need to learn a different API for each database. So, we can really expect that the outcome of their searches will be more important. This will also be a possibility towards big data analytics (which obviously depends on the availability of as much data as possible).

The social benefit is thus clearly present, though it is indirect in the sense that the OPTiMaDe API is a tool that will clearly contribute to making materials design easier and that materials design should indeed provide benefits to our society.

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Hot Colloids

Location: Ecole Normale de Lyon, Descartes Campus, ENS Descartes Campus 15 parvis Descartes, 69342 Lyon
Webpage: https://www.cecam.org/workshop-0-1564.html
Dates: June 11, 2018 to June 13, 2018

1 State of the art

Nanoscale heat transfer has attracted the attention of physicists, as it raises a number of new questions regarding thermal transport: violation of Fourier's law, balistic transport, phoretic motion, enhanced role of the interfaces. These questions arose essentially after the development of nanotechnologies during the nineties. In particular, heat generation by metallic nanoparticles in solution have many applications in a broad range of disciplines: biomedecine (thermal therapy treatments), physics (phoretic swimmers), chemistry (enhanced reactions) or engineering (nanofluids, energy conversion devices). Most of these applications rely on the properties of nanoparticles to strongly absorb light leading to controlled local heating. In turn, temperature gradients may be brought to very high levels 10⁹ K/m, and possibly drive local phase change. Experimentally, local mapping of the temperature field is often difficult, given the small time and length scales involved.

Computational studies conversely may reach nanoscale-picosecond timescales, and certainly help in understanding the physics of interfacial thermal transport. In order to match the experimental scales a multiscale approach combining molecular models and continuum approaches is highly suitable.

The broad range of applications makes the situation even more complex since each community develops its own models in a rapidly extending field.The aim of this workshop was to bring together scientists who work on optically heated colloidal nanoparticles for different purpose, and who belong to different communities, thermal sciences, soft matter/statistical physics and nano-optics, in order to break these frontiers.

2 Major outcomes

The workshop gathered almost 50 participants from 14 countries. As usual for CECAM workshops, most of the participants came from Europe. The idea behind the organization of the workshop was to gather researchers belonging to different communities, namely nano-optics, soft matter and statistical physics, thermal sciences. We were happy to realize that we reached an equilibrium between the different communities, and the participants made an effort not to stay in their confort zone. The major scientific points discussed during the meeting were as follows:

Nanofluids-dispersions of metallic nanoparticles in a solvent-still attract the attention of the community, for solar energy conversion purpose for instance (Sani,Mancin). The necessity to accurately model nanoparticles and possible ligands surrounding them was assessed (Asinari). The possibility to enhance the thermal conductivity of nanofluids was hotly debated. Still, the mechanisms were still not clear:are they predicted by effective medium theories (EMA) or is there some alternate microscopic mechanism beyond EMA?

Biomedecine represents a promising field of applications of hot nanoparticles (Rossi,Odershedde). Biological objects have been shown to be heated up to very high temperature without loss of integrity (Amblard). The need to probe locally the temperature around magnetic nanoparticles was outlined (Fresnais).

Collective effects turn out to have a detrimental effect on the efficiency of local heat generation (Chalopin).

Metallic nanoparticles being easily heated up by a laser, interesting new phenomena including temperature induced phase separation may be investigated (Hashimoto). Kapitza resistance is a classical nanoscale heat transfer problem (Bresme), but the question arose down to which nanoparticle size this quantitiy may be unambiguously defined. Beyond Kapitza resistance, heated nanoparticles may locally polarize water molecules, thus creating effective attractions between nanoparticles (Wirnsberger). In colloidal environments, nanobubble formation has been observed around hot nanoparticles (Orrit, Odershedde,Keblinski). An open question is wether or not is it possible to stabilize these small scale bubbles, with interesting applications in photoacoustic imaging.

Thermophoresis- drift of a colloid in a temperature gradient-is fully relevant to the dynamics of heated nanoparticles. It can be used to generate controlled temperature fields (Cichos).Thermoosmosis is also the main driving mechanism of artificially heated swimmers (Ripoll). Last, recent progress in our understanding of thermophoresis opens the way to build a microscopic picture of thermoosmosis (Würger,Fu).

To summarize, what appears as promising directions:

-thermophoresis and thermoosmosis in microfluidic devices

-quantifying local temperature field in a cell or inside a biological membrane

-understand the dynamics of vaporization around heated particles

-quantitative modeling of thermal transport properties of nanofluids

These questions arose from the interaction between experimentalists

and theoreticians.

At the end of the workshop, we were happy to realize that the scientific level of the presentations was very high while the small size of the event made the atmosphere very friendly and not too serious. This was a bit of a challenge to organize an interdisciplinary workshop gathering people from different communities, and we felt that mixing and discussion between communities occurred. We hope that the organization of the workshop will foster collaborations in the future.

3 Community needs

In terms of computational codes, people use either open source codes such as LAMMPS/GROMACS for molecular dynamics simulations, COMSOL for finite element calculations, or they develop their own code for specific purpose, essentially mesoscopic simulation models including DPD, SRD, dynamic density function theory or phase field.

One of the need of the community would be to couple one of these codes to an elementary electromagnetic code which may predict the heating level of nanoparticles, depending on the laser wavelength, intensity and nanoparticle size and shape.

As regards event organization, several possibilities of sequel events have been discussed. A possibility for the years to come is to organize a summer school dedicated to thermoplasmonics, with a significant contribution of modellers. This event may be organized

with an expert in nano-optics so as to attract this community. A second option is to organize a session on hot colloids during the

first international conference entirely dedicated to nanofluids (http://www.icnf2019.com/) taking place during summer 2019. Last,

the organization of small worskhops addressing challenges at the frontier between plasmonics and statistical physics may be envisaged. These workshops, intended to be technical, could be organized in the framework of CECAM. This will be the occasion to develop hybrid tools combining the electromagnetic response of the nanoparticles and traditional computational methods used in soft matter to study colloids.

4 Funding

As the topics addressed during the workshop cover different communities, different funding channels may be identified:

-for people doing either statistical mechanics or nano-optics, the typical channels include the national funding agencies or the European Community through call of proposals for excellence.

-researchers more involved in nanofluids, both experimentalists and theoreticians have already structured their community around a COST action (Nanouptake), and can also answer to less fundamental call of proposals (H2020).

-researchers studying biological objects may also respond to specific calls (health agencies).

In conclusion, although it was not discussed explicitly, there is clearly the possibility of joint project between communities. Researchers having rather fundamental perspective in the field may very well find an interest in building consortiums with researchers having more applied motivations.

5 Will these developments bring societal benefits?

The field has strong societal and economic impacts. There is a tremendous need to define solutions for thermal management at the nanoscale, and in particular for the design of liquid coolers. Recently, there has been a growing interest in the thermal transport properties of metallic colloidal suspensions. Nanofluids have caught the attention of physicists, as they display outstanding thermal conductivity which makes them interesting candidates for liquid coolers.

Light irradiated nanoparticles may be used to sterilize and treat water in remote areas. It has been shown very recently that gold nanoparticles may enhance water boiling significantly thanks to their plasmonic properties, with low-cost devices using sun light.

Metallic particles have also been shown to selectively destroy malignant cells when iluminated with high energy. Indeed, ultrafast boiling has been recently observed experimentally and numerically around intensely heated gold colloidal particles. The generation of fast expanding vapor nanobubbles has important applications in cancer cell therapy but also diagnostics. Indeed, bubbles may be used as contrast agents in ultrasonic detection methods.

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Multi-Scale Modelling of Flexible and Disordered Porous Materials

Location: Chimie ParisTech / PSL University 11 rue Pierre et Marie Curie 75005 Paris
Webpage: https://www.cecam.org/workshop-0-1645.html
Dates: June 11, 2018 to June 13, 2018

1 State of the art

An exponential growth in the number of reported nanoporous framework materials is observed within the last years. These materials open up new horizons in practically all branches of engineering, physics, chemistry, biology, and medicine. Compared with both dense and nanoporous inorganic materials, many framework materials are based on relatively weaker interactions and present large numbers of intramolecular degrees of freedom. All molecular assemblies and solids show some degree of flexibility, yet evidence is accumulating that there is a propensity among these framework materials to display large-scale dynamic behavior, typically called “flexibility”. This workshop covered phenomena that are very diverse both in terms of their microscopic origins and their macroscopic manifestations. This can also allow them to behave as meta-materials, exhibiting properties that are rare or not found in nature: negative thermal expansion, anomalous mechanical properties such as auxeticity or negative linear compressibility, negative adsorption, etc.

Just as there is flexibility in any molecular assembly, there is no such thing as a crystalline solid without defects and disorder. Recent years have demonstrated a large diversity in their nature, as well as the fact they can give rise to specific functionalities, such as improving adsorption affinity or catalytic activity. Computational chemistry is playing a big role in this exploration, with many of its tools being used alongside ex situ and in situ experimental techniques, including quantum chemistry calculations, first principles molecular dynamics, free energy methods, forcefield-based molecular simulations, as well as coarse-grained MD and other mesoscale modelling methods. Flexibility, defects and disorder are all related to entropy. To study these complex phenomena, both experimentally and theoretically, it is necessary to combine several characterization techniques at various scales to obtain a global picture.

2 Major outcomes

The focus of the discussion has been mainly on the state-of-the-art simulations techniques, their extension into multi-scale modelling schemes, and the way that these can help us address complex and cooperative phenomena in flexible and disordered porous solids. We have particularly highlighted to current lack of systematic effort to help bridge the modeling at various scales, i.e. to take for example data from DFT calculations as input for classical modeling, or to use quantitative information from molecular dynamics to build coarse-grained or mesoscale models. In particular, the main scientific points discussed and outcomes of the workshop are the following:

- Ab initio molecular dynamics (or first-principles MD) as the “gold standard” method is extremely useful, but still very demanding in computational effort. It can serve as benchmarks or to solve fundamental problems but there are still strong limitations in both length and time scales involved.
- Various parameterized methods have appeared meanwhile, ranging from atomistic force fields, parameterized from first principles to coarse-grained methods as well as neural network type potentials. This increases the variety of modelling strategies, however a systematic testing of these methods is not generally performed, and their performance and accuracy are not well established for now.
- The topics of presence of defects and disorder is moving into the focus of more and more research groups, and becomes topic of theoretical investigations. This is partly due to it getting more and more interesting from an application point of view, with examples of functionality being introduced into materials by controlled introduction of defects and/or disorder.
- The growth mechanisms of such systems is largely unclear yet, which is connected to that fact that the surface termination of MOFs is not well investigated both experimentally and theoretically. However, recent results indicate that all kinds of flexibility effects are affected by crystal morphology or size. Modelling of these effects is currently only in its infancy, and there are no “typical” methods to use for this; they will have to be developed and benchmarked.
- It needs to be seen to which extent periodic boundary conditions in typical simulation methods hamper the investigation of structural transformations e.g. due to temperature or guest adsorption. This is related to the issue of metastability vs. stability of phases in various conditions; there are systems for which full thermodynamic analyses have been performed (by a combination of experimental and theoretical methods), but this is still relatively rare in the published literature.

3 Community needs

The workshop clearly showed the advances made in the field from various sides (as discussed in the “Major outcomes” section) ranging from improved atomistic force fields, first coarse grained methods as well as “brute force” ab initio molecular dynamics simulations. Nevertheless a clear-cut route to the optimal multiscale simulation method is not visible, yet. As it is natural in an emerging field, different groups work with different methods on different problems. Since also the experimental investigations of flexibility effects (e.g. crystal size and morphology dependence of “breathing”) are still moving on, no clear “benchmarks” for theoretical methods really exist — even validation of novel methodologies is typically quite a complex task. From that overall picture one can conclude that the major community need is further networking both with respect to different theoretical methods (off different length and timescales) as well as to experimental groups, using a large variety of characterization methods — with particular focus on in situ, in operando, as well as tim- and space-resolved methods. All attendants confirmed the advantage of the concentrated and focused scientific atmosphere of the CECAM workshop in its particular format, indicating that such small and intense meetings are optimally suited for this network to grow.

4 Funding

Currently, funding ranges from national research grants for individual researchers to collaborative research centres, as well as individual ESR grants to e.g. the Marie Curie ITN DEFNET focusing on defects in network materials. Within the workshop, the focus was primarily on the scientific aspect, also because most of the attendees collaborate already within such a framework by one or the other way. Moreover, an important part of resources allocation is the use of national or supranational High-Performance Computing (HPC) resources — which are crucial in scientific progress in the workshop's area of focus, as well as for collaborations. Participants have expressed overall satisfaction with the current access to HPC resources, and the European PRACE program has been highlighted in particular. Thus, the overall funding strategy seems to be adequate.

5 Will these developments bring societal benefits?

Nanoporous materials find numerous applications as selective adsorbents and catalysts, substrates for biosensors and drug delivery, membranes and films in various nanotechnologies, which involve fluids adsorbed or confined to nanoscale pores. With their high tunability and on the other hand smaller thermal and chemical stability as compared to zeolites, they evolve as the "orthogonal" class of porous materials to established silicon based zeolites. As a particular example, gas or liquid separation processes are one of the most costly aspects in industrial synthesis of bulk chemicals, both from a financial but also from an ecological (energy need) point of view. MOFs will be seen here as alternatives very soon, but the understanding of flexibility (e.g. gate opening effects, which can increase the efficiency of such methods by a large amount) can only be achieved on an atomistic level by a combination of experimental and theoretical methods. On the theoretical side also this workshop clarified that novel multiscale simulation methods and workflows need to be developed, validated and applied to achieve this ambitious goal. These simulations methods shift some of the burden on the realization of actual experiments, including high-throughput materials synthesis and identification.

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Nano-Structured Soft Matter: A Synergy of Approaches to Amphiphilic and Block Copolymer Systems

Location: University of Lincoln, UK
Webpage: https://www.cecam.org/workshop-0-1574.html
Dates: June 25, 2018 to June 27, 2018

1 State of the art

An important class of soft materials is formed by molecules consisting of chemically distinct parts. In this workshop, we concentrated on two such materials: amphiphilic lipids and block copolymers, which can self-assemble into nano-structures (mesophases) of similar symmetries, but on different scales.

Controlling the properties of soft materials is relevant for a range of applications, such as pharmaceuticals, cosmetics and foodstuffs. Both lipids and block copolymers can form membranes. These can close into vesicles, which are important systems in biology and also in technological applications, for example as drug delivery vehicles.

Lipid mesophases usually contain more than one species, which tend to phase separate. From a biological perspective, lateral lipid organizations are known to play an important role in the membrane functionality. Most studies on lipid phase separation focus on simple geometries, such as lipid vesicles. Only very recently have lipids in more complex phases been theoretically investigated.

For block copolymers (BCPs), mesoscale and multiscale techniques have to be used, and much research has been done using coarse-grained models. Self-consistent field theory (SCFT) and field theoretical approaches can address much larger system sizes and molecular weights than molecular dynamics simulations. For even larger BCP system sizes, advances have been made using phase field models. In practical applications such as lithography, there is an interest in defects and their removal.

Vesicles have been formed from amphiphilic molecules using a wide range of techniques, including microfluidic templating, electro-formation from membranes and self-assembly in solution. Simplified theoretical models have proposed for BCP vesicular and micellar formation using versions of SCFT; however, most of the progress has been driven by experiment, and there is now a need for further theory and simulation to guide future investigations

2 Major outcomes

In the first session of the conference, experimental work that could potentially be explained or guided by simulations was presented. This session was strongly focused on biological systems. In two of the talks, the use of biological molecules to form structures with new and potentially useful properties was discussed, and results were shown on the production of a wide range of phases in lipid solutions and on the formation of porous networks from DNA. Work was also presented on the relationship between the self-assembly of polymer-peptide

conjugates and their interaction with biological systems, and on the use of vesicles to mimic and understand the behaviour of multicellular organisms.

The following session concentrated purely on the simulation of polymers. In the first talk, results were presented on the kinetics of pattern formation and defect annihilation in diblock copolymer melts. During the following presentation, a convincing theoretical explanation was provided of the experimental observation that polydisperse polymers produce more nearly monodisperse micelles. In the final two talks, the addition of fluctuations to field-based models was discussed, and it was shown that this leads not only to quantitative corrections to the original models but also to qualitatively new results, such as the prediction that certain morphologies can be stabilised by fluctuations in highly branched and asymmetric polymers.

During the third session, the role of curvature in membranes was discussed. The range of theoretical and simulation techniques used here was very broad and included microscopic techniques such as molecular dynamics and coarse-grained approaches such as hydrodynamic calculations and the Surface Evolver software. Another theme of this session was the interaction of membranes with particles or with external influences, such as light.

The next group of talks was simulation-based, and strategies were presented for the parameterisation of models to reproduce experimental results and for the formation of non-classical phases by the blending of different species or by using block copolymers with conformational asymmetry. The final talk of this session was perhaps the most fundamental of the conference and was concerned with the foundations of statistical mechanics and the application of counting problems to granular media.

In the final session, there was a stronger focus on dynamics and on the incorporation of realistic dynamics into theories originally formulated for statics. This part of the conference featured a number of talks by early career researchers and included a number of detailed comparisons of theory and simulation with experiment.

Each of the above sessions was followed by a broad-based question-and-answer session, and the limitations of the various models were also discussed; for example, different techniques are better adapted to molecules of different sizes. It was noted that the choice of the best simulation technique for a particular problem was not always clear and could be determined more by the code that was available to a particular group than by physical considerations. The final discussion covered a range of existing and future lines of investigation, in particular the adaptation of simulations to the more complex systems found in biology.

3 Community needs

Soft matter nano structure simulations are very challenging multiscale simulation from microscales MD level to mesoscale level. MD simulation tools like Lammps, NAMD, Gromacs and CP2K, where mesoscale software like SUSHI, CDS and DL_MESO are all open source and highly parallelised codes, we have invited few researchers from these software communities and there were a lot of common topics raised during the workshop discussions, like using multi-resolution mesh to capture interface between different phase, scalable numerical methods to bridge between microscale and mesoscale simulation on the future exascale computing architecture.

Working in this great challenge field of multiscale simulation requires a truly multidisciplinary approach and close interaction between researchers in physics, chemistry, biology, mathematics, engineering, materials and computational science and experiments. Having this kind of workshop annually would definitely help to advance the whole research field. This is

in particular true, as the field is very fast developing, and experimental systems are becoming more and more complex. Regular networking will be very beneficial for identifying new simulation pathways and potentially speedup development of new soft materials.

4 Funding

Several ideas were about paired (tandem) applications to corresponding national councils. Dr Greenall (Lincoln) and Dr Marques (Paris) are working on parallel applications to EPSRC in UK and French research council. Prof Zvelindovsky (Lincoln) and Dr Daoulas (Mainz) are planning DFG Volkswagen Foundation application in Germany, which can also support foreign applicants. Dr Vorselaars is planning on submitting an application to EPSRC after discussions with Canadians. Dr Pinna (Lincoln) is now working with Dr Honda (Japan) on modification of Japanese SUSHI code, which will form a part of UK Impact case for REF and in this case will bring income to Lincoln side after REF2021. Prof Wang (Colorado) and Prof Zvelindovsky (Lincoln) discus joint EPSRC-NSF application in materials science. Dr Paillusson (Lincoln) and Dr Kusumaatmaja (Durham) are discussing a joint EPSRC application.

5 Will these developments bring societal benefits?

The amphiphilic systems discussed during the workshop have a wide range of potential medical applications. For example, micelles and vesicles can be used as vehicles for the delivery of hydrophobic and hydrophilic drugs respectively, and self-assembled structures (for example, those formed by polymer-peptide conjugates) also have potential uses in regenerative medicine, antimicrobial systems and immune therapies. A question considered on several occasions during the conference was the penetration of molecules or small objects through membranes, and this has importance in understanding both how a cell might be invaded by a virus and how therapeutic agents could be transmitted to the cell interior. Finally, the interaction of lipids with light is important in photomedicine.

Outside the medical field, DNA frameworks could potentially be used in sensing, catalysis, photonics, energy storage and molecular sieving. A number of the block copolymer-based systems, especially those involving hydrogen bonding, could be used in precision lithography e.g. for the manufacture of integrated circuits. In this application, it is also important to understand how defects form and how they can be eliminated, and results on this question were also presented and discussed.

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Non-Adiabatic Quantum Dynamics: From Theory to Experiments

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1638.html
Dates: July 2, 2018 to July 6, 2018

1 State of the art

The increasing complexity of the systems being studied experimentally necessitates a strong synergy between experiment and theory. Over the past decade, there have been significant developments in experimental methodologies. Nonlinear spectroscopies, such as two dimensional electronic spectroscopy have been able to probe quantum coherences and the electronic couplings between different states. Vibrational spectroscopies have made it possible to follow molecular vibrations during a non-equilibrium dynamical process. Tools such as X-ray Free Electron Lasers and High Harmonic Generation have led to a paradigm shift in the capability of short wavelength techniques to deliver ultrafast dynamics with structural information.

The theoretical description of nonadiabatic phenomena calls for the treatment of coupled electronnuclear dynamics, and not just nuclear quantum effects. This can be achieved by solving the timedependent Schrödinger equation. While this can be achieved using the multi-configurational time dependent Hartree approach, such grid-based solutions are limited to a small number of nuclear degrees of freedom owing to the exponential scaling brought about by the direct product basis. In addition, in each case this potential must be computed a priori limiting the dynamics to models. To overcome this difficulty, many approximate methods based, to a greater or lesser extent, on trajectories have been developed. Among these trajectory surface hopping remains the most widely used method. However, path integral based methods such as ring polymer molecular dynamics have recently been extended to non-adiabatic systems using mean-field approximations and mapping variables. Wavefunction approaches based upon Exact Factorisation and Gaussian basis functions are also receiving much attention. There is also a great deal of interest in quantum-classical path integral and Liouville operator based methods.

2 Major outcomes

One of the most important outcomes from the workshop was the ability for experimentalists and theoreticians in the non-adiabatic quantum dynamics community to have lengthy discussions. This helped the two respective groups understand both the perspectives, limitations and language of the other. This will undoubtedly help increase the ability for synergy between experiment and theory in this area.

A major theme of the workshop was excited state dynamics of molecular systems. A number of talked exploiting either On-the-fly potentials (Shalashilin, Kirrander) or model potential energies (Fumanel, Thoss, Burghaht) were presented. The latter is highly appropriate for the smaller amplitude motion of photophysics while the latter has deemed more appropriate for photochemistry involving large amplitude motion of such as isomerisation and dissociation. However, these two approaches remain rather separated and, in many cases, hard to draw

direct comparison between the two. The presentation of Habershon described how machine-learning methods, specifically approaches such as kernel ridge regression (KRR), can be used to accelerate quantum dynamics simulations by providing efficient yet accurate approximations to potential energy surfaces. This enabled for small molecules the ability to perform simulations on comparative times as experiments. and provides an important links between model and on-the-fly potentials. Extending beyond gas phase studies usually performed for grid quantum dynamics, Santoro presented a mixed quantum/classical method for nonadiabatic quantum dynamics which correlated grid based quantum dynamics with molecular dynamics to provide a intuitive way of interpreting the effect of the environment on excited state dynamics.

A number of presentations on the quantum-classical ring polymer molecular dynamics (Richardson, Huo), quantum master equation formalism (Markland), quantum-classical path integral methods (Makri). These have recently been extended to include the description of multiple electronic surfaces and can treat highly complicated dynamical problems. Novel approaches with remove the need for Born- Oppenheimer potential energy surfaces were present (Kelly, Albareda). While in the early stages of development, these methods provide an exciting new perspective in the field.

From the experimental perspective, the major points discussed at the meeting were the potential for insight into ultrafast dynamics provides by new light sources and techniques. This included electron diffraction (Miller), X-ray spectroscopy (Marangos, Collet) and impulsive vibrational spectroscopies (Leonard). Examples of recent work included using the HHG spectroscopy technique to measure the fewfemtosecond timescale coupled electron-nuclear dynamics in a strong field ionised, electron diffraction of complex organic systems and solution phase reaction dynamics to identify major reaction modes and vibrational activity during photoisomerisation. Many of these examples are both accessible to theoretical treatment and benchmarking, and their underlying objectives are common with many of the theoretical work presented.

In terms of increasingly the synergy between experimental and theoretical work, a key challenge is using the simulations to calculate experimental observables and re-creating experimental conditions. Shalashilin outlined approaches for including the external field responsible for the pump and probe steps in experiments. Kirrander presented examples of this, using Gaussian wavepacket techniques to support chemical reaction dynamics probed using ultrafast scattering at X-ray Free-Electron Lasers (XFELs).

This demonstrated how the wavepacket limits the spatial resolution attainable in diffraction experiments, but despite the good agreement some fitting of the theoretical data was still required. This provides a fertile space for theory to understand the cause of this and propose possible solutions.

3 Community needs

This workshop is part of a longstanding series of CECAM workshops on this topic. In the last 5 years, they have provided a strong focal point for the community to develop around. They have naturally evolved into a balance of theory and application. This year's workshop in the area was the first to include experimentalists and consequently provided a new dimension to this series. In addition, this workshop demonstrated the strong future of the community as there was strong participation from early career researchers. Continuation of this series is therefore a strong need of the community along with the inclusion of experimentalists in future workshops. The theoretical non-adiabatic quantum dynamics community does not represent a major drain on the currently available HPC resources and therefore the present computational infrastructure does not represent a risk to the community. However, one of the

major needs is the requirement for a few community codes. Such codes for exist to some extent, e.g. Ab Initio Multiple Spawning, NEWTON-X, SHARC and CPMD, but many methods are not available and are combined to locally developed codes. With the development of codes such as Quantics, this is beginning to emerge, but work is still required to generate benchmarks for calibrating existing and new methods.

4 Funding

From the perspective of theoretical developments, typical funding channels in this area are focused upon national funding schemes. Given the relative low cost of the research, a significant amount is also performed without explicit funding. This does present challenges with continuity of researchers and code development. Experimental work in this area is also focused upon national funding schemes and regional funding, such as Horizon 2020 schemes. The possibility of joint research proposals was not explicitly discussed during the meeting, however collaborations between specific researchers were discussed during the extended breaks during the workshop. No new sources of funding were identified, however, the increasing ability to probe, calculate and interpret complicated systems is opening new avenues of potential funding, especially in applied research fields making it possible to access industry funding.

5 Will these developments bring societal benefits?

Both the experimental and theoretical non-adiabatic quantum dynamics community are founded upon fundamental science. However, while traditionally this fundamental knowledge has been focused upon objectives which far from direct societal benefits, the rapid developments in this field means that this impact is becoming increasingly possible. Indeed, Miller presented a way to drive the system from a solid to liquid so fast that nucleation could be arrested to as few as ten atoms. This observation led to a new concept in laser surgery that avoids explosive nucleation growth and cavitation induced shock wave damage that causes massive collateral damage in laser surgery. Consequently, the long held promise of the laser to achieve minimally invasive surgery has been achieved and without excessive fibroblast formation leading to scar tissue. In addition, various discussions of technologically relevant phenomenon such as singlet fission were held. This mechanism has significant potential in next generation solar cells.

The importance of coupled vibrational-electronic motion in this mechanism means that molecular design can only be achieved by using the understanding obtained from the non-adiabatic quantum dynamics community.

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Crystal Defects for Qubits, Single Photon Emitters and Nanosensors

Location: CECAM-DE-MM1P
Webpage: https://www.cecam.org/workshop-0-1561.html
Dates: July 9, 2018 to July 13, 2018

1 State of the art

Point defects acting as color centers in solids may realize single photon source and quantum bits that can be harnessed in quantum information processing and nanoscale sensor applications which may revolutionize the info-communication technology, biological research and therapy. The leading contender is the nitrogen- vacancy center in diamond which may be considered as a robust quantum tool. Several quantum algorithms and protocols for sensing have been already demonstrated by this center. However, researchers face many materials science problems in order to maintain the favorable intrinsic properties of this color center that can be perturbed by other defects either in bulk or at the surface of diamond that is difficult to resolve because of its chemical hardness and the concurrent stability of carbon allotropes.

Recently, theory-driven search for alternative materials could identify other quantum bit candidates in technologically mature wide band gap semiconductors, particularly silicon carbide, that have been recently demonstrated in experiments. However, the knowledge about these color centers is scarce and only the tight collaboration of experimental and atomistic simulation researchers would lead to a rapid progress in the field. The proposed workshop aims at bringing together world-leading experts in all these fields to improve interdisciplinary cooperation overcoming traditional boundaries between scientific disciplines.

We have been successful to achieve the following key objectives:

- Bring together researchers from materials growth, defect engineering, surface chemistry, quantum optics, spin physics and theory at phenomenological and atomic scale level to highlight recent progress and discuss challenges and opportunities in the host materials and the embedded defects from the aspect of realization and control of quantum bits for quantum information processing and sensing.
- To foster the exchange of methodological expertise and new developments between scientists working on different aspects of diamond, silicon carbide and related materials.
- To discuss possibilities for optimizing the materials properties and device design aided by theory. The interdisciplinary character of the workshop will help finding solutions for overcoming current limitations.
- Provide opportunity to form new worldwide interdisciplinary collaborations on solid state quantum bits for the mutual benefit of theoretical, experimental and applied researchers.

  The program consisted of 30 invited talks of 40 minutes (30+10) each and one poster session presenting 28 posters. In addition, many social events (reception and conference dinner) to allow for informal exchange were held. The invited talks were given by well-established scientists from the different theoretical and experimental communities, which acted as platform for interesting cross-/interdisciplinary discussions. The invited talks were followed by a poster session where the young researcher participants showed their scientific work/progress and exchange of ideas with a broad knowledge in computational chemistry, solid state physics and computational materials science. The organization was very compact

with the scientists accommodated in the same hotel fostering exchange and discussion between the participants also outside the meeting room.

Financial support from the DFG, Psi-k Network, and the German CECAM node multi- scale modelling from first principles, cecam-mm1p.de at the University Bremen is gratefully acknowledged.

2 Major outcomes

Initialization and readout of solid state qubits often relies on photoexcitation, thus understanding the excited states and levels is of paramount interest. An immediate quest of atomistic simulation techniques is to determine the excited states and levels from first principles that was one of the main discussion point at the conference. It was shown that many-body perturbation techniques are unable to address this issue properly for nitrogen-vacancy center in diamond and related centers in hexagonal boron nitride.

Another interesting point was the convergence issue in the calculation of photoluminescence sideband of color centers acting as solid state qubits. Instability in the degenerate electronic states may occur in color centers that manifests as dynamic Jahn-Teller effect. This effect has a great impact on the photoluminescence sideband and the intersystem crossing rates that was discussed in detail at the conference. Further development is required to calculate the intersystem crossing rate fully ab initio. We expect that the next 2-3 years this will be realized by combining the recent developments in calculating the excited state and the spin-orbit interaction. This would open the full description of solid state qubits for which the qubit is read out optically or electrically.

Experiment

On the experimental side, the workshop has demonstrated enormous effort in the advancement of solid state qubits for quantum communication and sensing.

Challenges and recent improvements on position-controlled creation of single and low ensemble of point defect qubits in bulk and nanostructured SiC have been discussed by Jörg Wrachtrup (University of Stuttgart) and Vladimir Dyakonov (University of Würzburg). Cutting edge experiments have been presented by Ronald Hanson (Delft University of Technology) on connecting point defect qubits for quantum networks and by David Awschalom (University of Chicago) on acoustic wave coupling of point defect qubits, a step toward quantum computers. Photoelectron detection of point defect qubits' signal is an important step forward integrated electric-quantum devises which was discussed by Fedor Jelezko (Ulm University). Recent experiments on novel single photon emitters in different host materials were presented by various speakers: emitters in hexagonal boron nitride by Lee C. Bassett (University of Pennsylvania) and Igor Aharonovich (University of Technology Sydney), SiV center in diamond by Christoph Becher (Saarland University), and emitters in silicon carbide by Brett C. Johnson (The Univeristy of Melbourne). Present status of silicon-based quantum device was discussed by Arne Laucht (University of New South Wales). New defects in 2D materials were discussed by Lee Bassett and for novel wide band gap semiconductors by Kai-Mei Fu (University of Washington). Quantum applications were back up by thoughtful interpretation of classical spectroscopy studies as well as their interpretation (Nguyen Tien Son).

Theory and computational studies

On the computational side, the theoretical groups as well have put a lot of effort to address the more and more the calculation of the heavily correlated excited state in qubits. This includes some key presentations at the workshop, given e.g. by Mike J Ford (University of

Technology, Sydney), Michel Bockstedte (University of Salzburg). The electron-phonon interaction and its role in the optoelectronic properties of solids were discussed by Michel Bockstedte (University of Salzburg), Shengbai Zhang (Rensselaer Polytechnic Institute, Troy), Audrius Alkauskas (Center for Physical Sciences and Technology, Vilnius), and Adam Gali (Wigner Research Centre for Physics, Hungarian Academy of Sciences). We note that a new field has been developed by directly calculating the spin dynamics of color centers from first principles parameters by Viktor Ivády (Linköping University & Wigner Research Centre for Physics, Hungarian Academy of Sciences) where the control of the spin using model Hamiltonians has been far developed by Martin Plenio (University of Ulm), Alex Retzker (The Hebrew University of Jerusalem) and Sophia Economou (Virginia Polytechnic Institute and State University, Blacksburg). Numerical models have been also developed to understand the relaxation times and coherence of the nitrogen-vacancy electron spin and its diffusion by Jeronimo R. Maze (Pontifical Catholic University of Chile) and Marcus W. Doherty (Australian National University).

III. Assessment of the results and impact on future direction of the field

Accurate description of the electronic states and levels, their coupling with phonons, spin-orbit interaction, radiative and non-radiative decay is a major obstacle in the optimization of defect qubits. In addition, the creation and conditions of stability of defect qubits is also of high interest for tight engineering of the formation of solid state qubits. Even advanced experimental techniques are not able to fully explore the physical mechanism of the initialization and readout processes of qubits, thus joint effort from experts in different fields, including both experimental and computational studies is required to efficiently advance this field. Atomistic simulations can also mediate engineering of qubits in solids and even predict new qubit candidates. To enable such collaborations, it is of crucial importance to organize interdisciplinary workshops like ours to act as platforms for exchanging ideas and for bringing together researchers from different subject areas who work on different aspects of the same topic. In the future, we will try to continue organizing workshop to achieve this goal on a biannual basis.

The workshop became a forum to discuss about possible solutions of improving the control of formation of qubits and the optimization of control of qubits.

IV. Infrastructure requirements to make advances in the field

As discussed above, the advancement of theories of the operation of solid state qubits requires the development of novel theories and codes which can i) capture the inherent complexity of intersystem crossing processes and ii) contain sufficiently accurate description of physico-chemical processes, including photon-electron interactions, electron-hole coupling, electron-phonon coupling, etc. The development of such theories and the resulting computer software will benefit the broad community of theoretical researchers, but also have important impacts on experimental studies and industry. However, to achieve this, a continued investment is required, as method and code development usually occur on a longer time scale compared to the study of applications. This also requires the training of masters and PhD students not only in physics, materials science or biology, but also in computer programming (including parallelization of software) and use of high-performance computing resources.

V. Impact to address the need of industry in driving economic growth

Progress in the field of many body physics, electron-phonon interaction and spin related properties is fundamental to many European industries connected to high- tech materials design and device applications. Examples are

- Sensors for automotives and semiconductor technology processing
- Defect engineering approaching single defect level in 3D and 2D materials
- Materials for secure (quantum) communication

- Single spin measurements for molecule identification and design of spin materials
- Hybrid nano/bio-sensors for medical applications

Such directions can be strengthened by focused research projects for the development of new materials and devices in key enabling technologies. The field of nanodevices is currently opening to new materials, especially 2D. The EU flagship on Quantum Technology is indeed expected with the aid of computational predictions to produce several new outcomes.

3 Community needs

The discussions at the workshop made it evident that two significant research directions have started to emerge in the field of computation studies for single point defect applications. First, for complete understanding the physics of know point defect qubits and single photon emitters, the community needs to carry out highly accurate calculations of the electronic structure and numerous of derived magneto- optical quantities in realistic models of single point defects. For the electronic structure calculation, the workhorse method today is the HSE06 hybrid functional, which provides reasonably convergent electronic structure in supercell models as

large as ~500 atom. For superb numerical accuracy one needs to apply either larger supercell, consisting of 1000-3000 atoms, or increasing the number of k-point for smapling the Brillouin-zone, e.g. to 2x2x2. For appropriate treatment of excited states, one need to apply high level approaches. Recent methodological developments made sophisticated calculations, such as GW+BSE and cRPA+CI, practically feasible on point defect supercell models. The second emerging direction is the identification of potential point defect for single defect applications. This direction requires a systematic search in the zoo of intrinsic and impurity related defect in 2D and 3D semiconductor hosts.

From these examples, it is evident that the community needs to invest enhanced computational power to be able to accurately and complete characterize point defects that have been investigated in experiment as well as to find candidates for extending the list of applicable point defect qubits and single photon emitters. While the theoretical studies are getting computationally more demanding it is necessary to clarify the needs and interest of experimental collaborators. Furthermore, to realize and test theoretical predictions, the community needs to tightly collaborate with experimentalists. These can be done on various forums, for example through the organization of CECAM workshops on this topic in the future.

4 Funding

The EU has launched the FET Flagship on Quantum Technologies as a part of Horizon2020, and the consortia of the first round of calls are being established where the leading scientists participated at the conference. In addition, EU QuantERA initiative fosters cooperation between theoretical and experimental groups on solid state qubits in Europe where again the consortia have been formed and started to work together. Future calls are expected to appear in the Quantum Technology and QuantERA where the cooperation was discussed between the participants in the social events and breaks of the conference.

Furthermore, national quantum technological programmes support research and development in the field in the European countries, the USA, Japan, China, Australia.

5 Will these developments bring societal benefits?

Our workshop contributes to the development of technologies based on solid state qubits that will have a number of societal and economic benefits, especially in terms of:

- Breakthrough in medical imaging and drug design and efficacy leading to corresponding breakthrough in disease diagnosis and treatments as well as low-cost diagnosis systems,
- Environment through optimized battery management, lower consumption electronics devices or reduction of electronic pollutions,
- Optimized wireless communications resulting from cognitive radio capabilities extended to the 5-25 GHz frequency range,
- Quantum communication with ultimate secure connection between partners that will influence the entire socio-economical system,
- Emergence of a new industry and new companies, thus creating new job opportunities. Quantum sensors and communication will be at the heart of Quantum internet of Things with a strong transformative effect on society in the long term.

Quantum technology is hence considered to be one of the most ground breaking technical developments currently, with dedicated impact on social developments in modern industrial societies. It thus appears to be advisable to include a session on the social impact of those technologies in upcoming events on this topic.

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International Workshop on Computational Electrochemistry

Location: CECAM-FI
Webpage: https://www.cecam.org/workshop-0-1612.html
Dates: July 9, 2018 to July 12, 2018

1 State of the art

Much work has been done on atomistic calculations of surfaces, interfaces and molecular adsorption. DFT usually grants a reasonable description of those. Even local and semilocal exchange-correlation density functionals can yield quantitatively accurate adsorption energies for a number of systems. However, this good description does not extend to surfaces with a net charge or where the position of the Fermi level is a tunable parameter. Obviously this imposes a serious drawback to modeling electrochemical interfaces where the effect of the potential is explicitly taken into account. In practice, one needs to resort to workarounds.

Seminal work was done in the 2000s, most notably by the Nørskov group in Denmark, and since then several approximations have been proposed. The simplest solution is to include potential differences only implicitly as an energy shift. Another way is through the inclusion of a constant external electric field within the electrode-water interface. One can also introduce an explicit excess charge (positive or negative) by changing the number of electrons in the calculation, which spontaneously accumulate on the metal surface. A different approach is to charge the electrode indirectly by introducing hydrogen atoms adsorbed on the surface metal sites.

On top of the issue of electrode potential, a crucial point in electrochemistry is how solvation, electrical double layer structure, counter-ions and pH effects are all taken into account. Implicit and explicit solvation models can be used, depending on available CPU resources. pH is usually only included implicitly because of system size limitations.

These combined issues make accurate computational electrochemistry modeling extremely challenging and all of these approaches have their own advantages and inconsistencies. In this workshop we looked at the latest developments and approaches to dealing with these effects.

2 Major outcomes

* The consensus is that, while the field is advancing, there is still much improvement to be done methodologically before the role of simulations in computational electrochemistry can shift from "rationalizing" experimental results to "doing a computational experiment". This was summarized by Axel Gross as "this has been and still is a field *towards*".

* In connection to the point above, in one of the "rump" sessions the participants identified the need for a "standardized test" that allows to establish and compare the performance of the very many approaches currently available. There was no consensus as to what this test should be.

* A major development with respect to early literature in the field seems to be the generalized adoption of dynamical solvent effects as a necessary ingredient in computational electrochemistry. That is, while early work often used static (i.e., ice-like) water and only few monolayers of solvent, current work uses molecular dynamics and many solvent "monolayers" to correctly include dynamical or entropic effects. There was for instance a special "rump" session on how to incorporate entropic effects into simulations.

* Another promising strategy to introduce electrode potential in simulations was presented by Mira Todorova, where a very wide gap insulator (neon in the example) is chosen as counter electrode. Because the gap is so large, the Fermi level is straddled by the conduction band mimimum and valence band maxima of the counter electrode for a wide range of applied potentials. This is in contrast to a typical two-metal electrode configuration, where the necessary presence of a global Fermi level in regular DFT calculations would mean the suppression of an applied electric field.

* A personal disappointment for one of the organizers (MAC), following up on the point above, was that the community has not explored the possibility of truly applying different Fermi levels on the different electrodes via non-equilibrium Green's functions. Somewhat related were some presented developments from Pasquarello's group at EPFL of "constant Fermi level" molecular dynamics, where fractional occupancies are changed throughout the MD so that the global Fermi level evolves towards a chosen value.

* Another identified trend is "doing more with less" with regards to solvation effects. In particular, implicit solvation models and joint density functional theory are being adopted in combination with explicit solvation to deal with extended solvent regions. Jarvist Frost from KCL, introduced the idea of using tight-binding to deal with extended systems and a new "hairy probe" formalism to deal with different electrochemical potentials at different electrodes.

* On the more applied side, people are striving to find CO2 reduction catalysts for fuel production, and also other molecules, such as NH3. We had several talks on calatyst search and characterization, including carbon nanotubes and novel oxides and perovskite materials and even an iron-based molecular catalyst. This area remains very active due to the obvious indutry applications.

* In the area of charge transfer we had contributions focusing on DFT-based parametrization of Marcus theory (e.g., constrained DFT), coupling the proton degrees of freedom to electron transfer phenomena (i.e., proton coupled electron transfer) and a new approach, "molecular" DFT. MDFT is conceptually related to joint DFT, where the molecular details of the solvent are kept but in a continuum level of description. It remains to be seen if these approaches will become generally adopted by the community.

3 Community needs

We feel that the community's need for HPC resources is well covered. It seems that getting CPU time for problems in electrocatalysis is not an issue because of the need for clean energy sources, offsetting carbon emissions, more efficient industrial processes and so on. These needs are usually well perceived by funding agencies and non-specialist committees (e.g., sitting at HPC infrastructure centers), as opposed to some more niche areas in electronic structure like development of highly accurate schemes (e.g., many-body or wave-function-based approaches).

It is possible that cross-talk with experimentalists is somewhat missing, and the community could benefit from it. In particular, with experimentalists doing fundamental work with well defined systems. We had an invited experimentalist, Víctor Climent, whose very fundamental

work on well-controled Pt electrochemistry was very well received by the audience. However, we also feel, from Víctor's feedback, that the computational work may have taken a path towards highly technical and theoretical approaches (e.g., fundamental developments in electronic structure theory) which makes cross-talk somewhat difficult. It would be useful to have some instrument (possibly in the form of a targetted workshop) available to bridge this communication gap.

We asked for anonymous feedback on the IWCE2018 workshop. The consensus was that the participants very much enjoyed this workshop and would welcome a similar event being held biannually in Europe. It would be good to have some level of CECAM commitment which allowed us to create a wider organizing committee involving people in several universities so that this event can rotate throughout Europe. The detailed feedback on the workshop can be obtained from Miguel Caro upon request.

4 Funding

Most participants seemed to be receiving funding majoritarily from their national research or science foundations and basic funding at their local institutions. Some participants also had European funding available to them, i.e., from the European Research Council. One or two speakers showed industry involvement in their work (for applied electrocatalysis). Joint funding opportunities were not openly discussed during the meeting, at least that we are aware of. Topics in electrocalatylis are always well suited for targeted calls related to clean and efficient energy production. Topics in analytical electrochemistry are also well received for targeted calls related to medical diagnostics and environment.

5 Will these developments bring societal benefits?

On the one hand, as we have mentioned before, some aspects of the computational side of the electrochemistry field are still far away from making a large direct impact on society, and many efforts are directed towards developing theory and methodologies towards accurate and affordable simulation of electrochemical systems. The potential impact on society once these methods are better established and more accurate is huge. We highlight the possibility to optimize biomolecule detection systems for in vivo health monitoring and diagnostics, but there are many others. On the other hand, the extensive work carried out on electrocatalysis for fuel production has the potential of impacting the development of new catalytical processes and materials. It is possible that cheap alternatives to Pt for water splitting may emerge from the myriad of different material systems which are currently being surveyed by the community. The community is also hard at work on finding semiconductors, mostly oxide based, for solar-energy-mediated water splitting. We feel that this direction may also have an impact on society in the near future, as new promising materials are being characterized via simulations.

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Frontiers and Challenges of Computing Metals for Biochemical, Medical and Technological Applications

Location: CECAM-FR-MOSER
Webpage: https://www.cecam.org/workshop-0-1519.html
Dates: July 11, 2018 to July 13, 2018

1 State of the art

Metal ions are critical across the fields of chemistry, biochemistry and material science. Metal ions are considered of extreme importance for metallo-drugs and metallo-enzyme functions. Moreover, metals are of utmost importance in technological applications that are expected to change our lives, like in the case of solar cells and next-generation batteries.

Nevertheless, while some fundamental aspects of metals in biology and chemistry have been investigated in depth, much remained to be understood on the mechanisms of recognition and selectivity for metal-aided processes. Also, the current force fields (when treated at the classical level), simulations of metallo-proteins can still produce artifacts. In this respect, predicting properties of metal complexes requires high-level computations at the quantum mechanical (QM) level. QM calculations are key for predicting the electronic structure properties of complex metal containing biological system. This knowledge is needed for designing of more efficient materials based on biomimicry and to create biotechnological application in the medical fields. In this context, our workshop has treated these complex topics with a focus on the role of metal ions in biological chemistry/ medicine, highlighting current limitations and major advances of computational simulations to treat atoms in proteins and new materials.

2 Major outcomes

The workshop reported several examples in which molecular simulation contributed to understanding biological processes where metals were playing a key role. These provided information on the atomic scale, furnishing also spatial and temporal resolution, inaccessible to experiments. This information may help develop new drugs, to design enzymes for biotechnological application in the medical and energy field.

Prof. Dyson EPFL, Lausanne, and Prof Davey, Singapore, Prof. N Russo, University of Calabri. have clearly shown that, although our understanding of the role of metallo-drugs ions in cancer has greatly improved in the last years, leveraging this knowledge to create novel therapeutics remains highly challenging. Trying to integrate experiment and theory synergistically is also a challenge.

The same was illustrated by Prof. V. Batista, Yale University USA, Prof. Rovira, University of Barcellona, Spain, Prof. Ramos University of Porto, Portugal, Dr. S. Raugei PNL, USA. In their presentation they showed how dissecting the function of complex biological molecules may lay the foundation to develop artificial biomimetic systems.

The workshop has been also devoted to show how a wise combination of computational methods of different level of accuracy can contribute to unravel electron transfer processes in complex macromolecules or their aggregates (Prof. J Blumberger UCL, London, UK, Prof R Wade, Heidelberg Institute for theoretical studies, Heidelberg, Germany, Dr. S. Raugei PNL, USA)

Challenges of simulations techniques to treat transition metal-based biomolecules have been addressed during the conference (Prof. Cui Boston University, USA). It was noted that approaches typically used in condensed matter physics, such as quantum Montecarlo, along with advanced quantum chemistry methods, lead to very exciting results in the field.

Several participants suggested that joint meetings between theoreticians and experimentalists might sprout new scientific research if they succeed in integrating highly diverse chemical and biophysical tools and approaches present in the community.

3 Community needs

1. The very large computational infrastructures available in Europe and USA allow addressing high-performance computing (HPC) -based investigations of metal-dependent biological phenomena with molecular simulations techniques. However, understanding the mechanism of a complex bioinorganic process usually requires the integration of several different computational techniques and not all of them perform equally well in supercomputing centers. Hence, local resources (e.g. at Universities) need to be tightly integrated with the supercomputing center. Unfortunately, this is not always the case.

2. We strongly need shared archives across Europe and USA reporting computational techniques to treat metal ions in biological systems (e.g. new ways to develop force fields for classical MD simulations)

3. The participants have underlined the success of this workshop. Prompted by this, a biannual series of workshops on experimental/computational approaches to metals in medicine has been strongly auspicated by the participants.

4 Funding

Typical channels to organize these future conferences would be CECAM, Psi-K. Specific cost actions on ‘structural and functional annotations of bioinorganic systems’ can also help in the organization of focused meetings. Funding for this kind of biological problems is available from the National Institute of Health and National Science Foundation in the USA. While in Europe they are provided by European Program Horizon2020, In Italy by Telethon, Italian Cancer Research Association (AIRC), Italian Ministry for Education and Research (MIUR).

5 Will these developments bring societal benefits?

Increasing our knowledge of metals ions in biomedicine, and biotechnological applications may greatly help develop the new societal challenges and it is of course of great significant societal benefit. It may reduce costs associated with healthcare treatments and to third persons taking care of ill people (relatives). Novel drugs may also largely help slow down the progress of the diseases and/or decrease side-effects, such as, for instance, the pain associated with neuroinflammation. This research is also obviously highly connected to pharmaceutical and technological industries. Funding opportunities for these topics can be sought from the latter, or by EU agencies, such as, for instance, the H2020 grants, Italian Ministry of Research, Italian Association for Cancer Research. Funding agencies for worldwide projects such as the Human Frontier Science Program.

Notably, this workshop had the participation of experimentalists. Such interdisciplinary interactions will hopefully lead to new collaborations, which may generate proposals for prestigious European grants, like the ERC Synergy. We believe that these multidisciplinary discussions may generate new interactions and collaborations that may end up in new research teams and efforts on metal-containing systems. Not only on the computational side, but also with practical extension toward applied technologies, which may generate a true impact on society, in the medium/long term.

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Interfacing Machine Learning and Experimental Methods for Surface Structures (IMPRESS)

Location: CECAM-AT
Webpage: https://www.cecam.org/workshop-0-1580.html
Dates: July 11, 2018 to July 13, 2018

1 State of the art

The structure of a surface determines its properties and its function. This holds especially true for organic films grown on inorganic surfaces. The adsorption is a complex processes determined by multiple physical phenomena. Thus, one and the same system often exhibits different motifs, depending on the details of the deposition. Such polymorphs exhibit different electronic properties, establishing a growing interest in elucidating the details of the adsorption structure.

Determining or predicting the structure of organic ensembles on surfaces is a challenging problem, both experimentally and theoretically. In the past years, computational structure search methods for inorganic/organic interfaces have made tremendous progress, which can be attributed to the advent of machine learning methods. Machine learning is now used to obtain cheaper, more accurate total energies, accelerate established techniques, and even to develop completely new search strategies. However, despite their success, most computational studies still focus on small model systems. A routine application to interfaces that are directly relevant to engineering problems is still challenging because of the occurrence of “real-world problems”, i.e. the imperfections of the interfaces.

Experimental groups also employ algorithms to convert their measured data into surface structures. These are specialized towards specific methods, and often do not provide unambiguous solutions. Moreover, the analysis of experimental data is often controversial and contains assumptions which themselves depend on the observed surface structure, and thus needs to be performed iteratively. As a result, the experimental algorithms are often just as sophisticated as computational structure search techniques. Since computational and experimental algorithms have, however, evolved to solve complimentary challenges efficiently, the respective method developers could greatly benefit from each other’s knowledge and expertise.

2 Major outcomes

The advent of machine learning has led to an unprecedented increase in accuracy and speed for global structure search endeavors. This has put many systems into reach that were previously intractable due to their size and/or complexity. As a consequence, the field of structure determination and prediction can now start to tackle questions that were previously outside of the realm of computational studies. Questions and topics discussed in the course of this workshop included:

> How can we extract physical meaningful information from machine-learning studies?

> What drives layer-by-layer formation in the case of organic thin film growth?

> Defects and grain boundaries: Which kind of defects need to be accounted for in computational studies?

> The Relevance of Transition States for Kinetic Processes of Molecules on Surfaces. Challenges for Experiments and Theory

> What efficient methods could be used for predicting the structure at a surface-molecule-surface (e.g. ZnO-organic superlattice).

> Multilayer and morphology: How can solid/liquid interfaces be modelled? What are good approaches to go beyond monolayer coverage?

The workshop included long, dedicated discussion sessions to deliberate these questions and exchange ideas. To each meeting an invited speaker was assigned as “chair” and discussion leader. The discussions proved to be very insightful, since the speakers tended to provide tutorial insights into the problem at hand from either the experimental or theoretical perspective. Even after extensive discussions, it is clear that many open challenges remain. In particular, robustness and transferability of machine-learned models is an issue; even more so, the question whether eventual insight gained from these models is trustworthy and accurate. Moreover, it remains unclear how thin layers beyond the direct interface (i.e., either a solid-liquid interface or multilayer) can realistically be modelled with a reasonable computational effort. An additional challenge that remains is the defect concentration at organic overlayers, that is difficult to assess in experiments and hardly ever reported in scientific studies, thus limiting the comparability and reproducibility of what could otherwise be invaluable benchmark data.

3 Community needs

The workshop brought together theoretical and experimental groups with a strong interest in structure determination at inorganic/organic interfaces. The large number of participants from both field testifies to the timeliness and relevance of this topic. It is clear that as of now, there is still a lack of awareness on the side of experimentalists as to what the limits and possibilities of new machine-learning methods are. At the same time, a similar lack of awareness might be attributed to the theoretical groups: Over the past years, it was common practice to neglect certain contributions, such as vibrational effects on adsorption energies or for thermal desorption experiments. Experience and training has thought us to neglect these contributions “by default”. In the light of the power of machine-learning methods, it is clearly time to re-evalute common practices; regular meeting between experimentalists and theoretical groups promote critical thinking in this direction.

A further aspect of this workshop was to intentionally bring together contributors from different regions and/or field, that were likely not to have met before. This did not only yield clear benefits for the exchange of idea and experience, but has also led to planning a number of new collaborations.

4 Funding

Small amounts of funding are readily available for networking activities. This community traditionally relies on funding from CECAM and Psi-K sources, given the good match between the subject matter and the scope of these two bodies. An emerging source of small-scale funding for this field are the novel European centres of excellence (CoEs) for 2/3
computational materials design such as NOMAD and Marvel: they have an interest in the methodology produced in this field, but many contributors work outside the CoEs.
There is no present plan for joint funding proposals at this stage: it is expected that groups will apply for individual funding (national and Horizon 2020) to advance their simulation tools before the community is ready for collaborative work.

5 Will these developments bring societal benefits?

Structure determination, both theoretical and experimental, is a core requirement to understand and improve a wide range of technologies. These include, inter alia, electro mobility – specifically batteries, where the interface between electrode and electrolyte is still poorly understood. Increasing the performance and/or lifetime of batteries by even a few percent is expected not only to have a massive economic impact (boosting, for example, the sales of electric cars), but also a big environmental effect (via the recycling of used batteries). Other applications include pharmaceuticals. There, polymorphism is, for instance an important pathway to govern the bioavailablity of drugs. Of similar importance is the so-called missing polymorph problem, which describes that sometimes, polymorphs that have been produced for years (and that have been approved by the drug agencies) no longer form in a given plant. For the companies, the only possible procedures are either finding a path to restore the polymorph, or undergoing a new approval process. Both strategies are extremely expensive. More importantly, however, until the problem is solved the drug may be unavailable, with corresponding health issues for the patients that rely on it.

These examples only constitute only two of the most tangible effects of polymorphism and underline the necessity for future and continuous research in the field of global structure search at interfaces.

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Frontiers of Coarse Graining in Molecular Dynamics

Location: CECAM-DE-MMS
Webpage: https://www.cecam.org/workshop-0-1615.html
Dates: July 23, 2018 to July 25, 2018

1 State of the art

The coarse graining of molecular dynamical systems, i.e., the systematic reduction of physical molecular models derived from first prinicples, plays a key role in making the systems accessible to numerical techniques, and developing a useful physical understanding of the involved processes.

Current computational approaches can be roughly classified into 1) kinetic or discrete coarse graining, which effectively “collapses” continuums of atomistic states into discrete macro-states, and 2) dynamic or continuous coarse graining, which projects the original dynamics onto a suitably-chosen reaction coordinate. An important subclass of the latter is known as geometric or phenomenological coarse graining, in which structurally related atoms are grouped into “beads” or “super-atoms”. A multitude of computional methods have been suggested for each of the classes, each with their own characterization of reduced models and their own theoretical justification. As such, each of these methods is valid in its own domain, but there is no broad consensus about what characterizes a “good” reduced model.

Related to that is the question about how to validate a coarse grained model. Current methods rely solely on the comparison of the dominant time scales of the full and reduced system, but the full system's time scales may be a) impossible to compute, and b) may not correspond to the specific property of interest. Due to these and other shortcomings, computational coarse graining methods are not used in practice by the computational molecular chemistry community. Instead, hand-picked reaction coordinates (like certain inter-atomic distances or the number of native side-chain contacts in peptides) are still state of the art. Of course, this procedure requires a lot of expert knowledge, is non-automatable, and difficult to verify rigorously.

2 Major outcomes

One central goal of our workshop was to bring together scientists involved in molecular (dynamics) coarse graining in different fields in order to learn from another the topics of large current interest and to initiate cross-fertilization. As a first step, we found in due course, an alignment of vocabulary is necessary, since similar or identical concepts were presented under different names (example: kinetic/discrete coarse graining etc.)

Guided by their intuitions, the different fields approach the problem of coarse graining in diverse manners, ranging from the functional-geometric view of aggregating atoms (or other groups of objects sharing structure or functions in the molecule) to the more high-level approaches that are justified by mathematical abstraction. Irrespective of the approach taken, we found that the community agrees that the ultimate aim is to achieve better physical

understanding. This is especially true now that machine learning starts to flourish (again), and „learning without understanding“ threatens to spread. Data science and physical understanding should go hand-in-hand, the former serving the latter. The interest in utilizing machine learning was strongly represented, and the arc between the functional- and the high-level coarse graining was nicely spanned by the participants Gregory Voth (learning optimal groupings of atoms for assembling coarse pseudo force fields) and Frank Noé (learning an optimal set of basis functions for the spectral analysis of transfer operators).

While the bulk of the efforts is using machine learning to some end in molecular dynamics, Eric Vanden Eijnden reversed this dependency in an original approach, in which he uses the theory of particle systems to understand the mechanisms of learning with deep neuronal networks.

Substantial efforts are made to accelerate (or otherwise enhance) sampling in complex high-dimensional systems. Discussions in the course of the workshop showed that novel coarse graining techniques yield a promising line of attack, e.g., reaction coordinates obtained in an automated manner can help search methods to prioritize and more efficiently explore state space (a collaboration initiated between the Max-Planck-Institute for Biophysics and the FU Berlin).

3 Community needs

One outcome of the workshop was that there are several different coarse graining approaches, but the problems these methods are applied to are vastly different. In order to be able to compare coarse graining techniques it would be beneficial to define a set of benchmark problems. Furthermore, due to the increasing complexity of the considered systems, also the size of the data sets grew significantly, necessitate large amounts of storage space, and are thus difficult to share. Additionally, machine learning approaches such as deep neural networks are computationally expensive and might require specialized hardware, e.g., Graphics Processing Units (GPUs) or Tensor Processing Units (TPUs). Another drawback of machine learning methods is that the results are often hard to interpret. Thus, collaboration between the machine learning experts and chemists is needed to further the understanding of complex molecular dynamics problems. Also, a regular exchange between the different coarse graining communities would help achieve the individual goals faster.

4 Funding

Coarse graining being a central topic in molecular dynamics, and molecular dynamics playing an important role in today’s pharmaceutical or material research, this very interdisciplinary field has ample funding opportunities. On a European level, Horizon 2020 is a considerable option, since the areas „Biotechnology“, „Health“, and „Key Enabling Technologies“ (e.g., materials) are all intensively served by molecular dynamics research. It seems that, the community rather separates into smaller, better manageable sub-communities, and organization of research activities on national levels is more prominent. All of us, organizers, being parts of the German research system, the main funding source for us is the DFG. There are numerous Priority Programmes related to molecular dynamics, and the topic plays an important role on the highest level of organized research: in Collaborative Research Centres — like the one about „Scaling Cascades in Complex Systems“, hosted by the FU Berlin.

5 Will these developments bring societal benefits?

Molecular dynamics simulations are predominant in the development of pharmaceutical products and can be used to create new or improve existing drugs (e.g., by reducing side effects). Furthermore, by simulating the effects of drugs, it is possible to reduce the number of experiments involving animals or human test subjects. Coarse graining leads to streamlined development processes since the complexity of the simulations can be reduced, and the optimization of system parameters can be carried out more efficiently. Moreover, problems that cannot be simulated in full detail, can be handled using coarse grained models. Molecular dynamics models can also lead to a better understanding of physical properties of materials such as friction and the development of new materials. Additionally, mathematical coarse graining techniques that do not exploit any specific properties of the molecules themselves can in the same way be applied to other problems, e.g., fluid dynamics problems and climate models.

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Emergence of Surface and Interface Structure from Friction, Fracture and Deformation

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1577.html
Dates: July 24, 2018 to July 27, 2018

1 State of the art

The topographic, morphological and chemical structure of surfaces and interfaces affect the mechanical behaviour of materials but cannot typically be systematically controlled. Few of the processes responsible are fully understood, often because they involve interactions across length and time scales. This topic was discussed from five perspectives:

1. Structure of fracture surfaces. This topic focused on the emergence of individual geometric features resulting from crack tip instabilities, such as oscillations of tip position in 2D or triangular protrusions found on a variety of materials in 3D, as well as the emergence of roughness on crack surfaces in glasses and hierarchical materials.

2. Emergence of surface roughness during plastic deformation. This was presented for metals and metallic glasses. Simulations showed the emergence of self-affine structures from homogeneous materials, and the creation of folds in polycrystalline samples. In experiments, surface and bulk deformation was visualized using metallic multilayers for contrast in microscopy or in-situ observation of surface cross-sections.

3. Evolution of interface morphology during frictional loading. This is intimately tied to plastic deformation and fracture. Observations of rock surfaces suggest a well-defined length-scale for the onset of brittle fracture. Simulations on 2D models show a similar transition and a potential explanation for these observations, pointing towards a unified wear model.

4. Emergence of structure from elastic instabilities. This was discussed in the context of folds and creases created during the deformation of soft solids.

5. Chemical structure at surfaces and interfaces. This was discussed in the context of fracture (hydrogen embrittlement) and friction (surface passivation during lubrication). Occurrence of tribochemical phenomena, and explicitly electronic-structure based simulations that reveal the relevant reaction mechanism were presented and amply discussed.

2 Major outcomes

Outcomes of the workshop aligned with the five perspectives above include:

1. Fracture. During the workshop it became clear that there a transition from understanding crack-path selection in two-dimensions to complex three-dimensional instabilities is underway. This poses a major challenge for experiments that typically look at post-mortem surface patterns after fracture has occurred in 3D, but often allow in situ observation in 2D. It is also a major challenge from a modelling point of view: most analytical models are derived for 2D and atomic-scale calculations are typically carried out in 2.5D. Multi-scale coupling relies to a certain extent on this 2.5D character because of the existence of small spatial regions to be modeled with accurate albeit expensive schemes. While these models can be even quantitatively predictive, there is a need for full 3D fracture simulations. It was demonstrated that both continuum scale phase-field models as well as large-scale atomistic models have started to bridge the gap from 2D to 3D models of fracture. There is a growing consensus that more work, requiring the incorporation of chemical and microstructural information into current models, is needed to identify the causes of geometric crack-path instabilities.

2. Plasticity. Experimental observation of pattern formation by plastic deformation on surfaces can be carried out in situ, but observation at interfaces (between grain boundaries or heterointerfaces) is presently limited to post-mortem analysis in oxidizing environments. The formation of folds is understood in terms of material heterogeneity (elastic and plastic moduli, Schmid factors) but novel results were presented that hinted at an influence of surface chemistry on these effects. Other phenomena, such as the formation of vortices during deformation, or the emergence of self-affine surface structure appear at present only to be understood in qualitative rather than quantitative terms.

3. Friction. Explaining frictional loading requires a combination of fracture and plastic deformation. While significant progress has been made in individual application areas (e.g., adhesive wear mechanisms), an overall systematic approach to scale-dependent strength is missing (see discussion of ‘Grand Challenges’ below).

4. Elastic instabilities. The formation of folds and creases (“rugae”) during the deformation of soft solids can be well described by conventional continuum models. Plastic instabilities can of course never be completely decoupled from the effect of the elastic matrix, requiring more studies of the interplay of elasticity and plasticity.

5. Chemical structure. Coupling of chemical and mechanical models of fracture and friction shows great potential, with highlight applications making quantitative predictions linking modelling and experiment. However, as discussed in more detail below, the multiscale challenge of unifying accurate models of e.g. individual tribochemical processes with long-range driving forces in complex loading geometries remains as urgent as ever. Moreover, while direct coupling of models does little to address the time scale challenge.

3 Community needs

We carried out a discussion session to assess the needs of the community, which as a result appear to include:

The idea of ‘virtual journals’ organised by the community to collate relevant articles, with the goal of promoting the diffusion of high-quality work out of community journals. This is an activity which CECAM might be interested in promoting/facilitating, perhaps along with hosting the associated research data.

Direct input from chemistry. When asked whom the participants would like to collaborate with but presently do not, the answer was overwhelmingly an expert in chemistry. This suggests that the community feels comfortable addressing mechanical aspects of structure formation but an understanding of chemomechanical effects is still in its infancy.

Better integration with experimental activities. It was recognised that there is also a distinct difference between experimental and theoretical approaches. Theory always requires models, either generic ones that explain a certain process or material specific ones, experiments live in the real world and are often complicated, e.g. by ambient chemistry or mechanical noise. For model validation, there is a need for simpler (theory-led) experiments on ultra-pure samples of simplified composition/microstructure.

Concrete recommendations for follow-up activities to nurture the burgeoning ‘multiscale mechanics of interfaces’ community include organising further workshops at CECAM, as well as proposing symposia at conferences such as MRS, MMM, DPG and EMRS. Setting up a COST action will also be explored.

Interestingly, when asked about how the field could benefit from present prominent trends in data science, machine learning and artificial intelligence, participants said it is useful to develop methods and carry out high throughput screening of complex experimental results (e.g. spectra or fractographic images) but not as a general research approach in a community whose primary focus is elucidating mechanisms.

4 Funding

Commonly agreed limitations of existing funding instruments were identified:

Difficulting of initiating relatively small-scale research projects across national borders, e.g. modelling-experiment collaborations with 2-3 partners, where setting up a consortium under e.g. the LEIT Horizon 2020 actions would not be appropriate. More joint calls between national funding agencies, or a similar action facilitated by the EC, would help to address this concern.

Competition between long-term fundamental research and immediate practical needs - it can be difficult to demonstrate the impact of projects which focus primarily on method development, but which in the long term are expected to enable significant technical progress.

Concerns were raised that the current drive towards an open-access culture in particular at high-impact journals will make publishing in these journals impossible for a broad community of researchers because of the cost associated with it.

5 Will these developments bring societal benefits?

One of the discussion topics we asked participants to consider was the identification of 'Grand Challenge' problems that would bring the community together to tackle problems of pressing societal, economic and technological benefit, such as a mechanistic understanding of scale-dependent strength, requiring cross community engagement to address the multiscale competition between plasticity and cleavage. Progress is needed for societal challenges ranging from optimisation of nanoscale manufacture through to prediction of earthquakes.

Other challenges identified with important societal impact include an improved understanding of fracture of hydrogels, used for a wide range of applications including tissue engineering, drug delivery and biosensors; effects of environment on crack growth though stress corrosion cracking, relevant from biomedical implants to mining; optimising surface properties of high performance materials such as high entropy alloys and metallic glasses.

Moreover, all the topics discussed can also be exploited for manufacturing, where requirements on surface finish contribute a large proportion of the cost of a part. Being able to produce custom interfaces in materials by controlling chemistry and deformation during manufacturing would enable materials with tailored mechanical properties. Advanced manufacturing techniques (e.g. 3D printing) may emerge from in-depth understanding of fundamental processes that shape surfaces in friction, fracture and deformation.

The participants were agreed that CECAM provides an ideal incubator/facilitator environment for creating the necessary interdisciplinary links, in a field with direct technological impact that only recently lends itself to detailed atomistic/molecular modelling, and can tap into expertise in materials (quantum) chemistry. On this basis, and looking ahead, the present set of organisers is contemplating planning another workshop, for 2020 (with planning to be carried out in spring 2019).

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CECAM/Psi-k Research Conference: Biomolecular Electronics (BIOMOLECTRO)

Location: Universidad Autónoma de Madrid, Madrid, Spain
Webpage: https://www.cecam.org/workshop-0-1522.html
Dates: August 27, 2018 to August 31, 2018

1 State of the art

The aim of our conference was to bring together theoreticians and experimentalists working on the electron transport through biomolecules such as proteins, peptides or DNA, as well as through bio-inspired devices and systems like bacterial nanowires.

The field of Biomolecular Electronics, the topic of our conference, is flourishing motivated by the unique opportunities that biomolecules offer in terms of redox and optical functionalities as well as specific chemical recognition and self-assembly. For instance, proteins have very rich physical properties (electrical and optical), which could potentially be used in nanoscale devices. In recent years, numerous experiments have shown that the electron transport through proteins is surprisingly effective. However, the transport mechanisms remain largely unknown. Indeed, numerous groups have started to investigate the electronic transport through individual peptides with the hope of clarifying their role in the transport through proteins. Nevertheless, no consensus has yet been reached on how conductive these molecules are.

Another key topic in Biomolecular Electronics is DNA-based electronics. The great interest in the DNA molecule as a possible component of molecular electronic devices is due to its unique recognition and self-assembling properties. After an initial phase of confusion and very disparate experimental results, new experiments are finally revealing the importance of different factors like sequence or the interaction with a substrate. Finally, an emerging topic in our field is that of bacterial nanowires or cable bacteria. These biological wires are electrically conductive appendages produced by a number of bacteria and whose purpose is to facilitate long-range extracellular electron transfer, the mechanism of which remains poorly understood.

2 Major outcomes

Our conference focused on the four topics of Biomolecular Electronics mentioned above. In the case of protein electronics, different speakers like D. Cahen (Weizmann Institute of Science), S. Lindsay (Arizona State University) or C. Nujhuis (University of Singapore) presented experimental results of the electronic transport through protein-based junctions that show that these molecules can sustain surprisingly high currents. Some of the presented results strongly suggest that the transport in these junctions may be dominated by quantum tunneling, contrary to the common wisdom in biology. In particular, D. Cahen presented very convincing data revealing that resonant tunneling is actually possible in these junctions. On the other hand, different talks on this subject (both experimental and theoretical) highlighted

the need for (ab initio) quantum mechanical calculations of the electron transport in protein-based junctions. These calculations, which constitute a formidable challenge for the theory and simulations, should finally clarify which transport mechanisms are actually operating in these systems.

In the context of peptides, speakers like N. Agraït (Universidad Autónoma de Madrid) or H. van der Zant (Technical University of Delft) showed preliminary experimental results on the electrical conductance of single-molecule junctions based on different amino acids and peptides. These results showed a high variability of the conductance values due, most likely, to the possibility of these molecules to bind in many different geometries in metallic electrodes. Moreover, these results and others, like those presented by S. Refaely (Berkeley), strongly suggest that these molecules are poorly conductive. These results are in marked contrast to those reported in many-molecule junctions, e.g., by D. Cahen. This has generated a puzzle that calls for new ab initio calculations of the electronic transport through peptide-based junctions.

Turning now to the topic of DNA-based electronics, J. Hitath (UC Davis) and D. Waldeck (University of Pittsburgh) presented a summary of their recent experimental results on the transport through single-DNA molecules that are helping to elucidate the role of the DNA sequence in the transport through these biopolymers. On the other hand, D. Porath (The Hebrew University of Jerusalem) presented very striking unpublished results that show that DNA dimers, in which a single DNA molecule is bonded to two metallic nanoparticles in a very controlled manner, can sustain very high current for lengths on the order of 30 nm. Moreover, he presented strong evidence that these currents actually proceed through the backbone of the molecules, which is completely at variance with the common wisdom and could constitute a new paradigm in DNA electronics.

M. Y. El-Naggar (University of Southern California), N. Malvankar (Yale University) and H. van der Zant (Technical University of Delft) presented very exciting experimental results on the electronic transport through bacterial nanowires and cable bacteria. These results demonstrated that different types of bacteria can actually transfer electrons over macroscopic distances. The fact that these results are not understood was also highlighted and although there are some hints about how electrons proceed through these biological cables, it is still unclear what the dominant transport mechanism is in these systems.

S. Skourtis (University of Cyprus), M. Elstner (Karlsruhe Institute of Technology) and J. Blumberger (University College London) discussed the relation between electron transfer and electron transport in biomolecules and identify some of the key challenges for the theory of electronic transport through biomolecular junctions. In particular, they emphasized the need for detailed quantum mechanical calculations and simulations that are absolutely crucial to identify and understand the possible transport mechanisms in these systems.

3 Community needs

One of the main conclusion of our conference is the fact that there are numerous open problems that require ab initio calculations/simulations to be properly addressed. In particular, there is an urgent need of ab initio calculations of the electronic structure and electronic transport through biomolecules. Many of these molecules, e.g. proteins, contain several thousand atoms and their modelling is usually out of the scope of present ab initio codes, which are mainly based on density functional theory (DFT). Moreover, biomolecules are very prone to fluctuations and their description requires the combination of molecular dynamic simulations with electronic structure calculations. So, in this sense, the existing codes definitely need to be optimized and adapted for the specific needs of the field of Biomolecular

Electronics. On the other hand, an ample use of HPC resources is absolutely needed so that theory can have an impact in this field. Moreover, the collaboration between different communities is certainly crucial in this case. In particular, the communities of electron transfer in biology and electron transport in molecular junctions must cooperate and share ideas and (theoretical and experimental) techniques.

Our conference has been regarded by the participants as a great success and it has been extremely useful identifying the key open problems of the field of Biomolecular Electronics. So, in this sense, there is a general consensus in this community on the need to organize more conferences on this subject. Moreover, this interdisciplinary topic is evolving very rapidly and focused conferences like ours are essential to keep track of the advances and to establish new collaborations. For these reasons, we believe that it would be highly desirable to organize a series of CECAM workshops on this topic.

4 Funding

As mentioned above, the field of Biomolecular Electronics is very interdisciplinary and the input of physicist, chemists and biologist is simply indispensable. Thus, a good part of the research in this field is actually done in the context of joint research proposals. However, so far most of the collaborations are bilateral and, during the conference, the need to launch new initiatives involving more partners was discussed. In this sense, we are aware of the fact that new collaborations were established during our meeting in Madrid and several groups are already working on joined proposal for ERC grants, bilateral programs (like the Israel-USA bilateral science foundation), and EU calls.

5 Will these developments bring societal benefits?

The main topics discussed in our meeting can be considered as basic science and most of the questions addressed so far in our field concern the basic understanding of the electron transport in bio-inspired systems. However, those problems are expected to be the basis for future biotechnological applications. For instance, an important line of research in our field is the use of electrical measurements for a rapid and cheap sequencing of DNA molecules. The research on this topic, if successful, could have a huge societal impact. On the other hand, the investigation of the impact of mutations and modifications of the biomolecules like proteins in their electronic transport could be the starting point for the development of unforeseen techniques to detect certain types of diseases. It is also worth mentioning that the results presented in our conference on the electron transport in bacterial nanowires or cable bacteria show that these bacteria could be used to create a new type of conductive biofilms that may find different applications in electronics and sensing. Finally, the chiral-induced spin selectivity discussed in our meeting has recently been shown to be the basis for a novel method to separate enantiomers without the need to use any chemical approach (simply using a magnetic field). Such a method might have a tremendous impact in chemistry.

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8th Workshop on Time-Dependent Density-Functional Theory: Prospects and Applications

Location: CECAM-DE-MM1P, CECAM-ES
Webpage: https://www.cecam.org/workshop-0-1594.html
Dates: August 28, 2018 to August 31, 2018

1 State of the art

There are many alternative schemes to approach the time-dependent, out-of-equilibrium, many-electron problem. Time-dependent density-functional theory (TDDFT) has a significant “market share” due to the same reasons that make conventional ground state density-functional theory (DFT) a successful scheme: the fairly good predictive power at a moderate computational cost. As a consequence, its use has quickly grown, and its reliability for many purposes has been sanctioned by many applications and benchmarks over the years. As the computational resources increase, however, various alternatives such as advanced post-Hartree Fock multi-configuration schemes or many-body perturbation theory techniques can be applied to larger systems, and may provide more precise results. Newer and more intriguing possibilities, such as the direct solution of the many-electron Schrödinger equation with quantum computers, and the use of machine learning techniques for the prediction of many properties, appear also in the horizon. It is therefore necessary to review the capabilities and perspectives of TDDFT.

2 Major outcomes

We have witnessed in this workshop (1) talks dedicated to the theretical foundations of TDDFT and its possible extensions; (2) talks dedicated to applications of TDDFT; (3) talks dedicated to alternatives to TDDFT; and (4) methodological topics.

The first session was entirely dedicated to the first of these groups: Ilya Tokatly discussed the combination of TDDFT with the quantum-mechanical treatment of the photon field, in order to address cavity quantum electrodynamics problems, whereas Carsten Ullrich presented research on the exchange-and-correlation functional – always the key fundamental problem of TDDFT. In a later session, Eric Suraud summarized theoretical results about the inclusion of dissipative effects in TDDFT. A very different theoretical problem was addressed by Ryan Requist: the issue of separating the electronic and nuclear wave function, typically handled by the Born-Oppenheimer approximation, can also be treated within an “exact” factorization scheme pioneered by Hardy Gross and collaborators in recent years within the TDDFT context. Ryan Requist presented new research, focusing on the approximation of the necessary functionals. Roi Baer also addressed a theoretical topic: a stochastic approach for evolving in real time non-interacting Fermions in open quantum systems under the influence of a bath. Finally, the work presented by Emmanuel Fromager also belongs to the group of theoretical developments: the use of DFT for ensembles in order to study the fundamental and optical gaps.

Various talks were dedicated to the second group mentioned above: applications of TDDFT. It became apparent, therefore, the wide applicability range of TDDFT, and how it can be used to approach non-equilibrium problems. Various examples were displayed: (1) the calculation of optical spectra of dyes in solution presented by Christine Isborn, who showed how solvent effects can be taken into acount; (2) the calculation of high-harmonic generation spectra from solids shown by Nicolas Tancogne-Dejean; (3) various applications of TDDFT in the realm of attosecond physics, summarized by Shunsuke Sato, (4) a review of the capabilities and shortcomings of TDDFT for the description of optical properties of materials, provided by Arjan Berger; (5) a discussion on the ability of TDDFT to describe non-linear optical properties of solids by Valerie Veniard; and (6) the problem of proton stopping power of materials, reviewed by André Schleife.

All previous talks centered on applications of TDDFT were good opportunities to discuss the shortcomings of the theory, whose origin is traced to the lack of a good approximation to the exchange and correlation potential, or to the lack of good approximations to some of the observables. Therefore, it is necessary to establish comparisons with other theories. Some examples: density functional perturbation theory from constrained DFT (David Strubbe), time-dependent two-particle density matrix theory (Joaquim Burgdörfer), the calculation of the spectral function from steady-state DFT (Stefan Kurth), reduced density matrix functional theory (Carlos Benavides-Riveros). But perhaps the most intriguing approach was the use of quantum computation techniques for the solution of highly correlated quantum-chemistry methods, described by Ivano Tavernelli. Although at an early stage both from the theoretical, software, and hardware perspectives, this scheme may be a revolutionary approach to the quantum chemical problem.

Finally, some time was dedicated to methodological advances: for example, Adrián Gómez Pueyo presented research on propagators for the TDDFT equations, and Peter Koval discussed the use of numerical atomic orbitals. We also emphasize that a younger generation of scientists was present, since the workshop takes place after a corresponding school. The students had the occasion of showing their research during a poster session, and one of them (Fumiyuki Ishii), selected by a vote, could present a talk.

3 Community needs

This workshop is part of a series of workshops dedicated to TDDFT, that started in 2004. It takes place every two years, a periodicity that we feel that is adequate to follow the advances in the topic. However, it always takes place in Europe, and there was a strong demand for a similar event taking place in the US, due to the difficulties in the travel, specially for students and young researchers. Fortunately, the demand was met in the last year by a similar event (a school on TDDFT followed by a workshop on first principles approaches to the electronic excited states problem) that took place in Telluride, Colorado. Part of the organizers of this event were present in Benasque, and the goal is to periodically repeat the US event, also every two years if possible. It should be noted, also, that a similar event is being planned in Asia (Tsukuba, Japan), by Prof. K. Yabana.

Regarding the community needs for software, nowadays many codes have implemented TDDFT, as we could learn from the presentations of the workshop, in which we could see results obtained with many different programs. The number of researchers that work on methodological software advances for TDDFT seems to be growing. Some of the results displayed during the presentations highlighted the good scalability of these programs. TDDFT is praised for its applicability to larger systems, but even in this case there is clear need to access high performance computing resources. This is not always the case for many researchers.

4 Funding

Unfortunately, we must repeat a main concern that was also a consensual comment of many researchers after the 2016 workshop: the difficulty of accessing funding through many of the usual channels, due to the basic-research nature of the discipline, and to the orientation of many of those channels to more applied science. Basic research in DFT or TDDFT is performed under the umbrella of large projects with a more technologically oriented topic, in which the basic science aspect is regarded as a necessary but marginal sub-project.

No particular funding proposal was discussed during the workshop.

5 Will these developments bring societal benefits?

TDDFT is already a mature scheme to describe electronic excitations from first principles, and has demonstrated its predictive power in a certain applicability domain. Software solutions have been developed over the years, and can be found both at the academic and industrial level. Therefore, its use benefits the industrial research on materials science and photo-chemistry, for example. One of the participants of the workshop did in fact come from an industry laboratory. There are numerous technological processes and areas in which the excited-state electronic-structure of atoms, molecules, and materials (the object of study of TDDFT) is relevant. For example, during this workshop, we could witness reports on the application of TDDFT to model the proton stopping power of materials – an area of interest for the study of radiation damage, and for the construction of containers of nuclear reactors. Also, the application of TDDFT to the excited state chemistry of molecules of biological relevance was discussed both during the workshop and during the previous school. In these and other areas, modelling based on TDDFT and related techniques may help industry, by easing the interpretation of the observations made in their research & development processes.

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Computational Biophysics on Your Desktop: Is That Possible?

Location: University of Trento - Dipartimento di Lettere e Filosofia - via Tommaso Gar, 14 - Trento, Italy
Webpage: https://www.cecam.org/workshop-0-1534.html
Dates: September 3, 2018 to September 6, 2018

1 State of the art

Computer simulations are a fundamental tool in many diverse branches of Physics and Chemistry. In particular, they are now routinely employed to study and predict the structural properties of biomolecules like DNA, RNA and proteins. This research is, in particular, stimulated by the increasing power of modern machines which offer the possibility to dig into the biomolecular processes at an unprecedented level of accuracy. Yet, this increasing power should not let the community forget that computer resources are nonetheless limited and/or of limited access, and that the quest for cheaper yet accurate methodologies needs to be pursued.

The workshop has reunited some of the leading experts in the field of biomolecular simulations with the intention of discussing the state-of-the-art in the design of accurate and efficient numerical algorithms. Particular emphasis has been put on discussing multi-scale methodologies, especially those tools which couple different parts of the same systems with different levels of resolution and accuracy. These tools appear promising to bypass computer limitations, yet may present some drawbacks which need to be carefully assessed in future investigations.

2 Major outcomes

The workshop has benefitted from contributions by an extremely rich and diversified list of speakers and audience: this favorable situation has in particular brought to the attention several key questions related to how to best model biomolecules and biomolecular aggregates as, for instance: proteins, protein complexes, RNA, DNA, chromatin and chromosomes. Thus, the workshop has offered to experienced and young researchers (including several PhD students) the opportunity to witness the evolution of the field of the last 20 years.

Notwithstanding the dramatic speed-up of modern super-computers, the workshop has made clear to everyone that, in order to achieve real progress and then move beyond the mere state-of-the-art, researchers are called for developing more efficient and, hence, less time- and resource-consuming algorithms.

This point has received special attention during the plenary talk by Prof. Giovanni Ciccotti (University "La Sapienza", Rome, Italy), which took the provocative title "Molecular Dynamics: Where From, Where To". Prof. Ciccotti, one of the founder fathers of modern Molecular Dynamics, has clearly pointed out that the achievement of the desired goals passes through the continuous search for improved algorithms and methods, rather than (solely) a brute-force boost of the computational power.

Another important point which has emerged during the workshop concerns the need for a closer integration between theoretical tools (which were the main actors of the workshop) and experimental results. In this respect, several talks focussed on the idea that traditional computational tools for the study of biomolecules, such as Monte Carlo or Molecular Dynamics, ought to be complemented by appropriate biases based on experimental data in order to get a more realistic depiction of the underlying molecular mechanisms. The pros and cons of these approaches have been extensively commented and discussed during the workshop.

To summarise, the workshop has presented a comprehensive analysis concerning which problems and questions need to be tackled in the next future.

3 Community needs

1) In general, the participants have clearly shown the need to move beyond the mere state-of-the-art and limitations of nowadays computer simulations. While Monte Carlo and/or Molecular Dynamics as currently intended have demonstrated how useful these tools are for understanding biomolecular processes, computer limitations or, as it happens more often, unfavourable local situations -where accessing to good computational resources is a recurrent problem- impose us to rethink the available algorithms and effect a true conceptual progress towards new and more efficient tools.
2) All the participants have shown clear appreciation for the workshop. In particular, they have enjoyed the friendly and sometimes informal atmosphere which has contributed to animate discussion and formulate questions. Prompted by this, a biannual series of workshops on computational approaches (possibly supplemented by some experimental contributions) to biomolecular processes has been strongly advocated by the participants.

4 Funding

The workshop has been funded by resorting to different channels: the CECAM-IT-SISSA-SNS node located at SISSA (Trieste, Italy), the University of Trento (Italy) through the 'Istituto Nazionale di Fisica Nucleare' (INFN) and the ERC-funded grant by one of the organisers (Dr. Raffaello Potestio).

For the organisation of similar events in the next future, we seek to identify other complementary/alternative sources of funding. These may include: the European Program Horizon2020, the Italian Ministry for Education and Research (MIUR).

5 Will these developments bring societal benefits?

Increasing our knowledge of biomolecules such as proteins, RNA, and DNA, and of the processes they are involved in within the restricted environment of the cell, is of capital importance. While experiments are, of course, the primary and indispensable source of information about these systems, computer simulations represent a complementary, and

increasingly often necessary, alternative. Moving forward the current state-of-the-art in computer simulations is then of great, significant societal benefit.

To make a few examples, understanding proteins may help reducing costs associated with healthcare treatments and strongly limit the side effects that the usage of certain drugs (e.g. antibiotics) can have on the environment. Similarly, understanding DNA folding within the cell is of crucial importance to understand genome mis-functions and lethal pathologies like cancer.

All this research is not only a conceptual challenge per se, rather it is highly connected to pharmaceutical and technological industries. We believe that the multidisciplinary discussions emerged during the workshop will generate interactions and collaborations that may end up in new research teams and efforts dedicated to biomolecular systems. These efforts will not only focus on the computational aspects, rather also look with interest at applied technologies with practical implications, which, in the medium/long term, may have a substantial impact on society.

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Excitonic Insulator: New Perspectives in Long-Range Interacting Systems

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1562.html
Dates: September 3, 2018 to September 5, 2018

1 State of the art

Fifty years ago a few outstanding physicists, including Leonid Keldysh and Walter Kohn, put forward a heretic paradigm of a strongly correlated insulator: If a narrow-gap semiconductor (or a semimetal with slightly overlapping conduction and valence bands) failed to fully screen its intrinsic charge carriers, then excitons---electron-hole pairs bound together by Coulomb attraction---would spontaneously form. This would destabilize the ground state, leading to a reconstructed 'excitonic insulator' (EI) that would exhibit a distinctive broken symmetry, inherited by the exciton character, as well as peculiar collective modes of purely electronic origin. Intriguingly, the excitonic insulator, which shares similarities with the Bardeen-Cooper-Schrieffer superconducting ground state, could display unusual macroscopic quantum coherence effects. So far, the observation of this phase has been elusive. The crux of the matter is the trade-off between competing effects in the semiconductor: as the size of the energy gap decreases, favouring spontaneous exciton generation, the screening of the electron-hole interaction increases, suppressing the exciton binding energy.

Very recently, novel low-dimensional systems and quantum devices seem to renew the promise of the excitonic insulator, as they combine optimal band structures, poor screening, truly long-ranged interactions, and giant excitonic effects. These include systems as diverse as carbon nanotubes, low-dimensional and van der Waals heterostructures, Dirac and Weyl materials, topological insulators. The field has just started exploding, as documented by the list of recent literature maintained at Cnr-Nano site: www.nano.cnr.it/index.php?mod=men&id=196.

By collecting the key actors of theoretical and experimental research, who are spread among different communities, this Workshop allowed the in-depth analysis of common themes and challenges, both theoretical and computational, to establish a roadmap to the EI.

2 Major outcomes

The workshop has put together leading scientists in the field, with expertise on:

(i) experimental spectroscopies (Abbamonte, Butov, Du, Eisenstein, Shapir, Sood);

(ii) first-principles methods: DFT and beyond-DFT (Cudazzo, Hellgren, Molinari, Olevano, Varsano), QMC (Sorella), DMFT (Kunes);

(iii) model/effective mass Hamiltonians and field theories (Bercioux, Fehske, Golez, Herbut, Khveshchenko, Littlewood, MacDonald, Neilson, Rontani, van Wezel).

Such diversity reflected in lively discussions, with many questions and comments after each talk. A key outcome was the awareness that a new field and scientific community is emerging,

and a more precise definition of the EI phase is needed as a basis for shared concepts and language. In a participated discussion session, consensus was reached that:

(1) The excitonic insulator is the Bose-Einstein condensate of excitons at equilibrium, well defined only if exciton states are, i.e. one is able to precisely asses the Hilbert space where excitons live, or associate them with a real pole of two-particle Green function, or provide their explicit wave function, or the like.

(2) In any realistic Hamiltonian inter-band terms occur that hybridize conduction and valence bands: these are similar to the mean-field EI order parameter but unrelated to excitons (e.g. they can be due to phonons). The ground state is an EI if these extrinsic terms are at least one order of magnitude smaller than the excitonic order parameter.

(3) The excitonic superfluid state is much harder to achieve, as it requires a huge degeneracy associated with the phase of the EI order parameter. As extrinsic inter-band terms pin this phase, they should be negligibly small (by orders of magnitude) with respect to the excitonic order parameter.

Condition (3) seems presently feasible only in bilayer systems (in either conventional or graphene-based heterostructures, cf. Butov, Du, Eisenstein, MacDonald, Neilson). Conditions (1) and (2) potentially apply to a much larger set of materials: transition metal dichalcogenides, such as TiSe2 (Abbamonte, Hellgren, Olevano, van Wezel) or Ta2NiSe5 (Golez, Sood), C nanotubes (Shapir, Varsano), unusual magnetic (Kunes) and ferroelectric materials (Fehske).

As a major outcome of the workshop, participants agreed that the critical feature shared by EI candidate materials is the long range of unscreened Coulomb interaction. This is in principle common to low-d materials –not necessarily strongly correlated in a conventional way— when weakly interacting with the environment. Therefore, it is likely that novel narrow-gap EI candidates will soon be discovered, making this field vibrant.

Main open issues at this time are:

(a) Experimental tests that can discriminate between the excitonic and phononic origin of the EI broken symmetry. This is especially urgent for excitons with finite center-of-mass momentum, since their condensation leads to a charge- or spin- density wave that may be confused with a Peierls-like distortion. The use of advanced ab initio tools to disclose the excitonic character of the phase transition (Varsano, Cudazzo, Hellgren, Olevano) was recognized as a breakthrough by the participants.

(b) What is the relation between the excitonic order and other types of order, e.g. those realized in topological insulators (Du, MacDonald), magnetic materials (Kunes), superconductors (Abbamonte, Littlewood)? Do they compete or coexist? The investigation of such fundamental question, relevant to other fields such as high-Tc superconductivity, is still in its infancy.

(c) What are the observable signatures of macroscopic quantum coherence in the EI? In addition to counterflow supercurrent measurements (Bercioux, Du, Eisenstein, Neilson, MacDonald), which may only be realized in bilayers, there could be other phenomena in principle relevant to bulk materials, e.g. in the time domain response if condensation leads to permanent macroscopic polarization.

3 Community needs

Whereas the EI topic is venerable, the field has just started exploding in the last two-three years. As a matter of fact, the participants recognized that this workshop was the first concrete opportunity to gather scientists who were so far spread among different communities. An obvious and immediate need is to consolidate networking. Establishing CECAM as the home

of a series of workshops on the topic would be very meaningful in view of the success of this first edition, where theoretical, computational and experimental talks have converged very effectively, and contributed to outlining the perspectives of simulations in this field.

Concerning computational infrastructures, the workshop has clearly shown that advances in the understanding of real EI materials essentially depend on massive, first-principles state-of-the-art calculations. Code development has progressed rapidly, and it should be noted that most of the first-principle codes adopted in this workshop for DFT and beyond DFT calculations, as well as QMC, are developed and made available open source in Europe. In view of the rapid evolution of the HPC and the future exascale perspectives, a massive effort is needed to ensure that these codes remain at the forefront of computational technologies. Some of the effort is supported in Europe through the H2020 CoEs, but this covers only a fraction of the actual needs, so it would be important to raise broader awareness in that direction. The same need of broader awareness exists for training and professional valorisation of the scientists who are investing not only in their research but also in the code evolution for the benefit of the whole community, and CECAM could certainly help in this direction. Finally, concerning HPC computer time, the amount that would be required is often much beyond the possibilities offered in Europe by PRACE and by the national HPC systems. Computational work in this field will provide eager users of the future EuroHPC scheme.

4 Funding

The research on the EI encompasses both fundamental and technological aspects. In this field the latter aspects are quite visionary, and rely on the exploitation of macroscopic quantum coherence in real materials, such as the occurrence of dissipationless current, or the possibility of encoding information using electronic collective degrees of freedom. Some of these long-term applications might fit in the H2020 FET scheme, even if the perspective of industrial interest at the moment is quite far. On the other hand, the core of the EI research has clearly a fundamental character, which may well fit curiosity-driven science programs such as the ERC scheme. The possibility of some kind of joint Europe-USA lobbying / networking has been informally discussed during the workshop. It is worth stressing that the EI theme seems particularly fit to proposals combining theory and experiments together. The organization of a second workshop could certainly foster joint funding actions.

5 Will these developments bring societal benefits?

The search for excitonic insulator phases could lead to novel manifestations of macroscopic quantum coherence, which historically have always led to breakthrough applications. In particular, exciton superfluidity would allow for the exploitation of quantum effects at temperatures much higher than those of the Bardeen Cooper Schrieffer state (since the exciton mass is much lighter than the Cooper pair mass). At variance with exciton-polaritons, where Bose-Einstein condensation occurs out of equilibrium, in the excitonic insulator excitons would condense at equilibrium, which makes any achievement in this field extremely appealing. Potential applications include the storage of information into the electronic collective modes of the EI and high-temperature dissipationless transport.

Furthermore, the research activity on the excitonic insulator will lead to unprecedented accuracy and understanding of screening, ground state properties, and excitations of a very important class of materials, which will be of relevance irrespective of the demonstration of the excitonic insulator phase.

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Normal Modes of Biological Macromolecules: Methods and Applications

Location: Institut Henri Poincare, Paris 5eme (CECAM-FR-MOSER).
Webpage: https://www.cecam.org/workshop-0-1554.html
Dates: September 12, 2018 to September 14, 2018

1 State of the art

It has been recognized that dynamics is essential for protein function.

Local motions such as amino-acid sidechain fluctuations can be studied with various experimental techniques, or predicted in silico by molecular dynamics (MD) simulations.

Global motions are more challenging. X-ray cristallography can for instance be used for determining the endpoints of a motion, but the process can prove slow. In principle, MD simulations could also be used for predicting these motions. However, such motions occur on a timescale which is well over the microsecond, that is, the timescale that can be reached nowadays, using standard supercomputers.

Apart from MD, another in silico technique has been used for predicting global motions, namely, normal mode analysis (NMA), which has the advantage of being much faster. Actually, NMA was among the very first in silico techniques used for trying to predict the motions of a biomolecule. At the time, the technique was limited by the amount of computer memory required, but the development of dedicated methods allowed its application to large systems and to the demonstration that the global motions provided by NMA are often similar to protein functional motions. It was then shown that comparable results can be obtained even when the protein is described with highly simplified models, such as elastic network models. The workshop noteworthy brought together the main developpers of these models.

2 Major outcomes

Main questions discussed: what NMA can give compared to MD simulations? how to make NMA results better known and easier to access for various communities of experimentalists, beyond structuralists? how to benchmark NMA results? Is it time to propose a set of NMA community tasks?

Other points addressed (too shortly for most of them): what bring physical forcefields to NMA, with respect to elastic network models (ENM) models ? is it useful to optimize the energy function of ENM models ? what would be an optimal coarse graining of these models? what non-linearity can bring to these models ? how to include the effect of the environment ? What about hybrid methods?

Applications to newly available techniques (like XFEL) or dynamical data (like chromosomal dynamics) were also discussed, with a focus of NMA applications to the protein-protein and protein-ligand docking problems.

Most new results presented were about the study of very large systems, like whole viral capsids or entire chromosomes. Noteworthy, several talks were dedicated to the comparative dynamics of related proteins, that is, to the study of the conservation/evolution of protein dynamics.

However, the main outcome of the workshop is an attempt to specify a list of NMA community tasks, namely:

1) Application-specific Benchmarks:

   a) Predictions of (anisotropic) B-factors

   b) Identification of flexible domains

   c) Identification of structural transitions in proteins and molecular assemblies in general. Protein-protein docking benchmark: the goal being to see how different NMA methods allow to predict the subspace of motions that lead a protein from the unbound to the bound state. Cryo-EM specific benchmark: the initial state comes from X-ray, and the final state from Cryo-EM. Benchmark with large-scale single-domain motions: something NMA-friendly.

2) Databases and webservers:

   a) Including modes in the PDB. PDBj (japan) already has it, but the interface can be improved significantly.

   b) Standardizing modes and hessian formats.

3 Community needs

Existing codes: several groups have made their methods available through websites or software repositories. What seems to miss is a (simple) way to compare results obtained with these various approaches.

HPC ressources: little needs for the moment, since the (successful) efforts in the field over the last twenty years have been about model simplification (coarse-graining). Development of hybrid methods (mixing NMA and MD, for instance) could change this but few efforts have at present been made along this line.

Outreach to other communities including experimentalists: this is an important issue since, although NMA is better known now, it is in the shadow of MD, which is widely recognized as a method of choice for studying the dynamics of biological macromolecules. Recent breakthroughs, noteworthy by the group of David Shaw, have moreover reinforced the opinion that MD is also the main, if not the only, method of the times to come.

Event organization: a couple of specialized workshops would be welcome. Noteworthy, a workshop focusing on NMA standardization and dissemination.

4 Funding

The possibility of joint research proposals was little discussed during the meeting. As several european groups contributed significantly to the development of ENMs, there were enough of them represented in the meeting to prepare a H2020 project. However, it would be difficult at present to convince non-specialists, including specialists of neighboring fields, that it is worth putting a significant amount of money on the development of NMA, so that it could become able to complement, if not rival with MD, in particular because in Europe, the usefulness of MD itself is still a matter of debate.

5 Will these developments bring societal benefits?

Being a method allowing to study the dynamics of biological macromolecules, NMA can prove useful in novel drug design processes. Compared to MD, being much quicker and easier to use, NMA can be included in large-scale studies. For instance, the whole protein databank can be studied with modest computing ressources. Moreover, since coarse-grained approaches have proven successful, very large systems can be routinely considered.

6 Participant list

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New Frontiers in Particle-Based Multiscale and Coarse-Grained Modeling

Location: Max Planck Institute for Polymer Research, Mainz, Germany (CECAM-DE-SMSM)
Webpage: https://www.cecam.org/workshop-0-1618.html
Dates: September 17, 2018 to September 19, 2018

1 State of the art

Particle-based computer simulations numerically integrate the time evolution of a system based on the interactions between its constituents. They offer the possibility to model the emerging complexity of phenomena occurring over many length- and time-scales. While an atomistic description can offer detailed insight, a thorough sampling of the relevant conformational space remains challenging for all but the smallest of systems. These limitations have motivated the development of coarse-grained (CG) models, where multiple atoms are lumped into one particle or bead. Coupling several models forms the basis of a multiscale approach, where models of different resolutions probe different length- and time-scales.

The main challenges in multiscale and CG modeling include representability and transferability. Representability describes the extent to which the model can reproduce various properties of the original system. Transferability refers to the model's accurate behavior beyond the state point or chemical composition it was parametrized from. Predictive modeling requires both aspects. Certain common assumptions that go into building CG models have imposed stringent constraints on the accuracy, e.g., the use of pairwise nonbonded potentials to reproduce the many-body potential of mean force.

While the modeling of structural, equilibrium properties has improved significantly over the last few decades, dynamics remains problematic. A CG model's smoother energy landscape leads to reduced molecular friction, accelerating arbitrarily the different kinetic processes. As a result, CG models are typically much faster, but with inconsistent dynamics. In parallel, recent technological and algorithmic developments (e.g., specific hardware or distributed computing) have allowed to probe extremely long time-scales of certain complex systems from atomistic simulations. This further hinders the impact of coarse-graining, due to ever-increasing interests in kinetic properties.

2 Major outcomes

Our format encouraged ample discussion: each 25-min talk was followed by a 20-min discussion. Further, we asked two prominent scientists in the field (Markus Deserno and Giovanni Ciccotti) to act as "critical pundits," challenging the speakers and raising certain critical points. The following summarizes several points in the discussion:

What is the objective behind structure-based coarse-graining? Some argued on the appeal of starting from small systems and partial information to reconstruct the underlying many-body potential of mean force (PMF). Others made a point that unless thermodynamic transferability was reached, the model was of little use. In all cases there was a consensus about the goal of reaching some additional physical insight into the driving mechanisms.

Clear targets/goals should be expressed/identified to reach predictive power:

State points

CG interactions that are transferable across systems

Modeling self assembly (e.g., establish/satisfy sequence-structure-property relationships)

CG seems most useful to describe interfaces between bulk phases. Yet CG models remain problematic at describing those. Interfaces often require heavy cross parametrization, making the process of building models and extending them to new materials/molecules tedious and inefficient. Two alternative solutions to describing interfaces were proposed, both involving local density as a mean-field many-body interaction term:

Ultra CG describes CG particles with several internal states. The example shown by Jaehyeok Jin switched between states depending on the local density.

Scott Shell presented a density-dependent potential, akin to a an embedded atom model for metals.

The challenge of enthalpy/entropy decomposition was raised several times. If a CG model averages over degrees of freedom, the conformational entropy must necessarily be reduced. Because the free energy is often a target quantity, CG models tend to compensate by means of enthalpic contributions. Efforts have recently been made at quantifying the loss of entropy. The distinction between two sources of loss was made:

Loss of entropy upon coarse-graining, i.e., due to the mapping;

Loss of entropy upon the projection of the many-body potential of mean force onto the interaction terms (e.g., bond, angle, pairwise interactions).

The challenge of coarse-graining the dynamics was raised in multiple talks. Several approaches were presented:

Mori-Zwanzig formalism, which arguably is the most rigorous way forward, but is computationally expensive (requires a memory kernel for the friction term in the Langevin equation) and requires many parameters to be optimized

The idea of better reproducing not only the free-energy minima, but also the barriers was brought forward. As such, a correct description of the static equilibrium properties would mechanically lead to consistent dynamics--up to a prefactor.

The use of Markov state models to analyze the dynamics of a CG system and possibly reweight given external reference information.

3 Community needs

Coarse-graining is a relatively mature field, and as such many codes/software exist. A lot of it is directly copy/pasted from software used for atomistic simulations. This can make for suboptimal situations, where the need for flexible CG potentials can be difficult to implement. As such, other software (e.g., LAMMPS, ESPResSo++) have been developed. In parallel, several pieces of software have been developed to build CG models, such as VOTCA or BOCS.

HPC resources are typically well used in coarse-graining, due to the long history of running molecular dynamics in HPC infrastructure. We note that CG typically requires much smaller resources, in practice few applications tend to go to extremely large system sizes. This may change as CG models become more accurate.

In terms of outreach, we had invited two scientists from the data-driven community: Gabor Csanyi and Phaedon-Stelios Koutsourelakis. The former is well known in the hard condensed matter community for his work on using machine learning to build interatomic potentials. Prof Koutsourelakis develops Bayesian methods to tackle coarse-graining problems. This raised many discussions linking force matching (a prominent structure-based CG method) with machine learning. We hope that the two fields will keep interacting in the future.

We see coarse-graining as being more relevant than ever in tackling soft-matter problems. The weak scale separation in soft matter makes the modeling extremely challenging, but offers the hope to gain more insight into these systems. We also note that computational materials discovery in soft matter is still almost nonexistent. We expect coarse-graining (possibly coupled to modern data-driven techniques) to help develop this field. As such we hope for the organization of more CECAM workshops going in the direction of computational materials design/discovery in soft matter around coarse-graining.

4 Funding

Given that this is a rather mature field, standard funding channels apply. We are not aware of active sources of funding specific to advancing coarse-grained modeling. There were no explicit, open discussions about upcoming calls in the general workshop forum.

However, the ongoing collaborations be tween a couple pairs of invited speakers were brought up several times. For example, Scott Shell and Will Noid discussed their work with a joint

Ph.D. student to address the challenge of optimizing the CG mapping. W e believe these types of discussions, made available by the extra discussion time between talks, may help to foster future joint proposals.

5 Will these developments bring societal benefits?

As discussed in “Community Need,” coarse-graining will be instrumental to develop the field of computational materials discovery in soft matter, ranging from novel types of plastics to organic electronics to drug design.

We organized the workshop to transitio n from method development to applications throughout. Thus, the latter half of the workshop examined various ways to apply

coarse-graining tools to advance the design of materials or understanding of biological processes. For example, Mehmet Sayar discussed the development of a CG model to study the aggregation properties of small peptides, implicated in neurodegenerative disorders. Juan de Pablo presented work dealing with defects in active matter , e.g., liquid crystaline materials, which is important for designing novel, light-activated materials for technological applications.

Phillipe Derreumaux discussed how a well-established CG model can be used to better understand the interactions between proteins and nucleic acids, with strong biomedical implications.

At the same time, as highlighted above, the discussion in the workshop indicated the importance of further methodological developments to maximize the societal impact of CG.

6 Participant list

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Heterogeneous Ice Nucleation: The Ultimate Challenge for Molecular Modelling?

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1547.html
Dates: September 18, 2018 to September 21, 2018

1 State of the art

The formation of ice has an impact across global phenomena such as climate change as well as on the microscopic details of water freezing within our own cells - which is of the greatest relevance for cryopreservation. Invariably, though, ice forms heterogeneously, thanks to the presence of impurities boosting the otherwise too low ice nucleation rate of pure water.

In the last few years we have achieved a good understanding of which substances can promote heterogeneous ice nucleation (HIN): however, we still lack the microscopic insight that would allow us to understand (and predict!) the ice nucleating ability of a given substrate. This is because experiments still struggle to characterize crystal nucleation, which happens on exceedingly small/short length/time scales (ns/nm). Conversely, molecular simulations, which could indeed provide invaluable insight, are hampered by the fact that:

- Accurate interatomic potentials/force fields describing water-water and water-substrate interactions at the same time are needed in order to perform reliable simulations of HIN, typically via classical molecular dynamics. Building such force fields has proven to be an incredibly challenging task.
- Nucleation is a rare event, as seconds, or days or even weeks are typically needed for a crystalline nucleus to reach its critical size and proceed toward crystallization. Thus, enhanced sampling techniques are almost always needed to tackle the time scale problem via molecular.
- We are very far away from being able to compare the results of simulations and experiments. For instance, one of the very few quantities that could in principle link the two is the nucleation rate, but a quantitative agreement still eludes us.

The aim of the workshop is to address these issues by devising practical strategies to further the scope, the reliability and the impact of molecular simulations of HIN, in order to bring the latter a step closer to experiments.

2 Major outcomes

Methodological advancements featured prominently throughout the Workshop. To be specific:

- The potential of novel enhanced sampling techniques such as multi-dimensional Forward Flux Sampling (Sarupria) and seeded molecular dynamics (Peters, Vega, Sosso) has been

discussed. Overall, the community feels that the tools to progress the field are there - but much more has to be done to develop these methodologies further. In this respect, a commun theme that emerged is the need for cross-validation, for instance in terms of ice nucleation rates, by using different techniques. An effort of this stature has been taken with respect to the nucleation rate of colloids, but achieving the same for ice nucleation, and particularly ice nucleation, is a formidable challenge. However, many participants feel that this is a necessity.

- The development of accurate force fields, not so much with respect to water, but chiefly in terms of water at interfaces. Recent advancements such as the novel force fields for ionic spieces in solution (Raiteri) have been presented, but it emerged from the discussions that we need different classes of force fields to deal with different systems/aspects of heteroegenous ice nucleation. The usefuleness and the pitfalls of coarse-grained force fields in the context of heterogeneous ice nucleation have both been reviewed, and the possibility of harnessing the increasingly popular framework of machine learning to deliver accurate/fast force fields enabling simulations of ice nucleation at complex interfaces has also been explored.
- The Workshop featured a substantial fraction of experimental contributions, which highlighted the need to further the current experimental techniques as well. This is key to the computational community, as in too many cases simulations take into account a single feature of the complex topology of the ice nucleating substrate, obviously limiting the scope of our simulations. Experimentalists are not yet in a position to pinpoint these ice nucleation sites, but the first achievements are starting to emerge (Kiselev)

Interestingly, a lot has been said during this Workshop about the homogeneous freezing if water into ice. This process, which represents the very first step toward the understanding of heteroegenous ice nucleation, has been investigated for decades, and yet many aspects remain to be clarified. For instance, the relevance of dynamics as opposed to structure in the context of nucleation has only recently been highlighted (Tanaka, Fitzner) - and more is needed to elucidate it and being able to translate that insight to heterogeneous ice nucleation.

A quite articulated debate took place about whether or not we can/should try to find a well-defined, tractable system representing a point of contact between experiments and simulations. The two are getting closer, but massive gaps do remain, and it is difficult to invest energies and funds in that respect. The idea is intriguing, but the challenges associated with making it happen will probably require a couple of decades to become tractable - where this timescale is associated with the pace by which both computational and experimental methods are evolving.

Sadly, it also became apparent that many aspect deserving further investigation from the community are difficult to fund: force field development, cross-validation and replication of older results make for a non-comprehensive list.

Finally, the level of complexity is exploding, both as it concerns inorganic substrates of relevance for atmospheric science (Murray, Koop) and biological interfaces for cryopreservation (Braslavsky, Davies). It is fair to say this meeting marked the beginning of a new wave of efforts, but the quest is a long one, and (almost) no one felt confident in saying that we have many certainties at the moment.

3 Community needs

- Computational infrastructure: two different streams within the community can be pinpointed in this respect. The first is the one seeking to investigate heterogeneous ice nucleation on model systems and idealised surfaces, more often than not employing coarse-grained models for water. Computationally speaking, not much is required to carry on this line of research. On the other hand, simulating ice nucleation on realistic, complex interfaces does require sheer amounts of computational power, which indeed is available to only an handful of research groups - albeit we recognize that the ease of accessing HPC facilities if improving quite rapidly.
- Networking: the involvement of experimental colleagues is absolutely key, and it does represent one aspect where much remains to be done. This is especially true given that the nucleation of ice impact very diverse fields and scientific ommunity which only rarely talk to each other. In this Workshop we put in the same room atmospheric scientists as well as cryobiologist, and the cross-fertilization originating from this interaction can easily be labeled as one of the most prominent achievements of the Workshop. The need for events bringing together the different aspect of heterogeneous ice nucleation is very clear.
- Event organisation: this Workshop built on an ice-oriented prequel (2014) where a number of participants were also present. Everyone was genuinely struck by the amount and quality of the progress in the field - which is quite an outstanding realisation, given the sheer amount of open questions still present within the field. There is definitely the will and the curiosity to take stock of this field again in a few years time, especially given the rate at which simulations are trying to make contact with experiments. We feel that the next few years are going to achieve much and define new challenges as well, and we thus advocate the need for a follow-up meeting within the space of 2-4 years.

4 Funding

The main hurdles in this respect are:

- Key aspects such as the development of new force fields and the cross-validation of computational results are exceedingly difficult to fund, given the ever-increasing focus of all funding agencies on "impact" - in conjunction with the inability of most funding body to recognize the sheer value of of methodological advancements in the long run.
- A quite frustrating reality that emerged from the Workshop is that the potential for collaborations, both EU-based and elsewhere, is just phenomenal. The community tends to focus on selected systems to study heterogenous ice nucleations, chiefly due to the availability of certain force fields. As such, there is the case for massive collaborative projects - which however remain incredibly difficult to fund via the conventional channels. Horizon2020 could be a way forward - but the dedicated EU/International funding opportunities are sorely needed.

5 Will these developments bring societal benefits?

The nucleation of ice impacts countless aspects of our society, from climate change to nanomedicine. Obviously, our computational efforts have little direct impact on these practical aspects - but are absolutely key to complement and guide the experimental endavours. To be specific, to this day we are not able to predict whether a given substrate will enhance the formation of ice - and/or to what extent. This is the probably the ultimate goal in the field, and will allow to improve a number of industrial applications.

One example with obvious societal benefit is that of cryopreservation, the process by which we store biological material (blood, embryos, tissues, staminal cells) via freezing: in that context, understanding heterogeneous ice nucleation will allow the design of a new generation of cryoprotective substances with the ability of minimize cellular damage upon freezing, with massive reverberation throughout the health sector, from blood storage to regenerative medicine.

The modelling of climate is another example: while the length scales probed by climate models are obviously enormous, being able to describe the kinetics of ice nucleation on different substrates is paramount to increase the accuracy and the predictive powers of these frameworks, which in turn carry a lot of weight in the attempt of tackling the pressing issue of climate change.

6 Participant list

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Charged Species in Bulk and at Interfaces: Mobility and Motility of Macromolecular Systems

Location: CECAM-AT
Webpage: https://www.cecam.org/workshop-0-1584.html
Dates: September 24, 2018 to September 27, 2018

1 State of the art

In the proposal for the present CECAM meeting, we mentioned the following main topics of interest that originated from the presentations and discussions of the previous CECAM meeting (held in Vienna in 2016):

(i) Fundamental theoretical and simulation problems in macromolecular electrostatics.

(ii) The role of electrostatics in biological (and neuronal) processes/systems.

(iii) Self-assembly and transport in complex synthetic charged macromolecules, used to create soft-matter functional materials in applied sciences.

The present workshop mainly focused on these subtopics of interest in processes where charge-charge interactions play an important role, including both structure formation in bulk, at interfaces, and on small molecular length scales, as well as dynamics and transport. The systems of interest ranged from synthetic- to biological macromolecules, as well as effects on very small scales, where for example hydration changes the electrostatic interactions between charged macromolecules on close approach.

A fundamental understanding of electrostatic interactions has already been partly achieved. Open questions are concerned with (i) electrostatic interactions for either strong coupling or in some cases (where the two extremes of weak and strong coupling are understood) for intermediate coupling strengths, (ii) electrostatic interactions between macromolecules with a complex architecture (like proteins), which are evidently orientation dependent, (iii) electrostatic interactions between charged species on close approach, where hydration plays an important role: for example, for enzymatic reaction rates and protein-ligand binding rates, and (iv) specific interactions between proteins and high-valence ions, which strongly affect the protein phase behavior and where most probably hydration plays an important role as well.

There is a lack of fundamental understanding an no consensus yet concerning electrostatic interactions involved in the

2 Major outcomes

We invited speakers (while some students were also given the chance to give short presentations of their work) who have been addressing the three topics mentioned above. In some more detail, the following topics have been considered:

(i) Fundamental theoretical and simulation problems in macromolecular electrostatics:

A comprehensive theory/simulation/experimental study of collective- and self-diffusion in suspensions of charge-stabilized colloidal spheres was addressed with hydrodynamic interactions, pressure, motility from time–dependent dynamics (G. Nägele). The comparison of simulations allowed for a critical evaluation of the accuracy of existing theories. A statistical mechanical theory of effective electrostatic interactions of ionic microgel particles (A. Denton) and charged, dendrimer-like DNA molecules (DL-DNA) (C. Jochum) are based on a sequential coarse-graining procedure by simulations. Fully atomistic simulations of interacting charged surfaces and ions in water are discussed to assess the validity of continuum models for the dielectric response at interfaces (R. Netz). For this, novel molecular dynamics (MD) simulation techniques allow to efficiently perform simulations at constant water chemical potential due to hydration of ions and the polarizability of the hydration layer. Thermal equilibrium of confined counterions in between the weak- and strong-coupling limit (E. Trizac) and pressure-induced liquid flow through a narrow long channel with charged walls (B. Werkhoven) are discussed. The electrical charge of surfaces in contact with surfactant-doped nonpolar liquids also plays an important role in electronic ink displays and liquid toner printing through interactions with charged inverse micelles (F. Strubbe).

(ii) The role of electrostatics in biological (and neuronal) processes/systems:

The dynamics of ion transport through membranes mediated by ion channels have been studied by MD computer simulations (J.-P. Machtens). Excitatory amino acid transporters (EAATs) terminate glutamatergic synaptic transmission and control synaptic glutamate concentrations. Protein aggregation pathways and the crystallization, gelation, and amorphous aggregation are induced by the addition of multivalent ions (F. Schreiber). Droplets made from recombinant coacervating charged proteins show a surprisingly complex behavior of oleosin (D. Hammer). Alzheimer's Disease is associated to the aggregation of small amyloid-ß (Aß) peptide into oligomers and fibrils (A. Horn). The interaction of different alkali metal ions with fibrillar Aß oligomers of different size by means of MD-simulations provide insights into the "sodium effect". Through atomistic simulations of diffusion of a receptor within a lipid membrane, the memory function enters the generalized Langevin equation as a mesoscopic approach in the post-synapse cascade (V. Calandrini). Furthermore, molecular simulations results were presented on DNA's and RNA's binding to proteins and small molecules with the relevance of electrostatic interactions (P. Carloni). The limitations of the various methods have been discussed in the difference between in-vitro and in-vivo experiments.

(iii) Self-assembly and transport in complex synthetic charged macromolecules, used to create soft-matter functional materials in applied sciences:

In a mixture solvent (water-oil) ions preferentially adsorb at the interface forming an extended electric double layer, reducing surface tension in the formation of mesophases (A. Onuki). The kinetics of dissolved ion species are solved for electrowetting of nanodrops in the breakup of charged and neutral droplets (J. Harting). The complex (electrostatic) interactions between various components in ionic surfactant micellar systems (surfactant monomers, counterions, and additives) are tuned to form molecular arrangements of individual molecules within the micelle and induce desired flow properties (P. Fisher). Also, the behavior of negatively c

3 Community needs

The scientific approach towards a quantitative understanding of suspensions of mixtures of complex macromolecules requires a concerted effort of soft-matter scientists from simulations, theory, and experiments. Especially the incorporation of biology expertise will become increasingly important. The processes in living organisms pose very interesting soft-matter problems, which are sometimes of such a high degree of complexity that simulations are indispensable to achieve a quantitative understanding. Moreover, in order to quantify the internal structure and the resulting interactions between molecules, quantum-based simulations are required. The output of these simulations can then be employed as an input for mesoscopic simulations in order to improve the understanding of the collective phenomena underlying the function of cells and living organism. Since many technological systems and all biological systems are water-based, electrostatic interactions often play an essential role. This CECAM workshop thus aimed of bringing scientists from different soft-matter disciplines together.

4 Funding

Ca. 4800 € has been spend for basic costs like printing, dinner, coffee breaks, by the TU Wien, while full travelling and housing costs of four invited speakers (2 from the USA, 1 from Canada, and 1 from Japan) and three participants from the ICS-3 in Jülich were paid from the ICS-3 at the Forschungszentrum Jülich (ca. 8000 €). The CECAM funding of 12000 € has been used to pay for part of the travelling/housing costs of the remaining participants, where the European scientists received a lump sum of 300 € and the scientists from outside Europe 800 €.

5 Will these developments bring societal benefits?

The societal relevance of the science of the workshop is twofold. Soft-matter based technologies are nowadays based on the very complex architecture (mostly synthetic) of macromolecules and mixtures of them, where in almost all of these, charge-charge interactions play an essential role. Further innovation and the development of new technologies in the field of smart soft-materials, which are of increasing importance in daily life (like self-healing materials, coatings, bio-mass fuel, sensors), requires a physics-based, quantitative understanding of their properties. Complex architectured macromolecules, mixtures of them, as well as their aggregates are essential for the functioning of living organisms. Also in these systems, electrostatic interactions and the resulting dynamics and kinetics are essential. A quantitative understanding of the relation between macromolecular interactions and the function of living organisms is essential for the long-term sustainable and rational design of medicine and of new therapies.

6 Participant list

Organizers

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Collective Behavior of Soft and Active Matter Under Confinement

Location: CECAM-DE-SMSM (Mainz, Germany)
Webpage: https://www.cecam.org/workshop-0-1563.html
Dates: September 24, 2018 to September 26, 2018

1 State of the art

Soft matter under confinement is ubiquitous in nature and technology, ranging from the crowded interior of biological cells to thin films of synthetic block copolymers. Confinement can either be imposed externally or it can emerge spontaneously through the collective self-organization of the constituents, e.g. the lipid bilayer formation. One crucial aspect of confined systems is the shape of the enclosing geometry, which can be, for example, planar, cylindrical or spherical. Further, the confining interface can be rigid, flexible, porous or semipermeable. Confined systems are characterized by a high surface to volume ratio, which can lead to strong deviations from the bulk behavior, even at regions far away from the confining interface. For example, the orientation of microdomains in block copolymer films can be controlled through the film thickness and the substrate properties. For nematic liquids, confinement frustrates global order and leads to the emergence of complex defect structures. Confinement also significantly influences the individual dynamics and collective behavior of active particle suspensions. For example, it was found that pusher types of swimmers (like spermatozoa) strongly migrate toward solid surfaces, and that self-propelled colloidal rods form transiently jammed clusters at planar channel walls. Microswimmers individually interact with surfaces through their self-generated hydrodynamic and chemical fields. Microswimmers are attracted or repelled from the walls depending on whether the swimmers are pushers or pullers. The combination of self-propulsion and confinement leads to new patterns of collective dynamics that are not observed in their passive counterparts. For instance, phoretic microswimmers speed up in confining channels.

2 Major outcomes

The work presented at our workshop can be roughly divided into two groups, i.e. passive and active matter systems under confinement, where both experimental and theoretical researchers presented their latest results. The major outcomes of some selected sessions are presented in the following.

Several presentations focused on the self-assembly of block copolymers (BCPs). For example, Marcus Müller showed that step-shear deformation of BCPs can result into novel, quasi-metastable morphologies that have no analog in the bulk phase behavior. Giang Vu demonstrated that the local orientation of the BCP microdomains is strongly coupled to the curvature of the confining geometry. In two other sessions, the behavior of nematic liquids under confinement was discussed. Teresa Lopez-Leon presented how the nematic order of cholesteric liquid crystals (LCs) gets disrupted when the cholesterics are confined to spherical shells, where stripes, fingers and skyrmions form organized, hierarchical patterns on the shell surfaces. This experimental work was supported by simulations by Zeynep Sumer, who

investigated the effect of surfactant adsorption on LC droplets. Kurt Binder demonstrated through simulations that lyotropic solutions of semiflexible polymers in spherical confinement exhibit a similar behavior like LC droplets.

Some talks concentrated on the role of long-range electrostatic interactions under confinement. Monica Olvera De La Cruz discussed the effect of confinement in surface polarization of water nanodroplets dispersed in oil. In this case, interfacial polarization leads to inter-droplet ion-ion attraction and eventual aggregation of droplets. Susan Perkin explained how confining highly concentrated electrolytes can be used to measure the screening length of electrostatic interactions. Lyderic Bocquet discussed the role of electrostatics on nanofluidic transport. The novel insights from his theory is that channel fluctuations enhance the water transport in nanopores.

The active matter talks comprised both dry matter and wet systems for which the hydrodynamic interactions are important. For dry systems, depending on the interparticle interactions and aligning rules with the walls distinctive patterns of collective behavior emerge. Angelo Cacciuto insights from simulations showed that confinement destabilizes long branched assembled structures in favor of compact clusters. Chantal Valeriani demonstrated that self-propelled particles of Vicsek model with an aligning rule with the wall are trapped on the wider opening side of the funnels. Yaouen Fily showed that in the strong confinement limit, when the persistence length of non-aligning active particles is much larger than the size of the box, particles stay on the boundary and align with the local boundary normal. This insight can be used to construct the box shape that yields any desired density distribution on the boundary.

In wet active matter, geometrical confinement strongly affects the interparticle hydrodynamic interactions. Juan P. Hernandez-Ortiz introduced a Green function formalism to include the effect of confinement in channels. This method was used to study the collective dynamics of confined chemotactic-driven active suspensions. Experimentally, Eric Clement discussed how applying an external magnetic field to magnetotactic bacteria confined in water droplets can be used to create rotatory motors and to harvest their swimming energy.

One open point of discussion was whether the framework of statistical thermodynamics can be directly applied to confined systems, since the thermodynamic limit cannot be reached in confined systems. Further, it was debated whether equilibrium structural properties in confined systems are affected by the presence of hydrodynamic interactions or not. These points were not resolved during our workshop and could serve as starting points for future initiatives.

3 Community needs

Discussions during our workshop have shown that there is a strong need for open software solutions, so that knowledge and methods can be better shared among various research groups. Such open source solutions also allow for peer review of the code, which can immensely help to identify and fix potential implementation mistakes. There are already several initiatives towards this direction in form of simulation packages like LAMMPS, GROMACS, HOOMD-blue etc., but closed source software is still prevalent in our field. Another big challenge is the lack of (standardized) reference data, which could be used for testing and analysis. There have been several attempts at establishing such databases in the past, but the utilization so far has been rather limited. A general framework to include the effect of long-range electrostatic and hydrodynamic interactions under confinement of arbitrary geometry is still missing and it needs further exchange of knowledge among the researcher active in this domain. We received very positive feedback on this workshop, and thus believe that a follow-up workshop on this topic should be organized in the near future.

4 Funding

Typically, funding is provided by national institutions, such as the National Science Foundation (NSF) or the German Research Foundation (DFG). For example, this workshop was co-financed by the Collaborative Research Center TRR146 (“Multiscale Simulation Methods for Soft Matter Systems”), which is funded by the DFG. To facilitate international collaborations, supranational or bilateral funding channels are highly desired, and several invited speakers discussed the possibility of joint research proposals.

5 Will these developments bring societal benefits?

By understanding the dynamical consequences of confinement, we can control the transport of fluids in nanopores and microfluidic devices used in various industrial applications. Additionally, confinement can be used to rectify the spontaneous flow generated by active particles. The topics discussed in our workshop are also relevant for a fundamental understanding of the behavior in crowded biological environments, such as cells and capsids.

6 Participant list

Organizers

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Topological Phases in Condensed Matter and Cold Atom Systems

Location: CECAM-FR-GSO
Webpage: https://www.cecam.org/workshop-0-1596.html
Dates: October 1, 2018 to October 13, 2018

1 State of the art

The 2016 Nobel Prize in Physics was awarded to pioneering work opening the field of topological phases of matter. This field has matured later on in the study of the fractional quantum Hall effect, which continues to deliver exciting physics, in the form of non-abelian excitations and the observation of neutral edge modes. Inspired by the quantum Hall effect, the study of non-abelian particles has branched into different topics, such as the study of topological phases emerging in (spin) lattice models and recently topological insulators and superconductors. During recent years, the field of topological phases has been boosted by the possible application to quantum computing. Implementing topological quantum computation in realistic experimental systems is one of the holy grails of the community.

Most notable are the newly discovered topological insulators (or superconductors), which combine physics from the quantum Hall effect and graphene. Currently, most of the interesting physics in topological insulators emerges from combining non-interacting band theory with the notion of topology, which has led to some spectacular results. However, the fact that most of the developments in the field of topological insulators have focused on the effects of the topological properties alone means that consideration of the consequences of adding electron interactions are largely missing. While the latter give rise to very interesting physics in their own right, combining them with topological structures will most certainly lead to many interesting discoveries. The fractional quantum Hall effect is a prime example of where this interplay indeed has led to very exciting new physics. Classifying topological phases in the presence of interactions is a daunting task, so that making even a little progress will greatly enhance our understanding of topological phases. This is one of the main questions that was be addressed during the workshop.

2 Major outcomes

Our workshop has fully confirmed that the field of topological phases in condensed matter physics and atomic gases is an extremely active field, where theoretical (both analytic approaches and simulations) and experimental progress go hand in hand. Since our previous CECAM workshop in 2013 and 2015, we have indeed noticed tremendous progress. We managed to gather again world-class physicists with different backgrounds - numerical, theoretical and experimental - and with the common interest of topological phases of matter. Reports of the very recent developments in the field were given and lively discussions have taken place. People left with interesting ideas from the discussions, which now have to be worked out in detail. The following topics emerged as key:

a) Fractional Chern insulators: The classification of topological phases in the presence of interactions is progressing steadily. New phases on lattices - with no fractional quantum Hall state equivalent - have been discussed in the course of the workshop.

b) Topological phases in quantum magnetism: Rapid progress is made in the field of frustrated magnetism showing that a number of quantum spin systems in low dimensions may host topological spin liquids.

c) New phases in cold atomic systems: The versatility of cold atomic matter is continuing to supply suprises. With the recent experiments on many-body localisation in cold matter, the promise of realising various new types of orders predicated on many-body localisation (such as 'eigenstate order') is in the air.

d) New entanglement-based theoretical tools: a number of new tools borrowed from quantum information and based on entanglement (Entanglement Spectrum, Tensor Networks, etc…) have enabled advances in the understanding of correlated systems and topological orders.

Networking & training to make advances:

We believe "Topo" workshops (at IES Cargèse or in a similar facility) every two or three years would serve the community well, as a regular platform to discuss the new developments in this rapidly growing field. We have managed to attract funding from a variety of sources, which has enabled us to put together an event allowing a considerable number of young scientists to benefit from the presence and availability of a strong roster of accomplished researchers.

Identification of key research areas (for the EU Horizon 2020 program) :

* The field of topological phases: Topological quantum computation solves, by construction, the problem of local decoherence. Implementing topological quantum computation in realistic experimental systems is one of the holy grails of the community.

* Numerical simulations with theoretical guidance of these complex many-body systems: density matrix renormalisation group and tensor network studies of cold atoms, topological spin liquids, fractional topological insulators, etc… are extremely dynamics fields currently being developed by our community.

3 Community needs

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4 Funding

Besides CECAM, for this workshop, we have obtained a partial funding by the french CNRS ("formation permanente") and by the Max Planck Institute (PKS, Dresden). This has allowed us to wave entirely the registration fees for all the invited lecturers and speakers. In addition, accommodation, lunches and coffee breaks have been provided for all participants. Local transportation between the airport and the center has also been covered for all invited speakers and beyond.

We will seek for such joint research proposal in the future.

5 Will these developments bring societal benefits?

Benefits for academics: A large fraction of the participants was PhD students, post-docs as well as young researchers. The program was particularly designed for them with very pedagogical lectures. The younger participants were also given the opportunity to present their work (contributed talks and two poster sessions) and, hence, to get better known in the community. Long breaks have also been beneficial to deep discussions between junior and more senior and/or experienced participants. We believe that the workshop has led to the initiation of new projects and new collaborations.

Economic benefits: The field of topological phases is still very much an area of fundamental research. While applications to the design of quantum computers have been proposed and are being pursued by research groups funded by Microsoft Corporation, it will be several years before this field and the research presented at the workshop will be of more immediate interest for commercial exploitation by European industry.

6 Participant list

Organizers

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CECAM-Lorentz Joint Workshop: Integrating Molecular Simulation with Machine Learning/Artificial Intelligence for Advance Material Design

Location: Lorentz Center, Leiden, The Netherlands
Webpage: https://www.cecam.org/workshop-0-1653.html
Dates: October 8, 2018 to October 12, 2018

1 State of the art

Rational design of advanced materials, such as smart energy materials, cognitive materials, bio-inspired materials, etc., requires the use of dedicated multiscale simulation methods spanning the range from atoms all the way to the continuum level. Currently, a limiting factor is handling of the big data that either goes into such

models or results from the predictions. Here the use of machine learning techniques and methods borrowed from the realm of artificial intelligence are needed to bring the field of computational material design ahead. The goal of this workshop was to connect several disciplinary lines and to bring together top researchers in the fields of

molecular simulation, machine learning, and artificial intelligence to develop unified methodology, covering the whole simulation pipeline, for the rational design of advanced materials. Establishing such an

interactive scientific network served as a solid foundation toward the ultimate goal of developing novel materials needed for efficient neuromorphic computers, improved photovoltaics, or biomedical applications.

2 Major outcomes

During the workshop we have (i) identified practical connections between molecular simulations (QM, MD) on the one hand and ML/AI on the other hand, (ii) discussed the major challenges and existing bottlenecks as well as ideas on how to improve these connections, from different disciplinary aspects, and (iii) established collaborations between people working in these different fields.

Below come the key points discovered interfacing ML/AI with MD and QM;

- We need a standard benchmark data set with analog or categorical target outputs for a realistic problem in MD modeling.

It should be big enough for serious cross validation, say k=8 or 10 in k-fold evaluation.

- Arrive at a minimum set of descriptors, categorical or analog that would describe the state of a non-trivial molecule according to consensus in the MD community. It is clear that this implies a subset of tasks and envisaged target model outputs.

- How to determine a correct network architecture or topology such as number of layers and convolution kernel sizes. We need tools esp. for MD.
- We need hands-on examples, not only of classification problems but also of potential-field estimation.
- It appeared that efficient sampling, i.e., improving the ratio of performance to training set size (“sample efficiency”), spares data, improving representations to be primary challenges in QM.
- It appeared that ML potentials are critically dependent on the quality of the QM input data, and as of today require significant effort to be developed in the first place
- ML makes instantaneous QM quality predictions
- Learning curves reveal quality of ML model
- QM Rate and offset depend on
  a. Uniqueness and target similarity (model dependent)
  b. Properties and structures (data dependent)
  c. Baseline (expert dependent)
- Models that combine QM with ML aim to deliver the accuracy of QM at the speed of ML by interpolating between a feasible number of reference calculations.
- The participants from different field of QM, MD, ML/AI, shared various in-house developed codes, open source softwares and teaches each other how to run their first ML/AI-QM or MD simulations and get hands on training models.

3 Community needs

This workshop initiated the integration of the molecular simulation with machine learning/artificial intelligence, as we were expecting. We believe that the participants intensely exchanged information/knowledge, already start testing proposed ideas on how to overcome the challenges and how their research will benefit being interfaced with different techniques within the simulation pipeline. However what was missing is required further is "event organization". We have realized that it is very important to organize a summer/winter-school for the PIs in which there are actual tutorial sessions. In such a setting, the PIs will get the chance to run and test various softwares used in other community supervised/guided by the experts form those fields. We believe that all three community of MD, QM, ML/AI will benefit from a series of CECAM workshops on similar topics as it has been clearly stated by various participants. However it should not be a brainstorming workshop but rather a practical workshop with series of tutorials/homework.

4 Funding

We have discussed the following points on the last day:

1) Double Degree PhD programs; A double doctorate is a doctorate in which supervisors from two universities supervise a PhD student on one project and for which these two universities each award a PhD degree.

2) Inspired by the workshop and the discussion that I had during the last day of the workshop, we came to the idea that now it might be a “right” time to initiate an ITN proposal on the topic "Machine learning for Chemistry”. So far we have 5 core partners committed and we will meet in Groningen in April 2019 to brainstorm the idea and discuss the logistics.

5 Will these developments bring societal benefits?

The workshop "Integrating Molecular Simulation with Machine Learning/Artificial Intelligence" organized at the LorenzCenter allowed us to establish an interactive scientific network and bring together top researchers in the fields of molecular simulation, machine learning, and artificial intelligence to develop unified methodology, covering the whole simulation pipeline. This is not only exciting but also a timely and critically needed initiatives that can play a significant role in shaping the science landscape for the better. For example, the Innovative Training Networks (ITN) on the topic "Machine Learning in Chemistry", that will be initiated in 2020 not only will serve as a solid foundation for a broad range of application, such as, developing novel materials needed for efficient neuromorphic computers by develop materials-centred systems paradigms for cognitive computing based on modelling and learning at all levels, improved photovoltaics solar cells, or biomedical applications.

6 Participant list

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Next Step in Random Walks: Understanding Mechanisms Behind Complex Spreading Phenomena

Location: CECAM-ISR
Webpage: https://www.cecam.org/workshop-0-1567.html
Dates: October 8, 2018 to October 11, 2018

1 State of the art

The workshop focused on discussion of spreading phenomena, which play either negative or positive role, depending on what is spreading, an invasive pathogen or holes in a semiconductor. There are many facets of spreading that have been studied in different fields. On the micro time-space scales compared with the lifetime of a single mover, an atom migrating over a substrate or a foraging animal, spreading splits into a set of point-like random processes, so that individual trajectories look like trajectories of random walkers. It was therefore very natural that the paradigm of random walks heavily influenced the development of the fields where spreading plays the key role – solid state electronics, turbulence, molecular biophysics, ecology, and others. It was observed in many labs that the obtained data do not fit the simple Gaussian model, so new tools and models were demanded. The complexity of the observed phenomena can be captured in more detail with such updates as continuous-time random and Lévy walks. These approaches have found a striking number of applications in diverse fields, including optics, dynamical chaos, turbulence, many-body physics (both quantum and classical ones), biophysics, behavioral science, and even robotics.

Existing models, such as Lévy walks and fractional Fokker-Planck equations, have a strong appeal – they are very well developed, they are famous and have very good reputations and agenda. It is very tempting therefore to use them immediately when an experimentalist or a field ecologist comes with the statistical data and ask “Could you please explain it with your theories?”. But even if the matching is perfect, it does not serve an explanation. The explanation is encoded in the data and in order to extract it, the theoretician has, first of all, to understand the process which produced this data.

2 Major outcomes

The main emphasis of the workshop was on changing the “cargo-cult” paradigm prevailing now on the field of anomalous diffusion and random walks when it comes to their practical applications. Namely, it is not that experimental data should be analyzed in the view of the existing random walk and diffusion models but models themselves have to be constructed in a way as to capture essential physics behind the emerging spreading. That simply means that physical mechanisms running the spreading have to be understood first by those theoreticians who want to describe them with their mathematical constructions. The focus of the proposed workshop is to leave the phenomenological stage of the theory and bring together experts who work on the basics mechanism still covering a large body of models and systems.

Spreading of cold atoms in dissipative optical potentials, discussed in the talk by Nir Davidson, is an example where this path is already taken. At first, a specific classical diffusion equation was derived to capture the specific cooling mechanism (essentially quantum by its nature) governing the dynamics of atoms; and then it was possible to demonstrate that on the microscopic level trajectories of individual atoms appear as Lévy walks. In such a way, a Lévy walk-like process has been derived from physics. Yet these experiments have also revealed that a simple LW description does not capture all features of the observed phase space dynamics. In a very different direction another microscopic origin of anomalous diffusion of bacteria was recently developed. These two examples are only part of a trend of a maturing field switching from phenomenological methods to deeper modeling, and our primary goal is to help diffuse these new ideas among the relevant practitioners.

The workshop lasted four days, comprising a total of 29 invited talks and a poster session. The covered topics included: continuous time random walk (Stanislav Burov); first passage under restart (Shlomi Reuveni and Alessandro Taloni); anomalous dynamics of ultra-cold atoms (Nir Davidson); anomalous chemical transport in geological porous media (Brian Berkowitz); quantum random walks (Yoav Lahini and Felix Thiel); dynamics of biomolecular folding and unfolding (Dmitrii E. Makarov, Michael Andersen Lomholt and Ronen Berkovich); anomalous diffusion in membranes and cytoplasm of biological cells (Ralf Metzler and Yael Roichman); super- and sub- diffusion in active networks (Rony Granek and Olivier Benichou); Levy flight random search (Aleksei Chechkin) and non Markovian random walks (Raphaël Voituriez).

The workshop program left significant time for discussions that was strongly appreciated by all participants. During the workshop the participants from abroad visited laboratories of the colleagues from the Tel Aviv University that will strengthen contacts between the groups.

3 Community needs

It is extremely important to construct opportunities for researches from different areas and background to meet and exchange knowledge and ideas. In fact the present policy for research funding, e.g. from the EU, push towards high level competences and excellence in specialized fields. Kinds of interdisciplinary are often stimulated but as a matter of fact call for funding are made on homogeneous areas (environment, nano, ICT, bio) so that the focus can be from different point of view but on narrow objectives.

The present workshop focused on spreading phenomena, which are transversal to many length and time scale, involving researchers from statistical physics, geophysics, condensed matter, mechanics of materials, biophysics and chemistry, working in theoretical, numerical and experimental areas. During this workshop we discussed what computational infrastructure is needed for efficient solution of problems in the area of spreading phenomena.

Last but not least, the workshop played an important role in keeping the integrity of the community of researchers working on such fields as random walks, diffusion, and stochastic processes.

Indeed, we plan a series of future workshops on these topics.

4 Funding

At the moment we see such field as random walks (especially Levy walks), anomalous diffusion, and stochastic processes as something coming back to life and becoming again ‘fashionable’, due to new contexts and constantly emerging applications.

A perspective direction are “Levy robotics” (use of Levy walks to develop new search algorithms for autonomous mobile robots), “First detection time in quantum random walks” (advancing such notions as “first passage time” into the field of quantum walks with a perspective to use this idea for quantum computations), “Quantum Levy walks” (generalization of the LW concept to quantum processes) , “Random walks with restarts as optimal strategies” (this concept has already spread into the quantum corner) .

On the international level, big a collaborative group can apply with such a projects as “Levy walks: new applications” (could include experimentalists and theoreticians from different fields, ranging from quantum optics to robotics) .

5 Will these developments bring societal benefits?

Topics addressed in the talks of the speakers are mostly belong to fundamental science. However, results in such applied fields as biophysics of plants (talk by Yasmine Meroz), quantum optics (talks by Nir Davidson and Yoav Lahini), hydrology (talk by Pierre E. Levitz) and geophysics (talk by Brian Berkowitz), were reported and discussed in the context of random walks and diffusion. This is an important component because – in a strategic perspective – these results could potentially lead to new technological solutions.

Starting from the seminal work by Pearson, random walks are almost genetically tied to to such subjects as human mobility and animal foraging. It is therefore important to promote also this facet of the studies and related them to recent advances in sociology and ecology. There were several talks, e. g., by Shlomi Reuveni (TAU) and V. Zaburdaev (University of Erlangen) on these aspects. These topics are also very good for outreach; they have high appeal for non-expert audience and therefore work for the benefit of the whole field, by exposing it to students and non-professionals.

6 Participant list

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Frontiers in Molecular Dynamics: Machine Learning, Deep Learning and Coarse Graining

Location: CECAM-ISR
Webpage: https://www.cecam.org/workshop-0-1628.html
Dates: October 10, 2018 to October 12, 2018

1 State of the art

2 Major outcomes

3 Community needs

4 Funding

5 Will these developments bring societal benefits?

6 Participant list

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Multiscale Simulations of Allosteric Regulatory Mechanisms in Cancer-Associated Proteins and Signaling Protein Networks

Location: CECAM-Lugano, Lugano, Switzerland
Webpage: https://www.cecam.org/workshop-0-1576.html
Dates: October 15, 2018 to October 17, 2018

1 State of the art

The phenomenon of allosteric communication is fundamental to many biological processes including the regulation of signal transduction networks.

While studies on allostery in protein systems are often focused on thermodynamic aspects of the mechanism, there is an increasing realization of the critical role of conformational dynamics, which is central to “entropy-driven” allostery.

The recent experimental breakthroughs in NMR technologies have enabled structural studies of large protein systems and conformational dynamic processes at atomic resolution that provide unique insights into allosteric mechanisms. Relaxation dispersion NMR methods developed over the past decade have enabled detection and characterization of rare and energetically excited conformational states that play significant role in dynamic activation of protein function and allosteric mechanisms. Recent time-resolved infrared spectroscopy experiments have indicated that the allosteric transitions occur on multiple timescales.

The growing evidence that dynamics-driven allostery may be common to many protein systems has further expanded our view of diverse allosteric mechanisms that are not limited to population-shift mediated exclusively through structural transitions that select and stabilize specific conformational states.

Theoretical and computational studies of allostery in biomolecular systems have witnessed a recent renaissance. Sequence-based approaches have unveiled that protein allostery may be mediated by coupled motions of evolutionary networks of functional residues. Network-based structural studies have also demonstrated that allosteric pathways may be formed through interactions of evolutionary conserved residues that are energetically coupled to mediate long-range communication. Elastic network models (ENM) and normal mode analysis (NMA) approaches, have provided a generalized formalism of allosteric communication in proteins and have identified that conserved low-frequency modes of collective motions are robust to sequence variations and capable of transmitting molecular signals over long distances. More recently, fully atomistic MD simulations, complemented by enhanced-sampling algorithms have provided further insight into the details of allosteric regulation and dysregulation of signaling proteins.

Computational studies have shown that examining proteins as dynamic regulatory machines fluctuating between allosteric states and modulated by ligand binding or mutations is critical to understanding the molecular principles of allostery. A significant body of computational studies of allosteric mechanisms has indicated that integration of physics-based and

experiment-informed simulations with network-based formalisms of allostery may provide a platform for atomistic characterization of allosteric states and regulatory mechanisms.

The allosteric regulation of protein kinases is of particular interest, due to their fundamental role in signal transduction networks and in cancer. Dysregulation of protein kinase activation by pathogenic mutations is involved in the initiation and propagation of most cancers. Recent advances in understanding allosteric regulation of protein kinases have facilitated efforts aiming in the discovery of allosteric kinase inhibitors that can provide target specificity and are at the forefront of the precision medicine initiative in oncology

The cancer-causing mutations can directly affect their allosteric activation, affect protein-protein interactions or their folding. The molecular mechanisms of allosteric kinase activation and its (dys)regulation by protein-protein interactions and cancer-causing mutations have been extensively studied by experiment and simulations. Still, the picture remains mostly qualitative and many aspects unclear. One is the role of chaperones. Hsp90-Cdc37 chaperones are recruited to misfolded or partially unfolded proteins and help their folding. Allosteric interactions of the Hsp90 with co-chaperones and protein kinase clients can determine regulatory mechanisms and cellular functions of many signaling proteins and cascades. But how do they interact with oncogenic mutations?

The organizers believe that integration of computational and structural approaches will advance the field by developing a novel research strategy for probing and validation of allosteric states and mechanisms at atomic resolution. A combination of state of the art models and simulations combined with structural and biophysical experiments are key to deeper understanding of allosteric regulation processes.

Our Workshop successfully brought together the top computational and experimental experts in the field to discuss the current status and the best avenues to further progress. A significant novelty was the focus on the role of misfolding and chaperones in regulating signaling protein activation.

2 Major outcomes

The workshop covered a number of topics, including:

a) Theoretical models and multiscale simulations of allosteric regulation and interactions in protein kinases and molecular chaperones;

b) Structural and biophysical studies of allosteric regulation in signaling networks;

c) Therapeutic applications of allosteric mechanisms of protein kinases and chaperones;

d) Integration of multiscale simulations with big data analysis and machine learning.

During the talks and in the two lively and successful round tables, the state-of-the-art of research in the field of signaling protein allosteric regulation was discussed, focusing on major recent advances both in experimental and computational techniques.

A number of successful cases in which the combination of experiments and theory provided an added insight to either of the two approaches were reported.

Specific case studies on the importance of allosteric regulation of kinases and other cancer-related proteins in drug-discovery were reported.

During the round tables the speakers had an open and enlightening discussion on open issues both in simulations and experiments of allosteric regulation and chaperone-mediated folding.

The transfer of knowledge from computer simulation experts to experimentalists and drug discovery experts was actively promoted.

3 Community needs

The participants to the workshop made clear that the use of Tier-0 HPC resources, such as those provided by PRACE in Europe and XSEDE in the US or specialized machines such as Anton-2 at De Shaw research are of fundamental importance to perform sufficiently accurate simulations leading to predictive atomistic models that can be used in drug discovery. In this respect, it was interesting to note how the models of RAS multimers obtained by Dr. Shan on Anton 2 are now being explored for the rational design of anti-cancer compounds and new start-up company has been set up to exploit the computational models.

One of the aims of this workshop was specifically to foster networking between computational and experimental communities. In this respect the workshop has been very successful as shown by the numerous follow-up collaborations of which we have been made aware of and some joint review papers that are being written.

The extremely positive and enthusiastic feedback from all speakers and participants and the overall success of the workshop provided a strong, consensual view to build on the current progress and continue with regular CECAM meetings on this topic. Many unresolved questions in the area require a strong cooperation between theory, computation and experiment. We believe that a series of CECAM workshops on this and related topics (combining structural, biophysical, genomic experiments with theoretical advances and new approaches to simulations to address biomedical open questions) should be considered for the immediate future and next workshop.

4 Funding

The high-profile participants to this workshop receive substantial funding from a number of European and international funding agencies.

These include H2020 (ERC, Humab Brain Project, MSC IT networks), the National Institutes of Health (NIH), the National Science Foundation, the Wellcome Trust, EPSRC, BBSRC, MRC, ANR, ISF, SNF, MIUR, etc.

The possibility of joint research proposal has been discussed explicitly during the meeting. However, while intra-H2020 grants facilitate such endeavours within the EU and the associated partners, this is currently more difficult with the US, due to the scarcity of true intercontinental calls (such as the Human Frontier Science Programme). A possible route is for EU and Israel -based researcher to participate as external collaborators in large NIH or NSF grants lead by US-based researchers.

Alternatively, the announced EU Horizon Europe framework should provide more opportunities to set up an international and inter-continental network of computational and experimental groups working on allosteric regulation with the focus on integration of experimental information into computational methods development. Some opportunities for funding might be available in the Future and Emerging Technologies (FET) Program of Horizon Europe.

5 Will these developments bring societal benefits?

The aims and central theme of this workshop are interconnected with the central socioeconomic impetus to generate unique interdisciplinary research and collaborative opportunities for cross-disciplinarily and large international collaborations in understanding mechanisms of regulation at various scales and resolution. A mix of innovative research reports and educational activities along with numerous personal interactions with top experts and round-table discussions provided unique opportunities and experiences for young researchers, postdocs and students.

As also shown by the many positive follow up mails from the participants, the workshop has successfully fostered progress beyond the state of the art in understanding the molecular mechanisms underlying allosteric regulation of cellular signaling networks and molecular chaperones.

The potential societal benefits of this are many and range from helping the design and discovery of novel and more effective anti-cancer agents to targeting cancer-causing genes in an effective and personalized manner (see for instance the example of RAS discussed above).

In the long term the novel collaborations, simulation platforms and theoretical knowledge inspired by the discussions and new collaborations promoted by the workshop might lead to more effective and less toxic therapies not only for cancer but also from other complex conditions, such as neuro-degenerative diseases.

6 Participant list

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Protein-Peptide Interactions: Peptide Identification, Binding Prediction and Design

Location: CECAM-FR-MOSER University Paris-Diderot Amphi Turing Bâtiment Sophie Germain 8 place Aurélie Nemours - 75013 Paris
Webpage: https://www.cecam.org/workshop-0-1570.html
Dates: October 16, 2018 to October 19, 2018

1 State of the art

In the recent years, biologics have emerged as a promising alternative to small compounds for the development of the next generation of therapeutic compounds. Among them, peptides are a specific class of molecules that are involved in cell signaling and trafficking, can act as antibiotics, or can target protein-protein interactions. Progress on peptide administration, stability, biodelivery and safety are encouraging the interest in peptide drug development.

On the in silico side however, peptide design faces specific challenges. Strategies for peptide design largely differ from those developed for small compounds. Owing to the largely differing physico-chemical properties of both classes of compounds (e.g. size, flexibility), the use of the protocols that have been optimized over decades for chemical drugs is largely inappropriate. Peptides largely escape the rule of five defined by Lipinsky for small compounds. In order to prevent rapid degradation and to improve membrane permeability it is often necessary to chemically modify peptides or to constrain their conformation (e.g. cyclisation), challenging current in silico methods for peptide modeling and design. Peptide structure modeling, peptide interaction with their targets, the design of peptide sequence variants with improved affinities, specificities and pharmacological profile, their combination with delivery vectors remain challenges to address that motivate the development of optimized and specific protocols.

Recent new algorithmic methods and developments result in improved force field description of peptides and proteins, much longer accessible simulation time scales for studies in aqueous solution but also promise to overcome some of the challenges for peptide design. The in silico peptide community is progressing rapidly, but so far, no synthesis of the specific efforts undertaken has been achieved, which motivates this application and could promote further in silico method advancements.

2 Major outcomes

The peptide-protein interactions workshop has provided the basis for a comprehensive overview on different challenging items of peptide drug development:

1/ In silico approaches to peptide modeling, with a highlight on the more challenging case of cyclic peptides. For these, various approaches relying on different backgrounds - robotics, molecular dynamics (MD), database search - have been presented, with a focus on the conformational space sampling using MD or robotics.

2/ In silico approaches to characterize protein-peptide interactions. Simulations based on coarse grained, all-atom representations, or a combination of both have been presented. Different strategies to take advantage of biologically available information, versus the blind docking of peptide have been discussed.

3/ Peptide design: Various MD protocols aiming at sequence optimization, driven either by experiment or by in silico approaches have been presented. The presentation of various ongoing applications guided or not by computational approaches, including a full success story of a drug approved december 2017 after almost 20 years efforts has highlighted the long road between candidate drug identification and dug approval. Experimental approaches addressing the difficult issues of peptide tissue distribution and cellular/organite internalization have also been presented.

Among the major outcomes:

- For cyclic peptides, the size of the peptide to cyclize seems presently critical. MD and robotics seem to presently better address the case of smaller peptides (5-7 amino acids). Experimentalists have reported that for them, one main issue is to reach a stable cyclic peptide whereras in silico approaches presently focus more on the relation between the conformational landscape and sequence. For longer peptides, the perspective of combining database approaches with MD has also emerged.

- For peptide-protein interactions, approaches relying on either coarse-grained, all atom representation, or protocols combining both point to: (i) the limits of current coarse grained representations to identify in a reliable manner the best poses, (ii) the added value of protocols combining both, some being reported able to generate identifiable atomic resolution poses. Interestingly, while flexibility of the peptide does not seem an issue any longer, flexibility on the receptor side is included in several protocols presented. Attempts to move towards the in silico quantification of the binding affinities, while presented in some cases, remains out of reach for the routine work.

- For in silico peptide design, simulations using Monte Carlo approaches in the sequence space are now challenged by emerging approaches addressing the full sequence space at a time. Whereas the results presented look promising, the effective blind design of candidate peptides using such approaches is still an objective. Reports of successful peptide design targeting protein-protein interfaces took advantage of the knowledge of the structure of the protein-protein complex to identify the initial candidate. The most impressive results reported have been reached by experimental design involving techniques such as phage display combined with QSAR approaches, or human expertise for peptide optimisation.

The workshop has strongly benefited from the presence of both experimentalists and theorists, sometimes highlighting a gap in the performance currently reachable by experimental methods (e.g. for peptide design) vs in silico approaches. Numerous fruitful discussions have been an opportunity to discuss the pros and cons of each paradigm, and to enlarge the network of collaborations. Both experimentalists and computational workers greatly benefited because the opportunities and limitations of experimental and computational approaches could be clearly communicated and were discussed extensively. More specifically, cyclic peptides and cell penetrating peptides have raised mutual interest from both sides.

3 Community needs

The in silico peptide community is progressing rapidly, but so far, no synthesis of the specific efforts undertaken had been achieved, which was a strong motivation to organize this workshop.

- The needs expressed in terms of computational infrastructures were rather limited, most groups relying on their own calculation resources. Note however that during this first meeting, the focus has not been put on identifying frontiers that could be overcome by important increase in computational resource.

- Discussions on how to keep on the community further federating have been tempered by the remark expressed by the head of CECAM-MOZER that chances to organize a series of CECAM workshops as a follow-up are low, when clearly, participants would have welcome such possibility. Possible directions identified during the discussions have been to propose sessions in regular meetings of the European Peptide Society for instance. These meetings seem to presently accept only few contributions from theorists, but the suggestion got a strong support from the experimentalists attending the workshop.

4 Funding

Funds to support the workshop, which encountered a larger success than expected in terms of applicants, came from various sources, and included CECAM-MOZER, academic societies (french GDR BIM - molecular bioinformatics), private companies (PEP-Therapy, a startup in the field) and the research laboratories of the organizers. The opportunity to apply to new upcoming sources, e.g. Horizon 2020 seems presently rather low because the community of peptide drug development is not presently well identified/structured, a reason this workshop was proposed. The opportunity to apply for instance for an Innovative Training Networks (H2020) is however under consideration.

5 Will these developments bring societal benefits?

Although the workshop has not created direct societal or economic benefits, the many extensive discussions have created new research ideas and potential routes for designing therapeutic peptides also interesting for the pharmaceutical industry. It is also interesting to note that one startup of the field contributed to the event, suggesting the interest of industry to the field. As pointed to by some talks, the development of new therapeutic peptides can be of large societal and economic benefit for treating various types of diseases, but the road to success from the early steps discussed in the workshop is long. Among their strong points, these new types of drugs are less expensive than biological treatments and they may have low side effects. Several applications to patented peptides have been presented. Several talks also described successful on-going drug developments addressing targets in the cell organelles or in the brain, i.e. overcoming the limitation of membrane permeation, opening new perspectives for applications.

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Ab Initio Spin Modelling

Location: CECAM-HQ-EPFL, Lausanne, Switzerland
Webpage: https://www.cecam.org/workshop-0-1549.html
Dates: November 26, 2018 to November 28, 2018

1 State of the art

Spin-polarized band structure calculations within density functional theory (DFT) with subsequent mapping onto a Heisenberg model have become the conventional method for the treatment of magnetism in materials. Although the formulae for the ab initio calculation of exchange parameters were written down 30 years ago by Liechtenstein, Katsnelson, Antropov and Gubanov, their evaluation and extension continue to attract considerable research. The Heisenberg model remains a central theme of magnetic research although its assumption of localized moments of constant magnitude interacting by static coupling parameters, may often be inappropriate. Dynamics and finite-temperature behaviour of the system are treated as separate problems using the methods of statistical physics.

Density functional theory is limited in its ability to treat strong correlation and temperature: in this context the development of GW and the combination of DFT with dynamical mean field theory, in particular, have had a significant impact in understanding complex magnetic materials. Significant efforts have been directed toward the calculation of the enhanced magnetic susceptibility using a range of post-DFT theories. Other state of the art research is concerned with relaxation of the spin magnitude and damping of magnetization dynamics, understanding spin dynamics on short timescales, introduction of quantum statistics in spin modelling and doing ab-initio finite temperature magnetism without recourse to a spin model.

2 Major outcomes

A wide variety of developments were discussed at the Workshop representing both advances in fundamental theory and understanding of magnetism and magnetic materials and also methodological improvements where new approaches have been implemented in computer codes.

Within conventional DFT, significant progress has been made in treating disordered materials and structures of different dimensionalities (Turek, Ernst) and the manifestation of (even low levels of) disorder on broadening of spin wave spectra was revealed.

Finite temperature magnetism was a central theme of the Workshop with discussions at the fundamental electronic structure level, where temperature relates to the electron system using the framework of DMFT (Minar, Di Marco). Ab initio calculations for treating finite temperature of the spin system were discussed in the disordered local moment theory (Staunton). Discussions of temperature and at the spin modelling level (Barker) and micromagnetic levels (Chantrell) highlighted the importance of using quantised thermostats in spin modelling and addressed the temperature dependence of macroscopic quantities, such as anisotropy, and how experimental data should be interpreted. The treatment of the electron-phonon interaction and its effect on electronic structure and magnetism was discussed in terms of an alloy analogy (Ebert) and via the inclusion of an explicit e-ph self energy.

The question of strong electronic correlation was addressed in detail (van Schilfgaarde) and when and how to use post-DFT methods, GW and DMFT, was discussed. The absence of spin-spin fluctuations in GW, which is seen in the failure of GW for NiO, was discussed as a motivation for the use of DMFT. The usefulness of advanced theory was demonstrated by pioneering calculations in perturbation theory for Fe (Friedrich) which provided a large amount of insight and a very useful benchmark for this important model system.

Advances beyond the conventional extended Heisenberg model were discussed (Etz, Lounis) and how these are relevant for different systems; the main direction for study is the evaluation of 3- and 4-spin interaction parameters. The importance of inclusion of dipole-dipole interactions in antiferromagnets was illustrated (Barker). Different ways of calculating the parameters for spin models were discussed in detail and some new methods were presented, including a new implementation of the Liechtenstein, Katsnelson, Antropov & Gubanov formula in the Siesta code (Szunyogh). The topic of non-collinear magnetism was covered in detail (Ebert) along with considerations of symmetry in antisymmetric and/or anisotropic exchange interactions.

3 Community needs

Calculations of magnetic systems using post-DFT theories are very demanding and much use is made of diverse, national level computer resources, however in various contexts, particular functionality is limited to particular software packages that vary significantly in their parallel performance. Different approaches, implemented in different codes, often make incompatible assumptions (eg, full potential or ASA) and it is difficult to bring conclusions and methods from one method into another -- eg, inclusion of GW or DMFT into existing KKR codes presents real challenges. In the other direction, inclusion of non-collinearity and relativistic effects has proven challenging to implement in methods for treating strong correlation. Theoretical and programming effort continues to be directed at these crossover problems.

The different methodologies have been developed by different communities -- theoretical spectroscopy, strong correlation, modelling of magnetism -- and a significant success of the workshop is in bringing these different communities together. A further conference or workshop in specifically concerning ab initio modelling of real materials would clearly be warranted (this being demonstrated by the very large number of applicants: there was space for about one third of the applicants), once the field has advanced further; at that time, bringing in experimentalists (especially those working with polarised neutron scattering) and industrial representatives (for example, from the hard disc drive business) would be tremendously profitable: a dialog between workers doing fundamental science and who write computer codes and the technologists who use them would be very useful.

4 Funding

Funding typically has been via national funding agencies and European networking activities. Representative examples are UK's Physics of Rare Earth and Transition Metal Magnets (warwick.ac.uk/pretamag) and Cost Action 1306 (EUSPEC). Much of the development and scientific activities are conducted as part of the academic work funded by universities and governmental research agencies: much of the work of fundamental, basic research. Nevertheless, a number of workers have projects financed jointly by commercial partners, notably from the magnetic recording industry.

5 Will these developments bring societal benefits?

The topic of magnetism is of basic, fundamental interest to condensed matter physics and plays a key role in innumerable technologies and devices. Permanent magnets in power transmission, in power generation and in data storage are prominent cases where optimal tuning of magnetic properties of materials already has huge economic and social consequences. The theoretical basis for the development of new materials, as well as new devices based on such materials, requires ab initio theory that is capable of describing particular materials with high predictive power.

The current Workshop contributed to advancing this capability by comparing different approaches and methods and bringing together some of the results of work in different sub-fields that have separated over time. By discussing critically different methods and theories, progress has been made in determining the limits of current capability and in achieving more robust modelling capabilities. At the same time, the comparison of methods means that research can be streamlined and focused on methods that have been proven effective: this particularly applies to issues such as the inclusion of temperature effects and disorder, and the relative accuracy of different methods for calculating Heisenberg parameters.

Real world material studies, in order to be relevant, increasingly require high accuracy and real predictive power for ever more complicated systems. The technologies discussed and developed at this Workshop aim to provide this capability. The implementation in prominent computer codes of some of the different methods discussed at the Workshop will provide also the tools for future researchers for a diverse range of material problems.

6 Participant list

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Modeling Metal-Based Nanoparticles: Environment and Dynamical Effects

Location: CECAM-FR-RA
Webpage: https://www.cecam.org/workshop-0-1589.html
Dates: December 3, 2018 to December 5, 2018

1 State of the art

Metal nanoparticles (NPs) can display exacerbated optical, reactivity, or magnetic properties relative to bulk materials. They have thus a great potential in physics (magnetic storage), chemistry (catalysis, fuel cells) and even medicine (imaging, biosensing, drug delivery/therapy). However, their practical use generally requires them to be deposited on a substrate or coated by organic ligands, e.g. to make them biocompatible. In addition to realistic environments, experimentalists are also now able to monitor the dynamical evolution of such nanoscale objects individually and in real time, or the kinetics of assemblies over macroscopically long durations. Computational modeling clearly lags behind such experimental advances, and the present workshop aimed at providing a view of the current state of the art in atomistic modeling of metal nanoparticles in their natural environment, emphasizing methodologies that are useful for probing long-time rearrangements and taking statistical aspects into account.
We thus aimed at bringing together scientists from rather different communities, namely chemistry-oriented researchers with a strong background in electronic structure and usually working on rather small systems, material scientists modeling larger nanostructures and possibly employing coarse-grained approaches, and finally statistical physicists developing methods for bridging the time scale gap.

2 Major outcomes

Two main sessions, among the six sessions of the workshop, were purposedly introduced by broad overview talks from experimentalists in the fields of deposition and manipulation of metal nanostructures and on nanocatalysis. These sessions revealed the diversity and complexity of phenomena that take place at the nanoscale, with nontrivial interactions between the metal nanoparticle and the insulating substrate or the surrounding environment. Predicting the shape of the nanoparticle, from which many properties derive, remains a difficult problem for supported nanoparticles or nanostructures surrounded by organic ligands. Moreover the possibly active role of the experimental probe (e.g. STM tip) was highlighted. The shape itself and how it should be tuned for chemical or biomedical applications were largely discussed.
Metal NPs on oxide supports were particularly scrutinized at various computational levels ranging from empirical force fields to density functional theory, and the results generally show the importance of dispersion corrections and magnetism in the latter case. Defects of the substrate and their role to pin the particle were also discussed.
The role of the substrate on the reactivity of the deposited nanoparticle was of major interest, in direct relation with catalytic applications such as the ever popular CO oxidation or ammonia synthesis. The possible benefit of reducing the nanoparticle size was also clearly demonstrated at least in experiments where the single-atom limit could even be an ideal goal.

A second major objective of the present workshop was to highlight and discuss the role of kinetics, either to address the non-equilibrium nature of some experiments in which the nanoparticles are explicitly far away from their optimal shape (as in the case of nanowires or nanoalloys with nonideal chemical ordering) or grow faster than the time needed to rearrange themselves. Kinetics of growth or chemical reactions can be addressed directly at the atomistic level of details, using if needed biasing schemes such as metadynamics, or through coarse grained descriptions based on kinetic Monte Carlo or Markov chain approaches. Overviews of path sampling and adaptive biased sampling methods provided the participants with current efforts in this specific field.
Among the systems covered in this workshop, nanoalloys received a specific attention owing to their greater versatility and tunability as both the shape and chemical ordering are tuned, making them currently an active topic. In particular, the specific time scales associated with rearrangement of the chemical ordering were probed using methods such as metadynamics. More generally, the competition between kinetic and thermodynamic stability was intensively debated with illustrative comparisons in the case of the growth of BCC metals or noble metal nanowires. Finally, several talks were devoted to the realistic modeling of metal nanoparticles interacting with proteins and peptides in the context of biomedical applications.

3 Community needs

It was very clear after the workshop that experimentalists have now the means to monitor, in real time, the evolution of individual objects deposited on substrates and manipulated either from the substrate or from external tools such as an STM tip. They also have the ability to characterize complex nanostructures at unprecedented levels of details, from the size selection in the gas phase at single atom level to the imaging and characterization also at the atomistic resolution.
Although theory and modeling can generally cope with individual and naked nanoparticles, a lot of progress is needed to address the time scales covered in experiments (reaching seconds or even days in some cases) and, at the same time, the presence of the environment that is essential for applications. Simplified approaches for kinetics based on approximations such as transition state theory may appear oversimplified and it is important that modern approaches based on the concepts of transition path sampling be known to the community of metal nanoparticles.
One major step already recognized towards the completion of this goal is the need for advancing sampling methods, however there is still some confusion between the physical meaning of trajectories obtained with heavy biasing as in metadynamics, and their time scales as well.
Deeper connections with the rare events community will be needed in the future, associated with efforts on the modeling community itself in order to simplify the description of interactions and reach experimentally relevant sizes and levels of complexity.

4 Funding

Future funding could be provided by contributing further to networks that are being developed currently at the european level.

One COST action on nanohybrids might be proposed in 2019, and there is little doubt that kinetic and environment aspects will be important owing to the development of in operando experimental techniques.

Similarly, one international research network co-managed by french CNRS and focused on nanoalloys will begin in 2019, with the capability of funding joint projects between teams.

Some fruitful discussions held during our workshop should also lead to applications for bilateral funding.

5 Will these developments bring societal benefits?

Metal nanoparticles are highly promising objects in a number of fields with a strong societal impact.

In materials science, magnetic nanoparticles can exhibit strong magnetic moments relative to their size, making them valuable for high density storage.

In catalysis, metal nanoparticles of transition and noble metals or their alloys are far more active than the corresponding bulk materials, and they will contribute to lowering the cost in expensive metals such as palladium. This will make them valuable as well in specific energy-related applications such as fuel cells.

Metal nanoparticles are also interesting for their optical properties, the emission range being tunable by changing the size and shape. Plasmonics at the nanoscale, which has become a very active field in the recent years, is already showing applications in screen technology.

Nanomedicine is also increasingly employing metal nanoparticles for applications in biosensing, bacterial control, diagnosis, imaging, detection, drug delivery or targeted cell treatment, again owing to their interesting electronic or magnetic features.

In most of these applications it is essential to ensure the nanoparticles are protected from outside perturbations by depositing them on substrates or coating them with organic ligands. Their kinetic stability over long times is also a prerequisite. This workshop aimed at addressing these two specific issues on a balanced perspective, focusing as in the traditional CECAM tradition on computational modeling but covering also the recent experimental state of the art.

6 Participant list

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E-CAM Workshops 2018

ESDW7: Quantum MD Part II

Location: CECAM-IRL, University College Dublin
Webpage: https://www.cecam.org/workshop-0-1407.html
Dates: March 21, 2018 to March 23, 2018

1 State of the art

Quantum dynamics simulations solve the time-dependent evolution equation, for the nuclei and, in non-adiabatic cases, the electrons, of a molecular system and can follow its fundamental behavior including, in principle, all quantum effects. These are often crucial for simulating fundamental reactivity, e.g. after a molecular collision, or the absorption of a photon, and are required for the understanding of many state-of-the-art experiments. This understanding is also becoming important for emerging technologies that need optimal properties of materials, for example in photo-activated technology molecules need to be engineered such that the energy flow into destructive pathways is suppressed. Other obvious uses are in technologies that rely directly on quantum properties, such as quantum computing.

Despite considerable advances in algorithms over the last couple of decades, quantum dynamics simulations still require large computational resources and suffer from poor scaling with respect to system size. Accurate calculations are restricted to treating only a few atoms. The field is also relatively fragmented, with few standard benchmarks and most work done as single codes within a research group. This complicates assessing the usefulness of approximate methods and comparing systematically their performance. The situation can be contrasted to the more mature field of quantum chemistry, in which the electronic problem is solved for static nuclei, where people work within the framework of a few large packages (Gaussian, Molpro, Qchem etc) with recognized benchmarks.

The field is, however, starting to change, with greater collaboration among the leading players, spurred also by a recent series of thematic workshops and schools held in the CECAM network. E-CAM is contributing to this transition via actions aiming at the systematic development of community software and dedicated state-of-the-art workshops.

2 Major outcomes

Training included lectures on scientific and HPC subjects (see also program).

The scientific topics included basic presentations of state-of-the-art performances of quantum dynamical algorithms and examples of their applications. Sparse grid based methods, to be used as a reference for current and new approximate methods and for exact solution of low dimensional problems, were also presented. A dedicated lecture was reserved to survey the current situation in potential parametrization at the empirical level and via machine learning. The problem of matching quantum dynamical methods with accurate first principle evaluation of the energy, forces, and non-adiabatic couplings was also discussed with reference both to current methods' performance and the characteristics of available, scalable, electronic structure packages.

A topic of specific interest for the participants was the description and implementation of mixed quantum-classical methods. Two lectures and several discussion sessions were devoted to

this and two main methods were considered: Wigner-Liouville dynamics and the exact factorization approach. These methods were selected also in view of specific modules to be developed at the workshop.

The software development training was provided by the E-CAM Software Manager (Alan O'Cais) and Software Developer (Liang Liang), in collaboration with experts from the Irish Supercomputing Center Ichec. The topics covered by the E-CAM experts included all the main tools deployed for software creation and development (the structure and operation of the GitLab repository and EasyBuild), performance analysis (Scalasca) and benchmarking (JUBE). Dr. O'Cais and Liang also provided continued assistance to the software development teams at the workshop with particular focus to identifying effective parallelisation strategies for the quantum dynamics E-CAM codes PaPIM and Quantics. The training provided by the Ichec experts focused instead on a four-part tutorial on OpenMP parallelization, which included hands on sessions.

The main scientific and strategic outputs of the meeting were:

- Mixed quantum-classical methods have consolidated their position as a well-established subtopic in quantum dynamics. The implementation of community level actions to ensure that this transition adopts fair evaluation criteria of the different approaches and is accompanied by a more systematic development of reliable, efficient, and sustainable software packages is timely. The EINFRA centers, and E-CAM in particular with its dedicated work package on quantum dynamics, can play a crucial role in this phase.
- Although some important technical difficulties remain to enable large scale calculations, recent progress and expert use of computational resources should rapidly favor progress. In particular:
  - Most mixed quantum-classical methods are based on the simultaneous propagation of multiple (hundreds of thousands of) independent trajectories each contributing to the final result via a weighted average computed at the end of the run or at fixed time intervals during the dynamics. This structure is ideally suited for massive parallelization and can exploit advanced High Throughput Schemes very effectively. The current developments in this area in E-CAM provide a unique opportunity for collaboration and implementation of new computational strategies and should be fully exploited.
  - First principles calculations of the electronic structure will also require advanced computational strategies and the optimal exploitation of HPC architectures. The added cost of the electronic structure evaluation, with its specific parallelization requirements, in fact, will probably lead to implementations combining the relatively trivial massive parallelization on the ensemble of trajectories with multi-nodal evaluation of the forces along each trajectory. Hybrid architecture exploitation (employing accelerators or GPUs for the electronic structure) should be explored.

3 Community needs

The following software development projects were pursued:

- Exact methods:
  - Implementation of iterative schemes for eigensolvers, Lanczos and Davidson (leader G. Worth)
  - Implementation of sparse (Smolyak) grids for exact dynamics via transformation between grid and basis representation (leader D. Lavergnat)
- Trajectory based methods:

- Path Sampling in the Wigner-Liouville dynamics, implementing new sampling methods aimed at mitigating the sign problem and optimizing convergence (leader D. MacKernan)
- Developments of the PaPIM E-CAM code (leader S. Bonella):
  - ♣ OpenPM parallelization in the initial condition sampling modules
  - ♣ New sampling schemes for initial condition based on Langevin dynamics
  - ♣ Inclusion of the quantum thermal bath method in the suite of available integration schemes in the code
  - ♣ Development of an interface (prototype with CP2K) for effective interfacing with first principle electronic structure codes
- Developments of the Quantics E-CAM code (leader G. Worth):
  - ♣ Interface with non-adiabatic surface hopping software package
  - ♣ Interface with Q-Chem package for first principle electronic structure

- Exact factorization methods (leader F. Agostini)
  - Integration of the method in the CPMD package for first principle electronic structure
  - Implementation of the algorithm for evolution of nuclear equations of motion.

Modules of industrial interest. After discussions with our partner, IBM the following modules are being developed to assist design of superconducting Qubits:

- LocConQubit: a toolbox of subroutines and functionalities that implements Local Control Theory for the construction of control pulses for tuning universal quantum gates.
- OpenQubit: patch to the LocConQubit suite to include effects of the environment in the simulation of the quantum gate.

The modules above (at various stages of development at the writing of this report) will be integrated in the E-CAM Quantum Dynamics modules, deliverables D3.3, D3.4. All modules are stored on our E-CAM software repository (https://www.e-cam2020.eu/software-library/).

4 Funding

A second face to face meeting took place March 21-23 2018 at University College Dublin. The meeting had two main objectives: (1) to ensure that the merging of modules in the E-CAM repository planned to fulfil the requirements of Deliverable D3.3 had been successfully completed and/or to resolve any pending issues in that connection; (2) discuss continuation of work and start planning calendar for new modules and their delivery also in view of the third ESDW in quantum dynamics, to be held at Maison de la Simulation, Paris in June 2018.

Both tasks were accomplished with no significant difficulties.

5 Will these developments bring societal benefits?

6 Participant list

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Scoping Workshop: Dissipative Particle Dynamics: Where Do We Stand on Predictive Application?

Location: CECAM-UK-HARTREE
Webpage: https://www.cecam.org/workshop-0-1635.html
Dates: April 24, 2018 to April 26, 2018

1 State of the art

Dissipative particle dynamics (DPD) has seen widespread uptake since its inception as a relatively simple and inexpensive coarse-grained modelling tool ideally suited to the study of soft condensed matter systems. DPD is perhaps unusual in that its development has been driven as much by the needs of industry as by academic research. Despite the scientific advances and the early industrial applications, there remain several open questions both in the foundations of the method and in advanced applications, which prevent the method being used in a predictive fashion in an industrial setting. These questions include:

- Do robust parameterization methods exist that enable predictive simulations?
- Can such coarse-grained potentials be extended to different families of compounds or are they molecule/system-dependent?
- Is the application of electrostatics in DPD solved or not?
- How do we treat solvents of different nature?
- Do many-body method play an important role in predictive applications?
- What is the real computational gain in DPD? Time and length scales?
- Many industrial applications of DPD involve interactions with surfaces; can DPD provide realistic representation of these?
- Does the software exist to support predictive simulations?
- Do we have analytics to extract appropriate data from simulations, e.g., viscosity
- How could we describe specific ion interactions or ion interactions beyond simple ad-hoc parameters?

The workshop aimed to bring together leaders on the DPD community from academia and industry to address these open questions and to develop pathways to overcome challenges.

2 Major outcomes

This workshop brought together the leaders in the field to ask the question, where can DPD offer predictive insight currently, and what is required to improve the method and application to enable improved predictive capability in the future? The workshop was dominated by discussion on four key areas; parameterization, applications, new methods and software. All of the talks were of high quality and covered topics such as the introduction of hydrogen-bonding into DPD, coupling DPD to higher length scale simulations and how to simulate surfaces effectively.

The workshop was able to answer most of the posed challenges.

- There are parameterization methods that enable predictive simulations although work is always ongoing
- Coarse-grained potentials should be considered system-dependent mot of the time
- The application of electrostatics is not solved, rather started.
- Progress is being made on solvents of different natures although there is plenty to do
- Many-body methods look like they should play an important role but are not yet fully exploited
- The computational gain is real but sacrifices must be made in accuracy
- Realistic representation of surfaces is important and some work has tackled this. However, more work is required
- In part, software does exist but more could be done (see community needs section)
- We have some good analytics but often not in an accessible repository and the tools can be extended (e.g., viscosity)
- Capturing specific ions effects are crucial to move the field on but no compelling strategy for parameterisation exists.

On this last point, the current best practice for charged ions is to assume they behave as charged water beads. Whilst the few groups who have simulated charge systems have used this approximation with good results, focussed work is required to be able to differentiate the behaviour of different ions. No consensus was reached at the workshop about how to tackle this challenge.

The workshop hosted a number of individuals from industrial organisations and the participants were impressed by the use of the DPD method in the research of BASF, Proctor & Gamble, Unilever and IBM. The first three of these organisations have produced workflows internal to their organisations to deploy the DPD method to key industrial challenges. The latter, IBM, are developing methodologies to parameterise the DPD method using experimental data in conjunction with the STFC Hartree Centre.

The need for clean, verified, experimental data was highlighted by a number of participants at the workshop. Currently, high-quality data is limited in the literature. The DPD community (and other communities) would benefit from good data (e.g., critical micelle concentrations, aggregation numbers, phase data) for pure surfactants. This data could be used to ratify simulation results and to train models.

A talk of particular note for the development of industrially useful predictive simulations was a GPU re-write of DL_MESO (sponsored by ECAM) with significant performance improvements. It is not unreasonable to assign an order of magnitude reduction in the cost of DPD simulations of DL_MESO calculations with this GPU dedicated version. With such a cost saving the application of DPD to industrial problems becomes more financially attractive.

The workshop assessed the community need for exascale. Most of the participants use very modest compute power, In the order of a couple of nodes. A smaller number of participants utilise 10-20 nodes at a time for simulations. The consensus was that exascale does not present a big step up for the community, rather that interesting scientific challenges need to be solved first. The main role exascale could play is in rapid screening of candidate systems for formulated product companies. This requires accurate models, efficient computation and appropriate workflows to be available.

3 Community needs

The DPD community needs discussed were separated into two related sections; software and support.

It was felt that identifying a European community code (e.g. DL_MESO or Espresso) to focus development upon would be highly desirable in two areas. Firstly, when lobbying the European commission for funding and secondly to ensure community developed functionality is available to all researchers in astable and well tested platform. The chosen community code would be the main European code of choice for DPD and could be validated with LAMMPS. Long-term funding would be required for this venture.

Whilst a number of analytics tools exist to extract data from simulation trajectories, these tools are often distributed across multiple research groups in different countries. Often poorly documented, these tools do not get utilised outside of the group from which they were developed. A positive outcome of the workshop would be if a repository could be developed and maintained where analytics codes could be deposited and used and further developed by other researchers. This should prevent many cases of the 're-invention of the wheel' in research projects. Note that there are a few general analytics tools available such as MD analysis and UMMAP.

In terms of usability of DPD methodologies, a significant amount of workshop time was dedicated to exploring the possibility of a dedicated user forum in which researchers around the globe could discuss challenges and successes as well as a portal for asking for help. This, coupled to a more informative set of tutorials was seen as a potential major boost to the community. A set of tutorial reviews were proposed to help with the latter point and the developers of DL_MESO and multiple workshop participants agreed to contribute.

4 Funding

Funding channels were not discussed with regards to scientific research as it was felt that the normal routes were appropriate.

However, long-term funding of community codes (see community needs section) was deemed to be a priority for the community. This funding would enable DPD codes chosen by the community to have well resourced development to ensure currentness and stability of the codes. No specific funding rules were identified but it was felt that the traditional routes did not facilitate software development well.

5 Will these developments bring societal benefits?

The potential impacts of developing and applying more predictive DPD models and methods is significant. The method has proven already to be beneficial to developing improved formulated products as can attested to by multiple industrial participants examples at the workshop. Further scientific developments and those made to simulation and analytics codes will lead to models which better represent industry products and processes which in turn will lead to an increased understanding of the mode of action of these products.

Improved simulation codes combined with an efficient strategies for tackling key scientific challenges will allow the development of improved models allowing scientists to design new products in-silico which will reduce the number of time consuming experiments that need to be performed.

Ultimately the impact will be to enhance de novo formulation design, shorten time to market, provide an adaptive response to supply chain variability, and encourage the adoption of formulation for sustainability. The ability to formulate virtually allows for acceleration of R&D processes, smoother development of new products, especially for high value manufacturing markets where growth arise

from high R&D intensive efforts.

The next few years will be particularly exciting. New methodologies are currently being developed to tackle scientific challenges and improved simulation codes and analytics methodologies are becoming available. It is therefore planned to repeat this workshop in three years' time, to review our success and look further ahead.

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Scoping Workshop: Solubility Prediction

Location: CECAM-FR-RA, Ecole Normale Supérieure de Lyon, France
Webpage: https://www.cecam.org/workshop-0-1497.html
Dates: May 14, 2018 to May 15, 2018

1 State of the art

Based on the Biopharmaceutics Classification System (BCS), over 75% of drug development candidates have low solubility, which is a major issue for drug development as formulation of low solubility compounds can be problematic. Other industries rely on value-added formulation and thus on solubility issues. Despite tremendous efforts, a definitive accurate and comprehensive approach to predicting solubility has proven elusive. This workshop has focused on the different approaches to predict solubility trends.

Recent work includes a systematic experimental approach to examine key thermodynamic functions such as sublimation and hydration properties as a function of structural modifications and a comprehensive computational approach to lattice energy estimation from molecular descriptors. A recent review has analysed simple predictive methods for the estimation of aqueous solubility and the specific use of a chemical informatics and theory to predict the solubility of drug like molecules.

Algorithms for solubility calculations have been carried out by two different general approaches: (i) the search of the concentration where the solute and the solid chemical potentials are equal and (ii) direct simulations of the solid and the solution at contact. Both these approaches have been discussed at length in the workshop.

In the complementary area of structure activity relationships, automatic model generation process for building QSAR models using Gaussian Processes were discussed, a powerful machine learning modeling method. The stages of the process that ensure models are built and validated within a rigorous framework were examined: descriptor calculation, splitting data into training, validation and test sets, descriptor filtering, application of modeling techniques and selection of the best model. The effectiveness of the automatic model generation process for two types of data sets commonly encountered in building ADME QSAR models was explored.

2 Major outcomes

In this workshop were discussed the tools that allow an unprecedented deconstruction of the relative importance of molecular solvation and crystal packing on solubility. Recent work includes a systematic experimental approach to examine key thermodynamic functions such as sublimation and hydration properties as a function of structural modifications and a comprehensive computational approach to solubility, from chemical informatics approaches to advanced molecular simulations.

Accumulating reliable experimental data of hydration and sublimation is essential to benchmark established as well as novel simulation tools. However, it has been underlined how challenging it is to compare experimental data with simulations results. Indeed, computing values are obtained for an ideal system, which is not what we measure experimentally. In addition, it is difficult to get a complete comprehensive coherent picture from experiments. Typically, the solid in equilibrium with a saturated solution is not necessarily in the same crystallographic phase or even in the chemical state than the one that was initially introduced. Re-precipitation can occur and the solid phase in equilibrium with the solution should be systematically fully characterized. Nevertheless, to ensure the development of novel simulation methodologies, hydration free energies are currently collected in an online database FreeSolv, ready to be used in a simulation benchmark.

Algorithms for solubility calculations have been carried out by two different general approaches. The thermodynamic approach seeks the concentration at which the electrolyte chemical potential, in solution, is equal to that of the pure solid. To compute the Gibbs free energy cost of the insertion of particles in a liquid, the thermodynamic integration is the workhorse and an alternative is the Wang Landau approach. A direct simulation of the solubility equilibrium can be modelled using the slab method that put in contact the saturated solution with the surface of the solid. The electrolyte concentration in the solution phase sufficiently far from the crystal surface is taken to be the solubility. It has been largely applied on the NaCl case. A controversy was relayed in the literature demonstrating that this approach is very demanding computationally, prone to size effect issues and requires very long simulation time to be able to reach the equilibrium.

Both strategies rely strongly on the quality of the force field used. OPLS has been developed to compute hydration energies of small organic molecules. It provides a good balance between the description of the liquid and the solid description. However, with the shift towards larger molecules (MW>500g/mol), this force field reaches its limitations. In addition, the typical Lennard-Jones potential used to deal with dispersion forces for practical reasons but it is too repulsive at short distance. Polarisability may also be key to reach a better quality in simulation data. A proposition is to use the Yukama potential with smeared charge and charge on spring for polarisability. Neural network appears as an alternative, but the large number of parameters implies the use of extensive experimental database eventually complemented with ab initio data.

Another major challenge that has been put forward is a good prediction of the crystal phases that can adopt an organic molecule. In AstraZeneca, this has been circumvented using systematically an amorphous phase to describe the solid phase. Recently, several approaches have been proposed to predict polymorphisms, either combining new order parameters and string method, either benefiting from conceptual DFT to understand better the crystal packing.

3 Community needs

To further progress, the scientific community needs to strengthen interaction between specialists in modelling but also with other communities (experimentalists, other field of applications than pharmaceutical). There is a clear need for open data, with the publication of raw data obtained by simulation as well as experiments to be able to re-investigate the influence of the scheme chosen to split data into training/validating set. Some semi-empirical approaches are currently not shared, impeding their further development in a participative scheme. Others are widely shared (see for instance bottledsaft.org).

There is a clear need for improved force field that are able to describe large molecules (MW > 500 g/mol) in solution as well as in solid phase. This is also true for ions, since for instance the force field to describe Na+ and Cl- should differ in water and in the NaCl phase. In addition, innovative algorithms to predict polymorphisms are a necessity. To assess the quality of the novel methods that are to be invented, good experimental references data are compulsory, spanning multiple families of molecules. Those developments would be better performed with dedicated series of CECAM workshop around force field development.

In addition to innovative methods, there is also a strong need in speeding-up the current methodologies and make them available in codes that can be transferred to industry through software engineering.

4 Funding

The funding's were not discussed during the workshop. A clear line that emerged is to intensify collaboration between academia and industry. Integrating research and innovation, with strong societal impact in health as well as sustainability, modelling solvation is clearly in the line of the H2020 priorities. A possibility would be to build an initiative training network around solvation.

An action has recently started in France to structure the scientific community around solvation (http://solvate.cnrs.fr) gathering around hundred researchers

5 Will these developments bring societal benefits?

During this workshop, we have seen that solubility issues can be found across several fields of applications, from pharmaceutical to specialty chemical industry.

In pharmaceutical industry, improved knowledge on solubility will help in designing efficiently production lines of novel drugs (it is key in purification steps). It is also key in the final formulation of a drug limiting aggregation issues, to favour highly concentrated solution and avoid injecting huge volume of solution to patients.

In specialty chemical industry, improved knowledge on solubility in water can drive the formulation of greener lubricants, detergents, etc. using water as a based instead of a oil-derived based (this shift occurred few years ago for painting, it is a general trend to avoid any hazard once those formulated product are at use). This drastic modification necessitates a complete revision of the additives of which properties are directly related to their solvation.

The development and use of modelling in those industrial contexts could be key to speed up the time to market of novel products, with health and sustainable benefits for the society as an end-user. Already at use in some companies, the benefits of a modelling study have to be balanced against the experimental duration and costs. In most cases, trends can be obtained rapidly with chemo-informatics approaches, even on a desktop PC and are already highly valuable. More advanced methods (based on MM-MD) would bring more insight on more

tricky cases, that can be also interesting topic of collaboration between industry and academia, challenging the state-of-the-art methodologies and triggering innovative developments.

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Scoping Workshop: Building the Bridge Between Theories and Software: SME as a Boost for Technology Transfer in Industrial Simulative Pipelines

Location: Istituto Italiano di Tecnologia, Genova, Italy
Webpage: https://www.cecam.org/workshop-0-1648.html
Dates: May 23, 2018 to May 25, 2018

1 State of the art

Statistical mechanics, electronic structure and multiscale modeling are three of the theoretical tools that enable understanding and modelling of physicochemical processes in computational chemistry/physics. Several theoretical/computational methods have emerged over the last decades. Despite their remarkable value in terms of novel ideas and theories, however, such approaches are often far from a practical applicability within industrial settings. This is mainly due to the fact that: i) these algorithms are often written in rather inefficient programming languages and therefore not fully optimized for new generation hardware architectures; ii) these methods can be very accurate from the physics standpoint, but quite far away from the industrial needs of finding a suitable trade-off between speed and accuracy. Therefore, companies in different areas are actively seeking more reliable, still rather fast, computational methods to reduce the overall costs of industrial R&D pipelines. This is, for example, the case in drug discovery, where companies are looking for innovative approaches to accurate kinetics and thermodynamics predictions, and in the material industry, where designing new nanostructures with improved features could greatly benefit from computational simulations. There exists, however, a clear and long-lasting gap between the theoretical chemistry/physics community and industries, which are looking for efficient, user-friendly, and professional software solutions to be utilized in many different areas. Against this scenario, small/medium enterprises (SMEs) that develop simulative software can play an increasingly key role not only in translating the science developed in academia into a proper technological transfer process, but also in building a scientific bridge between the industry requirements in terms of automation and the new theories and algorithms developed at an academic level. It is crucial to remark that transforming academic algorithms into usable software is not only a matter of software engineering, but often also means reconsidering the original theories and formalisms. In this context, software development SMEs, which have a clear mission towards top level science suitable for industrial settings, may represent the missing link in the pipeline from-theory-to-software.

In the present E-CAM workshop, we addressed in particular the following question: (1) which is the most appropriate propelling element of innovation, top-level academic science or industrial needs of accelerating R&D towards novel and cheaper products? Traditionally, the approach to technology is conceiving technology as a corollary of scientific research. However, there is compelling evidence that for several mid-term projects an industry-requirements-driven approach is largely feasible if not best suited. A tightly connected topic regards on how to match and synchronize curiosity driven research with industrial needs and

how to manage the resulting, possibly academic/industrial mixed, intellectual property. This led us to consider the further question (2) can this 'engineering' or 'politechnique' approach to science/technology transfer be the way to boost the technological SMEs European tissue?

[1] Kuhn et al., "A Real-World Perspective on Molecular Design", J. Med. Chem., 2016, 59 (9), pp 4087–4102

[2] Yibing Shan, Eric T. Kim, Michael P. Eastwood, Ron O. Dror, Markus A. Seeliger, and David E. Shaw. "How Does a Drug Molecule Find Its Target Binding Site?" J. Am. Chem. Soc., 2011, 133 (24), pp 9181–9183

2 Major outcomes

Talks from academia and industry were interleaved in the meeting. This allowed to complement and contrast experiences and knowledge coming from academia and industry.

Industrial requirements, expressed in particular by Pierre Ducrot and Richard Lewis both from the drug discovery field, emerged quite clearly and consisted in the need of fast albeit approximate methods for analysing ligands. This analysis should include both thermodynamic and kinetic properties with very high efficiency (overnight production of results). It was also stated that pharma companies are quite sceptical about the real effectiveness of machine learning when applied to docking or thermodynamics prediction.

The role of SME also emerged quite clearly. The discussions in particular involving Prof. Cruciani from Molecular Discovery underlined how, even though fundamental methodologies such the creation of an interaction field comes from academia, commercial products need to re-elaborate and recast methods to be effective. This observation created a certain consensus on the audience for which while the idea is coming from academia, the innovation, the application to the real-world problem often comes from the SME, whose success is tightly linked to its ability to address real industrial needs.

The role of software developers in SME and academia was also discussed. Different points of view emerged in the discussion. For some participants, software engineering is a fundamental component to any success in the computational field either commercial or academic software. For others, even for SME it is more important to hire personnel with a strong background in chemistry or physics, than in software developments.

There was also a consensus that EU funded Centers of Excellence for Computing Applications can provide an opportunity to enhance the expertise and scope of software vendors SMEs acting as a disseminator and co-developer of software and by providing a portal to broad scientific expertise that may not be present in the SME. An important collaborative opportunity was identified in the area of training and it was recommended that E-CAM initiates specific actions in this area. Exploratory discussions for training events with Scienomics and BiKi technologies were initiated.

Specific software development projects were also suggested to (1) create interfaces between E-CAM modules and commercial platforms for material design. This involved, in particular, matching the OPS E-CAM package with the Scienomics platform MAPS. A similar opportunity should be explored in the domain of material design by considering an interface between MAPS and the Quantum Monte Carlo package QMC-Pack. Furthermore, specific collaborative software developments to cross-enhance the functionalities of OPS and the PLUMED package for rare event calculations (topic of Work Package 1 in E-CAM) were also discussed. These developments should be implemented via E-CAM ESDWs.

3 Community needs

The following needs were highlighted by the academia and the industry participants.

Academia: (1) include in the research group software engineers able to properly code methods or ensure access to sustained consultancy and assistance in this area.; (2) identify means to ensure a certain degree of time continuity in the code development and maintenance; (3) identify and assist to assess the potential for technology transfer of in-house activities. The EU centers of excellence might provide an environment to systematize, host and enhance in-house software developments and foster technology transfer.

Industry: (1) increase the dialog between industry and academy; (2) seed academia with real world problems whose solution industry could benefit also in economic terms. There was unanimous consensus that SMEs are playing a significant role in bridging the two worlds. However, this kind can only work however with a proper “feedback-cycle”: academy talks with SME/Industry and vice-versa in a not interrupted loop to foster high level science that on the long term could be applied to industrial problems. Opportunities to create and sustain this cycle were indicated as still insufficient and absolutely crucial. In the discussion industrial participants, and in particular software vendors SMEs, raised the point that activities that are, or can be perceived, as establishing EU funded Centers of Excellence as competitors of SMEs should be avoided. The promotion of collaboratibe efforts in training, both of personnel of software vendors and joint training initiatives between CoEs and software vendors targeted at a broad range of industrialists was also indicated as a necessity.

4 Funding

From the academy side, there are several European initiatives that found computational methods ranging from material science to biological systems. Even if not a grant deliverer, CECAM constitutes a key resource to centralize in a common framework/place various research efforts in Europe and beyond and all the audience acknowledged the importance of such initiatives as E-CAM.

From an industrial perspective, it emerged that is rare or almost impossible to have an internal “methods development unit”; for this reason, SMEs can have a clear role in that industry can fund not only the software per se but also the development of new applied protocols and approached that differently they would not have been developed internally. This has been done by Molecular Discovery for instance. The economically capability of big pharma for instance is notable, however this funding from the private side can only be achieved if SME/academia clearly show to have addressed, or are in the process of addressing, problems that are considered key for the industry.

5 Will these developments bring societal benefits?

The potential benefit of the technologies and methods discussed is notable. For instance, in drug discovery, considering that the overall time needed to start from the target and arrive to a marketable drug is about 10 years and 1 billion of dollars of capitalization, it's then clear how computational methods, the ones presented at the meeting, can remarkably impact in economic terms. There are technological realities such as FEP as presented by Schrodinger and newer methods such as those delivered by BiKi Technologies. Also out of equilibrium method (Hummer's talk) and path sampling methods (D. Swenson) if properly tuned for the drug discovery requirements might have the potential to accelerate the drug discovery, hence impacting at an economical level.

To build the "bridge" as the title of the meeting states it is not an easy task and it was evident from the discussions that industry and academia are still distant, in particular in EU, whereas UK speakers seem more oriented and prone to build this necessary and fundamental bridge also starting from the kind of research is done on the labs.

There was not general consensus on which should be the driving force for innovation and thus to create long term benefits, nevertheless all the speakers realized the importance of delivering appropriate computational pipelines for the industrial tissue.

6 Participant list

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Extended Software Development Workshop: Quantum Dynamics

Location: CECAM-FR-MOSER Maison de la Simulation
Webpage: https://www.cecam.org/workshop-0-1641.html
Dates: June 18, 2018 to June 29, 2018

1 State of the art

Simulating the behavior of a microscopic system requires the development of approximations, algorithms, and computer softwares that beat the exponential growth of the numerical cost with the number of degrees of freedom to solve quantum-mechanical equations of motion. Building collaborations between theoreticians and computer scientists is, therefore, a critical step towards an optimal exploitation of the computational power available at high-performance computing (HPC) facilities, aiming at the study of molecular systems with increasing complexity.

Theoretically, the two main classes of approaches to solving the quantum molecular dynamical problem are wavepacket propagation schemes and trajectory-driven methods. The difference between the two classes lies in the way the nuclear degrees of freedom are treated, either fully quantum mechanically or within the classical approximation. In the first case, basis-functions contraction techniques have to be introduced to represent the nuclear wavefunction as soon as the problem exceeds 5 or 6 dimensions. In the second case, the nuclear subsystem is approximated classically, or semiclassically. Although leading to a loss of some information, this approximation offers the opportunity to access much larger systems for longer time-scales. In relation to trajectory-driven techniques, a significant amount of work has been proposed to recover some quantum-mechanical features via appropriately sampling the initial conditions from the Wigner distribution.

On the computational side, a large part of the cost of a calculation is spent to evaluate electronic properties. Also, the nuclear dynamics part of a calculation becomes itself a very costly computational task in the case of wavepacket propagation methods. Thus, algorithms for molecular dynamics simulations are not only required to reproduce realistically the behavior of quantum systems in general cases but also to scale efficiently on parallelized HPC architectures.

2 Major outcomes

The ESDW was organized in two parts.

During the first week, oral presentations focused on the more theoretical aspects of quantum molecular dynamics simulations. The points mentioned in the state-of-the-art section have been discussed, based on didactic lectures of 45 minutes, followed by 30 minutes of discussions. Each lecture provided a general overview of the presented topic, ensuring their accessibility not only to the experts in the field but also to the master and PhD students attending the workshop. In the first lecture, the multi-configuration time-dependent Hartree (MCTDH) method was introduced to the participants. MCTDH is undoubtedly among the most successful approaches to evolve (nuclear) wavefunctions fully quantum mechanically. Still,

alternative strategies for quantum dynamics simulations are continuously developed, for instance by identifying procedures to optimize the “space” where the wavefunction information is computed. In this context, the power of replacing Cartesian grids with Smolyak grids, effectively reducing the computational cost of the calculation, has been discussed in a second lecture. Various examples of trajectory-driven approaches were presented, ranging from the simplest, yet very effective, trajectory surface hopping and Ehrenfest schemes, to the more involved but indeed more accurate, coupled-trajectory mixed quantum-classical (CT-MQC), and quantum-classical Liouville equation (QCLE). One also finds, at the interface between wavepacket and trajectory schemes, methods like Gaussian-MCTDH, variational multi-configuration Gaussian (vMCG), or multiple spawning, which exploit the support of trajectories to propagate (Gaussian) wavepackets and allow to recover some of the information lost with a purely classical treatment; these strategies were introduced as well. Another theme of the theory lectures was on the sampling of initial conditions for trajectory-driven techniques, more specifically on how such sampling can be used to account for quantum nuclear effects, such as zero-point energy and tunneling, that are clearly missed in “classically”-based nuclear dynamics. In this context, approaches to sampling the Wigner distribution and the quantum thermal bath method have been presented.

The second week was dedicated to hands-on training on parallel computing. For these exercises, the supercomputer Poincaré (la Maison de la Simulation, Saclay), containing server-grade GPU accelerators, has been employed. In particular, two sessions of 3 slots each (90 minutes per slot) have been proposed on OpenACC and ScaLAPACK. Both practicals have, thus, focused on practical training of the use of parallel-computing techniques for GPUs and the use of the linear algebra library in parallel programming.

During both weeks, the afternoon sessions were entirely dedicated to code development. In particular, the participants of the ESDW have been involved in the development or finalization of the modules selected as 2018 deliverables for the ECAM work package 3 on Quantum Dynamics. The computer scientists attending the meeting provided the developers with strong support in optimizing their codes.

3 Community needs

The modules that have been developed at the ESWD are CTMQC, ModelLib, QCLE (single path), QQ Interface for Quantics, SHZagreb for Quantics, and OMP for Quantics.

CTMQC and QCLE (single path) are modules designed to perform excited-state molecular dynamics simulations in electron-nuclear systems. Nuclear trajectories are evolved under the effects of quantum-mechanical electrons differently, though, as CTMQC is based on the approximate quantum-classical solution of the exact factorization, whereas QCLE focuses on solving the quantum-classical Liouville equation. Both modules are currently not designed for ab initio simulations, that is, electronic-structure information is not computed on the fly but has to be pre-computed.

ModelLib is a library of model Hamiltonians that can, for instance, be employed for calculations based on CTMQC. A subset of model potentials included includes the Henon-Heiles model, phenol potentials, Tully models, vibronic models, and linear H-bond model.

The additional modules developed during the ESDW10 are interfaces and functionalities that were included in the Quantics software. Quantics is the quantum dynamics package performing MCTDH, G-MCTDH, and vMCG calculations, based on either pre-computed potential energy surfaces or on-the-fly computed electronic structure properties. Quantics (i) has been interfaced with QChem based on the module QQ Interface, (ii) allows to perform surface hopping calculations based on the module SHZagreb, and (iii) has been optimized for parallel calculations using OpenMP based on the module OMP Quantics.

The modules CTMQC, QCLE(single path), and OMP for Quantics have been designed to be fully compatible with HPC. For most modules, a merge request has been opened and deliverables documenting them will be submitted by the end of Summer 2018 for the ECAM work package on Quantum Dynamics.

4 Funding

The ESDW will be followed by a second face-to-face meeting of maximum two days with the aim of discussing the status of the 2018 deliverables and to prepare next-year ESDW (to be held, most likely, at one of the UK nodes of CECAM). Participants will be limited to those directly involved in the submission of the deliverables, and a few participants will be selected among those interested in the 2019 edition of the ESDW. In this way, the new group will be made familiar with the structure and procedures of an ESDW of the ECAM Quantum Dynamics work package.

5 Will these developments bring societal benefits?

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Extended Software Development Workshop: Intelligent High Throughput Computing for Scientific Applications

Location: Polytechnic University of Turin, Italy
Webpage: https://www.cecam.org/workshop-0-1650.html
Dates: July 16, 2018 to July 20, 2018

1 State of the art

High throughput computing (HTC) is a computing paradigm focused on the execution of many loosely coupled tasks. It is a useful and general approach to parallelizing (nearly) embarrassingly parallel problems. Distributed computing middleware, such as Dask or COMP Superscalar (COMPSs), can include tools to facilitate HTC, although there may be challenges extending such approaches to the exascale.

Across scientific fields, HTC is becoming a necessary approach in order to fully utilize next-generation computer hardware. As an example, consider molecular dynamics: Excellent work over the years has developed software that can simulate a single trajectory very efficiently using massive parallelization. Unfortunately, for a fixed number of atoms, the extent of possible parallelization is limited. However, many methods, including semiclassical approaches to quantum dynamics and some approaches to rare events, require running thousands of independent molecular dynamics trajectories. Intelligent HTC, which can treat each trajectory as a task and manage data dependencies between tasks, provides a way to run these simulations on hardware up to the exascale, thus opening the possibility of studying previously intractable systems.

This workshop aimed to produce four or more software modules related to intelligent HTC, and to submit them, with their documentation, to the E-CAM software module repository. These included modules adding HTC support to existing computational chemistry codes, where the participants brought the codes they are developing. They may also include modules adding new middleware or adding features to existing middleware that facilitate the use of HTC by the computational chemistry community. This workshop involved training both in the general topic of designing software to interface with HTC libraries, and in the details of interfacing with specific middleware packages.

The range of use for intelligent HTC in scientific programs is broad. For example, intelligent HTC can be used to select and run many single-point electronic structure calculations in order to develop approximate potential energy surfaces. Even more examples can be found in the wide range of methods that require many trajectories, where each trajectory can be treated as a task, such as:

* rare events methods, like transition interface sampling, weighted ensemble, committor analysis, and variants of the Bennett-Chandler reactive flux method;
* semiclassical methods, including the phase integration method and the semiclassical initial value representation;
* adaptive sampling methods for Markov state model generation;
* approaches such as nested sampling, which use many short trajectories to estimate partition functions.

The challenge is that most developers of scientific software are not familiar with the way such packages can simplify their development process, and the packages that exist may not scale to exascale. This workshop will introduce scientific software developers to useful middleware packages, improve scaling, and provide an opportunity for scientific developers to add support for HTC to their codes.

2 Major outcomes

In practice, many scientific programmers are not aware of the range of middleware to facilitate parallel programming. When HTC-like approaches are implemented as part of a scientific software project, they are often done manually, or through custom scripts to manage SSH, or by running separate jobs and manually collating the results. Using the intelligent high-level approaches enabled by distributed computing middleware can simplify and speed up development. Major topics that were covered included

* Concepts of HTC; how to structure code for HTC,

* Accessing computational resources to use HTC,

* Interfacing existing C/C++/Fortran code with Python libraries,

* Specifics of interfacing with Dask/PyCOMPSs,

* Challenges in using existing middleware at extreme scale.

Furthermore, middleware frameworks can meet the needs of many different computing infrastructures. For example, in addition to working within a single job on a cluster, COMPSs includes support for working through a cluster's queueing system or working on a distributed grid. Moreover, architecting a software package such that it can take advantage of one HTC library will make it easy to use other HTC middleware. Having all of these possibilities immediately available will enable developers to quickly create software that can meet the needs of many users.

This E-CAM Extended Software Development Workshop (ESDW) focussed on intelligent HTC as a technique that crosses many domains within the molecular simulation community in general, and the E-CAM community in particular. Teaching developers how to incorporate middleware for HTC matches E-CAM's goal of training scientific developers on the use of more sophisticated software development tools and techniques. The primary goals were:

1. To help scientific developers interface their software with HTC middleware.
2. To benchmark, and ideally improve, the performance of HTC middleware as applications approach extreme scale.

The second portion of the workshop focused exclusively on HTC enabled by Dask, and on the related libraries dask-jobqueue and jobqueue_features. The latter library is developed by E-CAM, largely in the context of the ESDW, and focusses on enabling MPI-aware tasks within Dask.

3 Community needs

The software package "jobqueue_features" (https://github.com/E-CAM/jobqueue_features) was entirely developed by E-CAM in collaboration with PRACE. There are a number of modules submitted to the E-CAM repository related to development work for this package:

* https://gitlab.e-cam2020.eu/e-cam/E-CAM-Library/merge_requests/83
* https://gitlab.e-cam2020.eu/e-cam/E-CAM-Library/merge_requests/84
* https://gitlab.e-cam2020.eu/e-cam/E-CAM-Library/merge_requests/85
* https://gitlab.e-cam2020.eu/e-cam/E-CAM-Library/merge_requests/86

with more related modules currently being prepared.

There are also user-related modules submitted

* https://gitlab.e-cam2020.eu/e-cam/E-CAM-Library/merge_requests/50
* https://gitlab.e-cam2020.eu/e-cam/E-CAM-Library/merge_requests/150

again with more modules under preparation.

4 Funding

The second face-to-face meeting took place at the beginning of July 2019. The workshop was 3.5 days long consisting of 1.5 days with three different Python libraries related to Dask:

Dask: https://docs.dask.org/en/latest/

Dask_jobqueue: https://dask-jobqueue.readthedocs.io/en/latest/

jobqueue_features: https://github.com/E-CAM/jobqueue_features

The last library is something that was developed between the two workshops by E-CAM. It allows the user to create tasks that call out to MPI programs, and easily configure the tasks to run on different types of resources (CPU/GPU/KNL). The final 2 days were a hackathon where you can work on your own use case with technical assistance.

Beyond this, future developments would be to continue to support jobqueue_features and expand it's capabilities and resilience.

5 Will these developments bring societal benefits?

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Extended Software Development Workshop: Atomistic, Meso- and Multiscale Methods on HPC Systems

Location: CECAM-DE-JUELICH
Webpage: https://www.cecam.org/workshop-0-1591.html
Dates: September 6, 2018 to September 7, 2018

1 State of the art

2 Major outcomes

3 Community needs

4 Funding

5 Will these developments bring societal benefits?

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State of the Art Workshop: Improving the Accuracy of Ab-Initio Predictions for Materials

Location: CECAM-FR-MOSER
Webpage: https://www.cecam.org/workshop-0-1643.html
Dates: September 17, 2018 to September 20, 2018

1 State of the art

Improving the accuracy of ab-initio methods for materials means to devise a global strategy which integrates several approaches to provide a robust, controlled and reasonably fast methodology to predict properties of materials from first principle. Kohn-Sham DFT is the present workhorse in the field but its phenomenological character, induced by the approximations in the exchange-correlation functional, limit its transferability and reliability.

A change of paradigm is required to bring the ab-initio methods to a predictive level.

The accuracy of XC functional in DFT should be assessed against more fundamental theories and not, as it is often done today, against experiments. This is because the comparison with experiments is often indirect and could be misleading. The emerging more fundamental method for materials is Quantum Monte Carlo because of: 1) its favourable scaling with system size with respect to other Quantum Chemistry methods; 2) its variational character which defines an accuracy scale and allows to progressively improve the results. However QMC being much more demanding in terms of computer resources, and intricate than DFT, a combined approach is still desirable where QMC is used to benchmark DFT approximations for specific systems before performing the production study by DFT.

A different aspect of accuracy is related to size effects: often relevant phenomena occurs at length and time scales beyond the one approachable by first-principle methods. In these cases effective force fields methods can be employed. Machine Learning methods can be used to extract those force fields from training sets provided by ab-initio calculations. Presently DFT-based training sets are used. Improving their accuracy will improve the ultimate accuracy at all scales.

This change of paradigm requires building a community of people with different expertises working in an integrated fashion. This has been the main aim of the workshop.

2 Major outcomes

The following is a partial list of the topics discussed at the workshop, and of their importance to develop the field of computational materials science from first principles.

1) Importance of computational benchmarks to assess the accuracy of different methods and to feed the machine learning and neural network schemes with reliable data;

2) Need of a common database, and need to develop a common language across different codes and different computational approaches;

3) Interesting capabilities for neural network methods to develop new correlated wave functions;

4) Cross-fertilizing combination of computational schemes in a multi-scale environment: from the elemental interactions described at very high-level by expensive approaches to the generation of effective potentials, keeping the accuracy of high-level methods but at much lower cost.

5) Recent progress in quantum Monte Carlo to further improve the accuracy of the calculations by taking alternative routes: transcorrelated Hamiltonians, multideterminantal expansions, pfaffian wave functions.

Limitations:

Lack of a common environment where to develop multi-scale approaches for the prediction of material properties. This workshop is one of the first attempts where such needs have been discussed, and possible solutions explored.

Open questions:

How to make the codes ready for the next high performance computing (HPC) generation? A fundamental limitation to the future expansion of HPC is the need to reduce energy cost per unit of computation, which requires new technologies. Some of these new technologies are based on accelerators, such as GPU's, which require in many case a complete rewriting of legacy scientific codes. This is a serious problem for the scientific community, requiring open and frank discussions, including a re-think of work recognition of computer code development as a major scientific endeavour.

How to develop a meaningful materials science database (which gathers both experimental and theoretical results)?

How to develop a common platform to merge different methods in a multi-scale spirit?

3 Community needs

The community of computational material science has increased in size tremendously in the past few decades. The drive for this expansion has been the development of ever more friendly computer codes, mainly based on density functional theory (DFT). Indeed, web of science is now reporting tens of thousands of papers per year based on DFT. By contrast, the quantum Monte Carlo (QMC) method, normally much more accurate than DFT, is only published in the hundreds/year, because of its much higher cost and also because of the intricacies of the method that make it more difficult to use. The number of workshops on QMC and the number of schools in which QMC is taught are also only a fraction compared to those on DFT. We believe that the community is now at a turning point where the extra accuracy offered by QMC is not only desirable, but also very much needed if serious progress is to be achieved in the computational design of new materials with bespoke properties. Only a few QMC codes (not even a handful) are currently supported through serious effort, and the community desperately need more formal recognition for code development in order to attract the best people to this endeavour. We are particularly focussing on QMC because we believe that it is the natural method capable of exploiting to the full the forecasted expansion in computer power in the next 10-20 years, but this is also a crucial point in time for this expansion, where new architectures require a complete re-thinking of computational approaches. A series of CECAM workshop may help to draw attention to these points.

4 Funding

Typical funding channels for the activities discussed at the meeting could be the Psi-k community and national funding schemes. In addition, since the ultimate goal of these activities will be to be able to design new materials entirely from first principles, it should be possible to target and persuade specific industries involved in the synthesis of new materials, including for example energy materials such as new batteries and new hydrogen storage materials. Industry funding could be targeted by offering to industry members of staff limited number of spaces to the workshops and requesting a registration fee.

5 Will these developments bring societal benefits?

The potential benefits of developing and handling computational tools able to predict material properties with a high level of reliability are numerous and of tremendous societal impact. During our workshop, a clearcut example was given by Xenophon Krokidis, who talked about the development of Scienomics, a software used to design and test new compounds in silico. This would allow a company to accelerate the R&D stage of its projects, cut ressources spent for checking the functionalities of a given material, and significantly shorten the "trial and error" time. The budget and time reductions yielded by the usage of a reliable material science software in the R&D is estimated to be of one order of magnitude, according to Krokidis's experience. This is a huge amount.

Thus, the efforts of bringing together the three different communities (ab initio quantum Monte Carlo, density functional theory, and machine learning) is definitely worth, in the perspective of improving the accuracy of ab initio predictions for materials.

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State of the Art Workshop: Large Scale Activated Event Simulations

Location: CECAM-AT
Webpage: https://www.cecam.org/workshop-0-1642.html
Dates: October 1, 2018 to October 3, 2018

1 State of the art

Running on powerful computers, large-scale molecular dynamics (MD) simulations are used routinely to simulate systems of millions of atoms providing crucial insights on the atomistic level of a variety of processes of interest in physics, materials science, chemistry and biology. For instance, MD simulations are extensively used to study the dynamics and interactions of proteins, understand the properties of solutions or investigate transport in and on solids. From a technological point of view, molecular dynamics simulations play an important role in many fields such as drug development, the discovery of new materials, oil extraction or energy production. Indeed, enormous amounts of data are produced every day by molecular dynamics simulations running on high performance computers around the world and one of the big challenges related to such simulations is to make sense of the data and obtain mechanistic understanding in terms of low-dimensional models that capture the crucial features of the processes under study. Another central challenge is related to the time scale problem often affecting molecular dynamics simulations. More specifically, despite the exponential increase in computing power witnessed during the last decades and the development of efficient molecular dynamics algorithms, many processes are characterized by typical time scales that are still far beyond the reach of current computational capabilities. The central goal of this ECAM-State-of-the-Art Workshop was to discuss computational approaches capable of addressing such time scale problems in complex systems in materials science and biophysics. Another important goal of the workshop was to debate about how to facilitate the use of simulation and modelling in industrial settings.

2 Major outcomes

Scientific discussions at the workshop centered around three fundamental computational challenges closely related to the time scale problem of classical MD simulation:

1) The calculation of the populations of metastable states of an equilibrium system. Such populations can be expressed in terms of free energies and hence this problem boils down to the efficient calculation of free energies. Sampling methods for such free energy calculations were discussed in several talks at the workshop.

2) The sampling of transition pathways between long-lived (meta)stable states and the calculation of reaction rate constants. Here the problem consists in sampling dynamical trajectories which can be very long for complex systems. Several talks discussed this problem and showed how path-based approaches can be used to study, for instance, the nucleation of gas hydrates, the crystallization of metals or the unbinding of a ligand from a protein. Simulations of such processes are facilitated by new scientific software tools, such as the Open Path Sampling (OPS) package, which provide flexible frameworks that can be easily extended and provide the tools required to handle large and complex systems.

3) The extraction of useful mechanistic information from the simulation data and the construction of low-dimensional models that capture the essential features of the process under study. Such models serve as the basis for the definition of reaction coordinates that enable in-depth studies of the process at hand. It has become evident during the workshop that new machine learning approaches have a huge potential for making progress on this very important problem. A number of talks discussed how to use supervised and unsupervised learning methods to identify collective variables that can be used to characterize complex molecular rearrangement.What has become clear in the talks and discussions during the workshop is that the key point in the application of machine learning methods to molecular simulations lies in the appropriate definition of descriptors on which the learning process is based. For instance, artificial neural networks have been shown to be able to provide very accurate and efficient representations of potential energy surfaces. A condition for the application of this approach, however, is that a set of molecular fingerprints is defined that contains sufficient information on molecular arrangements to make the energy prediction possible. The smart selection of descriptors is crucial in other machine learning approaches as well and it can be viewed as the interface between physics and chemistry and the world of machine learning.

The various themes discussed in the talks were picked up in two open discussion sessions on the first and second day of the workshop. The first discussion revolved on efficient path sampling methods and the identification of reaction coordinates. In particular, it was discussed how machine learning approaches can be used to make progress in this area and how extreme scale computational resources can be used efficiently to address these questions. Discussions on machine learning continued also in the second discussion, in which interactions between academia and industry was the other important topic. The workshop participants with industrial experience emphasized the importance of detailed project management and, in particular, the need to have very clear agreements about intellectual property rights. Industrial participants to the workshop also pointed out that small companies that develop software solutions can help to bridge the gap between academic research and industry. The workshop also reinforced contacts with scientists from non-academic research centers (T. Trnka [Software for Chemistry & Materials], M.G. Mota [Simune Atomistic Simulations], A. Pan [D.E. Shaw Research], Tim Conrad [Modal AG, Berlin]).

3 Community needs

The workshop demonstrated clearly that in order to make progress a community needs openly available codes that can be easily adapted, extended and combined. Until a few years ago, the field of rare event simulation lacked such a code, but in the mean time this deficit has been closed by the Open Path Sampling (OPS) and the PyRETIS package. It is crucial that these packages, which implement a wide range of path based methods, are interfaced with programs to generate dynamical trajectories (such as Gromacs, Lammps or CP2k) and to calculate collective variables (such as Plumed). Similarly, an open source software package (n2p2) is now available for the representation of atomistic potential energy surfaces. It is critical for the atomistic and molecular simulation community that development of these codes continues (for instance, within ECAM Extended Sowtware Development Workshops or similar CECAM activities) and that they are made ready for use on extreme scale computing infrastructure.

The availability of well documented and easily applicable software packages are also a condition for successful collaborations of academic researchers with industry.

4 Funding

The success of the ECAM Center of Excellence in the development of software tools for rare event simulations in the field of classical molecular dynamics has demonstrated that a collective effort is needed in order to develop high quality scientific software for the community. Such projects cannot be sustained by individual research groups and joint initiatives such as the European Centers of Excellence are needed to provide the funding for software development. The EuroHPC Joint Undertaking, a Europe-wide initiative to create a European HPC infrastructure which is starting at the moment, might provide opportunities in this direction in the future.

5 Will these developments bring societal benefits?

It is unlikely that short term societal benefits follow from the workshop. But in the long term, activities such our ECAM-State-of-the-Art Workshop on "Large Scale Rare Event Simulation" can have an important societal impact in several distinct ways, for instance:

- Many processes of importance in the fields of materials science and drug design are determined by rare events. So a detailed molecular understanding of new materials or drugs relies on our ability to study rare events in large-scale computer simulations. The simulation algorithms discussed in this meeting are an important step in this direction. In fact, several talks and discussions at the meeting touched on topics of direct economic relevance for instance the binding and unbinding of ligands to and from proteins and the catalytic properties of disordered substrates.
- The meeting also had a strong emphasis on the development of scientific software, mainly for transition path sampling and machine learning. Such software projects can have a huge impact on the research field and, in particular, on possible collaborations with industry.
- Early stage researchers working on the scientific software developments discussed in the workshop will have interesting job opportunities and will facilitate the transfer of knowledge from academic research to industry.

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