Scientific Report

ESF exploratory workshop: executive summary and assessment of results

"Bridging the gap between model systems and real systems in molecular science"

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Venue: L' école de physique, Les Houches, Chamonix, France

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In molecular science, smaller ("model") systems with a limited number of degrees of freedom allow more precise measurements of structure and dynamics as compared to bigger ("real") systems. The same statement is true for numerical modelling of molecules in condensed matter since *ab initio* (quantum chemistry) methods can be applied to smaller systems. Recently it has been demonstrated that a uniquely clear and detailed insight into the structure and dynamics of condensed matter systems can be obtained by combining neutron scattering and numerical investigations. The purpose of the workshop was therefore to bring together experimentalists and computational experts to investigate the possibilities of "passing-up" information and techniques from model systems to real systems (a bottom-up approach) and of defining model systems that are relevant fractions of real systems. Real systems could be broadly categorised as being of biological or technological interest.

From an original list of 24 participants, 22 scientists made it to the workshop. The ESF representative, Judith Howard was well-suited to this community. The list of participants was intended to cover a range of complementary experimental and computational techniques currently used in scientific investigation of condensed matter systems. Thus, in addition to neutron scattering, X-rays, optical methods and NMR were represented on the experimental side and both *ab initio* and force field methods were represented on the computational side. About one-third of the participants had dual experiment-simulation competence. The participants were equally split between model and real systems.

Since the purpose of the workshop was to discuss future directions in molecular science, as much time was dedicated to discussion as to presentation of recent results. In each session, broadly focussed on the different experimental and computational techniques, 2-3 talks were given back-to-back, followed by 45 minutes collective discussion of the presentations. In order to facilitate a more in-depth discussion, extended abstracts were submitted (typically 4 pages), which were distributed to all participants, before the meeting. The meeting was concluded with a round table discussion in which the participants summarised their views of the different gaps in molecular science.

A number of “technical results” were gleaned from the presentations and many, lively discussions.

The separation between model and real systems is not clear-cut and the same holds for other pairs of adjectives commonly used (small and big, simple and complex). All of these terms are relative in that smaller, simpler systems are regarded as model systems that allow a deeper understanding of some aspect of a bigger system of interest. On the other hand, bigger, more complex systems, which include some added functionality, are considered to be real versions of a smaller model system.

A more strict definition of a model system could be given as follows. In a model system, experiment allows essential aspects of structure and dynamics to be determined and the confrontation of experimental data and data obtained from ab initio, quantum chemistry calculations is possible so that an accurate, microscopic picture of structure and dynamics is derived.

Numerical modelling techniques, in particular molecular dynamics (MD) gives a microscopic description of systems of almost any size. Using force fields, several hundred thousand atoms, for example proteins in solution, can be simulated for tens of nanoseconds on typical PC clusters. Whether or not an understanding on the model system level, as defined before, is obtained depends on the validity of the force field.

Single ab initio calculations can also be performed on several hundred thousand atoms using linear scaling techniques, although an extensive series of calculations would be limited to about one thousand atoms. This size of system corresponds to small proteins and compact structures of DNA.

One obvious way of passing information up from model to real systems is to optimise the description of force fields, first against ab initio calculations and then against experimental data. The physical response of a force field calculation could also be compared with that of an ab initio calculation, for example finding the most stable conformation of the system. The large number of atoms that can now be treated by DFT gives considerable scope for defining model systems.

As suggested above, one of the limitations of any numerical method is the number of calculations that can be performed as this determines the timescale that can be accessed. This problem is particularly acute for ab initio MD in which only a few picoseconds can be simulated while force field based MD is limited to tens of nanoseconds. For some polymer problems, coarse-grain models in which atoms are no longer treated individually are required and by suppressing strong intra-molecular forces, longer timescales could be reached. Otherwise the reaction path has, for example, to be identified by Monte Carlo methods, and the corresponding time-scale is then deduced from the energy barrier.

Experimentally, model systems should allow measurements to be performed that discriminate between different structures or dynamics. For example, MD simulations readily reproduce quasi-elastic neutron scattering data of diffusive dynamics in real, polymeric systems, so this type of data is not a very rigorous test of the simulation. In contrast, inelastic measurements of low frequency collective excitations are less well reproduced by the same force fields and higher frequency modes are also problematic.

DFT methods allow precisely these higher frequency modes to be well reproduced, but the lack of dispersive interactions in DFT hampers the accurate calculation of the low frequency modes.

Molecular systems become complex when crystallinity and, in particular, short range order is lost. This was demonstrated by propanol, a simple molecule, which shows, in its glassy phase, dynamic responses similar to proteins, leading to the same success and problems for simulations as mentioned above.

When considering more complex model molecular structures, crystallinity and short range order become key parameters. Polymer fibres offer a high degree of crystallinity and interesting possibilities exist in this context for working on DNA and related polymers and oligomers. Generally, proteins and oligo-peptides seem to be more widely studied than oligo-nucleotides.

Moving up from model to real systems also brings difficulties in terms of sample preparation. For neutron scattering, the experimental technique allowing the most direct comparison between simulation and experiment, hundreds of milligrammes of sample are required, quantities for which the purchase or preparation may become financially prohibitive.

Abstracts of the papers presented at the meeting may be found here **Abstracts**

Assessment of results and future directions for molecular science

This workshop targeted the very broad field of molecular science, the issue being how information from smaller, simpler systems could be transferred to bigger, more complex systems. Every scientist is conscious of the need to get higher quality information, but the identification of simpler, relevant systems that afford this possibility is often a challenge. Since the goal is to obtain an accurate microscopic model of the system of interest, simulations must obviously be as accurate as possible and should be extended to bigger systems. Experiments on simpler molecular systems and ab initio calculations have a role to play in this context.

While the gap between model and real systems depends on the original system of interest and can therefore not be strictly defined, the gap between experiment and simulation is more evident and the need to bridge this gap is of fundamental importance. Not only do the experimentalists need simulators to make microscopic models, but the simulators need to remain in close contact with the experiments to know what kind of information can be obtained experimentally and what should therefore be extracted from simulations. In addition, the experimentalists that have become users of numerical codes in order to analyse their data, bridging the experiment-simulation gap themselves, need to be guided by the developers of new computational methods in order to ensure optimal use of the codes. Close contact between experimental and computational scientists will maximise the value of experiments and simulations, for example in identifying observables that are the most critical tests for calculations.

The various gaps that need to be bridged in molecular science have therefore been identified. Gaps can be closed by improving the precision of numerical methods and experimental techniques. The gap between numerical and experimental approaches can be closed by collaborative development of “data analysis” software. Finding new, relevant model systems to be investigated with existing numerical and experimental tools, which was the original goal of this workshop, constitutes the least well-defined gap, in that every investigator has his or her idea of a model system. All participants at this workshop were keen and willing to close these gaps. In spite of the broad range of scientists at the workshop, most participants found collaborators for their current projects.

Progress in this important field will be achieved through the combined effort of experimentalists and computational scientists. This effort should be structured and supported by national and international resources. The enthusiastic response of the participants indicates the need for conferences in this style with the very direct confrontation of experiment with simulation and extensive discussion/round table sessions. In addition this community is ready and willing to lobby at the level of the EU for support for this kind of science. The needs that were identified in order to make the necessary collaborations effective are first and foremost the availability of postdoctoral fellows and therefore the support for the corresponding positions that would be shared (delocalised) between different laboratories.

thurs am 1 (09:30-10:30)	**pause**	**thurs am 2 (11:00-12:30)**	**lunch**	**thurs pm 1 (14:00-15:30)**	**pause**	**thurs pm 2 (16:00-17:30)**	**more discussion then dinner at 19:00**
Introduction		Polymers: (Chair-Tarek)		Bio_1, expt+simul: (Chair-Kneller)		Structure: (Chair-Jobic)	
ESF (Howard)		Kearley		Smith		Fitch	
Johnson		Picken		Bon		Forsyth	
		Siebbeles		Tarek		Wilke	
		Gonzalez					
fri am 1	**pause**	**fri am 2**	**lunch**	**fri pm 1**	**pause**	**fri pm 2**	
Ab initio methods: (Chair-Johnson)		Small molecules/crystalline: Chair-Gale)		NMR, proton transfer and tunnelling: (Chair-Kearley)		Optics: (Chair-Trommsdorff)	
Gale		Jobic		Horsewill		Plazanet	
Parrinello		Navarro		Limbach		Ghomi	
		Johnson		Trommsdorff			
sat am 1	**pause**	**sat am 2**	**lunch**				
Bio_2, expt+simul: (Chair-Smith)		Round table discussion, perspectives … (Peter Trommsdorff, Don Kearley)		END			
Hunenberger							
Kneller							

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GALE Julian	40-50	UK	UK	M
GHOMI Mahmoud	50-60	F	F	M
GONZALEZ Miguel	30-40	Sp	F	M
HORSEWILL Anthony	40-50	UK	UK	M
HUNENBERGER Philippe	30-40	CH	CH	M
JOBIC Hervé	40-50	F	F	M
JOHNSON Mark	30-40	UK	F	M
KEARLEY Gordon	50+	UK	NL	M
KNELLER Gerald	40-50	D	F	M
LIMBACH Hans-Heinrich	50+	D	D	M
NAVARRO Amparro	30-40	Sp	Sp	F
PARRINELLO Michele	50+	I	CH	M
PICKEN S.J.	40-50	NL	NL	M
PLAZANET Marie	20-30	F	F	F
SIEBBELES Laurens	40-50	NL	NL	M
SMITH Jeremy	40-50	UK	D	M
TAREK Mounir	30-40	Marocco	CH	M
TROMMSDORFF Hans-Peter	50+	D	F	M
WILKE Steffen	40-50	D	UK	M