Report on the workshop "Numerical methods in molecular simulation" (7-11 april 2008, Bonn, Germany)

April 22, 2008

1 Summary

1.1 Organizational details

The workshop took place in Bonn, in the framework of the HIM Junior Hausdorff Semester Program, from 7th April to 11th April. See the webpage:

`http://cermics.enpc.fr/~stoltz/Bonn/workshop.html`

It was organized by:

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- Tony Lelièvre[1,3],
- Mathias Rousset[4],
- Gabriel Stoltz[1,3].

with the following institutional affiliations:

- (1) CERMICS, Ecole Nationale des Ponts et Chaussées, 6 et 8 av. Blaise Pascal, 77455 Marne la Vallée, FRANCE.
- (2) LAMI, Ecole Nationale des Ponts et Chaussées, 6 et 8 av. Blaise Pascal, 77455 Marne la Vallée, FRANCE.
- (3) INRIA Rocquencourt, MicMac project-team, B.P. 105, 78153 Le Chesnay, FRANCE.
- (4) INRIA Lille Nord-Europe, Simpaf project-team, Parc Scientifique de la Haute Borne 40, avenue Halley bat. A, Park Plaza 59650 Villeneuve d'Ascq, FRANCE.

1.2 Scientific program

The purpose of the workshop was to study numerical questions raised by molecular dynamics simulations. Such simulations represent today a huge part of the CPU time used by scientists but this field has not yet been covered a lot by numerical analysts and experts in scientific computing. These simulations are related to many unexplored and interesting topics in numerical analysis and scientific computing.

The workshop consisted in four lectures and sixteen contributed talks. The lectures were given by:

- Wim Briels: *Coarse graining of soft matter systems*,
- Pierre Del Moral: *Particle Rare Event Stochastic Simulation Methods*,
- Arnaud Guillin: *Long time behavior of Markov processes: Various approaches*,
- Raz Kupfermann: *Averaging and coarse-graining: the mathematics of modeling.*

1.3 Scientific content and achievements

During this workshop, the following topics have been covered:

- Numerical and theoretical analysis of sampling algorithms,
- Model reduction and effective dynamics,
- Monte-Carlo methods for quantum chemistry,
- Free energy computation.

One of the main achievement of this workshop was to bring together people from various communities, ranging from mathematics to computational biology, including numerical analysis, mathematical physics and chemistry. Many students attended the workshop and had the opportunity to learn from this mixed program.

1.4 Funding of the workshop

The workshop was hosted by the Hausdorff Institute for Research. This institution paid for local expenses (hotel and per diem) for all participants, and the travel expenses for the four lecturers listed in section 1.2. We asked for a ESF grant of 9500 euros to cover the travel expenses of the other participants. The funding of the ESF is acknowledged on the workshop webpage, and was also acknowledged on the printed program given to each participant.

2 Description of the scientific content of and discussion at the event

2.1 Numerical and theoretical analysis of sampling algorithms

Many problems in molecular dynamics consist in computing the average of some functional with respect to a probability measure in a high-dimensional space. Monte Carlo methods are the method of choice, and particularly Markov Chain Monte Carlo methods which are based on stochastic perturbations of deterministic molecular dynamics. The lecture of Arnaud Guillin reviewed the mathematical techniques that can be used to measure the convergence rate of the above sampling techniques.

The sampling efficiency is however usually limited by some metastability in the dynamics. The system typically spends a lot of time in one metastable state, before hopping to another, and the interesting part of the dynamics is this rare event. For example, the difference of free energy between these two states is an important quantity to compute, since it is related to the likelihood of these states. Cosmin Marinica presented one method to overcome such metastabilities, and its application to the case of interstitial atoms in metals.

More generally, Pierre Del Moral, in his lecture, introduced a general mathematical framework to improve straightforward sampling strategies by selecting several replicas of a same system, simulated synchronously in parallel. A possible application is simulated annealing, for which Andreas Eberle presented recent refined mathematical convergence results.

Finally, Aline Kurtzmann discussed the convergence of some self avoiding random walks. This seems to be a convenient mathematical framework for proving the convergence of some adaptive methods to compute free energy differences.

2.2 Model reduction and effective dynamics

One difficulty in molecular simulation is the presence of a large spectrum of time and space scales. Two lectures were devoted to model reduction and effective dynamics, as well as many contributed talks. To classify the numerous contributions, it is convenient to distinguish between equilibrium properties (lecture by Wim Briel, talks by Markos Katsoulakis and Dimitrios Tsagkarogiannis) and dynamics or dynamical properties (lecture by Raz Kupferman and talks by Carsten Hartmann, Cedric Bernardin, Greg Pavliotis and Stephan De Bievre).

Another interesting distinction is whether the effective properties are recovered through some time scale separation (typically, slow vs. fast times) or through some thermodynamic limit (when the number of particles goes to infinity).

Two prototypical applications were considered in many talks: coarse graining of polymer chains, and reduction of the number of degrees of freedom for heat baths. Polymer chains are typically long and complicated molecules, which are computationally expensive to simulate. It is interesting to have some reduced description of the (non newtonian) polymeric fluids by resorting to some dumbbell model where a polymer is viewed as a chain of 'blobs', each 'blob' standing for a portion of the chain. The aim of the coarse graining procedure is to propose a reasonable interaction between the blobs. Heat baths described by a collection of deterministic oscillators are another interesting example. Such models are interesting to derive constant temperature dynamics from deterministic systems.

2.3 Monte Carlo for quantum chemistry

The Diffusion Monte Carlo (DMC) method is a stochastic method to estimate the ground state energy E_0 of a N-body Schrödinger hamiltonian $H = -\frac{1}{2}\Delta + V$ with high accuracy. It consists in writing E_0 as the long-time limit of an expectation value of a drift-diffusion process with a source term, and in numerically simulating this process by means of a collection of random walkers with some interacting selection mechanism. As for a number of stochastic methods, a DMC calculation makes use of an importance sampling function ψ_I which is used as a drift potential in the random walkers motion, and hopefully approximates some ground state ψ_0 of H.

In the fermionic case, the DMC method is biased, except in the special case when the nodal surfaces (the zeros) of ψ_I coincide with those of a ground state of H (Fixed Node Approximation (FNA)). The mathematical analysis of the FNA has been presented by Benjamin Jourdain, as well as a careful numerical analysis of a benchmark one dimensional system. Roland Assaraf complemented this talk by presenting a new method to compute energy derivatives (hence, linear response properties), which were until now plagued by statistical errors. Finally, Sylvain Maire presented another application of the above mentioned strategies to compute ground state energies in a different context.

2.4 Free energy computation

For systems in the canonical ensemble, many methods exist to compute free energy differences between two metastable states indexed by a reaction coordinate. One can roughly distinguish between four classes of method : thermodynamic integration (which uses constrained dynamics and homogeneous Markov processes), perturbation methods (which are basically importance sampling methods), out of equilibrium dynamics (like the Jarzynski method, typically based on non-homogeneous Markov processes) and adaptive methods (like the Wang Landau method, adaptive biasing force method, metadynamics, typically based on non-linear Markov processes). Many questions are raised by these methods and their discretizations.

Manuel Athènes presented new path sampling techniques to enhance the accuracy of Jarzynski like methods. Volodymyr Babin and Chris Chipot described new applications of adaptive biasing methods in molecular biology. Finally, Paul Fleurat-Lessard compared the results obtained on a simple benchmark system with different parametrizations of a thermodynamic transformation.

3 Assessment of the results and impact of the event on the future direction of the field

This workshop was the opportunity for applied scientists (be they physicists, biologists or chemists) to learn how mathematicians assess the quality of some modeling assumption or dynamics. The applied mathematicians, on the other hand, were confronted to new and challenging problems, which were presented in a pedagogical manner. The interactions that grew out of the workshop led to the following research tracks:

- Many techniques are now available to perform efficient model reductions at equilibrium. In particular, the error related to the approximation of effective hamiltonian by two-body potentials can now be assessed. This give a rationale for a systematic derivation of coarse-grained potentials for complex systems such as biological molecules and polymers.

- On the other hand, except in special cases where a clear separation of scales is artificially introduced, most remains to be done on the reduction of *d*ynamics. In particular, no systematic study of closure approximations on the dynamics has been undertaken. This is a very relevant subject for future research.

- In molecular dynamics, practicionners are not used to simulating many replicas of the same system in parallel, and to use information exchange to accelerate the convergence of the algorithms. There are now plenty of techniques which have proven their efficiency for complex Monte Carlo computations, especially in quantum chemistry. In particular, it would be interesting to apply these techniques for free energy computations and coarse-graining.

- To study the convergence of stochastic dynamical systems to equilibrium, many methods exist, but they are in general not able to distinguish between local effects and global properties. For example, techniques based on functional inequalities lead to bounds which only rely on the properties of the sampled potential outside a bounded set of the configuration space. This is clearly not sufficient to obtain sharp results, especially to understand metastability. Techniques to obtain estimates using local properties of the sampled measure need to be developed.

4 Final program of the meeting and participants list

Table 1: Participants list

Participant	Institution	Country
Benedicte Aguer	Laboratoire Painleve et INRIA, Villeneuve d'Ascq	France
Roland Assaraf	Laboratoire de Chimie Théorique, Paris 6	France
Manuel Athènes	CEA Saclay	France
Volodymyr Babin	Dpt of Physics, North Carolina State University	USA
Cedric Bernardin	UMPA, ENS Lyon	France
Wim Briels	University of Twente	The Netherlands
Christophe Chipot	Université Henri Poincaré, Nancy	France
Ismaïla Dabo	CERMICS - ENPC	France
Stephan De Bièvre	Université de Lille	France
Pierre Del Moral	INRIA Bordeaux	France
Andreas Eberle	Universität Bonn	Germany
Paul Fleurat-Lessard	Laboratoire de Chimie, ENS Lyon	France
Arnaud Guillin	Université de Marseille	France
Carsten Hartmann	Institut für Mathematik, Freie Universität Berlin	Germany
Benjamin Jourdain	CERMICS - ENPC	France
Markos Katsoulakis	Dpt of Mathematics and Statistics, U. Massuchussetts	USA
Raz Kupferman	Institute of Mathematics, The Hebrew University	Israel
Aline Kurtzmann	Mathematical Institute, Oxford	UK
Frédéric Legoll	LAMI - ENPC	France
Tony Lelièvre	CERMICS - ENPC	France
Sylvain Maire	Université du sud Toulon-Var	France
Cosmin Marinica	CEA Saclay	France
Kimiya Minoukadeh	CERMICS - ENPC	France
Andrei Osipov	Institute of Mathematics, The Hebrew University	Israel
Greg Pavliotis	Department of Mathematics, Imperial College	UK
Mathias Rousset	INRIA Lille	France
Raphaël Roux	CERMICS - ENPC	France
Gabriel Stoltz	CERMICS - ENPC and IMPMC, Paris 6	France
Dimitrios Tsagkarogiannis	MPI Leipzig	Germany

Table 2: Final program

Monday	
09:30-10:30	Welcome and coffee
10:30-11:00	Opening remarks
11:00-12:30	Wim Briels
	Coarse graining of soft matter systems
12:30-14:00	Lunch
14:00-15:30	Arnaud Guillin
	Long time behavior of Markov processes: Various approaches
15:30-16:00	Coffee break
16:00-16:45	Chris Chipot
	Reaction coordinates versus order parameters in free energy calculations
16:45-17:30	Aline Kurtzmann
	Self-interacting diffusions
18:30-20:00	Wine and bretzel reception at HIM

Tuesday	
09:00-10:30	Wim Briels
	Coarse graining of soft matter systems (2)
10:30-11:00	Coffee break
11:00-11:45	Cosmin Marinica
	Stability and mobility of small interstitials clusters in iron
11:45-12:30	Paul Fleurat-Lessard
	A chemist view on reaction path
12:30-14:00	Lunch
14:00-15:30	Arnaud Guillin
	Long time behavior of Markov processes: Various approaches (2)
15:30-16:00	Coffee break
16:00-16:45	Volodymyr Babin
	Adaptively Biased Molecular Dynamics for Free Energy Calculations
16:45-17:30	Manuel Athènes
	Mapping equilibrium and non-equilibrium entropy landscapes from path-sampling

Wednesday	
09:00-10:30	Pierre Del Moral
	Particle Rare Event Stochastic Simulation Methods
10:30-11:00	Coffee break
11:00-11:45	Benjamin Jourdain
	Numerical analysis of the QMC method in a simple case
11:45-12:30	Roland Assaraf
	Toward an exact calculation of energy derivatives in Diffusion Monte Carlo
12:30-14:00	Lunch
14:00-15:30	Raz Kupferman
	Averaging and coarse-graining: the mathematics of modeling
15:30-16:00	Coffee break
16:00-16:45	Sylvain Maire
	A Monte Carlo method to compute principal eigenelements of some linear operators
16:45-17:30	Andreas Eberle
	Quantitative approximations of evolving probability measures

Thursday	
09:15-10:45	Pierre Del Moral
	Particle Rare Event Stochastic Simulation Methods (2)
10:45-11:00	Coffee break
11:00-11:45	Carsten Hartmann
	Model reduction for partially-observed stochastic differential equations
11:45-12:30	Markos Katsoulakis
	Coarse-graining and reconstruction for many-particle stochastic systems
12:30-14:00	Lunch
14:00-15:30	Raz Kupfermann
	Averaging and coarse-graining: the mathematics of modeling (2)
15:30-16:00	Coffee break
16:00-16:45	Dimitrios Tsagkarogiannis
	Reconstruction schemes for coarse-grained models
20:00-22:00	Conference dinner

Friday	
09:00-09:45	Cedric Bernardin
	Fourier law for Hamiltonian microscopic dynamics perturbed by a conservative noise
10:00-10:45	Greg Pavliotis
	From ballistic to diffusive motion in periodic potentials
10:30-11:00	Coffee break
11:00-11:45	Stephan De Bievre
	Motion through an oscillator chain: diffusion and linear response
11:45-12:00	Closing remarks