Report of the School “Progress on simulating activated processes”.

Summary

The school “Progress on simulating activated processes” has gathered about fifty students from more than fifteen European and non European countries. The aim of the school was to present modern methods for studying termally activated processes in atomistic and molecular simulations. Methods for simulating reaction path connecting a specific reactant and product as well as methods for exploring free energy landscape were discussed.
The school consisted of lectures alternated with lab sessions. In addition, thanks to the fact that students and teachers shared the resort facilities, scientific discussions were allowed, and occurred, during all the day.

Description of the event

The school progress on activated processes has been held in Casaprota, Rieti (IT) between May 26th-30th. The aim of the school was to present modern techniques for studying reactions and processes that occur on scale of times that exceed those accessible by atomistic and molecular simulations even using the most powerfull supercomputers available nowadays.

It was decided to have only a small number of teachers and to give them the time needed to go into details on the subjects of their lectures. Tthe teachers of the school were Prof. Giovanni Ciccotti (univ. “La Sapienza”, Roma - IT), Prof. Christoph Dellago (Univ. Of Wien, Wien - AU), Prof. Eric Vanden-Eijnden (Courant Institut, New York, USA). The teachers were assisted by Dr. M. Gruenwald and Dr. M. Venturoli for the lab sessions. The detailed program of the school is given in appendix I.

The School gathered about fifthy participants at different level of career (PhD students, post-doctoral fellows and senior researchers) from 16 countries. Most of the participants were European citizens but several of them were from Asia and the US. The list of participants is given in appendix II. The research fields of participants were very diverse, ranging from solid state physics to biology, from material science to applyed mathematics. This fact contributed in crating a active “community” which discussed of theoretical and applicative aspects of the techniques presented in the school.

The main objective of the school was to present in a comprehensive way basic theories and (some) modern methods for simulating rare events. Since these methods are founded on ideas and methods dating back to 70s and 80s, we added a lecture in which the basic concepts are presented.

We started presenting the transition state theory, both in its complete formulation and also presenting usual approximations (e.g. variational transition state theory, harmonic approximation, etc.). Then, it was also presented the transition path theory, which is the theoretical playground of the transition path sampling and the family of string methods.

Then the program consisted mainly into two parts, the class of algorithm connected to the transition path sampling and the class of algorithm connected to the string method. Lectures and laboratories allowed students to become familiar with the subtle theoretical aspects as well as the implementation details of the methods. Small but complete codes (Fortran and Matlab versions) were provided to the students for possible future use in their research.

The program was completed with two methods for calculating free energy surface landscape: methods based on the Jarzinsky equality and the temperature accelerated molecular dynamics

Finally, we are in the procees of preparing lecture notes of the school. At the moment we cannot say yet whether these notes will be published or simply made available to the students.

Two sessions of short talks given by participants were also organised (10 talks of 15 minutes). The aim of these sessions was two-fold. The first aim was to give the participants the opportunity of presenting their work. The second aim was to discuss their work in the conceptual framework presented in the school and verifying the applicability of some of the methods discussed to these research works. Details of these sessions are given in appendix I.

Assessment of the results and impact of the event

Participants with a more applicative focus were put in contact with modern techniques that can be very beneficial for their research. Thanks to the residential scheme, they were allowed to discuss with the teachers and other participants in detail about general aspects possible application of the methods to their research. This will prompt them to start using these modern techniques immediately. At the same time, researchers focused on the development of methods for simulations were confronted with a large landscape of possible applications of their work, so forcing them to cope with the miriad of very specific application details that usually make a method very useful in real applications.
Since the school involved a large number of young researchers, and since they have had time to establish connections with others participants and with the teachers, we expect that the school will facilitate the adoption of these modern techniques in computational research in Europe in all those fields that are connected with atomistic and molecular simulations.

Appendix I: Program of the school

Giovanni Ciccotti

1. Barriers, paths, and simulations: A story of rare events
   - Rare events, reaction coordinates, barriers, and rate constants
   - Computer simulation approaches: Blue Moon, Bennett
   - Locating metastabilities and transition states: The search of reactive paths

Christoph Dellago

1. Transition state theory
   - Reaction rate constants: Macroscopic versus microscopic description
   - TST reaction rate constant
   - Harmonic approximation
   - RRKM theory
   - Variational transition state theory
   - Dynamical Corrections: reactive flux formalism

2. Transition path sampling
   - Transition path ensemble
   - Sampling the transition path ensemble: Monte Carlo simulation in trajectory space
   - Kinetics from the transition path ensemble
   - Transition interface sampling
   - Partial path sampling
   - Forward flux sampling
   - Discrete path sampling
   - TPS Applications

3. Rare events in trajectory space
   - Jarzynski's nonequilibrium work theorem
   - Crooks theorem
   - Biasing nonequilibrium trajectories

Eric VandenEijnden

1. Transition State Theory
   - Metastability, reactive trajectories and effective dynamics
   - Transition state rate constant
   - Variational TST and free energy
   - Dynamical corrections
   - Practical implementation and error estimates

2. Transition Path Theory
    - Probability density of reactive trajectories and committor function
    - Probability current of reactive trajectories, probability flux and reaction rate
    - Variational characterization of the committor function
    - Practical aspects: Localization assumption and collective variables

3. String Method
    - The basic idea: evolving curves while controlling their parametrization
    - Zerotemperature string method
    - Using collective variables
    - Finitetemperature string method
    - Generalization to nonequilibrium systems

4. Temperature accelerated molecular dynamics
    - Basic equations and justification
    - Free energy reconstruction: histogram methods vs integration

Short Talks

- **Attilio-Vittorio Vargiu**: Mechanisms and free energy of drug/DNA unbinding investigated by
metadynamics.

- **Fabio Pietrucci**: Enzyme-ligand interaction by bias exchange metadynamics
- **Fabrizio Marinelli**: A thermodynamic and kinetic model from bias exchange metadynamics: application to the Ace-ala-ala-ala-Nme peptide and to TRP-cage miniprotein folding.
- **Eric Hajjar**: Accelerated Molecular Dynamic Simulations of antibiotic diffusion through protein channels; applications and challenges.
- **Jan-Hendrik Prinz**: Enhanced Phase Space Sampling Using Metastability
- **Alexandre Sivak**: Self-Point Defects Diffusion in BCC Iron
- **Darko Simonovic**: Computing Diffusion Coefficient of Rare-Earth Elements in Aluminum
- **Emad Noorizadeh**: An ergodic sampling method for molecular dynamics
- **Ekaterina Persyianova**: Statistical description of the shape of moving dislocation

Appendix II: list of participants

Austria

Geiger Philipp (PhD student)

Grünwald Michael (PhD student)

Lechner Wolfgang (PhD student)

Denmark

Greisen Per Jr. (PhD student)

France

Rotenberg Benjamin (Post-Doc)

Hajjar Eric (Post-Doc)

Manuel Athens

Germany

Held Martin (PhD student)

Prinz Jan-Hendrik (PhD student)

Wigger Jan-Frederik (PhD student)

Fishbach Martin (PhD student)

Hungary

Bartok-Partay Livia (PhD student)

Bartok-Partay Albert (PhD student)

Italy

Marinelli Fabrizio (PhD student)

Orlandini Sergio (PhD student)

Pietrucci Fabio (Post-Doc)

Vargiu Attilio Vittorio (Post-Doc)

Sterpone Fabio (Post-Doc)

Cammarata Antonio (PhD student)

Giulio Trigila (PhD student)

Mugnai Mauro Lorenzo (PhD student)

Ippolito Mariella (Post-Doc)

Agostini Federica (PhD student)

Maddalena Venturoli

Simeoni Mirko (Post-Doc)

Michele Monteferrante (Post-Doc)

Michele Di Pierro (PhD student)

Grazia Cottone

Walter Rocchia

Russian Federation

Gribova Nadezda (Post-Doc)

Lebedeva Irina (PhD student)

Chulkin Dmitriy (Post-Doc)

Ekaterina Persiyanova (PhD student)

Sivak Alexander (Post-Doc)

Czech Republik

Kuntova Zdenka (Post-Doc)

Spain

Domene Carmen (Post-Doc)

USA

Bellucci Michael (PhD student)

United Kingdom

Noorizadeh Emad (PhD student)

Serbia and Montenegro

Simonovic Darko (PhD student)

Colombia

Cossio Pilar (PhD student)

Malaysia

Yew Zu Thur (PhD student)

India

Kumar Amit (Post-Doc)

Iran

Maleki Armin (PhD student)

Organisers and Teachers

Vanden Eijnden Eric

Dellago Christoph

Ciccotti Giovanni

Bonella Sara

Meloni Simone