SIMBIOMA network

Report of the workshop « Simulation of biological matter », as part of the general conference CCP2007, the international conference on computational Physics, organized from september 5th, till 8th, in Brussels.

Summary

The workshop funded by ESF, through its RNP SIMBIOMA, was held as one part of the general conference CCP2007, which was attended by 328 participants (registred). The complete programme of the conference has been forwarded separately to ESF, here we focus on the specific aspects related to the simulation of biological matter. Note that another CCP2007 session was dedicated to applications of Wang-Landau algorithms to protein foldings, there was also a session dedicated to nanofluidics implying some biological content. Around 10 posters directly related to the SIMBIOMA sessions were presented. Their titles can be found in the extended conference abstract list which is being sent separately.

The conference will have proceedings and part of the lectures provided in this session will be reproduced in the special issue of CPC (Computer Physics Communications, Elsevier) related to CCP2007. This issue will appear early 2008, with M. Mareschal as special guest editor. R. Lavery, I. Pagonabarraga, P. Carloni and U. Roethlisberger have papers accepted in this issue.

Scientific content

Here are the abstracts of the talks presented inside the SIMBIOMA session.

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Mechanics and function in biomacromolecules

Structure is clearly a major factor in determining how biological molecules interact with, and act on, their molecular environment. However, structure also implies specific mechanical properties which can also play a role in these processes. Experimentally, molecular mechanics is less easy to study, although single molecule experiments are now making significant headway in this area. Computer simulations offer another promising route to understanding the mechanics of macromolecules and their possible functional roles. I will present recent work we have carried out on enzymatic proteins and on protein-nucleic acid interactions which both highlight the very heterogeneous nature of macromolecular deformations and suggest how this heterogeneity has been exploited by evolution to promote specific

interactions or reactions. The techniques we have used range from computationally inexpensive coarse-grain elastic models to large-scale grid calculations on all-atom models.

Berend Smit

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Mesoscopic simulations of the interactions between transmembrane peptides

In this presentation we describe the development of a mesoscopic model of a phospholipid membrane. Using Dissipative Particle Dynamics we show that this model gives a realistic description of the phase behavior of membranes [1]. We use this model to study the interactions between transmembrane peptides. In particular we show how the interactions between the peptides depend on the hydrophobic mismatch, which is defined as the difference between the hydrophobic thickness of the membrane and the hydrophobic length of the peptide.

[1] Venturoli, M., Sperotto, M. M., Kranenburg, M., & Smit, B. *Mesoscopic models of biological membranes* Phys. Rep. **437**, 1-54 (2006).

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A coarse-grained protein and solvent model for protein-protein interactions

In order to study protein-protein interactions, we present the development of a new reduced protein model that represents each amino-acid residue with one to three coarse grains, whose physical properties are derived in a consistent bottom-up procedure from the higher resolution all-atom AMBER force field. The resulting potential energy function is paiwise additive and includes distinct Van-der-Waals and Coulomb terms. The Van-der-Waals effective interactions are deduced from preliminary molecular dynamics simulations of all possible aminoacid homodimers. They are best represented by a soft $1/r^6$ repulsion and a gaussian attraction, with parameters obeying Lorentz-Berthelot mixing rules. For the Coulomb interaction, coarse grain charges are optimized for each separate protein in order to best represent the all-atom electrostatic potential outside the protein core. This approach leaves the possibility of using any implicit solvent model to describe solvation effects and electrostatic screening. The coarse-grained force field is tested carefully for a few homodimeric complexes and it does reproduce satisfactorily the specificity of the all-atom underlying potential, in particular within a Poisson-Boltzmann/Surface Area solvation model. It also provides per se an efficient and discriminating scoring energy function for protein-protein docking, that remains pertinent at both the global and refinement stage. A numerically efficient coarse-grained water model, based on polarisable pseudo-particles, is introduced too. It is shown to describe quantitatively solvation free-energies and electrostatic screening. The coarse-grained protein and solvent models are used consistently for molecular dynamics simulations of protein-protein association in solution.

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Cooperative dynamics in biofluids: from filaments to propellers

I will discuss how mesoscopic simulation methods can be implemented to study the collective behavior of suspended objects of biophysical interest on the time scales in which they evolve. I will in particular consider the interaction between semiflexible filaments (which constitute simplified models of biopolymers, and which can be also be used to analyze cooperative motion of flagella) and a the dynamics of suspensions od self propellers which interact dissipatively through the embedding solvent.

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Investigating neuro-degenerative diseases with molecular simulation

This contribution describes recent computational studies related to proteins involved in Parkinson's Disease (PD). The first focuses on the interplay between dopamine and alpha-synuclein (AS), which plays a central role in PD. The second deals with the protein DJ-1, whose mutations are present in patients suffering from familiar PD [1]. Computational methods are used to investigate the relationship between such mutations and the protein oligomeric state, which may be important for the progression of the disease.

REFERENCES

1. F.E. Herrera, S. Zucchelli, A. Jezierska , A.S. Lavina , S Gustincich, P. Carloni, *J. Biol Chem.* 2007 (Epub)

Ursula Röthlisberger : DFT methods in biological simulations

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Protein-DNA recognition : breaking the combinatorial barrier	Cyril Delembre Richard Lavery* Krystyna Zakrzewska	richard.lavery@ibcp.fr
On the nature of the	V. Carnevale	carloni@sissa.it

reaction intermediate in the HIV-1 protease : a quantum chemical study	S. Raugei S. Piana P. Carloni*	
Cooperativity and hydrodynamic interactions in externally driven semiflexible filaments*	I. Lopis M. Consentino Lagomartinopaul I. Pagonabarraga*	ipagonabarraga@ub.edu

Future trends in the field

As seen from the abstracts presented, the biological simulations require several levels of description, ranging from quantum modeling (at least within DFT approaches) towards mesoscoping modeling, where length and time scales are closer to what is directly experimentally observed. There is a consensus in the community present at the conference that biology is one of the major field of applications of the new methods developed nowadays. More specifically, it was stressed in the discussions

• Embedding quantum description within a classical force-field simulations is becoming routine work, as long as non-adiabatic effects are excluded. The case of diabatic quantum dynamics remains a theoretical challenge for chemists and physicists

• the field will profit from new algorithms developed in critical phenomena, such as Wang-landau algorithms, in particular in the fundamental questions arising in the understanding of protein folding and alike

• more and more mesoscopic modeling is being done, reaching a point where contact to experiments will be done in a quantitative way. Multiscale developed in materials research will be of tremendous importance for reaching those scales of simulations, with a satisfactory level of precisions.

• Protein-membrane, and protein-protein interactions are topics of great importance where a real progress can bee xpected in the coming years, for the reasons listed above

• Connections to systems biology type of approaches has been mentionned but remain, at this time, virtual. It might become more and more real once methods and algorithms develop.

Final programme

See the file `ccp2007_resumes_total02-09.pdf`, sent separately.