Multi-Scale modelling of biological processes

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Proposal

1.1 Introduction and motivation

A new generation of experimental techniques is now capable to provide unique information on the dynamics and stability of proteins and molecular assemblies, during cellular processes. Despite these progresses a full and microscopic understanding of how the cellular crowded environment influences these functional processes, e.g. molecular transport or pathogenic misfolding and aggregation, is still lacking. A support from in silico molecular modelling is therefore necessary. However, from the computational point of view, in order to study processes at the cellular level, and beyond, and shake hands with the experimental studies, it is necessary to deploy innovative multi-scale strategies. For this purpose, we have recently proposed and developed a computational scheme that by coupling particle and fluid dynamics can play with the several scales involved in the study of cellular processes. The methodology combines particle **Particle Dynamics** and **Lattice Boltzmann** description of fluid dynamics, ultimately leading to a **Multi-Scale** strategy to biological and non-biological solutions under flow or no-flow conditions. The methodology is currently implemented in an in-house developed code, MuPhy. This code, not yet public, has however been been shared in the context of several international collaborations involving the proposers and other European researchers. The cases-studies approached by the method is vast, ranging from the unfolding of protein under perturbing shear flow, to the dynamics of red blood cells in arterial system. **The goal of the present proposal is to support a first meeting among the actors active in this network of punctual collaborations, and therefore support the constitution of a community centred on the developed multi-scale methodology.**

1.2 State of the art

The quantitative description of flowing matter traditionally relies upon two basic pillars: **continuum fluid mechanics** and **atomistic/molecular dynamics**. The former describes matter as a collection of space-filling (continuum) fields, say density, pressure and flow, whereas the latter explicitly acknowledges the discrete nature of the microscopic constituents of matter, i.e., atoms and molecules. By definition, they deal with very different ranges of space and time scales, which we denote generically as macro and micro, respectively. Nowadays, because of the growing computer power and the development of efficient algorithms, we are experiencing, from the numerical point of view, a possible overlap between the scales.

The multi-scale modelling of soft and condensed matters deals with this grey zone where the boundary between micro and macro is fuzzy. This zone that we generally referred to as meso-scale is the playground for different computational strategies. For instance, within the particles based approach, an atomistic model can be coupled with coarser descriptions, e.g. coarse-grained models of different resolutions [1, 2]. This embedded scheme that evokes what back in time proposed for mixed quantum-classical simulations [3] has been applied to bio-systems [1] and liquids [5].

In our strategy, we propose a more radical approach, where two different physical descriptions of reality are brought together. This multi-scale modelling that we label LBPD, for Lattice Boltzmann Particle Dynamics is based on the coupling of fluid and particle dynamics [6,7]. The LB part takes care of the continuum sector, typically the flow solvent, while the PD is in charge of molecular motion. The distinctive trait of LBPD is that both micro and macro descriptions are inherently based on mesoscale (coarse-grained) representation of both solvent and molecular components. In other words, LBPD is strongly rooted within the two pillars of kinetic theory: the Boltzmann equation and stochastic particle dynamics. While this approach was originally designed to study polymer physics [6], only recently and thanks to our effort, it has been exported to the field of bio-simulations. At the molecular scale this corsair attempt has benefitted of the parallel development of an efficient coarse-grained model for proteins, able to reproduce their internal flexibility as well as their intermolecular interactions [8].

1.3 **Objectives**

So far, the methodology has been applied to challenge intriguing biophysical problems like the aggregation of amyloid peptides a key process in the development of Alzheimer diseases, the behaviour of crowded protein solutions, the unfolding of small proteins under shear, the haemodynamic, polymer translocation. Willing to test the potentiality of the methodology at different time and length scales, a set of punctual collaborations has been also established and is allowing to treat systems never explored. This includes the problem of electro-diffusion in neurons, the functional response of proteins under physiological shear, the flow of physiological fluids such as blood in arteries and air in the nasal cavity, the translocation of DNA in nano-pores, and many others, multi-phase and charged fluids, bigels, and so on.

Each of these challenges is requiring ad hoc developments of special features that are enriching the base methodology. For instance, the problem of electro-diffusion in neuron requires the coupling among the LB description at nanoscales, the Enskog level of description of molecular fluids to include hard-core correlations, and electrostatics as the basic mechanism that moves matter in nano-spaces.

The objective of the meeting is to create a first contact among the actors of these collaborations so to share the on-going research, and the technical/conceptual problems involved in each line of research. This meeting must be intended as a nucleation event so to boost the emergence of a mini-community cantered around the LBPD methodology.

The meeting will cover two days. The work will start in the morning with a public seminar by S. Succi (Rahman Prize for Computational Physics 2017). In the afternoon half of the invited participants will present their research with a talk of 40 min followed by informal discussion. At the end of the afternoon an informal discussions time-slot will be organized so to stimulate discussion on practical experiences, e.g. computational performances, further methodological developments etc. The meeting will continue for

half day (morning) with the second round of talks from the invited participants (four talks). The talk of the invited participants will be open to the hosting laboratory members, and specific invitations to join the discussion will be sent to researchers of the Paris area and active in the field of multi-scaling. During the meeting an informal poster session will be held during a coffee break where the students of F. Sterpone lab will present their work on multi-scaling. During the afternoon of the second day, depending on the participants, discussions about the on-going collaborative works will take place in the spaces at the LBT.

Bibliography

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1.4 Participant List

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2. *Financial Support*

We request a funding of **4,000 Euros**. This funding has been estimated according to the following costs:

1. Travel costs for 6 foreigners participants (3000 Euros)
2. Lunch/Diner meeting day for participants (700 Euros)
3. Coffee breaks (300 Euros)

The cost for accommodation will be covered with extra independent financial support