Molecular simulations - en route to the computational microscope

Luca Monticelli*[1]

[1]Molecular Microbiology and Structural Biochemistry (MMSB) – Centre National de la Recherche Scientifique - CNRS, Université Claude Bernard - Lyon I (UCBL) – 7 passage du Vercors 69007 Lyon, France

Résumé

Computer simulations at the atomistic and molecular level can describe biological systems with sub-nanometer spatial resolution and femtosecond time resolution. Pioneered by Warshel, Levitt, Karplus, and others in the 1970's, molecular simulations were initially used to investigate the motions of a few hundred atoms on picosecond time scales; nowadays they can include tens of millions of atoms, and reach time scales of milliseconds. The enormous progress in length and time scales accessible to molecular simulations is due to the fast development of computer technology and to the evolution of simulation software and methodologies. Progress has also been significant in the accuracy of the predictions afforded by molecular models, leading some scientist to use the term "computational microscope" referred to molecular simulations. I will present examples of how molecular simulations are used today in biology, focusing on the dynamic view of biological membranes studied in my laboratory. I will highlight the role of methodological development, exemplified by the commitment to the improvement of force fields at the all-atom and coarse-grained level; then I will mention applications of current methodologies to problems of biological and pharmaceutical relevance, such as membrane permeation of drugs and pollutants, the interaction of synthetic materials with cellular membranes, and the biogenesis of lipid droplets. I will conclude by indicating some of the limitations of current molecular models, and suggesting avenues for future development.

Mots-Clés: molecular simulation, molecular dynamics, coarse, grain, biological membrane, membrane permeation, lipid droplet

*Intervenant