THE USE OF MOLECULAR DYNAMICS SIMULATIONS IN THE REFINEMENT OF CRYSTALLOGRAPHIC STRUCTURES

Fernandes, C.L. [1], Becker, C.F. [1], Menegon, G. [1], Lima, L.M.T.R. [3], Verli, H. [1,2]
[1]Centro de Biotecnologia, UFRGS, Porto Alegre, Brazil; [2]Faculdade de Farmácia, UFRGS, Porto Alegre, RS; [3]Faculdade de Farmácia, UFRJ, Rio de Janeiro, RJ

Most of the current knowledge about three-dimensional (3D) structures of biological macromolecules is originated from X-ray crystallography. Probably the most critical step of such methodology is to produce a crystal of the macromolecule. However, the supersaturation of the protein solution and the packing of molecules in the crystal may originate a series of non-biological intermolecular contacts, capable to distort the macromolecule conformation. An additional technique in the characterization of the 3D structure and conformation of macromolecules, capable to mimic the biological environment, is the molecular dynamics (MD). Such technique, generally starting from an X-ray obtained structure, is capable to describe its conformational dependence on the surrounding medium as a time dependent variable. In this context, our group has applied MD in the study of several proteins, including the antithrombin, the HIV-1 matrix protein, the *Apis mellifera* melittin, the E2 proteins from papillomaviruses and the suramin-thrombin complex. In all cases, MD simulations were capable to describe a series of conformational modifications, as folding and unfolding of secondary structure elements, deoligomerzation and ligands reorientation. As all these conformational modifications are plentifully supported by experimental data, we propose the use of MD simulations as an important tool for the refinement of crystallographic structures of macromolecules.