Molecular Monte Carlo Simulations (and Their Surroundings): Developments and Applications to Systems of Biological Interest

Julian Tirado-Rives
Department of Chemistry, Yale University, New Haven, CT 06520, USA

Molecular Simulations have contributed greatly to our understanding and use of biological systems and processes. The generation of an appropriate ensemble to study the properties of a given system can in principle be done by using Monte Carlo (MC) or Molecular Dynamics (MD) algorithms. However, since the first Molecular Dynamics simulation of the protein BPTI in 1977[1] the field has been dominated by MD. This talk will illustrate some of the algorithmic and functional differences between the MD and MC methods, selected aspects of the development of the MCPro software package[2] to conduct MC simulations of biomolecules, including methodology that can be generally applied to other systems and methods. In particular the evolution of the OPLS force fields,[3] and QM/MM calculations.[4]

The development and use of some of these methods will be illustrated through selected applications to study enzymatic reaction mechanisms, protein-ligand binding and ultimately Structure Based Drug Design.[5]

1. McCammon, J. A.; Gelin, B. R.; Karplus, M. *Nature* **1977**, *267*, 585-590. doi:10.1038/267585a0
2. Jorgensen, W. L.; Tirado-Rives, J. *J. Comput. Chem.* **2005**, *26*, 1689-1700. doi:10.1002/jcc.20297.
3. Robertson, M. J.; Tirado-Rives, J.; Jorgensen, W. L. *J. Chem. Theory Comput.* **2015**, *11*, 3499-3509. doi:10.1021/acs.jctc.5b00356.
4. Vilseck, J. Z.; Kostal, J.; Tirado-Rives, J.; Jorgensen, W. L. *J. Comput. Chem.* **2015**, *36*, 2064-2074. doi:10.1002/jcc.24045.
5. Cole, D. J.; Tirado-Rives, J.; Jorgensen, W. L. *Biochim. Biophys. Acta, Gen. Subj.* **2015**, *1850*, 966-971. doi:10.1016/j.bbagen.2014.08.018.