[P31] Pump-Probe Molecular Dynamics Simulations of Allosteric Proteins in GROMACS

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Allostery is a broad phenomenon common to all folded proteins under some conditions [1]. It is characterized by the fact that an action in one part of the molecule causes an effect at another site. Allosteric effect can involve changes in the mean conformation (enthalpic effects) but also changes in the dynamic fluctuations about the mean conformation (entropic effects) [2]. Since it occurs on timescales of microseconds, its study by conventional molecular dynamics is very time-consuming. Pump-probe molecular dynamics (PPMD) overcomes this difficulty by exciting selected atoms or residues with a set of oscillating forces of a specified magnitude, direction, and frequency. This oscillation is transmitted throughout the structure by the sparse network of interconnected residues. The transmission of the impulse to other parts of the protein is probed at various sites using the Fourier transform of the atomic motions. Subsequently a coupling profile can be determined using the covariance terms [3] and the degree of interaction between interconnected residues can be quantified [4].

We had implemented PPMD method in the mdrun program of GROMACS package. Another GROMACS program was introduced to provide FFT analysis of PPMD trajectory. Several sets of tests were made and finally it led to a reasonable data. Currently we are testing the influence of different setups and chosen parameters like frequency, amplitude, direction, force field, solvent treatment, etc. We also plan to map allosterically interconnected parts in G-protein coupled receptors (targets of more than one third of all medical drugs available on the market). Last but not least PPMD method is going to be implemented in the form of web server for the wider academic community.

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