Peptide's dynamics between structural transitions

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Motivation: Folding and conformational changes of peptides and proteins are predominantly determined by the φ and ψ dihedral angles' dynamics of the backbone of the biopolymer. The angle values are bounded by the steric restrictions of the backbone and the side chains. This is reflected in specific distributions of the points on the Ramachandran φ-ψ plots where most of the points are concentrated at restricted areas characteristic to each aminoacid. Dynamically this results in a situation when the biomolecule exhibits well separated periods of stationary fluctuations and quick transitions between them (Fig. 1). Elucidating the dynamical structure of the system's trajectories at these regimes is very important because they define the proteins' conformations and functioning.

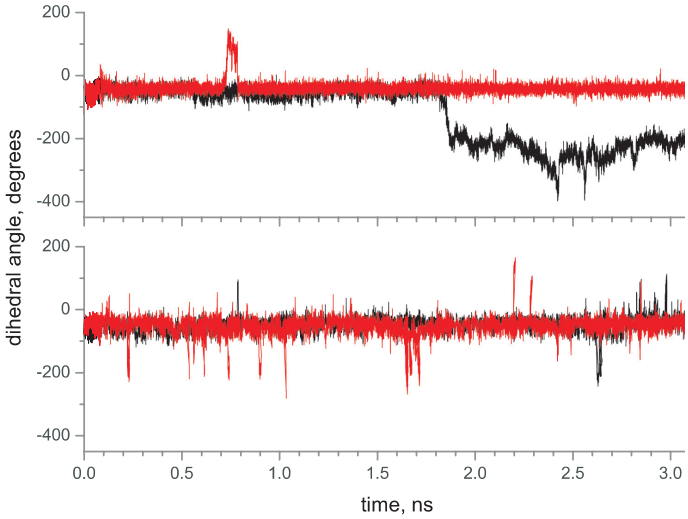

Figure 1. Time evolution of two representative dihedral angles of a 21-residue peptide showing two regimes of fluctuations for each angle. Top: no perturbation; bottom: minimal perturbation.

Method: A 21-residue peptide $A_5(A_3RA)_3A$, that is known to fold in 0.8 μs[1], was MD simulated in explicit water using GROMACS[2]. The dynamics in the stationary regimes are investigated by preventing the molecule of making the transitions. This is done by the perturbations of the trajectory just before the transitions occur. The perturbations are minimal: the velocity of only one atom of the system was randomly rotated by a few degrees (this keeps the system on the same energy surface). We find that despite such a small perturbation (these changes happen few dozens of times on a 6 ns run) it is possible to keep the molecule in the same dynamic regime without entering conformational transitions. It would be reasonable to assume that periodic random perturbations of the same type would have the same effect on the system.

Results: 1. Perturbations at the start of the transitions prevent the transitions; most of the times only one perturbation is enough, however for some transitions several attempts are required to prevent the transition. 2. Periodic perturbations do not prevent the biomolecule from the transitions. 3. Perturbations of water atoms have the same effect as the perturbations of the peptide's atoms. We suggest the following interpretation of these results: 1. The dynamics in the stationary regimes are not random, otherwise the periodic perturbations would have the same effect as the perturbations before the transitions. 2. Most of the trajectories in the stationary regimes quickly (not by random exploration) lead to a transition because the jumps between the trajectories caused by the periodic perturbations do not prevent the transitions. 3. Dynamically water is as important as the peptide itself since perturbing the water atoms have the same qualitative effect as the perturbations of the peptide's atoms.

References:

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