DYNAX: A New System for Biomolecular Dynamics Simulation in Solution

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1 Introduction

One of the ordinary methods to understand accurately the intermolecular interactions and transition undergoing in a biomolecule is the dynamics simulations carried out with the assistance of computers. The advent of more powerful and low cost computers has made this type of simulations routine work and many semiempirical potential functions are being continuously improved in order to reduce even more the processing time and express more accurately intermolecular interactions. However many such simulation systems still oversimplify the interaction of the protein atoms with the solvent. In this work we have developed a new system for biomolecular dynamics simulation whose main characteristic is the use of a new potential energy proposed to explicitly take into account the solvent effect on the structural characteristics of biomolecules.

2 Solvent Effect

The main characteristics of our potential function are the consideration of the solvent as a continuum medium, and the computation of the solvent effect as the sum of two interaction energy terms: (i) A hydrophobic interaction term and (ii) a solute-solvent electrostatic interaction term [1]. The hydrophobic interaction term is calculated as a function of the solvent accessible surface area (SASA) of the protein, while the electrostatic interaction term is computed by means of the generalized Born equation [2].

3 Dynamics Simulation

Protein dynamics calculates the motion of the atoms in a protein by generating the changes of the atomic coordinates as a function of time. At each time step, new positions and velocities of each of the atoms are determined by solving the equations of motion using the old positions, the old velocities and the accelerations, always under the restriction imposed by the law of energy conservation.

To compute new positions, velocities and accelerations of the atoms composing the protein, we use the elemental Newton equation and the formula proposed by Beeman to solve the resulting differential equation [3].

Protein dynamics simulations using the system developed in this work has allowed us to define two new characteristics for polypeptides in function of which particular properties of protein folding can be expressed. These two characteristics are:

(1) The Fluctuating Hydrogen Bond: As effect of long term dynamics (2 ps) several hydrogen bonds are broken and new formed, being a characteristic of the particular protein the number of these

fluctuating hydrogen bonds. Furthermore, its calculation is a measure of the stability of a determined conformer.

(2) The Fluctuating SASA: Dynamic simulations using our system allow the definition of this new property, which is directly related to the solvent pressure on the atoms constituting the protein. The calculation of the fluctuating SASA for regions in the protein allows the computation of a fluctuating solvent-protein configuration.

4 Results and Discussion

Several properties and new parameters can be obtained by the dynamics simulations of proteins. One such calculation is the rate of ordering and reordering of the protein in what are called secondary structure elements of protein structures, (α helices, β sheets, coils, etc.). Our system also allows to path the trajectory followed by interprotein segments, such as sense anti-sense peptides, leading to new insights in the field of protein engineering and specifically in protein folding processes.

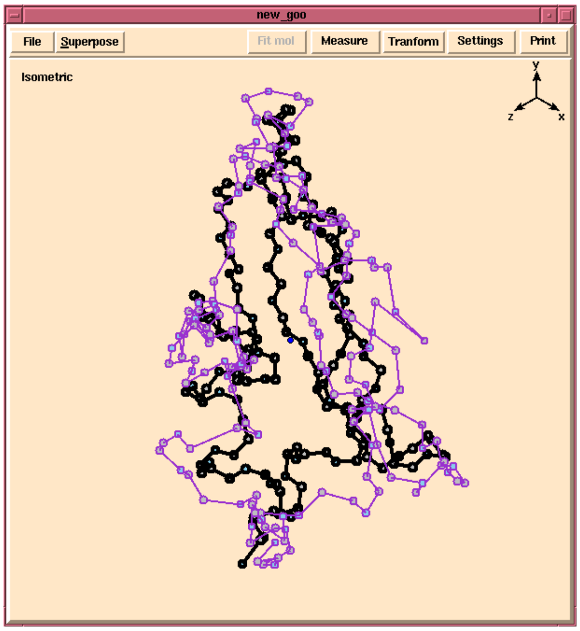

Figure 1: Dynamics Simulations of BPTI,using Dynax (2ps).

References

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