Protein Folding studies using a Grid Computing Platform

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ABSTRACT

During the last years computational simulations based on the atomic description of biological molecules have been resulted in significant advances on the comprehension of biological processes. It is well known, however, that a molecular system has a great number of conformations due to the great number of degrees of freedom in the rotations around chemical bonds, leading to several local minima in the molecular energy hyper-surface. It has been proposed that proteins, among the great number of possible conformations, expresses their biological function when their structure is close to the conformation of global minimum energy. In order to solve this kind of problem, in this work it is used a new strategy based on the Simulated Annealing methods. These methods have been well suited to a large extent of optimization problems, specially those containing many local minima. In particular, it is applied the Generalized Simulated Annealing method (GSA) [4] for the search of the minimum energy conformation in peptides. Some software tools are employed in this study, such as the Molecular Force Field GROMOS96 and the GSA algorithm implemented in the molecular simulation program, THOR, developed by the Laboratory of Biological Physics IBCCF - UFRJ.

In the GSA procedure, an artificial temperature is introduced, which is gradually cooled, being extremely convenient for eventually detrapping from local minima. The torsion angles are then randomly displaced according to a visiting distribution. These jumps can be accepted or not according to an acceptance probability. The cooling is adjusted by the parameter q_T, while the visiting distribution function and the acceptance probability function are adjusted by the parameters q_V and q_A, respectively. The efficiency of the GSA procedure consists on the right choice of these parameters.

Recent work presents a successful investigation for the helical propensities of polyalanines [2]. That work presents a q_V and q_A parameter choices that reaches global minimum for more than 50% GSA simulations, where the helical structure can be obtained by using only a few steps compared with conventional methods.

In order to search the better q_T, q_V and q_A parameters for the global otimization of a polyalanine, containing 18 residues, we need over 8.000 hours processing time using an Athlon 1000 MHz processor. Besides, we pretend applying the method to larger and heterogeneous polypeptides. To make possible the global optimization of a protein, a GRID environment is being developed for the execution of THOR processes through the middleware MYGRID [1]. MYGRID is a user-centric grid middleware that provides a global execution environment which permits the remote execution of a large amount of parallel tasks through the machines that the user has access. So as to investigate THOR execution on a GRID environment, we successfully run 60 THOR execution simulation on a 57 GRID machines environment [3].

Massive calculations for the prediction of protein structure in a GRID may be an important step in order to fill in the huge gap between the knowledge of the aminoacids sequence that compose proteins and the determination of tridimensional structures through experimental methods, such as X-ray Crystallography and Nuclear Magnetic Resonance.

This work search the better q_T, q_V, and q_A parameters for the global optimization of a polyalanine containing 18 residues, which is the first step toward a THOR-GSA simulations in a GRID environment

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