

ProMode: A Database of Normal Mode Analysis of Proteins

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1 Introduction

Computer simulation of protein molecules plays an important role to understand the principle of architecture of protein structures and their functions. There are several conventional methods to simulate the protein dynamics by computer, for example, Monte Carlo simulation (MC), molecular dynamics (MD), and normal mode analysis (NMA). The MC and MD are more reliable than the NMA, because the NMA is based on the harmonic approximation (in other words, the MC and MD can cover much wider area of conformational space of the protein than the NMA). However, many studies have shown that the results from the NMA are qualitatively reasonable in most cases, compared to those from the MC and MD. Fortunately, the NMA is much less time-consuming in computation and more systematic and more adequate than the MC and MD for the analysis when it is intended to carry it out routinely for many proteins. In this context we are constructing a database of the NMA of the proteins called *ProMode*. In the database the results of the NMA are being collected so that the dynamical structures of the proteins can be investigated in comparison of various proteins.

2 Method and Results

2.1 Regularization and Energy Minimization

For the NMA in *ProMode* we use a full-atom molecular model of a protein. The most time-consuming part in the NMA is to obtain the energy-minimum conformation very close to the one of the corresponding Protein Data Bank (PDB) data (we refer to this procedure as regularization and energy minimization of PDB data). We use the program FEDER/2 developed by us [2] for this purpose, because the regularization and energy minimization can be carried out rapidly and efficiently.

Since the PDB data have slightly different bond lengths and bond angles from the standard values used in our calculation (note that calculation is carried out in fixing the bond lengths and bond angles to these standard values, because FEDER/2 treats dihedral angles as independent variables), the conformational energy minimization starting from the PDB data leads to the three-dimensional structure deviating from the PDB data slightly or sometimes drastically. In order to obtain the energy-minimum conformation very close to that of the PDB data for the NMA, we carry out the restrained energy minimization. Finally we perform the energy minimization without any artificial restraints to obtain the energy-minimum conformation, for which the NMA is performed.

2.2 Normal Mode Analysis

In the NMA, once the normal mode vectors, their frequencies and their amplitudes are obtained, various properties can be calculated easily. At present the following properties are available in *ProMode*.

- (1) Averages over all modes
 - a) mean fluctuations of atom positions and their mutual correlations.
 - b) mean fluctuations of dihedral angles.
- (2) Properties related to each normal mode vibration
 - a) fluctuations of atom positions and their mutual correlations
 - b) fluctuations of dihedral angles
 - c) results from DynDom
 - d) animation of normal mode vibrations

In this database the program DynDom [1] is used to analyze the results from the NMA. DynDom defines domains of the proteins from the dynamical aspects. The hinge axes and amino acid residues involved in the hinge bending motions are also defined. In *ProMode* the two conformations, the energy-minimum and the fluctuated ones in each normal mode vibration are used as input data for DynDom.

The numerical results from the NMA are available, and also shown in graphic charts and diagrams in the web pages (*ProMode* is tentatively uploaded in PDBj [4]). It is also possible to see the animation of normal mode vibrations and dynamical domains defined by DynDom, if the plug-in free software Chime [3] is installed in your browser.

3 Discussion

The static pictures of three-dimensional structures of proteins directly derived from PDB have provided useful information about the principle of protein architecture and their functions. However, the approach to the proteins only from the static aspect is not sufficient. The dynamic pictures are necessary. Although the PDB data provide such a kind of information through temperature factors, what we can obtain from it for the dynamics is limited. This is the reason why the dynamics simulation is required to derive the information about protein dynamics from the PDB data.

However, the simulation requires much computer resources and experts to perform it. Although a comparative study of various proteins is expected to provide the new aspects for the proteins, it is quite difficult to perform the MC and MD for many proteins. We expect that *ProMode* is useful especially for the protein researchers not familiar to the dynamics simulation. The observation of protein motions through the animation of the normal mode vibrations may give the impact on them. Although the MC and MD simulations may be necessary to understand the biologically significant motions in connection with the normal mode vibrations and to confirm the observed facts in the NMA, *ProMode* can play a role as the first step to approach to the protein structures from the dynamical aspects.

References

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