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KOSMOS: Macromolecular Morph Server*

Sangjae Seo** and Moon Ki Kim**, ***

**Department of Nano Science and Technology, Sungkyunkwan University

E-mail:bumsei@skku.edu

*** School of Mechanical Engineering, Sungkyunkwan University

300 Cheoncheon-dong Suwon, South Korea

E-mail:mkkim@me.skku.ac.kr

Abstract

Based on various elastic network models such as full atom, backbone, C α coarse-grained and hybrid one, KOSMOS is the first web server to provide both normal mode analysis and transient pathway generation of macromolecules including proteins and nucleic acids. In the hybrid model, a system is decomposed into rigid cluster domains and flexible regions. Translation-rotation of rigid clusters and local movement of point masses are both taken into account. One can access databases with various simulation options not only to retrieve simulation outputs using JMOL plug-in, but also to download computed parameters and atomic coordinates in the PDB format. As an example, vibration modes and translocation mechanism of ribosome are investigated through KOSMOS web server.

Key words: Elastic Network Model, Morph Server, Protein Dynamics

1. Introduction

Normal mode analysis (NMA) has been one of the powerful computational approaches for the study of dynamics of macromolecules (Ma, 2005; Bahar and Rader, 2005). Many researchers have demonstrated that the lowest frequency normal modes of proteins are strongly correlated with large amplitude conformational transitions, which are implicated in biological functions of proteins. In particular, the large scale conformational changes play crucial roles in ligand binding, signal transduction and allosteric responses of proteins such as chaperonin GroEL, hemoglobin and aspartate transcarbamylase (Ma and Karplus, 1998; Chunyan et al., 2003; Thomas et al., 1996).

Despite of the effectiveness of NMA, computational cost, especially in case of large protein structure, is still the major challenge. Noteworthy, several studies have shown that the computational burden can be reduced dramatically by separating rigid domains from flexible bodies. The first attempt was the rotations-translations of blocks approach (RTB) proposed by Sanejouand group (Tama et al., 2000). RTB considered consecutive amino-acid residues as a pure rigid body block. The block normal mode (BNM) method (Li and Cui, 2002) was proposed to reduce the storage size in diagonalization step of RTB method by the projection matrix. The cluster NMA (Schuyler and Chirikjian, 2004) and hybrid normal mode analysis (HNMA) technique (Kim et al., 2005) have been developed to overcome several limitations in RTB and BNM method. cNMA and HNMA can directly convert Cartesian coordinate into rigid clustering, vice versa, without any projection, whereas RTB and BNM method transform the full Hessian matrix into a reduced subspace. Here, we introduce KOSMOS as the first web server built upon the HNMA technique for the various purposes.

2. Method

KOSMOS performs NMA of macromolecules based on elastic network models (ENMs). Firstly, the coordinates of C α and phosphate are sampled from input file for representing amino acids and nucleotides, respectively. All the representative atoms are then networked with virtual linear springs. The connectivity among atoms is determined by a distance cutoff rule. The