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An Effective Modification to Multiscale Elastic Network Model and Its Evaluation Based on Analyses of Protein Dynamics

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Abstract : Dynamics plays an essential role in function exertion of proteins. Elastic network model (ENM), a harmonic potential-based and cost-effective computational method, is a valuable and efficient tool for characterizing the intrinsic dynamical properties encoded in biomacromolecule structures and has been widely used to detect the large-amplitude collective motions of proteins. Gaussian network model (GNM) and anisotropic network model (ANM) are the two often-used ENM models. In recent years, many ENM variants have been proposed. Here, we propose a small but effective modification (denoted as modified mENM) to the multiscale ENM (mENM) where fitting weights of Kirchhoff/Hessian matrixes with the least square method (LSM) is modified since it neglects the details of pairwise interactions. Then we perform its comparisons with the original mENM, traditional ENM, and parameter-free ENM (pfENM) on reproducing dynamical properties for the six representative proteins whose molecular dynamics (MD) trajectories are available in http://mmb.pcb.ub.es/MoDEL/. In the results, for B-factor prediction, mENM achieves the best performance among the four ENM models. Additionally, it is noted that with the weights of the multiscale Kirchhoff/Hessian matrixes modified, interestingly, the modified mGNM/mANM still has a much better performance than the corresponding traditional ENM and pfENM models. As to dynamical cross-correlation map (DCCM) calculation, taking the data obtained from MD trajectories as the standard, mENM performs the worst while the results produced by the modified mENM and pfENM models are close to those from MD trajectories with the latter a little better than the former. Generally, ANMs perform better than the corresponding GNMs except for the mENM. Thus, pfANM and the modified mANM, especially the former, have an excellent performance in dynamical cross-correlation calculation. Compared with GNMs (except for mGNM), the corresponding ANMs can capture quite a number of positive correlations for the residue pairs nearly largest distances apart, which is maybe due to the anisotropy consideration in ANMs. Furtherly, encouragingly the modified mANM displays the best performance in capturing the functional motional modes, followed by pfANM and traditional ANM models, while mANM fails in all the cases. This suggests that the consideration of long-range interactions is critical for ANM models to produce protein functional motions. Based on the analyses, the modified mENM is a promising method in capturing multiple dynamical characteristics encoded in protein structures. This work is helpful for strengthening the understanding of the elastic network model and provides a valuable guide for researchers to utilize the model to explore protein dynamics.

Keywords : elastic network model, ENM, multiscale ENM, molecular dynamics, parameter-free ENM, protein structure
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