Stochastic Analysis of Native State Protein Dynamics

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INTRODUCTION

Proteins have been of great interest due to being the building blocks of all living organisms and having special functions in the cell. to understand the behaviour of these long chain molecules, especially the dynamics were investigated. Since the time scale of dynamics of the protein chains were in nanoseconds, the experimantal approaches were insufficient. Thus new computational approaches were proposed. In this project, a stochastic analysis was proposed to determine the protein dynamics near the native state. Through this study, it was aimed to determine the fast and slow mode behavioır of the molecule and to estimate the hotspots and hinge points of the molecule, which play crucial role in stability and functionality of the molecule, respectively.

METHODOLOGY

Stochastic analysis of the protein dynamics require a time dependent data of the fluctuations. Since no experimental data available, a computational method, off-lattice Monte Carlo algorithm was used to obtain a fluctuation data in virtual time which was accepted to represent the real time domain. The MC algorithm yield an output including the time dependent coordinates of each residue on the backbone chain. From this data, the time dependent fluctuations and the spectral density functions of these fluctuations were computed for each residue in x-y-z directions. It was proposed that the area under the spectral density funtion curve for the entire frequency range would correlate with the experimental measurement of mean square fluctuations, B-factors; area under the curve for low frequency region and the high frequency region would correlate with the slow and fast mode fluctuations, respectively. The bahviour of different modes were to be compared with another computational method GNM, which the validity has been accepted for years.

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RESULTS

The results of the method proposed were first compared with the experimental measurements, B-factors. The correlation coefficients for two different runs were calculated as 0.485 and 0.509. From the graphs of comparison of these results it was observed that the method could mimic the behaviour of the experimental measurements with good match of the minima and maxims of the experimental curve. The comparison of the slow mode behaviour obtained with the proposed method with that of GNM were resulted with correlation coefficients of 0.722 and 0.624 (figure 1); the from the curves a perfect match of behaviour of the results was obatined. The fast mode analysis was unsatisfactory. The results yield no correlation with the results obtained from GNM.

CONCLUSION

The proposed mtethod of analysing the dynamic behaviour of native state protein was satisfactory for determining the global motion of the molecule. No information about the fast modes of the molecule could be obtained. For further studies, the results from MC simulation for a higher sampling frequency may be analysed.

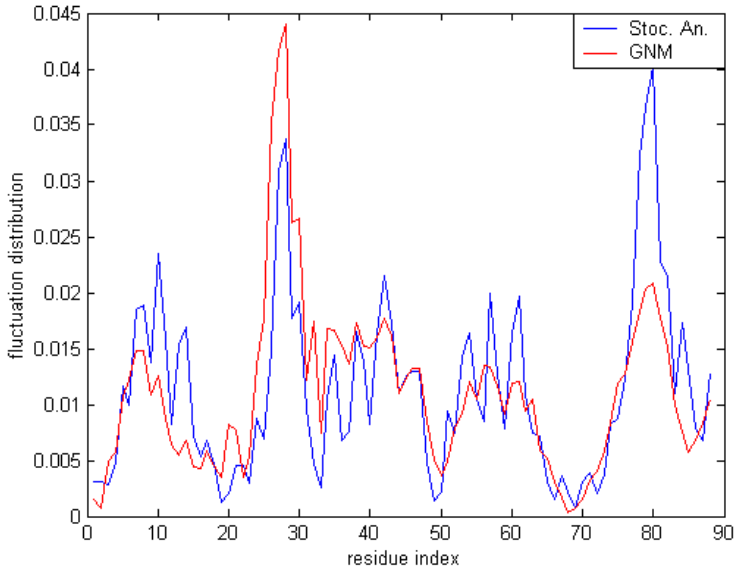

Figure 1. Comparison of the slow mode behaviour obtained by proposed method and GNM (corrcoef=0.722).