Biophysical aspect of coexistence of stability and flexibility of protein

Bagher Davaeil

Institute of Biochemistry and Biophysics, University of Tehran, Tehran, Iran

"Presented at the Postgraduate Biophysical Seminars, Autumn 98 (2019)"

Abstract

Introduction: The functional structure of proteins has the lowest energy levels with their most stable states. Protein stability refers to their thermodynamic stability, which is related to the net balance of forces. Alongside this, the protein structure has remarkable flexibility that is critical for its function. Protein flexibility refers to concerted changes that affect a few degrees of freedom, modifying the overall structure without destroying it. The relation between protein stability, flexibility and function remains one of the most challenging for scientists. This article provides a summary of the information that will help us to understanding this content.

Methods: In this study, based on the results obtained from X-ray crystallography techniques, NMR and molecular dynamic simulations (for measuring flexibility) as well as DSC and CD (for stability measurement) the subject has been investigated.

Results and discussion: The physicochemical stability and biological functions of proteins are thought to be intimately related to their global flexibility, intramolecular fluctuations and various other dynamic processes. Dynamics is concerned with timescale, amplitude and direction of motions, while flexibility is typically described in terms of thermodynamics, fluctuations and equilibrium events.

Studies have shown that the function of some proteins is strongly affected by their flexibility, and with reduced flexibility, protein function also decreases. This is especially important for enzymes that have binding sites for the substrate. Most studies have found a direct relationship between conformational stability and protein function. However concurrent changes in flexibility and stability and their affect on protein function remain a scientific challenge for researchers.

Conclusion: Due to the complex nature of proteins a certain degree of flexibility and stability is required for proteins to function at their best.

Keywords: protein flexibility, protein stability, protein function

References:

- 1. Tim J. Kamerzell, C. Russell midaaugh. Department of Pharmaceutical Chemistry, University of Kansas, The Complex Inter-Relationships Between Protein Flexibility and Stability, November 2007
- 2. Andrey Karshikoff, Lennart Nilsson and Rudolf Ladenstein. Department of Biosciences and Nutrition, Karolinska Institutet, Huddinge, Sweden. Rigidity versus flexibility: the dilemma of understanding protein thermal stability. June 2015
- 3. Satya P. Gupta, Protein Flexibility: A Challenging Issue of Drug Discovery. Current Chemical Biology, 2018, 12, 3-134.
- 4. Kaare Teilum, Johan G. Olsen, Birthe B. Kragelund. Protein stability, flexibility and function. Biochimica et Biophysica Acta 1814 (2011) 969–976
- 5. Shlomi Reuveni,1 Rony Granek,2 and Joseph Klafter1. Proteins: Coexistence of Stability and Flexibility, published 19 May 2008