Poster I-69

Datamining the Fourth Dimension from Crystal Structures: Function-Structure-Entropy Relationships in Membrane Proteins

Authors:
Ilan Samish (*Dept of Biochemistry & Biophysics, School of Medicine & Dept of Chemistry, School of Arts and Scienc*)
Avigdor Scherz (*Weizmann Institute of Science, Rehovot, Israel*)

Short Abstract: We show how variation in conformational flexibility is involved in dynamic mechanisms of membrane-proteins. Intra-protein cavities within photosynthetic-reaction-centers are involved entropic-reorganization facilitating acclimatization of energy conversion to ambient temperatures. More generally, carefully-normalized high temperature-factors in membrane-proteins point at pivotal loci to dynamic mechanisms.

Long Abstract:
Crystal Structures, the major source of protein structural information, are often regarded as static snapshots of dynamic macromolecules. Consequently, studying protein local dynamics is generally confined to short time-scale, computationally-heavy simulations. Alternatively, here we data-mine membrane-protein crystal structures for local functional variation in intrinsic flexibility. First, the mechanism conveying dynamic function in photosynthetic reaction centers is studied. In these complexes a group of hitherto unrecognized, evolutionary-conserved, intra-protein cavities and adjacent packing motif jointly impart crucial localized flexibility1. As demonstrated for mesophiles and thermophiles, the entropic reorganization allows for acclimatization of the energy conversion to the ambient temperatures. The electron-transfer shifts to non-Arrhenius behaviour above the physiological temperature thus avoiding photo-damage due to reaction over-acceleration - a phenomenon abolished when blocking the cavities1. Second and more generally, normalized B-factors in a non-redundant dataset of helical membrane proteins were assessed. Rather than normalizing according to the full structure, only the transmembrane backbone segments were used thus isolating the unique properties of these regions. Residues with high B-factors point at pivotal loci of dynamic functions, e.g. conformational gating, bond cleavage and proton pathways. These evolutionary-conserved residues are often involved in local structural deformations of the transmembrane helices, thus decreasing the rigidifying constraints of the helix. Last, variation in local flexibility along electron transfer pathways explains the dilemma between two apposing requirements - optimizing rigid geometry required for donor to acceptor wave-function overlap and conferring flexibility to quickly dissipate heat thus avoiding a back-reaction. In photosynthetic complexes the first fast and low-delta-G steps take part along a rigid microenvironment while the latter slow and high-delta-G steps take part along a flexible microenvironment. Cumulatively, datamining local variation in intrinsic flexibility is possible and provides a key tool to study the dynamic mechanism intrinsic to all multi-span helical membrane proteins.

1. Kerner, O. *, Samish, I. *, Kaftan, D. *, Holland, N., Sai, P. S. M., Kless, H. & Scherz, A. (2006). Protein Flexibility Acclimatizes Photosynthetic Energy Conversion to the Ambient Temperature. Nature (In Publication). *Equal contribution to this study.