The role of electrostatics in homo-dimeric proteins

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Introduction:

The living cell is an extremely complicated system and is comprised of hundreds of thousands of types of biological macromolecules, which constantly interact with each other to maintain the function of the cell, reflecting the dynamics of cellular networks. The interactions are very specific and frequently a particular protein macromolecule is able to recognize its partner among hundreds of thousands of candidates. At the same time, the recognition process is fast and thus some protein-protein interactions may be electrostatically guided, perhaps through a long-range force that selects and brings the interacting partners together. The best candidate for such a guiding long-range force is the electrostatic force. A rough estimate of the electrostatic energy of interaction between two molecules carrying a unit net charge and positioned at a distance 10A away from each other results in almost 1 [KJ/mol], which is much more than any other energy component contributes to the binding at such distances.

Thus, electrostatic forces and energies are essential for the interactions of virtually all biological macromolecules. The central role of electrostatics is due to the fact that most biological macromolecules, especially DNA and RNA, are highly charged. However, they are not easy to calculate because the association occurs in a water phase at specific salt concentration and pH. In addition to contributing to the binding free energy, the long-range electrostatic interactions can steer protein molecules toward their pre-binding orientations. However, some complexes are formed of identical macromolecules (homo-complexes), while others involve different entities (hetero-complexes). The main difference between these two cases is the net charge and the distribution of the charges of the monomers, which for homo-dimers is the same for both monomers, while for hetero-complexes the monomers frequently carry opposite net charges.

Many biological processes involve electron translocation on long distances. Typically the electron is delivered via electron carriers, small molecules or proteins, either across the water phase or the lipid-protein moiety. Experimental and computational investigations suggest that the shortest path is not typically utilized; rather longer trajectories are energetically more favorable. Here we investigate the role of electrostatics in two aspects: as a driving force and as a guiding environment. It is demonstrated that in case of large molecular assemblages, as mitochondria complex, the electrostatic field lines provide “electrostatic tunnel” from the electron donor to the electron acceptor sites. The tunnel does not necessary facilitate the electron transport, but provides navigation of the electron carrier throughout the complex lipid-protein moiety.

Results (ongoing project)

The electrostatic field lines forming a guiding funnel to deliver the positively charged spermidine into the active sites of spermine synthase