Electrostatics and Amino Acid Pair Distributions in Proteins

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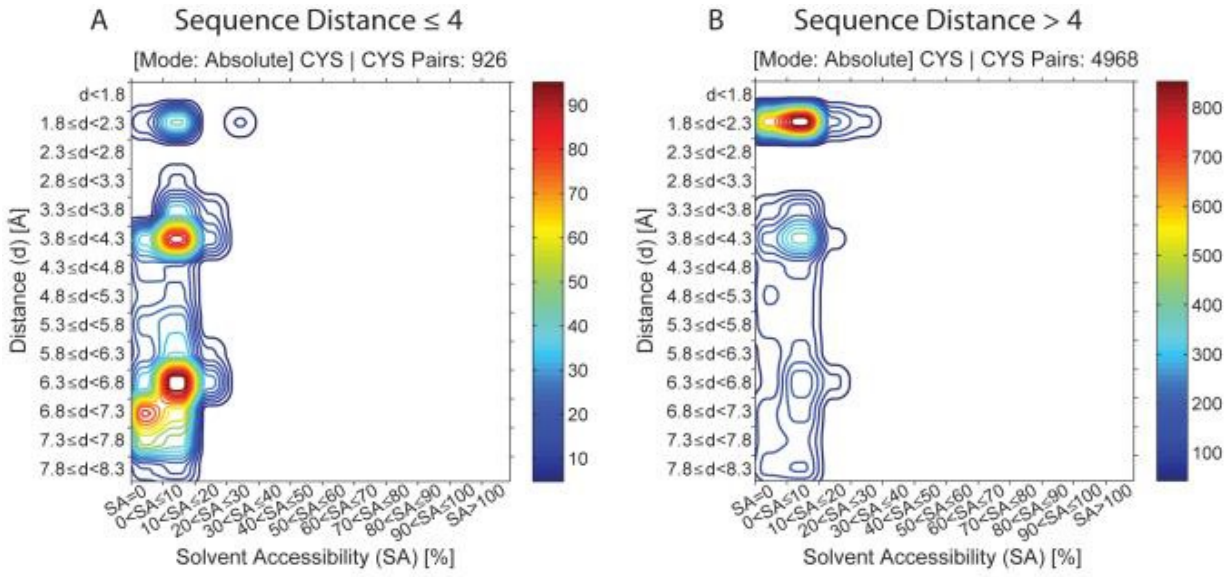
We have studied the role of pH dependent electrostatics in proteins. We have in particular studied how electrostatics influence the enzymatic activity of triglyceride lipases both in solution and at substrate interfaces. The latter represents a particular complex situation, since enzymatic products dissolve in the substrate phase. The talk will introduce the general principles of protein electrostatics and how we can improve our understanding of both enzyme function as well as receptor protein ligand interaction.
Our most recent work represents a novel approach to protein structure analyses. We have organized an 8-dimensional data cube with protein 3D-structural information from 8706 high-resolution non-redundant protein-chains with the aim of identifying packing rules at the amino acid pair level. The cube contains information about amino acid type, solvent accessibility, spatial and sequence distance, secondary structure and sequence length. We are able to pose structural queries to the data cube using the program ProPack. The response is a 1, 2 or 3D graph. Whereas the response is of a statistical nature, the user can obtain an instant list of all PDB-structures where such pair is found. The user may select a particular structure, which is displayed highlighting the pair in question. The user may pose millions of different queries and for each one he will receive the answer in a few seconds. In order to demonstrate the capabilities of the data cube as well as the programs, we have selected well known structural features, disulphide bridges and salt bridges, where we illustrate how the queries are posed, and how answers are given. Motifs involving cysteines such as disulphide bridges, zinc-fingers and iron-sulfur clusters are clearly identified and differentiated. ProPack also reveals that whereas pairs of Lys residues virtually never appear in close spatial proximity, pairs of Arg are abundant and appear at close spatial distance, contrasting the belief that electrostatic repulsion would prevent this juxtaposition and that Arg-Lys is perceived as a conservative mutation



Distribution of the observed spatial distance (Å) and solvent accessibility of the protein shell where 923 Cys-Cys pairs located at a sequence distance ≤4 residues (4A) and at a sequence distance >4 residues (4B) are found.

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