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Structure-function relationships in proteins and peptides

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The main goal of the project is the theoretical description on molecular level of non-covalent interactions and their role in structure-function relationships in proteins. The physical bases of molecular adaptability of extremophilic organisms will also be on focus. Special emphasis will be placed on electrostatic interactions and their interplay with the other non-covalent interactions. Both folded and unfolded (denatured) states of proteins will be subject of investigations.

Research objectives:

I. Development of theoretical and computational method for prediction of ionisation equilibria in ***native proteins***. On focus will be the factors causing ***cooperative ionisation***, a phenomenon of extreme importance for understanding on molecular level of functional properties, such as stability and enzymatic activity. Special attention will be paid on the coupling of electrostatic interactions with the ***structural (conformational) flexibility*** of the protein molecules. Phenomena, such as pH-dependent conformational changes, will also be of special interest.

II. Investigation of the non-covalent interactions in ***unfolded proteins.*** Unfolded proteins are poorly investigated on molecular level, which contradicts their importance in the context of biological functionality, including structural stability of native proteins. Stability, solubility, and intermolecular interactions of proteins with unstructured segments in their native forms will be on focus, as well.

III. Investigation on ***protein-membrane interactions***, membrane pore formation induced by proteins and peptides, membrane penetration of cationic peptides, as well as the interactions of surfactant proteins and synthetic peptides with model membrane structures.

IV. ***Molecular basis of environmental adaptability of organisms:*** Elucidation of the driving forces responsible for the change of the structural stability of proteins upon change of the environmental pressure (change of pH, temperature, salt concentration).

Papers related to the project:

1. Moutsatsou, P., Papoutsi, Z., Kassi, E., Heldring, N., Tsiapara, A., Melliou, E., Chrousos G.P., Chinou, I., Karshikoff, A., Nilsson, L. & Dahlman-Wright K. (2010). Fatty acids derived from royal jelly are modulators of estrogen receptor functions. *PLoS ONE* **5**, e15594. **PDF**
2. Nilsson, L. & Karshikoff, A. (2011). Multiple pH regime molecular dynamics simulation for p*K* calculations. *PLoS ONE* **6**, e20116. **PDF**

3. Bachvarov, B.I., Kirilov, K.T. & Ivanov, I.G. (2011). Codon and codon pairs usage in bacteria. In: *Encyclopedia of DNA Research* (Duncan S. J. and P. H. Wiley, eds) Nova Science Publishers, Inc, NY. in press

4. Wuxiuer, Y., Morgunova, E., Cols, N., Popov, A., Karshikoff, A., Sylte, I., Gonzàlez-Duarte, R., Ladenstein, R. & Winberg, J.-O. (2012). An intact eight-membered water chain in drosophilid alcohol dehydrogenases is essential for optimal enzyme activity. *FEBS Journal* **279**, 2940–2956. **Abstract**

5. Lilkova, E., Nacheva, G., Petkov, P., Petkov, P., Markov, S., Ilieva, N. & Litov, L. (2012). Metadynamics study of mutant human interferon-gamma forms. *Computers and Mathematics with Applications* **64**, 272–277. **PDF**

6. Nacheva, G., Lilkova, E., Petkov, P., Petkov, P., Ilieva, N., Ivanov, I. & Litov, L. (2012). *In silico* studies on the stability of human interferon-gamma mutants. *Biotechnol. & Biotechnol. Eq.* **26**, 200-204 **PDF**

7. Jordanova, A., Tenchov, B. & Lalchev, Z. (2011). Effects of interaction and surface morphology of mixed DPoPE /Poloxamer 188 monolayers and thin liquid films. *Soft Matter* **7**,.7003-7012. **Abstract**

8. Georgiev, G. As., Vassilieff, C., Jordanova, A., Tsanova, A. & Lalchev Z. (2012). Foam Film study of Albumin Inhibited Lung Surfactant Preparations. Effect of added Hydrophilic Polymers. *Soft Matter* **8**, 12072–12079. **Abstract**