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VABILO NA PREDAVANJE
V OKVIRU DOKTORSKEGA ŠTUDIJA
KEMIJSKE ZNANOSTI

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z naslovom:

Impact of Hydrophobicity on Nonnative Interactions, Evolutionary Switches, and Effects of Hydrostatic Pressure in Protein Folding

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Vljudno vabljeni!

Impact of Hydrophobicity on Nonnative Interactions, Evolutionary Switches, and Effects of Hydrostatic Pressure in Protein Folding

Hydrophobic interactions are a major -- though not necessarily the dominant -- driving force in protein folding. I will present recent advances in applying atomic and coarse-grained simulation approaches to investigate the impact of hydrophobicity on protein folding, using primarily three systems to gain insight into the underlying general principles: (i) Bacterial colicin-immunity proteins Im7 and Im9 are homologous, but they fold by different mechanisms. Im7 tends to fold in a three-state manner via an intermediate but Im9 folding is two-state-like. Our model suggests that nonnative effects in Im7 folding are caused by a higher local hydrophobicity concomitant with a lower local native contact density [1]. (ii) How novel folds of proteins may evolve is addressed by modelling the folding behaviours of 12 experimentally well-characterized GA/GB sequences covering a switch from an all-alpha GA fold to an entirely different four-beta + alpha GB fold. In agreement with experiment, our model exhibits conformational switching upon a single L45Y substitution. The fold preference shows a gradual sequence-dependent change in our model, in line with the latent evolutionary potential concept [2]. Our theoretical perspective thus provide a coherent physical picture for rationalizing and predicting nonnative effects and conformational switches [3,4]. (iii) Based on explicit-water atomic simulation of volumetric effects of hydrophobic association [5], an implicit-water atomic chain model is developed to embody effects of the particulate nature of water and other aspects of solvation on a polypeptide. The model was tested by Langevin dynamics simulations of a 16-residue polyalanine. Consistent with prior experiment [6], coil-helix transition in our simulation is associated with an average volume decrease; but the transition process entails a robust positive activation volume. Thus pressure likely stabilizes helices of short peptides but is expected to slow down their formation. General ramifications of our theoretical findings for pressure effects on globular protein folding will also be explored.

References:
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[6] Neumaier, Buttner, Bachmann & Kiefhaber (2013) PNAS 110:20988-20993