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Forces in **SFB**₃₃
Biomolecular Systems

"Programming and Controlling the Supramolecular Assembly of Peptides"

by
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Abstract:

The rational, or de novo design of proteins is a challenging in a number of respects: we do not understand the forces that stabilise the folded states of proteins relative to their unfolded states; we do not have "rules" that relate protein sequence to structures, as we do for DNA-based assemblies; and predicting the pathways that unfolded proteins might take en route to their folded functional states is not trivial. On top of this, there are practical problems of producing de novo peptides and proteins because of potential issues with solubility, stability and cytotoxicity. So why bother? What makes de novo protein design such an interesting research area in the face of these difficulties? Well, for a start, clearly it is a challenge. Second, it provides the acid test of our understanding of the protein-folding problem. Third, natural proteins are by far the most varied and versatile of the natural biomolecules in terms of structures that they can adopt and functions that they perform, which makes them interesting targets to mimic. Finally, nature could not have sampled all of the possible protein-sequence-and-structure space, which leaves open exciting possibilities for creating new protein structures and functions. But where do we start on this formidable problem?

The approach to protein design that my group takes is to choose small and relatively straightforward protein-folding motifs—notably, the α -helical coiled coils. We then develop mathematical descriptions and sequence-to-structure relationships for them. In turn, we use these as frameworks and rules to generate well-characterised peptide components. We then use the components as a toolkit to create larger, more-complicated, and, hopefully, useful assemblies. Thus, in many respects we are taking a synthetic-biology approach to the protein-design problem.

This talk will outline the biological inspiration, physical models and chemical aspects of this approach; our progress in setting up the toolkit; and how we are using the components to design new protein folds, peptide-based assemblies and biomaterials.

Friday, February 15th, 2013, 13:00

Room PH 127

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