Designing Protein-Protein Interaction Specificity

The past 15-20 years have witnessed remarkable advances in computational, structure-based protein design. These have included the design of well-folded proteins that exhibit functions including ligand binding, protein binding, DNA binding and catalysis. A challenge confronting computational design is how to address interaction specificity, i.e. how to favor the interaction of a designed protein with some partners or substrates over others that might be closely related. This talk will describe how we have explored specificity design using the human bZIP transcription factors as a model. A novel formulation of the problem that borrows techniques from materials and computer science led us to the successful design and testing of numerous specific anti-bZIP synthetic peptides.