

Learning From Nature to Engineer Proteins

As we get a more complete picture of how proteins accomplish myriad complex tasks in cells, from catalysis to mechanical force generation, we are more inspired to engineer similarly “smart” molecules for specific needs. Being able to do so would have a transformative impact on nanotechnology, drug discovery as well as basic science. Thus, learning the design principles of natural proteins, and building on these to engineer new molecules with desired properties is of critical importance. I will describe several undertakings towards these general goals. 1) An essential task for cellular proteins is to recognize “correct” from “incorrect” interaction partners. In an effort to understand this process, we have designed peptide binding partners for human bZIP transcription factors that selectively recognize just one out of 20 closely related bZIP families. 2) The universe of natural protein structures consists of highly recurring structural motifs, one reason for which is the *designability* of these motifs – i.e. the relative ease with which they can be stabilized with natural amino acids. Using a computational method for rapidly estimating designability, we have engineered peptides that self-assemble into a pre-defined structural array around single-walled carbon nanotubes. Further, we are exploring the possible use of our designability metric in identifying incorrectly predicted regions in modeled protein structures, without knowing the correct answer.