How might new protein folds evolve without detrimental effects on the biological function being performed by the original structural fold?

Recent studies by many laboratories indicate that selection of latent "promiscuous" traits can be an efficient route to new function, and that the adaptive conflict between the old and new folds can be resolved by gene duplication and intrinsic kinetic effects of sequence-space topology. Intense research in the past one and a half decade has also demonstrated that not all proteins function as folded structures.

Intrinsically disordered proteins (IDPs) or protein regions perform critical physiological functions, especially for the regulation of cellular processes in higher organisms. Remarkably, some IDPs function not only as individual molecules, but also collectively by undergoing reversible liquid-liquid phase separation in the living cell.

The resulting high-IDP phase forms a major component of membraneless organelles such as P granules and nucleolus that, by creating their own IDP-rich compartments, stimulate critical biological functions.

To gain physical insight into these newly discovered and fascinating phenomena, I will discuss recent effort in using computational models and analytical theory to elucidate how new protein folds might have arisen in evolution and how biologically functional phase separation of IDPs is governed by their genetically coded amino acid sequences.