How phosphorylation affects protein-peptide interactions

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Large-scale proteomics and transcriptomics studies have unraveled that about half of all proteins in biological cells are targets of post-translational modifications. Since this may have crucial consequences on the protein interactions involving the respective proteins, this severely complicates our understanding of the cellular protein interactome. However, only few model systems have so far been characterized in structural and thermodynamic terms. This project aims at exploring the potential and limitations of molecular dynamics simulations to contribute to the systematic proteomic mapping of the consequences of post-translational modifications on the cellular protein interactome. Here, we are focusing on the interaction of PDZ domains that bind to hundreds of other proteins in human cells. Based on X-ray crystallographic data for PDZ:peptide complexes, we study how well molecular dynamics computer simulations can capture the influence of peptide phosphorylation on their binding to PDZ domains in structural and energetic terms.