

**Presentation title:** Structure, unstructure and systems biology

**Date:** Wednesday 6 July 2011

**Abstract:**

Genomics and systems biology have made great progress in recent years. At the same time, constant progress has been made in structural biology. Combining expertise from these fields can be very insightful and modern bioscience is increasingly becoming an integrative discipline. I will describe some recent progress on the boundary of the fields of protein structure (and unstructure) and systems biology.

Many protein interactions, in particular those in signaling networks, are mediated by peptide recognition domains. These recognize short, linear amino acid stretches on the surface of their cognate partners with high specificity. Residues in these stretches are usually assumed to contribute independently to binding, which has led to a simplified understanding of protein interactions. Conversely, in large binding peptide data sets different residue positions display highly significant correlations for many domains in three distinct families (PDZ, SH3 and WW). These correlation patterns reveal a widespread occurrence of multiple binding specificities and give novel structural insights into protein interactions. For example, a new binding mode of PDZ domains can be predicted and structurally rationalized for DLG1 PDZ1.

While protein structure is very important for peptide binding domains, the regions they bind are usually unstructured (intrinsically disordered). These regions are widespread, especially in proteomes of higher eukaryotes, and have been associated with a plethora of different cellular functions. Aside from general importance for signaling networks, they are also important for such diverse processes as protein folding or DNA binding. Leveraging knowledge from systems biology can help to structure the phenomenon. Strikingly, disorder can be partitioned into three biologically distinct phenomena: regions where disorder is conserved but with quickly evolving amino acid sequences ("flexible disorder"), regions of conserved disorder with also highly conserved amino acid sequence ("constrained disorder") and, lastly, non-conserved disorder.