

Pepsite: A structural method to predict peptide/protein binding

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Protein-protein interactions are vital for all cellular mechanisms. A major class of such interactions are those where a globular domain in one protein binds to a short peptide stretch in another. Phosphorylation/dephosphorylation events, other post-translational modifications, and dozens of signalling, targeting & trafficking procedures are known to occur by way of this kind of interaction. Often proteins sharing an interaction partner contain a common peptide pattern or linear motif known to mediate the interaction. For example, SH3 domains bind to a PxxP pattern, WW domains to PPxY, 14-3-3 domains to RxSxP, etc. The availability of hundreds of new peptides known or predicted to interact with a particular protein, in addition to the fact that structural genomics initiatives, and the general increased pace of structure determination, have provided representative structures for many if not most globular domains suggests the need for methods that specifically fit a peptide onto the surface of a 3D structure.

We describe just such an approach here. The method involves constructing 3D-profiles capturing the preferred environment for each amino acid when bound as a peptide from a database of protein/peptide structure. These profiles are then used as probes to find candidate binding sites of each residue of a particular peptide on proteins surfaces, which are then combined to suggest the potential binding site and rough orientation of this peptide. The method performs well in a benchmark, and we show that it is capable of identifying the true binding site of peptides and roughly orient them on protein surfaces.