How do soluble proteins bind to lipid membranes? Computational approaches for mapping and predicting protein-membrane interfaces

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Unlike transmembrane proteins, peripheral proteins bind at the surface of cell or organelle membranes transiently. They can be enzymes such as e.g. phospholipases or membrane-targeting domains such as Pleckstrin Homology or C2 domains. The prototypical peripheral membrane binding site is described as a combination of clusters of basic and hydrophobic amino acids but we know that this model does not hold for all peripheral proteins. In fact, and unlike protein-protein or protein-DNA interfaces, interfacial binding site of peripheral proteins are still poorly characterized both in terms of amino acid composition and structural patterns.

We aim at updating the text-book model for peripheral interfacial binding site and use a combination of computational tools and experimental data. We use molecular simulations on a hand-full of proteins and enzymes, and bioinformatics analyses on larger datasets of protein structures. I will present a summary of our progresses so far, including (i) the role and energetic contributions of aromatic amino acids, (ii) the overestimated role of unspecific electrostatics and (iii) the idea that protruding hydrophobes are a structural pattern distinguishing membrane-binding from non-membrane binding protein surfaces.