Anchoring spots mapping on protein surfaces: Application in docking
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The currently accepted model of molecular recognition processes includes at least two steps: the formation of an encounter complex, which is dominated by the energetic contribution of hot-spots, and an induced-fit step in which additional structural rearrangements occur. Hot spot residues tend to form anchoring spots that consist of a protruding anchor residue of one molecule that packs tightly in a pocket on the surface of the binding partner. The predictions of anchoring spots are expected to contribute significantly to protein-protein/peptide docking, protein engineering, and advance our understanding of molecular recognition processes. To predict anchoring spots we scatter thousands of amino acid copies on the entire protein surface and select anchoring spots by several cycles of energy minimization and clustering. We use an empirical scoring function designed specifically for the context of protein-protein interactions in which the anchor residue is treated as a fragment attached to a hypothetical protein through adequate account of the solvation and dielectric shielding effects. Applying the procedure on unbound protein structures show that (1) correct anchoring pockets were identified in the unbound protein and accurate anchoring spots were predicted despite the structural rearrangements expected occur upon complex formation; (2) the ranks of the correct anchoring spots are high, especially for red-hot anchoring-spots, and the calculated interaction energies are in line with alanine mutation data; (3) anchoring spots involving amino acids R, E, D, Y, W and H require a more restricted binding environment and therefore are better predicted than others.