Combining NMR docking data with EPR distances and in silico calculations for a more complete model of colicin protein-protein interactions

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Currently atomic resolution structures of protein-protein interactions are commonly limited to X-ray crystallography with its unnatural buffers, pHs and forced crystalline structure. Meanwhile NMR developments have allowed for solution based structures of small complexes to be developed [1] however ab initio information still remains a developing field [2,3]. Site-directed spin labelling (SDSL) in combination with the electron paramagnetic resonance (EPR) technique pulsed electron double resonance (PELDOR) allows for the precise measurement of intra and intermolecular distances up to 12 nm. Whilst new in silico methods allow the comparison of computation and experimental data [4]. By combining SDSL and distance measurements across multiple sites within protein-protein complexes a three dimensional model can be built to discriminate the NMR ensemble built from NMR docking experiments resulting in a more complete binding complex model [5]. Using the well-characterised system, of colicin E9 DNase domain and its cognate inhibitor, Im9 [6] a comprehensive solution is being developed to combine NMR docking models, with EPR distance constraints and in silico computations which are comparable to X-ray crystallographic models. Before expansion into full colicin E9 and non-cognate binding immunity proteins Im2, Im7 and Im8.