On the role of electrostatics in molecular recognition

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Electrostatic interactions are important for understanding molecular interactions, since they are long-range interactions and can guide binding partners to their correct binding positions. The macromolecular binding involves two processes: initial molecular recognition, which brings the binding partners in close proximity to each other and physical binding, which results in the 3D structure of the corresponding complex. Here we report a development of a combined tool, DelPhiForce Molecular Dynamics simulation tool, the DFMD, and demonstrate its efficiency in case of protein small molecule and protein-protein binding. Furthermore, we study the electrostatic force profile (the force as a function of the distance between binding partners) in case of dynein microtubule binding domain and microtubule and on a set of 275 protein complexes using recently developed DelPhiForce tool. It is demonstrated that at large distances between the partners, the electrostatic force (magnitude and direction) is consistent among the protocols used and the main factors contributing to it are the net charge of the partners and their interfaces. However, at short distances, where partners form specific pair-wise interactions or de-solvation penalty becomes significant, the outcome depends on the precise balance of these factors. Based on the electrostatic force profile, we group the cases into four distinctive categories, among which the most intriguing is the case termed “soft landing”. In this case, the electrostatic force at large distances is favorable assisting the partners to come together, while at short distance it opposes binding, and thus slows down the approach of the partners toward their physical binding.