# Literature Review

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## 1. Binding Affinity

Different methods for predicting binding affinity (BA) have been used, varying in accuracy and computational cost. **Exact methods** such as **free energy perturbation** and **thermodynamics integration** can be very accurate, but have limited application due to their computational cost. Mostly for low throughput studies and for small drug binding or mutation [1]. Are TCR complexes small enough for this approach? If not on a large scale, could it be used as a final accurate process once a good candidate has been selected?

Methods based on empirical functions are much faster - **empirical, force-field-based potentials, statistical potentials, scoring functions used in docking**. Lots of references given by [1]. The main weaknesses of these methods are that they usually neglect factors such as conformational changes upon binding, allosteric regulation, and solvent and co-factor effects, which may all contribute to the binding strength.

### 1.0.1 Allosteric regulation

Regulation of an enzyme by binding an effector molecule at a site different to the enzyme's active site. The site which the effector binds is the allosteric site.

Binding between two proteins is mainly defined by their contact region, the interface and it is indeed the network of contacts between surface residues that holds complexes together, defines their specificity and contributes to their interaction strength [1].

**RESEARCH:** Critical Assessment of Prediction of Interactions (CAPRI) experiment (Janin et al., 2003)

**RESEARCH:** Scoring functions of docking. Conservation of contacts at interface across docking models has been shown to improve ranking of docked models (Oliva et al., 2013; Chermak et al., 2014). Also included in ZRANK pipeline (Hwang et al., 2010) [1].

**RESEARCH:** Effect of non-interacting surface (NIS) on BA (Kastritis et al., 2014; Marillet et al., 2015).

## References

1. Vangone, A. & Bonvin, A. M. Contacts-based prediction of binding affinity in protein-protein complexes. *eLife* **4.**