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.

References

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