

# **[L15] Computational Approaches to the Chemical Equilibrium Constant in Protein-Ligand Binding**

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The physiological role played by protein-ligand recognition has motivated the development of several computational approaches to the ligand binding affinity. Some of them, termed rigorous, have a strong theoretical foundation but involve too much computation to be generally useful. Some others alleviate the computational burden by introducing strong approximations and/or empirical calibrations, which also limit their general use. Moreover, it seems to be difficult to correlate their predictive power with the level of approximation introduced. Here, we present a general framework for the quantitative interpretation of protein-ligand binding based on statistical mechanics. Within this framework, we re-derive self-consistently the fundamental equations of some popular approaches to the binding constant and pinpoint the inherent approximations. Our analysis represents a first step towards the development of variants with optimum accuracy/efficiency ratio for each stage of drug discovery.