

**P014** Using Simulation Cell Theory to Calculate the Thermodynamics of Protein-Ligand Binding.

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The association of molecules is of central importance in biology and pharmacology. Methods to predict the affinity of such associations would be of great practical value. However, entropic changes upon binding are difficult to estimate and are often neglected. Here we apply our recently developed method, simulation cell theory, to evaluate the entropy of a ligand when bound to a protein and when free in solution. In this approach the average magnitudes of the forces and torques acting on the ligand are evaluated from a molecular dynamics simulation of the system. An entropic contribution from water may also be evaluated by a similar route. The protein contribution to entropy is neglected. The difference in entropy of the bound and free states gives the entropy change of binding. The two systems studied are the benzene-T4 lysozyme complex and major urinary protein (MUP) with a series of pyrazine derivatives.