Computing absolute binding affinities via non-equilibrium un-binding simulations F. MARTY YTREBERG, University of Idaho — We demonstrate that non-equilibrium unbinding simulations can be used to accurately estimate equilibrium absolute binding affinities ($\Delta G$). Utilizing the FKBP protein bound to two different ligands we estimate $\Delta G$ within less than 1.0 kcal/mol of experimental values. The methodology is straight-forward, requiring no modification to many modern molecular simulation packages. The approach makes use of a physical pathway, eliminating the need for complicated alchemical decoupling schemes. These results suggest that non-equilibrium simulation could provide a viable means to accurately estimate protein-ligand binding affinities.