MULTISCALE MODELING AS AN AVENUE TO EXPLORE ENZYME STRUCTURE / FUNCTION RELATIONSHIPS. H. Lee Woodcock, Department of Chemistry, University of South Florida, 4202 E. Fowler Ave CHE205, Tampa, FL 33620.

Combining theoretical models that treat different spatial and temporal scales is increasingly important for addressing complex biochemical problems. Herein we introduce a general framework for carrying out multiscale calculations and describe its implementation in CHARMM. This functionality, termed MSCALE, generalizes both additive and subtractive multiscale schemes (e.g. QM/MM ONIOM-type), and extends support to classical force fields, coarse grained modeling, and mixtures of them all. MSCALE is completely parallelized with each subsystem running as an independent, but connected calculation. This new facility is fully integrated with free energy perturbation (FEP) methods, Hessian based methods, and the use of periodicity and symmetry, which allows the calculation of accurate pressures. We demonstrate the utility of this new technique with four examples; (1) subtractive QM/MM and QM/QM; (2) multi-force field alchemical FEP; (3) integration with AMBER and TINKER; and (4) mixed resolution (i.e. coarse grain / all-atom) normal mode analysis.