HIGHLANDS IN CHEMISTRY SEMINAR SERIES

H. LEE WOODCOCK

UNIVERSITY OF SOUTH FLORIDA

"Making the inaccessible, accessible: Novel Techniques for Obtaining Accurate QM/MM Free Energies at Affordable Costs"

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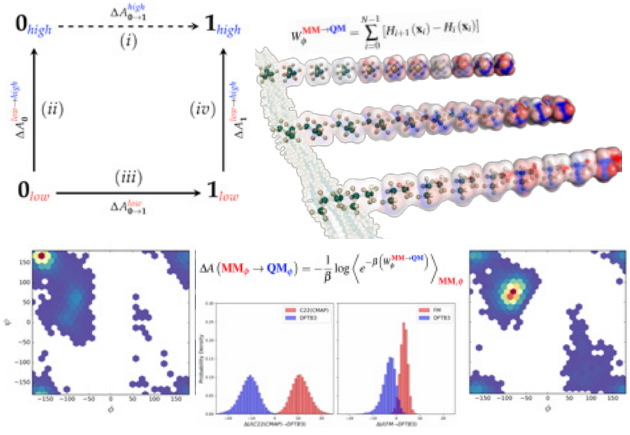
2:30PM

HAHN HALL NORTH 140

FACULTY HOST:
VALERIE WELBORN

The use of the most accurate (i.e., QM or QM/MM) levels of theory for free energy simulations (FES) is typically not possible. Primarily, this is because the computational cost associated with the extensive configurational sampling needed for converging FES is prohibitive. To ensure the feasibility of QM-based FES, the "indirect" approach is generally taken, i.e., necessitating the computation of ΔA(MM→QM). Ideally, this step is performed with standard Free Energy Perturbation (FEP) as it only requires simulations to be carried out at the low level of theory, however, work from several groups over the past few years has conclusively shown that FEP is ill-suited to this task. As such, several alternative strategies and approximations have arisen to mitigate difficulties with FEP. In this presentation, I will discuss our recent developments to this end with particular emphasis on (1) using more robust techniques to compute ΔA(MM→QM), (2) improving MM descriptions of QM systems, and (3) critically examining a common approximation (i.e., the Interaction Energy Hypothesis) that has been widely used to circumvent tackling the challenging problems from (1) and (2).



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