LAUFER CENTER
FOR PHYSICAL AND QUANTITATIVE BIOLOGY

Seminar 2015

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Tuesday, July 28, 2015

2:00 PM

Laufer Center Lecture Hall 101

Host: Ken Dill

Refreshments following seminar

Laufer Hub 110

Reconciling Theory and Experiment: The Search for Certainty in an Uncertain World

Despite continuing advances in biophysical techniques it is still not possible to directly observe the energetic and dynamic properties of individual atoms in biomolecular systems using experimental approaches. As a consequence, everything we know (or think we know) regarding biomolecular systems at an atomic level is to a greater or lesser degree a model. The question then becomes to what extent can the models used to interpret experimental data be trusted? For example, while the overall structure of a protein may be resolved in near atomic detail, the position, orientation and/or conformation of a small molecular ligand (cofactor, substrate, inhibitor etc.) bound to such a protein is often much less certain.1 Electrostatics are generally ignored in structure refinement. In other cases there is systematic bias in how data is used or interpreted. The variation in the area per lipid in theoretical calculations of membrane systems is much less than the variation in the experimental data on which they are based.2 This is not only a problem for experimentalists but represent a fundamental challenge to theoreticians attempting to validate computational models.3,4 Using a range of examples the talk will illustrate how the theoretical or structural model models we use can bias our interpretation of experimental data, but how when used appropriately molecular simulations, provide a unique means to test and challenge our interpretation of experimental data leading to increased certainty in some cases, new insights into the true nature of biomolecular systems in action in others.5,6

1. Malde, A.K. and Mark, A.E. (2011) Challenges in the determination of the binding modes …….. J. Comp. Aided Mol. Des. 25, 1-12.
2. 2. Poger, D. and Mark, A. E. (2010) On the Validation of Molecular Dynamics Simulations of Saturated and cis-Monounsaturated …….. J. Chem. Theory Comput. 6, 325-336.
3. 3. Nair, P,C., Malde, A.K. and Mark, A.E. (2011) Using theory to reconcile experiment: the structural and thermodynamic basis of ligand ….. (PNMT). J. Chem. Theory Comput. 7, 1458-1468
4. 4. O'Mara, M. L. and Mark, A. E. (2012) Effect of environment on membrane protein structure: P-glycoprotein under physiological conditions. J. Chem. Theory Comput., 8, 3964-3976.
5. 5. Sengupta, D., Leontiadou, H., Mark, A. E. and Marrink, S. J. (2008) Toroidal Pores Formed by Antimicrobial Peptides Show Significant Disorder. Biochim. Biophys. Acta., 1778, 2308-2317.
6. 6. Brooks, A. J., et al. (2014) A new cytokine receptor activation paradigm: activation of JAK2 by the Growth Hormone Receptor. Science, 344, 1249783

For a disability related accommodation, please call 631-632-5400

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