Preface: Special Topic on Reaction Pathways

Cecilia Clementi[1,a)] and Graeme Henkelman[2,b)]
[1]*Department of Chemistry, Rice University, Houston, Texas 77005, USA*
[2]*Department of Chemistry, University of Texas at Austin, Austin, Texas 78712, USA*

(Received 29 September 2017; accepted 2 October 2017; published online 16 October 2017)

This Special Topic Issue on Reaction Pathways collects original research articles illustrating the state of the art in the development and application of methods to describe complex chemical systems in terms of relatively simple mechanisms and collective coordinates. A broad range of applications is presented, spanning the sub-fields of biophysics and material science, in an attempt to showcase the similarities in the formulation of the approaches and highlight the different needs of the different application domains. *Published by AIP Publishing.* https://doi.org/10.1063/1.5007080

In the last few decades, our ability to generate high resolution data by computer simulation has dramatically increased. In the field of biophysics, it is now possible to use molecular dynamics (MD) simulation to fold small proteins,[1,2] study large conformational changes in macromolecules,[3] or protein-ligand and protein-protein association[4] *in silico*. In the fields of chemistry and material science, where bond-breaking reactions are of particular interest, there have been significant advances in the accuracy and scale of electronic structure calculations of activated processes, with applications to understanding materials such as batteries[5] and catalysts.[6]

The advances in simulation have in turn stimulated a surge of interest in data analysis methods,[7] to extract essential information from the data in order to enable quantitative predictions and connect with experimental results. In particular, both in biophysics and in material science, it is desirable to characterize complex molecular mechanisms in terms of reaction pathways.[8] The systems of interest are generally composed by a large number of atoms, and the analysis of the reaction mechanisms requires a reduction in the dimensionality of the simulation data to a few collective variables that describe the molecular processes under consideration.

In this Special Topic Issue of *The Journal of Chemical Physics*, we have compiled examples of work where the definition of collective variables and reaction pathways is essential to understand molecular mechanisms, with application both in biophysics and in material science.

While methods developed in these two different sub-fields of chemistry bear significant similarities and have sometimes a common origin, there are also important differences associated with the different application domains. One important distinction among these methods is based on the requirement of the knowledge of (meta)stable states in the system of interest. In the field of biophysics, it is desirable to sample the phase space relevant for a molecular system, to map all the main metastable states and the rates of interconversion between them. For a material scientist, it is very often the time evolution of a system which is important, including the final states which are not known *a priori*. In catalysis, for example, one typically knows the initial structure of the catalysts and the reactions, and what you want to know is the active site under steady state conditions and the products that form.

In both biophysical and material science systems, the definition of reaction coordinates and reaction pathways typically rely on the existence of a separation of time scales.[9] The slow processes are usually of interest, and most methods propose to find the important slow dynamical "directions" while averaging over the faster processes. Transition state theory, for example, can be used to separate the fast vibrational time scale from the slower state-to-state kinetics. For the rough landscapes found in biophysical systems, the use of collective variables, spectral methods, Markov state models, and transition path theory is central to a description of the slowest time evolution.[7,10,11] Here, we recognize that there are similarities as systems in both fields become increasingly complex, and an aim of this Special Issue is to explore common ground between methods used in what could appear to be very diverse fields.

C.C. group is supported by NSF (Grant Nos. CHE-1265929, CHE-1738990, and PHY-1427654) and the Welch Foundation (Grant No. C-1570). G.H. group is supported by NSF (Grant Nos. CHE-1534177, CHE-1505135, and DMR-1410335) and the Welch Foundation (Grant No. F-1841).

[1]D. E. Shaw, P. Maragakis, K. Lindorff-Larsen, S. Piana, R. O. Dror, M. P. Eastwood, J. A. Bank, J. M. Jumper, J. K. Salmon, Y. Shan, and W. Wriggers, "Atomic-level characterization of the structural dynamics of proteins," Science **330**, 341–346 (2010).
[2]K. Lindorff-Larsen, S. Piana, R. O. Dror, and D. E. Shaw, "How fast-folding proteins fold," Science **334**, 517–520 (2011).
[3]Y. Meng, D. Shukla, V. S. Pande, and B. Roux, "Transition path theory analysis of c-src kinase activation," Proc. Natl. Acad. Sci. U. S. A. **113**, 9193–9198 (2016).
[4]N. Plattner, S. Doerr, G. De Fabritiis, and F. Noé, "Complete protein–protein association kinetics in atomic detail revealed by molecular dynamics simulations and markov modelling," Nat. Chem. **9**, 1005–1011 (2017).
[5]A. Urban, D.-H. Seo, and G. Ceder, "Computational understanding of li-ion batteries," NJP Comput. Mater. **2**, 16002 (2016).

[a)]Electronic mail: cecilia@rice.edu
[b)]Electronic mail: henkelman@utexas.edu

[6]J. K. Nørskov, T. Bligaard, J. Rossmeisl, and C. H. Christensen, "Towards the computational design of solid catalysts," Nat. Chem. **1**, 37–46 (2009).
[7]F. Noé and C. Clementi, "Collective variables for the study of long-time kinetics from molecular trajectories: Theory and methods," Curr. Opin. Struct. Biol. **43**, 141–147 (2017).
[8]M. A. Rohrdanz, W. Zheng, and C. Clementi, "Discovering mountain passes via torchlight: Methods for the definition of reaction coordinates and pathways in complex macromolecular reactions," Ann. Rev. Phys. Chem. **64**, 295–316 (2013).
[9]C. Schütte, A. Fischer, W. Huisinga, and P. Deuflhard, "A direct approach to conformational dynamics based on hybrid Monte Carlo," J. Comput. Phys. **151**, 146–168 (1999).
[10]J. D. Chodera and F. Noé, "Markov state models of biomolecular conformational dynamics," Curr. Opin. Struct. Biol. **25**, 135–144 (2014).
[11]W. E and E. Vanden-Eijnden, "Transition-path theory and path-finding algorithms for the study of rare events," Ann. Rev. Phys. Chem. **61**, 391–420 (2010).