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Capturing Chemical Reactivity and Entropy with Machine Learning Potentials

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Chemical reactions drive fundamental processes in both nature and industry. Understanding these reactions is crucial across diverse fields, from the chemistry of life's origins to the synthesis of pharmaceuticals and advanced materials. However, unraveling reaction mechanisms, thermodynamics, and kinetics—especially in complex environments involving solvents—poses significant challenge Experimental methods often lack the resolution to fully characterize transition states and energy landscapes, while quantum-level simulations are computationally prohibitive for large systems and long timescales. Recent advances in machine learning, particularly the development of machine learning interatomic potentials (MLIPs),1,2 offer a paradigm shift by providing quantum-accurate force fields at a fraction of the computational cost. These MLIPs enable molecular dynamics simulations that are several orders of magnitude faster than traditional ab initio methods, thus bridging the gap between quantum accuracy and accessible dynamical timescales. However, generating reliable reactive MLIPs remains nontrivial due to the complexity of chemical reactions and the need for extensive, diverse training datasets capturing all relevant reactive events.3 Here, we introduce ArcaNN (Automated training of Reactive Chemical Architectures with Neural Networks),4 a robust and flexible framework designed to automate and optimize the training of MLIPs for chemical reactions. ArcaNN integrates enhanced sampling techniques to efficiently explore reactive configurational space, coupled with a concurrent learning strategy that ensures adaptive refinement of the training set. The workflow orchestrates the key stages of training, exploration, and labelling, greatly reducing human intervention and making the generation of reactive MLIPs accessible to a broader scientific community. We apply this framework to organic reactions including the SN2 reaction, the Claisen rearrangement, and alkene hydroboration, explicitly modelling solvent molecules in a fully reactive manner. We will discuss the ability to generate long-timescale trajectories and trace accurate thermodynamic and especially entropic contribution along reaction coordinates,5 providing a more comprehensive picture of chemical processes. Overall, ArcaNN represents an advancement in the training of MLIPs for chemical reactivity, enabling detailed, efficient, and automated investigations of complex reactions in condensed-phase environments under realistic dynamical conditions.

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