Path-metadynamics combined with machine learning to unravel complex reaction mechanisms

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Abstract
Metadynamics is more than a versatile tool to enhance the sampling of activated molecular transitions and reveal the underlying free energy landscape spanned by multiple collective variables (CVs). With its ever-growing list of applications and methodological extensions, metadynamics has also provided us through the years with a detailed understanding of the dynamics of rare fluctuations in many-particle systems. Still, the performance of the method depends crucially on the quality of the CVs. Finding good CVs requires enhanced sampling data, but enhanced sampling requires good CVs; a notorious chicken-and-egg problem.

In this talk, I will present three approaches based on supervised learning [1], unsupervised learning, and reinforcement learning [2], to find CVs and sample transition paths. By combining machine learning methods with path-metadynamics [3], also the chicken-and-egg problem is efficiently tackled.

References
[1] Discovering collective variables of molecular transitions via genetic algorithms and neural networks. *J. Chem. Theory Comput.* **17**, 2294-2306 (2021)
[2] Path Integral Stochastic Optimal Control for Sampling Transition Paths. *arXiv:*2207.02149 [q-bio.BM]
[3] Advances in enhanced sampling along adaptive paths of collective variables. *J. of Chem. Phys.* **149**, 072320 (2018)