# Metastability and partial differential equations

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In these lectures, I will describe various mathematical questions arising from sampling algorithms used in computational statistical physics. In this context, the goal is to compute averages of observables with respect to Boltzmann-Gibbs measures (thermodynamic quantities) or statistics over paths (dynamic quantities). In both cases, this requires, *a priori*, the simulation of high-dimensional diffusion processes over very long time scales. Numerical methods aim to bridge these discrepancies in space and time scales between the atomic and macroscopic levels.

After a brief overview of the challenges posed by molecular dynamics simulations, I will present mathematical questions related to:

- **Free energy adaptive biasing techniques:** These techniques require studying the long-time behavior of Fokker-Planck equations, which are nonlinear due to mean-field interactions. I will present results based on entropy methods [LRS08] and more recent approaches using gradient flows [LLM25].
- **The quasi-stationary distribution approach to metastability**: This approach [DGLLPN17] is useful for rigorously linking Langevin-type dynamics with jump Markov models (kinetic Monte Carlo), and for analyzing algorithms designed to efficiently sample exit events from metastable states. Dorian Le Peutrec will present, in particular, recent joint work on the parametrization of kinetic Monte Carlo using Eyring-Kramers exit rates [LLPN25]. I will also discuss ongoing work on the so-called narrow escape problem [LRS24].

In both cases, I will highlight open problems, particularly those related to generalizing results to hypoelliptic operators (kinetic Langevin dynamics).

## References

[DGLLPN17] G. Di Gesù, T. Lelièvre, D. Le Peutrec, and B. Nectoux. Jump markov models and transition state theory: the quasi-stationary distribution approach. *Faraday discussions*, 195:469–495, 2017.

[LLM25] T. Lelièvre, X. Lin, and P. Monmarché. Convergence rates for an adaptive biasing potential scheme from a wasserstein optimization perspective, 2025. https://arxiv.org/abs/2501.17979.

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[LRS08] T. Lelièvre, M. Rousset, and G. Stoltz. Long-time convergence of an adaptive biasing force method. *Nonlinearity*, 21:1155–1181, 2008.

[LRS24] T. Lelièvre, M. Rachid, and G. Stoltz. A spectral approach to the narrow escape problem in the disk, 2024. https://arxiv.org/abs/2401.06903.