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Robust Active Force Detection with the Overdamped Langevin Equation

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The Overdamped Langevin equation describes the inertialess motion of a particle under deterministic drift and thermal noise. The deterministic drift is the result of the combined action of active forces and the diffusivity gradient (the "spurious" force). For biological applications, it is important to distinguish between the two components, because the former indicates specific interactions, while the latter is due to a heterogeneous environment, in which these interactions take place. The spurious force is always proportional to the diffusivity gradient, but the proportionality coefficient is only known for equilibrium systems. This leads to a range of possible spurious force values in out-of-equilibrium systems and leads to ambiguity in the interpretation of the observed drift. This ambiguity is known as the Itô-Stratonovich dilemma.

In this work, we do not try to resolve the dilemma, but analyze the information that can be extracted about the active forces in an *a priori* unknown out-of-equilibrium system. To this end, we propose a Bayesian method that marginalizes over all possible values of the spurious force and allows robust identification of active forces in both equilibrium and out-of-equilibrium setups. Under certain assumptions, the main result can be obtained in an analytical form. The method has a significantly decreased false positive rate of active force detection as compared to conventional approaches. We illustrate the practical value of the method by integrating it into an open-source software project and applying it to both numerical trajectories and experimental single-biomolecule tracks recorded on the cell membrane.

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