Soft Matter

PAPER

View Article Online
View Journal | View Issue

Cite this: *Soft Matter*, 2017, **13**, 2174

Received 23rd January 2017, Accepted 17th February 2017

DOI: 10.1039/c7sm00174f

rsc.li/soft-matter-journal

# Maximum likelihood estimations of force and mobility from single short Brownian trajectories†

Raphael Sarfati,[a] Jerzy Bławzdziewicz[b] and Eric R. Dufresne*[c]

We describe a method to extract force and diffusion parameters from single trajectories of Brownian particles. The analysis, based on the principle of maximum likelihood, is well-suited for out-of-equilibrium trajectories, even when a limited amount of data is available and the dynamical parameters vary spatially. We substantiate this method with experimental and simulated data, and discuss its practical implementation, strengths, and limitations.

## 1 Introduction

Brownian particles are ubiquitous in soft matter and biological sciences, from colloidal particles to fluorescently-tagged molecules. The trajectories of these particles contain precious information about their structure and interactions. For example, particle sizes are routinely quantified by measuring diffusion coefficients of a dilute suspension in a well-characterized fluid.[1,2] Alternatively, when the particles are well-characterized, the trajectory of a Brownian particle can probe the solvent's rheological properties.[3] Analysis of Brownian trajectories can also reveal the conservative and dissipative forces acting on particles due to external fields[4] or interactions with other particles.[5]

Since Brownian trajectories are stochastic, their analysis is necessarily statistical. The physical theory describing the statistics of Brownian particles is well-established.[6] When particles fluctuate near an equilibrium position, conservative forces acting on them are readily extracted using Boltzmann statistics.[7] In the absence of external forces, the dissipative forces acting on particles can be calculated from their diffusion coefficient using the Stokes–Einstein relation. More generally, the Smoluchowski equation describes the trajectory of Brownian particles when conservative forces and diffusion coefficients vary over space.[8] In this case, conservative and dissipative forces can simultaneously be determined from the distribution of displacements at each configuration.

Importantly, this requires the measurement of many trajectories through the same system configuration. This approach has been successfully implemented for micron-sized colloidal particles, which can be repeatedly trapped in the desired configuration and released using optical traps.[5,9–11] However, in some cases Brownian particles cannot be manipulated with optical traps, and in others the laser will perturb the rest of the system. In such situations, one requires a method to determine the forces with less data, typically a single trajectory.

Maximum likelihood estimators have recently been shown to be powerful tools for measuring the diffusion coefficient of Brownian particles.[12–14] They are more efficient and more accurate than the conventional approach, where one determines a diffusion coefficient by calculating a mean-squared displacement and fitting. Given a discretely sampled trajectory, maximum likelihood estimators provide an explicit analytical expression for the best estimate of the diffusion coefficient. This approach explicitly accounts for common experimental artifacts such as localization error from exposure time-induced blurring,[12] finite trajectory length,[13] or limited photon statistics.[14]

We recently introduced a method, based on the same principle, to estimate force and diffusion parameters from single Brownian trajectories.[15] Our numerical approach allows one to efficiently estimate spatially varying dynamical parameters. It can provide useful results for even short trajectories, because it assumes a specific functional form for the spatial dependence of the dynamical parameters. One can readily characterize the statistical error and bias in these estimates through the analysis of ensembles of simulated data. Here, we provide a detailed description of our numerical maximum likelihood analysis (MLA) of Brownian trajectories. First, we provide a simple review of the principles of Brownian motion and maximum likelihood. Second, we demonstrate the method based on simulations and experimental data, including the analysis of

[a] Department of Applied Physics, Yale University, New Haven, CT 06520, USA
[b] Department of Mechanical Engineering, Texas Tech University, Lubbock, TX 79409, USA
[c] Department of Materials, ETH Zürich, 8092 Zürich, Switzerland. E-mail: ericd@ethz.ch

† Electronic supplementary information (ESI) available: Materials & methods, and mathematical derivations. See DOI: 10.1039/c7sm00174f