Bayesian inference of optical trap stiffness and particle friction

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Bayesian inference provides a principled way of estimating the parameters of a stochastic process that is observed at discrete points in time. The overdamped Brownian motion of a bead confined in an optical trap is generally modelled as an Ornstein-Uhlenbeck process and is measured directly in experiment. Here we present Bayesian methods for determining the parameters of this process, the trap stiffness and the particle friction coefficient, using exact likelihoods. Maximum aposteriori estimates are obtained analytically by exploiting sufficient statistics. Our method obviates the need for Monte Carlo sampling and is, consequently, orders of magnitude faster. The viscosity of the ambient fluid can be estimated from the particle friction, given the bead radius. We apply our method to experimental data and find excellent consistency with the fluctuation-dissipation theorem and good agreement with commonly used non-Bayesian methods.

I. INTRODUCTION

Since the seminal contributions of Rayleigh, Einstein, and Langevin, stochastic processes have been used to model physical phenomena in which fluctuations play an essential role. Examples include the Brownian motion of a particle, the fluctuation of current in a resistor, and the radioactive decay of subatomic particles. A central problem is to infer the parameters of the process from partially observed sample paths, for instance, the diffusion constant from a time series of positions, or the resistance from a time series of current measurements, and so on. Bayesian inference provides a principled solution for this inverse problem, making optimal use of the information contained in the partially observed sample path.

The Ornstein-Uhlenbeck process is commonly used to model the sample paths of a harmonically confined Brownian particle. This process has a mean regression rate λ and a volatility σ which correspond, in the physical application, to the stiffness k of the harmonic potential and the friction γ of the particle. Since the friction of a particle of radius a is given by $\gamma = 6\pi\eta a$, where η is the viscosity of the ambient fluid, any estimation of the friction also provides an estimate of the viscosity of the medium, given the particle radius. Thus, the viscosity, which is defined as the response of the fluid to an externally imposed shear, can be inferred from the observation of harmonically confined Brownian fluctuations. This, of course, is a consequence of the relation between response and fluctuation that prevails in a physical system in thermal equilibrium.

In this paper, we apply Bayesian inference to the problem of estimating the parameters of the Ornstein-Uhlenbeck process from time series that represent partially observed sample paths. This is of great current experimental relevance, since harmonic confinement of micron-sized spheres is easily achieved using optical tweezers. A reliable estimation of the trap stiffness is a necessary first step when using tweezers in force measurements. Bayesian methods, using Monte Carlo sampling, have been proposed earlier to this end. Here, we present a method that does not require sampling, exploits the sufficient statistics of the problem, and provides exact maximum a posteriori estimates using these statistics. Consequently, the method is both extremely fast and accurate, being able to jointly estimate the trap stiffness and the particle friction from a time series with a million points in less than a millisecond. Further, the fluctuation-dissipation relation provides a stringent internal consistency check on the accuracy of the estimation. We apply our method to experimental data to find estimates that have excellent internal consistency. These estimates are in good agreement with commonly used non-Bayesian calibration methods.

The remainder of the paper is organized as follows. In the next section we recall several key properties of the sample paths and distributions of the Ornstein-Uhlenbeck process. In Section III, we present the Bayesian method and follow, in section IV, with its application to experimental data. We conclude with a discussion of future directions in Bayesian inference in optical tweezer experiments.

II. ORNSTEIN-UHLENBECK PROCESS

The Langevin equation for a Brownian particle confined in a potential U is given by

$$m\dot{v} + \gamma v + \nabla U = \xi \tag{1}$$

where $\xi(t)$ is a zero-mean Gaussian white noise with variance $\langle \xi(t)\xi(t')\rangle = 2k_BT\gamma\delta(t-t')$ as required by the fluctuation-dissipation theorem. In the limit of vanishing inertia and a harmonic potential, $U = \frac{1}{2}kx^2$, we obtain the overdamped Langevin equation

$$\dot{x} = -\frac{k}{\gamma}x + \sqrt{\frac{2k_BT}{\gamma}}\zeta(t) \tag{2}$$

where $\zeta(t)$ is now a zero-mean Gaussian white noise with unit variance. This is the Ornstein-Uhlenbeck process, whose sample paths obey the Ito stochastic differential equation,

$$dx = -\lambda x dt + \sigma dW \tag{3}$$

where W is the Wiener process, $\lambda = k/\gamma$ is the mean-regression rate and $\sigma = \sqrt{2k_BT\gamma^{-1}}$ is the volatility. The particle diffusion coefficient D is related to the friction γ by the Einstein relation $D = k_BT\gamma^{-1}$ and so $2D = \sigma^2$. In problems involving Brownian motion, it is convenient to work with the diffusion coefficient, rather than the volatility, and henceforth we infer D rather than σ directly.

The transition probability density $P_{1|1}(x't'|x\,t)$ obeys the Fokker-Planck equation $\partial_t P_{1|1} = \mathcal{L}P_{1|1}$ where the Fokker-Planck operator is

$$\mathcal{L} = \frac{\partial}{\partial x}\lambda x + \frac{\partial^2}{\partial x^2}D. \tag{4}$$

This gives probability of a path segment ending at the point x' at time t', given that it started at the point x at time t. The solution is a normal distribution,

$$x't'|x\,t \sim \mathcal{N}\left(xe^{-\lambda(t-t')}, \frac{D}{\lambda}[1-e^{-2\lambda(t-t')}]\right),$$

where $\mathcal{N}(a,b)$ is the univariate normal distribution with mean a and variance b. This solution is exact and holds for arbitrary values of $|t-t'|$, unlike the Euler approximation used in which is accurate only when $\lambda|t-t'| \ll 1$. The stationary distribution $P_1(x)$ obeys the steady state Fokker-Plank equation $\mathcal{L}P_1 = 0$ and the solution is a normal distribution,

$$x \sim \mathcal{N}\left(0, \frac{D}{\lambda}\right) = \mathcal{N}\left(0, \frac{k_BT}{k}\right)$$

where $\sigma^2/2\lambda = k_BT/k$ has been used to obtain the equality above. Comparing the forms of $P_{1|1}$ and P_1 it is clear that former tends to the latter for $|t-t'| \to \infty$, as it should.

III. BAYESIAN INFERENCE

Consider the time series $X \equiv (x_1, x_2, \ldots, x_N)$ consisting of observations of the sample path $x(t)$ at the discrete times $t = n\Delta\mathrm{t}$ with $n = 1, \ldots, N$. Then, using the Markov property of the Ornstein-Uhlenbeck process, the probability of the sample path is given by

$$P(X|\lambda, D) = \prod_{n=1}^{N-1} P_{1|1}(x_{n+1}|x_n, \lambda, D)P_1(x_1|\lambda, D)$$

The probability $P(\lambda, D|X)$ of the parameters, given the sample path, can now be computed using Bayes theorem, as

$$P(\lambda, D|X) = \frac{P(X|\lambda, D)P(\lambda, D)}{P(X)} \tag{5}$$

The denominator $P(X)$ is an unimportant normalization, independent of the parameters that we henceforth ignore. Since both k and γ must be positive, respectively for stability and positivity of entropy production, we use informative priors for λ and σ, $P(\lambda, \sigma) = H(\lambda)H(\sigma)$, where H is the Heaviside step function. This assigns zero probability weight for negative values of the parameters and equal probability weight for all positive values. The logarithm of the posterior probability, after using the explicit forms of $P_{1|1}$ and P_1, is

$$\begin{aligned}\ln P(\lambda, D|X) = \frac{N-1}{2}\ln\frac{\lambda}{2\pi D I_2} - \frac{\lambda}{2DI_2}\sum \Delta_n^2 \\ + \frac{1}{2}\ln\frac{\lambda}{2\pi D} - \frac{\lambda}{2D}x_1^2\end{aligned} \tag{6}$$

where we have defined the two quantities

$$I_2 \equiv 1 - e^{-2\lambda\Delta t}, \quad \Delta_n \equiv x_{n+1} - e^{-\lambda\Delta t}x_n. \tag{7}$$

and the sum runs from $n = 1, \ldots, N$ as earlier.

The maximum aposteriori (MAP) estimate $(\lambda^\star, D^\star)$ follows from the stationary conditions $\partial \ln P(\lambda, D|X)/\partial\lambda = 0$ and $\partial \ln P(\lambda, D|X)/\partial D = 0$, while the standard error of this estimate is obtained from the matrix of second derivatives evaluated at the maximum. The exact solution of the stationary conditions yields the MAP estimate to be

$$\begin{aligned}\lambda^\star &= \frac{1}{\Delta t}\ln\frac{\sum x_n^2}{\sum x_{n+1}x_n} \\ D^\star &= \frac{\lambda^\star}{N}\left(\frac{\sum \Delta_n^2}{I_2} + x_1^2\right) \\ k^\star &= \frac{\lambda^\star}{D^\star}\end{aligned}$$

where both I_2 and Δ_n are now evaluated at $\lambda = \lambda^\star$. This completes our description of the Bayesian procedure for jointly estimating λ and D.

An alternative Bayesian procedure for estimating the trap stiffness alone results when X is interpreted not as a time series but as an exchangeable sequence, or, in physical terms, as repeated independent observations of the stationary distribution $P_1(x)$. In that case, the posterior probability, assuming an informative prior that constrains k to positive values, is

$$\ln P(k|X) = \frac{N}{2}\ln\frac{k}{2\pi k_B T} - \frac{1}{2}\frac{k}{k_B T}\sum_{n=1}^{N} x_n^2 \tag{8}$$

The MAP estimate follows

$$k^\star = \frac{N k_B T}{\sum_{n=1}^{N} x_n^2} \tag{9}$$

This procedure is independent of the sampling time and is equivalent to the equipartition method when the Heaviside prior is used for k. A comparison of the estimates obtained from these independent procedures provides a check on the assumptions implicit in Ornstein-Uhlenbeck process: harmonicity of the potential and thermal equilibrium, that is, stationarity with a Gibbs distribution. A disagreement between the two methods signals a breakdown of either or both of the above assumptions.

The posterior probabilities in both methods can be written in terms of the four quantities $T_1(X) = \sum x_{n+1}^2$, $T_2(X) = \sum x_{n+1}x_n$, $T_3(X) = \sum x_n^2$ and $T_4(X) = x_1^2$, which, therefore, are the sufficient statistics of the problem. The entire information in the time series X relevant to estimation is contained in these four statistics. There use reduces computational expense enormously as only four numbers, rather than an entire time series, is required. The combination of exact likelihoods, analytical MAP estimates, and the use of sufficient statistics provides an accurate and efficient method, together with a self-consistency criterion, for estimating parameters from the time series of particle positions.

IV. DATA ACQUISITION

The optical tweezers system is constructed around a Zeiss inverted microscope (Axiovert.A1) with a 100x 1.4 numerical aperture (NA) objective lens tightly focusing laser light from a semiconductor laser at 1064 nm (Lasever, maximum power 500 mW) into the sample chamber. The sample chamber is built using a standard glass microscope slide and cover slip that are attached to each other using double sided tape. The back aperture of the objective is slightly overfilled so as to maximize the trapping intensity. The sample consists of a dilute (1:10000) dispersion of polystyrene beads of diameter 3 μm in 10\% NaCl-water solution. Details of our experimental set up including the beam-coupling optics is available in Ref.~\cite{rsi12}. The total power available at the trapping plane is around 15 mW. Detection of Brownian motion of a single trapped bead is performed by back-focal plane interferometry using the back-scattered intensity of a detection laser at 671 nm that co-propagates with the trapping laser. Note that the detection laser power is maintained at much lower levels than that required to trap a bead independently. The back-scattered signal from a trapped bead is collected on a position sensitive photodiode that we construct by placing a knife-edge in front of a Thorlabs PDA100A-EC Si-photodiode (bandwidth 2.4 MHz) so that a portion of the signal is obstructed by the knife-edge. The The position of the knife-edge determines whether we measure the x or y component of the Brownian motion of the bead with the edge being flipped by 90 degrees to choose between the coordinate being measured. To reduce cross-talk between the orthogonal components, we use an acousto-optic modulator that is placed in the conjugate plane of the microscope \cite{rsi12} to sinusoidally scan the trapping beam (and thus the single trapped bead) in the x-direction, and measure the response in the photodiode with the knife-edge placed to detect the y-component of motion. The detected signal is minimized so that the effects of cross-talk are almost entirely negligible. The large bandwidth of the photodiode, that is typically much faster than most available commercial quadrant photodetectors, addresses concerns about photodiode response time and associated requirements of data filtering. The data from the photodiode is logged into a computer using a National Instruments DAQ system.

V. RESULTS

Since the seminal of contributions of Rayleigh, Einstein, and Langevin, stochastic processes have been used to model physical phenomena in which fluctuations play an essential role. Examples include the Brownian motion of a particle, the fluctuation of current in a resistor, and the radioactive decay of subatomic particles. A central problem is to infer the parameters of the process from partially observed sample paths, for instance, the diffusion constant from a time series of positions, or the resistance from a time series of current measurements, and so on. Bayesian inference provides a principled solution for this inverse problem, making optimal use of the information contained in the partially observed sample path.

VI. DISCUSSION

- use of exact likelihood removes the need to sample at high frequencies. this is the limitation of Euler approximation used in the paper of the French group. accuracy.
- use of analytical MAP estimates removes the need for Monte Carlo sampling, speed.
- use of sufficient statistics reduces the entire time series to four numbers, efficiency.
- joint probability obtained, can marginalize out friction if that is not known and treat it as a nuisance parameter
- can do many more complicated models, e.g. air trapping etc, using Bayesian inference.