FORMA and BEFORE: expanding applications of optical tweezers

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Abstract: We introduce two methods based on statistical inference to calibrate optical tweezers. Both outperform well-established methods and cover a broader application field, including non-conservative force fields and out of equilibrium systems.

1. Force reconstruction via Maximum Likelihood estimator

We recently introduced force reconstruction via maximum-likelihood-estimator analysis (FORMA) to calculate the force field acting on a Brownian particle by analyzing its trajectory displacements. FORMA exploits the linear relationship between the time series of the position of a Brownian particle x_n and drag forces $f_n = \gamma \frac{\Delta x_n}{\Delta t_n}$ at instant n in the vicinity of an equilibrium point:[1]

$$f_n = -\kappa x_n + \sigma w_n \tag{1}$$

Where κ is the stiffness of the force field and $\sigma = \sqrt{\frac{2D\gamma^2}{\Delta t_n}}$, $D = 6\pi\eta R$, $D = k_B T/\gamma$, R is the radius of the particle, η is the viscosity of the medium in which the particle is moving; and finally, w_n is a Gaussian random number of zero mean and unit variance. Using a Maximum likelihood estimator, we find the solution:

$$\kappa^* = -\frac{\sum_n x_n f_n}{\sum_n x_n^2} \tag{2}$$

Using the calculated κ^* one can estimate the diffusion as:

$$D^* = \frac{1}{N} \sum_n \frac{\Delta t_n}{2\gamma^2} \left[f_n + \kappa^* x_n \right] \tag{3}$$

FORMA has proven to be faster, more precise, more accurate, and ten-fold less data-intensive than autocorrelation function method (ACF), power spectrum density method (PSD), mean squared displacement method (MSD), and potential method. Furthermore, with FORMA, we have characterized the force field's conservative and non-conservative components, having relevant advantages over well-established techniques. In Fig. (1), we can see the application of FORMA to characterize the force field generated by a speckle pattern that features non-conservative components due to the presence of optical vortices and unstable equilibrium points. Another key advantage of FORMA is that its application does not depend on the fine-tuning of a fitting parameter, which is the case of ACF, PSD, and MSD [1].

2. FORMA, the case of a flat prior in Bayes approach

In the context of inference statistics, FORMA uses a linear non-Bayesian approach to estimate the properties of the force field and the diffusive properties of the particle. Recently, we have developed a method that uses Bayesian inference to expand and generalize FORMA.

[1] This equation is valid in the vicinity of an equilibrium point $\mathbf{F}_0(x) = 0$; however, it can be applied to any other point by adding the correspondent term of the force at that point $\mathbf{F}_0(x) = \mathbf{F_0}$.

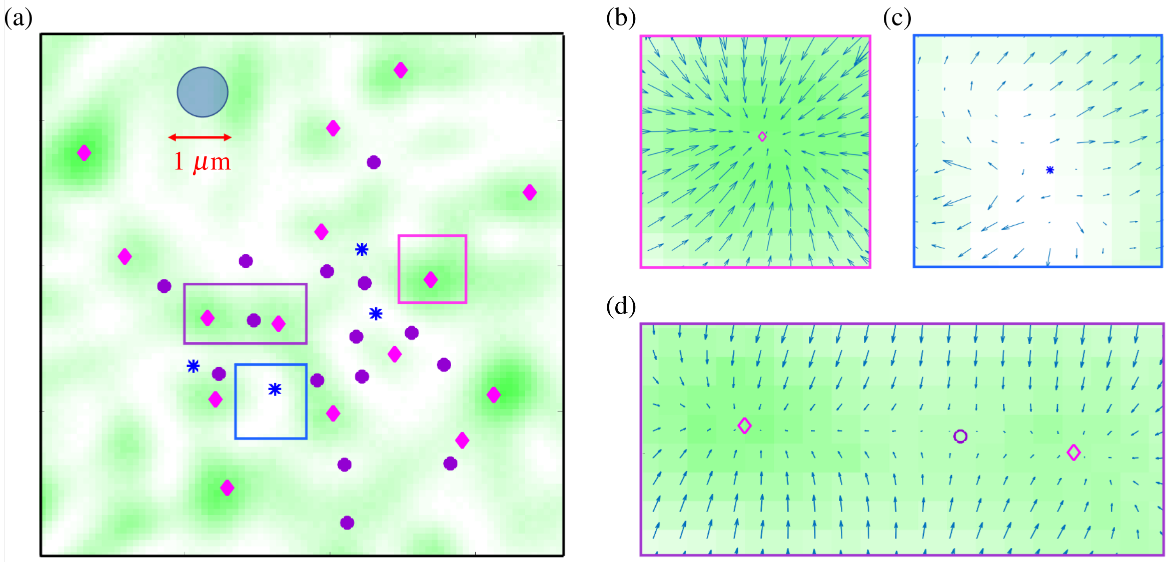

Fig. 1. FORMA has been used to characterize non-conservative force fields as the ones generated by a speckle pattern. A $1\mu m$ polystyrene particle was suspended in water and exposed to a speckle pattern formed by a spatial light modulator. The markers in (a) represent equilibrium points i.e., where $\mathbf{F}_0(\mathbf{r}) = 0$. In (b), we see the characteristic force field of a stable equilibrium point, specifically an attractor; in (b), we see an unstable equilibrium point as all force lines are repelled from inside out, and in (c), we see a saddle point which happens to be in the middle of the line that connects two attractors.

With Bayesian Force Reconstruction (BEFORE), we have derived formulas for the posterior distribution for a set of parameters $\{D, \gamma, \kappa\}$ denoted by θ, also called a model. The posterior distribution $P(\theta|\mathbf{x}, \mathbf{f})$ gives us the probability that a model θ explains the data-set provided by the vector pair $\{\mathbf{x}, \mathbf{f}\}$.

Assuming $P_0(\theta)$ to be the prior distribution for the model, by Baye's rule, the posterior distribution is given by:

$$P(\theta|\mathbf{x}, \mathbf{f}) = \frac{\mathcal{L}(\mathbf{f}|\mathbf{x}, \theta) P_0(\theta)}{\int d\theta' \mathcal{L}(\mathbf{f}|\mathbf{x}, \theta') P_0(\theta')} \tag{4}$$

where $\mathcal{L}$ is the likelihood of observing a vector $\mathbf{f}$ given the vector of positions $\mathbf{x}$ and the set of parameters θ. FORMA actually can be derived from a flat prior distribution; thus, the posterior distribution is proportional to the likelihood $\mathcal{L}$ given by:

$$\mathcal{L}(\mathbf{f}|\mathbf{x}, \theta) = \sqrt{\frac{\prod_n \Delta t_n}{(4\pi D\sigma^2)^N}} \exp\left[-\sum_n \frac{\Delta t_n}{4D\sigma^2}(f_n + \kappa x_n)^2\right] \tag{5}$$

Using more informative priors, BEFORE can provide reasonable estimates of the parameters even when little data is available; it can also be generalized to more than one dimension and be used for time series with any time interval Δt.

Both FORMA and BEFORE represent an approach for calibration of optical tweezers using statistical inference techniques. Their advantages become relevant whenever we have few data points, out of equilibrium systems, non-conservative forces, underdamped regime, or inhomogeneous time sampling. All these advantages will allow expanding experiments towards more complex scenarios such as biological systems, time-varying conditions, and active baths [2].

References

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