



Analyses of Single Molecule Torque and Twist Precision using Nanotechnology

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ABSTRACT

Unprecedented insights into the structure, purpose, interactions, and mechanical characteristics of biological macromolecules have been made possible by single-molecule manipulation techniques. Techniques that permit rotation and torque measurements, such as the optical torque wrench (OTW) and several variations of magnetic (torque) tweezers have recently been added to the single-molecule toolset. Although single-molecule approaches' systematic evaluations of their location and force precision have garnered a lot of attention, they have received significantly less attention when it comes to their angle and torque precision. Here, we suggest using the Allan deviation as a technique to systematically quantify the precision of angle and torque measurements made on single molecules. We discover that both methods can produce torque accuracy when we apply the Allan variance method to experimental data from our implementations of (electro) magnetic torque tweezers and an OTW. Superior to 1 pnm. The OTW offers the best torque precision for measurement periods (10 s), after which drift becomes a limiting issue. The OTW is capable of measuring torque on (sub) millisecond timescales. Magnetic torque tweezers, with their exceptional stability, offer the finest torque precision for extended measuring durations. Utilizing the Allan deviation provides a tool to optimise measurement protocols for a specific instrument and application and allows for critical evaluations of the torque precision as a function of measurement duration across different measurement modalities.

Keywords: Spectroscopy; Macromolecules; Torque; Nanotechnology

INTRODUCTION

The structure, function, relationships, and mechanical characteristics of biological macromolecules may now be studied in unprecedented depth thanks to methods for manipulating single molecules. Numerous single-molecule manipulation methods naturally work in the space of (linear) extension and force, most notably optical tweezers and atomic force microscopy. However, because biological macromolecules routinely experience torsion, the molecular motors that move along them must be able to go forward under the weight of accumulated twist and torque. A variety of techniques that allow measurements have been used to quantify these phenomena of torque and rotation angle have lately been created [1]. The rotor-bead-tracking assay, optical torque tweezers, and different magnetic tweezers extensions, such as magnetic torque tweezers, freely orbiting magnetic tweezers, and electromagnetic torque tweezers, are examples of such approaches. The field of torque- and twist-measuring techniques would benefit from a better understanding of the achievable precision in angular detection and the determination of torque, much like the field of force spectroscopy, which has benefited from systematic analyses of the position and force precision of single-molecule techniques.

Here, we suggest Allan deviation (AD) (38-49) as a standard for systematically quantifying the accuracy of angle and torque measurements made with single molecules. The AD enables us to analyse the torque precision across several measurement modalities as a function of measurement time that depend on specific physical concepts. It offers an intuitive and straightforward way to measure and evaluate precision because it is a real space quantity and has the same units as the relevant observable [2].

Using the AD methodically gives an experimental user a very useful tool for optimizing the measurement process for a specific Nanotechnology, in addition to permitting direct quantitative comparisons of various torque and twist measurement strategies. Here, we use simulated traces to examine the AD approach and demonstrate its use with various magnetic torque tweezers (MTT), electromagnetic torque tweezers (eMTT), and an optical torque wrench implementations (OTW). We arrive at clear suggestions using the AD analysis, such as the ideal in-plane magnetic field strength in the eMTT and the ideal trapping laser power in the OT [3].

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MATERIALS AND METHODS

Definition and Properties

A discrete form of Equation 1 is used in practise to estimate the AV from a data set with a finite number of measurements. The data are divided into M bins of m data points each in the simple form of the AV, and the value of each bin is the mean over its m data points [4]. The AV is estimated by the mean-square difference between adjacent bins. Where q_i is the mean of the i th bin of length $m\tau_s$ and τ_s is the sampling period. The integration time is assumed to be equal to the sampling period. This assumes no dead time in between frames for camera-based detection in the magnetic tweezers, which is reasonable given how often dead time is compared to integration time. The scenario is considerably different for photodiode-based detection in the OTW because, despite a very quick effective integration time, the photodiode is only read out at 100 kHz [5]. This rate's inverse is comparable to a dead time because no signal averaging takes place at such period. As a result, in the OTW, the integration time is much less than the dead time. However, the use of Eq. 2 is still appropriate in all circumstances [6].

Analytic Expression for the AV

Using numerical solutions to the related over damped Langevin equation, we generate stochastic time traces of rotational motion to evaluate our AD analysis and demonstrate the consequences of different system parameters. We discretize time into time steps Δt in order to replicate the rotation angle as a function of time $q(t)$. The discretized overdamped Langevin equation yields the angle at time step $I = 1$, $q_1 = 1$ [7].

AD Measurements with Magnetic Tweezers

The alignment of super paramagnetic micron-sized beads or microspheres with an externally applied magnetic field is necessary for the magnetic tweezers' ability to apply torque. Both MTT and use a mostly vertical-oriented field produced by a cylindrical magnet and a minor horizontal field produced by an electromagnet in the case of the MTT or a side magnet in the case of the latter Nanotechnology. The in-plane field produces an angular trap that is sufficiently faint to be used in research with DNA and other delicate molecules. When a molecule of interest that is tethered between a surface and a bead is subjected to twist, torque measurements in MTT and eMTT rely on measuring the rotational angle of the bead and analysing changes in the equilibrium angle position of the bead inside the trap [8]. The angle AD can be derived simply from the angular traces, however the torque AD requires calibrated trap stiffness because the torque is calculated as the product of the angular shift and the trap stiffness. Therefore, limitations in angular tracking will also impact torque precision.

AD Measurements with Optical Tweezers

The OTW is an improvement on traditional optical tweezers that applies and measures torque by taking advantage of the exchange of angular momentum between a nanofabricated, birefringent particle and a polarised trapping beam. There are no equivalent particles for the OTW, in contrast to the magnetic tweezers, which use common commercially available magnetic beads (whose magnetic anisotropy regulates the possible torque levels and in which a variety of diameters provides control over the drag coefficient). Instead, a variety of fabrication techniques, materials

(such as quartz SiO₂ (0.009), vaterite CaCO₃ (0.1), calcite CaCO₃ (-0.16), and rutile TiO₂ (0.26; optical birefringences specified in parentheses), shapes (such as spherical, cylindrical, etc.), and dimensions are typically used to create birefringent dielectric particles on demand (with a size scale of a few micrometres being most prevalent). Our specially designed device uses cylindrically rutile TiO₂ nanoparticles that are shaped. The optical tweezers in the OTW capture a birefringent cylinder whose long axis is parallel to the direction of light transmission [9]. The rutile TiO₂ cylinder's angular position is clamped by the linear polarization of the trapping laser, and rotation of this polarization regulates the particle's rotation about its long axis Nanotechnology. The exchange of angular momentum inside the trap may be directly measured by the imbalance between the left and right circularly polarised components in the trap's output, which also serves as a gauge for the optical torque applied to the particle. We fixed the linear polarization's direction in the AD measurements and observed the variations around this equilibrium point [10].

RESULTS

The AD is the square root of the AV, which employs data, averaged over variable time intervals t and is calculated from the difference between neighboring time intervals. Although there are various ways to evaluate precision, we believe AD to be a particularly practical measure for a number of reasons [11]: As a real space quantity, the AD is immediately in the same units as the measured quantity of interest; it is also effective in detecting low frequency, long-time scale drifts (43), which are crucial for single-molecule measurements of torque and twist; and it provides a direct and intuitive measure of the precision expected for a measurement of a given duration. The AD can be easily calculated from the unprocessed experimental data without the necessity for a priori calibration [12].

The use of AD to quantify the angle and torque precision of single-molecule measurements is explored in the section that follows. First, we discuss the idea of AD and validate our methodology by presenting the outcomes of stochastic simulations Nanotechnology. The precision of three different single-molecule torque spectroscopy technique MTT, eMTT, and an OTW—is then compared using AD.

DISCUSSION

Analyzing the AD offers information on the best measurement time and parameters, as well as the precision that can be achieved. If the trace is averaged long enough, the AD can be arbitrarily minimal for a hypothetical measurement without drift because it gets smaller in the thermal limit as $t \rightarrow \infty$. This would suggest that the level of precision that could be achieved experimentally could be extremely high. In reality, noise other than the white noise produced by thermal fluctuations will interfere and prevent further precision gains. Due to the additive nature of the AD, drift will begin to predominate over the thermal limit at a certain averaging period t ; over longer timeframes, the precision will no longer improve with averaging but rather deteriorate. Then indicates the highest possible precision and, hence, the ideal measurement time. Different drift sources will have different signals in the AD. For instance, if there were linear drift, the AD should rise with $t^{1/2}$, as seen in the OTW traces. The AD scales as $t^{-1/2}$ if the predominant source of noise has a $1/f$ character, as we see at around 2 s in the AD plots for the OTW data set in. In this study, we introduce the

application of the AD to assess the effectiveness of various torque measurement equipment. Even for extremely long measurement times, drift appears to not appreciably limit the readings in the MTT and eMTT studies.

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