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Dynamic Force Sensing Using an Optically Trapped Probing System

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Abstract

This paper presents the design of an adaptive observer that is implemented to enable real-time dynamic force sensing and parameter estimation in an optically trapped probing system. According to the principle of separation of estimation and control, the design of this observer is independent of that of the feedback controller when operating within the linear range of the optical trap. Dynamic force sensing, probe steering/clamping, and Brownian motion control can, therefore, be developed separately and activated simultaneously. The adaptive observer utilizes the measured motion of the trapped probe and input control effort to recursively estimate the probe-sample interaction force in real time, along with the estimation of the probing system's trapping bandwidth. This capability is very important to achieving accurate dynamic force sensing in a time-varying process, wherein the trapping dynamics is nonstationary due to local variations of the surrounding medium. The adaptive estimator utilizes the Kalman filter algorithm to compute the time-varying gain in real time and minimize the estimation error for force probing. A series of experiments are conducted to validate the design of and assess the performance of the adaptive observer.

Index Terms

Adaptive estimation; force measurement; Kalman filtering; optical tweezers; state feedback

I. Introduction

A single-beam gradient-force optical trap was first reported in 1986 [1]. It employed a tightly focused near-infrared laser beam (e.g., at wavelength = 1064 nm) to trap and manipulate individual microscopic dielectric particles. Optical forces on the order of a few piconewtons (pNs) to hundreds of pNs were generated in optical tweezers and soon demonstrated for noninvasive trapping and manipulation of a single living cell [2]. With calibration [3], the optical trap formed on a microscopic particle has also been employed as a force transducer and proven to be a useful research tool in many research disciplines [4].

Recently, based on the advancement in 3-D position detection [5], [6], sample scanning [7], and laser beam steering [7]–[11] technologies, new optically trapped probing systems have been developed [7], [9], [11] for biological research. The unparalleled subpiconewton (sub-pN) force resolution of these systems is essential to many biological studies, including the study of motor proteins at a single molecular level [12], the measurement of mechanical property of biopolymers [13], and the investigation on cell mechanics and mechanotransduction [14], [15]. In a reported 2-D probing system [7], a microscopic particle was optically trapped to serve as the measurement probe. The probe–sample interaction force was measured, using a linear spring model, from the relative probe position with respect to the trapping equilibrium. It was then employed for feedback control to achieve 2-D force clamp, applying constant load of several pNs on the sample.

This force transduction capability is not only superior in terms of resolution, when compared to the widely used atomic force microscopes (AFM) [16], but also naturally available in 3-D. Although new design of micromanipulators [17] may help AFM on its multiaxis applications [18], they are still not as flexible as 3-D optically trapped probes. Furthermore, since the measurement probe of the trap is held by a laser beam, there is no mechanical link involved. Manipulation of biological samples in a 3-D complex environment [19] and even trapping inside living organisms [20] become possible. The authors of this paper recently reported a 3-D probing system, wherein the optically trapped microscopic probe was propelled by a three-axis rapid laser steering system [11]. The actuators in the steering system consist of a deformable mirror (DM) enabling axial steering and a two-axis acousto-optic deflector (AOD) for lateral steering. This steering system serves two functions. First, high-bandwidth active control of the trapped probe's Brownian motion is achieved to enhance probing resolution and trapping stability. Second, large range 3-D steering of the measurement probe is realized to enable contouring complex 3-D trajectories. It is thus possible to transform the 3-D optically trapped probing system to a scanning probe system if real-time dynamic force sensing and force control of the system can be implemented.

Caused by random thermal noise, the optically trapped probe exhibits seemingly random movement, also known as the Brownian motion [21], in an aqueous solution. It is the major limiting factor on the measurement precision in many applications [22]. Moving averaging or low-pass filtering is often applied such that high-frequency fluctuations in the measurement data are effectively attenuated [7], whereas the information fidelity of the dynamic process could be compromised. Moreover, since it is based on Hooke's law to calculate the probe–sample interaction force [4], the commonly employed linear spring model ignores trapping dynamics. Consequently, it is valid only for quasi-static force sensing. This paper, on the other hand, presents the design and implementation of a disturbance observer that is employed to realize real-time dynamic force sensing. It therefore not only enables research on time-varying biological processes but also serves as the essential technology that leads to force feedback control, making the automatic scanning of the optically trapped probe in an unknown environment possible, similar to what has been accomplished by AFM [16].

The observer utilizes the measured motion of the probe along with the input control effort to recursively estimate the probe–sample interaction force via a closely related disturbance term, whose dynamics is augmented into the dynamic model of the probing system. According to the principle of separation of estimation and control [23], the design of this observer is independent of that of the feedback controller when operating within the linear range of the optical trap. Probe steering [11], Brownian motion control [24], [25], and force sensing can, therefore, be developed separately and activated simultaneously. Moreover, since a significant change of trapping dynamics [26] may occur in many applications as a result of the variation in local environment [3], an adaptive estimation algorithm [27] is

implemented to enable joint state-parameter estimation so that the probe-sample interaction and the trapping bandwidth of the probing system can be estimated simultaneously in real time. The adaptive observer utilizes the Kalman filter [23], [28], [29] to compute the time-varying gain in real time and minimize the estimation error in force probing. It evolves from the recursive weighted least-squares method and results in the best linear unbiased and maximum likelihood estimation in the case when both process and measurement noises satisfy the white Gaussian condition [28].

The design of the adaptive observer for dynamic force sensing using an optically trapped probing system and the experimental demonstration of its performance are presented hereinafter. The rest of the paper is organized as follows. Section II briefly introduces the probing system setup, wherein a discrete system model is derived. The adaptive observer for joint state-parameter estimation is designed and then optimized using the Kalman filter algorithm in Section III. Section IV presents the experimental results to evaluate the performance of the adaptive dynamic force sensing. Finally, conclusion is summarized in Section V.

II. PROBING SYSTEM OVERVIEW

A. Experimental Setup

The optical trapping system employed in this investigation is built around an inverted microscope (Eclipse TE2000-U, Nikon, Japan) with two trapping lasers and one measurement laser [11]. The primary trapping laser (2.5 W 1064 nm) passes a unique three-axis laser steering device, which consists of a two-axis AOD for lateral manipulation of the trapped probe and a DM for axial actuation. The actuation range is designed and calibrated to be over 20 μm along the two lateral axes and over 10 μm along the axial direction. The bandwidth of the two lateral axes is over 50 kHz, characterized by an actuator time delay of $\sim 12 \mu\text{s}$ [25], and the associated resolution is 0.016 nm (1σ). The axial resolution is 0.16 nm, while the bandwidth is enhanced to over 3 kHz by the model cancellation method [11]. A water-immersion objective lens focuses the laser beam to form a stable trap at the specimen plane, whose position is controlled by a closed-loop three-axis piezoelectric stage with a travel range of $100 \mu\text{m} \times 100 \mu\text{m} \times 20 \mu\text{m}$. The stage's 3-D position is commanded and measured by a host computer at a 5 kHz updating rate via a high-speed parallel I/O (PIO) interface [30]. The 830 nm measurement laser is aligned with the primary trapping laser to detect the probe's absolute position from its stationary focus. The measurement principle is based on 3-D back-focal-plane interferometry [5], wherein a quadrant photodiode (QPD) detector is used. The QPD signal is conditioned by a filtering and amplification circuit to improve the measurement sensitivity and resolution. After conditioning, the signal's bandwidth is up to 150 kHz.

A field programmable gate array (FPGA)-based embedded system (Stratix II, Altera, San Jose, CA) then samples the QPD signal through its analog-to-digital (AD) channels (ADS8365, Texas Instruments, Dallas, TX). Real-time estimation and control algorithms for dynamic force probing, probe regulation, as well as Brownian motion suppression are all implemented in the FPGA, which sends the result to the host computer for data logging and analysis through a customized parallel digital communication. Despite the computational complexity of the real-time algorithms, the FPGA's parallel processing structure allows high-precision floating-point calculation with a high loop rate of 208.3 kHz, which is limited only by the conversion time of the AD channels. High-speed steering of the primary trapping laser and active control of the probing system were experimentally demonstrated and reported in [11] and [25], respectively. Hence, this paper focuses on dynamic force sensing with the probing system and its applicability to control.

B. Discrete System Model

In order to estimate the probe–sample interaction from the probe’s dynamic response, the dynamic model of the probing system is needed for the analysis and design of the observer. The probe’s motion is known to be governed by the Langevin equation [21], in which the 3-D motion can be decomposed into three components along the xyz directions. For simplicity, only the equation of motion along the x -axis is presented as follows:

$$\underbrace{m\ddot{x}(t)}_{\rightarrow 0} = - \underbrace{\gamma\dot{x}(t)}_{\text{viscous drag force}} + \underbrace{F_L(t)}_{\text{random thermal force}} + \underbrace{F_E(t)}_{\text{external force}} + \underbrace{F_{OT}(x-u)}_{\text{optical trapping force}}. \quad (1)$$

In this equation, the viscous drag $\gamma\dot{x}$ dominates over the inertia force $m\ddot{x}$ due to the microscopic size of the probe. Since γ , the probe’s damping coefficient, is a function of local temperature [3] and influenced considerably by the wall effect [4], the dynamics of the trapped probe can be altered significantly with the variation of the local environment. The Langevin force F_L is the white Gaussian thermal noise causing the probe’s Brownian motion, and F_E is the external probe–sample interaction force to be estimated by the observer designed in this paper. Finally, F_{OT} is the laser trapping force that dynamically balances all the other forces. The force has a profile that is close to linear between its two extrema, which occur at ± 500 nm from the equilibrium in our setup [25]. The force field can, therefore, be modeled as a linear spring for the trapped probe [9], [25], $F_{OT} = -k_{OT}(x - u)$, where u is the trapping equilibrium that can be manipulated by the system’s laser steering devices for active control and k_{OT} is the trapping stiffness. Consequently, (1) is linearized as

$$\gamma\dot{x} + k_{OT}x = k_{OT}u + F_E(t) + F_L(t). \quad (2)$$

The stiffness k_{OT} depends on the applied laser power, the probe size, and refractive index mismatch between the probe and the surrounding medium. It is usually calibrated by various means [4] prior to undertaking force probing. It can, however, be seen in (2) that direct linear-spring model-based measurement of F_E using calibrated trapping stiffness is only valid for quasi-static cases, wherein the drag and thermal forces can be filtered.

Alternatively, F_E can be estimated with an observer, into which the trapping dynamics described by (2) is incorporated to achieve dynamic force sensing. Fig. 1 illustrates the combined estimation and control structure of the probing system, in which the result of the adaptive observer is independent of the time-varying control effort of the system and is fed into the controller to improve the control performance.

As the probe’s motion is measured and sampled into the digital system to enable estimation and control, a discrete system model is derived from (2) and included in the observer. Similar to the derivation in [25], the measurement delay and steering dynamics are taken into account. The filter of the QPD signal conditioning circuit induces a small time delay to the signal in its passband, which is larger than the Nyquist frequency of the digital system. Therefore, measurement dynamics other than the time delay τ_m is neglected [25]. The sampling and calculation in the digital controller as well as the AOD steering cause additional delays [25]. All these delays in the loop in Fig. 1 are lumped into a total time delay τ_T which is $28.8 \mu\text{s}$ for our probing system [25]. This τ_T is the latency from the moment when the measured probe motion x_m is sampled to the time when new measurement begins to be affected by the control effort u_c , computed based on the old one. Therefore, the system equation between two consecutive samplings, $t \in [t_{k-1}, t_k)_{k=1,2,\dots}$, evolves from (2)

$$\gamma \dot{x}_m(t) + k_{OT} x_m(t) = k_{OT} u_c [x_m(t_{k-1} - \tau_T)] + F_{E'}(t) + F_{L'}(t) \quad (3)$$

where $F_{E'}(t) = F_E(t - \tau_m)$ and $F_{L'}(t) = F_L(t - \tau_m)$ are the time-shifted terms due to the measurement delay. It is worth noting that the axial DM's dynamics is more complicated than a pure steering delay. It was calibrated to be eighth-order [11]. Nevertheless, as long as the actuator dynamics is included to correctly determine the trapping equilibrium u from the control effort u_c , the same approach as presented in this paper can be applied to design the observer for the axial direction.

The discrete system model is then established using (3), which is a linear ordinary differential equation between the samplings. Based on the principle of superposition, the sampled displacement at each time instant $t_k, k=1,2,\dots$ is decomposed into three distinct components, i.e., $x_m[k] = x_{md}[k] + d[k] + v[k]$, where x_{md} is the deterministic part of the displacement, driven by the trapping force F_{OT} to move from previously sampled position $x_m[k-1]$ toward the equilibrium u , d is the disturbed motion of the probe due to the external force F_E , and v is the additive random fluctuation of the probe caused by the thermal force F_L within the period $[t_{k-1}, t_k]$. Hence, the three components at t_k are the solutions to the following three equations from time t_{k-1}^+ until approaching time t_k^- , given their respective initial conditions, namely $x_{md}(t_{k-1}^+) = x_m[k-1]$, $d(t_{k-1}^+) = 0$ and $v(t_{k-1}^+) = 0$

$$\gamma \dot{x}_{md}(t) + k_{OT} x_{md}(t) = k_{OT} u_c [x_m(t_{k-1} - \tau_T)], t \in [t_{k-1}, t_k]$$

$$\gamma \dot{d}(t) + k_{OT} d(t) = F_{E'}(t) U(t - t_{k-1}), t \in [t_{k-1}, t_k]$$

$$\gamma \dot{v}(t) + k_{OT} v(t) = F_{L'}(t) U(t - t_{k-1}), t \in [t_{k-1}, t_k]. \quad (4)$$

The use of the unit step function $U(t - t_{k-1})$ and zero initial condition in the last two equations of (4) reflects the fact that the initial probe position $x_m[k-1]$ at t_{k-1} has been the joint consequence of all forces before time t_{k-1} , which means that both d and v are solely caused by their respective sources within current time interval. When the system's sampling period, $\tau_s = t_k - t_{k-1}$, is chosen such that $\Delta = \tau_T/\tau_s$ is an integer, the discrete autoregressive moving average with exogenous input system model is derived as

$$x_m[k] = \phi x_m[k-1] + (1 - \phi) u_c \{x_m[k-1 - \Delta]\} + d[k] + v[k] \quad (5)$$

where $\phi = \exp(-(k_{OT}/\gamma)\tau_s)$ is the state transition coefficient associated with the open-loop trapping bandwidth $f_c = k_{OT}/2\pi\gamma$ [26]. This model explains how the current sample of probe motion x_m is determined by its previous state, the control effort u_c , the external disturbance d , as well as the thermal noise v . In all the experiments presented in this paper, τ_s is set to 14.4 μ s to reduce the amount of data for analysis, so Δ is 2. Derived from (4), the discrete white Gaussian noise term v in (5) is characterized by its autocorrelation function [25]

$$R_v[i, j] = \frac{k_B T}{k_{OT}} (1 - \phi^2) \cdot \delta[i, j] = \begin{cases} \frac{k_B T}{k_{OT}} (1 - \phi^2), & i=j \\ 0, & i \neq j \end{cases} \quad (6)$$

where $k_B = 1.38 \times 10^{-23} \text{ J} \cdot \text{K}^{-1}$ is the Boltzmann constant and T is the absolute temperature. The disturbance term is also obtained from (4), $d[k] = h(t) * F_{E'}(t) = \int_{t_{k-1}}^{t_k} h(t) F_{E'}(t - \tau) dt$, where $h(t) = (1/\gamma) \exp[-k_{OT}/\gamma(t - t_{k-1})]$ is the impulse response function of (4). If F_E varies slowly within the system's small sampling interval, it can be measured by its mean value in each sampling period, which, as shown by the aforementioned convolution, can be scaled from $d[k]$

$$F_E(t - \tau_m | t_{k-1} \leq t < t_k) \approx \bar{F}_E[k] = \frac{k_{OT}}{1 - \varphi} d[k]. \quad (7)$$

III. Adaptive Estimation Algorithm

As seen from (7), in order to determine the dynamic force F_E both the disturbance term d and the parameter φ of the system model (5) need to be known in real time. The trapping stiffness k_{OT} in the equation, which can be calibrated before-hand, is invariant if the laser power is kept constant, whereas the probe's damping coefficient γ , as a function of local temperature and influenced by the wall effect, makes φ vary. The adaptive estimation algorithm for joint estimation of d and φ is hence presented in this section.

An established approach to disturbance estimation is to augment the system model with the dynamics of the disturbance, which becomes a virtual state variable to be estimated by a state observer [23]. It can also be applied to parameter estimation, with the inclusion of a suitable update law of parameter variation in the system model [31]. Hence, as long as the convergence of the estimator can be guaranteed, adaptive estimation is feasible. In our design, the disturbance dynamics is described by a general autoregressive (AR) model

$$d[k] = \sum_{i=1}^p c_i d[k - i] + w_1[k] \quad (8)$$

where c_i 's are the designed model parameters and w_1 is the process noise with variance $\sigma_{w_1}^2$. This noise results from the random source and/or unmodeled dynamics of the disturbance.

Although *a priori* knowledge of the actual dynamics is desirable for accurate estimation, it is not mandatory [23]. The only constraint to assure the existence of convergent estimators, d to be observable, is evident in (5). Thus, for slow-varying external force, the first-order AR model can be employed [32]:

$$d[k] = d[k - 1] + w_1[k]. \quad (9)$$

The model has an integrator structure. With small process noise w_1 , it predicts a nearly constant disturbance, and any state of the disturbance can be eventually reached via random walk [21]. Similarly, since parameter variation caused by the environmental change is often even slower, it is represented by the first-order model of the same type

$$\varphi[k] = \varphi[k - 1] + w_2[k]. \quad (10)$$

In the case that fast-varying disturbance needs to be estimated, a natural extension of (9) to the second-order AR model is to include d 's rate of change

$$d[k] = d[k-1] + \beta(d[k-1] - d[k-2]) + w_1[k] = (1+\beta)d[k-1] - \beta d[k-2] + w_1[k] \quad (11)$$

where β is a weighting factor very close to but less than 1. Model analysis shows that (11) is an integrator cascaded with a stable first-order low-pass filter. The time constant of the filter, decided by β , determines the effective period of the historical rate of change employed for estimation. When compared to the first-order model, this second-order AR model is a better approximation of rapid change and thus suitable for dynamic force sensing.

In our implementation, the general AR disturbance model (8) and the first-order AR parameter update law (10) are used to expand the system model (5), and an estimator, also known as a Luenberger observer [23], is designed accordingly. It is worth noting that in our probing system, the state x_m is measured with high resolution; hence, it is acceptable to construct a reduced-order estimator [23], in which only d and ϕ are estimated. The augmented system is thus derived in a state-space canonical form as

$$\begin{pmatrix} d_f[k] \\ d[k] \\ d_1[k] \\ \vdots \\ d_{p-1}[k] \\ \varphi[k] \end{pmatrix} = \underbrace{\begin{bmatrix} c_1 & c_2 & \cdots & c_p & 0 \\ 1 & 0 & \cdots & 0 & 0 \\ \vdots & \ddots & \ddots & \vdots & \vdots \\ 0 & \cdots & 1 & 0 & 0 \\ 0 & 0 & \cdots & 0 & 1 \end{bmatrix}}_{\Phi_d} \underbrace{\begin{pmatrix} d_f[k-1] \\ d[k-1] \\ d_1[k-1] \\ \vdots \\ d_{p-1}[k-1] \\ \varphi[k-1] \end{pmatrix}}_{\mathbf{d}_f[k-1]} + \underbrace{\begin{pmatrix} w[k] \\ w_1[k] \\ 0 \\ \vdots \\ 0 \\ w_2[k] \end{pmatrix}}_{\mathbf{w}[k]} + \underbrace{\begin{pmatrix} d[k] \\ \varphi[k] \end{pmatrix}}_{\mathbf{d}[k]} = \underbrace{\begin{bmatrix} 1 & 0 & \cdots & 0 & 0 \\ 0 & 0 & \cdots & 0 & 1 \end{bmatrix}}_{\mathbf{T}_d} \mathbf{d}_f[k]$$

$$\underbrace{x_m[k] - u_c[k - \Delta - 1]}_{y[k]} = \underbrace{(1 x_m[k - 1] - u_c[k - \Delta - 1])d[k] + v[k]}_{H_d[k]}. \quad (12)$$

The first equation of (12), $\mathbf{d}_f[k] = \Phi_d \mathbf{d}_f[k-1] + \mathbf{w}[k]$, is the state-space model of the augmented variables. Its state matrix Φ_d can be derived according to the linear disturbance model and the update law of parameter variation employed. The second one, $\mathbf{d}[k] = \mathbf{T}_d \mathbf{d}_f[k]$, is a transform equation that singles the two variables d and ϕ out for estimation. The last one, $y[k] = \mathbf{H}_d[k] \mathbf{d}[k] + v[k]$, is derived from (5) as the measurement equation of the observer, whose order is reduced by removing the state x_m from the estimation. Subsequently, for the joint estimation of the vector $\mathbf{d}$, a Luenberger observer is formulated to correct the model-based prediction $\Phi_d \hat{\mathbf{d}}_f[k-1]$ with measurement innovations ($y[k] - \mathbf{H}_d[k] \mathbf{T}_d \hat{\mathbf{d}}_f[k]$) in real time, so that the estimation $\hat{\mathbf{d}}$ can quickly converge to the true states of $\mathbf{d}$

$$\hat{\mathbf{d}}_f[k] = \Phi_d \hat{\mathbf{d}}_f[k-1]$$

$$\hat{\mathbf{d}}[k] = \mathbf{T}_d \hat{\mathbf{d}}_f[k] + \mathbf{L}[k](y[k] - \mathbf{H}_d[k] \mathbf{T}_d \hat{\mathbf{d}}_f[k]). \quad (13)$$

$\mathbf{L}$ in (13) is a 2×1 feedback gain vector of the estimator, which depending on the design may or may not be constant.

When employing (13), the convergence of the estimation on d is easily guaranteed by choosing proper gains, whereas the convergence of $\hat{\phi}$ demands an additional persistent excitation condition in $\mathbf{H}_d$ [27]. This condition is typically required for system identification [31], whereas it is satisfied in our system due to the fact that the probe's motion is subject to a persistent thermal force excitation. Hence, unbiased adaptive estimation of the dynamic external force F_E and trapping dynamics can be obtained from (7) and (13).

The Kalman filter algorithm, which evolves from the recursive weighted least-squares method, is employed to compute the estimator's gain so as to achieve efficient adaptive estimation with (13). In the case that $\mathbf{w}$ in (12) is the white Gaussian and uncorrelated to the white Gaussian noise v of the measurement equation, the algorithm produces the best linear unbiased as well as maximum likelihood estimation [28]. The estimation error $\mathbf{e}[k] = \mathbf{d}[k] - \hat{\mathbf{d}}[k]$ is, therefore, minimized in the sense of its mean square, and the estimator is asymptotically efficient among all possible ones, whether linear or nonlinear [28].

Adapted from the standard Kalman filter [23], the gain update equation for (13) is

$$\mathbf{L}[k] = \mathbf{P}[k] \mathbf{H}_d^T[k] R_{v_0}^{-1} \quad (14)$$

where $R_{v_0} = \sigma_v^2 = R_v[0, 0] = \frac{k_B T}{k_{OT}} (1 - \hat{\varphi}^2)$ and

$$\mathbf{P}[k] = E(\mathbf{e}[k] \mathbf{e}^T[k]) = \mathbf{M}[k] - \frac{\mathbf{M}[k] \mathbf{H}_d^T[k] \mathbf{H}_d[k] \mathbf{M}[k]}{\mathbf{H}_d[k] \mathbf{M}[k] \mathbf{H}_d^T[k] + R_{v_0}} \quad (15)$$

The gain $\mathbf{L}$ computed by (14) is time varying and does not converge to a steady-state value since $\mathbf{H}_d$ is shown in (12) to be influenced by the persistently excited probe motion. It therefore needs real-time update. Using the Kalman filter algorithm to determine $\mathbf{L}$ can also lead to whitening the innovations process in the observer (13) [28] and result in optimal tracking for the variation of $\mathbf{d}$ [29].

$\mathbf{P}$ given by (15) is the 2×2 error covariance matrix of $\hat{\mathbf{d}}$, after the estimation has been corrected by the latest measurement innovations in (13). It is an indicator of the estimation accuracy as well. In (15), the estimation error $\mathbf{e}[k]$ is a 2×1 vector, and $\mathbf{M}$ is the 2×2 error covariance matrix prior to the innovations, which is propagated from $\mathbf{P}$ of the previous step based on the model prediction

$$\mathbf{M}[k] = \mathbf{T}_d \Phi_d \mathbf{T}_d^T \mathbf{P}[k-1] \mathbf{T}_d \Phi_d^T \mathbf{T}_d^T + \mathbf{R}_{w_0}. \quad (16)$$

$\mathbf{R}_{w_0} = \text{diag} \{ \sigma_{w_1}^2, \sigma_{w_2}^2 \}$ in (16) is the covariance matrix of the process noise $\mathbf{w}$, which needs to be white Gaussian for achieving optimal estimation. However, due to the lack of noise information in practice, $\mathbf{R}_{w_0}$ usually accounts for all unknown dynamics in model (12). Its value then needs to be tuned, according to $\mathbf{P}$, such that model (12) approximates the augmented system dynamics in the case that the actual one is not exactly known. The quality of the estimation can consequently be assured, in spite of being suboptimal. The estimation performance in this suboptimal scenario is illustrated by Fig. 4(b) and discussed further in Section IV-A.

IV. Experimental Results

The adaptive estimator designed in Section III, (13)–(16), along with various feedback controllers was implemented in the probing system's FPGA. The system is capable of achieving simultaneously dynamic force sensing, active Brownian motion control, and force-fed position clamping in our current implementation, whereas force feedback control for automatic scanning will be implemented in the near future. A series of experiments were conducted to assess the performance of the adaptive observer. The results of dynamic force probing and its effects on position clamping are presented in Section IV-A Adaptive estimation of a nonstationary process is shown in Section IV-B.

A. Dynamic Force Sensing

The probing system was employed to measure external forces, which were generated from viscous drag [33], [34]. Viscous drag force can be controlled by regulating the movement of the medium surrounding the measurement probe. It can be theoretically calculated and is often employed in force calibration for optical traps [34]. According to Stoke's law [33], $F_{\text{drag}} = \gamma v_s = 6\pi\eta a v_s$, where a is the trapped probe's radius, η is the viscosity of surrounding medium, and v_s is the flow speed of the medium. In our experiments, the medium flow was induced by the motion of the setup's piezostage while the measurement probe was stabilized by the optical trap. The external force F_E was controlled by regulating the speed of the stage. Its theoretical value was calculated and served as the benchmark for the evaluation of force sensing.

In the first experiment, a 1.87 μm diameter probe was trapped by the system with ~ 32 mW laser power at focus. The piezostage was commanded to move along the y -axis with a speed of 250 $\mu\text{m/s}$ for 0.4 s, stop for 0.8 s, and then retreat to its initial position with the same speed. The motion profile of the stage is shown in the inset of Fig. 2(b). This motion exerted ~ 4 pN drag force on the probe, calculated and shown as the black dashed line in Fig. 2(b). The force amplitude is comparable to what can be generated by a single motor protein [7] and is only a fraction of the ± 50 pN force range of our setup [25]. The first-order disturbance model (9) was utilized for dynamic force estimation and the experiment was performed twice. Active control was turned OFF first and then enabled for comparison. Fig. 2(a) shows the dynamic response of the probe. Without active control, the probe exhibited large thermal fluctuation (blue solid line, darker in gray scale) and was displaced by the external force until a new force balance established. Subsequently, two control laws were activated. The first one was the proportional Brownian motion control [11], [24], which enhances trapping stability and the spatial resolution of the probing by suppressing the probe's thermal fluctuation. The resulting motion of the probe exhibited smaller thermal fluctuation (green solid line, lighter in gray scale), reduced over 50% in terms of its standard deviation σ_y . The second control objective was position clamping by the force feedback, wherein the estimated external force was utilized as a feedback signal to steer the laser focus and generate the needed optical force for disturbance rejection. The probe's collective displacement, caused by the external drag force, therefore disappeared except for four barely noticeable pulses occurring at the beginning and end of the piezostage's two ramp movements.

Estimated forces with and without the control in action are drawn correspondingly in the solid blue/darker line and green/lighter line in Fig. 2(b). They accorded well with theoretical calculation (black dashed line) in general, whereas slight deviation from the theoretical curve took place sporadically due to the fact that the system was very sensitive to all external force, whether under our control or not. These results validate the probing system's capability of sensing dynamic force from noisy measurements. In addition, the estimation tracks the force variation in real time, with its settling time (within 5%) < 30 ms. Since the

stepwise external force and constant trapping dynamics in this experiment are exactly modeled by (9) and (10), $\mathbf{w}$ in (12) contains only white Gaussian noise and the result of estimation is optimal. Despite having very different probe motion, the green/lighter line in Fig. 2(b) illustrates that the estimation is unaffected by feedback control and validates the principle of separation of estimation and control. Dynamic force sensing, Brownian motion control, and position clamping can, therefore, be achieved simultaneously, whereas the force sensing performance during control would be much degraded were quasi-static linear-spring method employed.

When applying the probing system to investigate an unknown process, due to the lack of prior knowledge of the dynamics of the process, the estimation using the Kalman filter may only lead to suboptimal results. In order to evaluate the performance of the estimator in this situation, another experiment was performed. A 5 Hz cosine drag with ~ 5 pN peak force was exerted on a $1.95 \mu\text{m}$ probe by oscillating the stage in sine wave with $10 \mu\text{m}$ amplitude along x - and y -axis, respectively. Since F_E was a simple harmonic force, the accurate model $d[k] = 2 \cos(\omega_d \tau_s) d[k-1] - d[k-2] + w_1[k]$ should be used for the estimator design, where ω_d is the angular frequency of the force and equals to $10 \pi/\text{s}$ in this experiment. However, in an effort to measure arbitrary dynamic force, the first-order model (9) and second-order model (11) were employed in (12) for the x - and y -axis estimation respectively. Due to the modeling error, w_1 was no longer white Gaussian and the resultant force sensing was not optimal for both axes. Nevertheless, both observers, as illustrated in Fig. 3(b) and Fig. 4(b), worked properly and yielded satisfactory results: they both followed the dynamic trend of the external force in real-time with sub-pN resolution. When further comparing the difference between the two results that used different disturbance models, it is clear that the latter [Fig. 4(b)] did not exhibit the 16 ms estimation delay of the former [Fig. 3(b)], although the resolution was a little worse, 0.2 pN versus 0.1 pN (1σ). As a result, the large oscillation of the uncontrolled probe, over 200 nm peak-to-peak (p-p) as demonstrated by the blue/darker line in Fig. 4(a), could be eliminated almost perfectly (green/lighter line) through disturbance rejection using the second-order model. In contrast, a small residual vibration was still present after enabling the control that employed the first-order model for dynamic force sensing, which is shown by the green/lighter line in Fig. 3(a).

B. Adaptive Estimation of Time-Varying Processes

In addition to dynamic force sensing, the adaptive estimation algorithm presented in Section III can be employed to simultaneously detect the dynamic parameter variation of the optical trap. This capability is very important to achieving accurate dynamic force sensing in a time-varying process, in which the trapping dynamics is nonstationary due to local variations of the surrounding medium. It is especially helpful to the investigation of active biological systems, in which morphological change and energy transfer occur constantly. This section presents experimental results that validate the effectiveness of the adaptive estimation algorithm.

When approaching the liquid/solid interface, the trapped probe's damping coefficient γ undertakes significant change and so does the trapping bandwidth (corner frequency). This change is determined by Faxen's law [4]

$$\gamma = \frac{6\pi\eta a}{1 - \frac{9}{16} \left(\frac{a}{h}\right) + \frac{1}{8} \left(\frac{a}{h}\right)^3 - \frac{45}{256} \left(\frac{a}{h}\right)^4 - \frac{1}{16} \left(\frac{a}{h}\right)^5} \quad (17)$$

where h is the distance from the center of the probe to the interface. In the experiment, h was controlled by the piezo sample stage. The theoretical variation of γ , obtained from (17), was used to validate the estimation result.

Fig. 5 shows the adaptive estimation result of such a time-varying process. A $1.87\text{ }\mu\text{m}$ probe was trapped with $\sim 32\text{ mW}$ laser power at focus; the Brownian motion control and position clamping were activated simultaneously. The boundary of the surrounding medium, as formed by a cover slip fixed on the piezo sample stage, was moved $5\text{ }\mu\text{m}$ axially by the stage toward the trapped probe in 3 s, stayed at about 200 nm away from the probe's lowest point for 1.5 s, and then retreated back to its initial position with the same slow speed. The optical trap's corner frequency f_c was expected to decline and then recover in the process. It was computed from the estimated state transition coefficient ϕ by $f_c = -\ln \phi / (2\pi\tau_s)$ and drawn in Fig. 5(a). As illustrated in the figure, corner frequencies of both x - and y -axis vary up to almost 50%, and the changes synchronize with the stage motion shown in the inset of Fig. 5(a). It is worth noting that the difference between the two corner frequencies was not due to the convergence error of the adaptive estimation, but came from the slight asymmetry of the trapping laser focus. Since no external force was intentionally applied in the two lateral directions, the force sensing results on both axes in Fig. 5(b) illustrate only sub-pN disturbance of unknown source and estimation noise.

The adaptive estimation result of this nonstationary process is further validated in two ways. First, the probe's motion was recorded after the two controls were disabled and the stage retreated. It was transformed to its double-sided power spectral density using the fast Fourier transform algorithm. The corner f_c was then fitted [26] to be 435.7 Hz for x -axis, as shown in Fig. 6. The x -axis adaptive estimation result at the beginning and end of the controlled probing experiment, illustrated in Fig. 5(a), gives the same value. It proves the convergence of the adaptive estimator and demonstrates that this convergence is unaffected by adding active feedback control to the probing system.

Second, the estimated damping coefficients are compared to the theoretical calculation in Fig. 7. It shows that the estimated results from both x - and y -axes data are very close to the theoretical value (black dashed line) despite the difference in the corner frequency illustrated in Fig. 5(a). The two estimates also coincide with the theoretical value along the time axis in Fig. 7, when the latter is delayed by 140 ms . The convergence time of the parameter estimation accounts for this delay and dictates the adaptability of the estimator to the change of the trapping dynamics. The estimated result exhibits larger fluctuation when the probe is closer to the boundary surface. This fluctuation is due to the variation of the probe-surface distance caused by the probe's Brownian motion, whose amplitude is approximately $\pm 60\text{ nm}$ p-p along the z -axis [11]. According to (17), with the probe being in the vicinity of the solid surface, the small change of h alters γ significantly.

V. CONCLUSION

An adaptive observer was designed and implemented for an optically trapped probing system to realize simultaneous real-time dynamic force sensing and trapping dynamics estimation. The observer utilized the measured motion of the trapped probe along with the input control effort to recursively estimate the probe-sample interaction force. The estimated external force was employed as a feedback signal to steer the laser focus and generate the needed optical force for disturbance rejection, achieving precise position clamping. The adaptive estimation also worked compatibly with the Brownian motion control, which enhances trapping stability and probing resolution. This ability of joint state-parameter estimation is very important to achieving accurate dynamic force sensing in a time-varying process. It is especially helpful to the investigation of active biological systems, in which morphological change and energy transfer occur constantly.

A series of experiments were conducted to validate the capabilities of the probing system in terms of dynamic force sensing, position clamping, and parameter estimation. Satisfactory

results were demonstrated for both x - and y -axes to signify promising real-time force probing and regulation applications. Specifically, even if the optimal estimation condition could not be satisfied when the process noise of the external force deviates from the white Gaussian model, the force sensing result of our estimator still has an ultra-high resolution of 0.2 pN (1σ) and no palpable latency. To further improve this performance, application-specific modeling of the external force needs to be studied, so that the white Gaussian noise condition for optimal estimation can be met.

Although not presented in this paper, comparable performance for the z -axis was also obtained by including the dynamic model of the z -actuator (i.e., DM) in the design of the observer. To do so, $u_c[k - \Delta - 1]$ in (12) was replaced by $\hat{u}[k - \Delta_z - 1]$, which was calculated from the z -axis u_c using the calibrated eighth-order model of the DM. Since the DM is open-loop stable [11], $\hat{u}$ converges to the actual trapping equilibrium u along the z -axis regardless of the initial condition; therefore, the convergence of the estimation is unchanged by the actuator's dynamics. The control performance is, however, affected due to the DM's relatively small bandwidth [11].

In addition to enabling disturbance rejection for position clamping, dynamic force sensing also lays the foundation of force feedback control that is needed in automatic scanning. Along with three-axis steering, it enables the transformation of the 3-D optically trapped probing system to a scanning probe system, which is capable of intra/extracellular scanning, mechanical property measurement of subcellular organelles, and molecular interaction control. Using the same technique as presented in this paper, similar force sensing capability can also be developed for different probing apparatus, e.g., magnetic tweezers [35]. Other applications of the adaptive estimation algorithm include the adaptive Brownian motion control [25], by which the control performance was self-tuned to sustain its optimality in a complex environment.

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Fig. 1.
Combined estimation and control structure of the optically trapped probing system.

Fig. 2.

Dynamic force sensing of step force changes along the y-axis with the first-order disturbance model: (a) dynamic response of the probe, (b) estimated force compared to the theoretically computed external force, and inset shows the stage's y-axis motion for drag force generation.

Fig. 3.

Dynamic force sensing along the x -axis with the first-order disturbance model: (a) dynamic response of the probe subject to oscillating force, (b) estimated force compared to the theoretically computed external force, and inset shows the stage motion along the x -axis for drag force generation.

Fig. 4.

Dynamic force sensing along the y-axis with the second-order disturbance model: (a) dynamic response of the probe subject to oscillating force. (b) estimated force compared to the theoretically computed external force, and inset shows the stage motion along the y-axis for drag force generation.

Fig. 5. Joint state-parameter estimation of a time-varying process with probe control enabled: (a) estimated (open-loop) corner frequencies along the x - and y -axis, (b) estimated external force, and inset shows the z -axis stage motion.

Fig. 6.

Power spectrum analysis of the x -axis motion of the trapped 1.87 μm probe at the initial position of the probing experiment (active control is off).

Fig. 7.

Validation of parameter estimation: estimated damping coefficients are compared to the theoretical calculation. The theoretical result is delayed by 140 ms to take account of the convergence time of the estimation.