Robotic Manipulation of Micro/Nanoparticles Using Optical Tweezers with Velocity Constraints and Stochastic Perturbations

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Abstract— Various control approaches have been developed for micro/nanomanipulations using optical tweezers. Most existing methods assume that the micro/nanoparticles stay trapped during manipulations, and stochastic perturbations (Brownian motion) are usually ignored for the simplification of model dynamics. However, the trapped particles could escape from the optical traps especially in motion due to several possible reasons: small trapping stiffness, stochastic perturbations, and kinetic energy gained during manipulation. This paper investigates the conditions under which micro/nanoparticles will stay trapped while in motion. The dynamics of the trapped particles subject to stochastic perturbations is analyzed. Dynamic trapping is considered and the maximum manipulation velocity is determined from a probabilistic perspective. A controller with certain velocity bound is proposed, the stability of the system is analysed in presence of stochastic perturbation. Experimental results are presented to show the effectiveness of the proposed control approach.

I. INTRODUCTION

Extensive attention has been drawn recently to the manipulation of micro/nanoparticles including biological cells with the rapid developments in technology. Compared with traditional manual manipulations using micropipettes, systems integrated with robotic technology and biomedical equipments make micro/nanomanipulations easier yet more accurate and efficient.

Many techniques have been developed for the purpose of micromanipulation, including magnetic tweezers [1], dielectrophoresis (DEP) [2], [3], atomic force microscopy (AFM) [4], [5], and optical tweezers [6]. Optical tweezers are becoming popular for manipulations of micro/nanoparticles such as biological cells. A tightly focused laser beam can generate forces to trap and manipulate micro/nanoparticles around the vicinity of the beam focus [7]. As a result, a freely diffusing micro/nanoparticle can be trapped and manipulated by changing the position of the beam focus. This simple non-contact manipulation method with high precision has therefore been utilized extensively for biomedical applications, such as cell transportation [8], cell sorting [9], [10], cell responses to external stimuli [11], and cell-cell interactions [12], to name a few.

Various automatic control systems and approaches have been developed over the past few years, allowing researchers

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to accomplish more complicated applications. In [13], a three-axis steering system was developed and the trapped micro/nanoparticle serves as a measurement probe. Brownian motion control of an optically trapped probe was reported [14] and an optimal controller was proposed to minimize the variance of the probe's Brownian motion. Automated manipulation of multiple non-spherical objects was proposed in [15] by using multiple-force optical clamps. A stochastic dynamic programming framework was proposed for automated particle transport operations in [16]. Automated cell transportation was reported in [17] with calibrated optimal motion parameters and a modified path planning algorithm. An integrated closed-loop controller was developed in [18], allowing the transition from trapping to manipulation without any hard switching from one controller to another. Vision based observer technique was developed in [19] to estimate the velocity of cell without the need of camera calibration. In [20], dynamic interaction between the cell and the manipulator of laser source was studied and a setpoint control approach was proposed, which was further extended to a region reaching controller. An automated arraying approach was developed in [21] to place groups of microparticles into a predefined array with right pairs using holographic optical tweezers. Cell patterning of a group of cells was considered in [22] with a multilevel-based topology design, which can form various desired patternings with rotation and scaling capabilities. An indirect pushing based automated micromanipulation of biological cells was reported in [23] so the exposure of the cell to the laser beam could be minimized. Real-time path planning was investigated for coordinated transport of multiple particles [24].

Most existing optical manipulation approaches ignored the random effect of Brownian motion, and control methods were developed assuming the trapped particle will never escape, which might not be always valid. Saturated controllers can be implemented to alleviate this problem but there is no theoretical result so far to analyse the stability of the optical manipulation system in the presence of Brownian motion. A trapped particle might escape especially in motion due to various possible reasons, including small trapping stiffness, random Brownian motion, and kinetic energy gained in motion, which should all be investigated carefully.

In this paper, Brownian motion is studied for an optically trapped micro/nanoparticle from stochastic perspective. A maximum manipulation velocity is determined considering the stochastic behavior of the trapped micro/nanoparticle in order to achieve dynamic trapping with a desired probability. A controller constrained by the maximum manipulation

velocity is proposed to keep the micro/nanoparticle trapped for a given time. The stability of the system is investigated and experimental results are presented to illustrate the performances of the proposed control approach.

II. THEORY AND MODEL DESCRIPTION

In this section, the Brownian motion is defined as a stochastic process. The dynamics of a freely diffusing particle in fluid is presented, and earlier work regarding static optical trapping of particles is briefly reviewed.

A. Brownian motion

Definition 1: A standard Brownian motion (one-dimensional) is a stochastic process $\{W_t : t \geq 0\}$ with the following properties:

1) W_t is continuous in the parameter t, and $W_0 = 0$;
2) for every $0 \leq t_1 < t_2 < t_3 < \cdots < t_n$, the increments $W_{t_2} - W_{t_1}, W_{t_3} - W_{t_2}, \cdots, W_{t_n} - W_{t_{n-1}})$ are independent random variables;
3) for each $0 \leq s < t < +\infty$, the increment $W_t - W_s$ is a Gaussian random variable with mean 0 and variance $t - s$.

Assume there exists no external potential, the Brownian particle is considered as "free", and the motion of the "free" Brownian particle in one dimension is modeled by the Langevin equation [25]:

$$m\ddot{x} = -\gamma\dot{x} + F, \tag{1}$$

where x is the particle position, $F = \sqrt{2k_B T_{temp}\gamma}\xi$ is the Brownian force, k_B is the Boltzmann's constant, T is the absolute temperature, γ is the drag coefficient, and $\xi = \frac{dW_t}{dt}$ is the stochastic Gaussian white noise satisfying

$$\langle\xi(t)\rangle = 0, \tag{2}$$
$$\langle\xi(t)\xi(t')\rangle = \delta(t - t'). \tag{3}$$

For manipulation of micro/nanoparticles, the Reynolds number is always low ($Re \ll 1$) for the environment, and thus the inertia effect in (1) can be ignored, which yields

$$\dot{x} = \frac{F}{\gamma}, \tag{4}$$

Note that the inertia term will be ignored in the rest of the paper.

B. Static trapping

Static trapping of a micro/nanoparticle refers to the case when the laser does not move, as shown in Fig.1. The potential energy U of the gradient force is determined by many factors, including intensity and wavelength of the incident light, particle size, and the refractive indices of the particle and the medium. The condition for a stable static trapping in a single beam trap was discussed in [6]. One necessary and sufficient condition is that the potential well of the gradient force should be much larger than the kinetic energy of the Brownian particles, which is given in Boltzmann factor $\exp(-U/k_B T_{temp}) \gg 1$, where k_B is the Boltzmann constant and T_{temp} is the absolute temperature.

This requirement can be seen as requiring the time to pull the particle into a optical trap much less than the time for the particle to diffuse out of the trap because of Brownian motion [6]. Therefore the minimum energy for a stable static trapping in a single beam trap could be calculated as $|U|_{min} > 10k_B T_{temp}$ [6].
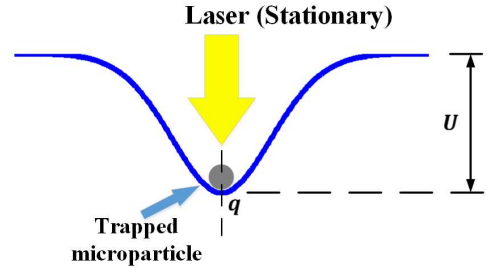

Fig. 1. Static trapping of micro/nanoparticle

III. DYNAMIC TRAPPING

When the optical trap is moving together with the laser, the trapped particle gains additional kinetic energy due to the motion, making it easier to escape from the optical trap, which is considered as a *dynamic trapping* problem. The trapped particle should be manipulated within a certain threshold velocity, otherwise it may escape from the optical trap if manipulated at a high velocity. The following sections are devoted to the study of this threshold velocity.

A. Micro/nanoparticle dynamics in optical trap

Consider a micro/nanoparticle that is trapped by an optical trap as shown in Fig. 2. The dynamics in one dimension is given by

$$\dot{x} = \frac{k(x,q)}{\gamma}(q - x) + \sqrt{2D}\xi \tag{5}$$

where q is the laser position, $D = \frac{k_B T_{temp}}{\gamma}$, and $k(x,q)$ is the optical trapping stiffness defined as [18]

$$k(x,q) = \begin{cases} k_c, & \|q - x\| \leq R \\ k_c e^{-k_R(\|q-x\|-R)^2}, & \|q - x\| > R \end{cases} \tag{6}$$

where k_c and k_R are positive constants, and R is the trapping radius. An illustration of the trapping stiffness and trapping force are shown in Fig. 3.(a) and Fig. 3.(b) respectively.

In this section, we consider the regime when $\|q-x\| \leq R$, that is, when the trapping stiffness is maximum and constant, such that the optical trap can be considered as a spring with constant stiffness.

B. Dynamic trapping and maximum manipulation velocity

As can be seen from (5), the velocity of the cell is a stochastic process due to the Brownian motion, therefore the maximum velocity for dynamic trapping should be computed taking into account the stochastic perturbations.

Assume that the laser moves with a positive constant velocity v, such that its position is given by $q = vt + x_0$, where x_0 is the initial position of the trapped particle. For a
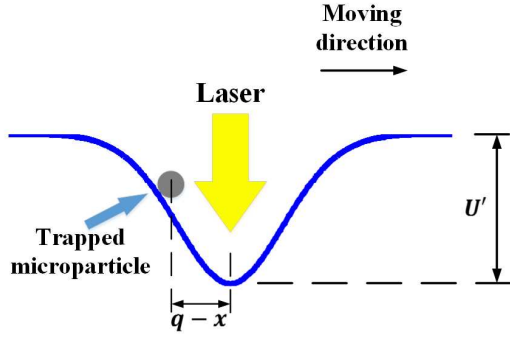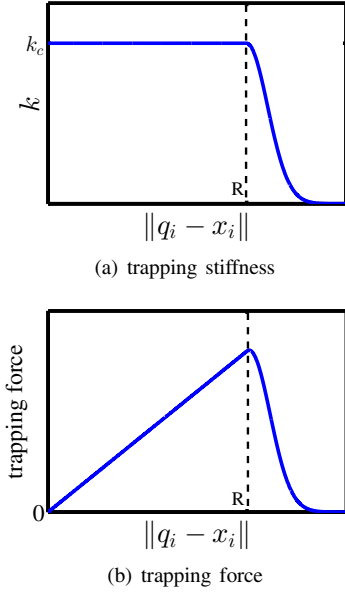
Fig. 2. Dynamic trapping of micro/nanoparticle

(a) trapping stiffness

(b) trapping force

Fig. 3. Trapping stiffness and trapping force

given time T, consider the event that the particle is trapped until time T, i.e. $\{\forall t \leq T, \|q - x\| \leq R\}$.

In this event, we have from equations (5) and (6) that

$$\dot{x} = \frac{k_c}{\gamma}(q - x) + \sqrt{2D}\xi \tag{7}$$

where $x = x_t + x_0$, and x_t is the time-varying part of the particle position.

Define next $y = x - q + v\frac{\gamma}{k_c}$. Substituting y in the above equation leads to

$$\dot{y} + v = \frac{k_c}{\gamma}(-y + v\frac{\gamma}{k_c}) + \sqrt{2D}\xi, \tag{8}$$

which results in

$$\dot{y} = -\frac{k_c}{\gamma}y + \sqrt{2D}\xi. \tag{9}$$

Thus y follows a Langevin equation [25]. Rewriting this in the form of stochastic differential equation yields

$$dy_t = -\rho y_t dt + \sqrt{2D}dW_t \tag{10}$$

where $\rho = \frac{k_c}{\gamma}$.

Now we consider the probability $P(\{\forall t \leq T, \|x - q\| \leq R\})$ when the laser is moving at a constant velocity v. Since $x - q = y - v\frac{\gamma}{k_c}$, the probability is thus $P(\{\forall t \leq T, \|y - v\frac{\gamma}{k_c}\| \leq R\})$. As long as $y^2 < (R - v\frac{\gamma}{k_c})^2$, one has $\|y - v\frac{\gamma}{k_c}\| \leq R$, which yields the inequality

$$P(\{\forall t \leq T, \|y - v\frac{\gamma}{k_c}\| \leq R\})$$
$$\geq P(\{\forall t \leq T, y^2 < (R - v\frac{\gamma}{k_c})^2\}). \tag{11}$$

Let $m = (R - v\frac{\gamma}{k_c})^2$. Using results on finite time stability (cf. chapter III in [26]), one obtains

$$P(\{\forall t \leq T, y^2 < m\}) = 1 - P(\{\forall t \leq T, \sup y^2 \geq m\})$$
$$\geq (1 - \frac{y_0^2}{m})e^{-\Phi_T/m}, \tag{12}$$

where $y_0 = v\frac{\gamma}{k_c}$, $\varphi_t = 2D$, and $\Phi_T = \int_0^T \varphi_s ds$. Therefore we have

$$P(\{\forall t \leq T, \|y - v\frac{\gamma}{k_c}\| \leq R\}) \geq (1 - \frac{y_0^2}{m})e^{-\Phi_T/m} \tag{13}$$

For a desired probability of dynamic trapping, a maximum velocity v_{max} can be thus calculated by (13).

For example, consider an experimental setting with room temperature $300K$ and a spherical microbead with diameter of 5 μm. If $T = 1$s and $P_{desired} = 0.95$ then v_{max} is given by $v_{max} = 4.6319R$ s^{-1}.

Note that the bound on v_{max} just obtained is a sufficient bound based on the Lyapunov analysis of [26]. Tighter bounds can be obtained by studying directly the escape time of equation (9), which is one of our current topics of investigation.

Proposition 1: A micro/nanoparticle is dynamically trappable in one dimension for a given time T with a desired probability, if its velocity is bounded by the value of v_{max} determined by (13).

To ensure dynamic trapping in two dimensions, the trapping radius should be reduced to the value of $\frac{\sqrt{2}}{2}R$ along each direction x_i, $i = 1, 2$. The micro/nanoparticle is dynamically trappable along direction x_i with the probability p_i as calculated in (12). The trapped particle is considered escaped when it escapes from either direction, therefore the probability for dynamic trapping in two dimensions is simply $p_1 p_2$. This also applies for manipulation in three dimensions.

IV. MANIPULATION CONTROLLER DESIGN WITH DYNAMIC TRAPPING

Consider a trapped micro/nanoparticle in two dimensions with fixed vertical position. Similar to the one dimensional case, the dynamics of the trapped particle is given by

$$\dot{\boldsymbol{x}} = \boldsymbol{\Gamma}^{-1}k(\boldsymbol{x}, \boldsymbol{q})(\boldsymbol{q} - \boldsymbol{x}) + \boldsymbol{\Gamma}^{-1}\boldsymbol{F}, \tag{14}$$

where $\boldsymbol{x} = [x_1, x_2]^T$ is the position of the particle, $\boldsymbol{q} = [q_1, q_2]^T$ is the position of laser beam, $\boldsymbol{\Gamma} =$

$diag(\gamma_1, \gamma_2)$ is a damping coefficient matrix, and $k(\boldsymbol{x}, \boldsymbol{q}) = diag(k_1(x_1, q_1), k_2(x_2, q_2))$. $\boldsymbol{F}$ denotes the two-dimensional Brownian force $\boldsymbol{F} = \sqrt{2k_BT}[\sqrt{\gamma_1}\xi_1, \sqrt{\gamma_2}\xi_2]^T$, and ξ_1 and ξ_2 are distinct and independent white noises.

Definition 2: Given a positive constant M, a function $s : R \rightarrow R : \zeta \mapsto s(\zeta)$ is defined to be a saturation function with bound M, if it is nondecreasing, and satisfies the followings:
1) $\zeta s(\zeta) > 0, \forall \zeta \neq 0$;
2) $|s(\zeta)| \leq M, \forall \zeta \in R$.

A saturation vector is defined as $\boldsymbol{sat}() = [s_1(), s_2()]^T$ where $s_i(), i = 1, 2$ is strictly increasing continuously differentiable saturation function defined as

$$s_i(x) = \begin{cases} M_i - 1 + tanh(x - M_i + 1), \\ \qquad\qquad x > M_i - 1 \\ x, \quad -M_i + 1 \leq x \leq M_i - 1 \\ -M_i + 1 + tanh(x + M_i - 1)), \\ \qquad\qquad x < -M_i + 1 \end{cases} \quad (15)$$

An illustration of saturation function $s_i()$ is shown in Fig. 4. It can be seen that the saturation function $s_i()$ is an odd function, and is linear within the non-saturation zone, i.e. $[-M_i + 1, M_i - 1]$. It can be seen that $\|s_i()\| \leq M_i$, where $M_i = v_{max\{i\}}, i = 1, 2$ in both directions.
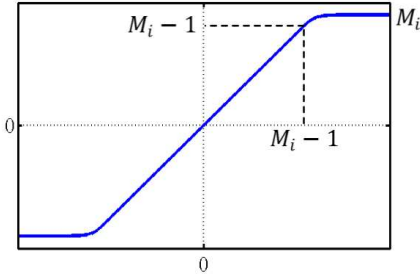

Fig. 4. Saturation function

The desired velocity of the particle $\dot{\boldsymbol{x}}_d$ is designed to be always within the non-saturation zone $[-M_i + 1, M_i - 1]$ in both dimensions, satisfying the follows:

$$sup \|\dot{\boldsymbol{x}}_d\| < \|\boldsymbol{v}_{max}\| = \sqrt{v_{max\{1\}}^2 + v_{max\{2\}}^2} \quad (16)$$

where $\boldsymbol{x}_d(t)$ is the desired trajectory of the particle.

However, $\dot{\boldsymbol{x}}_d$ is bounded does not necessarily indicate the boundedness of $\dot{\boldsymbol{x}}$. Consider the transient phase, i.e. when the initial position of the micro/nanoparticle $\boldsymbol{x}_0$ is far from the initial position of the desired trajectory. The large initial position error might result in a high initial velocity which could cause the trapped particle to escape at the beginning of the manipulation, even though the desired velocity satisfies equation (16). Therefore, a controller should be appropriately defined to ensure the boundedness of $\dot{\boldsymbol{x}}$.

The position input for the laser beam is proposed as

$$\boldsymbol{q} = \boldsymbol{x} - k^{-1}(\boldsymbol{x}, \boldsymbol{q})\boldsymbol{\Gamma} \cdot \boldsymbol{sat}(K_p\Delta\boldsymbol{x} - \dot{\boldsymbol{x}}_d). \quad (17)$$

where $\Delta\boldsymbol{x} = \boldsymbol{x} - \boldsymbol{x}_d$.

Substituting (17) into (14) yields

$$\dot{\boldsymbol{x}} = -\boldsymbol{sat}(K_p\Delta\boldsymbol{x} - \dot{\boldsymbol{x}}_d) + \boldsymbol{D\Xi}, \quad (18)$$

where $\boldsymbol{D} = diag(\sqrt{2D_1}, \sqrt{2D_2})$, $D_i = \frac{k_BT}{\gamma_i}$ for $i = 1, 2$, and $\boldsymbol{\Xi} = [\xi_1, \xi_2]^T$.

Then we have:

$$\Delta\dot{\boldsymbol{x}} = \dot{\boldsymbol{x}} - \dot{\boldsymbol{x}}_d = -\boldsymbol{sat}(K_p\Delta\boldsymbol{x} - \dot{\boldsymbol{x}}_d) - \boldsymbol{sat}(\dot{\boldsymbol{x}}_d) + \boldsymbol{D\Xi}, \quad (19)$$

which can be written in the form of stochastic differential equation

$$d(\Delta\boldsymbol{x}) = -(\boldsymbol{sat}(K_p\Delta\boldsymbol{x} - \dot{\boldsymbol{x}}_d) + \boldsymbol{sat}(\dot{\boldsymbol{x}}_d))dt + \boldsymbol{D}d\boldsymbol{W}. \quad (20)$$

where $\boldsymbol{W} = [W_1, W_2]^T$ denotes the two-dimensional Wiener process with distinct and independent W_1 and W_2.

Define a Lyapunov-liked function candidate as:

$$V(t) = \frac{1}{2}\Delta\boldsymbol{x}^T\Delta\boldsymbol{x}. \quad (21)$$

Theorem: Consider a system described by (14) with control input described in (17), then $\forall t \geq 0$

$$E[V(t)] \leq \frac{D_1 + D_2}{\lambda_1} + [V(0) - \frac{D_1 + D_2}{\lambda_1}]^+ e^{-2\lambda_1 t} \quad (22)$$

where $E[V(t)]$ is the expected value of $V(t)$, and $[.]^+ = max(0, .)$.

Proof:
We derive an inequality on $\mathscr{L}V(t)$ where $\mathscr{L}$ denotes the differential generator of the Itô process [26].

$$\begin{aligned} \mathscr{L}V(t) &= -\frac{\partial V}{\partial \Delta\boldsymbol{x}}(\boldsymbol{sat}(K_p\Delta\boldsymbol{x} - \dot{\boldsymbol{x}}_d) + \boldsymbol{sat}(\dot{\boldsymbol{x}}_d)) \\ &\quad + \frac{1}{2}tr((2D_1 + 2D_2)I_2) \\ &= -\Delta\boldsymbol{x}^T(\boldsymbol{sat}(K_p\Delta\boldsymbol{x} - \dot{\boldsymbol{x}}_d) \\ &\quad + \boldsymbol{sat}(\dot{\boldsymbol{x}}_d)) + 2(D_1 + D_2). \end{aligned} \quad (23)$$

It can be clearly seen that the first term in (23) can be written in the form of $-(k_1\Delta x_1^2 + k_2\Delta x_2^2)$ with positive k_1 and k_2. Then we have $\mathscr{L}V(t) \leq -\lambda_1\|\Delta\boldsymbol{x}\|^2 + 2(D_1 + D_2)$, where $\lambda_1 = \min(k_1, k_2)$.

Then we have:

$$\mathscr{L}V(t) \leq -2\lambda_1 V(t) + 2(D_1 + D_2). \quad (24)$$

Since the function $V(t)$ contains stochastic process term, it is difficult to calculate the value of $V(t)$, instead, we consider the expected value E of $V(t)$. Then we have:

$$E[V(t)] - V(0) = E[\int_0^t \mathscr{L}V(s)ds], \quad (25)$$

Therefore one has $\forall u, t, 0 \leq u \leq t < +\infty$

$$\begin{aligned} E[V(t)] - E[V(u)] &= E[\int_u^t \mathscr{L}V(s)ds] \\ &\leq E[\int_u^t (-2\lambda_1 V(s) + 2(D_1 + D_2))ds] \\ &= \int_u^t (-2\lambda_1 E[V(s)] + 2(D_1 + D_2))ds \end{aligned} \quad (26)$$

Based on the Gronwall-type lemma [27], we have $\forall t \geq 0$:

$$E[V(t)] \leq \frac{D_1 + D_2}{\lambda_1} + [V(0) - \frac{D_1 + D_2}{\lambda_1}]^+ e^{-2\lambda_1 t} \quad (27)$$

As a result, it can be concluded that the mean square error between the particle trajectory and the desired trajectory is bounded, and the system described by (14) and (17) is stable.

V. Experiments

Experiments were performed to demonstrate the effectiveness of the proposed control approach for micro/nanoparticle manipulations.

A. Experimental setup

A robotic aided cell manipulation system (Elliot Scientific) mounted on an anti-vibration table (Thorlabs) was used in our experiments as shown in Fig. 5. Main sensors of this system include a microscope (Nikon Eclipse T*i*) and a CCD camera (Basler AG) with a resolution of 640×480 and frame rate of 30 fps. An oil immersion objective len of $100 \times$ magnification was used to observe the microenvironment. The size of each pixel under 100x was 0.074 μm, and the size of the field of view is 47.36 μm in length and 35.52 μm in width. A motorized stage (Marzhauser Wetzlar) can be controlled manually with a joystick or programmed by the computer to achieve desired movements. A highly focused laser beam (Ytterbium Fibre Laser, IPG Photonics) can be generated with the near-infrared wavelength of 1070 nm. Multiple traps can be generated as well to manipulate multiple micro/nanoparticles concurrently. Labview is used for various purposes, including programming, localization of cell positions, and data recording, etc.
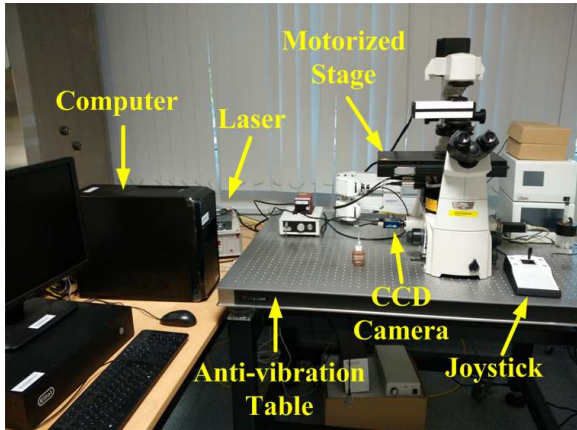

Fig. 5. Experimental setup

B. Results

Spherical latex microbeads with 5 μm diameter (Life Technologies, Singapore) were used in the experiments. Deionized water was used as the medium fluid. The laser power was set as 0.1 W. The maximum velocity for 5 μm microbead was determined with $P_{desired} = 0.95$. The trapping stiffness was measured at 1.3 pN/μm, and the trapping radius was measured at 5.2 μm with imaging processing technique. The calculated maximum velocity for the 5 μm microbead over $T = 1$s was $v_{max} = 24$ μm/s.

The microbead was trapped and moved to a fixed point. The position of the motorized stage remained fixed and the laser trap was manipulated. The control parameter was set as $K_p = 10$. The upper left corner was defined as the origin (0,0), and the update frequency of the laser trap was 30 Hz.

The 5 μm microbead was initially positioned at (15 μm, 10 μm) as shown in Fig. 6.(a), and the desired fixed point was set as (35 μm, 20 μm). In the first case, the proposed controller was used without a velocity bound. As shown in Fig. 6, the laser beam was manipulated with a high velocity and resulted in the escape of the initially trapped microbead after only 0.1 second. In the second case, the velocity bound for the proposed controller was set to 24 μm/s for dynamic trapping. As shown in Fig. 7, the microbead was manipulated with a lower velocity. The microbead was dynamically trapped at all time and finally reached at the desired position after 1.5 seconds. These results indicated the necessity of an appropriate velocity bound even if the desired velocity is zero in setpoint control.
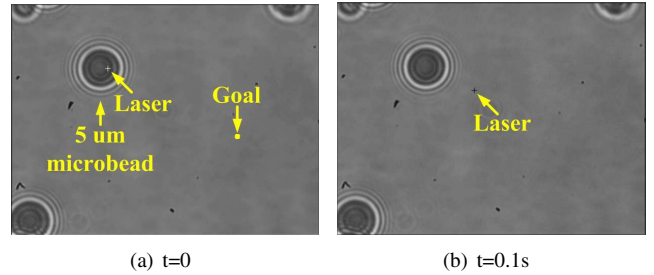

(a) t=0   (b) t=0.1s

Fig. 6. First case: fixed point control without velocity bound

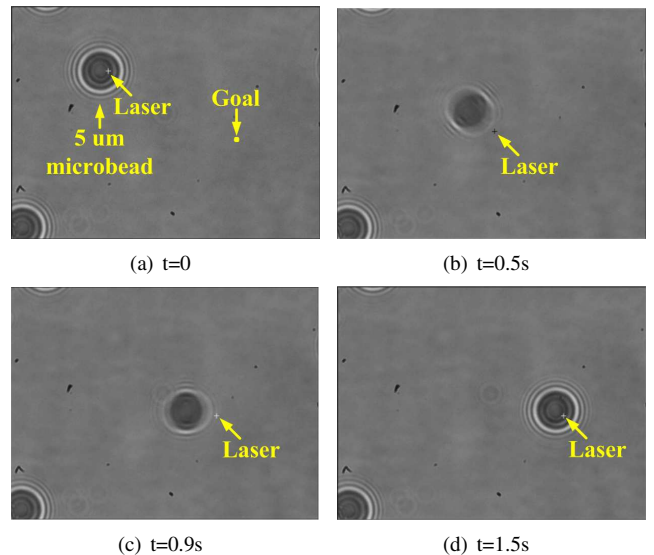(a) t=0   (b) t=0.5s

(c) t=0.9s   (d) t=1.5s

Fig. 7. Second case: fixed point control with velocity bound

The experimental results were obtained and analyzed. The positional errors were shown in Fig. 8 for the second case,

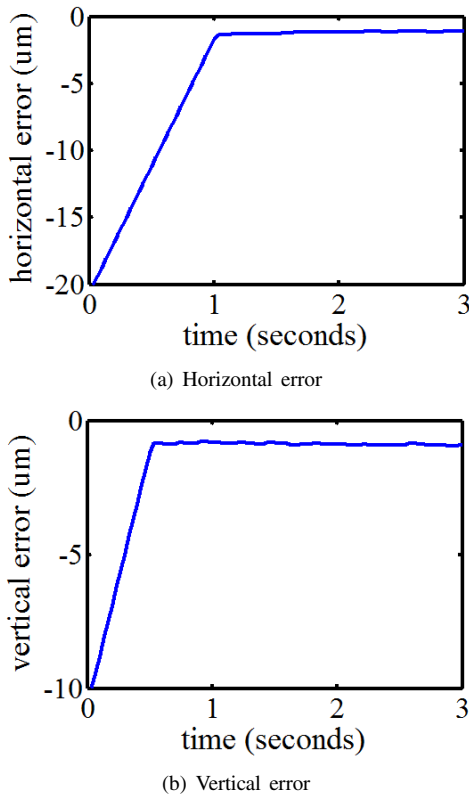illustrating the stability and boundedness of the proposed approach.

(a) Horizontal error

(b) Vertical error

Fig. 8.   Positional errors

VI. CONCLUSIONS

In this paper, the effect of stochastic perturbations on the stability of optical manipulation for micro/nanoparticles has been investigated. Dynamic trapping has been studied when the laser beam is in motion and the maximum manipulation velocity is determined such that a trapped micro/nanoparticle will not escape for a given time with a desired probability. A controller was proposed with appropriate velocity bound and the system was shown to be stable and bounded. Experiments were presented to demonstrate the necessity and effectiveness of the proposed control approach.

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