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Observer Based Adaptive Control for Optical Manipulation of Cell

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Abstract—In this paper, an observer based adaptive control method is proposed for optical manipulation of cell. The dynamics of the robotic manipulator of the laser source is introduced in the optical tweezers system, so that a closed-loop control method is formulated and solved, and a backstepping approach is used to derive a control input for the manipulator. The interaction between the cell dynamics and the manipulator dynamics leads to a fourth-order overall dynamics, and hence a nonlinear observer is constructed to avoid the use of high-order derivatives of the positions in the control input. Stability of the closed-loop system is analyzed by using Lyapunov-like analysis. Simulation results are presented to illustrate the performance of the proposed control methods.

I. INTRODUCTION

Optical tweezers are scientific instruments which can manipulate microscopic objects based on the principle of optical trap [1]. Several automatic optical manipulation systems and control methods using optical tweezers have been developed in recent years. In [2], the optical micromanipulation was modeled as an infinite-horizon partially observable Markov decision process, and a stochastic programming method was introduced for the real-time path planning of cell motion. An automatic cell sorting system based on dual-beam trap was introduced in [3], and an image-processing system using thresholding, background subtraction and edge-enhancement algorithms was developed for identification of single cells. In [4], the dynamics of the trapped cell was analyzed, and a PID closed-loop feedback controller and a synchronization control technology was proposed for cell transportation. With the multiple trapping technology based on the computer-generated holographic optical-tweezers arrays [5], Arai et al. [6] developed an automatic system to flock micro-scale particles. In [7], a simple feedback controller was proposed for the positioning of a microscopic particle. In [8], the performance of proportional control, LQG control and nonlinear control in particle positioning was compared, and the dynamics of trapped particle was modeled as a first-order system by ignoring the particle mass. In [9], a region reaching control method was used to flock multiple micro particles towards a static region. In [10], an automated optical trapping technique was developed based on computer vision and multiple-force optical clamps.

In existing optical tweezers systems, open-loop controllers are employed for laser source without the consideration of

manipulator dynamics of the laser source. The first study investigating the closed-loop dynamic interaction between the robotic manipulator and the trapped cell is proposed in [11], and the dynamics of manipulator of laser source is introduced into optical tweezers system, so that the position of the laser beam is controlled by closed-loop control techniques. However, the interaction between the cell dynamics and the manipulator dynamics leads to a fourth-order overall dynamics, and hence high-order derivatives of the positions are required for the torque input of the robotic manipulator.

In this paper, we propose an observer based adaptive control scheme for optical manipulation of cell. A nonlinear observer is proposed for the optical tweezers system, so as to eliminate the requirements of high-order derivatives which is sensitive to noise. The proposed control method based on the nonlinear observer is able to manipulate the cell to track the desired trajectory. Stability of the closed-loop system is analyzed by using Lyapunov-like analysis, with the consideration of the dynamics of both the cell and the manipulator of the laser source. Simulation results are presented to illustrate the performance of the proposed control methods.

II. DYNAMICS OF CELL AND ROBOTIC MANIPULATOR

The basic principle of optical trap is based on the transfer of momentum from photons to microscopic objects, when a focused light travel through the object that is immersed in a medium. The refraction of the photons at the boundary between the object and the medium, results in a stable trap of the object.

The cell dynamics for the optical trapping is described by the following equation [7], [11]:

$$\mathbf{M}\ddot{\mathbf{x}} + \mathbf{B}\dot{\mathbf{x}} + k_1(\mathbf{x} - \mathbf{q})e^{-k_2\|\mathbf{x} - \mathbf{q}\|^2} = \mathbf{0}, \quad (1)$$

where $\mathbf{M} \in \mathbb{R}^{2 \times 2}$ denotes the inertia matrix, and $\mathbf{B} \in \mathbb{R}^{2 \times 2}$ represents the damping matrix, and k_1 and k_2 are positive constants, and $\mathbf{x} = [x_1, x_2]^T \in \mathbb{R}^2$ is the position of the cell, and $\mathbf{q} = [q_1, q_2]^T \in \mathbb{R}^2$ is the position of the laser. Both $\mathbf{M}$ and $\mathbf{B}$ are positive definite. The parameter k_1 is related to the laser intensity, and k_2 is related to the waist of the beam dimensions. The terms $\mathbf{M}\ddot{\mathbf{x}} + \mathbf{B}\dot{\mathbf{x}}$ in equation (1) is linear in a set of physical parameters $\boldsymbol{\theta}_d = [\theta_{d1}, \dots, \theta_{dl}]^T \in \mathbb{R}^l$ as:

$$\mathbf{M}\ddot{\mathbf{x}} + \mathbf{B}\dot{\mathbf{x}} = \mathbf{Y}_d(\dot{\mathbf{x}}, \ddot{\mathbf{x}})\boldsymbol{\theta}_d, \quad (2)$$

where $\mathbf{Y}_d(\dot{\mathbf{x}}, \ddot{\mathbf{x}}) \in \mathbb{R}^{2 \times l}$ is a dynamic regressor matrix.

Existing manipulation techniques treat the position of the laser beam $\mathbf{q}$ as the control input and open-loop controllers are designed to move the laser source. In this paper, the manipulator dynamics is introduced into the optical tweezers system and then the position of the laser beam is controlled by closed-loop robotic manipulation techniques. The dynamics of the robotic manipulator of the laser beam is described as:

$$\mathbf{M}_q \ddot{\mathbf{q}} + \mathbf{B}_q \dot{\mathbf{q}} = \mathbf{u}, \quad (3)$$

where $\mathbf{M}_q \in \mathbb{R}^{2 \times 2}$ denotes the inertial matrix and $\mathbf{B}_q \in \mathbb{R}^{2 \times 2}$ represents the damping matrix, and both $\mathbf{M}_q$ and $\mathbf{B}_q$ are positive definite, and $\mathbf{u} \in \mathbb{R}^2$ is the control input for the manipulator. As illustrated in Fig. 1, the variable $\mathbf{q}$ is set as the position of the laser beam with respect to the stage, and it can be adjusted by moving either the laser module or the stage. Note that equation (3) is also linear in a set of physical parameters as:

$$\mathbf{M}_q \ddot{\mathbf{q}} + \mathbf{B}_q \dot{\mathbf{q}} = \mathbf{Y}_q(\dot{\mathbf{q}}, \ddot{\mathbf{q}}) \boldsymbol{\theta}_q, \quad (4)$$

where $\mathbf{Y}_q(\dot{\mathbf{q}}, \ddot{\mathbf{q}}) \in \mathbb{R}^{2 \times n}$ is a dynamic regressor matrix, and $\boldsymbol{\theta}_q = [\theta_{q1}, \dots, \theta_{qn}]^T \in \mathbb{R}^n$ denote a set of physical parameters.

Fig. 1. A typical optical tweezers system.

III. ADAPTIVE CONTROL OF OPTICAL MANIPULATION

The optical tweezers system constitutes of two subsystems as described by equations (1) and (3) respectively, and hence the overall system is of fourth order. In this paper, the control method design is introduced in two steps. Firstly, based on the cell dynamics in equation (1), a desired position input for the trapped cell $\mathbf{q}_d$ is developed to ensure the convergence of the tracking error. Then a backstepping procedure is used to derive a torque input $\mathbf{u}$ based on a nonlinear observer.

A. Desired Position Input for Trapped Cell

First, a reference vector is proposed as:

$$\dot{\mathbf{x}}_r = \dot{\mathbf{x}}_d - \alpha_x \Delta \mathbf{x}, \quad (5)$$

where $\mathbf{x}_d$ is the desired position, and $\Delta \mathbf{x} = \mathbf{x} - \mathbf{x}_d$, and α_x is a positive constant. Next, a sliding vector is defined as:

$$\mathbf{s}_x = \dot{\mathbf{x}} - \dot{\mathbf{x}}_r = \Delta \dot{\mathbf{x}} + \alpha_x \Delta \mathbf{x}. \quad (6)$$

Differentiating equation (6) with respect to time yields:

$$\dot{\mathbf{s}}_x = \ddot{\mathbf{x}} - \ddot{\mathbf{x}}_r. \quad (7)$$

By using the sliding vector, the dynamics of trapped cell in equation (1) can be represented as:

$$\mathbf{M} \dot{\mathbf{s}}_x + \mathbf{B} \mathbf{s}_x + \mathbf{Y}_d(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r) \boldsymbol{\theta}_d + k_3(\mathbf{x} - \mathbf{q}) = \mathbf{0}, \quad (8)$$

where $k_3 = k_1 e^{-k_2 \|\mathbf{x} - \mathbf{q}\|}$ is a positive time-varying gain. The equation (8) can be written as:

$$\mathbf{M} \dot{\mathbf{s}}_x + \mathbf{B} \mathbf{s}_x + \mathbf{Y}_d(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r) \boldsymbol{\theta}_d + k_3 \mathbf{x} = k_3 \Delta \mathbf{q} + k_3 \mathbf{q}_d, \quad (9)$$

where $\Delta \mathbf{q} = \mathbf{q} - \mathbf{q}_d$ represents an input perturbation to the cell dynamics. The system in equation (9) can be viewed as controlled by $k_3 \mathbf{q}_d$ with the perturbation $k_3 \Delta \mathbf{q}$.

The desired position input for the trapped cell is proposed as:

$$\mathbf{q}_d = \mathbf{x} - k_3^{-1} \mathbf{K}_p \Delta \mathbf{x} - k_3^{-1} \mathbf{K}_d \mathbf{s}_x + k_3^{-1} \mathbf{Y}_d(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r) \hat{\boldsymbol{\theta}}_d, \quad (10)$$

where $\mathbf{K}_p$ and $\mathbf{K}_d$ are positive definite matrices. The estimated parameters $\hat{\boldsymbol{\theta}}_d$ are updated using the following update law:

$$\dot{\hat{\boldsymbol{\theta}}}_d = -\mathbf{L}_d \mathbf{Y}_d^T(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r) \mathbf{s}_x, \quad (11)$$

where $\mathbf{L}_d$ is symmetric positive definite.

Substituting the desired position input for the trapped cell into equation (9), we have:

$$\mathbf{M} \dot{\mathbf{s}}_x + \mathbf{B} \mathbf{s}_x + \mathbf{K}_p \Delta \mathbf{x} + \mathbf{K}_d \mathbf{s}_x + \mathbf{Y}_d(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r) \Delta \boldsymbol{\theta}_d = k_3 \Delta \mathbf{q}. \quad (12)$$

B. Control Input of Robotic Manipulator of Laser Beam

We can now use the desired position input for the trapped cell $\mathbf{q}_d$ to design a control input $\mathbf{u}$ for the manipulator. Note that the interaction between the cell dynamics described by equation (1) and the manipulator dynamics described by equation (3) leads to a fourth-order overall dynamics. Therefore, an estimated desired position input $\hat{\mathbf{q}}_d$ is employed by developing an observer instead of using $\mathbf{q}_d$ directly, so as to eliminate the use of high-order derivatives in the control input of manipulator.

An observer is developed to update $\hat{\mathbf{q}}_d$ as:

$$\begin{cases} \dot{\hat{\mathbf{q}}}_d = \boldsymbol{\eta} + \beta \mathbf{e} \\ \dot{\boldsymbol{\eta}} = \hat{\mathbf{M}}_{qo}^{-1}(\mathbf{u} - \hat{\mathbf{B}}_{qo} \boldsymbol{\eta} + \mathbf{K}_e \mathbf{e}), \end{cases} \quad (13)$$

where $\mathbf{e} = \mathbf{q}_d - \hat{\mathbf{q}}_d$ is the observation error, and $\boldsymbol{\eta}$ is an auxiliary variable, and β is a positive constant. The matrices

$\hat{M}_{q_o}$ and $\hat{B}_{q_o}$ are the approximate models for M_q and B_q respectively, which are updated through the update laws:

$$\begin{aligned}\dot{\hat{\theta}}_{M_{q_o}} &= -L_{M_{q_o}} N_{M_{q_o}}(\dot{\eta})z, \\ \dot{\hat{\theta}}_{B_{q_o}} &= -L_{B_{q_o}} N_{B_{q_o}}(\eta)z,\end{aligned}\quad (14)$$

where $z = \dot{q} - \eta$, and $\hat{\theta}_{M_{q_o}}$ and $\hat{\theta}_{B_{q_o}}$ are the vectors of estimated parameters, and $L_{M_{q_o}}$ and $L_{B_{q_o}}$ are positive definite matrices, and the matrices $N_{M_{q_o}}(\dot{\eta})$ and $N_{B_{q_o}}(\eta)$ are defined as:

$$\begin{aligned}N_{M_{q_o}}(\dot{\eta}) &= \begin{bmatrix} \dot{\eta}_1 & 0 \\ 0 & \dot{\eta}_2 \end{bmatrix}, \\ N_{B_{q_o}}(\eta) &= \begin{bmatrix} \eta_1 & 0 \\ 0 & \eta_2 \end{bmatrix}.\end{aligned}\quad (15)$$

Using the estimated desired position input $\hat{q}_d$, the closed-loop equation for the desired position input of the laser beam described by equation (12) can be rewritten as:

$$\begin{aligned}M\dot{s}_x + B s_x + K_p \Delta x + K_d s_x + Y_d(\dot{x}_r, \ddot{x}_r) \Delta \theta_d \\ = k_3 \Delta q = k_3 [q - \hat{q}_d - (q_d - \hat{q}_d)] = k_3 (\Delta \hat{q} - e),\end{aligned}\quad (16)$$

where $\Delta \hat{q} = \hat{q} - q_d$.

Next, a reference vector $\dot{\hat{q}}_r$ is defined as:

$$\dot{\hat{q}}_r = \dot{\hat{q}}_d - \alpha_q (q - \hat{q}_d), \quad (17)$$

where α_q is a positive constant, and the derivative of $\dot{\hat{q}}_r$ is obtained as:

$$\ddot{\hat{q}}_r = \ddot{\hat{q}}_d - \alpha_q (\dot{q} - \dot{\hat{q}}_d). \quad (18)$$

A sliding vector is then defined as:

$$\hat{s}_q = \dot{q} - \dot{\hat{q}}_r = \dot{q} - \dot{\hat{q}}_d + \alpha_q (q - \hat{q}_d), \quad (19)$$

and the control input of robotic manipulator is proposed as:

$$u = -K_q \Delta \hat{q} - K_s \hat{s}_q + Y_q(\dot{\hat{q}}_r, \ddot{\hat{q}}_r) \hat{\theta}_q, \quad (20)$$

where K_s and K_q are positive definite matrices, and the uncertain dynamic parameters $\hat{\theta}_q$ are updated as follows:

$$\dot{\hat{\theta}}_q = -L_q Y_q^T(\dot{\hat{q}}_r, \ddot{\hat{q}}_r) \hat{s}_q. \quad (21)$$

Using the sliding vector $\hat{s}_q$, equation (3) can be expressed as:

$$M_q \dot{\hat{s}}_q + B_q \hat{s}_q + Y_q(\dot{\hat{q}}_r, \ddot{\hat{q}}_r) \theta_q = u. \quad (22)$$

Substituting equation (20) into equation (22), the closed-loop equation for the control input of the robotic manipulator is obtained as:

$$M_q \dot{\hat{s}}_q + B_q \hat{s}_q + K_q \Delta \hat{q} + K_s \hat{s}_q + Y_q(\dot{\hat{q}}_r, \ddot{\hat{q}}_r) \Delta \theta_q = 0. \quad (23)$$

Next, multiplying both sides of equation (13) with $\hat{M}_{q_o}$ and using equation (3), we can get the closed-loop observer dynamics for $\hat{q}_d$ as:

$$\begin{aligned}M_q \dot{z} + B_q z + K_e e &= (\hat{M}_{q_o} - M_q) \dot{\eta} + (\hat{B}_{q_o} - B_q) \eta \\ &= -N_{M_{q_o}}(\dot{\eta}) \Delta \theta_{M_{q_o}} - N_{B_{q_o}}(\eta) \Delta \theta_{B_{q_o}},\end{aligned}\quad (24)$$

where $\Delta \theta_{M_{q_o}} = \theta_{M_{q_o}} - \hat{\theta}_{M_{q_o}}$ and $\Delta \theta_{B_{q_o}} = \theta_{B_{q_o}} - \hat{\theta}_{B_{q_o}}$.

C. Stability Analysis

Now that the closed-loop equations of the optical tweezers system described by equations (16), (23) and the closed-loop equation of the observer described by equation (24) have been obtained, we can proceed to analyze the stability.

A Lyapunov function candidate V is proposed as:

$$\begin{aligned}V &= \frac{1}{2} s_x^T M s_x + \frac{1}{2} \Delta x^T K_p \Delta x + \frac{1}{2} \Delta \theta_d^T L_d^{-1} \Delta \theta_d \\ &+ \frac{1}{2} \hat{s}_q^T M_q \hat{s}_q + \Delta \hat{q}^T (\frac{1}{2} K_q + \alpha_q K_s) \Delta \hat{q} + \frac{1}{2} \Delta \theta_q^T L_q^{-1} \Delta \theta_q \\ &+ \frac{1}{2} z^T M_q z + \frac{1}{2} \Delta \theta_{M_{q_o}}^T L_{M_{q_o}}^{-1} \Delta \theta_{M_{q_o}} + \frac{1}{2} \Delta \theta_{B_{q_o}}^T L_{B_{q_o}}^{-1} \Delta \theta_{B_{q_o}}.\end{aligned}\quad (25)$$

Differentiating V with respect to time, we have:

$$\begin{aligned}\dot{V} &= s_x^T M \dot{s}_x + \Delta x^T K_p \Delta \dot{x} - \dot{\hat{\theta}}_d^T L_d^{-1} \Delta \theta_d + \\ &+ \hat{s}_q^T M_q \dot{\hat{s}}_q + \Delta \hat{q}^T (K_q + 2\alpha_q K_s) \Delta \hat{q} - \dot{\hat{\theta}}_q^T L_q^{-1} \Delta \theta_q \\ &+ z^T M_q \dot{z} - \dot{\hat{\theta}}_{M_{q_o}}^T L_{M_{q_o}}^{-1} \Delta \theta_{M_{q_o}} - \dot{\hat{\theta}}_{B_{q_o}}^T L_{B_{q_o}}^{-1} \Delta \theta_{B_{q_o}}.\end{aligned}\quad (26)$$

Substituting closed-loop equations (16), (23), (24) and the update laws (11), (14) and (21) into equation (26), we have:

$$\begin{aligned}\dot{V} &= -s_x^T (B + K_d) s_x - \alpha_x \Delta x^T K_p \Delta x + k_3 s_x^T \Delta \hat{q} \\ &- k_3 s_x^T e - \hat{s}_q^T B_q \hat{s}_q - \Delta \hat{q}^T K_s \Delta \hat{q} \\ &- \Delta \hat{q}^T (\alpha_q K_q + \alpha_q^2 K_s) \Delta \hat{q} - z^T B_q z - z^T K_e e.\end{aligned}\quad (27)$$

Note that $z = \Delta \hat{q} + \beta e$, and thus equation (27) can be rewritten as:

$$\begin{aligned}\dot{V} &= -s_x^T (B + K_d) s_x - \alpha_x \Delta x^T K_p \Delta x + \\ &k_3 s_x^T \Delta \hat{q} - k_3 s_x^T e - \hat{s}_q^T B_q \hat{s}_q - \Delta \hat{q}^T K_s \Delta \hat{q} \\ &- \Delta \hat{q}^T (\alpha_q K_q + \alpha_q^2 K_s) \Delta \hat{q} - z^T B_q z \\ &- \Delta \hat{q}^T K_e e - \beta e^T K_e e \\ &= -\alpha_x \Delta x^T K_p \Delta x - \hat{s}_q^T B_q \hat{s}_q - z^T B_q z \\ &- [s_x^T \Delta \hat{q}^T \Delta \hat{q}^T e^T] P [s_x^T \Delta \hat{q}^T \Delta \hat{q}^T e^T]^T,\end{aligned}\quad (28)$$

where $P \in \mathbb{R}^{8 \times 8}$ is:

$$P = \begin{bmatrix} B + K_d & -\frac{k_3}{2} I & 0 & \frac{k_3}{2} I \\ -\frac{k_3}{2} I & \alpha_q K_q + \alpha_q^2 K_s & 0 & 0 \\ 0 & 0 & K_s & \frac{1}{2} K_e \\ \frac{k_3}{2} I & 0 & \frac{1}{2} K_e & \beta K_e \end{bmatrix}, \quad (29)$$

where $I \in \mathbb{R}^{2 \times 2}$ is an identity matrix. Let the controller parameters α_q , K_q , K_s , β and K_e are chosen so that

$$\begin{aligned}\alpha_q \lambda_{\min}[K_q + \alpha_q K_s] &> \frac{k_1^2}{4 \lambda_{\min}[B]}, \\ \beta \lambda_{\min}[K_s] &> \frac{1}{4} \lambda_{\max}[K_e],\end{aligned}\quad (30)$$

then $\dot{V} \leq 0$, where $\lambda_{\min}[\bullet]$ and $\lambda_{\max}[\bullet]$ denotes the minimum and the maximum eigenvalues of the matrix respectively. We are now in the position to state the following theorem:

Theorem: The input of the robotic manipulator (20), with the adaptive observer described by (13) ensures the convergence of the closed-loop system. That is, $\Delta x \rightarrow 0$, $\Delta \dot{x} \rightarrow 0$ and $\Delta q \rightarrow 0$ as $t \rightarrow \infty$ when the control parameters α_q , K_q , K_s , β and K_e are chosen to satisfy condition (30).

Proof: Since equation (30) is satisfied, we have $V > 0$ and

$\dot{V} \leq 0$, and hence V is bounded. The boundedness of V ensures the boundedness of s_x , $\Delta\theta_d$, Δx , $\hat{s}_q$, $\Delta\hat{q}$, $\Delta\theta_q$, z , $\Delta\theta_{M_{qo}}$, $\Delta\theta_{B_{qo}}$. The boundedness of s_x and Δx ensures the boundedness of $\Delta\dot{x}$. Therefore, Δx is uniformly continuous. Since Δx is bounded, $\dot{x}_r$ is bounded. Since $\Delta\dot{x}$ is bounded, $\ddot{x}_r$ is bounded. In addition, the boundedness of $\hat{s}_q$ and $\Delta\hat{q}$ ensures the boundedness of $\Delta\dot{q}$. The boundedness of $\Delta\dot{q}$ and z ensures the boundedness of e . From equation (16), it is obtained that $\dot{s}_x$ is bounded. Therefore, s_x is uniformly continuous. From equation (28), it is easy to verify that $s_x, \Delta x \in L_2(0, +\infty)$. Then it follows from [12], [13] that $s_x \rightarrow 0$ and $\Delta x \rightarrow 0$ which also indicates that $\Delta\dot{x} \rightarrow 0$. $\triangle\triangle\triangle$

Remark: One common assumption in optical manipulation is that the optical trapping is maintained throughout the task. To allow the laser beam to start from an initial position that is far away from the cell and automatically trap then manipulate the cell, the desired position input is proposed as:

$$q_d = x - k^{-1}(x, q) a K_p \Delta x - k^{-1}(x, q) a K_d s_x + k^{-1}(x, q) Y_d(\dot{x}_r, \ddot{x}_r) \hat{\theta}_d, \quad (31)$$

where $k(x, q)$ is a time-varying stiffness, and s_x is the sliding vector which is defined as:

$$s_x = \dot{x} - \dot{x}_r = \dot{x} - \dot{x}_d + \alpha_x \frac{a}{a^2 + \delta} \Delta x, \quad (32)$$

where $\dot{x}_r = \dot{x}_d - \alpha_x \frac{a}{a^2 + \delta} \Delta x$ is a reference vector, and δ is a very small positive constant.

In equations (31) and (32), a is an auxiliary variable which is defined as:

$$a = \begin{cases} 1, f_r(x, q) \leq 0, \\ 1 - \frac{\{[f(x, q)]^N - [(\kappa b)^{n-b^n}]^N\}^N}{[(\kappa b)^{n-b^n}]^N}, f(x, q) < 0, f_r(x, q) > 0, \\ 0, f(x, q) \geq 0, \end{cases} \quad (33)$$

where $N \geq 6$ is an even integer, and $\kappa < 1$, b are positive constants, and

$$\begin{aligned} f(x, q) &= \|x - q\|^{n-b^n} \leq 0, \\ f_r(x, q) &= \|x - q\|^{n-(\kappa b)^n} \leq 0, \end{aligned} \quad (34)$$

represent trapping region functions and corresponding reference functions with the order n . If the position of the cell is outside the trapping region, $f(x, q) > 0$, and the laser should be moved towards the cell for trapping. If the cell is inside the trapping region, $f(x, q) \leq 0$, the cell is trapped by the laser, and the trapped cell can be transported along the desired trajectory. From equation (33), the auxiliary variable a smoothly increases from 0 to 1 when the cell transits from outside to inside the trapping region, and vice versa.

When the cell is far away from the laser beam, $a = 0$, and $Y_d(\dot{x}_r, \ddot{x}_r)$ reduce to zero. From equations (31) and (32), the desired position input is specified as:

$$q_d = x. \quad (35)$$

That is, the desired position input is the position of the cell, and hence the laser moves towards the cell to trap it. After

the cell is trapped by the laser beam, $a = 1$, and the desired position input in equation (31) becomes:

$$q_d = x - k_c^{-1} K_p \Delta x - k_c^{-1} K_d s_x + k_c^{-1} Y_d(\dot{x}_r, \ddot{x}_r) \hat{\theta}_d, \quad (36)$$

where k_c is a positive constant. That is, the laser beam drives the trapped cell towards the desired trajectory. Therefore, the desired position input q_d described by equation (31) is able to trap then manipulate the biological cell, as illustrated in Fig. 2. The stability analysis can be found in [14] and is omitted here.

Fig. 2. Trapping and manipulation of biological cells. $\triangle\triangle\triangle$

IV. SIMULATION

Numerical simulation has been carried out to verify the performance of the proposed control methods. The optical tweezers system is illustrated in Fig. 3. In Fig. 3, the cell is placed on a motorized stage and the laser beam is fixed downwards, and the relative distance between the laser beam and the stage is dependent on the variation of the stage position. The motorized stage thus act as a robotic manipulator, and we can control the relative distance between the laser beam and the stage. In the simulation, the variable q is set as the position of the laser beam with respect to the motorized stage.

Fig. 3. The optical tweezers system. The laser beam is fixed downwards, and the relative distance between the laser beam and the stage is dependent on the variation of the stage position.

The parameters of the cell dynamics in equation (1) were set as: $M = \text{diag}\{10^{-10}, 10^{-10}\} \text{kg}$, $B = \text{diag}\{1.8 \times 10^{-9}, 1.8 \times 10^{-9}\} \text{kg/s}$, $k_1 = 2.77 \times 10^{-5}$ and $k_2 = 6.93 \times 10^9$. The parameters of the manipulator dynamics in equation (3) were set as: $M_q = \text{diag}\{0.02218, 0.011386\} \text{kg}$ and $B_q = \text{diag}\{0.04749, 0.04023\} \text{kg/s}$.

In the simulation, an adaptive observer was introduced to estimate the desired position input $\hat{q}_d$. Both the cell and the laser were located at $(150 \mu\text{m}, -150 \mu\text{m})$ initially, so the cell was trapped by the laser. After that, the trapped cell was moved to track the desired trajectory:

$$\begin{cases} x_{d1} = 200 + \frac{15\cos(0.3t)}{1+\sin^2(0.3t)} \mu\text{m}, \\ x_{d2} = -150 + \frac{15\sin(0.3t)\cos(0.3t)}{1+\sin^2(0.3t)} \mu\text{m}. \end{cases} \quad (37)$$

The parameters of the adaptive observer in equations (13) and (14) are set as: $\beta = 3$, $K_e = 0.01I$, $L_{M_{qo}} = 10^{-8}I$, $L_{B_{qo}} = 10^{-8}I$, while the initial estimates of the dynamic parameters of the robotic manipulator were: $\hat{M}_{qo} = \text{diag}\{0.02, 0.01\} \text{kg}$, and $\hat{B}_{qo} = \text{diag}\{0.05, 0.04\} \text{kg/s}$.

The parameters of the desired position input for the trapped cell in equations (10) and (11) were proposed as: $\alpha_x = 1$, $K_p = 2 \times 10^{-6}I$, $K_d = 10^{-6}I$, $L_d = 10^{-10}I$, and the parameters of the control input for the manipulator in equation (20) were set as: $\alpha_q = 1$, $K_q = 0.6I$, $K_s = 0.01I$, $L_q = 10^{-5}I$.

The path of the laser and the trapped cell is shown in Fig. 4, and the tracking error is shown in Fig. 5. From Fig. 4 and Fig. 5, it is seen that the cell was successfully transported to follow the desired trajectory. The torqued applied on the robotic manipulator is shown in Fig. 6.

V. CONCLUSIONS

In this paper, we propose an observer based adaptive control method for optical manipulation of cell. A closed-loop control system is formulated by introducing the manipulator dynamics into the optical tweezers system. An observer is developed to avoid the use of high-order derivatives in the control input of the robotic manipulator. The stability of the closed-loop system is analyzed by using Lyapunov-like analysis, with the consideration of the dynamics of both the cell and the manipulator of the laser source. Simulations are carried out to verify the performance of the proposed control methods.

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(a) $t=0$ s: initial positions

(b) $t=1$ s: the cell is trapped by the laser beam

(c) $t=20$ s: the cell position converges to the desired trajectory

Fig. 4. The positions of the cell and the laser beam at different time instants.

Fig. 5. The tracking error.

Fig. 6. The torque applied on the manipulator of the laser source.

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