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Dynamic Region Control for Robot-Assisted Cell Manipulation Using Optical Tweezers

X. Li and C. C. Cheah

Abstract—Current manipulation techniques of optical tweezers treat the position of the laser beam as the control input and an open-loop kinematic controller is designed to move the laser source. In this paper, a closed-loop robotic control method for optical tweezers is formulated and solved. While robotic manipulation has been a key technology driver in factory automation, robotic manipulation of cells or nanoparticles is less well understood. The proposed formulation shall bridge the gap between traditional robot manipulation techniques and optical manipulation techniques of cells. A dynamic region controller is proposed for cell manipulation using optical tweezers. The desired objective can be specified as a dynamic region rather than a position or trajectory, and the desired region can thus be scaled up and down to allow flexibility in the task specifications. Experimental results are presented to illustrate the performance of the proposed controller.

I. INTRODUCTION

Optical tweezers [1] are very useful tools in cell manipulation because of the capability of manipulating tiny particles without causing damage to the particles. By using a highly focused laser beam, optical tweezers are able to trap particles as diverse as atoms, molecules, bacteria, viruses [2], and hence optical tweezers have been successfully applied in biological sciences and nanotechnology for realization of various manipulation tasks, such as the cell separation [3], evaluation of nonsticky substrate coatings by moving live dissociated neurons [4], the membrane elasticity analysis of human red blood cells [5], study of mechanical and structural properties of DNA [6], [7], etc.

However, due to the laborious work of cell manipulation, the manual operation with optical tweezers tends to induce the operator fatigue and thus the reduction of success rate. To improve the efficiency, several automatic optical manipulation systems and control methods using optical tweezers have been developed in recent years. In [8], 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. A modified A-star path planning algorithm was proposed to transport cell in [9], and the force applied on the trapped cell was also analyzed. An automatic cell sorting system based on dual-beam trap was introduced in [10], and an image-processing system using thresholding, background subtraction and edge-enhancement algorithms was developed for identification of single cells. In [11], 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 [12], Arai et al. [13] developed an automatic system to flock micro-scale particles. In [14], a simple feedback controller was proposed for the positioning of a microscopic particle. In [15], 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 [16], a region reaching control method was used to flock multiple micro particles towards a static region. In [17], an automated optical trapping technique was developed based on computer vision and multiple-force optical clamps.

In this paper, we propose a dynamic region control method for cell manipulation with optical tweezers. The proposed controller is able to manipulate the trapped cell to follow the dynamic moving region while the size of the region can be varied for specific manipulation tasks. The contributions of the paper are twofold. First, unlike the existing methods that assume open-loop control of the position of laser source, the dynamics of robotic manipulator is introduced into optical tweezers system so that a closed-loop control problem can be formulated and solved. The proposed formulation shall bridge the gap between traditional robot manipulation techniques and optical manipulation techniques of cells. Second, the desired objective is specified as a dynamic region instead of a trajectory or point. This allows flexibility in the specifications of the desired tasks. In cases where high accuracy is required, the desired region can be specified arbitrarily small and thus the proposed region based cell manipulation technique is a generalization of conventional techniques. Stability of the closed-loop system with consideration of the dynamics of both the cell and the manipulator of the laser source is analyzed by using Lyapunov-like analysis. Experimental results for various manipulation tasks are presented to illustrate the performance of the proposed control methods.

II. DYNAMICS OF TRAPPED CELL AND ROBOTIC MANIPULATOR

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

It is well known that the trapping works only when the cell is located in a small neighborhood of the centroid of the focused laser beam, and the cell dynamics for the optical trapping is described by the following equation [14]:

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

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. Note that in optical manipulation, there is no interaction between the cell and the laser beam when the cell is located far away from the laser. This is described by the term $k_1(\mathbf{x} - \mathbf{q})e^{-k_2\|\mathbf{x} - \mathbf{q}\|^2}$ in equation (1), which is regulated by the Gaussian potential energy. 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.

In existing manipulation techniques, the position of the laser beam $\mathbf{q}$ is treated as the control input and an open-loop kinematic controller is designed to move the laser source. In this paper, the robot 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. The dynamics of the robotic manipulator described by 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 dynamics regressor matrix, and $\boldsymbol{\theta}_q = [\theta_{q1}, \dots, \theta_{qn}]^T \in \mathbb{R}^n$ denote a set of physical parameters.

III. DYNAMIC REGION CONTROL METHOD

The main idea of the proposed control method is to specify the desired objective as a dynamic region which provides flexibility in the specifications of the cell manipulation tasks.

A. Dynamic Region Functions

In most cases, the size and the position of the desired region is time-varying. Let us define a dynamic region as specified by the following inequality functions:

$$\mathbf{f}(\Delta\mathbf{x}_S) = [f_1(\Delta\mathbf{x}_{S1})f_2(\Delta\mathbf{x}_{S2}) \cdots f_m(\Delta\mathbf{x}_{Sm})]^T \leq \mathbf{0} \quad (5)$$

where $\Delta\mathbf{x}_{Si} = \mathbf{S}^{-1}(\mathbf{x} - \mathbf{x}_{oi}) = \mathbf{S}^{-1}\Delta\mathbf{x}_i$, $\mathbf{x}_{oi}$ is the reference point of $f_i(\Delta\mathbf{x}_{Si})$ ($i = 1, 2, \dots, m$), m is the total

number of objective functions, $\mathbf{S}(t)$ is a symmetric scaling matrix that is nonsingular, and $\mathbf{S}^{-1}$ is the inverse of the scaling matrix. The functions $f_i(\Delta\mathbf{x}_{Si})$ are scalar functions with continuous partial derivatives. Note that the desired region is a single region specified as the intersections of all the objective functions. Therefore, all desired regions must be specified at the same speed of $\dot{\mathbf{x}}_o$ so that the desired shape is preserved. Various desired regions such as sphere, cube, cylinder etc. can be formed by choosing the appropriate functions.

For example, when the desired region is designed as a rectangle, the inequality functions in equation (5) can be specified as:

$$\begin{aligned} f_1(\Delta\mathbf{x}_{S1}) &= (x_{S1} - x_{o1})^2 - b_1^2 \leq 0, \\ f_2(\Delta\mathbf{x}_{S2}) &= (x_{S2} - x_{o2})^2 - b_2^2 \leq 0, \end{aligned}$$

where b_1 and b_2 are the individual regional bounds for each axis, and

$$\begin{bmatrix} x_{S1} - x_{o1} \\ x_{S2} - x_{o2} \end{bmatrix} = \mathbf{S}^{-1} \begin{bmatrix} x_1 - x_{o1} \\ x_2 - x_{o2} \end{bmatrix}. \quad (6)$$

When the desired region is designed as a circle, the inequality function in equation (5) can be specified as:

$$f(\Delta\mathbf{x}_S) = (x_{S1} - x_{o1})^2 + (x_{S2} - x_{o2})^2 - R^2 \leq 0, \quad (7)$$

where R is the radius of the circle.

Equation (5) specifies a moving region, where the reference points $\mathbf{x}_{oi}$ are time-varying, and the size of the moving region can be varied by adjusting the scaling matrix. In an application where the high precision is required, it is possible to define the region arbitrarily small. When the precision is not critical, the region could be scaled up so that less control effort is required.

The potential energy function for the desired regions described in equation (5) can be specified respectively as:

$$P(\Delta\mathbf{x}_S) = \sum_{i=1}^m P_i(\Delta\mathbf{x}_{Si}), \quad (8)$$

where

$$P_i(\Delta\mathbf{x}_{Si}) = \frac{k_{pi}}{N} [\max(0, f_i(\Delta\mathbf{x}_{Si}))]^N. \quad (9)$$

That is,

$$P_i(\Delta\mathbf{x}_{Si}) = \begin{cases} 0, & f_i(\Delta\mathbf{x}_{Si}) \leq 0, \\ \frac{k_{pi}}{N} [f_i(\Delta\mathbf{x}_{Si})]^N, & f_i(\Delta\mathbf{x}_{Si}) > 0, \end{cases}$$

where k_{pi} are positive constants, and $N \geq 4$ is a constant integer so that $P(\Delta\mathbf{x}_S) \in C^2$. The above energy function is lower bounded by zero. Note that $P(\Delta\mathbf{x}_S) = 0$ if all the functions in equation (5) are satisfied.

Partial differentiating the potential energy function described by (9) with respect to $\Delta\mathbf{x}_S$ yields:

$$\left(\frac{\partial P_i(\Delta\mathbf{x}_{Si})}{\partial \Delta\mathbf{x}_S}\right)^T = \begin{cases} 0, & f_i(\Delta\mathbf{x}_{Si}) \leq 0, \\ k_{pi} [f_i(\Delta\mathbf{x}_{Si})]^{N-1} \left(\frac{\partial f_i(\Delta\mathbf{x}_{Si})}{\partial \Delta\mathbf{x}_S}\right)^T, & f_i(\Delta\mathbf{x}_{Si}) > 0. \end{cases}$$

Therefore,

$$\begin{aligned} \left(\frac{\partial P(\Delta \mathbf{x}_S)}{\partial \Delta \mathbf{x}_S} \right)^T &= \sum_{i=1}^m \left(\frac{\partial P_i(\Delta \mathbf{x}_{Si})}{\partial \Delta \mathbf{x}_S} \right)^T \\ &= \sum_{i=1}^m k_{pi} [\max(0, f_i(\Delta \mathbf{x}_{Si}))]^{N-1} \left(\frac{\partial f_i(\Delta \mathbf{x}_{Si})}{\partial \Delta \mathbf{x}_S} \right)^T \triangleq \Delta \boldsymbol{\xi}, \end{aligned} \quad (10)$$

where $\Delta \boldsymbol{\xi}$ denotes the region error which drives the trapped cell towards the desired region. After the cell is inside the region, the gradient of the potential energy is zero and hence $\Delta \boldsymbol{\xi}$ also reduces to zero.

B. Desired Position Input for Trapped Cell

Using the region error, we propose a dynamic region control method for cell manipulation. Firstly, based on the cell dynamics (1), a desired position input for the trapped cell $\mathbf{q}_d$ is developed to ensure the convergence of the region error. Then based on the robot dynamics (3), a backstepping procedure is used to derive a torque input $\mathbf{u}$ applied on the robotic manipulator of the laser source to guarantee that the actual position input $\mathbf{q}$ tracks the desired position input $\mathbf{q}_d$.

First, a reference vector is proposed as:

$$\dot{\mathbf{x}}_r = (\dot{\mathbf{x}}_o - \dot{\mathbf{S}}\dot{\mathbf{S}}^{-1}\Delta\mathbf{x}) - \alpha_x \mathbf{S}\Delta\boldsymbol{\xi}, \quad (11)$$

where $\dot{\mathbf{S}}^{-1}$ is the time derivative of $\mathbf{S}^{-1}$, and α_x is a positive constant.

Next, a sliding vector is defined as:

$$\mathbf{s}_x = \dot{\mathbf{x}} - \dot{\mathbf{x}}_r = \Delta\dot{\mathbf{x}} + \dot{\mathbf{S}}\dot{\mathbf{S}}^{-1}\Delta\mathbf{x} + \alpha_x \mathbf{S}\Delta\boldsymbol{\xi}. \quad (12)$$

Differentiating equation (12) with respect to time yields:

$$\dot{\mathbf{s}}_x = \ddot{\mathbf{x}} - \ddot{\mathbf{x}}_r. \quad (13)$$

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

$$\mathbf{M}\dot{\mathbf{s}}_x + \mathbf{B}\mathbf{s}_x + \mathbf{Y}_d(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r)\boldsymbol{\theta}_d + k_3(t)(\mathbf{x} - \mathbf{q}) = \mathbf{0}, \quad (14)$$

where $k_3(t) = k_1 e^{-k_2 \|\mathbf{x} - \mathbf{q}\|^2}$ is a positive time-varying gain.

The equation (14) can be written as:

$$\mathbf{M}\dot{\mathbf{s}}_x + \mathbf{B}\mathbf{s}_x + \mathbf{Y}_d(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r)\boldsymbol{\theta}_d + k_3(t)\mathbf{x} = k_3(t)\Delta\mathbf{q} + k_3(t)\mathbf{q}_d, \quad (15)$$

$$\mathbf{M}\ddot{\mathbf{x}} + \mathbf{B}\dot{\mathbf{x}} + k_3(t)\mathbf{x} = k_3(t)\Delta\mathbf{q} + k_3(t)\mathbf{q}_d, \quad (16)$$

where $\Delta\mathbf{q} = \mathbf{q} - \mathbf{q}_d$ represents a input perturbation to the cell dynamics. The system in equation (15) can be viewed as controlled by $k_3(t)\mathbf{q}_d$ with the perturbation $k_3(t)\Delta\mathbf{q}$.

By using the region error, the desired position input for the trapped cell is proposed as:

$$\mathbf{q}_d = \mathbf{x} - k_3^{-1}(t)\mathbf{S}^{-1}\Delta\boldsymbol{\xi} - k_3^{-1}(t)\mathbf{K}_v\mathbf{s}_x + k_3^{-1}(t)\mathbf{Y}_d(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r)\hat{\boldsymbol{\theta}}_d \quad (17)$$

where $\mathbf{K}_v$ is a positive definite matrix. The estimated parameters $\hat{\boldsymbol{\theta}}_d$ are updated using the following update law:

$$\dot{\hat{\boldsymbol{\theta}}}_d = -\mathbf{L}_d \mathbf{Y}_d^T(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r)\mathbf{s}_x, \quad (18)$$

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

Substituting the desired position input for the trapped cell into equation (15), we have:

$$\mathbf{M}\dot{\mathbf{s}}_x + \mathbf{B}\mathbf{s}_x + \mathbf{S}^{-1}\Delta\boldsymbol{\xi} + \mathbf{K}_v\mathbf{s}_x + \mathbf{Y}_d(\dot{\mathbf{x}}_r, \ddot{\mathbf{x}}_r)\Delta\boldsymbol{\theta}_d = k_3(t)\Delta\mathbf{q} \quad (19)$$

To analyze the stability of the trapped cell system, a Lyapunov-like function candidate V_1 is proposed as:

$$V_1 = \frac{1}{2}\mathbf{s}_x^T \mathbf{M} \mathbf{s}_x + P(\Delta \mathbf{x}_S) + \frac{1}{2}\Delta\boldsymbol{\theta}_d^T \mathbf{L}_d^{-1} \Delta\boldsymbol{\theta}_d. \quad (20)$$

Differentiating V_1 with respect to time, we have:

$$\begin{aligned} \dot{V}_1 &= \mathbf{s}_x^T \mathbf{M} \dot{\mathbf{s}}_x - \dot{\boldsymbol{\theta}}_d^T \mathbf{L}_d^{-1} \Delta\boldsymbol{\theta}_d + \sum_{i=1}^m k_{pi} [\max(0, f_i(\Delta \mathbf{x}_{Si}))]^{N-1} \\ &\quad \times (\dot{\mathbf{S}}^{-1} \Delta\mathbf{x} + \mathbf{S}^{-1} \Delta\dot{\mathbf{x}})^T \left(\frac{\partial f_i(\Delta \mathbf{x}_{Si})}{\partial \Delta \mathbf{x}_S} \right)^T. \end{aligned} \quad (21)$$

Substituting equations (12), (18) and (19) into above equation, we have,

$$\begin{aligned} \dot{V}_1 &= -\mathbf{s}_x^T (\mathbf{B} + \mathbf{K}_v) \mathbf{s}_x - [\Delta\dot{\mathbf{x}} + \dot{\mathbf{S}}\dot{\mathbf{S}}^{-1}\Delta\mathbf{x} + \alpha_x \mathbf{S}\Delta\boldsymbol{\xi}]^T \\ &\quad \times \mathbf{S}^{-1} \Delta\boldsymbol{\xi} + \sum_{i=1}^m k_{pi} [\max(0, f_i(\Delta \mathbf{x}_{Si}))]^{N-1} \times \\ &\quad (\dot{\mathbf{S}}^{-1} \Delta\mathbf{x} + \mathbf{S}^{-1} \Delta\dot{\mathbf{x}})^T \left(\frac{\partial f_i(\Delta \mathbf{x}_{Si})}{\partial \Delta \mathbf{x}_S} \right)^T + \mathbf{s}_x^T k_3(t) \Delta\mathbf{q} \\ &= -\mathbf{s}_x^T (\mathbf{B} + \mathbf{K}_v) \mathbf{s}_x - \alpha_x \Delta\boldsymbol{\xi}^T \Delta\boldsymbol{\xi} + \mathbf{s}_x^T k_3(t) \Delta\mathbf{q}. \end{aligned} \quad (22)$$

We are now in a position to state the following lemma:

Lemma: *The desired position input for the trapped cell (17) and the update law (18) for the trapped cell system described by equation (19) guarantee the convergence of $\Delta\boldsymbol{\xi} \rightarrow 0$ as $t \rightarrow \infty$ if $\Delta\mathbf{q} = \mathbf{0}$.*

Proof: If $\Delta\mathbf{q} = \mathbf{0}$, we have $V_1 > 0$ and $\dot{V}_1 \leq 0$. Since $V_1 > 0$ and $\dot{V}_1 \leq 0$, V_1 is bounded. Hence, $\mathbf{s}_x$, $\Delta\boldsymbol{\theta}_d$ and $P(\Delta \mathbf{x}_S)$ are bounded. From equation (9), $f_i(\Delta \mathbf{x}_{Si})$ is also bounded. The boundedness of $f_i(\Delta \mathbf{x}_{Si})$ ensures the boundedness of $\mathbf{x}$ if $\mathbf{x}_o$ is bounded. Hence, $\frac{\partial f_i(\Delta \mathbf{x}_{Si})}{\partial \Delta \mathbf{x}_S}$ is also bounded. Therefore, from equation (10), $\Delta\boldsymbol{\xi}$ is bounded. In addition, $\hat{\boldsymbol{\theta}}_d$ is bounded from equation (18). Since $\mathbf{x}$ and $\Delta\boldsymbol{\xi}$ are bounded, $\dot{\mathbf{x}}_r$ is bounded if $\dot{\mathbf{x}}_o$ is bounded. Since $\mathbf{s}_x$ is bounded, from equation (12), $\dot{\mathbf{x}}$ is bounded. Since $\frac{\partial f_i(\Delta \mathbf{x}_{Si})}{\partial \Delta \mathbf{x}_S}$, $\mathbf{x}$, $\dot{\mathbf{x}}$ are bounded, $\Delta\boldsymbol{\xi}$ is bounded. Then $\ddot{\mathbf{x}}_r$ is bounded. From equation (19), we can conclude that $\dot{\mathbf{s}}_x$ is bounded since $\Delta\boldsymbol{\xi}$, $\mathbf{s}_x$, $\mathbf{q}_d$ and $\Delta\boldsymbol{\theta}_d$ are all bounded. Hence, $\ddot{V}_1$ is bounded since $\dot{\mathbf{s}}_x$, $\mathbf{s}_x$, $\Delta\boldsymbol{\xi}$, $\Delta\boldsymbol{\xi}$ are bounded. Therefore, $\dot{V}_1$ is uniformly continuous. Applying Barbalat's lemma [18], we have $\dot{V}_1 \rightarrow 0$ which also indicates: $\Delta\boldsymbol{\xi} \rightarrow \mathbf{0}$ and $\mathbf{s}_x \rightarrow \mathbf{0}$. From equation (10), $\Delta\boldsymbol{\xi} \rightarrow \mathbf{0}$ indicates that $f_i(\Delta \mathbf{x}_{Si}) \leq 0$ or $\frac{\partial f_i(\Delta \mathbf{x}_{Si})}{\partial \Delta \mathbf{x}_S} \rightarrow \mathbf{0}$. Moreover, $\frac{\partial f_i(\Delta \mathbf{x}_{Si})}{\partial \Delta \mathbf{x}_S} \rightarrow \mathbf{0}$ is only satisfied when $\Delta \mathbf{x}_S \rightarrow \mathbf{0}$. Either $f_i(\Delta \mathbf{x}_{Si}) \leq 0$ or $\Delta \mathbf{x}_S \rightarrow \mathbf{0}$ implies that the cell is inside the desired region. Therefore, $\mathbf{x}$ converges to the moving desired region if $\Delta\mathbf{q} = \mathbf{0}$. ■

C. 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 robot control input $\mathbf{u}$ which will ensure the convergence of $\Delta\mathbf{q}$ to zero.

First, another sliding vector by using the desired position input is proposed as:

$$\mathbf{s}_q = \dot{\mathbf{q}} - \dot{\mathbf{q}}_r = \dot{\mathbf{q}} - \dot{\mathbf{q}}_d + \alpha_q \Delta\mathbf{q}, \quad (23)$$

where α_q is a positive constant.

Next, the control input for the robotic manipulator of laser beam is proposed as:

$$\mathbf{u} = -\mathbf{K}_s \mathbf{s}_q - \mathbf{K}_p \Delta \mathbf{q} + \mathbf{Y}_q(\dot{\mathbf{q}}_r, \ddot{\mathbf{q}}_r) \hat{\boldsymbol{\theta}}_q, \quad (24)$$

where $\mathbf{K}_s$ and $\mathbf{K}_p$ are positive definite matrices, and the estimated parameters $\hat{\boldsymbol{\theta}}_q$ are updated by the following update law:

$$\dot{\hat{\boldsymbol{\theta}}}_q = -\mathbf{L}_q \mathbf{Y}_q^T(\dot{\mathbf{q}}_r, \ddot{\mathbf{q}}_r) \mathbf{s}_q. \quad (25)$$

The region error $\Delta \boldsymbol{\xi}$ and the desired position input $\mathbf{q}_d$ in equation (17) are continuous, and hence the control input $\mathbf{u}$ in equation (24) is also continuous without inducing any vibration or chattering that is not desirable for micromanipulation.

By using the sliding vector $\mathbf{s}_q$, the manipulator dynamics in equation (3) can be rewritten as:

$$\mathbf{M}_q \dot{\mathbf{s}}_q + \mathbf{B}_q \mathbf{s}_q + \mathbf{Y}_q(\dot{\mathbf{q}}_r, \ddot{\mathbf{q}}_r) \boldsymbol{\theta}_q = \mathbf{u}. \quad (26)$$

Substituting the control input (24) into equation (26), the closed-loop equation is given as:

$$\mathbf{M}_q \dot{\mathbf{s}}_q + (\mathbf{B}_q + \mathbf{K}_s) \mathbf{s}_q + \mathbf{K}_p \Delta \mathbf{q} + \mathbf{Y}_q(\dot{\mathbf{q}}_r, \ddot{\mathbf{q}}_r) \Delta \boldsymbol{\theta}_q = \mathbf{0}. \quad (27)$$

To prove the stability of the overall system, a Lyapunov-like function candidate is proposed as:

$$V_2 = V_1 + \frac{1}{2} \mathbf{s}_q^T \mathbf{M}_q \mathbf{s}_q + \frac{1}{2} \Delta \mathbf{q}^T \mathbf{K}_p \Delta \mathbf{q} + \frac{1}{2} \Delta \boldsymbol{\theta}_q^T \mathbf{L}_q^{-1} \Delta \boldsymbol{\theta}_q, \quad (28)$$

where V_1 is defined in equation (20).

Differentiating V_2 in equation (28) with respect to time, we have:

$$\dot{V}_2 = \dot{V}_1 + \mathbf{s}_q^T \mathbf{M}_q \dot{\mathbf{s}}_q + \Delta \mathbf{q}^T \mathbf{K}_p \Delta \dot{\mathbf{q}} - \dot{\boldsymbol{\theta}}_q^T \mathbf{L}_q^{-1} \Delta \boldsymbol{\theta}_q. \quad (29)$$

Substituting equations (22), (23), (25) and (27) into equation (29), we have:

$$\begin{aligned} \dot{V}_2 &= -\mathbf{s}_x^T (\mathbf{B} + \mathbf{K}_v) \mathbf{s}_x - \alpha_x \Delta \boldsymbol{\xi}^T \Delta \boldsymbol{\xi} + \mathbf{s}_x^T k_3(t) \Delta \mathbf{q} \\ &\quad - \mathbf{s}_q^T [(\mathbf{B}_q + \mathbf{K}_s) \mathbf{s}_q + \mathbf{K}_p \Delta \mathbf{q}] + \Delta \mathbf{q}^T \mathbf{K}_p \Delta \dot{\mathbf{q}} \\ &= -\alpha_x \Delta \boldsymbol{\xi}^T \Delta \boldsymbol{\xi} - \mathbf{s}_q^T (\mathbf{B}_q + \mathbf{K}_s) \mathbf{s}_q \\ &\quad - \begin{bmatrix} \mathbf{s}_x^T & \Delta \mathbf{q}^T \end{bmatrix} \begin{bmatrix} \mathbf{B} + \mathbf{K}_v & -\frac{k_3(t)}{2} \mathbf{I} \\ -\frac{k_3(t)}{2} \mathbf{I} & \alpha_q \mathbf{K}_p \end{bmatrix} \begin{bmatrix} \mathbf{s}_x \\ \Delta \mathbf{q} \end{bmatrix}. \end{aligned} \quad (30)$$

Note that $k_3(t) = k_1 e^{-k_2 \|x - q\|^2} \leq k_1$. Therefore, if we choose the controller parameters $\mathbf{K}_v$, α_q and $\mathbf{K}_p$ sufficiently large so that

$$\lambda_{\min}[\mathbf{K}_v + \mathbf{B}] > \frac{k_1^2}{4}, \quad (31)$$

$$\alpha_q \lambda_{\min}[\mathbf{K}_p] > 1, \quad (32)$$

then the matrix $\begin{bmatrix} \mathbf{B} + \mathbf{K}_v & -\frac{k_3(t)}{2} \mathbf{I} \\ -\frac{k_3(t)}{2} \mathbf{I} & \alpha_q \mathbf{K}_p \end{bmatrix}$ is positive definite and hence $\dot{V}_2 \leq 0$. The notation $\lambda_{\min}[\mathbf{A}]$ denotes the minimum eigenvalue of matrix $\mathbf{A}$.

We can now state the following theorem:

Theorem: If the manipulator input $\mathbf{u}$ given by equations (24), (25), (17) and (18) is applied on the robot-assisted cell manipulation system (1), (3), then the closed-loop system

gives rise to the convergence of $\Delta \boldsymbol{\xi} \rightarrow 0$ and $\mathbf{q} \rightarrow \mathbf{q}_d$ as $t \rightarrow \infty$ when the control parameters $\mathbf{K}_v$, α_q and $\mathbf{K}_p$ are chosen to satisfy conditions (31) and (32).

Proof: Since $V_2 > 0$ and $\dot{V}_2 \leq 0$, V_2 is bounded. Hence, $\mathbf{s}_q$, $\Delta \mathbf{q}$ and $\Delta \boldsymbol{\theta}_q$ are bounded. Since $\dot{\mathbf{x}}$, $\Delta \dot{\boldsymbol{\xi}}$, $\dot{\mathbf{s}}_x$ and $\dot{\hat{\boldsymbol{\theta}}}_d$ are all bounded (as shown in the previous section), $\dot{\mathbf{q}}_d$ is bounded. Since $\Delta \mathbf{q}$ and $\dot{\mathbf{q}}_d$ are bounded, $\dot{\mathbf{q}}_r$ is bounded. Then $\dot{\mathbf{q}}$ is bounded because $\mathbf{s}_q = \dot{\mathbf{q}} - \dot{\mathbf{q}}_r$. Similarly, it can be shown that $\dot{\mathbf{q}}_d$ is bounded, which also indicates that $\dot{\mathbf{q}}_r$ is bounded. From the closed-loop equation (27), $\dot{\mathbf{s}}_q$ is bounded. Therefore, $\dot{V}_2$ is also bounded since $\mathbf{s}_x$, $\dot{\mathbf{s}}_x$, $\Delta \boldsymbol{\xi}$, $\Delta \dot{\boldsymbol{\xi}}$, $\mathbf{s}_q$, $\dot{\mathbf{s}}_q$, $\Delta \mathbf{q}$ and $\Delta \dot{\mathbf{q}}$ are all bounded. It is thus concluded that $\dot{V}_2$ is uniformly continuous. Applying the Barbalat's lemma [18], we have $\dot{V}_2 \rightarrow 0$ as $t \rightarrow \infty$, which also indicates that $\Delta \mathbf{q} \rightarrow 0$ and thus $\Delta \boldsymbol{\xi} \rightarrow 0$. ■

IV. EXPERIMENT

The proposed control method was implemented in an optical tweezers system as shown in Fig. 1. The system is constituted of three modules for sensing, control and execution. The sensing module consists of a microscope and an IEEE 1394 digital camera (FOculus, FO124SC), and the cell positions can be obtained through image processing. The control module consists of a phase modulator for HOT device and a stepping motor controller for the laser beam. The execution module consists of a holographic optical trapping (HOT) device (Arryx, BioRyx200). All of the mechanical components are supported by an anti-vibration table in a clean room. The optical tweezers were controlled to manipulate the yeast cell, and the cell was trapped from the beginning. In the experiments, the position of the laser beam is fixed, and the desired position input $\mathbf{q}_d$ in equation (17) is applied on the motorized stage to vary the relative distance between the laser beam and the cell.

Fig. 1. A robot-tweezer manipulation system.

In the first experiment, the trapped cell was controlled to follow a moving region. The desired region is specified as:

$$f(\Delta \mathbf{x}_S) = (x_{S1} - 3.75t)^2 + (x_{S2})^2 - 2^2 \leq 0, \quad (33)$$

where the scaling matrix was specified as an identity matrix. The control parameters were set as: $\mathbf{L}_d = \text{diag}\{10^{-7}, 10^{-7}\}$, $N = 4$, $k_p = 0.0008$, $\alpha_x = 1$,

$K_v = \text{diag}\{0.14, 0.14\}$. The snapshots of the trapped cell at different time instants are shown in Fig. 2. The results indicate that the trapped cell was transported within the moving desired region. The tracking error is defined as $\sqrt{(x_{S1} - 3.75t)^2 + (x_{S2})^2}$, which is shown in Fig. 3.

In the second experiment, the center of the circular region was fixed while the radius was decreasing. Therefore, the trapped cell was being dragged towards the center without the specification of trajectory. The desired region is specified as:

$$f(\Delta x_S) = (x_{S1})^2 + (x_{S2})^2 - 10^2 \leq 0, \quad (34)$$

where the scaling matrix was specified as $S^{-1}(t) = \text{diag}\{\frac{1}{1+0.94t}, \frac{1}{1+0.94t}\}$. The control parameters were set as: $L_d = \text{diag}\{10^{-7}, 10^{-7}\}$, $N = 4$, $k_p = 6 \times 10^{-8}$, $\alpha_x = 1$, $K_v = \text{diag}\{0.1, 0.1\}$. The tracking error is defined as $\sqrt{(x_{S1})^2 + (x_{S2})^2}$, which is shown in Fig. 4. The snapshots of trapped cell at different time instants are shown in Fig. 5. From Fig. 4 and Fig. 5, it is seen that the tracking error decreased as the region reduced.

V. CONCLUSIONS

In this paper, we have proposed a dynamic region control method for cell manipulation with optical tweezers. The dynamics of robotic manipulator of the laser beam is introduced into the optical tweezers system so that a closed-loop control system is formulated. A dynamic region is formulated for specific manipulation tasks while the size of the region can be varied to provide flexibility. Experimental results are presented to illustrate the performance of the proposed control method.

REFERENCES

- [1] A. Shikin, J. M. Dziedzic, J. E. Bjorkholm and S. Chu, "Observation of a single beam gradient force optical trap for dielectric particles," *Optics Letters*, Vol. 11, pp. 288-290, 1986.
- [2] A. Ashikin, "History of Optical Trapping and Manipulation of Small-Neural Particle, Atoms, and Molecules," *IEEE Journal on Selected Topics in Quantum Electronics*, Vol. 6, No. 6, pp. 841-856, 2000.
- [3] M. Murata, Y. Okamoto, Y. Park, N. Kaji, M. Tokeshi and Y. Baba, "Cell separation by the combination of microfluidics and optical trapping force on a microchip," *Analytical and Bioanalytical Chemistry*, Vol. 394, pp. 277-283, 2009.
- [4] J. Pine and G. Chow, "Moving live dissociated neurons with an optical tweezer," *IEEE Transactions on Biomedical Engineering*, Vol. 56, No. 4, pp. 1184-1188, 2009.
- [5] Y. Tan, D. Sun, J. Wang and W. Huang, "Mechanical characterization of human red blood cells under different osmotic conditions by robotic manipulation with optical tweezers," *IEEE Transactions on Biomedical Engineering*, Vol. 57, No. 7, pp. 1816-1825, 2010.
- [6] S. Chu, "Laser manipulation of atoms and particles," *Science*, Vol. 253, pp. 861-866, 1991.
- [7] C. Rusu, R. Oever, M. J. Boer, H. V. Jansen, J. W. Berenschot, M. L. Bennink, J. S. Kanger, B. G. Grooth, M. Elwenspoek, J. Greve, J. Brugger and A. Berg, "Direct integration of micromachined pipettes in a flow channel for single DNA molecule study by optical tweezers," *Journal of Microelectromechanical Systems*, Vol. 10, No. 2, pp. 238-245, 2001.
- [8] A. G. Banerjee, A. Pomerance, W. Losert and S. K. Gupta, "Developing a stochastic dynamic programming framework for optical tweezer-based automated particle transport operations," *IEEE Transactions on Automation Science and Engineering*, Vol. 7, No. 2, pp. 218-227, 2010.

Fig. 2. Experiment 1: Positions of the trapped cell at various time instants.

Fig. 3. Experiment 1: The tracking error.

Fig. 4. Experiment 2: The tracking error.

- [9] Y. Wu, Y. Tan, D. Sun and W. Huang, "Force analysis and path planning of the trapped cell in robotic manipulation with optical tweezers," *2010 IEEE International Conference on Robotics and Automation*, pp. 4119-4124, 2010.
- [10] S. C. Grover, A. G. Skirtach, R. C. Gauthier and C. P. Grover, "Automated single-cell sorting system based on optical trapping," *Journal of Biomedical Optics*, Vol. 6, No. 1, pp. 14-22, 2001.
- [11] S. Hu and D. Sun, "Automatic transportation of biological cells with a robot-tweezer manipulation system," *The International Journal of Robotics Research*, Vol. 30, 2011 (online).
- [12] E. R. Dufresne, G. C. Spalding, M. T. Dearing, S. A. Sheets and D. G. Grier, "Computer-generated holographic optical tweezer arrays," *Review of Scientific Instruments*, Vol. 72, No. 3, pp. 1810-1816, 2001.
- [13] F. Arai, K. Onda, R. Iitsuka and H. Maruyama, "Multi-beam laser micromanipulation of microtool by integrated optical tweezers," *2009 IEEE International Conference on Robotics and Automation*, (Kobe, Japan), pp. 1832-1837, 2009.
- [14] C. Aguilar-Ibanez, M. S. Suarez-Castanon and L. I. Rosas-Soriano, "A simple control scheme for the manipulation of a particle by means of optical tweezers," *International Journal of Robust and Nonlinear Control*, 2010.
- [15] A. Ranaweera and B. Bamieh, "Modeling, identification and control of a spherical particle trapped in an optical tweezer," *International Journal of Robust and Nonlinear Control*, Vol. 15, pp. 747-768, 2005.
- [16] H. Chen, J. Chen, Y. Wu and D. Sun, "Flocking of micro-scale particles with robotics and optical tweezers technologies," *The 2010 IEEE/RSJ International Conference on Intelligent Robots and Systems*, pp. 6155-6160, 2010.
- [17] Y. Tanaka, H. Kawada, K. Hirano, M. Ishikawa and H. Kitajima, "Automated manipulation of non-spherical micro-objects using optical tweezers combined with image processing techniques," *Optics Express*, Vol. 16, No. 19, pp. 15115-15122, 2008.
- [18] J. J. E. Slotine and W. Li, *Applied Nonlinear Control*. Englewood Cliffs, New Jersey: Prentice Hall, 1991.

(a) $t=1.54$ s

(b) $t=9.24$ s

(c) $t=16.9$ s

(d) $t=23.1$ s

Fig. 5. Experiment 2: Positions of the trapped cell at various time instants.