Virtual Haptic Cell Model for Operator Training

Ben Horan, Daniel Lowe, Quan-Zen Ang, Marzieh Asgari, Ali Ghanbari and Saeid Nahavandi

Centre for Intelligent Systems Research, Deakin University, Australia

Corresponding: ben.horan@deakin.edu.au

***Abstract* – Microrobotic cell injection is an area of growing research interest. Typically, operators rely on visual feedback to perceive the microscale environment and are subject to lengthy training times and low success rates. Haptic interaction offers the ability to utilise the operator's haptic modality and to enhance operator performance. Our earlier work presented a haptically enabled system for assisting the operator with certain aspects of the cell injection task. The system aimed to enhance the operator's controllability of the micropipette through a logical mapping between the haptic device and microrobot, as well as introducing virtual fixtures for haptic guidance. The system was also designed in such a way that given the availability of appropriate force sensors, haptic display of the cell penetration force is straightforward. This work presents our progress towards a virtual replication of the system, aimed at facilitating offline operator training. It is suggested that operators can use the virtual system to train offline and later transfer their skills to the physical system. In order to achieve the necessary representation of the cell within the virtual system, methods based on a particle-based cell model are utilised. In addition to providing the necessary visual representation, the cell model provides the ability to estimate cell penetration forces and haptically display them to the operator. Two different approaches to achieving the virtual system are discussed.**

Keywords – Cell injection, haptic training, virtual training, haptic virtual fixtures

1 INTRODUCTION

Microrobotic cell injection facilitates the manipulation of biological cells and is an area of growing research interest [1-4]. Typically, microrobotic cell injection is controlled manually where an operator remains limited to their visual sense to perceive and operate in the microscale environment. Research suggests that it takes approximately one year for an operator to be appropriately trained in the cell injection process and success rates remain low [1, 5].

Autonomous cell injection has been proposed as an alternative to manual cell injection. Autonomous cell injection offers benefits inherent to system autonomy including high throughput, minimal operator intervention, and the ability to work as part of an automated lab environment. The work by [4] presented a novel system for the autonomous injection of individual cells. The work focused on mouse embryos and used image processing to locate the cell nucleus and micropipette tip. While such autonomous cell injection does represent a worthwhile research effort, benefits relating to real-time human operator control are not utilised.

This work is distinct from such an approach in that rather than replacing the operator, haptic interaction is introduced to enhance human-in-the-loop cell injection. Human-in-the-loop control natively caters to flexibility, adaptation, and utilisation of human level judgement and intuition. Haptics relates to the human's ability to feel and touch, and haptic technologies interact with human's haptic sensory modality through tactual, force-based and proprioceptive information. Haptic technologies have been utilised in a vast diversity of applications including procedural operator training [6], mobile robotic teleoperation [7-9], and medical simulation and training [10-13].

Our earlier work presented a haptically enabled system for assisting the operator with certain aspects of the cell injection task [14-16]. Some works, such as those of [17, 18], focused on providing the operator with real-time haptic feedback of cell penetration forces. Despite such research efforts, appropriate lab-ready force sensors are not yet readily available. It is for this reason that our system haptically assists the operator independent of real-time measurement of cell penetration forces. The system is however, designed to support the haptic display of cell penetration forces given the availability of appropriate sensors.

Aside from assisting the operator during real-time cell injection, the same concepts can be employed for offline virtual operator training. Using a virtual replication of the cell injection system, it is suggested that operators can train offline in a similar way to which they would with the physical system. After receiving adequate training, operators can then transfer their skills to the similar physical system. Such a training system offers several benefits including reduced training costs, low maintenance and the ability to augment the virtual environment with training aids and other information.

Haptically enabled virtual operator training has been proposed for many applications including surgical drilling [19], laparoscopic procedures [12], complex machining tasks [6] and minimally invasive surgery [11]. It is apparent that in order to be effective, the virtual training environment needs to be adequately realistic. Approaches to the virtual representation of the micromanipulator and micropipette, haptic virtual fixtures [15, 16] and the cell are discussed in this paper.

The cell within the virtual training environment needs to behave in a similar way to the corresponding real cell and, as such, an appropriate cell model is required. The work by [20] presented a non-linear MSD cell model to estimate cell interaction forces during the injection task. In [21] boundary element modelling was used to estimate cell interaction forces. In this work, the virtual cell needs to provide visual and force responses to penetration similar to those of the corresponding real cell. This is achieved within the virtual environment using methods based on a particle-based cell model [22]. As a result, the virtual cell visually deforms in response to penetration as well providing as an estimate of the interaction forces. These forces can be haptically displayed to the operator and correspond to those which may be measured by force sensors later integrated to the physical system.

This paper presents our progress towards a virtual replication of the physical haptically enabled cell injection system, aimed at facilitating offline operator training. It is suggested that operators can use the virtual system to train offline and later transfer their skills to the physical system.

2 PHYSICAL HAPTIC CELL INJECTION SYSTEM

The haptic cell injection system, as presented in our previous works [14-16], is depicted by Fig. 1. The system consists of an MP-285 micromanipulator from Sutter Instruments, a venturi vacuum pump (UN816, KNF), a PMI-200 pressure microinjection system (Dagan), an A601f-2 CMOS camera (Basler) mounted on top of the SZX2-ILLB optical microscope (Olympus), a PC (Intel Core Duo CPU 2.66GHz, 4GB RAM) with a PCI-6259 DAQ card (National Instruments), and a Phantom Omni haptic device (SensAble Technologies).

Fig. 1: Haptic microrobotic cell injection system as presented in [14-16]

The system allows operators to intuitively control the micropipette's motion while haptic virtual fixtures provide haptic assistance during the cell injection task. This is achieved through the two distinct components below.

(1) The mapping framework enables the operator to control the micromanipulator using the haptic device. The mapping results in an intuitive method to control the movement of the micropipette in a manner similar to conventional handheld needle insertion (as opposed to using rotary encoders or modified joystick).

(2) Haptic feedback/assistance in the form of haptic virtual fixtures is rendered to the operator during the cell injection process. Given the availability of appropriate real-time force sensors, haptic feedback may also include display of the cell interaction forces.

2.1 Haptic Virtual Fixtures

The haptic virtual fixtures introduced in our earlier works [15, 16] aim to provide the operator with real-time haptic assistance for certain aspects of the cell injection task. Aside from real-time assistance, the haptic virtual fixtures are applicable to the virtual training system. As is the case for the physical system, the virtual fixtures can assist the operator with certain aspects of the virtual cell injection task. Then, after sufficient training, the operator can transfer their training experience to the physical system offering the same virtual fixtures. In this paper, the following three haptic virtual fixtures [15] are considered.

- The planar virtual fixture attempts to prevent the operator from exceeding the desired insertion depth inside the cell. The virtual plane is orthogonal to the conical virtual fixture axis of symmetry and the injection target location lies within the plane.
- The axial virtual fixture can be enabled by the operator using either of the buttons on the haptic device's stylus. When enabled (only available when the micropipette tip is within the cell and no other haptic forces are active) the axial virtual fixture attempts to constrain the user along the micropipette's direction of insertion.
- The conical potential field virtual fixture applies forces to the operator's hand so as to guide the micropipette's tip to the desired penetration point on the cell's surface. Aside from guiding the operator to the penetration point, large repulsive forces near the virtual fixture's surface attempt to prevent the micropipette's tip from moving outside of the conical volume.

It is worthwhile to acknowledge, that if deemed appropriate, the operator is able to overpower the virtual fixtures to exercise independent actions.

It should also be noted that the virtual fixtures complement the haptic display of cell interaction forces. Given the availability of such real-time force sensing (or model-based estimation as per the following section) integration is straightforward.

3 VIRTUAL TRAINING SYSTEM

In order to realise an effective virtual training system it needs to be adequately realistic. To this end, this section discusses our approaches to virtual representation of the biological cell, micromanipulator and micropipette, and haptic virtual fixtures.

3.1 Haptic Cell Model

The virtual cell needs to exhibit behaviour similar to that of the corresponding real cell. In this work this is achieved using methods based a particle-based cell model [22] able to be tuned according to experimental data. It should be noted that other cell models may be employed, however should first be assessed for their real-time computational capability. In addition to providing the necessary visual representation, the cell model enables interaction forces to be estimated and haptically displayed to the operator.

The methods employed within the virtual environment to represent the virtual cell are based on the below-described cell model.

- The cell membrane is considered as a viscoelastic layer and modelled using the Discrete Element Method (DEM). The DEM has proven to be effective for many applications including modelling the cell wall of plant cells [23]. The layer is divided into discrete particles using a meshing algorithm and neighbouring particles are connected by spring-dashpots.

- The structure inside the cell is considered as a Kelvin-Voigt material (viscous and elastic properties) with a small compressibility factor. To model the cell interior a mass is assumed at the centre of the sphere linked to all membrane particles through spring-dashpots. The incompressibility condition is modelled as a hydraulic pressure applied to the membrane.

Each particle is connected to the four adjacent membrane particles as well as to the centre mass. These connections model elastic and damping interactions between adjacent particles. By applying these interactions and solving equation (1), the position of each node is determined.

$$M_{m,k}\ddot{\vec{r}}_{m,k} + B_{m,k}\dot{\vec{r}}_{m,k} + K_{m,k}\vec{r}_{m,k} = \vec{F}^{ext}_{m,k} + \vec{F}^{comp}_{m,k} \quad (1)$$

where $M_{m,k}$ is the mass of the particle (m,k), $\vec{r}_{m,k} = [x_{m,k},\ \ y_{m,k},\ \ z_{m,k}] \in R^3$ is the position vector of each particle, $F^{ext}_{m,k} \in R^3$ is the external force applied to the cell at the node (m,k) which may arise from the micropipette, cell holding device or any other external force from the surrounding environment, $B_{m,k}$ is the damping factor at each point, $K_{m,k}$ represents the tension factor between particle (m,k) and its neighbouring particles, and $F^{comp}_{m,k} \in R^3$ is the hydraulic force applied to the membrane due to incompressibility condition of the liquid inside the cell.

To ensure that the cell's volume has no considerable changes during penetration, the cell volume is considered as an incompressible liquid. The compressibility β is given by

$$\beta = -\frac{1}{V}\frac{dV}{dP} \quad (2)$$

where V is the cell volume and dV and dP are the changes in cell volume and hydraulic pressure respectively.

V is evaluated at each iteration to determine dV, and given an appropriate value for β, equation (2) can determine dP. Given the relation between force and pressure, $F^{comp}_{m,k}$ can then be derived.

The model can be tuned according to forces and deformations obtained from suitable cell injection experiments, such as those in [24].

In order to represent the virtual deformation of the cell membrane during cell injection (and to determine the corresponding interaction forces), the virtual micropipette's tip is tracked and fed as an input to the model.

The virtual cell is implemented using methods based on the above-described model.

3.2 Virtual Training Environment using Webots

The virtual training environment was initially developed using Webots robot simulation software [25]. Webots was chosen based on its use of ODE physics and the provision of a wide range of robot related functionality. The virtual system developed in Webots, including the micromanipulator, micropipette and cell, are shown in Fig. 2.

Fig. 2: Virtual system developed using Webots

Webots enabled rapid realisation of most of the virtual system's components, including the micromanipulator and micropipette. The deformable cell was achieved using a sphere mesh surface where cell data (particle position, velocity, etc.) is managed by a supervisor robot controller which responds to physics events such as collisions. At each update of the Webots graphics loop, the supervisor controller updates vertex positions of the sphere mesh to represent cell deformations (according to the cell model). The major limitation is the slow update rate (< 1 frame/sec) resulting in inadequate real-time interaction with the virtual cell. Several attempts were made to improve the update rate including reducing cell model complexity, reducing the visualisation update rate, representing aggregate cell particle position data with a less complex mesh, etc. Despite these attempts, satisfactory graphical and physics representations could not be achieved together.

3.3 Virtual Training Environment using C++ and DirectX

The second virtual training environment was developed as custom software using C++ and DirectX 9.0c (Windows platform) and achieved greater control over graphics rendering. The virtual cell was implemented using a similar method to the Webots implementation where a cell class comprising a set of particles in a mass-spring-damper system updates its data in response to physics events, and vertices of a sphere mesh are updated at each graphics frame using the particle position data.

In this software, the cell utilises a "render" method able to be called at each graphic frame update, as well as allowing the class to access the graphics API directly. This resulted in a large improvement in graphical performance. In the absence of Webots' ODE physics, a custom system using a Verlet numerical integration scheme is used.

Fig. 3 depicts the virtual cell undergoing deformation as the micropipette penetrates the cell. Fig. 3 (a-c) shows progressive deformation before penetration, and (d) shows the cell after penetration. The cell is rendered as semi-translucent after the operator has successfully penetrated the cell membrane.

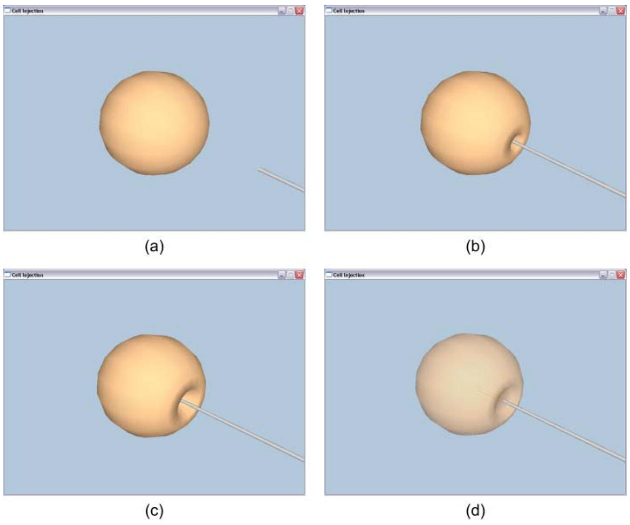

Fig. 3: Deformation of the virtual cell in response to penetration (a-c) Cell before penetration, and (d) Cell after penetration

The virtual cell also enables the haptic rendering of a scaled cell interaction force. Note: before contact (Fig. 3 (a)) and after penetration (Fig. 3 (d)), the rendered cell interaction force is zero.

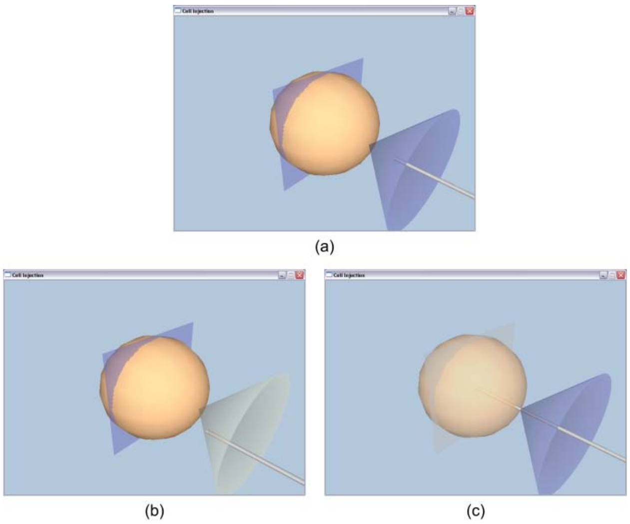

Fig. 4: Virtual cell with graphical representation of virtual fixtures (a) No collision with virtual fixtures, (b) Attempting to penetrate the conical virtual fixture surface, and (c) Attempting to penetrate the planar virtual fixture

The haptic virtual fixtures of [15] were implemented within the virtual training environment as shown by Fig. 4. The operator is able to toggle them on and off using the keyboard, and the colour of the virtual fixtures changes to reflect the amount of force the operator imparts on the virtual fixture.

4 CONCLUSION

This paper presents our progress towards a virtual replication of a physical haptically enabled cell injection system, aimed at facilitating offline operator training. In order to represent the cell within the virtual environment methods based on a particle-based cell model were utilised. The haptic virtual fixtures of our earlier work were implemented in the virtual environment. Two different approaches to achieving the virtual training system were discussed. It is suggested that operators can use the virtual system to train offline and later transfer their skills to the physical system.

REFERENCES

[1] P. Scherp and K. H. Hasenstein, "Microinjection - a tool to study gravitropism," *Advances in Space Research*, vol. 31, pp. 2221-2227, 2003.

[2] Y. Xie, *et al.*, "Force Sensing and Manipulation Strategy in Robot-Assisted Microinjection on Zebrafish Embryos," *IEEE/ASME Transactions on Mechatronics*, vol. PP, pp. 1-9, 2010.

[3] X. Liu, *et al.*, "Orientation Control of Biological Cells Under Inverted Microscopy," *IEEE/ASME Transactions on Mechatronics*, vol. PP, pp. 1-7, 2010.

[4] Y. Sun and B. J. Nelson, "Biological Cell Injection Using an Autonomous MicroRobotic System," *The International Journal of Robotics Research*, vol. 21, pp. 861-868, 2002.

[5] N. D. Tran, *et al.*, "Efficiency of Chimeraplast Gene Targeting by Direct Nuclear Injection Using a GFP Recovery Assay," *Mol Ther*, vol. 7, pp. 248-253, 2003.

[6] A. Balijepalli and T. Kesavadas, "Value-Addition of Haptics in Operator Training for Complex Machining Tasks," *Journal of Computing and Information Science in Engineering*, vol. 4, pp. 91-97, 2004.

[7] B. Horan, *et al.*, "Haptic Control Methodologies for Telerobotic Stair Traversal," *International Journal of Intelligent Control and Systems*, vol. 13, pp. 3-14, 2008.

[8] Z. Najdovski, *et al.*, "Method and Apparatus for Haptic Control: Patent," WO/2008/074081, 2008.

[9] S. K. Cho, *et al.*, "Teleoperation of a Mobile Robot Using a Force-Reflection Joystick With Sensing Mechanism of Rotating Magnetic Field," *IEEE/ASME Transactions on Mechatronics*, vol. 15, pp. 17-26, 2010.

[10] A. Mor, *et al.*, "Interacting with 3-Dimensional Medical Data - Haptic Feedback for Surgical Simulation," in the proceedings of the *First PHANToM Users Group Workshop*, 1996.

[11] C. Basdogan, *et al.*, "Haptics in minimally invasive surgical simulation and training," *IEEE Computer Graphics and Applications*, vol. 24, pp. 56-64, 2004.

[12] C. Basdogan, *et al.*, "Virtual environments for medical training: graphical and haptic simulation of laparoscopic common bile duct exploration," *IEEE/ASME Transactions on Mechatronics*, vol. 6, pp. 269-285, 2001.

[13] A. Gupta and M. K. O'Malley, "Design of a haptic arm exoskeleton for training and rehabilitation," *IEEE/ASME Transactions on Mechatronics*, vol. 11, pp. 280-289, 2006.

[14] B. Horan, *et al.*, "Towards haptic microrobotic intracellular injection," in the proceedings of the *ASME & IDETC/CIE International Design Engineering Technical Conferences & Computers and Information in Engineering Conference*, 2009, pp. 135-142.

[15] A. Ghanbari, *et al.*, "Haptic guidance for microrobotic intracellular injection," in the proceedings of the *3rd IEEE RAS and EMBS International Conference on Biomedical Robotics and Biomechatronics*, 2010, pp. 162-167.

[16] A. Ghanbari, *et al.*, "Haptic microrobotic intracellular injection assistance using virtual fixtures," in the proceedings

of the *11th International Conference on Control Automation Robotics & Vision*, 2010, pp. 781-786.

[17] A. Pillarisetti, "Force Feedback Interface for Cell Injection," in the proceedings of the *World Haptics Conference*, 2005, pp. 391-400.

[18] S.-Y. Cho and J.-H. Shim, "A new micro biological cell injection system," in the proceedings of the *IEEE/RSJ International Conference on Intelligent Robots and Systems*, 2004, pp. 1642-1647.

[19] C. Sewell, *et al.*, "The effect of virtual haptic training on real surgical drilling proficiency," in the proceedings of the *Second Joint EuroHaptics Conference and Symposium on Haptic Interfaces for Virtual Environment and Teleoperator Systems*, 2007.

[20] M. Ammi, *et al.*, "Evaluation of 3D Pseudo-Haptic Rendering using Vision for Cell Micromanipulation," in the proceedings of the *IEEE/RSJ International Conference on Intelligent Robots and Systems*, 2006, pp. 2115-2120.

[21] J. Kim, *et al.*, "Haptic Feedback Based on Physically Based Modeling for Cellular Manipulation Systems " in *Haptics: Perception, Devices and Scenarios*. vol. 5024, M. Ferre, Ed., ed: Springer, 2008, pp. 661-667.

[22] M. Asgari, *et al.*, "3D Particle-Based Cell Modelling for Haptic Microrobotic Cell Injection," in the proceedings of the *15th International Conference on Mechatronics Technology*, 2011.

[23] P. Van Liedekerke, *et al.*, "Particle-based model to simulate the micromechanics of biological cells," *Physical Review E,* vol. 81, p. 061906, 2010.

[24] L. Xinyu and et al., "Vision-based cellular force measurement using an elastic microfabricated device," *Journal of Micromechanics and Microengineering,* vol. 17, p. 1281, 2007.

[25] O. Michel, "Webots: Professional Mobile Robot Simulation," *Journal of Advanced Robotics Systems,* vol. 1, pp. 39-42, 2004.