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Micro-Robotic Cell Injection Training in a CAVE^{TM}

Syafizwan Faroque[1,2]*, Ben Horan[1], Michael Mortimer[1], and Mulyoto Pangestu[3]

[1]School of Engineering, Deakin University, Geelong, Australia
[2]Department of Community College Education, Ministry of Higher Education, Putrajaya, Malaysia
[3]Department of Obstetrics and Gynaecology, Monash University, Melbourne, Australia

Abstract

This paper focuses on the design of an evaluation made to a large-scale virtual reality micro-robotic cell injection training system. The aim of the evaluation is to empirically investigate the usability and effectiveness of three distinct display configurations and the input controller employed in the system. The data was gathered through a set of experiments with human participants. Participants' performance against metrics such as success rate and magnitude of error was considered in the evaluation. For the experiments, participants were randomly divided into six equal sized groups where each group was provided with a specific combination of display configuration and haptic guidance mode. The participants performed ten injections and the time and position of the virtual micropipette tip were recorded. Data was analysed using descriptive statistics and performance comparison between groups was conducted. Additionally three groups also underwent two subsequent sessions, training and post-training, as a basis to evaluate the effectiveness of the training with haptic guidance by comparing participants' performance before and after the training session. The implementation of the designed evaluation has contributed to the conclusions drawn which suggest the proposed large-scale virtual reality system as a feasible training tool for micro-robotic cell injection procedure, and recommendations for future work are proposed.

Keywords: Evaluation design, skills training, virtual reality, haptics, cell injection

Corresponding Author:
Syafizwan Faroque; email:
smohdfar@deakin.edu.au

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1 Introduction

Cell injection is a biological procedure where certain amount of foreign substance is injected into a cell for applications such as cell biological research, intracytoplasmic sperm injection and transgenics [1]. Currently training for the micro-robotic cell injection procedure is conducted physically using real cells and equipment which generally subject to challenges concerning cost, flexibility and ethics compliance.

This paper presents a virtual training system for the procedure as an alternative to the conventional training approach. The introduced large-scale virtual reality (VR) micro-robotic cell injection training system provides an immersive, in-depth, attractive and motivational approach for motor skill training by utilising state-of-the-art technology available. One of the advantages of using large displays is it provides more detailed image representations which can increase sense of presence and understanding of the virtual environment [2] such as the micropipette's orientation and relative position as well as improving participants' spatial awareness. In addition the utilisation of gross motor skill when using the large workspace input controller provides several benefits such as less sensitivity to unintentional and insignificant movements such as vibration, tremors and minor deviations.

2 Large-scale VR Micro-robotic Cell Injection Training System

Our recent work introduced a large-scale virtual reality (VR) training system [3] which was developed by utilising the state-of-the-art facilities available in the CADET VR Lab, Deakin University, Australia [4. The setup consists of four large 3.2 m × 2.4 m screens able to be arranged in two screen arrangements, CAD wall and Cave^{TM}. The CAD wall arrangement utilised three screens combined to form a large 9.6 m × 2.4 m flat display. In the CAVE^{TM} arrangement, two side screens are folded to form a cube-like display.

The virtual environment displays a replication of a cell injection setup consists of a virtual cell and basic bio-manipulation equipment such as microscope, micro-robot, micropipette and cell holding dish. The user will have a view of the environment and able to zoom in to concentrate on the areas of interest.

In order to replicate the cell interaction in a virtual environment, a spring-based cell model was utilised. The virtual cell is modelled to visually deform in response to micropipette contacts as well as providing interaction force estimations where the contact force can be haptically displayed to the user while performing the procedure.

2.1 Display Configurations

There are three display configurations available for the large-scale VR system, 2D, 3D and CAVE-like. The 2D display configuration projects a two-dimensional image in CAD wall arrangement. The user is provided with a magnified top view similar to what can be seen from a microscope during an injection. Similarly the 3D display configuration provides a three-dimensional image in CAD wall arrangement. The CAVE-like display configuration provides a three-dimensional multiple viewpoints of the virtual environment across three of the four screens in the CAVE^{TM} arrangement.

The front screen displays a magnified top view similar to the view provided by the 2D and 3D display configurations. Meanwhile the left and floor screens display a view from behind and side of the micropipette respectively. With this display configuration the user is able to obtain a more immersive virtual environment where the display from three different angles are provided simultaneously while injection is performed.

2.2 Large Workspace Input Controller

An INCA 6D [5] haptic device is employed to interact with the virtual environment. The haptic device can provide up to 6-DOF force feedback to the user within large workspace. The interface was achieved by mapping the orientation and position between the haptic device and the virtual micropipette. As such the virtual cell injection procedure can be performed by holding the INCA 6D handle to control the virtual micro-robot which holds the micropipette. The implemented mapping enables the user to experience an intuitive handling of the micropipette as if they are holding the micropipette, as opposed to the traditional rotary encoders. When performing the procedure with the haptic device user have the options to either enabling or disabling the haptic guidance.

In the haptic guidance enabled mode, the user is provided with virtual fixtures (VFs) and force feedback which serve as physical guidance of the user's control in order to achieve appropriate penetration and deposition points, and to estimate the penetration force. The first is a cone-shaped VF which guides the user to follow the ideal trajectory where it allows the micropipette to move inside its conical guided region. Once the micropipette entered the guided region the conical wall prevents the micropipette from going through it. As such, as the user commands the micropipette to approach the cell, the conical VF encourages them to follow an optimised trajectory to the penetration point on the cell membrane, where the apex of the cone is. Once the micropipette's tip has reached the penetration point, and the user attempts to pierce the cell membrane, they will feel a simulated reaction force feedback, followed by a sudden force drop representing the rupture and penetration of the cell membrane. The user then needs to move the micropipette as straight as possible towards the deposition point inside the cell. In order to prevent the user from overshooting the deposition point, which can cause damage to the cell, a planar VF is provided. The planar VF attempts to prevent the micropipette tip from passing the deposition point at the cell centre.

3 User Training Evaluation Design

This section presents the design of an evaluation aimed to investigate the effectiveness of the large-scale VR system as a training tool for micro-robotic cell injection. Firstly participants are randomly divided into six groups, 2DN, 2DH, 3DN, 3DH, CAN and CAH, as shown in Figure 2.

The 2DN and 2DH groups perform virtual cell injection in 2D display configuration with haptic guidance disabled and enabled respectively. Likewise, the 3DN and 3DH groups perform injections in 3D display configuration with haptic guidance disabled and enabled respectively, and the CAN and CAH groups perform injections in CAVE-like display configuration with haptic guidance disabled and enabled respectively.

The first part of the evaluation considers the success rates and learning curves of the six groups of participants, each of which performs injections with a different display configuration and haptic guidance mode combination. The participants' performance when using each display configuration are then compared in the second evaluation. To obtain a fair comparison, the six groups are assigned into two clusters. The first cluster comprises of the haptic guidance disabled groups, 2DN, 3DN and CAN, and the second cluster comprises of the haptic guidance enabled groups, 2DH, 3DH and CAH. It is anticipated that the participants who are provided with haptic guidance will achieve better performance than those who are not. This is also supported by the results discussed in [6,7] where the participants who utilised the haptic device with haptic guidance during injection performed significantly better than other participants who utilised the keyboard and haptic device without haptic guidance. Therefore the analysis is performed separately for each cluster to distinguish the performance level of participants who were provided with different haptic guidance modes. For example, participants' performance for the first cluster are only compared to each other since all groups in the cluster performed injections without haptic guidance albeit different display configuration. The third evaluation compares the performance between the haptic guidance enabled and haptic guidance disabled groups in each display configuration. Therefore, three clusters are formed where each cluster consists of both haptic guidance enabled and haptic guidance disabled groups for a particular display configuration. The first, second and third clusters consist of 2DN and 2DH groups, 3DN and 3DH groups, and CAN and CAH groups, respectively. Each cluster is considered separately in order to investigate the effects of providing haptic guidance to users as both groups in a cluster were provided with the same display configuration. For example, both groups in the first cluster, 2DN and 2DH, were provided with 2D display configuration where the latter group was provided with haptic guidance during injection.

Finally the fourth evaluation considers participants' performance improvement after undergoing training provided with the haptic guidance. For the purpose of the fourth evaluation, a series of additional injection trials, categorised as training and post-training sessions, conducted for 2DN, 3DN and CAN. The magnitude of error metric is compared between the pre-training and post-training sessions to investigate participants' performance progress in terms of accuracy.

3.1 Measures of Participants' Performance

For the purpose of this evaluation the diameter of the virtual cell is assumed to be 2 μm which is considered to be a small cell based on the fact that real cell diameters range from 1 to 100 μm [8]. The relatively small virtual cell is intentionally chosen on the basis that smaller cells present a more difficult scenario for the bio-operator and therefore a more valuable study. As such the virtual cell has a radius of 1 μm and is centred at the origin (0, 0, 0) of the virtual environment.

Two performance metrics considered in the evaluation are the magnitude of error, *E* and success, *S*. For an injection, *S* and *E* are considered based on the final position of the micropipette tip, *F*. The value of *F* is determined by the participant, through pressing a button on the haptic device when they believe to have reached the best deposition point and are ready for deposition. An injection is considered successful when *F* is located inside the cell, given by $|F| = \sqrt{x^2 + y^2 + z^2} < 1$ μm, indicating that the participant managed to penetrate the cell membrane and stop inside the cell for deposition.

Additionally, once the cell has been penetrated, so as to avoid damage the micropipette should not allowed to be retracted or pushed forward in any direction beyond the cell membrane. As such for each injection, observation is made to verify that multiple penetrations in any direction had not occurred. Aside from direct observation of each injection, the position data are also examined to ensure no multiple penetrations occurred during an injection. This is achieved by analysing whether |*F*| becomes greater than 1 μm after it crossed the threshold to be less than 1 μm.

Herein accuracy is considered as the inverse to error where high accuracy corresponds to low error and vice versa. An ideal injection is achieved when the micropipette tip ends at the centre of the cell, *C*. As such the magnitude of error, *E*, is determined by the distance between *F* and *C* which can be obtained by $E = |F| = \sqrt{x^2 + y^2 + z^2}$.

4 Experiments and Results Summary

A set of experiments with human participants conducted at the CADET VR Lab, Deakin University where participants' performance improvement against metrics such as success rate and magnitude of error was considered in the evaluation. The evaluations were granted low risk human research ethics approval by the Human Ethics Advisory Group (HEAG), Faculty of Science, Engineering & Built Environment, Deakin University. All participants were screened to ensure that they had no prior exposure to any physical cell injection activity in order to obtain a set of participants who have the same entry level experience with the procedure as new people being trained in the procedure. Their demographic data were also obtained to be used in the analysis. Participants were video recorded and interviewed during the experiments in order to obtain useful qualitative data.

Eighteen participants were recruited for the experiments and randomly divided into six groups of three, 2DN, 2DH, 3DN, 3DH, CAN and CAH. Each group had a specific combination of display configuration and haptic guidance mode. Participants were asked to perform ten injections and the time and position of the virtual micropipette tip were recorded at a sampling rate of 50 Hz. In addition to the ten injections performed by all

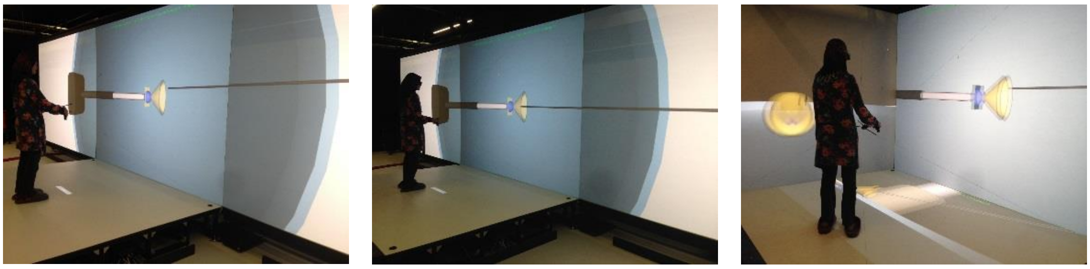

Figure 1: Display configurations: 2D, 3D and CAVE-like (from left to right).

	2DN	3DN	CAN	2DH	3DH	CAH
Magnitude of Error (µm)	0.555216	1.063526	0.468659	0.348023	0.324408	0.348082
Success Rate (%)	90	73	100	100	100	100

Table 1: Overall scores for all groups.

	Pre-training (µm)	Training (µm)	Post-training (µm)	Improve (%)
2D	0.56	0.34	0.40	27
3D	1.06	0.32	0.80	25
CAVE-like	0.47	0.34	0.36	24
Mean	0.70	0.33	0.52	25

Table 2: Results for pre-training, training and post-training.

groups, the participants in the 2DN, 3DN and CAN groups also underwent subsequent training and post-evaluation sessions. To achieve the purpose of this evaluation the first ten injections for the three groups were redefined as a pre-training session. The participants of the three groups then undertook a training session which consisted of an additional ten injections with haptic guidance enabled in the same display configuration as their pre-training session. Finally, a post-evaluation session was undertaken where participants performed ten more injections with haptic guidance disabled. Pre-training, training and post-training sessions, as the name of the sessions imply, were used to evaluate the performance of the participants before, during and after the training with haptic guidance enabled respectively. Doing so provides the basis to evaluate the effectiveness of the training with haptic guidance.

In general the results demonstrated that participants achieved significant success rates between 73 to 100% across the experiments demonstrating strong performance levels for the micro-robotic cell injection task. It was also observed that the participants' accuracy improved between 24 to 27% after undergoing training with haptic guidance enabled mode.

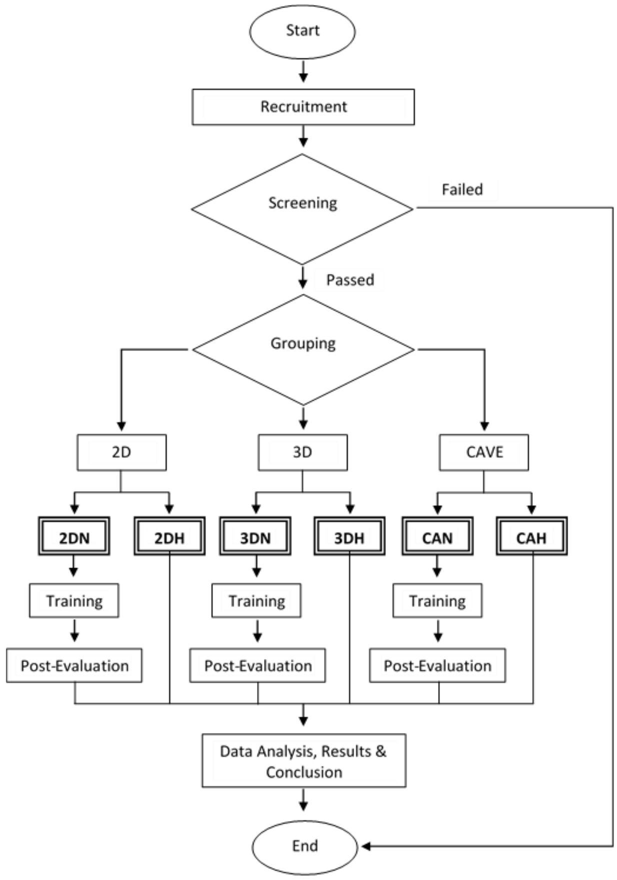

Figure 2: Flowchart of the experiments design.

The findings of this study indicate that the large-scale VR micro-robotic cell injection training system introduced herein, specifically using a large workspace haptic device, INCA 6D as the input control method can benefit bio-operators, especially to better understand spatial relationship of the virtual environment. It is also suggested that the acquired skills, knowledge and understanding from the virtual training such as the spatial awareness, depth estimation and hand-eye coordination can be transferred into physical micro-robotic cell injection or similar real tasks.

5 Conclusions

This paper presents the design of an evaluation for a large-scale virtual reality micro-robotic cell injection training system. The evaluation aims to consider the practicality of the three display configurations and the large workspace input controller employed in the system. Results obtained from the evaluation has contributed towards concluding that the proposed large-scale VR system is a feasible training tool for micro-robotic cell injection procedure. Future work can revolve around aiding bio-operators in improving their spatial awareness. The correlation between visual workspace size and bio-operator's performance can be studied, as well as investigating different potential input control methods.

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