A modular architecture for biomanipulation

Release 1.00

Yixin Gao[1], Russell H. Taylor[1], and Rajesh Kumar[1]

August 15, 2010

[1]Johns Hopkins University, Baltimore, MD

Abstract

The Johns Hopkins University Surgical Assistant Workstation (SAW) modular software framework provides support for robotic devices, imaging sensors and a visualization pipeline for rapid prototyping, primarily for surgical research systems. We extend the SAW architecture for "steady hand" micromanipulation in biomanipulation laboratory tasks. The proposed system integrates direct "steady-hand" manipulation, teleoperation, and automated manipulation in a single two-handed system. System architecture, implementation and initial performance measurement experiments are detailed.

Contents

1 Introduction

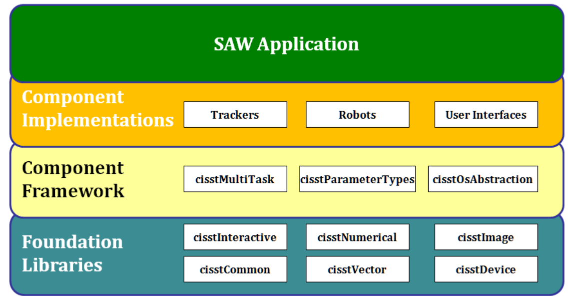

Figure 1: Architecture overview of Surgical Assistant Workstation (SAW) framework

We seek to develop and evaluate methods for performing micrometer scale bio-manipulation tasks using cooperative manipulation and vision based augmentation. These tasks form the basic enabling components of methods for cell manipulation in the development of transgenic models, cancer research, fertilization research, cytology, developmental biology and a wide range of other biological sciences research. Micromanipulation is also common in in-vitro tasks in biological and genetic engineering research where genetic materials and various markers are commonly microinjected into single cells. Development of the means to enable accurate delivery of genetic material into cells would greatly improve efficiency of these tasks. Teleoperation, and automated delivery are common enabling methods for such micromanipulation. There is significant art in automatically handling micro-cellular and other micrometer sized objects using highly structured environments as well as vision based methods. Although art has reported augmentation [1, 2, 3, 4, 5, 6, 7], only visual feedback from the high-magnification stereo microscope is available in commercially available teleoperated systems.

Automated techniques for micromanipulation do not translate well between models or beyond a specific automated task. Automation requires great amounts of structuring of the task, which adds cost, complexity and time. Additional steps introduced by a new paradigm also increase the risks of damage, contamination and cell death. While literature has often paid attention to only the most complex portion of these tasks e.g. injection portion in a microinjection task which also involves selecting and pick a cell from a group of cells, reorienting it such that the pronucleus is accessible, injecting and replacing the cell in another section of the petri dish. These remaining portions are equally important. By contrast, our proposed methods do not modify the current task work flow.

The flexibility needed for multiple micromanipulation paradigms (teleoperation, direct control, or automation) and multiple models and tasks motivates our extensions of the Surgical Assistant Workstation (SAW) modular software framework [8, 9] here. SAW uses component-based design [10] and provides a large collection of implemented components including collaborative and telesurgical robots, and a 3D user interface toolkit. SAW also provides integrated support for robotic devices, imaging sensors, and a visualization pipeline for rapid prototyping of telesurgical research systems [9].

2 Methods

Our framework will also allow us combine sensor-enabled and sensor-less manipulation at the limits of conventional sensing. Sensing enables feedback from both recognition of tools and targets as well as detection of events in the task sequence, but it also introduces additional error/noise and complexity. Sensing based strategies are easier to implement due to the availability of sensory feedback. Where sensor feedback is not available, the alternative calls for much more difficult planning with fewer sub-goals that can be analyzed before the task execution.

2.1 Hardware

A biomanipulation system (Figure 2) consists of a high resolution inverted mono/stereo microscope configured on a sturdy vibration free base with appropriate tools (a holding pipette and an injecting pipette for microinjection) attached to the mechanical micromanipulators. Our proposed prototype (Figure 2) integrates two robotic micromanipulators with an inverted stereo microscope. The user will manipulate each robot by grasping a force sensor instrumented handle which will also integrate a force sensor for sensing environment forces. Two 3-D joysticks allow evaluation of teleoperation in comparative performance experiments. The specifications of the system are detailed in Table 1.

We use a Leica DMIL inverted trinocular microscope with Integrated Modulation Contrast optics (10X and 40X objectives, 10X eyepieces, up to 400X magnification). An Osprey-240e video capture card captures NTSC video (600x480, 30fps) from an analog camera attached to the third visual channel of the microscope. Two Thorlab MT3-Z8 DC 3DOF micromanipulators are integrated with the microscope. Narishige instrument holders attached to the micromanipulators using a custom universal joint mechanical adaptor provide the ability to attach micropipettes. A Galil DMC-2183 motion controller is used to control the micromanipulators via Ethernet using a Windows workstation (E5300, 2.4Hz, 4GB RAM).

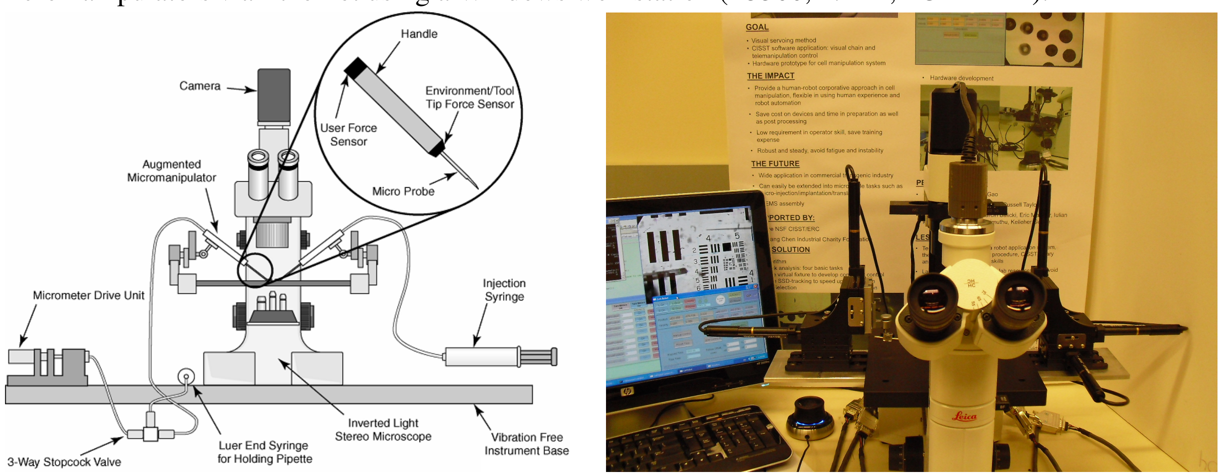

Figure 2: Micromanipulation System sketch, and hardware in integration.

Metric	Last Generation	Current Prototype
No. of Manipulators	1	2 (L,R)
Degrees of freedom	3(XYZ), passive adjustments	3 (XYZ), passive adjustments
Workspace	100mm×100mm×100mm	12mm×12mm×12mm
Position Resolution	0.5μm	0.029μm
Precision	2.5μm	0.15μm
Maximum Velocity	40mm/sec	3mm/sec
User Force Sensing	0.01N-1N	0.01N-1N
End-effector Assembly	Custom	Custom
Control Modes	Steady-Hand, Collaborative, Automatic	Additional Tele-manip., Vision guided modes
Video	Inverted Trinocular Microscope	Inverted Trinocular Microscope

Table 1: The Specifications of current prototype and previous generation system

2.2 Software

The cisst/SAW platform independent libraries support a wide range of devices while preserving the flexibility for a user to integrate new elements into custom applications. SAW components can be classified in three categories: 1) foundation libraries, 2) component-based framework and 3) component implementations (see Figure 1). We extend the SAW for use in laboratory tasks by modifying the video pipeline, as well as by adding new robotic control methods. The cisstMultitask library provides a safe and efficient framework for multi-threading design based on component based design. Each task in an application specifies ”provided” and ”required” named interfaces to communicate with other tasks. All communication between tasks and devices in cisstMultiTask are performed using thread safe commands and component encapsulation[8].

We aim to create a hybrid framework for performing micromanipulation tasks combining automated and interactive tasks as appropriate for best task performance. We design the three pipelines of our framework based on the cisstMultitask mechanisms - the force sensing pipeline including a devSpaceNavigator task for using a 3D SpaceNavigator joystick input for telemanipulation, the vision pipeline which uses a svlFilter-based image processor filter that provides image processing for target segmentation, and a robot control pipeline which provides the robot control using the GalilTools libraries for communicating with the hardware. A user interface task provides graphical user interface for interactive input and integrates these pipelines as tasks. The task manager connects the ”provided” and ”required” interfaces of these tasks to facilitate the communication between the pipelines. The interfaces and information flow are shown in figure 3.

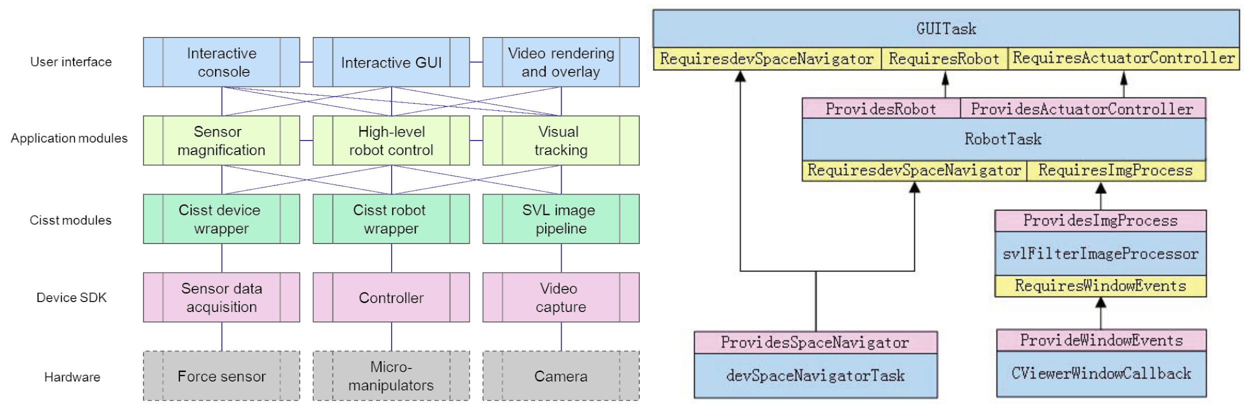

Figure 3: The software architecture for micromanipulation

2.3 Task analysis

We assume the targets e.g. cells and micro-particles approximate disks, and are therefore nearly circular in projection. Here, we also assume simple tool models e.g. a conical micro-pipette, and a cylindrical holding pipette with a spherical end. In considering a common microinjection procedure, there are four common subtasks: ”selection” aims to identify the cells and safely navigate to it; ”separation” moves two or more adhered cells apart by pushing the adhering cell away from the selected cell; ”orientation” reorients the cell to achieve an easier, shorter path to the target, and ”injection” places the injecting pipette at an identified location using a safe trajectory. These four tasks form basic elements of our cell manipulation task and allow integration of visual tracking, virtual fixtures, and selective automation (Figure 4).

2.4 Force Sensing and Telemanipulation

Each robot will be augmented with two force sensors. The user force sensor (Bokam DX-46X series) senses the user forces applied on the control handle, and the tip force sensor captures the environmental forces, such as the cell membrane pressure force when injecting into a cell. These sensors are currently being integrated.

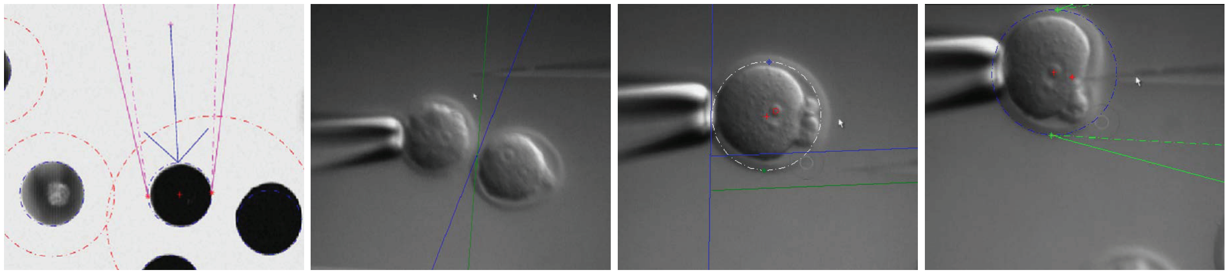

Figure 4: Selection, separation, orientation, and injection tasks with visual virtual fixtures and target guidance overlays.

We use 3Dconnexion 3D SpaceNavigator (3 axis translation and rotation, 2 buttons) devices as teleoperation masters for teleoperated control

2.5 Vision Pipeline

The vision pipeline extends the stereo vision library (SVL) video pipeline for real-time image acquisition, processing and rendering of the acquired images in the user interface in real-time. The SVL library already provides methods for simple image manipulation, such as resizing, cropping, and filtering [9]. We create new image processing filters using the *svlFilterBase* and *mtsTaskFromCallback* that are embedded in the SVL pipeline by the stream manager. Custom image filters for target detection, tracking, visual virtual fixtures and graphical overlays, and user input have been developed for biomanipulation.

2.6 Robot control

We enable four robot control modes for comparison of different control strategies and current conventional teleoperation:

1. Teleoperation - The robot complies with scaled user forces. The master input for teleoperation is provided with 3D SpaceNavigator. Teleoperation is widely used in transgenic lab research and commercial systems.

2. Automated - The movement of the micromanipulators is automated. The target velocity and position of the actuator are designated using the user interface, or from automated image segmentation/tracking.

3. ”Steady-Hand”- A pseudo-admittance control law [1] combines the user handle and environment force sensor inputs. This direct manipulation modes integrates human and robot collaboration by allowing direct input as well as augmented control.

4. Collaborative - We allow the user to supervise task execution. For example, the user may select the the target cell from a group of cells, or designate the point of injection on the cell membrane. The user is then guided to these targets in either teleoperated or steady-hand modes using information extracted from the images.

2.7 The User Interface

The user interface contains three main sections (Figure 3) - the command console, the interactive graphic panel, and the video rendering window. The GUI wraps FLTK (Fast Light Toolkit) widgets in our multitask framework. The user can switch between different control mode, observe the actuator states, and view live video from the trinocular inverted microscope. In addition, callback such as the position of the mouse click or the keyboard input are captured and processed as needed for the above control modes. Figure 5 shows the command panel and the video window.

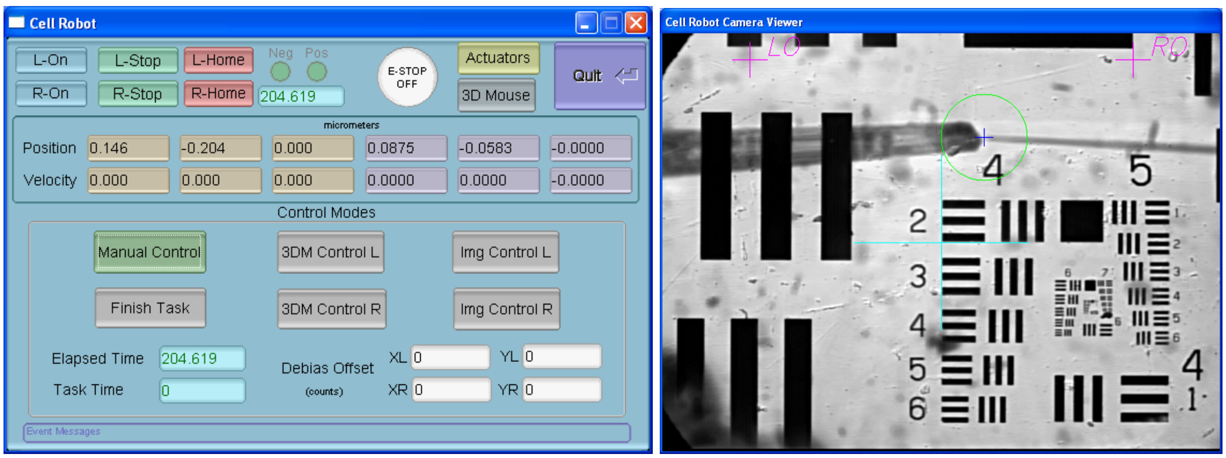

Figure 5: Current user interface command panel, and the video window showing live trinocular video from the inverted microscope.

3 Experiments

We have performed preliminary experiments to assess the performance of the assembled prototype in automated, and teleoperated modes while the force sensors enabling the other control modes are integrated into the prototype.

Axis	Left -	Left +	Right -	Right +
$X/\mu m$	0.02	0.03	-0.02	-0.02
$Y/\mu m$	0.03	-0.07	0.02	-0.06
$Z/\mu m$	-0.03	-0.13	0.05	0.11

Table 2: Positioning accuracy for forward (+) and backward (-) motion for micromanipulators with tuned parameters.

3.1 Calibration

Robot calibration: Our micromanipulators use conventional DC motors, and can be controlled very accurately. After Calibration of the PID gains, we performed initial positioning accuracy assessment. Average positioning errors are listed Table 2. We are able to control our robots within 5 encoder counts. Recall that the encoder resolution is 0.029μm, so that the positioning precision is approximately 0.15μm.

Robot Camera Registration: We define a global coordinate frame at the optical center of the focal plane of the microscope allowing natural integration of the image and robot workspace. The XYZ directions are defined along the positive motion directions of the left micromanipulator. The right robot base frame is translated by a calibrated offset, and rotated by 180 degrees about Z axis. During these calibration experiments, we limit ourselves to the focal plane of the microscope ($Z = 0$). Let Let (x_{pix}, y_{pix}) denote the image pixel coordinates relative to the image origin located at the upperleft corner, and and let (X_r, Y_r) denote the corresponding micromanipulator coordinates. We segment image coordinates $(X_{offset}, Y_{offset}, 0)$ of the left and right tool instrument tips by moving the instrument tips at the origin on the image. Therefore,

$$\begin{bmatrix} X_r^i \\ Y_r^i \\ Z_r^i \end{bmatrix} = \begin{bmatrix} X_{offset}^i \\ Y_{offset}^i \\ 0 \end{bmatrix} + \begin{bmatrix} S_x^i & 0 & 0 \\ 0 & S_y^i & 0 \\ 0 & 0 & 0 \end{bmatrix} \begin{bmatrix} x_{pix}^i - x_o^i \\ y_{pix}^i - y_o^i \\ 0 \end{bmatrix} \quad (1)$$

where $i = l, r$ denotes the left or right robot. In the focal plane, there are only 2 scale parameters to estimate: S_x and S_y. We use a 1951 USAF resolution test chart to estimate these parameters. The chart has pattern of line pairs of various scales at perpendicular orientations. We drive the instruments to line intersections to acquire multiple observation and estimate the parameters as $S_x = 99.8842$ and $S_y = 101.2153$.

3.2 Preliminary experiments

After calibration we can use two of the control modes - teleoperation, and automated guidance to target. The accuracy and utility of these modes is tested in common instrument positioning tasks. The user is asked to move the tool tip from the origin to a known target, and then move back to the origin. In the teleoperation mode, a 3D SpaceNavigator device drives the actuator until the user is satisfied the tool tip is at the target position. In the automated mode, the user selects the target position with a mouse, and the robots are then moved to the target position. The user may re-select the target until they are satisfied the instrument tip is at the target. Both modes are used with both left and right micromanipulators.

Task completion times and accuracy of positioning in both modes by one user are presented in Table 3. The automated mode outperform telemanipulation in both task completion times, and accuracy. This indicates a supervisory collaborative approach will likely allow integration of automated sensing, user supervision and robotic accuracy in a flexible manner and outperform current conventional teleoperation. Additional experiments with the prototype are currently in progress.

Target	Left Micromanipulator				Right Micromanipulator			
	Automated		Teleoperated		Automated		Teleoperated	
	Accuracy	Time	Accuracy	Time	Accuracy	Time	Accuracy	Time
(78,91)	1.4325	3.0813	15.834	21.2627	1.3658	10.187	18.9182	16.8719
(148,91)	1.4924	2.4925	21.8054	11.7809	1.3663	9.2622	22.2007	9.2045
(217,92)	1.4758	3.3384	12.4753	17.3188	1.1332	7.3466	12.895	8.8645
(369,191)	2.3074	6.5461	18.5461	18.214	1.4817	4.2176	15.8814	10.7677
(358,317)	2.2504	7.6377	14.1949	18.1687	1.2874	6.5799	9.6145	16.362
(351,416)	2.032	9.3204	11.6592	20.6088	0.8176	8.7453	14.446	11.6606
(398,191)	1.7313	7.1291	10.1136	20.521	0.9761	4.1773	10.7425	18.315
(382,317)	2.2125	6.6992	10.1008	12.8867	1.3275	6.5825	9.9669	12.3803
(369,417)	1.5274	8.7859	12.6755	19.6283	1.1375	8.7334	14.5476	15.6057
(504,393)	1.9965	9.0533	15.4664	16.2795	1.3498	8.415	10.292	11.6354
(581,392)	1.7621	10.1583	13.54	15.6921	0.1691	8.1738	12.6684	15.527
Avg	1.8382	6.7492	14.2192	17.4874	1.1284	7.4928	13.8339	13.3813

Table 3: Positioning accuracy (μm) and task completion time (sec) for positioning task in automated and teleoperated modes.

4 Conclusion

We detail the prototyping of a two handed micromanipulation using the JHU SAW framework and cisst libraries. Although designed primarily for surgical systems, these libraries have also provided us with the tools to quickly create a two-handed micromanipulation system that will support the evaluation of automated, telemanipulated, steady-hand, and collaborative modes of micromanipulation at the limit of conventional sensing and manipulation. Upon completion of force-sensor integration, we aim to investigated both sensor-enabled, and sensor-less strategies of bimanual task execution at the micrometer scale using a range of biomanipulation tasks outlined here.

References

[1] A. Kapoor, R. Kumar, and R.H. Taylor. Simple Biomanipulation Tasks with Steady Hand Cooperative Manipulator. In *MICCAI*, pages 141–148, 2003. 1, 3

[2] H.B. Huang, Dong Sun, J.K. Mills, and Shuk Han Cheng. Robotic cell injection system with position and force control: Toward automatic batch biomanipulation. *IEEE Transactions on Robotics*, 25(3):727–737, 2009. 1

[3] Y Xie, D Sun, C Liu, H Y Tse, and S H Cheng. A Force Control Approach to a Robot-assisted Cell Microinjection System. *The International Journal of Robotics Research*, 2009. 1

[4] Z. Lu, P.C.Y. Chen, J. Nam, R. Ge, and W. Lin. A micromanipulation system with dynamic force-feedback for automatic batch microinjection. *Journal of micromechanics and microengineering*, 17(2):314–321, 2007. 1

[5] L. Mattos, E. Grant, and R. Thresher. Semi-automated blastocyst microinjection. In *Proceedings 2006 IEEE International Conference on Robotics and Automation*, pages 1780–1785, 2006. 1

[6] Y. Sun and B.J. Nelson. Biological cell injection using an autonomous microrobotic system. *The International Journal of Robotics Research*, 21(10-11):861–86X, 2002. 1

[7] R. Kumar, A. Kapoor, and R.H. Taylor. Preliminary experiments in robot/human cooperative microinjection. In *Proceedings of IEEE/RSJ International Conference on Intelligent Robots and Systems (IROS 2003)*, volume 3, pages 3186–3191, 2003. 1

[8] A Deguet, R Kumar, R Taylor, and P Kazanzides. The *cisst* libraries for computer assisted intervention systems. In *MICCAI Workshop on Systems and Arch. for Computer Assisted Interventions*, Midas Journal: http://hdl.handle.net/10380/1465, Sep 2008. 1, 2.2

[9] B Vagvolgyi, S DiMaio, A Deguet, P Kazanzides, R Kumar, C Hasser, and R Taylor. The Surgical Assistant Workstation: a software framework for telesurgical robotics research. In *MICCAI Workshop on Systems and Arch. for Computer Assisted Interventions*, Midas Journal: http://hdl.handle.net/10380/1466, Sep 2008. 1, 2.5

[10] Clemens Szyperski. *Component Software: Beyond Object-Oriented Programming*. Addison-Wesley, 2002. 1