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Computerized control system and interface for flexible micromanipulator control

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ABSTRACT

Micro- and nanomanipulators are essential for a broad range of applications requiring precise micro- and nanoscopic spatial control such as those in micromanufacturing and single cell analysis. These manipulators are often manually controlled using an attached joystick and can be difficult for operators to use efficiently. This paper describes a system developed in MATLAB to control a well-known, commercial micromanipulator in a user friendly and versatile manner through a graphical user interface (GUI). The control system and interface allows several types of flexible movement controls in three-axis, Cartesian space, including single movements, multiple queued movements, and mouse-following continuous movements. The system uses image processing for closed loop feedback to ensure precise and accurate control over the movement of the manipulator's end effector. The system can be used on any electronic device capable of running the free MATLAB Runtime Environment (MRE) and the system is extensible to simultaneously control other instruments capable of serial communication.

1. Introduction

Micro- and nanomanipulators provide the ability to maneuver and position micro- and nanoscale objects to precise locations and orientations. Used in conjunction with optical and electron microscopes, these ultrahigh-precision positioning instruments enable functions critical for many micro- and nanoscale applications, such as manufacturing and biomedicine. In manufacturing, manipulator systems have been employed to automate the maneuvering and positioning of small objects in order to produce patterns, structures, and devices. For example, Cappelleri et al. developed caging grasps for micro assembly capable of accurately positioning micro objects using an array of probes [1,2].

In biomedicine, manipulators are commonly utilized to maneuver and position small probes inside living cells and tissue. Cell injection is a large area of research; Wang et al. developed a method of carrying out cellular injection using probes at a high rate and with minimal user intervention [3]. Grippers are used in addition to pipettes for biological applications. For example, Kim et al. developed a nanonewton microgripper to analyze the properties of biomaterials [4].

The goal of micro- and nanomanipulator automation is to create a system requiring only minimalistic intervention, optimally none, to carry out a specific desired function. In this way, automation of predefined tasks increases precision and throughput while reducing variability and time. Most automation requires computer vision algorithms to access the position of manipulation targets. Wang et al. also developed high-throughput automatic injection systems and demonstrated their use on zebrafish embryos [5–7] and contributed image processing techniques for injection automation [8]. Mattos et al. developed image processing techniques to improve their automated injection process of blastocyst cells [9–13].

However, situations exist, especially in the development and utilization of new tools and techniques, where the automation and control of these manipulators, and other related equipment, needs to be flexible and adaptable. For example, in our own work towards developing carbon nanotube (CNT)-based probes for single cell analysis [14–20], micro- and nanomanipulators are routinely used to maneuver the functional end of the probes in order to interface with single living cells in an undetermined manner, often requiring on-the-fly repositioning or customized movements based on qualitative visual feedback. Here, the tips of CNT-based probes are manually maneuvered in Cartesian space by the manipulator's joystick and positioned within the intracellular environments of single living cells under an optical or fluorescence microscope to perform functions or analysis with tertiary instruments.

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New probe-based single cell analysis techniques, as well as traditional cell physiology techniques such as patch clamp electrophysiology, involve continuous interactions with multiple instruments simultaneously. The user is required to often switch attention and focus between the microscope, the micro- or nanomanipulator, tertiary instruments (e.g. electrophysiology amplifier), and computer screen (often displaying the field of view from a microscope camera and/or graphical user interface of tertiary instruments), making the work difficult and laborious. Although many commercial microscopes and tertiary instruments come equipped with some form of graphical user interface (GUI) for use on standard computer workstations, no such interface has been provided for micro- or nanomanipulator control. Moreover, no interface exists as an expandable platform for the inclusive control of multiple instruments.

The purpose of this paper is to present a new system layout developed in MATLAB to provide an intuitive and accessible GUI for micro and nanomanipulator control through a standard computer workstation. Through the GUI, a user with minimal prior knowledge can directly control the manipulator or select from customizable control functions for real-time control with a mouse. The system and GUI can be adapted to multiple applications with relative ease and configured to include control over additional instruments as needed. The computer-based system is intended to provide a user-friendly, expandable control platform for micro- and nanomanipulators over a wide range of applications in both research and education.

2. Materials and methods

2.1. System layout

A typical configuration for performing micro- or nanomanipulator operations, as shown in Fig. 1, was used to develop the Manipulator Control system. The system consists of four primary components: a manipulator and its control unit (Eppendorf TransferMan NK 2), a microscope (Zeiss Observer.A1m), a camera (Point Grey Chameleon), and a computer (Dell with Intel Core i5-2400 @ 3.1 GHz) to interface with all of the controllable components. The software was developed in MATLAB R2011a. The microscope is mounted on a vibration isolation table in order to minimize detrimental vibrations during manipulation operations. The computer and manipulator controller are located near the microscope but separated from the vibration isolation table. Each system component is a commercially available device with no hardware modifications.

While each of the system components can be reasonably interchanged and the control software adapted to the new equipment, the current implementation assumes a number of things about each of the components. The camera must be a device recognizable by MATLAB, which requires that it provide video information and accept computer commands through MATLAB's Image Acquisition Toolbox. This restriction prevents cameras with proprietary communication protocols from being used with the GUI. The camera utilized in this particular hardware configuration was selected because the manufacturer provides control drivers, which specifically allow for open interfacing. There are however many microscope cameras which use restrictive or proprietary communication and control schema. To access information from more restrictive camera systems, it would be necessary to run a separate executable from the control software or develop device drivers which can allow MATLAB to interface with the camera.

The control scheme of the manipulator controller and its method of digital communication are critical to the design of the GUI. The selected control unit utilizes an absolute positioning system, wherein all movement commands sent to the manipulator are interpreted as a request to place the needle tip at the specified location in three-dimensional space by travelling at a specified velocity along each axis. The control software is designed to generate movement commands according to this control scheme. However, coordinate information is maintained both for the current position of the needle and the movement location, so that it would be possible to extend the software to support a manipulator which utilizes a relative positioning system. Additionally, the means by which the system is calibrated has been managed in such a way that it could be readily adapted to a relative positioning system. The manipulator selected has a range of travel of approximately 20 mm along each axis and can travel at up to 7.50 mm/s. The finest possible resolution of movement is approximately 40 nm. This allows for sufficient movement of the manipulator tip over a wide range of magnifications while also providing fine resolution for accurate manipulations at high optical magnifications. The Eppendorf TransferMan control unit is programmed to receive serial communication. Besides movement commands and coordinate requests, the control unit can receive commands to perform a number of other functions including connecting and disconnecting or toggling between manual and computerized control.

The schematic view of the system, shown in Fig. 2, illustrates the flow of information between components. The host computer controls the manipulator and camera using the control program developed in MATLAB. The computer interfaces with the

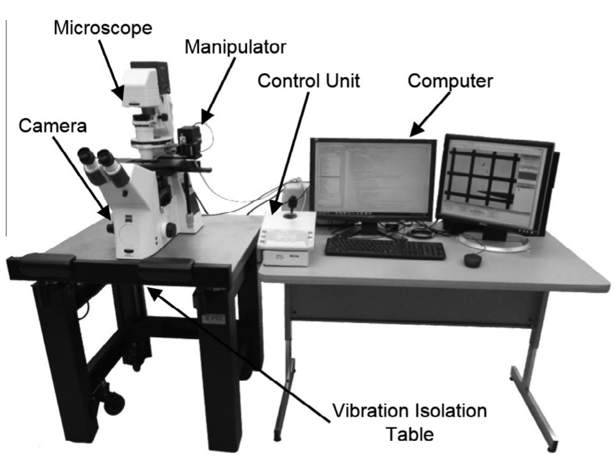

Fig. 1. System layout used in the development of the nanomanipulator GUI. The layout consists of a microscope, camera, manipulator with control unit, and a standard computer workstation containing the Manipulator Control software.

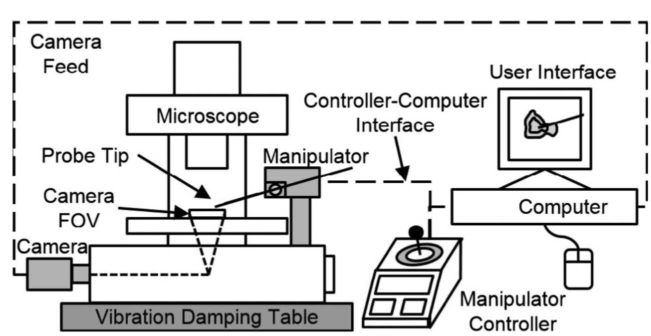

Fig. 2. System layout illustrating the transfer of information between system components. The camera observing the microscope slide is directly connected to the computer, which is in turn connected to the manipulator controller. The manipulator controller processes either signals from the computer or the manual input device depending on which method of control is enabled.