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Packaging and Characterization of Mechanically Actuated Microtweezers for Biomedical Applications

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Abstract—**This paper presents the successful design, fabrication, and packaging of a mechanically actuated micro-electro-mechanical-systems (MEMS) microtweezer, and its use in a variety of biological environments. This complete and low cost MEMS system has minimal manufacturing complexity and it can be augmented to any standard micromanipulator or positioning system. Characterization of the system shows that precise and controlled tool actuation is achieved with maximal tip closing forces of 367 mN. The system's performance and ease of use can provide the means to create and enhance a multitude of experimental preparations previously not possible.**

I. Introduction

Microtweezers and similar microtools offer an attractive option to meet the increasing need to manipulate micro-sized objects such as cells, tissues, fluorescent markers, chemicals, biological structures and other constructs.. The packaging system presented in this paper allows previously developed MEMS microtools [1] to be used in a variety of biomedical research applications, potentially replacing crude blunt and dropper type instruments as well as expensive and functionally-limited optical positioning equipment. As these tools provide acuity of control, repeatability, and miniaturization, they can also play a more direct role in experimentation, such as isolating material and tissue samples for chemical and mechanical characterization and manipulation. Microtools tailored to these fields will allow for a significant variety of experimental preparations previously not thought possible. In addition to benefiting biomedical research, these devices could be adapted to support remote, minimally invasive surgical and dissection procedures, both in a clinical and experimental setting.

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Currently, cost and ease of use are major barriers for instruments in this market. Previously developed microtweezers require the use of electrostatic force, electrothermal force, laser power, or shape memory alloy for microtweezer actuation [1-11]. These power and control requirements complicate the microtool fabrication and consequently limit microtool design, size, and material set. In addition, these mechanisms can dissipate heat into the local environment or generate unintended electrostatic fields which limit the device's application space. The microtweezers reported in this paper employ a micro-mechanical actuation mechanism based on position, precluding the need for thermal or electrically sensitive materials, or for complex controllers. Tool tips are opened and closed due to their position within a sleeve, or box, and the relative motion of these two components can be delivered through a micro-cam drive system. This system consists of a luer based tool packaging and docking station, which allows plug-n-play docking of various microtools as well as rotation along the microtool axis, and an actuator, or micrometer/motor attached to a tether-cable system. Because such a mechanism can be controlled either by a knob or motor, it could benefit from both the inherent tactile precision of a human user, or the automation of a computerized controller. These components can augment any standard micropositioner, allowing positioning in three-plus dimensions, plus the tool actuation and rotation. Given the simplicity of design and low-cost manufacturing requirements, these potentially disposable tools address needs in a variety of bio-medical, clinical, and experimental markets.

II. Device Design

A. MEMS Microtool Design

Previous work demonstrated the successful fabrication of a prototype microtweezer, which consisted of a tool body that contains the tool tips and the tool box that houses the tool body. The inner channel of the tool box contacts with the tool tips to actuate the microtool [9]. A new tweezer design is presented (Fig. 1, 2) which has modified channel and tweezer geometries to allow for larger tool sizes and provide improved control and linearity of tool actuation. The channel contains two segments: a regular drive section, and an over-drive section which provides additional actuation range to allow tool tips with larger separations between them to close completely. In addition, a new fabrication process presented in this paper replaces a single 13-step process [9]

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where the body and box are produced together, with two shorter more efficacious processes where the parts are produced independently. This reduces the number of alignment steps from four to two and process integration issues but more importantly allows increased flexibility and customization of tool components, which can range in tip shape (forceps, serrated, notched), separation (µm-mm), and thickness. This more modular design also creates a platform that permits integration of sensors, such as surface microelectrodes, and allows for a variety of (and potentially different) body and box materials.

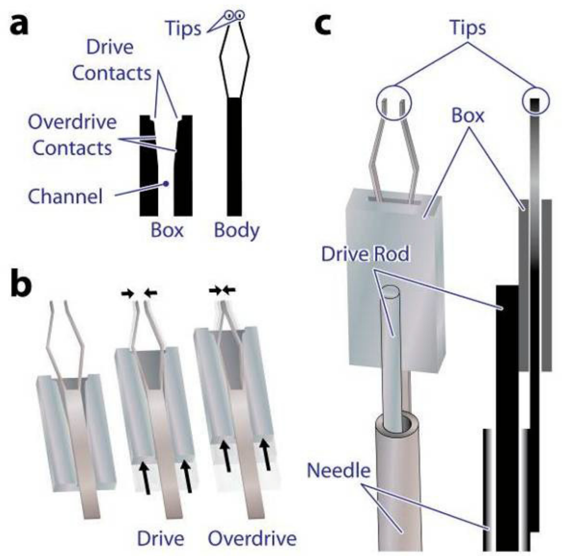

Fig. 1. (a) Schematic of wide-gap MEMS microtweezer showing key features and geometries, (b) box and tool tips actuation with arrow size demonstrating benefit in tip closing resolution compared to box actuation, and (c) packaging of microtool with needle and drive rod.

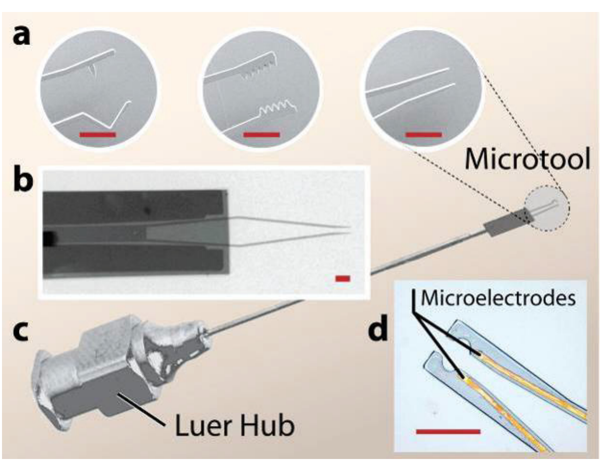

Fig. 2. (a) SEM images of various tip shapes, (b) X-Ray of assembled microtweezers, (c) Luer needle packaging for microtweezers, and (d) Bright field image of SU-8 multielectrode microtweezers. All microtweezers shown have thicknesses of 25 µm, and beam widths of 40 µm. All red scale bars are 200 µm.

The selection of materials is important not only for the mechanical and material properties, such as tensile strength, elastic modulus, and surface attraction, but also for biological compatibility. The microtool body fabricated in this study has tips that are 40 µm wide and 25 µm thick. The body and box channel widths are 300 µm and 330 µm respectively.

B. MEMS Packaging Design

Once the tool body is inserted into the channel of the tweezer box, the assembled MEMS device can then be attached to the tool packaging. This package allows simplified connection to the docking station through a luer system. The packaged microtool (Fig. 2, 3) consists of three main components: 1) a female luer hub, which houses the micro-drive mechanism, 2) an attached stainless steel hollow needle which provides both a physical structure in which to adhere the fixed body of the microtool, and 3) a durable tract in which to allow translation of precise linear actuation of the drive system to the microtool. The tool body is glued to the end of the needle, and the drive rod running through the needle track is glued to the tool box. The motion of the drive rod relative to the needle shaft is translated to the tool box, which is then displaced relative to the tool body. Through this motion, the walls of the box channel make contact with the tool tips causing them to close.

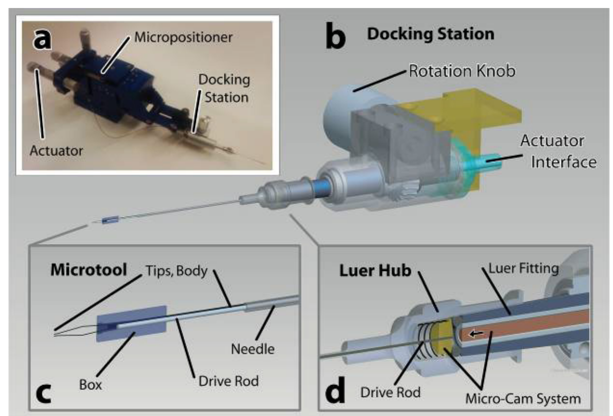

Fig. 3. (a) Photograph of complete system attached to Signatone micropositioner, and schematics of the (b) docking station, (c) MEMS microtool packaging, and (d) the luer system.

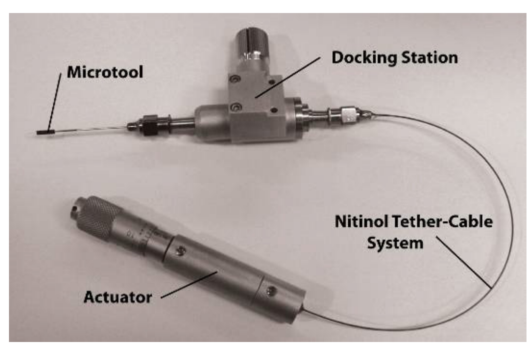

Fig. 4. Photograph of complete packaging and actuation system.

C. Docking Station and Actuator

The docking station both physically and functionally connects the microtool component to a mechanical controller. This interface has minimal manufacturing complexity, an industry standard luer interface providing modular plug and play docking of various microtool components, and a linear-actuation-based micro-cam drive mechanism allowing precise and controlled mechanical actuation of docked microtools. The docking station also provides a novel ability to rotate the microtool about its axis (Fig. 3, 4). The drive mechanism that travels throughout this docking system can be controlled by a manual or programmable actuator system connected to the rear of the docking station. This interfacing system can be attached to any standard micropositioning or imaging stage, micromanipulator, or robotic arm. The actuator currently employed in this system is composed of a micrometer head attached to a nitinol cable tether-cable system, allowing relative linear driving to the docking station.

III. FABRICATION PROCESS

Traditional photolithography and micromachining processes were used to fabricate the MEMS microtools. The tool body and the box were fabricated separately using similar planar fabrication processes, both starting with the depositing of a sacrificial photoresist layer for lift off and electrical isolation, and an electroplating seed layer made of Cr/Cu. The subsequent fabrication processes involve the creation of a series of molds in which Ni is electroplated to form the multiple layers of the box or the single layer of the tweezer. The process flow is illustrated in Fig. 5.

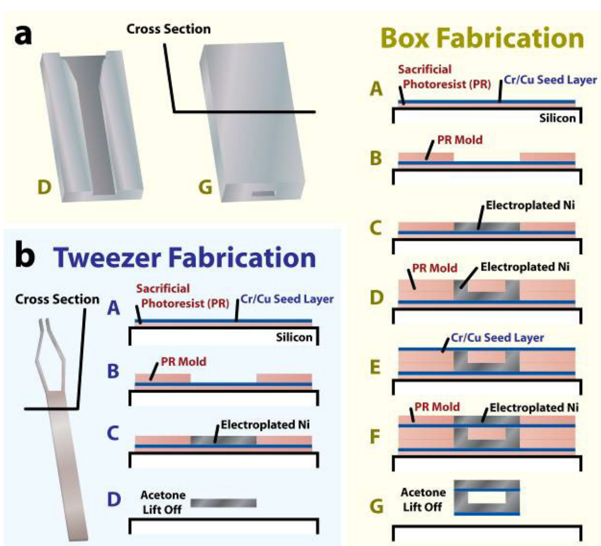

Fig. 5. Fabrication processes of Ni (a) box and (b) body.

IV. MECHANICAL EVALUATION

A. Tip Actuation and Closing

Tweezer and box geometries were designed to provide nearly linear closing of the tips through both regular and overdrive actuation. Tip actuation was modeled using a series of equations dependent on the geometries of the tool tips and the relative position of the body and box. The separation of the tips is shown based on the actuation distance of the box (Fig. 6). For a tweezer with a tip separation of 330 µm, a box actuation of 1.09 mm is required to close the tips, and this mechanical advantage can allow increased actuation resolution.

B. Tip Forces

Following assembly of the packaged MEMS devices, docking station, and actuator, the forces exerted by the inner faces of the tweezer tips were measured under a variety of actuation schemes using the MTS NanoUTM system (Oak Ridge, TN) (Fig. 6). Quickly oscillating tip deflections of 125 µm (oscillating period for 250 µm open-close movement averaged less than 1.5 sec) delivered via the manual actuator showed average maximal forces of 367 µN with a standard deviation of 1.1 µN. This force suggests a beam spring constant of 2.936 N/m. While this small spring constant enables manipulation of delicate microstructures like biological constructs, the tip force is strong enough to overcome the adhesion of cells to substrates [12] and to lift solid structures over 10 mg.

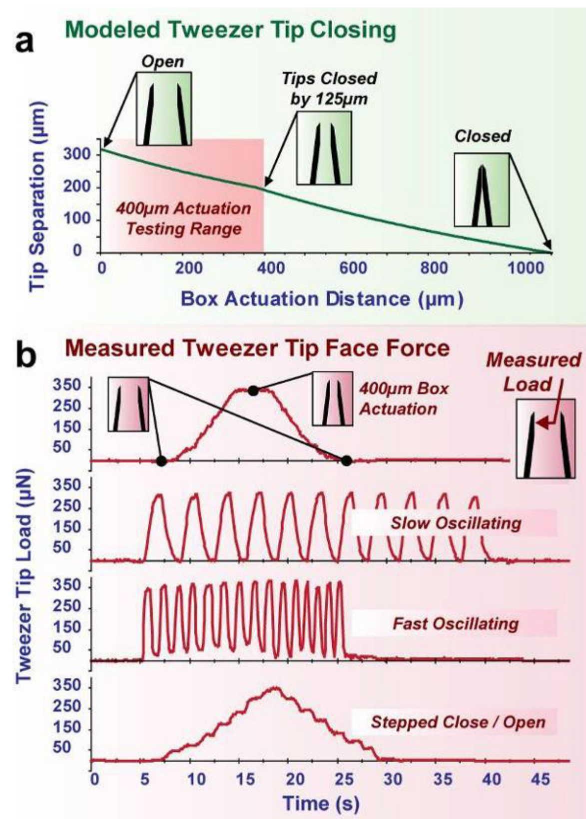

Fig. 6. (a) Modeling data for separation of tips based on actuation distance of box, and (b) measured force on inner face of closing tweezer tip. Average maximal forces from 125 µm tip deflections were 321 µN, 367 µN, 339 µN, and 335 µN for oscillating, fast oscillating, slow close/open, and stepped close/open actuations respectively.

V. MANIPULATION OF MICROSTRUCTURES

Attaching the microtweezer system to a Signatone (Lucas Signatone, Gilroy, CA) micromanipulator with an additional control knob for tweezer actuation (Fig. 3a) has allowed for use in a variety of biomedical experimental applications. This positioning system has been used to precisely direct the microtool's location and use within cell cultures, and to micromanipulate a variety of devices and biological samples (Fig. 7). Proposed experiments include using tweezers to assess the mechanical properties of biological structures through immobilization and interfacing, and use of tweezers themselves to induce mechanical injury onto single neurons.

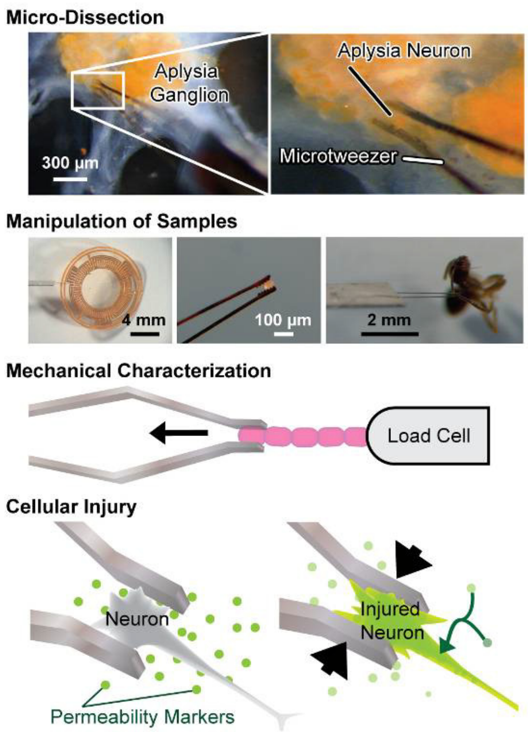

Fig. 7. Photographs and schematics demonstrating the wide range of applications for just one version of the microtweezer. Microtweezers are shown dissecting cells, manipulating various objects (microdevice, mineral, ant), inducing strain in a biological construct, and applying prescribed forces and strains into neurons which take up fluorescent markers following plasma membrane permeability from injury. Microtweezers have thickness of 25 µm, and beam widths of 40 µm.

VI. Future Directions

A single neuron injury study that uses the microtweezer system is planned. Following tweezer insertion and positioning into a 2D cortical neuron-astrocyte co-culture, a servo motor could be used to actuate the microtool to induce prescribed strains and forces, and thus, mechanical injury, on individual neurons within the culture. The cellular uptake of permeability dyes introduced into the tissue environment can be monitored during these injuries to quantify the degree of mechanical damage in the cell membranes of the neurons. Simultaneous electrical data can also be collected from the neurons using inserted probes or a microelectrode array. Following live-dead assays, correlations can be made between the levels of permeability dye uptake, electrophysiological responses, and injury rates. Such a neuronal injury study could provide a multi-faceted approach to elucidate the role of neuronal plasma membrane disruptions and their functional consequences.

VII. Conclusion

A novel microtweezer system is presented in this paper. This system relies on a mechanical micro-cam mechanism to actuate the microtool tips. In addition to providing enhanced functionality and ease of attachment to micromanipulators and micropositioners, this system has multiple advantages over previously developed systems including low cost, durability and flexibility, and modularity. Given the material composition and mechanics, the longevity of the tool (while not examined here), is also expected to exceed silicon based alternatives [13]. Due to its elegant device design, this system provides a platform in which to integrate additional functionality and sensors [1] that can enhance its already large application space.

Characterization of the system shows that prescribed, repeatable actuations and forces can be induced with the microtool tips. This performance and the system's ease of use can provide the means to create and enhance a multitude of experimental preparations. This includes a planned investigation that uses the microtweezer system to induce prescribed strain injuries into cortical neurons to examine the role of neuronal plasma membrane disruption in traumatic and spinal cord injury.

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