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► **To cite this version:**

Edison Gerena, Stéphane Régnier, Sinan Haliyo. Interactive Laser-actuated micro-robots for Experimental Biology. International Symposium on Optomechatronic Technology (ISOT) 2021, International Society for Opto-Mechatronics (ISOM), Nov 2021, Besançon, France. hal-03417350

HAL Id: hal-03417350

<https://hal.sorbonne-universite.fr/hal-03417350>

Submitted on 12 Nov 2021

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Interactive Laser-actuated micro-robots for Experimental Biology

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Abstract

Recent breakthroughs in biotechnology are rising the demand for single-cell manipulation techniques such as cell isolation and 3D orientation. Significant challenges remain for these applications, mainly due to the physics involved and the size constraints imposed by the environment. The precision required at those dimensions have a cost in term of workspace, grasping strategies and control schemes. Furthermore, there is an increasing demand to manipulate objects in confined environments like micro-fluidic devices, rendering external actuators unusable. In this presentation, an interactive optical robotic system is introduced. It implements untethered actuation and wireless sensing for microobjects in a confined liquid medium.

1. Introduction

Cell Biophysics is an emerging interdisciplinary science, in which physics and chemistry are employed to understand biological mechanisms, to assay cell response to events, characterize activation status in different settings or coming from different healthy or patient individuals. As such, adding to established spectroscopic and micro-scopic techniques, a new range of mechanical techniques and devices has emerged in recent years to investi-gate, measure and map mechanical forces in cells and decipher their role in cell function and fate. In this context, the ability to manipulate and characterize individual biological objects is become a major scientific challenge. The need to perform tasks such as single-cell deformation, stimulation, rotation, or transportation, has called for new emerging techniques that allow working at the unicellular scale.

Among these devices, robotic micromanipulators have become an ubiquitous tool in many experiments as they offer the only means to access the samples for manipulation, physical characterization, extraction... Using needles or glass pipettes as end-effectors, robotic systems give the opportunity to directly process a sample such as an isolated cell, a bacterium, making possible a wide range of mechanical, chemical or electrical stimuli and measurements [1]. However, these tools are complex to integrate in an experimental set-up and have dimensions many times larger than samples. It is thus quite complicated to design such an experiment as well as mastering the proper use of these devices. Additionally, using electro-mechanical sensors directly on the samples is quite difficult as those are prone to be affected by the liquid environment, provide low sensitivity and precision, and low signal-to-noise ratio. In addition, interfacing and communicating with the physical sensors through the sample chamber is highly challenging.

Optical techniques may greatly overcome these difficulties by providing wirelessly both the actuation and sensing. Optical tweezers [2] avoid many of the limitations of competing techniques as they offer much greater versatility. Optical trapping relies on an immaterial electromagnetic field produced by a highly focused laser beam. A highly focused laser produces a localized three-dimensional electromagnetic field that stably traps microscopic objects. This object is then actuated by deflecting the focal point of the laser. The optical forces can be modeled, and three-dimensional trap stiffness can be estimated analytically or numerically [3]. Motion tracking allows the force to be inferred. A trapped microsphere can serve as a force probe to examine the physical characteristics of a target object, such as the stiffness of cells, thus enabling a broad variety of potential applications, especially in biology or medical science. Optical Tweezers have successfully been applied in a large range of bio-manipulation experiments [4], such as the trapping of red blood cells and the immobilization of bacterial cells for nanoscopy.

Optical Microrobots is an evolution of optically trapped simple probes mentioned above. These are microscale floating 3D structures elaborated with optical ‘handles’ and actuated by optical tweezers. Using the laser tweezers as the actuation principle, and real-time motion tracking for sensing, these can be controlled in closed-loop or be teleoperated, in complete 6 degrees of freedom.

2. Interactive optical robotic system

In order to take the full advantage of these optical robots, our team has produced a robotic optical trapping system by carefully take in to account the sensor feedback, actuation and control issues (Fig. 1.A). It include a real-time 3D force measurements using event-based vision sensors. These bio-inspired sensors are frame-free and

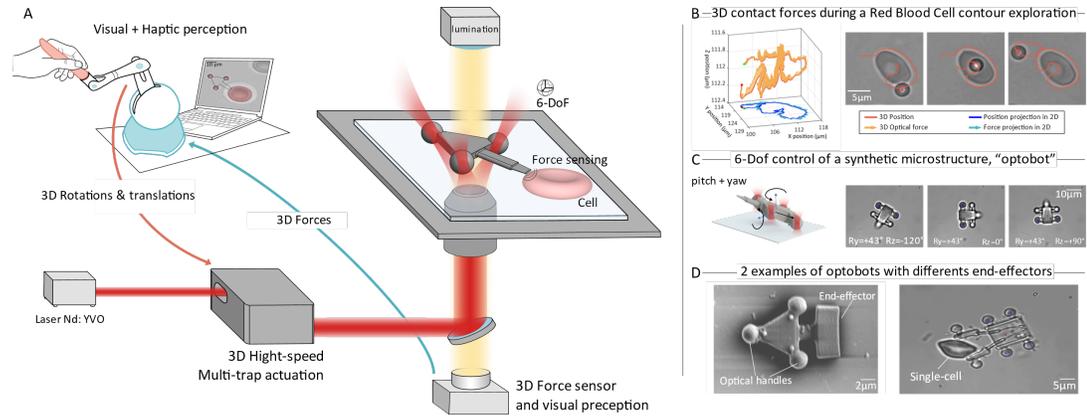


Figure 1: Unicellular laser-micromanipulation system.

eliminate data redundancy by design and allow for 2D tracking at the rate in the order of tens of kilo-Hertz [5]. The integration of such a sensor in laser trapping set-up provide high-bandwidth 3D motion tracking [6]. External forces applied on the trapped object are inferred with piconewton resolution in nanonewton range in practically real-time, up-to 300 Hz sampling rate. Haptic exploration tasks in biological (Fig. 1.B) and not-biological objects [7] has been performed.

An active solution for 3D high speed actuation of optical tweezers with MOEMS [8] has also be proposed. It allows to generate more than 15 time-shared traps in 3D with low latency and high bandwidth. The 3D motion of the focal spot is obtained by the synchronization of the orientation of a galvanometer mirror and the focusing or defocusing of a deformable mirror. This actuation technique is useful in applications where the 3D orientation of microscopic objects is needed, such as cell surgery or 3D tomographic imaging of living samples. The individual 3D manipulation of multiple objects, and the 6DoF manipulation of optical robots is depicted in Fig 1.C. A teleoperation interface for interactive bio-manipulation is also implemented [9]. The system provides a straightforward human/machine interaction through a tele-robotic solution allowing dexterous manipulation of synthetic and biological objects in an efficient and intuitive way. Teleoperation control is implemented with an Omega 7, a haptic device with 7-DoF (including an active two-finger grip) and force feedback, and is ensured by a hard real-time operating system. Traps can be grouped and controlled in a variety of ways for specific purposes.

Optical robots have dimensions in the same range of samples and can be simply introduced in the medium. Two diferents examples are show in Fig. 1.D. Compared to simple spherical probes, these can be equipped with custom designed end-effectors, for example sharp probes, mechanical sensors or injectors, shovels... to carry out different stimuli and measurements directly on the bio-samples. These Optical robots can be used collectively to induce mechanical stimuli, squeeze, or bring samples in contact and directly measure their responses at high temporal and force resolution, with eventually through haptic devices for “feeling” the force and dynamics of the cell surface. Looking further forward, they can include internal mobilities, to do tools like grippers, or active components like a micromotor or a pump. This represents a huge potential for experimental biology, as the user will virtually be able to reach inside the Petri Dish and manipulate single specimens, while collecting information on interaction forces.

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