

# New Optical Sensor for Monitoring the Micropipette Motion

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**Abstract**—A novel noncontact sensor is developed to monitor the displacements of a drawn glass pipette tip. These pipettes are commonly used in various cellular-injection applications, from *in vitro* fertilization to cloning. The physics of the underlying cellular-piercing process, however, is quite complex and presently not fully understood primarily due to the absence of appropriate motion sensors. A high-sensitivity noncontact sensor is needed to study this delicate microdynamics. We report here on an optical microdevice, which is developed for this objective. In the core of the sensing, properly positioned four photodiodes receive the light, which emanates from the target micropipette. Appropriate electronics and sensitivity-enhancement techniques are also utilized. The experimental results are presented from a preliminary test study on a prototype setup. These results are very encouraging in that we can already report submicrometer-level motion-detection capability.

**Index Terms**—Intracytoplasmic sperm injection (ICSI), *in vitro* fertilization (IVF), microinjection, micropipette, microsensors, optical-fiber transducers.

## I. INTRODUCTION AND MOTIVATION

IN recent years, we have observed that cellular piercing has become a standard procedure in nuclear or subcellular-transfer operations and in intracytoplasmic sperm injection (ICSI). An enhanced version of the process, which is also known as “piezo-assisted ICSI,” is proven to increase the success rate beyond the earlier deployments of the ICSI procedure (what is also known as the “conventional ICSI”) [1], [2]. The piezo-assisted procedure is, in fact, important progress toward automated and repeatable deployment of microinjection operation. However, there are a number of points in the physics of the procedure which need further investigation. An important utility for such investigations is a nonintrusive sensor to monitor the microdynamics of the tip of the very pliable glass pipette. This need is the primary motivation of the present paper.

We should also mention about an interesting earlier discovery over piezo-assisted cell piercing in which using a very small amount of mercury in the pipette tip is shown to improve the method substantially [3], [4]. However, mercury being a highly-toxic substance, this enhancement is very cautiously utilized today. In order to investigate the effects of mercury in the piercing process, the author’s group has done an earlier study. The results from that study show that piezo-actuated impulsive axial forcing generates more intensive transverse displacements

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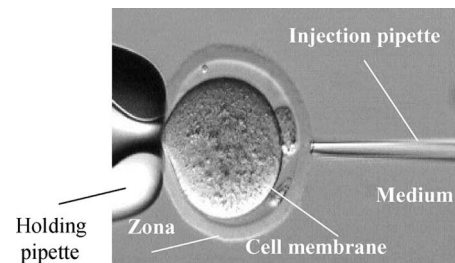


Fig. 1. Cellular-injection setup.

than the axial motion. These movements are transmitted and further exaggerated through the flexible pipette tip [5], [9]. In these studies, the lateral oscillations at the glass-pipette tip are detected by digital microscopic-imaging techniques. There are, however, several constraints in this detection mechanism such as the frame speed of camera, signal-processing efficiency, adverse lighting condition, and only one-dimensional (in transverse motion) sensing ability [6].

In this paper, we develop a new methodology to monitor the tip motion of the glass pipette in three-dimensional (3-D) sense by using laser-optics technology. A crucial requirement in this sensor is its “noncontact” nature, so that the physics of cell piercing is not disturbed by the sensory presence. The bandwidth of the sensor has to be high enough to capture all critical pipette-tip behavior, in the air and also *in situ*. *In situ* deployment obviously refers to the most realistic situation, where the biological cell and the neutral medium (such as mineral oil) are all in direct contact with the pipette tip. The sensor we propose in this paper should still be dynamically responsive under these conditions. Understanding the tip motion of the pipette is essential in improving the cell-piercing procedure. More importantly, we anticipate that such a monitoring scheme can lead us to develop different pipette designs and cell-piercing procedures.

### A. Description of the Piezo-Assisted Cellular Piercing

Cellular piercing is done using two glass pipettes [3]–[5], which are also called the holding and the injection pipettes (Fig. 1). They vary in size and shape. For example, for ICSI on mice oocytes, the *injection pipette* has a tip with 10- $\mu\text{m}$ -outer and 8- $\mu\text{m}$ -inner diameters. The *holding pipette*, which has a tip with 50–100- $\mu\text{m}$  outer and 10- $\mu\text{m}$  inner diameters, immobilizes the oocyte by a slight suction. The injection pipette is pressed on the membrane and a dimple is generated. A piezo-activated axial pulse is given to the pipette, which then pierces the membrane. In our earlier investigations to monitor the position of