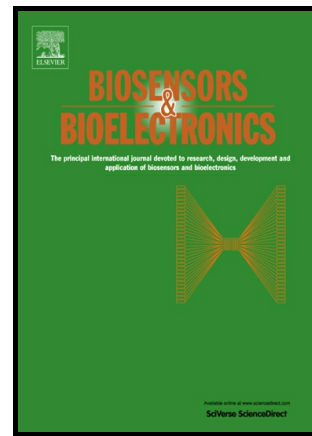


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## Versatile on-Stage Microfluidic System for Long Term Cell Culture, Micromanipulation and Time Lapse Assays

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### Abstract

We report here a versatile on-stage microfluidic cell culture and assay system which is compatible with different microscopes and sensors, can simultaneously perform steps of long term cell culture, high throughput time lapse cell assays/ imaging, and cell micromanipulations. With the system, we cultured a variety of cells for different periods of time and monitored their cell morphology, migration and division. We also performed a series non-invasive real time in situ time lapse assays and micromanipulations on different cells. They include: the first time lapse imaging and measurements on the instantaneous variations of morphology, biomechanical properties and the intracellular protein of human red blood cells in responding to pH fluctuation, drug action and electromagnetic radiation; the first continuous time lapse Raman micro-spectroscopy on a CHO cell in different phases of its entire life cycles; the micro-transfection of GFP into B16 cells and the follow up observation of the cell's morphology and expressed GFP fluorescence varying with incubation time and cell generations. The performance of these experiments not only demonstrated the capability of the system, but also proposed a variety of novel methods for obtaining time- and spatially-resolved information about the cellular and molecular heterogeneity and transformation during development or stimulations.

### Keywords

Microfluidic cell culture and assay system; Long term cell culture; Time lapse cell assay; Cell micromanipulation

### 1. Introduction

To explore cellular processes and dynamic events, long term continuous monitoring of living cells on a microscope stage is strongly desired nowadays. Meanwhile, to study the cell responses to different physical and chemical stimulations at single-cell level, on stage cell assay and manipulation are also required so that the steps of cell culture and assay/manipulation can be performed simultaneously. However, it poses a number of significant biotechnological and bioengineering challenges in such experiments. For they need to have an onstage cell culture system to provide a clean, sterile,

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