

Abstract

Controlled Contact between Beads and Cells for the Characterization of Receptor–Ligand Bonds [†]

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Abstract: The controlled contact between two micro-sized objects, such as beads and cells, and the assessment of their adhesion status is demonstrated in this research. The controlled contact is carried out in a microfluidic channel under flow conditions and makes use of a combination of hydrodynamic traps, flow drag force and dielectrophoretic (DEP) force to maintain the two objects in contact for the desired duration in a first step. Then, the pair objects are separated in the second step in order to explore their adhesion status. Adhesion events are mediated by the bond formed between a receptor and its ligand, and their binding kinetic parameters can be extracted from the measurements using the proposed device.

Keywords: microfluidics; hydrodynamic traps; dielectrophoretic traps; cell–cell adhesion; receptor–ligand binding kinetics

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1. Introduction

The binding between a membrane-bound receptor and its ligand mediates cell–cell adhesion, communication, and cell adaptation to its environment. Failure of the receptors to properly function threatens the homeostasis of the organism, and our understanding of the resulting pathologies relies on our capability to study the associated binding kinetics. Current methods for the controlled contact between two objects, such as atomic force microscopy, optical tweezers, or a dual pipette assay, are typically cumbersome, slow, and leave no hope for scalability [1].

2. Discussion

We thus propose a microfluidic device for the controlled contact between two objects. The operation of the device is illustrated in Figure 1 and starts with the hydrodynamic trapping of the first type of object in custom vertical traps (a) made using an innovative fabrication process [2]. This type of trap is totally transparent and has no effect on other particles once filled with a cell. The second type of object is directed to and trapped in contact with the first object using the DEP force created by the electrodes patterned in their vicinity (b–c) [3]. The forced contact is released by stopping the voltage applied to the electrodes and letting the flow drag the second type of object (d). A receptor–ligand

binding event is assessed by observing the adhesion state after the forced contact is released. A scanning electron microscope (SEM) image of the device is shown in Figure 1e.

The concept is demonstrated by measuring the lifetime of pairs formed by cancer cells and T-cell clones that are TCR-specific to cancer cell peptides, as illustrated in Figure 2.

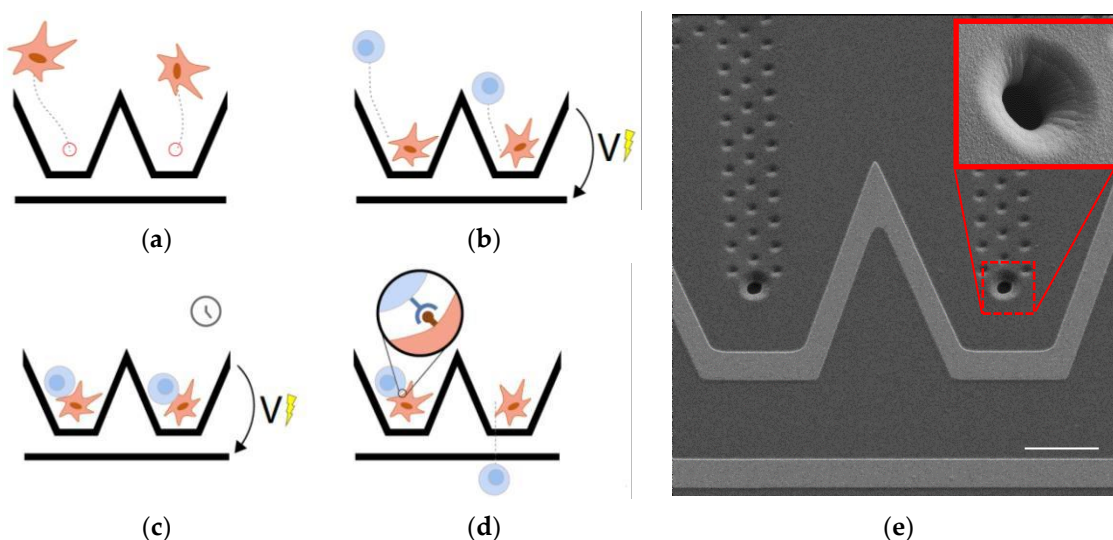


Figure 1. (a–d) Process for the controlled contact between two cells and the exploration of their adhesion status after a defined, forced contact time. (e) SEM image of the proposed device with the hydrodynamic trap highlighted in the inset and the electrodes used for the DEP manipulation patterned in their vicinity.

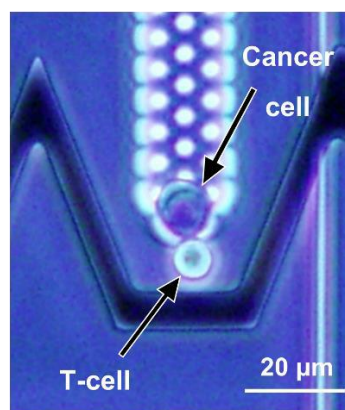


Figure 2. This microscopy picture represents the controlled contact between a cancer cell (in the hydrodynamic trap) and a T-cell (manipulated by DEP) using the proposed device.

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