



**HAL**  
open science

## Controlled Contact between Beads and Cells for the Characterization of Receptor–Ligand Bonds

Clémentine Lipp, Laure Koebel, Romain Loyon, Aude Bolopion, Laurie Spehner, Michaël Gauthier, Christophe Borg, Arnaud Bertsch, Philippe Renaud

► **To cite this version:**

Clémentine Lipp, Laure Koebel, Romain Loyon, Aude Bolopion, Laurie Spehner, et al.. Controlled Contact between Beads and Cells for the Characterization of Receptor–Ligand Bonds. Proceedings, 2024, 97 (1), pp.2504 - 3900. 10.3390/proceedings2024097189 . hal-04790907

**HAL Id: hal-04790907**

**<https://hal.science/hal-04790907v1>**

Submitted on 19 Nov 2024

**HAL** is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.



Distributed under a Creative Commons Attribution 4.0 International License

Abstract

# Controlled Contact between Beads and Cells for the Characterization of Receptor–Ligand Bonds <sup>†</sup>

Clémentine Lipp <sup>1</sup>, Laure Koebel <sup>2</sup>, Romain Loyon <sup>3</sup>, Aude Bolopion <sup>2</sup>, Laurie Spehner <sup>3</sup>, Michaël Gauthier <sup>2</sup>, Christophe Borg <sup>3</sup>, Arnaud Bertsch <sup>1</sup> and Philippe Renaud <sup>1,\*</sup>

- <sup>1</sup> Laboratory of Microsystems LMIS4, Ecole Polytechnique Fédérale de Lausanne (EPFL), Lausanne, Switzerland; clementine.lipp@epfl.ch (C.L.); arnaud.bertsch@epfl.ch (A.Bertsch)
- <sup>2</sup> Institut FEMTO-ST, Département AS2M, Univ. Bourgogne Franche-Comté, CNRS, Besançon, France; laure.koebel@femto-st.fr (L.K.); aude.bolopion@femto-st.fr (A.Bolopion); michael.gauthier@femto-st.fr (M.G.)
- <sup>3</sup> Établissement Français du Sang Bourgogne Franche-Comté, Unité RIGHT, UMR INSERM 1098, Besançon, France; romain.loyon@efs.sante.fr (R.L.); laurie.spehner@efs.sante.fr (L.S.); christophe.borg@efs.sante.fr (C.B.)
- \* Correspondence: philippe.renaud@epfl.ch
- <sup>†</sup> Presented at the XXXV EUROSENSORS Conference, Lecce, Italy, 10–13 September 2023.

**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

**Citation:** Lipp, C.; Koebel, L.; Loyon, R.; Bolopion, A.; Spehner, L.; Gauthier, M.; Borg, C.; Bertsch, A.; Renaud, P. Controlled Contact between Beads and Cells for the Characterization of Receptor–Ligand Bonds. *Proceedings* **2024**, *97*, x. <https://doi.org/10.3390/xxxxx>

Academic Editors: Pietro Siciliano and Luca Francioso

Published: date



**Copyright:** © 2024 by the authors. Submitted for possible open access publication under the terms and conditions of the Creative Commons Attribution (CC BY) license (<https://creativecommons.org/licenses/by/4.0/>).

## 1. Introduction

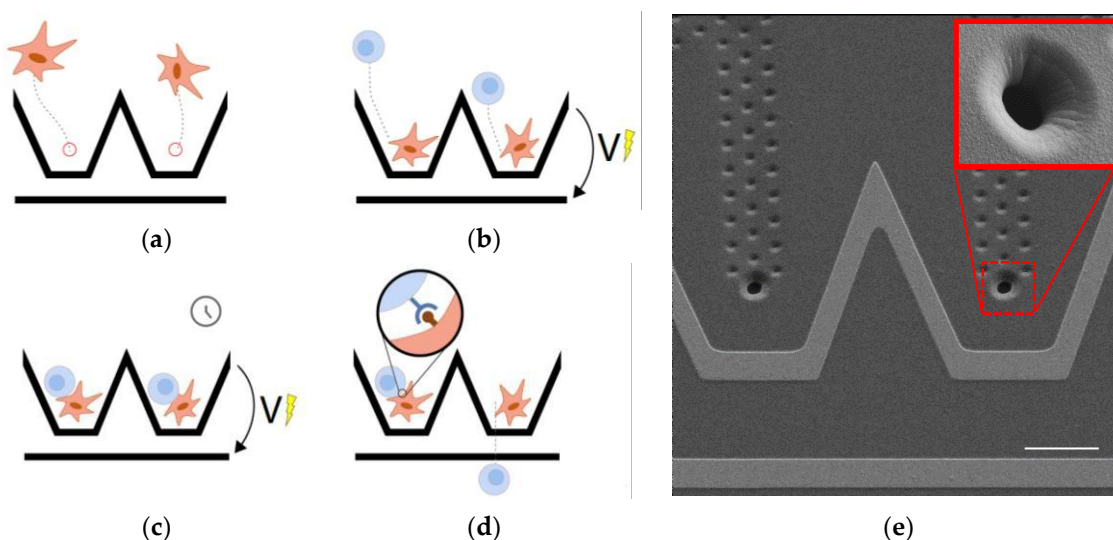
The binding between a membrane-bound receptor and its ligand mediates cell–cell adhesion, communication, and cell adaptation to its environment. Failure of the receptors to properly function threatens the homeostasis of the organism, and our understanding of the resulting pathologies relies on our capability 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

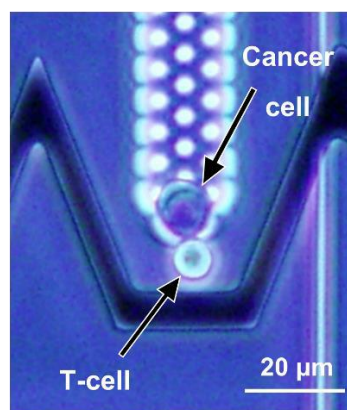
We thus propose a microfluidic device for the controlled contact between two objects. The operation of the device is illustrated in Figure 1 and starts with the hydrodynamic trapping of the first type of object in custom vertical traps (a) made using an innovative fabrication process [2]. This type of 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.

**Author Contributions:**

**Funding:** This study was supported by the EIPHI Graduate School under Contract ANR-17-EURE-0002, by the French Agence Nationale de la Recherche and the Swiss National Science Foundation through the CoDiCell project (contract “ANR-17-CE33-0009” and “FNS 00021E\_175,592/1”, respectively), and by the French ROBOTEX network and its Micro and Nanorobotics center under Grant ANR-10-EQPX-44-01.

**Institutional Review Board Statement:**

**Informed Consent Statement:**

**Data Availability Statement:**

**Conflicts of Interest:** The authors declare no conflicts of interest.

## References

1. Liu, B.; Chen, W.; Zhu, C. Molecular force spectroscopy on cells. *Annu. Rev. Phys. Chem.* **2015**, *66*, 427–451.
2. Lipp, C.; Uning, K.; Cottet, J.; Migliozi, D.; Bertsch, A. Renaud, P. Planar hydrodynamic traps and buried channels for bead and cell trapping and releasing. *Lab A Chip* **2021**, *21*, 3686–3694.
3. Lipp, C.; Koebel, L.; Bertsch, A.; Gauthier, M.; Bolopion, A.; Renaud, P. Dielectrophoretic Traps for Efficient Bead and Cell Trapping and Formation of Aggregates of Controlled Size and Composition. *Front. Bioeng. Biotechnol.* **2022**, *10*, 910578.

**Disclaimer/Publisher's Note:** The statements, opinions and data contained in all publications are solely those of the individual author(s) and contributor(s) and not of MDPI and/or the editor(s). MDPI and/or the editor(s) disclaim responsibility for any injury to people or property resulting from any ideas, methods, instructions or products referred to in the content.