Handling of Living Cells in a Microfluidic Chip with a Nozzle-Diffuser Micropump

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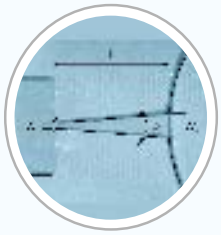
Abstract: We study the transport of mammalian cells using a reciprocating micropump with nozzle-diffuser elements. The effect of the pumping action on cell viability and proliferation, as well as on the damaging of cellular membranes is quantified using four types of well-established biological tests: a trypan blue solution, the tetrazolium salt WST-1 reagent, the LDH cytotoxicity assay and the calcium imaging ATP test. The high viability levels obtained after pumping indicate that the nozzle-diffuser micropump can be appropriate for handling living cells in cell-on-a-chip applications.

Principle of the Nozzle-Diffuser Micropump[1]

A diffuser micropump is a « positive displacement pump » that uses two nozzle/diffuser elements instead of mechanical valves.

The nozzle/diffuser element is a fluidic channel constriction that has a different fluidic resistance in the diffuser (direct) and nozzle (reverse) direction.

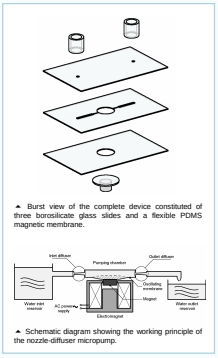


Schematic diagram

The diffuser micropump consists of 3 glass layers and a flexible silicone membrane:

- the central glass layer contains the fluidic network;
- the top glass layer has the fluidic connections;
- the membrane is attached to the bottom glass layer.

The micropump is actuated with an external electromagnet placed below.



Burst view of the complete device constituted of three borosilicate glass slides and a flexible PDMS magnetic membrane.

Schematic diagram showing the working principle of the nozzle-diffuser micropump.

Microfabrication Technique[2]

Due to its *chemical inertness*, glass is undeniably the favourite material for Lab-On-Chip biomedical applications.

Our microfabrication technique is based on:

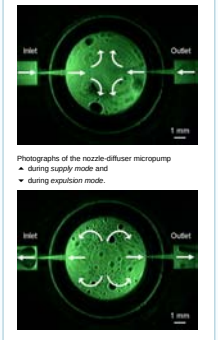
- Microstructuration of fluidic channels by **powder blasting**.
- Multi-layered microchip assembly by **glass fusion bonding**.

Characterization of the micropump

The fabricated prototypes were characterized by pumping **water**:

- Resonant frequency of ~ 50 Hz;
- A maximum back-pressure of 50 mbar was obtained;
- A maximum water flow rate of 1 mL was measured.

Furthermore, the micropump demonstrated good tolerance to bubbles and was even self-priming.



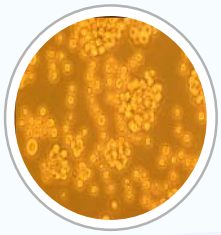
Photographs of the nozzle-diffuser micropump during *supply mode* and during *expulsion mode*.

Pumping of Mammalian Cells[3]

The viability and cytotoxicity of mammalian cells were evaluated for different pumping conditions.

4 types of biological assays were used in our experiments:

- Trypan blue solution;
- Tetrazolium salt WST-1;
- LDH cytotoxicity test;
- Calcium imaging ATP test.

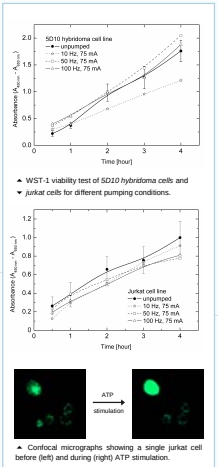


Mammalian cells viability and proliferation assays

The WST-1 cell proliferation reagent and the LDH cytotoxicity assay were used to systematically study the behaviour of jurkat cells and hybridoma cells as a function of pumping parameters (actuation current and frequency).

The viability of jurkat cells was further confirmed by the calcium imaging ATP test.

High viability levels were obtained after pumping (in the 80% range), even for the most sensitive cells.



WST-1 viability test of *5D10 hybridoma cells* and *jurkat cells* for different pumping conditions.

Confocal micrographs showing a single jurkat cell before (left) and during (right) ATP stimulation.

1. A. Olsson, *"Valve-less Diffuser Micropumps,"* Ph.D. thesis, KTH, Stockholm, Sweden, 1998.

2. C. Yamahata *et al.,* "Glass valveless micropump using electromagnetic actuation," *Microelectronic Engineering* ***78-79*** *(3)*: 132-137, 2005.

3. C. Yamahata *et al.,* "Pumping of mammalian cells with a nozzle-diffuser micropump," *Lab On a Chip* ***5*** *(10)*: 1083-1088, 2005.

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