Rapid-prototyped macro-valves for fluidic control of µ-3D cardiac tissues-on-chip

Amélie Bocquet [1,2]*, Anke R. Vollertsen [1] , Tom Boonen [1], Marcelo C. Ribeiro [1] and Mathieu Odijk [2]

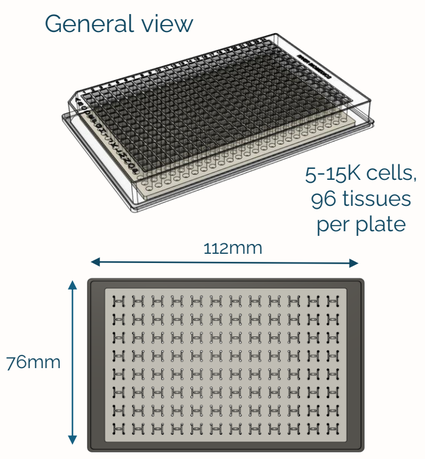
1 River BioMedics BV, Enschede, the Netherlands,

2 BIOS Lab on a Chip group, University of Twente, Enschede, the Netherlands

***Contact: amelie.bocquet@riverbiomedics.com**

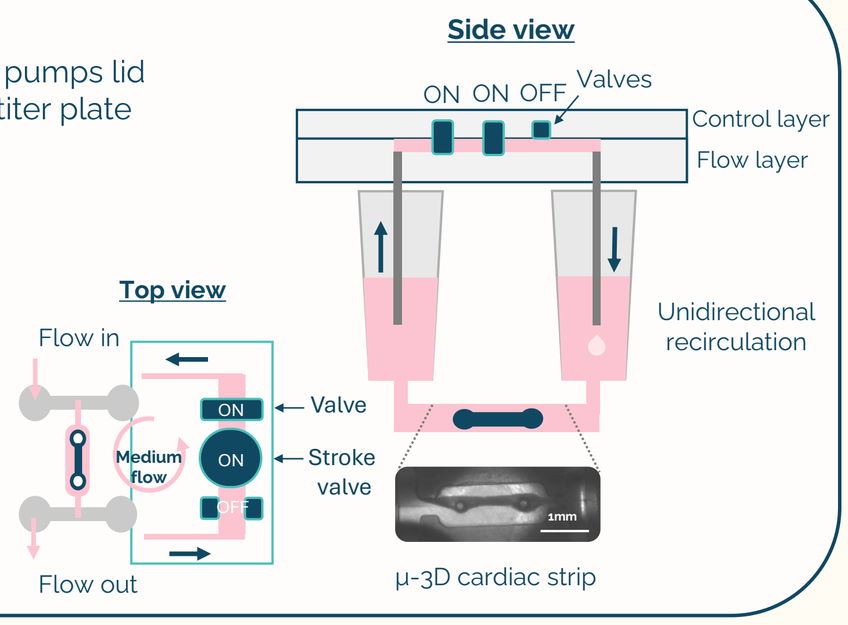
INTRODUCTION

- Multiplexed standardized Organs-on-Chip (OoC) platforms are developed by Biotech companies to enable high-throughput drug screening.
- Rocker plates and pipetting robots face challenges in precise flow recirculation and shear stress control.
- **Can optimizing fluid flow control in OoCs well-plates significantly increase experimental throughput ?**

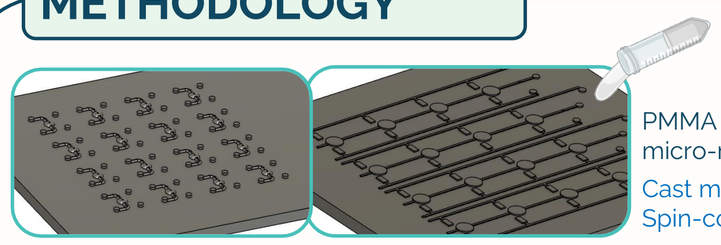


OBJECTIVES

- Develop multiplexed peristaltic pumps lid for micro 3D cardiac strip microtiter plate model
  - **Active and precise control over fluid flow**
  - 96-well plate standard
  - Rapid-prototyping fabrication
  - Upscaled production (injection molding)
  - Flexible and biocompatible material
  - Low molecule absorption



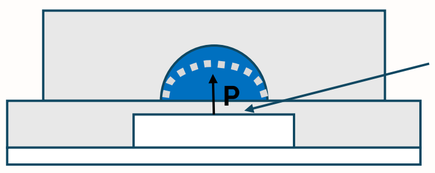
METHODOLOGY



PDMS

PMMA (poly(methyl methacrylate)) mold designs micro-milled

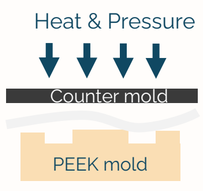
Cast mold PDMS 7:1 on flow layer mold (left)
Spin-coat PDMS 10:1 on control layer mold (right)



Schematic side view of an open PDMS (Polydimethylsiloxane) Quake valve [1] cross section

- Flow layer with flow channel in blue
- Flexible membrane which can **deflect under pressure to close flow channel**
- Control layer contains control channels which can be pressurized with water
- Glass slide

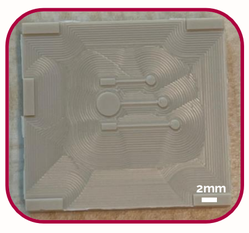
FlexDym™

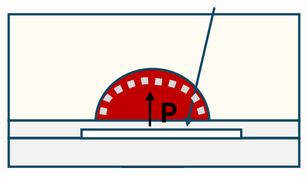


FlexDym™ 250µm sheet

Hot embossing in Sublym Machine ©EdenTech

PEEK (polyetheretherketone) mold design micro-milled





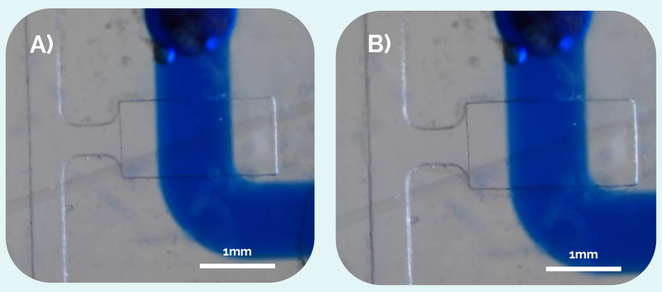
Schematic side view of an open FlexDym™ Quake valve cross section

- Flow layer made of PMMA or PS (polystyrene) with flow channel in red
- FlexDym™ 250µm control layer pressurized with air
- FlexDym™ 2mm

PRELIMINARY RESULTS

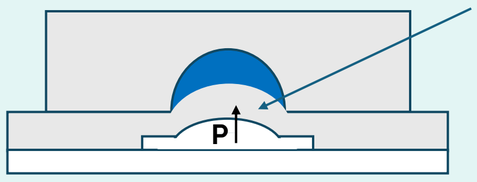
Final device & valve actuation

Final PDMS microfluidic device with 16 integrated peristaltic pumps, made with 2mm x 1mm x 200µm macro-valves.

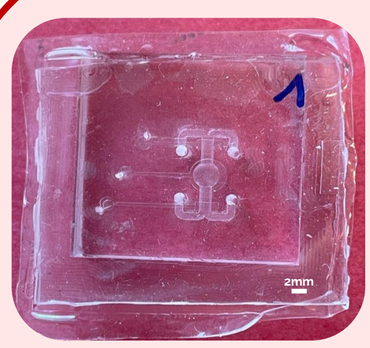


A) Open valve, B) Valve still open under 1.2 bar pressure in control channels containing water. Half-round flow channels 250µm high, 1000µm wide, are filled with blue food colouring.

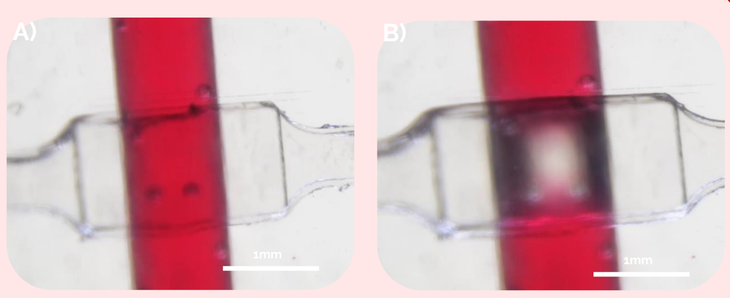
Membrane thickness analysis



The PDMS membrane thickness was analysed under VK-X 3000 Keyence microscope. On the same chip, the membrane had different heights going from around 300µm to 800µm. The membrane is too thick and not flexible enough, which means that it can't expand properly, leading to poor valve closure.



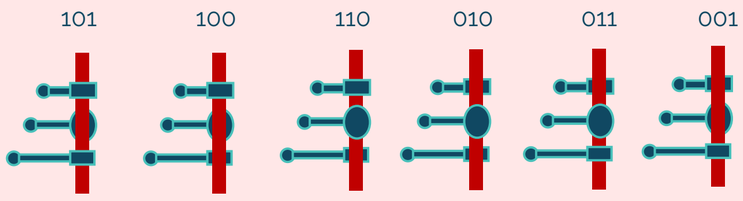
Final FlexDym™ - PMMA microfluidic device with 1 integrated peristaltic pump, made with 2mm x 1mm x 180µm macro-valves.



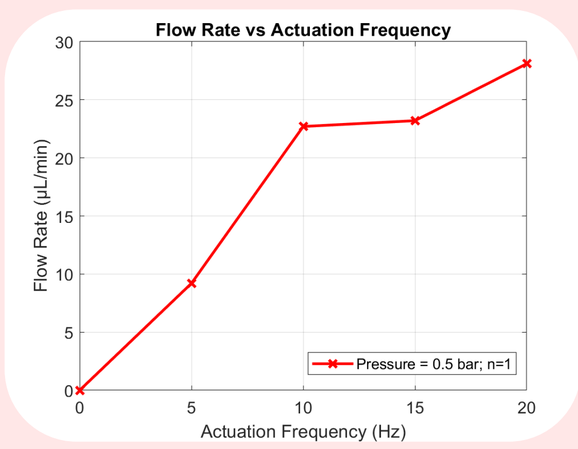
A) Open valve, B) Closed valve under 1.2 bar pressure in control channels containing air.

Basic design with a FlexDym™ membrane and Polystyrene flow layer with half round flow channels 300µm high, 1000µm wide, are filled with red food colouring.

Flow rate measurements



Peristaltic pump 6-phase actuation pattern [2].
1: valve actuated (closed), 0: valve normally open.



- Flow rate up to 28µl/min, under 0.5 bar pressure, at 20Hz actuation.
- Delamination occurred at the bottom valve.

Flow rate measurements within PMMA recirculation chip with a FlexDym™ membrane

CONCLUSION & OUTLOOK

- **FlexDym™ is a promising material** as it offers low molecule absorption, scalability via injection molding, and biocompatibility [3].
- This technology is adaptable to every kind of OoCs model in a 96-well plate.

- Our current challenges are to find an optimized protocol to overcome bonding issues and fabricate those devices using FlexDym™ reliably.
- In the future, this technology is destined to be **upscaled to fit a 96-well plate** and bring automated nutrient delivery to the µ-3D cardiac tissues in River BioMedics microtiter plate.

This work is part of the **TRANSITION-3DcardiacHTS project** (HORIZON-EIC-2022-TRANSITION-01), funded by the European Innovation Council (EIC) and SMEs Executive Agency (EISMEA).

Follow us

River BioMedics

BIOS Lab on a Chip group

European Innovation Council

UNIVERSITY OF TWENTE.

Organ-on-Chip Centre Twente

[1] Thorsen, T. et al. Science (New York, N.Y.), 298(5593), 580–584 (2002).
[2] Bossink E.G.B.M. et al. Microsyst Nanoeng 8, 54 (2022).
[3] Emma Thomée, PhD Thesis, Université de Strasbourg (2021). NNT : 2021STRAF050 . tel-03934758