From Finger Prick Sampling to On-Body and Ultimately Implantable Chem/Bio-Sensors: The Key Role of Active Fluidics in Realising the Long-Term Functional Platforms of the Future

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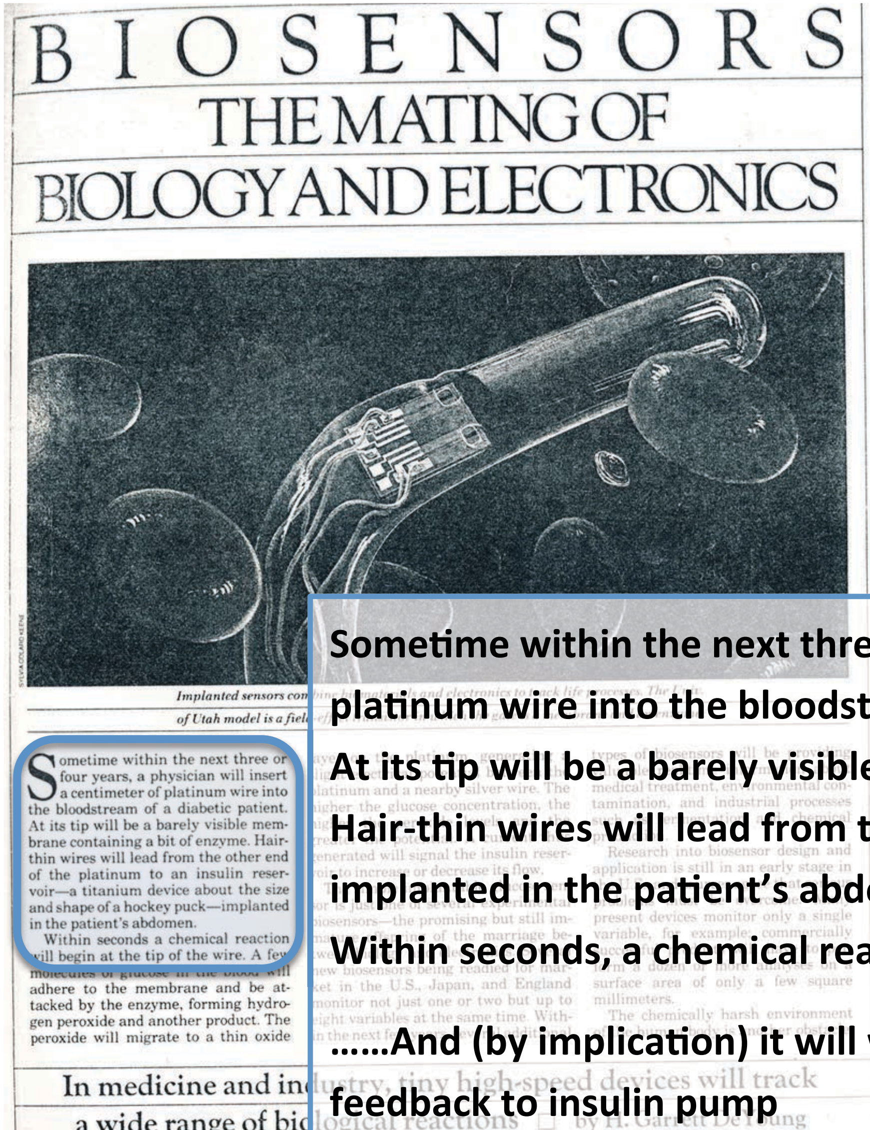
The (broken) promise of biosensors…..



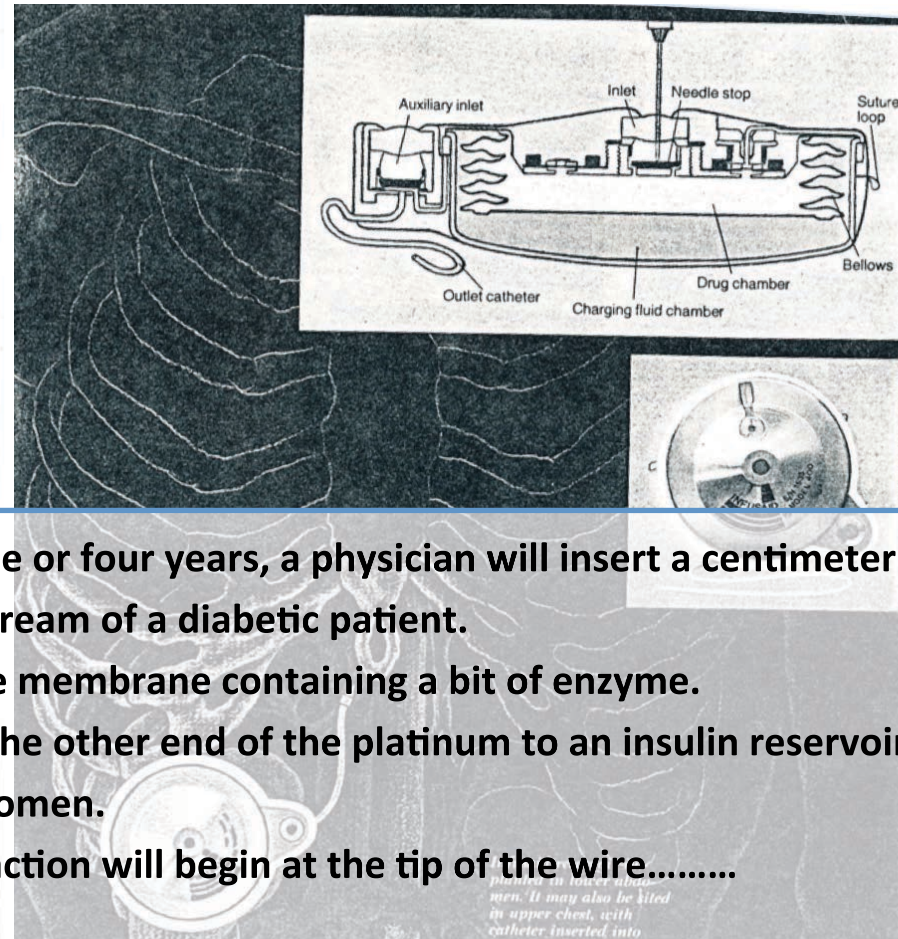
BIOSENSORS

THE MATING OF BIOLOGY AND ELECTRONICS

Sometime within the next three or four years, a physician will insert a centimeter of platinum wire into the bloodstream of a diabetic patient. At its tip will be a barely visible membrane containing a bit of enzyme. Hair-thin wires will lead from the other end of the platinum to an insulin reservoir—a titanium device about the size and shape of a hockey puck—implanted in the patient's abdomen. Within seconds a chemical reaction will begin at the tip of the wire. A few … adhere to the membrane and be attacked by the enzyme, forming hydrogen peroxide and another product. The peroxide will migrate to a thin oxide

In medicine and industry, tiny high-speed devices will track a wide range of biological reactions □ by H. Garrett DeYoung

High Technology, Nov. 1983, 41-49



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At its tip will be a barely visible membrane containing a bit of enzyme.

Hair-thin wires will lead from the other end of the platinum to an insulin reservoir implanted in the patient's abdomen.

Within seconds, a chemical reaction will begin at the tip of the wire………

……And (by implication) it will work for years reliably and regulate glucose through feedback to insulin pump

Current Approach: Finger Prick Sampling

- e.g. Diabetes: ca. 7% of world population
- USA: population 300 million
- Ca. 20 million diabetics
- Personal control of condition using finger prick test => blood sample + glucose biosensor

- Say four measurements per day = 80 million/day
- Per year = ca. 30 Billion measurements/yr
- Each sensor used ONCE

Abbott Freestyle 'Libre'

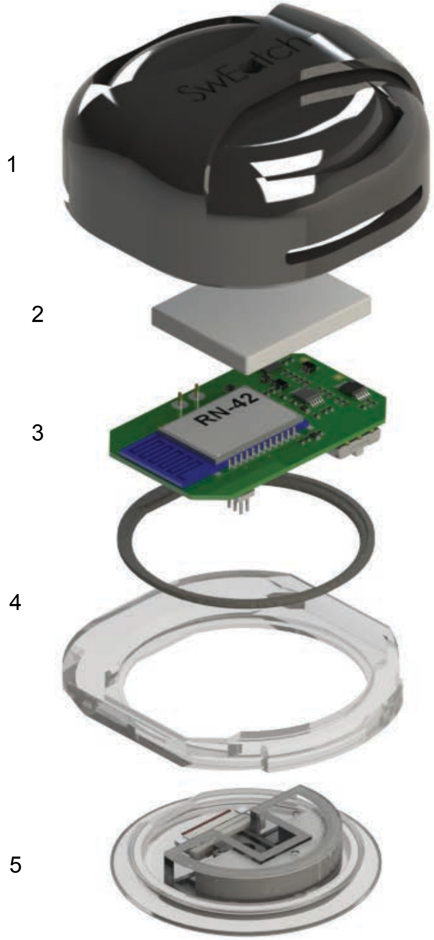
The days of routine glucose testing with lancets, test strips and blood are over.[2]

Welcome to flash glucose monitoring!

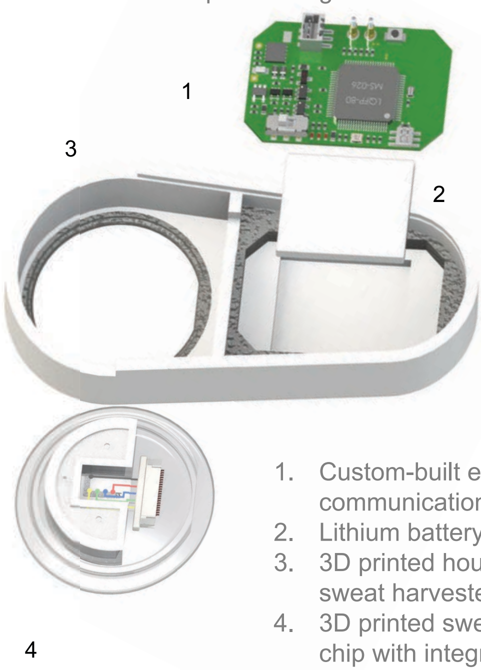
- 'Small fibre' used to access interstitial fluid
- Data downloaded at least once every 8 hr via 1s contactless scan (1-4 cm)
- Waterproof to 1 metre
- Replace every 2 weeks

Current state-of-the-art for patch based glucose sensing is 2-weeks use outside the body Implants require 10 years inside the body

Sweatch……



1. 3D printed housing
2. Lithium battery
3. Custom-built electronics with wireless communication (Shimmer)
4. 3D printed mount will silicon inner seal to house the sweat harvester
5. 3D printed sweat harvesting device and microfluidic chip with integrated sensor



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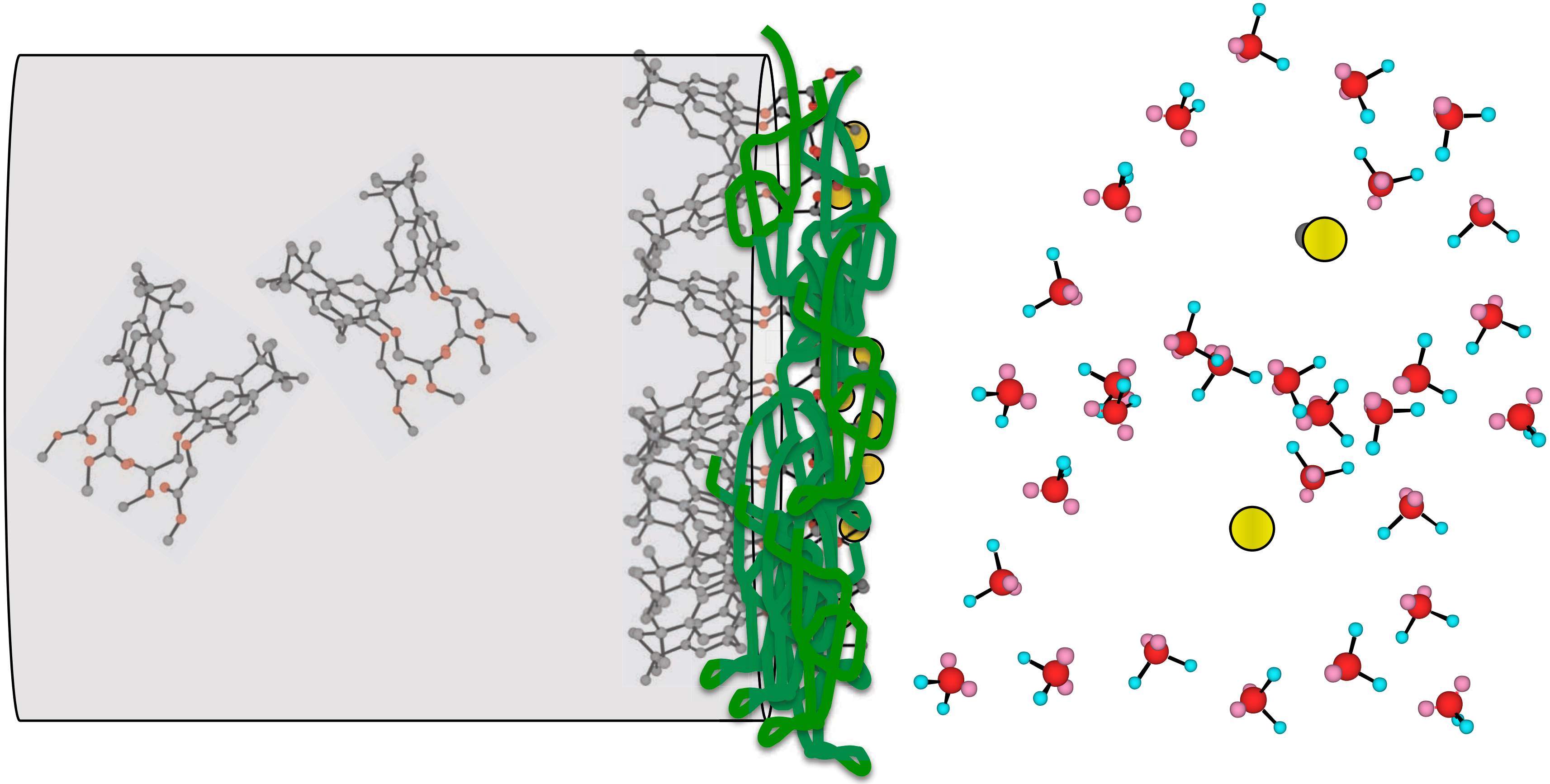
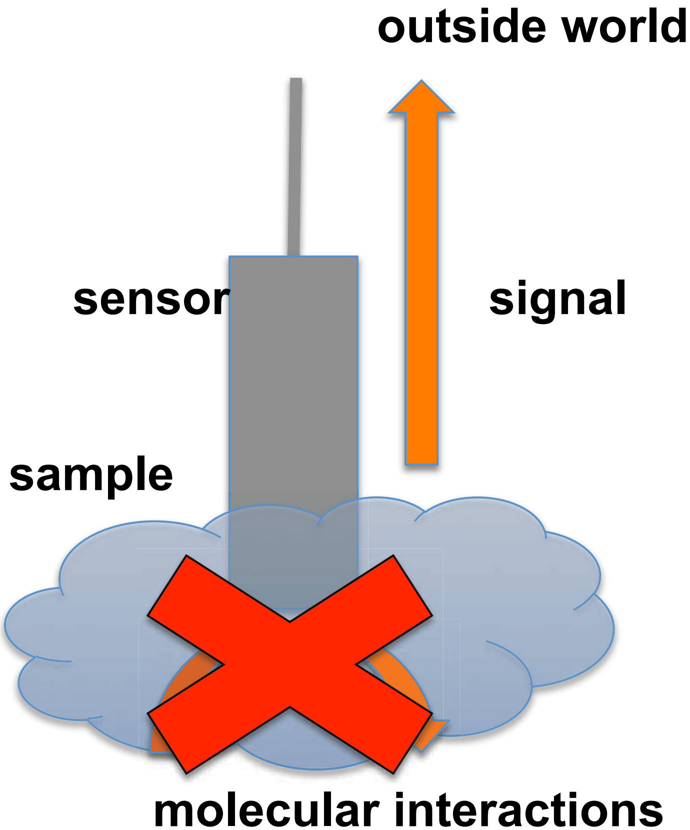
See Poster Margaret mcCaul, et al…

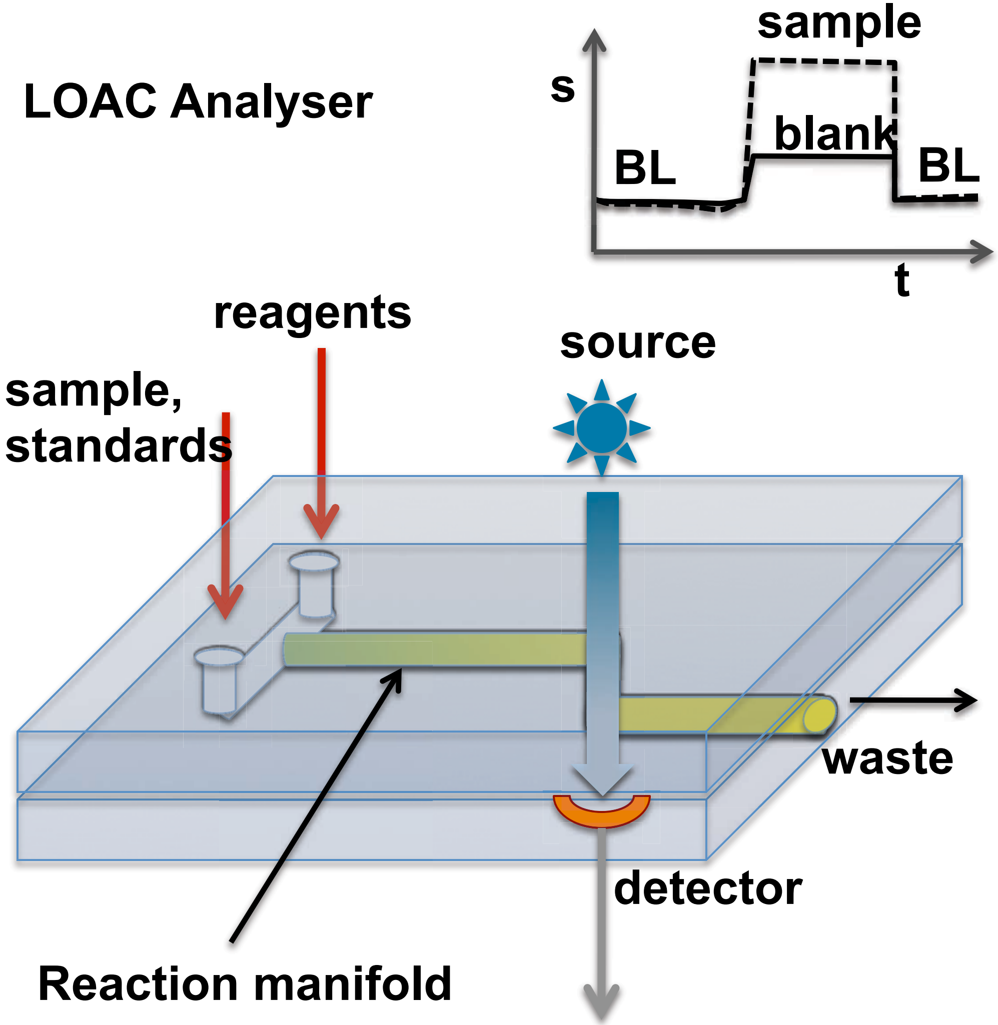
Control of membrane interfacial exchange & binding processes



Remote, autonomous chemical sensing is a tricky business!

Direct Sensing vs. Reagent Based LOAC/ufluidics



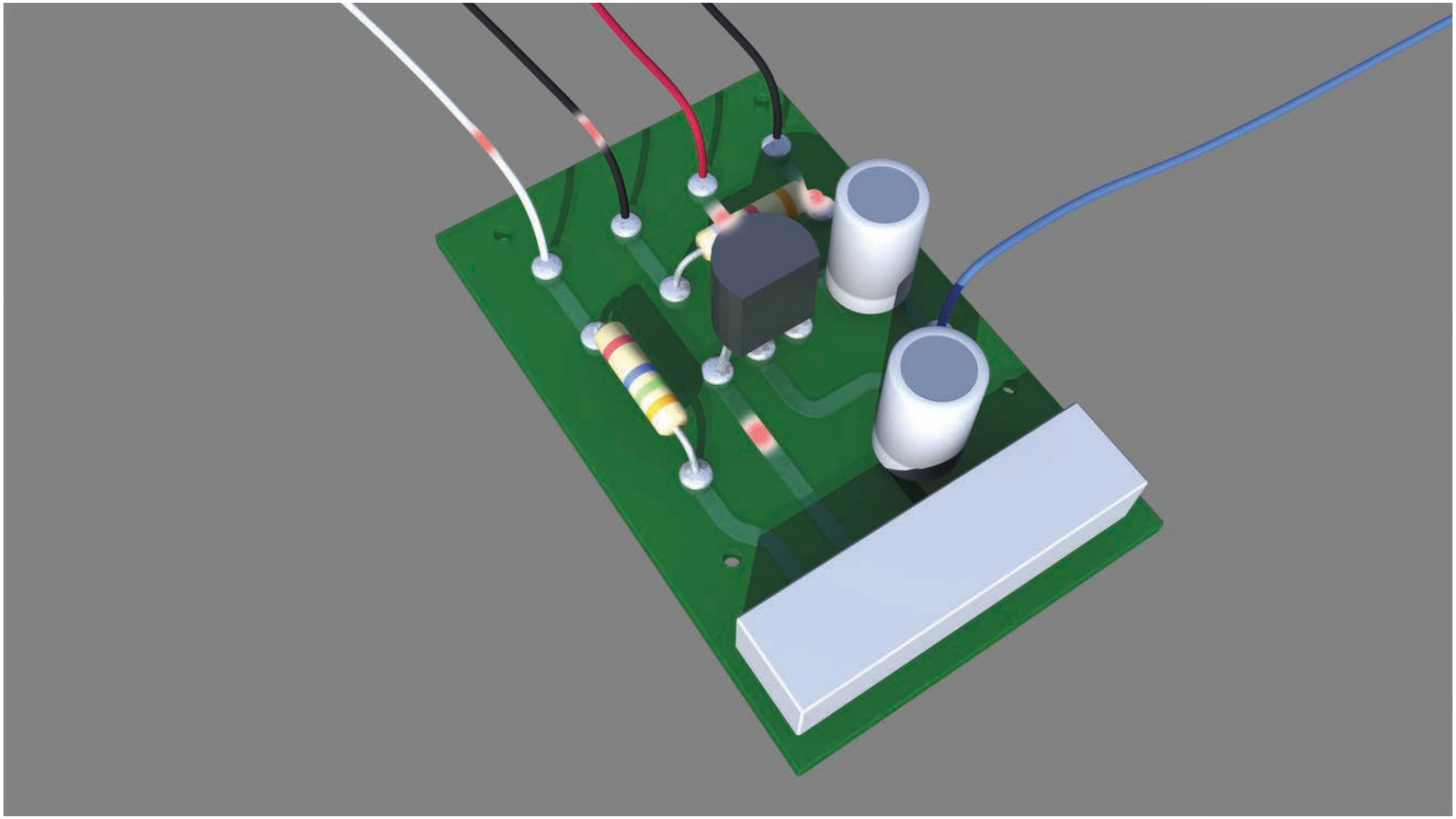


Microfluidics, to date, has been largely focused on the development of science and technology, and on scientific papers, <u>rather than on the solution of problems</u>

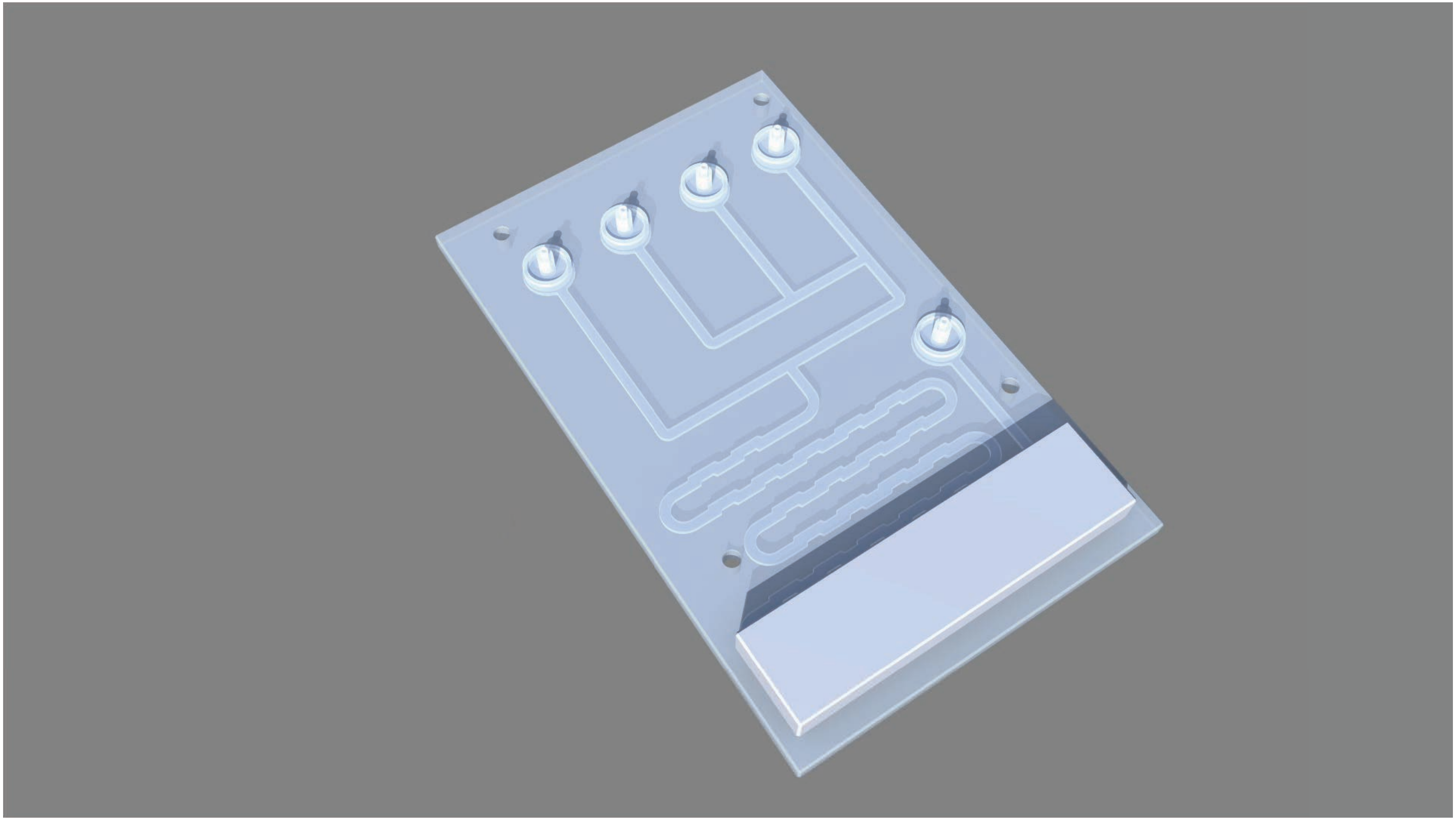
Editorial 'Solving Problems', George Whitesides, Lab Chip 10 (2010) 2317-2318

Microfluidics – Evolution….

Engineering Inspired → **BioInspired**

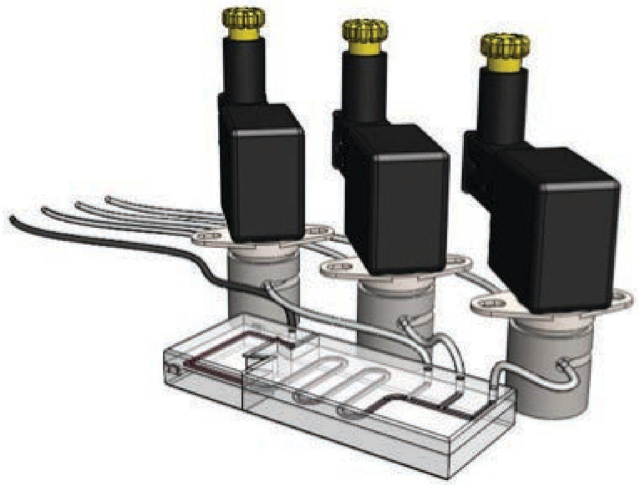


But not everything is integrated…..



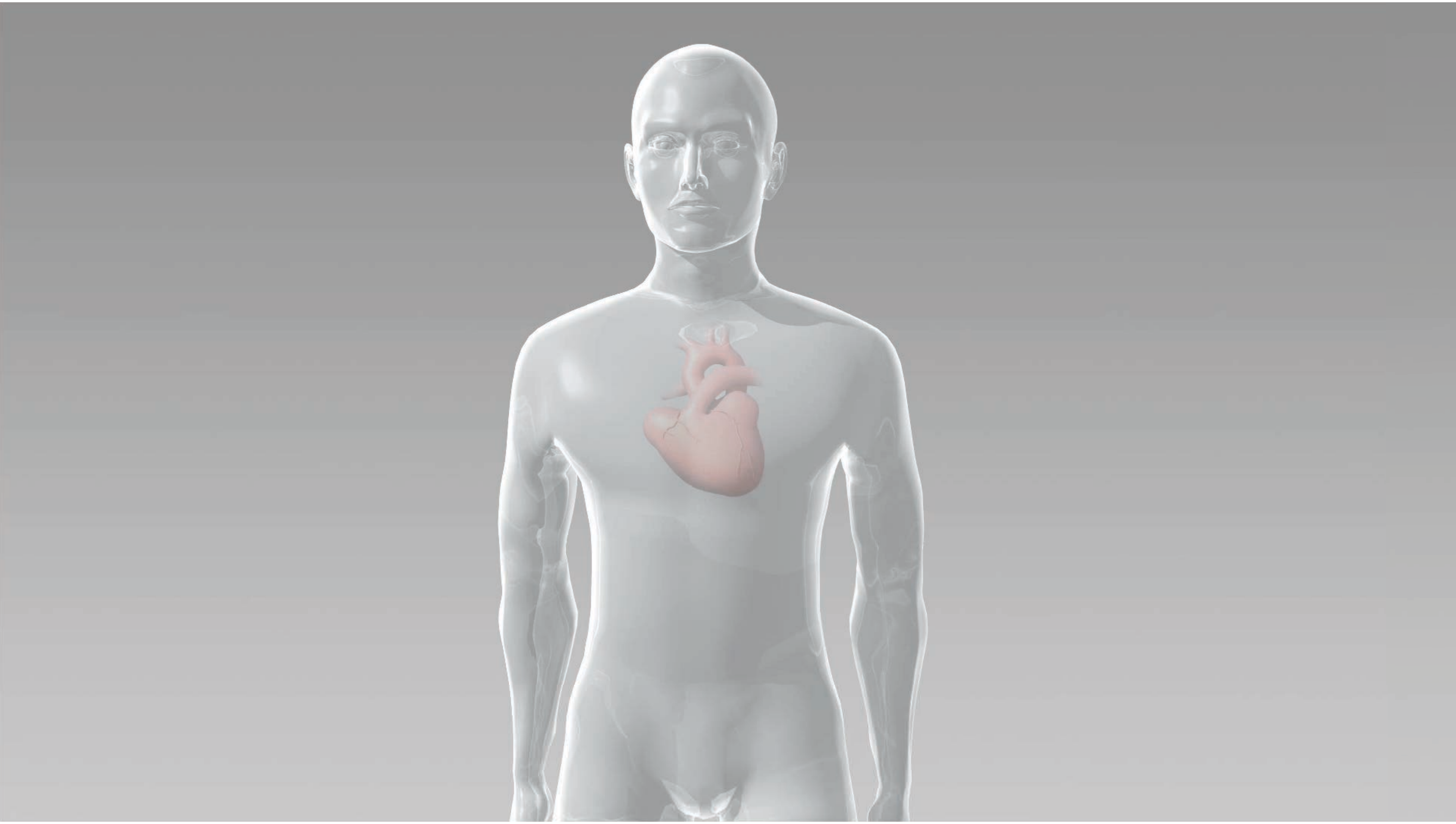
How to advance fluid handling in LOC platforms: re-invent valves (and pumps)!

- **Conventional valves cannot be easily scaled down - Located off chip: fluidic interconnects required**
  - Complex fabrication
  - Increased dead volume
  - Mixing effects
- **Based on solenoid action**
  - Large power demand
  - Expensive

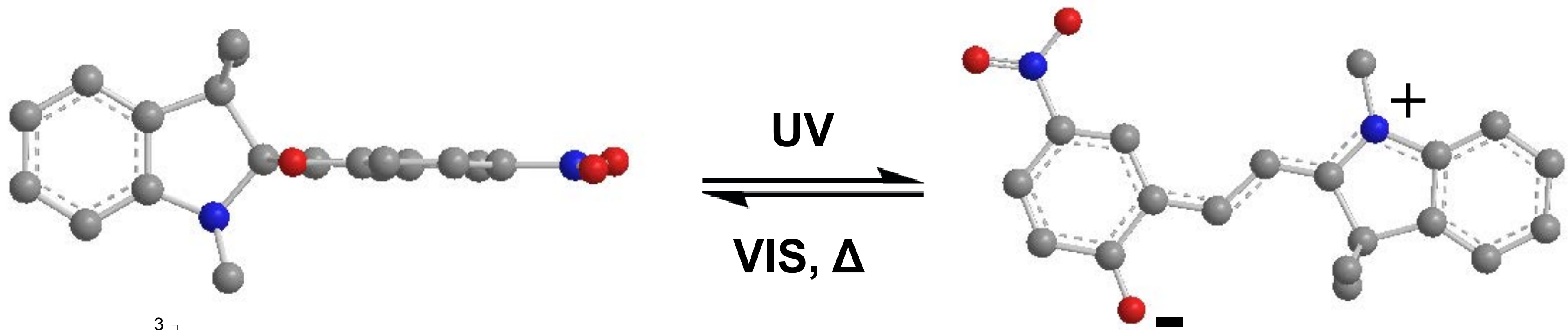


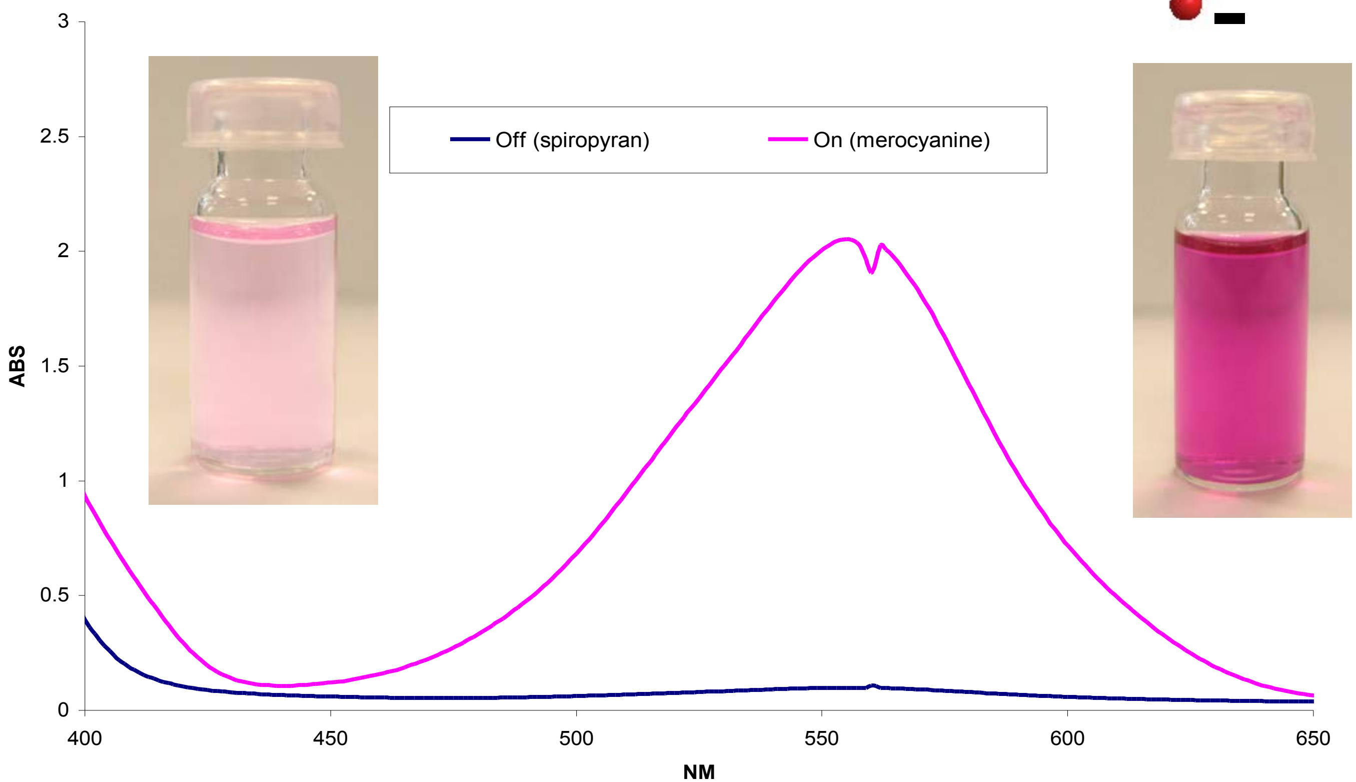
Solution: soft-polymer (biomimetic) valves fully integrated into the fluidic system

Bioinspired Fluidics



Photoswitchable Soft Actuators

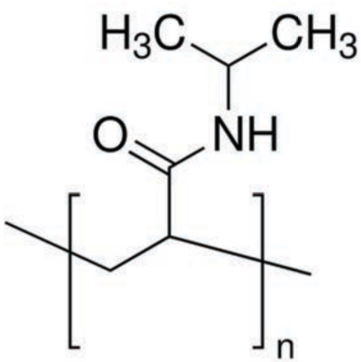




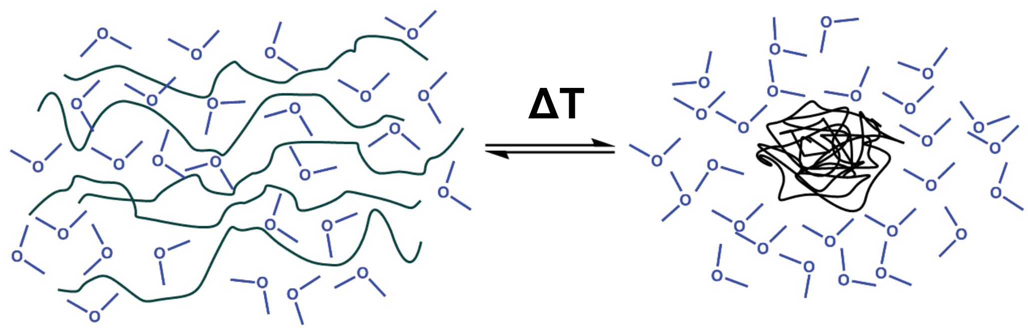
Poly(*N*-isopropylacrylamide)

- **pNIPAAM exhibits inverse solubility upon heating**
- **This is referred to as the LCST (Lower Critical Solution Temperature)**
- **Typically this temperature lies between 30-35^{o}C, but the exact temperature is a function of the (macro)molecular microstructure**
- **Upon reaching the LCST the polymer undergoes a dramatic volume change, as the hydrated polymer chains collapse to a globular structure, expelling the bound water in the process**

pNIPAAM

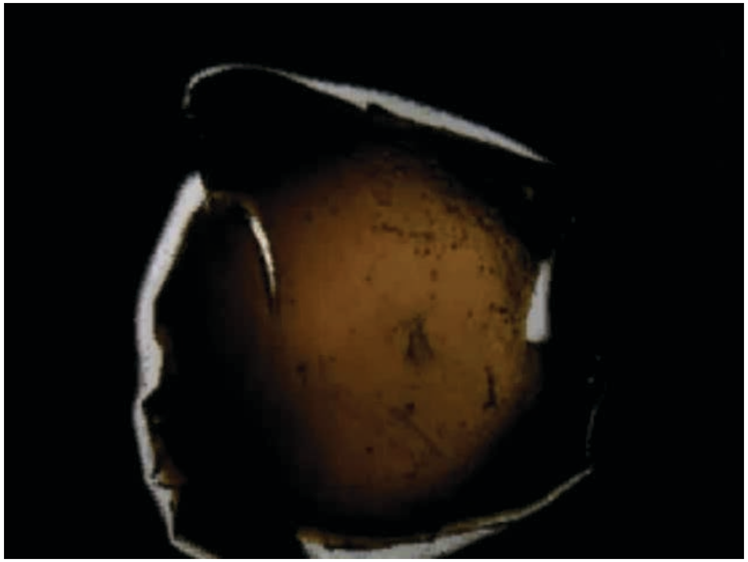


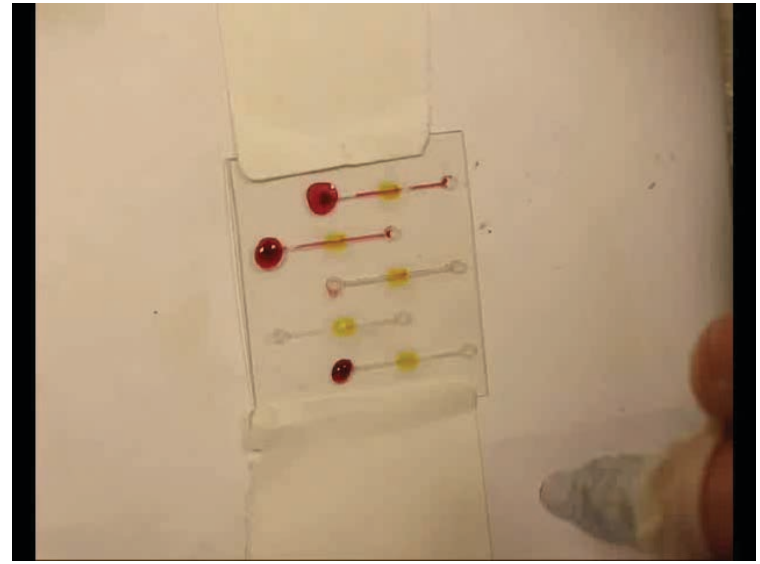
Hydrophilic **Hydrophobic**

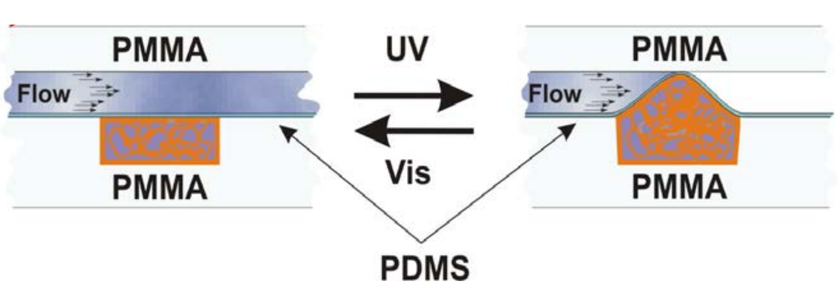


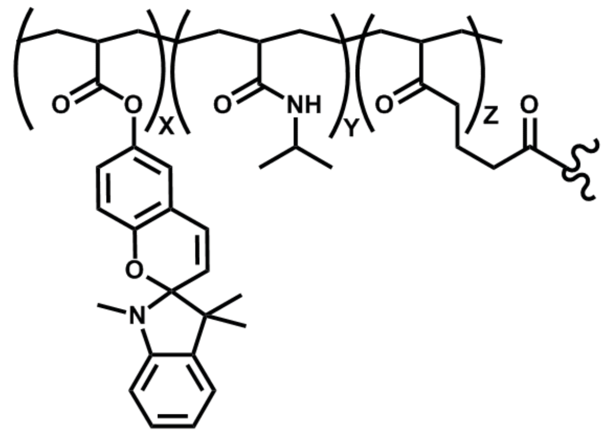
Hydrated Polymer Chains **Loss of bound water -> polymer collapse**

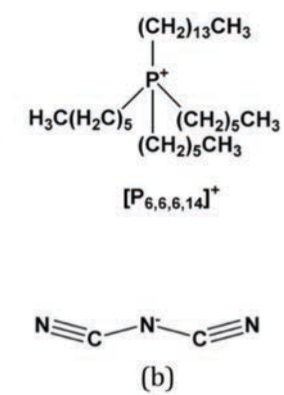
Photo-actuator polymers as microvalves in microfluidic systems









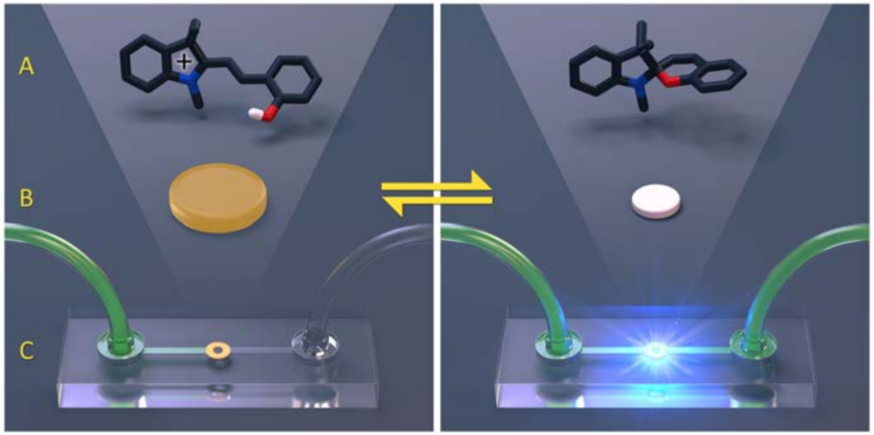


trihexyltetradecylphosphonium dicyanoamide $[P_{6,6,6,14}]^+[dca]^-$

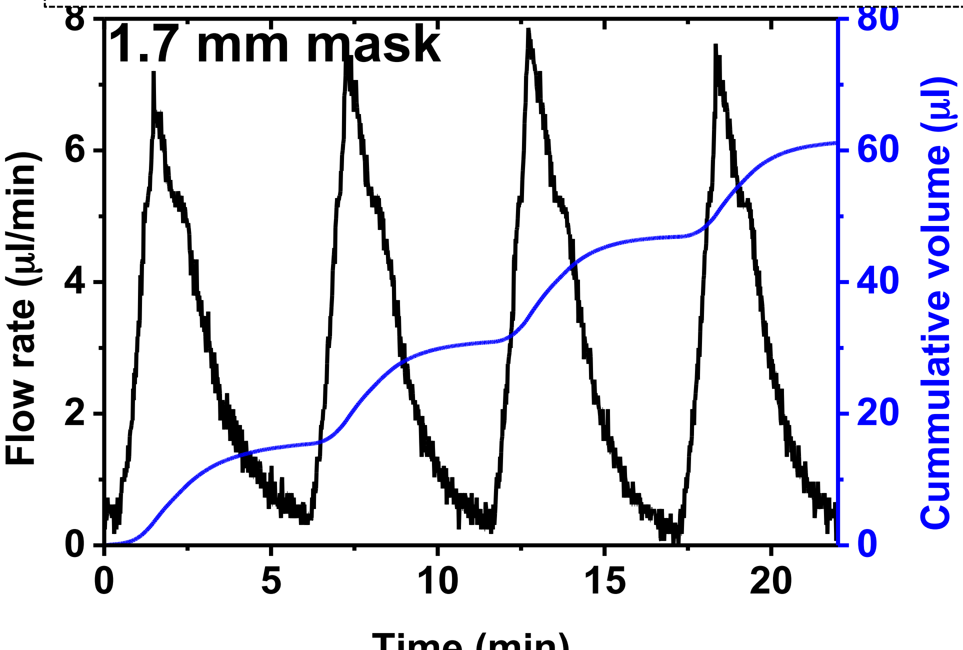
Ionogel-based light-actuated valves for controlling liquid flow in micro-fluidic manifolds, Fernando Benito-Lopez, Robert Byrne, Ana Maria Raduta, Nihal Engin Vrana, Garrett McGuinness, Dermot Diamond, Lab Chip, 10 (2010) 195-201.

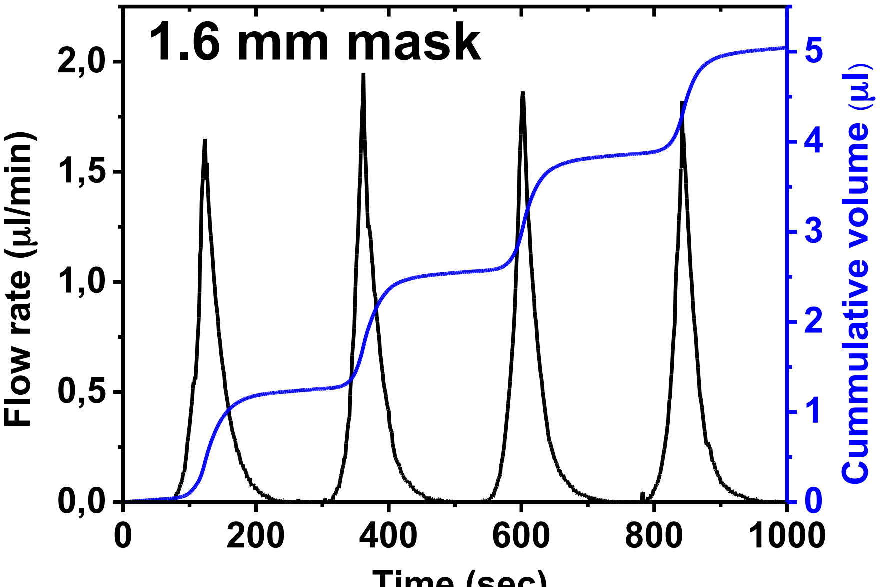
Valve Optimisation

**First example of actuating polymer gels as reusable valves for flow control on minute time scales
(> 50 repeat actuations)**

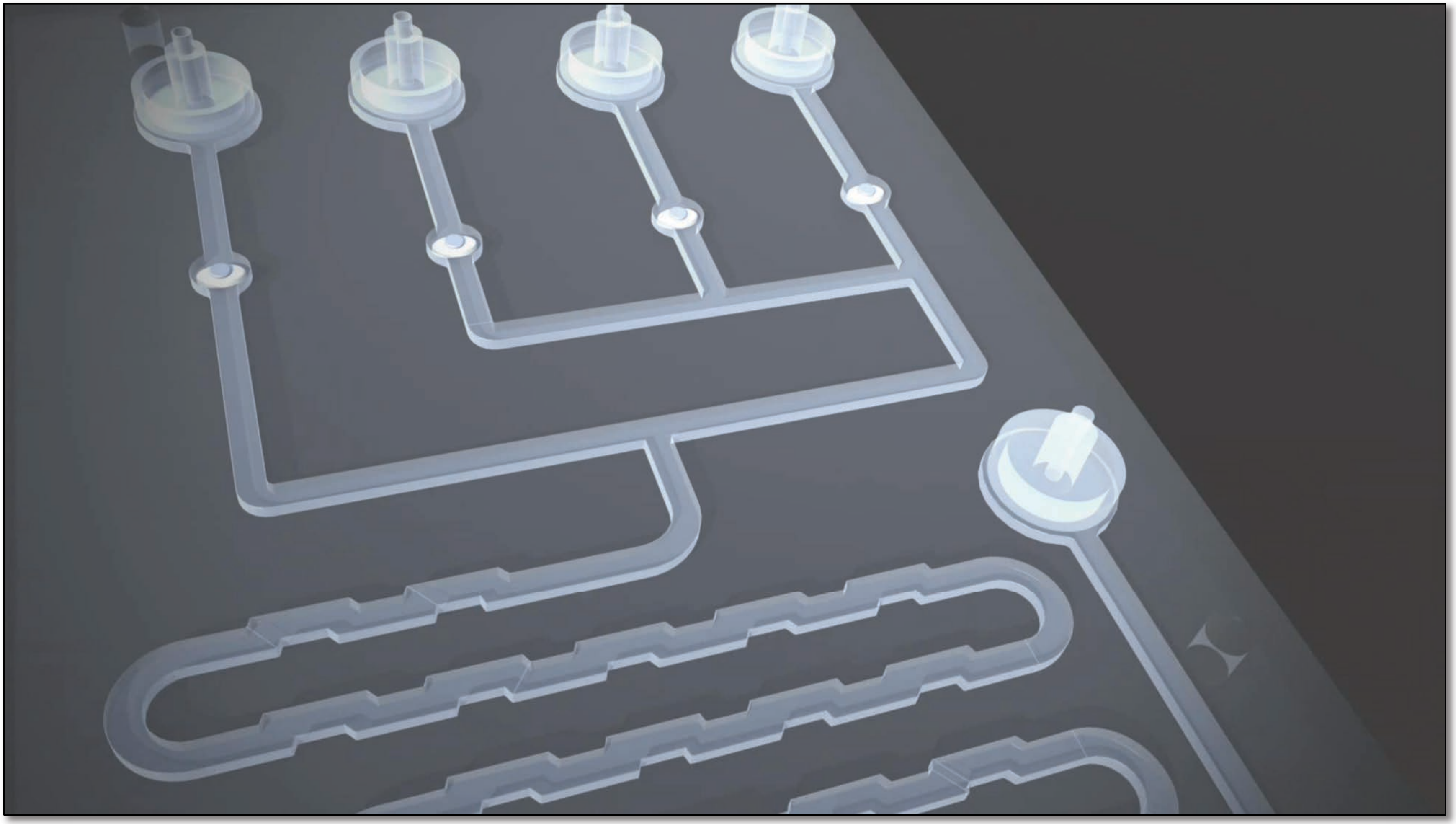


From *'Molecular Design of Light-Responsive Hydrogels, For in Situ Generation of Fast and Reversible Valves for Microfluidic Applications*', J. ter Schiphorst, S. Coleman, J.E. Stumpel, A. Ben Azouz, D. Diamond and A. P. H. J. Schenning, Chem. Mater., 27 (2015) 5925−5931. **(cover article)**

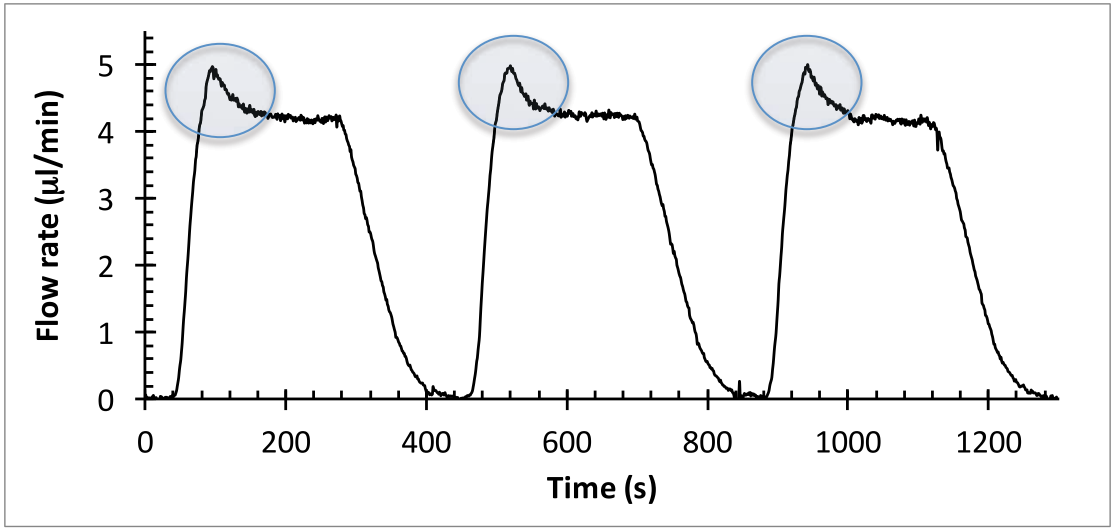




Photovalve Operation



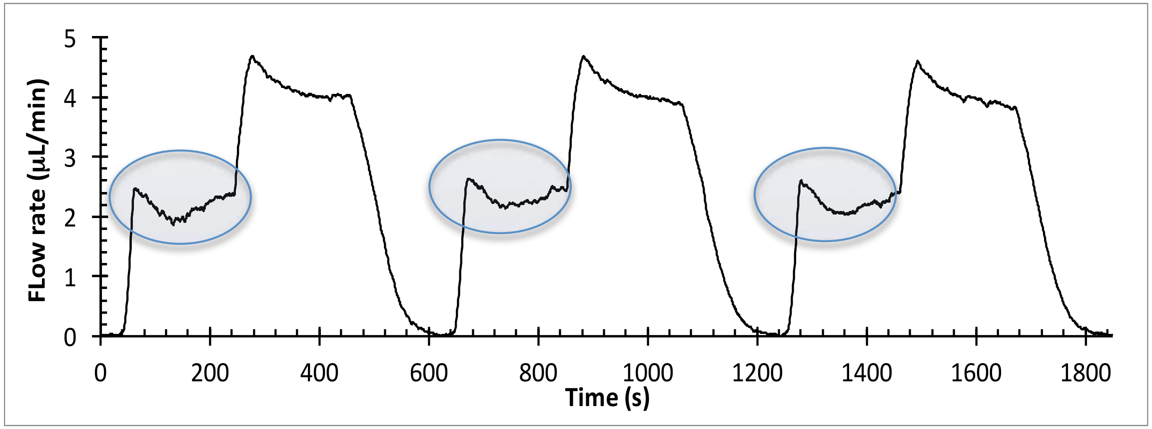
Photocontrolled Flow rate



- 60s LED on
- **180s pulsed LED (1s on, 2s off)**
- 180s LED off

Levels out ca. 4.0 µl/min

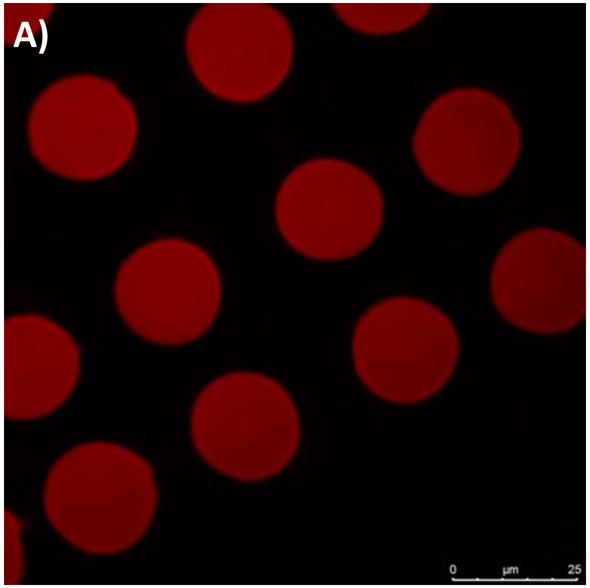
- 30s LED on
- **180s pulsed LED (1s on, 2s off)**
- 30s LED illumination
- **180s pulsed LED (1s on, 2s off)**
- 180s LED off

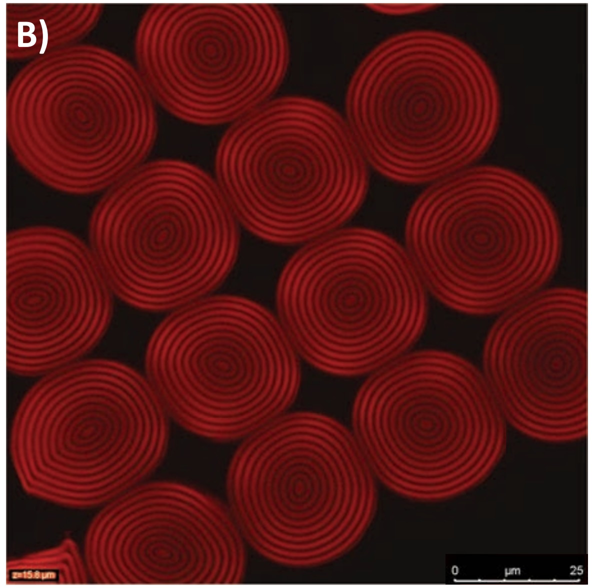


(1) Overshoot, and (2) Steady-state flow rate for this pulse sequence is ca.4.0 µL/min

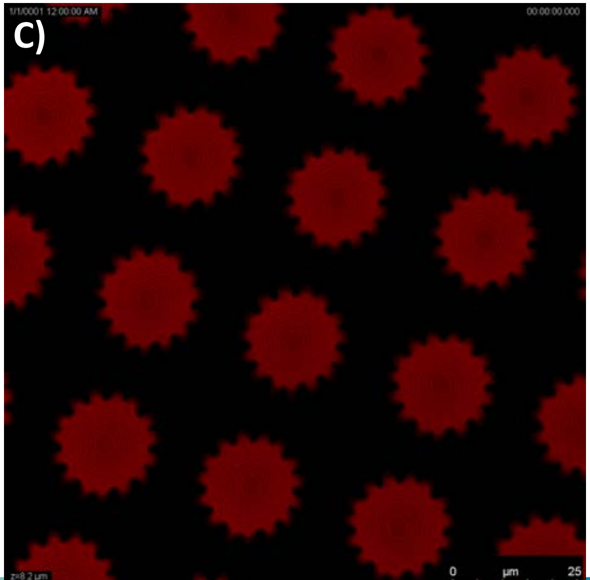
Coleman, S.; ter Schiphorst, J.; Ben Azouz, A.; Bakker, S.; Schenning, A. P. H. J.; Diamond, D. Tuning Microfluidic Flow by Pulsed Light Oscillating Spiropyran-Based Polymer Hydrogel Valves. Sensors and Actuators B: Chemical 2017, 245, 81–86.

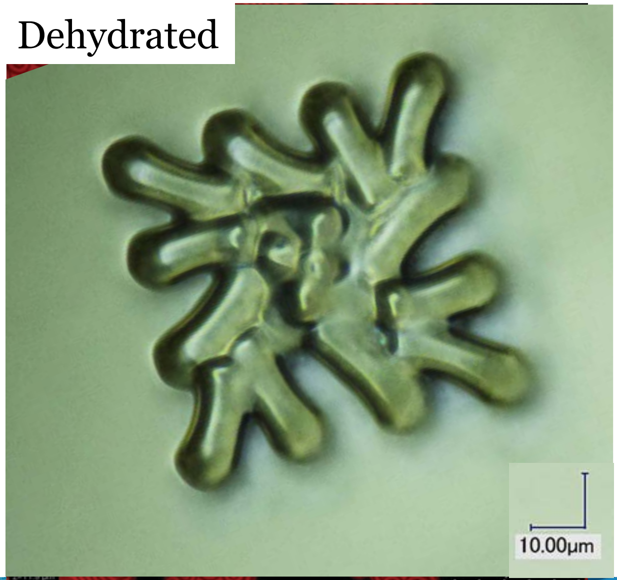
Endo-Skeleton Controlled Actuation





Microscope images of micro-scale pillar array fabricated in PIL hydrogels by 2-PP showing the collapsed pillars before hydration (left) and after hydration (middle and right). The concentric contour slicing pattern used to create the microstructure is visible in the swollen hydrated structures and are very clear in the high resolution STED image (right) of rodamine modified hydrogels. The hydration process is fully reversible and shows shape-memory behaviour. (DCU unpublished results)





The future?

Flexible Conformable Displays…
Flexible, Conformable Fluidics

But ultimately
3D 'Soft' Self-Aware
Fluidics….

Thanks to…..

- Members of my research group: Simon Coleman, Peter McCluskey, Colm Delaney, Nigel Kent, Jeff Whyte, Aymen Ben Azouz, Jeroen ter Schiphorst, Albert Schenning

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MASK
Project no: 269302
Materials and Advanced Sensor Knowledge Exchange