‘Bio-inspired Microfluidics’

Dermot Diamond

Insight Centre for Data Analytics, National Centre for Sensor Research
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Invited Seminar Presented at the NBMC Workshop;

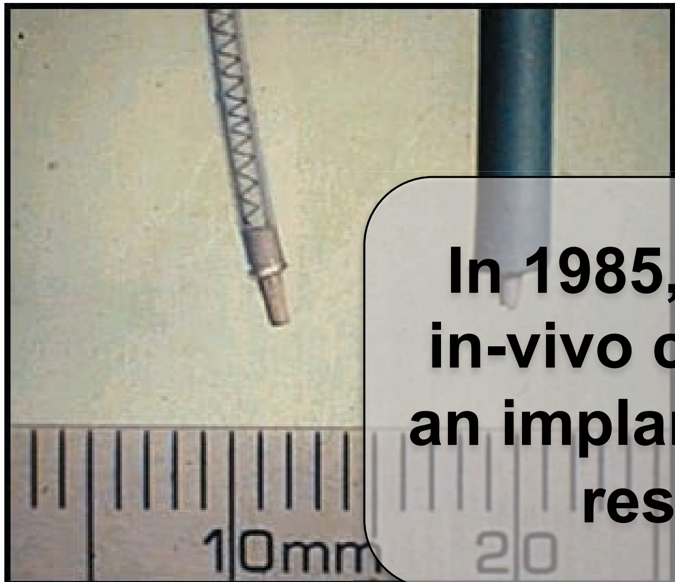
‘Blood, Sweat and Tears’

Lockheed Martin, Arlington, Virginia

November 2-3 2016

Blood Analysis; Implantible Sensors

In 1985, the use model for reliable in-vivo continuous monitoring with an implantable chemical sensor was restricted to a day or two



1985: Catheter Electrodes for intensive care – function for 24 hrs

Dr. David Band, St Thomas's Hospital London

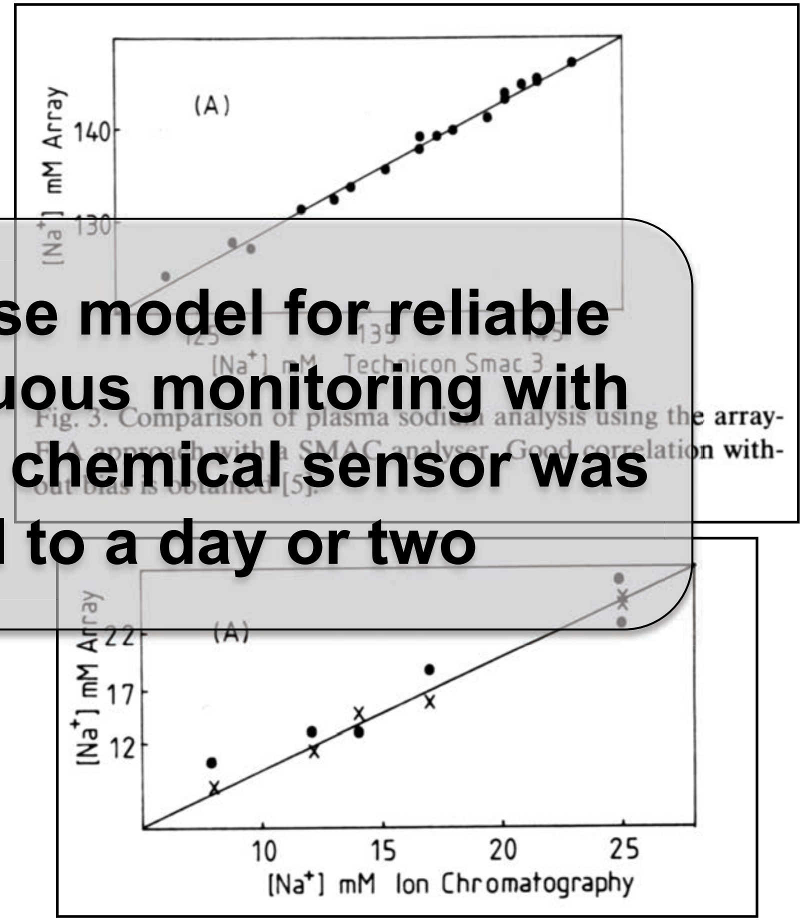
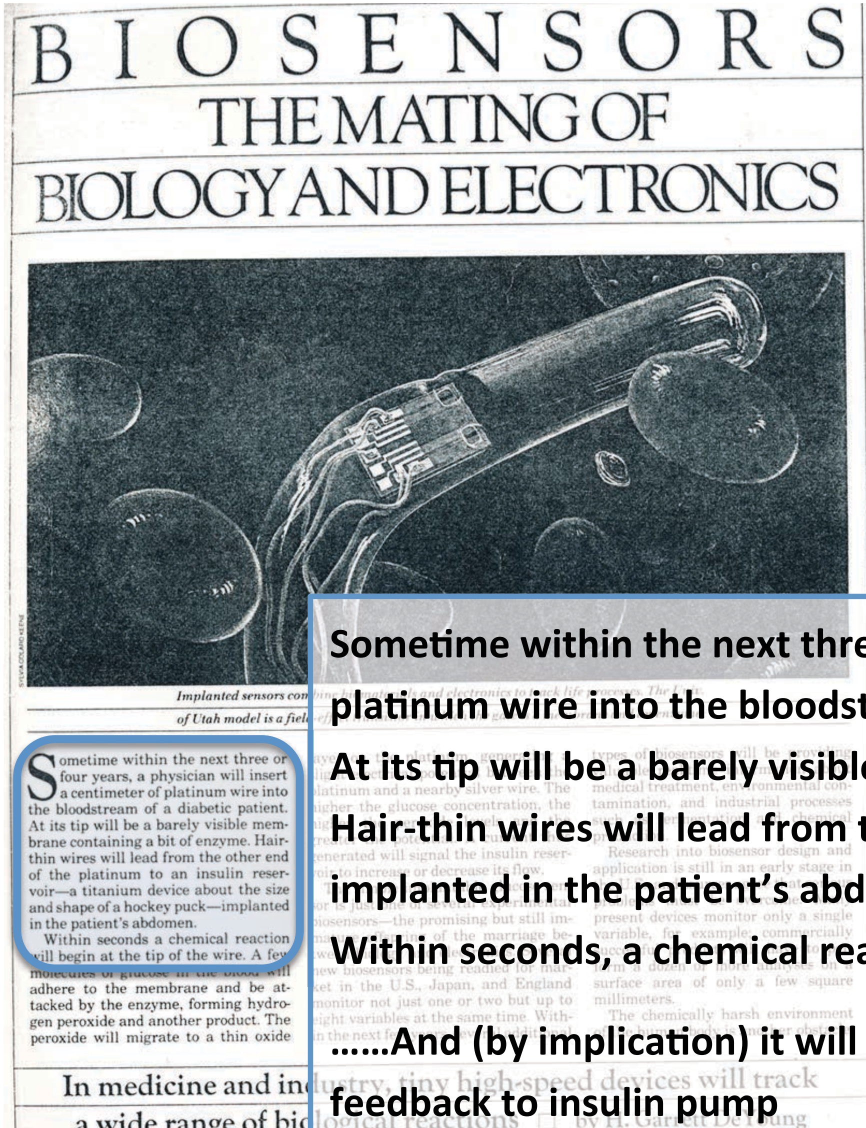


Fig. 3. Comparison of plasma sodium analysis using the array-FIA approach with a SMAC analyser. Good correlation without bias is obtained [5].

Anal. Chem., *64* (1992) 1721-1728.

Ligand (and variations of) used in many clinical analysers for blood Na^+ profiling

The (broken) promise of biosensors…..



BIOSENSORS

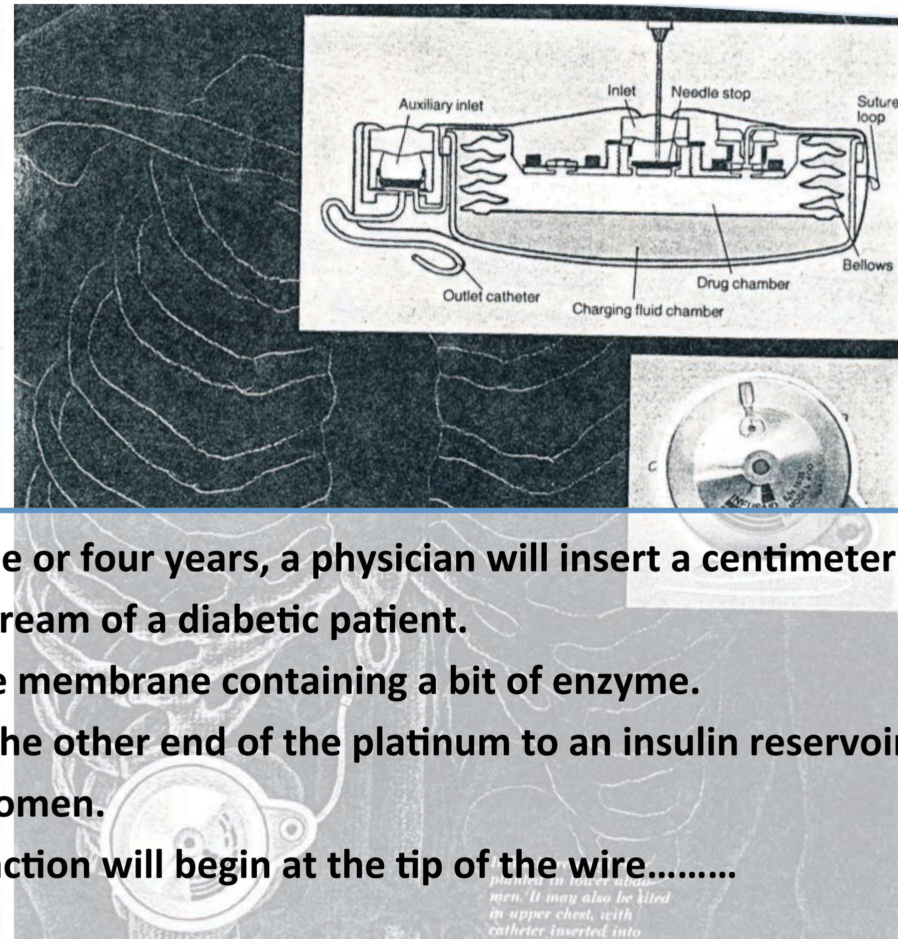
THE MATING OF BIOLOGY AND ELECTRONICS

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 molecules of glucose in the blood will 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



Sometime within the next three or four years, a physician will insert a centimeter of platinum wire into the bloodstream of a diabetic patient.

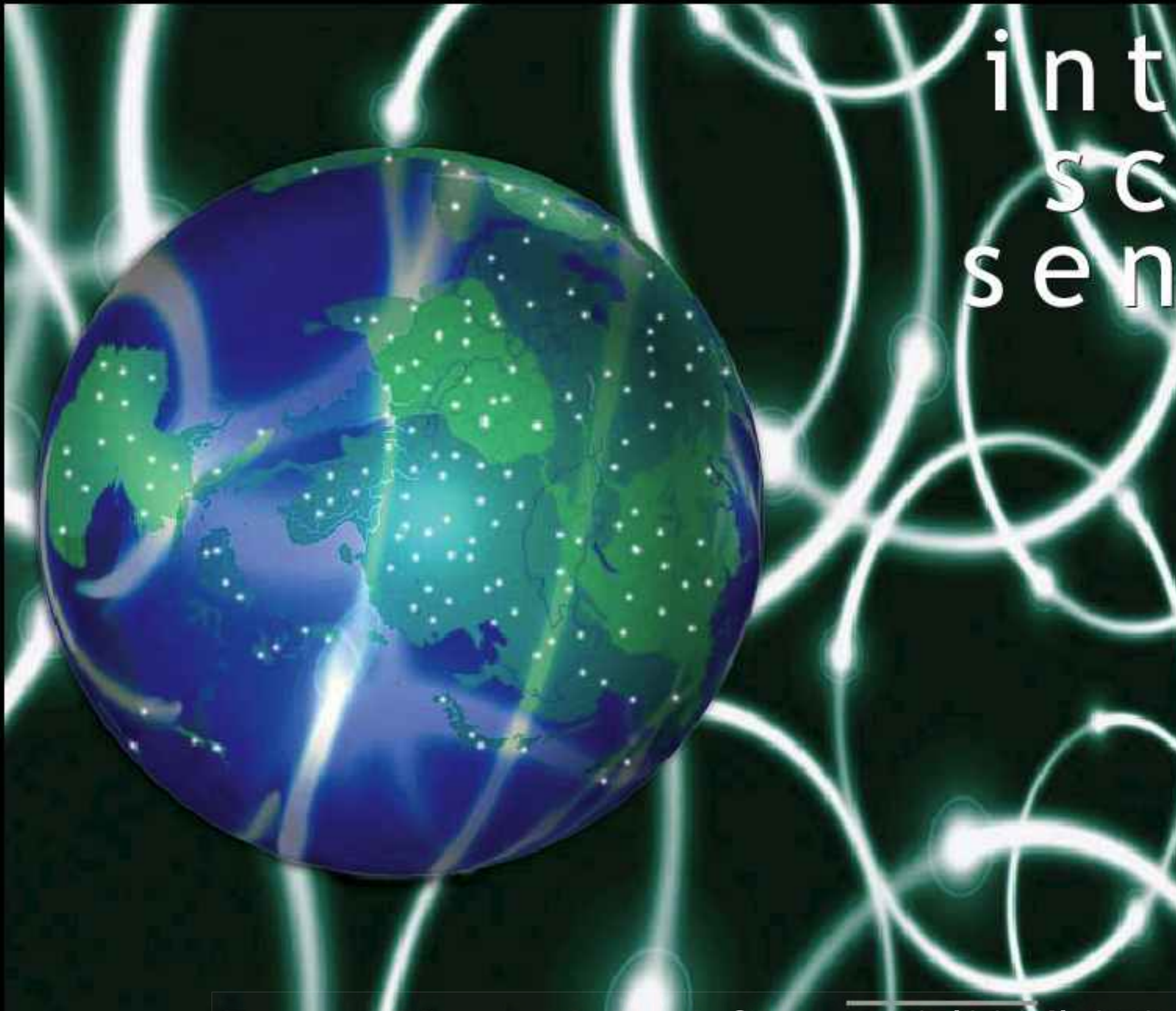
At its tip will be a barely visible membrane containing a bit of enzyme.

Hair-thin wires will lead from the other end of the platinum to an insulin reservoir 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

Keynote Article: August 2004, Analytical Chemistry (ACS)



internet scale sensing

Dermot Diamond
Dublin City University
(Ireland)

Incredible advances in digital communications and computer power have profoundly changed our lives. One chemist shares his vision of the role of analytical science in the next communications revolution.

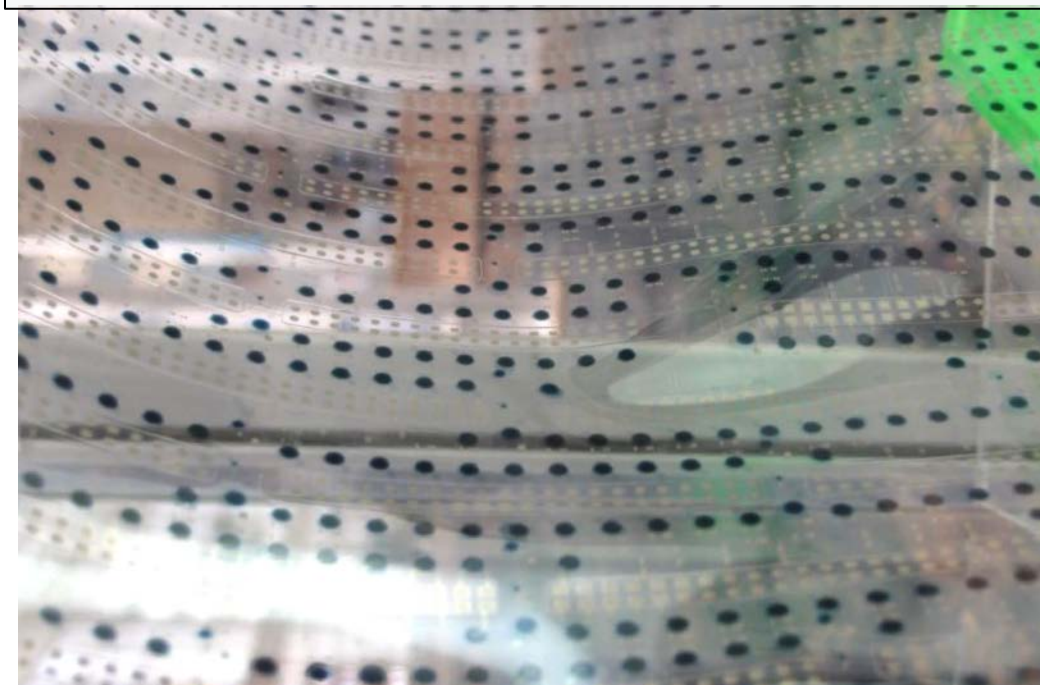
Digital communications networks are at the heart of modern society. The digitization of communications, the development of the Internet, and the availability of relatively inexpensive but powerful mobile computing technologies have established a global communications network capable of linking billions of people, places, and objects. Email can instantly transmit complex documents to multiple remote locations, and websites provide a platform for instantaneous notification, dissemination, and exchange of information globally. This technology is now pervasive, and those in research and business have multiple interactions with this digital world every day. However, this technology might simply be the foundation for the next wave of development that will provide a seamless interface between the real and digital worlds.

The crucial missing part in this scenario is the gateway through which these worlds will communicate: How can the digital world sense and respond to changes in the real world? Analytical scientists—particularly those working on chemical sensors, biosensors, and compact, autonomous instruments—are

Dermot Diamond, Anal. Chem., 76 (2004) 278A-286A
(Ron Ambrosio & Alex Morrow, IBM TJ Watson)

Glucose Sensors

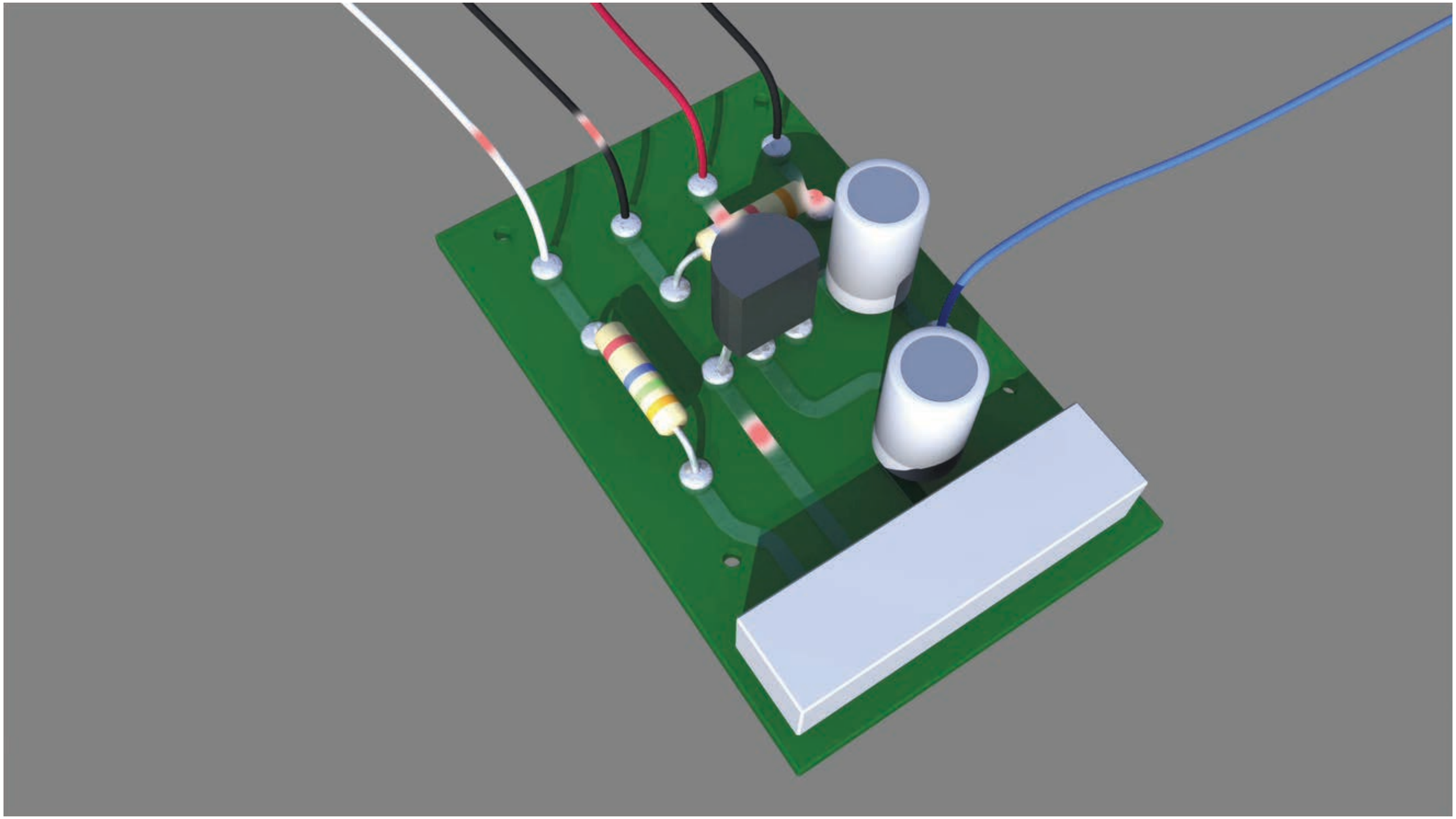
Abbott Diabetes (Ireland)
manufactures 100,000's of electrodes per week using high volume printing to deposit highly accurate amounts of materials in precise locations; (carbon tracks and substrate layer, glucose oxidase enzyme layer, mediator layer..)



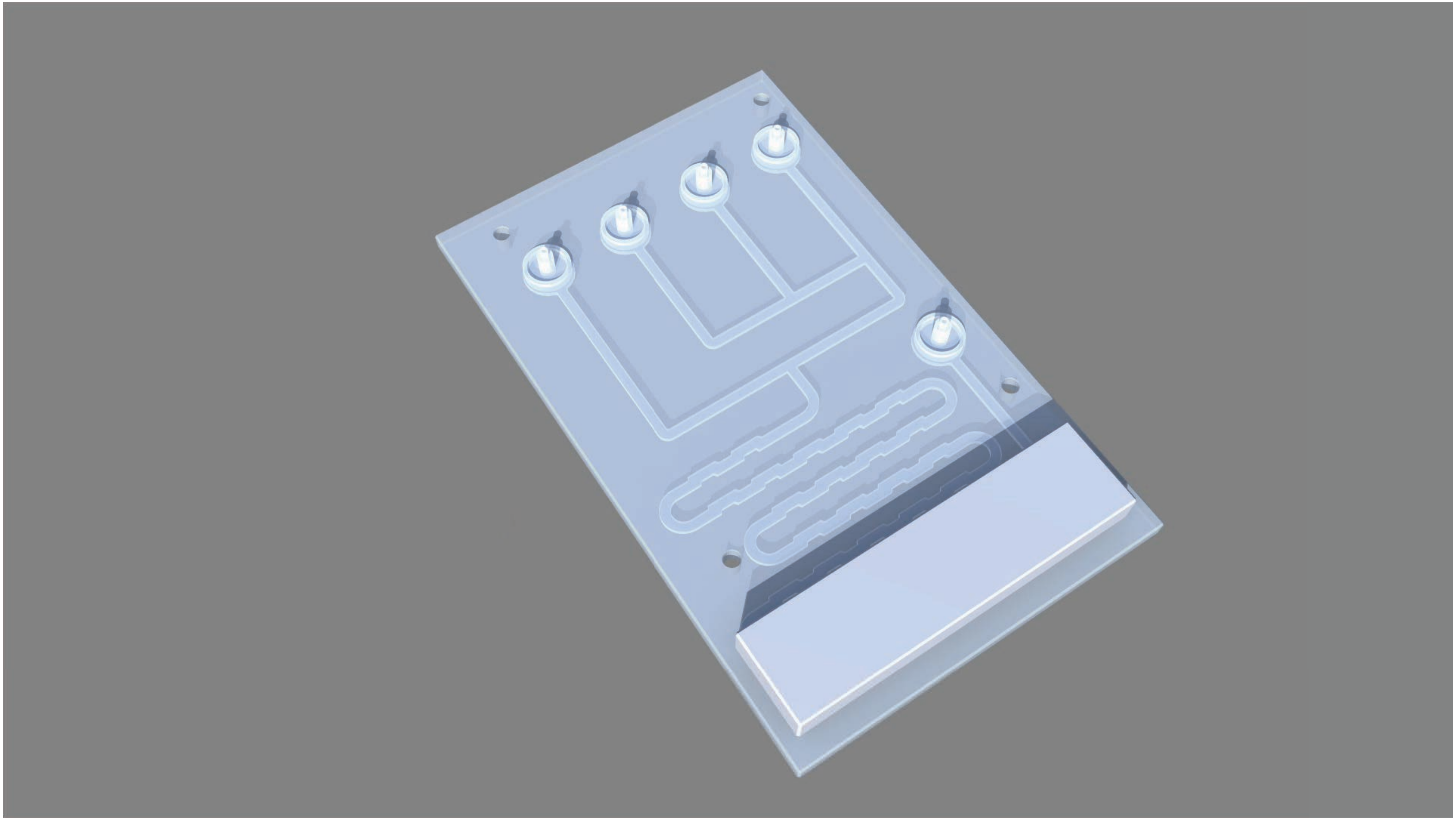
Accuracy in use depends on;
- **Very reproducible manufacturing with stable, reliable materials**
- **Testing of representative sub-populations of sensors**
- **Single shot use model**

Microfluidics – Evolution….

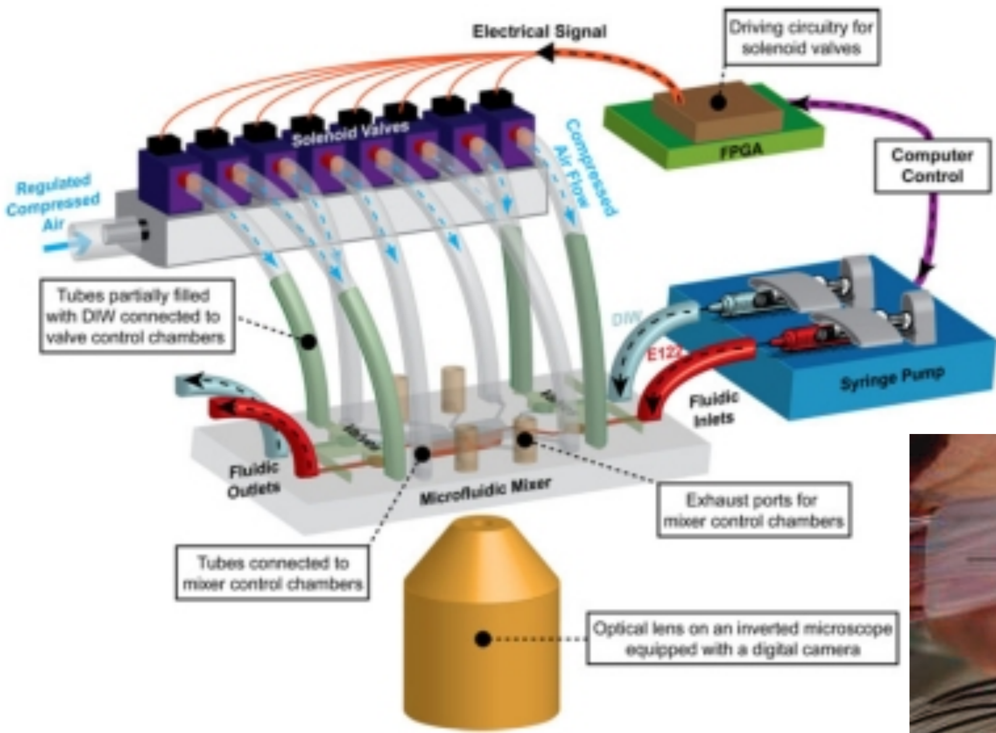
Engineering Inspired → **BioInspired**



But not everything is integrated…..



But not everything is integrated…..

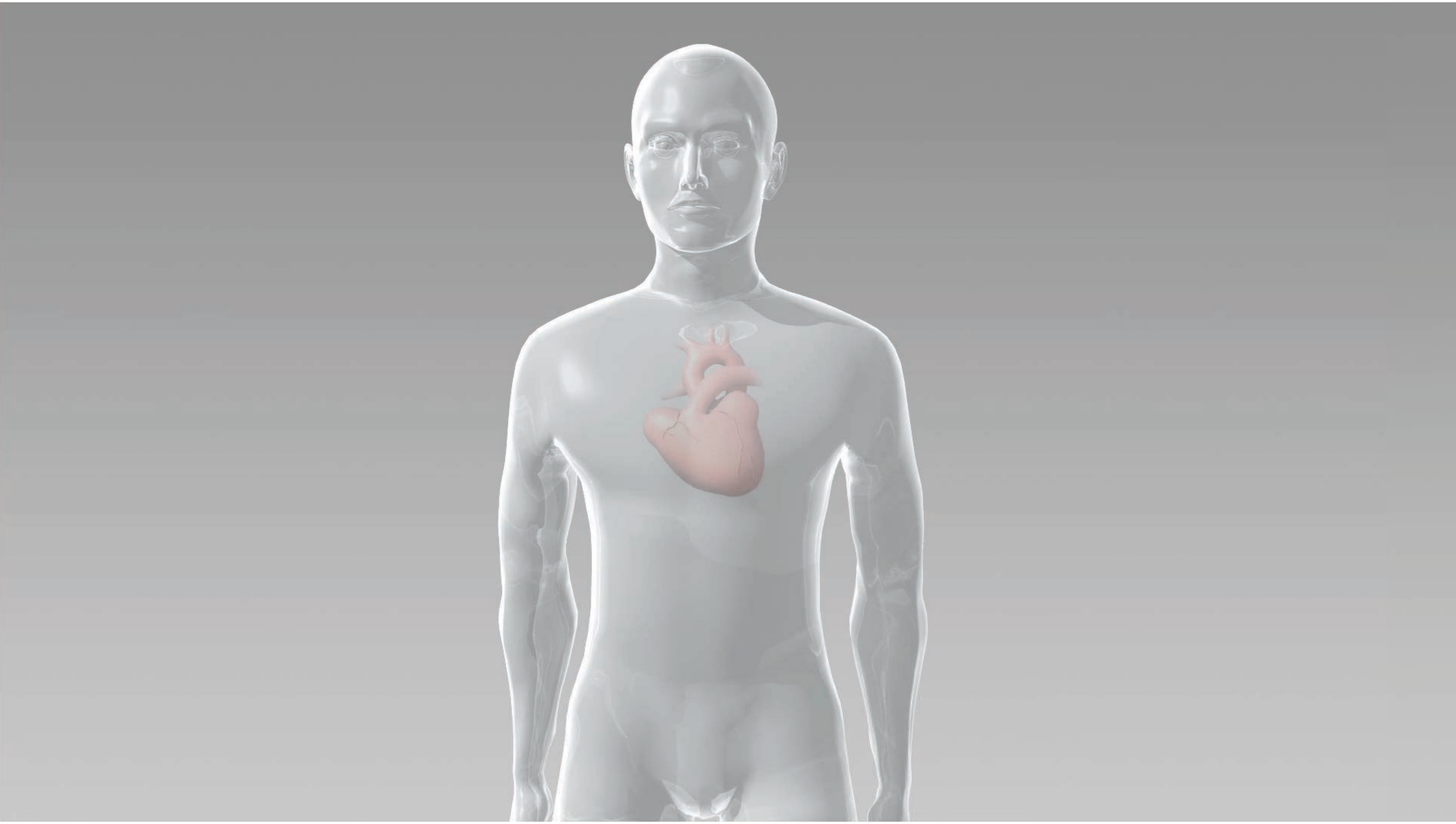


- Many components are located off-chip
- Detectors, pumps, valves….
- Hard Materials

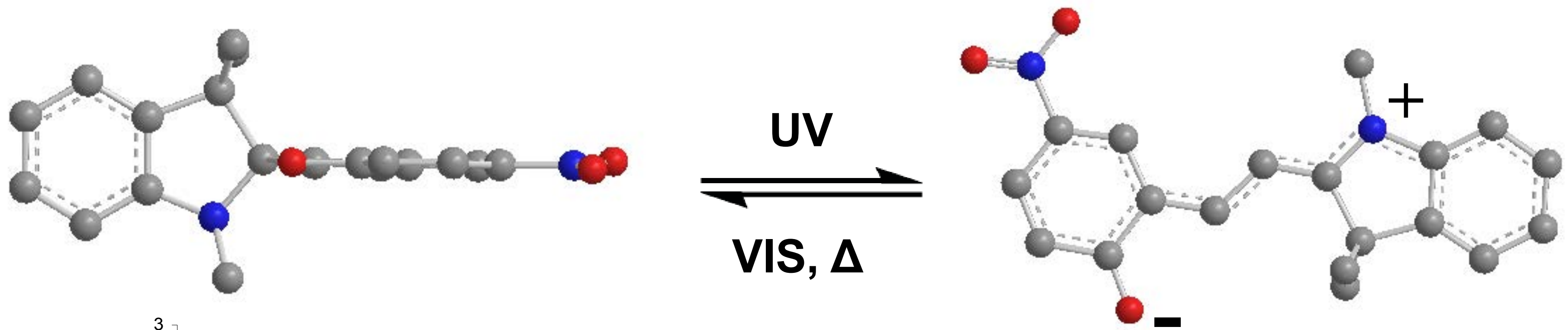
- Fluidic Interconnects can get very messy
- Most of the 'Chip' has no function

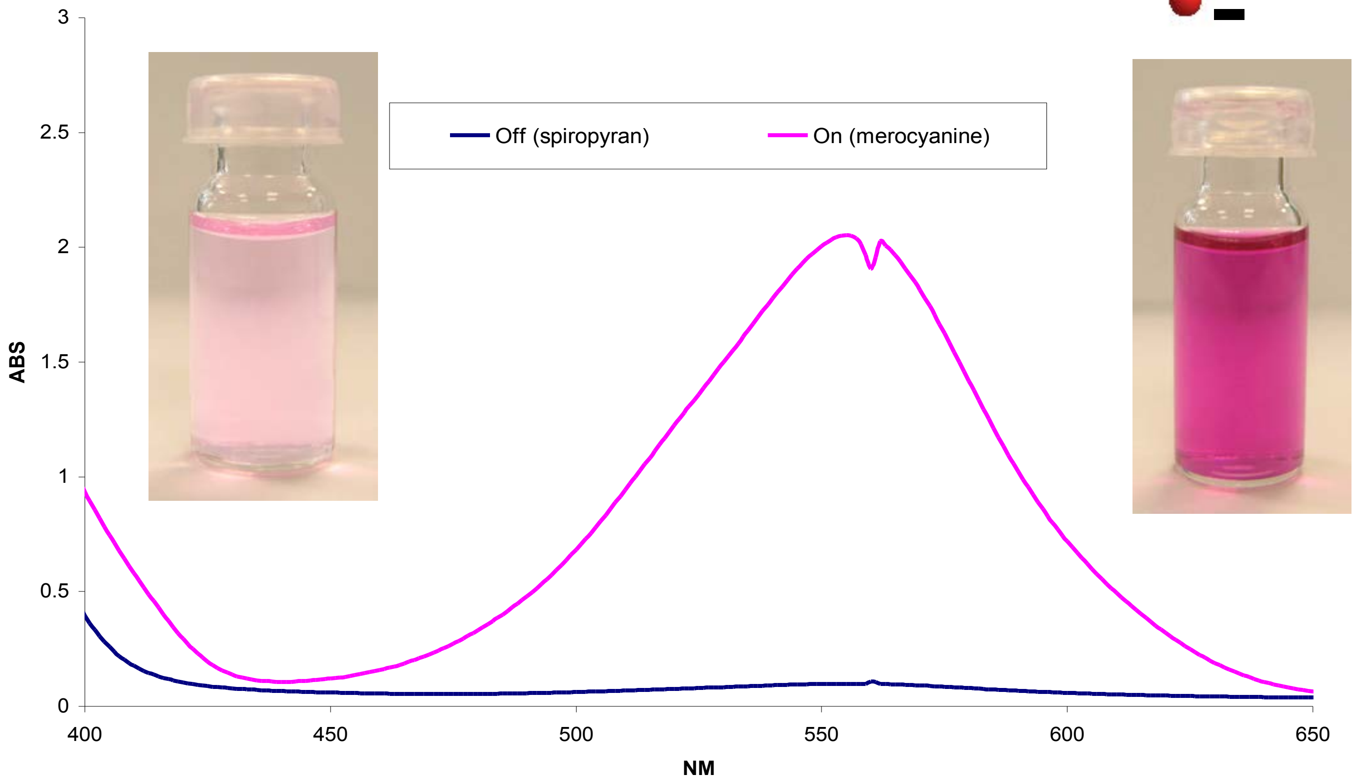
http://www.eetimes.com/document.asp?doc_id=1171478

Bioinspired Fluidics



Photoswitchable Actuators

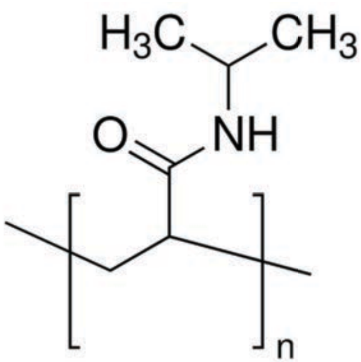




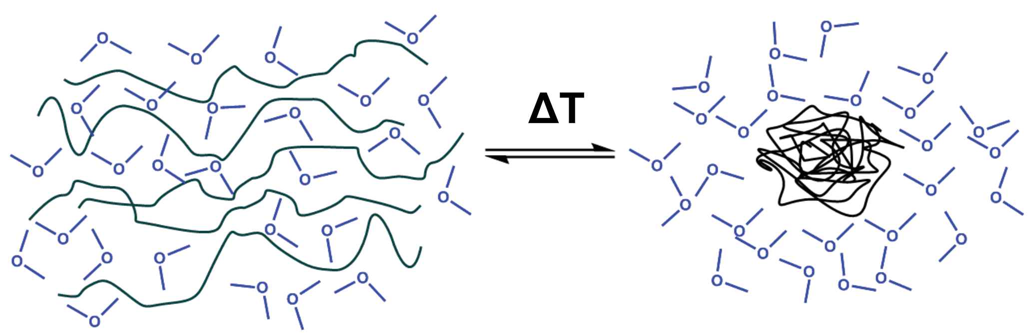
Poly(*N*-isopropylacrylamide)

- **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

Integrated Soft Gel Photovalves

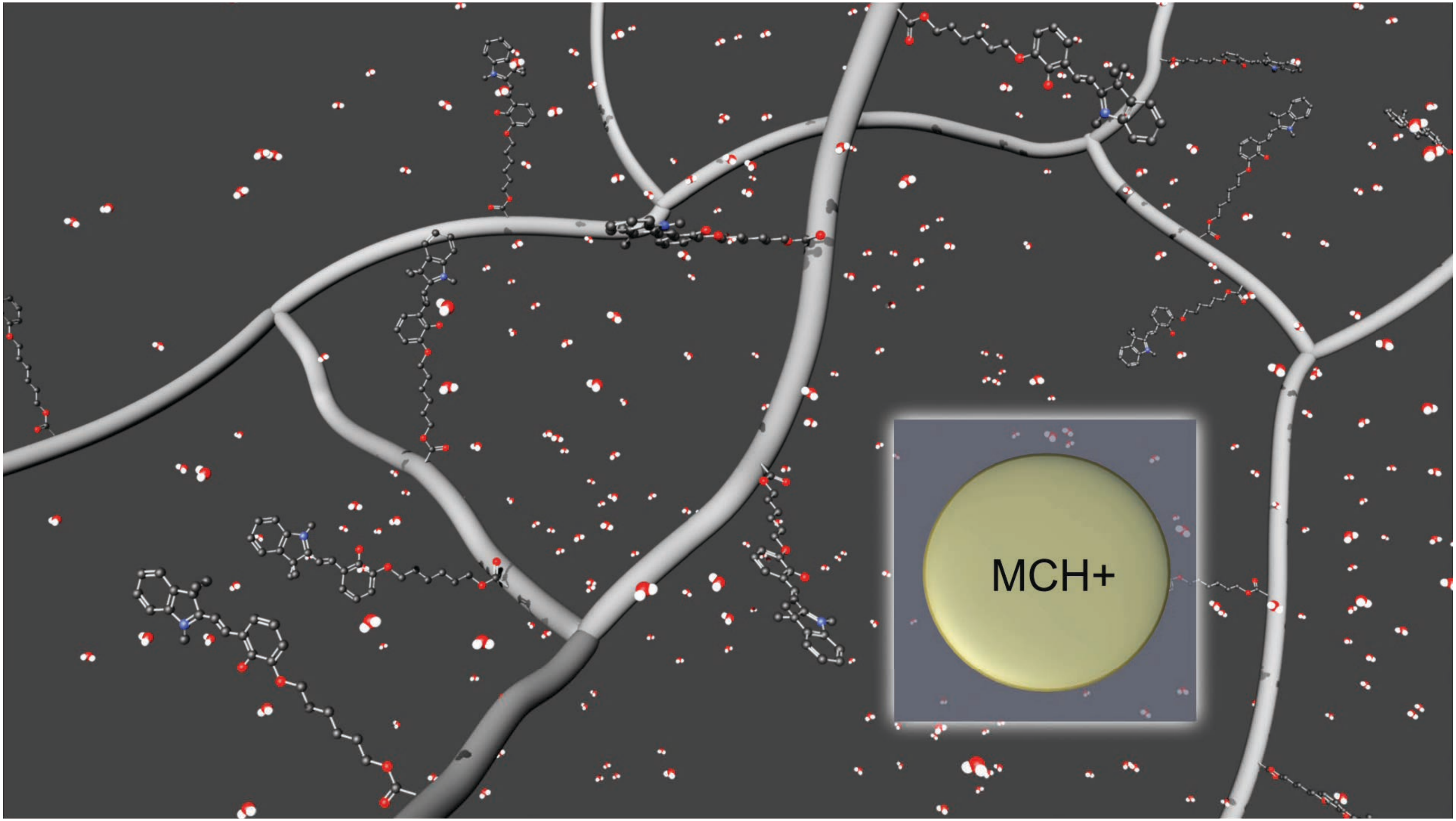
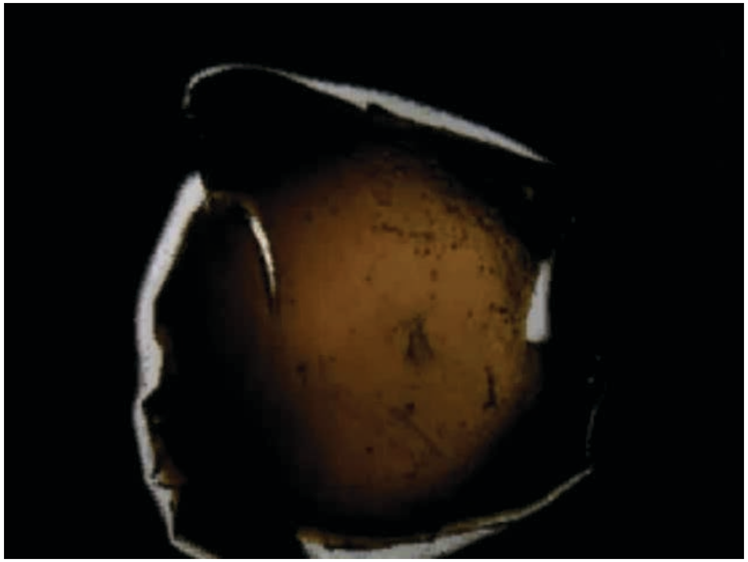
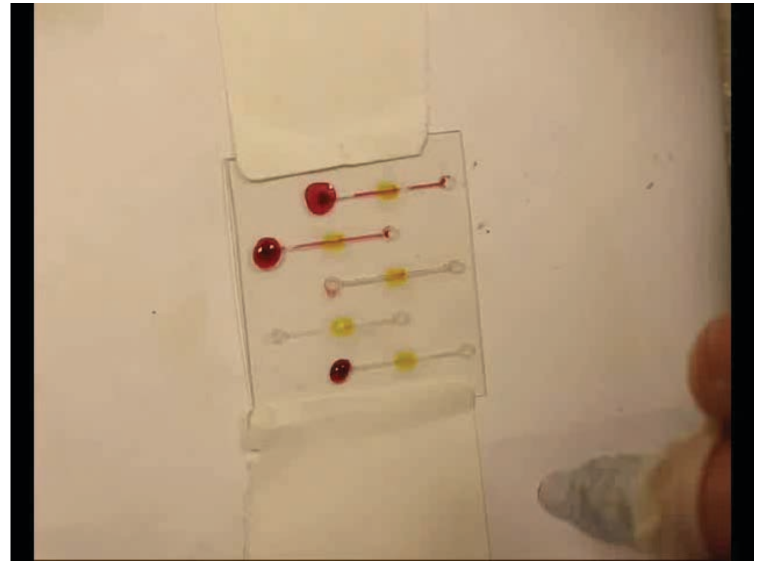
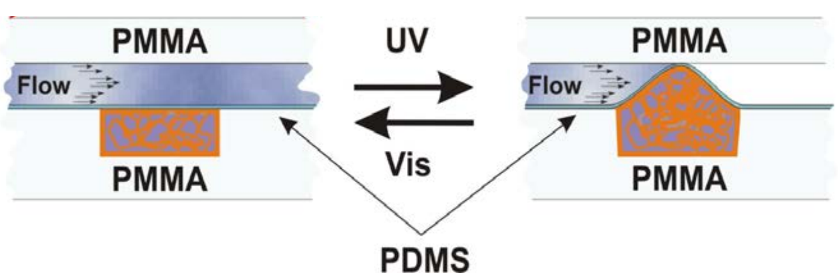
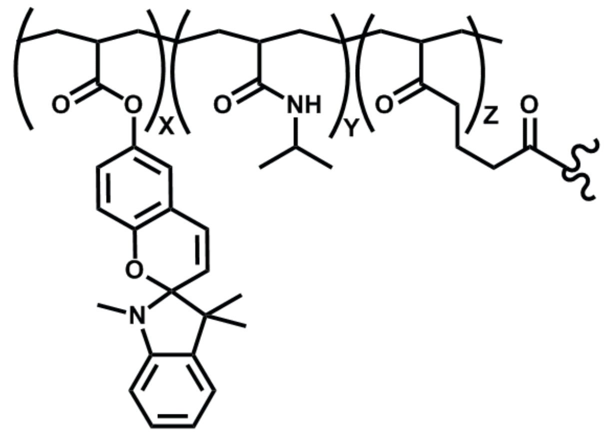


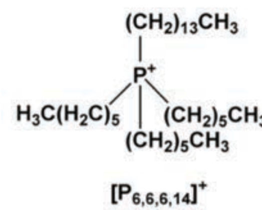
Photo-actuator polymers as microvalves in microfluidic systems

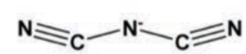










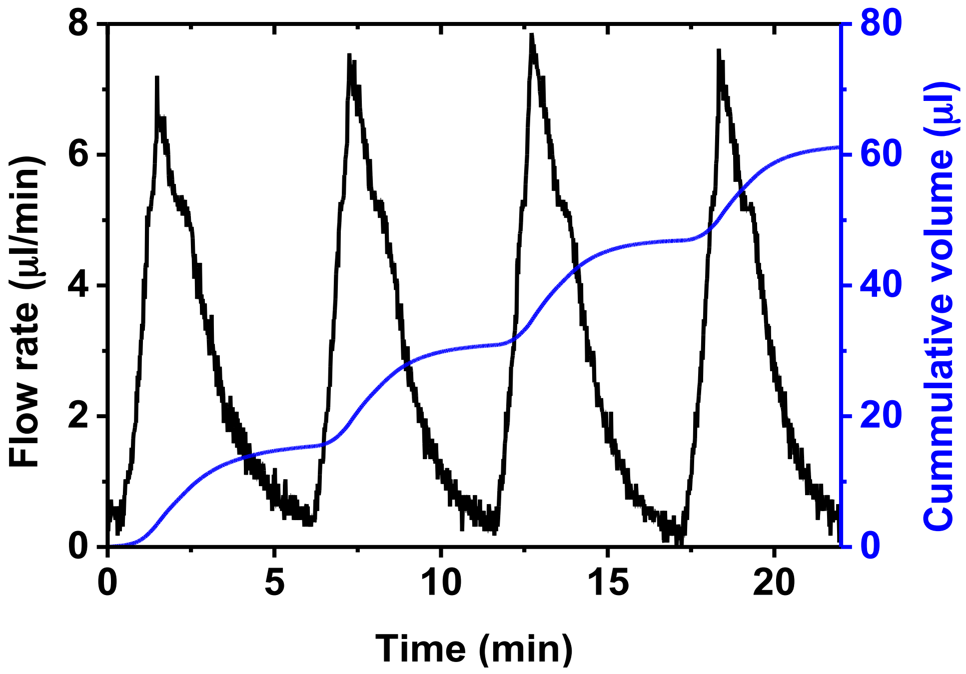


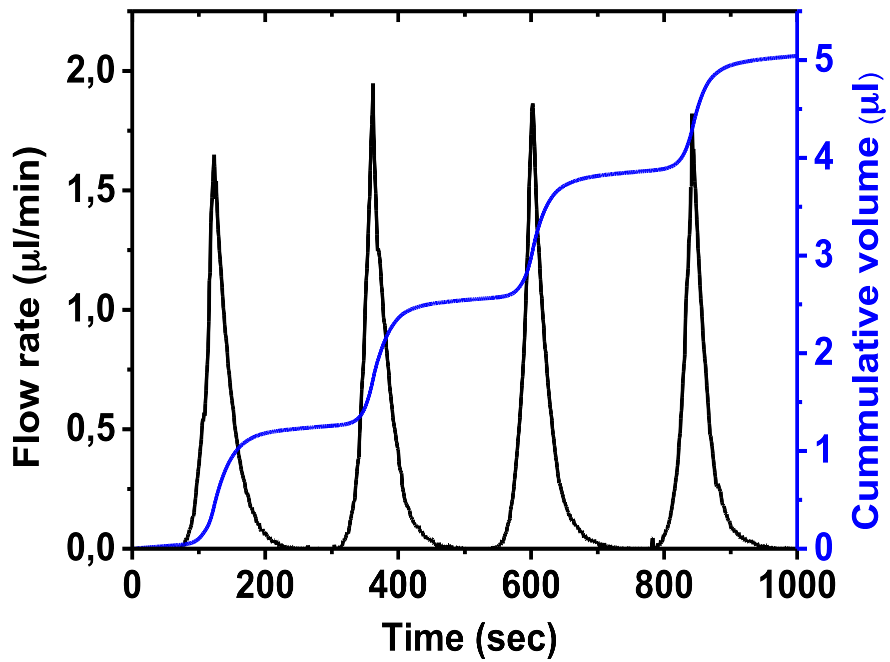
(b)

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.

Optimisation of valve dimensions





1.7 mm mask **1.6 mm mask**

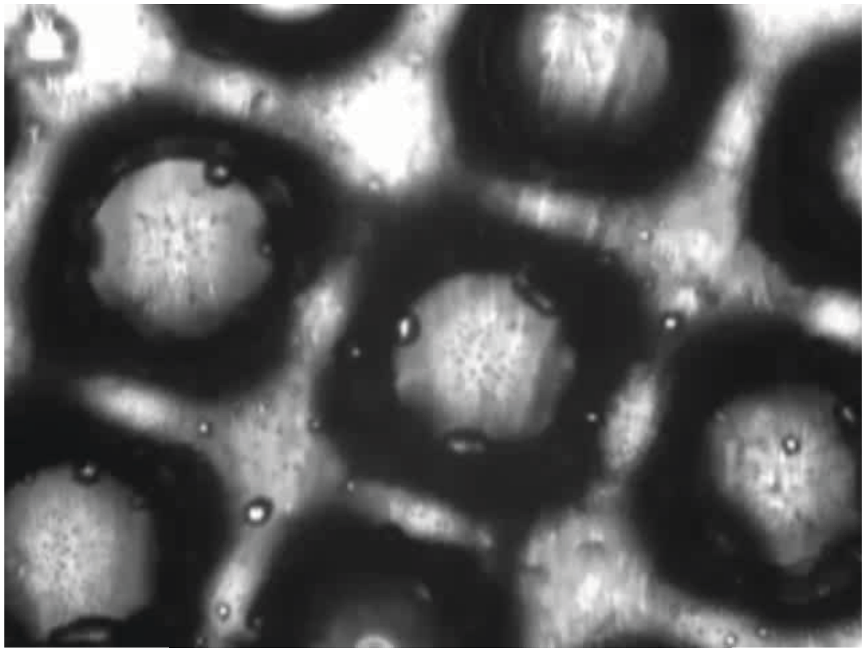
First example of actuating polymer gels as reusable valves for flow control on minute time scales (> 50 repeat actuations)

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)**

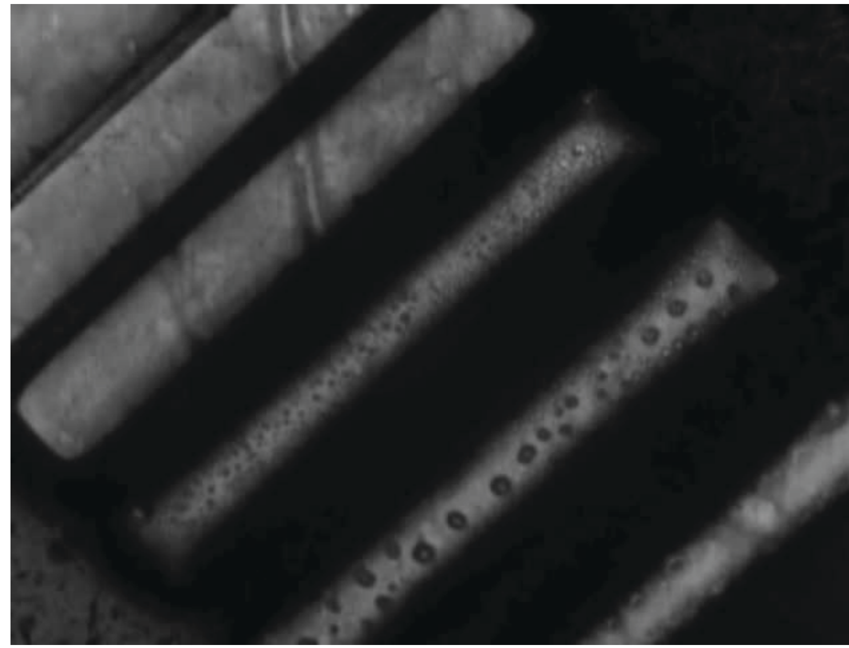
Functional Organic Materials and Devices, Department of Chemical Engineering and Chemistry, and Institute for Complex Molecular Systems, Eindhoven University of Technology

INSIGHT Centre for Data Analytics, National Center of Sensor Research, Dublin City University, Dublin 9, Ireland

Flexible creation of μ-dimensioned features in flow channels using in-situ photo-polymerisation



Ntf2 pillars speed x3



DCA lines speed x4

With Dr Peer Fischer, Fraunhofer-Institut für Physikalische Messtechnik (IPM), Freiburg

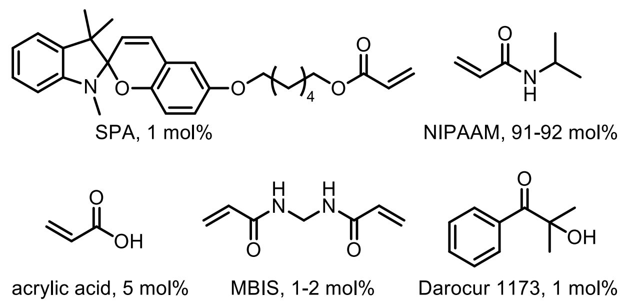
Photocontrol of Assembly and Subsequent Switching of Surface Features

ACS APPLIED MATERIALS & INTERFACES
Research Article
www.acsami.org

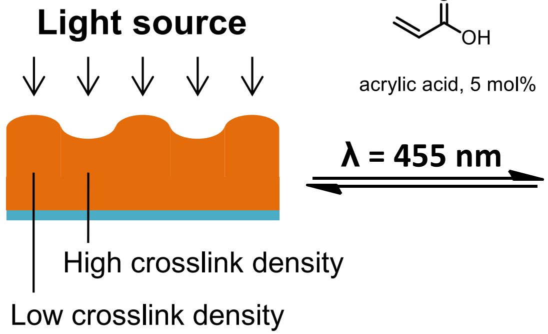
ACS applied materials & interfaces, 6 (2014) 7268-7274

Photoswitchable Ratchet Surface Topographies Based on Self-Protonating Spiropyran–NIPAAM Hydrogels

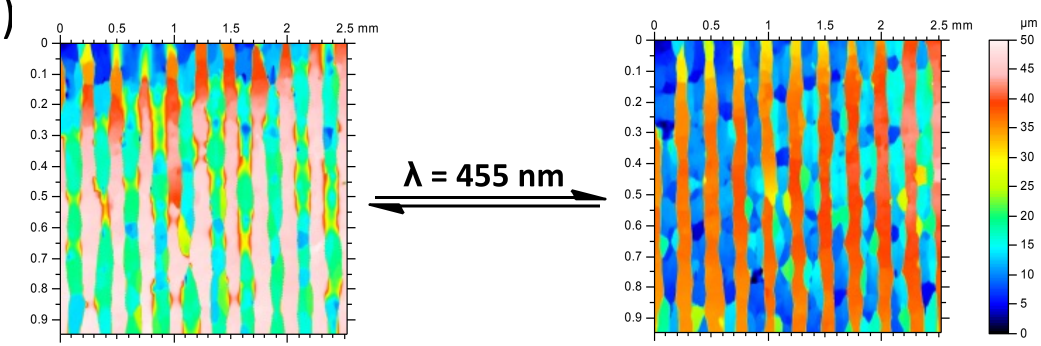
Jelle E. Stumpel,[†] Bartosz Ziółkowski,[‡] Larisa Florea,[‡] Dermot Diamond,[‡] Dirk J. Broer,[*,†,§] and Albertus P. H. J. Schenning[*,†,§]

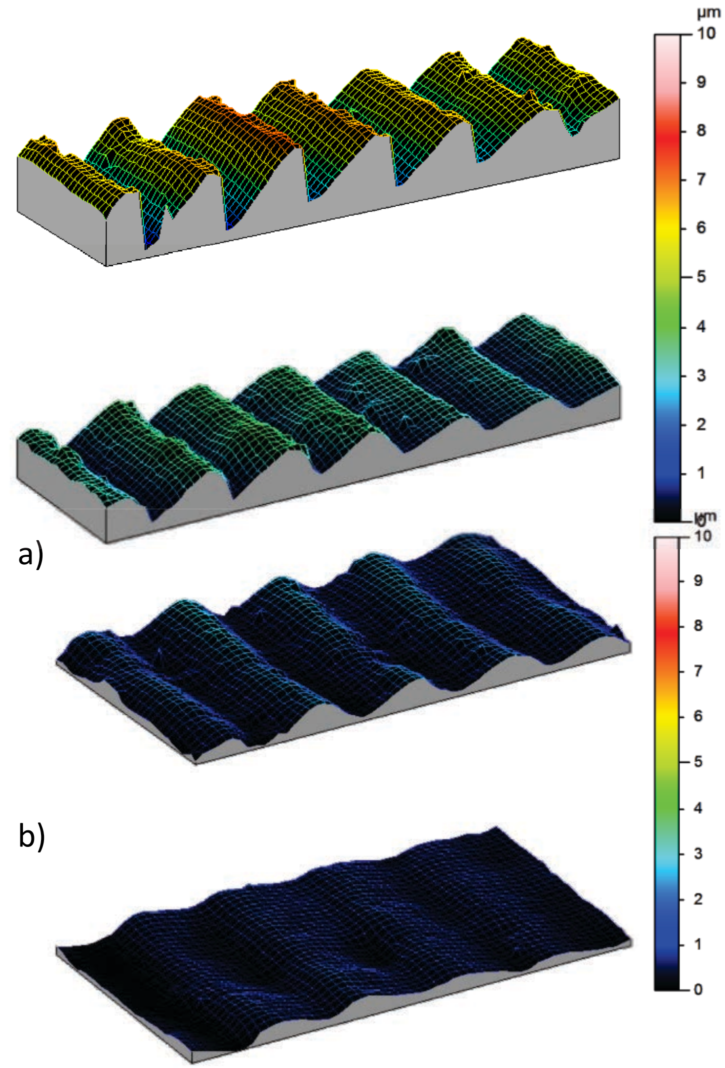


a)

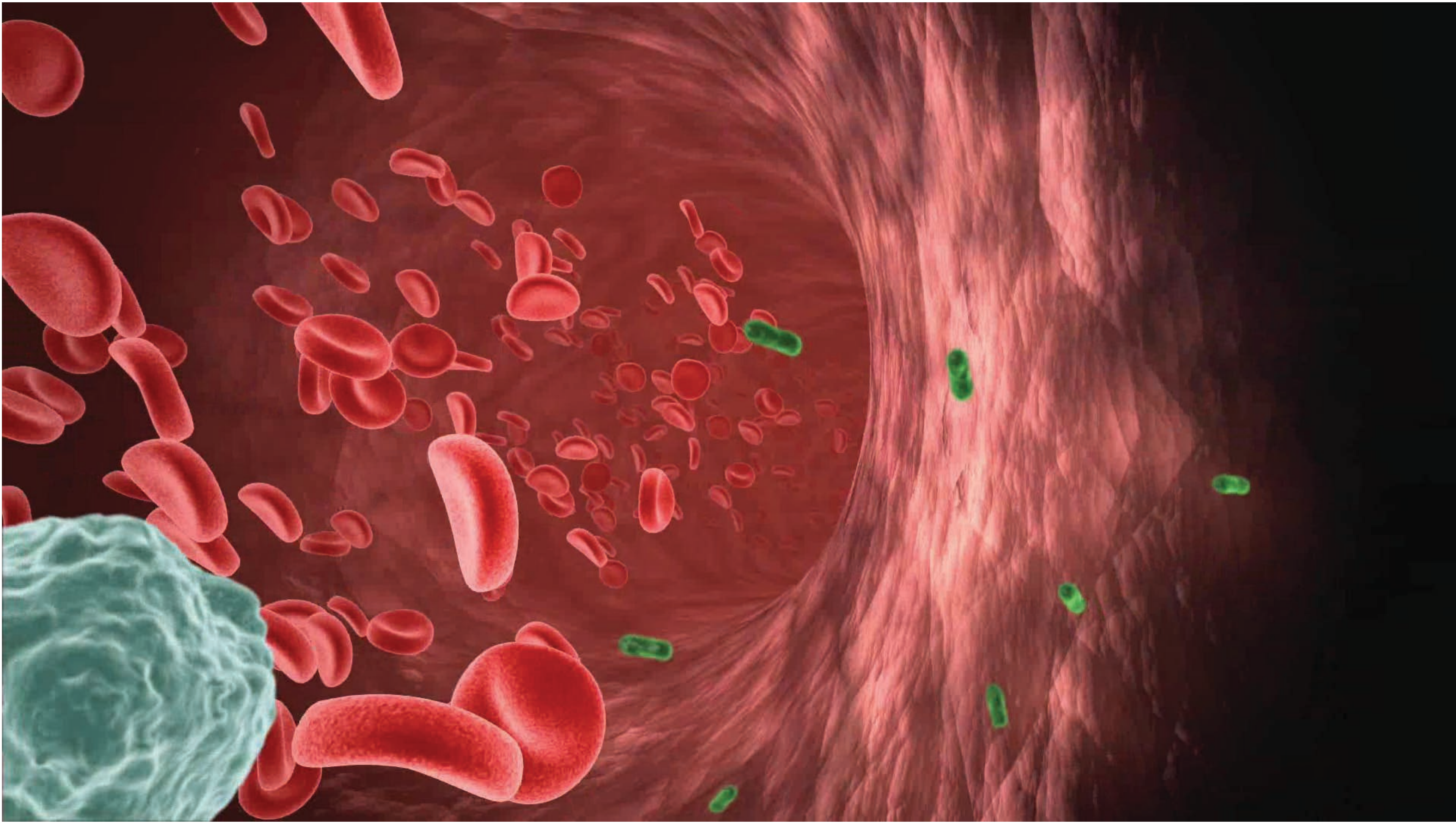


b)

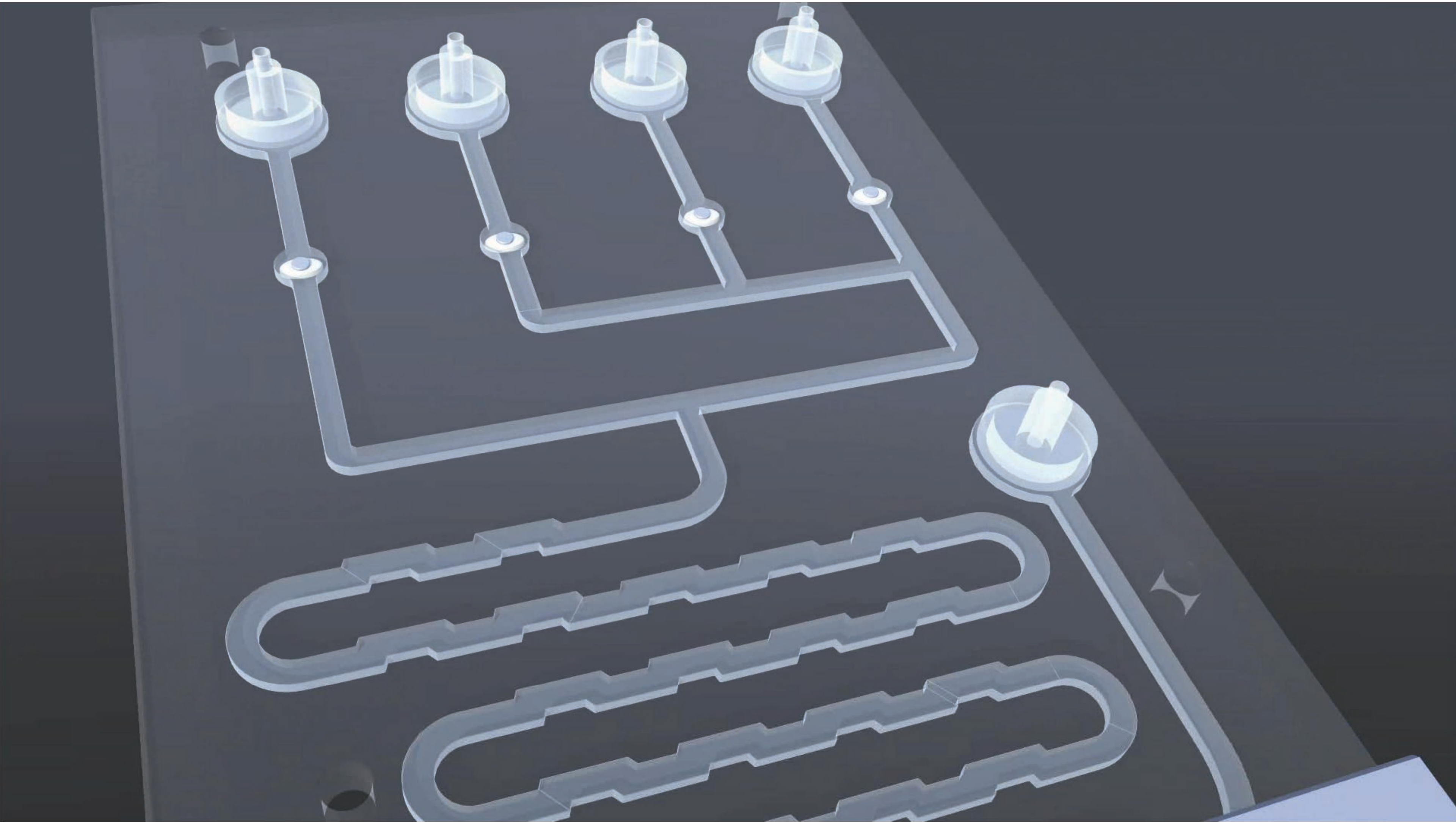




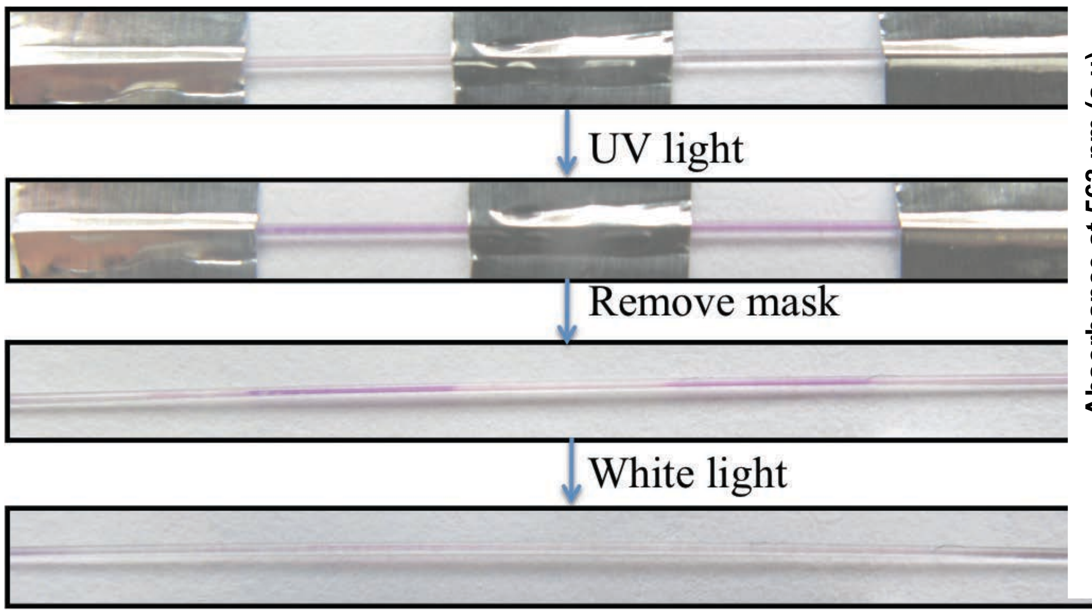
Self-Maintenance: Immune Response

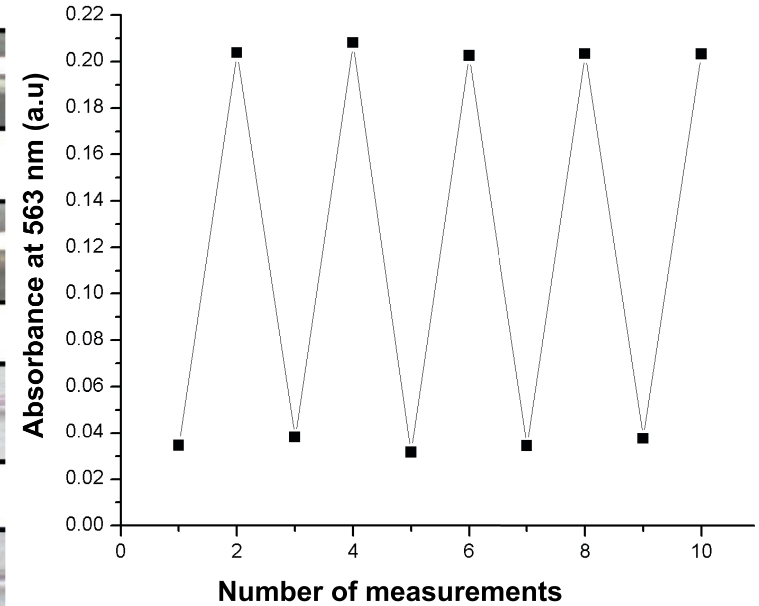


Activate the Channel Walls… Switchable Binding and Release



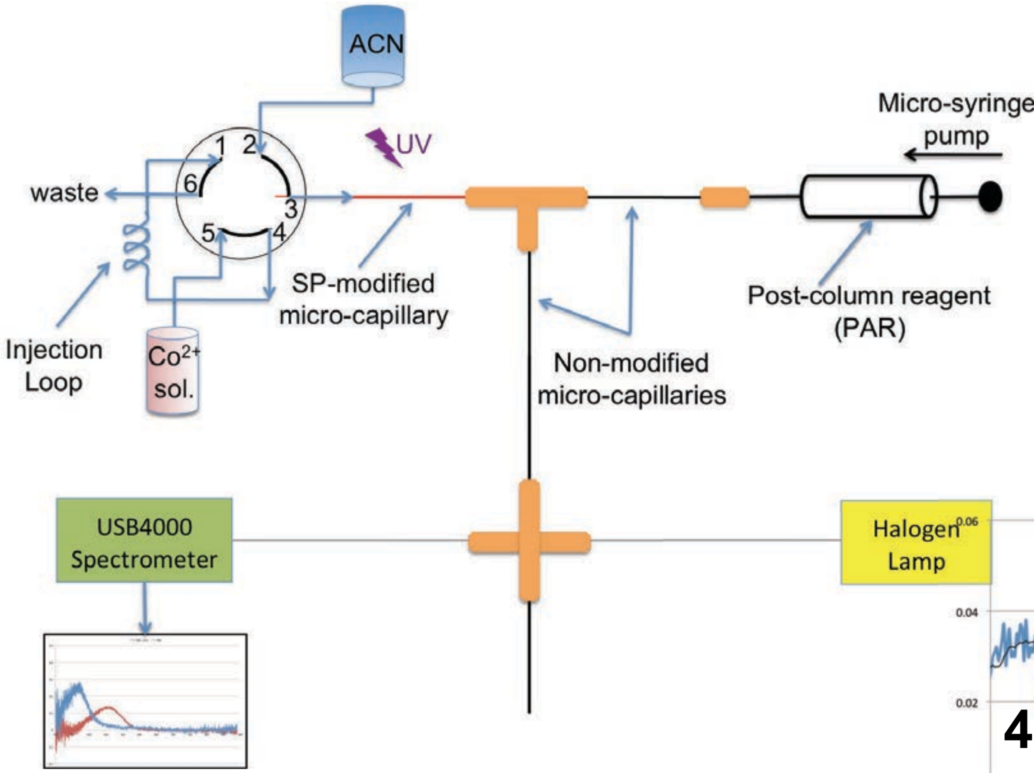
ROMP Chemistry – thick SP polymer 'brush' films

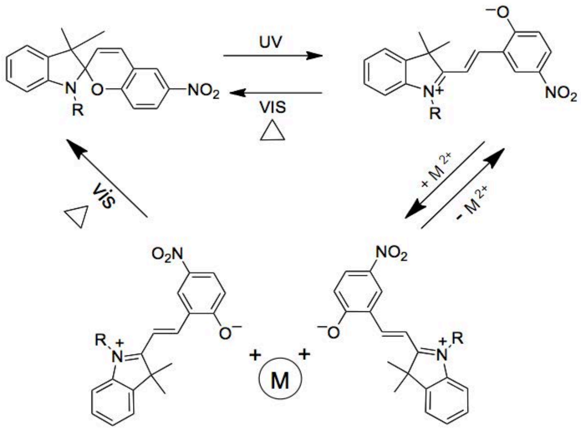


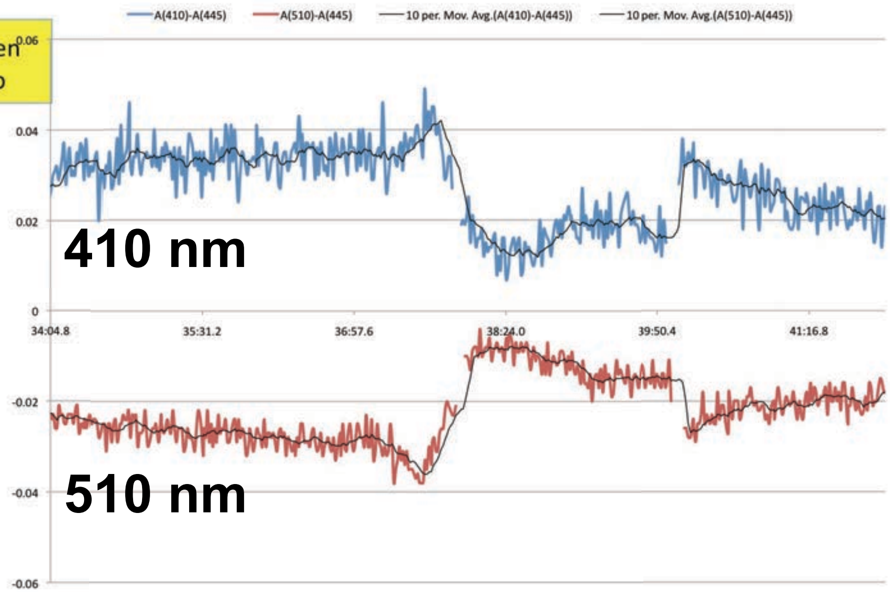


L. Florea, A. Hennart, D. Diamond, F. Benito-Lopez, Sens. Actuators B: Chem., 2011, DOI:10.1016/j.snb.2011.12.055

Switchable Uptake and Release – ‘Post Column’ Detection





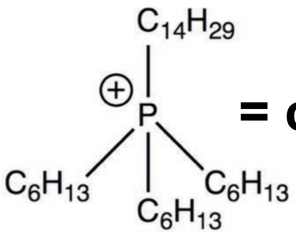


Co^{2+} + PAR ➔ PAR-Co^{2+}

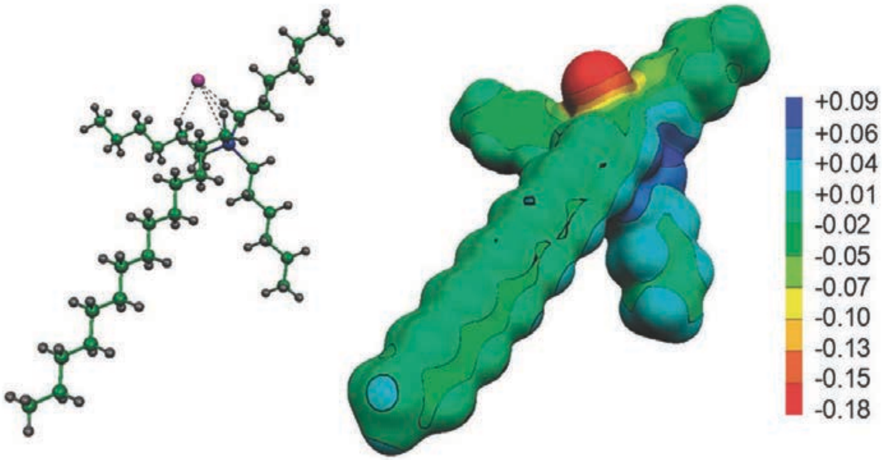
410 nm 510 nm

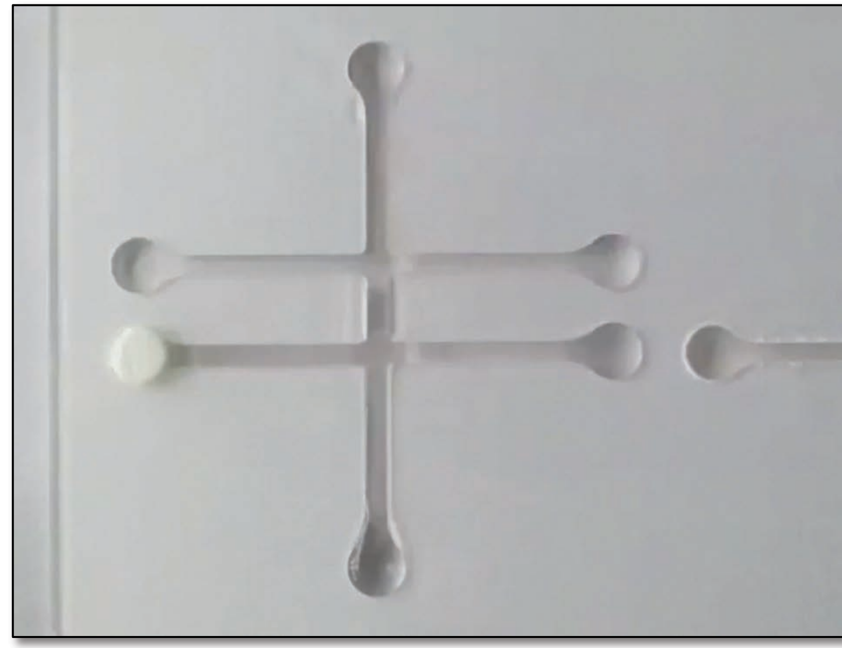
Self Aware Fluidics…

Chemotaxis – Autonomous Movement to a Plume Source with IL Droplets



= cationic surfactant



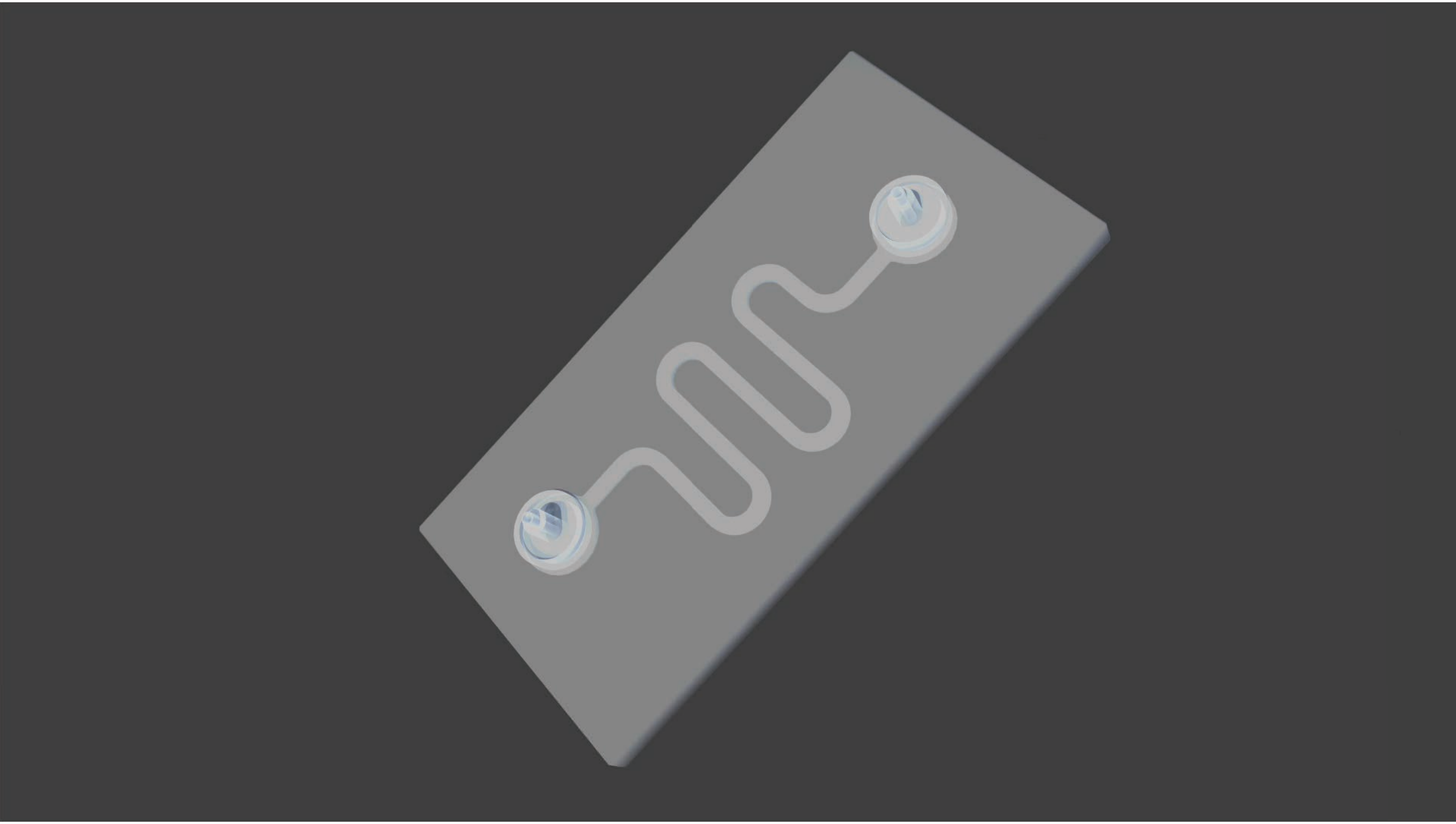


Trihexyl(tetradecyl)phosphonium chloride ($[P_{6,6,6,14}][Cl]$) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the Cl^- ion which is created using a polyacrylamide gel pad soaked in 10^{-2} M HCl; A small amount of NaCl crystals can also be used to drive droplet movement.

Electronic structure calculations and physicochemical experiments quantify the competitive liquid ion association and probe stabilisation effects for nitrobenzospiropyran in phosphonium-based ionic liquids, D. Thompson et al., *Physical Chemistry Chemical Physics*, 2011, 13, 6156-6168.

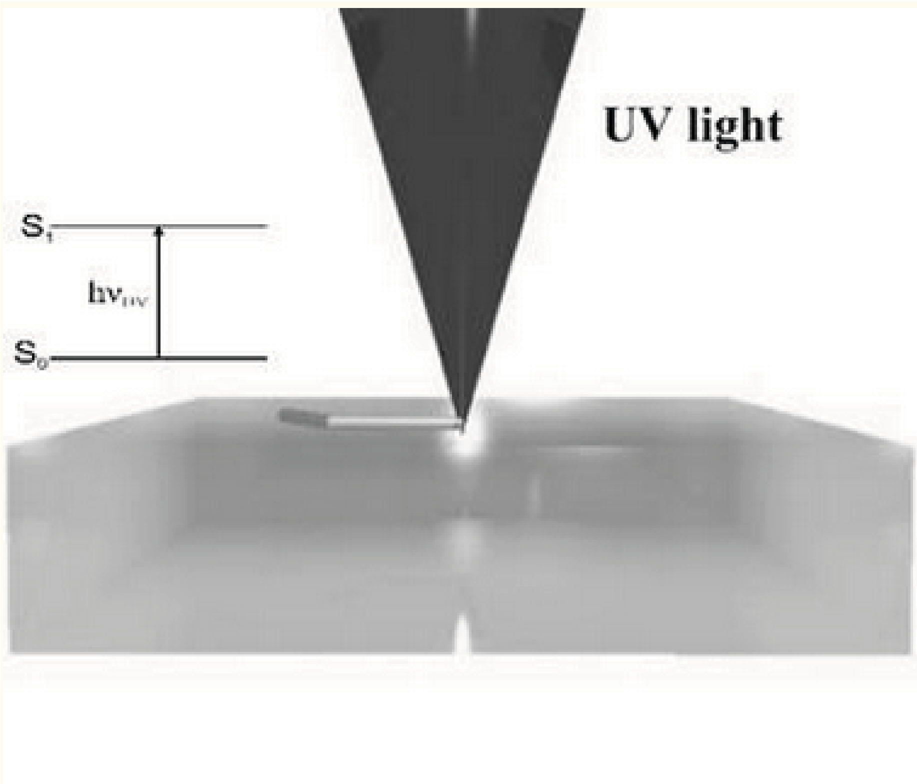
Electrochemical Generation of Cl^- gradients on demand…

2D Rigid to 3D Flexible Microfluidics??



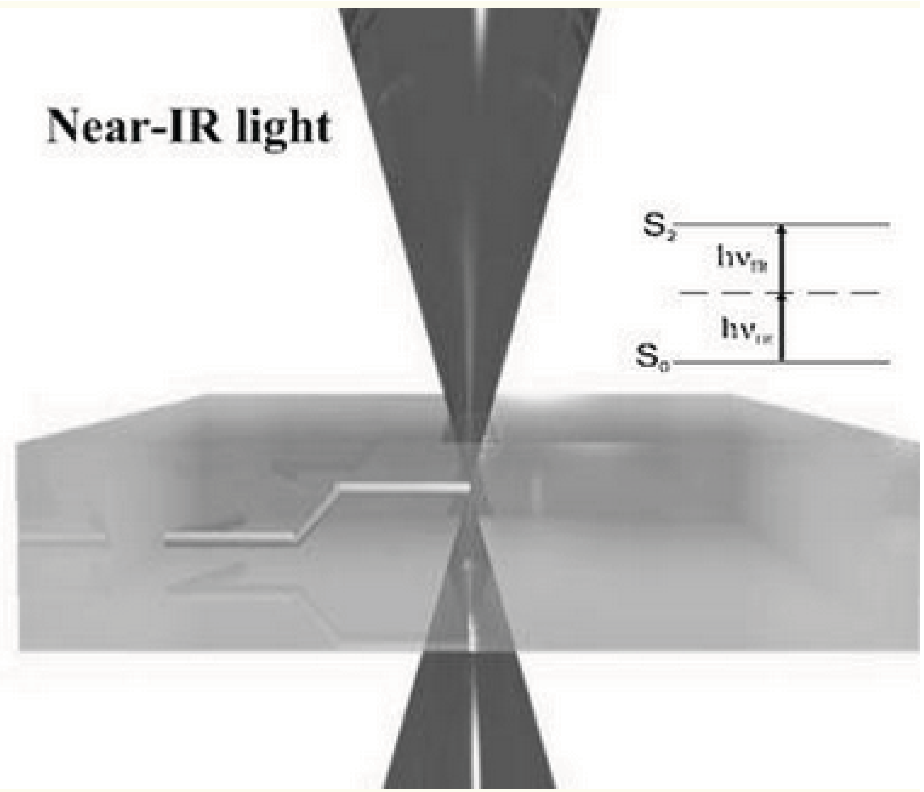
Background

Stereolithography



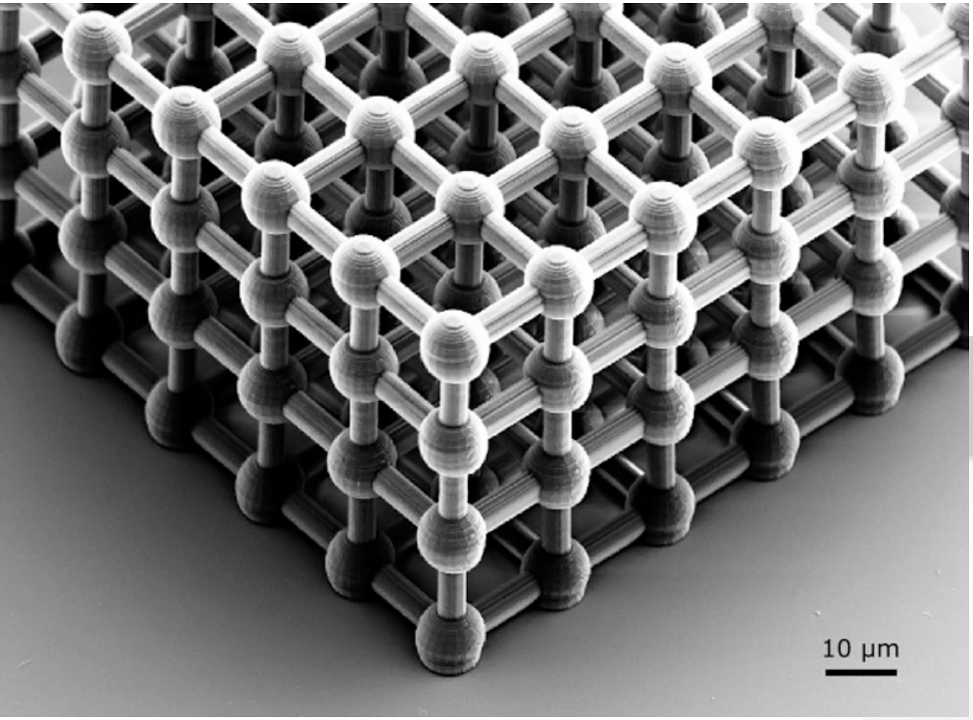
- Single photon absorption
- 2D patterns

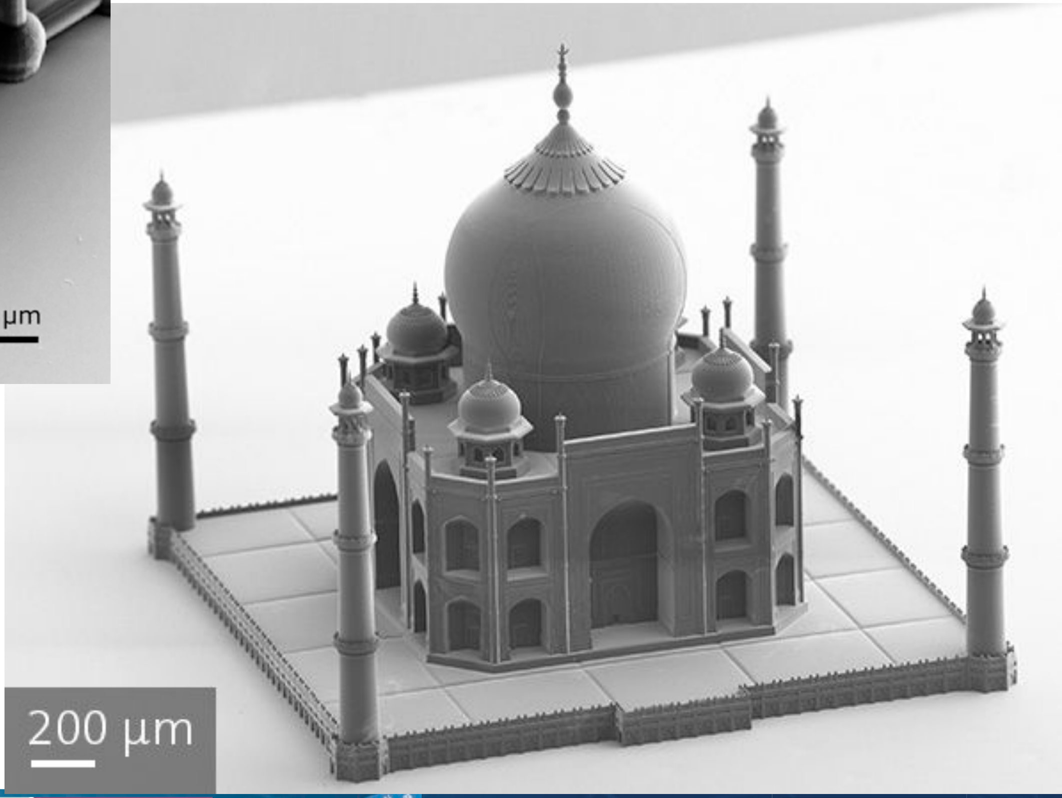
Two-photon polymerisation



- Two photon absorption
- 3D structures

Background



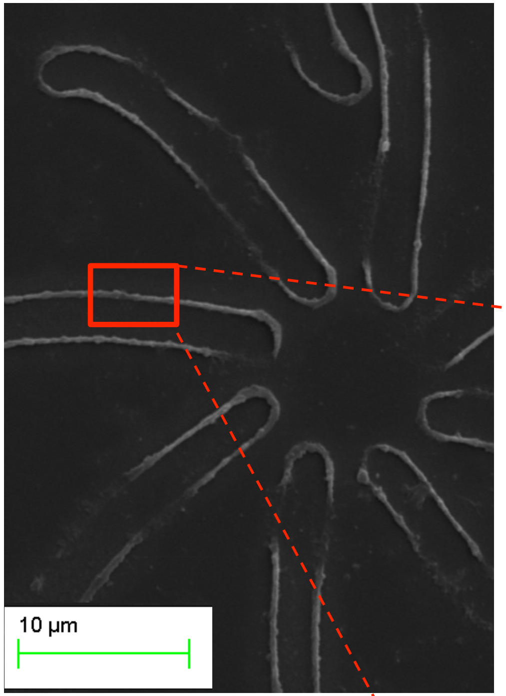


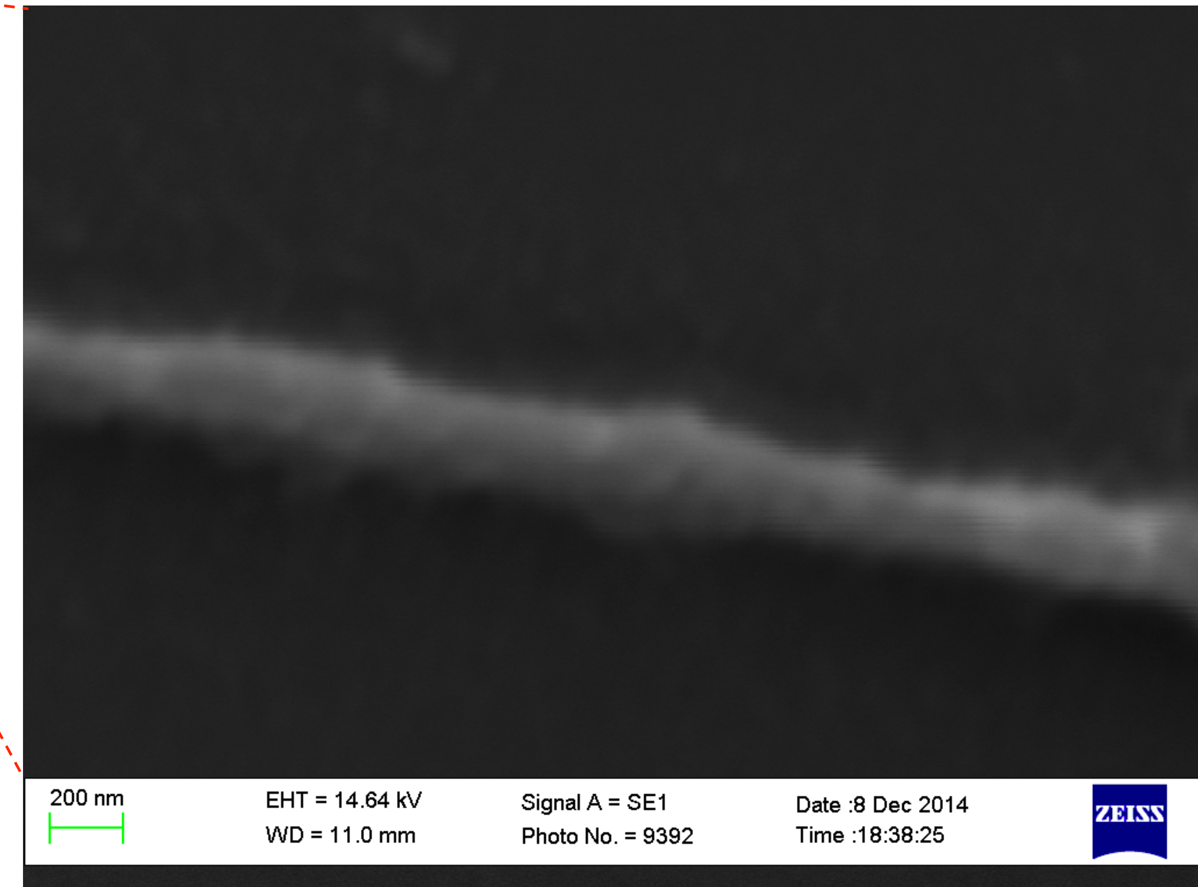
http://www.nanoscribe.de/

The Exciting Potential of Stimuli-responsive Materials and Biomimetic Microfluidics

Larisa Florea[1], Vincenzo Curto[2], Alexander J. Thompson[2],
Guang-Zhong Yang[2], and Dermot Diamond[1]*
[1]Insight Centre for Data Analytics, NCSR, Dublin City University
[2]The Hamlyn Centre for Robotic Surgery, Imperial College London, London, SW7 2AZ

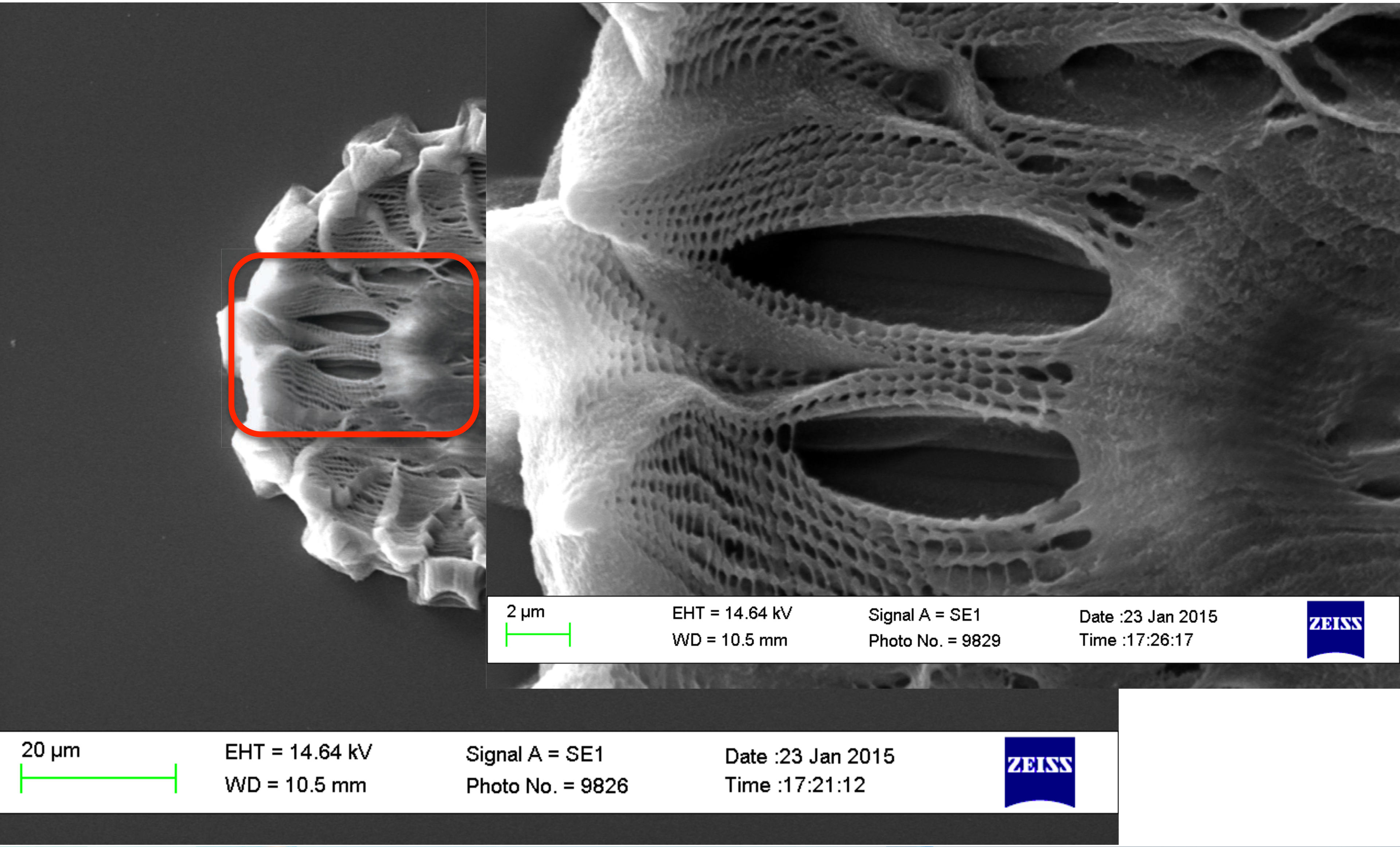
Submitted to Euronanoforum, Riga, Latvia, June 2015





Creating 3D soft gel structures with a line resolution of ca. 200 nm

‘Daisy’ – Micro/Nano Scaled Porous Structure




‘Micro-Rose’
2 µm
EHT = 14.64 kV
WD = 10.5 mm
Signal A = SE1
Photo No. = 9753
Date :23 Jan 2015
Time :12:31:01
ZEISS
2 µm
EHT = 14.64 kV
WD = 10.5 mm
Signal A = SE1
Photo No. = 9755
Date :23 Jan 2015
Time :12:33:11
ZEISS
‘Micro-Stoma’
2 µm
EHT = 14.64 kV
WD = 11.0 mm
Signal A = SE1
Photo No. = 9763
Date :23 Jan 2015
Time :12:39:59
ZEISS
2 µm
EHT = 14.64 kV
WD = 11.0 mm
Signal A = SE1
Photo No. = 9764
Date :23 Jan 2015
Time :12:40:59
ZEISS

Time to re-think the game!!!

- New materials with exciting characteristics and unsurpassed potential…
- Combine with emerging technologies and techniques for exquisite control of 3D morphology
- And greatly improved methods for characterisation of structure and activity
- Learn from nature – e.g. more sophisticated circulation systems for 'self-aware' sensing devices!
- Integrate flexible electronics, fluidics, photonics

Develop disruptive '**revolutionary**' solutions
In parallel to '**evolutionary**' improvements

Thanks to…..

- Members of my research group
- NCSR, DCU
- Science Foundation Ireland, INSIGHT Centre & Enterprise Ireland
- EU Framework Funding
- Academic and Industry Research Partners

nbmc, FlexTech, semi

MASK
Project no: 269302
Materials and Advanced Sensor Knowledge Exchange