Bio-Inspired Active Fluidic Systems based on Stimuli-Responsive Materials

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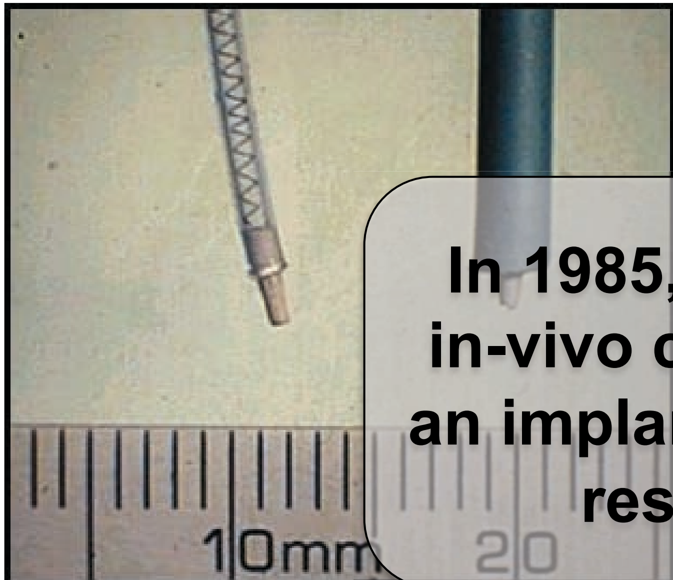
Invited lecture presented at

67th Irish Universities Chemistry Research Colloquium
Maynooth University

25th June 2015

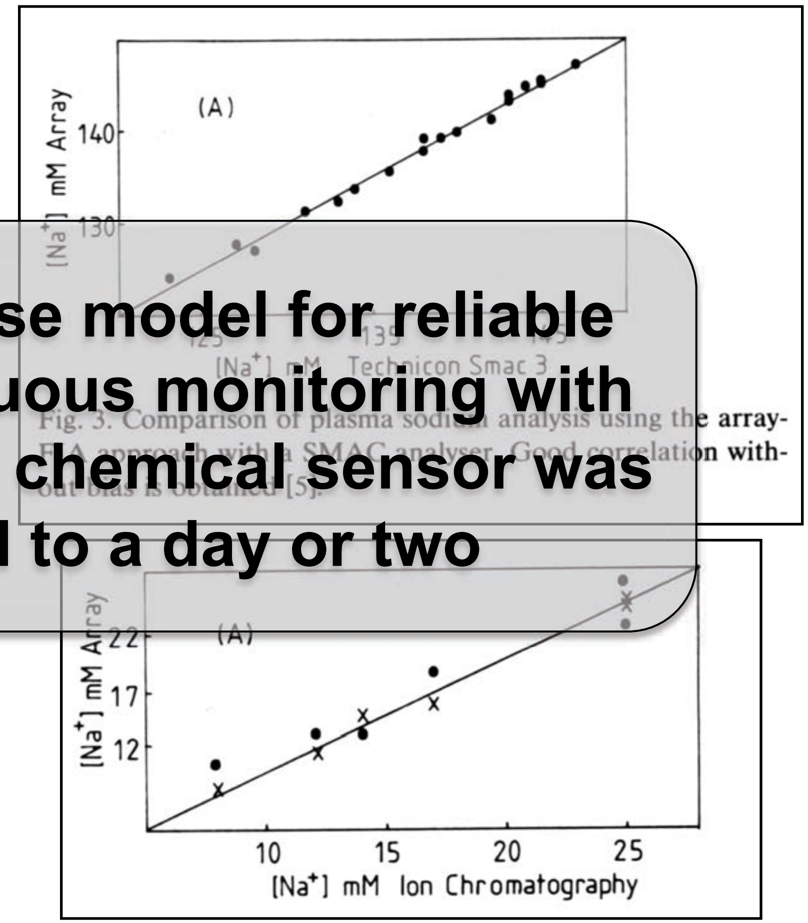
Blood Analysis; Implantible Sensors



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

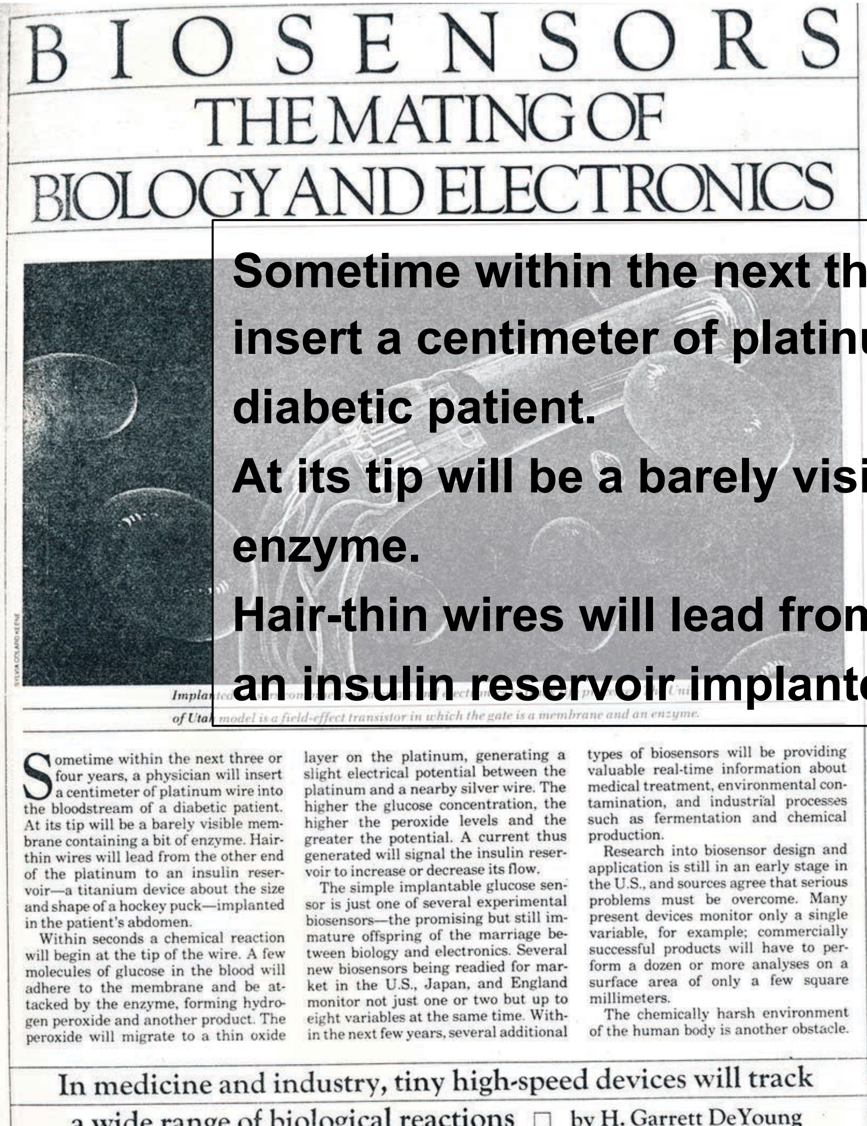
Dr. David Band, St Thomas's Hospital London



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

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

The promise of biosensors…..



BIOSENSORS

THE MATING OF BIOLOGY AND ELECTRONICS

…model is a field-effect transistor in which the gate is a membrane and an enzyme.

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 layer on the platinum, generating a slight electrical potential between the platinum and a nearby silver wire. The higher the glucose concentration, the higher the peroxide levels and the greater the potential. A current thus generated will signal the insulin reservoir to increase or decrease its flow.

The simple implantable glucose sensor is just one of several experimental biosensors—the promising but still immature offspring of the marriage between biology and electronics. Several new biosensors being readied for market in the U.S., Japan, and England monitor not just one or two but up to eight variables at the same time. Within the next few years, several additional types of biosensors will be providing valuable real-time information about medical treatment, environmental contamination, and industrial processes such as fermentation and chemical production.

Research into biosensor design and application is still in an early stage in the U.S., and sources agree that serious problems must be overcome. Many present devices monitor only a single variable, for example; commercially successful products will have to perform a dozen or more analyses on a surface area of only a few square millimeters.

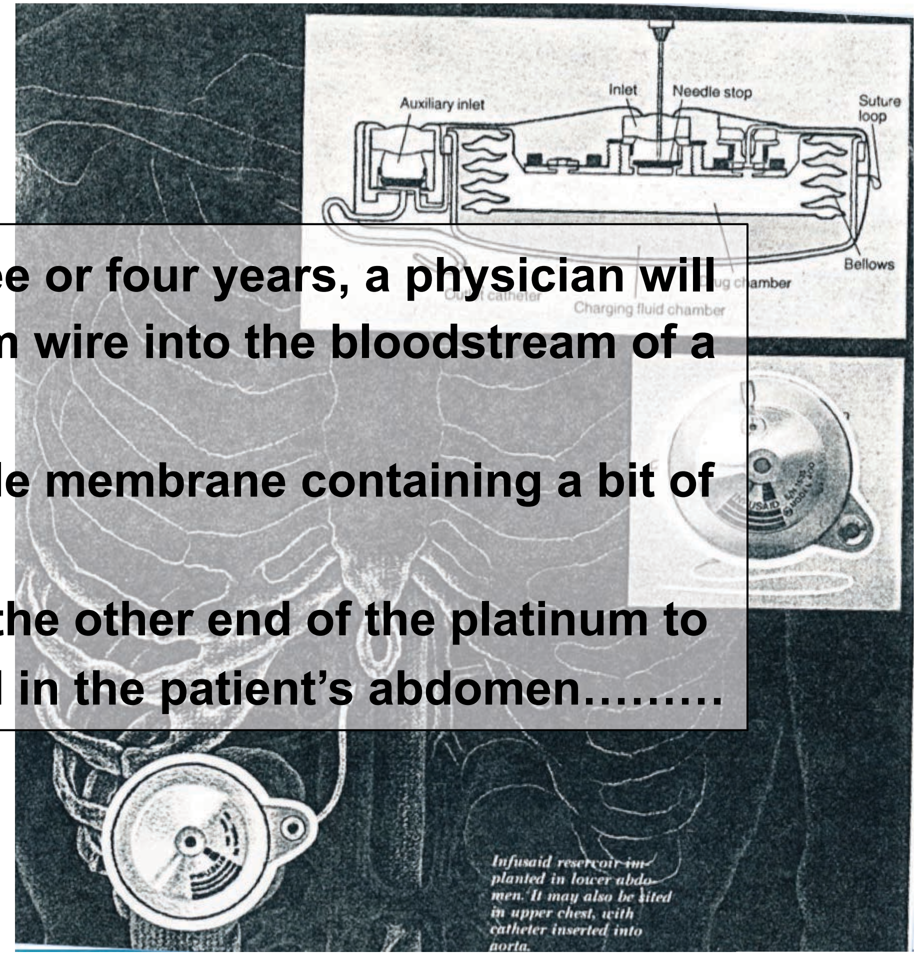
The chemically harsh environment of the human body is another obstacle.

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

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………



High Technology, Nov. 1983, 41-49

On-skin patches ….

Jicheng Yu et al., www.pnas.org/cgi/doi/10.1073/pnas.1505405112 (May 2015)

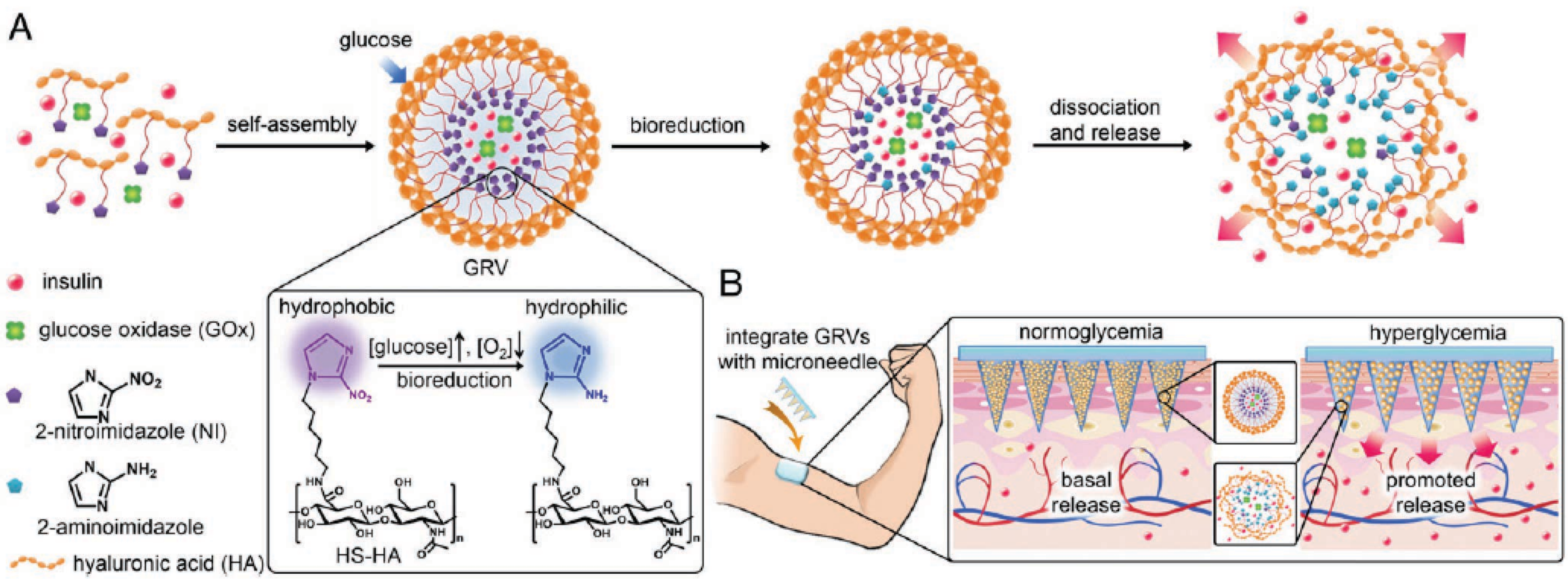
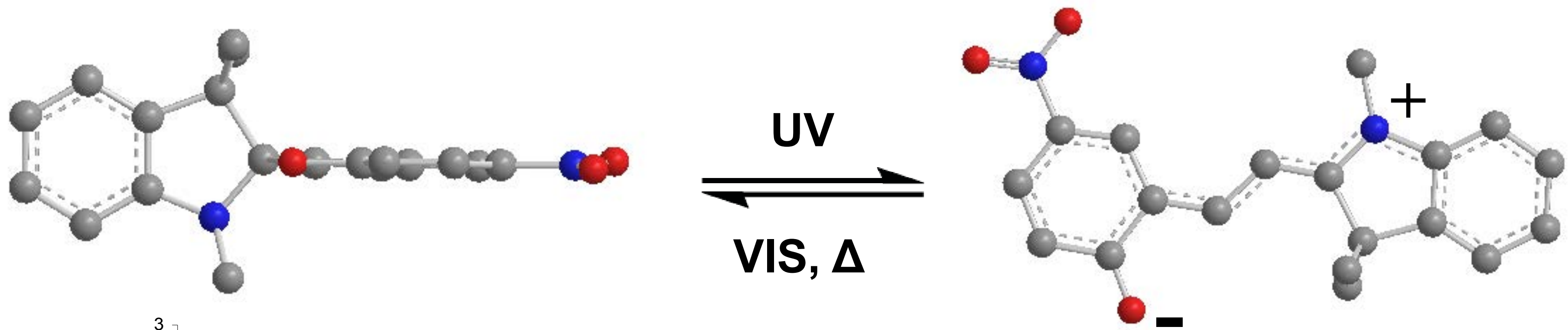
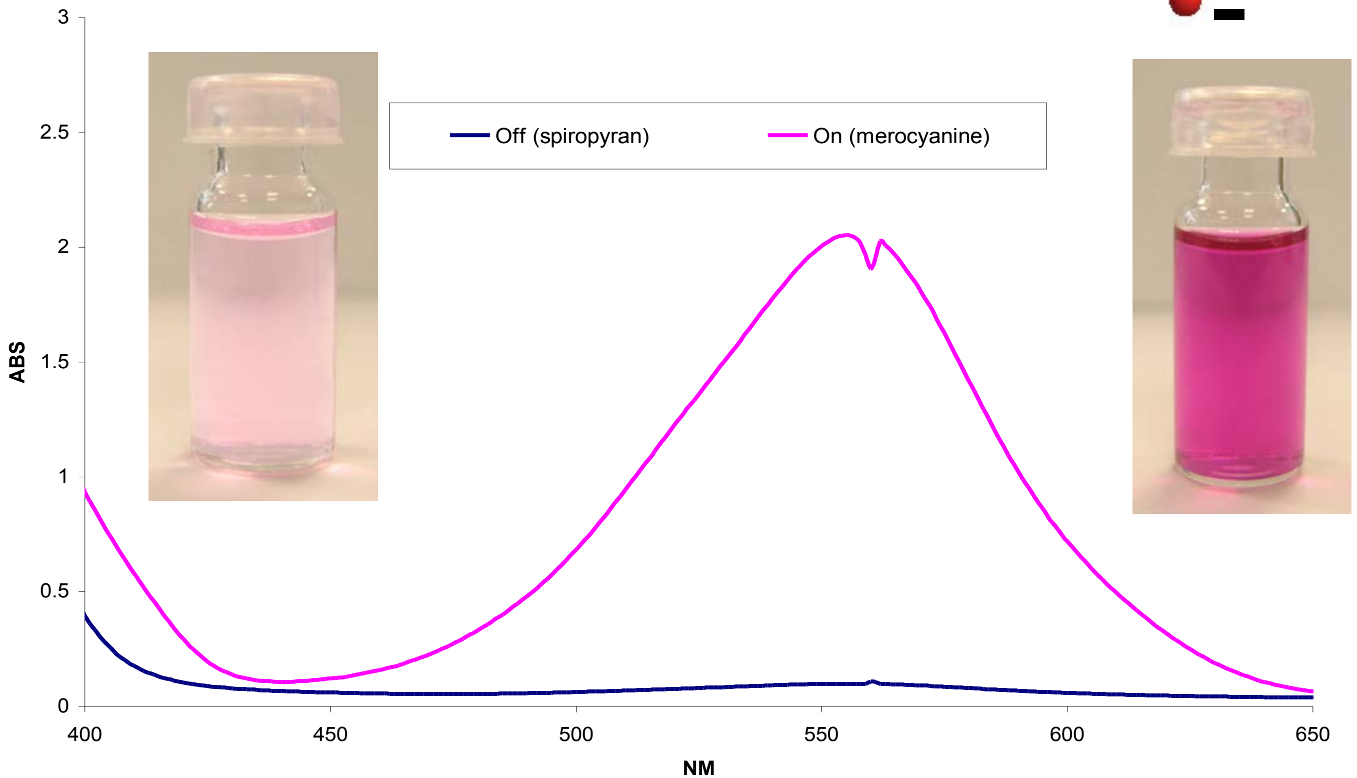


Fig. 1. Schematic of the glucose-responsive insulin delivery system using hypoxia-sensitive vesicle-loading MN-array patches. (*A*) Formation and mechanism of GRVs composed of HS-HA. (*B*) Schematic of the GRV-containing MN-array patch (smart insulin patch) for in vivo insulin delivery triggered by a hyperglycemic state to release more insulin.

Photoswitchable Actuators





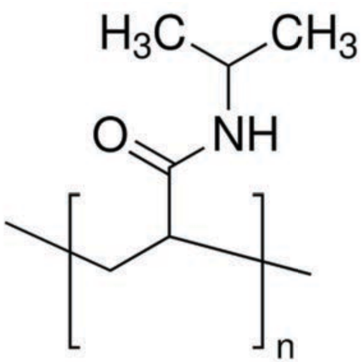
Famous Molecule….

From Prof. Thorfinnur Gunnlaugsson, TCD School of Chemistry
Spotted on Nickelodeon Cartoons February 2015

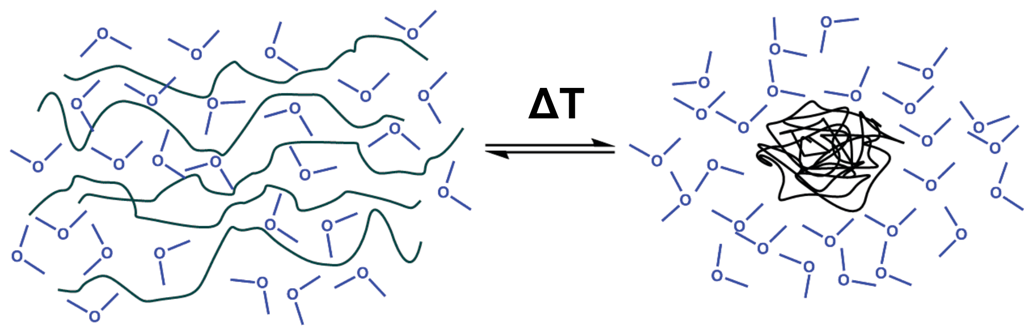
Poly(*N*-isopropylacrylamide)

- **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

Polymer based photoactuators based on pNIPAAm

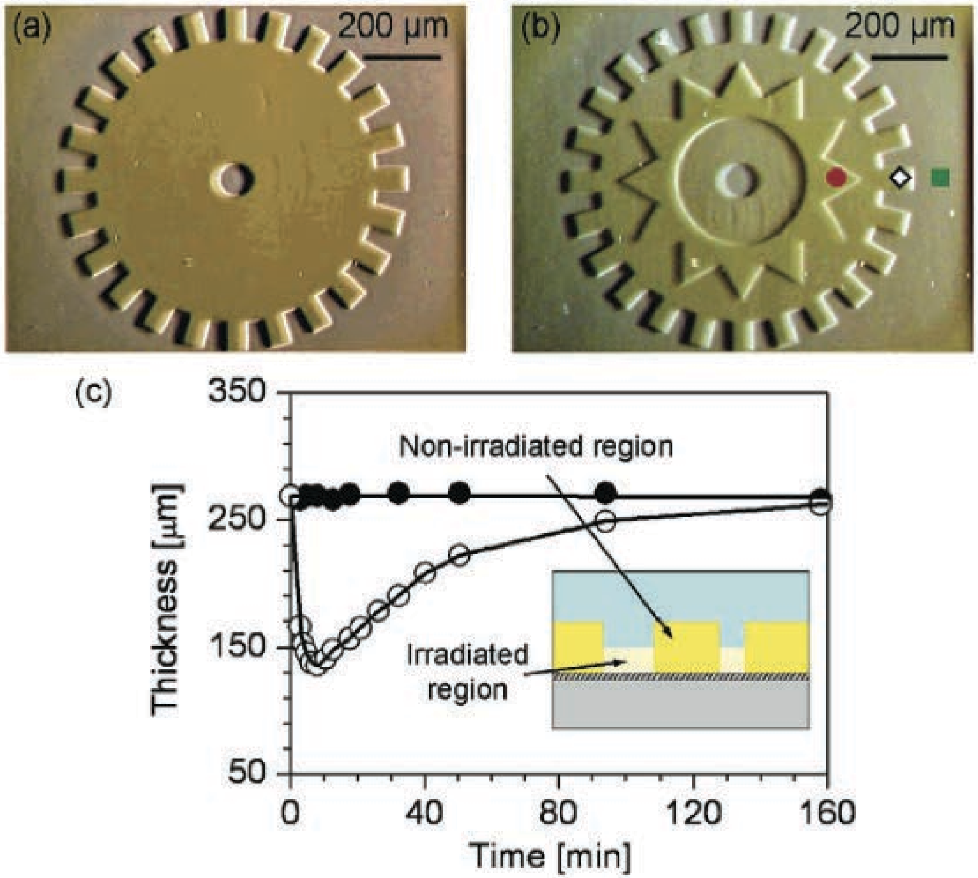
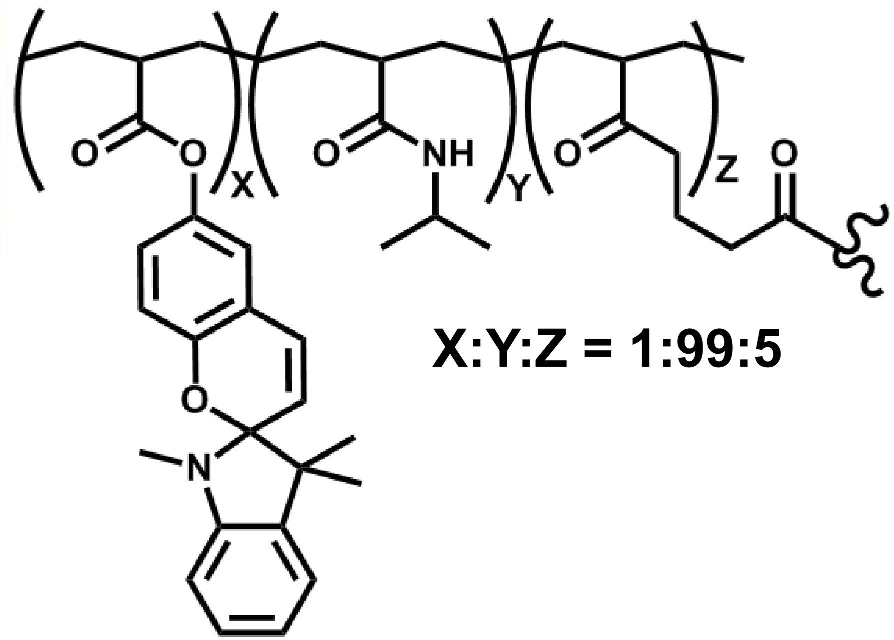


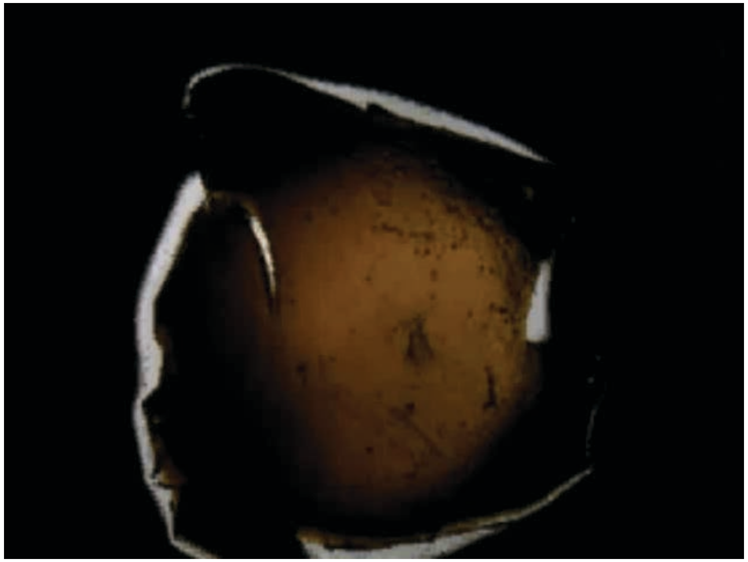
Figure 3. (a, b) Images of the pSPNIPAAm hydrogel layer just after the micropatterned light irradiation. Duration of irradiation was (●, red) 0, (◊) 1, and (■, green) 3 s. (c) Height change of the hydrogel layer in (●) non-irradiated and (○) irradiated region as a function of time after 3 s blue light irradiation.

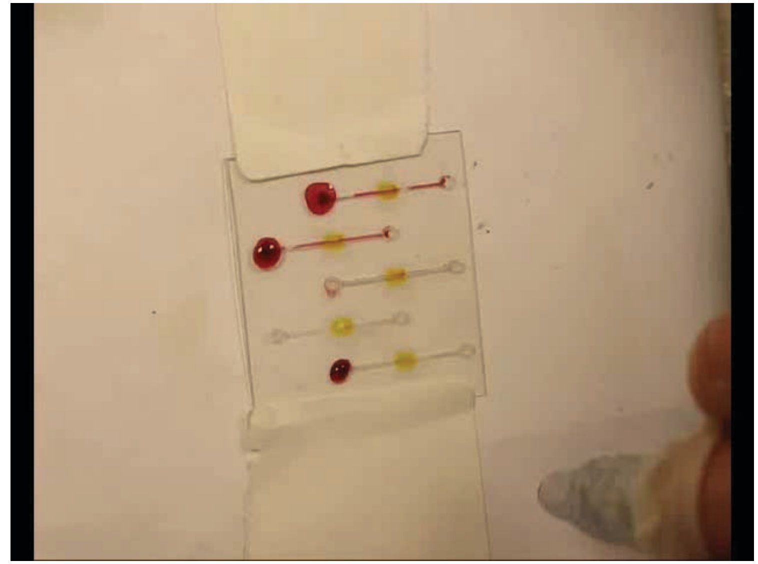


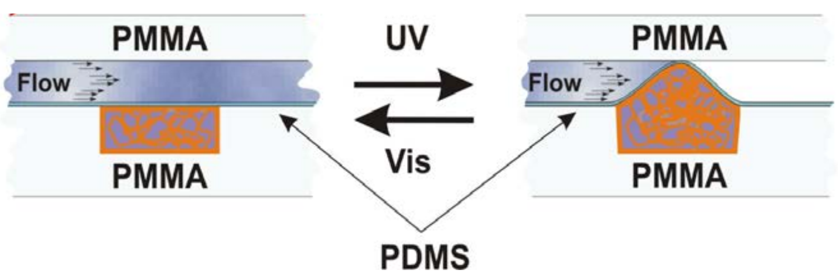
X:Y:Z = 1:99:5

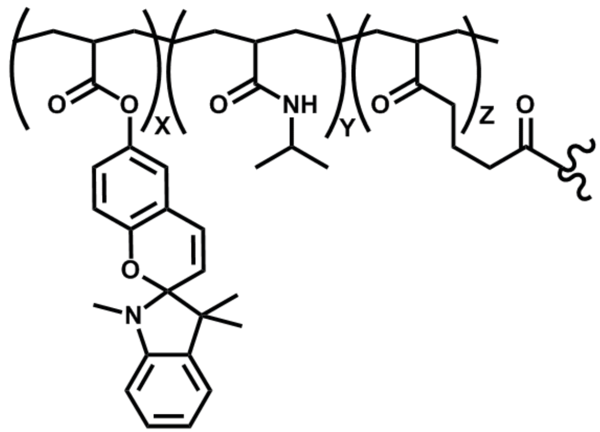
poly(N-isopropylacrylamide) (PNIPAAm)
Formulation as by Sumaru et al[1]
***1) Chem. Mater.*, 19 (11), 2730 -2732, 2007.**

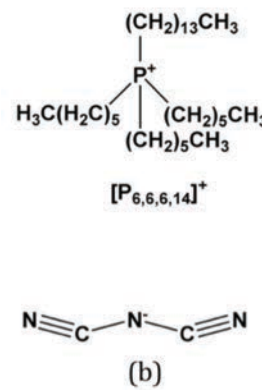
Photo-actuator polymers as microvalves in microfluidic systems







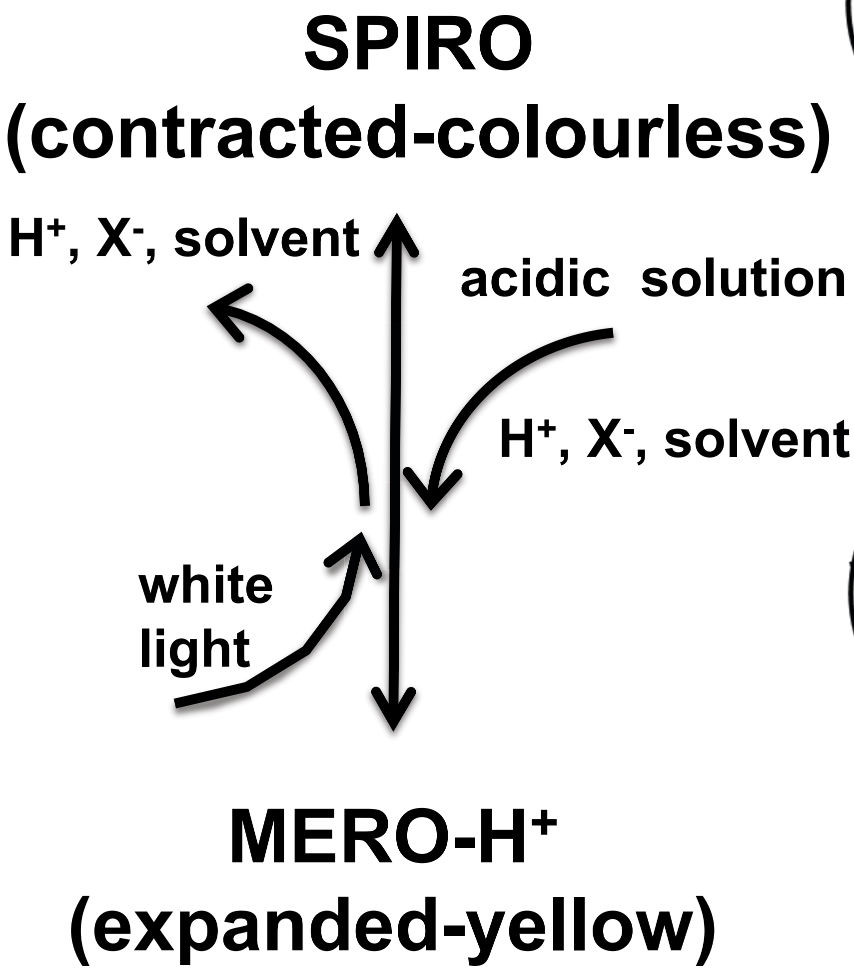


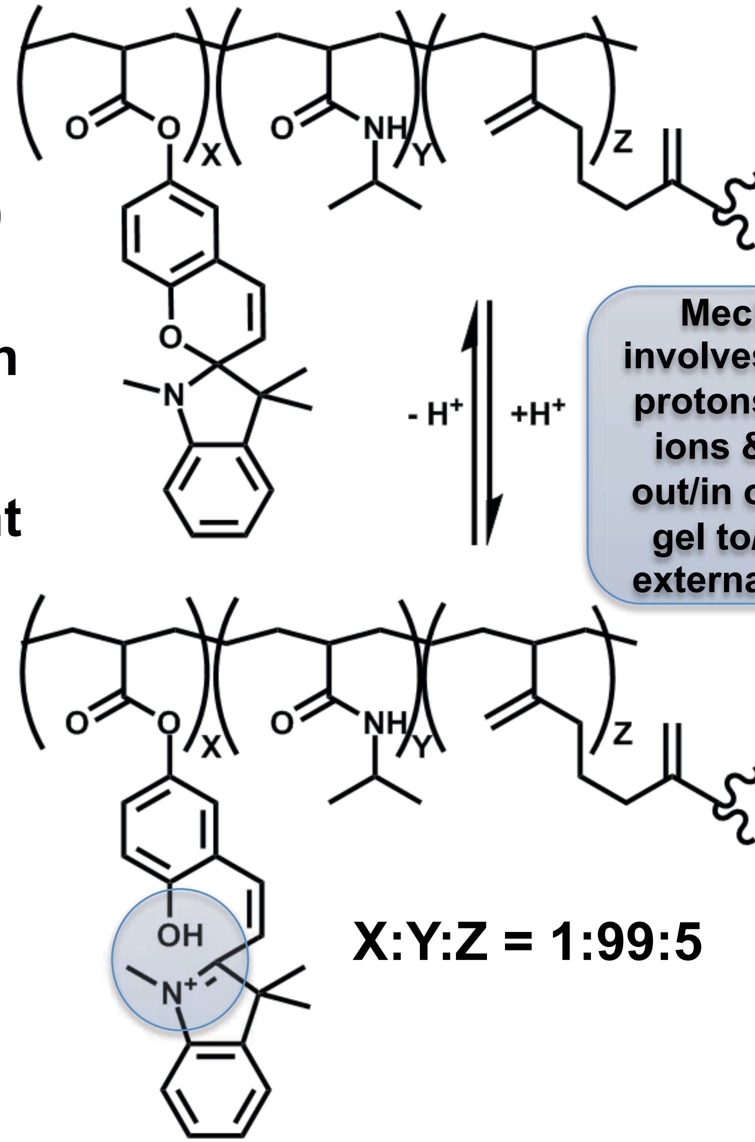


trihexyltetradecylphosphonium dicyanoamide $[P_{6,6,6,14}]^+[dca]^-$

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.

Actuation Mechanism

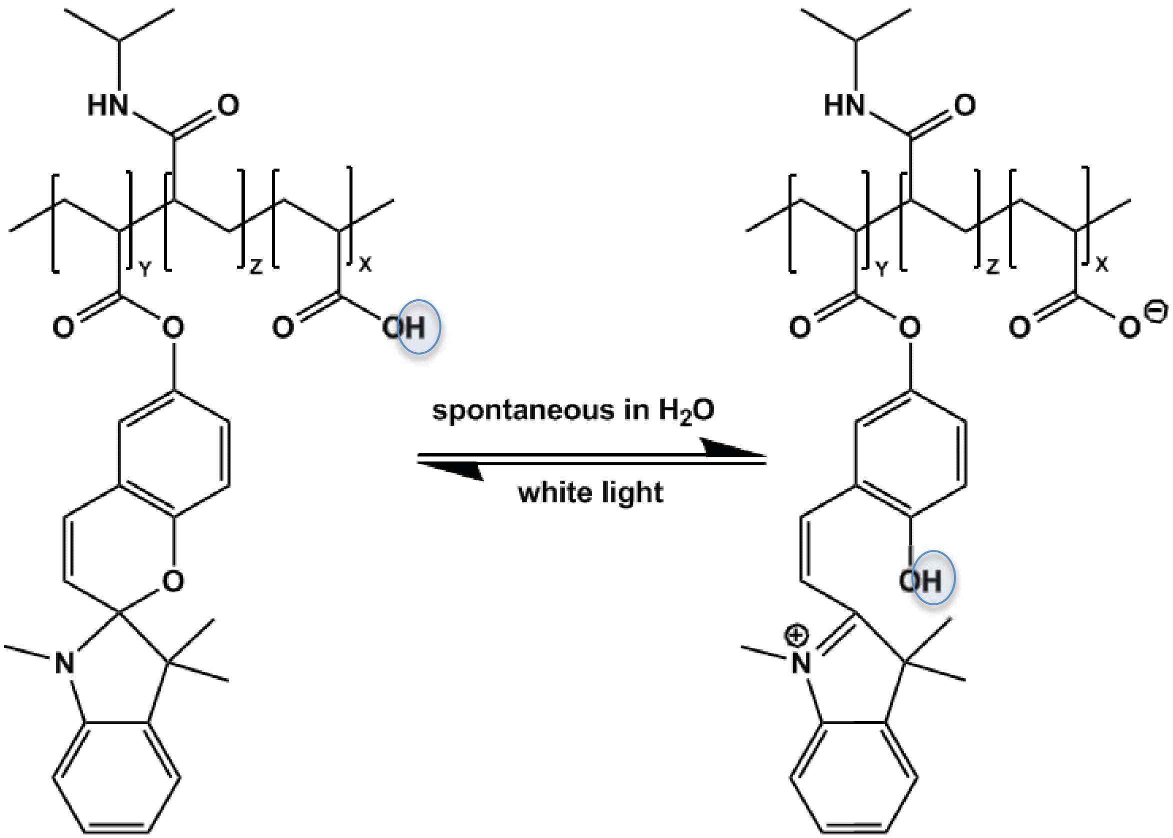


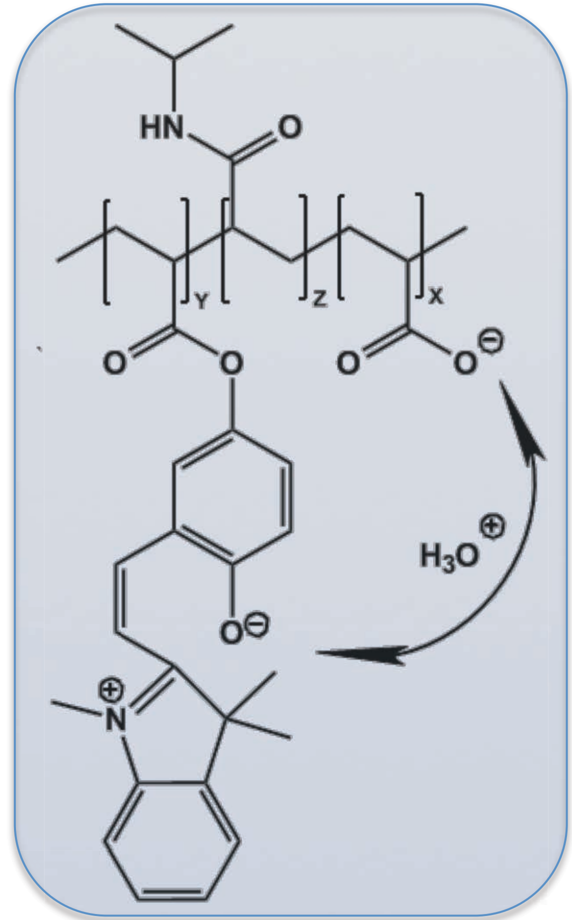


Mechanism involves diffusion protons, counter ions & solvent out/in of the bulk gel to/from the external solution

Self protonating photoresponsive gel

Ziolkowski *et al*., Soft Matter, 2013, 9, 8754–8760





Previously proton source was external (acidic soln. required)
Protons, counter ions & solvent diffuse into/out of the gel

Now the proton exchange is 'internalised'
The proton population is essentially conserved

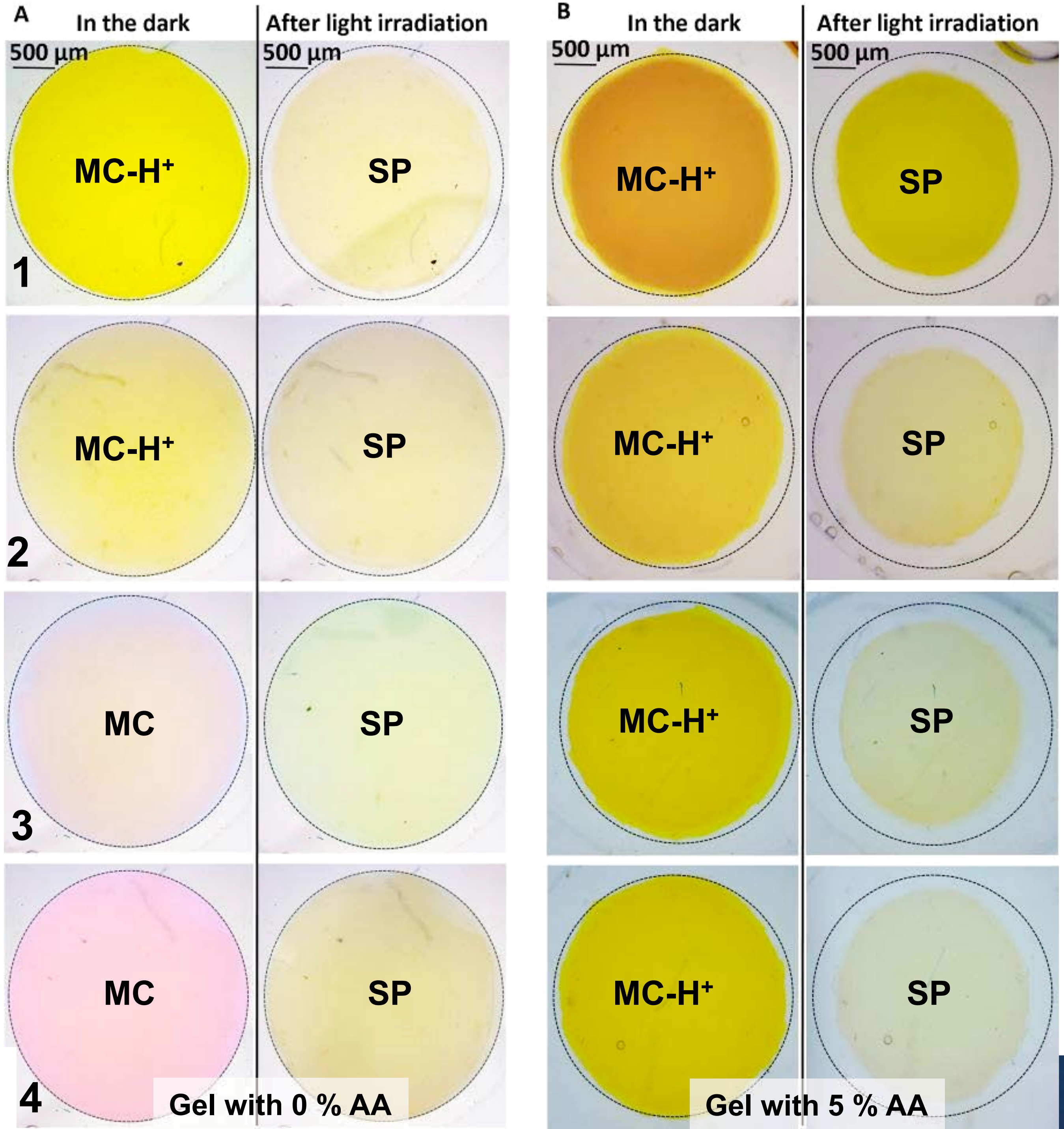
Effect of AA-modification on Actuation Cycling in non-acidified water

A: Un-modified Gel (left): Colour gradually changing from yellow to purple as H^+ leaves the gel on each cycle.

Actuation stops after initial cycle

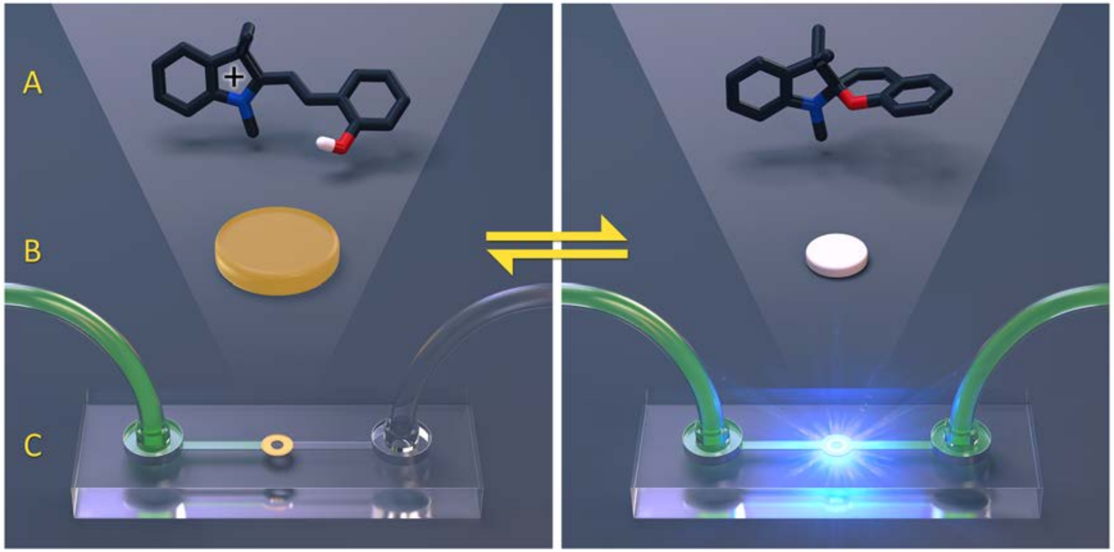
B: Modified Gel (Right) Colour remains essentially the same, as H^+ stays in the gel during cycling

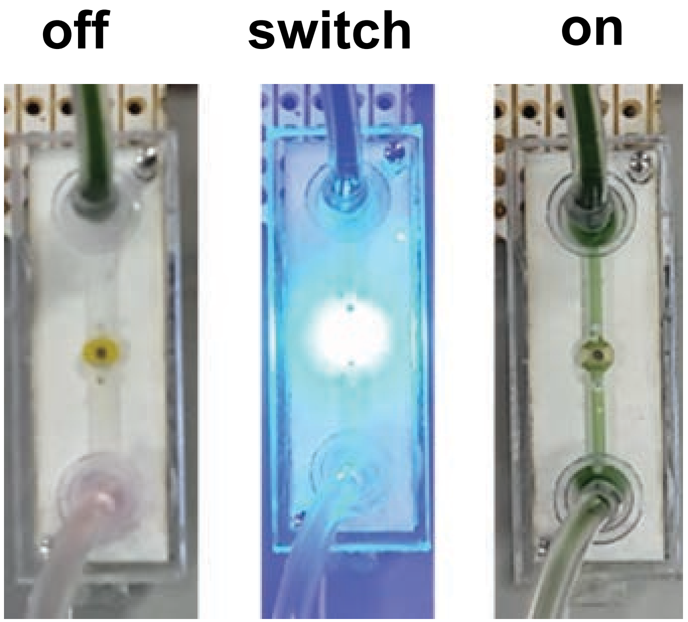
Actuation efficiency is retained over multiple cycles



Ziolkowski *et al.*, Soft Matter, 2013, 9, 8754–8760

Reversible Photo-Switching of Flow

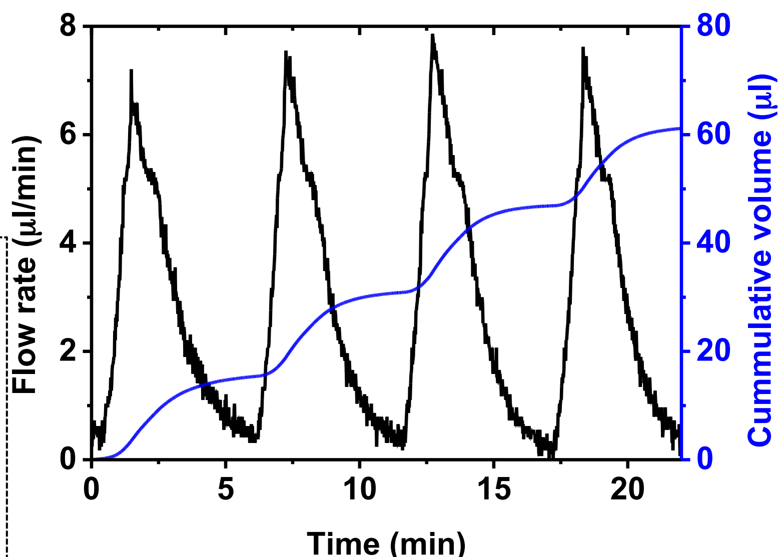




Above: scheme showing switching process protonated $MC\text{-}H^+$ photoswitched to SP triggering p(NIPAAM-*co*-AA-*co*-SP) gel contraction and opening of the channel.

Right, Top: Photos of the valve in operation before (flow OFF) and after (flow ON) one minute of blue light irradiation.

Right, Bottom: Flowrate and cumulative volume measurements showing repeated opening and closing of microvalve: 1 min blue light irradiation opens valve followed by ~5.5 min thermal relaxation to close.



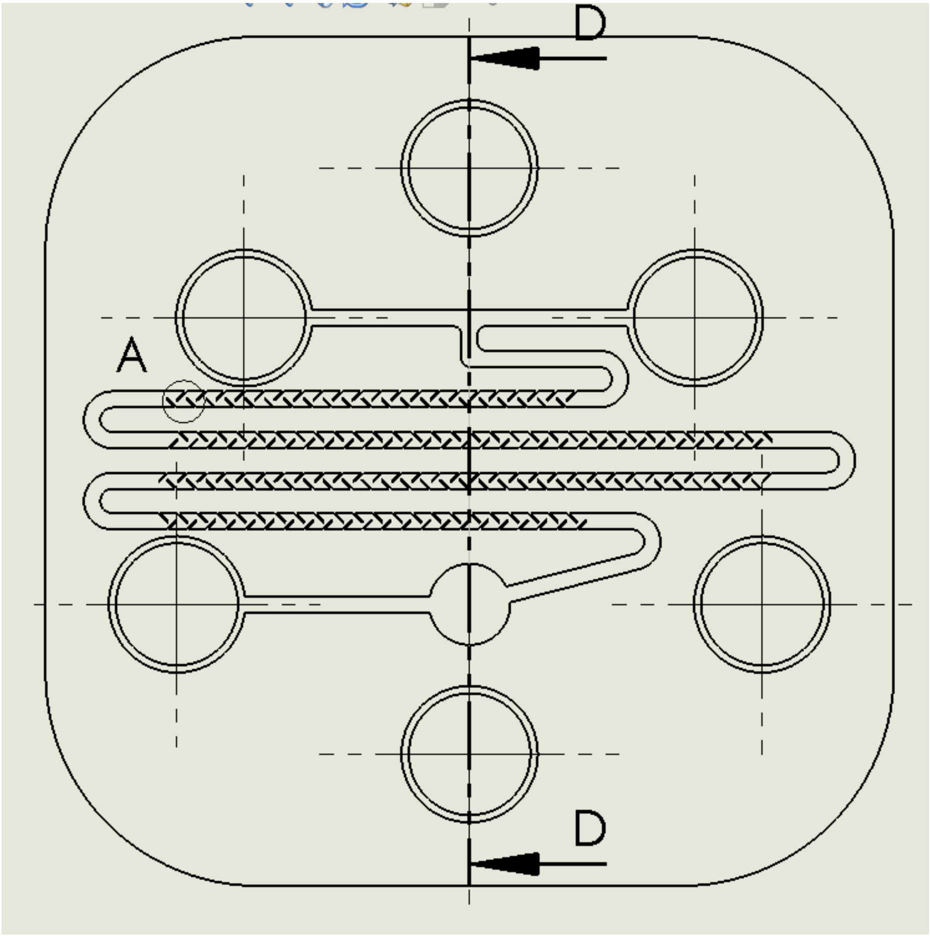
From: 'Molecular design of light-responsive hydrogels, for in-situ generation of fast and reversible valves for microfluidic applications ' Chemistry of Materials (2015), accepted.

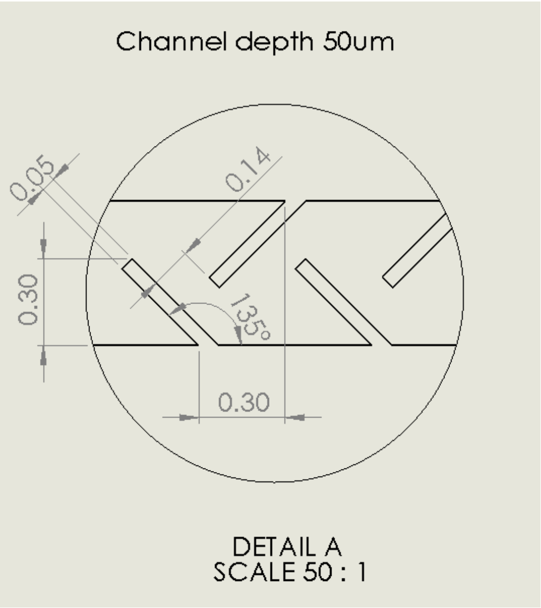
Jeroen ter Schiphorst,[†,#] Simon Coleman,[‡,#] Jelle E. Stumpel,[†] Aymen Ben Azouz,[‡] Dermot Diamond[*,‡] and Albertus P.H.J. Schenning[*,†,§]

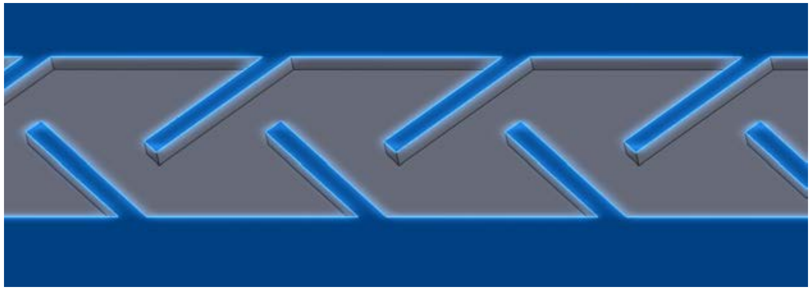
†Functional Organic Materials and Devices, §Institute for Complex Molecular Systems, Eindhoven University of TechnologyEindhoven, The Netherlands

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

Mixing Baffles







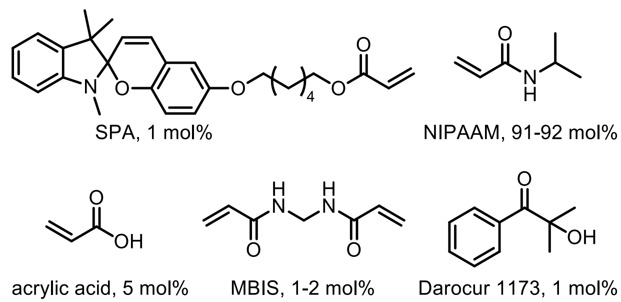
Photocontrol of Assembly and Subsequent Switching of Surface Features

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

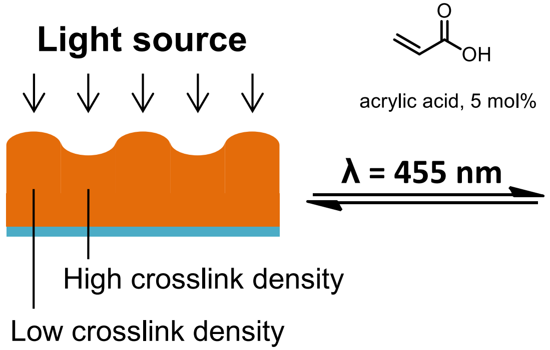
ACS applied materials & interfaces, 6 (2014) 7268-7274

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

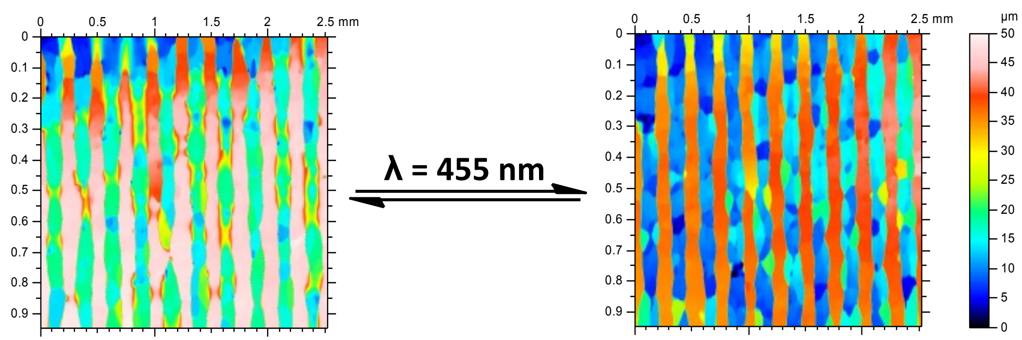
Jelle E. Stumpel,[†] Bartosz Ziółkowski,[‡] Larisa Florea,[‡] Dermot Diamond,[‡] Dirk J. Broer,[*,†,§] and Albertus P. H. J. Schenning[*,†,§]

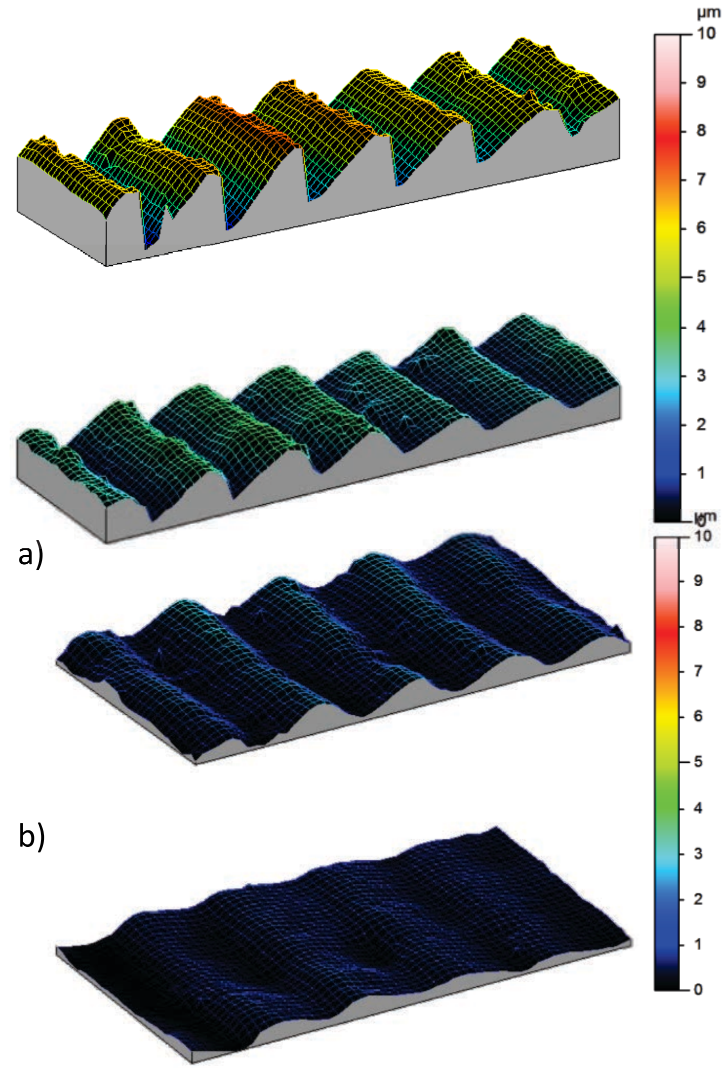


a)

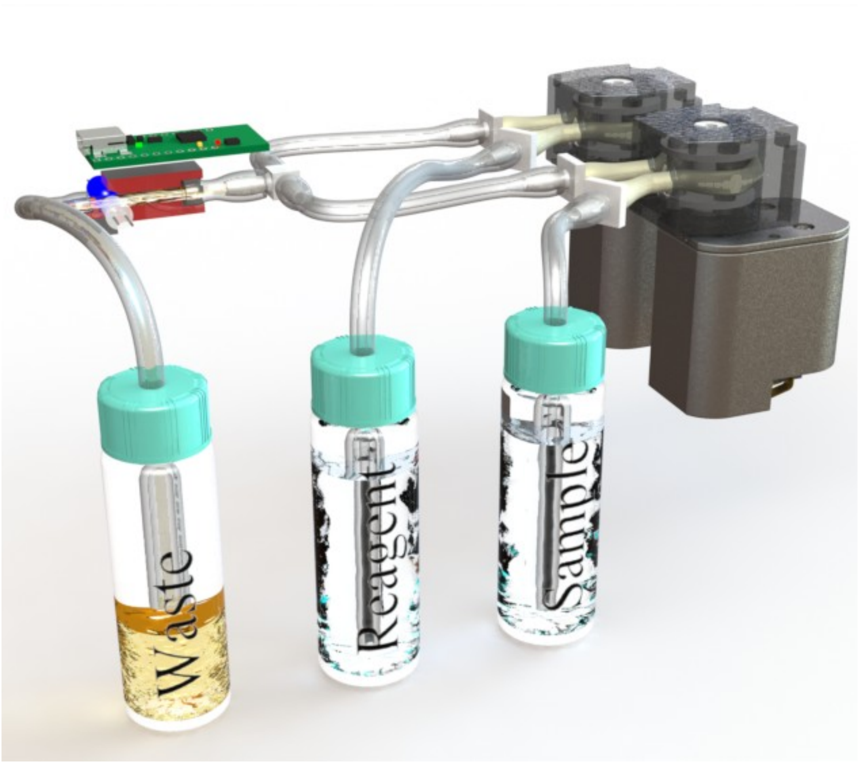


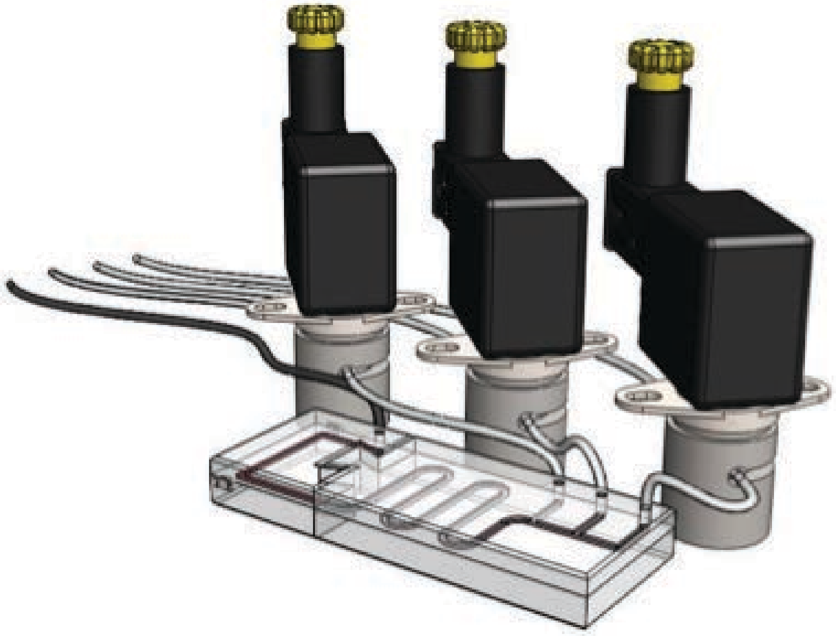
b)



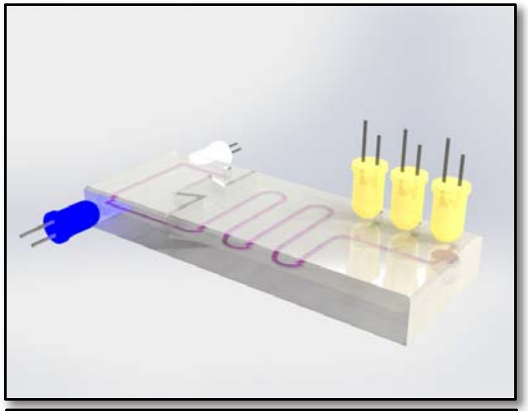


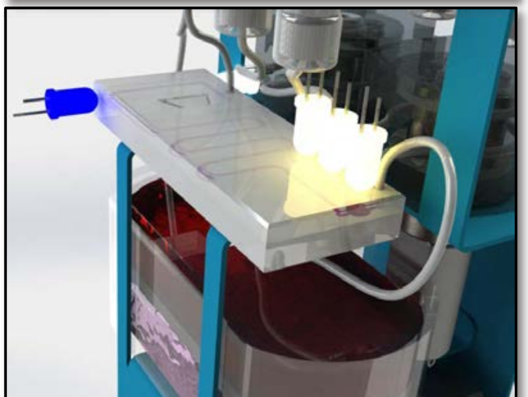
We must go from this:

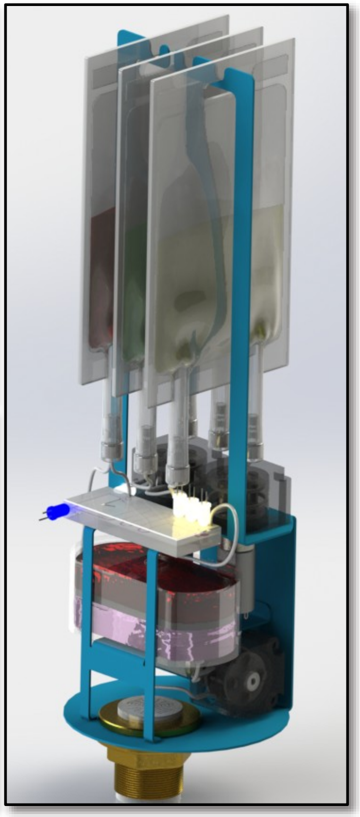


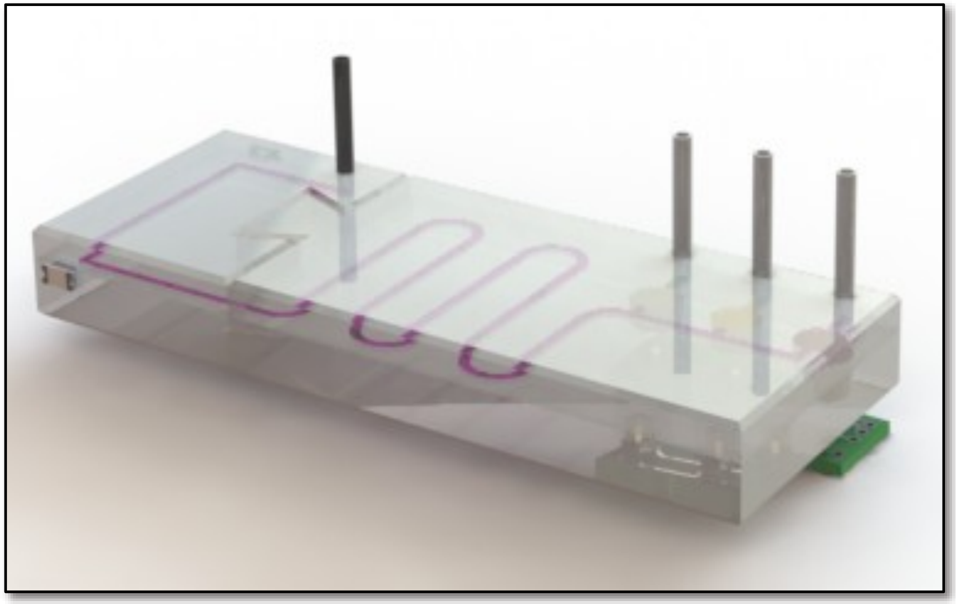


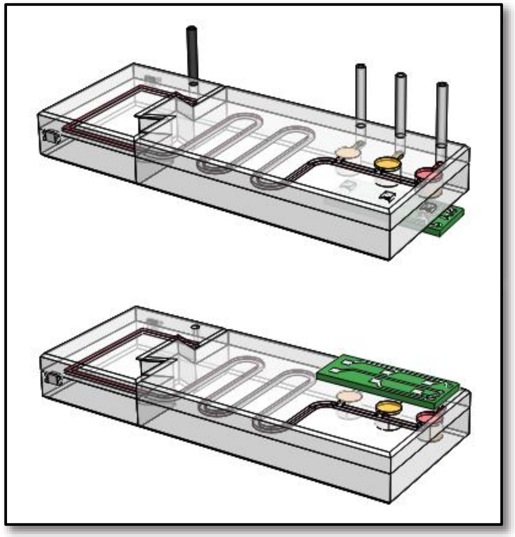
To Photo-Fluidics & Detection











- **Fluidic handling completely integrated into the microfluidic chip**
  - **Valves actuated remotely using light (LEDs)**
  - **Detection is via LED colorimetric measurements**
  - **Photo-controlled uptake and release**

And Ultimately – to Bioinspired Multi-Functional Fluidics

- **In the future, the fluidic system will perform much more sophisticated 'bioinspired' functions**
  - System diagnostics, leak/damage detection
  - Self-repair capability
  - Switchable behaviour (e.g. surface roughness, binding/release),
- **These functions will be inherent to the channels and integrated with circulating smart micro/nano-vehicles**
  - Spontaneously move under an external stimulus (e.g. chemical, thermal gradient) to preferred locations

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

We have the tools – now we need creativity!