‘Sensing the Molecular World - Challenges and Opportunities’

Dermot Diamond

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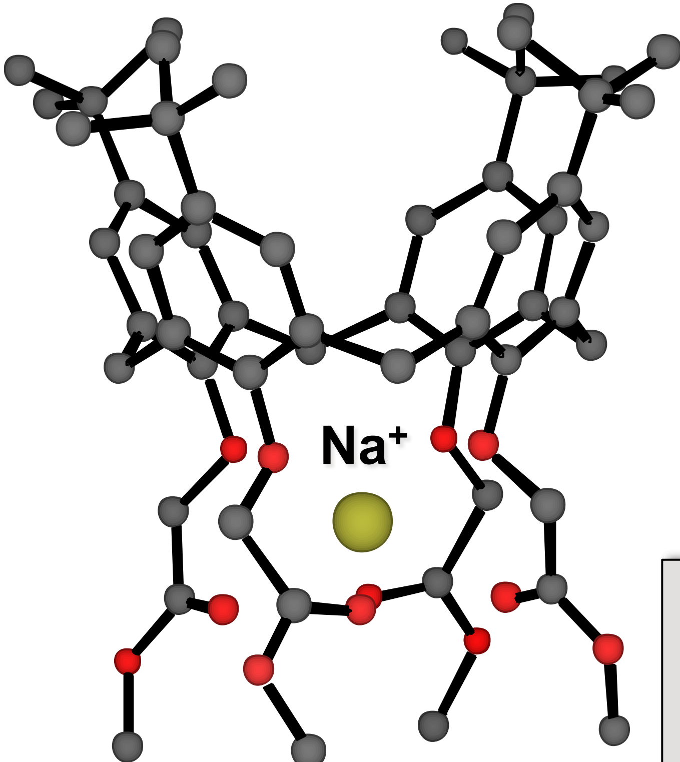
Dublin City University, Dublin 9, Ireland

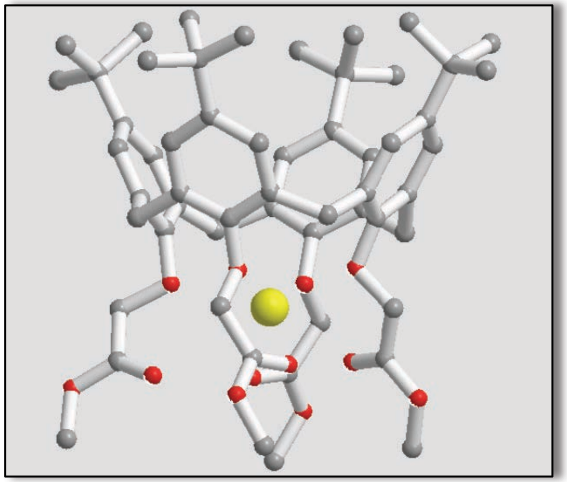
Invited Seminar Presented at GE Global Research

November 4th 2016

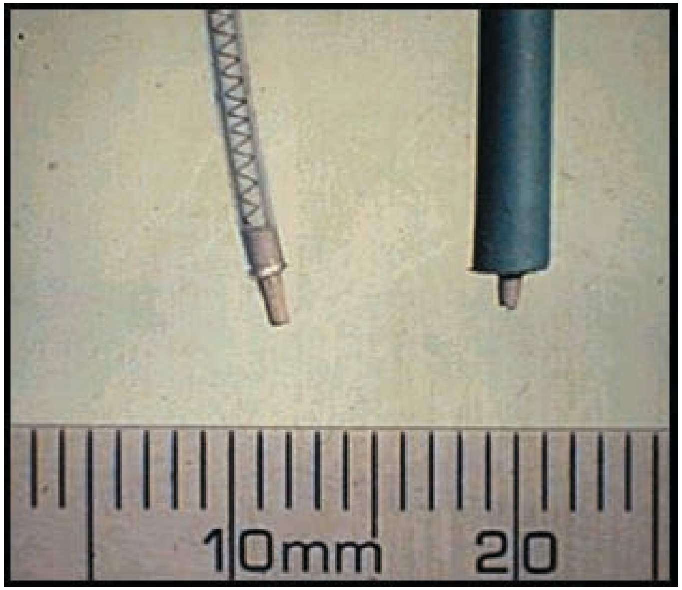
Calixarene Ionophores – controlling the selectivity



$$H_3C-O-\underset{\underset{O}{\|}}{C}-CH_2-$$



Blood Analysis; Implantible Sensors



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

Dr. David Band, St Thomas's Hospital London

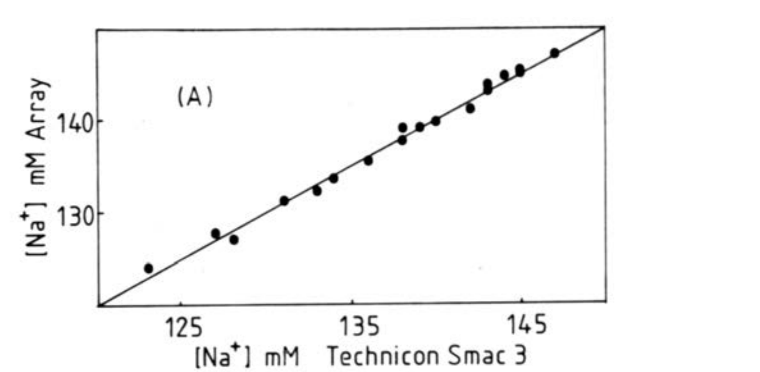
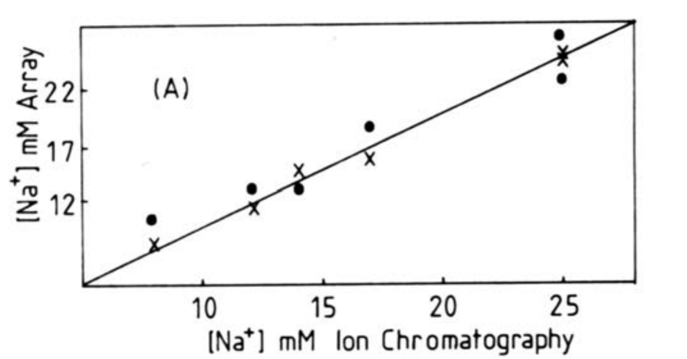


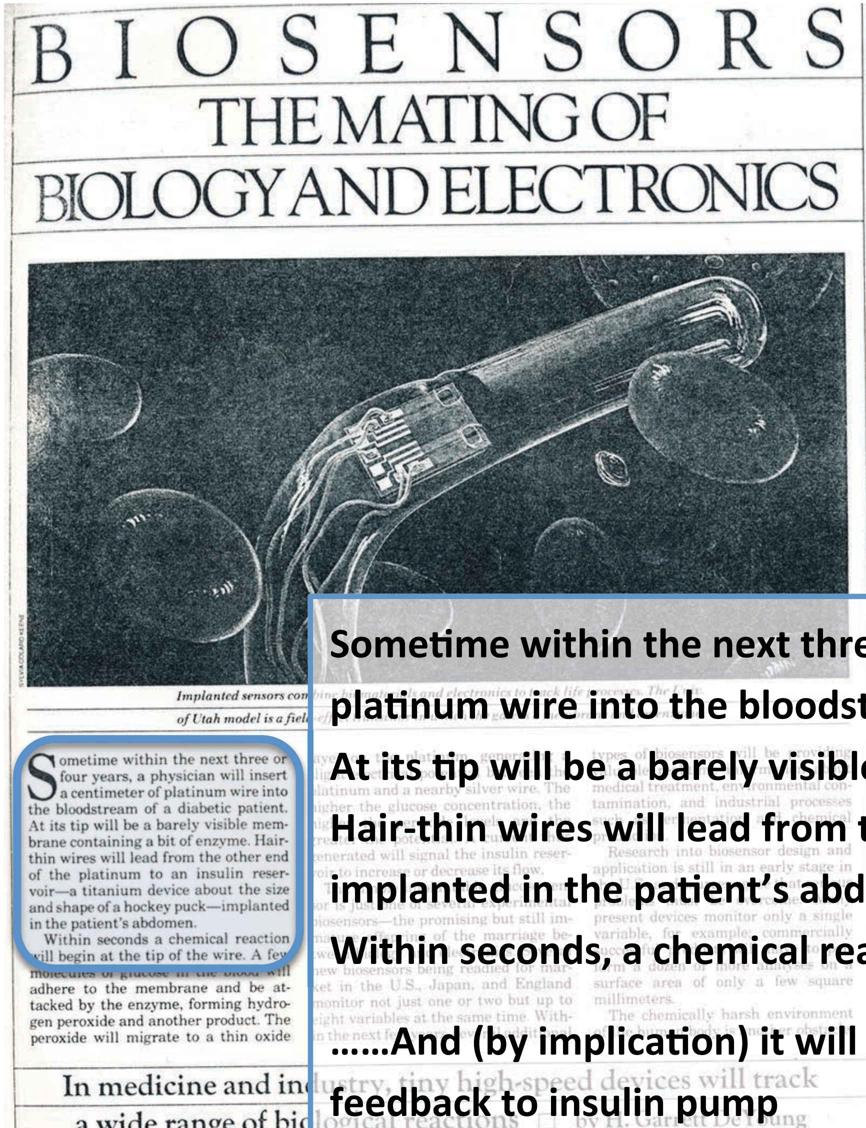
Fig. 3. Comparison of plasma sodium analysis using the array-FIA approach with a SMAC analyser. Good correlation without bias is obtained [5].



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

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

The (broken) promise of biosensors…..

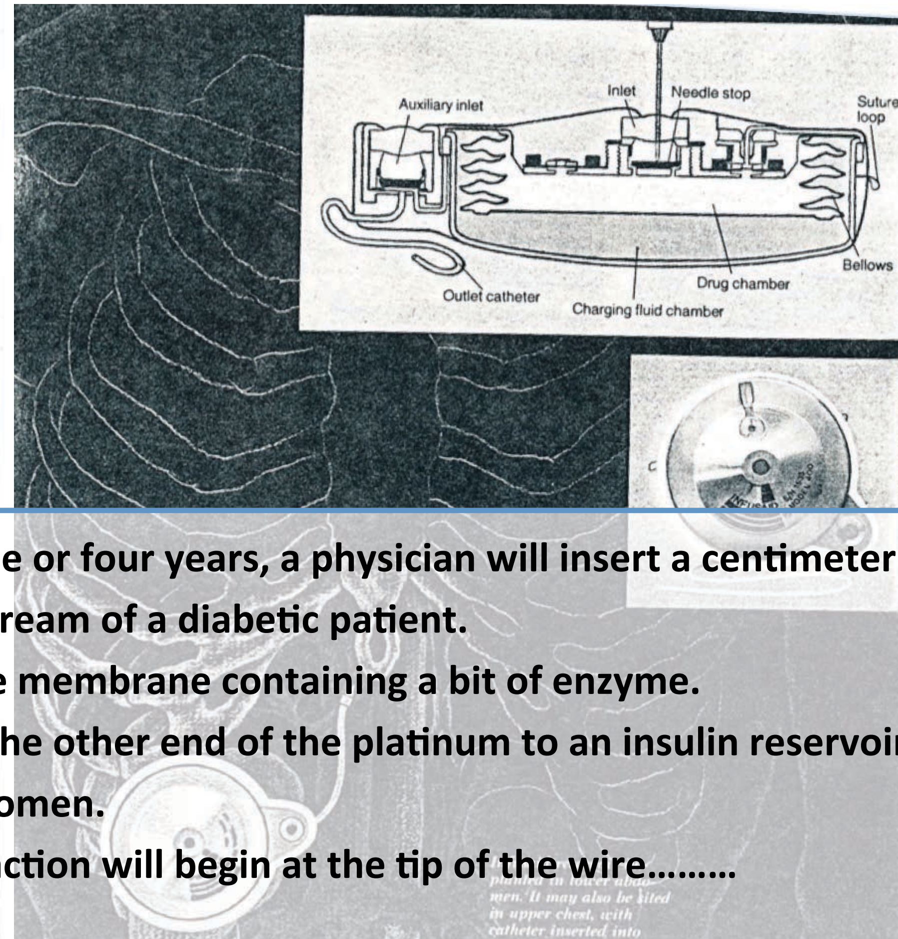


BIOSENSORS
THE MATING OF BIOLOGY AND ELECTRONICS

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.

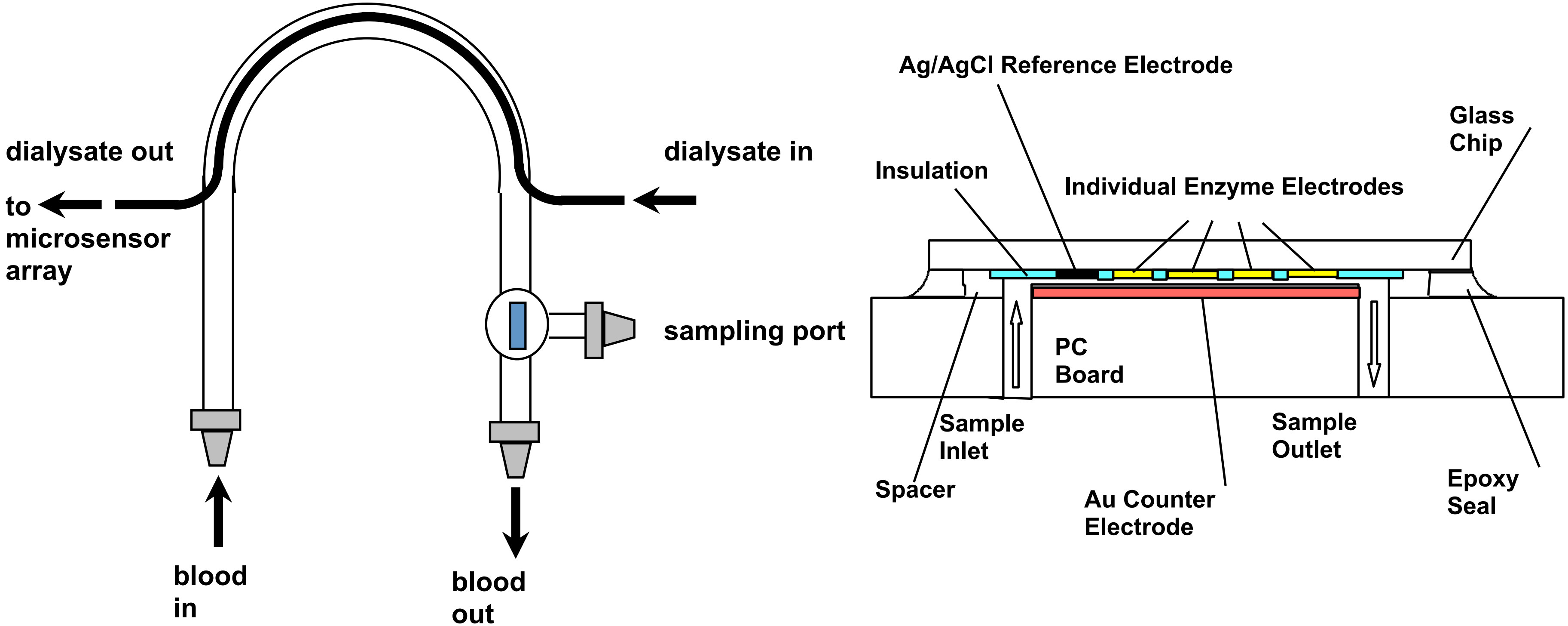
At its tip will be a barely visible membrane containing a bit of enzyme.

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

Microdialysis sampling via arterio-venus shunt

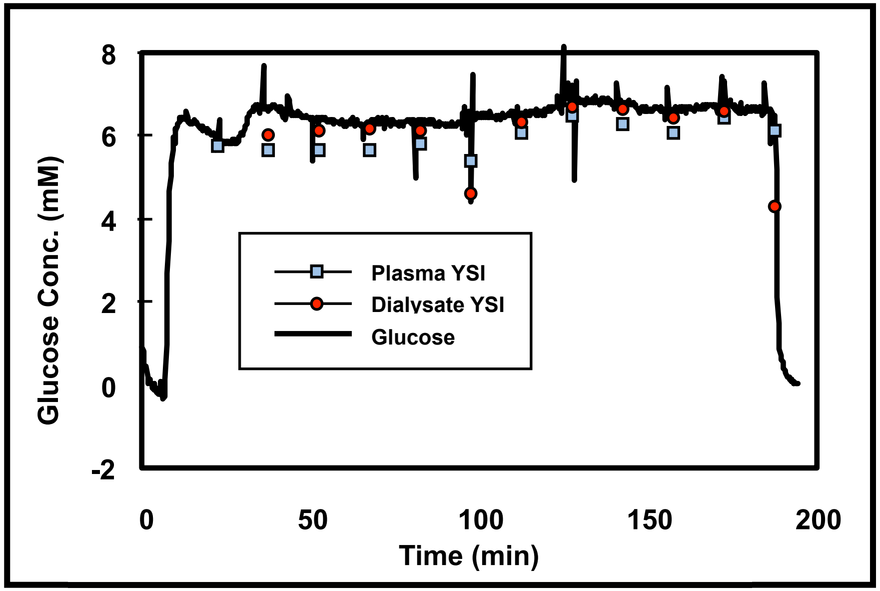


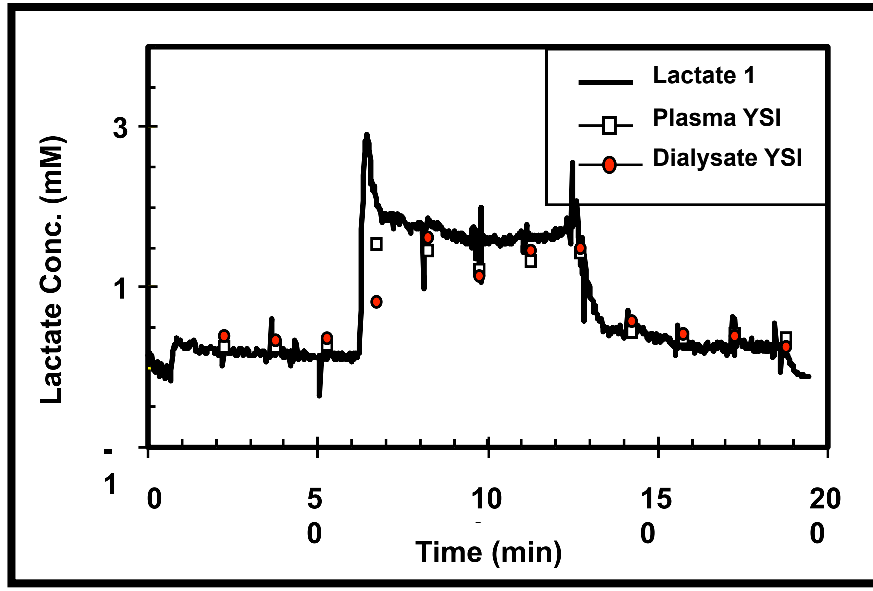
Novel Instrumentation for Real-Time Monitoring Using Miniaturised Flow Cells with Integrated Biosensors, R. Freaney, A. McShane, T.V. Keavney, M.McKenna, K. Rabenstein, F.W. Scheller, D. Pfeiffer, G. Urban, I. Moser, G. Jobst, A. Manz, E. Verpoorte, M.W. Widmer, D. Diamond, E. Dempsey, F.J. Saez de Viteri and M. Smyth, Annals of Clinical Biochemistry, 34 (1997) 291-302.

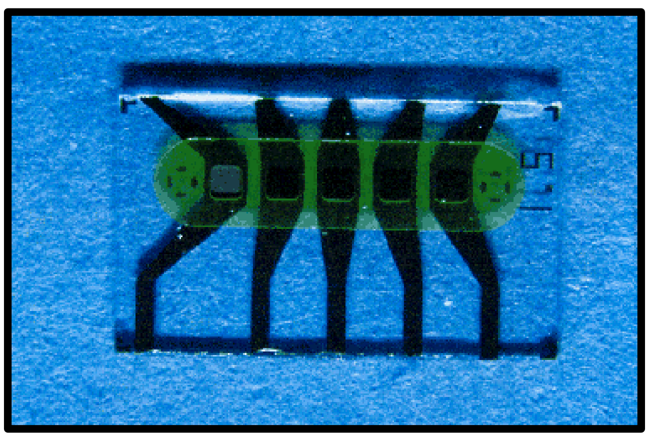
In Vitro Optimisation of a Microdialysis System with Potential for On-Line Monitoring of Lactate and Glucose in Biological Samples, E. Dempsey, D. Diamond, M.R. Smyth, M. Malone, K. Rabenstein, A. McShane, M.McKenna, T.V. Keavney and R Freaney, Analyst, 122 (1997) 185-189.

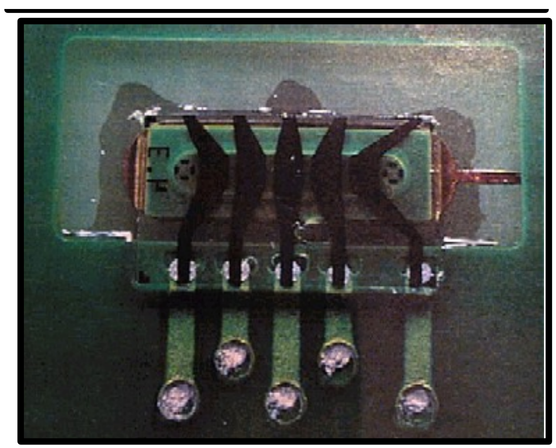
Design and Development of a Miniaturized Total Chemical-Analysis System for Online Lactate and Glucose Monitoring in Biological Samples, Ethna Dempsey, Dermot Diamond, Malcolm R. Smyth, Gerald Urban, Gerhart Jobst, I. Moser, Elizabeth MJ Verpoorte, Andreas Manz, HM Widmer, Kai Rabenstein and Rosemarie Freaney, Anal. Chim. Acta, 346 (1997) 341-349.

Real Time Blood Glucose and Lactate









System functioned continuously for up to three hours!

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.

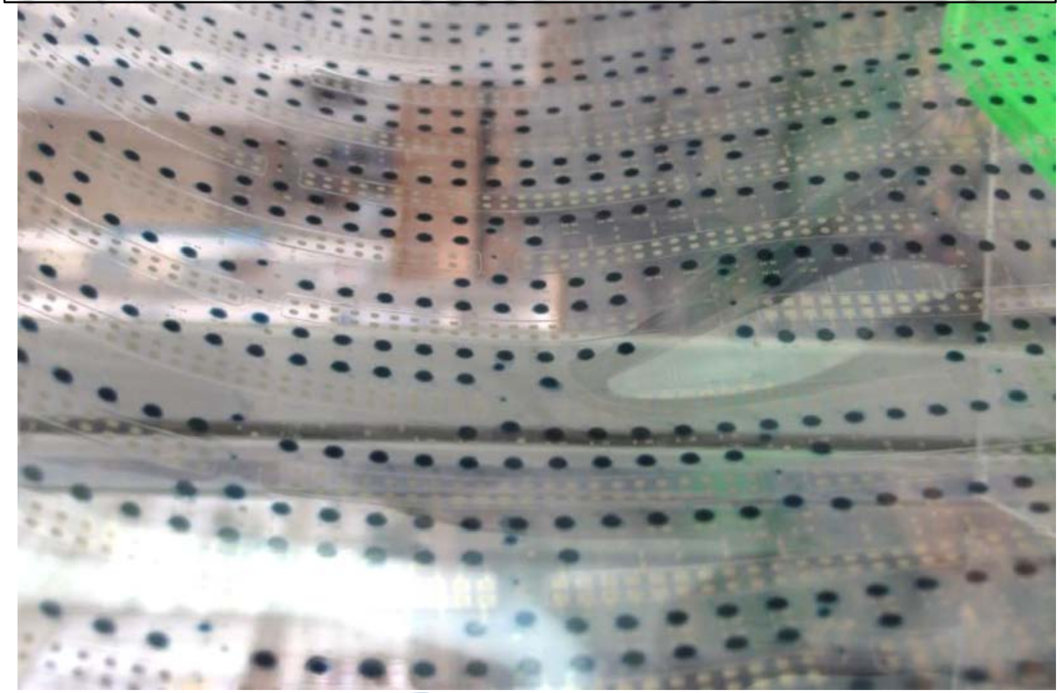
Digital communications networks are at the heart of modern society. The digitization of communications, the development of the Internet, and the availability of relatively inexpensive but powerful mobile computing technologies have established a global communications network capable of linking billions 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 - 2016

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

Abbott Freestyle 'Libre'

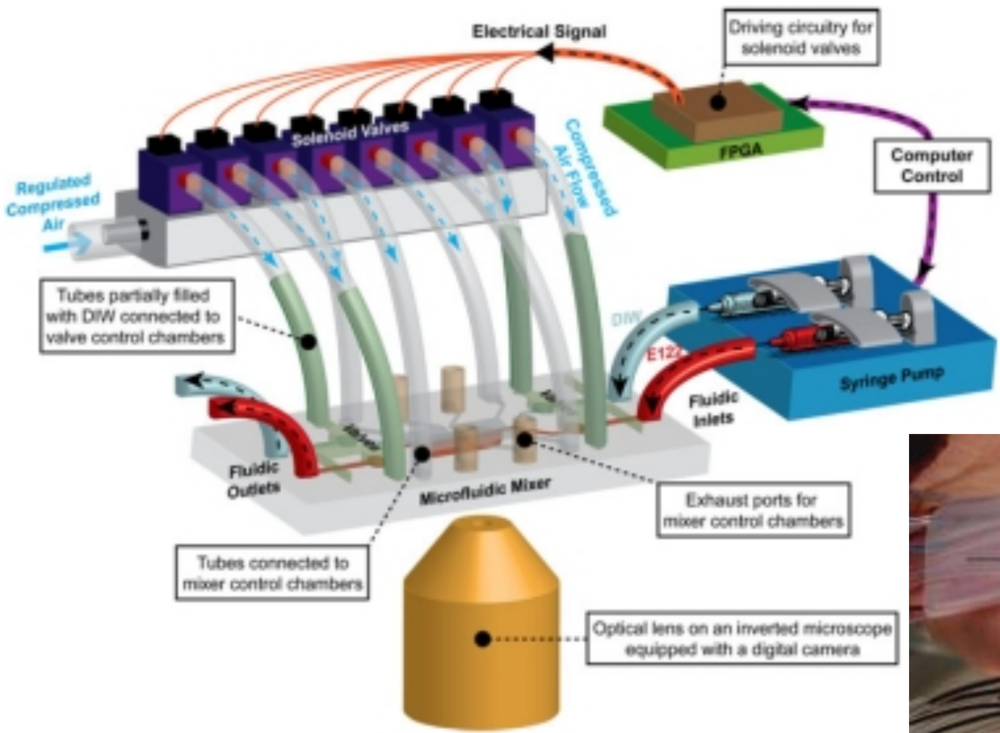
The days of routine glucose testing with lancets, test strips and blood are over.[2]

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

See http://diatribe.org/drugdevice-name/freestyle-libre

But not everything is integrated…..

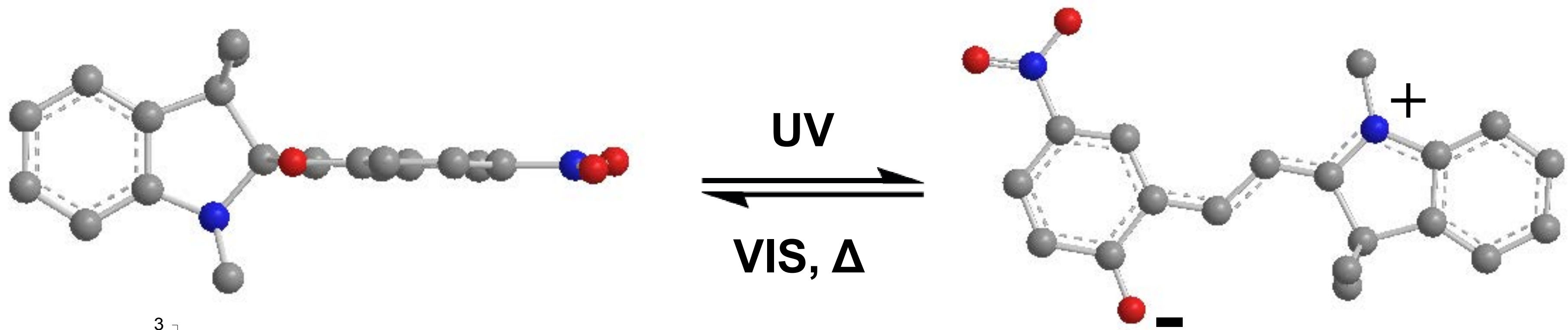


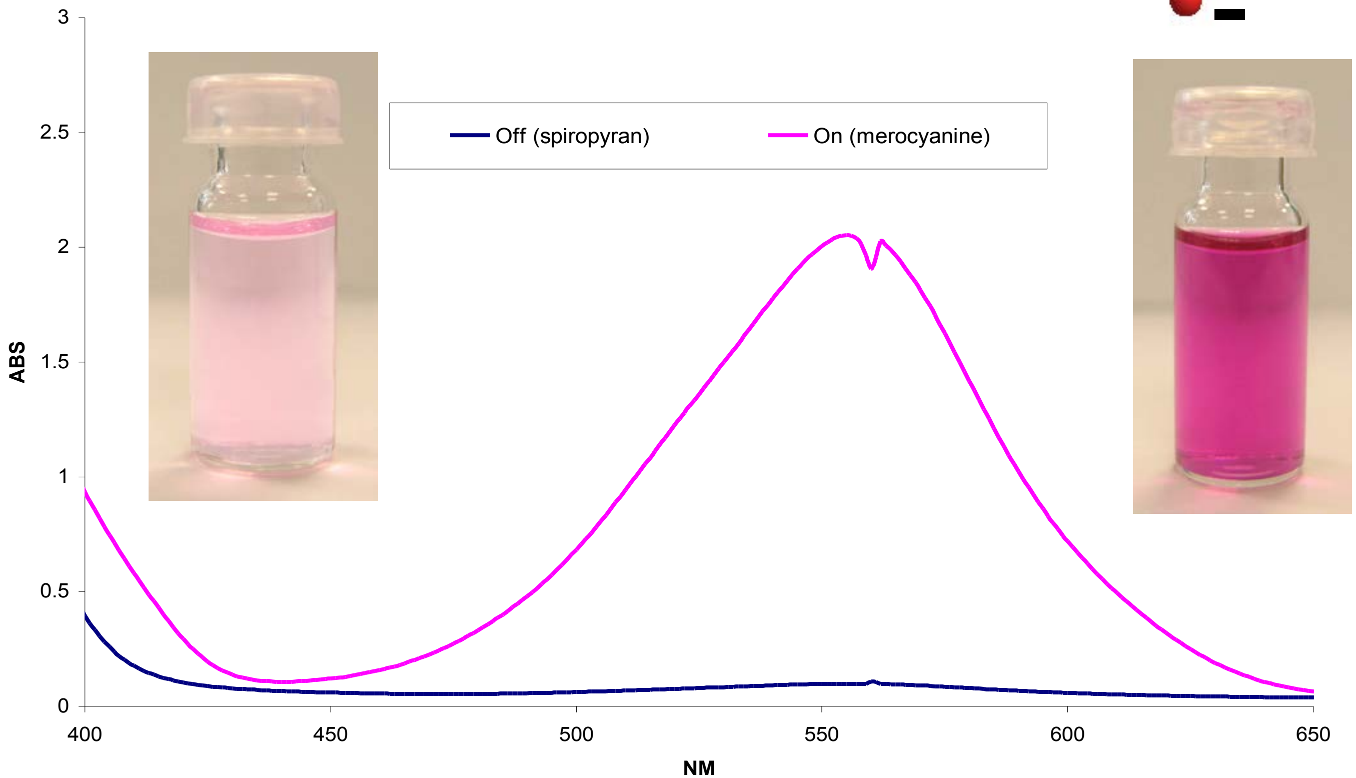
- Many components are located off-chip
- Detectors, pumps, valves….
- Hard Materials

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

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

Photoswitchable Actuators

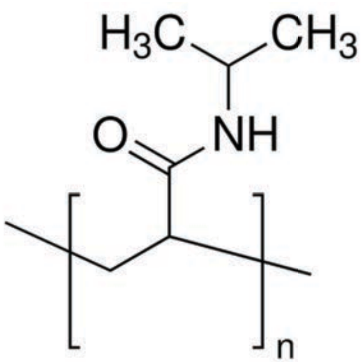




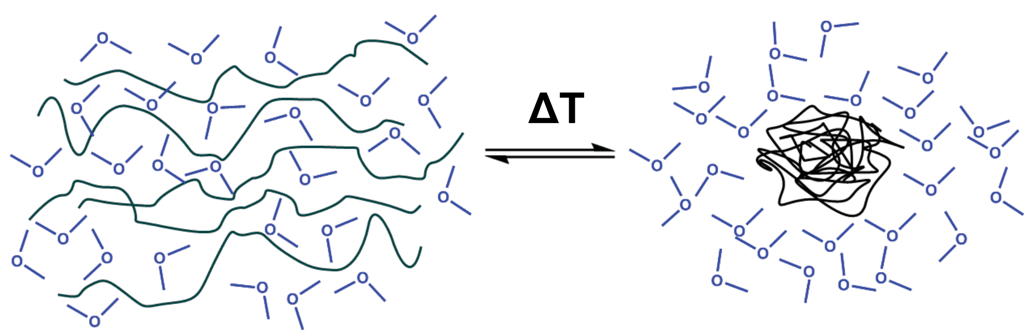
Poly(*N*-isopropylacrylamide)

- **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



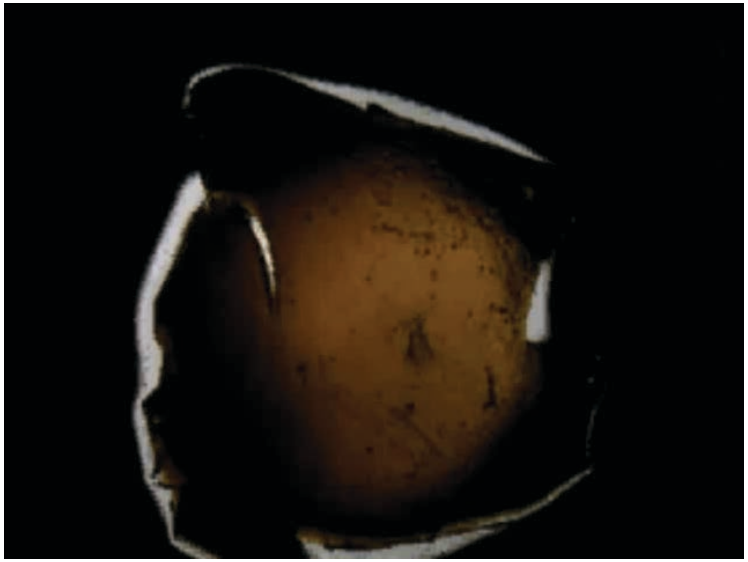
Hydrophilic **Hydrophobic**

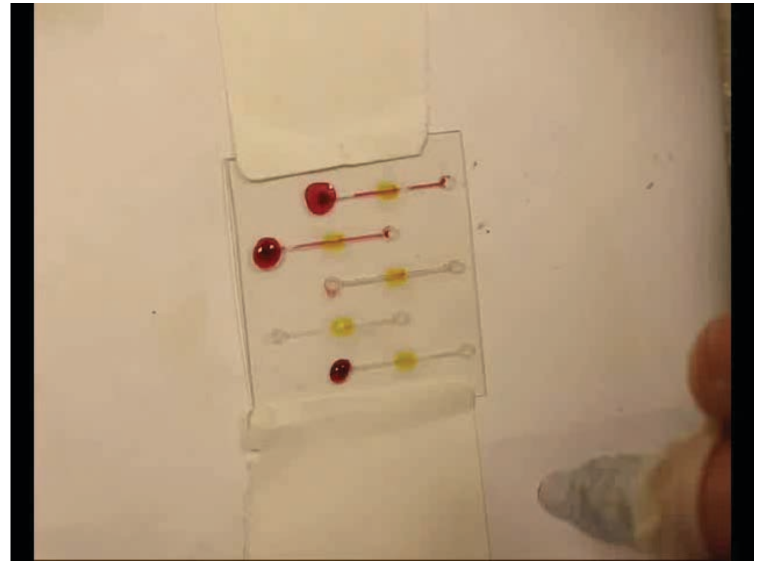


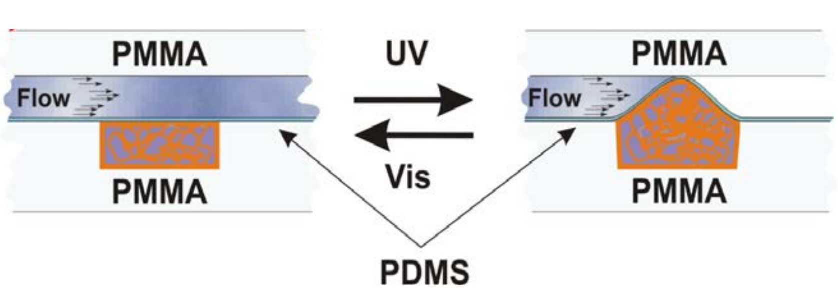
Hydrated Polymer Chains

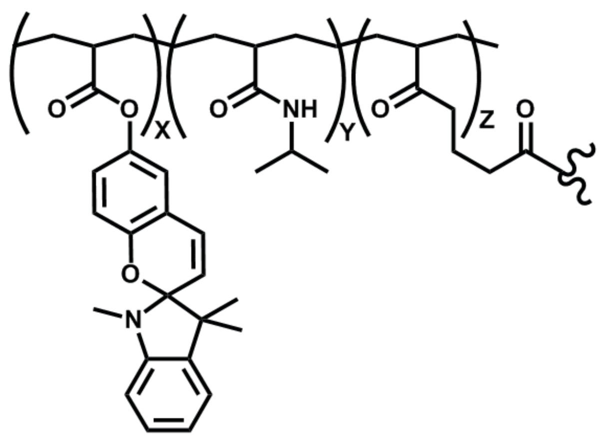
Loss of bound water -> polymer collapse

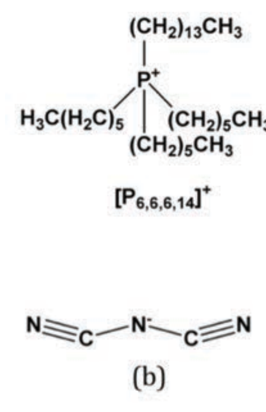
Photo-actuator polymers as microvalves in microfluidic systems







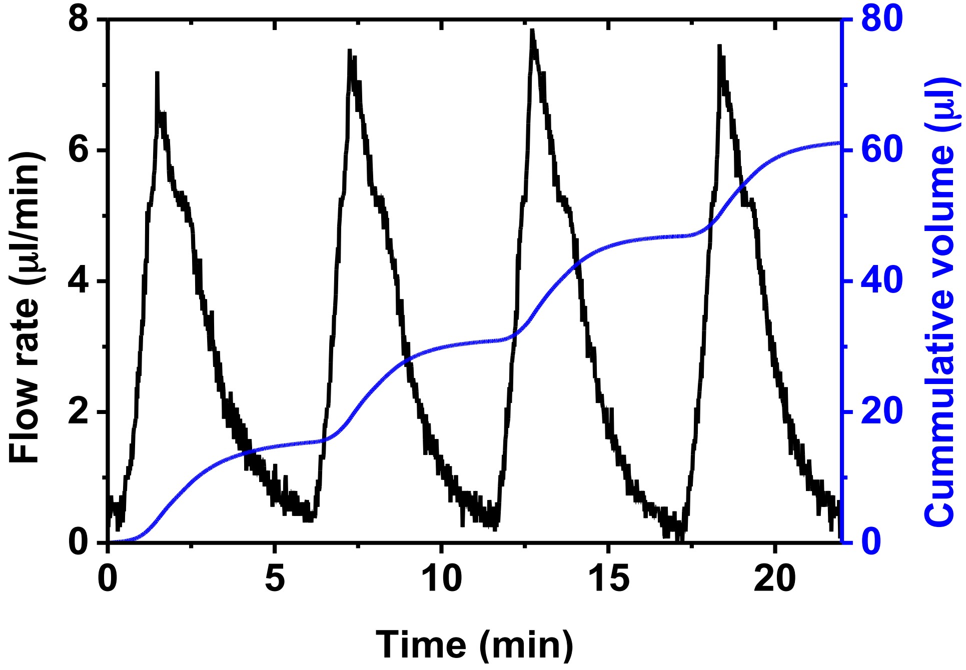


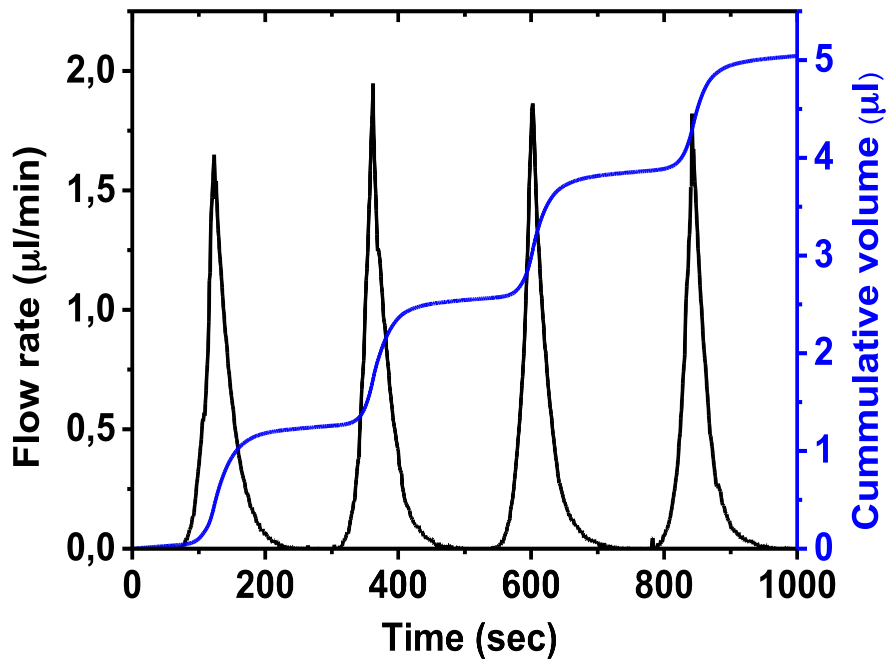


trihexyltetradecylphosphonium dicyanoamide $[P_{6,6,6,14}]^{+}[dca]^{-}$

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.

Optimisation of valve dimensions





1.7 mm mask **1.6 mm mask**

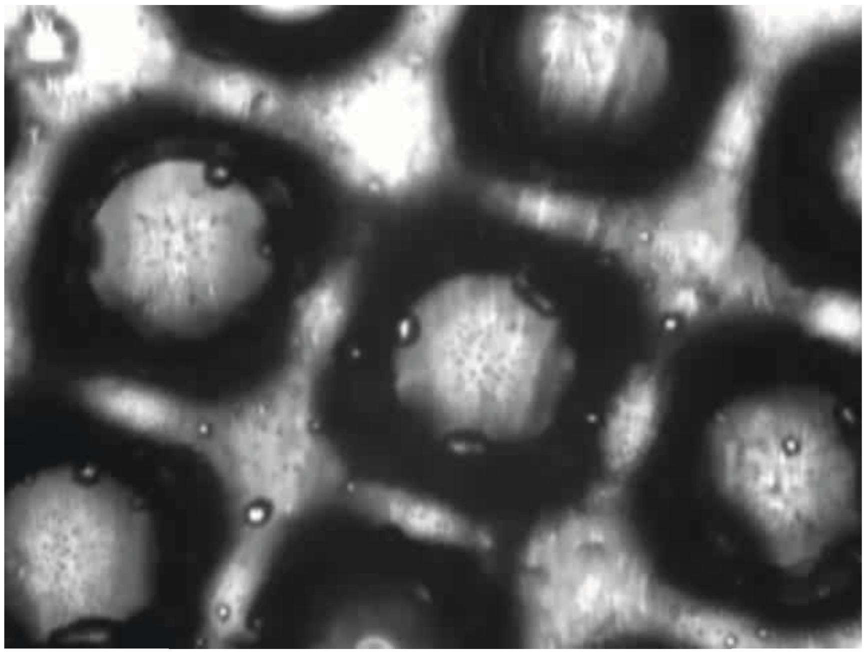
First example of actuating polymer gels as reusable valves for flow control on minute time scales (> 50 repeat actuations)

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)**

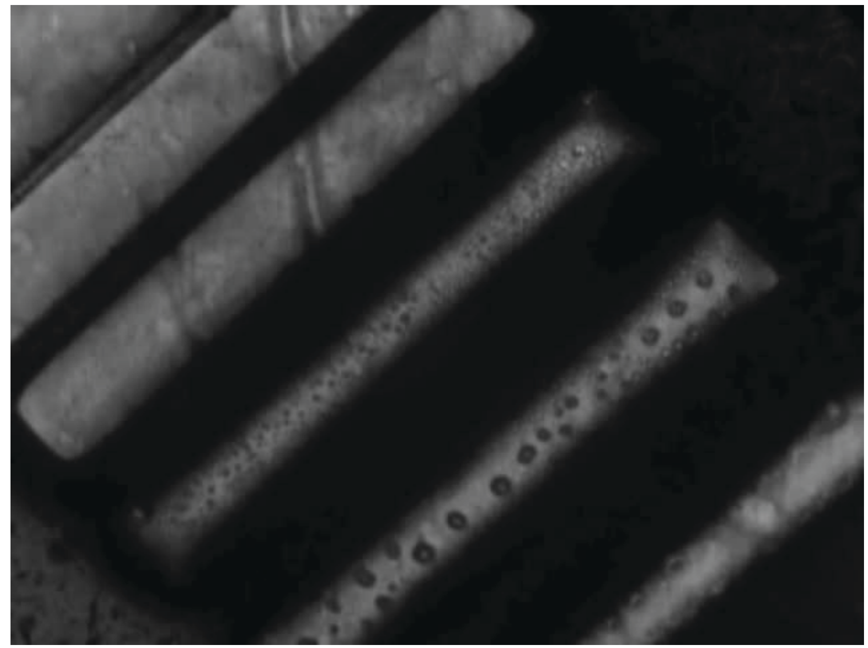
Functional Organic Materials and Devices, Department of Chemical Engineering and Chemistry, and Institute for Complex Molecular Systems, Eindhoven University of Technology

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

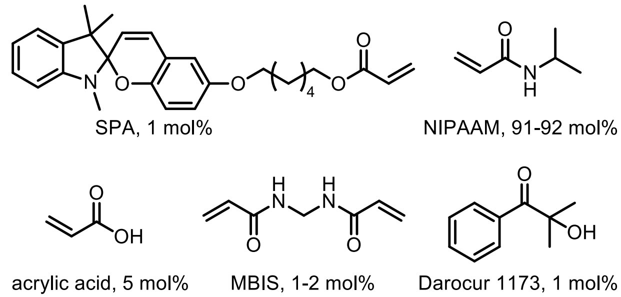
Photocontrol of Assembly and Subsequent Switching of Surface Features

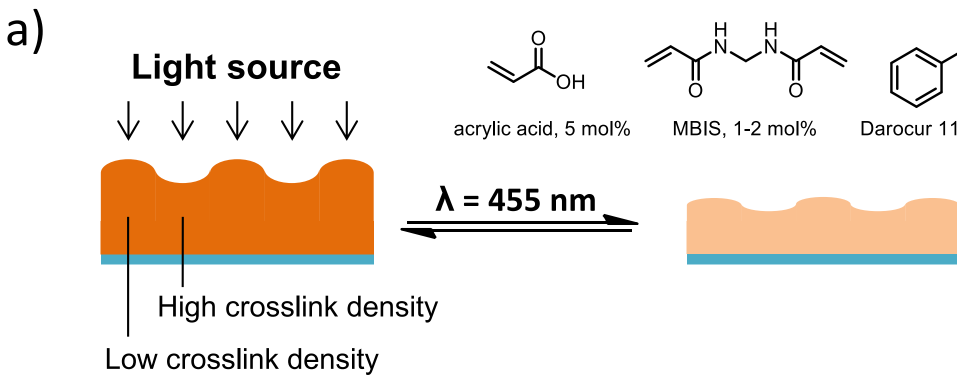
ACS APPLIED MATERIALS & INTERFACES
Research Article
www.acsami.org

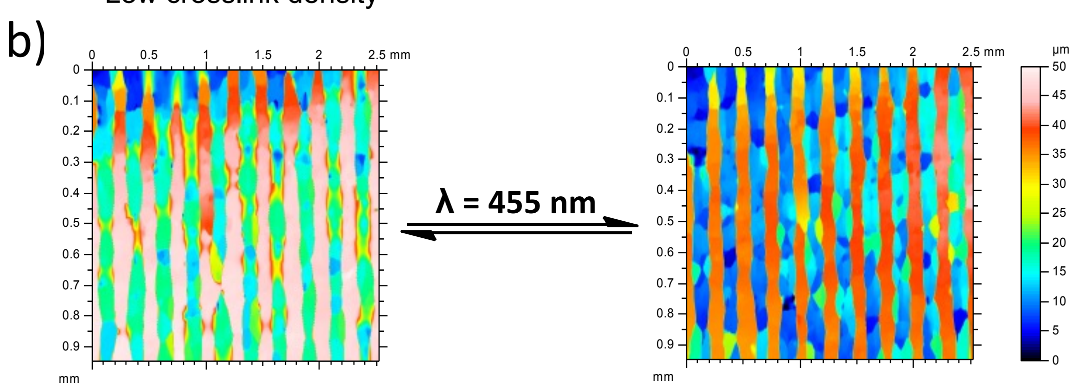
ACS applied materials & interfaces, 6 (2014) 7268-7274

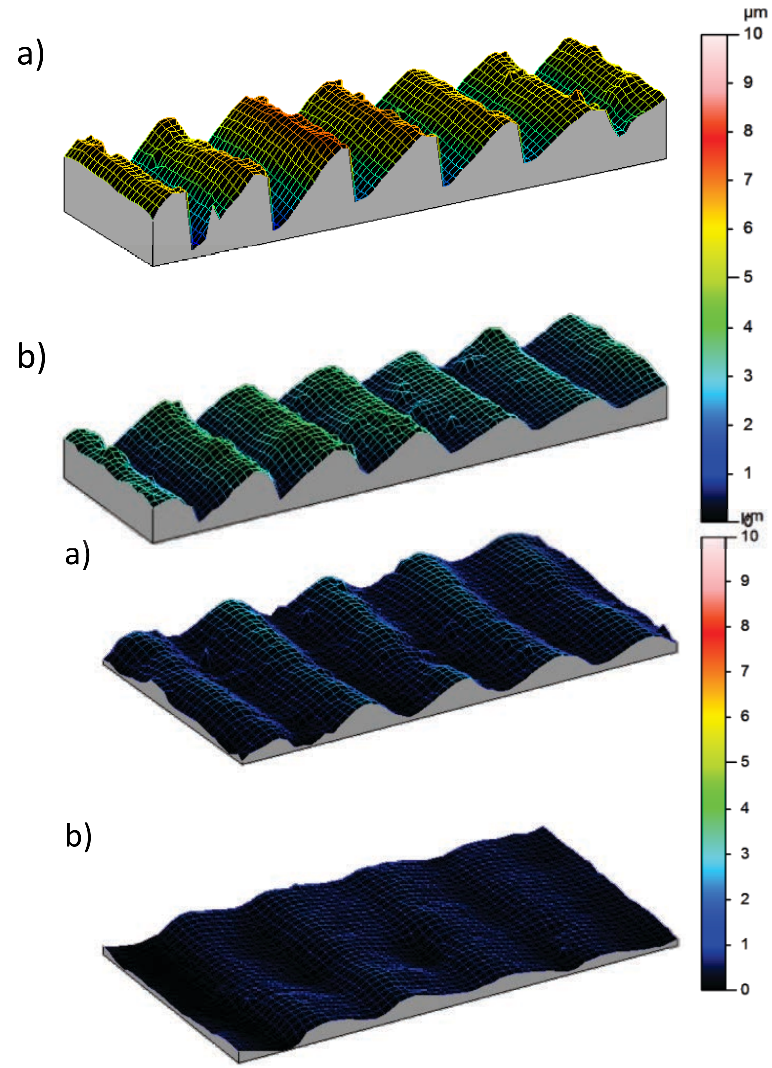
Photoswitchable Ratchet Surface Topographies Based on Self-Protonating Spiropyran–NIPAAM Hydrogels

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



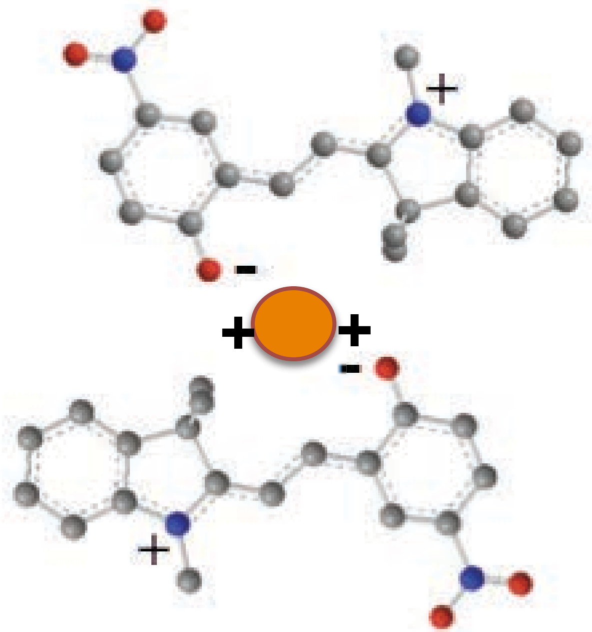


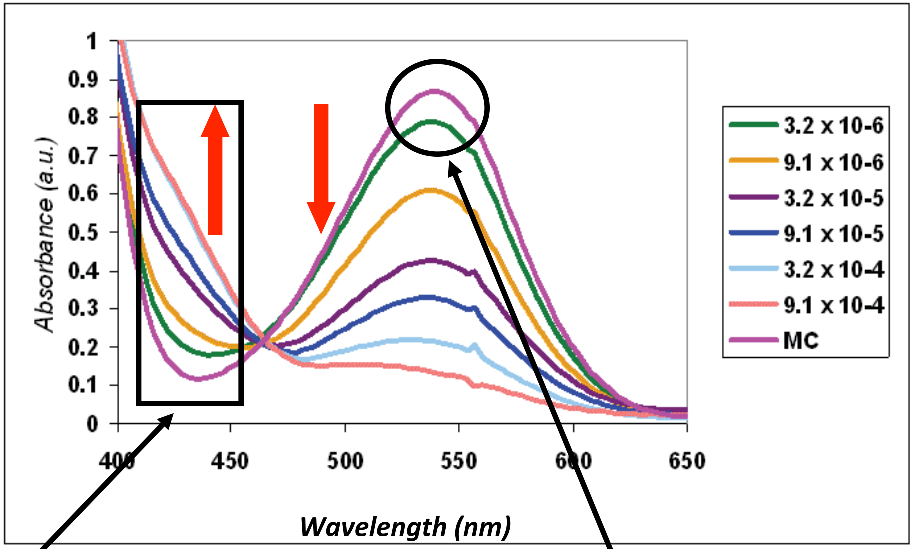




Spiropyran and Metal Ions

The binding of many metals, such as Cu^{2+} and Co^{2+}, to the phenolate of the MC form has been demonstrated

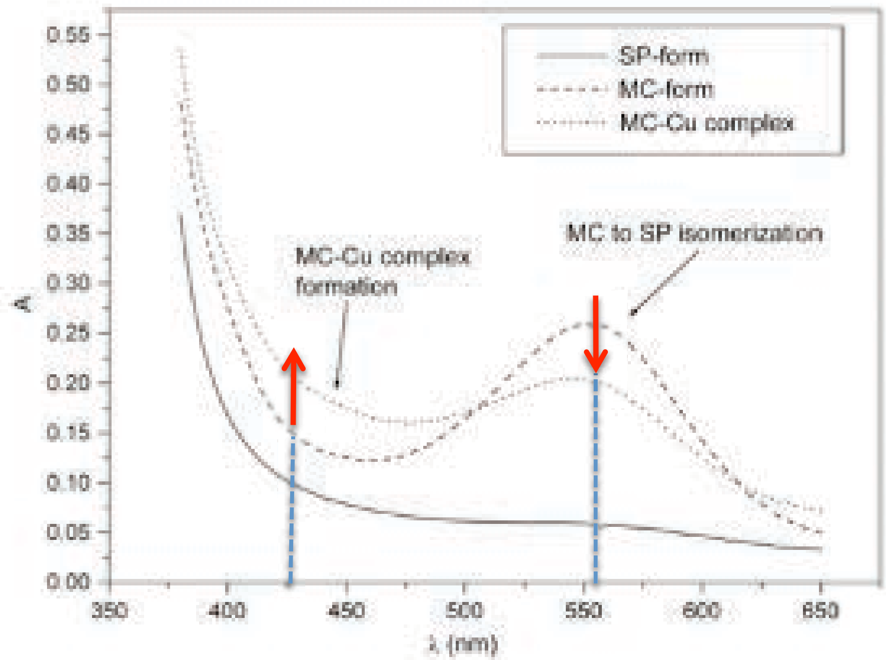


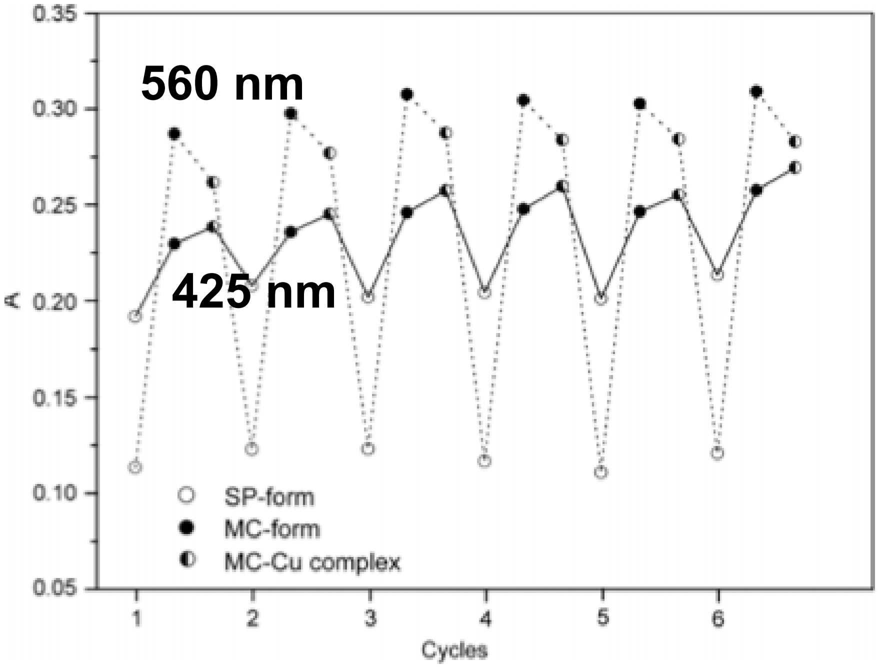


Increase in absorbance below ~460 nm due to formation of MC-Cu^{2+} complex

Decrease at 540 nm as free MC concentration decreases

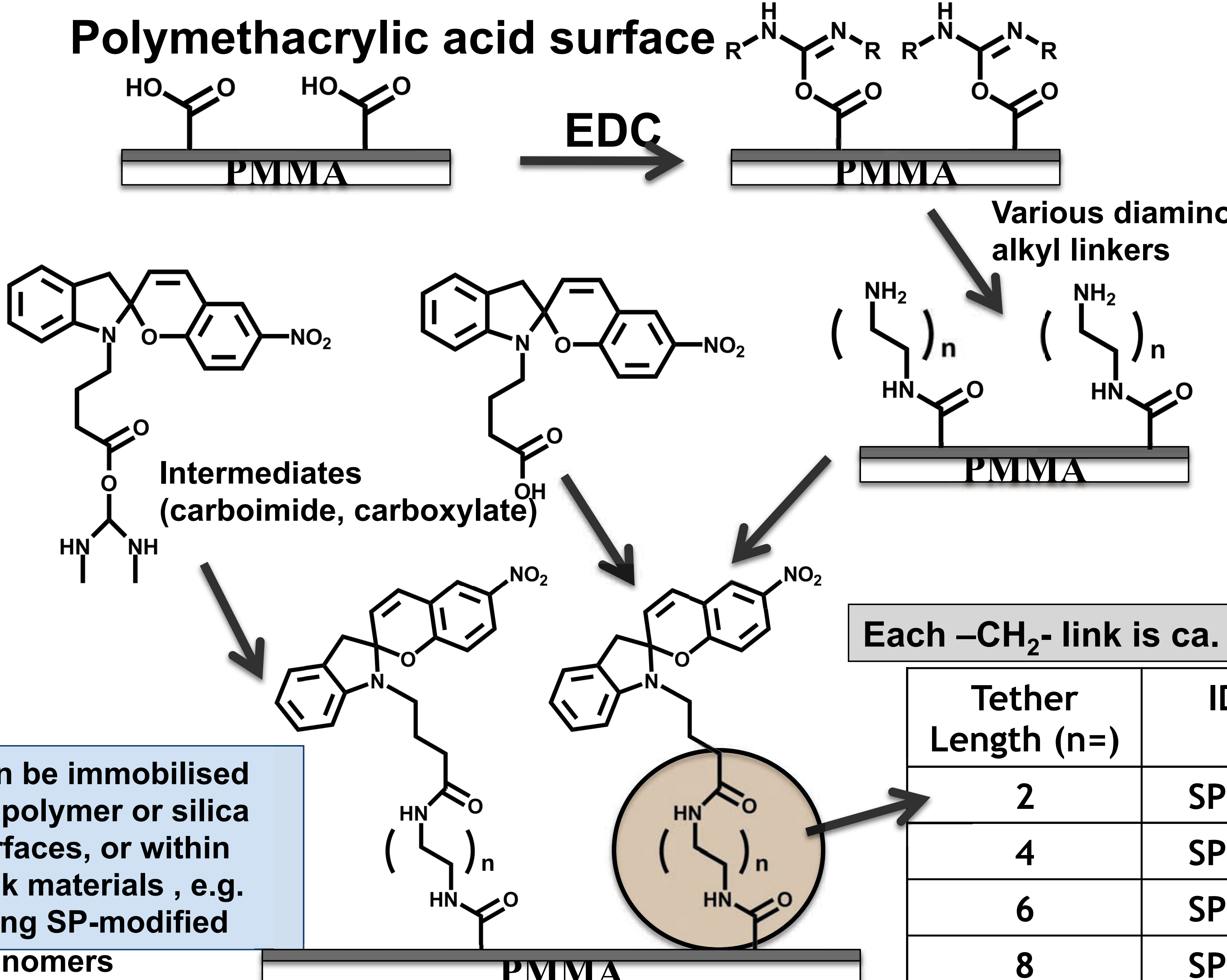
Detection of switching between SP/MC/MC-Cu^{2+} states using the 'Discophotometer





Photonic Modulation of Surface Properties: A Novel Concept in Chemical Sensing, Aleksandar Radu, Silvia Scarmagnani, Robert Byrne, Conor Slater, King Tong Lau and Dermot Diamond, J. Phys.D; Appl. Phys., 40 (2007) 7238-7244.

Polymethacrylic acid surface



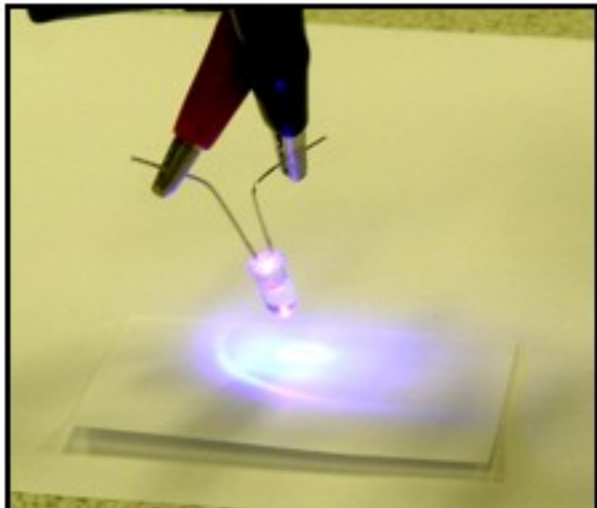
Each –CH_2- link is ca. 1.5 Å

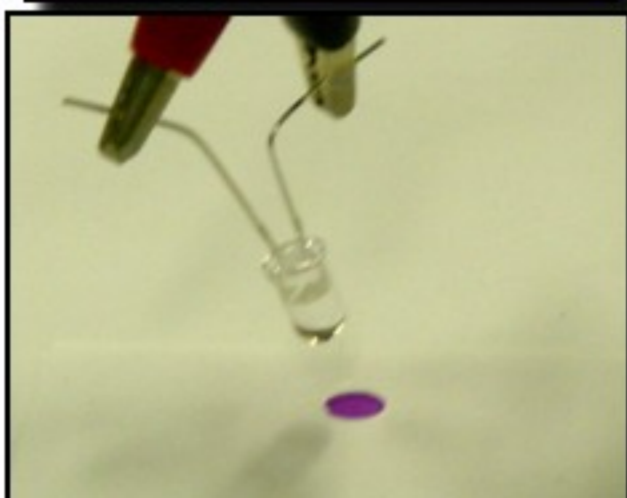
Tether Length (n=)	ID
2	SP-2
4	SP-4
6	SP-6
8	SP-8

Can be immobilised on polymer or silica surfaces, or within bulk materials , e.g. using SP-modified monomers

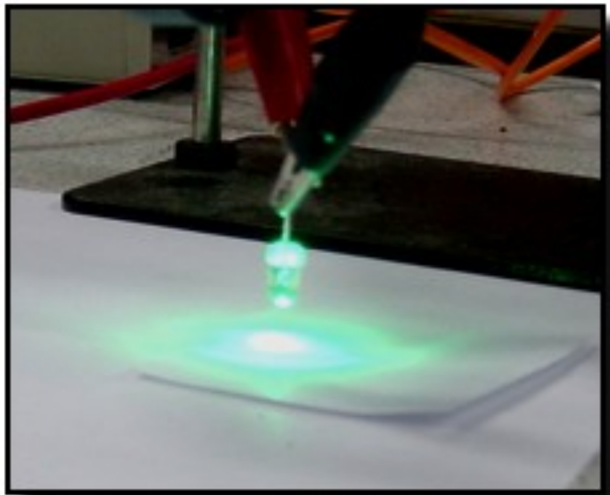
Switching SP-Doped Films

UV LED 380 nm

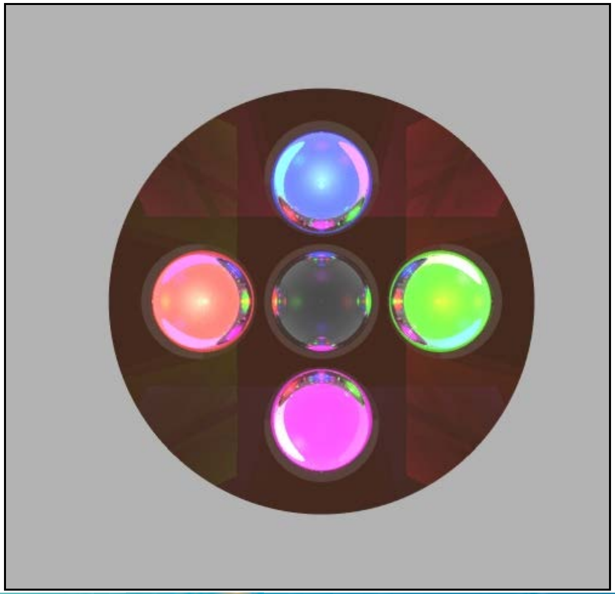


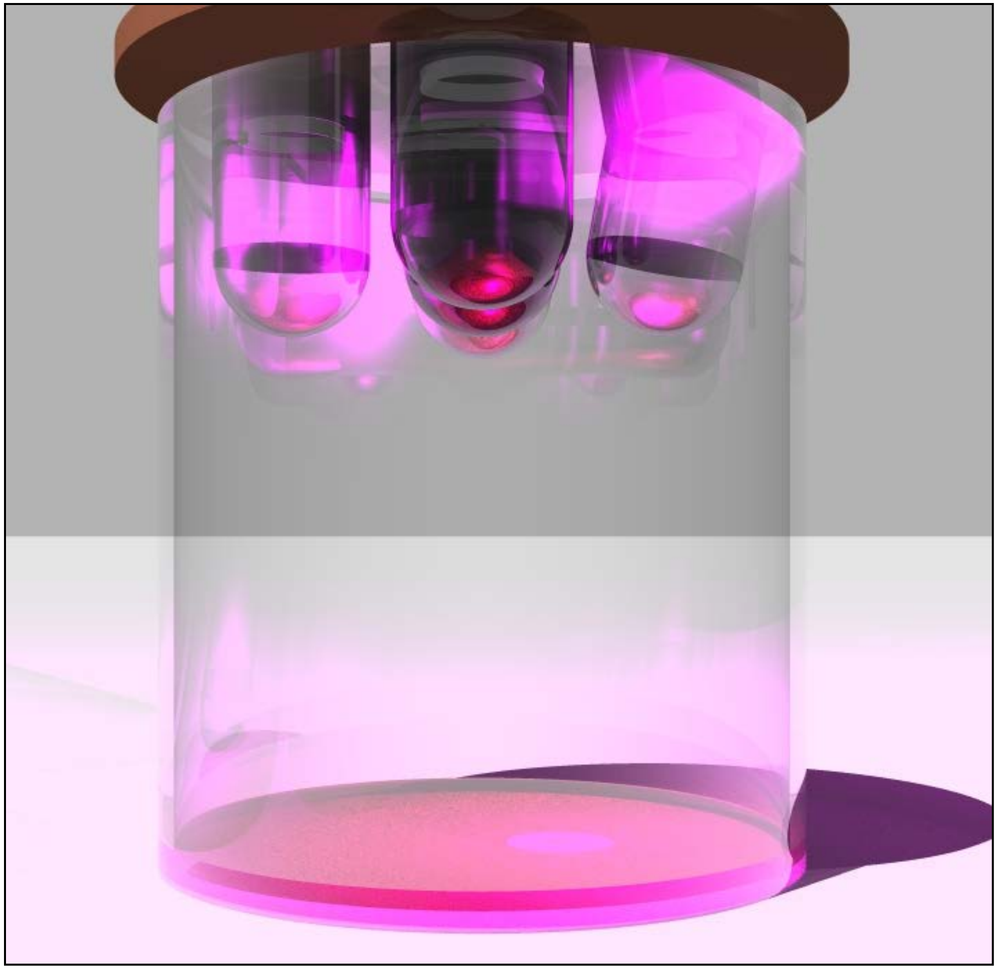


Green LED 523 nm

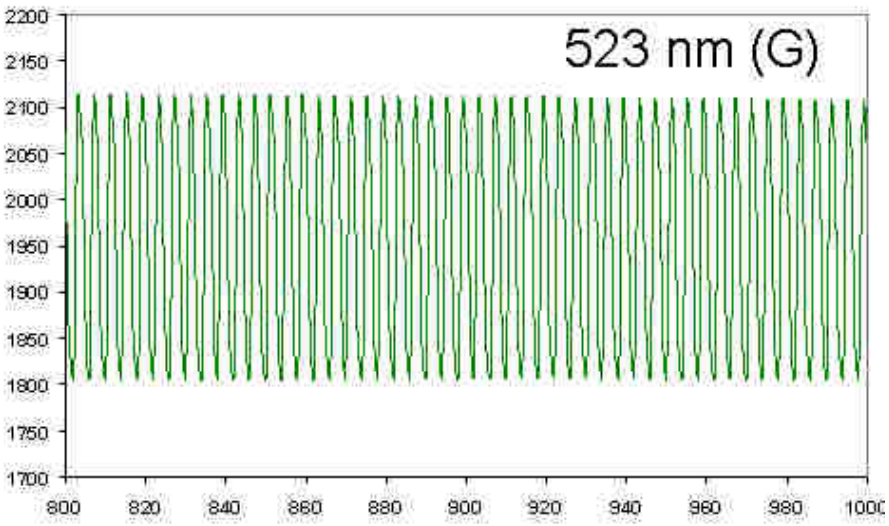


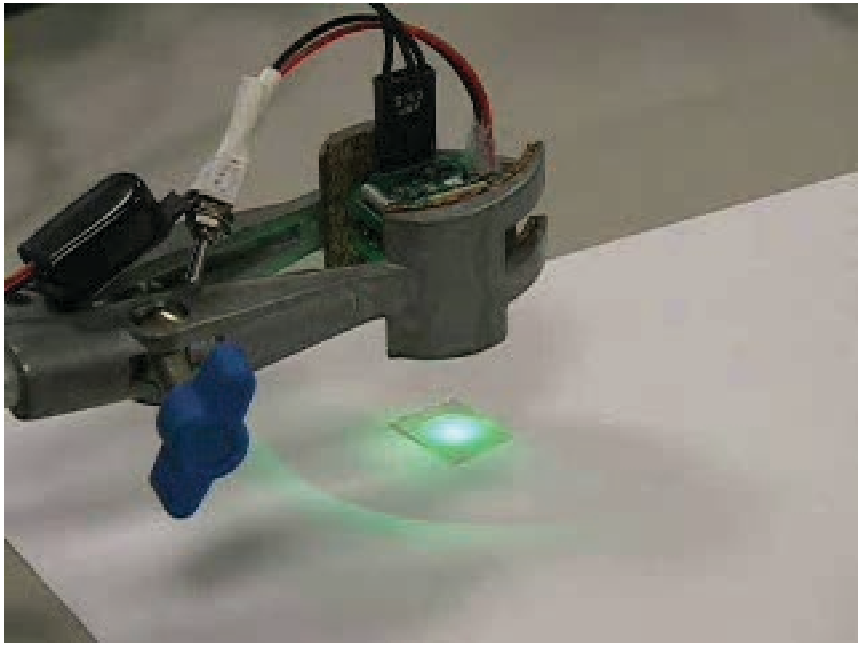
LED-Based Device for Switching and Monitoring SP-MC: The Discophotometer





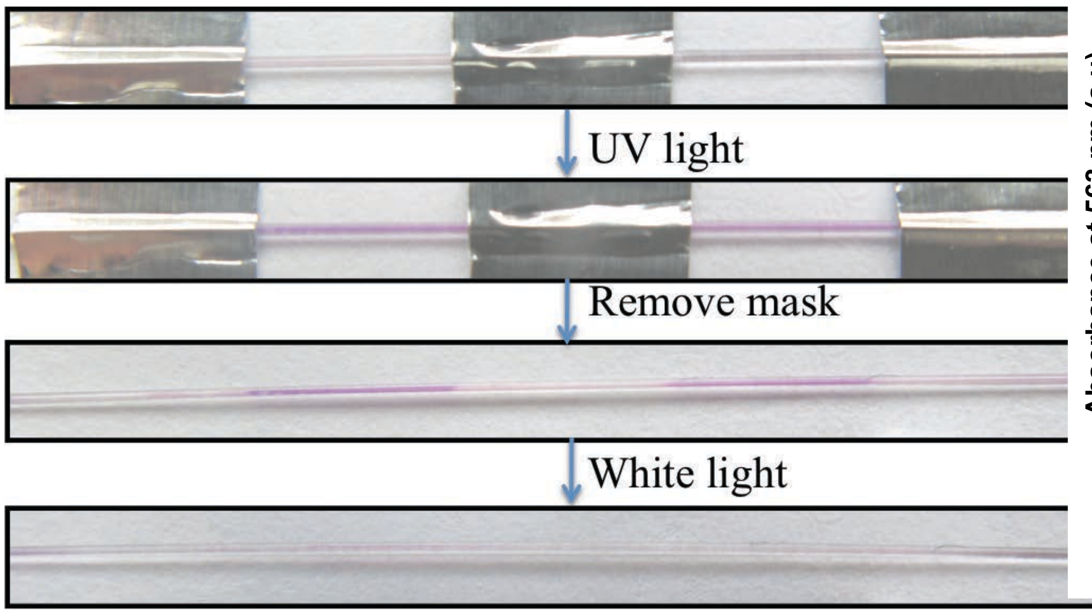
Multiple Switching of SP-MC using LEDs

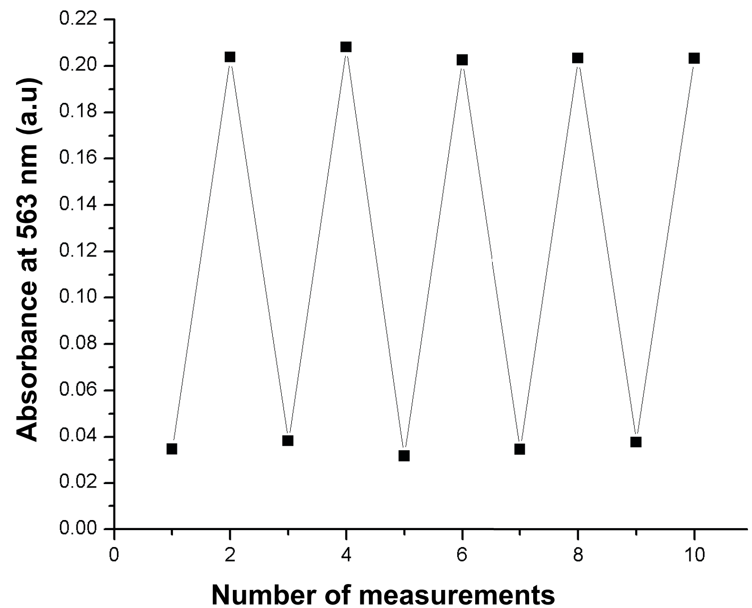




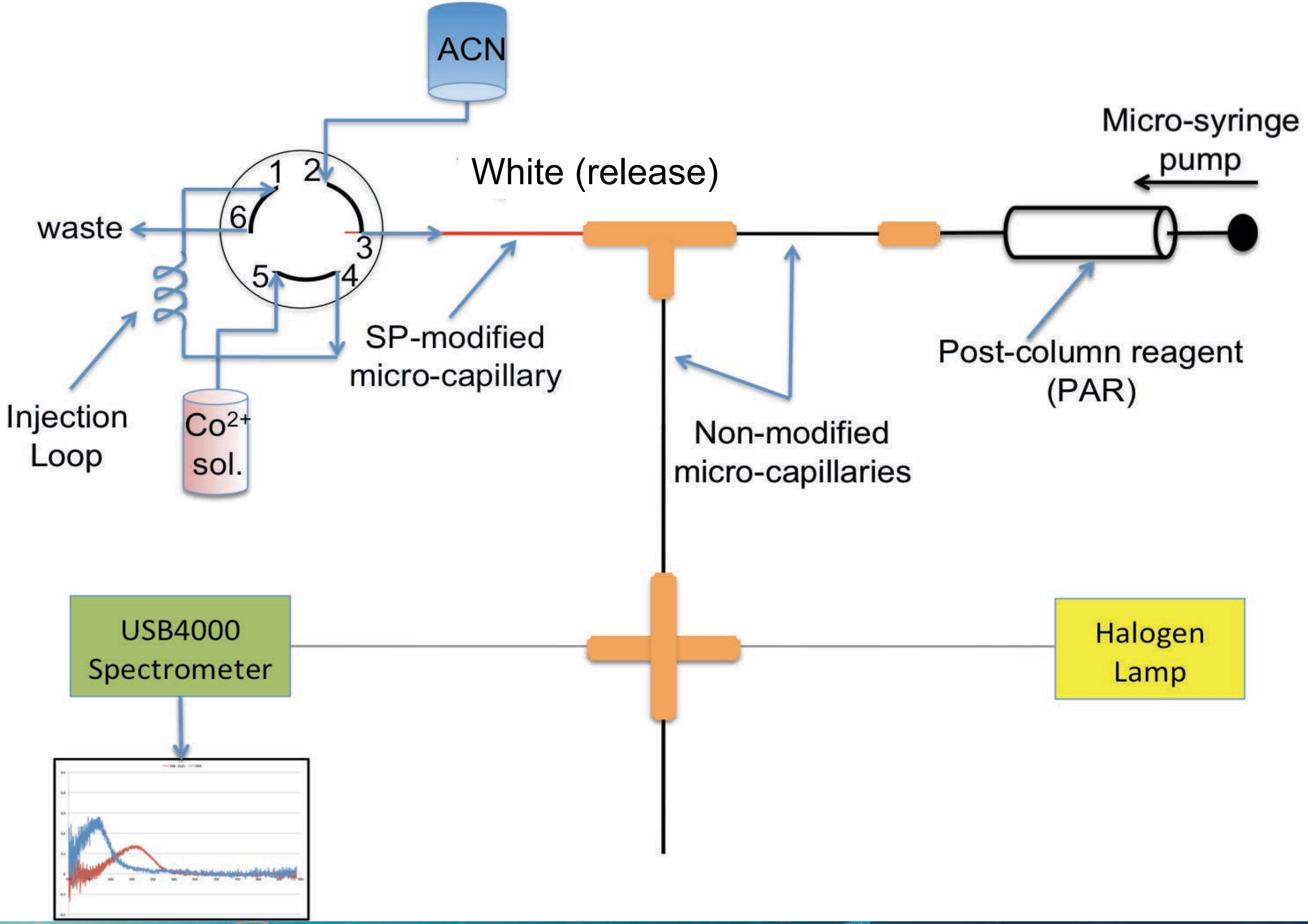
- Take measurements R,G,B (flash <1s)
- UV LED ‘on’ 10 s; wait 10 s; repeat measurements
- Green LED ‘on’ 10 s; wait 10 s; repeat measurements
- Green channel more sensitive as expected
- >2,000 repeat switches performed on a single surface

ROMP Chemistry – thick SP polymer 'brush' films

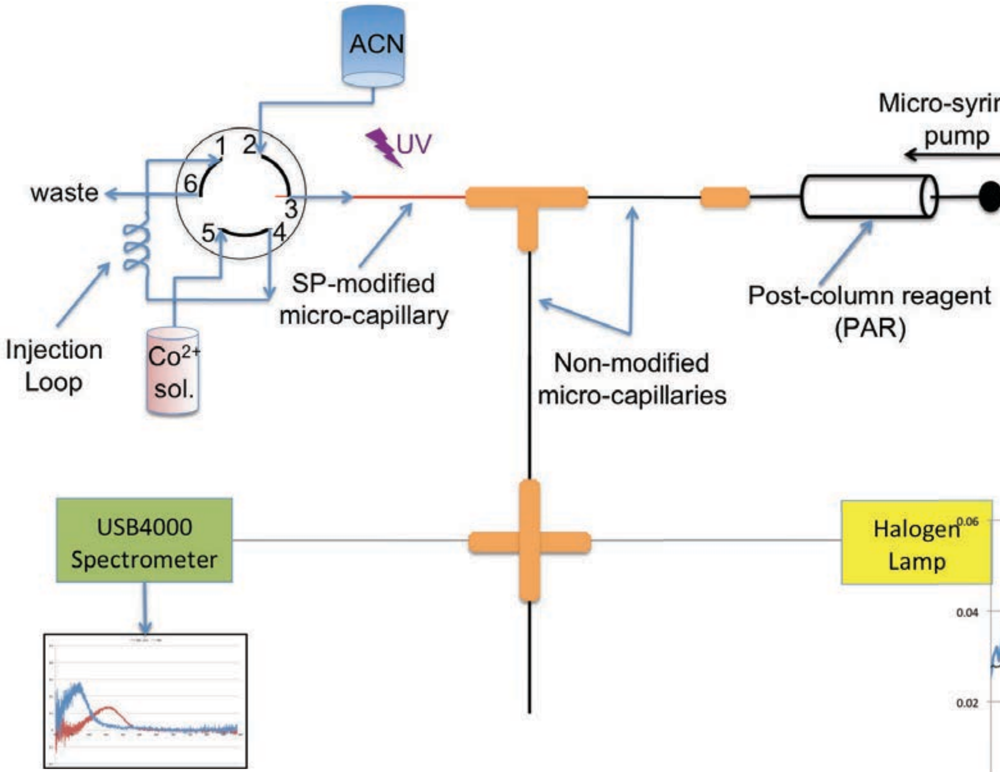


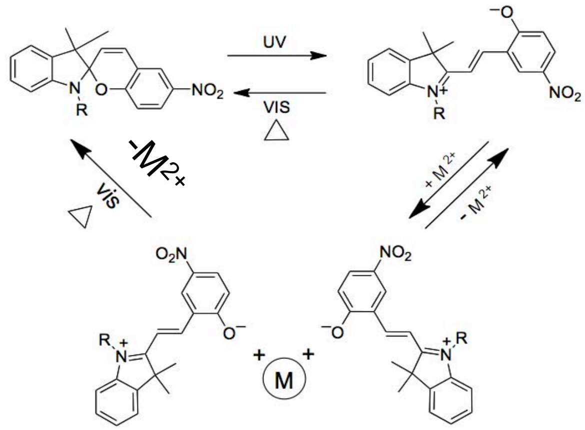


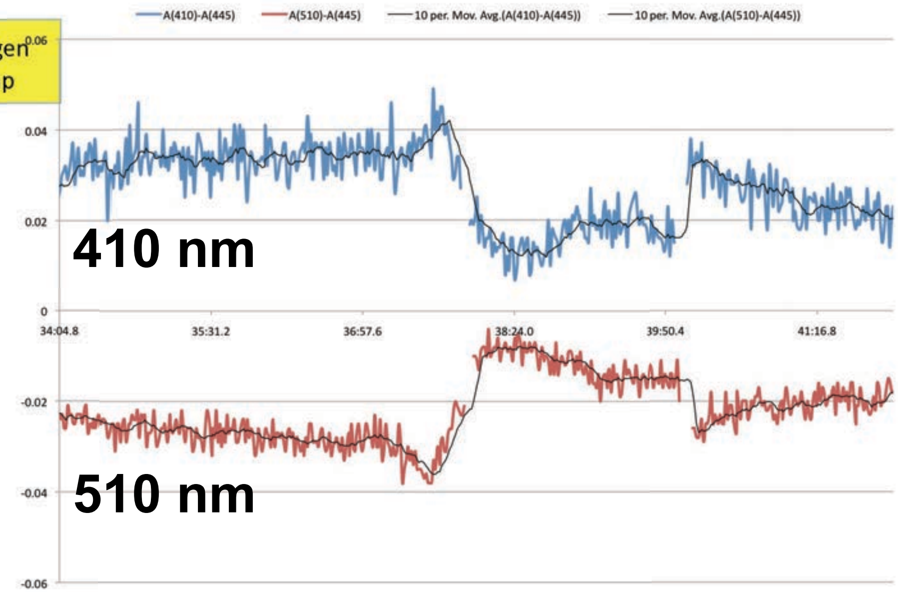
L. Florea, A. Hennart, D. Diamond, F. Benito-Lopez, Sens. Actuators B: Chem., 2011, DOI:10.1016/j.snb.2011.12.055


ACN
Micro-syringe pump
White (release)
1
2
3
4
5
6
waste
SP-modified micro-capillary
Post-column reagent (PAR)
Injection Loop
Co2+ sol.
Non-modified micro-capillaries
USB4000 Spectrometer
Halogen Lamp

Switchable Uptake and Release – 'Post Column' Detection



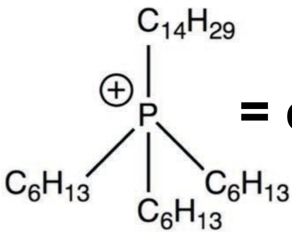




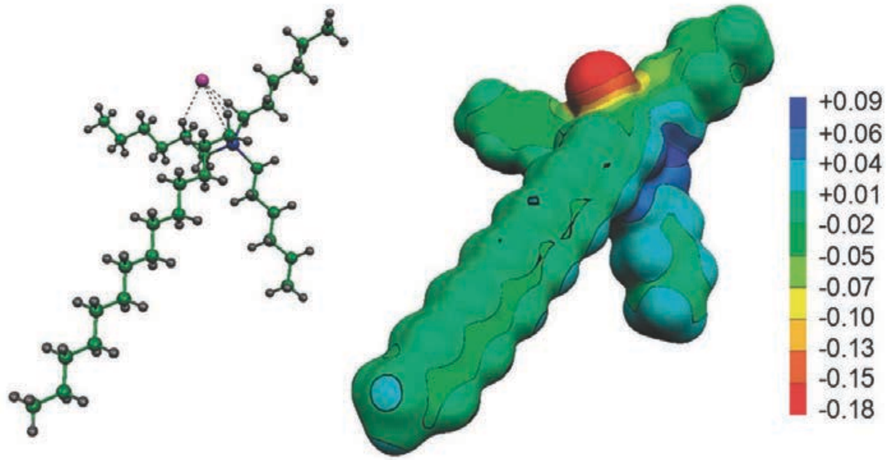
Co^{2+} + PAR ➔ PAR-Co^{2+}

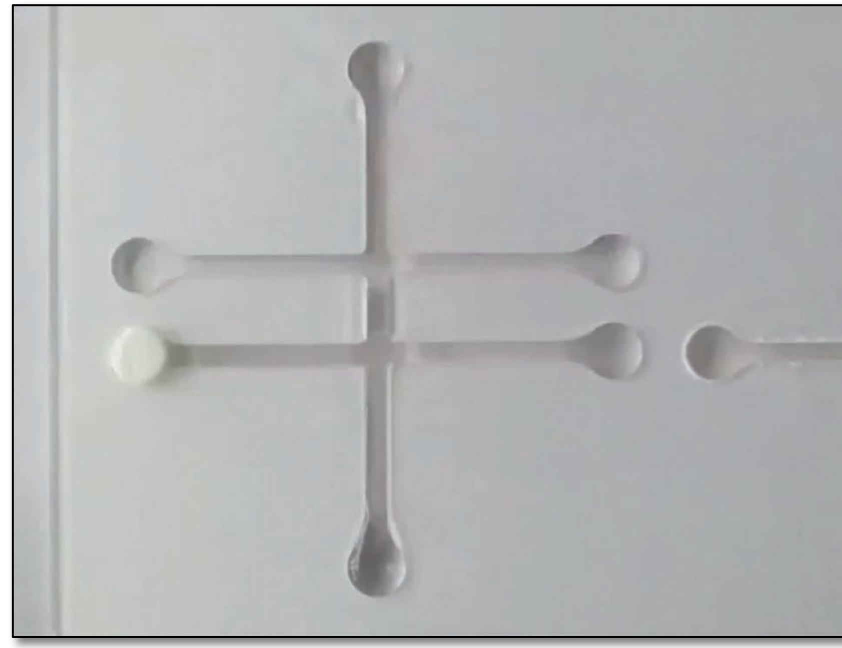
410 nm 510 nm

Chemotaxis – Autonomous Movement to a Plume Source with IL Droplets



= cationic surfactant

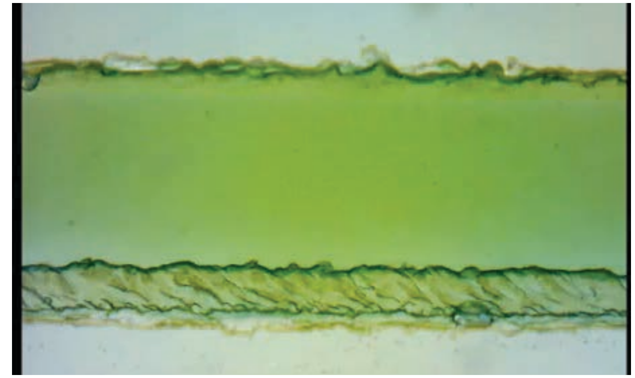


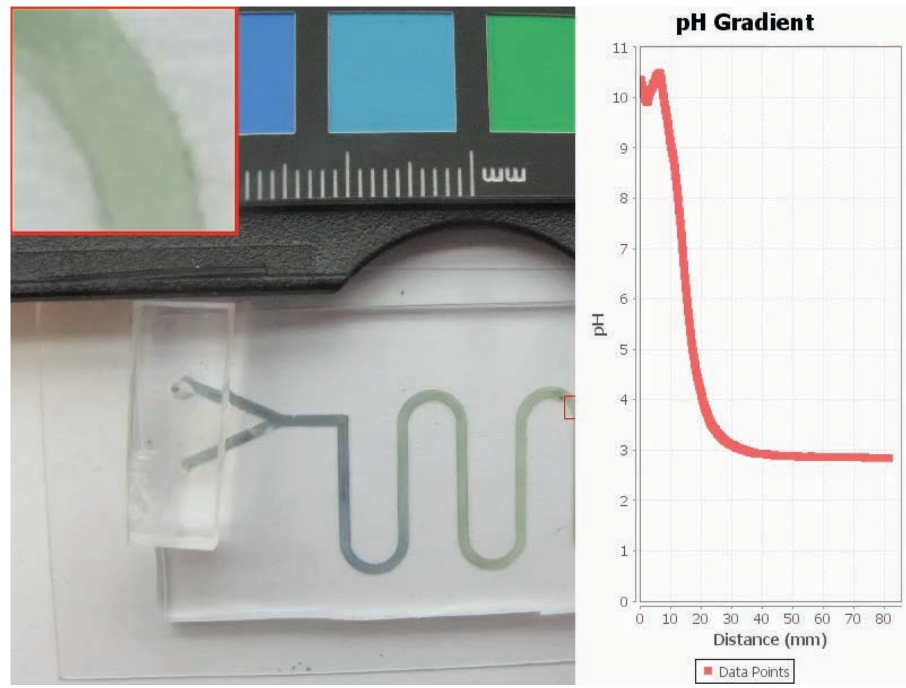


Trihexyl(tetradecyl)phosphonium chloride ($[P_{6,6,6,14}][Cl]$) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the Cl^- ion which is created using a polyacrylamide gel pad soaked in 10^{-2} M HCl; A small amount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

Channels that can sense…



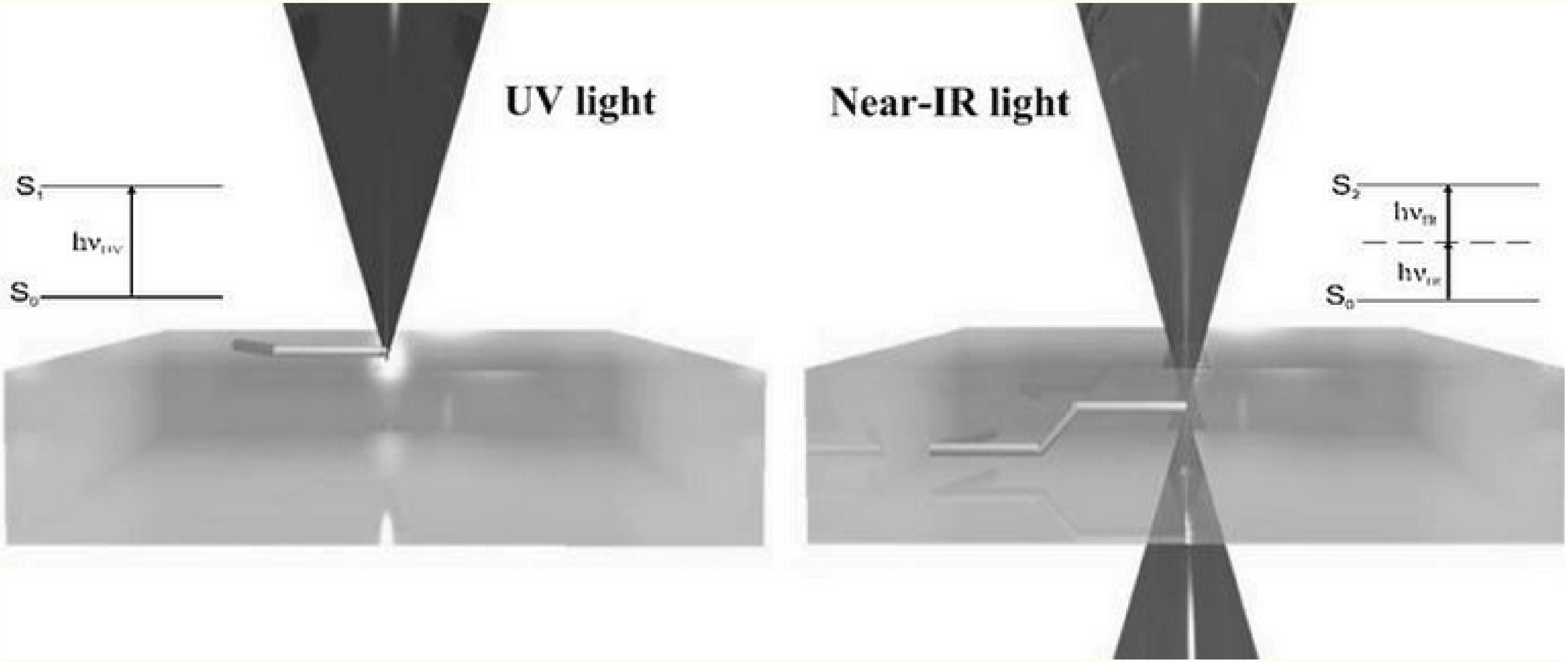


- PANi deposited on channel walls - Channels are now inherently responsive e.g. pH sensitive
- Status can be determined at any location within the channels using low cost digital imaging
- Presented at: µTAS 2011 (MicroTAS) Conference, Seattle, October 2-6, 2011

Background

Stereolithography

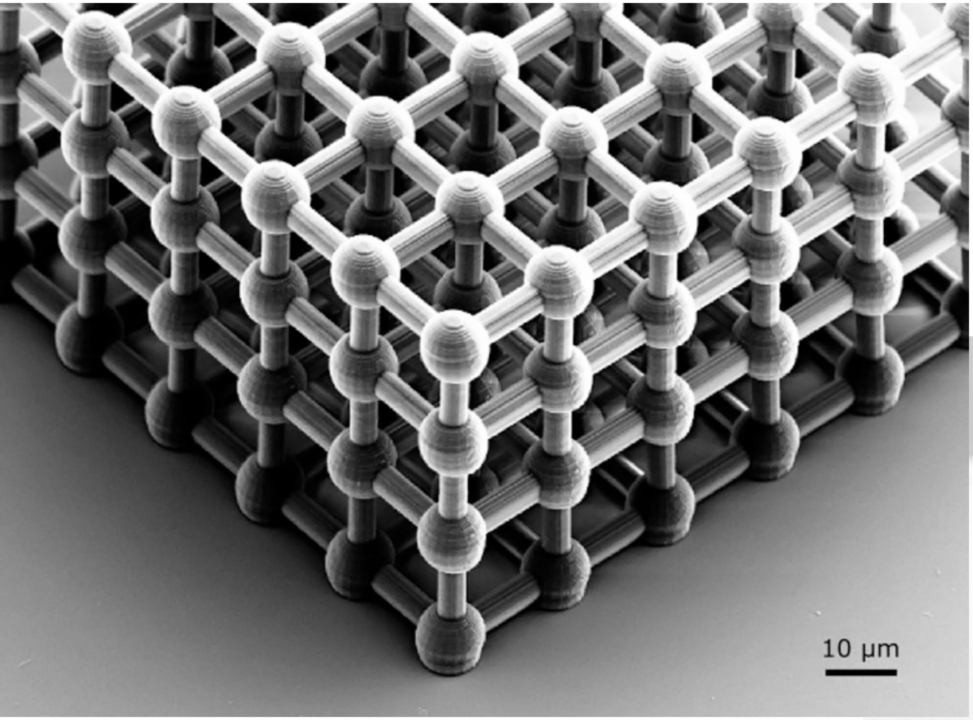
Two-photon polymerisation

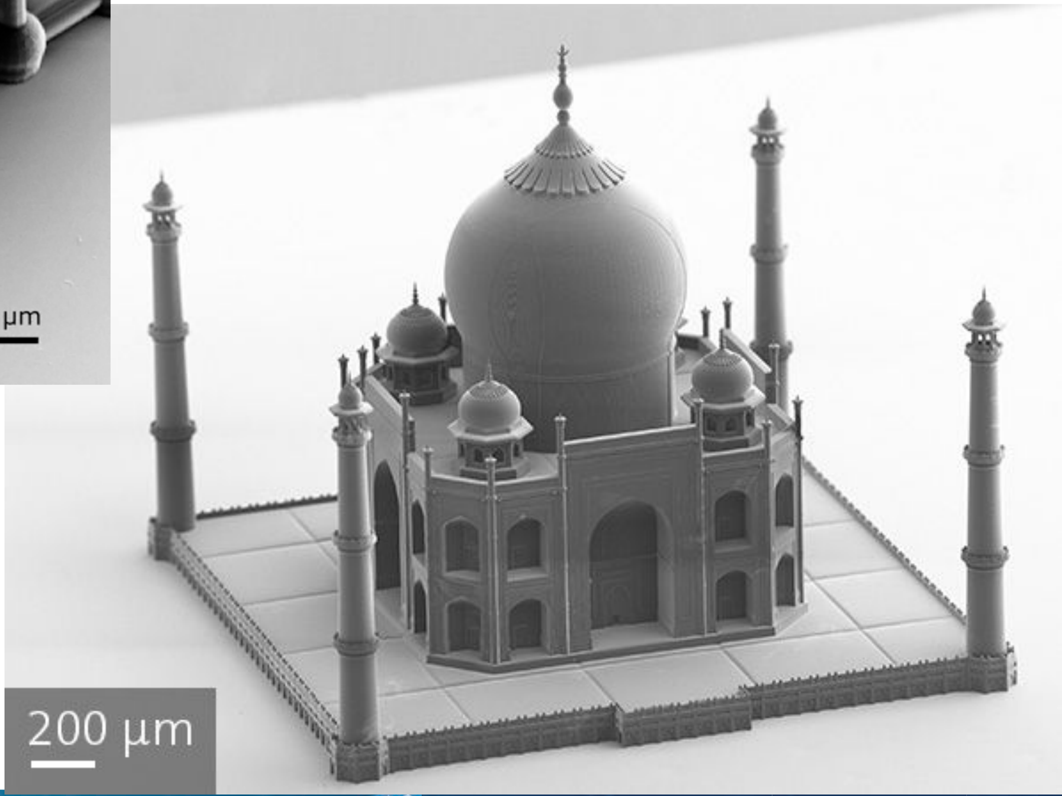


- Single photon absorption
- 2D patterns

- Two photon absorption
- 3D structures

Background





http://www.nanoscribe.de/

Near Term Applications (5Years)

Data and Information; IOT

Outside: On-Body

- Smart Bandages
- Sensorised Contact Lens
- platforms patches/watches
- Sensorised Splints/ dentures
- Smart Textiles/ Clothing

Inside: Implants/In-vivo

- Smart Stents
- Self-Aware Transplant
- Platforms and Implants
- Post-Operative IC (days)
- Medium term Convalescence (weeks)

Devices and Platforms

MATERIALS

Physics Chemistry Biology Engineering (photonics, electronics, fluidics, 4D materials)

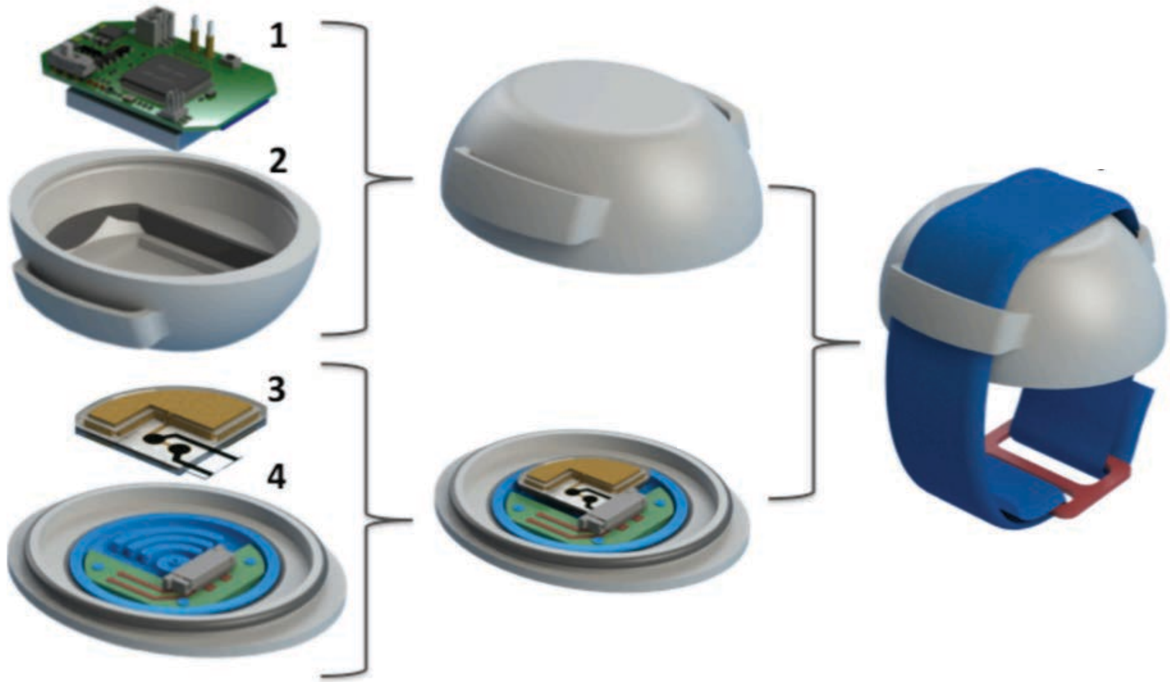
SWEATCH Device

1. Custom-built electronics with wireless communication (Shimmer)

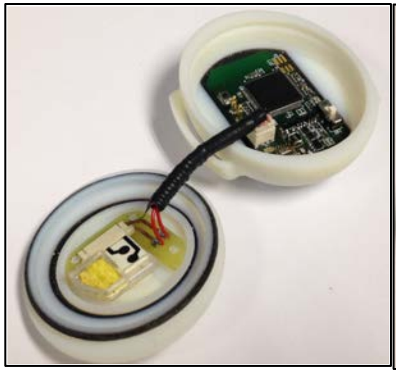
2. 3D printed casing

3. Microfluidic chip + ISE

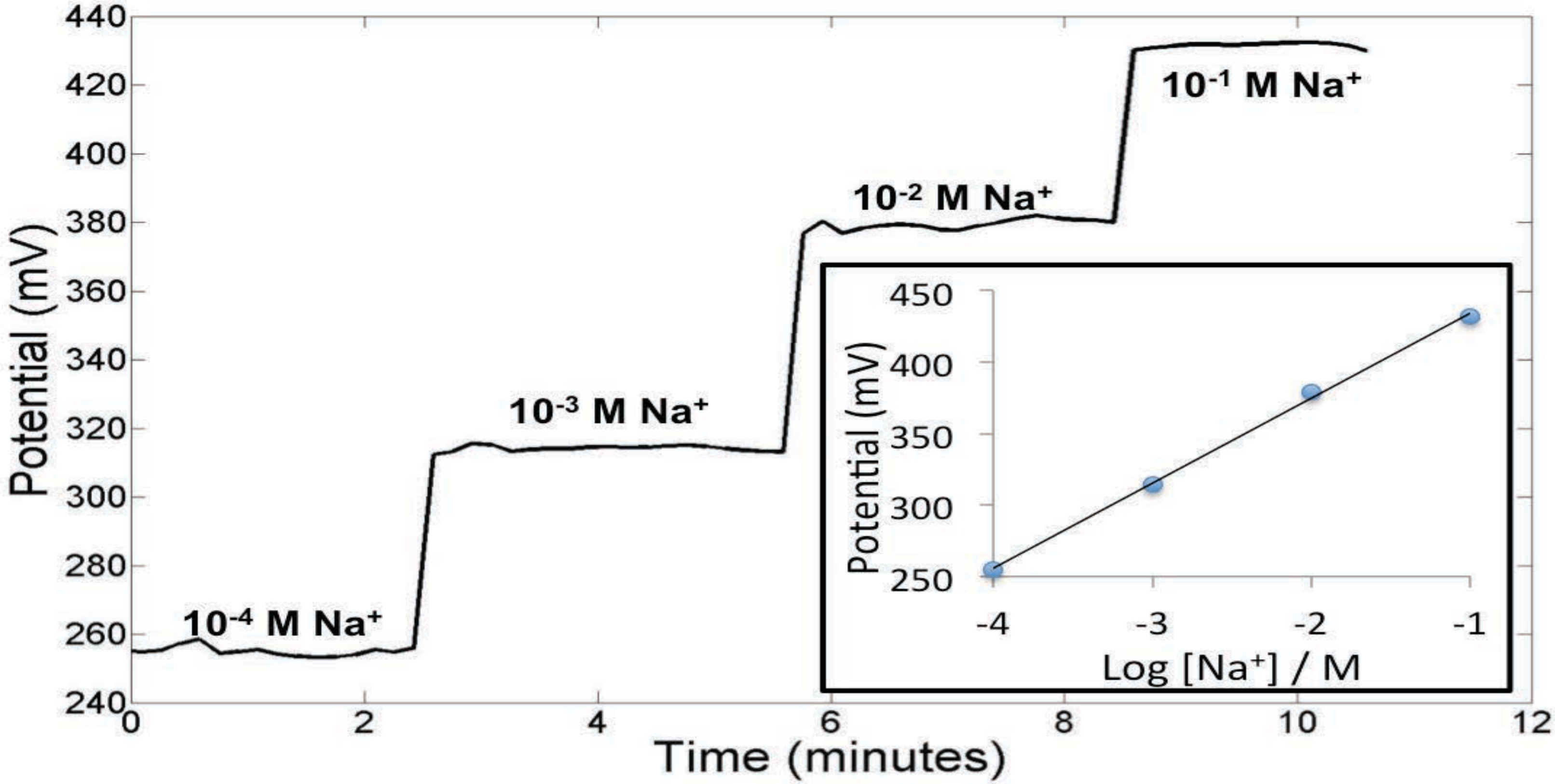
4. 3D printed sweat harvester and sensor connections



- Rapid prototyping techniques such as laser ablation and 3D printing are utilised to custom build various components including casing and sweat harvesting device *(the Australian National Nanofabrication Facility – Materials node and the Nano-Bioanalytical Research Facility (NRF) in Dublin City University)*

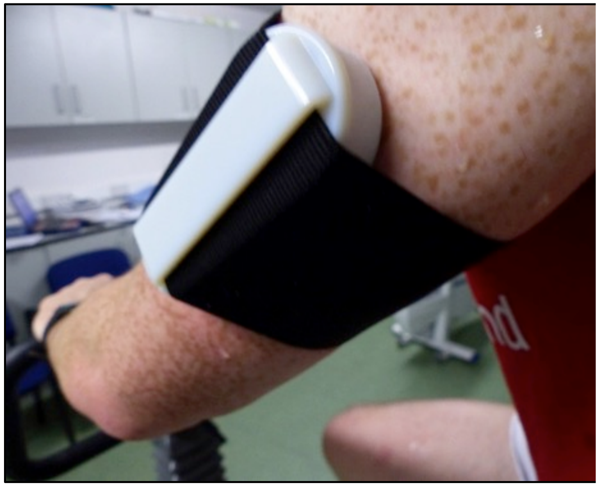


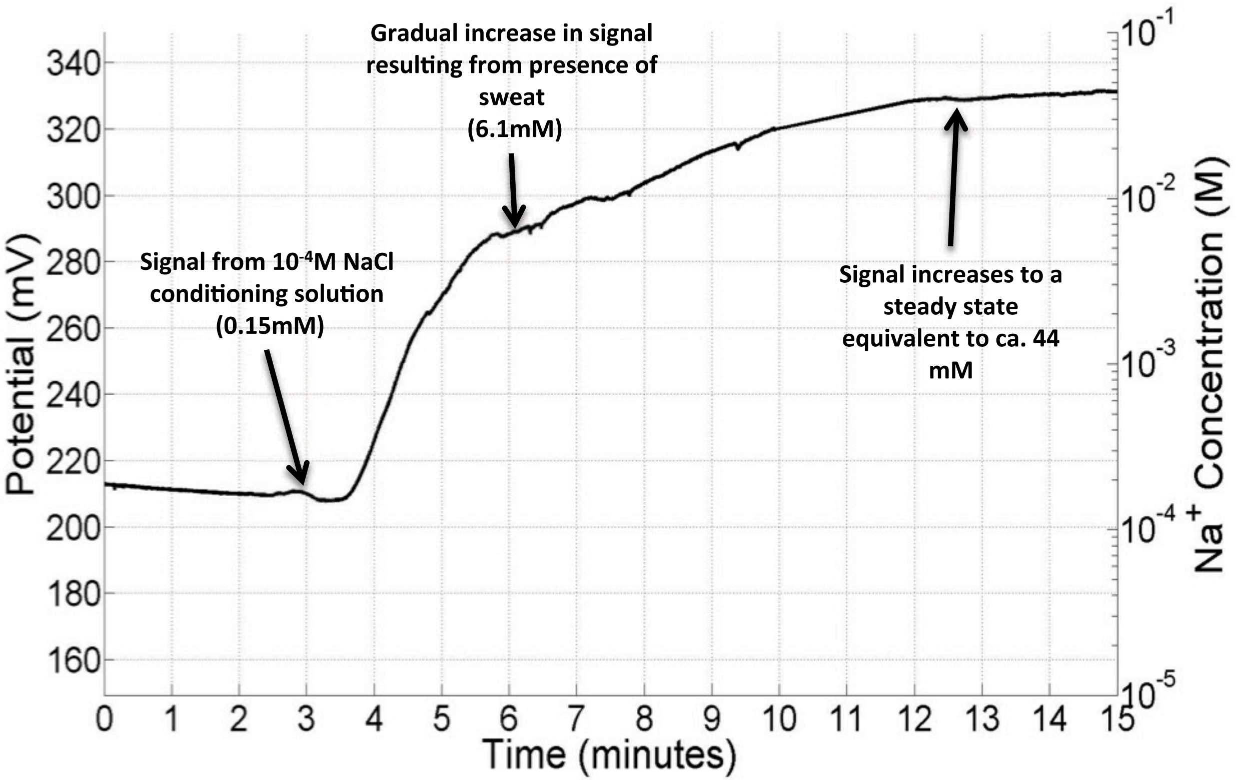
Sensor Calibration



- Calibration of a Na^+ SS-ISE and SS-RE output signal using the Shimmer board, giving a slope of 56.98mV and an R2 value of 0.99.

On Body Trials





Tom Glennon, Conor O Quigley, Margaret McCaul, Giusy Matzeu, Stephen Beirne, Gordon G. Wallace, Florin Stroiescu, Niamh O Mahoney, Paddy White, and Dermot Diamond, 'SWEATCH': A Wearable Platform for Harvesting and Analysing Sweat Sodium Content, Electroanalysis, 28 (2016) DOI: 10.1002/elan.201600106

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**

Thanks to &

MASK
Project no: 269302
Materials and Advanced Sensor
Knowledge Exchange