Microfluidic Platforms based on Biomimetic Materials and Principles

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Invited Lecture presented at
10th Annual Electromaterials Science Symposium, 'ACES 2015',
AIIM Facility, Innovation Campus, Squires Way, North Wollongong

Keynote Article: August 2004, Analytical Chemistry (ACS)

internet scale sensing

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(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)

pH sensing – wasn't that solved by Nikolskii in the 1930's?

EVENT	DATE
Launch (San Francisco)	September 2013
PHASE 1: Innovation Phase	
Registration opens	January 1, 2014
Early-bird Registration deadline	March 2014
OA Solutions Fair and Kick-Off Event	March 2014

Overview

Competition Guidelines

Competition Schedule

Registration Process

OVERVIEW

The Challenge: Improve Our Understanding of Ocean Acidification

The Wendy Schmidt Ocean Health XPRIZE is a $2 million global competition that challenges teams of engineers, scientists and innovators from all over the world to create pH sensor technology that will affordably, accurately and efficiently measure ocean chemistry from its shallowest waters… to its deepest depths.

There are two prize purses available (teams may compete for, and win, both purses):

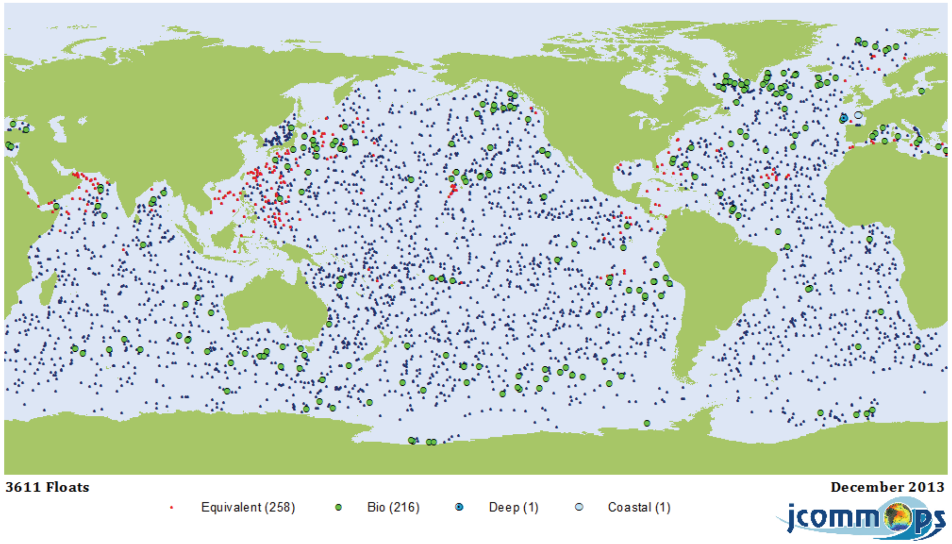
A. $1,000,000 Accuracy award – Performance focused ($750,000 First Place, $250,000 Second Place): To the teams that navigate the entire competition to produce the most accurate, stable and precise pH sensors under a variety of tests.

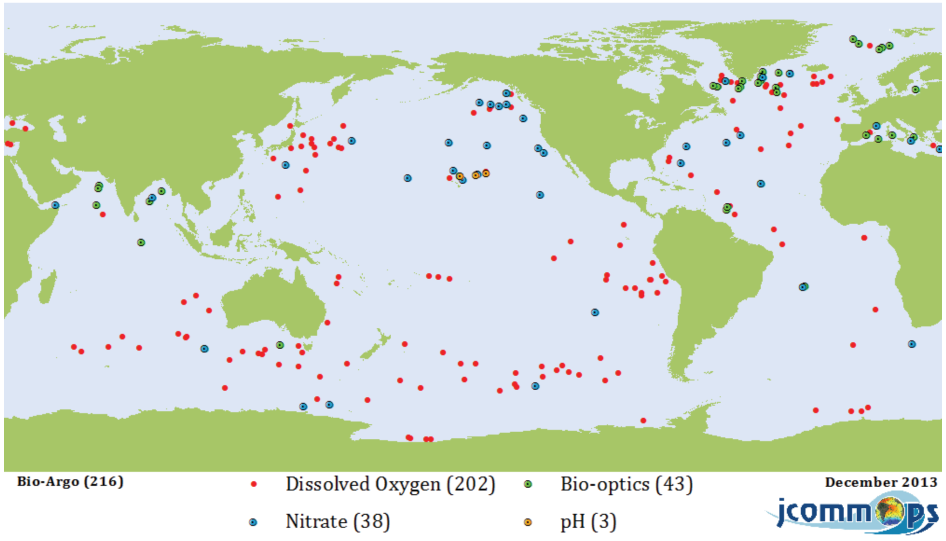
Wendy Schmidt Ocean Health XPRIZE

$2,000,000 up for grabs!
Task is to provide a way to do reliable measurements of pH in the ocean environment

The winner will almost certainly be a reagent based platform, not a conventional chemical sensor

Argo Project (accessed March 9 2014)





- **Ca. 3,600 floats: temperature and salinity**
- **Only 216 reporting chem/bio parameters (ca. 6%)**
- **Of these nitrate (38), DO (202), Bio-optics (43), pH (3)**

@€60K ea!

DO is by Clark Cell (Sea Bird Electronics) or Dynamic fluorescence quenching (Aanderaa)

See https://picasaweb.google.com/JCOMMOPS/ArgoMaps?authuser=0&feat=embedwebsite

'calibration of the DO measurements by the SBE sensor remains an important issue for the future', Argo report 'Processing Argo OXYGEN data at the DAC level', September 6, 2009, V. Thierry, D. Gilbert, T. Kobayashi

And for nutrients….

Personal health Monitoring….

Implantable artificial organs, medical devices, sensors….capable of functioning autonomously and reliably for years….constantly monitoring our health status and reporting to cloud databases….

Artificial Pancreas

Used a Technicon segmented flow colorimetric glucose analyser

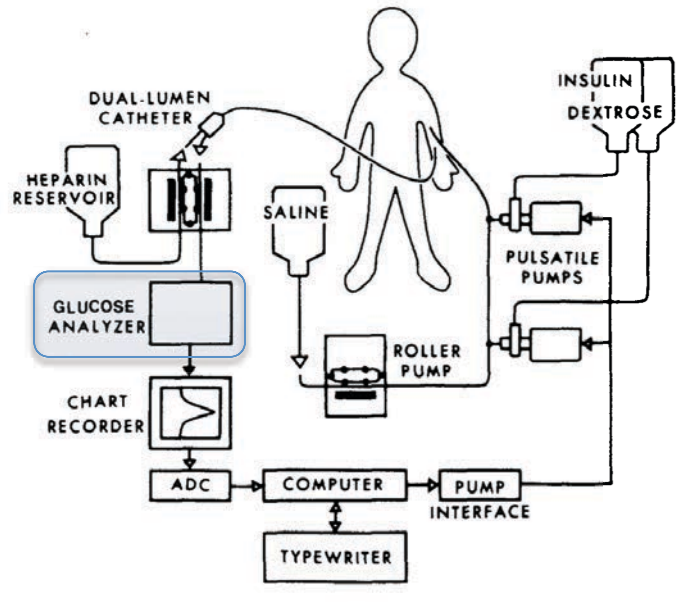
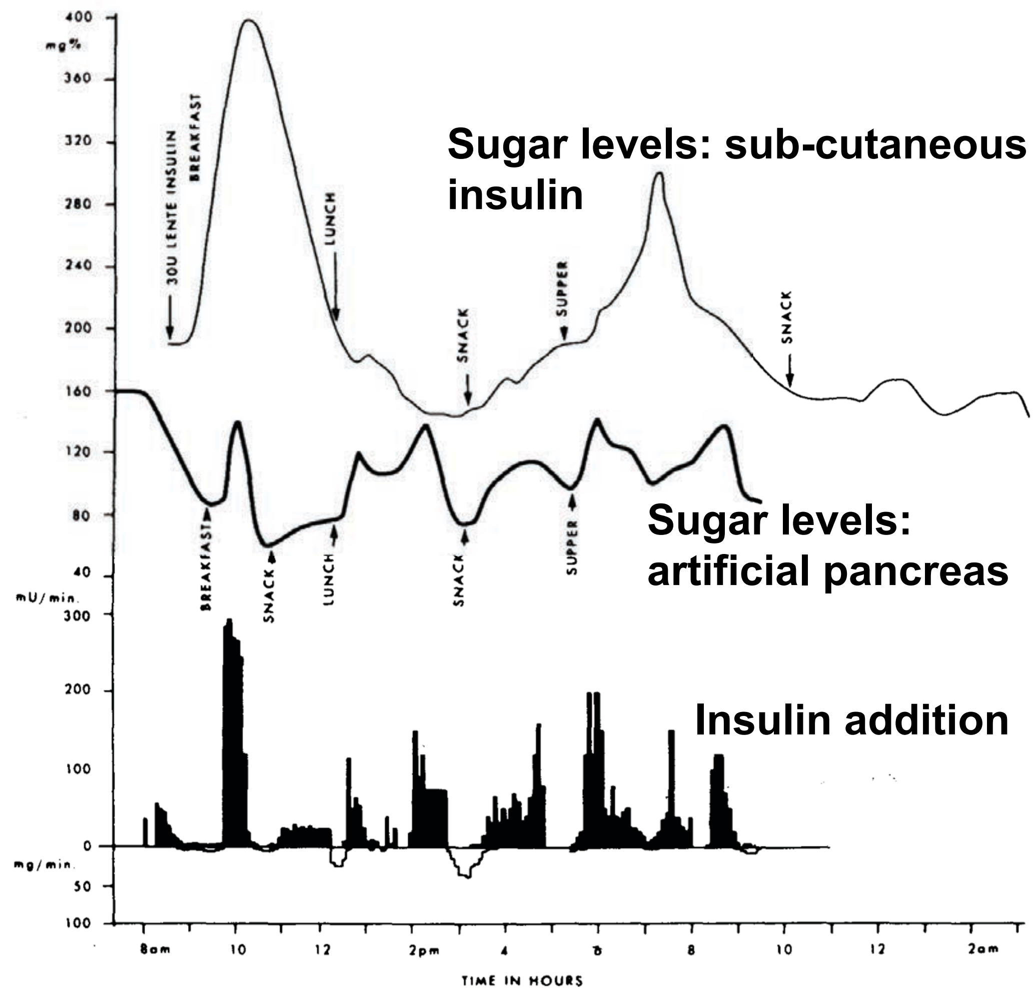


FIG. 1. Schematic diagram of apparatus used for monitoring and automatic regulation of blood sugar.

A. M. ALBISSER, M.A.SC., PH.D., AND ASSOCIA



A M Albisser, B S Leibel, T G Ewart, Z Davidovac, C K Botz, W Zingg, H Schipper, and R Gander
Clinical Control of Diabetes by the Artificial Pancreas
Diabetes May 1974 23:5 397-404; doi:10.2337/diab.23.5.397 1939-327X (Toronto)

Adam Heller

Subcutaneous sampling of interstitial fluid using microneedles to access the fluid through the skin without causing bleeding

San Francisco Business Times; Tuesday, April 6, 2004

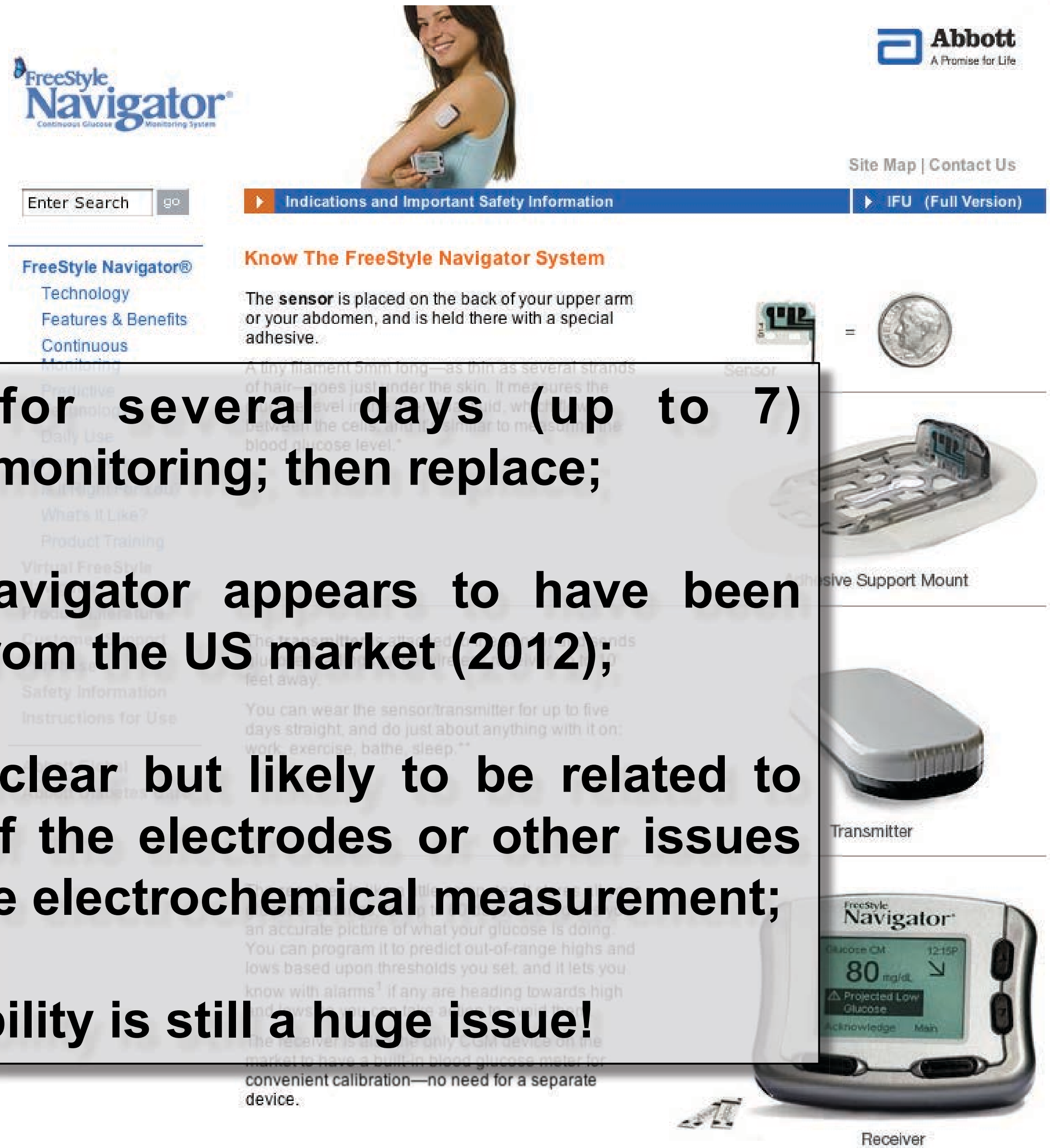
‘Abbott completes TheraSense acquisition’

Abbott Laboratories said Tuesday it completed its $1.2 billion acquisition of Alameda-based TheraSense Inc. after a majority of shareholders approved the transaction a day earlier.

- **Abbott Press Release September 29, 2008**
- Abbott Park, Illinois — Adam Heller, Ph.D., a professor at the University of Texas in Austin who created the technology that led to the development of Abbott's FreeStyle Blood Glucose Monitoring Systems® and FreeStyle Navigator® Continuous Glucose Monitoring System, today received the 2007 National Medal of Technology and Innovation from President George W. Bush in an award ceremony at the White House.

Freestyle Navigator

- Combines microfluidics with a micro-dimensioned filament sampling unit which is designed to minimise incidence of infection (therefore can be left in place for 5 days).
- Measures glucose in interstitial fluid (not blood). Diabetics have poor peripheral blood supply, therefore this is a major advance.
- Wireless communications used to harvest data continuously, and relay to carers and specialists. Enables trending, aggregation, warning….



Target is for several days (up to 7) continuous monitoring; then replace;

Freestyle Navigator appears to have been withdrawn from the US market (2012);

Reasons unclear but likely to be related to biofouling of the electrodes or other issues related to the electrochemical measurement;

Biocompatibility is still a huge issue!

Apple, iWatch & Health Monitoring

Independent.ie — Wednesday 7 May 2014

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Independent.ie › Business › Technology

Apple hiring medical device staff, shares break $600 mark

0 Comments | Recommend 7 | Tweet 89 | g+1 3 | Share

Apple Inc CEO Tim Cook

May 7th 2014

'Over the past year, Apple has snapped up at least half a dozen prominent experts in biomedicine, according to LinkedIn profile changes.

Much of the hiring is in sensor technology, an area Chief Executive Tim Cook singled out last year as primed "to explode."

Industry insiders say the moves telegraph a vision of **monitoring everything from blood-sugar levels to nutrition, beyond the fitness-oriented devices now on the market.'**

"This is a very specific play in the bio-sensing space," said Malay Gandhi, chief strategy officer at Rock Health, a San Francisco venture capital firm that has backed prominent wearable-tech startups, such as Augmedix and Spire.

'Healthkit' personal health information platform developed in collaboration with Mayo Clinic

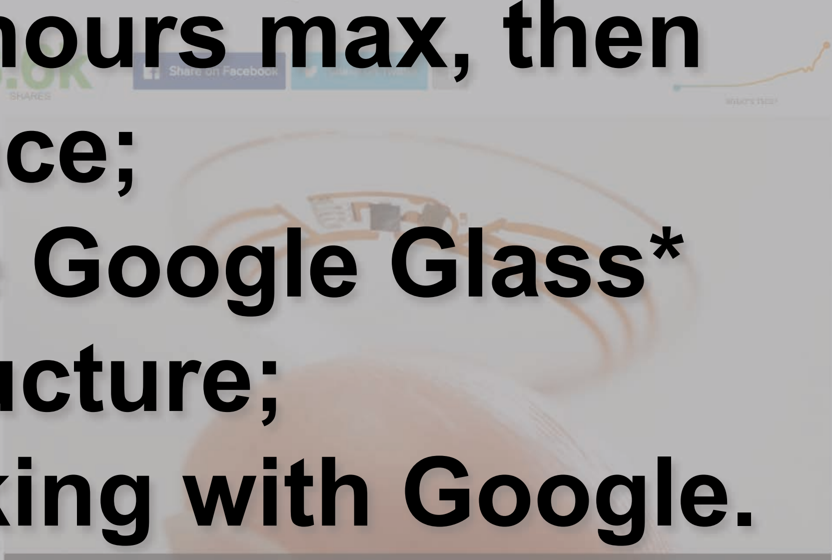
Google Contact Lens

United States Patent Application ***20140107445***
Kind Code A1 Liu; Zenghe April 17, 2014
Microelectrodes in an Ophthalmic Electrochemical Sensor

Abstract

An eye-mountable device **includes an electrochemical sensor embedded in a polymeric material** configured for mounting to a surface of an eye. The electrochemical sensor includes a working electrode, a reference electrode, and a reagent that selectively reacts with an analyte to generate a sensor measurement related to a concentration of the analyte in a fluid to which the eye-mountable device is exposed.

Google Smart Contact Lenses Move Closer to Reality



Google's Smart Contact Lens is like your contact lens, except it's a whole lot smarter.

- **Use model is 24 hours max, then replace;**
- **likely to leverage Google Glass* infrastructure;**
- **Novartis now working with Google.**

***Google Glass project has been abandoned!** **(Jan 15 2015) see** https://plus.google.com/+GoogleGlass/posts/9uiwXY42tvc

A contact lens with embedded sensor for monitoring tear glucose level, M. Cowan, I. Landesmaki and B. A. Parviz, ***Biosensors & Bioelectronics*, 2011, 26**, 3290-3296.

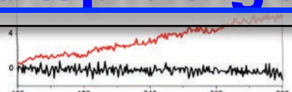


Fig. 2. Images of the sensor as it goes through surface functionalization and the related measured responses: (a) sequential images of sensor pre-treatment with GOD/titania/Nafion®; (b) measured amperometric response for the sensor just incubated with GOD; (c) measured amperometric response for the sensor prepared with GOD/titania/Nafion®; (d) measured amperometric response for the sensor prepared with GOD/titania sol–gel film; (e) three controls (signals for buffer) for the same pre-treatment of (b), (c), and (d); (f) the enlarged view of curve (b) and control of (b) for 120–360 s.

http://www.gmanetwork.com/news/story/360331/scitech/technology/google-s-smart-contact-lenses-may-arrive-sooner-than-you-think

After decades of intensive research, our capacity to deliver successful long-term deployments of chemo/bio-sensors in remote locations is still very limited

MicroTAS/Lab on a Chip/Microfluidics

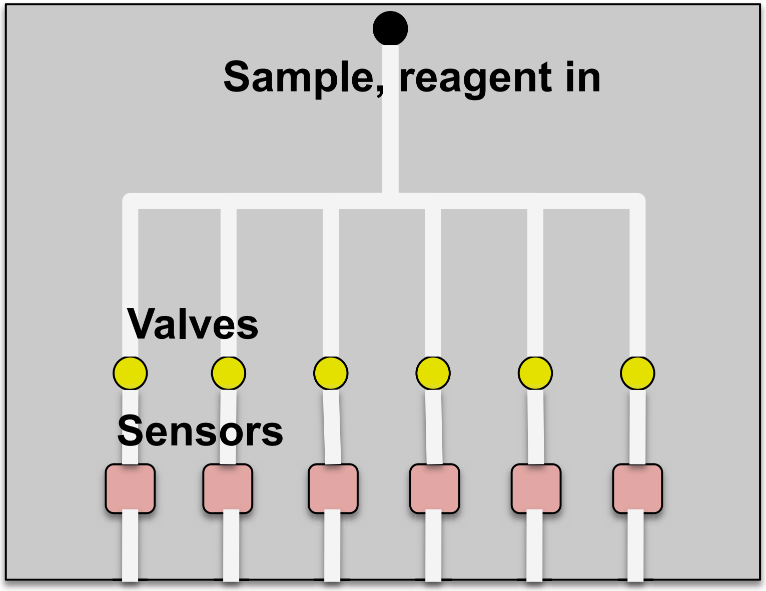
Many people, myself included, expected that the ability to manipulate fluid streams, in microchannels, easily, would result in a proliferation of commercial LoC systems, and that we would see applications of these devices proliferating throughout science. In fact, it has not (yet) happened.

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

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

Use Arrays of Sensors….?

- If each sensor has an in-use lifetime of 1 week….
- And these sensors are very reproducible….
- And they are very stable in storage (up to several years)….

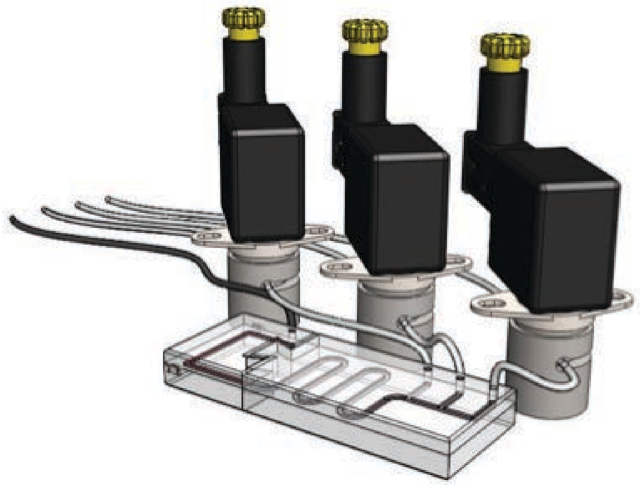


Then 50 sensors when used sequentially could provide an aggregated in-use lifetime of around 1 year

But now we need multiple valves integrated into a fluidic platform to select each sensor in turn

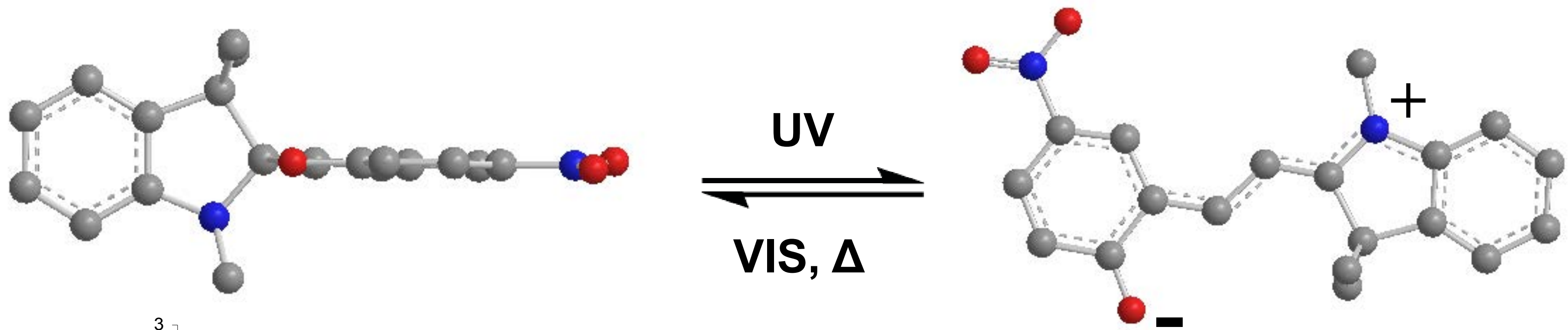
How to advance fluid handling in LOC platforms: re-invent valves (and pumps)!

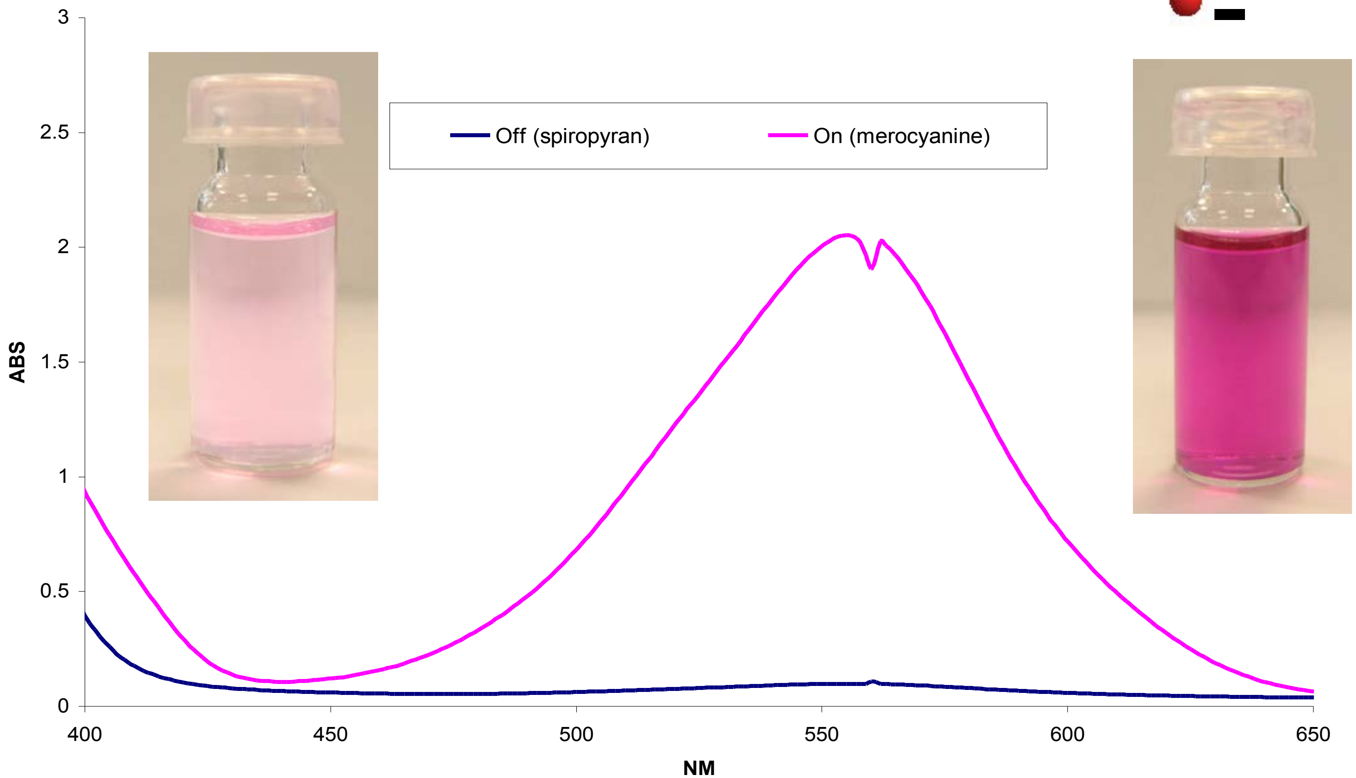
- **Conventional valves cannot be easily scaled down - Located off chip: fluidic interconnects required**
  - Complex fabrication
  - Increased dead volume
  - Mixing effects
- **Based on solenoid action**
  - Large power demand
  - Expensive



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

Photoswitchable Materials

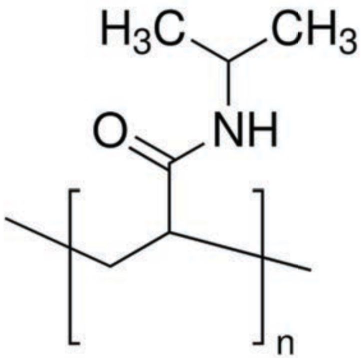




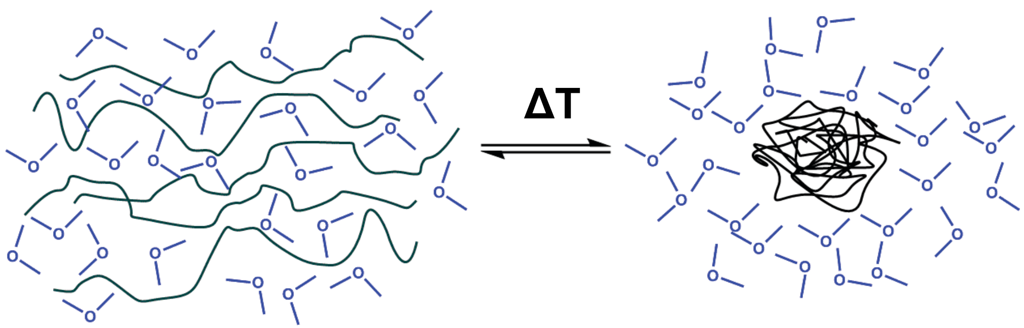
Poly(*N*-isopropylacrylamide)

- **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

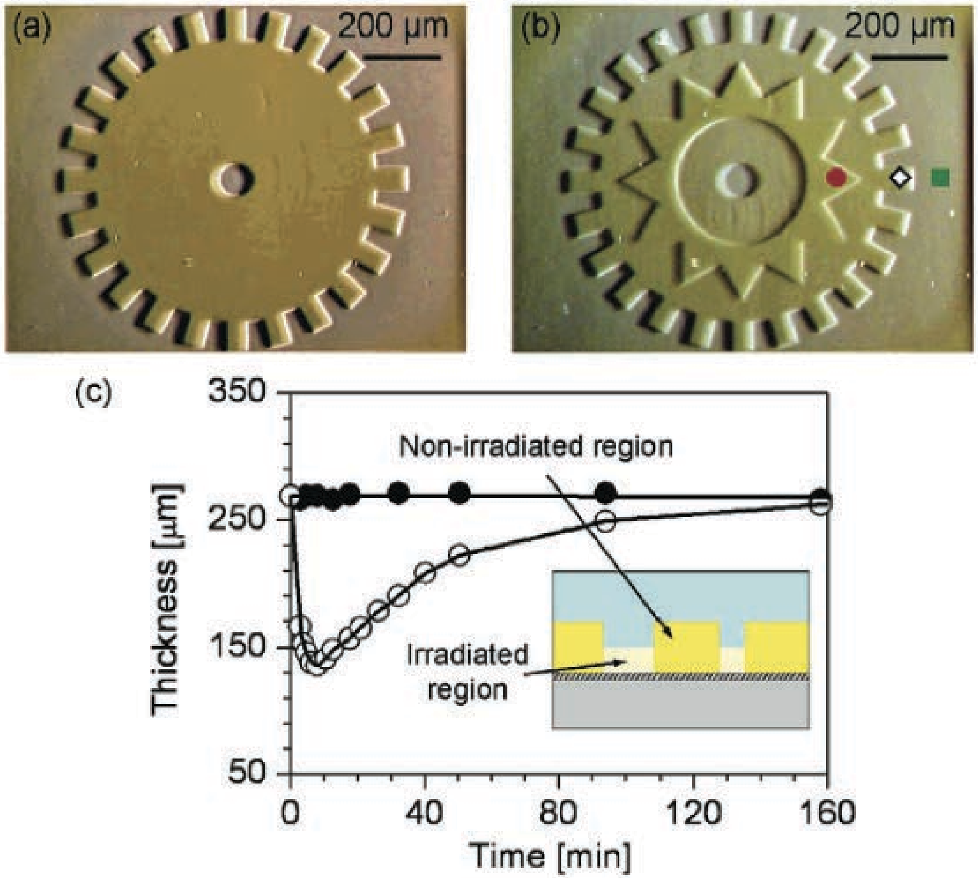
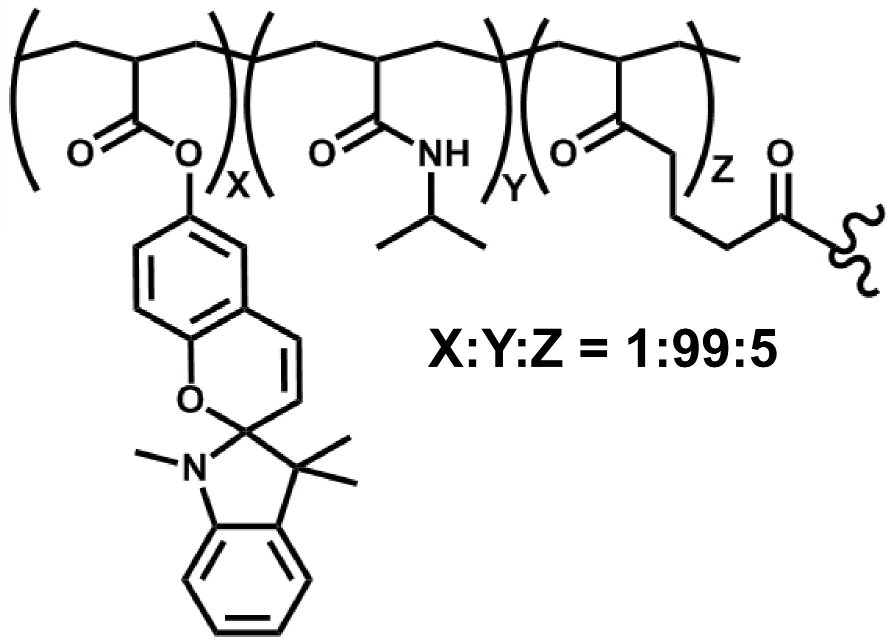


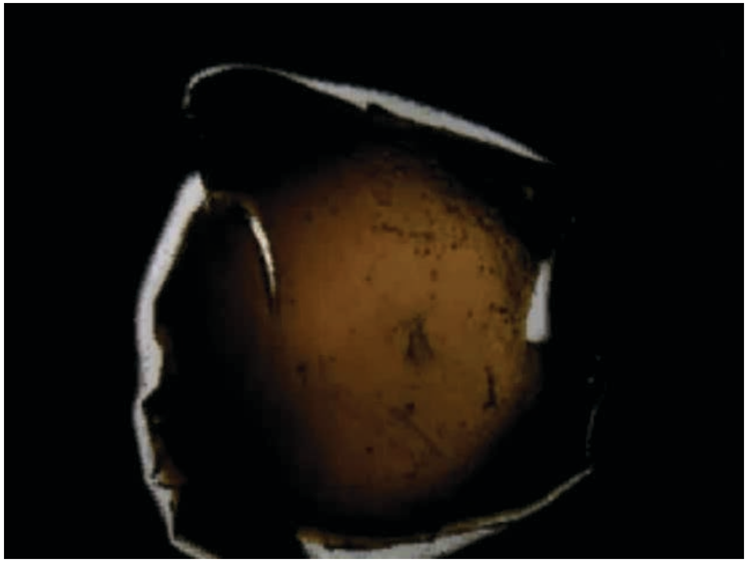
Figure 3. (a, b) Images of the pSPNIPAAm hydrogel layer just after the micropatterned light irradiation. Duration of irradiation was (●, red) 0, (◇) 1, and (■, green) 3 s. (c) Height change of the hydrogel layer in (●) non-irradiated and (○) irradiated region as a function of time after 3 s blue light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

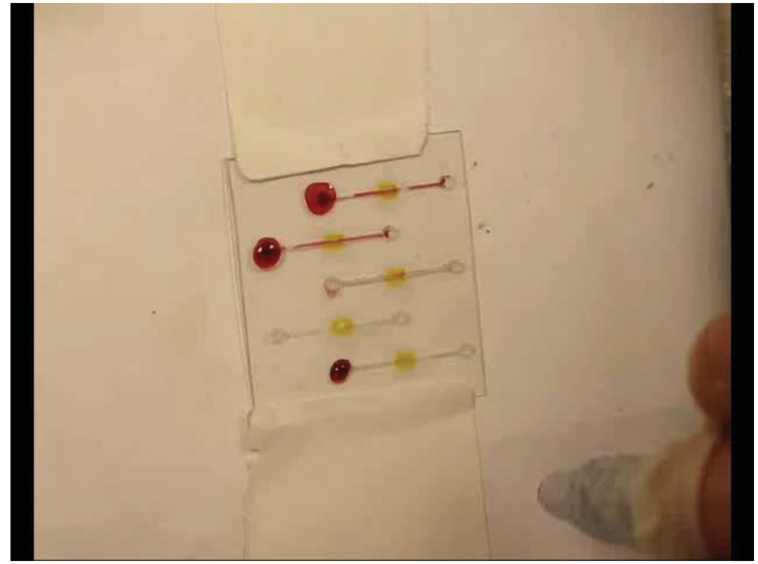


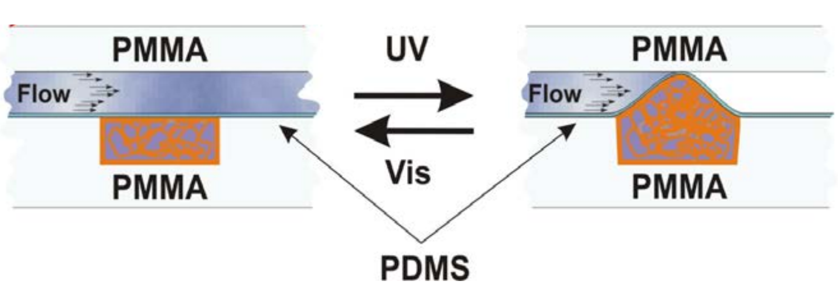
poly(N-isopropylacrylamide) (PNIPAAm)
Formulation as by Sumaru et al[1]

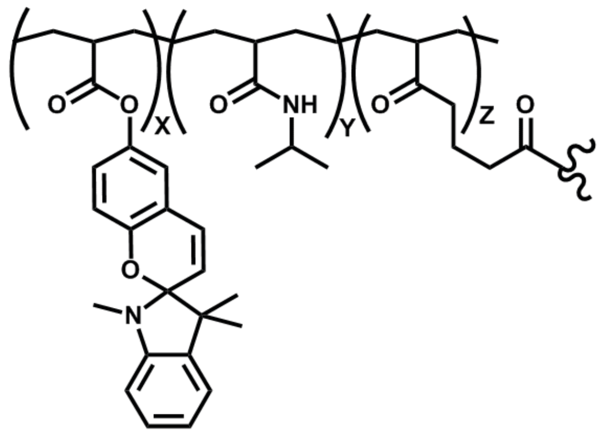
***1) Chem. Mater.*, 19 (11), 2730 -2732, 2007.**

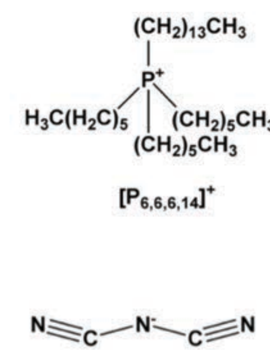
Photo-actuator polymers as microvalves in microfluidic systems









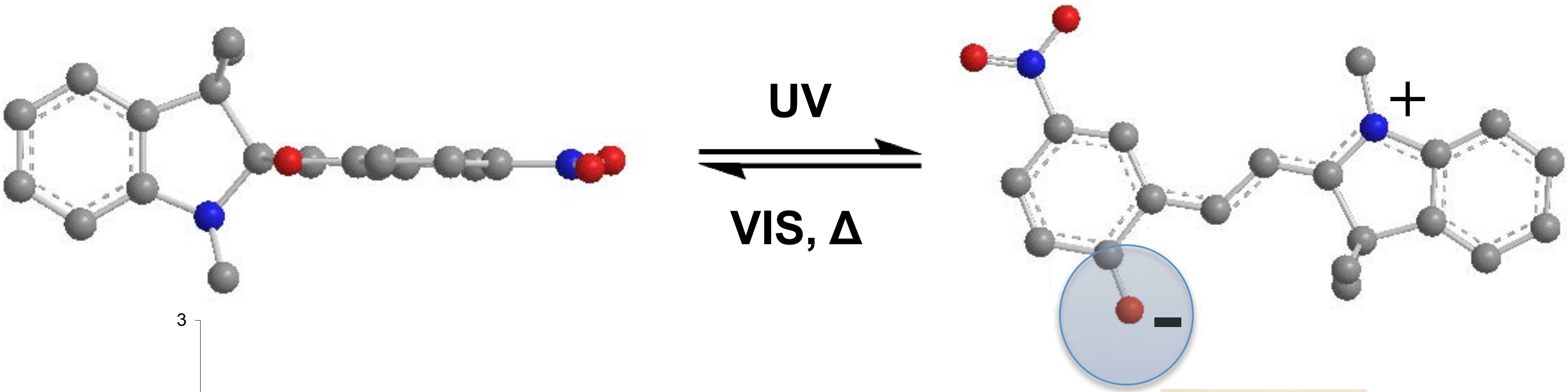


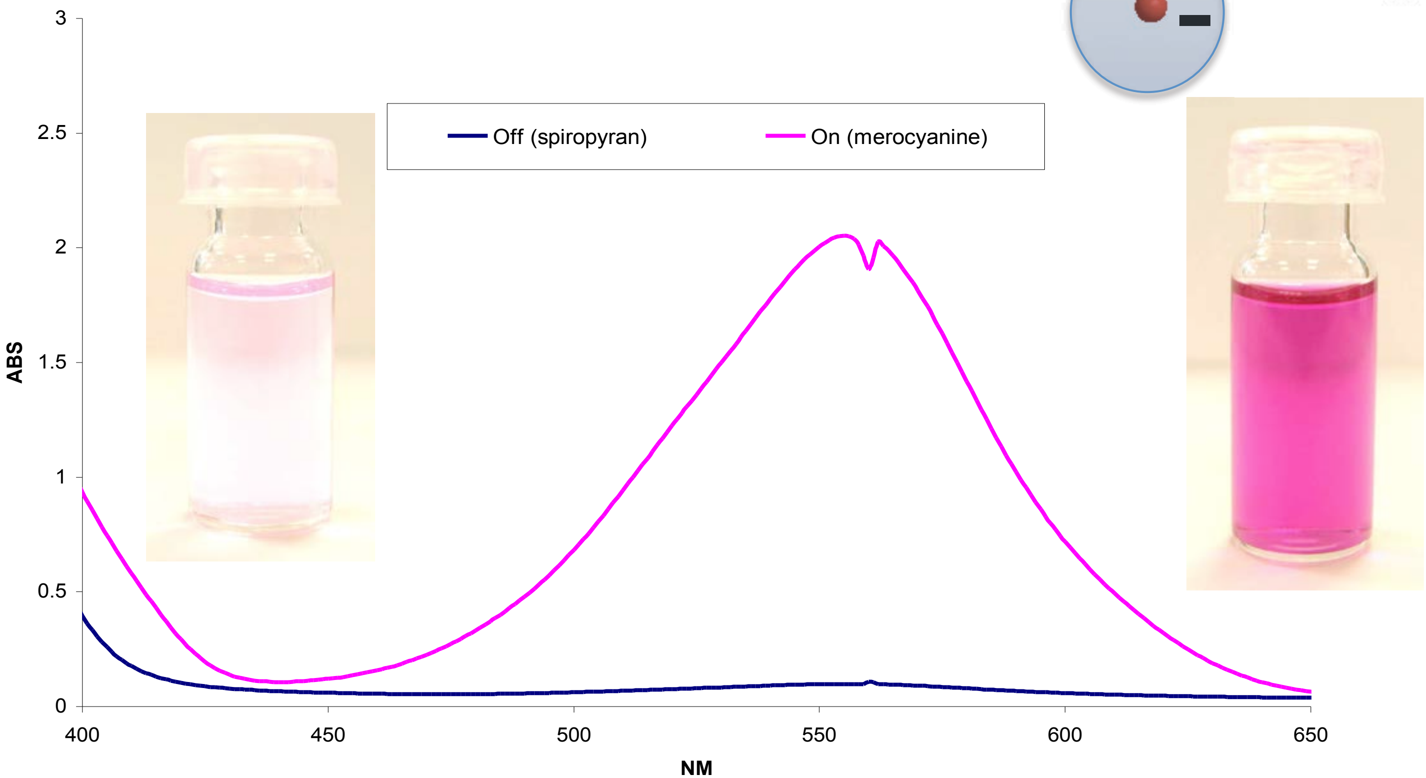
(b)

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.

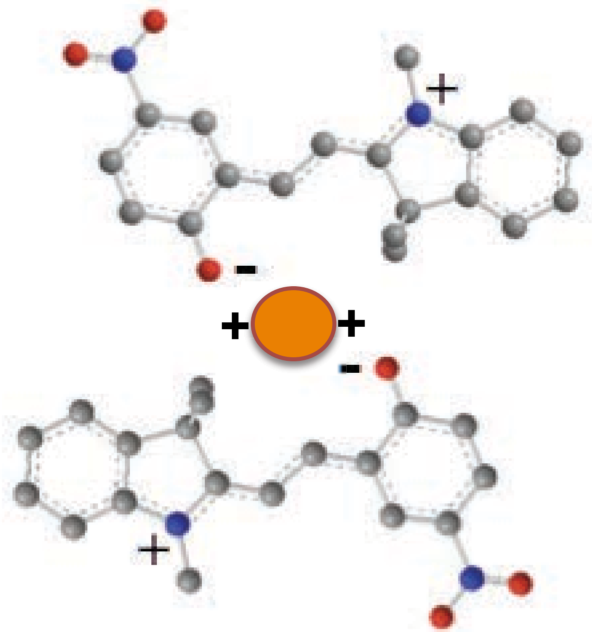
Photoswitchable Binding

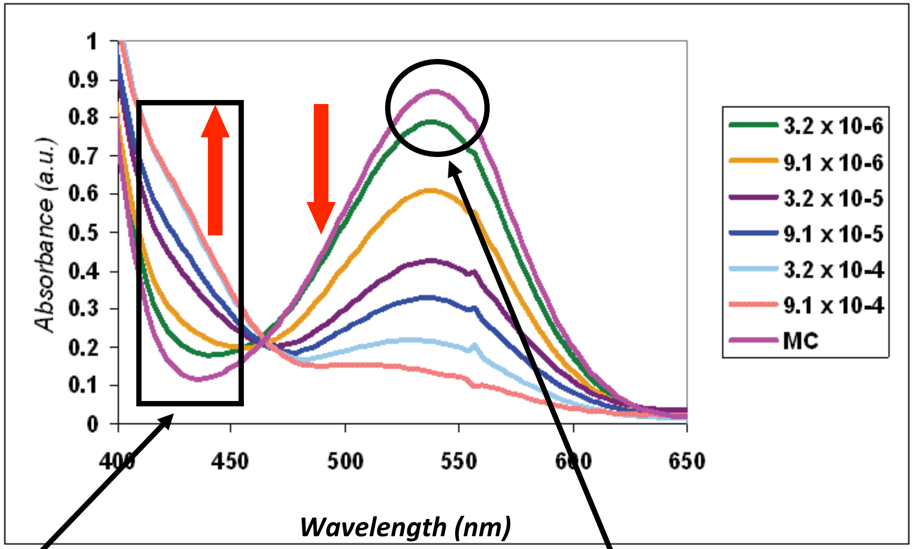




Spiropyran and Metal Ions

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

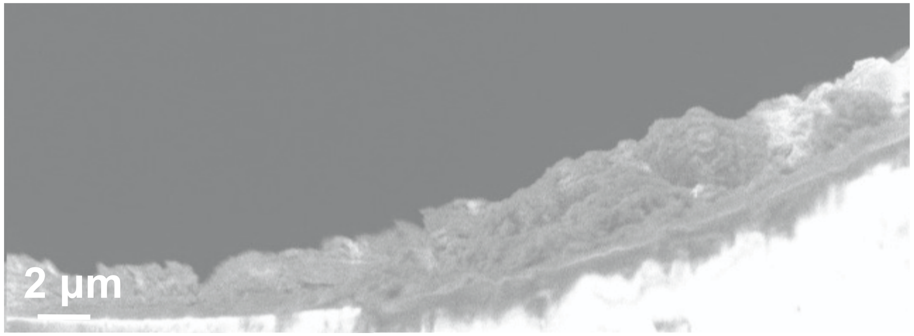


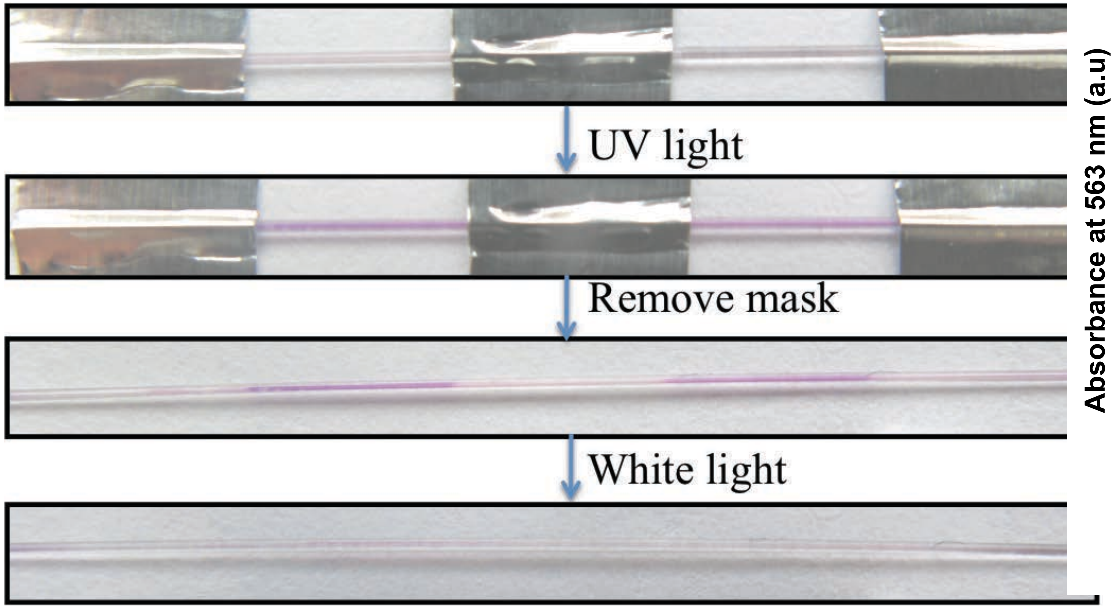


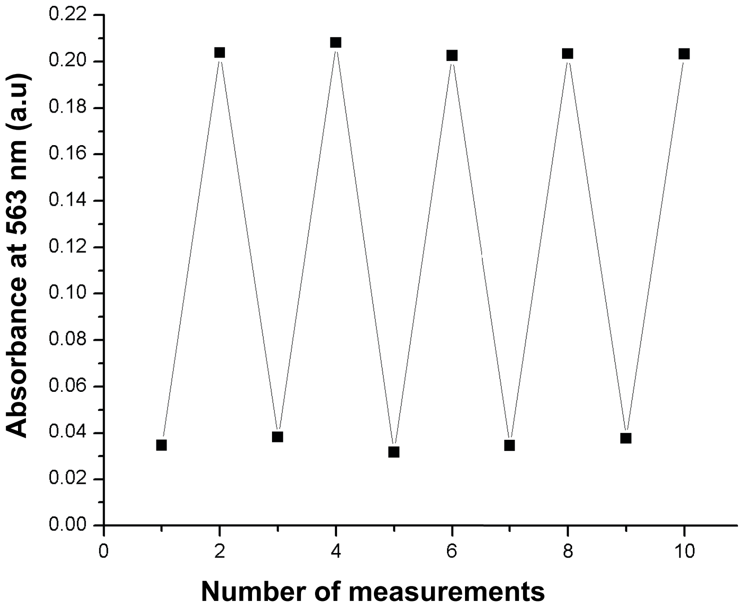
Increase in absorbance below ~460 nm due to formation of MC_2-Cu^{2+} complex

Decrease at 540 nm as free MC concentration decreases

Characterisation

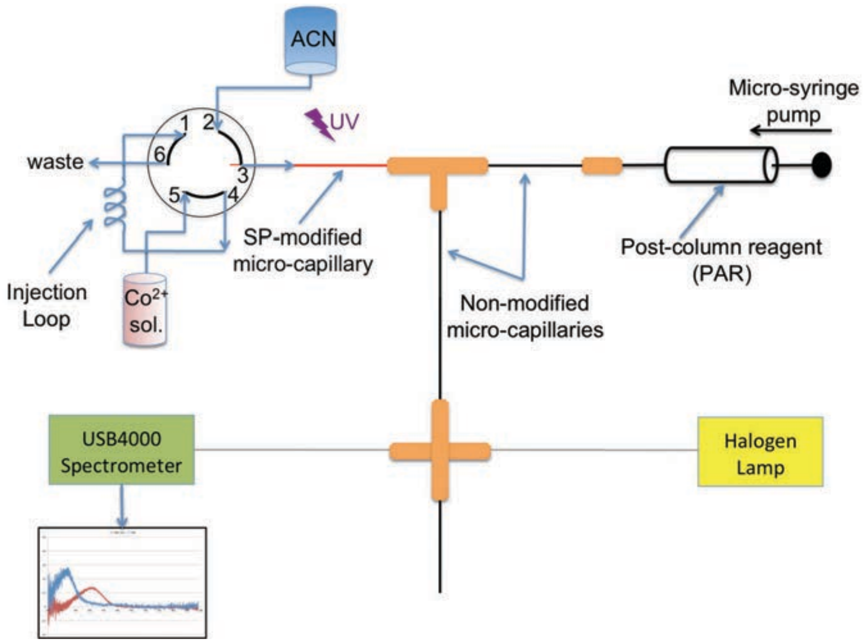


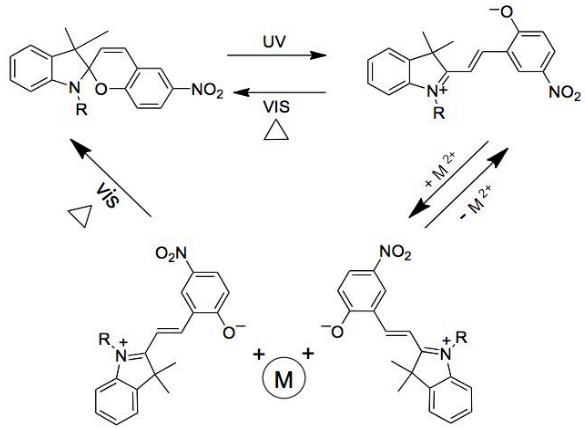


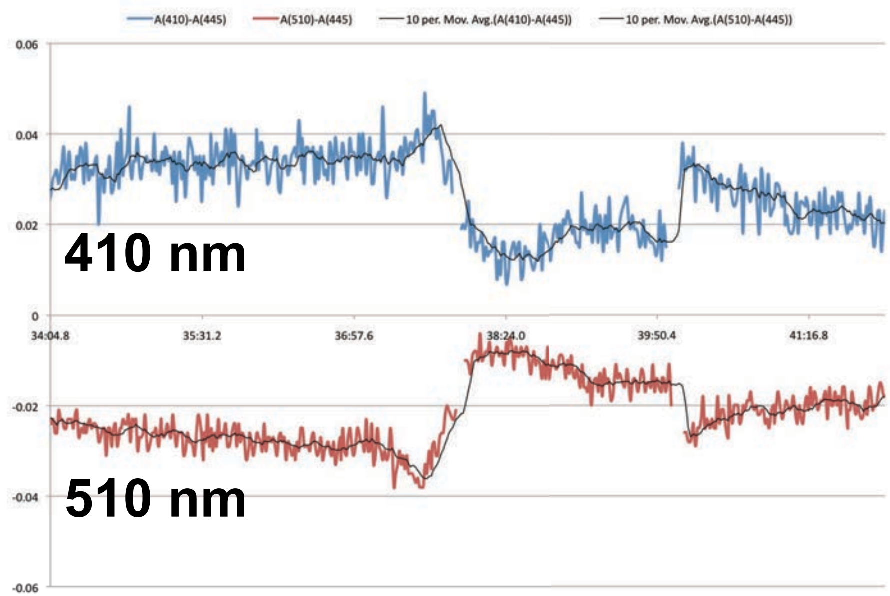


L. Florea, A. Hennart, D. Diamond, F. Benito-Lopez, Sens. Actuators B: Chem., 2011, DOI:10.1016/j.snb.2011.12.055

Uptake and Release – ‘Post Column’ Detection



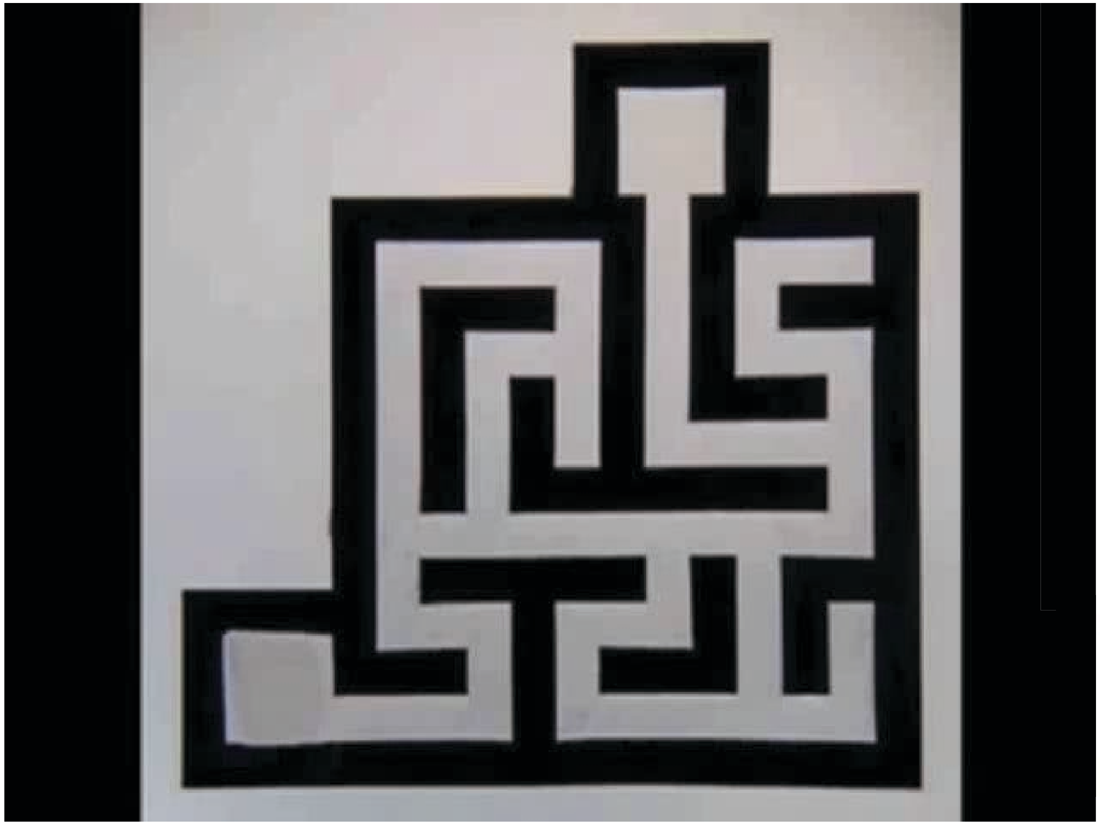




Co^{2+} + PAR ➔ PAR-Co^{2+}

410 nm 510 nm

Chemotactic Systems



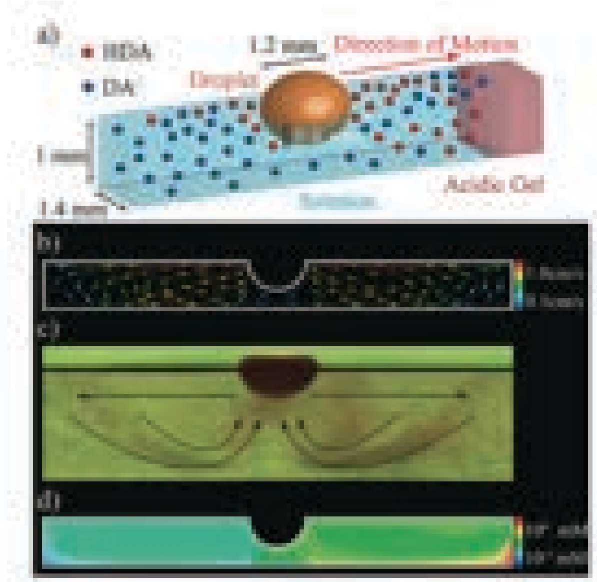


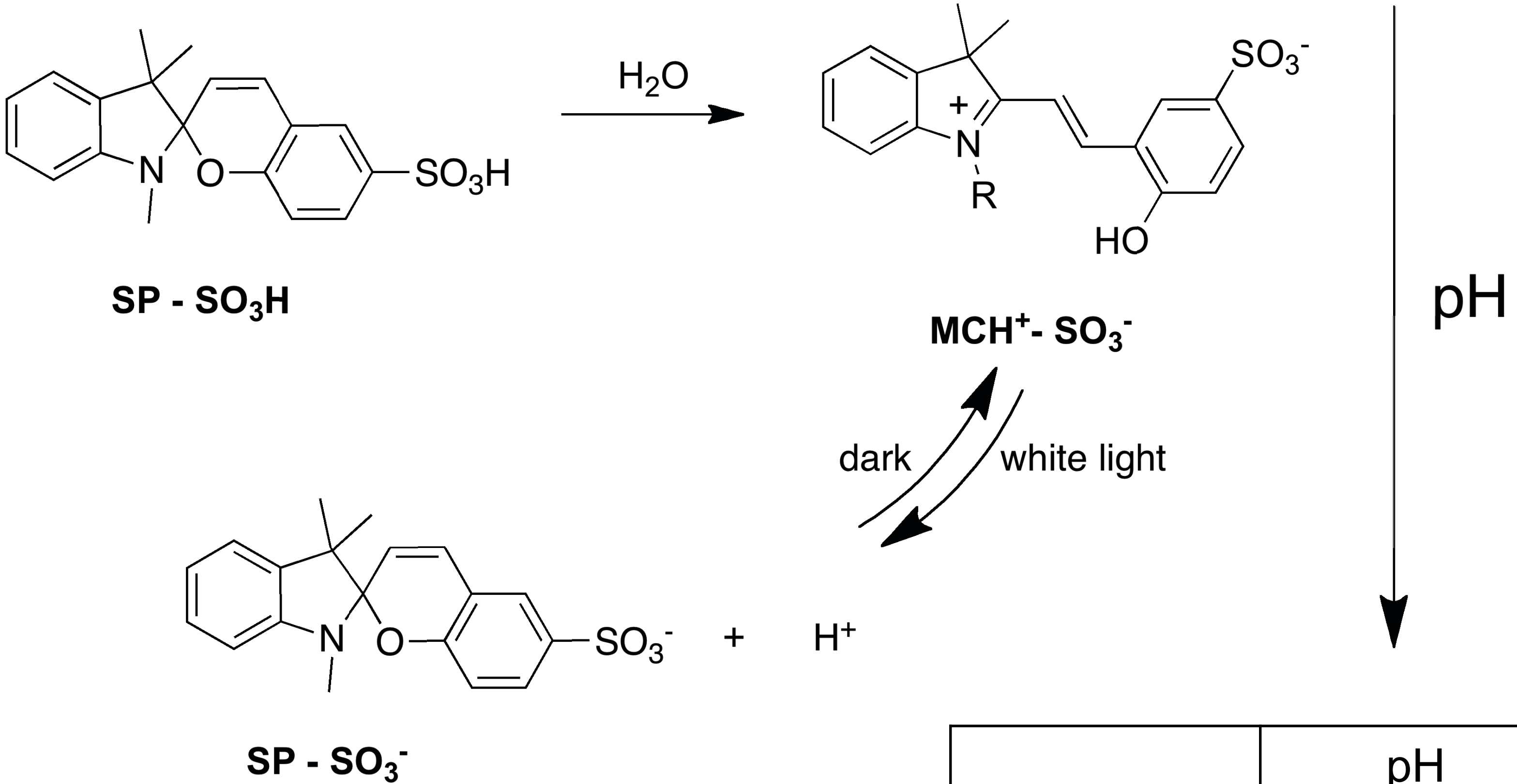
Figure 2. (a) Scheme of a droplet in a channel. The presence of HDA at the liquid−air interface gives rise to convective flows. Since more HDA is present in the direction facing the source of acid, the flows and forces are asymmetric. (b) Velocity field based on the theoretical model described in the main text (calculated using the Fluent computational fluid dynamics package from Ansys). (c) Experimental image of the convection rolls visualized using Neutral Red indicator (see also video 3 in the SI). (d)

Published on Web 11/01/2010 (speed ~x4): channels filled with KOH (pH 12.0-12.3 + surfactant; agarose gel soaked in HCl (pH 1.2) sets up the pH gradient; droplets of mineral oil or DCM containing 20-60% 2-hexyldecanoic acid + dye. Droplet speed ca. 1-10 mm/s; movement caused by convective flows arising from concentration gradient of HDA at droplet-air interface (greater concentration of HDA towards lower pH side); **HDA <-> H^+ + DA^-**

Maze Solving by Chemotactic Droplets; Istvan Lagzi, Siowling Soh, Paul J. Wesson, Kevin P. Browne, and Bartosz A. Grzybowski; **J. AM. CHEM. SOC. 2010, *132, 1198–1199***

Fuerstman, M. J.; Deschatelets, P.; Kane, R.; Schwartz, A.; Kenis, P. J. A.;Deutch, J. M.; Whitesides, G. M. *Langmuir 2003, 19, 4714.*

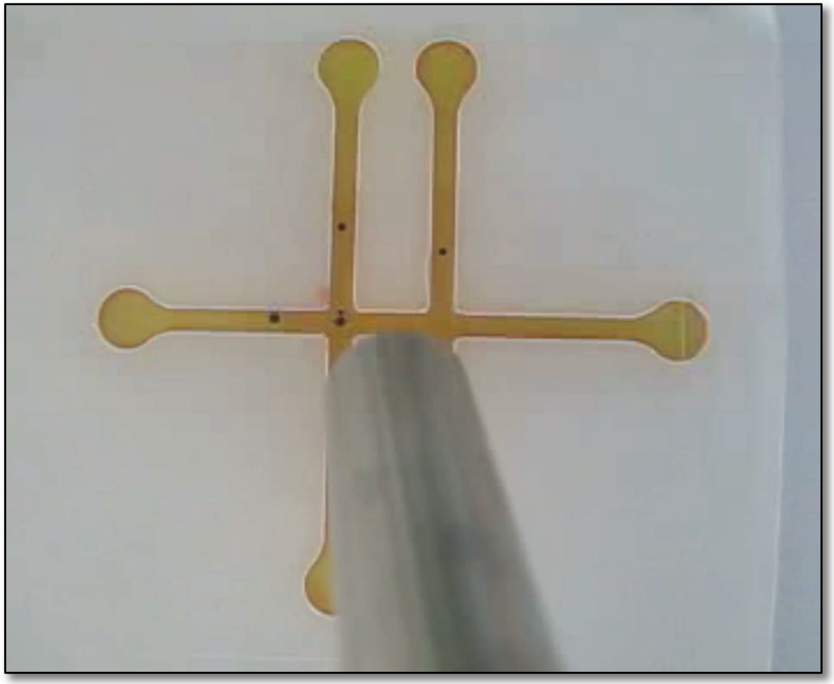
Photo-modulation of pH

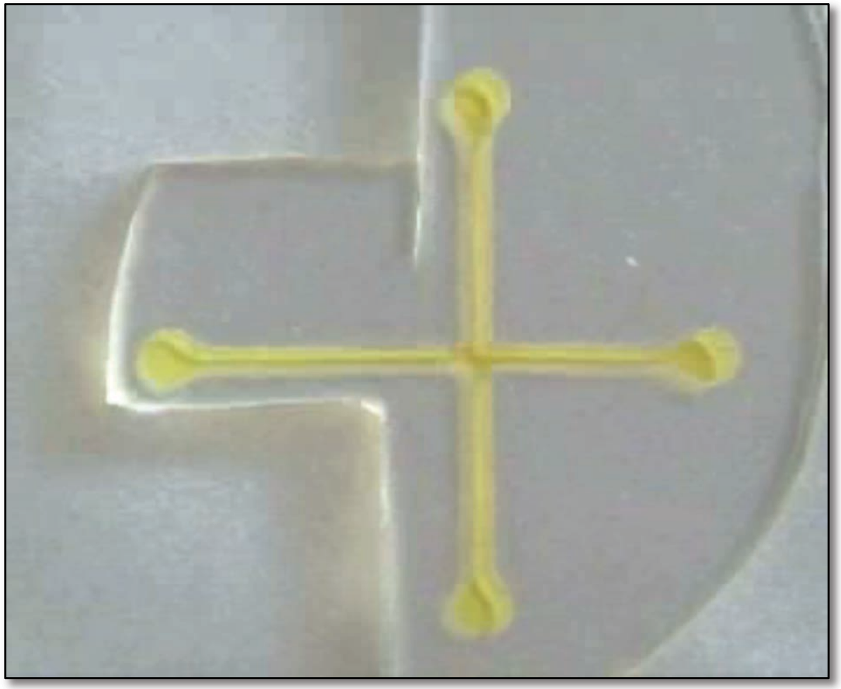


	pH
H_2O	6.5
MCH^+-SO_3^-	4.8
SP-SO_3^-	3.4

Channel Solution: Spiropyran Sulfonic Acid 10^{-3}M (H_2O)

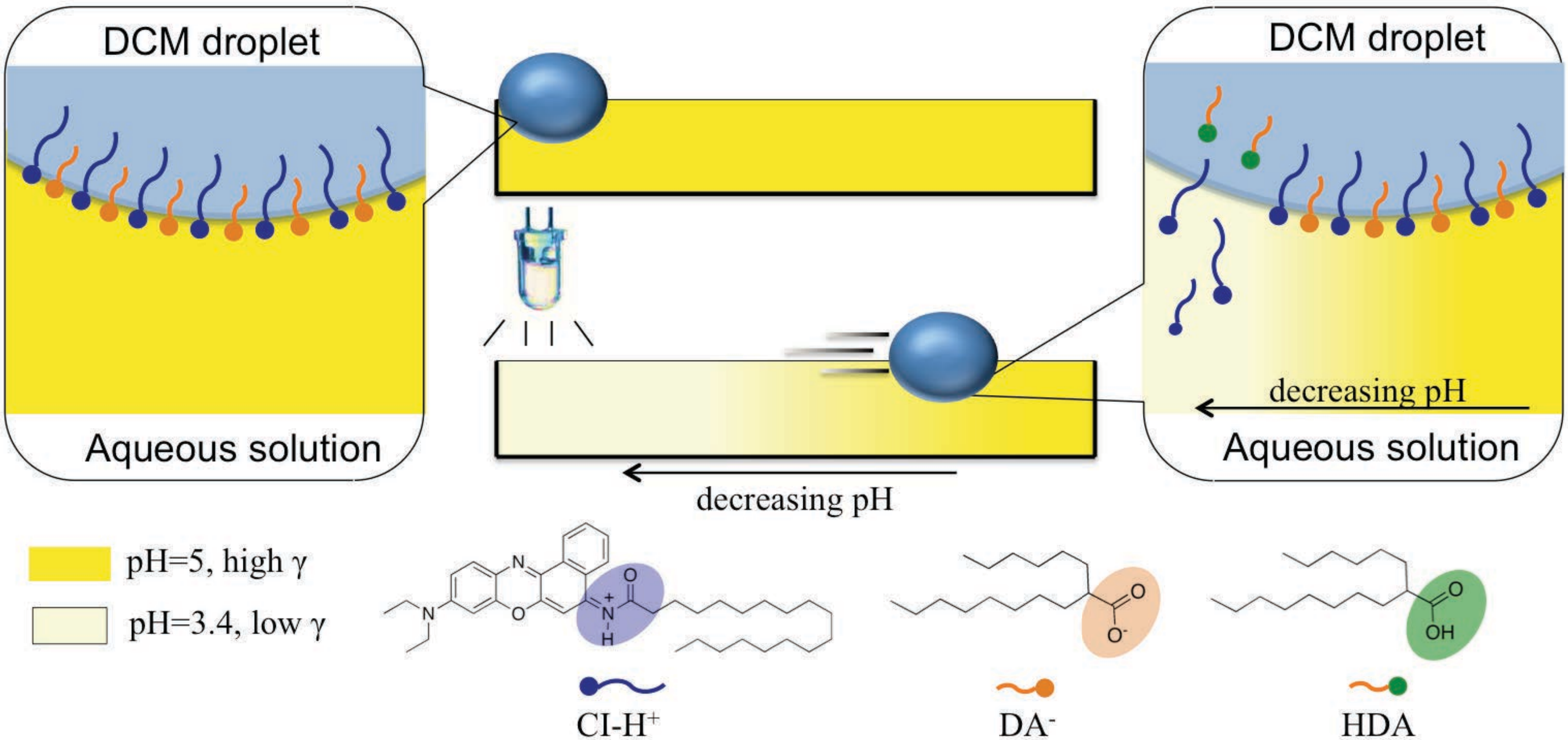
Movement of Droplets in Channels using Light





- We use light to create a localised pH gradient
- This disrupts an ion pair at the droplet interface
- Surfactant is expelled and movement of the droplet occurs
- Interested in exploring how to use droplets for sensing and for transport & release of active components

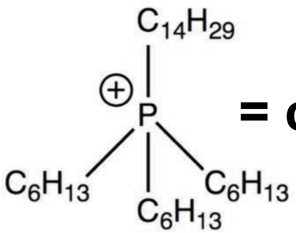
Mechanism of Photo-Stimulated Droplet Movement (with David Officer, UOW)



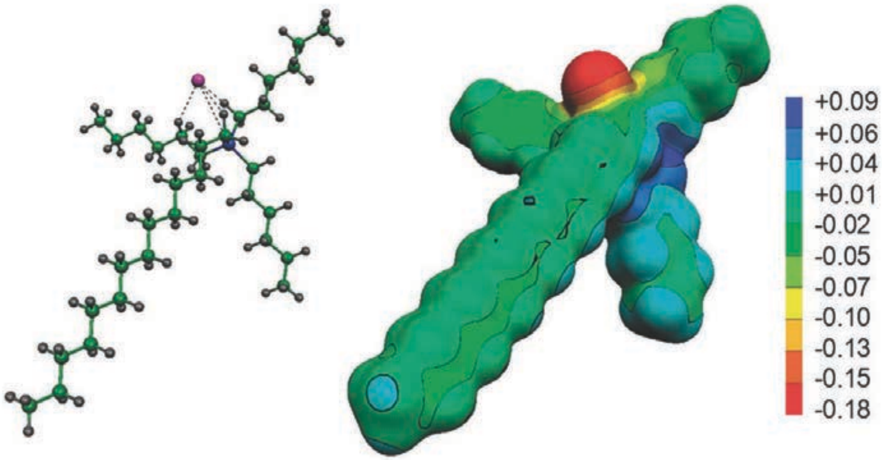
N-OCTADECANOYL-NILE BLUE

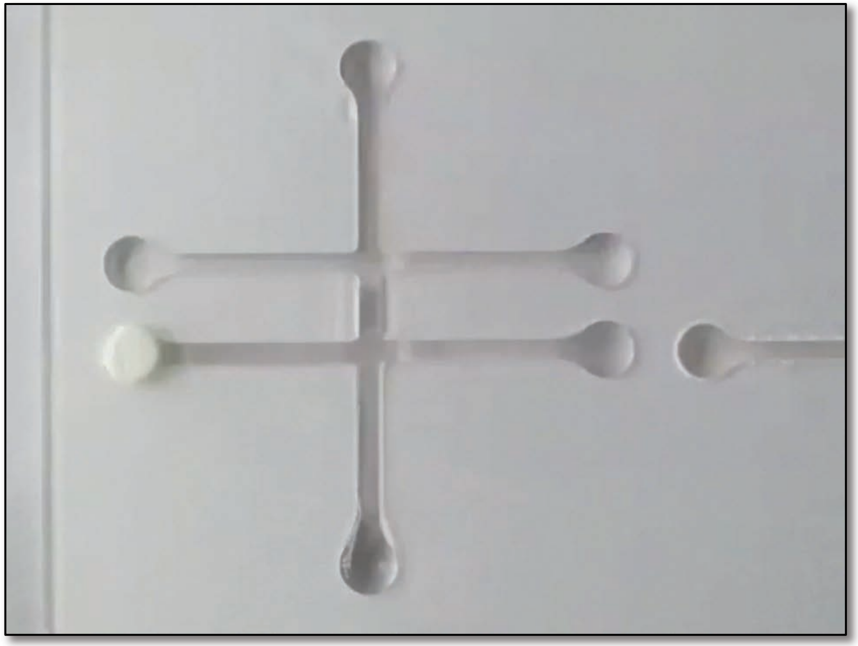
Photo-Chemopropulsion – Light-Stimulated Movement of Microdroplets, *Larisa Florea, Klaudia Wagner, Pawel Wagner, Gordon G. Wallace, Fernando Benito-Lopez, David L. Officer, and Dermot Diamond, Adv. Mater. 2014, DOI: 10.1002/adma.201403007*

We can do the same with IL Droplets



= cationic surfactant





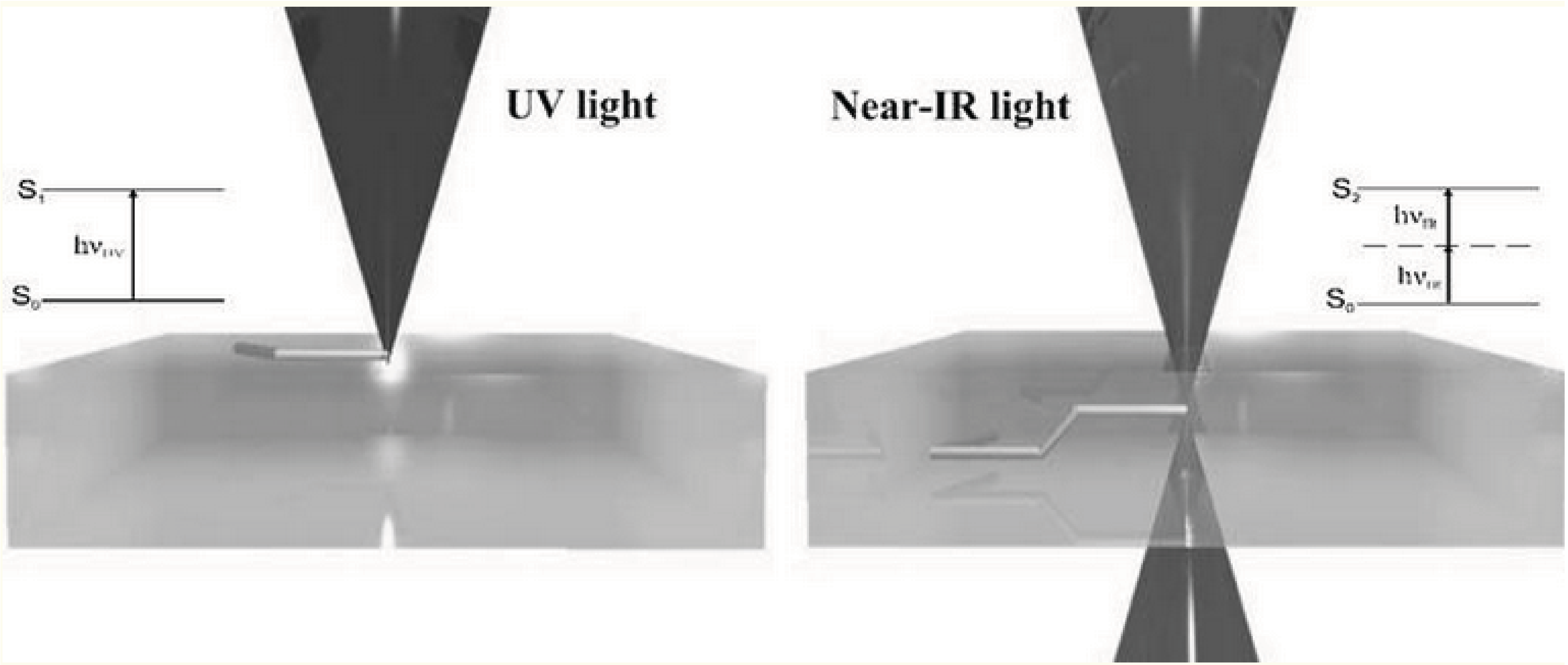
Trihexyl(tetradecyl)phosphonium chloride ([$P_{6,6,6,14}$][Cl]) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the Cl^- ion which is created using a polyacrylamide gel pad soaked in 10^{-2} M HCl; A small amount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

Background

Stereolithography

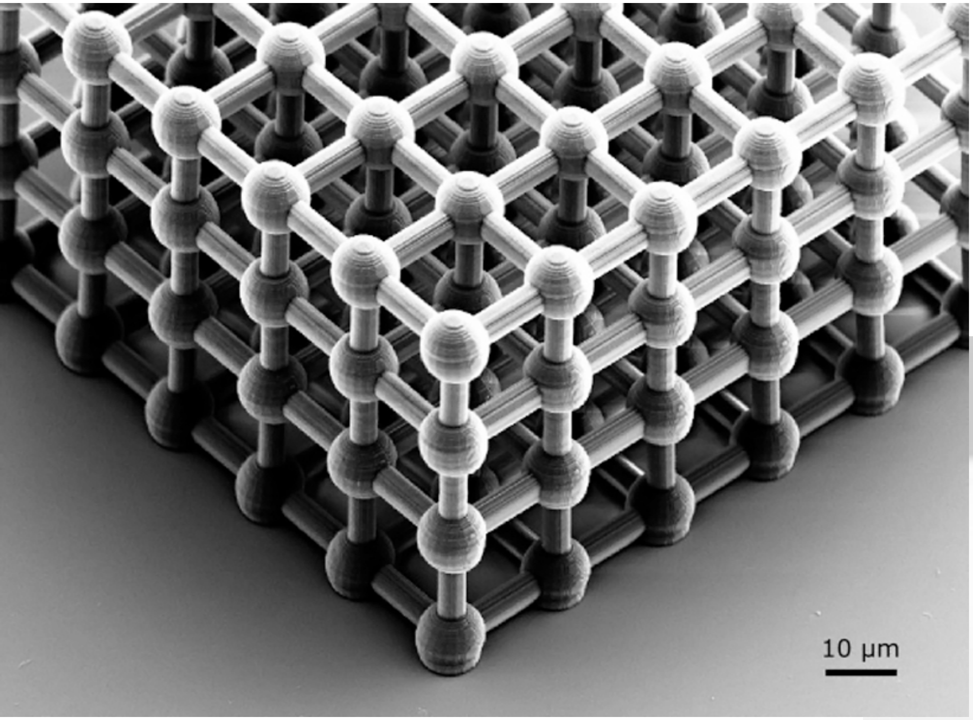
Two-photon polymerisation

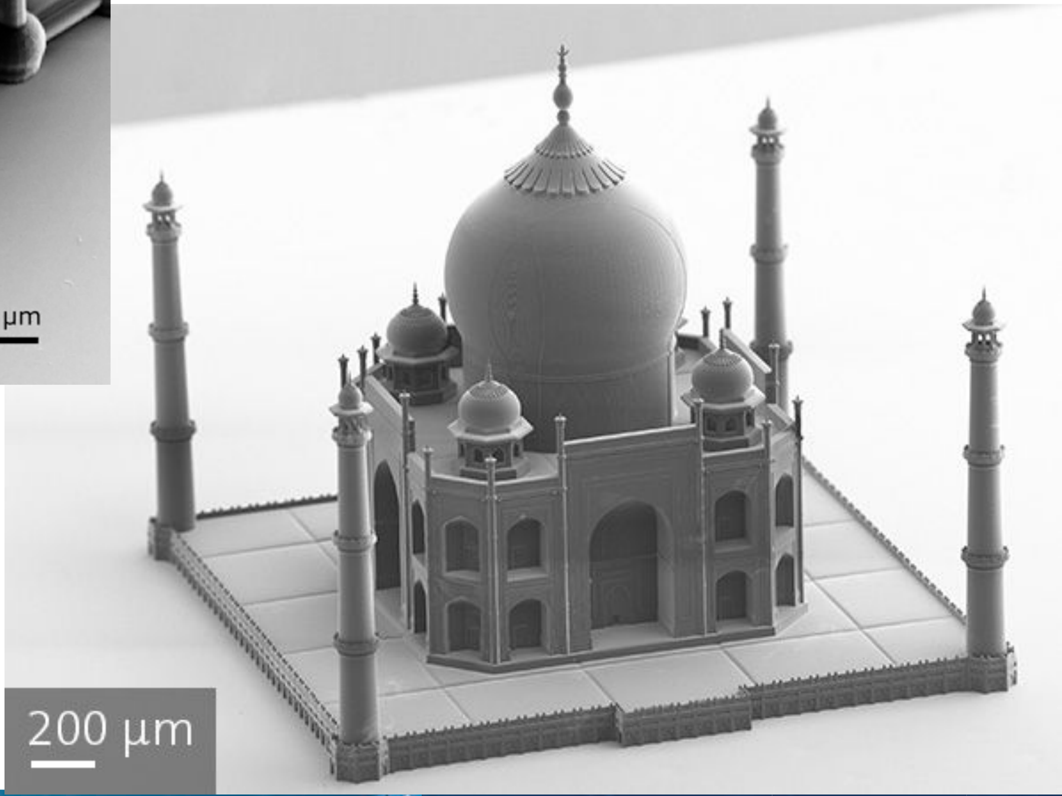


- Single photon absorption
- 2D patterns

- Two photon absorption
- 3D structures

Background





http://www.nanoscribe.de/

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!