NCSR
National Centre for Sensor Research

Insight

The Exciting Potential of Stimuli-Responsive Materials and Biomimetic Microfluidics

Larisa Florea, Simon Coleman, Wayne Francis, Simon Coleman, Aishling Dunne and Dermot Diamond,

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

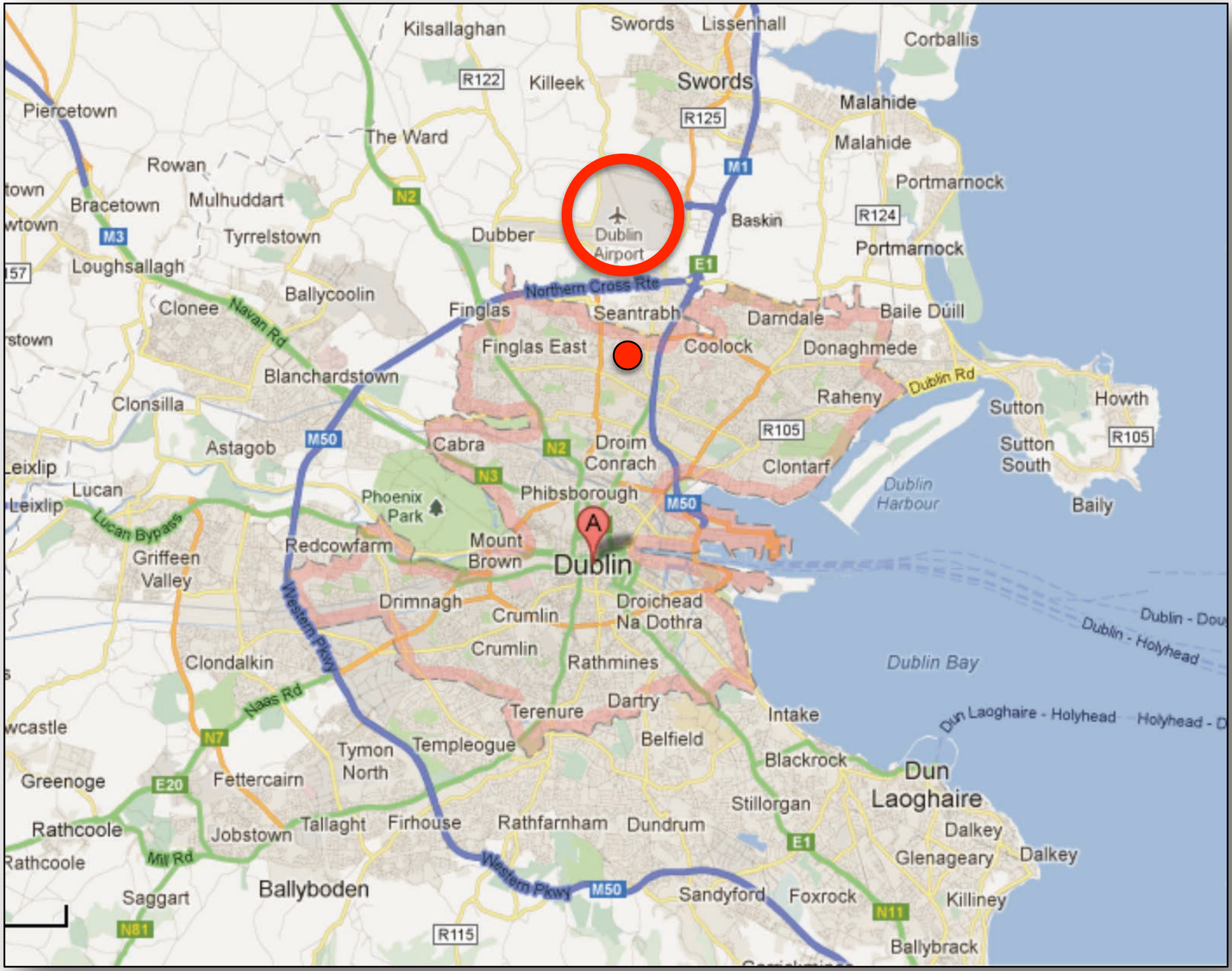
Invited lecture presented at

EuroNanoForum Sensors Workshop
University of Latvia

Riga, Latvia, 9th June 2015

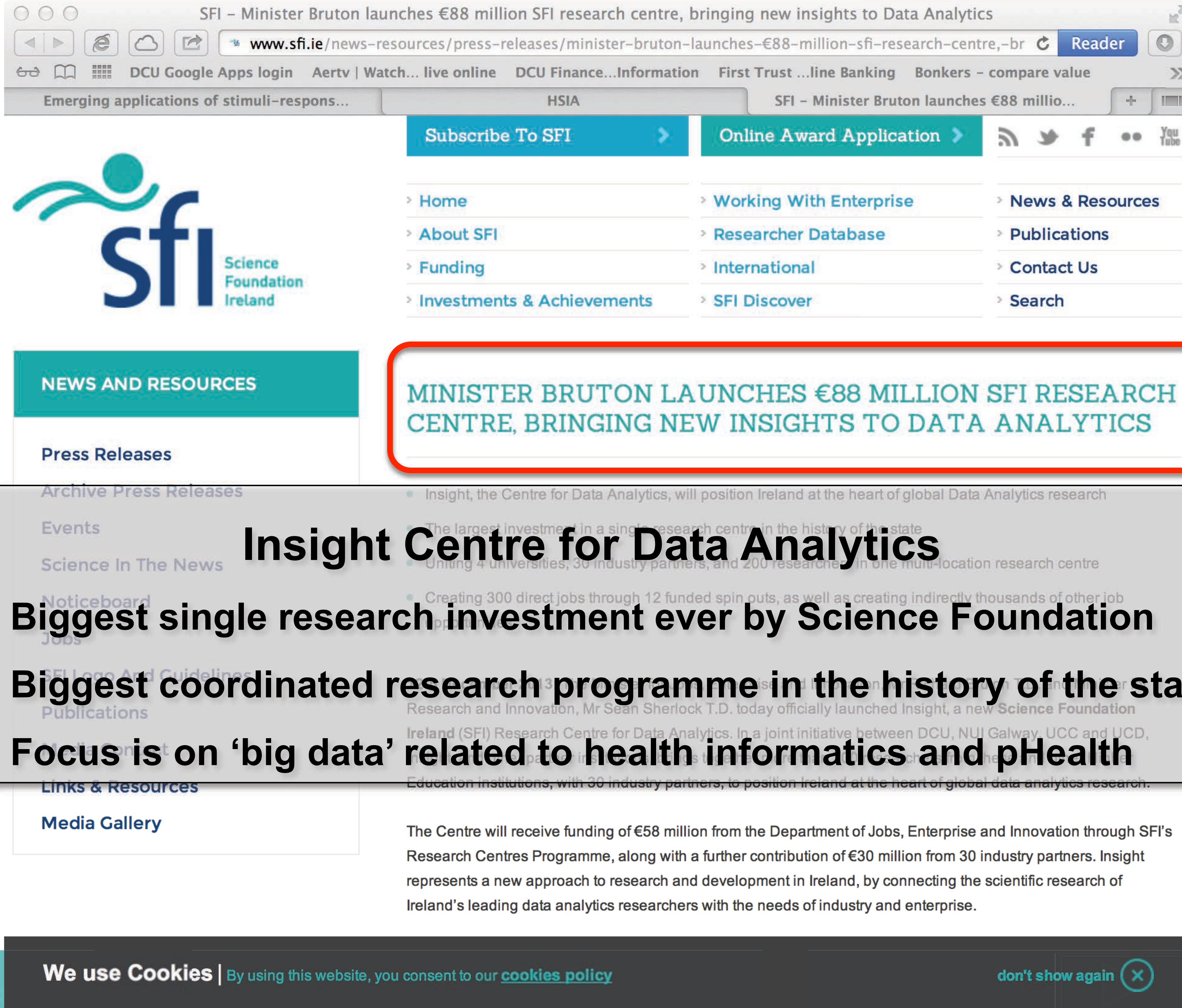
sfi DCU UCC OÉ Gaillimh NUI Galway UCD DUBLIN

Dublin & DCU Location



Insight Centre for Data Analytics

- Biggest single research investment ever by Science Foundation
- Biggest coordinated research programme in the history of the state
- Focus is on ‘big data’ related to health informatics and pHealth



NAPES Consortium

DCU · institutCurie · TelLab · WIS Williams Industrial Services · TU/e · CIC microGUNE Microtechnologies Cooperative Research Center · UNIVERSITÀ DEGLI STUDI DI MILANO · Aquila Bioscience

Funded under grant agreement No. 604241 of the European Union's Seventh Framework Programme

Keynote Article: August 2004, Analytical Chemistry (ACS)

internet scale sensing

Dermot Diamond
Dublin City University
(Ireland)

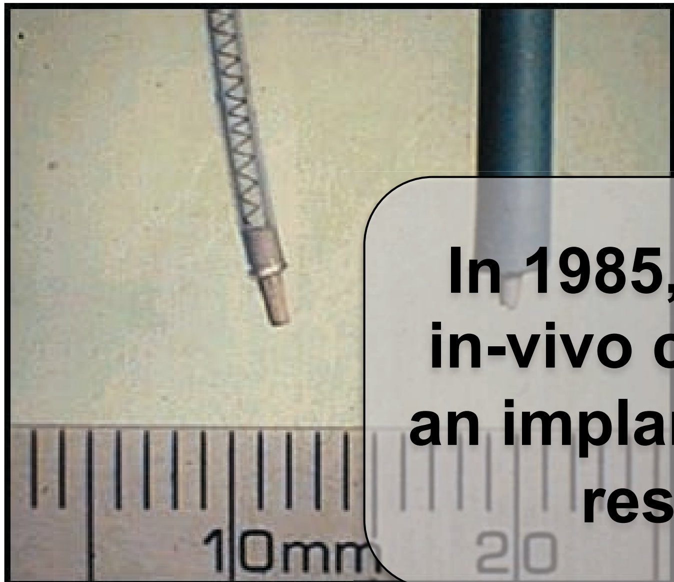
Incredible advances in digital communications and computer power have profoundly changed our lives. One chemist shares his vision of the role of analytical science in the next communications revolution.

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)

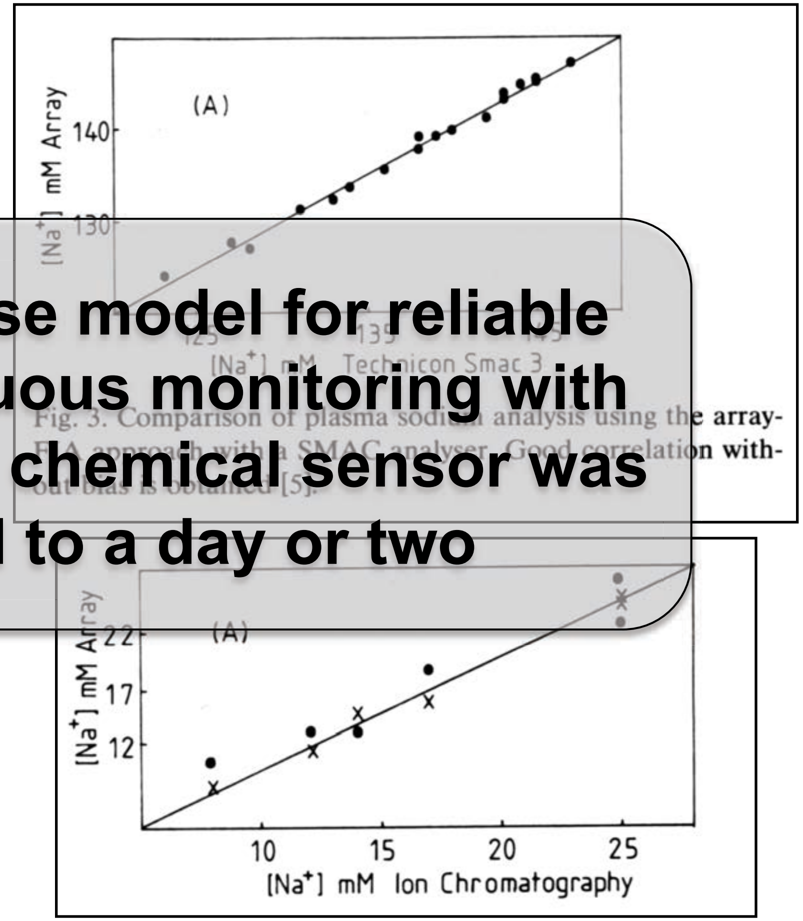
Blood Analysis; Implantible Sensors



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

Dr. David Band, St Thomas's Hospital London

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



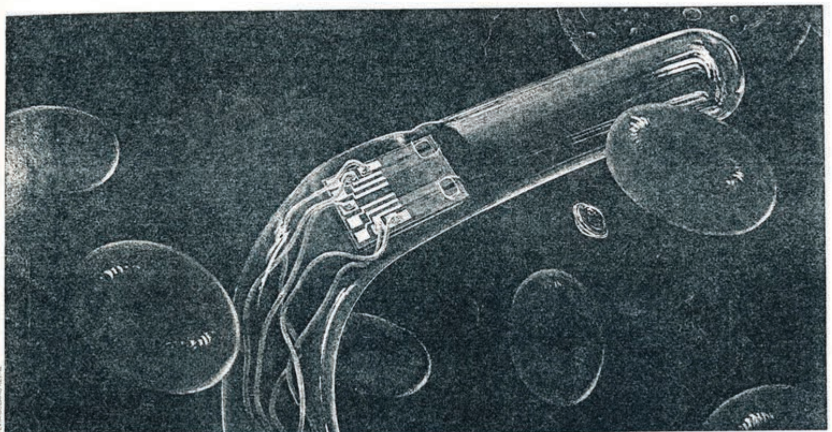
Anal. Chem., *64* (1992) 1721-1728.

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

The promise of biosensors…..

B I O S E N S O R S

THE MATING OF BIOLOGY AND ELECTRONICS



Implanted sensors combine biomaterials and electronics to track life processes. The Univ. of Utah 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.

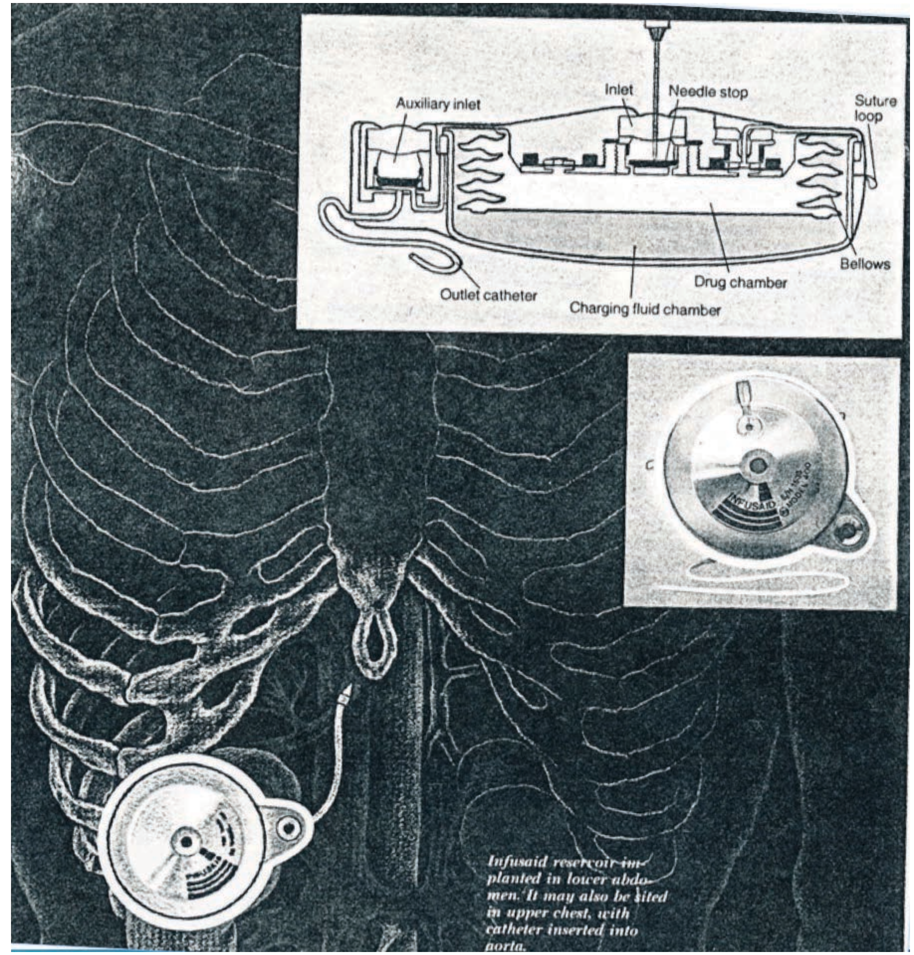
Within seconds a chemical reaction will begin at the tip of the wire. A few molecules of glucose in the blood will adhere to the membrane and be attacked by the enzyme, forming hydrogen peroxide and another product. The peroxide will migrate to a thin oxide layer on the platinum, generating a slight 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



Infusaid reservoir implanted in lower abdomen. It may also be sited in upper chest, with catheter inserted into aorta.

High Technology, Nov. 1983, 41-49

Apple, iWatch & Health Monitoring

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.

How will they integrate biosensing with the iWatch…..?

Google Contact Lens

United States Patent Application ***20140107445***

Kind Code A1 Liu; Zenghe April 17, 2014

Microelectrodes in an Ophthalmic Electrochemical Sensor

Abstract

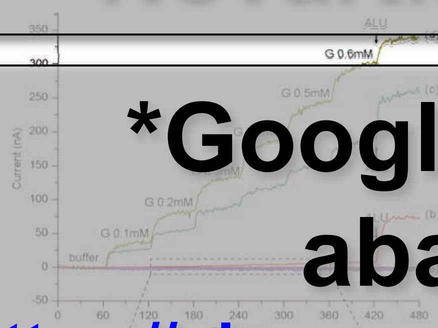
An eye-mountable device **includes an electrochemical sensor embedded in a polymeric material** configured for mounting to a surface of an eye. The electrochemical sensor includes a working electrode, a reference electrode, and a reagent that selectively reacts with an analyte to generate a sensor measurement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

- **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



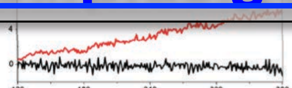
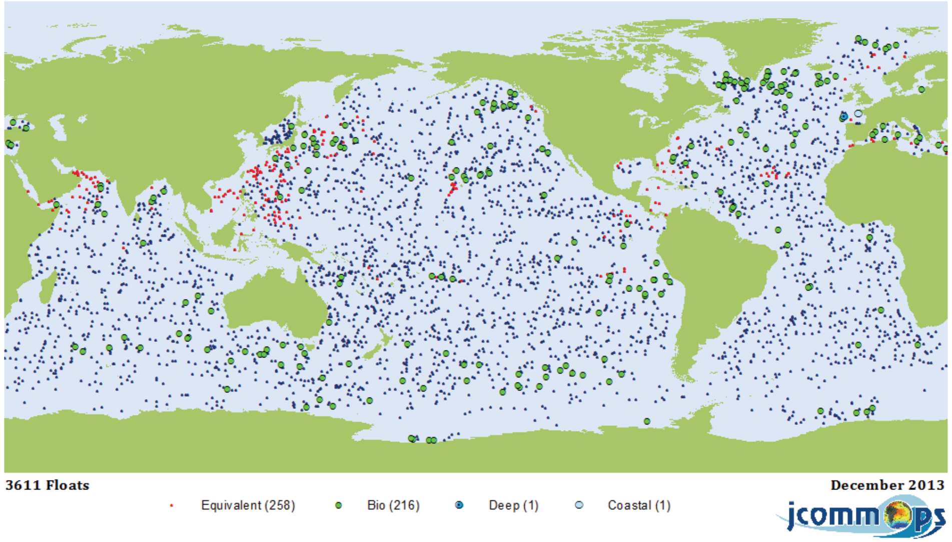


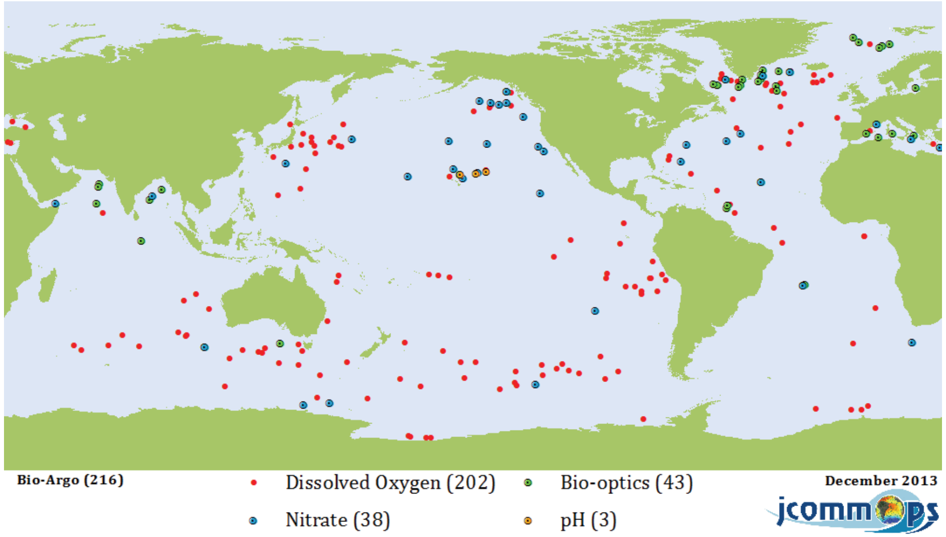
Fig. 2. Images of the sensor as it goes through surface functionalization and the related measured responses: (a) sequential images of sensor pre-treatment with GOD/titania/Nafion®; (b) measured amperometric response for the sensor just incubated with GOD; (c) measured amperometric response for the sensor prepared with GOD/titania sol–gel film; (d) measured amperometric response for the sensor prepared with GOD/titania/Nafion®; (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.

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

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

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)**

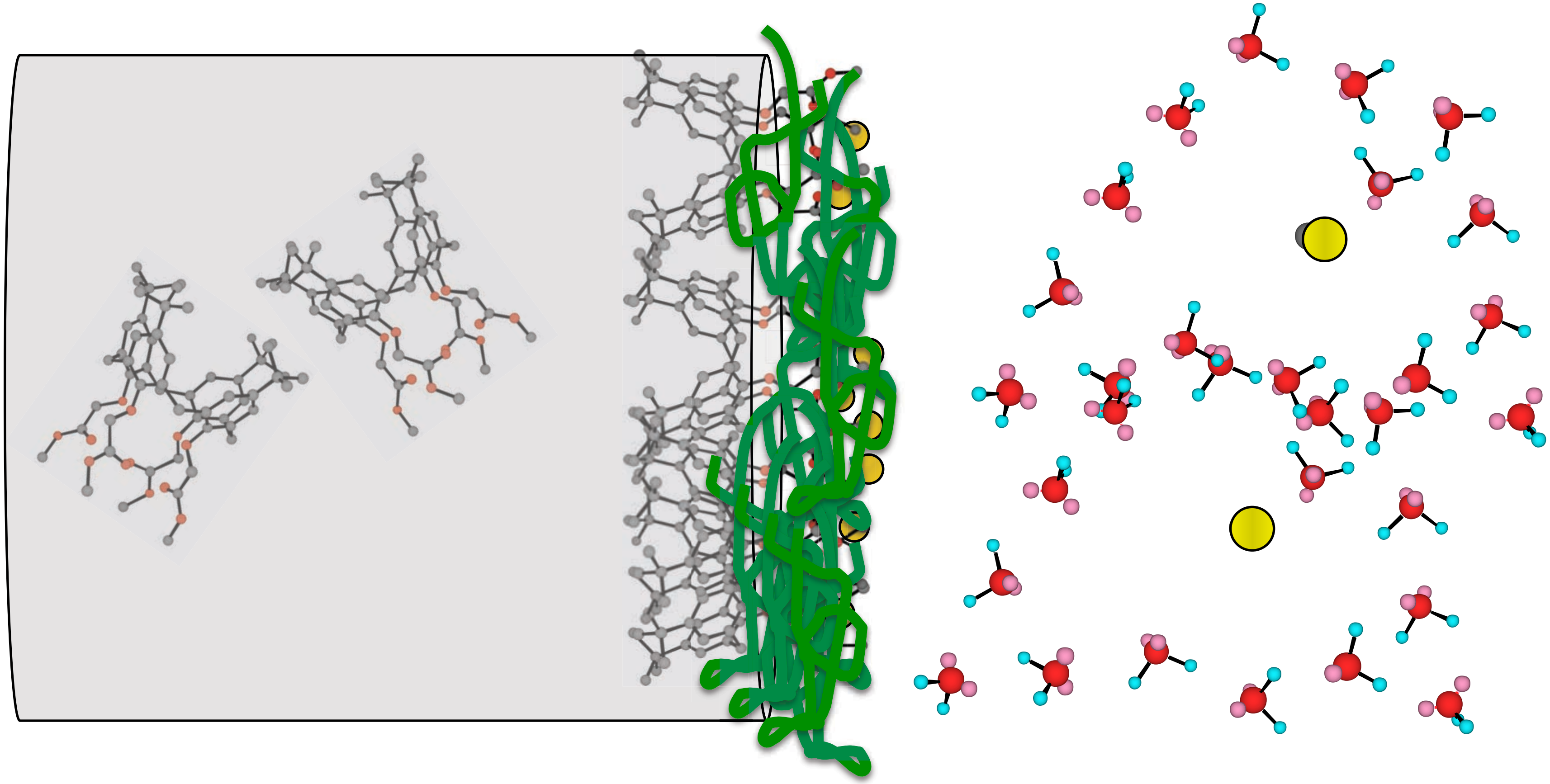
@€60K ea!

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

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

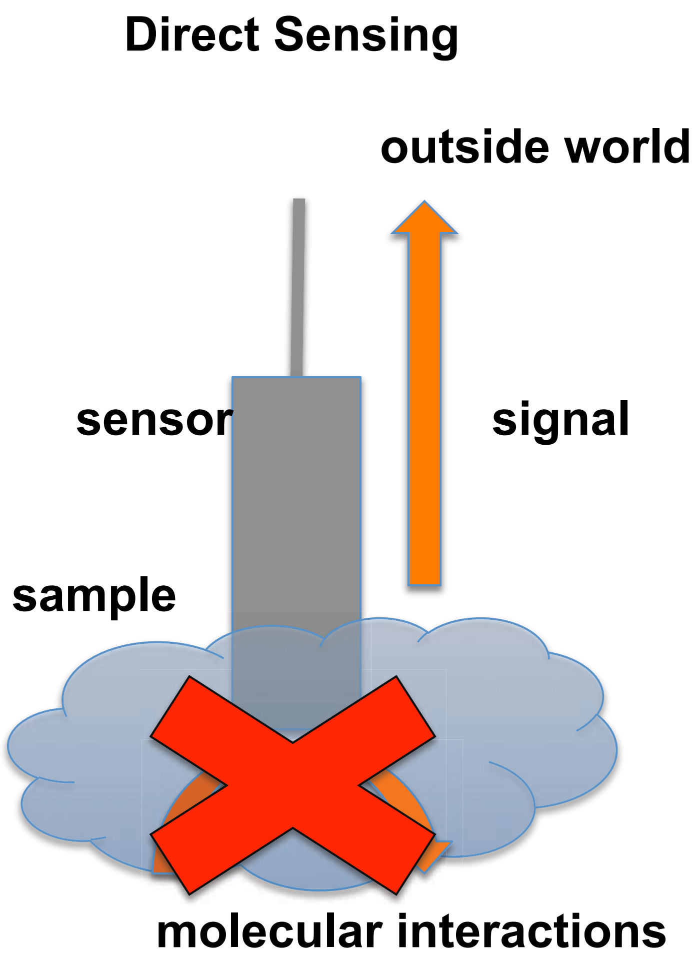
‘calibration of the DO measurements by the SBE sensor remains an important issue for the future’, Argo report ‘Processing Argo OXYGEN data at the DAC level’, September 6, 2009, V. Thierry, D. Gilbert, T. Kobayashi

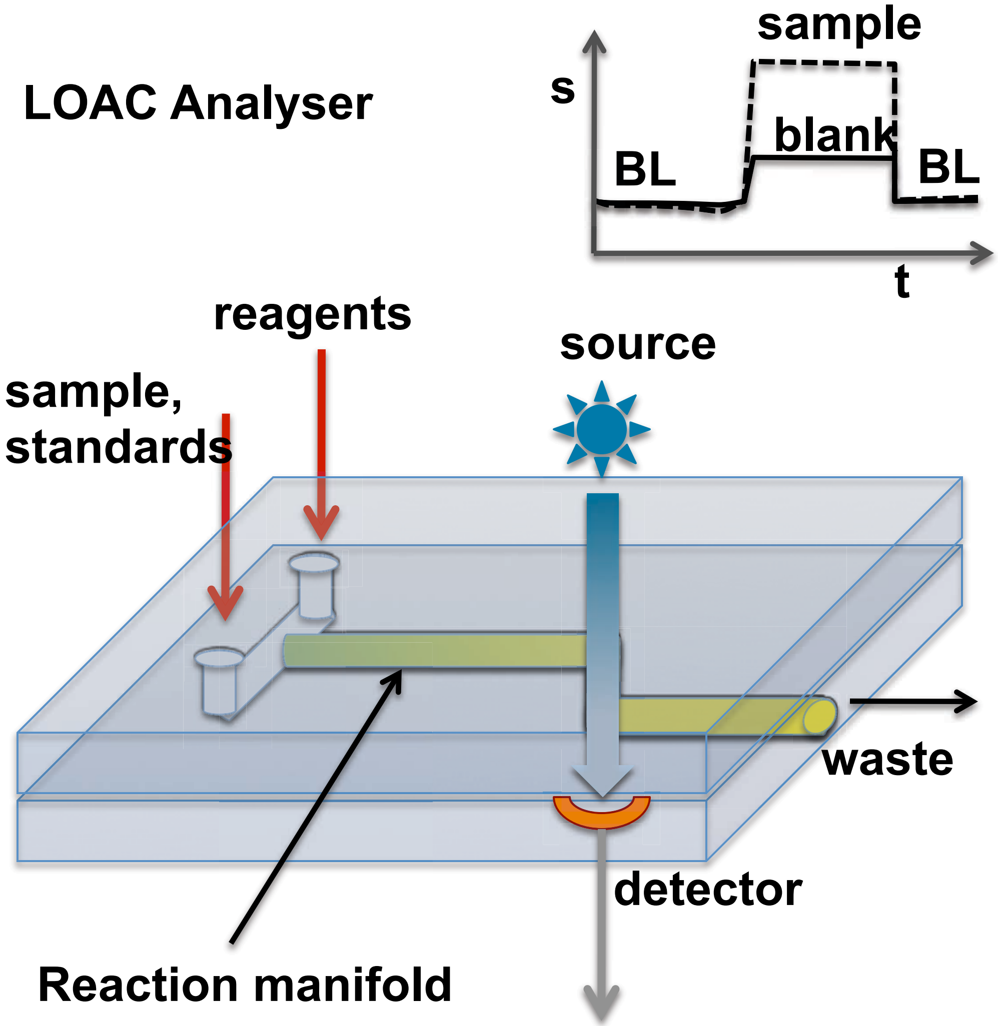
Control of membrane interfacial exchange & binding processes



Remote, autonomous chemical sensing is a tricky business!

Direct Sensing vs. Reagent Based LOAC/ufluidics





Phosphate: The Yellow Method

Mixture (Reagent)

$(NH_4VO_3) + (NH_4)_6Mo_7O_{24}.4H_2O$, HCl conc.

+

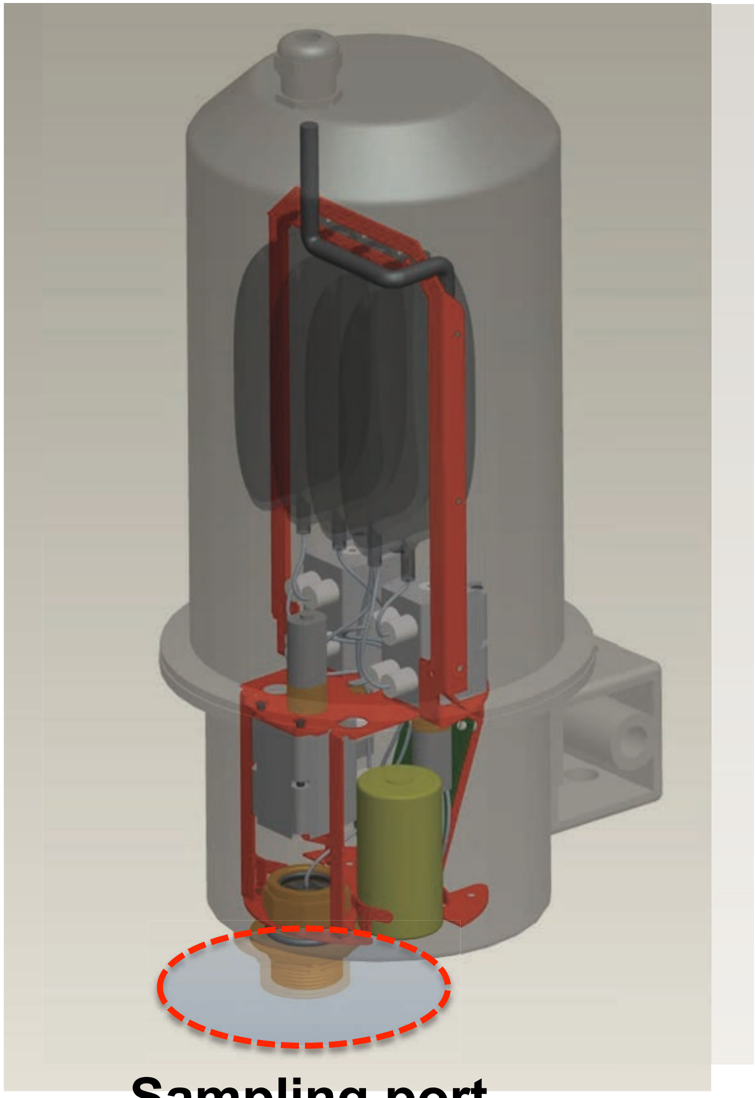
Sample

$H_2PO_4^-$

$$(NH_4)_3PO_4.NH_4VO_3.16MoO_3$$

- Yellow vanaomolybdophosphoric acid is formed when ammonium metavanadate and ammonium molybdate (mixture) reacts with phosphate (acidic conditions)
- In conventional (molybdate) method, **ascorbic acid** is used to generate the well-known deep blue complex (**v. fine precipitate**)
- **Could not be exploited in LOAC devices until UV-LEDs became available!!!!**

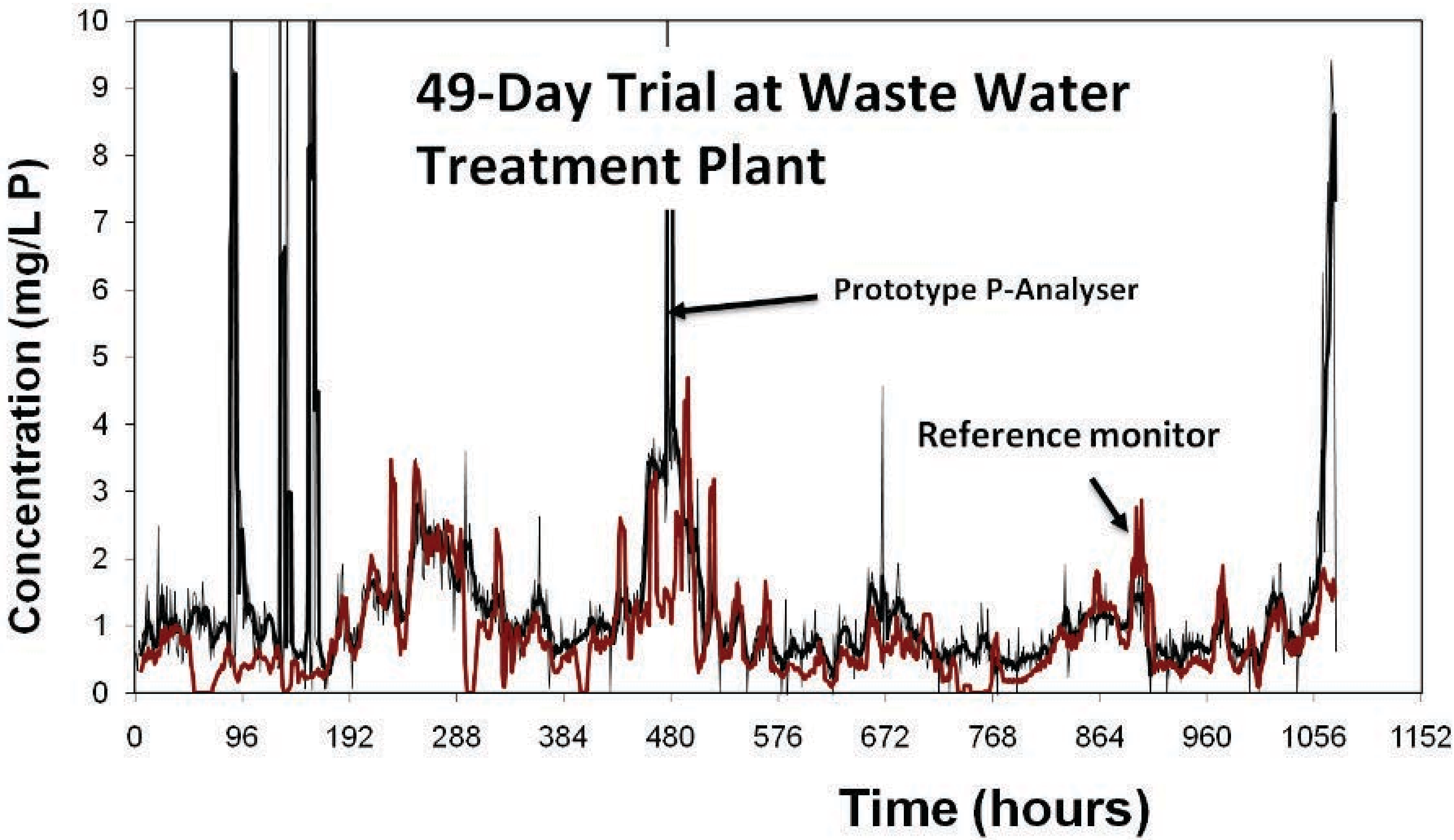
2nd Generation Analyser: Design



Deployment at Osberstown WWTP

- Phosphate monitoring unit deployed
- System is fully immersed in the treatment tank
- Wireless communications unit linked by cable
- Data transmitted to web

Autonomous Chemical Analyser

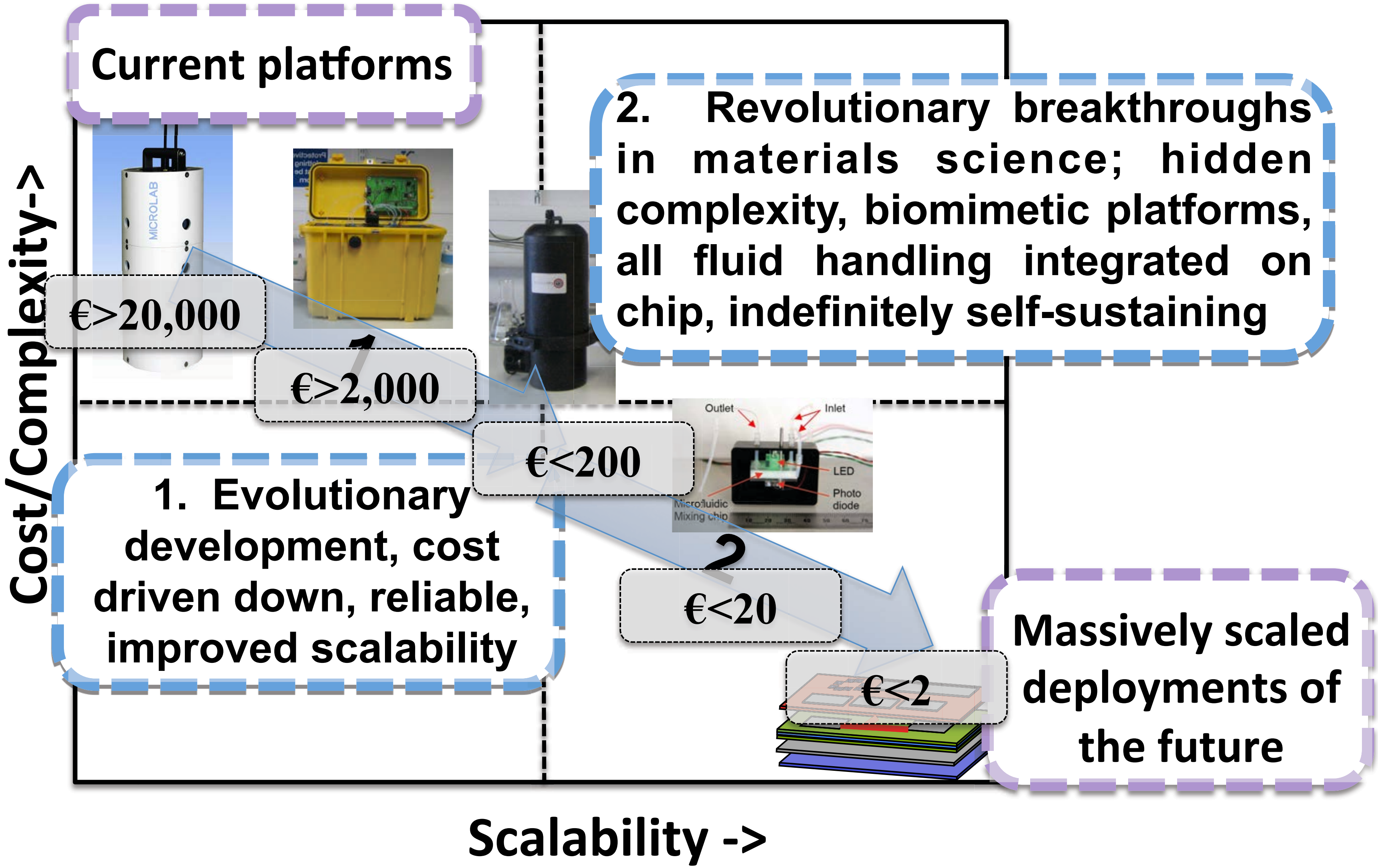


Phosphate monitoring using the Yellow Method

Osberstown – 3 week deployment

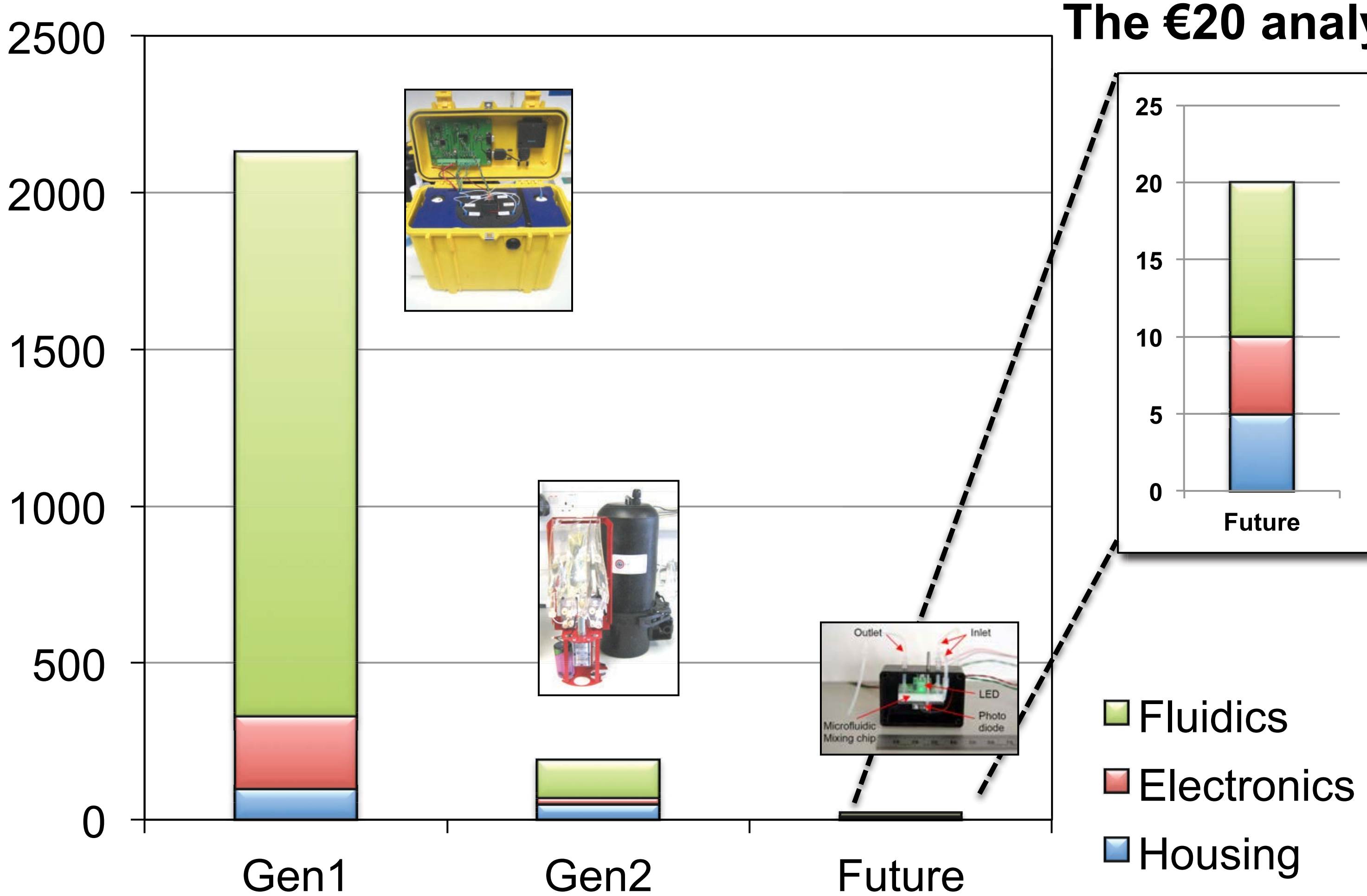
Biofouling of sensor surfaces is a major challenge for remote chemical sensing – both for the environment and for implantable sensors

Achieving Scale-up



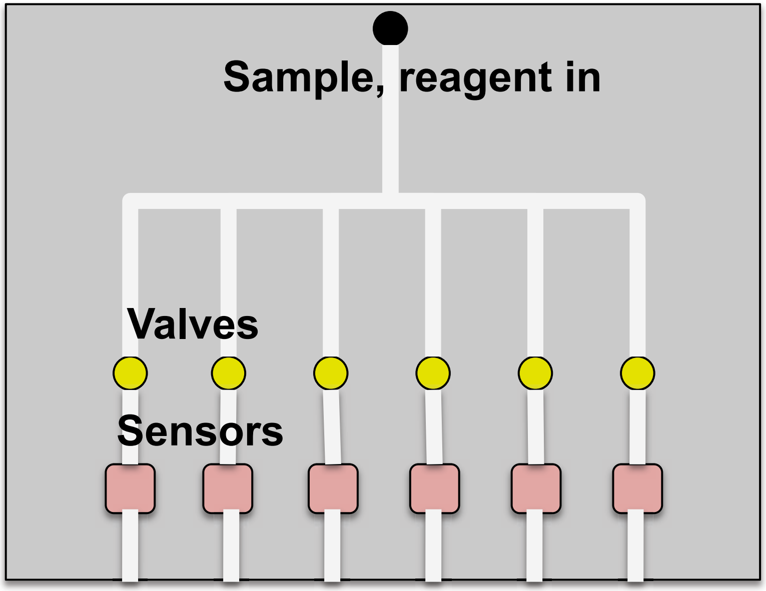
Cost Comparison Analyser (€)

The €20 analyser



Extend Period of Use via 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)….

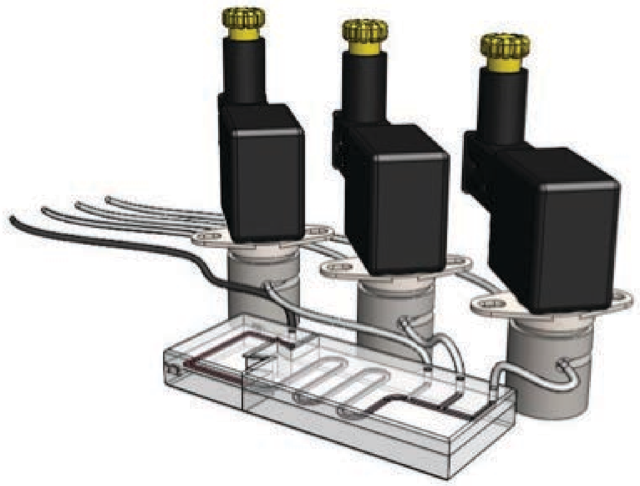


Then 50 sensors when used sequentially could provide an aggregated in-use lifetime of around 1 year

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

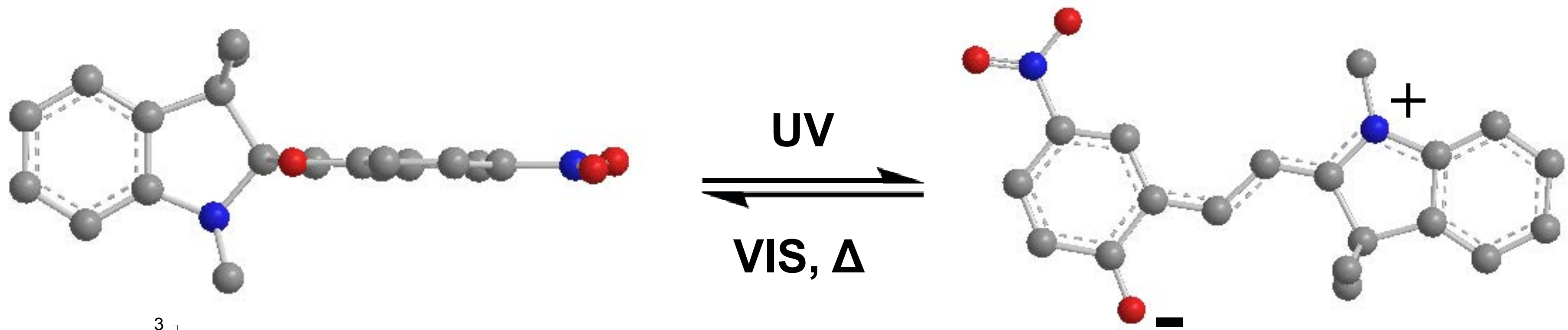
How to advance fluid handling in LOC platforms: re-invent valves (and pumps)!

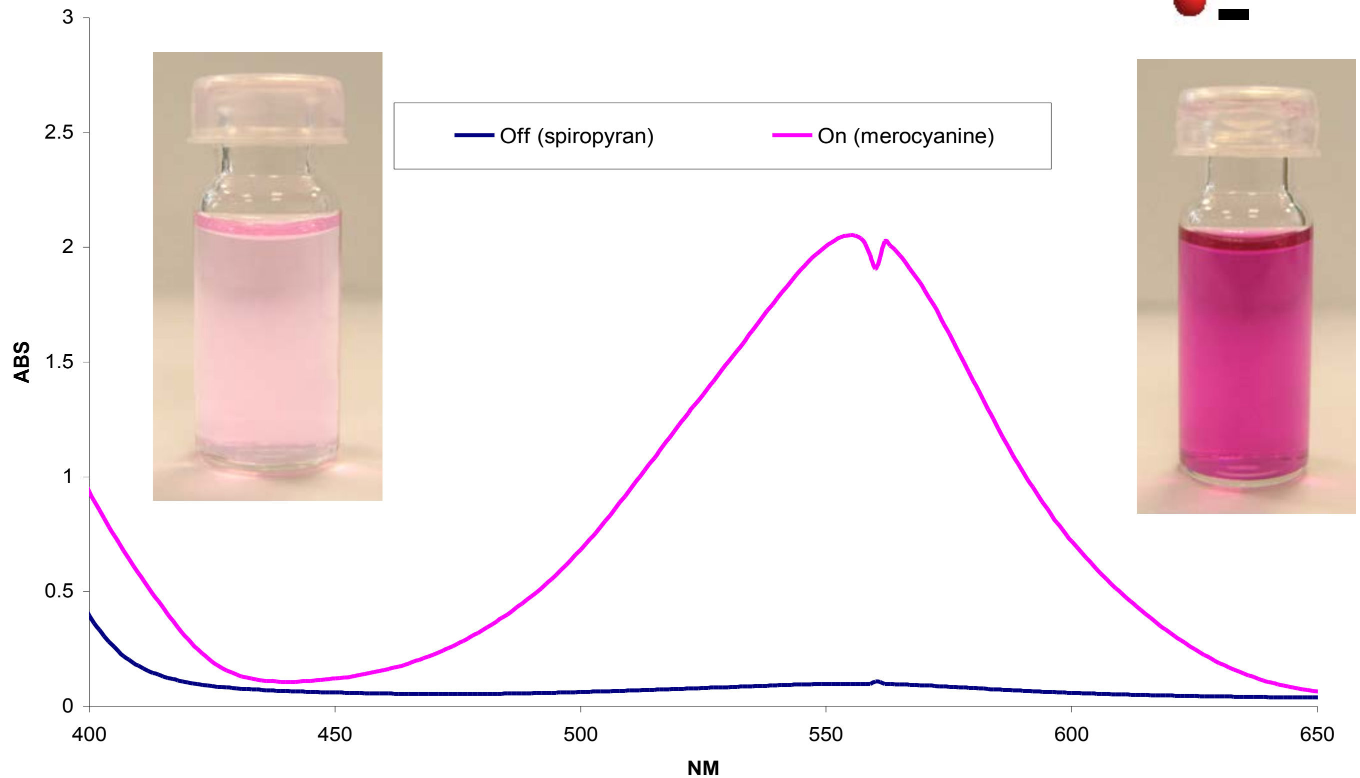
- **Conventional valves cannot be easily scaled down - Located off chip: fluidic interconnects required**
  - Complex fabrication
  - Increased dead volume
  - Mixing effects
- **Based on solenoid action**
  - Large power demand
  - Expensive



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

Photoswitchable Actuators





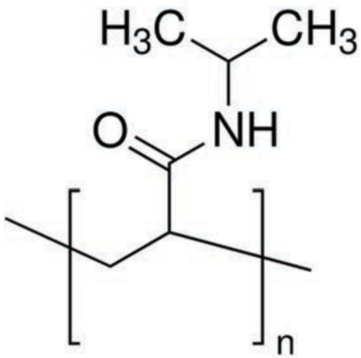
Famous Molecule….

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

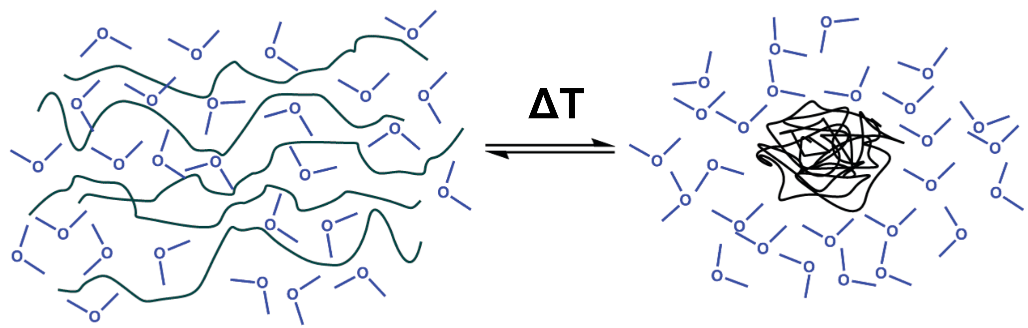
Poly(*N*-isopropylacrylamide)

- 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

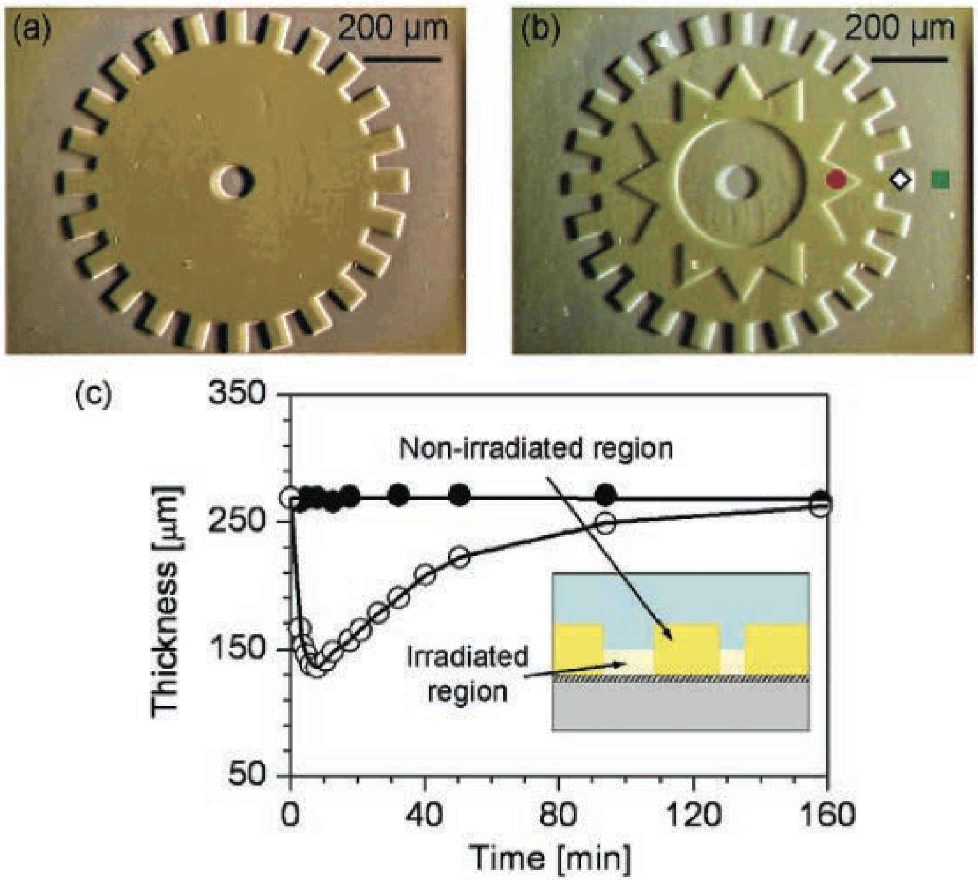
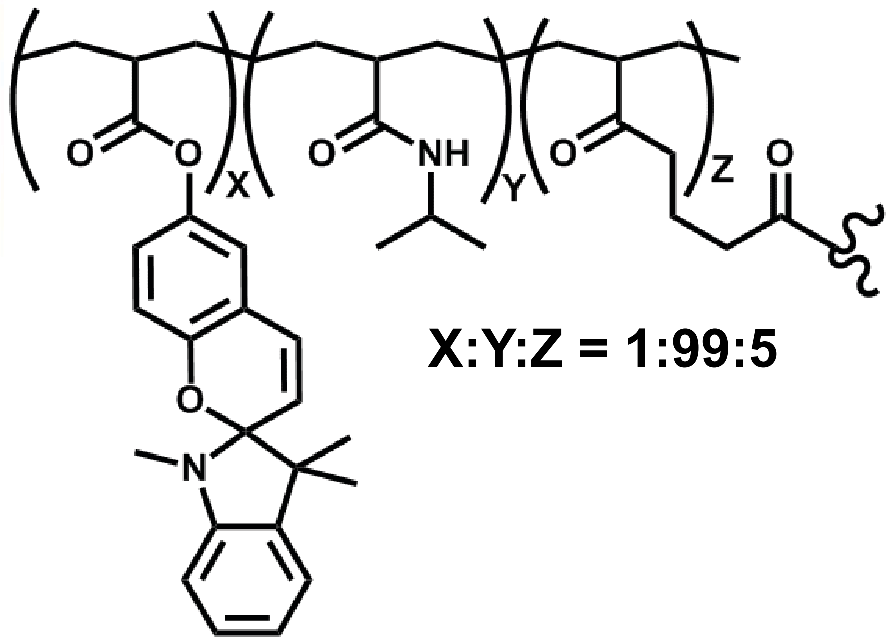


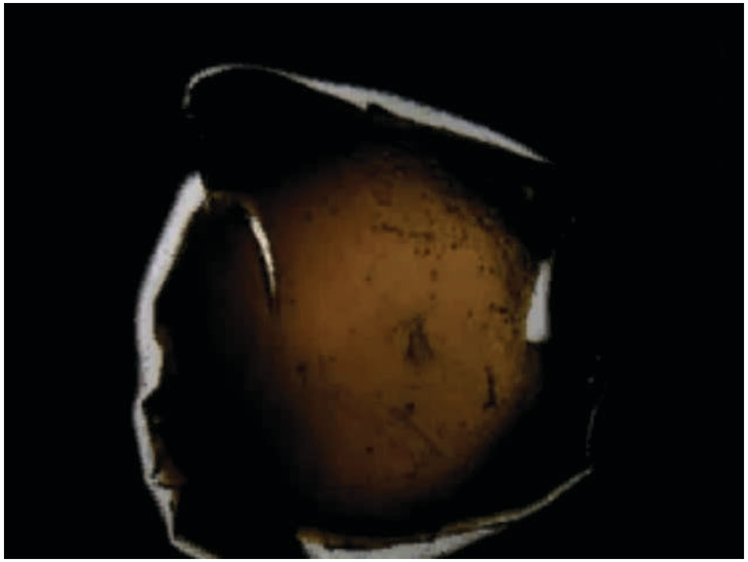
Figure 3. (a, b) Images of the pSPNIPAAm hydrogel layer just after the micropatterned light irradiation. Duration of irradiation was (●, red) 0, (◇) 1, and (■, green) 3 s. (c) Height change of the hydrogel layer in (●) non-irradiated and (○) irradiated region as a function of time after 3 s blue light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

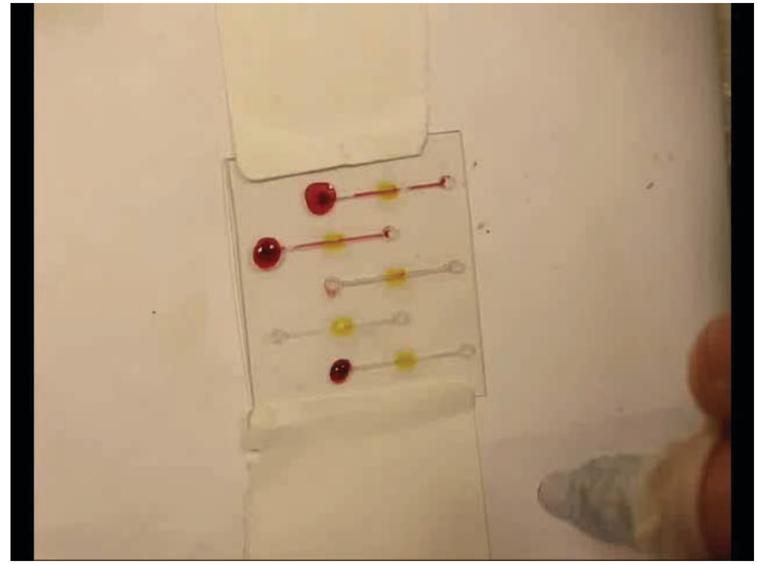


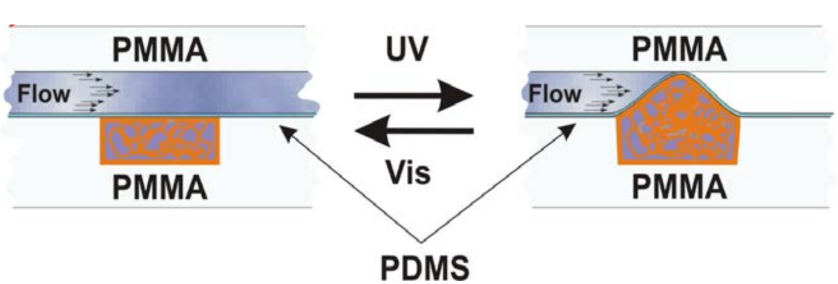
X:Y:Z = 1:99:5

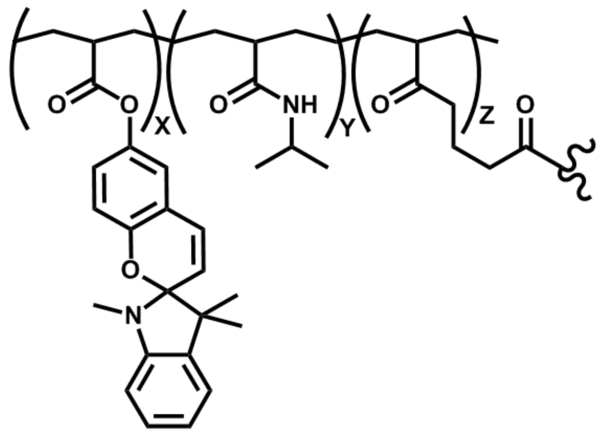
poly(N-isopropylacrylamide) (PNIPAAm)
Formulation as by Sumaru et al[1]
***1) Chem. Mater.,* 19 (11), 2730 -2732, 2007.**

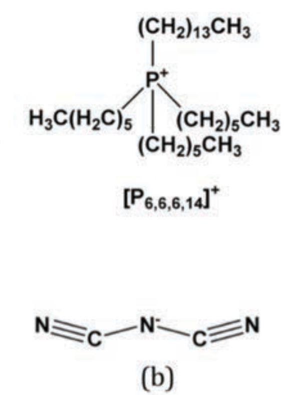
Photo-actuator polymers as microvalves in microfluidic systems







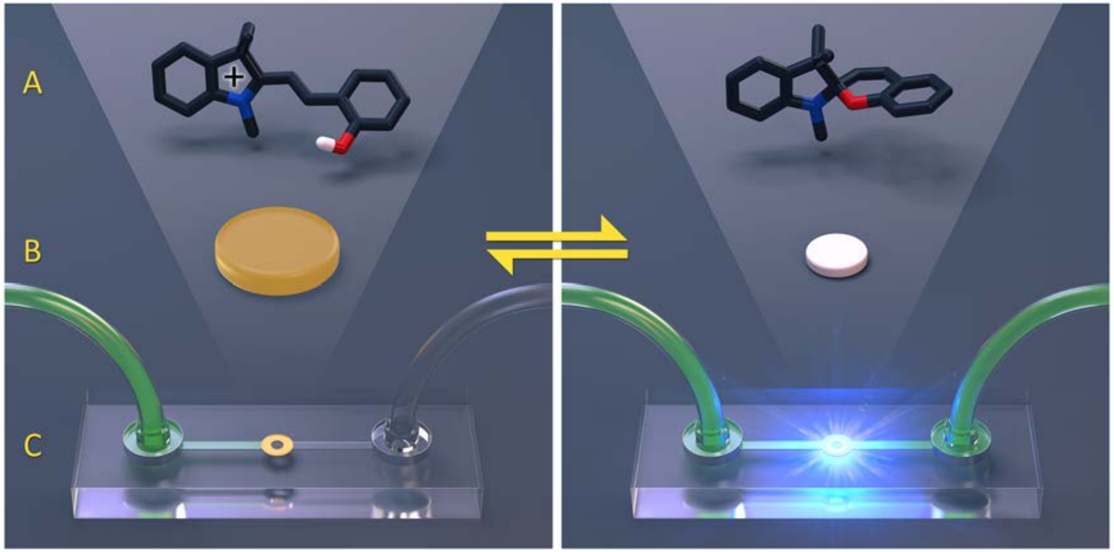




trihexyltetradecylphosphonium dicyanoamide $[P_{6,6,6,14}]^{+}[dca]^{-}$

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.

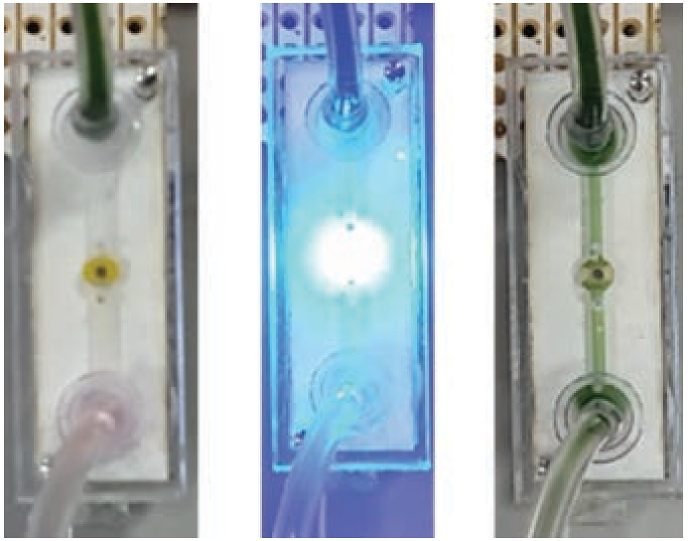
Reversible Photo-Switching of Flow

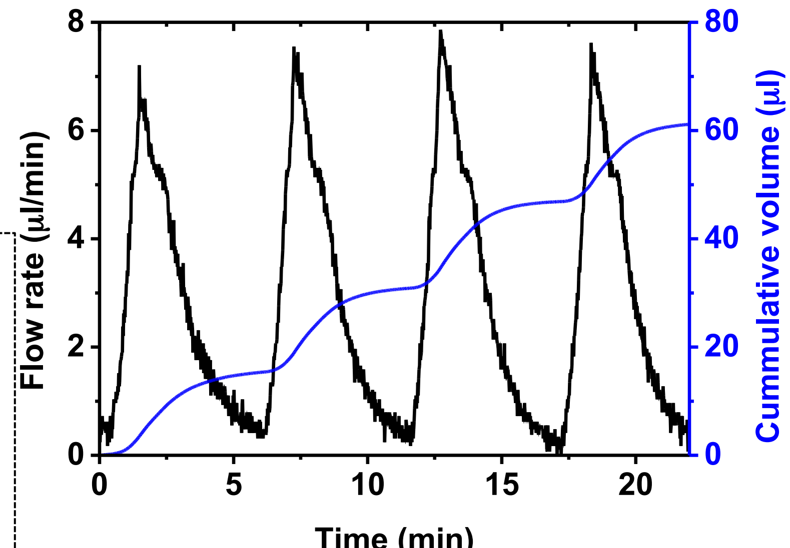


Above: scheme showing switching process protonated MC-H$^+$ photoswitched to SP triggering p(NIPAAM-*co*-AA-*co*-SP) gel contraction and opening of the channel.

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 ' (submitted for publication)

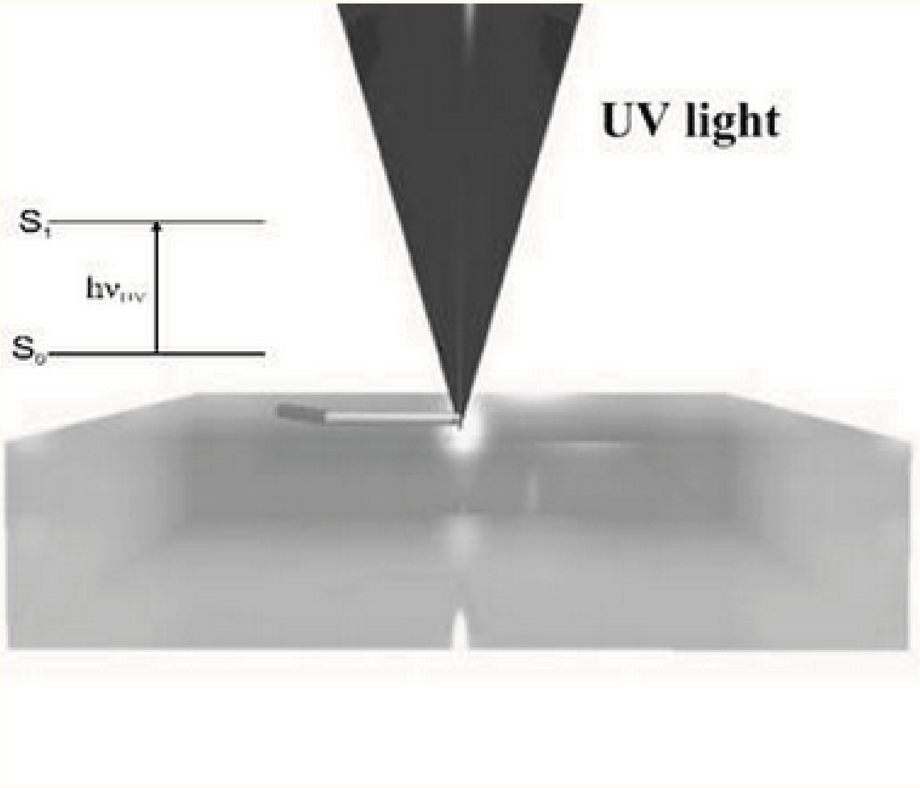
Jeroen ter Schiphorst,[†,#] Simon Coleman,[‡,#] Jelle E. Stumpel,[†] Aymen Ben Azouz,[‡] Dermot Diamond[*,‡] and Albertus P.H.J. Schenning[*,†,§]

†Functional Organic Materials and Devices, Department of Chemical Engineering and Chemistry, and §Institute for Complex Molecular Systems, Eindhoven University of Technology, P.O. Box 513, 5600 MB, Eindhoven, The Netherlands

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

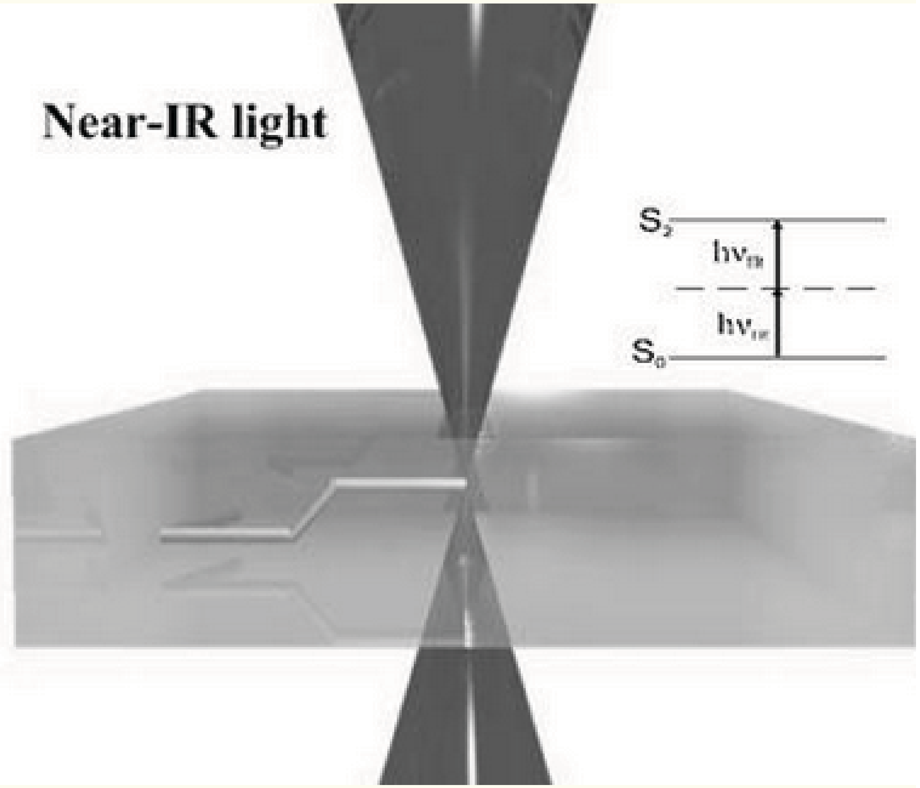
Background

Stereolithography



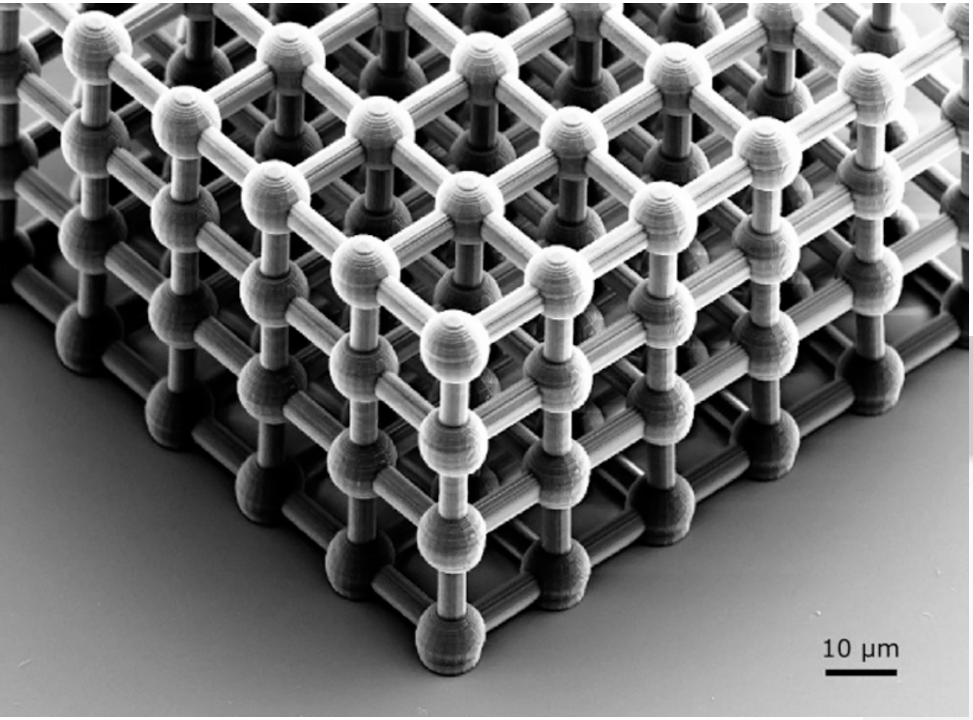
- Single photon absorption
- 2D patterns

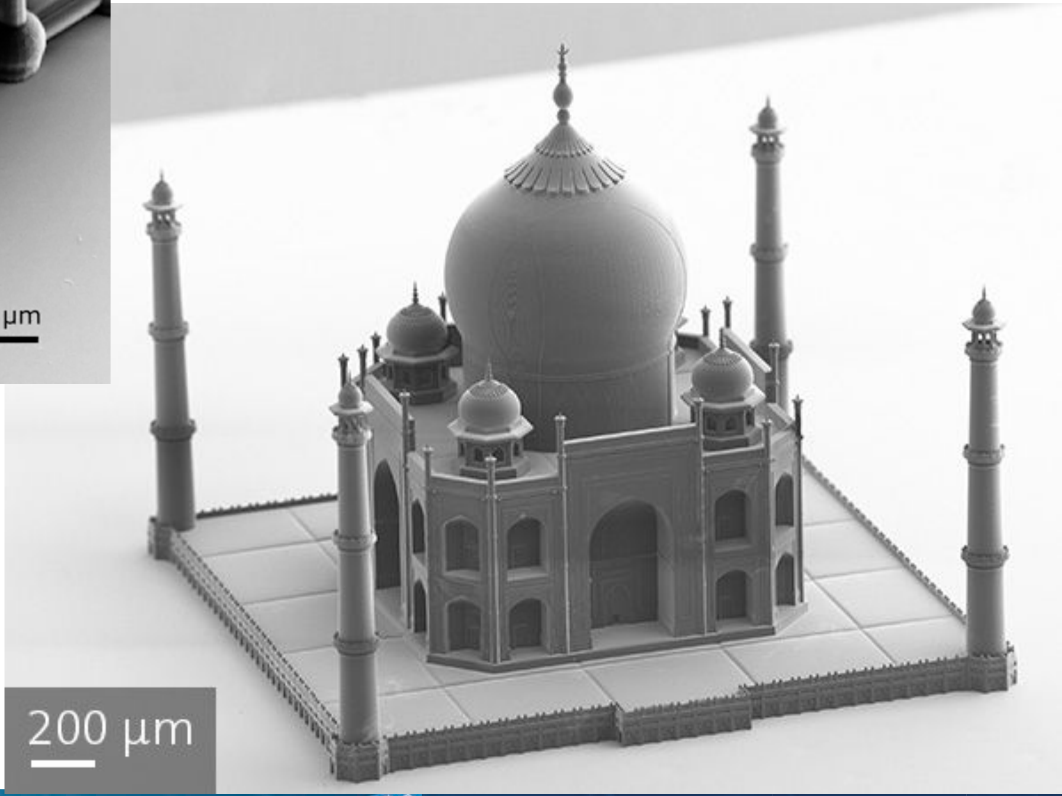
Two-photon polymerisation



- 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
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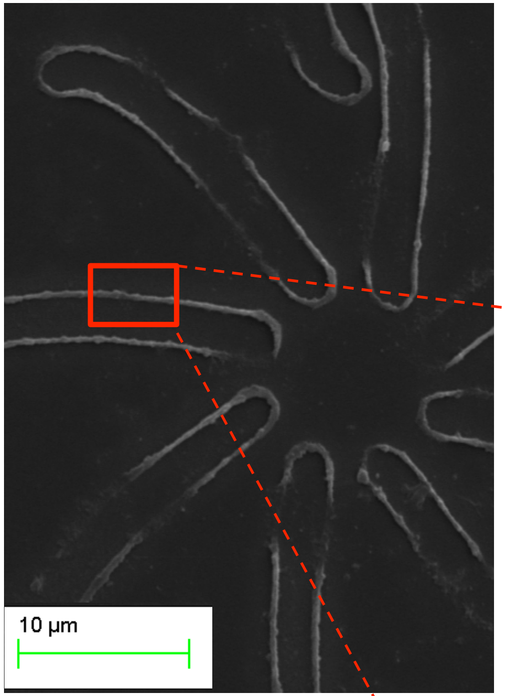
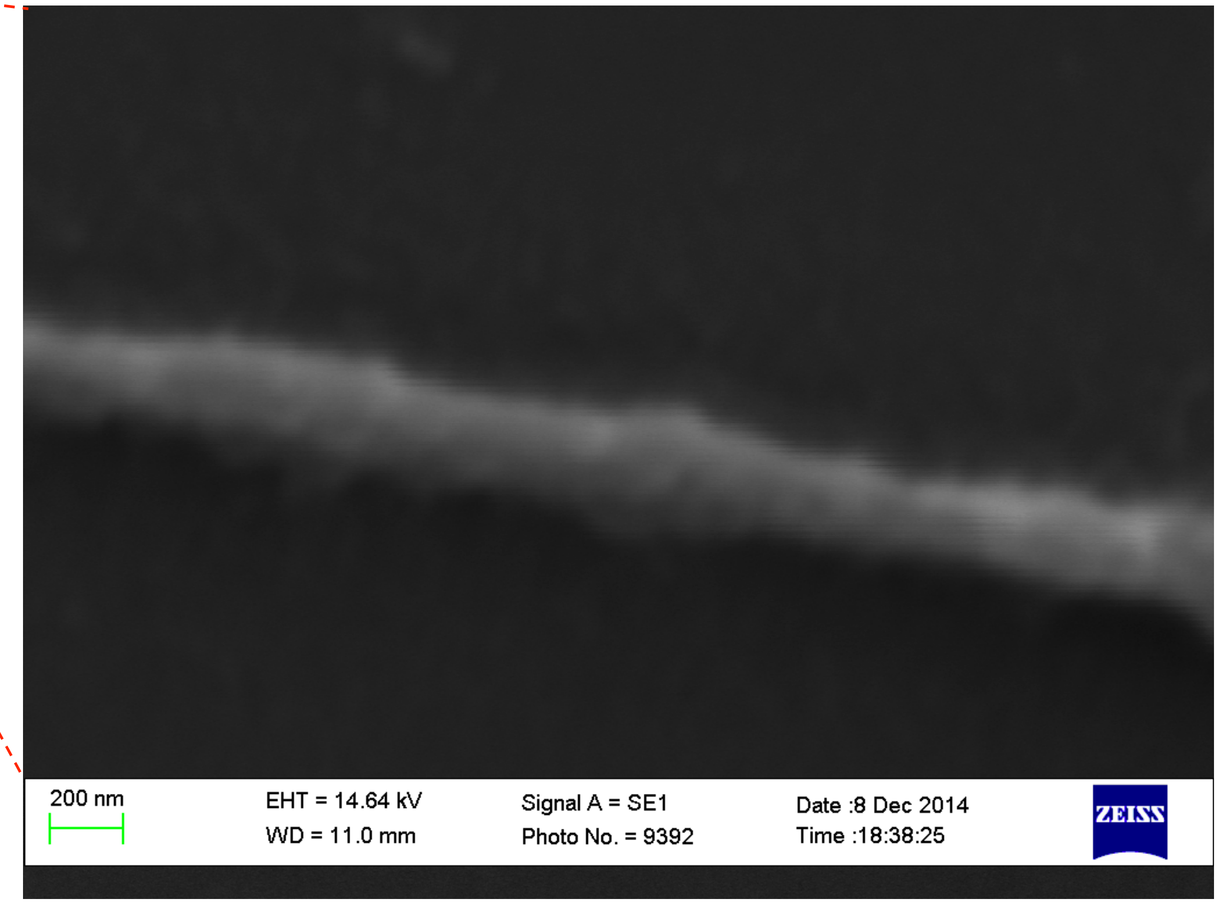
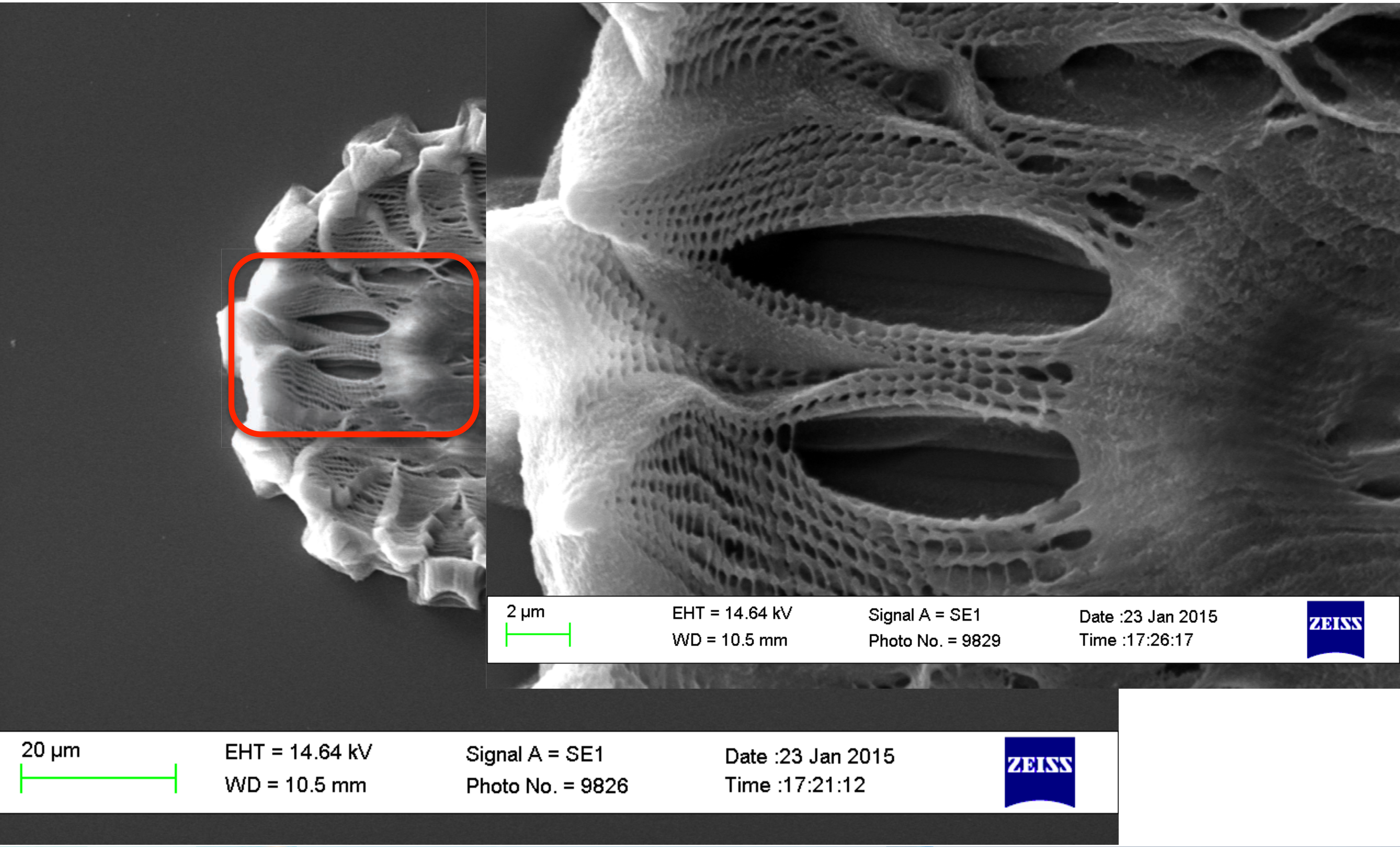
Submitted to Euronanoforum, Riga, Latvia, June 2015





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

‘Daisy’ – Micro/Nano Scaled Porous Structure

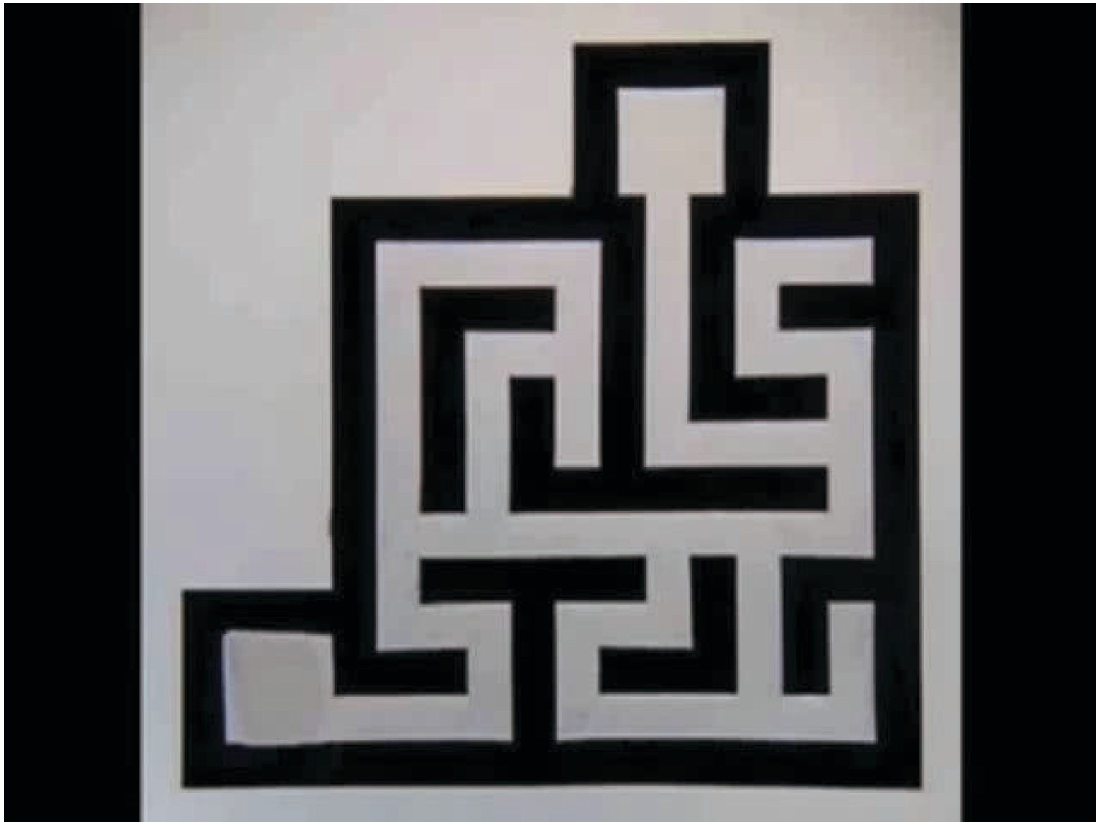


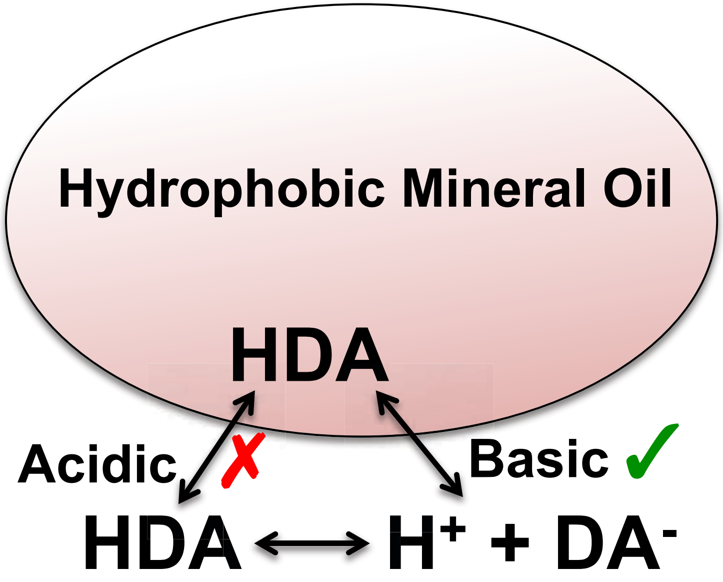

‘Micro-Rose’
2 µm
EHT = 14.64 kV
WD = 10.5 mm
Signal A = SE1
Photo No. = 9753
Date :23 Jan 2015
Time :12:31:01
ZEISS
2 µm
EHT = 14.64 kV
WD = 10.5 mm
Signal A = SE1
Photo No. = 9755
Date :23 Jan 2015
Time :12:33:11
ZEISS
‘Micro-Stoma’
2 µm
EHT = 14.64 kV
WD = 11.0 mm
Signal A = SE1
Photo No. = 9763
Date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

Multi-Functional Fluidics

- **At present, the fluidic system's function is to;**
  - Transport reagents, samples, standards to the detector
  - Perform relatively simple (but important) tasks like cleaning, mixing
  - Switching between samples, standards, cleaning solutions
- **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

Chemotactic Systems





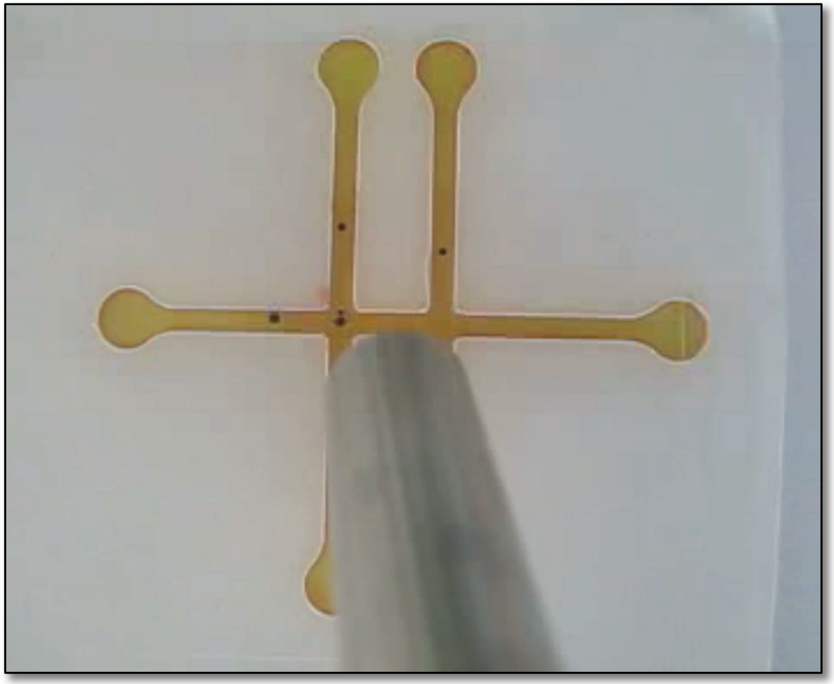
In a pH gradient, DA^- is preferentially transferred to the aqueous phase at the more basic side of the drop.

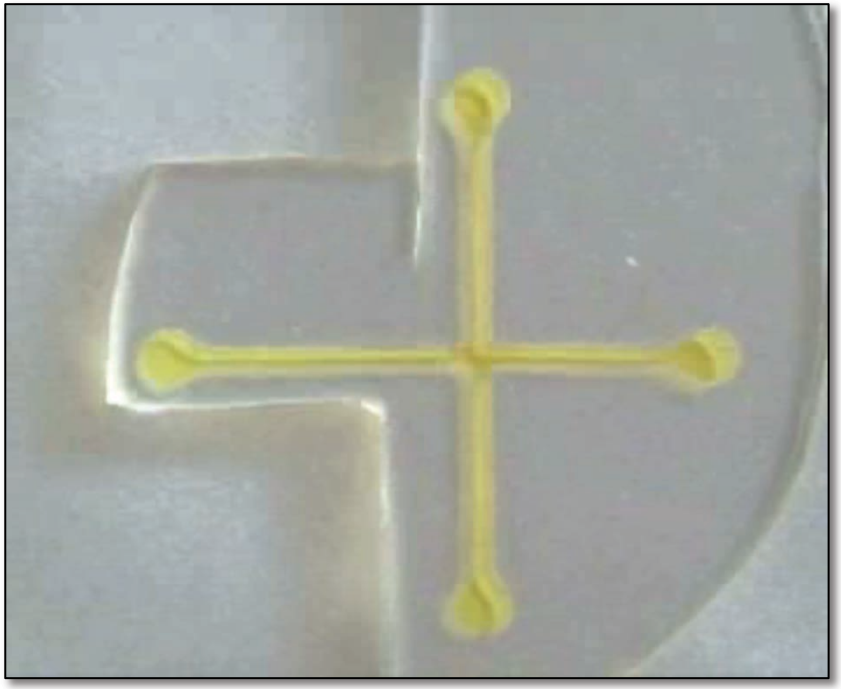
Published on Web 11/01/2010 (speed ~x4): channels filled with KOH (pH 12.0-12.3 + surfactant; agarose gel soaked in HCl (pH 1.2) sets up the pH gradient; droplets of mineral oil or DCM containing 20-60% 2-hexyldecanoic acid + dye. Droplet speed ca. 1-10 mm/s; movement caused by convective flows arising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

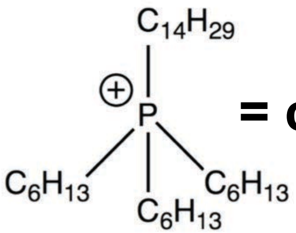
Movement of Droplets in Channels using Light



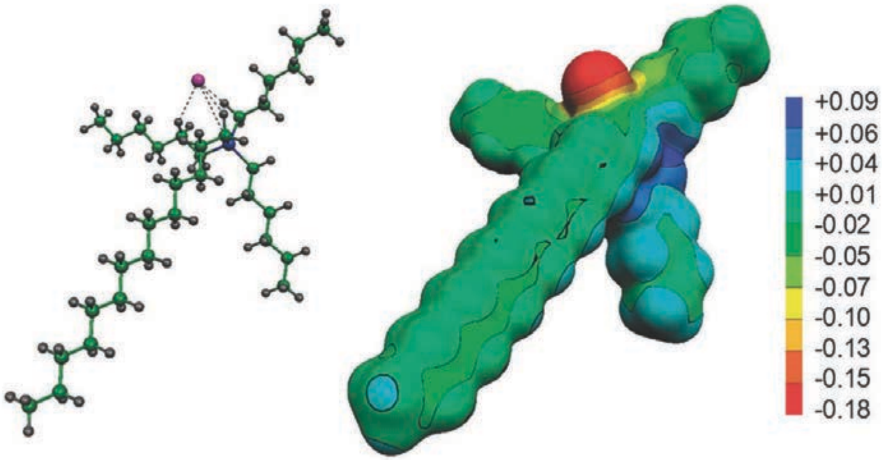


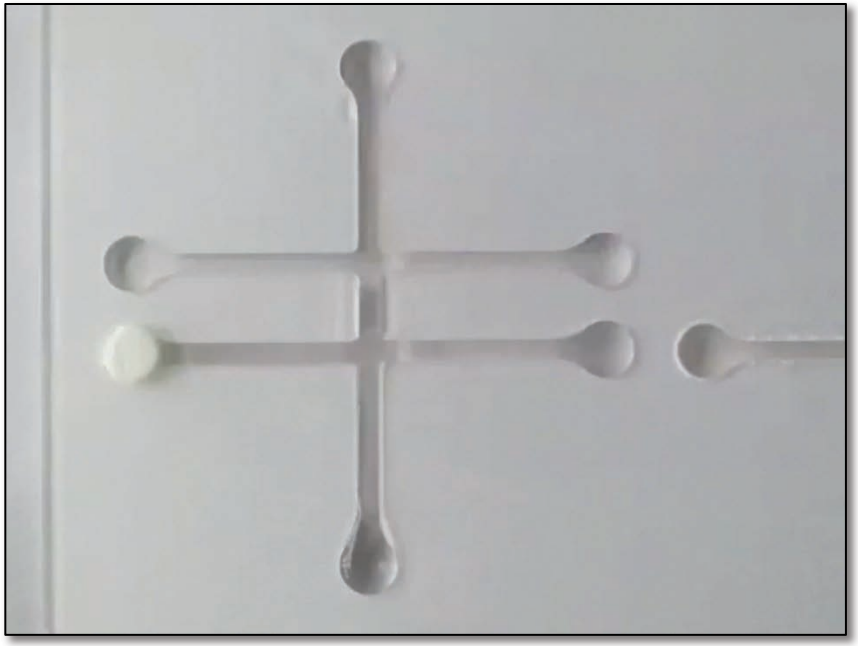
- We use light to create a localised pH gradient
- This disrupts an ion pair at the droplet interface
- Surfactant is expelled and movement of the droplet occurs
- Interested in exploring how to use droplets for sensing and for transport & release of active components

We can do the same with IL Droplets



= cationic surfactant

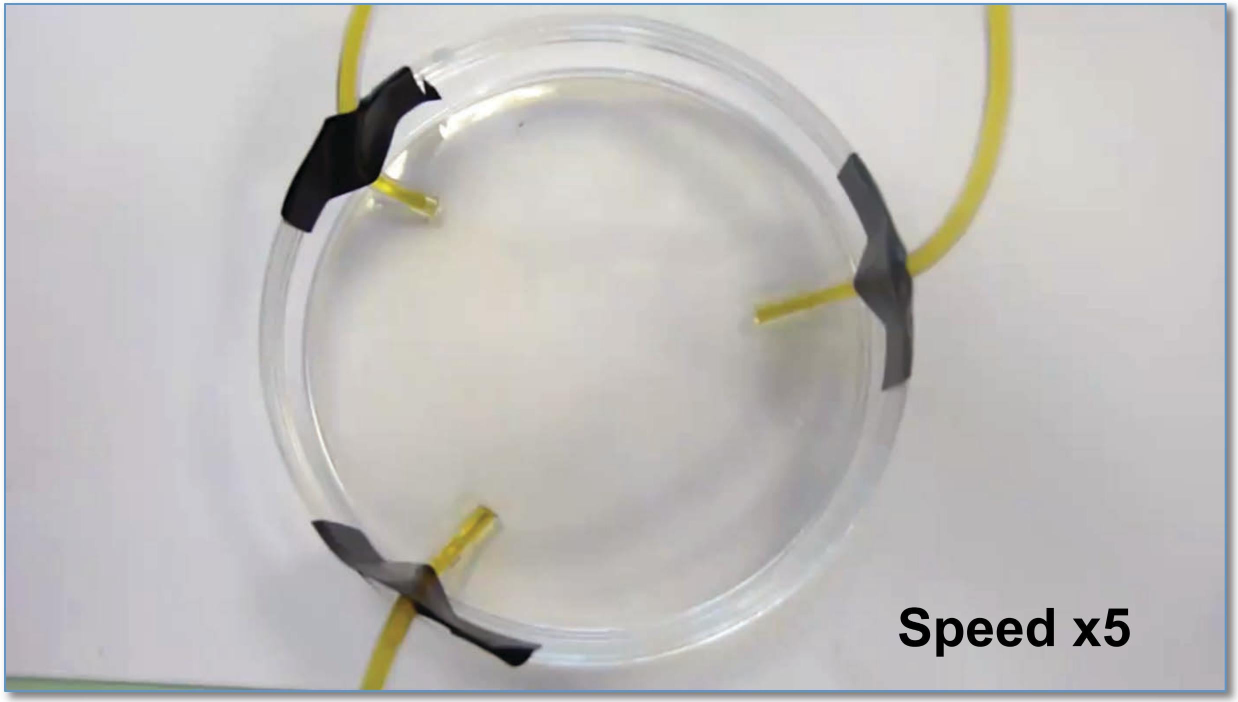




Trihexyl(tetradecyl)phosphonium chloride ($[P_{6,6,6,14}][Cl]$) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the Cl^- ion which is created using a polyacrylamide gel pad soaked in 10^{-2} M HCl; A small amount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

2D chemotactic droplet movement

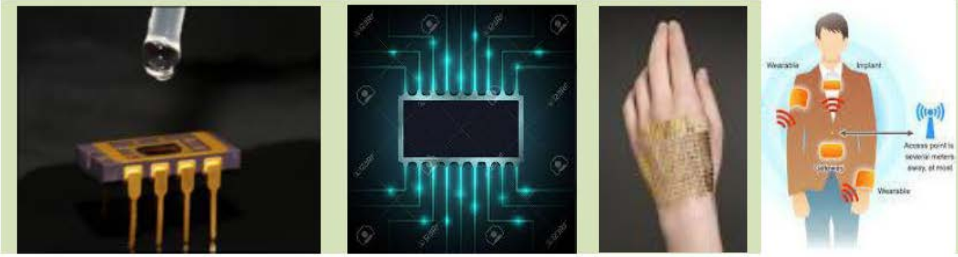


- NaOH in petri dish; HCl with indicator dye added from tubes in sequence
- Droplet moves spontaneously towards acidic locations
- In 2/3 cases, the droplet enters the source tube
- Droplets can be loaded with monomeric units that polymerise inside the tubing sealing off the source of the 'leak'

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!



The European Sensor Systems Cluster (ESSC)

European Sensor Systems Cluster - *ESSC*

Vision, Objectives, Strategies, Priorities and Challenges of EU Cluster

Cluster launched at Preparatory Workshop on 27 November 2014 in Brussels sponsored and observed by EC DG Research and Innovation

AMA Conference 2015 - SENSOR+TEST Trade Fair

Room Tunis, Session Time: 12:00 - 13:30

Nuremberg/Germany, 19 May 2015

Vision, Objectives and Position Paper

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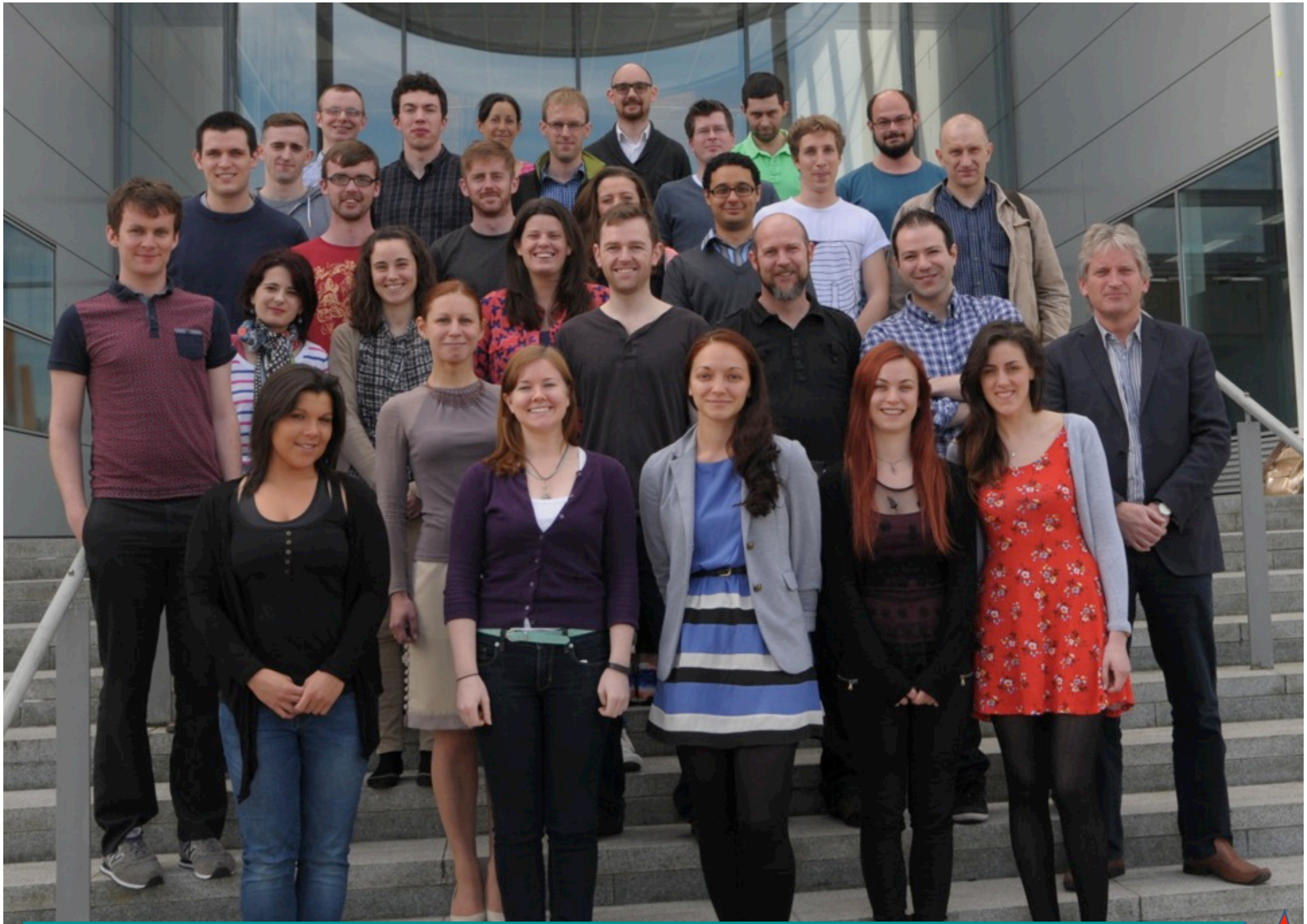
www.cluster-essc.eu



Thanks for listening