Stimuli-responsive Polymers: The Key to realising low-cost autonomous chemical sensing platforms with revolutionary capabilities

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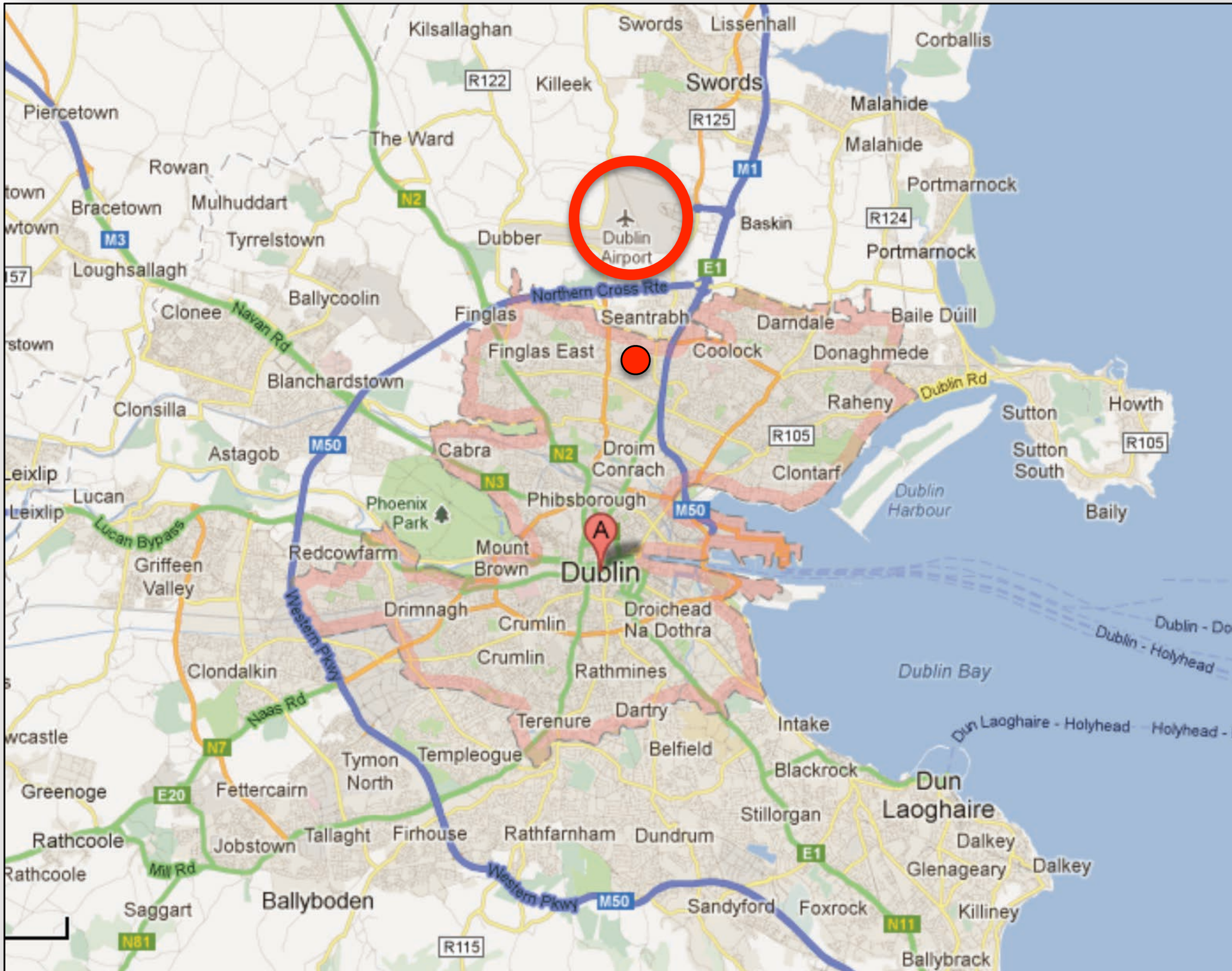
Dublin City University

Invited Keynote Lecture presented at
AMPT2014 Dubai, UAE
17-20 November 2014

Dublin & DCU Location



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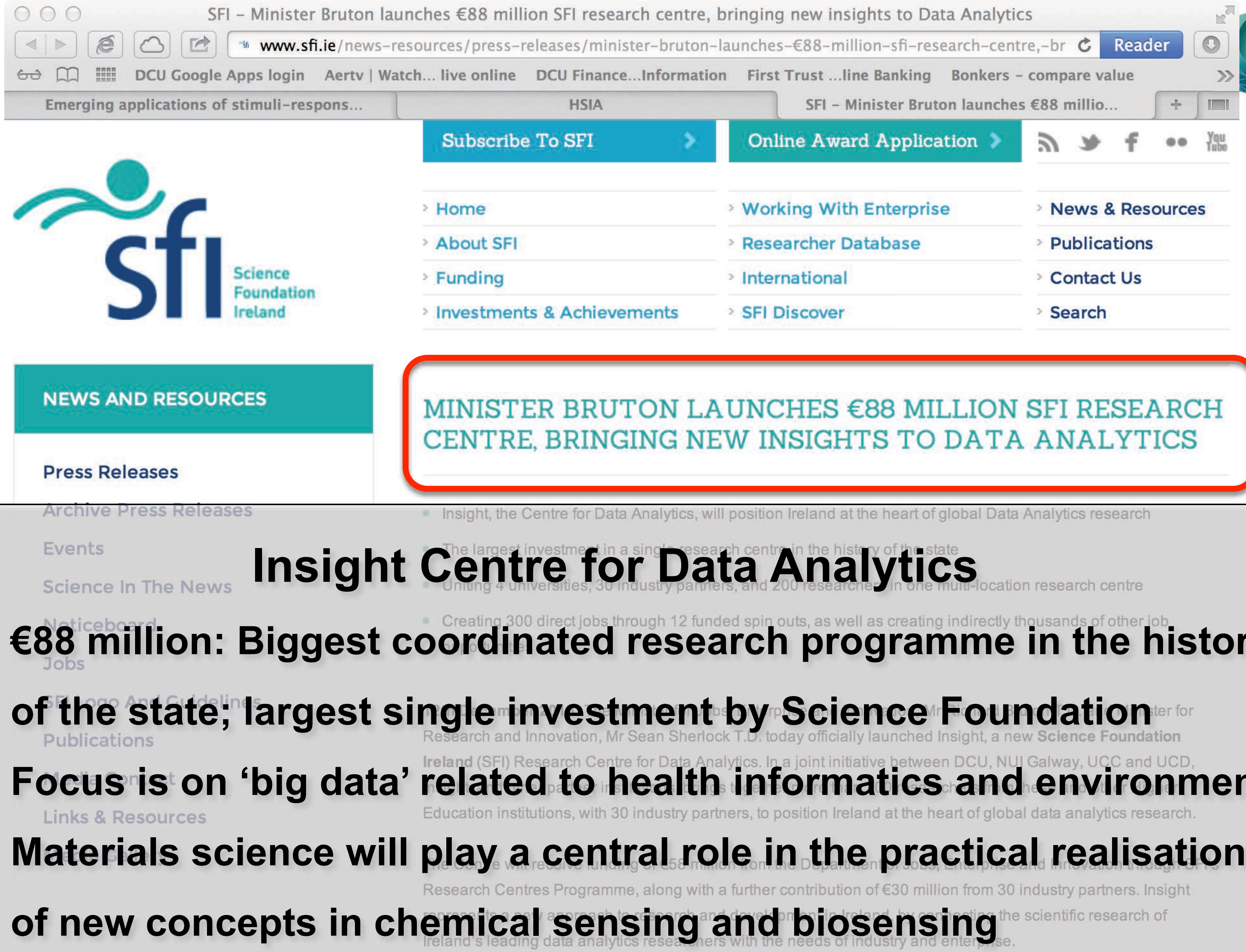
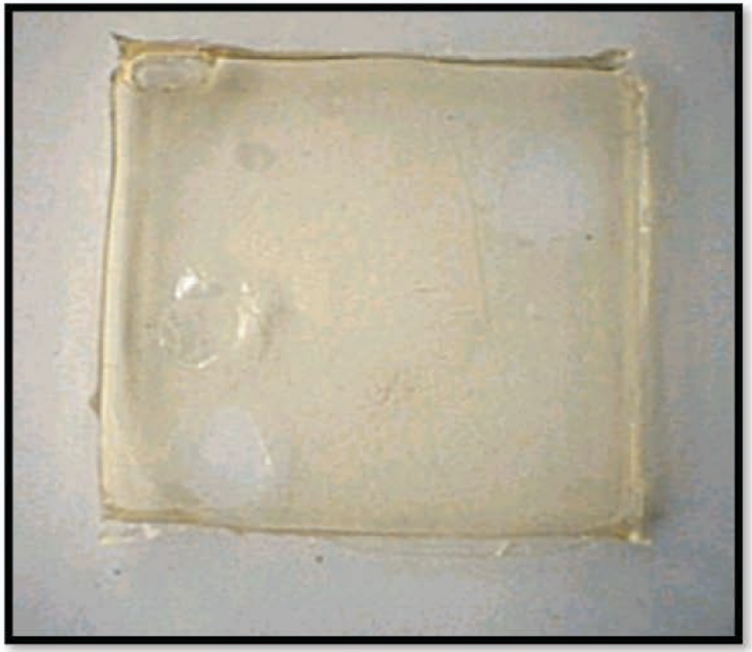
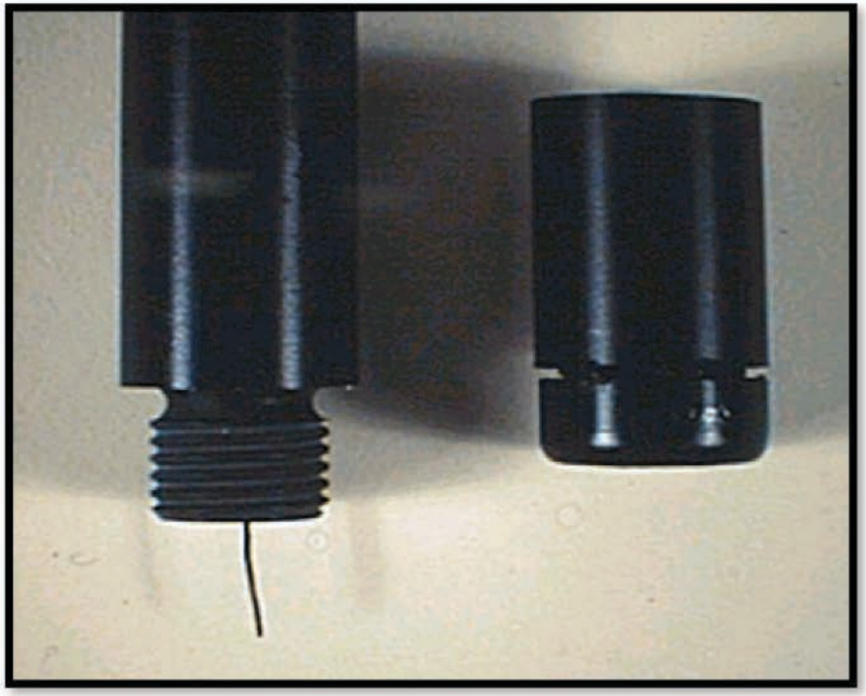


Insight Centre for Data Analytics

- €88 million: Biggest coordinated research programme in the history of the state; largest single investment by Science Foundation
- Focus is on 'big data' related to health informatics and environment
- Materials science will play a central role in the practical realisation of new concepts in chemical sensing and biosensing

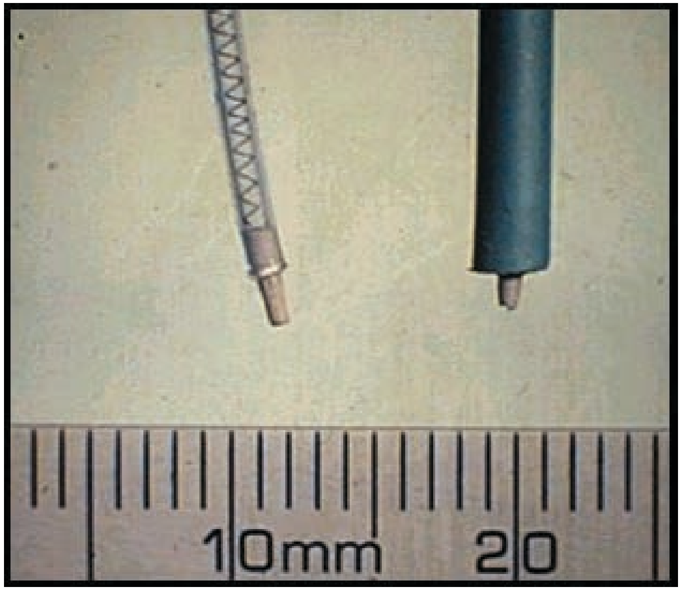
PVC - Membrane ISEs





Typical membrane cocktail (%w/w); PVC:33%, NPOE (plasticiser):66%; ionophore/exchanger: 1% (ratio at least 2:1 by mole); dissolve in a volatile solvent e.g. THF and cast membrane from this solution

Blood Analysis; Implantible Sensors



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

Dr. David Band, St Thomas's Hospital London

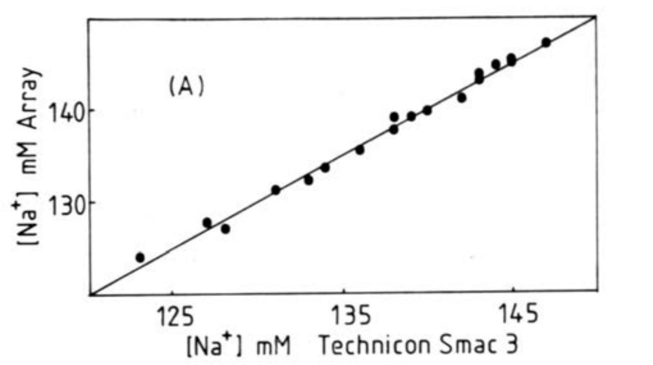
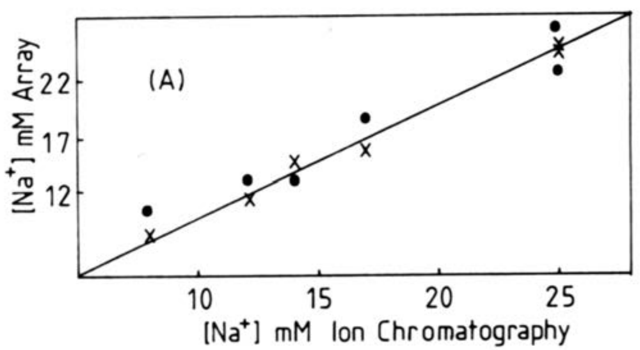


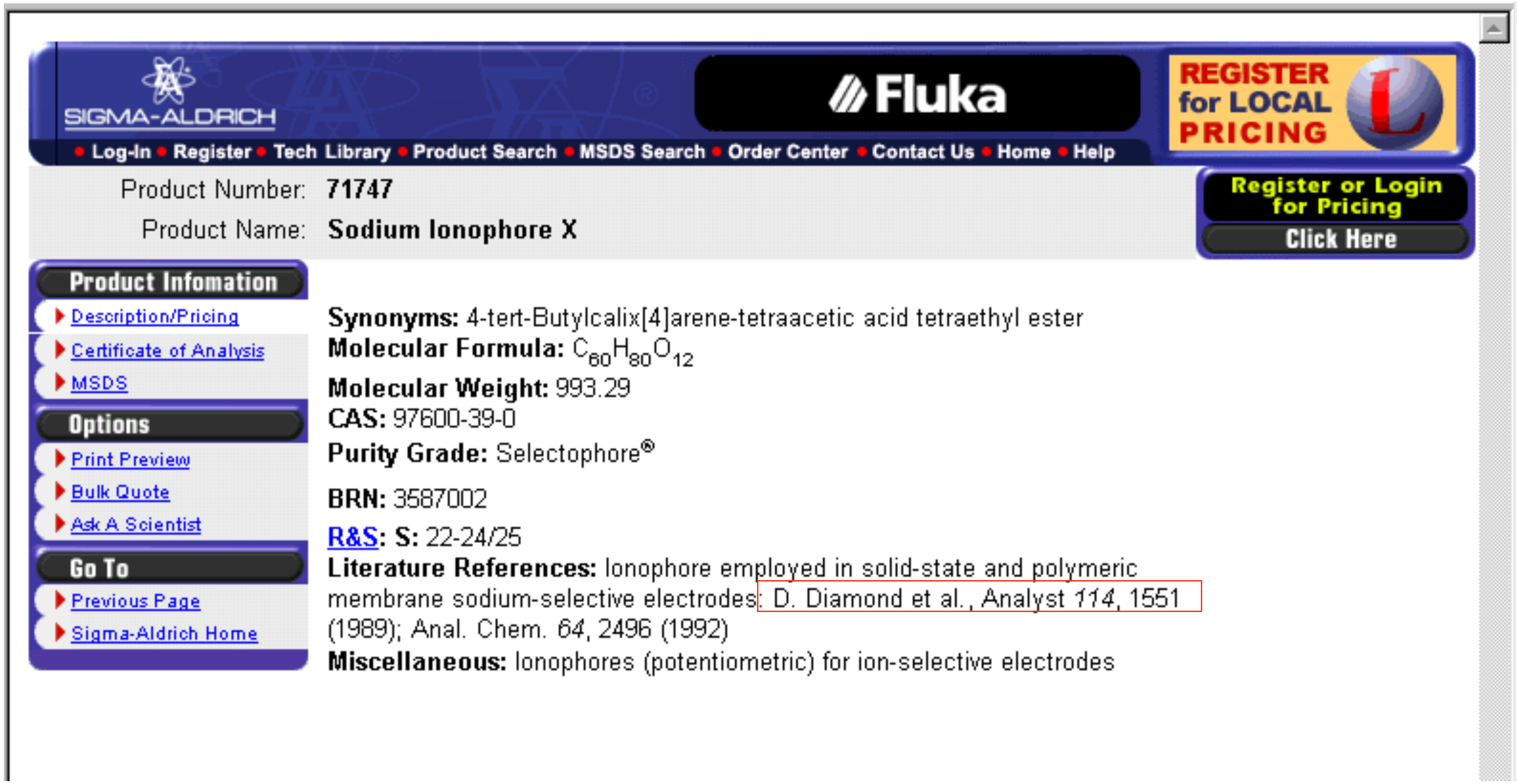
Fig. 3. Comparison of plasma sodium analysis using the array-FIA approach with a SMAC analyser. Good correlation without bias is obtained [5].



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

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

Fame at last!!



- **Best ionophore for sodium**

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.

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

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.

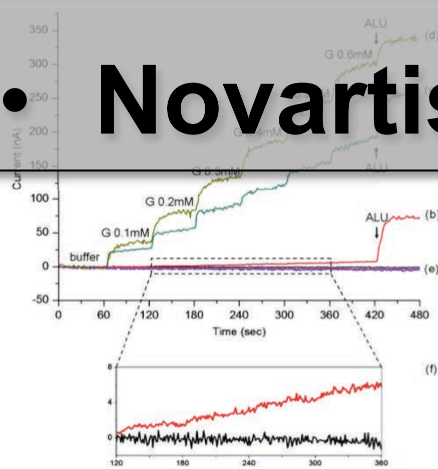
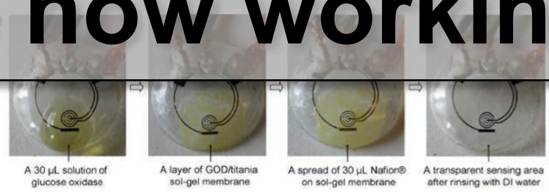


Fig. 2. Images of the sensor as it goes through surface functionalization and the related measured responses: (a) sequential images of sensor pre-treatment with GOD/titania/Nafion®; (b) measured amperometric response for the sensor just incubated with GOD; (c) measured amperometric response for the sensor 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, **H. F. Yao, A. J. Shum, M. Cowan, I. Lahdesmaki and B. A. Parviz, *Biosensors & Bioelectronics*, 2011, 26**, 3290-3296.

BY LANCE ULANOFF
1 DAY AGO

technology.

Known among scientists as "Ophthalmic Electrochemical Sensors," these contact lenses will feature flexible electronics that include sensors and an antenna. The sensors are designed to read chemicals in the tear fluid of the wearer's eye and alert her, possibly through a little embedded LED light, when her blood sugar falls to dangerous levels.

SEE ALSO: 7 Incognito Wearables You'd Never Guess Were Gadgets

According to the patent:

> "Human tear fluid contains a variety of inorganic electrolytes (e.g., Ca.sup.2+, Mg.sup.2+, Cl.sup.-), organic solutes (e.g., glucose, lactate, etc.), proteins, and lipids. A

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

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):

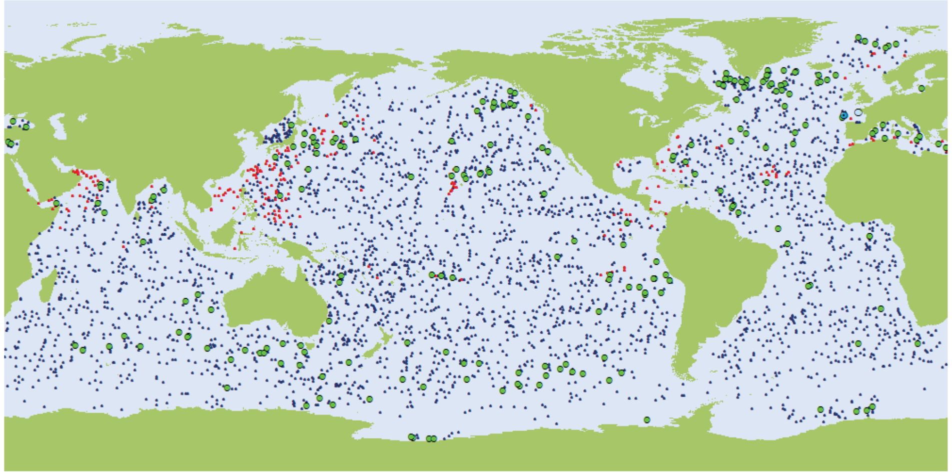
A. $1,000,000 Accuracy award – Performance focused ($750,000 First Place, $250,000 Second Place): To the teams that navigate the entire competition to produce the most accurate, stable and precise pH sensors under a variety of tests.

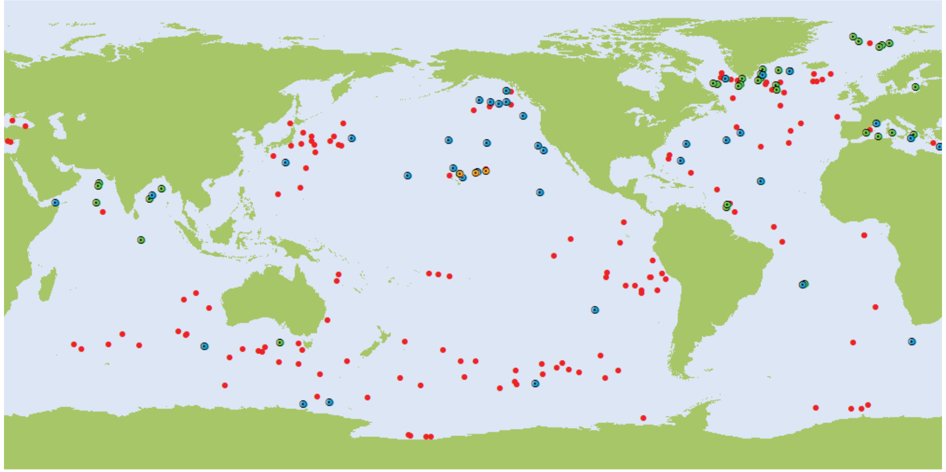
Wendy Schmidt Ocean Health XPRIZE

$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!

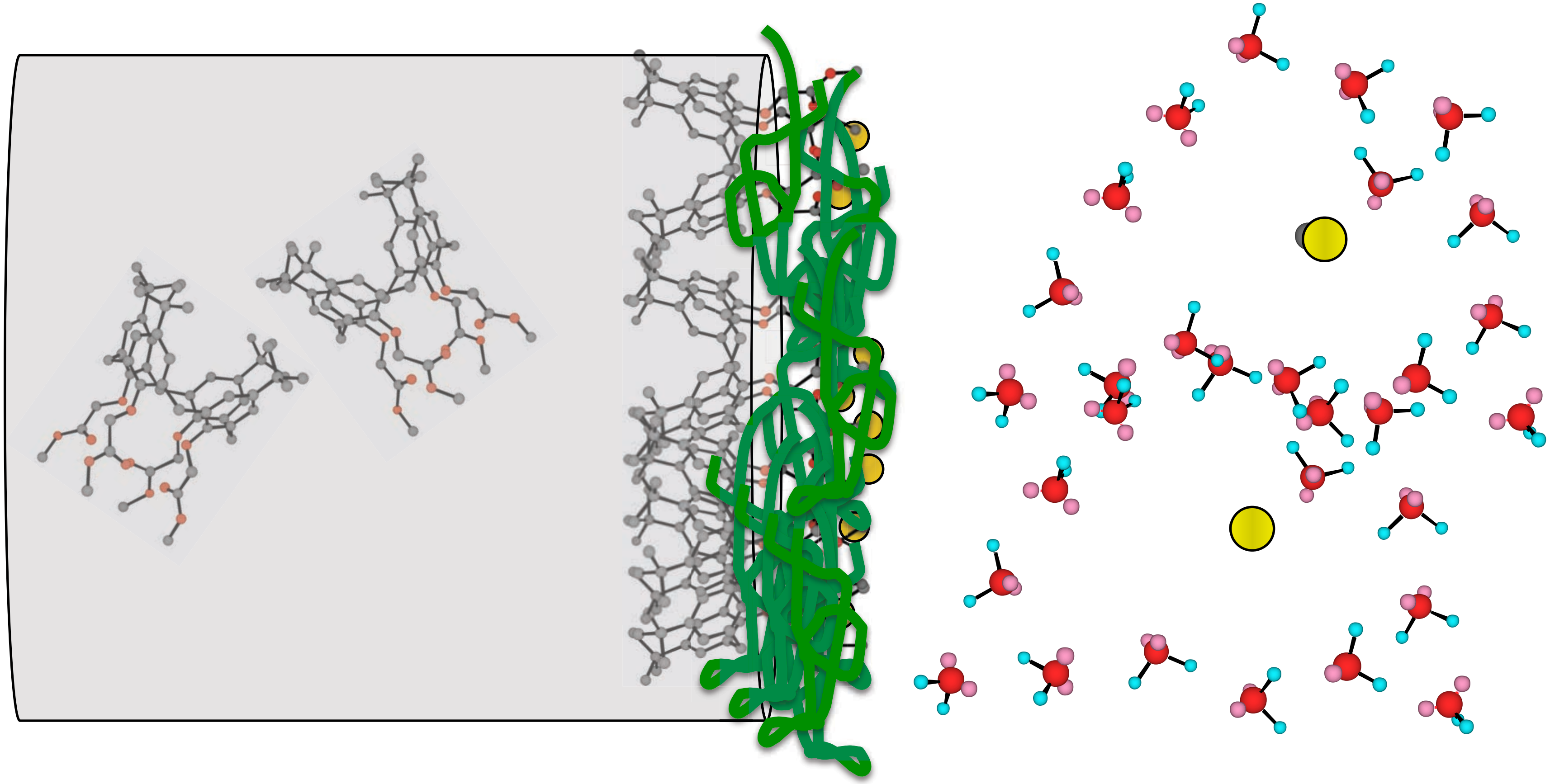
DO is by Clark Cell (Sea Bird Electronics) or Dynamic fluorescence quenching (Aanderaa)

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

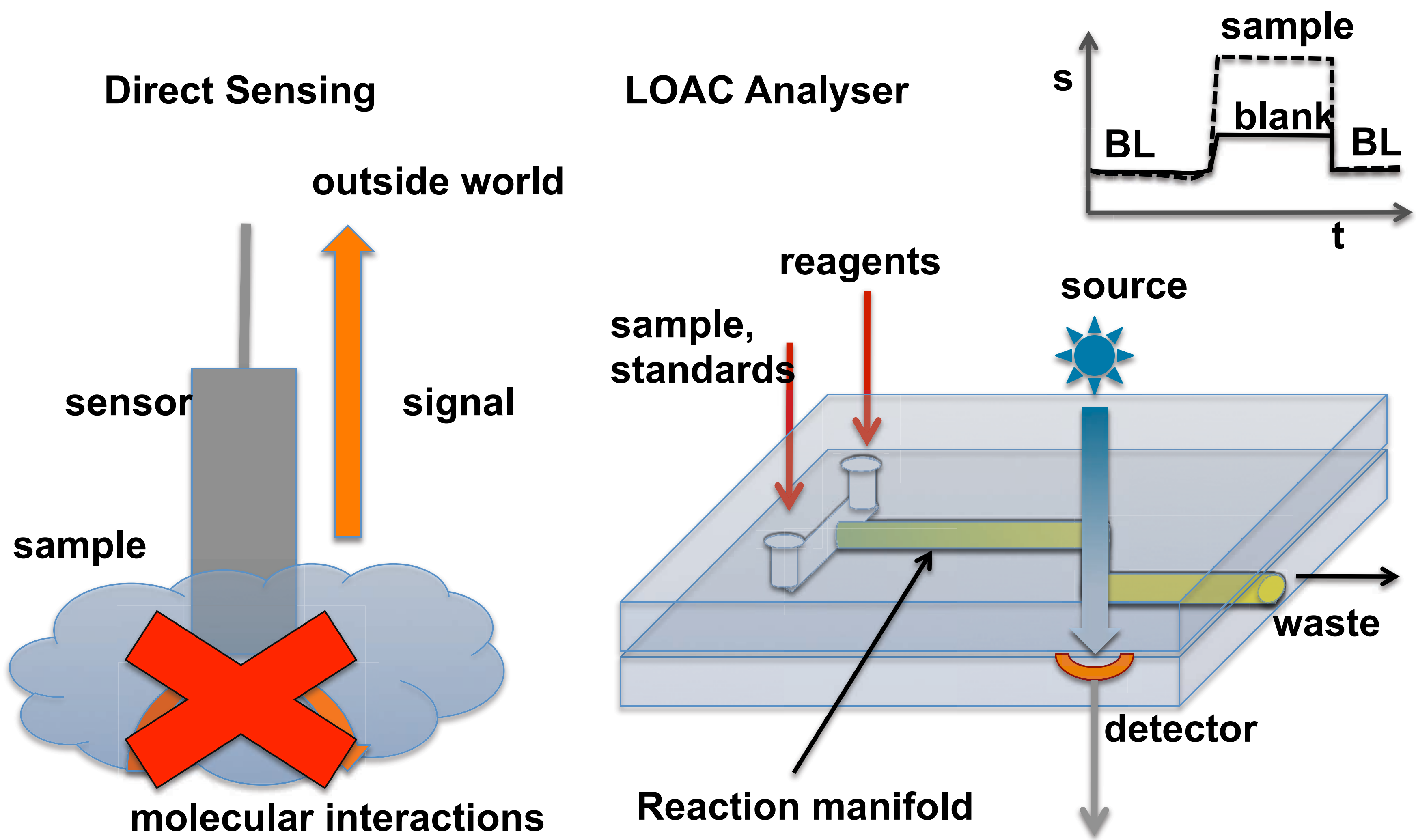
After decades of intensive research, our capacity to deliver successful long-term deployments of chemo/bio-sensors in remote locations is still very limited

Control of membrane interfacial exchange & binding processes

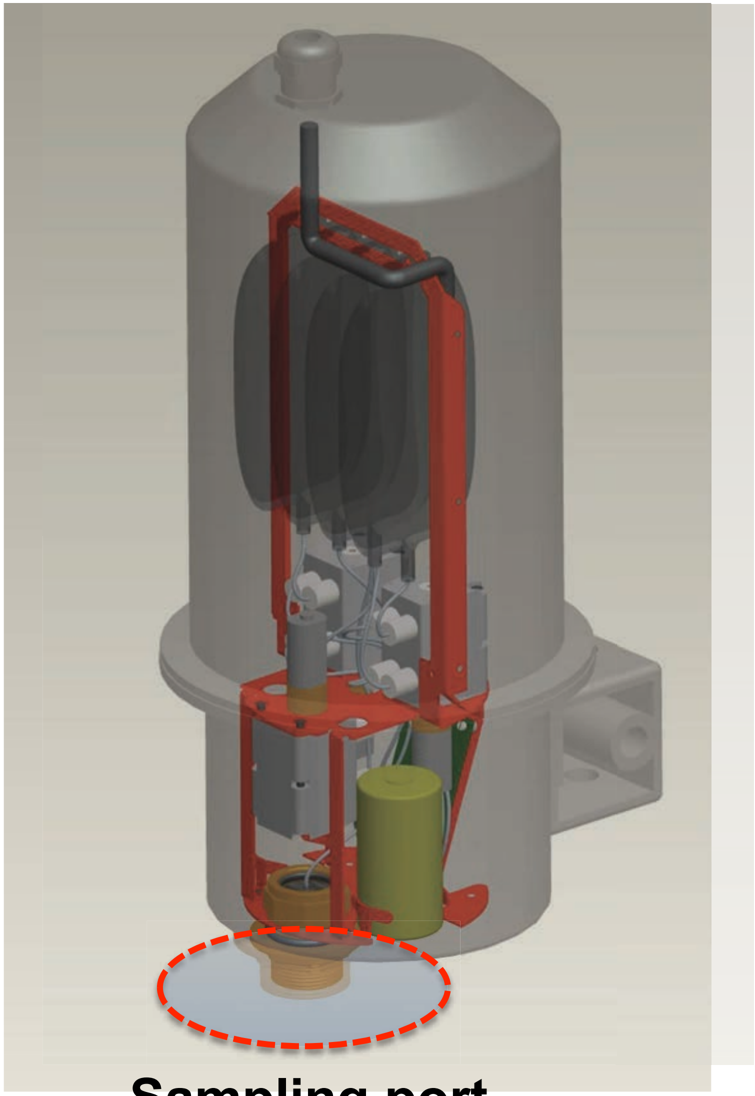


Remote, autonomous chemical sensing is a tricky business!

Direct Sensing vs. Reagent Based LOAC/ufluidics



Autonomous platform – water Analysis



Sampling port

Phosphate: The Yellow Method

Mixture (Reagent)

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

\+

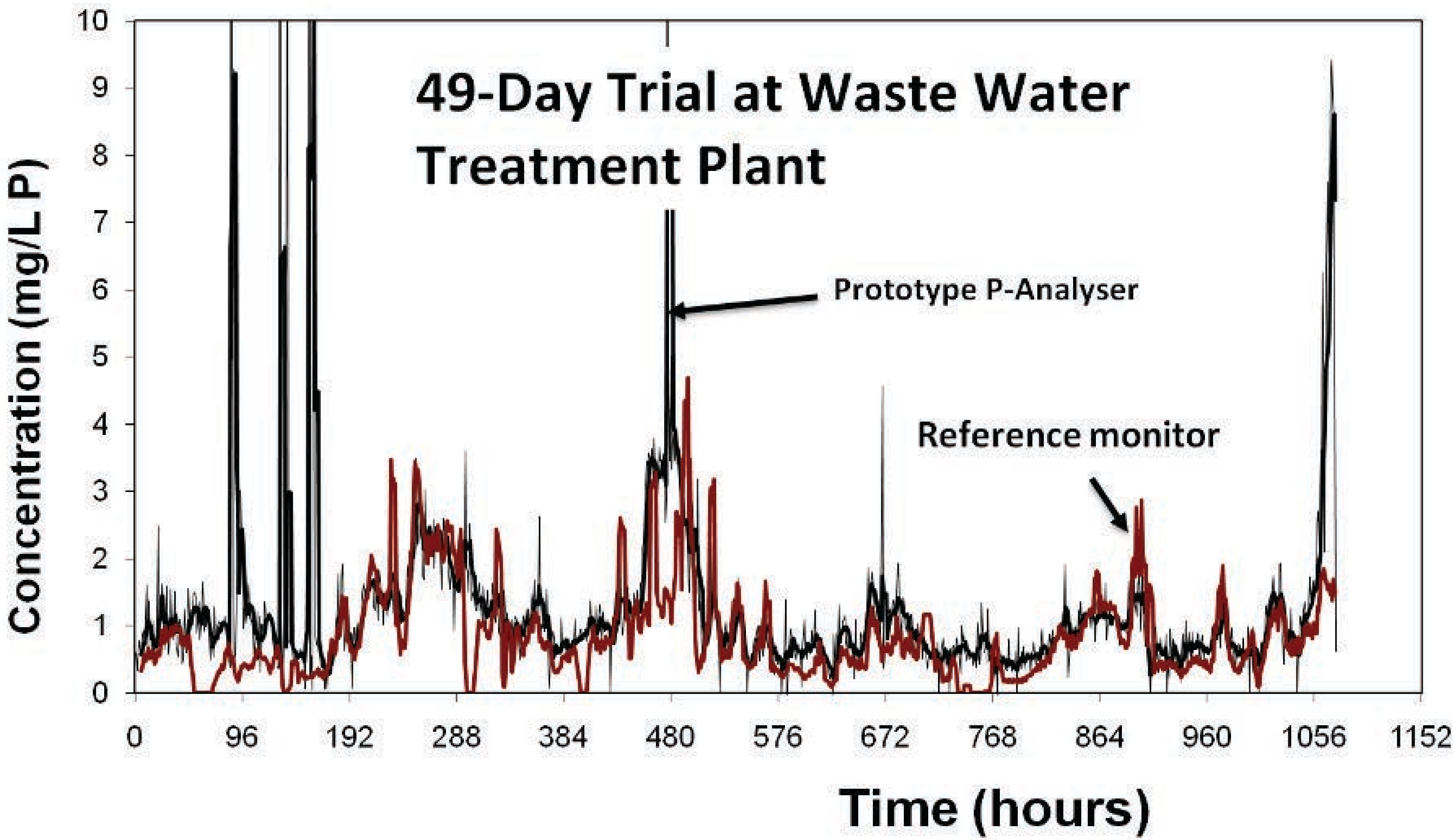
Sample

(KH_2PO_4)

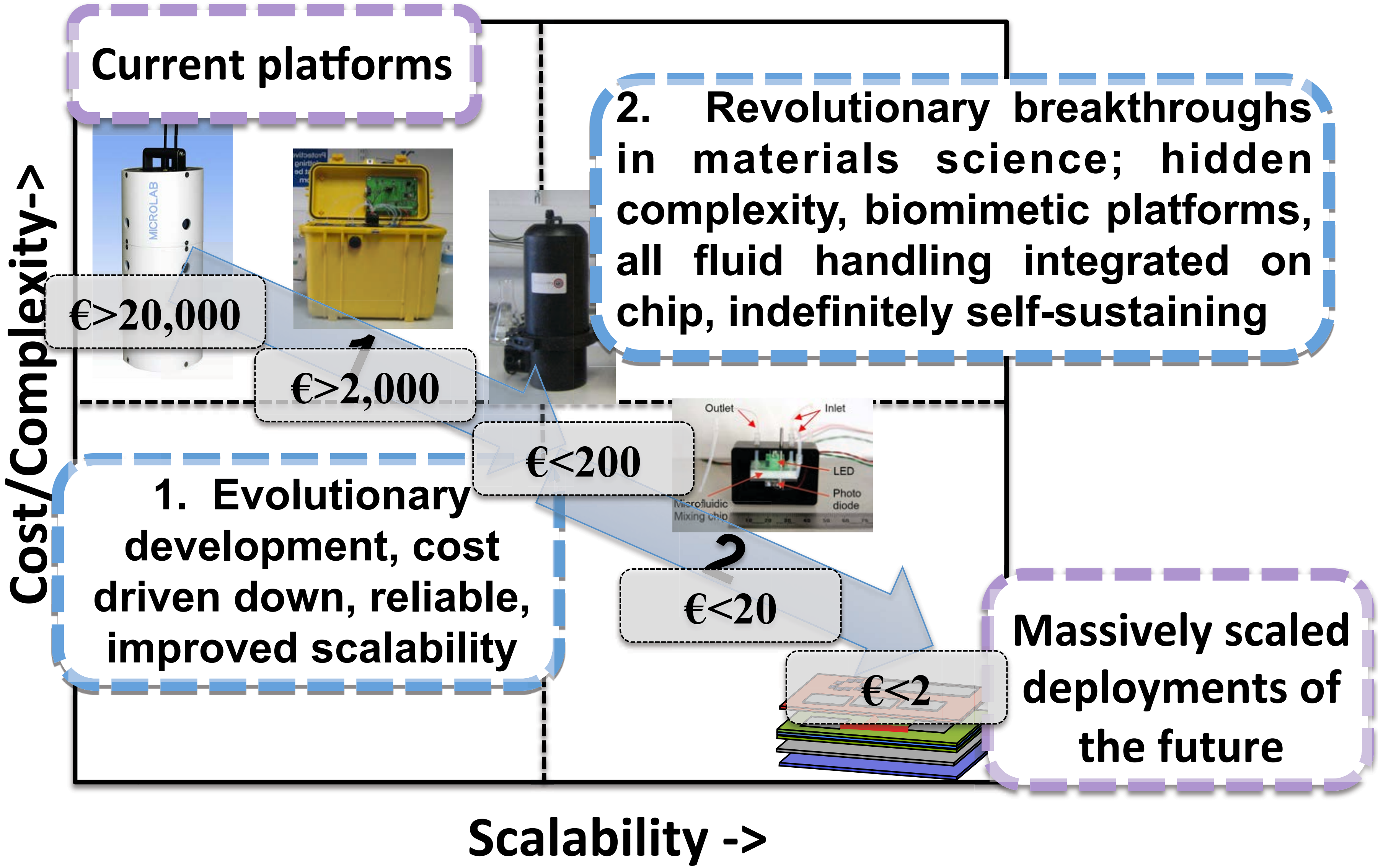
$(NH_4)_3PO_4.NH_4VO_3.16MoO_3$

- 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**)

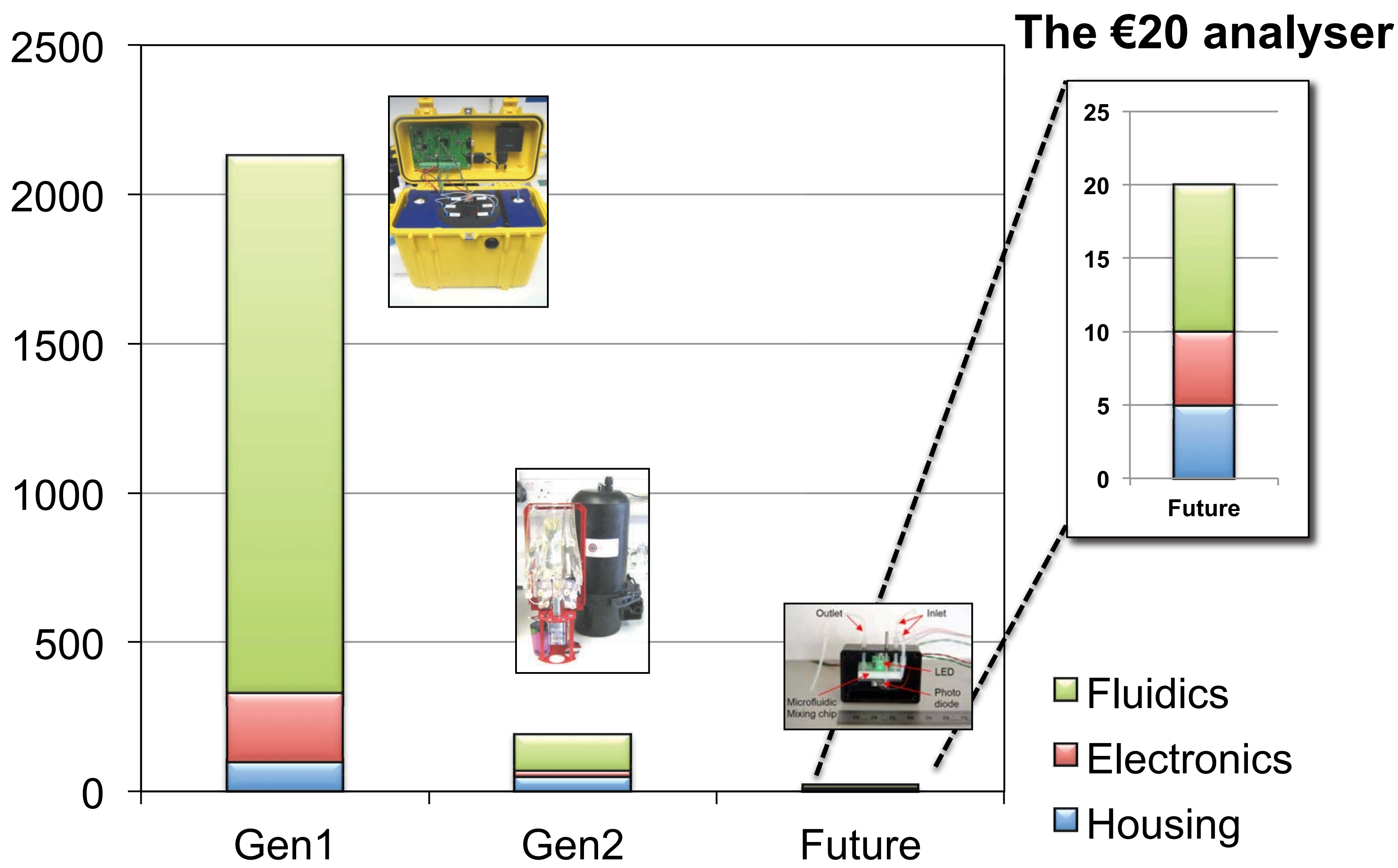
Autonomous Chemical Analyser



Achieving Scale-up

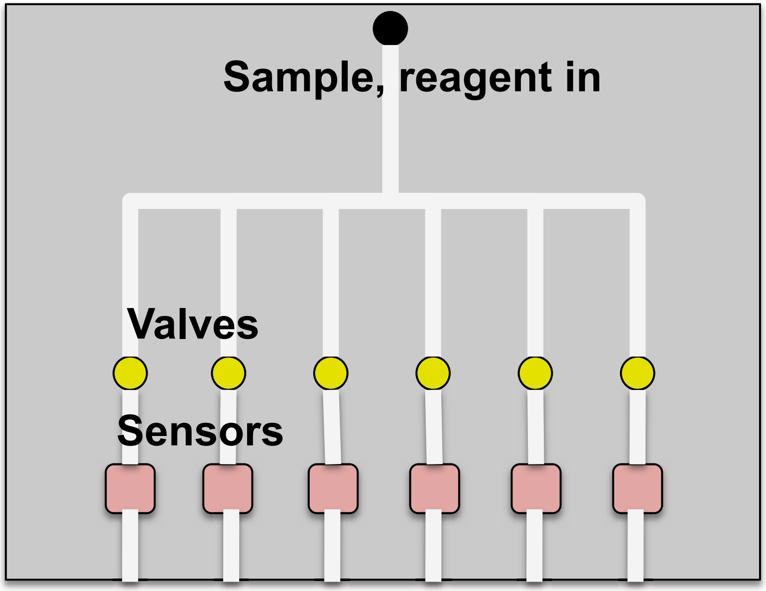


Cost Comparison Analyser (€)



Use Arrays of Sensors….?

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

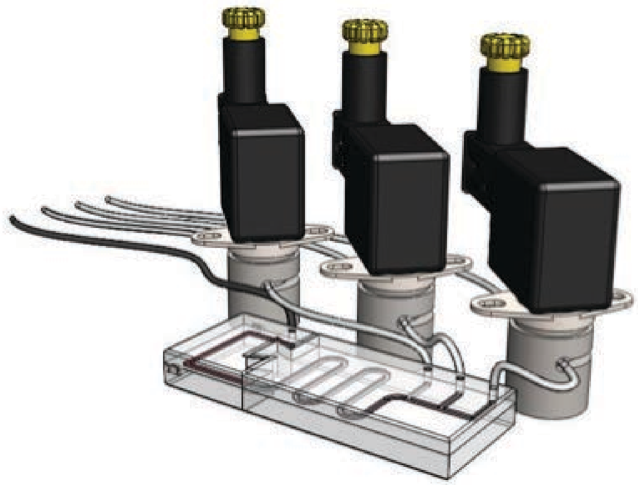


Then 50 sensors when used sequentially could provide an aggregated in-use lifetime of around 1 year

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

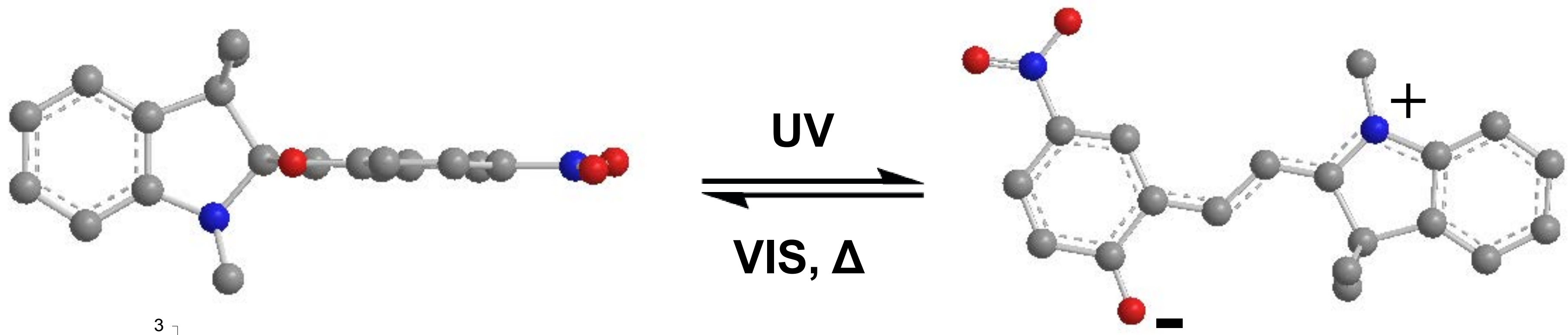
How to advance fluid handling in LOC platforms: re-invent valves (and pumps)!

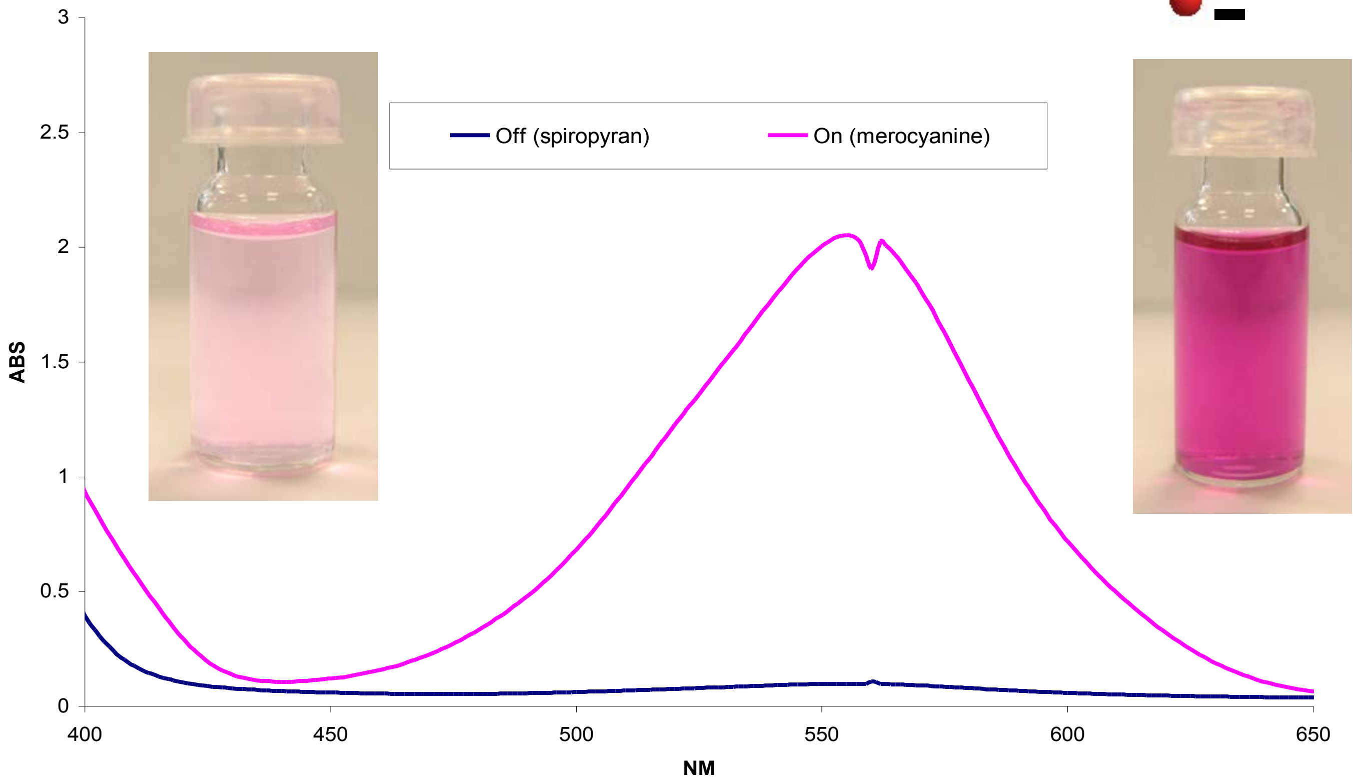
- **Conventional valves cannot be easily scaled down - Located off chip: fluidic interconnects required**
  - Complex fabrication
  - Increased dead volume
  - Mixing effects
- **Based on solenoid action**
  - Large power demand
  - Expensive



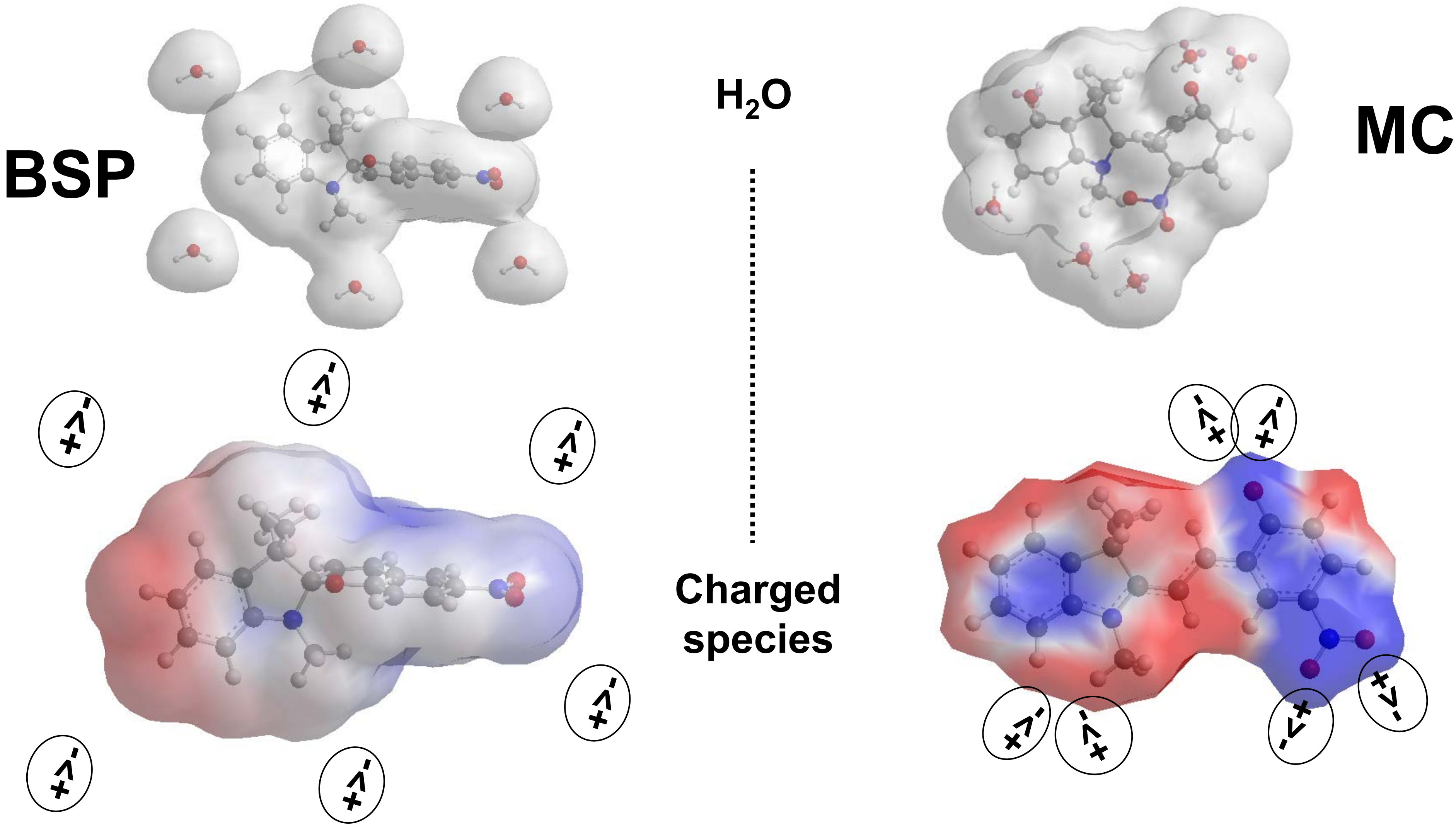
Solution: soft-polymer (biomimetic) valves fully integrated into the fluidic system

Photoswitchable Materials





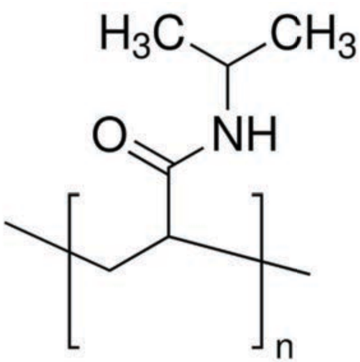
Non-specific (BSP) and specific (MC) Interactions

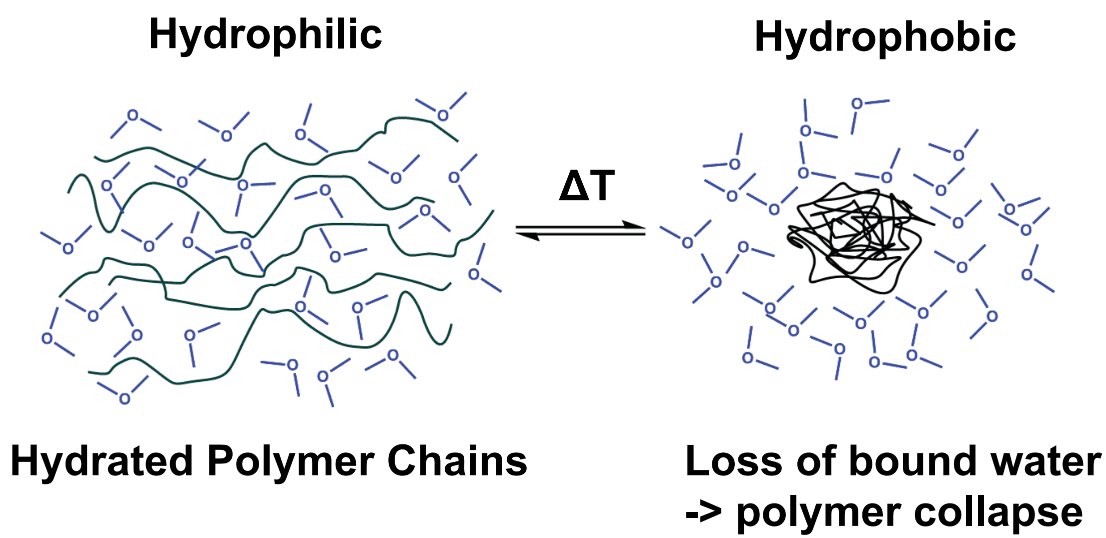


Poly(*N*-isopropylacrylamide)

- **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





Polymer based photoactuators based on pNIPAAm

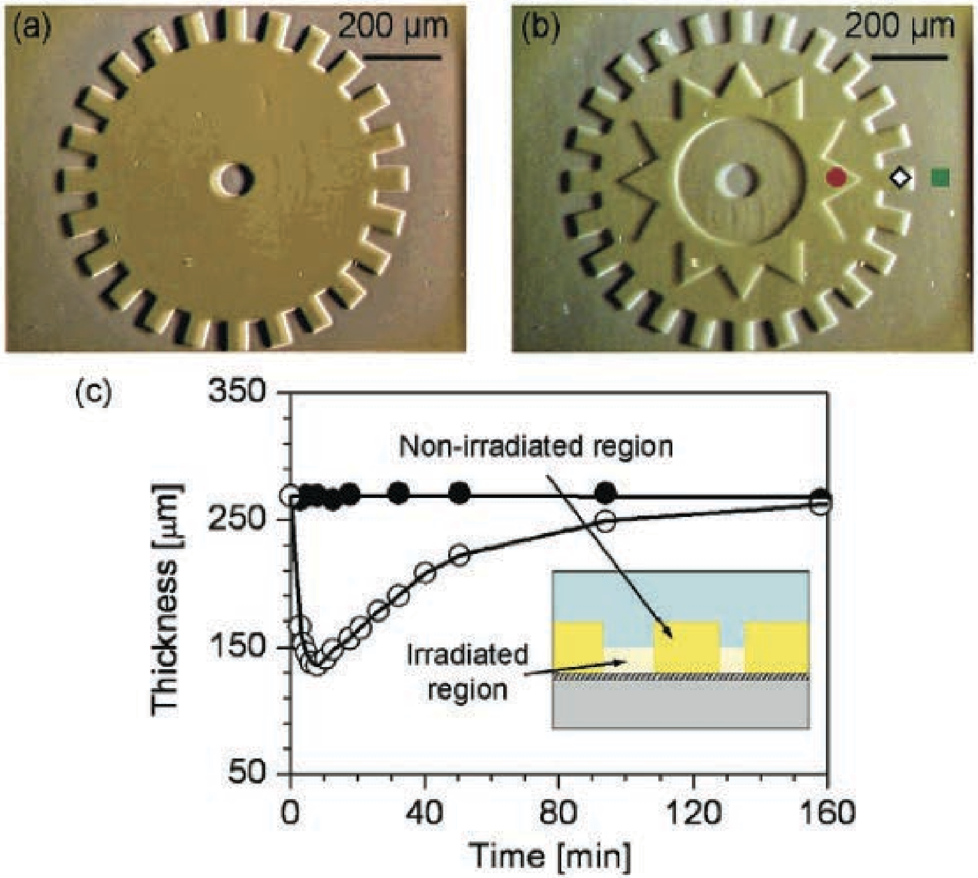
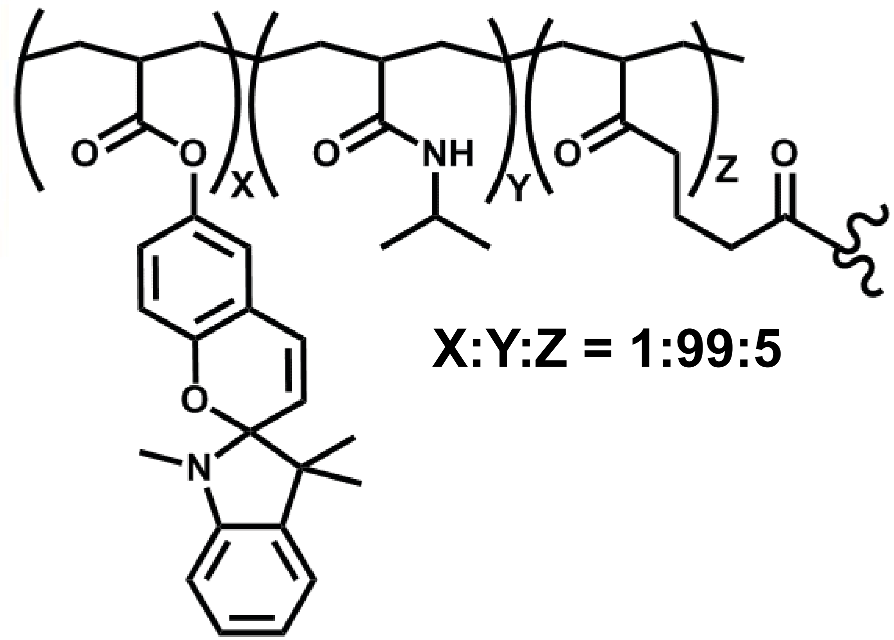


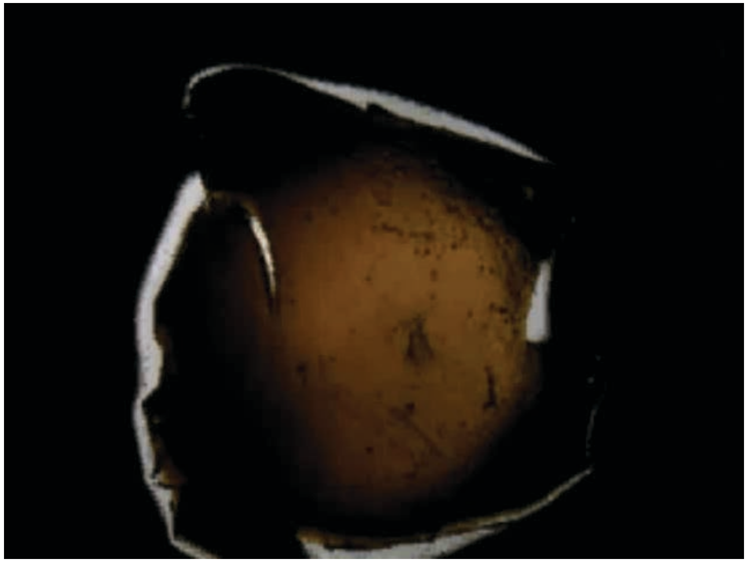
Figure 3. (a, b) Images of the pSPNIPAAm hydrogel layer just after the micropatterned light irradiation. Duration of irradiation was (●, red) 0, (◇) 1, and (■, green) 3 s. (c) Height change of the hydrogel layer in (●) non-irradiated and (○) irradiated region as a function of time after 3 s blue light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

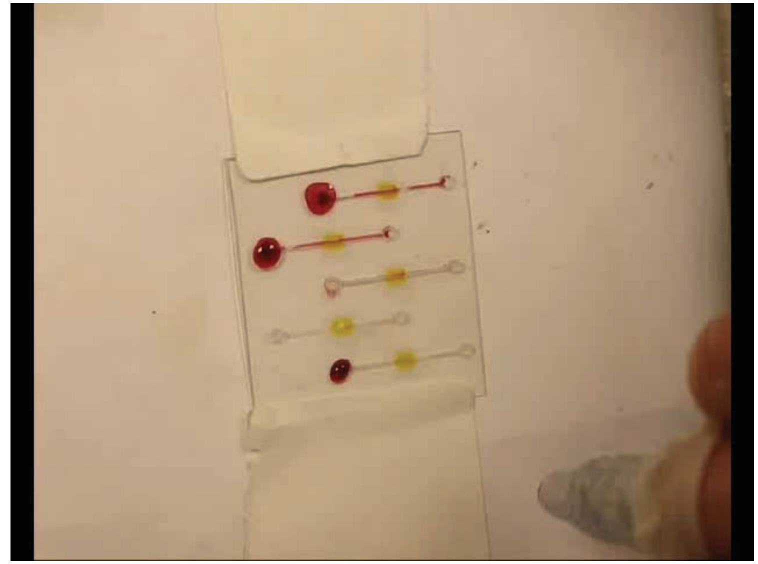


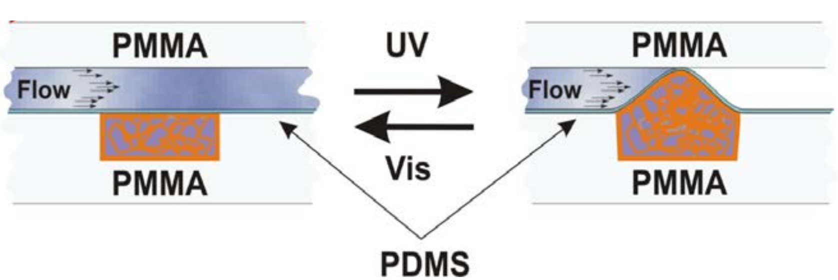
X:Y:Z = 1:99:5

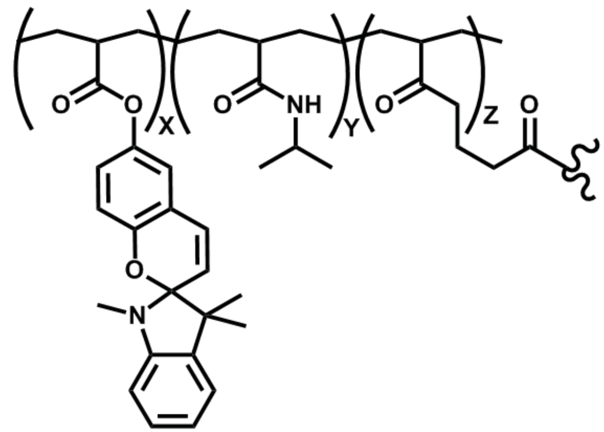
poly(N-isopropylacrylamide) (PNIPAAm)
Formulation as by Sumaru et al[1]
***1) Chem. Mater.*, 19 (11), 2730 -2732, 2007.**

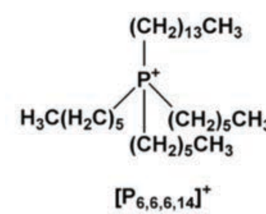
Photo-actuator polymers as microvalves in microfluidic systems

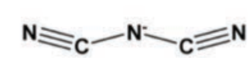












(b)

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.

Photocontrol of Assembly and Subsequent Switching of Surface Features

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

Stumpel et al., 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[*,†,§]

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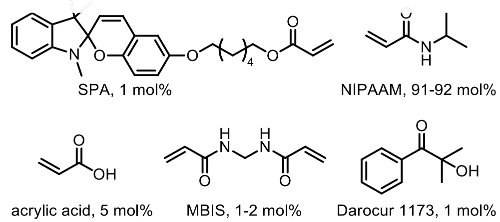
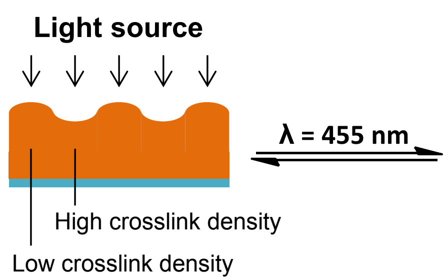
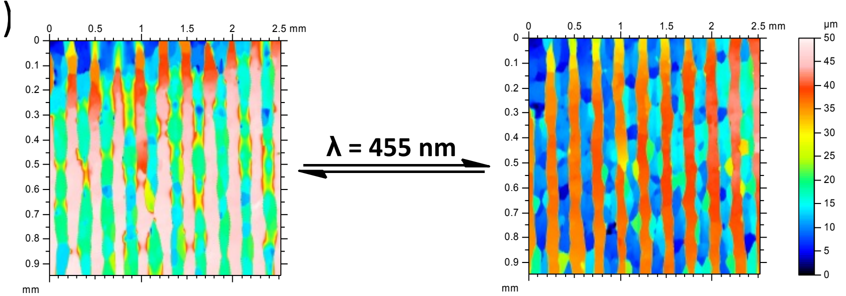
[§]Institute for Complex Molecular Systems and Laboratory of Macromolecular and Organic Chemistry, Eindhoven University of Technology, P.O. Box 513, 5600 MB Eindhoven, The Netherlands

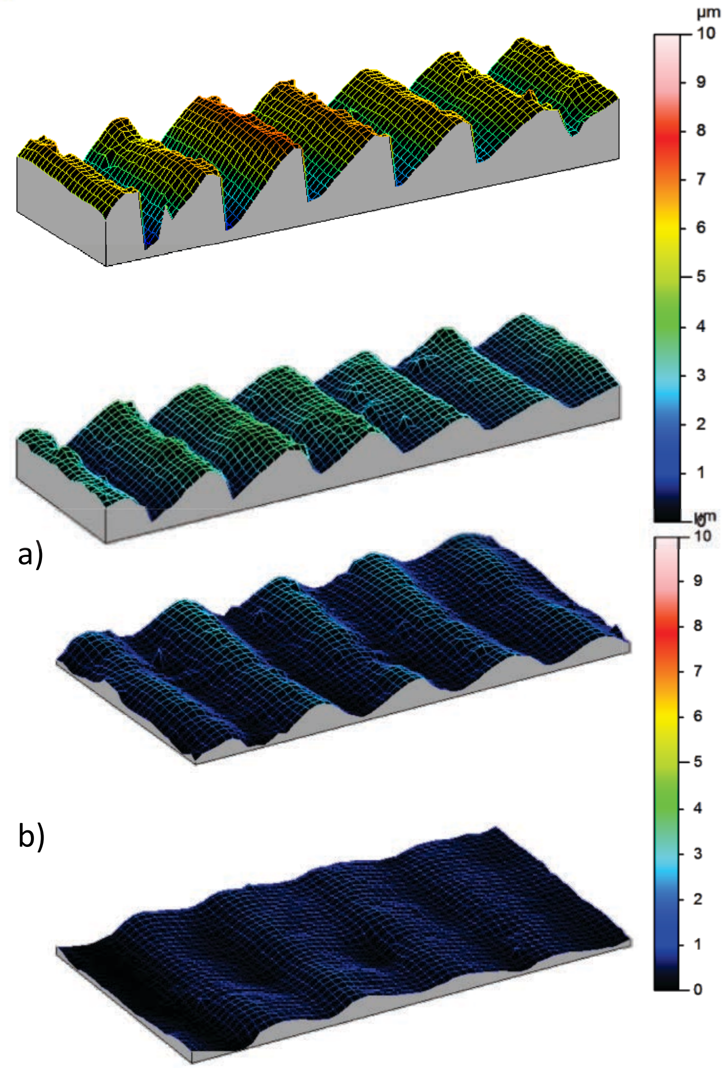


a)



b)

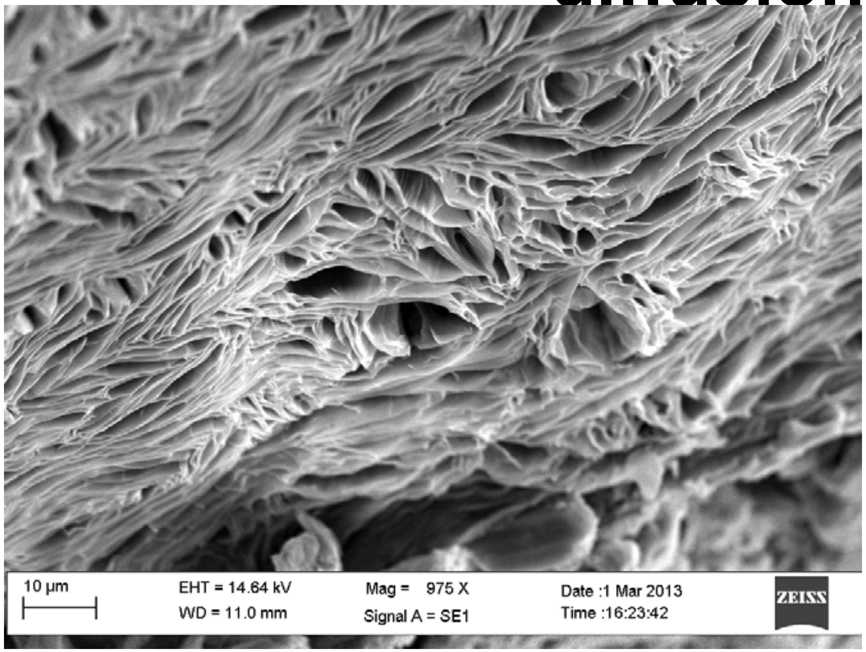


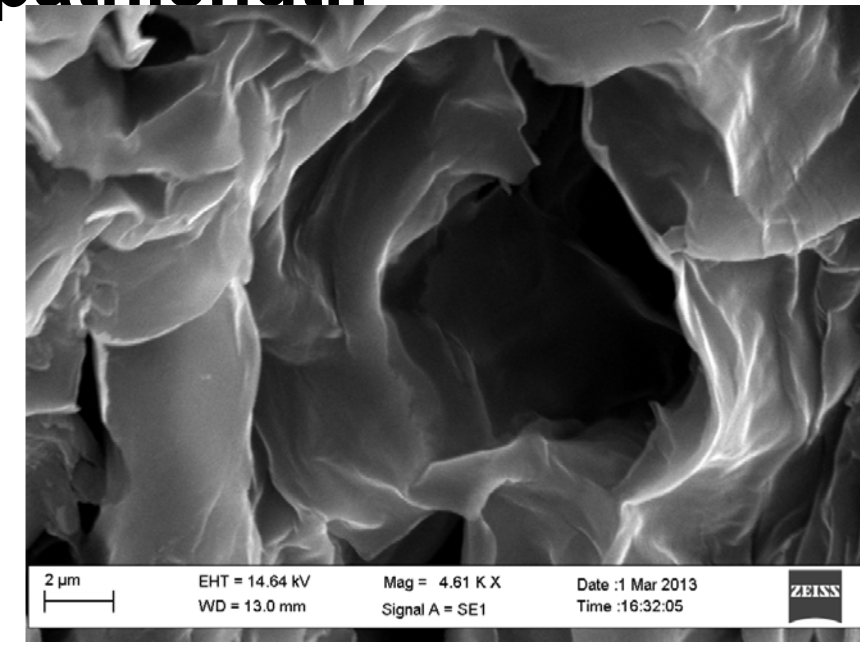


So far, so good: but what are the limitations?

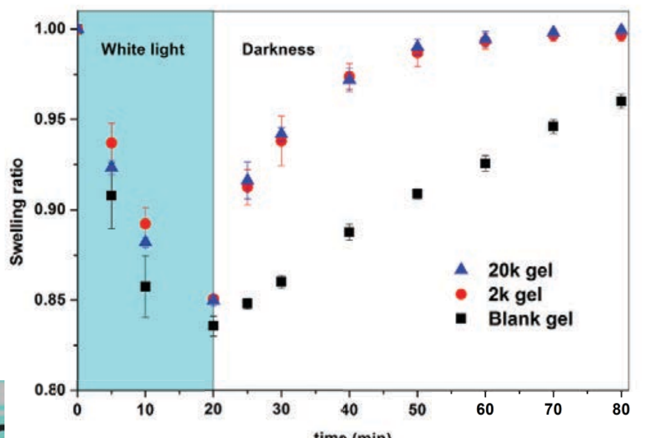
- Response time for re-swelling is slow - 10's of minutes due to diffusion mechanism
- Swelling requires protonation of the MC to $MC\text{-}H^+$ within the ionogel by the external bathing solution – which must be acidic, typically pH 3
- These issues more or less limit the applicability of the valves to single use

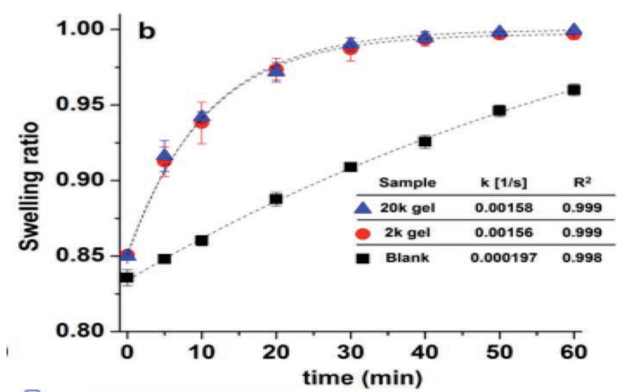
Improve response time: Porous Gels → reduce diffusion pathlength





Highly porous pNIPAAm gel structures generated using PEG as the porogen. This dramatically increases the surface area to bulk ratio, reducing the diffusion pathlength for water to penetrate to the gel interior, which in turns results in faster swelling/contraction rates

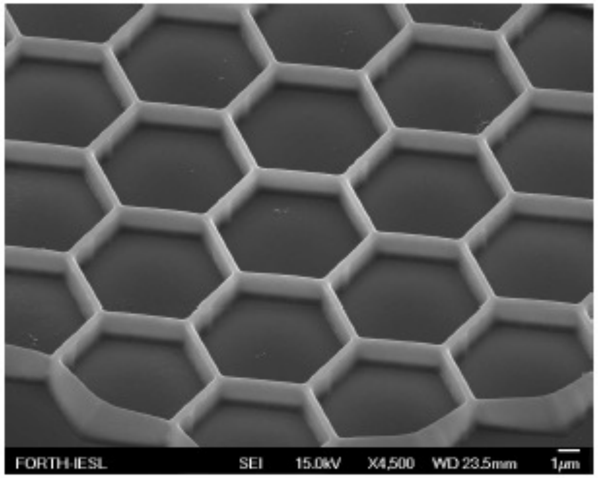




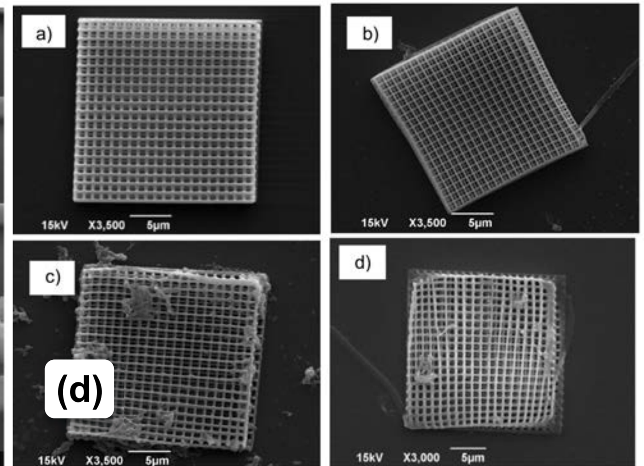
On the re-swelling side; highly porous gels now recover ca. an order of magnitude faster;

k = 1.6×10^{-3} S^{-1} vs. 2.0×10^{-4} S^{-1}

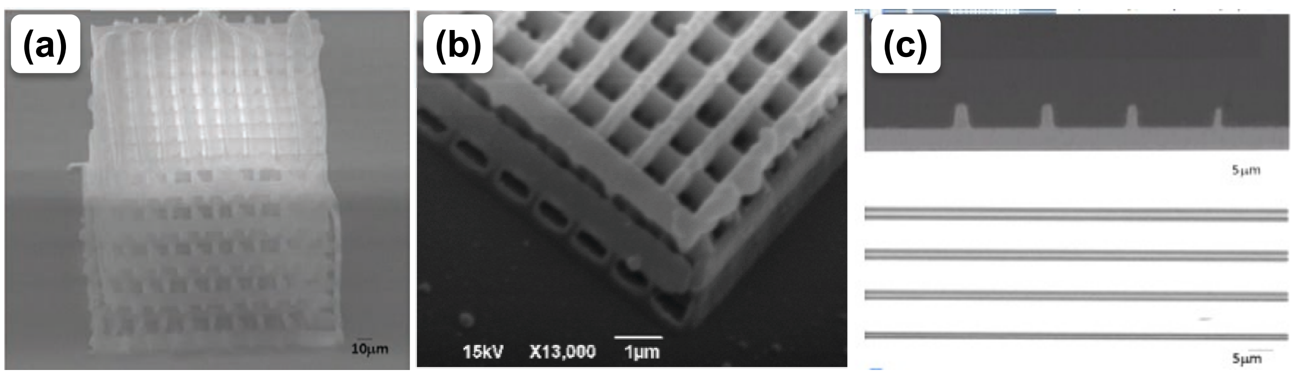
Reduce scale – improve response time
3-d Spiro-doped sol-ionogels



SEM of surface pattering produced by multi-photon polymerisation of hybrid graphene-doped ionogels



SEM images of woodpiles fabricated from material D containing a) 0%, b) 20%, c) 40% and d) 50% IL

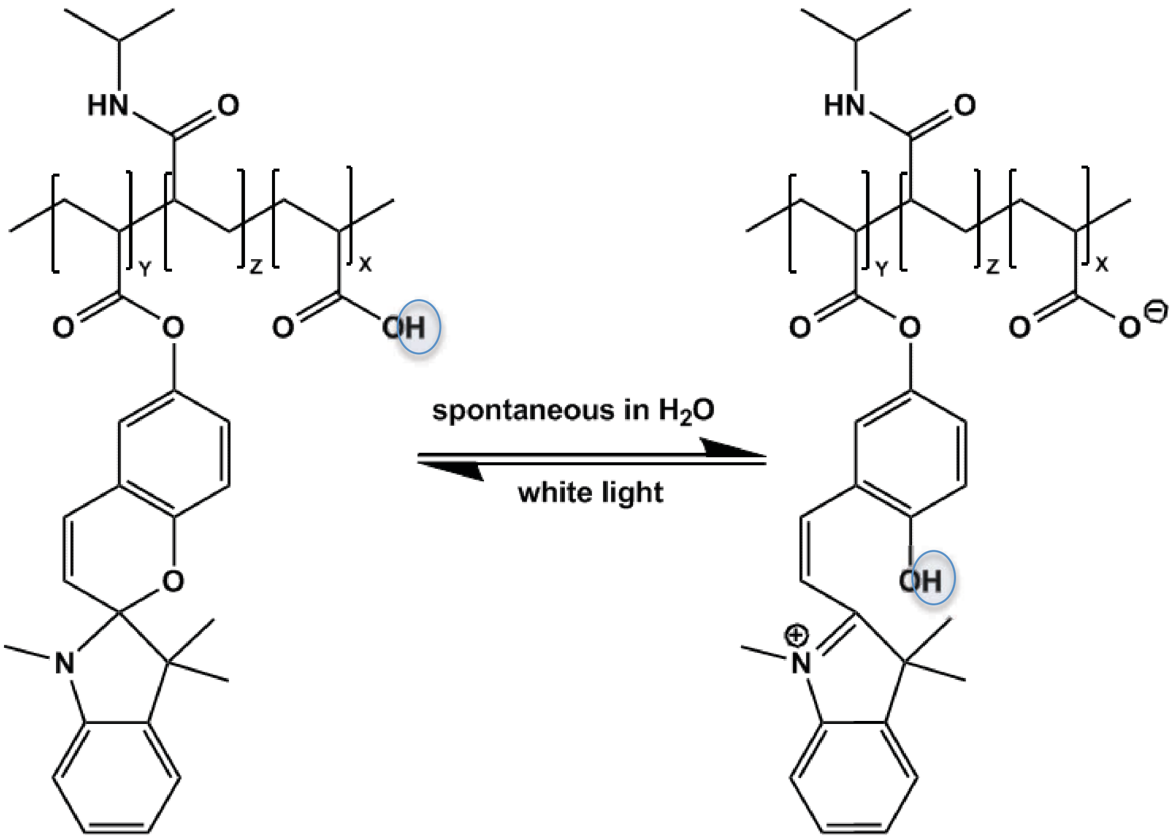


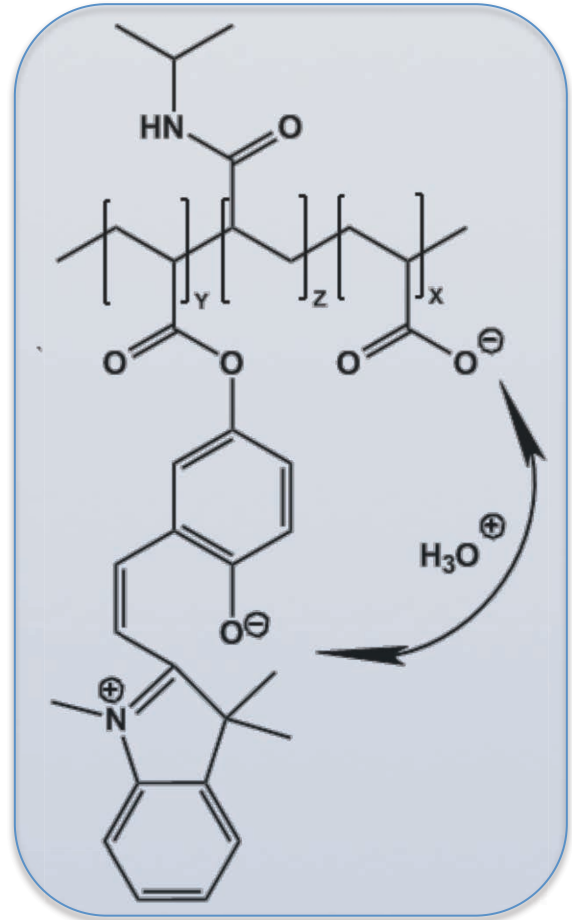
Two photon polymerised (2PP), patterned ionogels (a) and (b), and (c) feature resolution down to 150 nm or less; (d) spiropyran co-polymerised in a gel 'woodpile' structure.

The ionogels were based on photo-curable silicato-zirconate hybrid sol-gel materials and phosphonium (trihexyltetradecylphosphonium dicyanamide [$P_{6,6,6,14}$][DCA] ionic liquid (IL). To optimise the dispersion of graphene within the ionogel matrices, aqueous solutions of graphene were prepared, as opposed to the conventional graphene powder approach, and employed as catalysts for the hydrolysis and condensation reactions occurring in the sol-gel process.

With Gabija Bickauskait *and* Maria Farsari, Institute of Electronic Structure and Laser, Foundation for Research and Technology Hellas, N. Plastira 100, GR-70013 Heraklion, Crete, Greece

Improve pH range: 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

Spontaneous Reformation of Acidified Merocyanine during Actuation Cycling in non-acidified water

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

Gel with 0 % AA

Colour gradually changing from yellow to purple as H^+ leaves the gel on each cycle

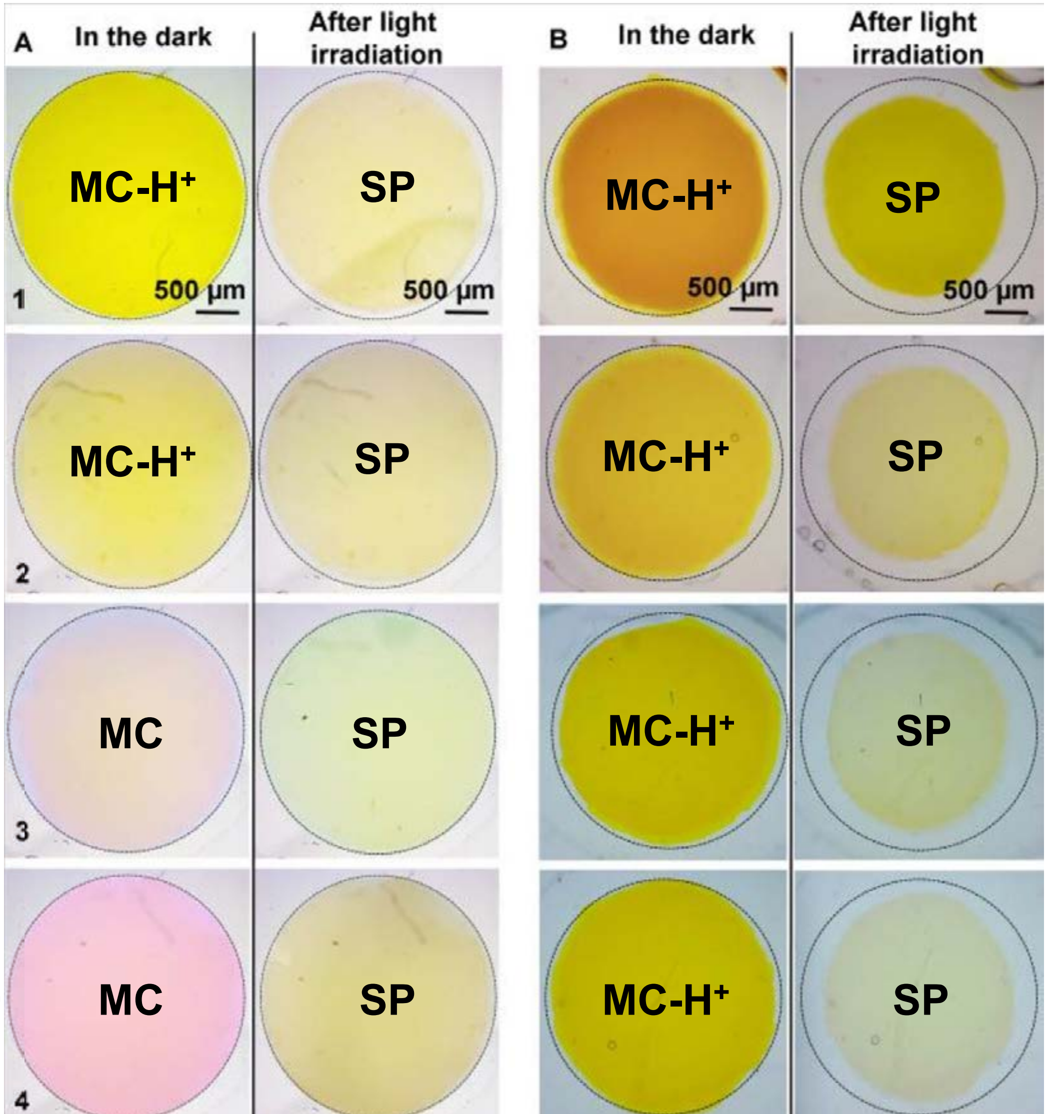
Switching changes from primarily

$MC\text{-}H^+ \rightarrow SP + H^+$

to

MC -> SP

Gel actuation stops



Gel with 5 % AA

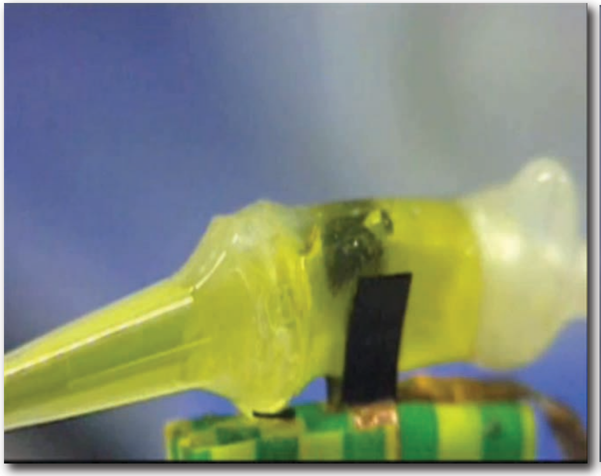
Colour remains essentially the same, as H^+ stays in the gel during cycling

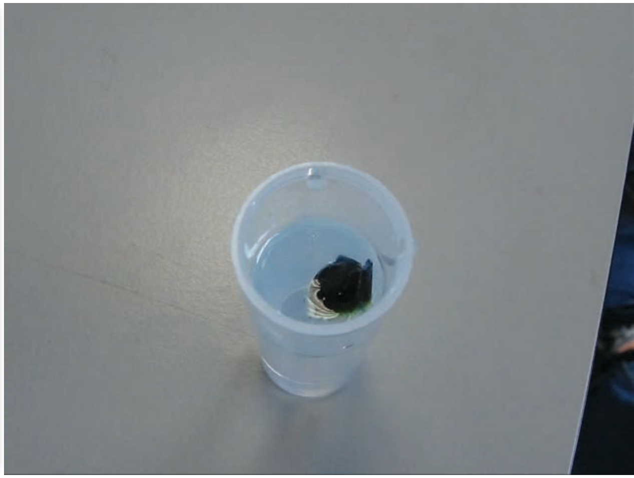
Switching stays primarily as

$MC\text{-}H^+ \rightarrow SP + H^+$

Gel actuation continues

Biomimetic low-power soft pump





Low Power control of fluid movement in channels and on surfaces is possible using electrochemically switched actuators!

Internet-scale Sensing: Are Biomimetic Approaches the Answer?, Sonia Ramirez-Garcia and Dermot Diamond, Journal of Intelligent Material Systems and Structures, 18 (2) (2007) 159-164.

Biomimetic, low power pumps based on soft actuators, Sonia Ramirez-Garcıa and Dermot Diamond, Sensors and Actuators A 135 (2007) 229–235.

Even better is to use the power of chemistry! ‘Beating Heart’ with no external power requirement; solvent exchange in a ionogel polymer causes a rhythmic movement

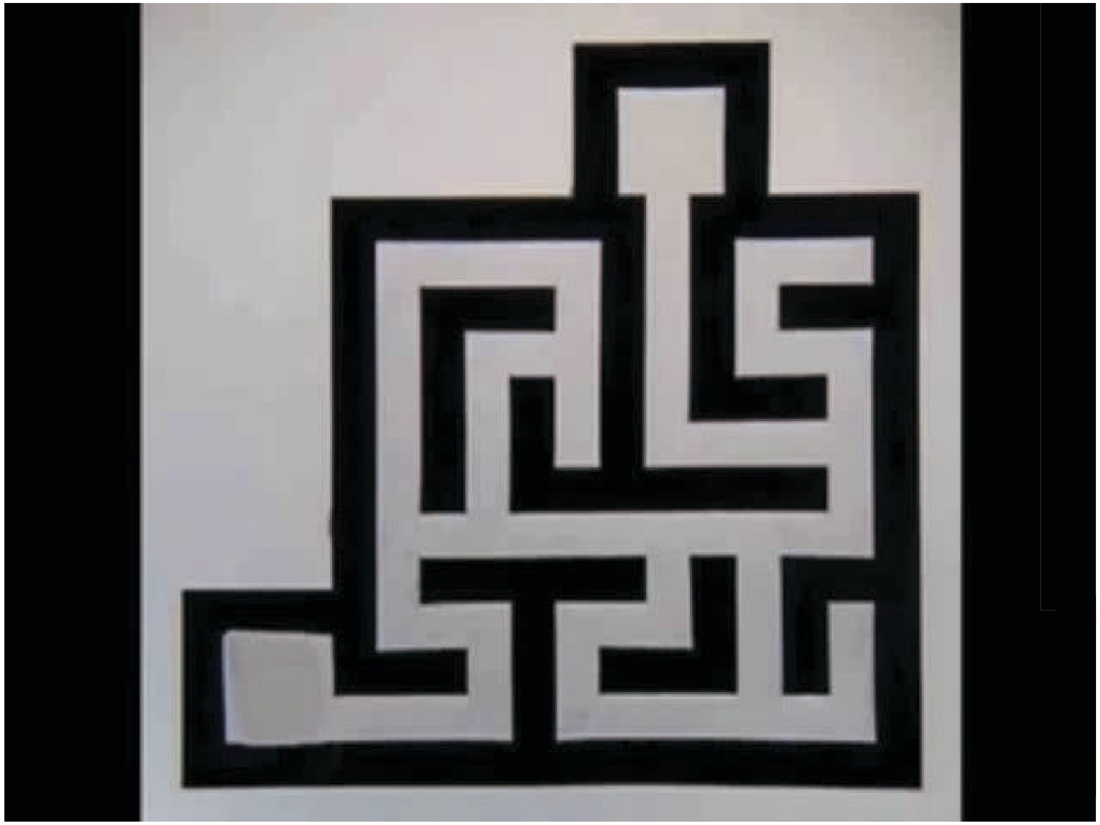
Why move the solvent at all?

[sample]/mol l^{-1}	Ratio H_2O/Sample
$1.0x10^{-6}$	$5.56x10^{7}$
$1.0x10^{-9}$	$5.56x10^{10}$
$1.0x10^{-12}$	$5.56x10^{13}$

Strategy:
Move multifunctional micro/ nano-vehicles such as beads, vesicles, micelles, capsules, droplets through the sample to perform tasks……

- **These vehicles should be able to;**
  - Spontaneously move under an external stimulus (e.g. chemical, thermal gradient) to preferred locations
  - Report selective binding of guest species
  - Release active payload to modify local environment

Chemotactic Systems



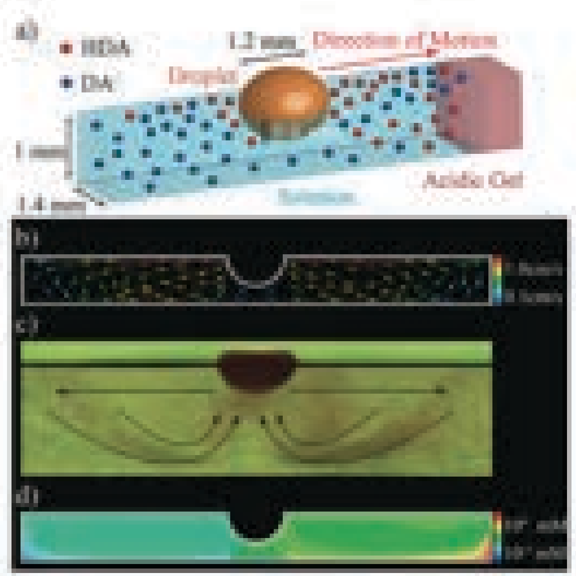


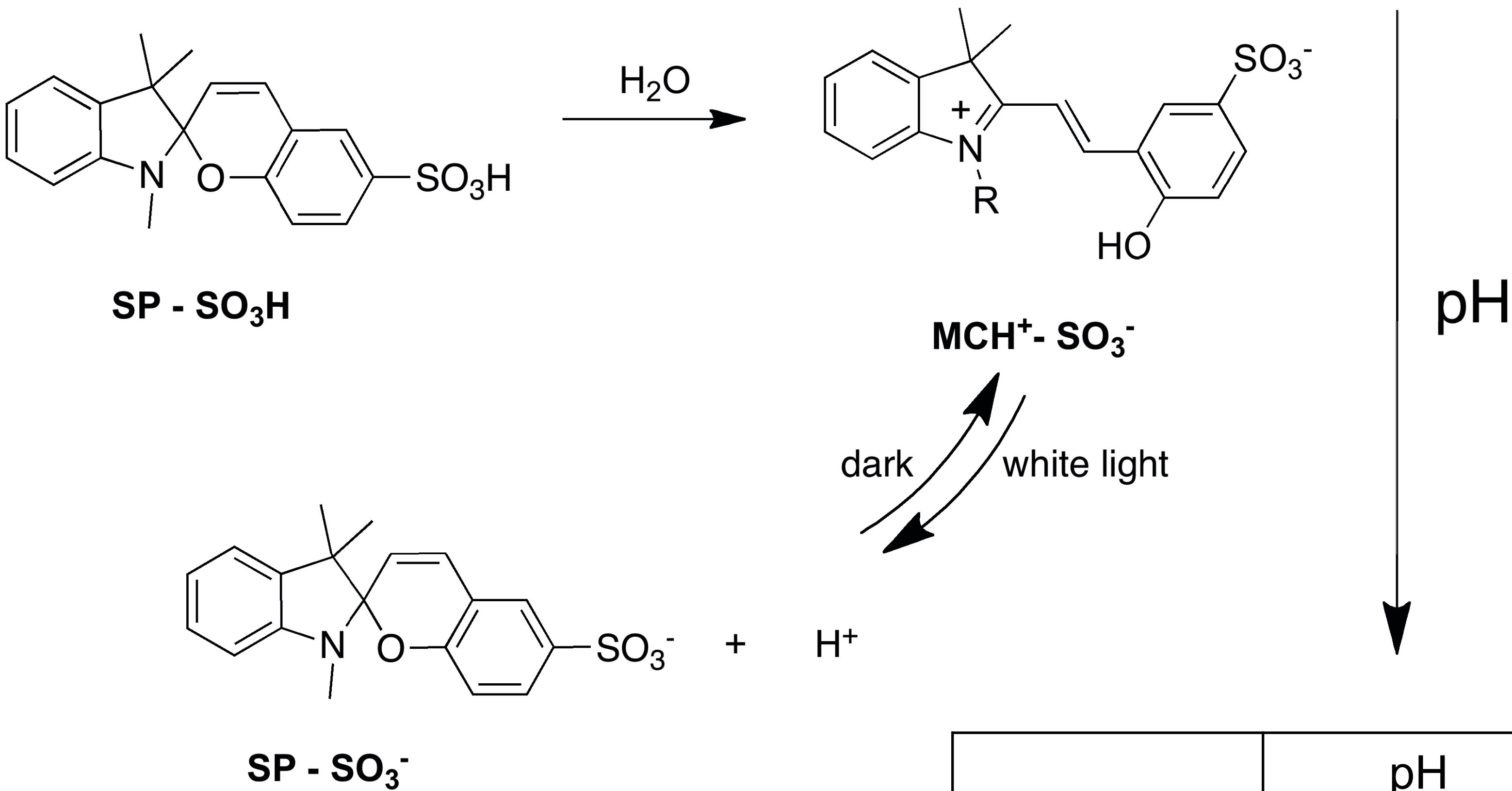
Figure 2. (a) Scheme of a droplet in a channel. The presence of HDA at the liquid−air interface gives rise to convective flows. Since more HDA is present in the direction facing the source of acid, the flows and forces are asymmetric. (b) Velocity field based on the theoretical model described in the 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.*

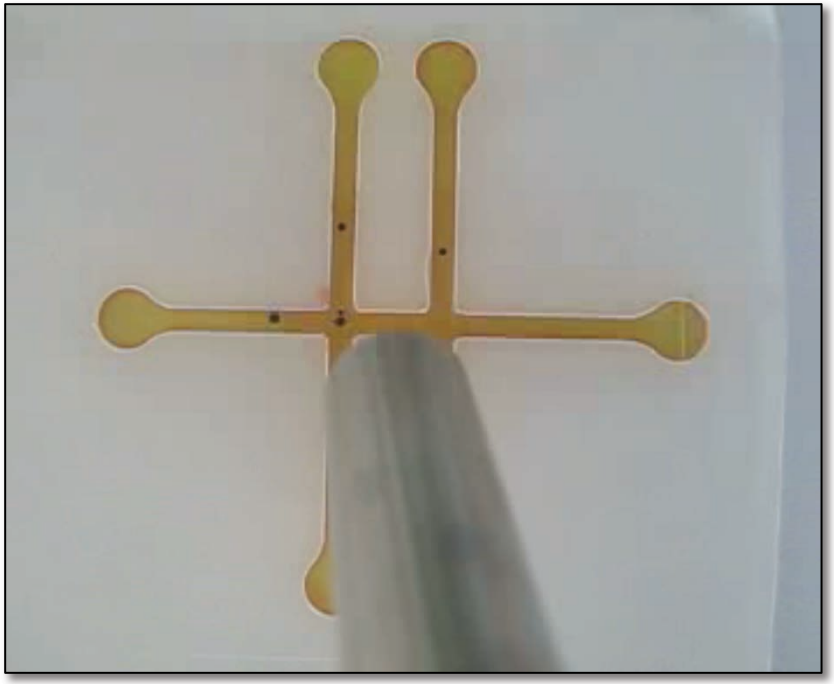
Photo-modulation of pH

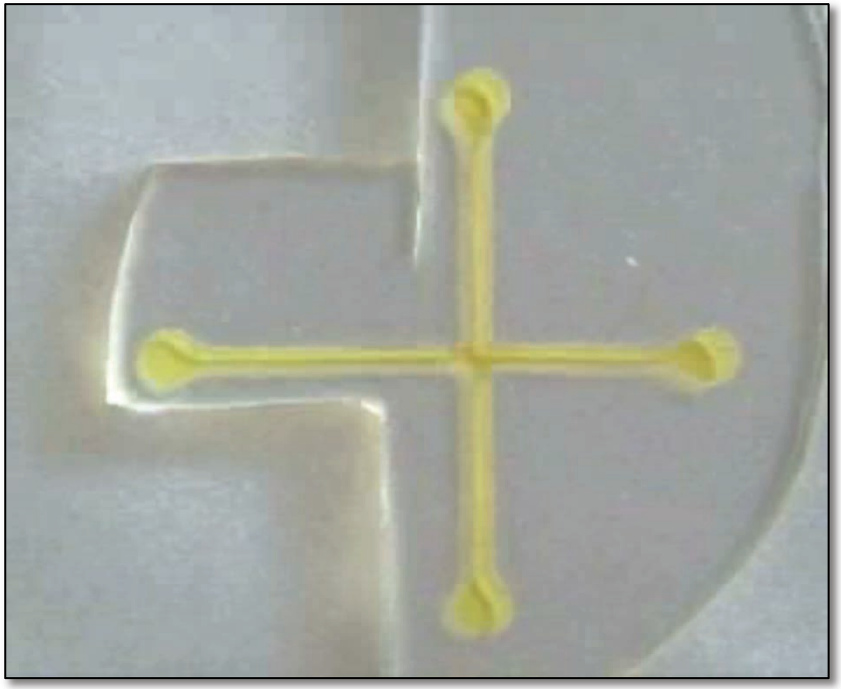


	pH
H_2O	6.5
MCH^+-SO_3^-	4.8
SP-SO_3^-	3.4

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

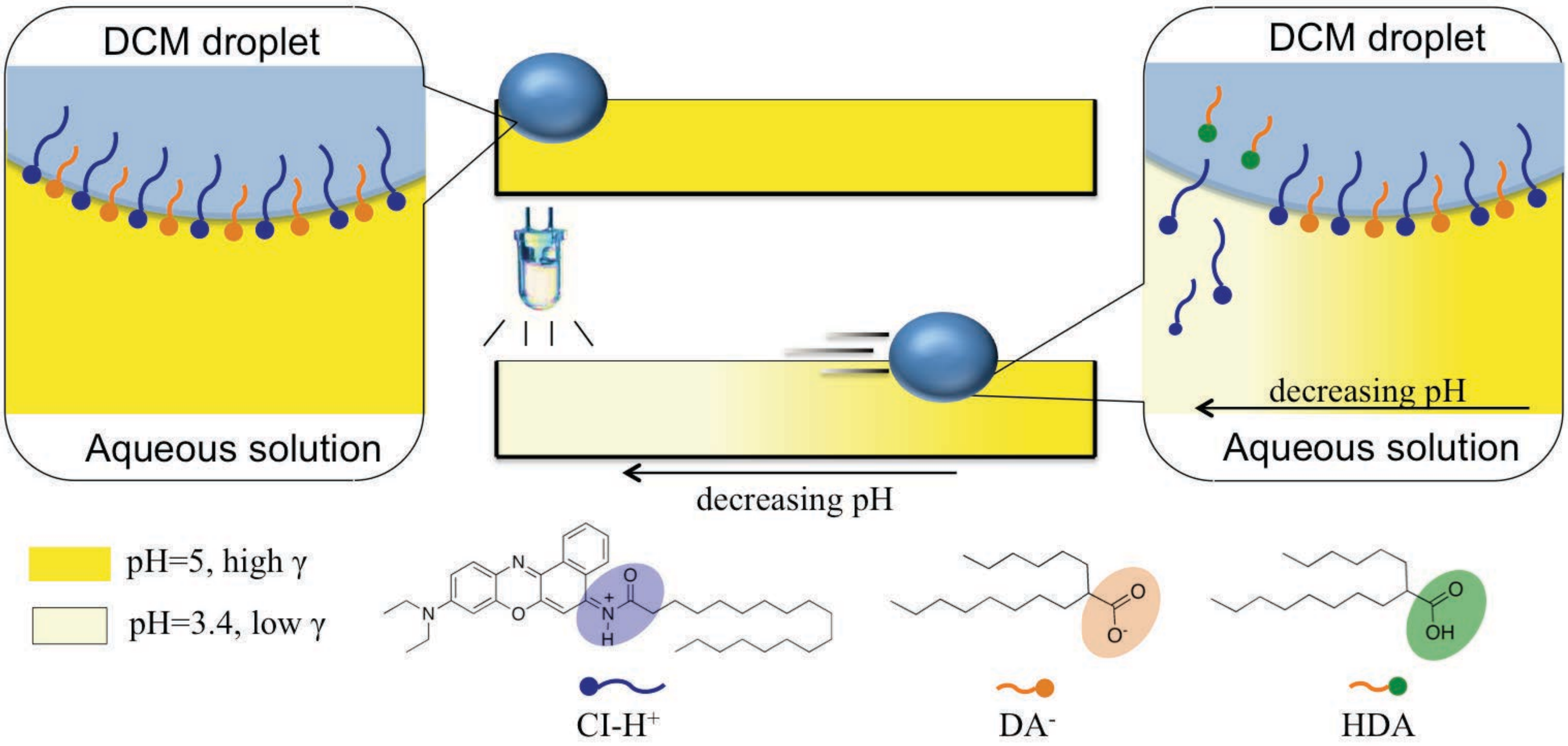
Movement of Droplets in Channels using Light





- 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

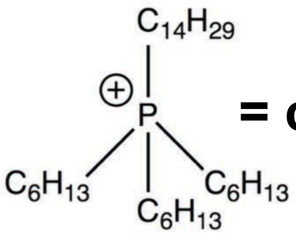
Mechanism of Photo-Stimulated Droplet Movement (with David Officer, UOW)



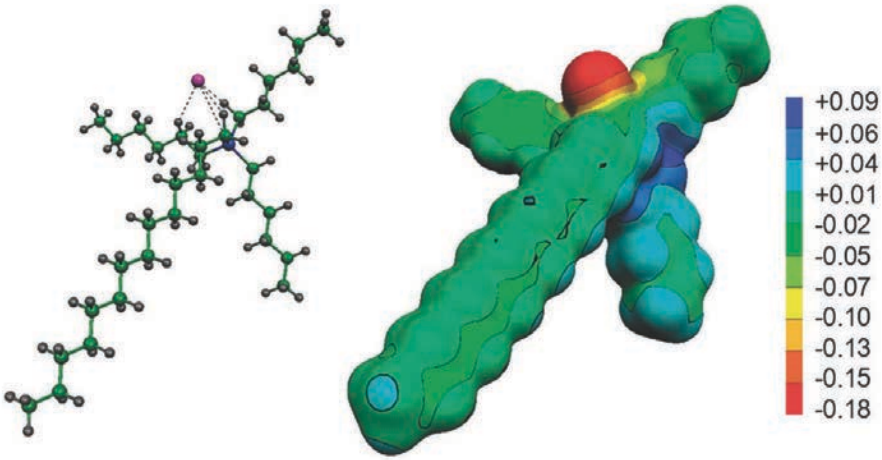
N-OCTADECANOYL-NILE BLUE

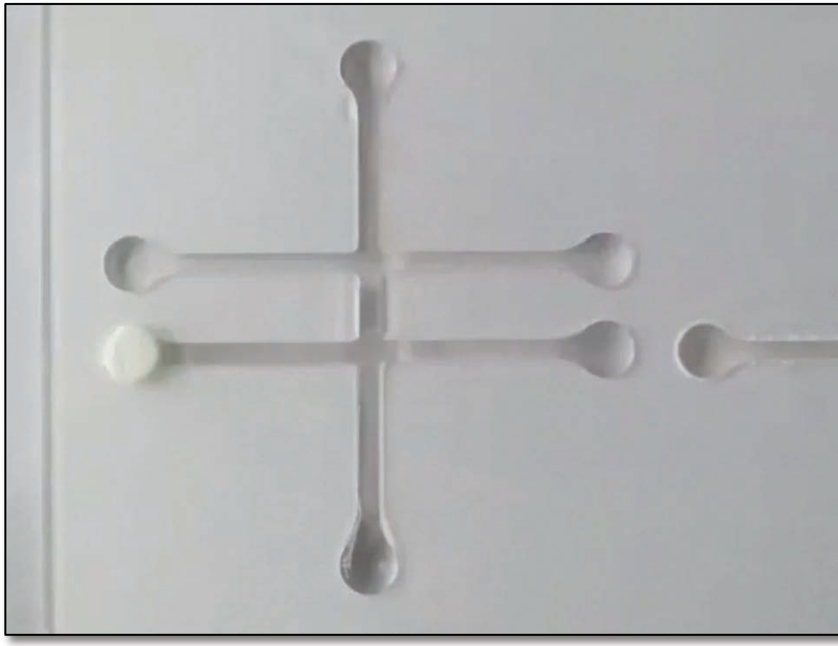
Photo-Chemopropulsion – Light-Stimulated Movement of Microdroplets, *Larisa Florea, Klaudia Wagner, Pawel Wagner, Gordon G. Wallace, Fernando Benito-Lopez, David L. Officer, and Dermot Diamond, Adv. Mater. 2014, DOI: 10.1002/adma.201403007*

We can do the same with IL Droplets



= cationic surfactant

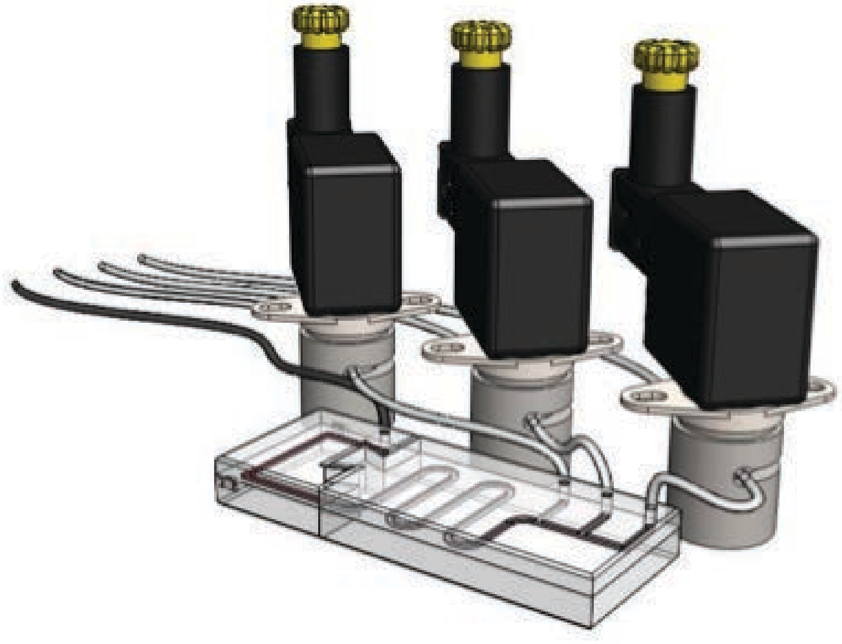




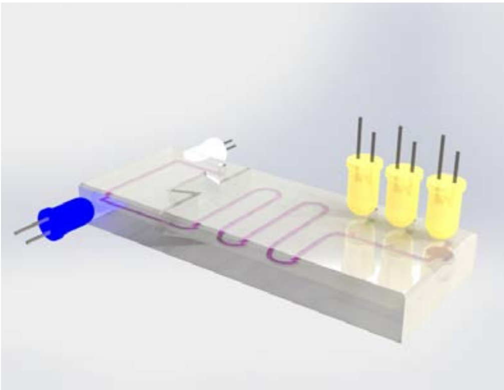
Trihexyl(tetradecyl)phosphonium chloride ($[P_{6,6,6,14}][Cl]$) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the Cl^- ion which is created using a polyacrylamide gel pad soaked in 10^{-2} M HCl; A small amount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

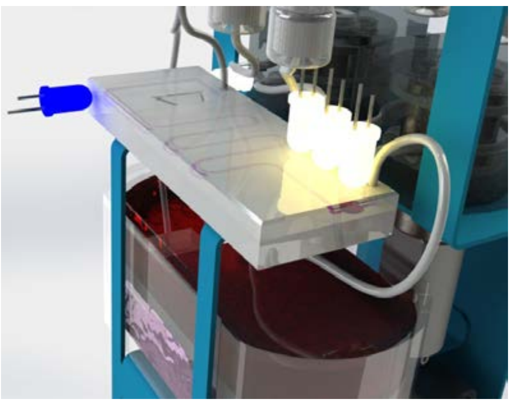
Electronic structure calculations and physicochemical experiments quantify the competitive liquid ion association and probe stabilisation effects for nitrobenzospiropyran in phosphonium-based ionic liquids, D. Thompson et al., *Physical Chemistry Chemical Physics*, 2011, 13, 6156-6168.

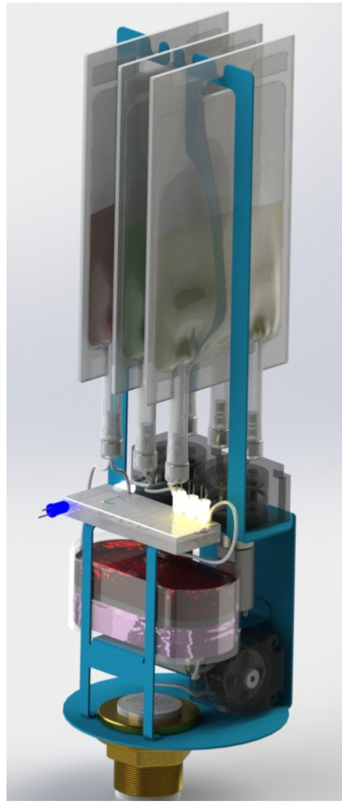
Can we go from this:



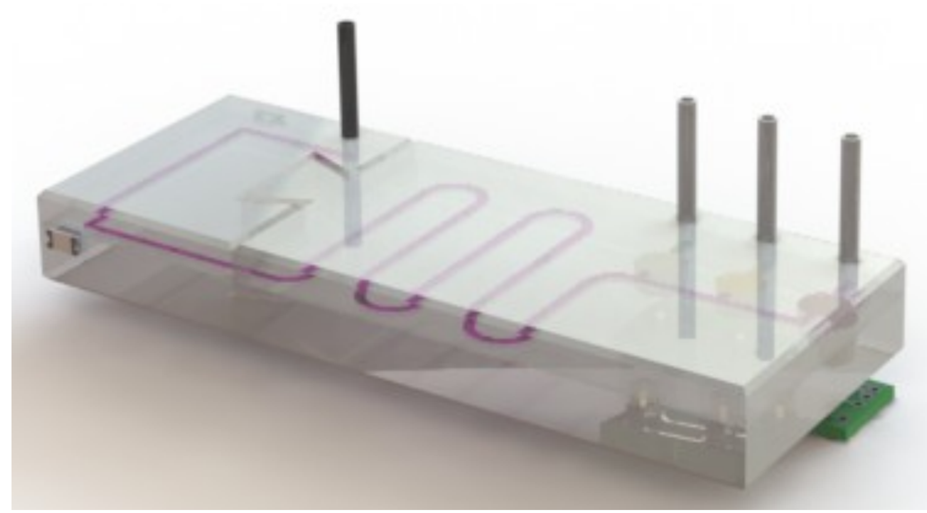
To Photo-Fluidics & Detection

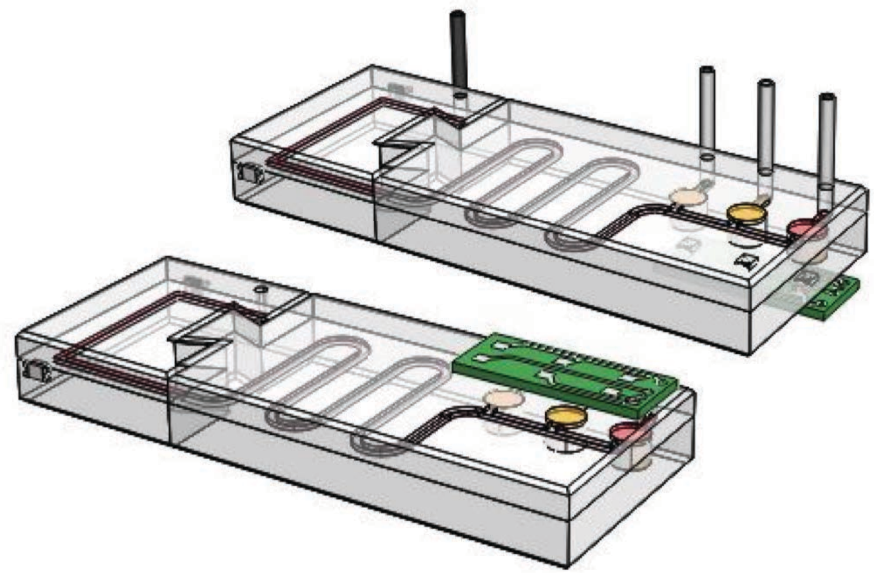






Fluidic Chip is completely sealed – no need for interconnects to detection/flow components





- **Fluidic handling completely integrated into the microfluidic chip**
- **Valve structures created post chip fabrication by in-situ photopolymerisation**
- **Valves actuated remotely using light (LEDs)**
- **Detection is via LED colorimetric/fluoescence measurements**

NAPES Consortium

NAPES
NEXT GENERATION ANALYTICAL PLATFORMS FOR ENVIRONMENTAL SENSING

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TU/e

CIC microGUNE
Microtechnologies Cooperative Research Center

UNIVERSITÀ DEGLI STUDI DI MILANO

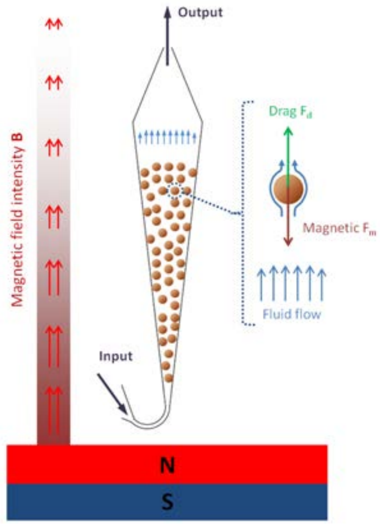
Aquila Bioscience

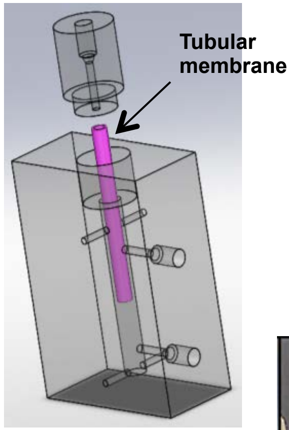
Funded under grant agreement No. 604241 of the European Union's Seventh Framework Programme

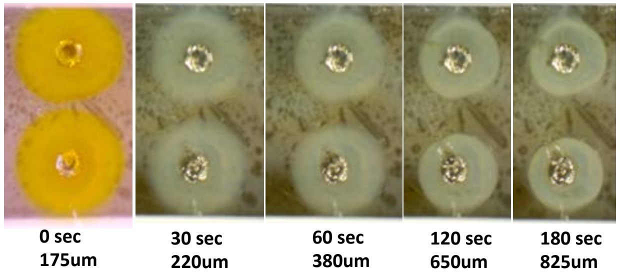
SEVENTH FRAMEWORK PROGRAMME

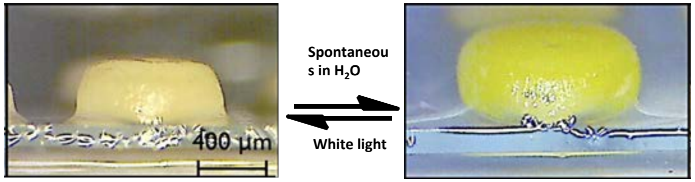
Integration of Novel platform Components

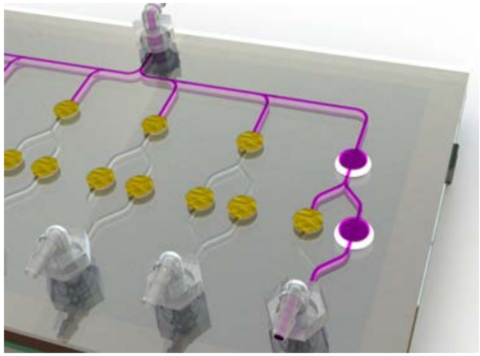
NAPES
NEXT GENERATION ANALYTICAL PLATFORMS FOR ENVIRONMENTAL SENSING

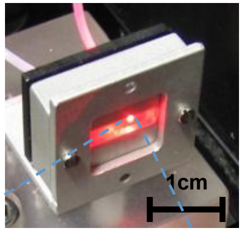


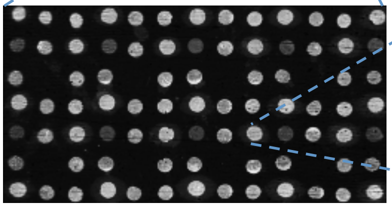


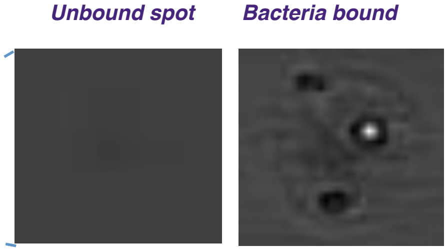


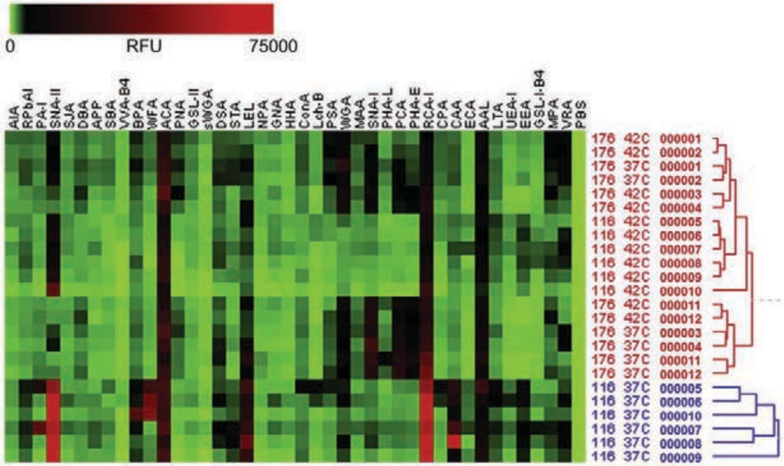










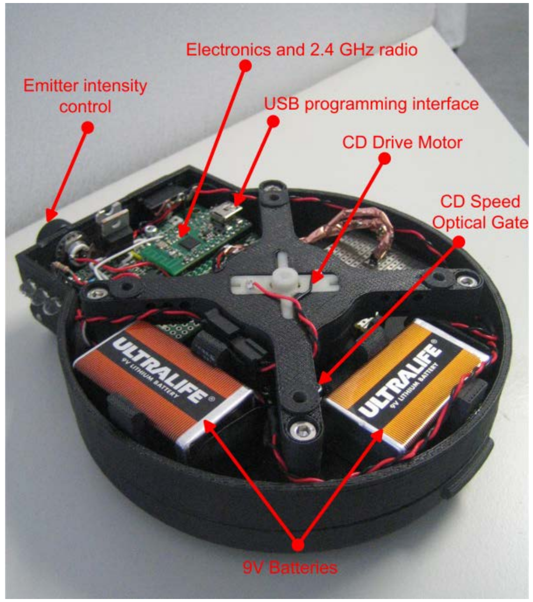


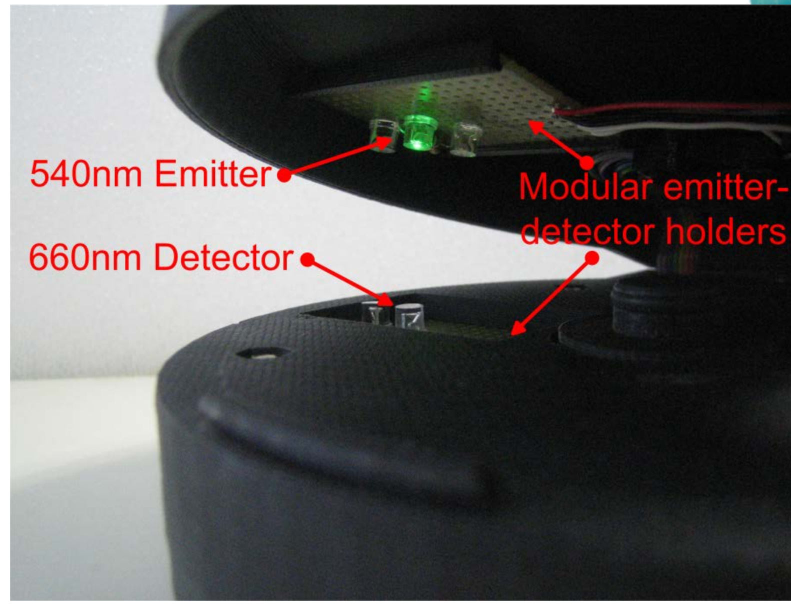
Funded under grant agreement No. 604241 of the European Union's Seventh Framework Programme

SEVENTH FRAMEWORK PROGRAMME


shimmer

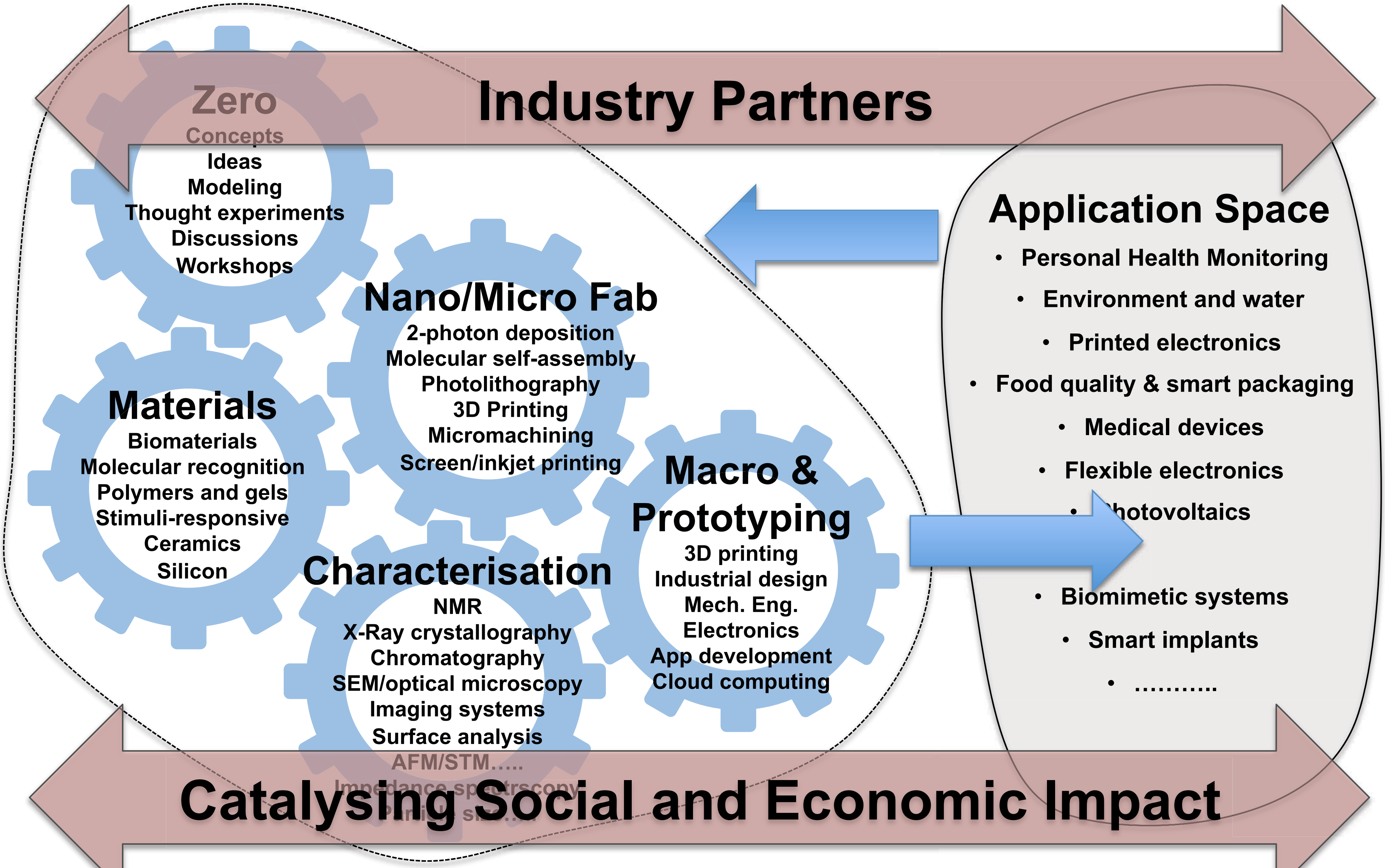

Linksulin



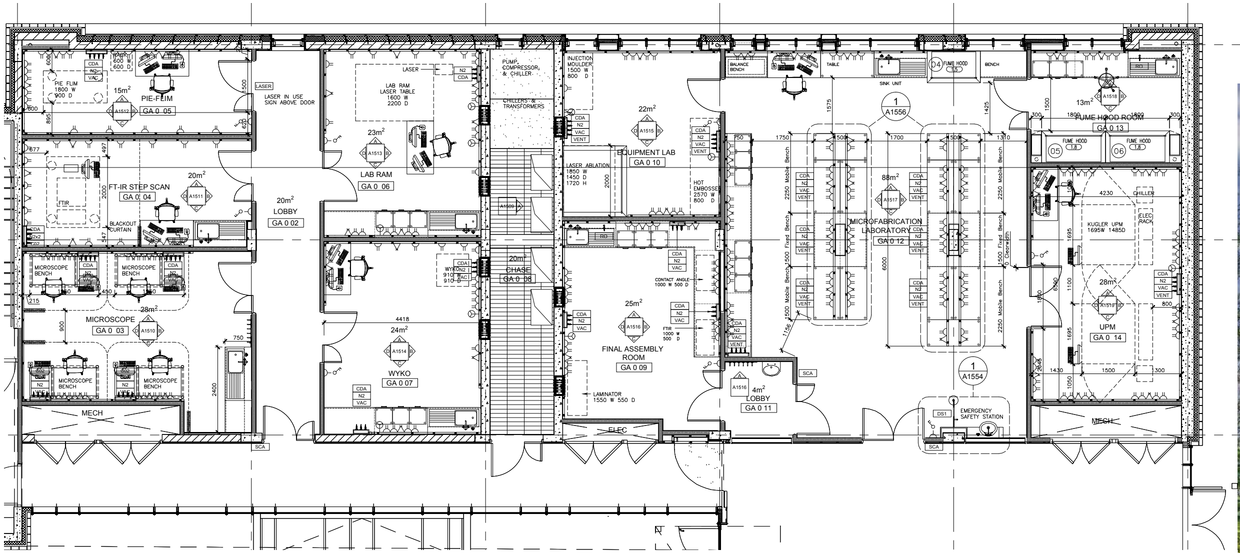


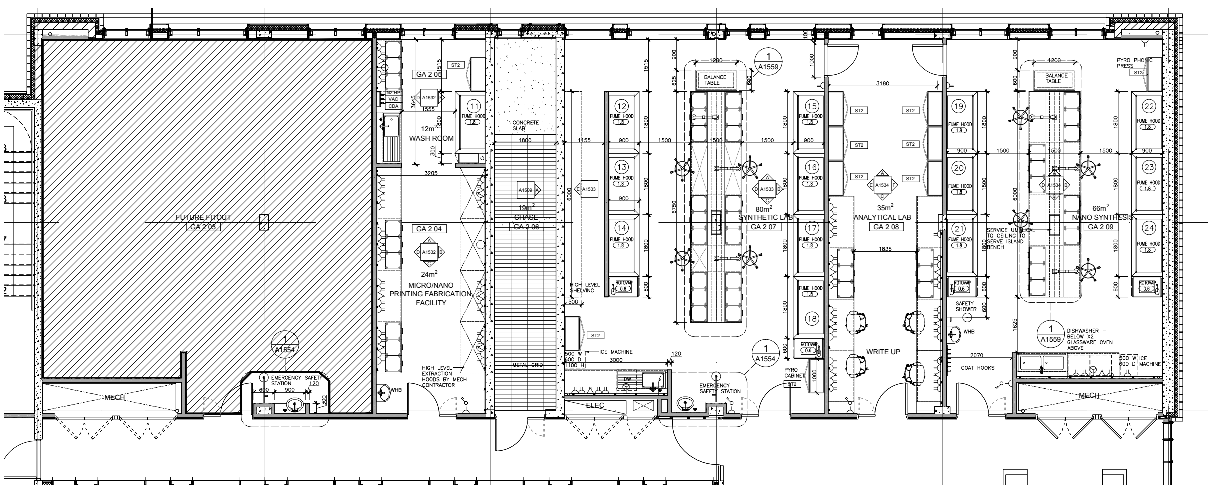
Centrifugal Microfluidic Analysis System

Getting it all to Work Together…



NRF Building (Autumn 2014)





Thanks to…..

Thanks for the invitation

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