

Stimuli-Responsive Materials and Biomimetic Fluidics: Key Building Blocks of Futuristic Autonomous Chem/Bio-Sensing Platforms

Larisa Florea, 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 seminar presented at

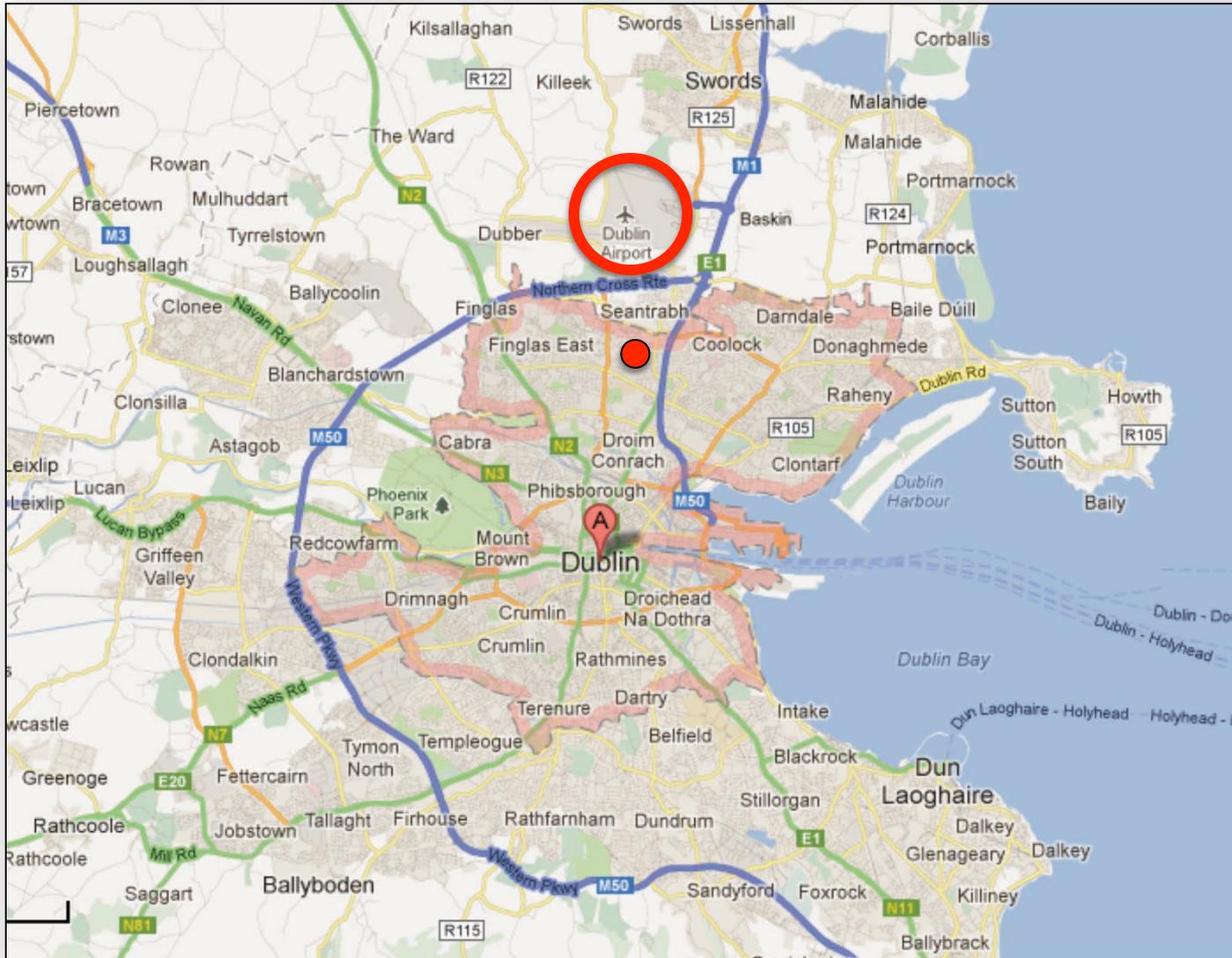
Dipartimento di Chimica e Chimica Industriale, Università degli Studi di Pisa, Italia

27th May 2015





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NEWS AND RESOURCES

MINISTER BRUTON LAUNCHES €88 MILLION SFI RESEARCH CENTRE, BRINGING NEW INSIGHTS TO 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**

Insight, the Centre for Data Analytics, will position Ireland at the heart of global Data Analytics research

The largest investment in a single research centre in the history of the state

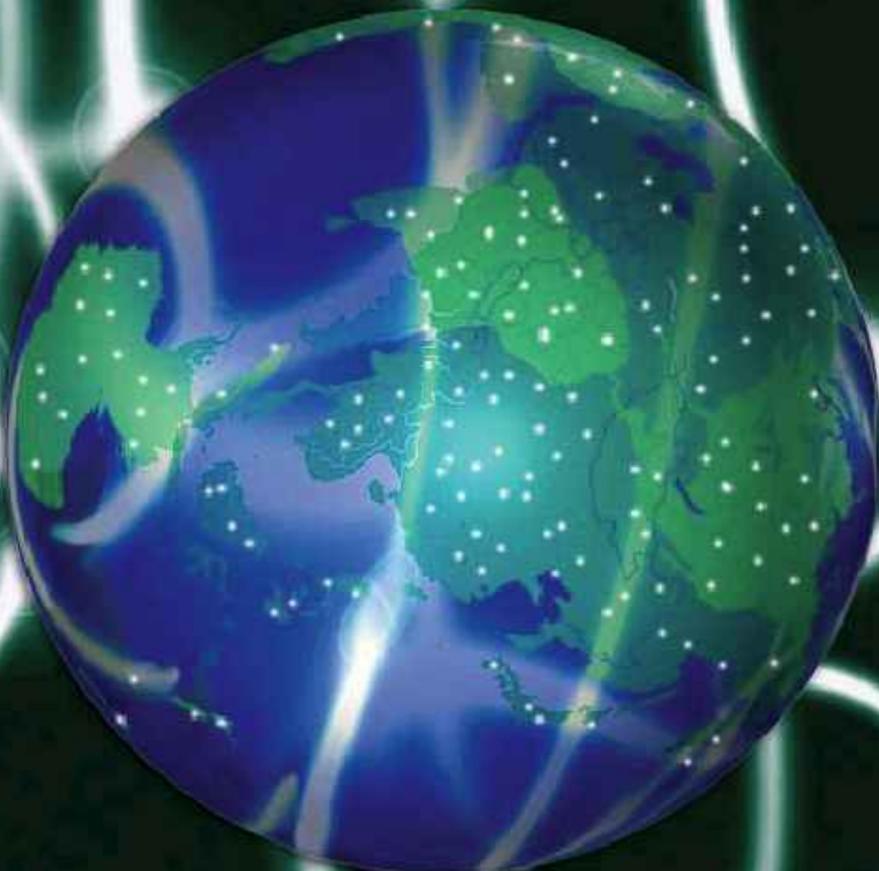
Uniting 4 universities, 30 industry partners, and 200 researchers in one multi-location research centre

Creating 300 direct jobs through 12 funded spin outs, as well as creating indirectly thousands of other job

Research and Innovation, Mr Sean Sherlock T.D. today officially launched Insight, a new Science Foundation Ireland (SFI) Research Centre for Data Analytics. In a joint initiative between DCU, NUI Galway, UCC and UCD, Education institutions, with 30 industry partners, to position Ireland at the heart of global data analytics research.

The Centre will receive funding of €58 million from the Department of Jobs, Enterprise and Innovation through SFI's Research Centres Programme, along with a further contribution of €30 million from 30 industry partners. Insight represents a new approach to research and development in Ireland, by connecting the scientific research of Ireland's leading data analytics researchers with the needs of industry and enterprise.

Keynote Article: August 2004, Analytical Chemistry (ACS)



internet 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.

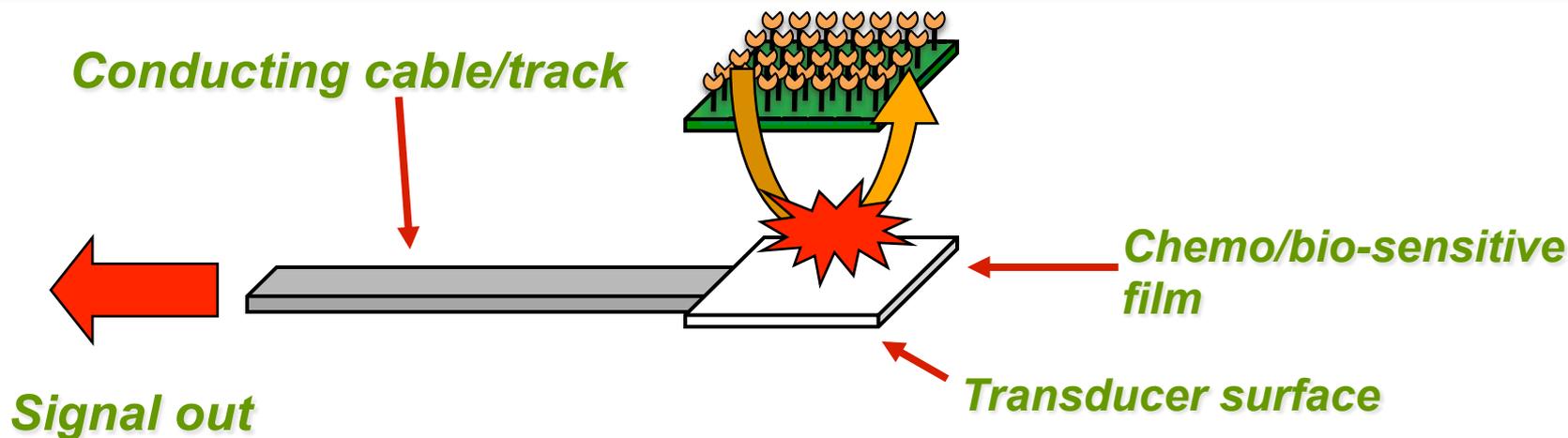
Digital communications networks are at the heart of modern society. The digitalization of communications, the development of the Internet, and the availability of relatively inexpensive but powerful mobile computing technologies have established a global communications network capable of linking billions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

What is a Chemo/Bio-Sensor?

'a device, consisting of a transducer and a chemo/bio-sensitive film/membrane, that generates a signal related to the concentration of particular target analyte in a given sample'

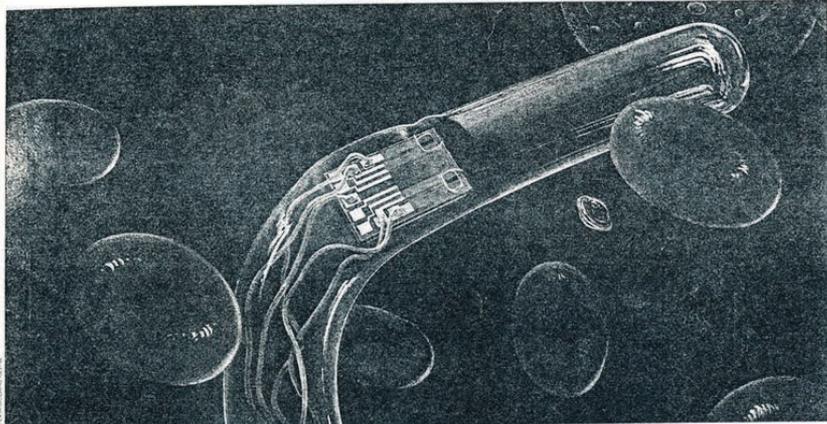


Chemo/Bio-sensing involves selective **BINDING & TRANSDUCTION** on the device surface; this also implies the target analyte **MUST** meet the device surface (**LOCATION & MOVEMENT**). It provides a signal observable in the macroscopic world (**COMMUNICATION**)



The promise of biosensors.....

BIOSENSORS THE MATING OF BIOLOGY AND ELECTRONICS



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

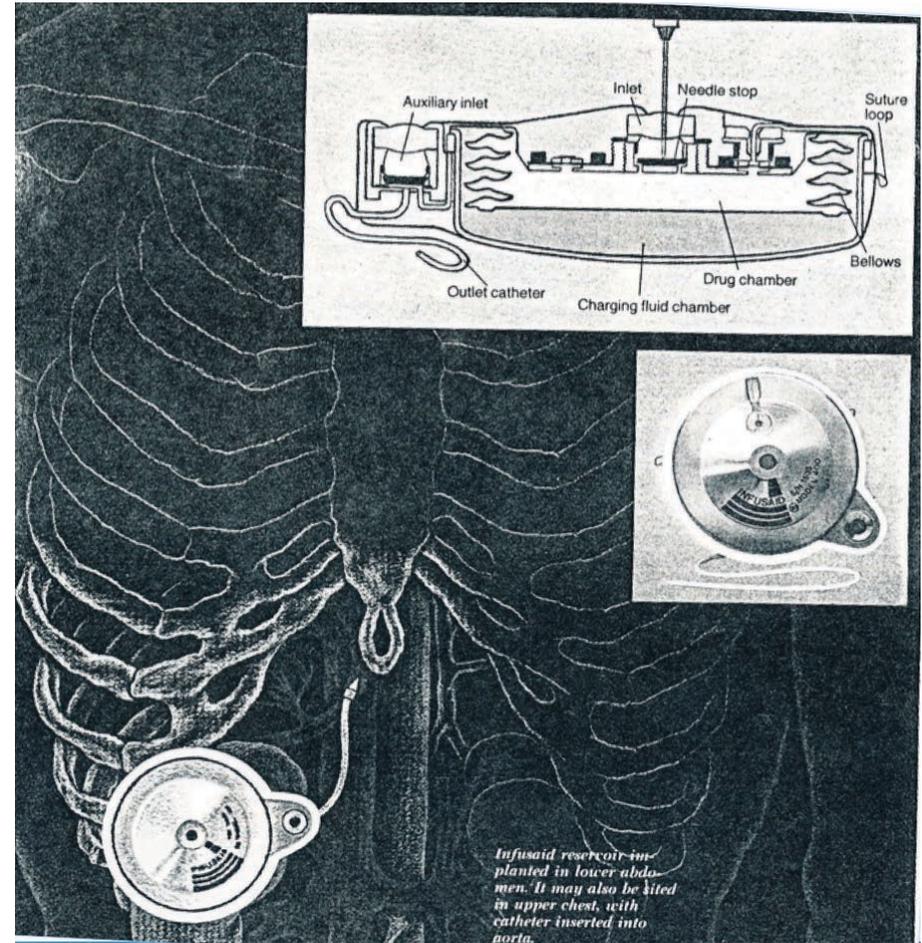
layer on the platinum, generating a slight electrical potential between the platinum and a nearby silver wire. The higher the glucose concentration, the higher the peroxide levels and the greater the potential. A current thus generated will signal the insulin reservoir to increase or decrease its flow.

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.



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

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

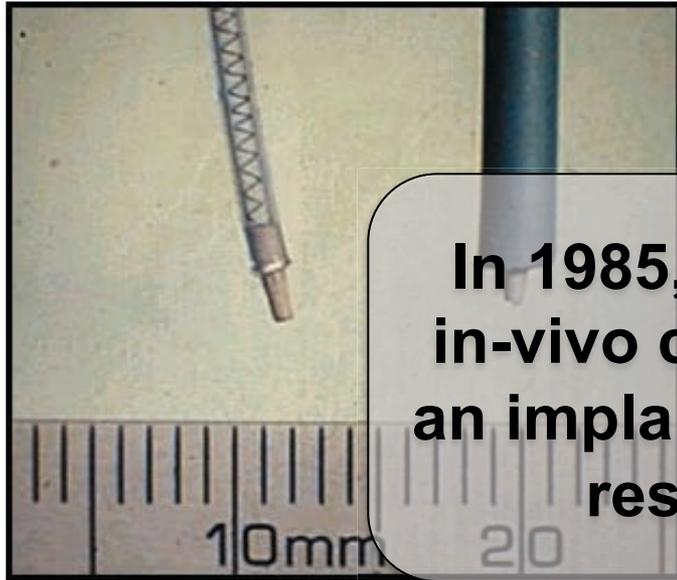


OÉ Gaillimh
NUI Galway





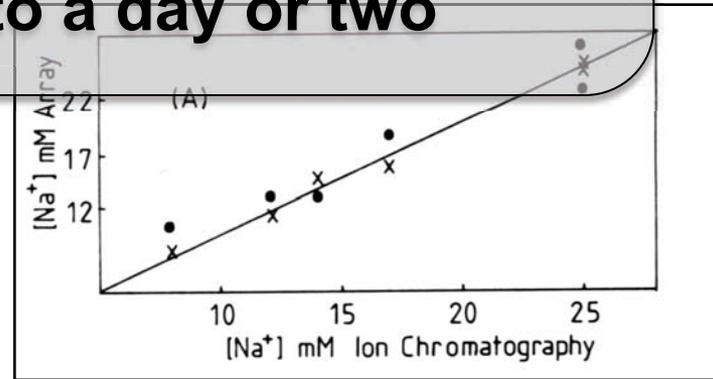
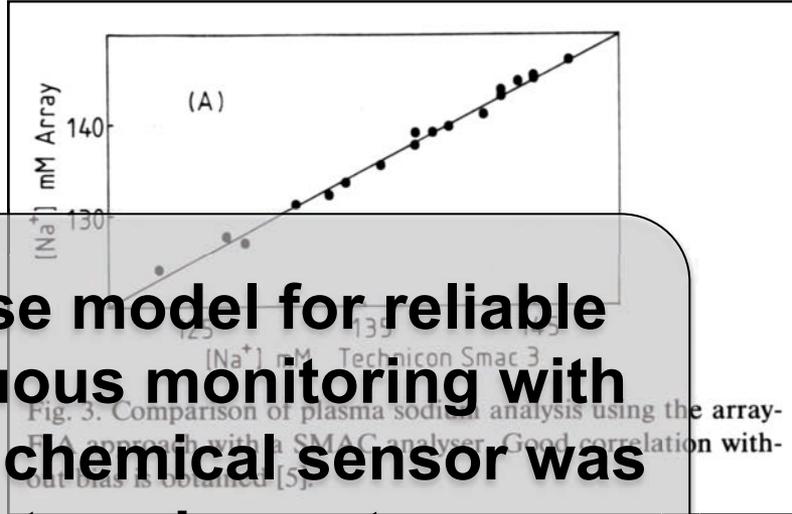
Blood Analysis; Implantable Sensors



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

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

Dr. David Band, St Thomas's Hospital London



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

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





From implantable to sub-cutaneous...



Up to now, implantable pumps for clinical application and suitable for the delivery of insulin have not been developed. However several groups are working on the development of both implantable dosing units and an implantable glucose sensor. Intravascular blood glucose sensing is difficult owing to the complex technology involved, and the foreign-body reaction of blood. The measurement of glucose in tissue would be easier to handle, but it has not been established whether the extravascular tissue concentration of glucose is sufficiently significant to serve as an input signal for a closed-loop system. Only when these questions have been answered and a suitable pumping and dosing unit have been developed, can the closed-loop system for the control of blood glucose be realised and miniaturised for implantation.

An implantable artificial pancreas, W. Schubert, P. Baurischmidt, J. Nagel, R. Thull, M. Schaldach;

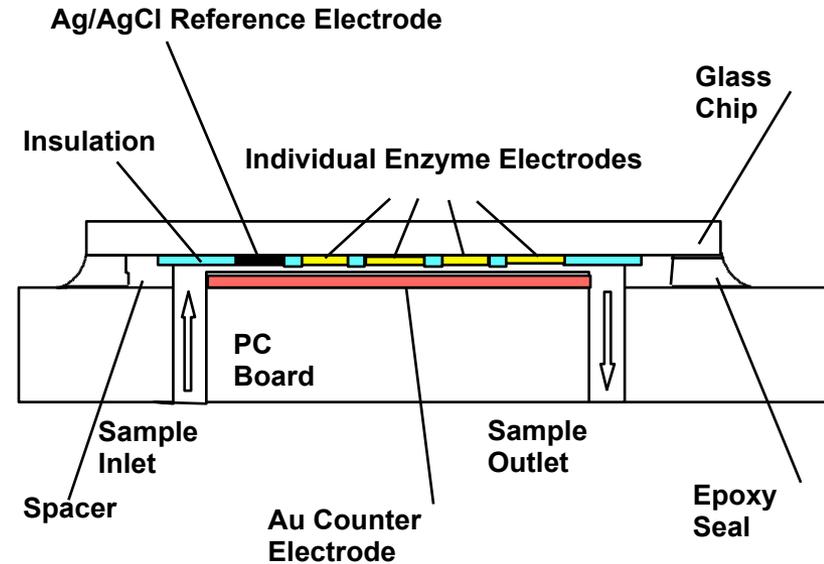
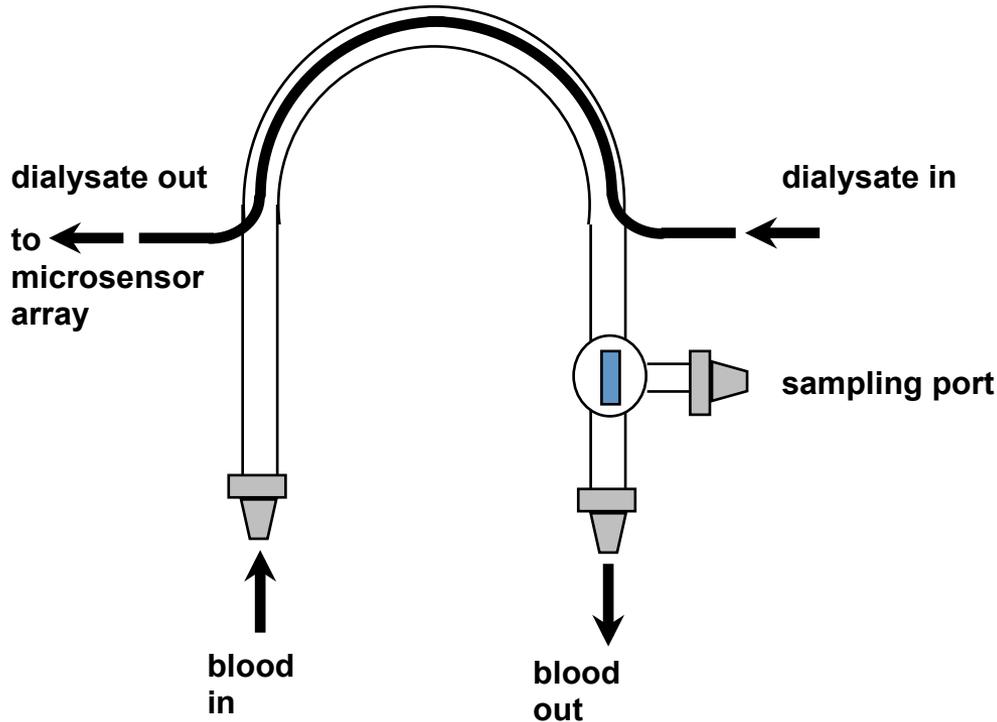
Medical and Biological Engineering and Computing, July 1980, Volume 18, Issue 4, pp 527-537

'Intravascular blood glucose sensing is difficult owing to the complex technology involved and the foreign body reaction of blood.'

'The measurement of glucose in tissue would be easier to handle, but it has not been established whether the extravascular tissue concentration of glucose is sufficiently significant to serve as an input signal for a closed-loop system'



Microdialysis sampling via arterio-venous shunt



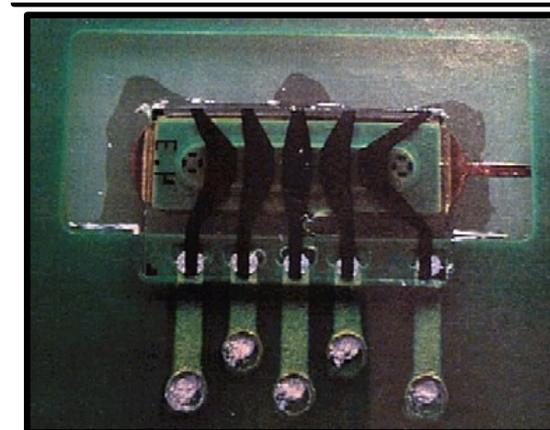
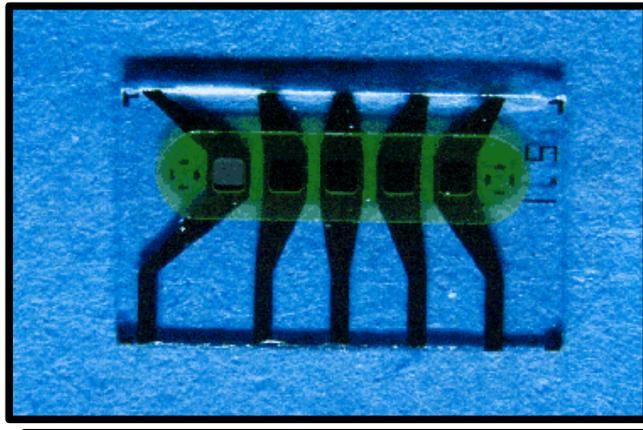
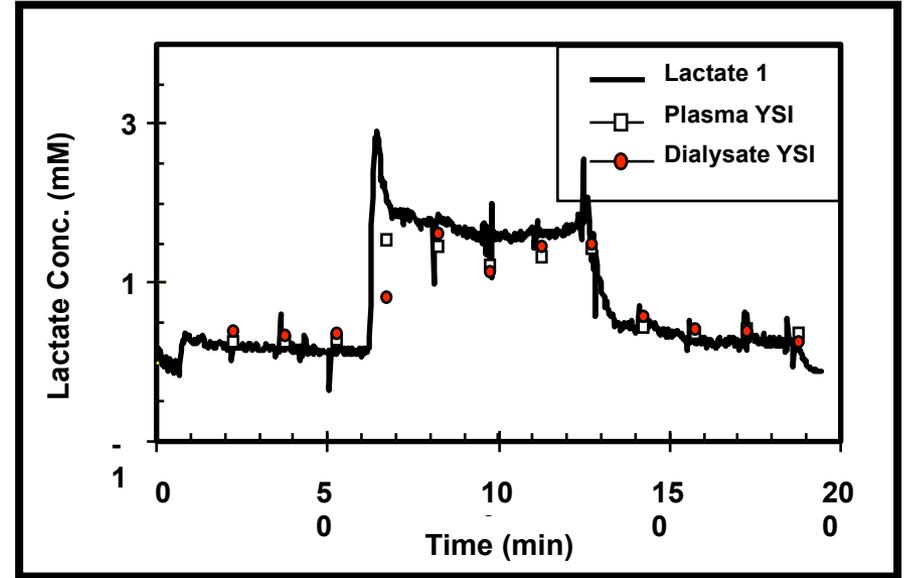
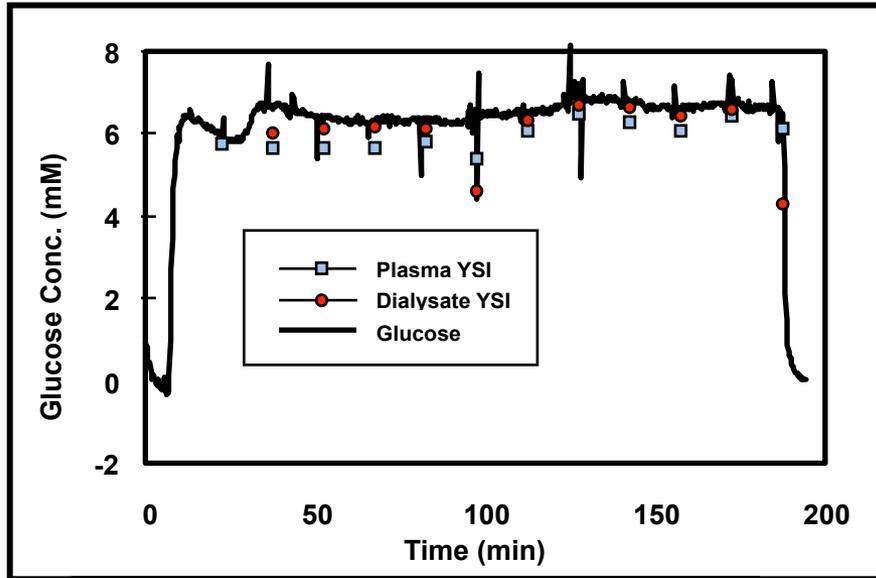
Novel Instrumentation for Real-Time Monitoring Using Miniaturised Flow Cells with Integrated Biosensors, R. Freaney, A. McShane, T.V. Keavney, M. McKenna, K. Rabenstein, F.W. Scheller, D. Pfeiffer, G. Urban, I. Moser, G. Jobst, A. Manz, E. Verpoorte, M.W. Widmer, D. Diamond, E. Dempsey, F.J. Saez de 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!



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'

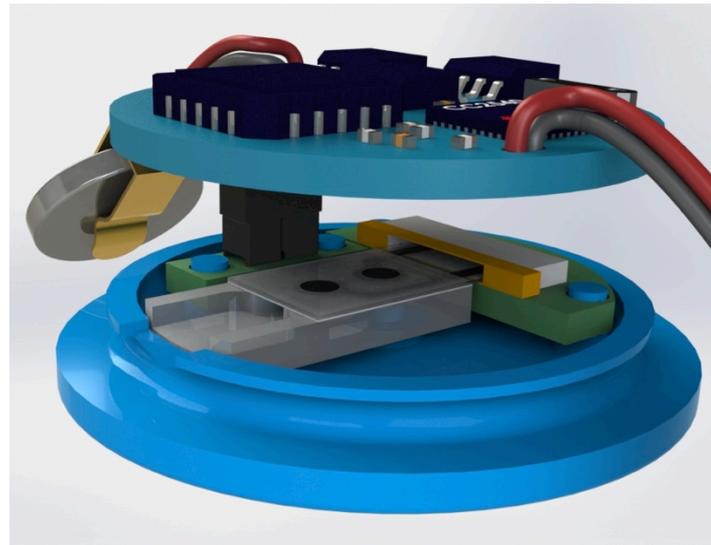
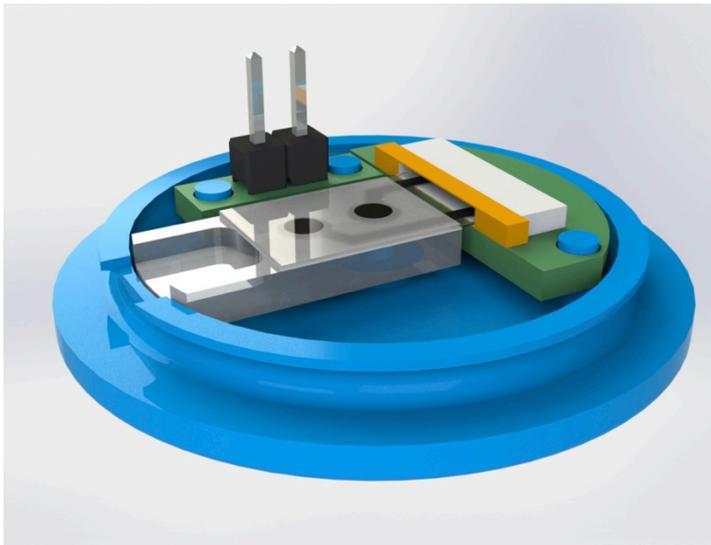
Abbott Laboratories said Tuesday it completed its \$1.2 billion acquisition of Alameda-based TheraSense Inc. after a majority of shareholders approved the transaction a day earlier.

- **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.



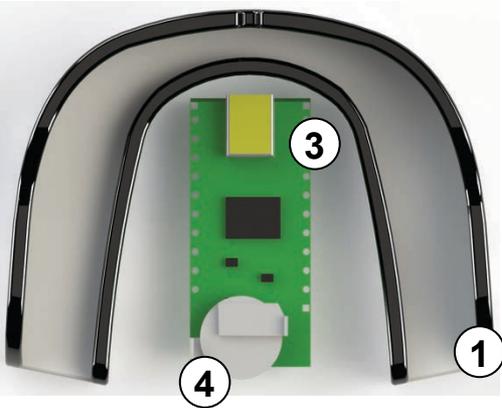


Next Generation: Watch Fluidic Sensor Concept (Shimmer)

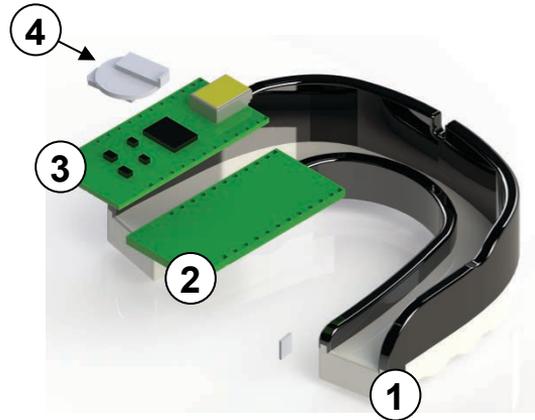




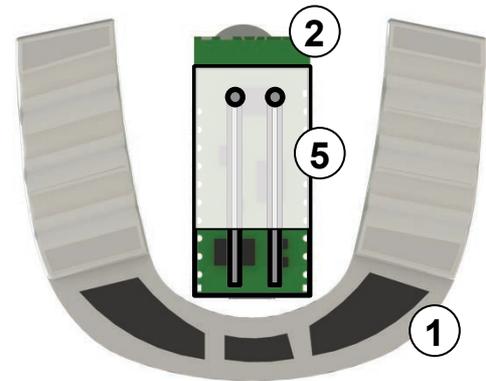
Smart Gumshield



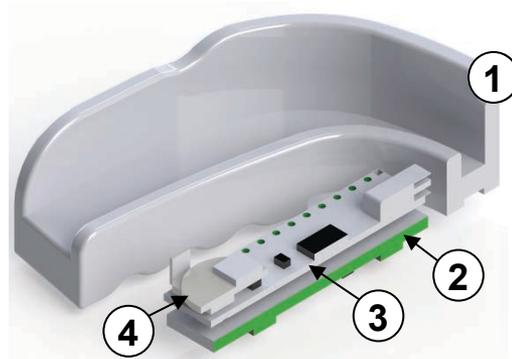
(a) Top View



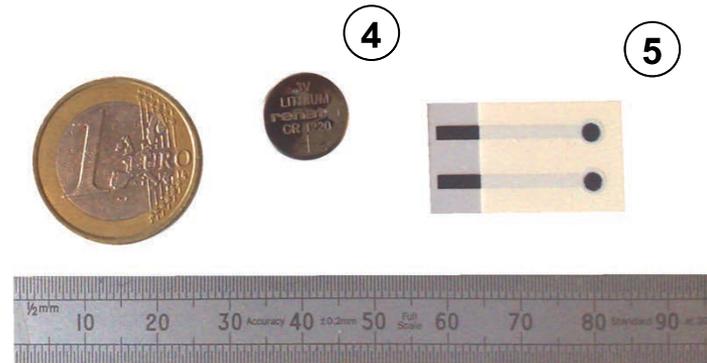
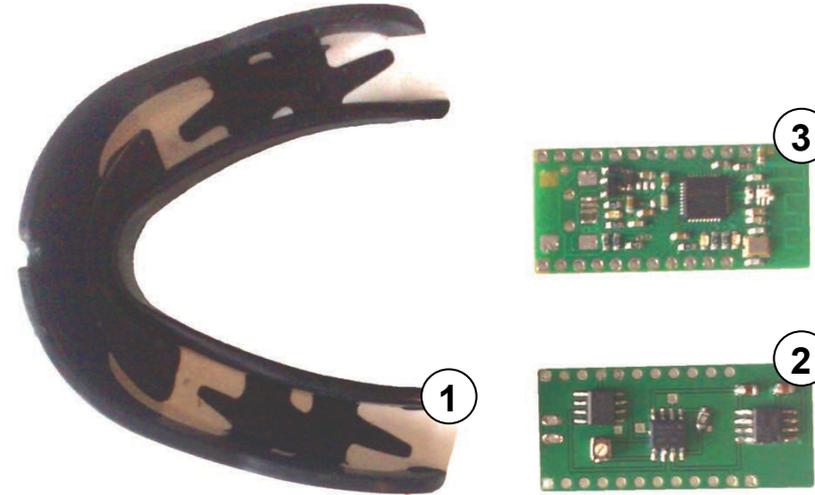
(b) Exploded View



(c) Bottom View



(d) Assembled Sectional View



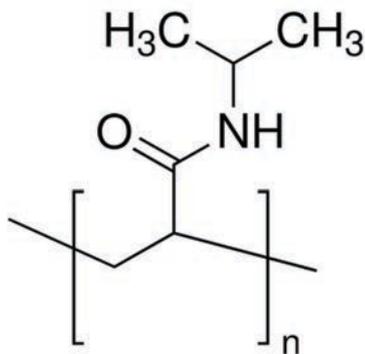
(e) Photo of components laid out



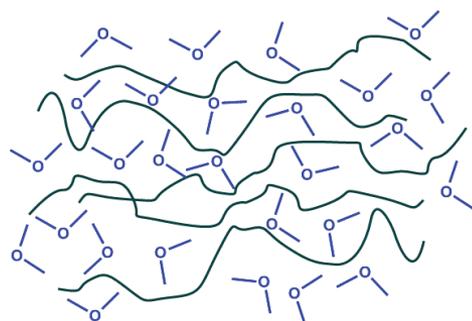
Poly(*N*-isopropylacrylamide)

- pNIPAAm exhibits inverse solubility upon heating
- This is referred to as the LCST (Lower Critical Solution Temperature)
- Typically this temperature lies between 30-35°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



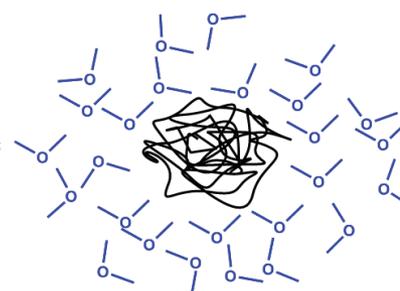
Hydrophilic



Hydrated Polymer Chains



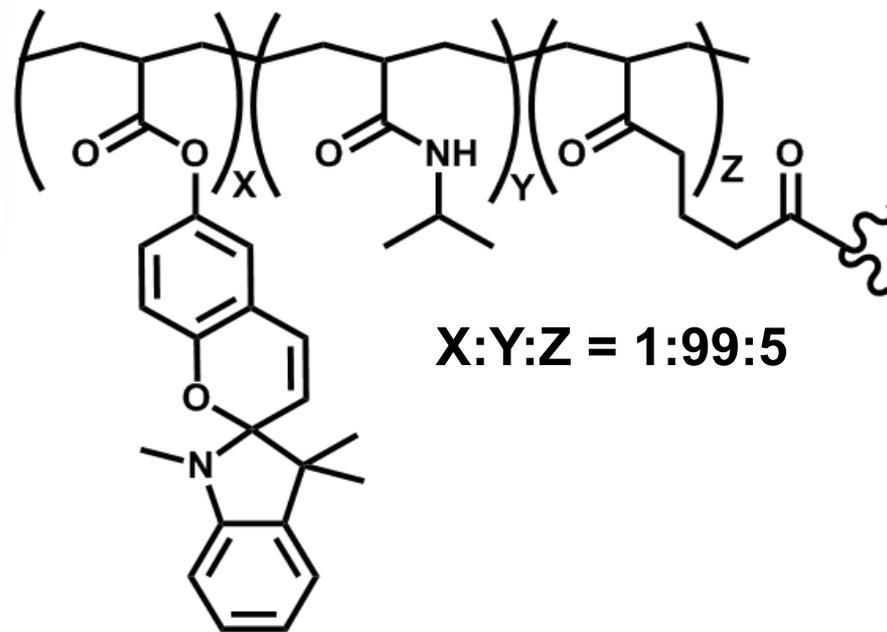
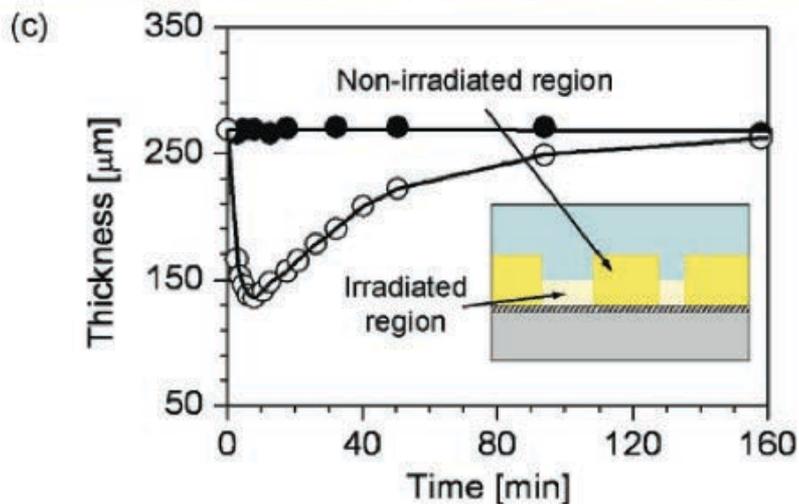
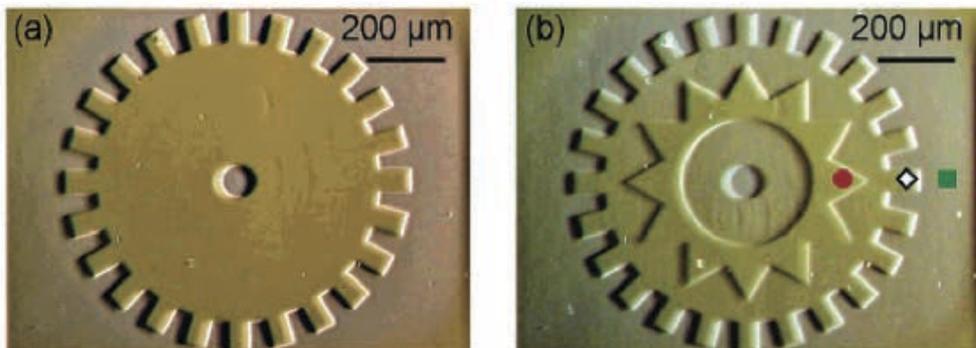
Hydrophobic



Loss of bound water
-> polymer collapse



Polymer based photoactuators based on pNIPAAm



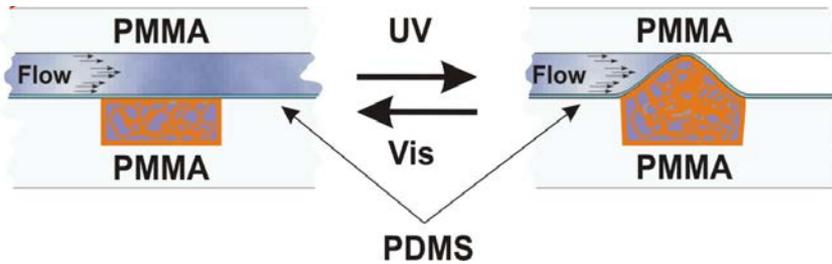
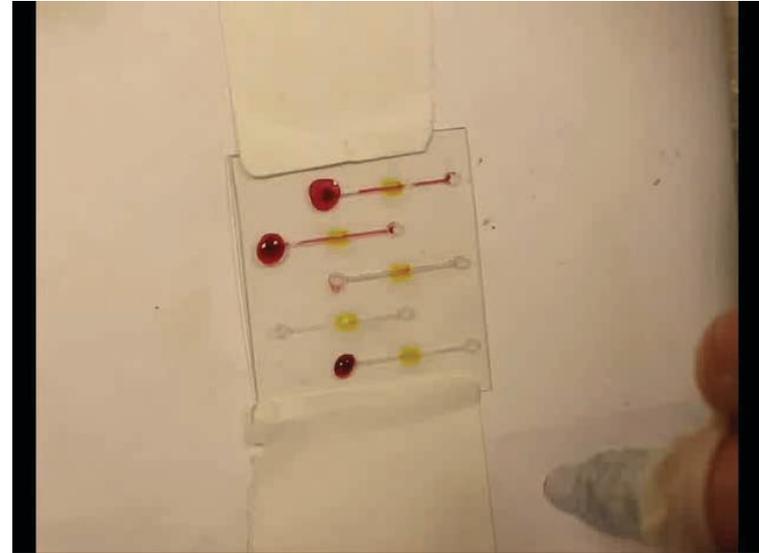
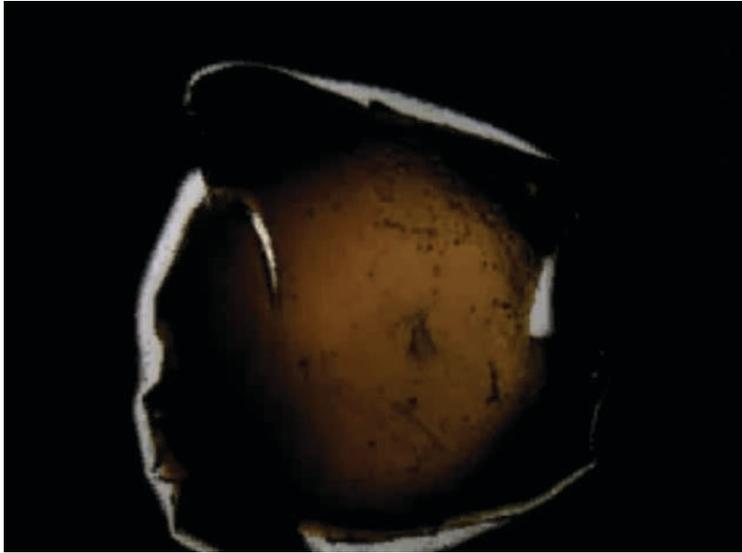
poly(N-isopropylacrylamide) (PNIPAAm)
Formulation as by Sumaru et al¹

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

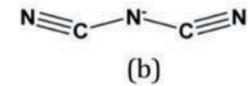
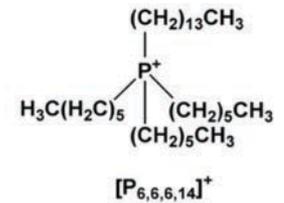
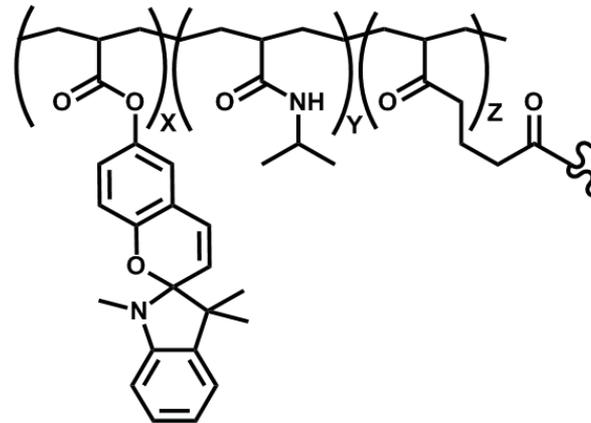
Figure 3. (a, b) Images of the pSPNIPAAm hydrogel layer just after the micropatterned light irradiation. Duration of irradiation was (●, red) 0, (◇) 1, and (■, green) 3 s. (c) Height change of the hydrogel layer in (●) non-irradiated and (○) irradiated region as a function of time after 3 s blue light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



Photo-actuator polymers as microvalves in microfluidic systems



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

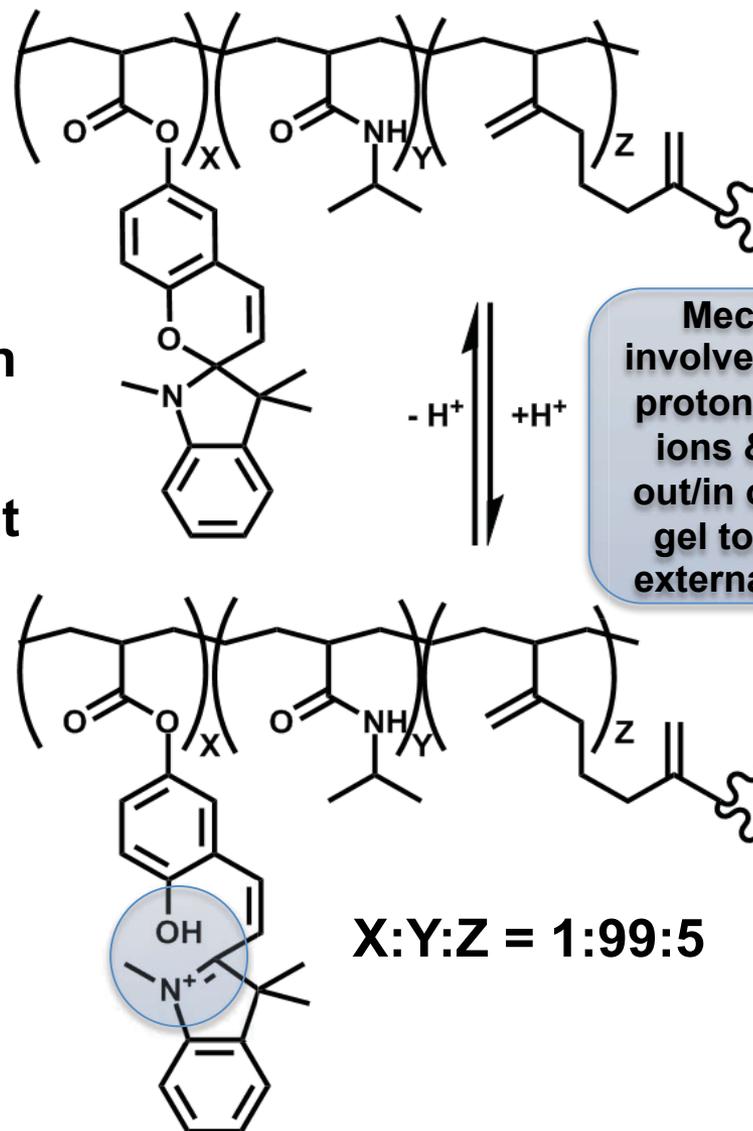
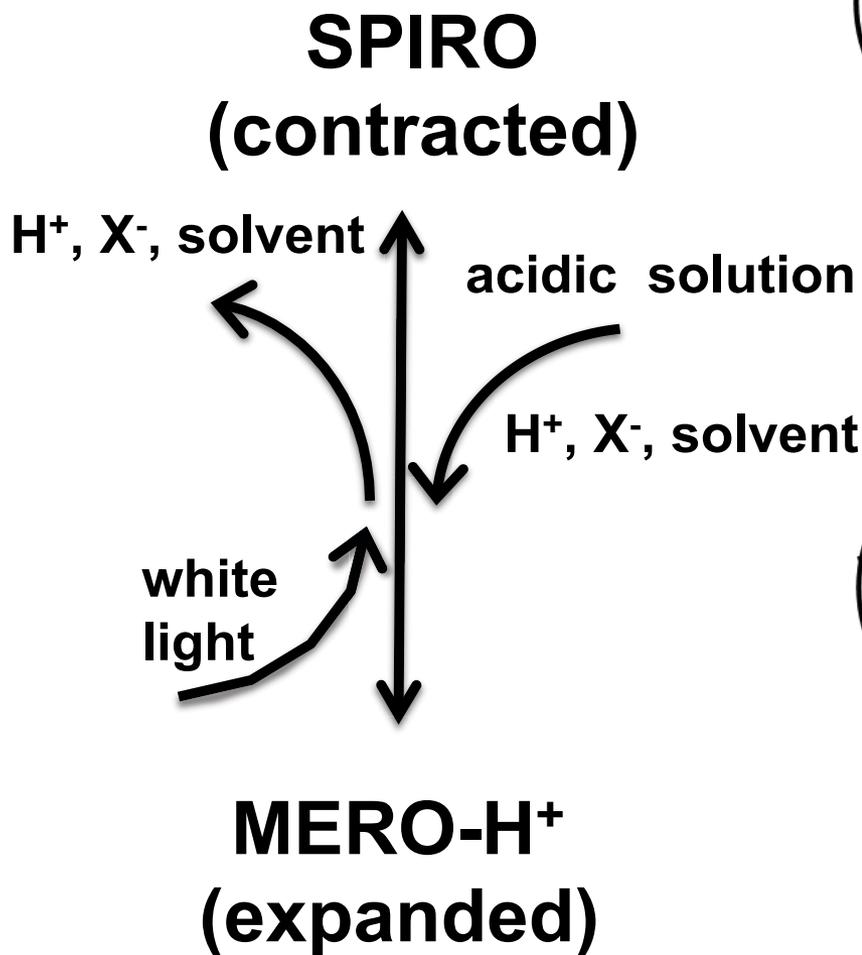


Ionogel-based light-actuated valves for controlling liquid flow in micro-fluidic manifolds, Fernando Benito-Lopez, Robert Byrne, Ana Maria Raduta, Nihal Engin Vrana, Garrett McGuinness, Dermot Diamond, Lab Chip, 10 (2010) 195-201.





Actuation Mechanism



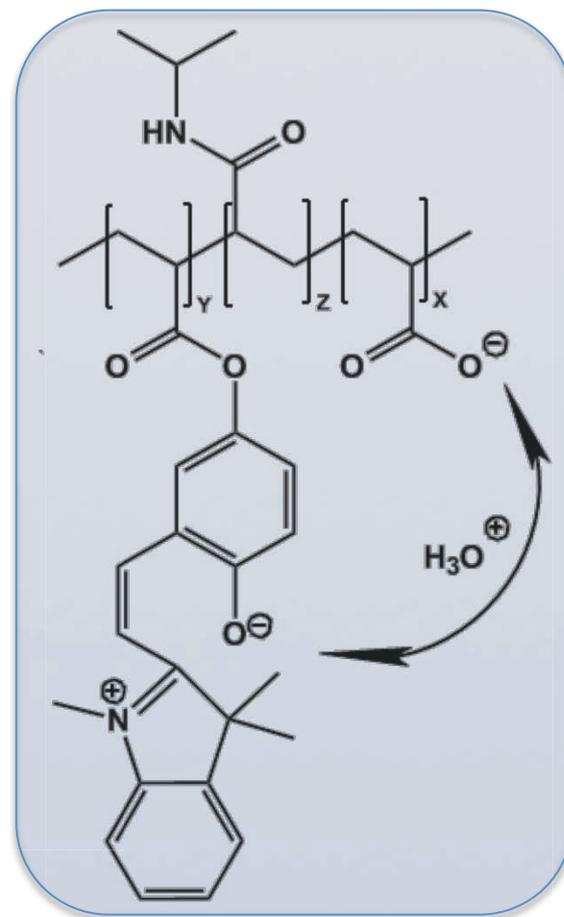
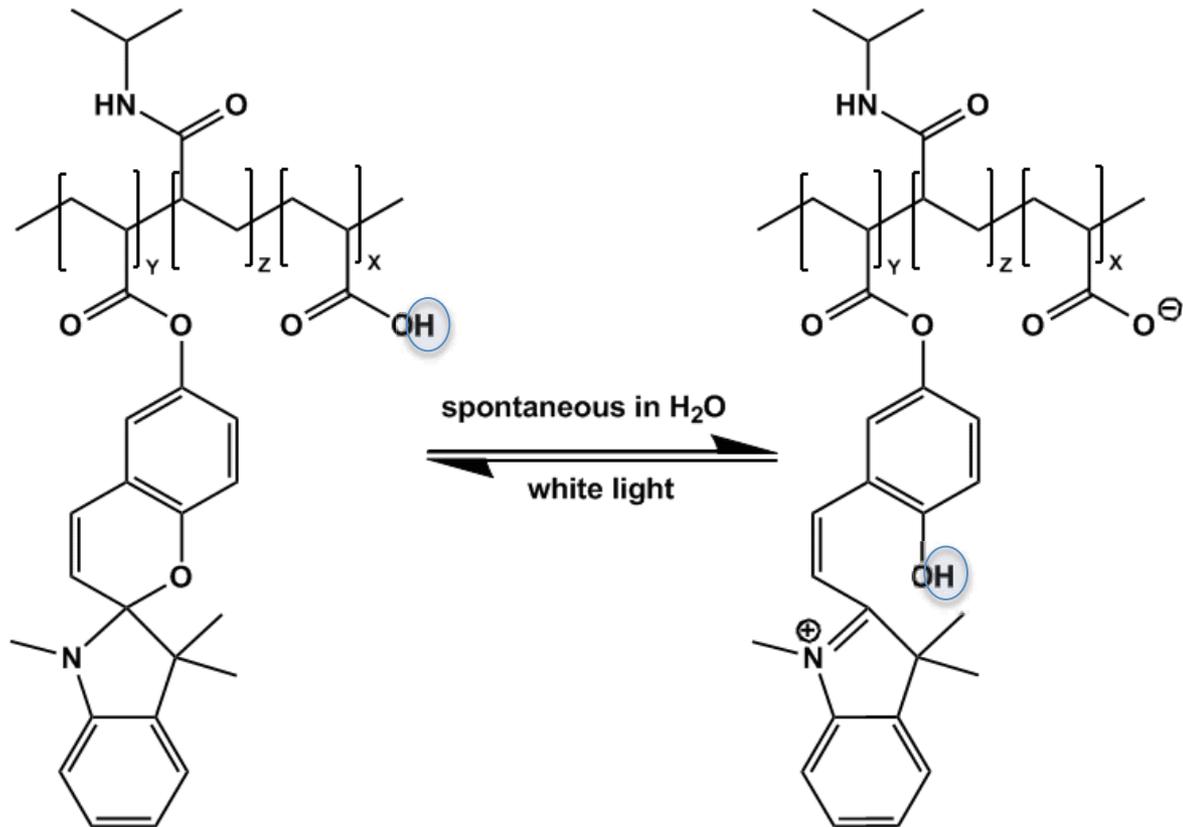
Mechanism involves diffusion protons, counter ions & solvent out/in of the bulk gel to/from the external solution





Self protonating photoresponsive gel

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



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

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





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

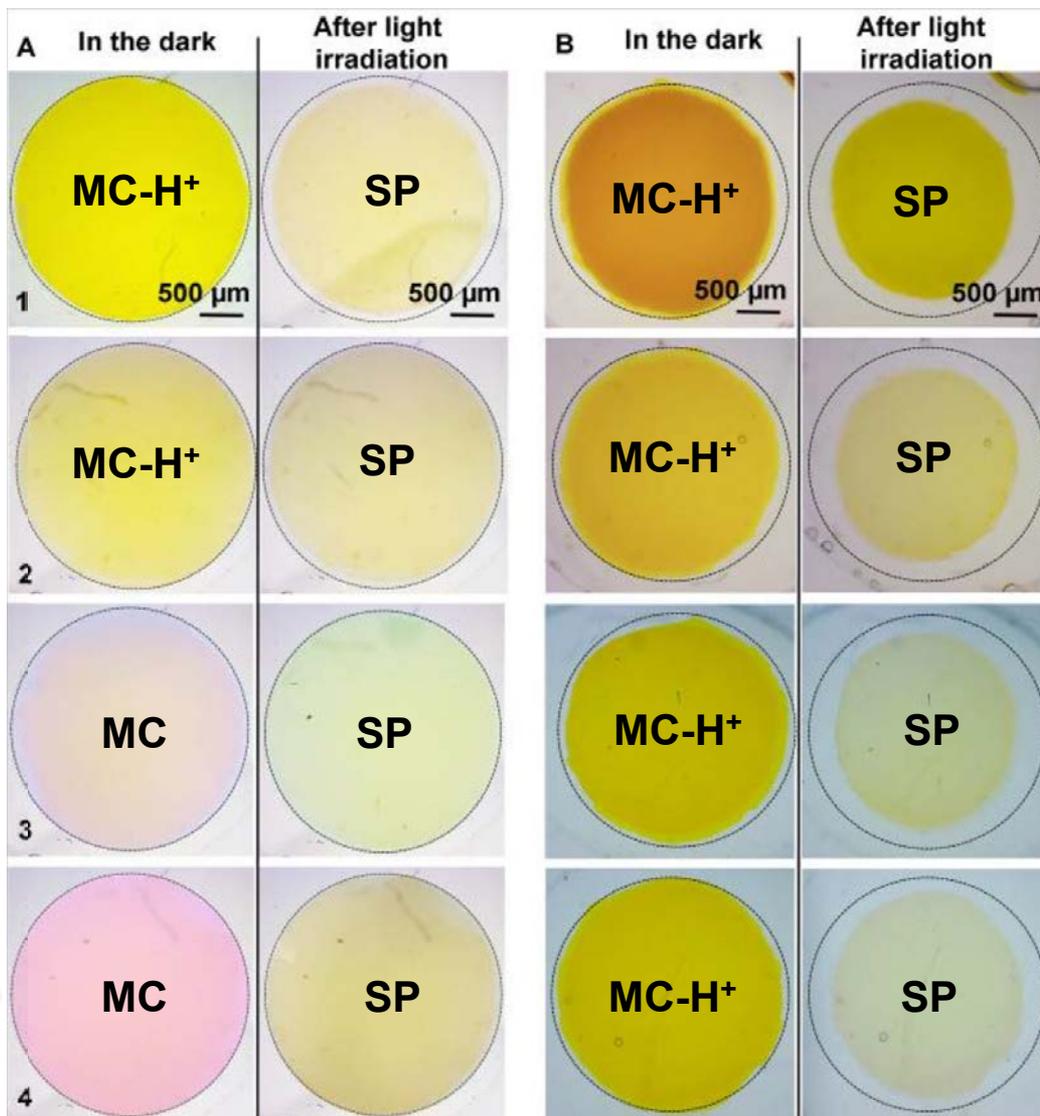
Switching changes from primarily

MC-H⁺ -> 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-H⁺ -> SP+H⁺

Gel actuation continues





Why move the solvent at all?



[sample]/mol l ⁻¹	Ratio H ₂ O/Sample
1.0x10 ⁻⁶	5.56x10 ⁷
1.0x10 ⁻⁹	5.56x10 ¹⁰
1.0x10 ⁻¹²	5.56x10 ¹³

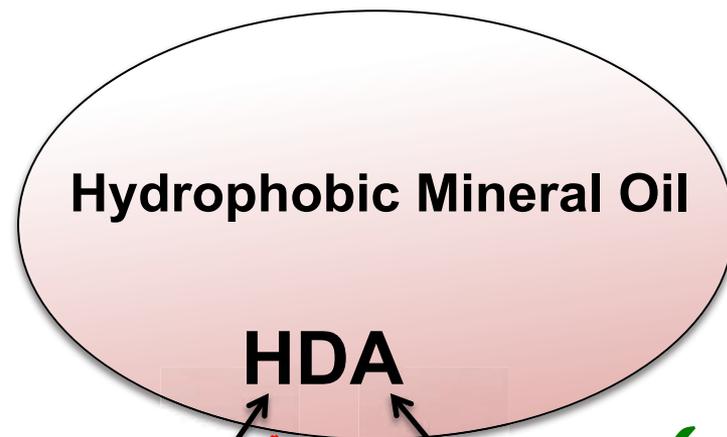
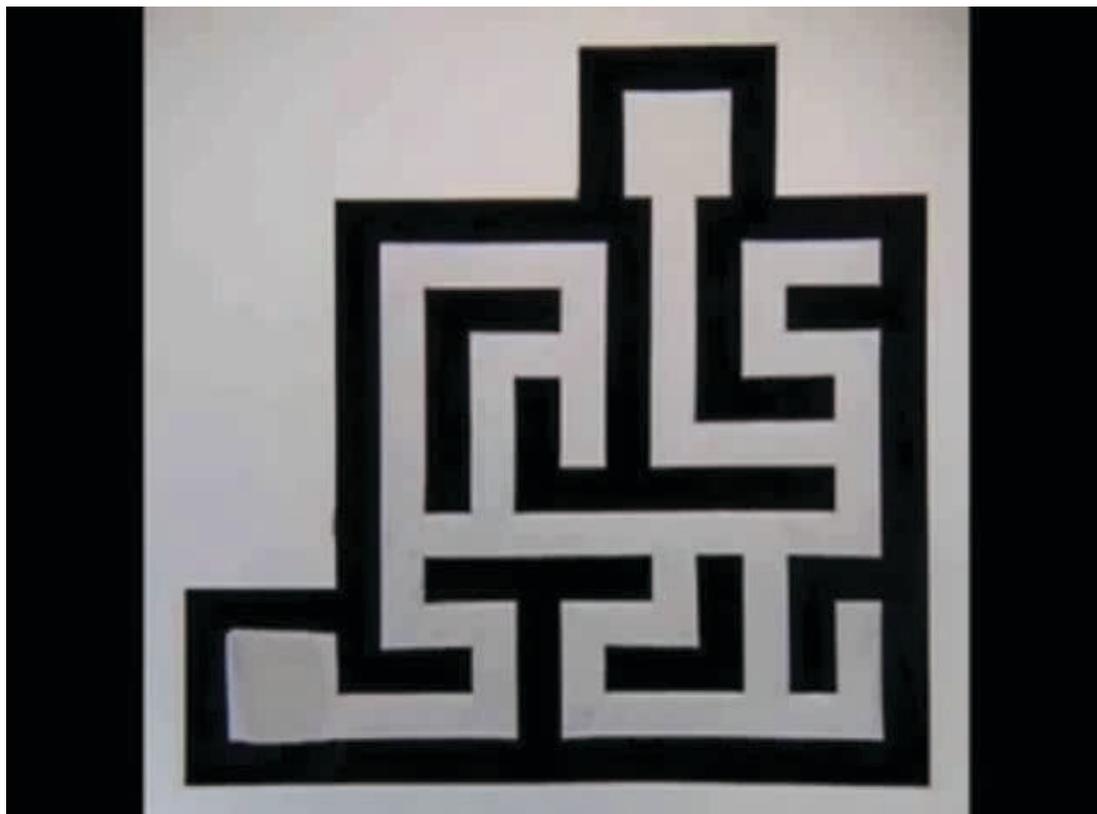
Strategy:

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



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 \sim 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); $\text{HDA} \leftrightarrow \text{H}^+ + \text{DA}^-$

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.



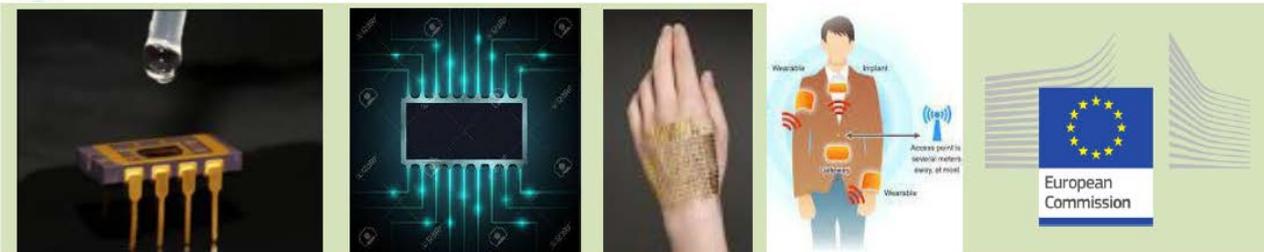


Time to re-think the game!!!

- **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

**EuroNanoForum, Riga, Latvia,
June 9-12**

Vision, Objectives and Position Paper

Michele Penza - Chairman of the ESSC

michele.penza@enea.it

ENEA, Materials Technologies, Brindisi - Italy





Sensor Research Clustering: Steering Committee

Chairman: Michele Penza

Observer: Hans Hartmann Pedersen (EC)

Towards to a cluster on Characterization

Environmental sensors

• D. Diamond

Indoor quality sensors

• A. Schütze (O. Martimort)

Health and safety

(A. Mello)

Monitoring

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Integration and commercialization

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