

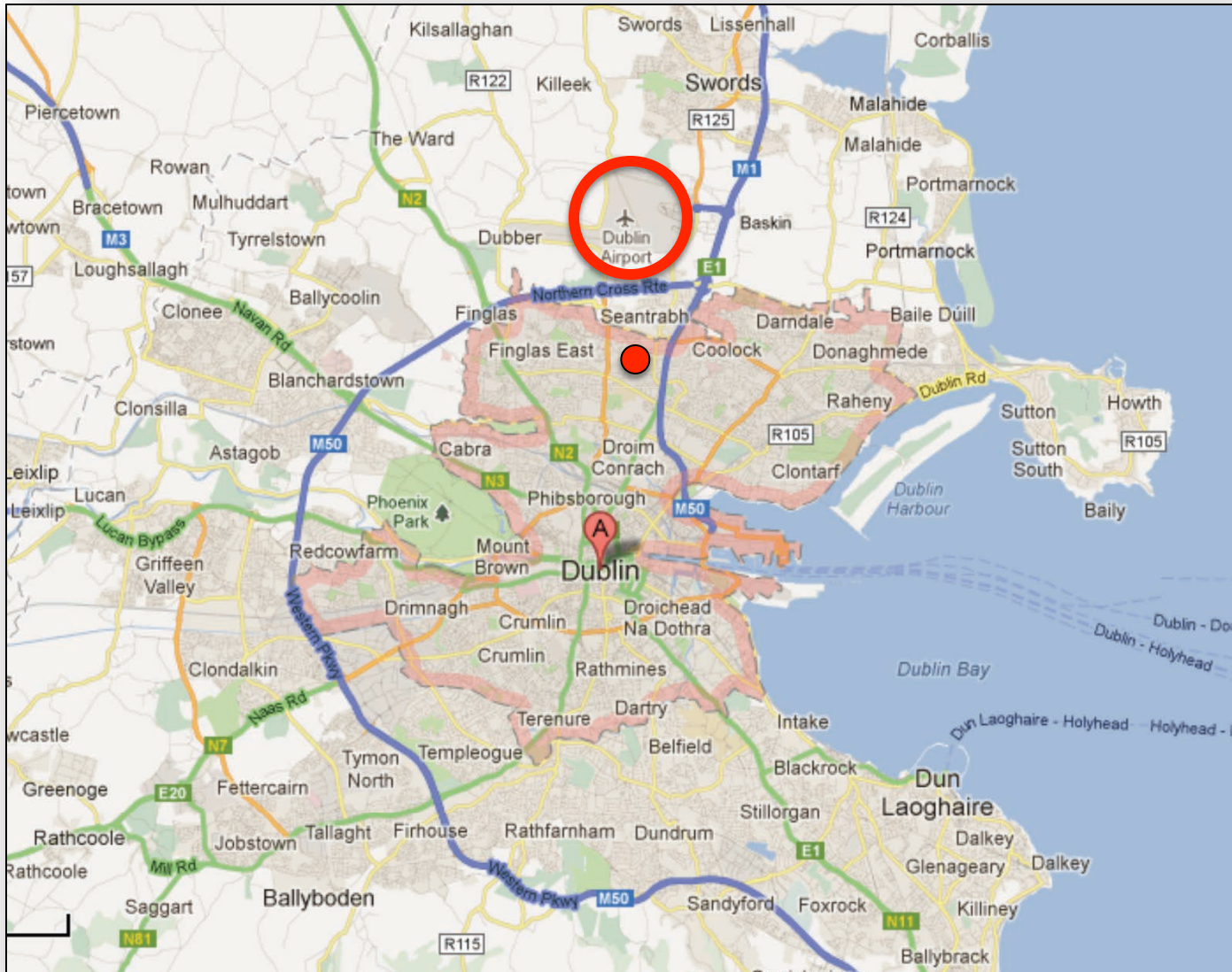
# **Wearable Platforms for Biomarker Monitoring – Challenges and Opportunities**

**Prof. Dermot Diamond  
Director National Centre for Sensor Research  
Funded Investigator, INSIGHT Centre for Data Analytics  
Dublin City University**

**Invited Plenary Lecture presented at  
2015 Flexible and Printed Electronics Conference  
Monterey, California, 23-26 February 2015**



# Dublin & DCU Location





## 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.

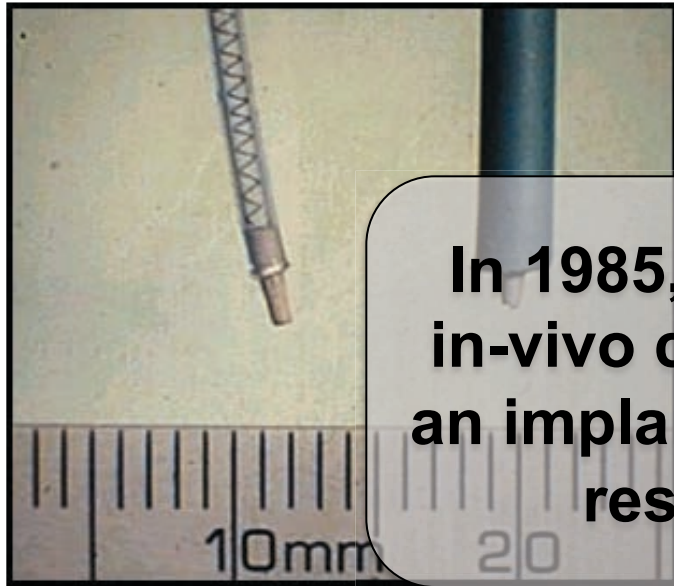
Digital communications networks are at the heart of modern society. The digitalization of communications, the development of the Internet, and the availability of relatively inexpensive but powerful mobile computing technologies have established a global communications network capable of linking billions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



# 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

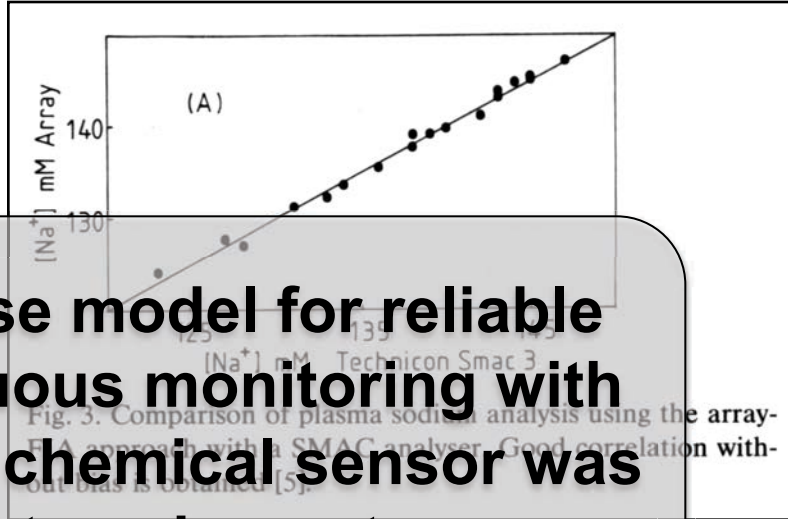
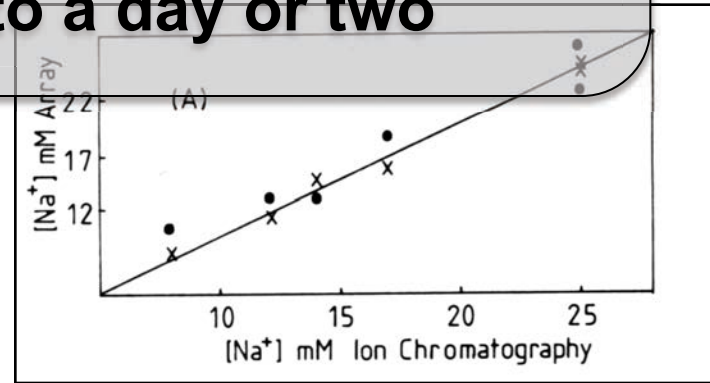


Fig. 3. Comparison of plasma sodium analysis using the array-FIA approach with a SMAC analyser. Good correlation with-out bias is obtained [5].



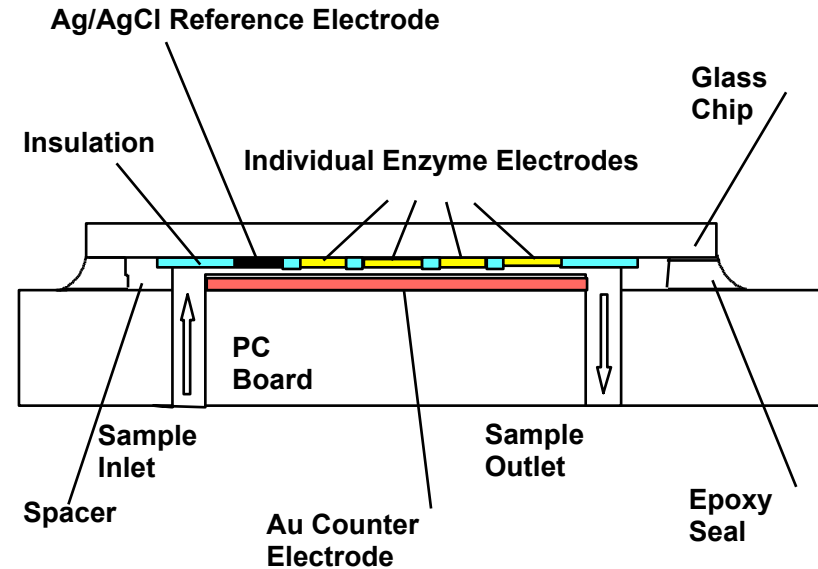
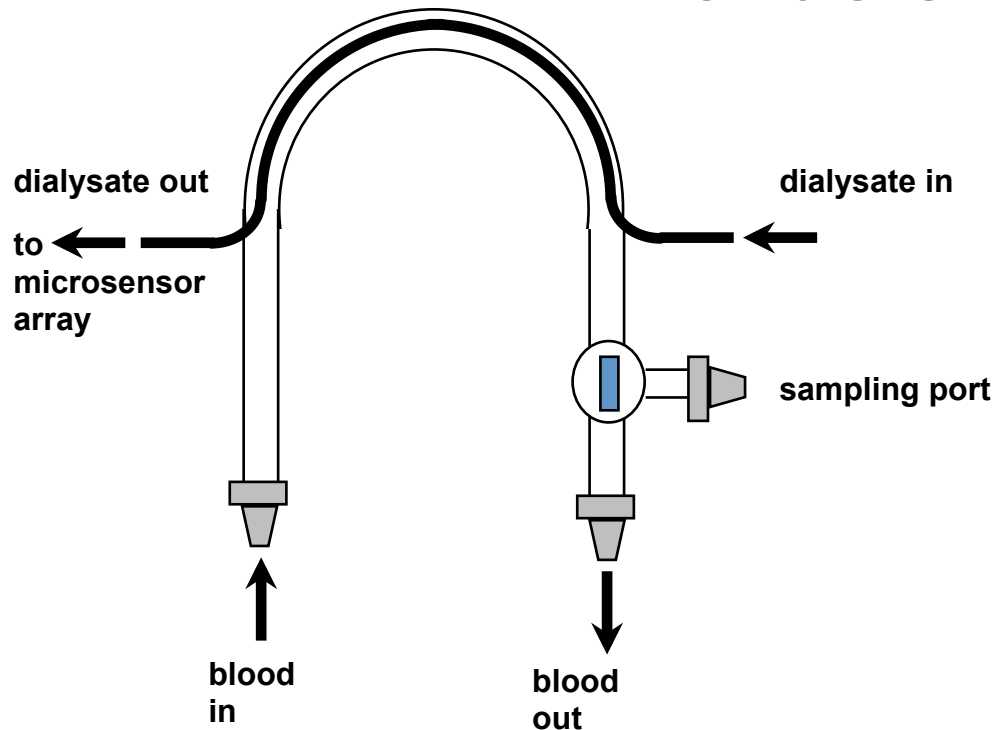
*Anal. Chem.*, **64** (1992) 1721-1728.

Ligand (and variations of) used in many clinical analysers for blood  $\text{Na}^+$  profiling





# Microdialysis sampling via arterio-venous shunt



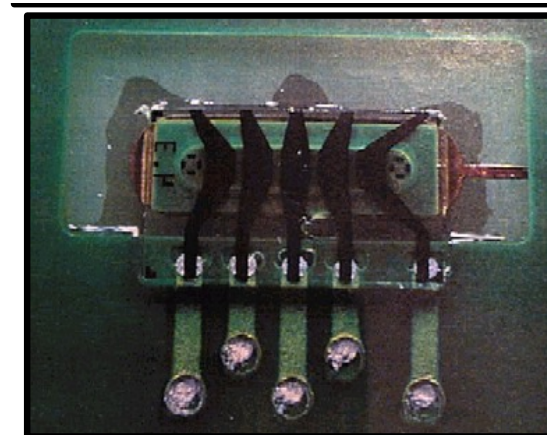
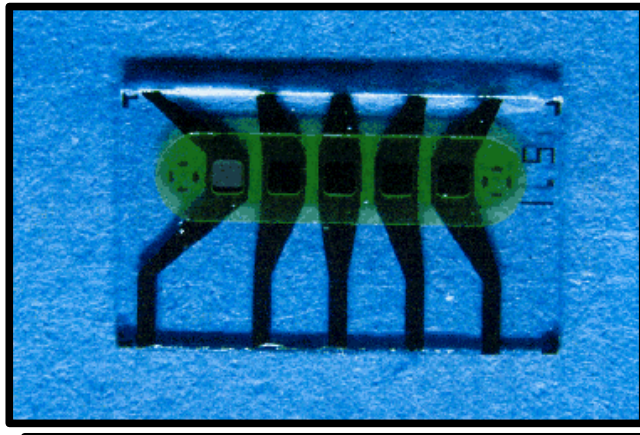
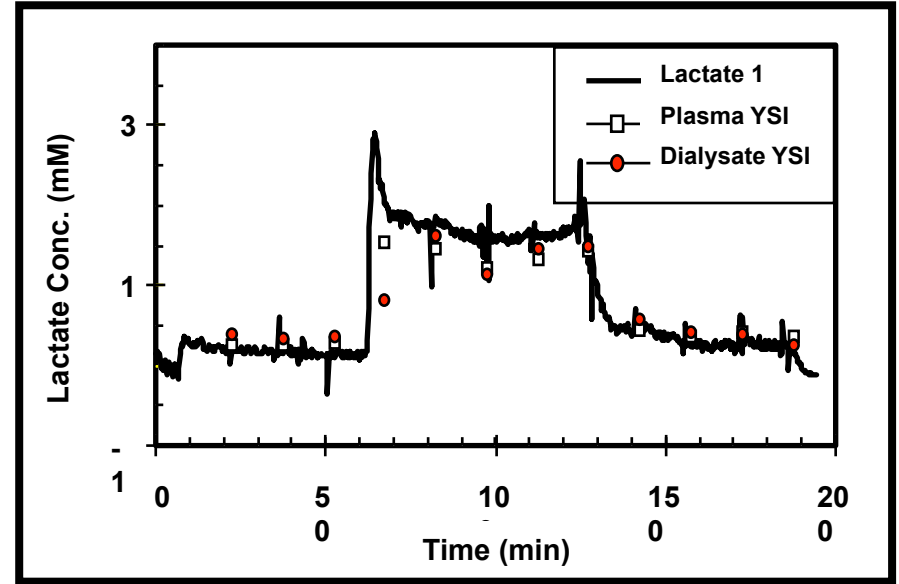
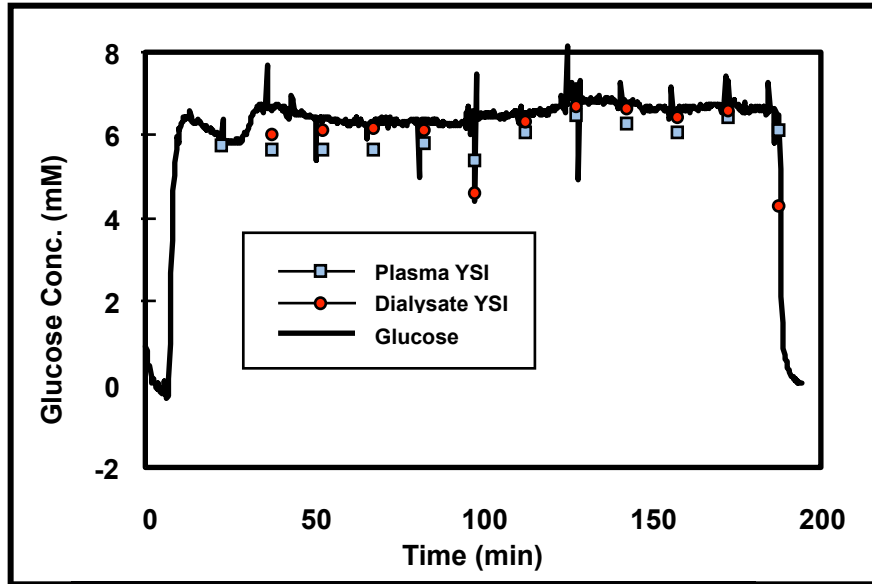
**Novel Instrumentation for Real-Time Monitoring Using Miniaturised Flow Cells with Integrated Biosensors**, R. Freaney, A. McShane, T.V. Keavney, M. McKenna, K. Rabenstein, F.W. Scheller, D. Pfeiffer, G. Urban, I. Moser, G. Jobst, A. Manz, E. Verpoorte, M.W. Widmer, D. Diamond, E. Dempsey, F.J. Saez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



# Artificial Pancreas



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

Used a Technicon segmented flow colorimetric glucose analyser

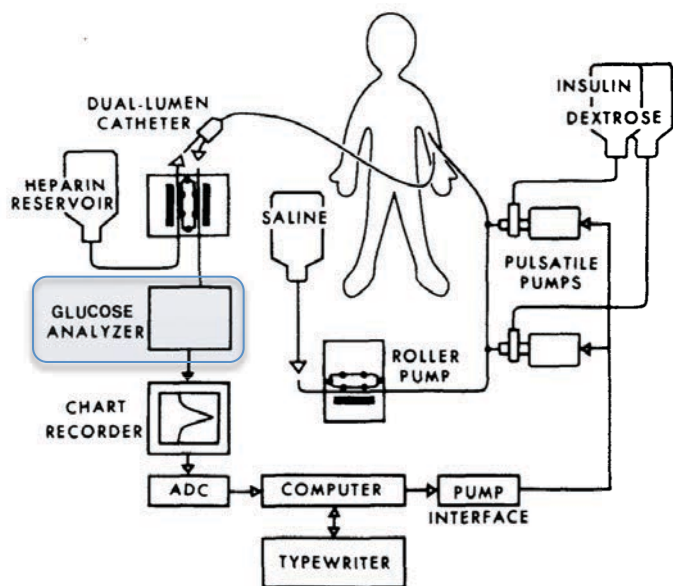
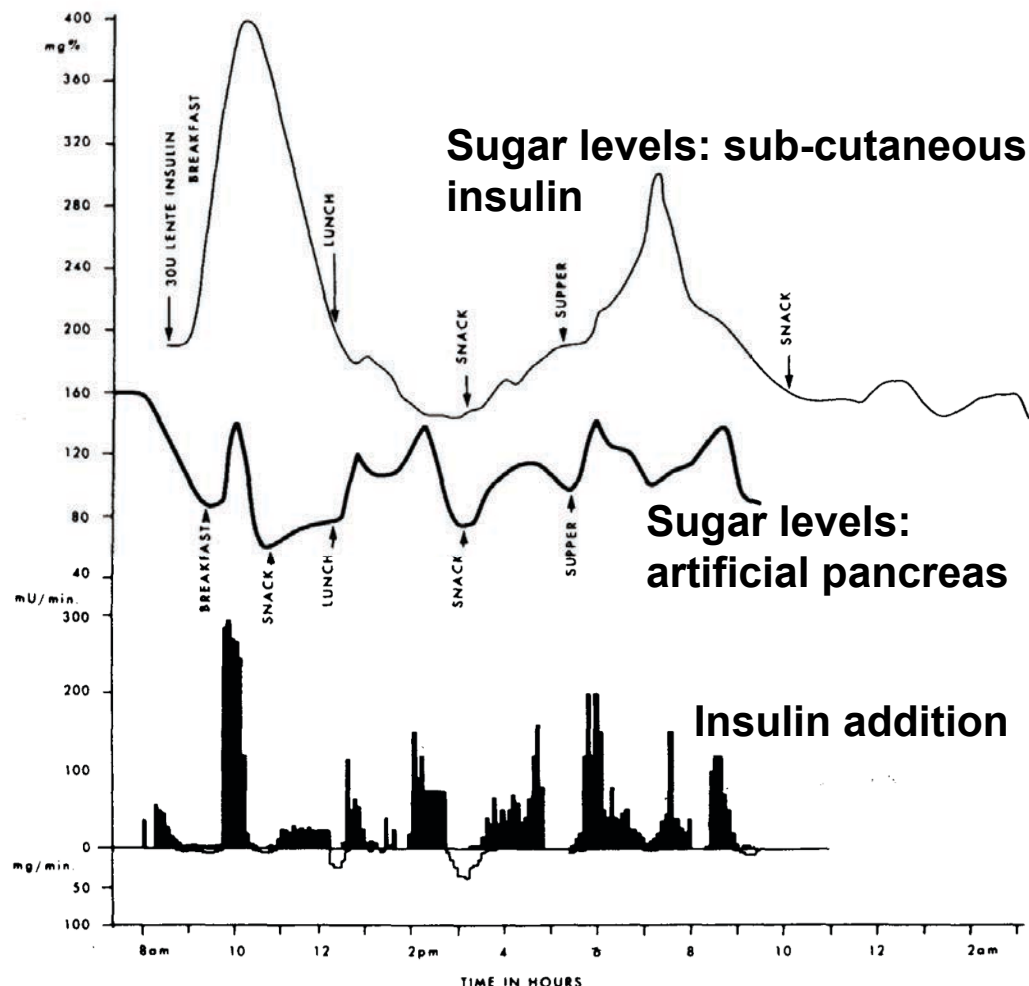


FIG. 1. Schematic diagram of apparatus used for monitoring and automatic regulation of blood sugar.



A M Albisser, 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)





# Implantable Artificial Pancreas



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.'**

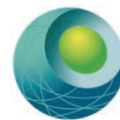
**'The measurement of glucose in tissue would be easier to handle, but it has not been established whether the extravascular tissue concentration of glucose is sufficiently significant to serve as an input signal for a closed-loop system'**







# 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



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Indications and Important Safety Information

IFU (Full Version)

FreeStyle Navigator®

Know The FreeStyle Navigator System

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

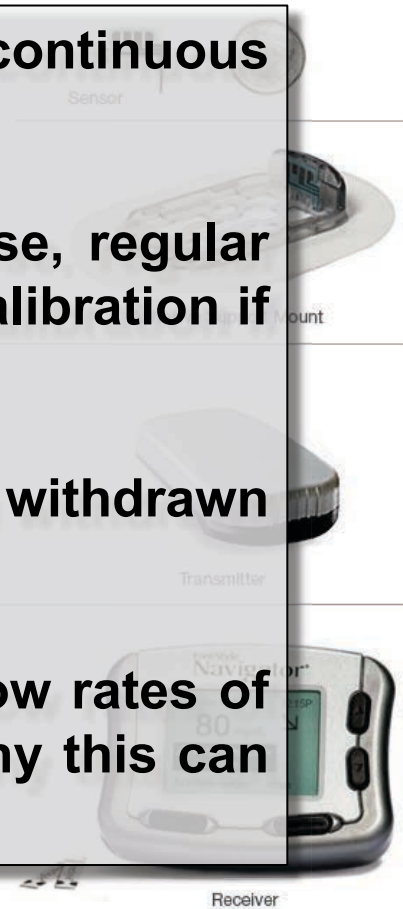
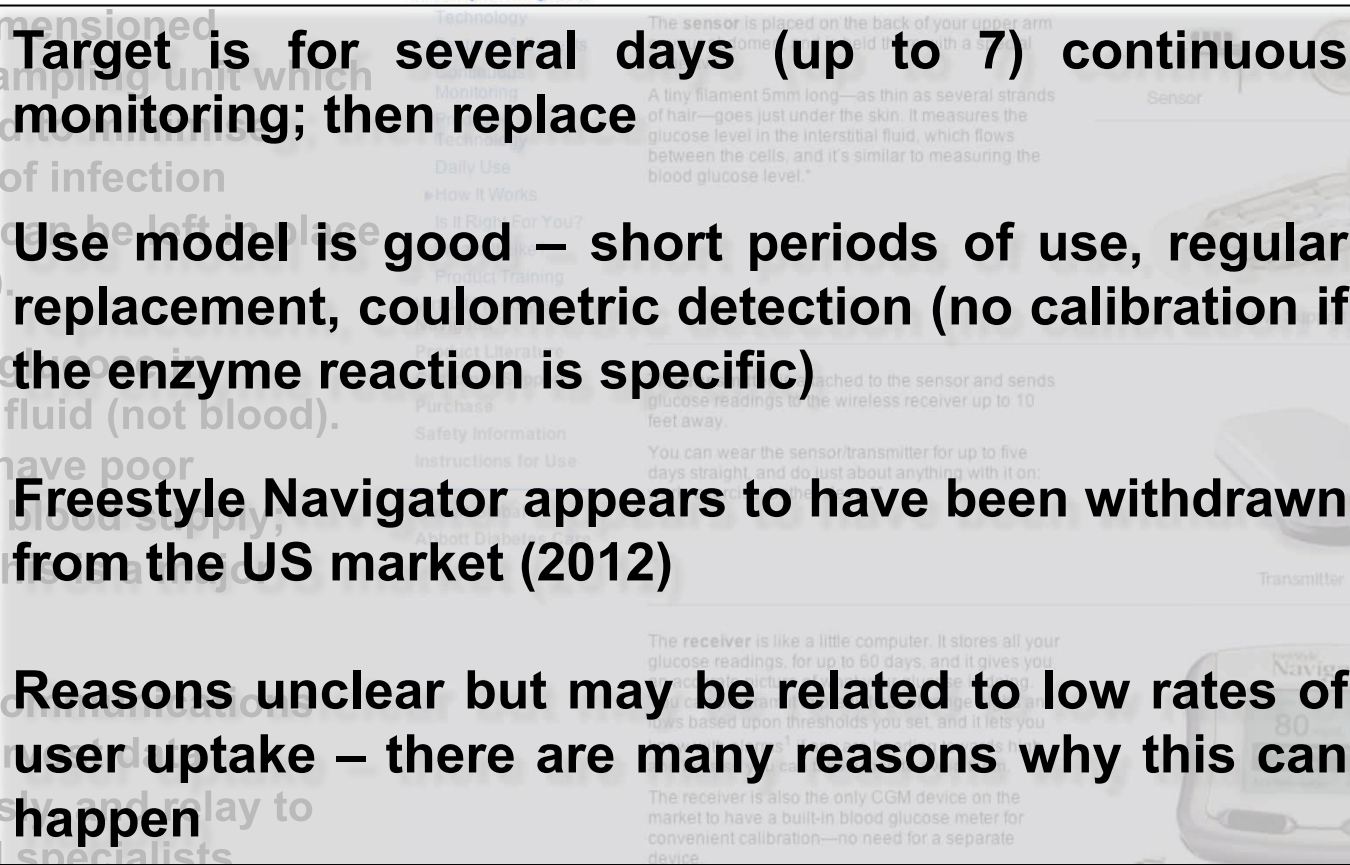
Use model is good – short periods of use, regular replacement, coulometric detection (no calibration if the enzyme reaction is specific)

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

Reasons unclear but may be related to low rates of user uptake – there are many reasons why this can happen

Enables trending, aggregation, warning....

- Combines microfluidics with a micro-dimensioned filament sensor is designed to minimize incidence of infection (therefore for 5 days)
- Measures interstitial fluid (not blood). Diabetics have poor peripheral blood supply, therefore t advance.
- Wireless communication used to have continuous data relay to carers and specialists. Enables trending, aggregation, warning....





# Apple, iWatch & Health Monitoring

Independent.ie 

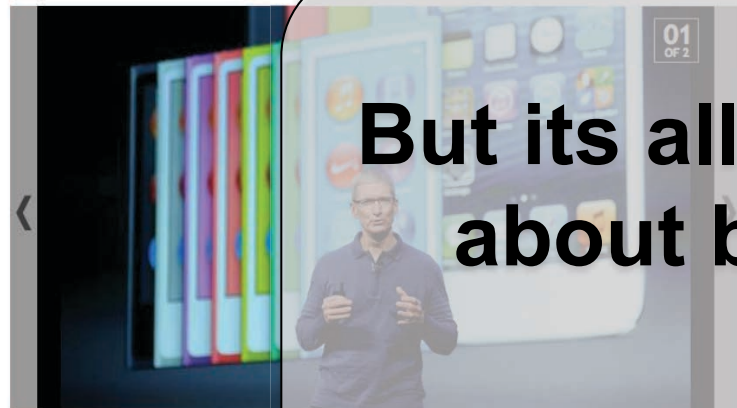
Wednesday 7 May 2014

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Independent.ie Business Technology

## Apple hiring medical device staff, shares break \$600 mark

0 Comments Recommend 7 Tweet 89 +1 Share



Apple Inc CEO Tim Cook

**But its all gone very quiet about biosensors.....**

**'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.





# Google Contact Lens

United States Patent Application 20140107445

Google Smart Contact Lenses Move

Kind Code A1 Liu; Zenghe April 17, 2014

Microelectrodes  
Sensor

Abstract

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

Closer to Reality

Use model is 24 hours max, then replace;

likely to leverage Google Glass\* infrastructure;

Novartis now working with Google.

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

\*Google Glass project has been abandoned! (Jan 15 2015) see

<https://plus.google.com/+GoogleGlass/posts/9uiwXY42tvc>

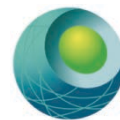


A contact lens with embedded sensor for...  
M. Cowan, T. Laitinen, and B. A. Parviz,  
*Biosensors & Bioelectronics*, 2011, 26, 3290-3296.

Google's plan to bring smart contact lenses to diabetes sufferers inched closer to reality as...  
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 light, whenever her blood sugar falls to dangerous levels.

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

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 120–360s.



**After decades of intensive research, our capacity to deliver chemo/bio-sensors capable of long-term autonomous use of in remote locations is still very limited.**

**Blood is by far the best diagnostic medium, but no sensor will function acceptably for more than a few days continuous exposure to blood**

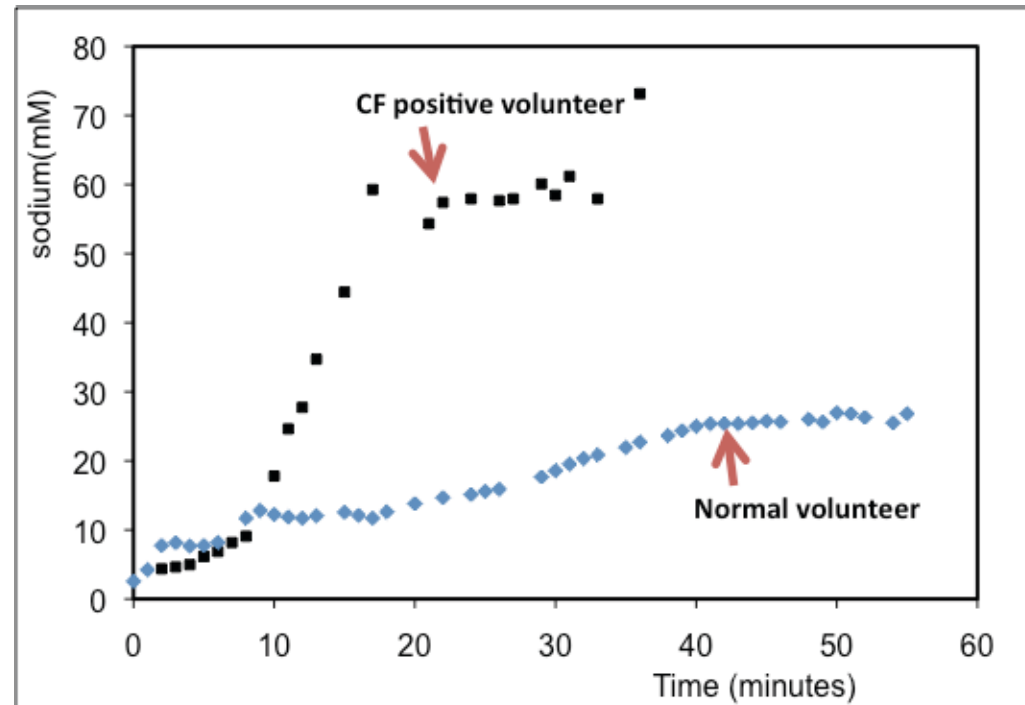




# Na<sup>+</sup> monitoring in sweat using wearable sensor



- **Measurements successfully made with CF-positive and normal volunteers**
  - clear difference between CF+ and normal levels
- **Elevated levels of Na<sup>+</sup> found in sweat of CF+ volunteers as expected**
- **Enables electrolyte loss to be estimated when combined with sweat rate/volume data**
- **Important for rehydration**
- **Interesting observations**
  - elevated viscosity of sweat of CF+ volunteers
  - sweat rate much lower – in some cases no sweating occurred
  - could not exercise as long as normal volunteers



- **Diagnostic CF threshold >60mM [Na<sup>+</sup>] reached**
- **Issue with initial delay**
  - arises from inherent delay in onset of sweating
  - contribution from device 'dead-volume'

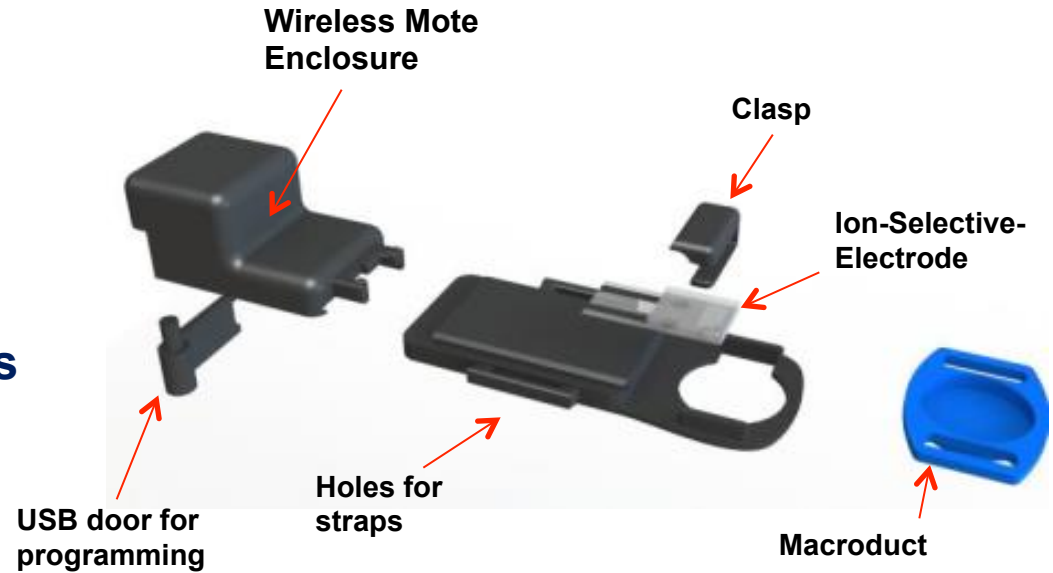




# Na<sup>+</sup> Monitoring in Sweat

Real time monitoring of Sodium in Sweat through screen printed potentiometric strips:

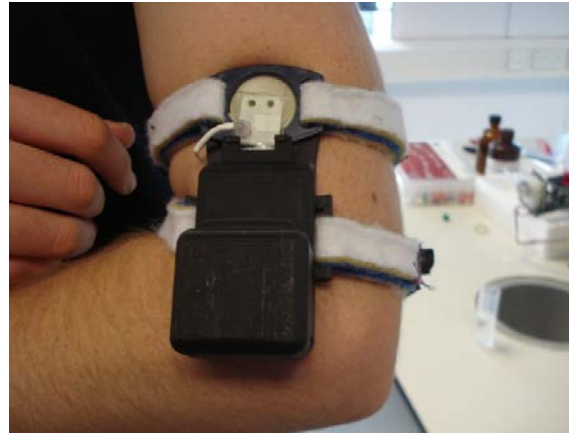
- Monitoring of athletes during exercise
- Monitoring clinical conditions e.g. Cystic Fibrosis patients



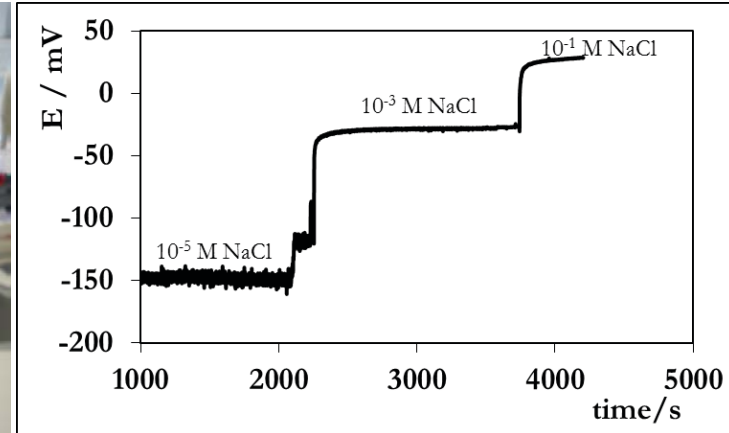
Macroduct sweat sampling unit (Wescor Corporation) Speed x4



Pilocarpine based sweat sampling



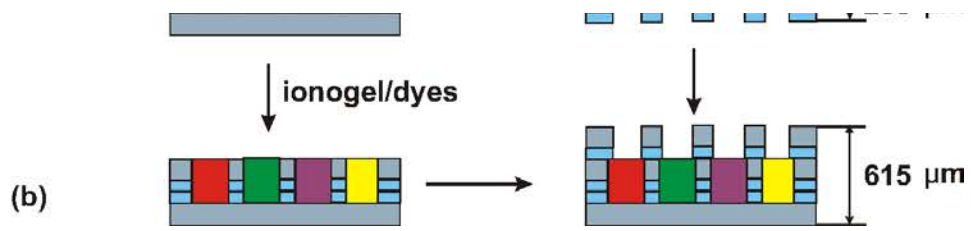
Exercise based sweat sampling



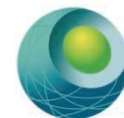
Sensor calibration



# Microfluidic pH Sensor fabrication

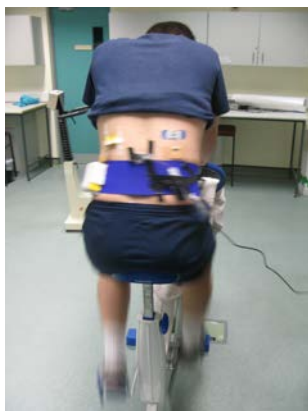
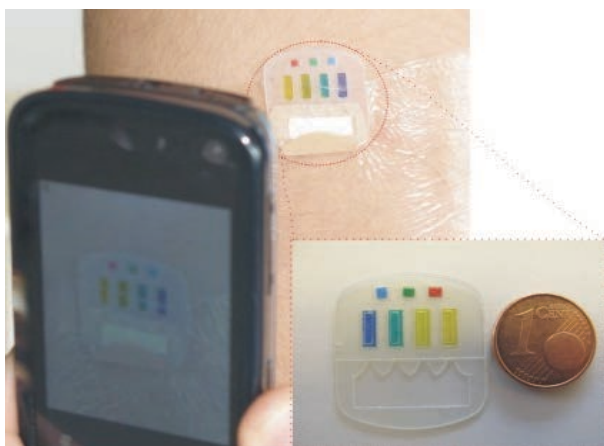






# pH Monitoring via Smart Phone App

- COLOUR CHANGE VISIBLE BY EYE
- SMARTPHONE APP TO DETECT pH AUTOMATICALLY
- REAL TIME VIDEO ANALYSIS IS POSSIBLE



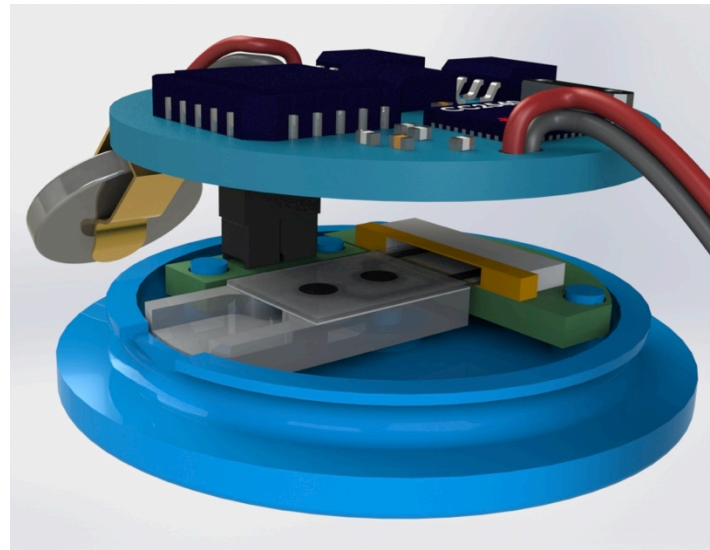
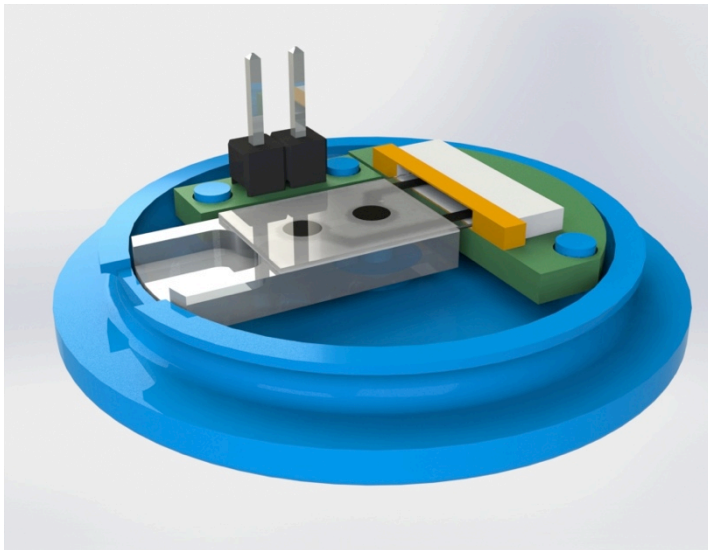
Time [min]	pH Meter	Dyes Prediction (pH)	% RE
20	6.38	5.89	7.68
30	5.8	5.56	4.14
40	5.67	5.67	0.00
50	5.95	5.63	5.38

**SWEAT pH DETERMINATION USING THE BARCODE IN AN ATHLETE DURING A 50 MIN TRAINING PERIOD**



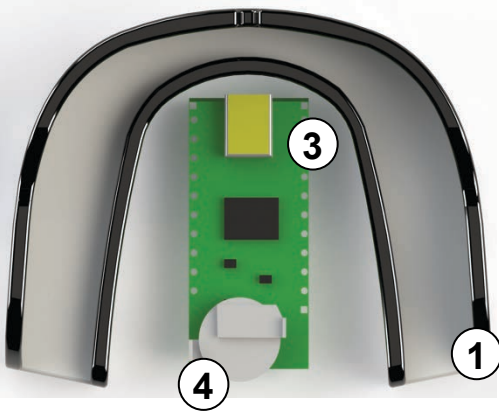


# Next Generation: Watch Fluidic Sensor Concept (Shimmer)

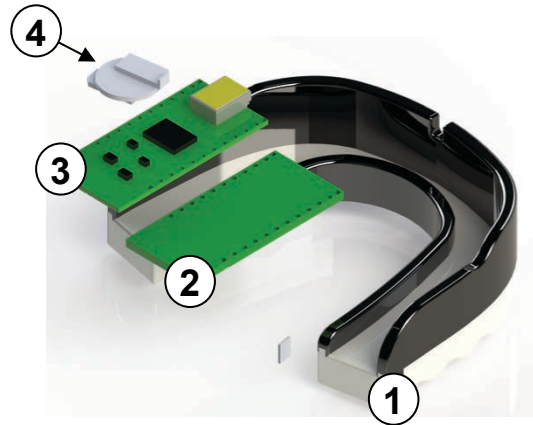




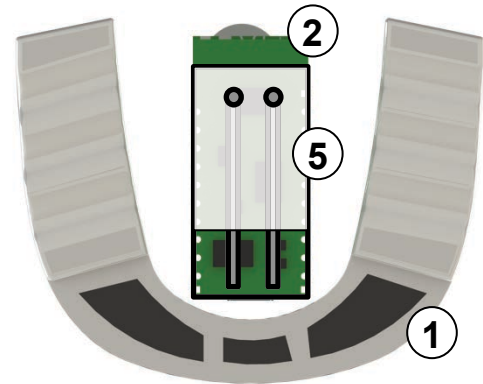
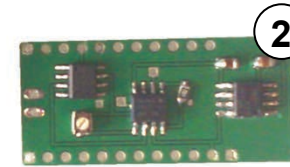
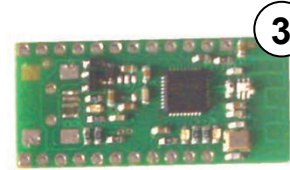
# Smart Gumshield



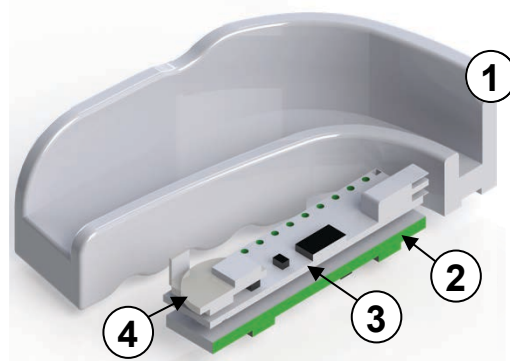
(a) Top View



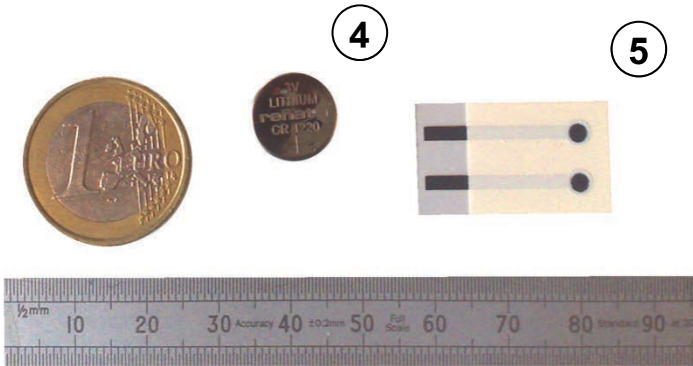
(b) Exploded View



(c) Bottom View



(d) Assembled Sectional View

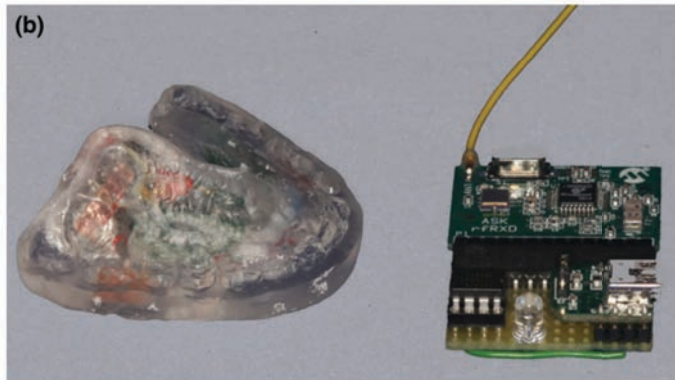
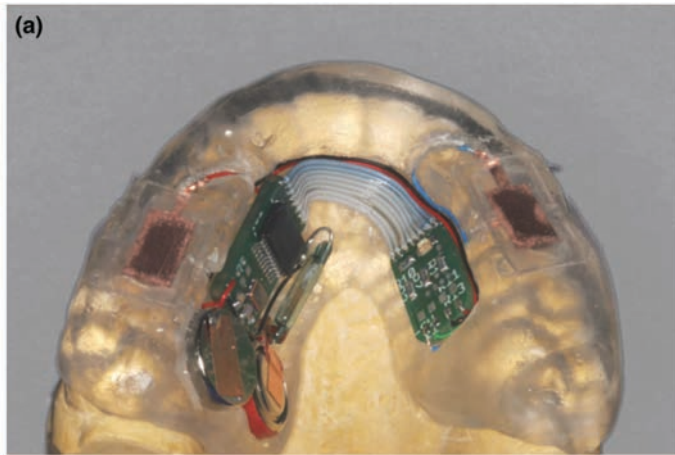


(e) Photo of components laid out

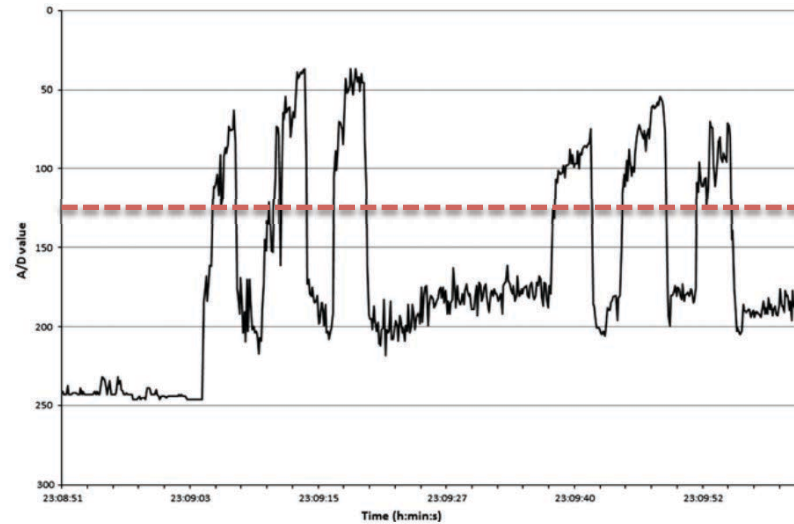




# Smart Splint – Preliminary In-Vivo Data



**Fig. 1.** (a) First prototype splint with electronics exposed before hermetic sealing (b) splint containing sensors and wireless receiver circuit.



**Fig. 2.** *In vivo* response of wireless sensor-containing occlusal splint to forces simulating phasic bruxism, as described in Table 1. The *x*-axis shows the time line of the recording, and the *y*-axis is the analogue-to-digital value of the device output, which represents the resistance of the sensor.

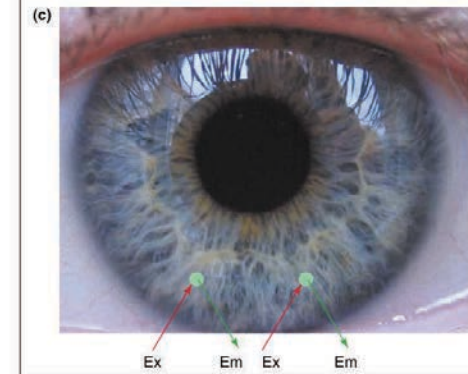
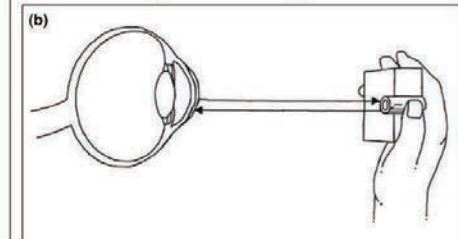
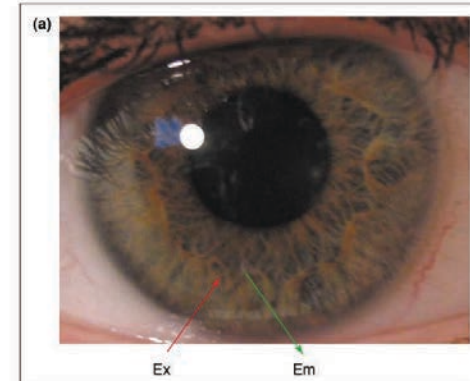
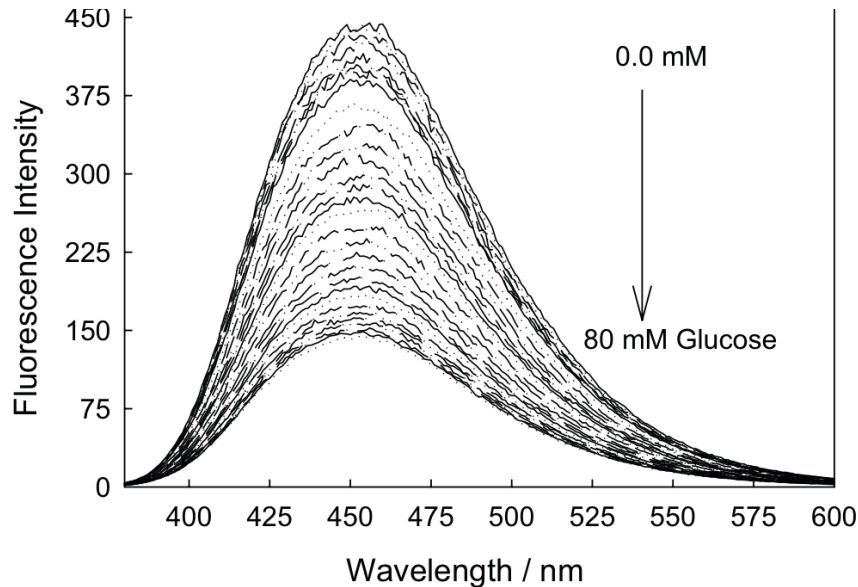
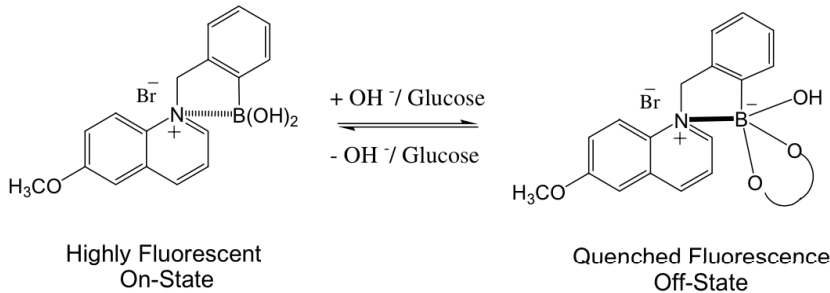
- **Event detection algorithm -> number of, severity, duration...**
- **Convert this to a score (where on scale the person is)**
- **Track effect of interventions on this score**

**A sleep bruxism detection system based on sensors in a splint – pilot clinical data, Journal of Oral Rehabilitation 2015 42; 34--39**  
P. MCAULIFFE\*, J. H. KIM†, D. DIAMOND†, K. T. LAU† & B. C. O'CONNELL\* \*Department of Restorative Dentistry & Periodontology, Dublin Dental University Hospital, Trinity College Dublin, and †National Centre For Sensor Research, Dublin City University





# Optically Responsive Contact Lens for Diabetics



Series of papers by Ramachandram Badugu, Joseph R. Lakowicz, and Chris D. Geddes [1] & Jin Zhang of the University of Western Ontario [2] based on boronic acid quinolinium receptors: Under alkaline conditions (pH9) saccharide diols bind to form the B<sup>-</sup> centre which interacts strongly with the N<sup>+</sup> centre, quenching the fluorescence emission.

[1] Noninvasive continuous monitoring of physiological glucose using a monosaccharide-sensing contact lens, R. Badugu, J.R. Lakowicz, C.D. Geddes, *Analytical Chemistry*, 76 (2004) 610-618.

[2] Jin Zhang\*, William Hodge, Cindy Hutnick, and Xianbin Wang, "Non-invasive diagnostic technology for diabetes through monitoring ocular glucose", *J. Diabetes Sci. Tech.* 5,166, (2011)

Potential methods for non-invasive continuous tear glucose monitoring. (a) Boronic acid doped contact lenses. (b) Schematic of a possible tear glucose-sensing device. The hand-held device works by flashing a light into the eye (Ex) and measuring the emission (Em) intensity. (c) Sensor spots on the surface of the lens can be included to monitor other analytes in addition to glucose, such as drugs, biological markers, Ca<sup>2+</sup>, K<sup>+</sup>, Na<sup>+</sup>, O<sub>2</sub> and Cl<sup>-</sup>. Sensor regions could also allow for ratiometric, lifetime or polarization based fluorescence glucose sensing.

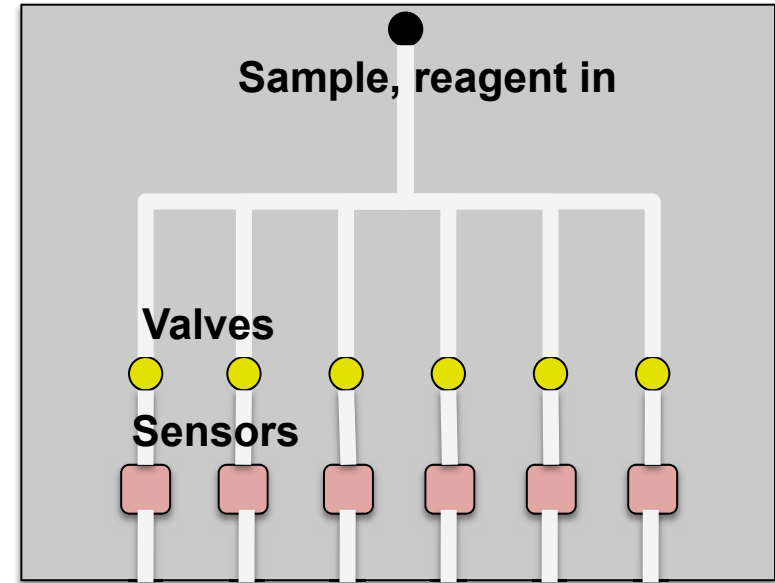




# Extend Period of Use via Arrays of Sensors....?

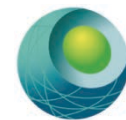


- If each sensor has an in-use lifetime of 1 week....
- And these sensors are very reproducible....
- And they are very stable in storage (up to several years)....



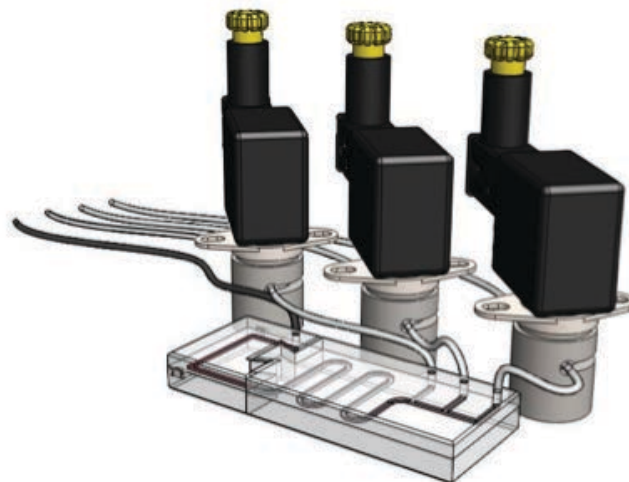
**Then 50 sensors when used sequentially could provide an aggregated in-use lifetime of around 1 year**

**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)!

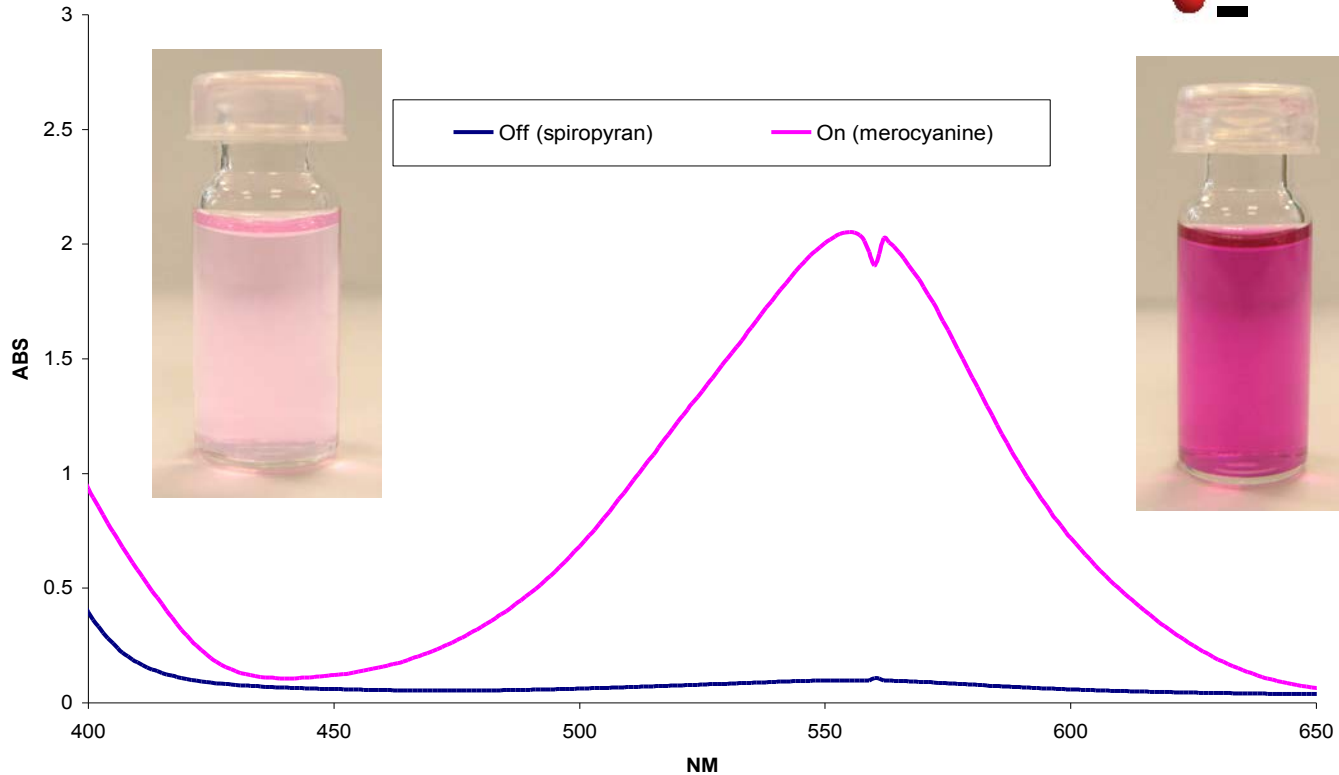
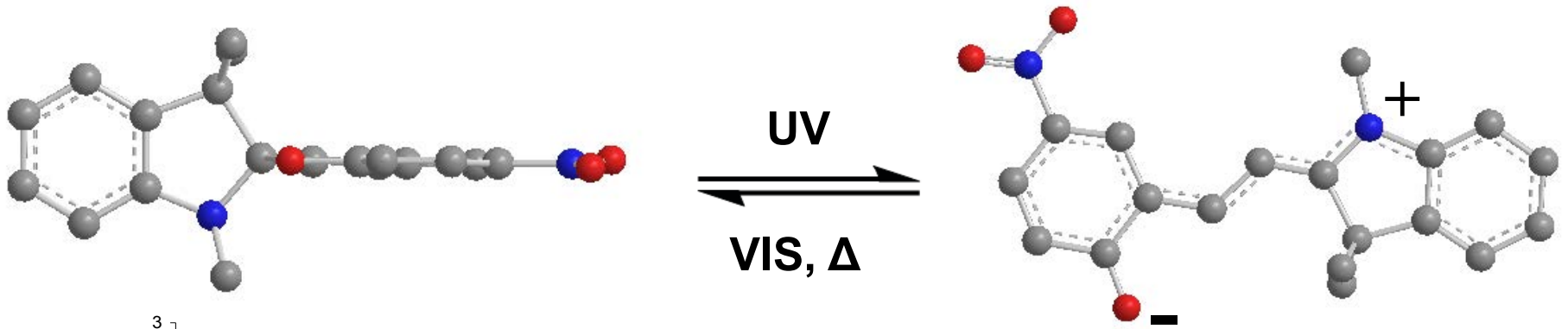
- **Conventional valves cannot be easily scaled down - Located off chip: fluidic interconnects required**
  - Complex fabrication
  - Increased dead volume
  - Mixing effects
- **Based on solenoid action**
  - Large power demand
  - Expensive



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



# Photoswitchable Materials



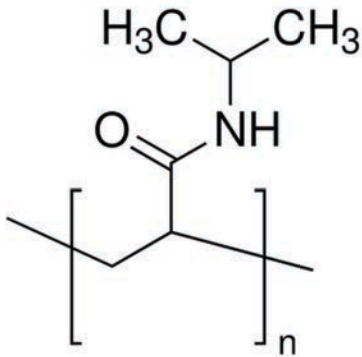




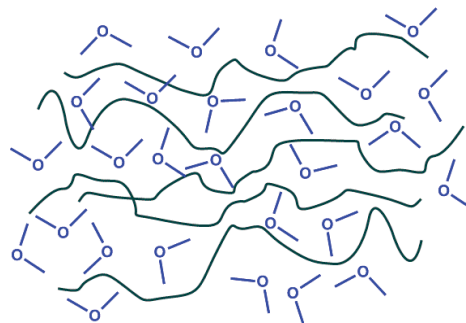
# Poly(*N*-isopropylacrylamide)

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



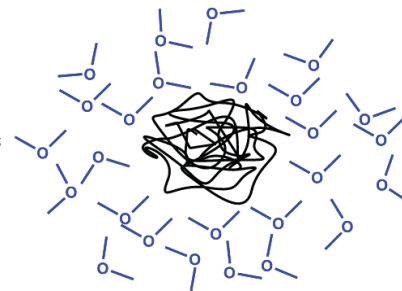
Hydrophilic



Hydrated Polymer Chains



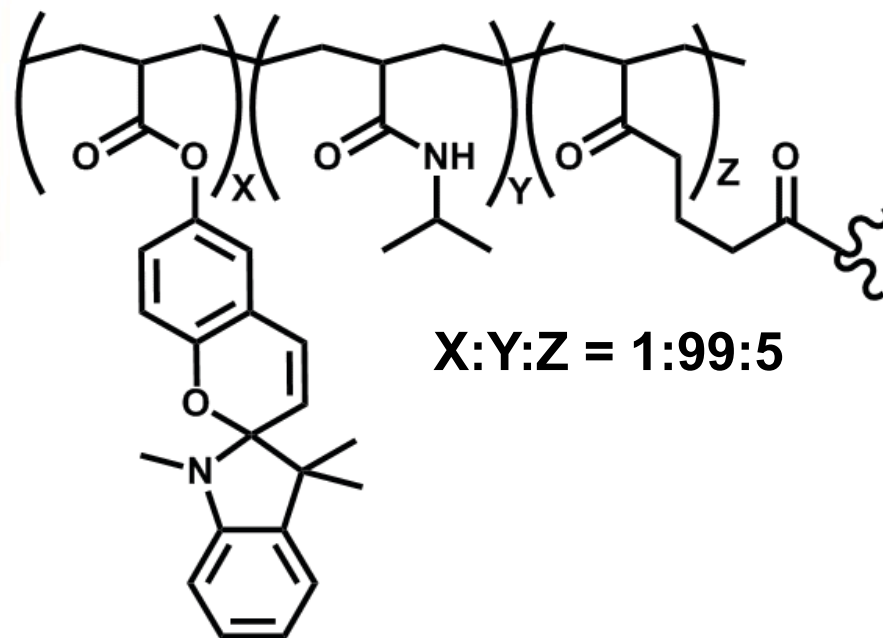
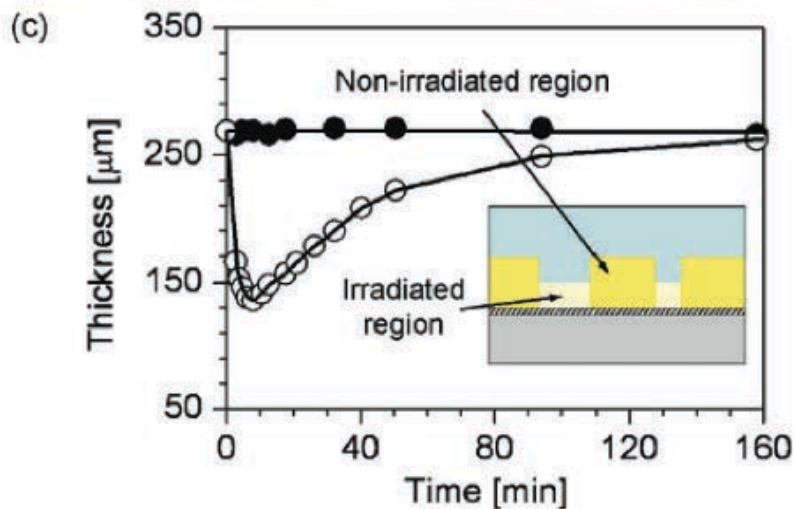
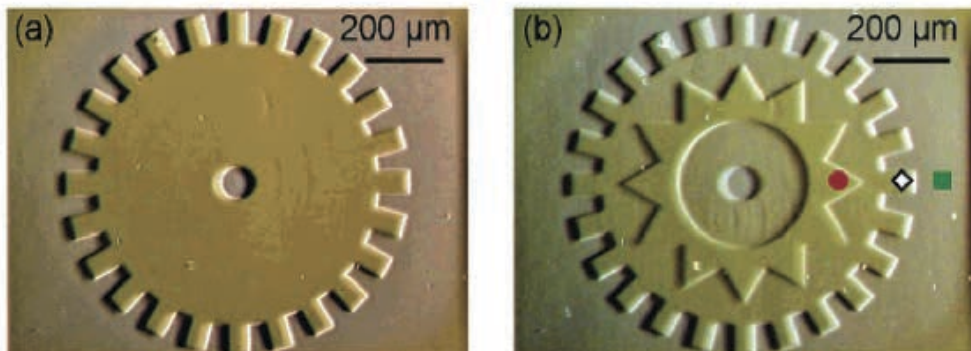
Hydrophobic



Loss of bound water  
-> polymer collapse



# Polymer based photoactuators based on pNIPAAm



poly(N-isopropylacrylamide) (PNIPAAm)  
Formulation as by Sumaru et al<sup>1</sup>

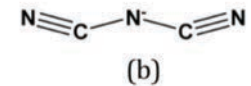
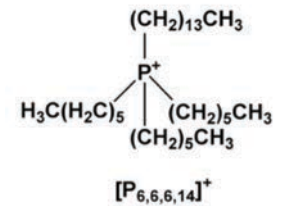
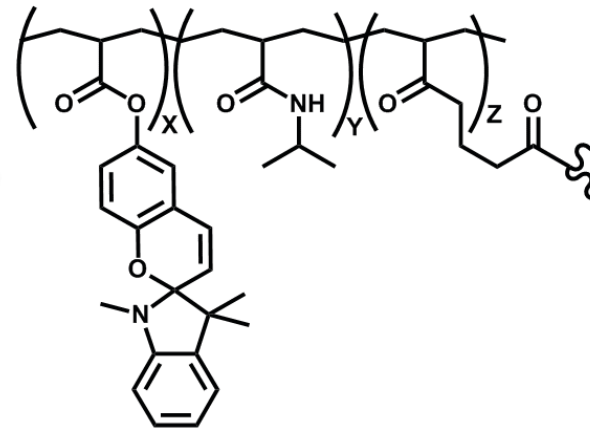
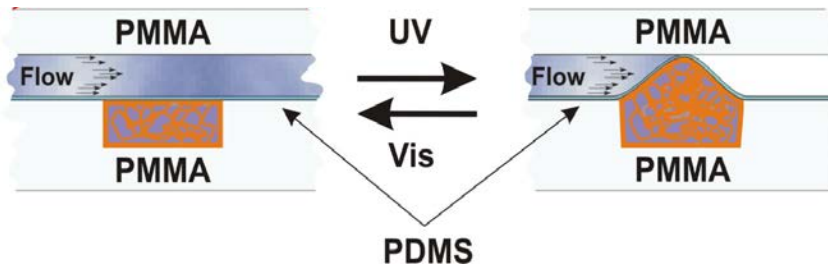
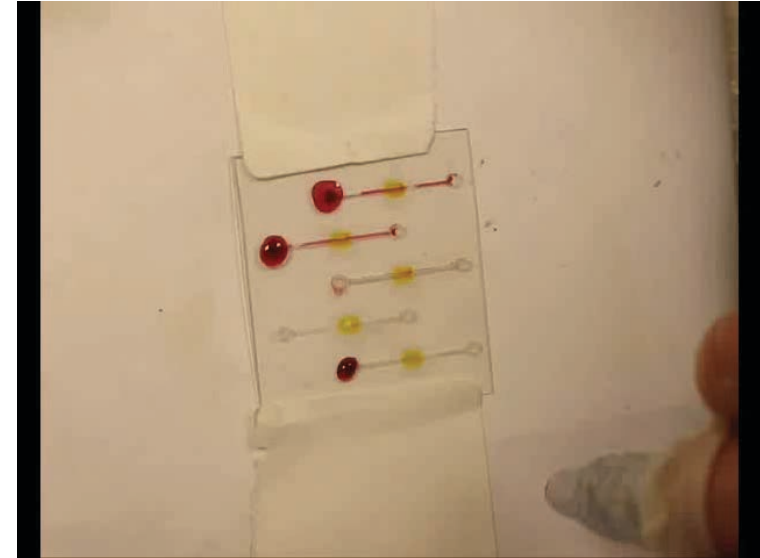
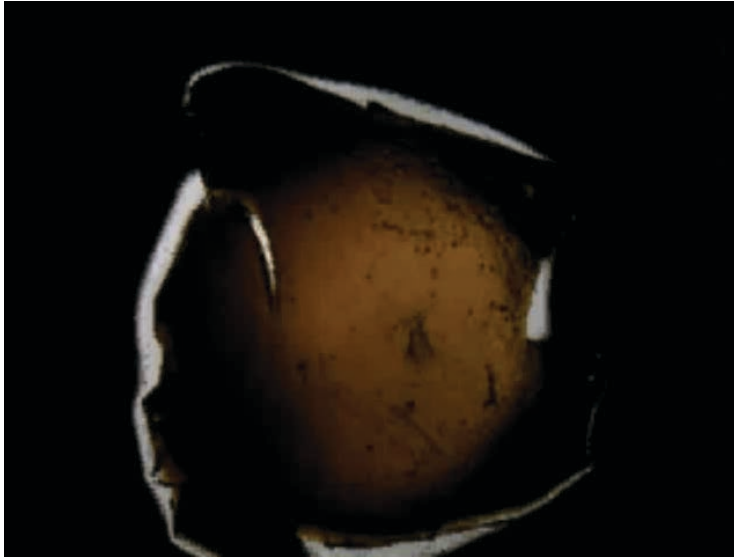
1) *Chem. Mater.*, 19 (11), 2730 -2732, 2007.

**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



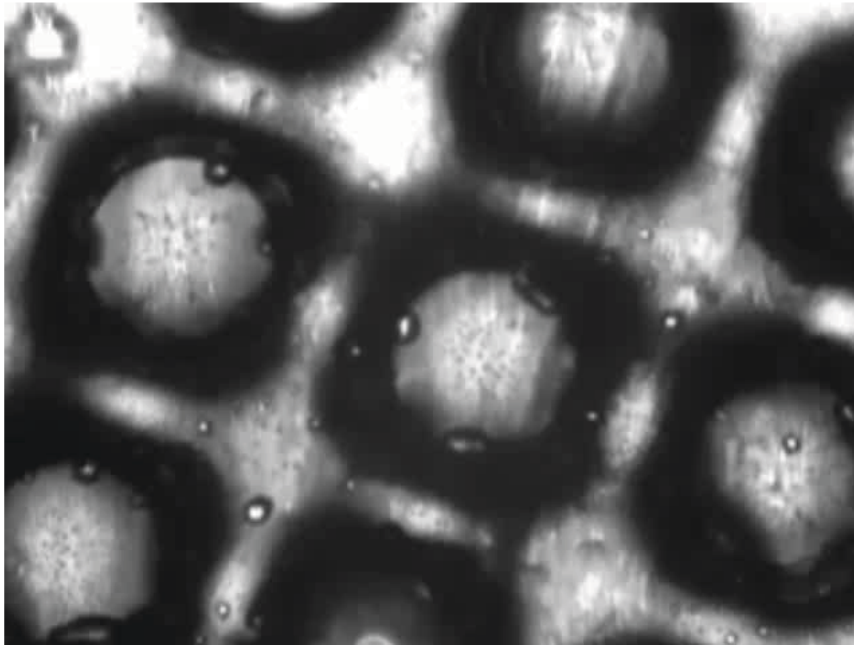
trihexyltetradecylphosphonium dicyanoamide  $[\text{P}_{6,6,6,14}]^+[\text{dca}]^-$

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.

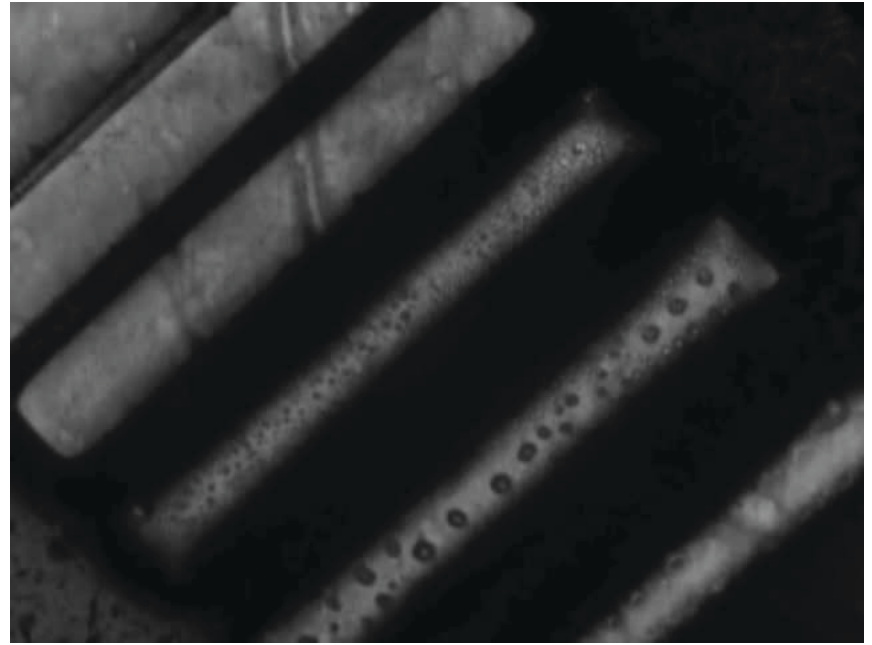




# Flexible creation of $\mu$ -dimensioned features in flow channels using in-situ photo-polymerisation



Ntf2 pillars speed x3

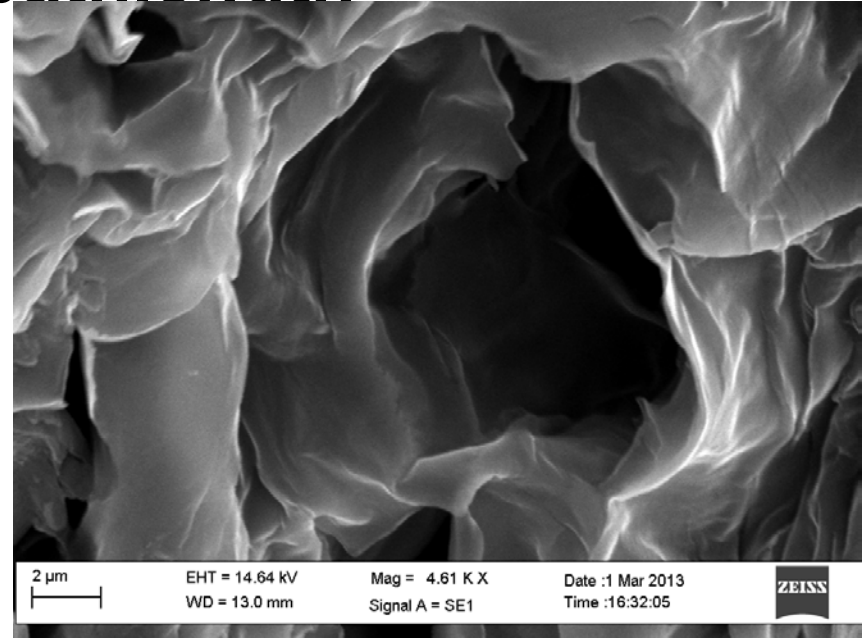
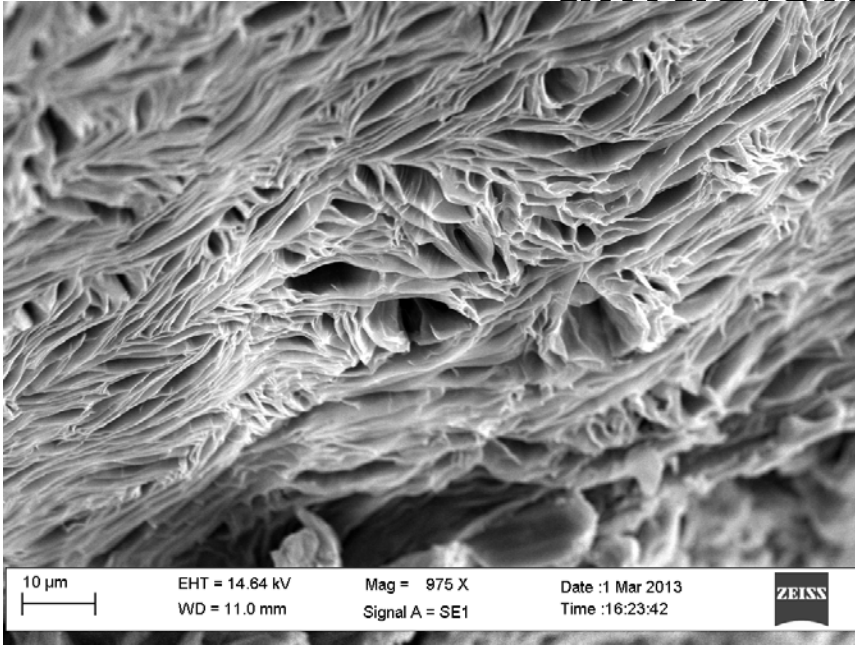


DCA lines speed x4

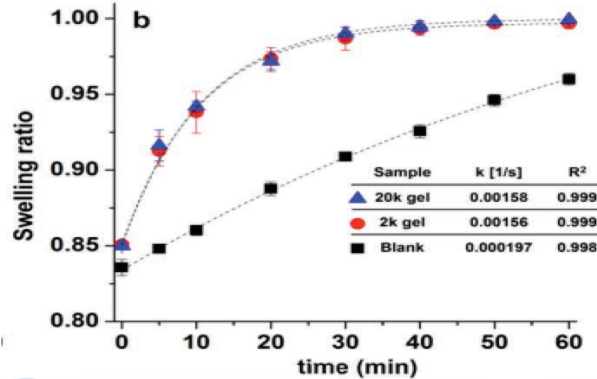
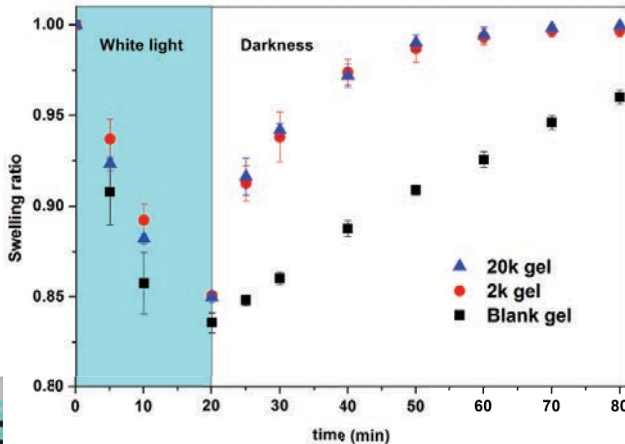
With Dr Peer Fischer, Fraunhofer-Institut für Physikalische Messtechnik (IPM), Freiburg



# 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

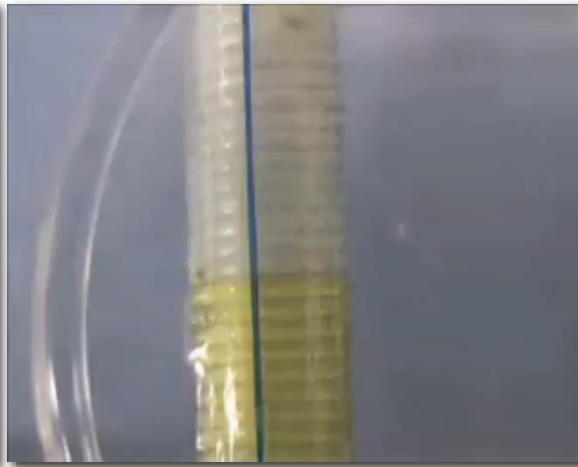


On the re-swelling side; highly porous gels now recover ca. an order of magnitude faster;

$k = 1.6 \times 10^{-3} \text{ S}^{-1}$   
vs.  $2.0 \times 10^{-4} \text{ S}^{-1}$



# 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.

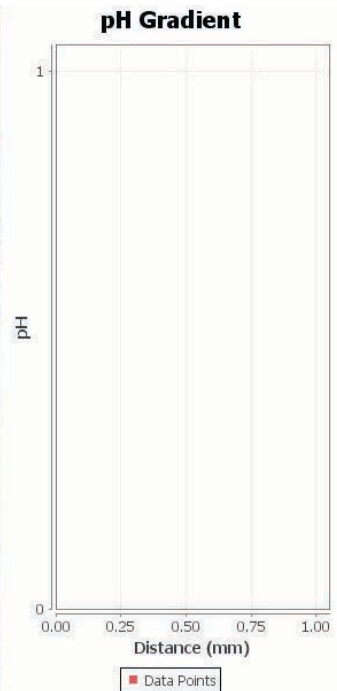
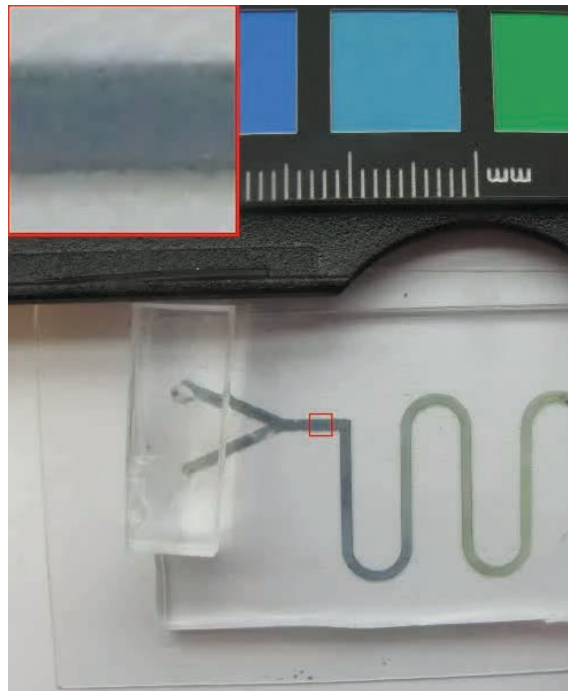
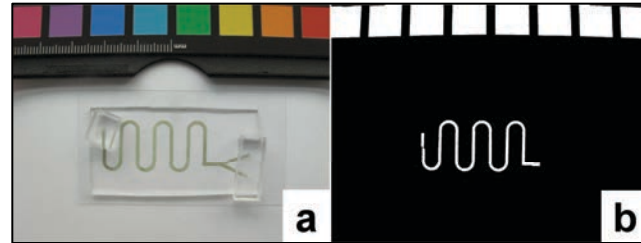
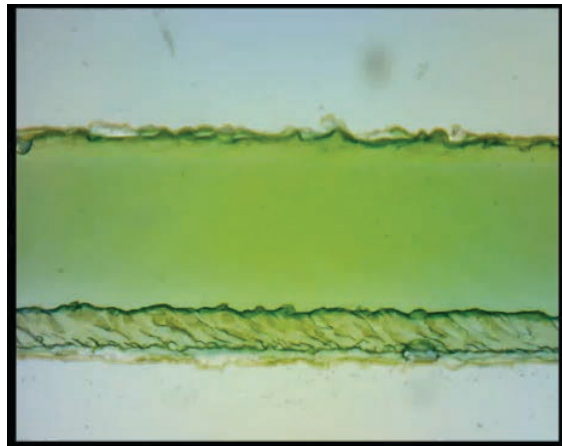
Biomimetic, low power pumps based on soft actuators, Sonia Ramirez-Garcia and Dermot Diamond, *Sensors and Actuators A* 135 (2007) 229–235.

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





# Inherently sensing flexible channels

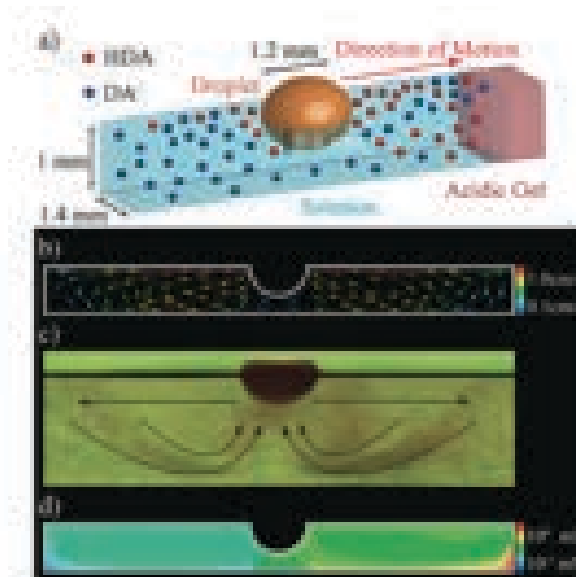
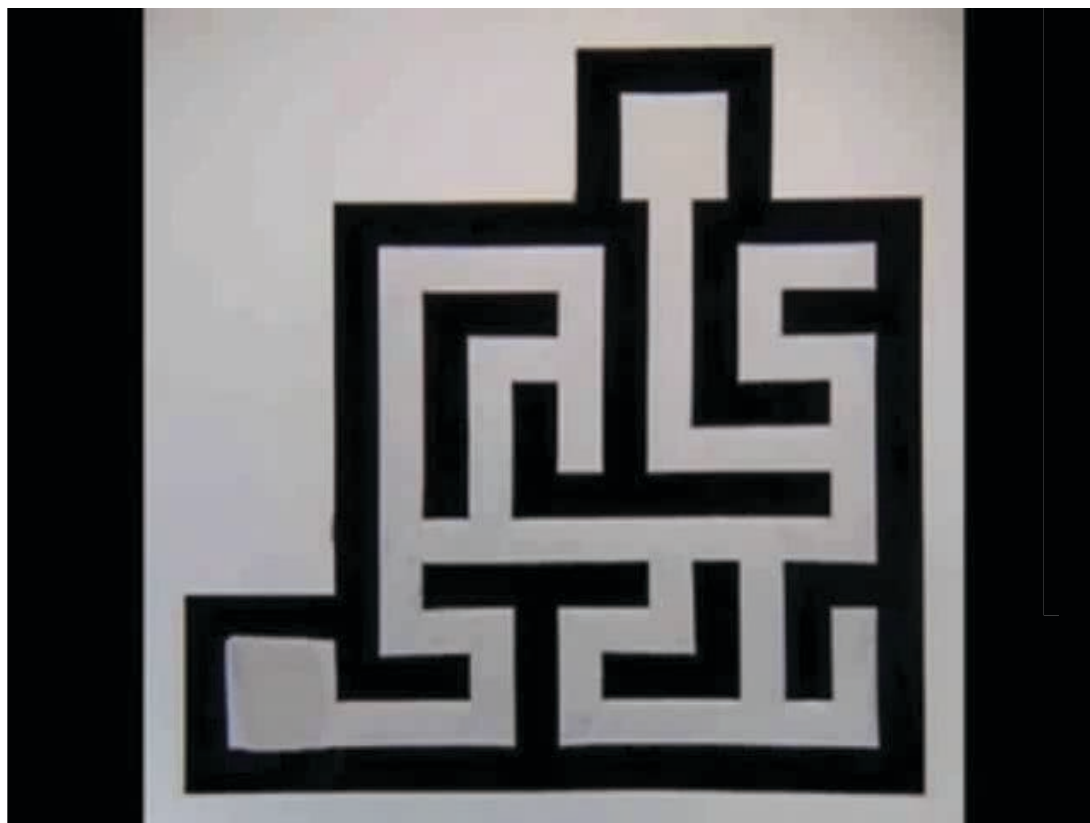


- PANi deposited on channel walls - Channels are now inherently responsive e.g. pH sensitive
- Status can be determined at any location within the channels using low cost digital imaging





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

**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

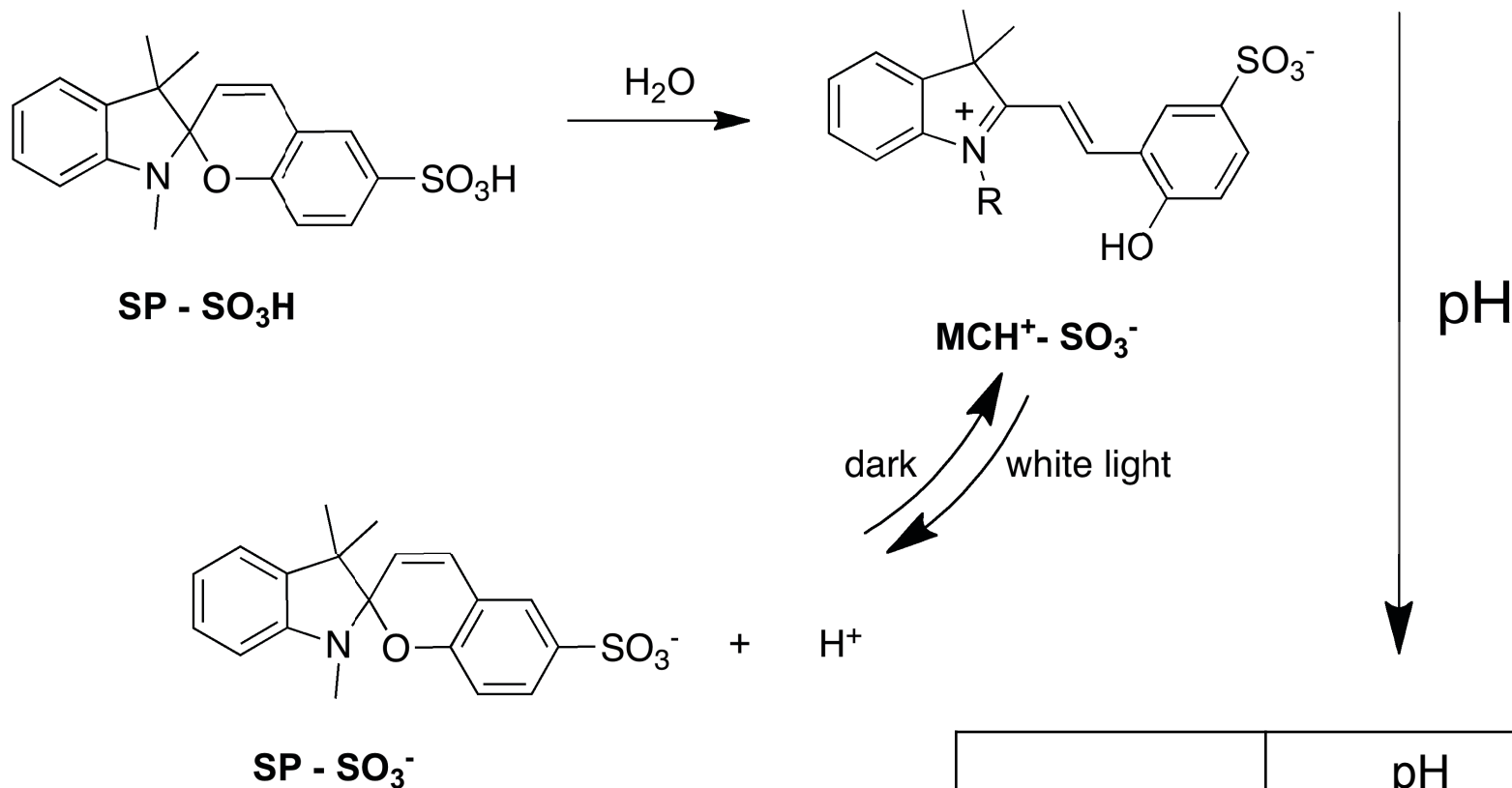
Fuerstman, M. J.; Deschatelets, P.; Kane, R.; Schwartz, A.; Kenis, P. J. A.; Deutch, J. M.; Whitesides, G. M. *Langmuir* 2003, 19, 4714.







# Photo-modulation of pH



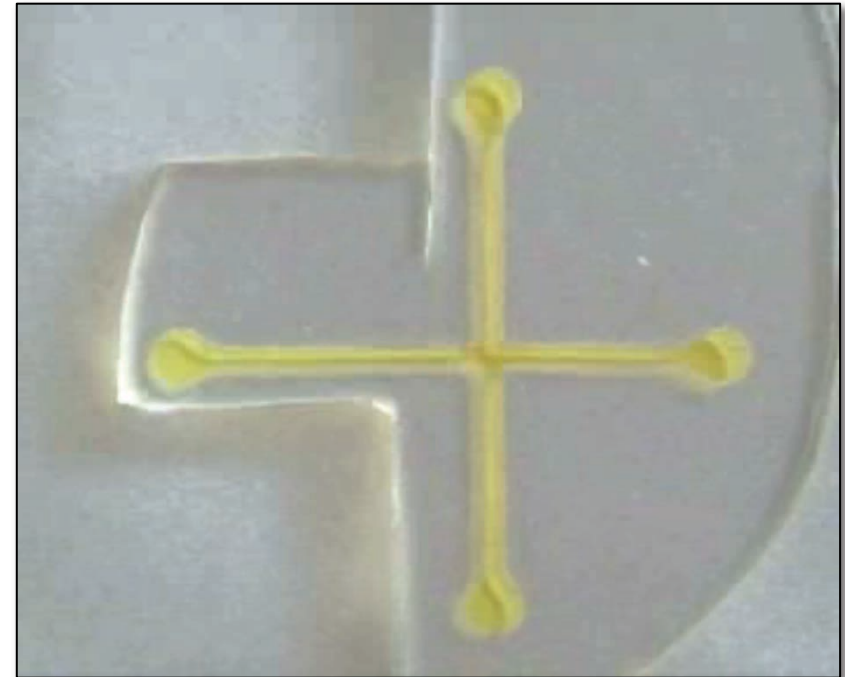
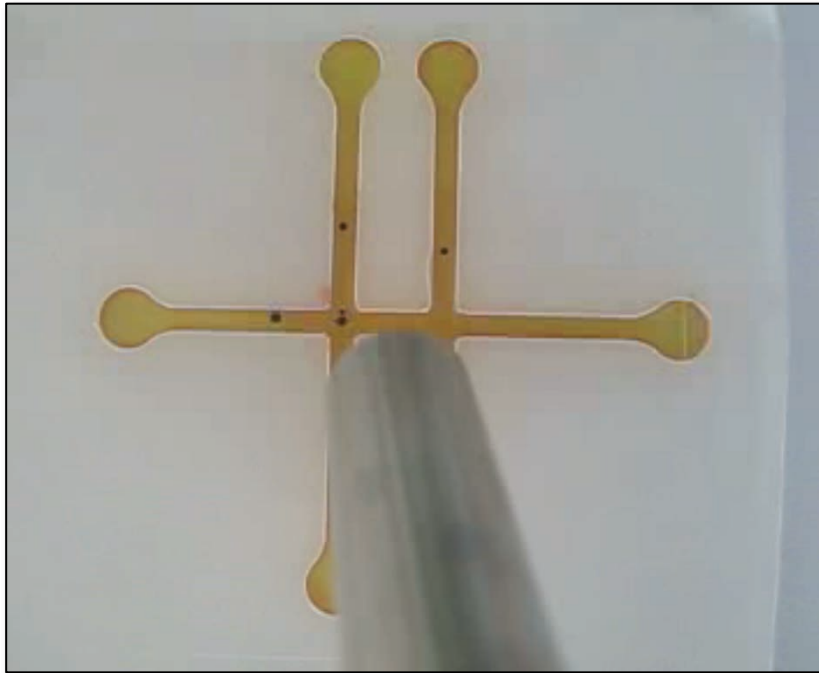
**Channel Solution: Spiropyran Sulfonic Acid  $10^{-3}\text{M}$  ( $\text{H}_2\text{O}$ )**

	pH
$\text{H}_2\text{O}$	6.5
$\text{MCH}^+\text{-SO}_3^-$	4.8
$\text{SP-SO}_3^-$	3.4

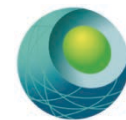




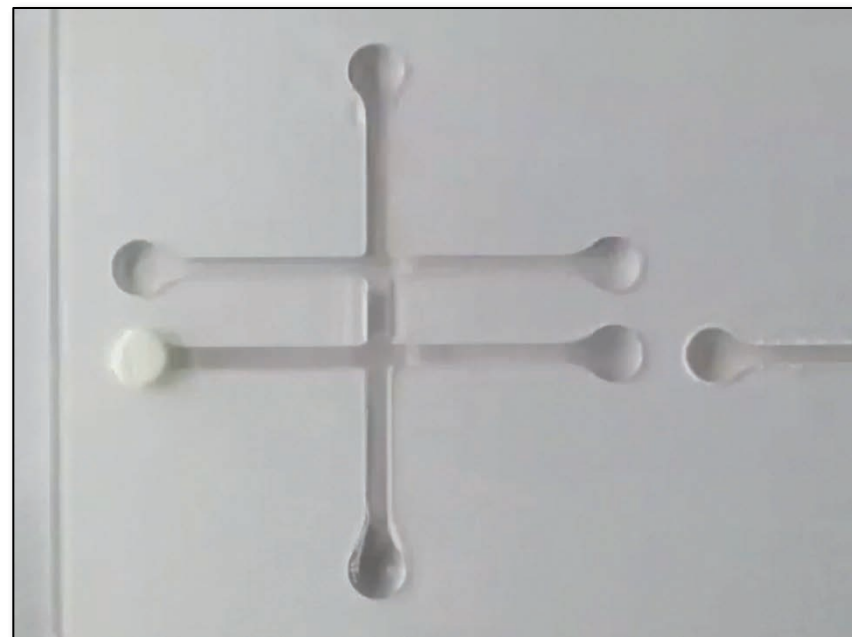
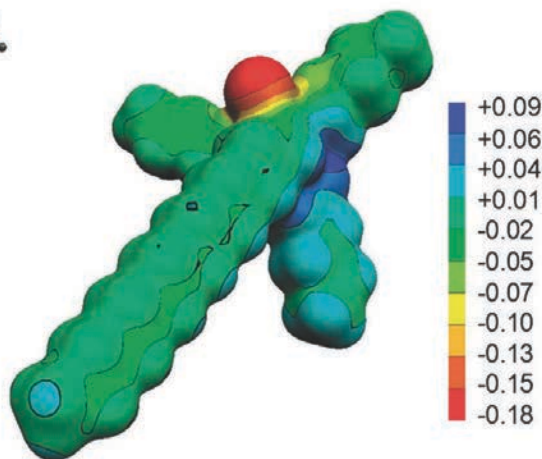
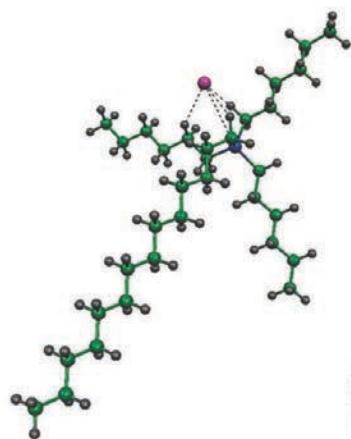
# Movement of Droplets in Channels using Light



- 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

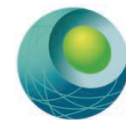


Trihexyl(tetradecyl)phosphonium chloride ( $[\text{P}_{6,6,6,14}][\text{Cl}]$ ) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the  $\text{Cl}^-$  ion which is created using a polyacrylamide gel pad soaked in 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



# Photocontrol of Assembly and Subsequent Switching of Surface Features



ACS APPLIED MATERIALS & INTERFACES

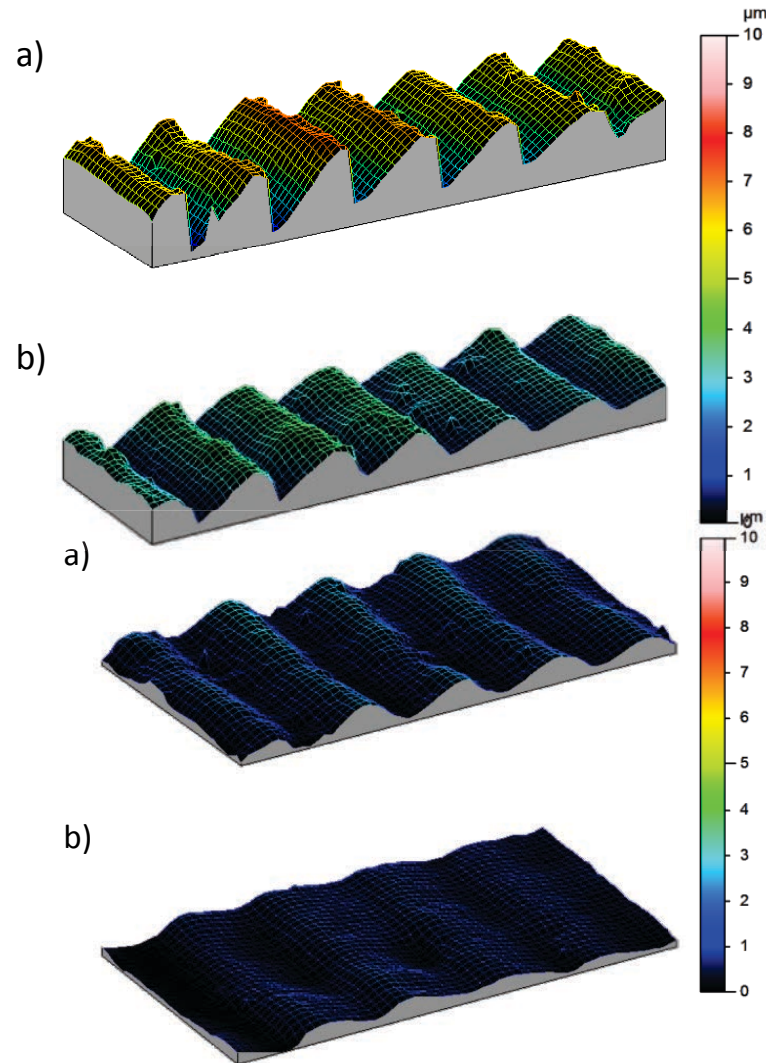
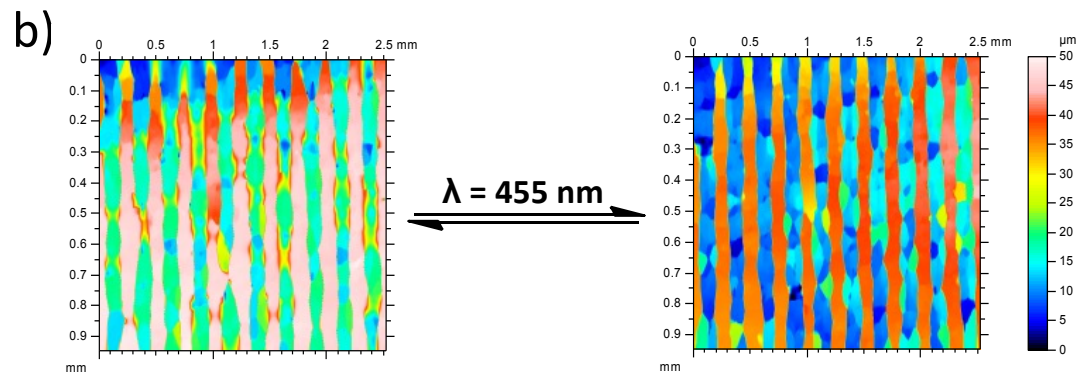
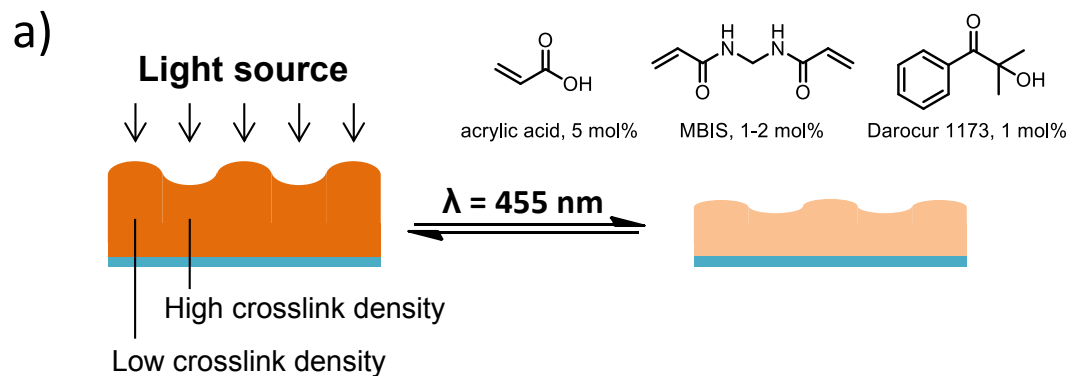
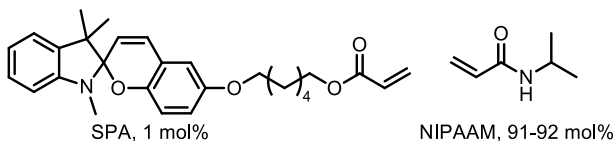
Research Article

www.acsami.org

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

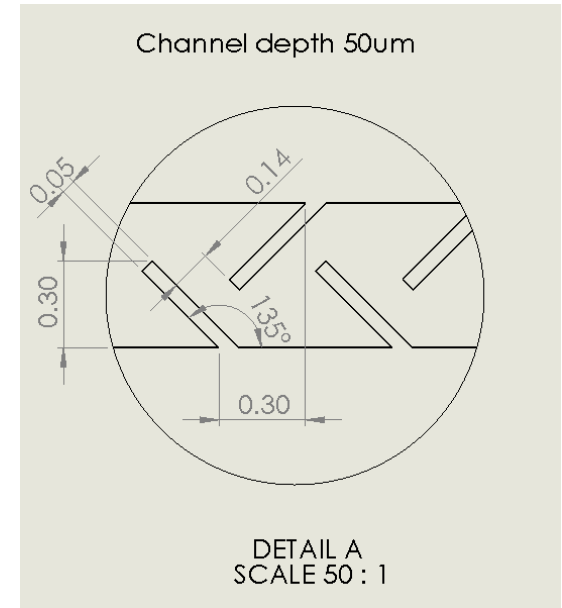
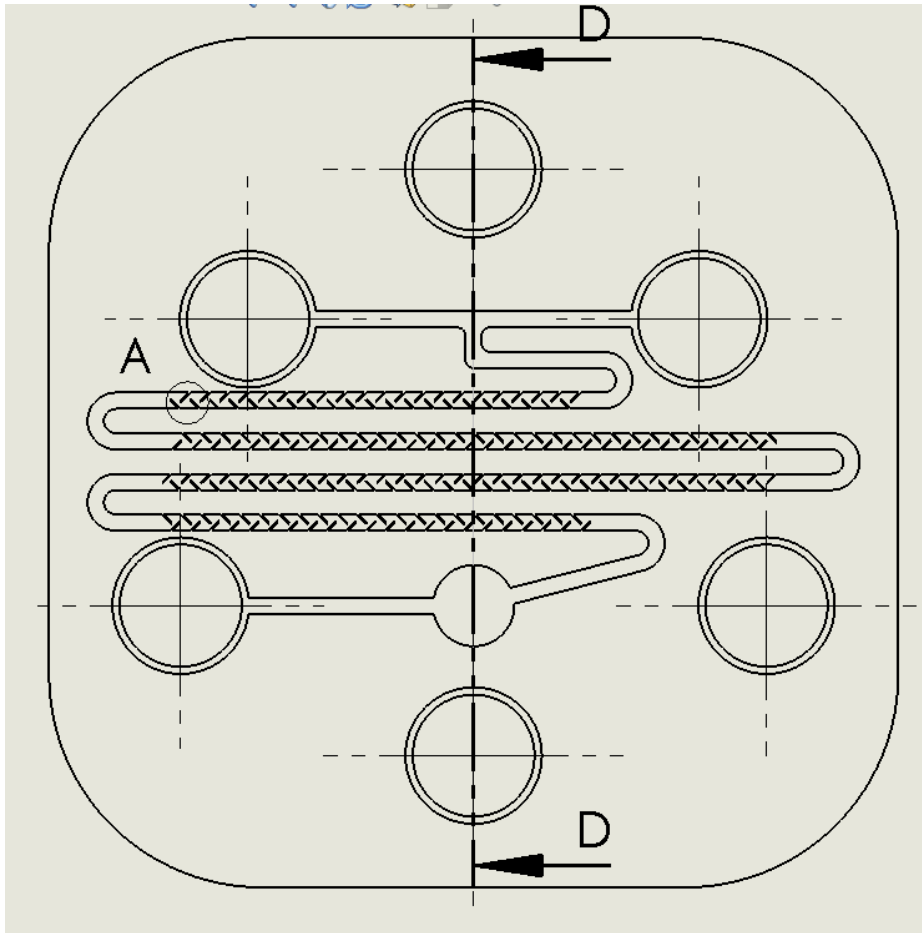
## Photoswitchable Ratchet Surface Topographies Based on Self-Protonating Spiropyran–NIPAAm Hydrogels

Jelle E. Stumpel,<sup>†</sup> Bartosz Ziolkowski,<sup>‡</sup> Larisa Florea,<sup>‡</sup> Dermot Diamond,<sup>‡</sup> Dirk J. Broer,<sup>\*,†,§</sup> and Albertus P. H. J. Schenning<sup>\*,†,§</sup>



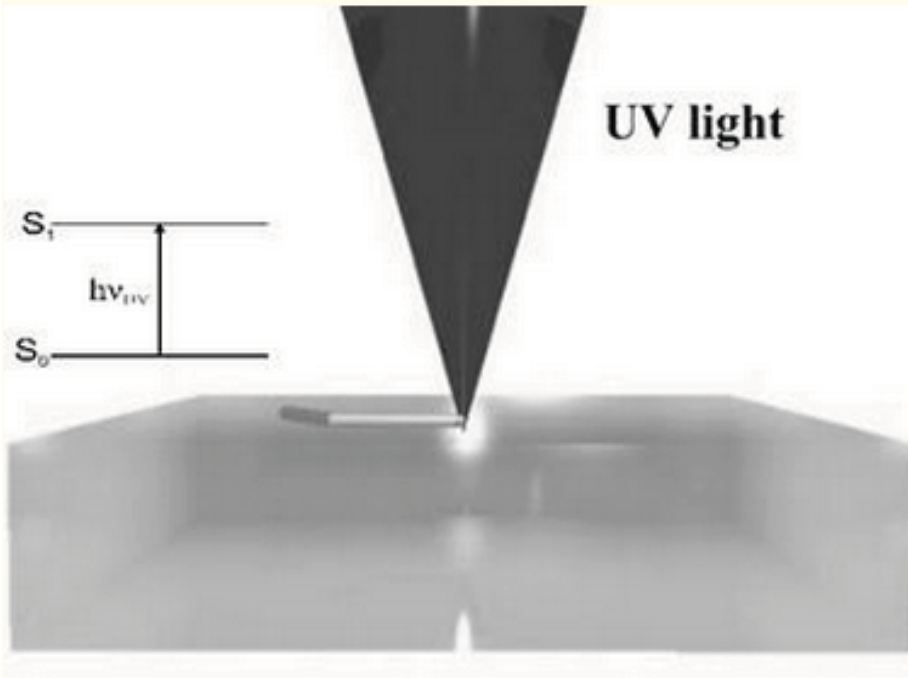


# Mixing Baffles



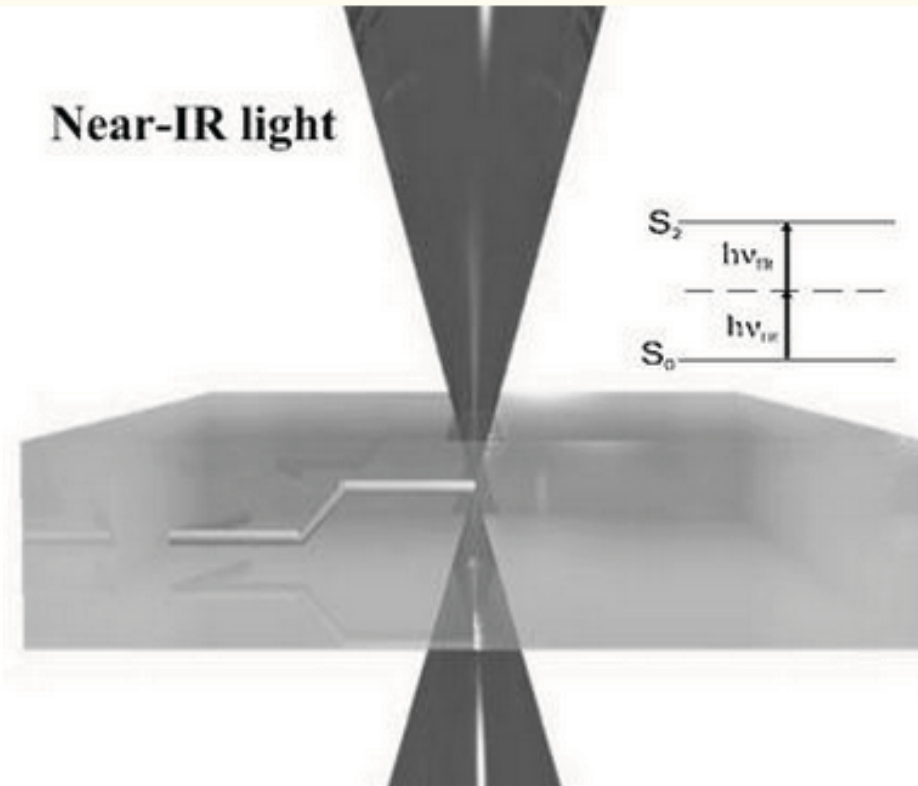
# Background

## Stereolithography



- Single photon absorption
- 2D patterns

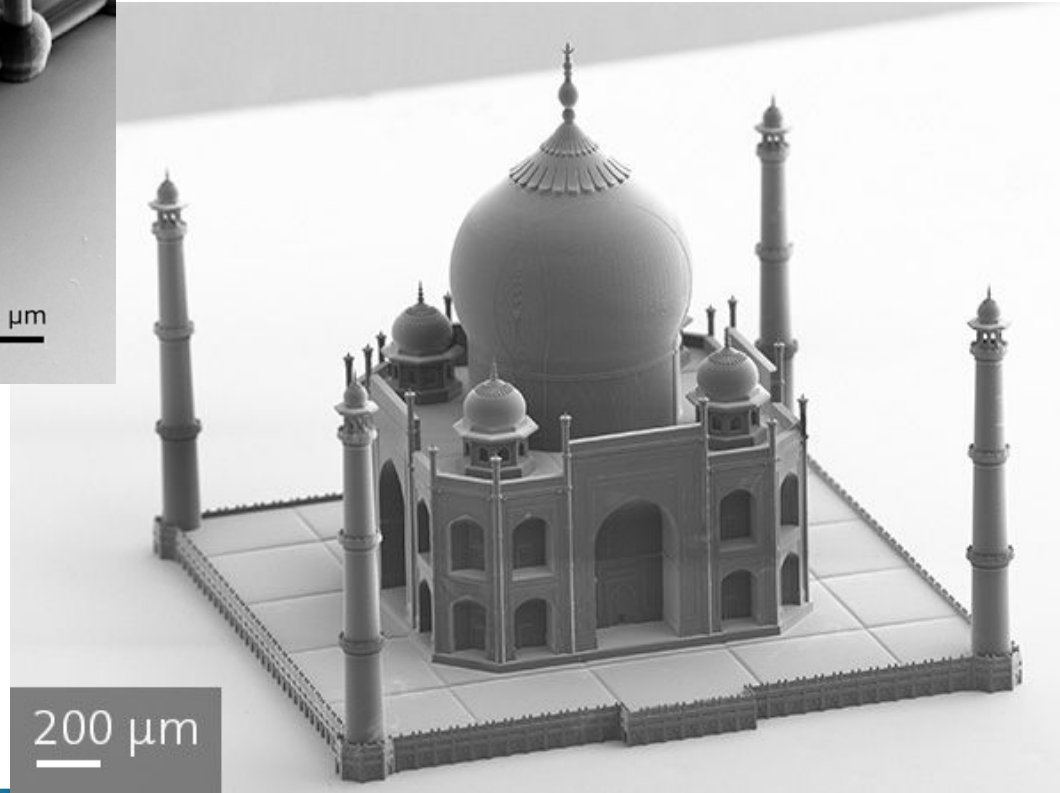
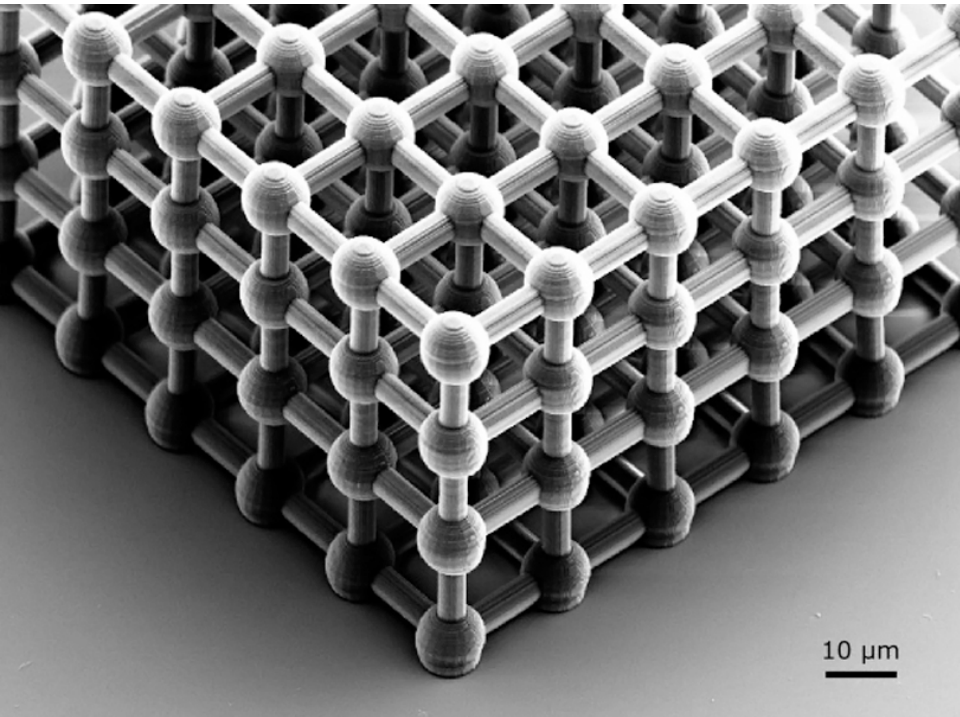
## Two-photon polymerisation



- Two photon absorption
- 3D structures

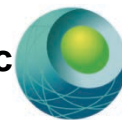


# Background



<http://www.nanoscribe.de/>





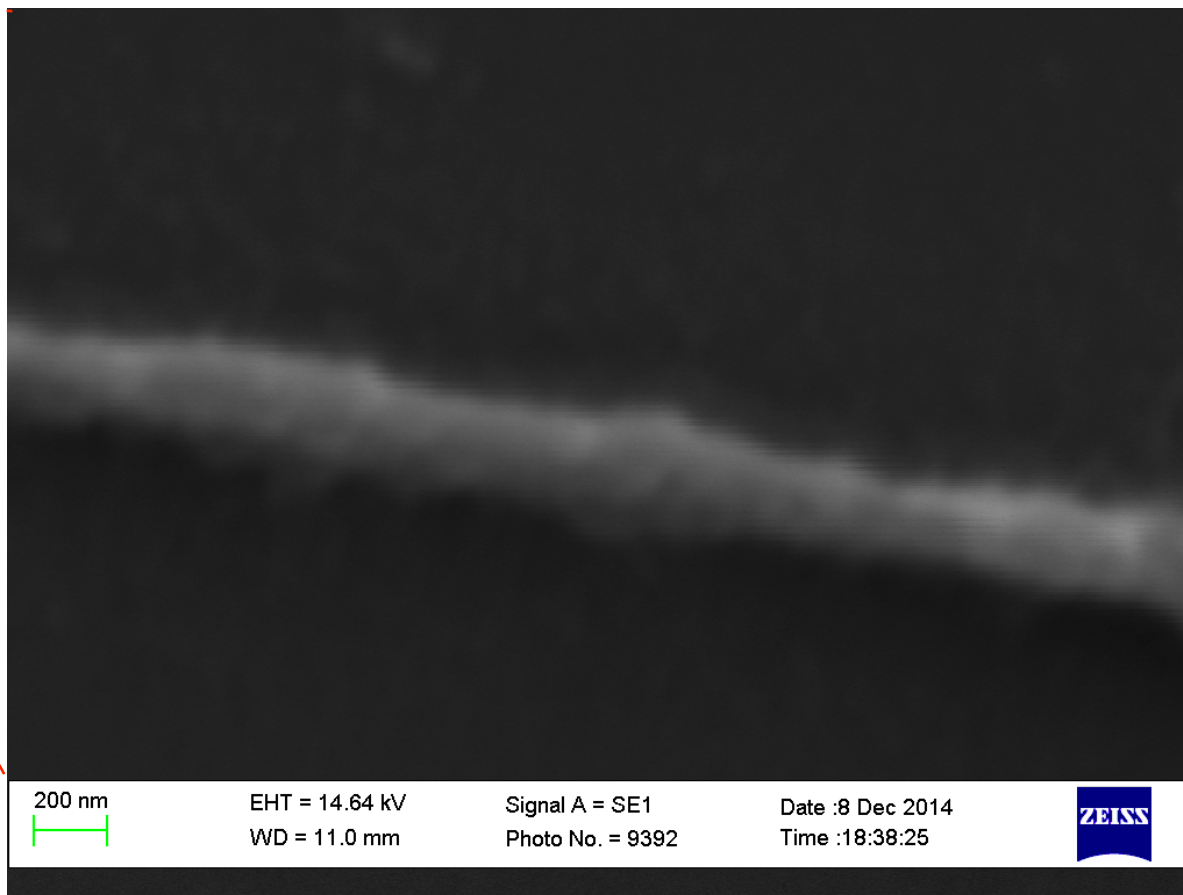
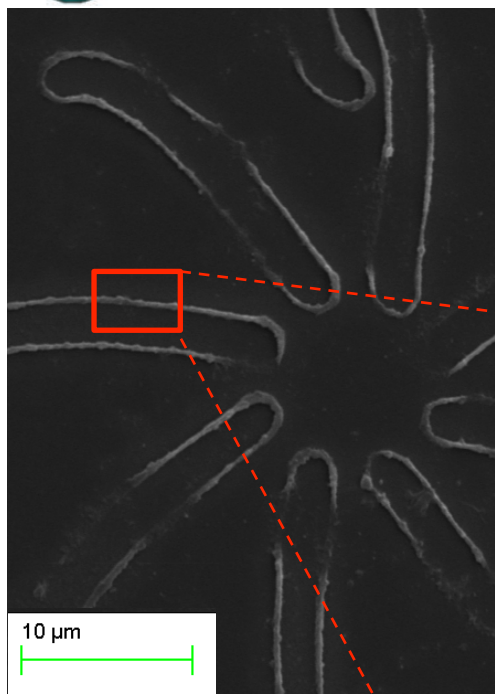
# The Exciting Potential of Stimuli-responsive Materials and Biomimetic Microfluidics

Larisa Florea<sup>1</sup>, Vincenzo Curto<sup>2</sup>, Alexander J. Thompson<sup>2</sup>,  
Guang-Zhong Yang<sup>2</sup>, and Dermot Diamond<sup>1\*</sup>

<sup>1</sup>Insight Centre for Data Analytics, NCSR, Dublin City University

<sup>2</sup>The Hamlyn Centre for Robotic Surgery, Imperial College London, London, SW7 2AZ

Submitted to Euronanoforum, Riga, Latvia, June 2015

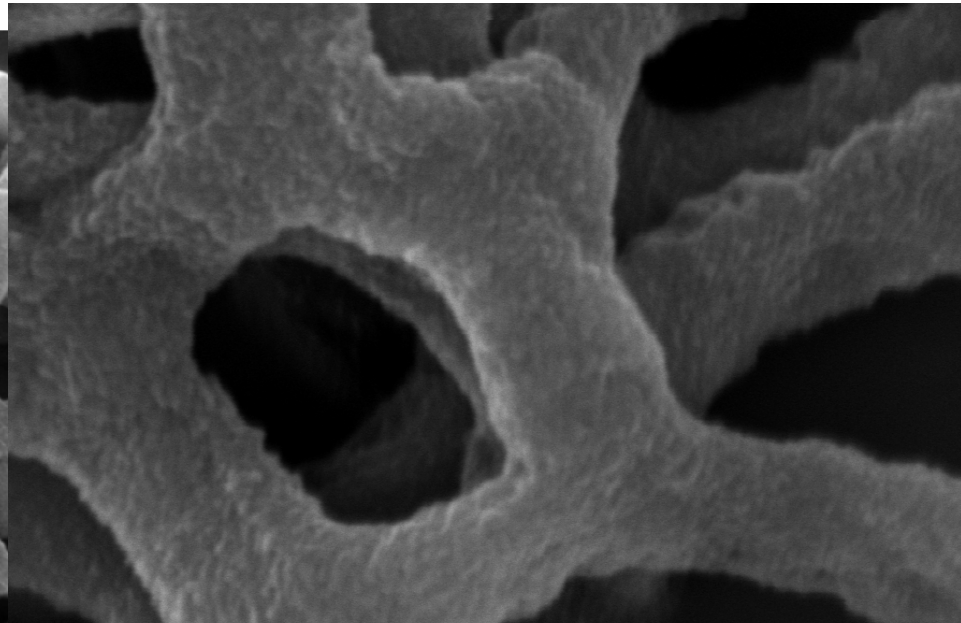
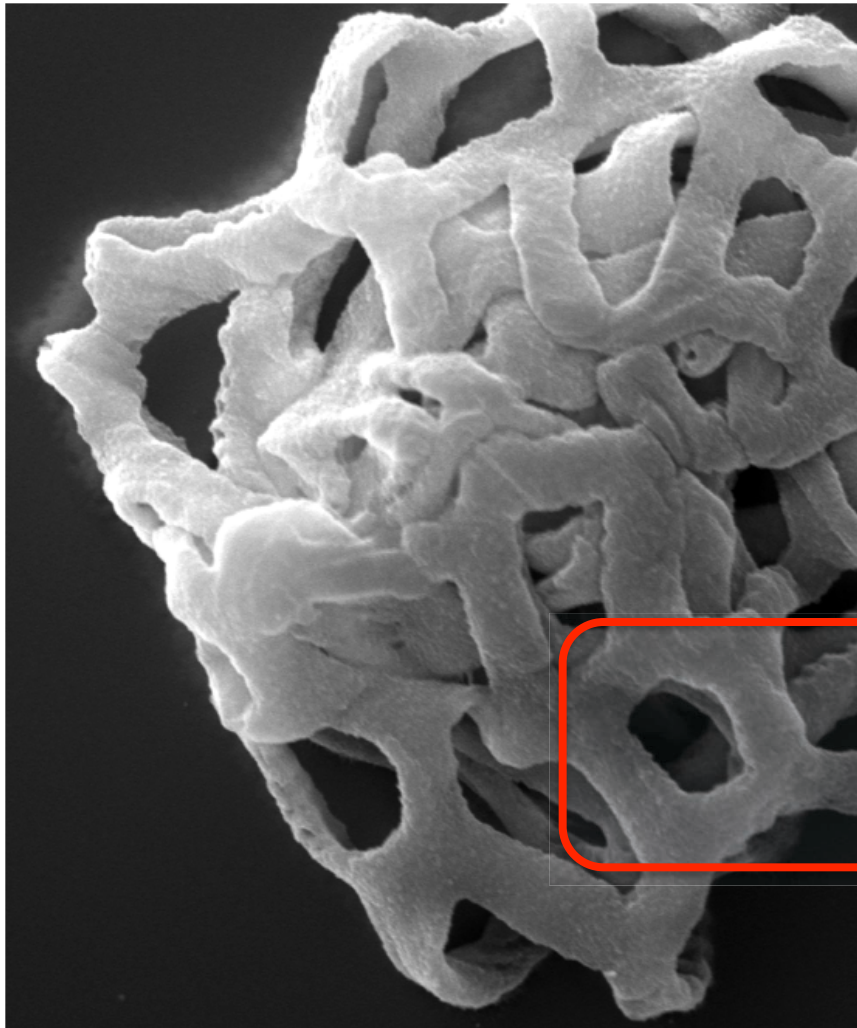


**Creating 3D soft gel structures with a line resolution of ca. 200 nm**





# Globular Porous Structure

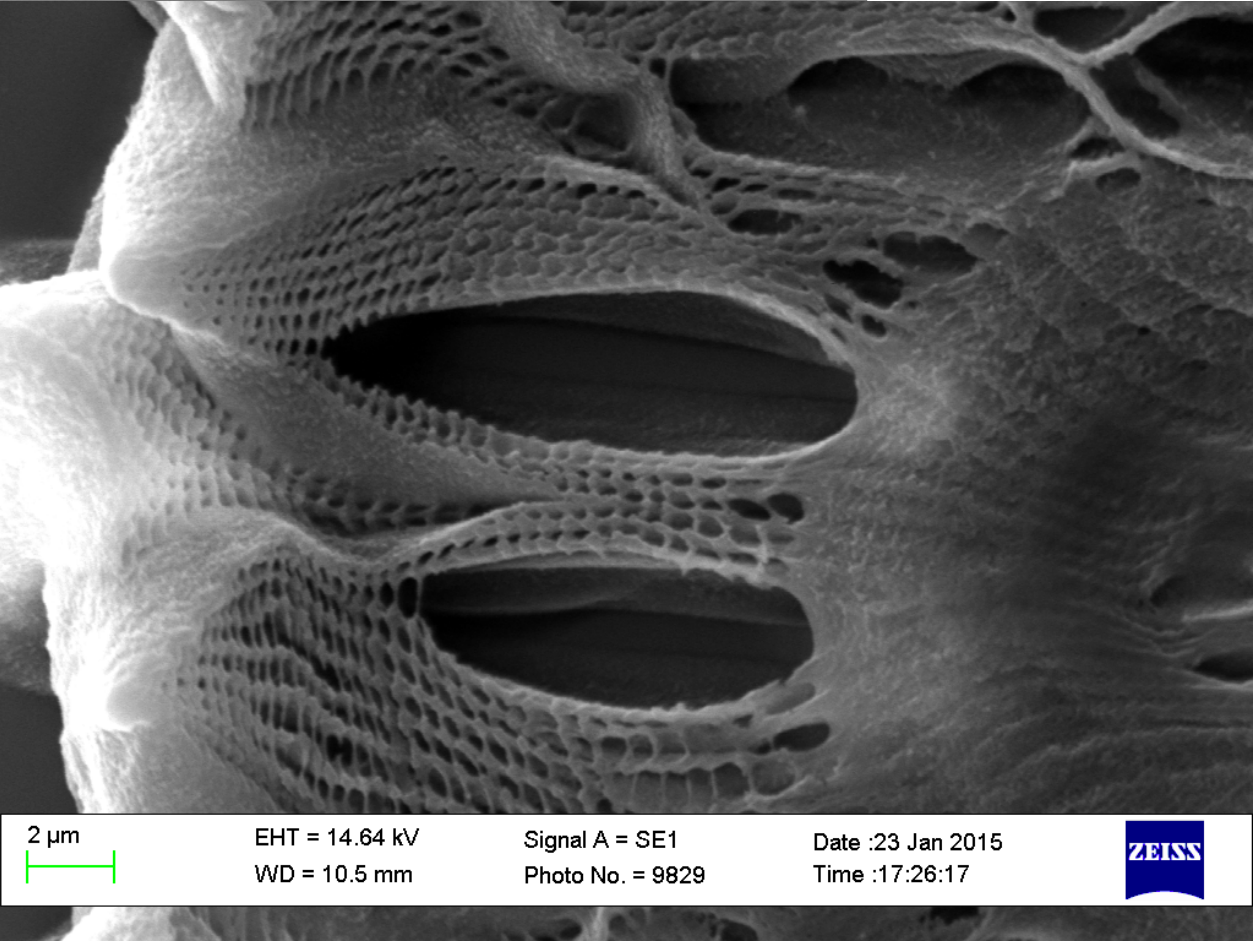
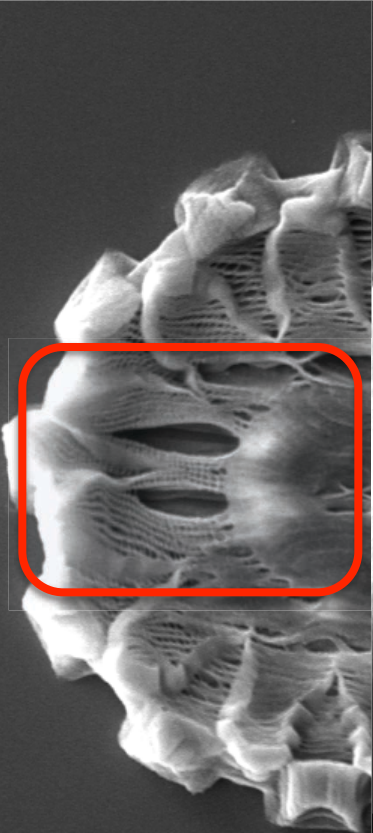


1  $\mu$ m      EHT = 14.64 kV      Signal A = SE1      Date :23 Jan 2015  
WD = 10.5 mm      Photo No. = 9807      Time :16:55:41      ZEISS

2  $\mu$ m      EHT = 14.64 kV      Signal A = SE1      Date :23 Jan 2015  
WD = 10.5 mm      Photo No. = 9805      Time :16:53:15      ZEISS



# 'Daisy' – Micro/Nano Scaled Porous Structure



2  $\mu$ m

EHT = 14.64 kV  
WD = 10.5 mm

Signal A = SE1  
Photo No. = 9829

Date :23 Jan 2015  
Time :17:26:17



20  $\mu$ m

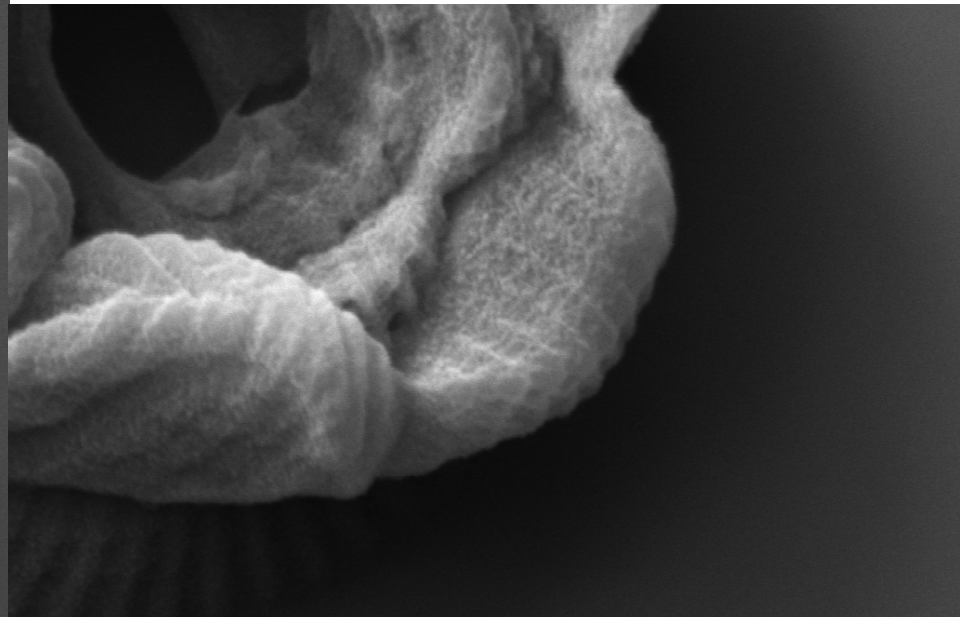
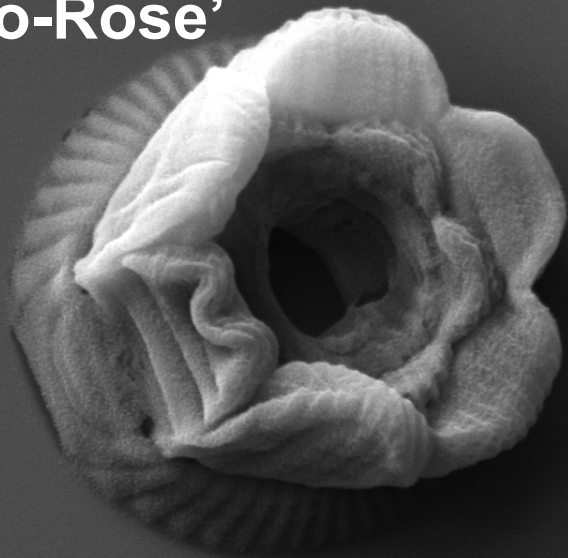
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WD = 10.5 mm

Signal A = SE1  
Photo No. = 9826

Date :23 Jan 2015  
Time :17:21:12



# 'Micro-Rose'



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WD = 10.5 mm Photo No. = 9753 Time :12:31:01 ZEISS

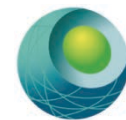
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WD = 10.5 mm Photo No. = 9755 Time :12:33:11 ZEISS

# 'Micro-Stoma'



2  $\mu$ m EHT = 14.64 kV Signal A = SE1 Date :23 Jan 2015  
WD = 11.0 mm Photo No. = 9763 Time :12:39:59 ZEISS

2  $\mu$ m EHT = 14.64 kV Signal A = SE1 Date :23 Jan 2015  
WD = 11.0 mm Photo No. = 9764 Time :12:40:59 ZEISS



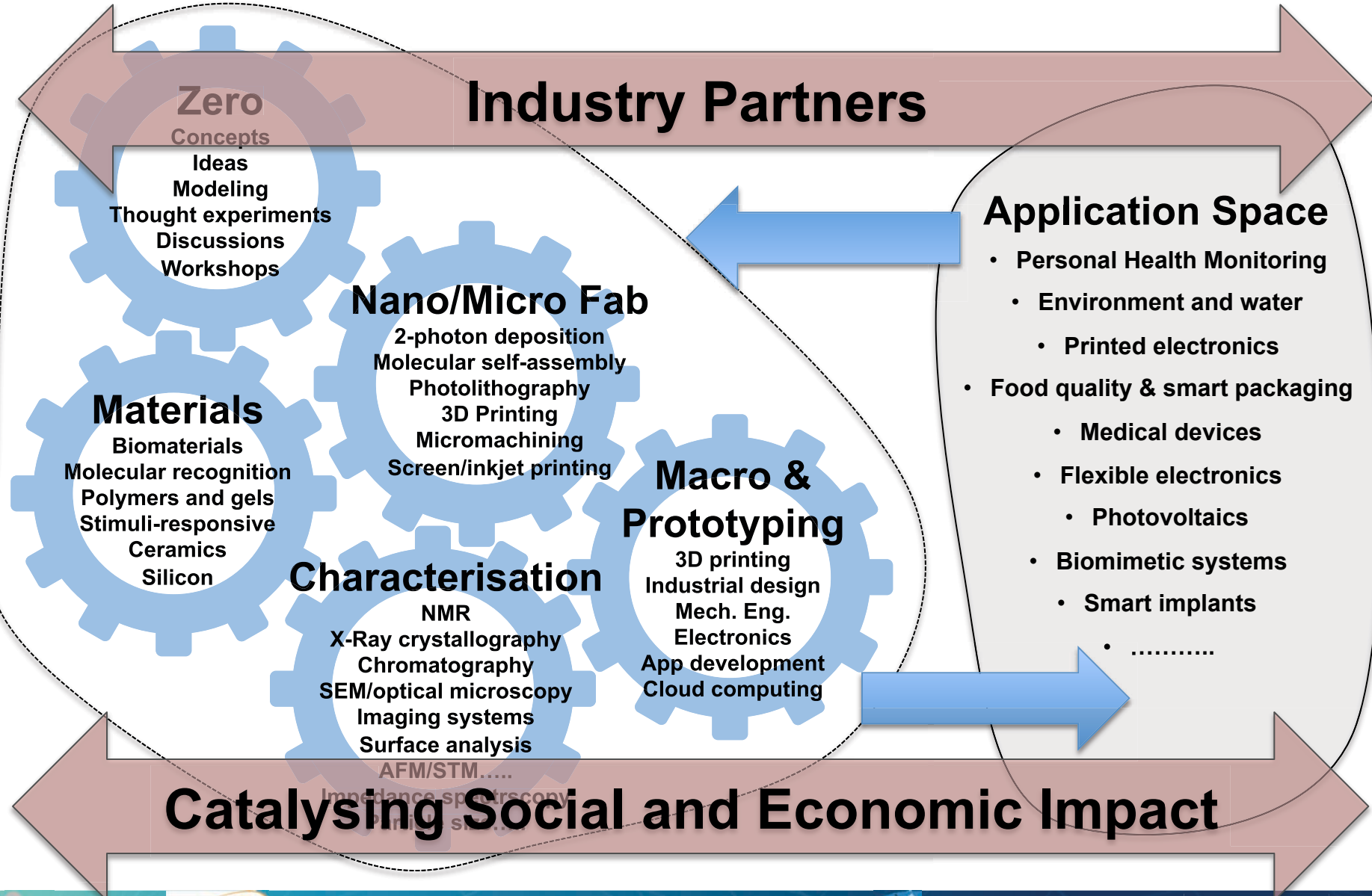
# Time to re-think the game!!!

- **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!**



# Getting it all to Work Together...





# Thanks to.....



**Thanks for the invitation**



OÉ Gaillimh  
NUI Galway

