From ‘Devices' to 'Self-Aware, Bioinspired MicroSystems': What does the future hold for Optical Sensing?

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Presented at

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GRAZ, Austria

March 20-23, 2016

Single Use vs. Continuous Monitoring

Chemical Sensors & Biosensors

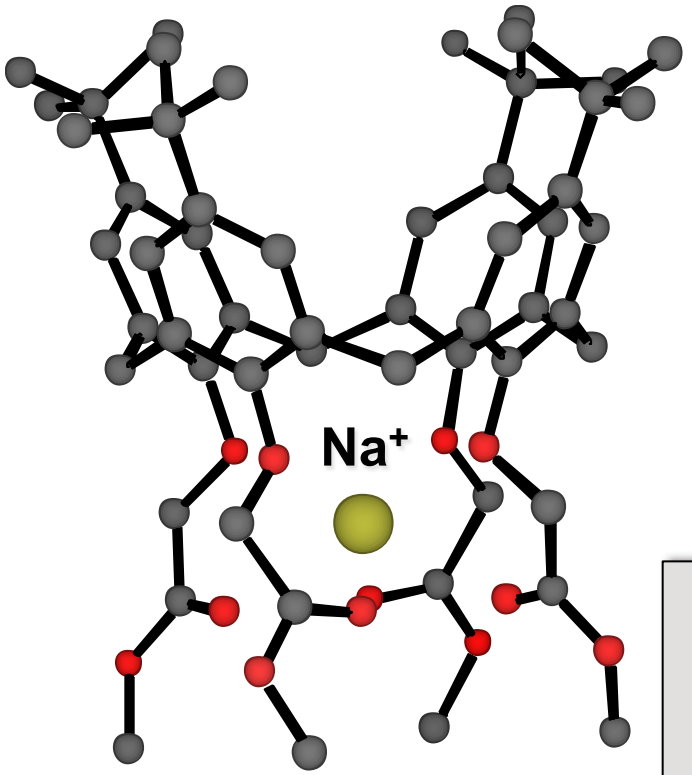
Single Use Measurements and Diagnostics

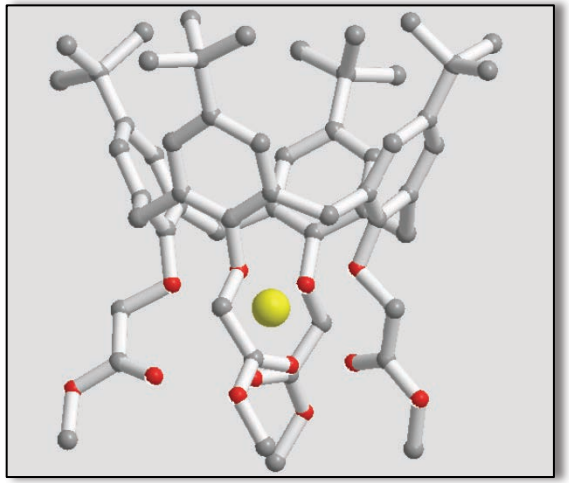
Physical Sensors & Transducers

Continuous Monitoring & Sensor Networks

Can we do long-term in-situ sensing with Chemical Sensors & Biosensors

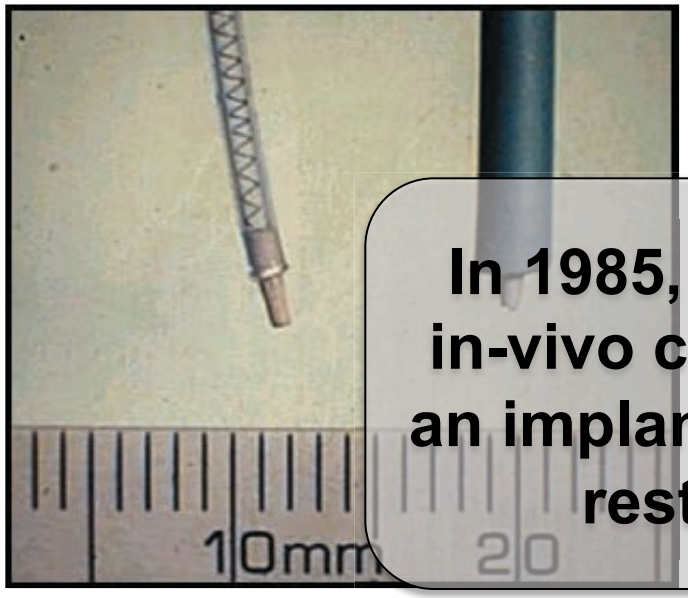
Calixarene Ionophores – controlling the selectivity





$H_3C—O—\underset{\underset{O}{\|}}{C}—CH_2—$

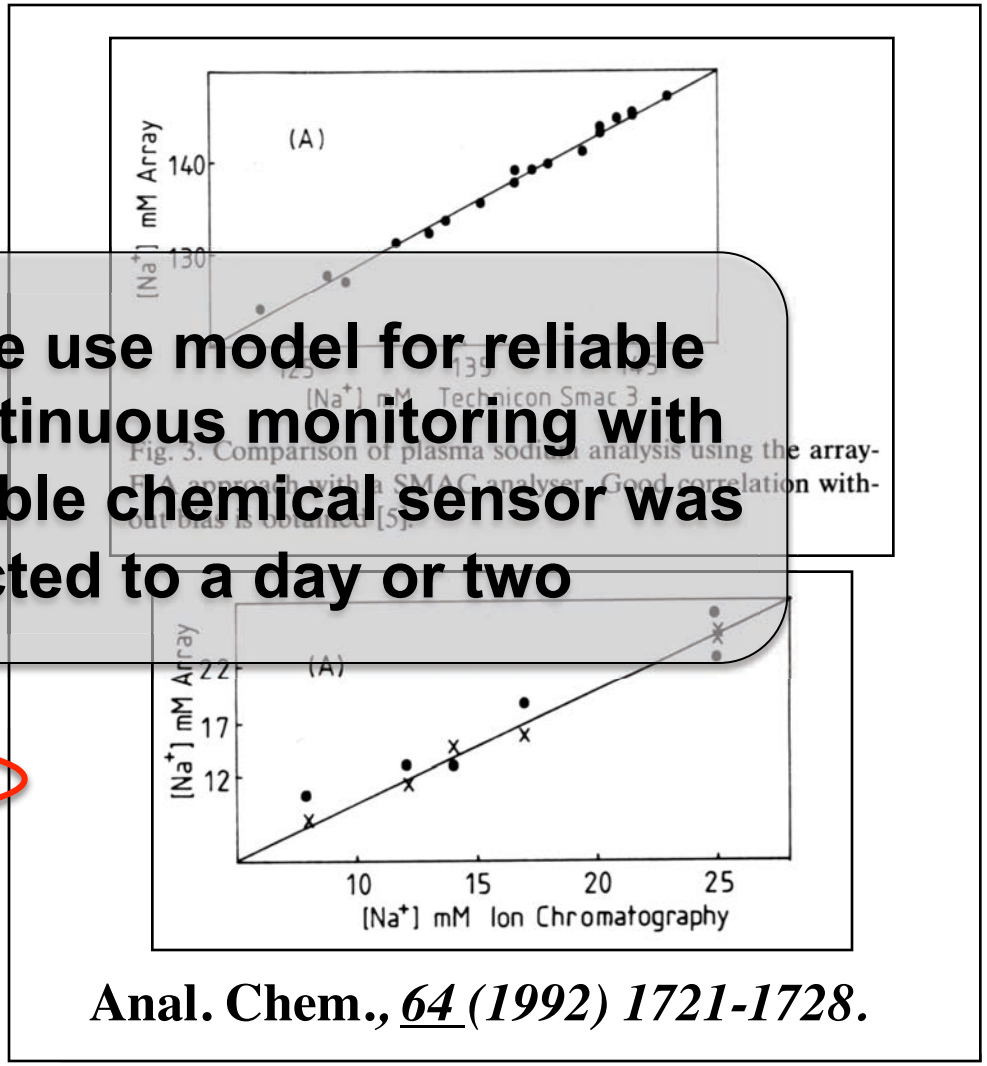
Blood Analysis; Implantible Sensors



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

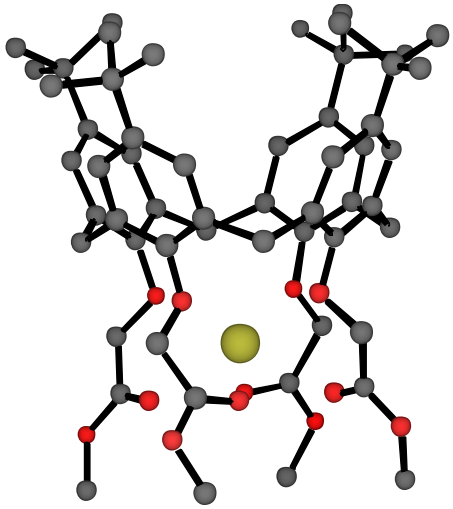
Dr. David Band, St Thomas's Hospital London

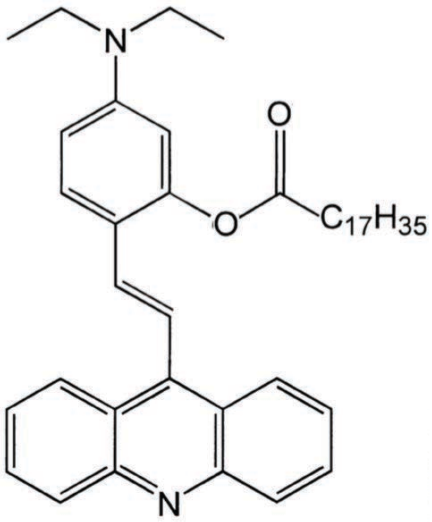


Anal. Chem., *64 (1992) 1721-1728.*

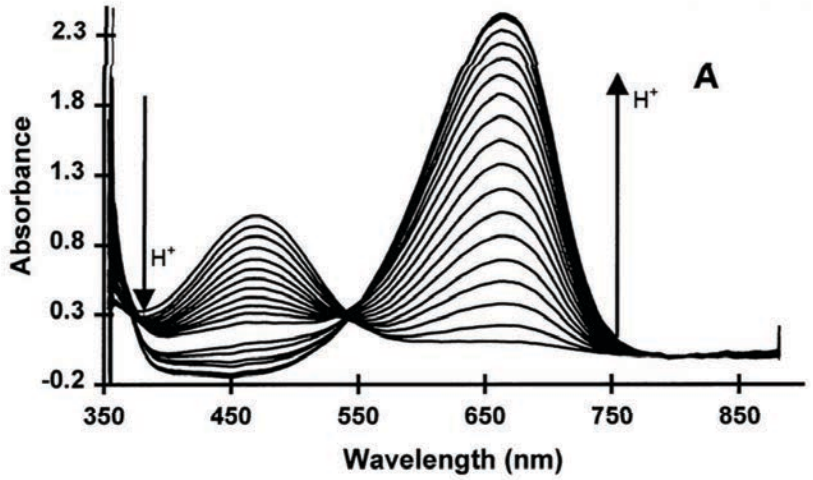
Ligand (and variations of) used in many clinical analysers for blood Na^+ profiling

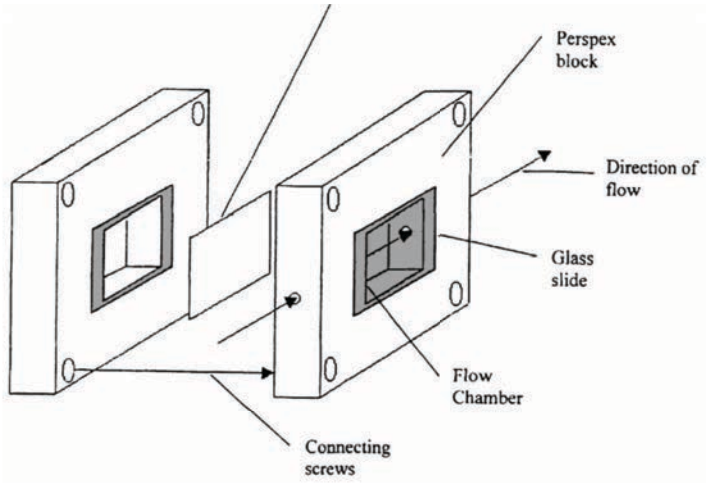
Coupling ion complexation to Acridine Dye protonation

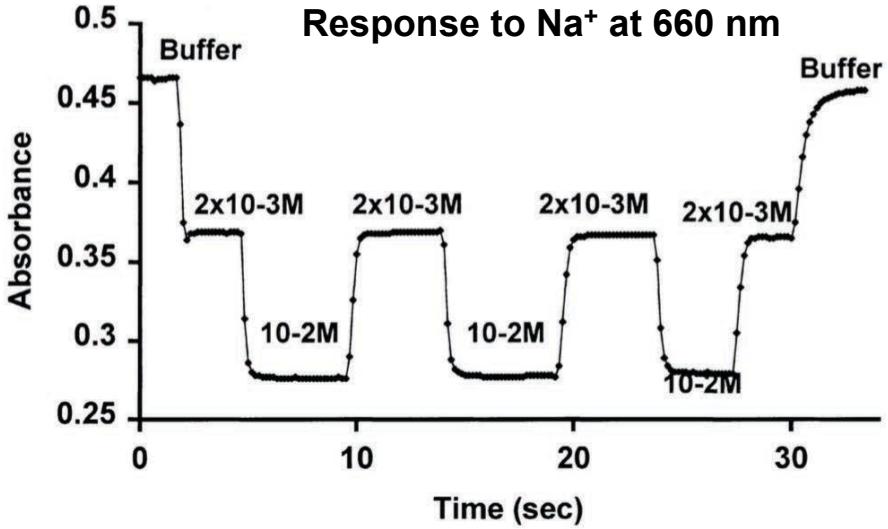




S. O'Neill et al. / Analytica Chimica Acta 398 (1999) 1–11

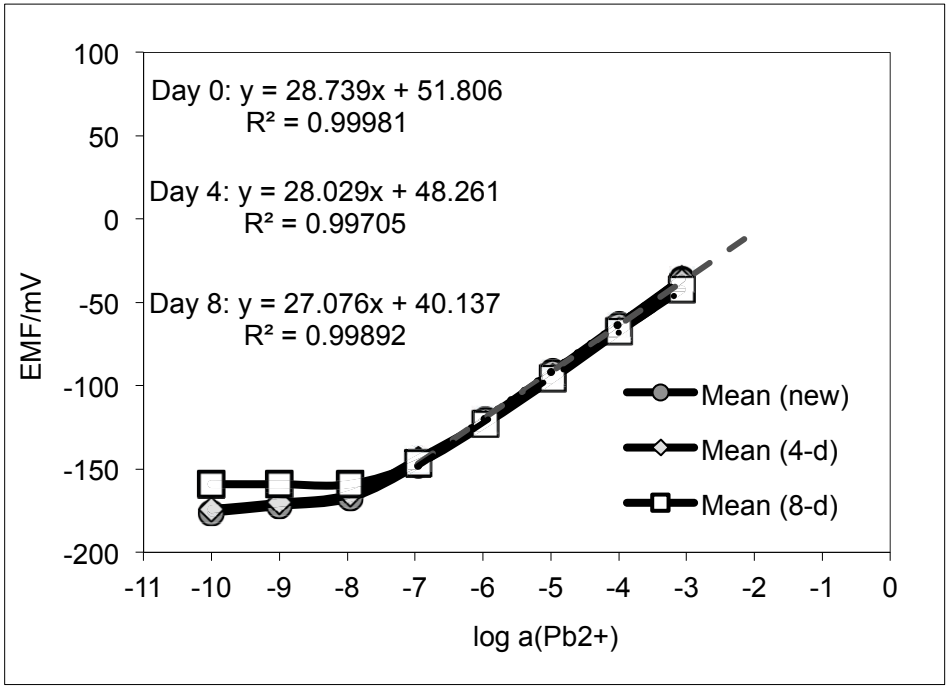


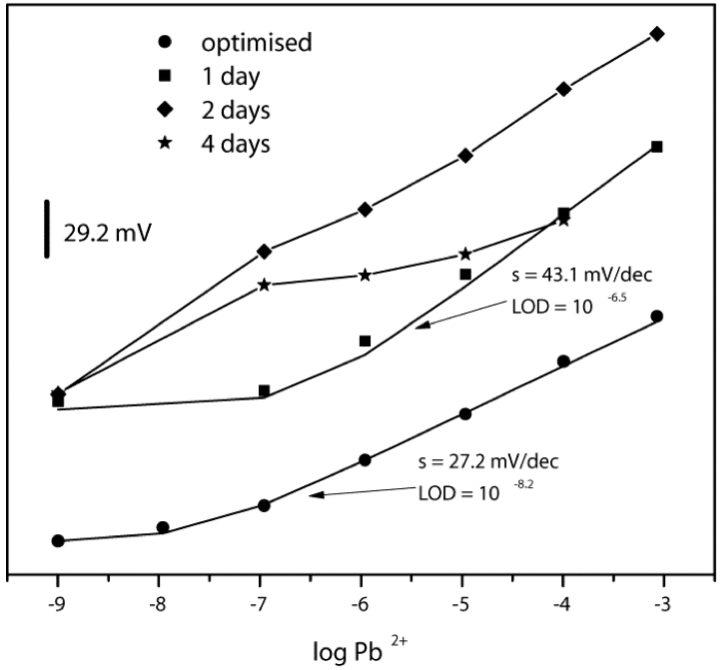




Change in Electrode Function over Time

See Electrochimica Acta 73 (2012) 93–97



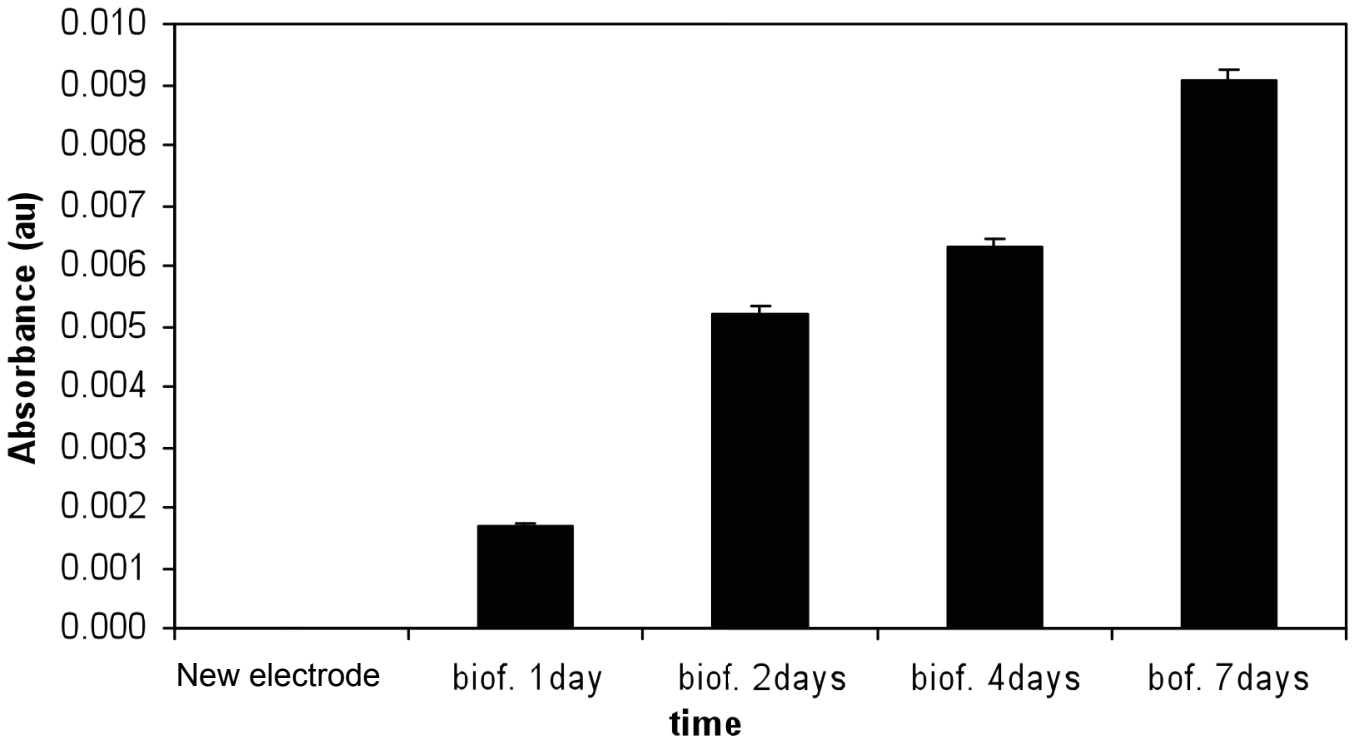


stored in 10^{-9}M Pb^{2+}, pH=4

Continuous contact with river water

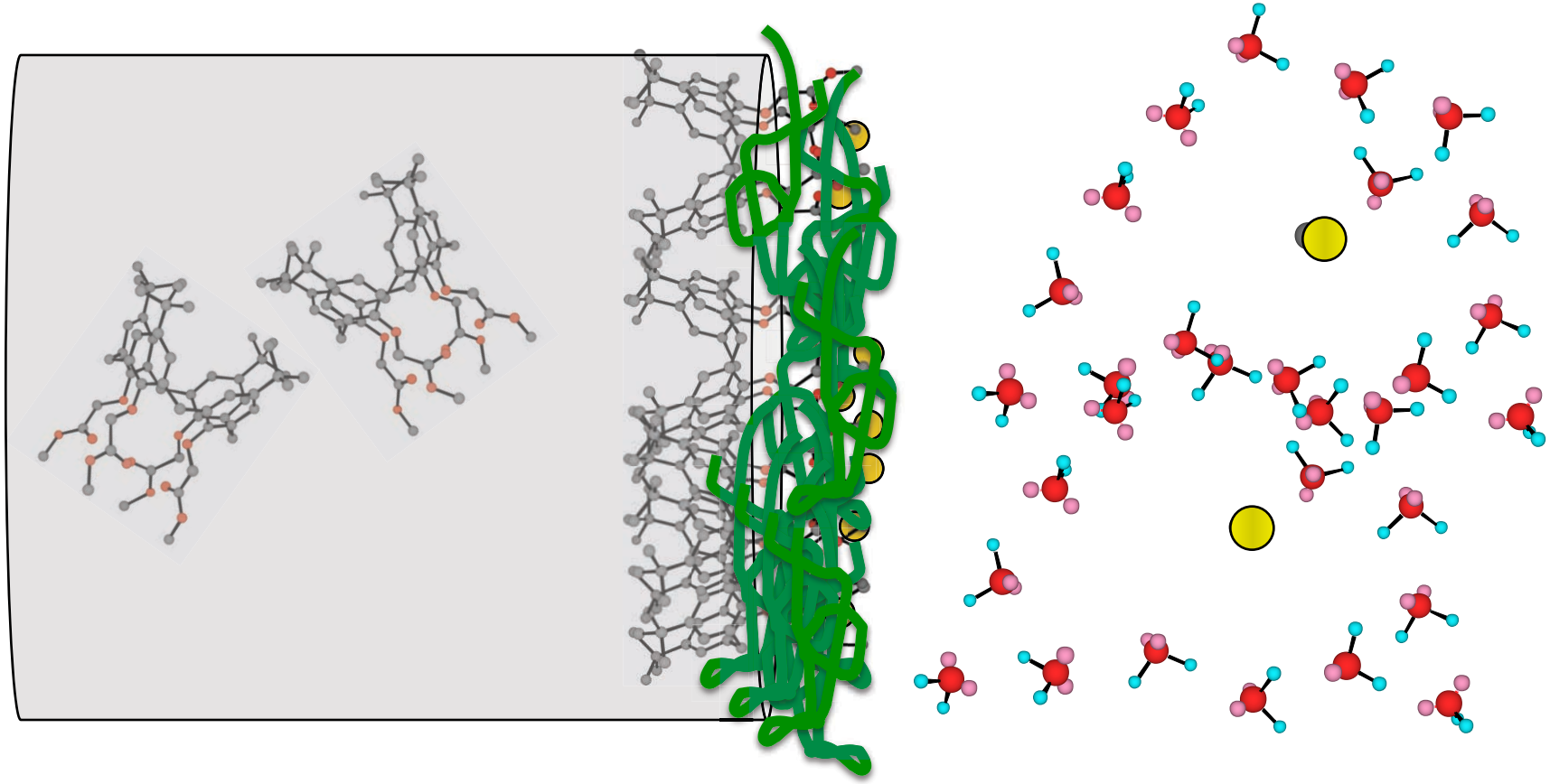
Conventional PVC-membrane based ISEs

Biofilm Formation on Sensors



- Electrodes exposed to local river water (Tolka)
- 'Slime test' shows biofilm formation happens almost immediately and grows rapidly

Control of membrane interfacial exchange & binding processes

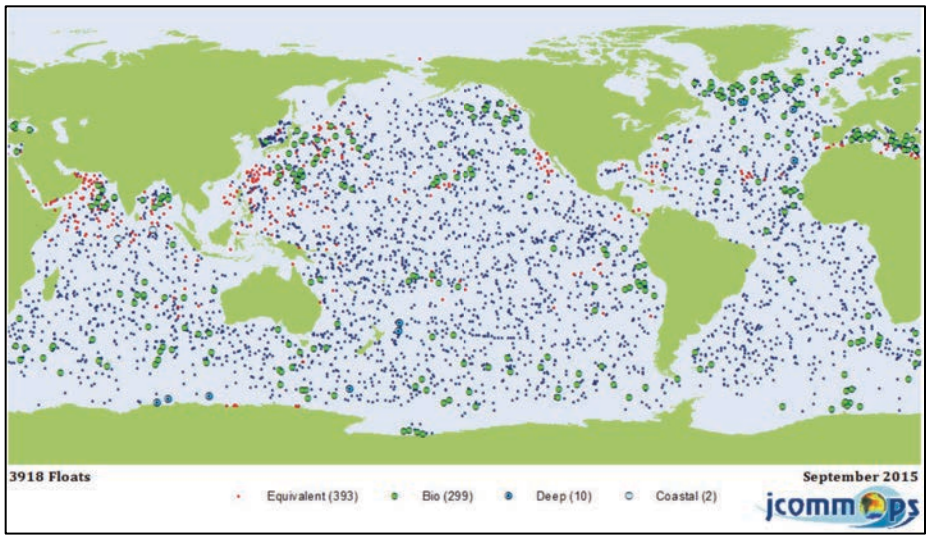


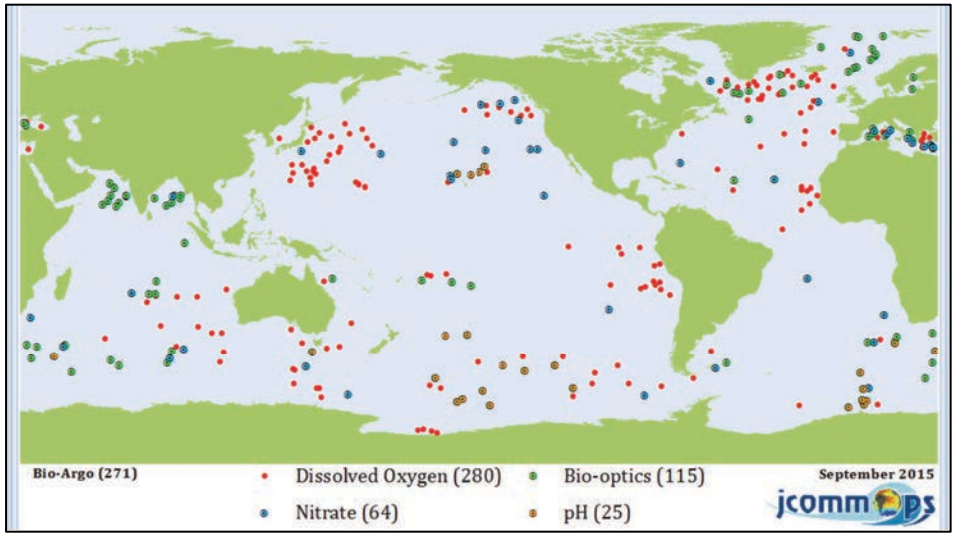
Remote, autonomous chemical sensing is a tricky business!

Osberstown – 3 week deployment

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

Argo Project (accessed March 20 2016)





- Ca. 4,000 (3918) floats: temperature and salinity
- Bio/Chem: Nitrate (64), DO (280), Bio-optics (115), pH (25)

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

@€60K ea!

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

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.

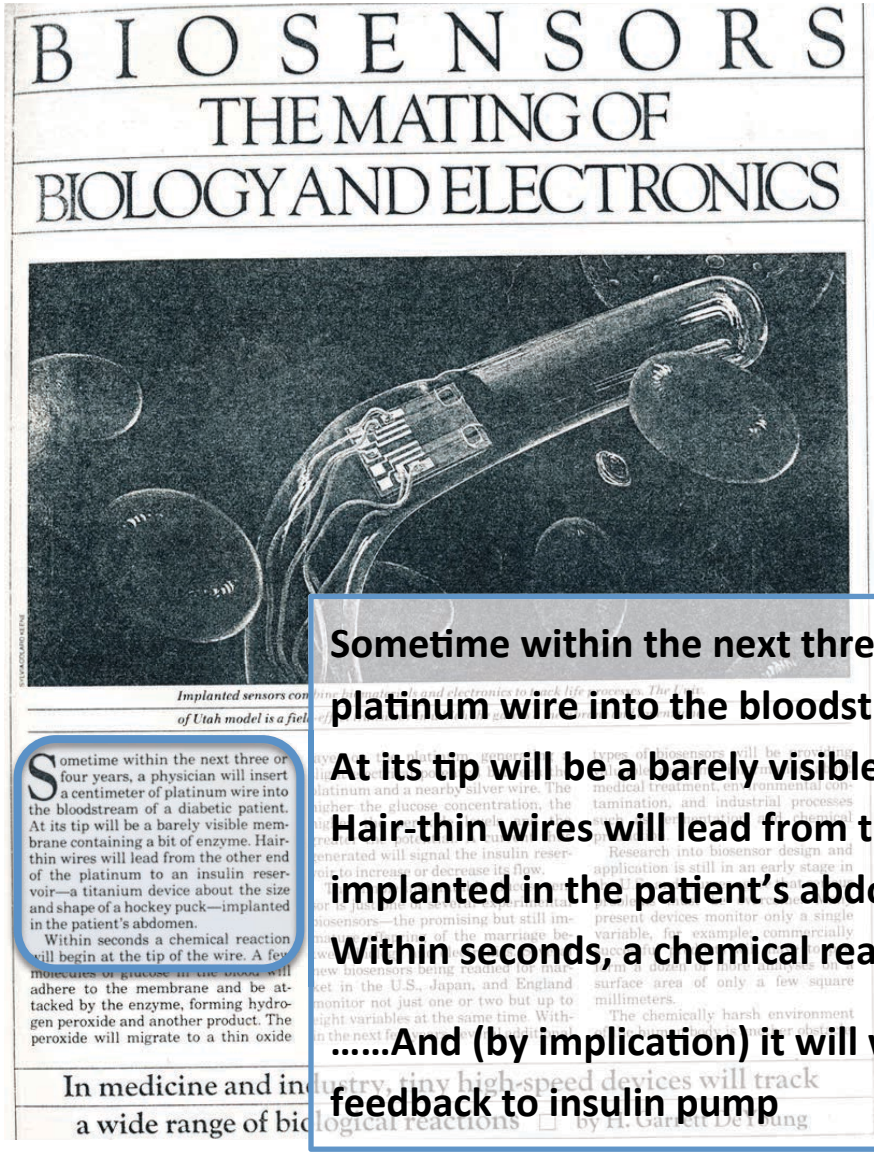
Wendy Schmidt Ocean Health XPRIZE

$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

And for nutrients….

The (broken) promise of biosensors…..


BIOSENSORS

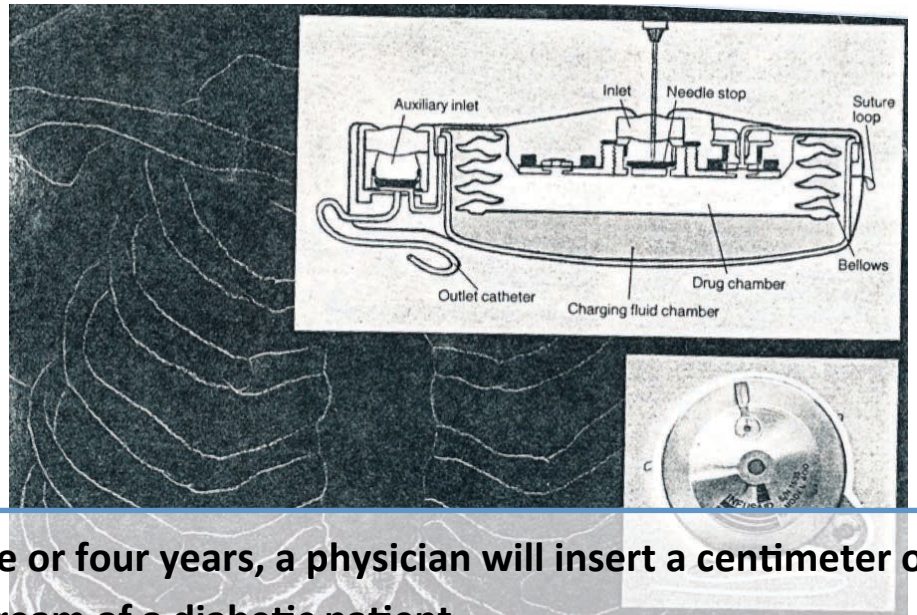
THE MATING OF BIOLOGY AND ELECTRONICS

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

In medicine and industry, tiny high-speed devices will track a wide range of biological reactions

High Technology, Nov. 1983, 41-49



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 implanted in the patient's abdomen.

Within seconds, a chemical reaction will begin at the tip of the wire……..

……And (by implication) it will work for years reliably and regulate glucose through feedback to insulin pump

Abbott Freestyle ‘Libre’

The days of routine glucose testing with lancets, test strips and blood are over.[2]

Welcome to flash glucose monitoring!

How to use the FreeStyle Libre System

The FreeStyle Libre system utilises advanced technology that is easy to use.

1 Apply sensor
with applicator

●○○

- A thin flexible sterile fibre (5mm long) is inserted just below the skin. Most people reported that applying the sensor was painless[6]
- The 14-day sensor stays on the back of your upper arm and automatically captures glucose readings day and night.
- The sensor is water resistant and can be worn while bathing, swimming and exercising[7]

[6] Most people did not feel any discomfort under the skin while wearing the FreeStyle Libre sensor. In a study conducted by Abbott Diabetes Care, 93.4% of patients surveyed (n=30) strongly agree or agree that while wearing the sensor, they did not feel any discomfort under their skin. [29 persons have finished the study; 1 person terminated the study after 3 days due to skin irritations in the area where the sensor touched the skin.]
[7] Sensor is water-resistant in up to 1 metre (3 feet) of water for a maximum of 30 minutes

- ‘Small fibre’ used to access interstitial fluid
- Data downloaded at least once every 8 hr via 1s contactless scan (1-4 cm)
- Waterproof to 1 metre
- Replace every 2 weeks

HYPEwatch: Apple, iWatch & Health Monitoring

How will they integrate biosensing with the iWatch……?

Apple Inc CEO Tim Cook

May 7th 2014

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

Apparent 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***

Kind Code A1 **Liu; Zenghe** **April 17, 2014**

Microelectronic contact lens and sensor system for detection of an analyte in tear fluid

Sensor

Abstract

An eye-mountable device includes an electrochemical sensor embedded in a polymeric material configured for mounting on a surface of the 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 tear fluid when the eye-mountable device is engaged.

- **Contact lens use model is 24 hours;**
- **Leverage Google Glass*;**
- **Novartis now working with Google.**

- ***Google Glass project abandoned!**

(Jan 15 2015) see

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

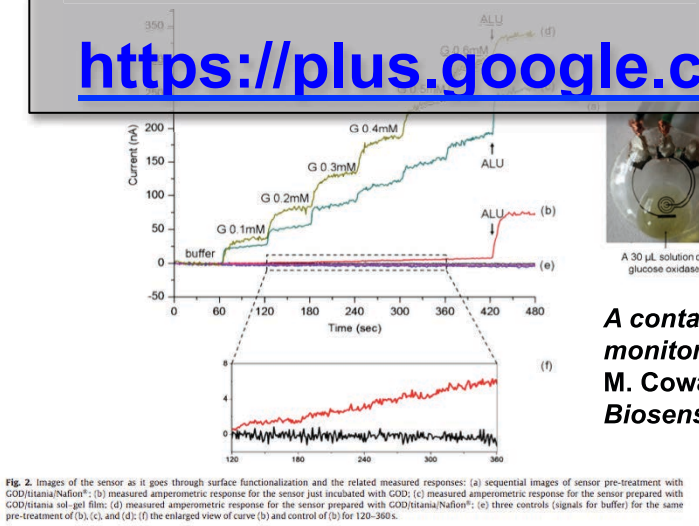
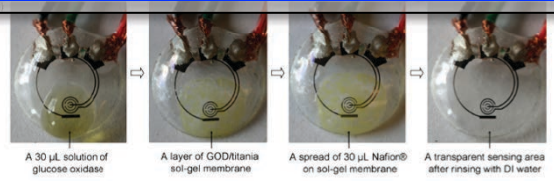


Fig. 2. Images of the sensor as it goes through surface functionalization and the related measured responses: (a) sequential images of sensor pre-treatment with GOD/titania/Nafion®: (b) measured amperometric response for the sensor just incubated with GOD; (c) measured amperometric response for the sensor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



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

Google Smart Contact Lenses Move Closer to Reality

BY LANCE ULANOFF

1 DAY AGO

the company secured two patents last week for the cutting edge, biometric sensor 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:

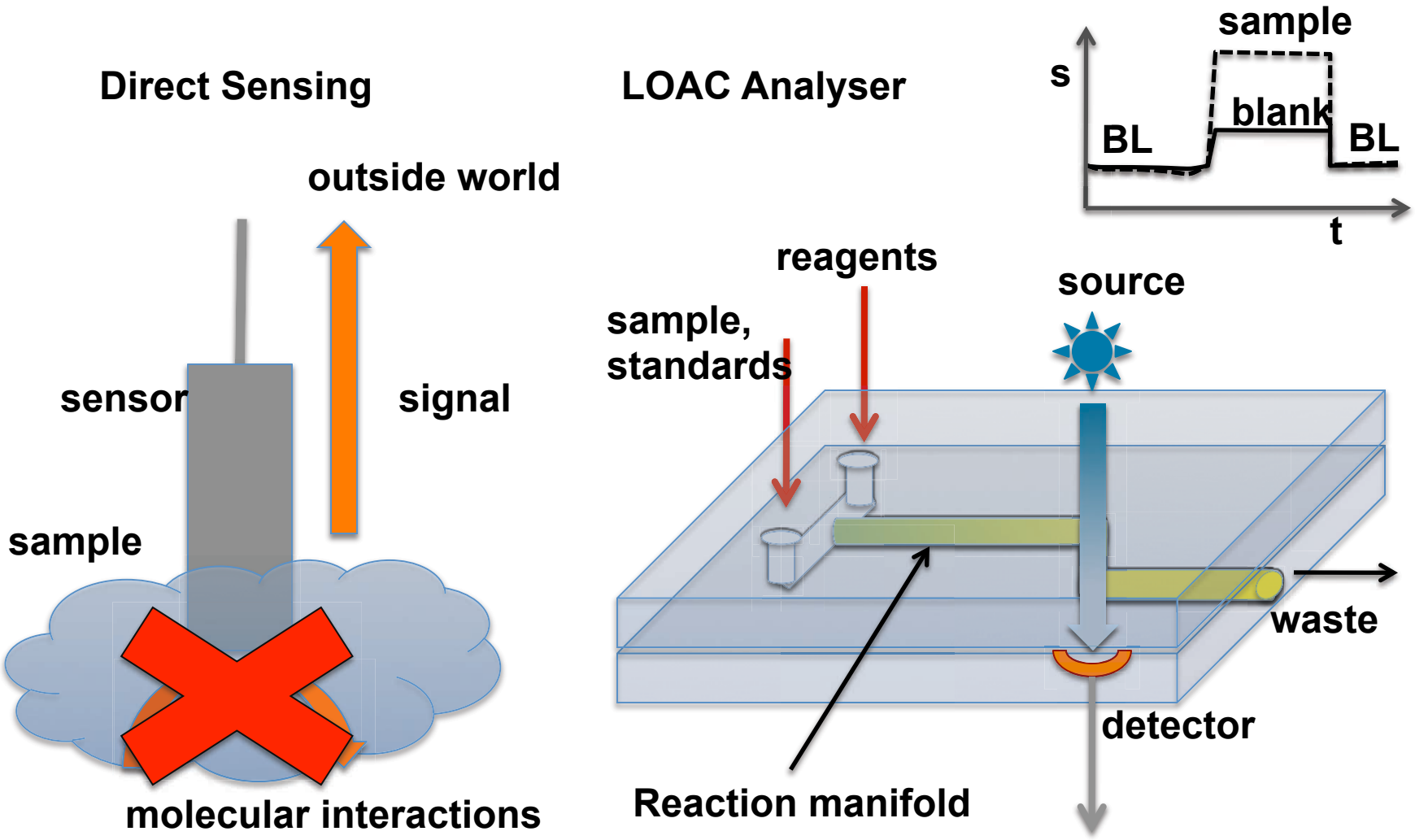
> "Human tear fluid contains a variety of inorganic electrolytes (e.g., Ca.sup.2+, Mg.sup.2+, Cl.sup.-), organic solutes (e.g., glucose, lactate, etc.), proteins, and lipids. A

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

What is the core issue??

- Simple, bare chem/biosensors do not function reliably EXCEPT as single shot short-term use devices – regular recalibration required (if they manage to keep functioning)
- Sensor surfaces change as soon as they are exposed to the real world – biofouling, interferents, leaching of components….
- Current systems work for days (after decades of research)
- Implants must work for 10 years! Environmental Sensors are far too expensive

Direct Sensing vs. Reagent Based LOAC/ufluidics



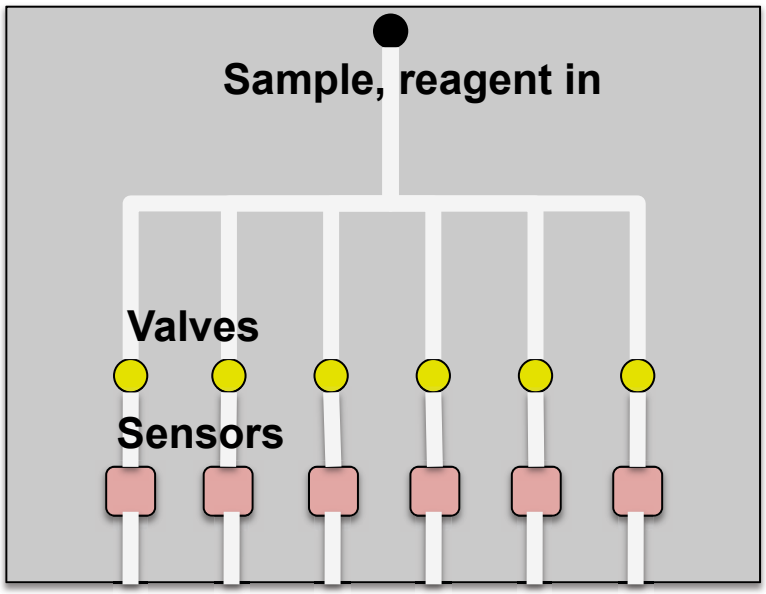
MicroTAS/Lab on a Chip/Microfluidics

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

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

Extend Period of Use via Multiple short-use Sensors….?

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

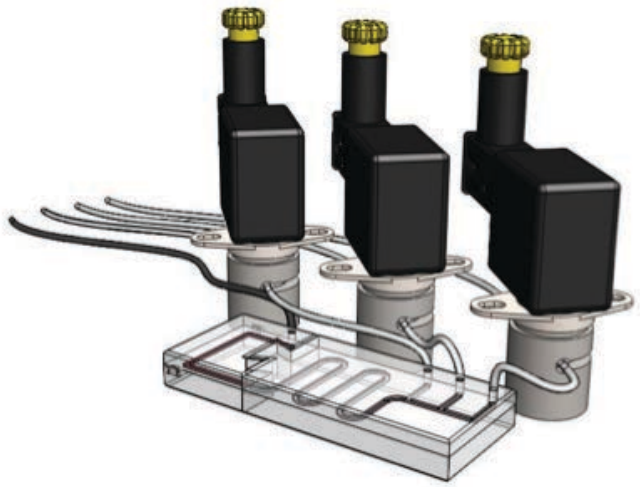


Then 50 sensors when used sequentially could provide an aggregated in-use lifetime of around 1 year

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

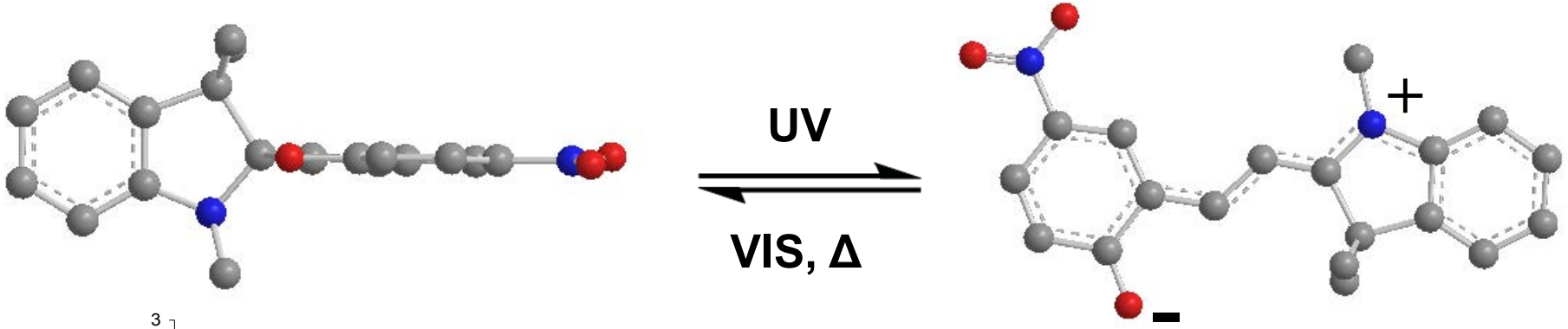
How to advance fluid handling in LOC platforms: re-invent valves (and pumps)!

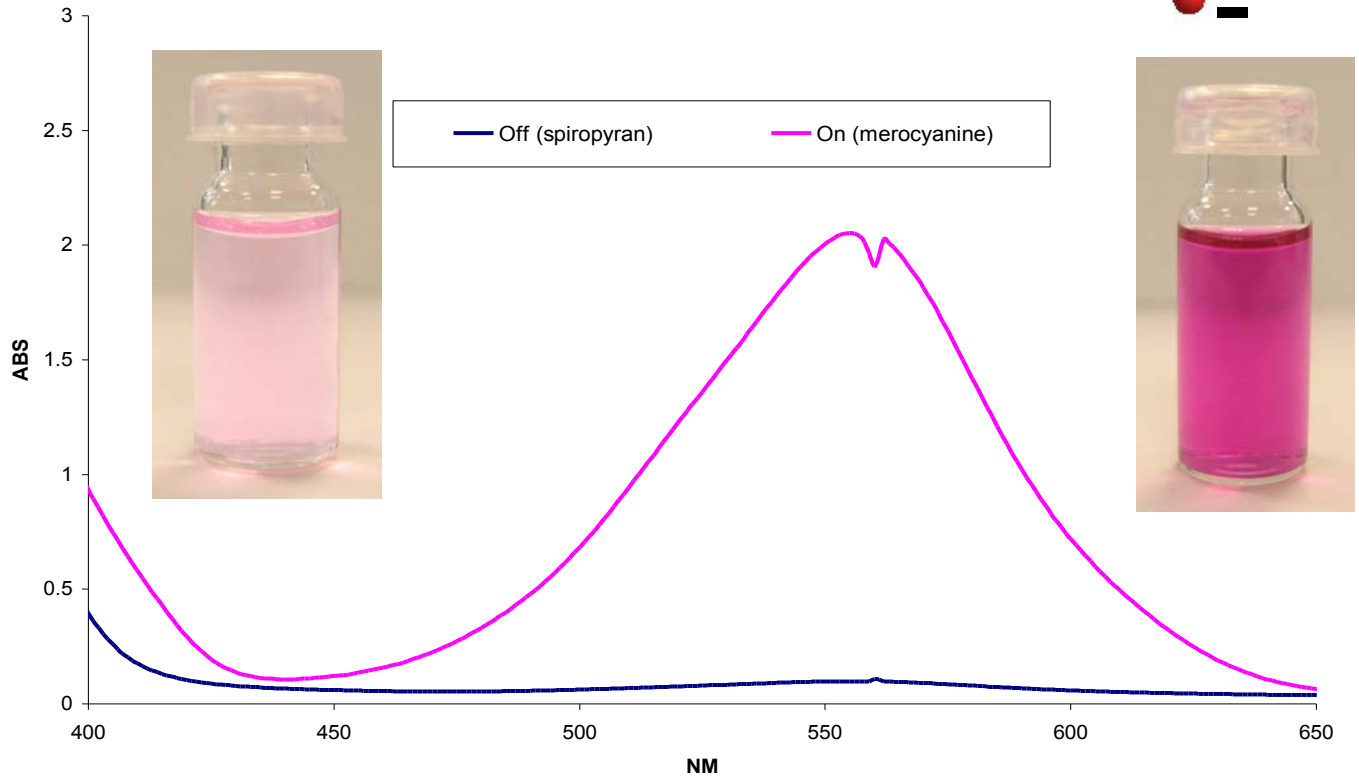
- **Conventional valves cannot be easily scaled down - Located off chip: fluidic interconnects required**
  - Complex fabrication
  - Increased dead volume
  - Mixing effects
- **Based on solenoid action**
  - Large power demand
  - Expensive



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

Photoswitchable Actuators





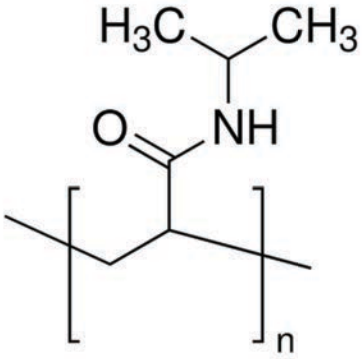
Famous Molecule….

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

Poly(*N*-isopropylacrylamide)

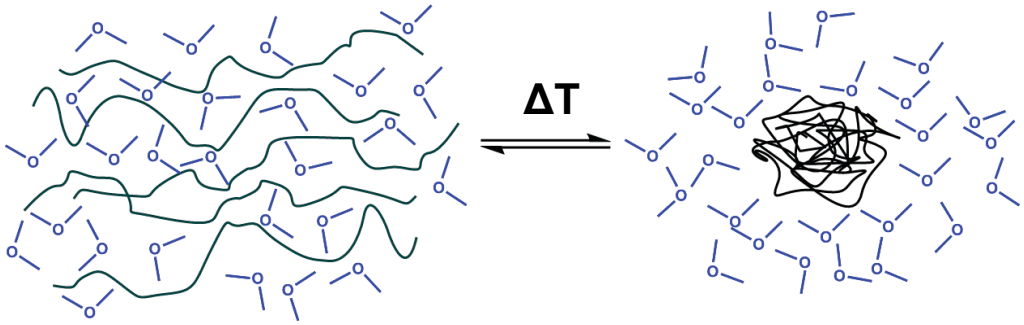
- pNIPAAM exhibits inverse solubility upon heating
- This is referred to as the LCST (Lower Critical Solution Temperature)
- Typically this temperature lies between 30-35^{o}C, but the exact temperature is a function of the (macro)molecular microstructure
- Upon reaching the LCST the polymer undergoes a dramatic volume change, as the hydrated polymer chains collapse to a globular structure, expelling the bound water in the process

pNIPAAM



Hydrophilic

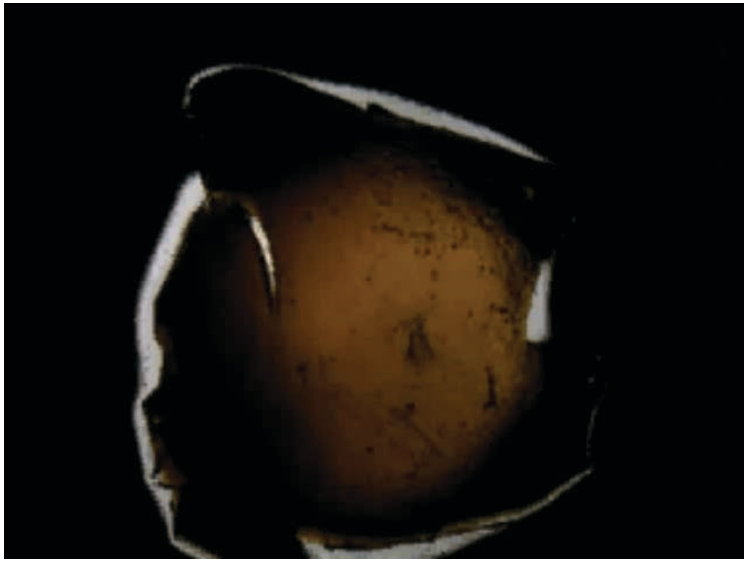
Hydrophobic

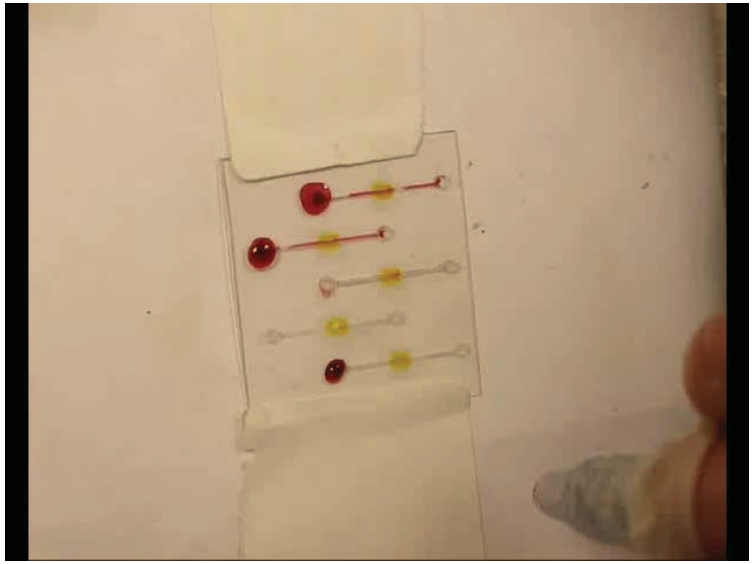


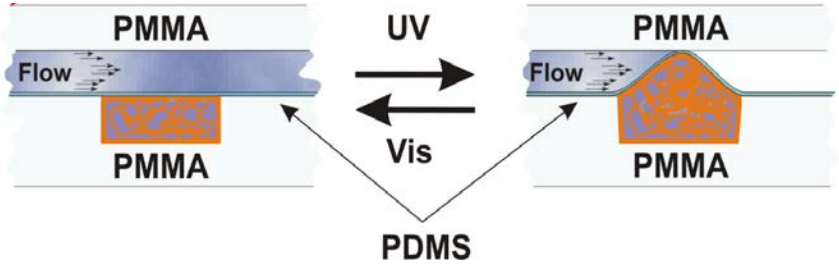
Hydrated Polymer Chains

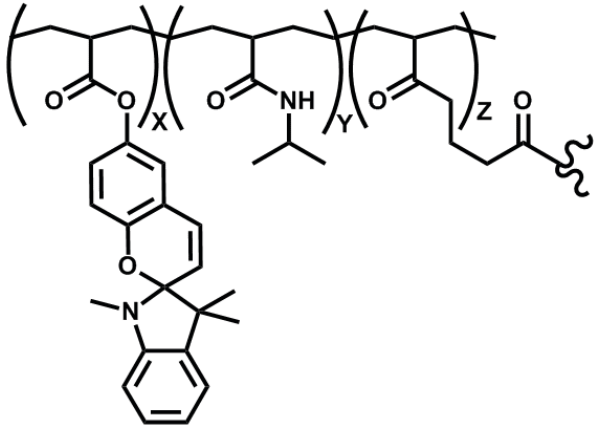
Loss of bound water -> polymer collapse

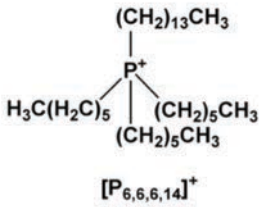
Photo-actuator polymers as microvalves in microfluidic systems

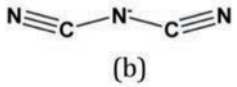








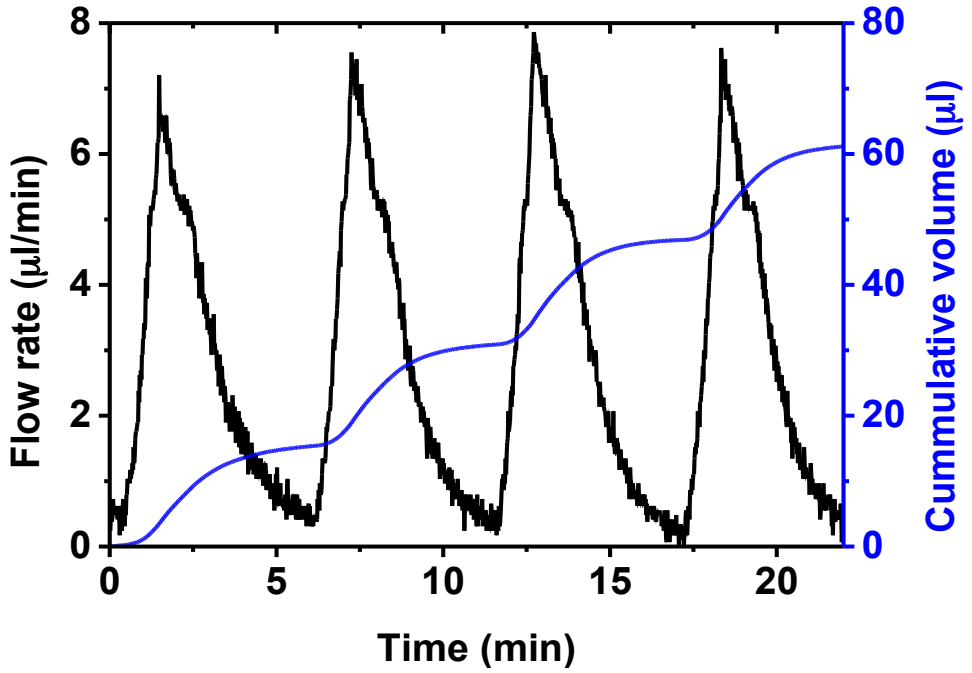




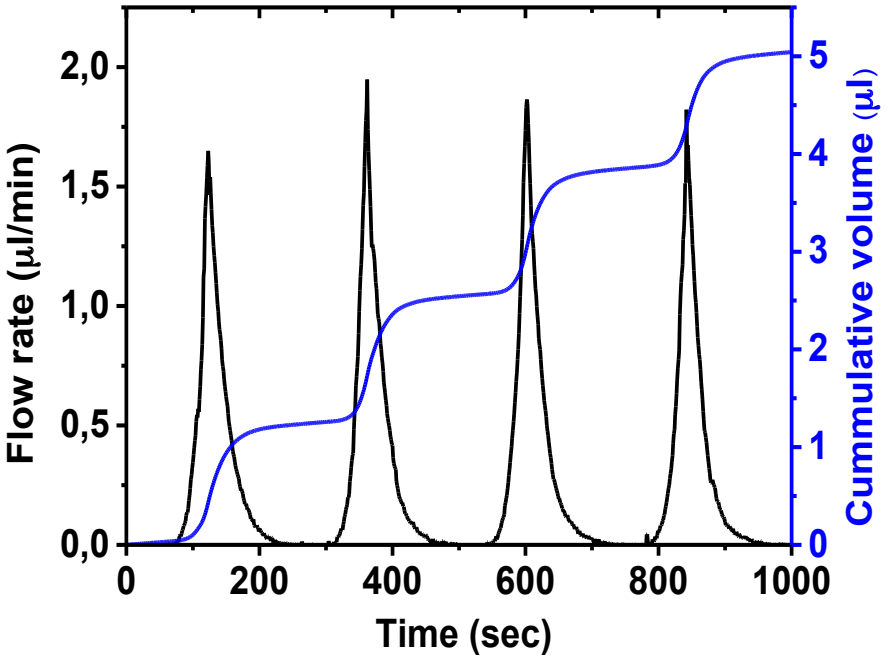
trihexyltetradecylphosphonium dicyanoamide $[P_{6,6,6,14}]^+[dca]^-$

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.

Optimisation of valve dimensions



1.7 mm mask



1.6 mm mask

First example of actuating polymer gels as reusable valves for flow control on minute time scales (> 50 repeat actuations)

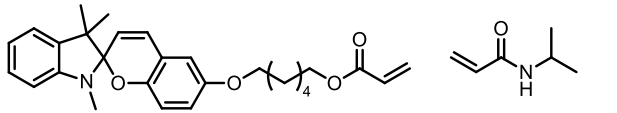
Photocontrol of Surface Features – Channel Surfaces Become 'Active'

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

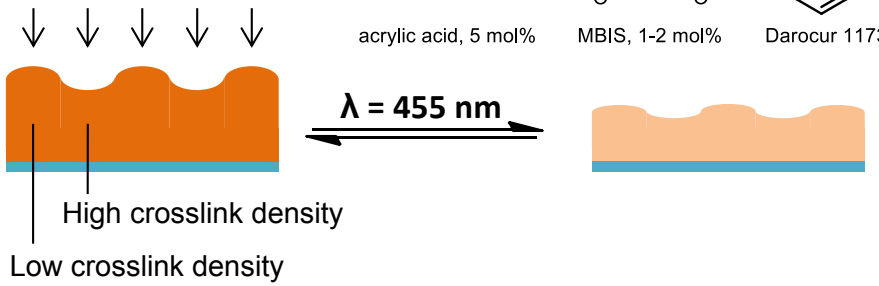
Jelle E. Stumpel,[†] Bartosz Ziółkowski,[‡] Larisa Florea,[‡] Dermot Diamond,[‡] Dirk J. Broer,*[,†,§] and Albertus P. H. J. Schenning*[,†,§]

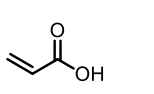


SPA, 1 mol%

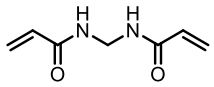
NIPAAM, 91-92 mol%

a)

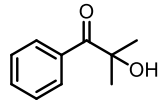




acrylic acid, 5 mol%

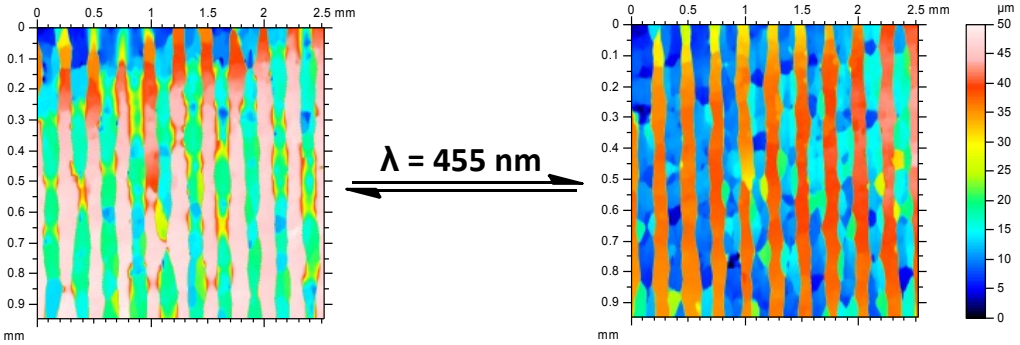


MBIS, 1-2 mol%

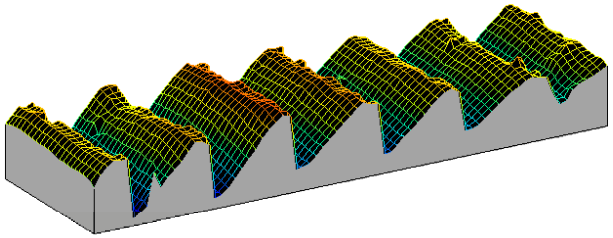


Darocur 1173, 1 mol%

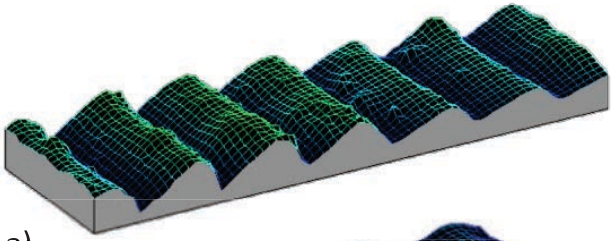
b)



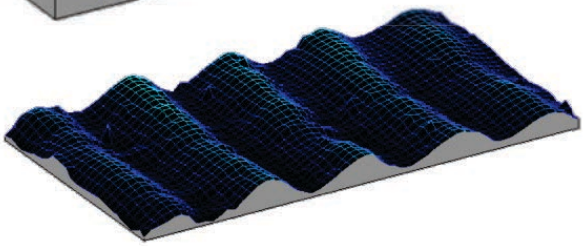
a)



b)

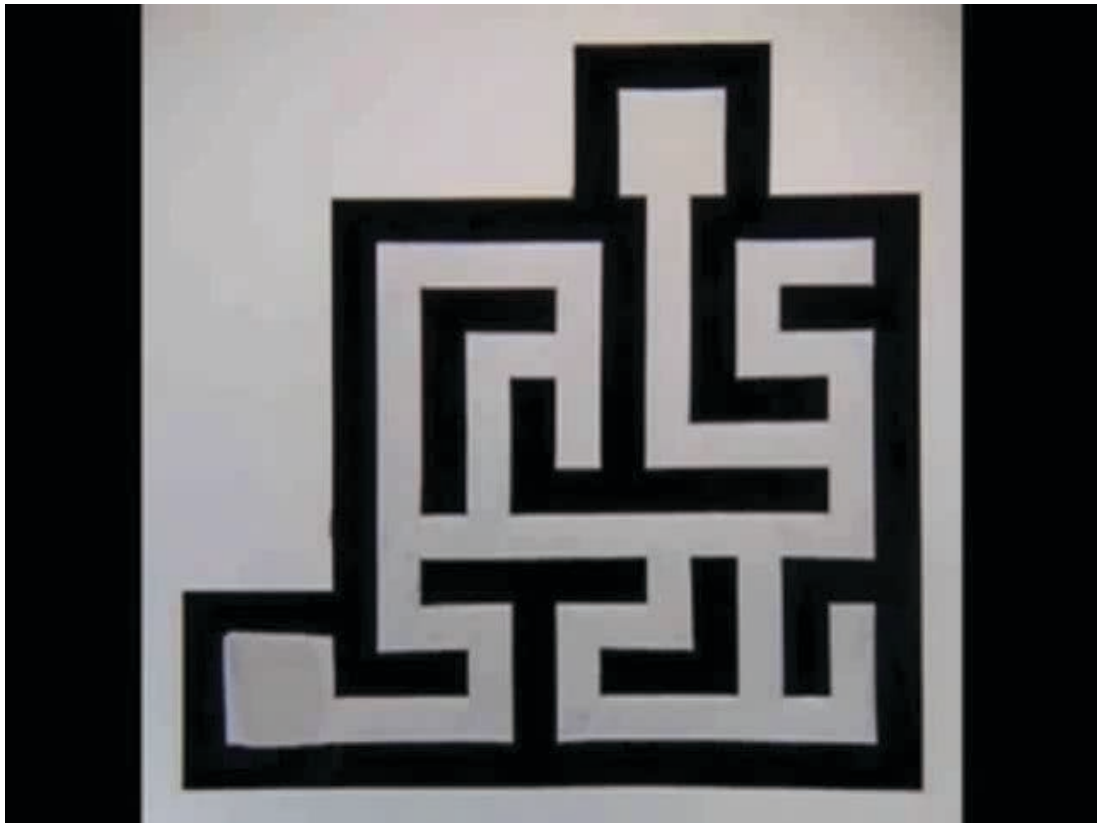


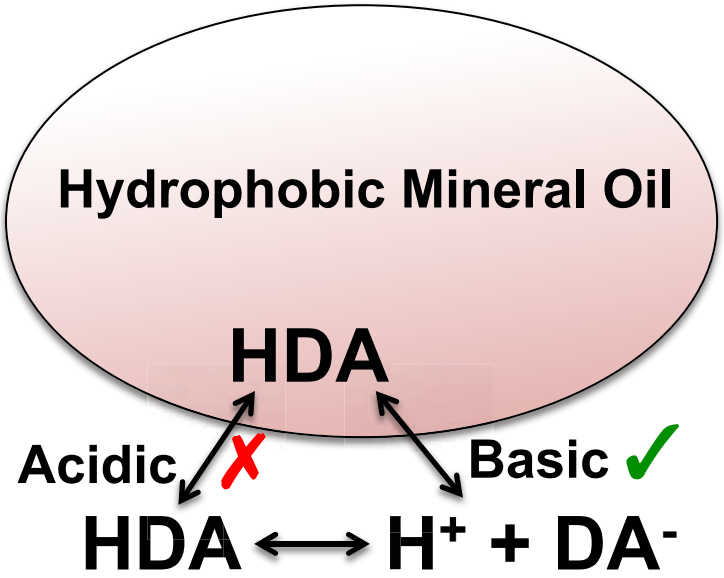
a)



b)

Chemotactic Systems





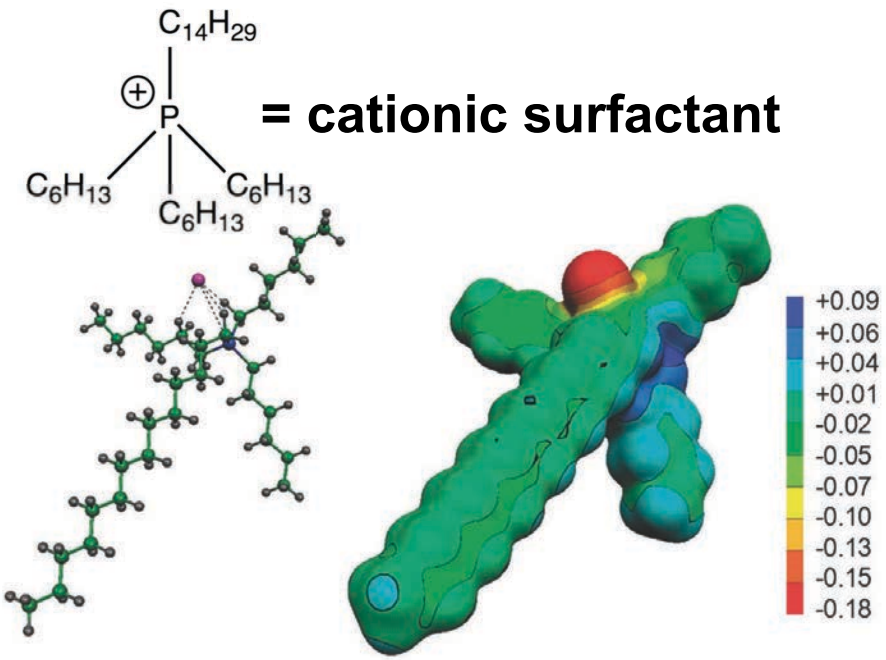
In a pH gradient, DA^- is preferentially transferred to the aqueous phase at the more basic side of the drop.

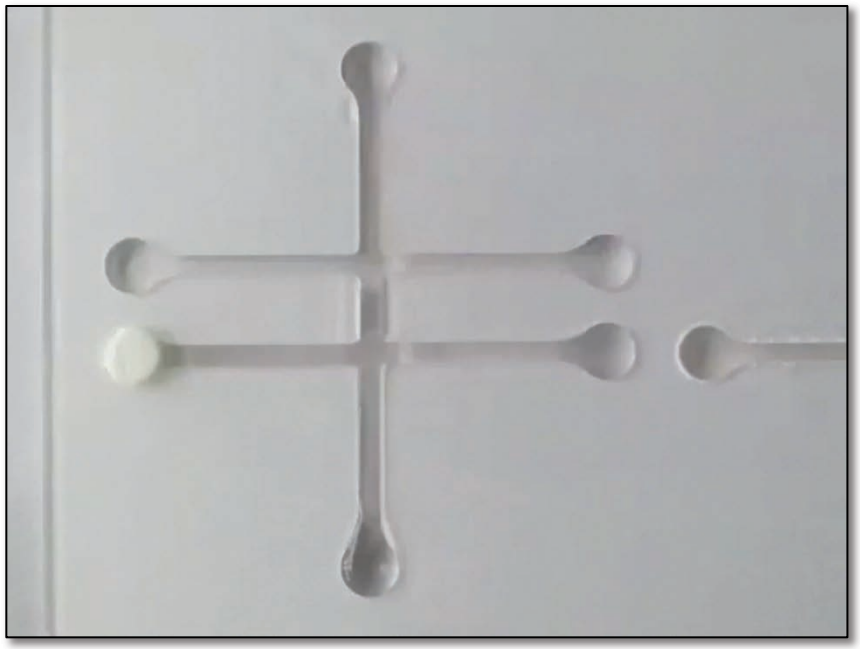
Published on Web 11/01/2010 (speed ~x4): channels filled with KOH (pH 12.0-12.3 + surfactant; agarose gel soaked in HCl (pH 1.2) sets up the pH gradient; droplets of mineral oil or DCM containing 20-60% 2-hexyldecanoic acid + dye. Droplet speed ca. 1-10 mm/s; movement caused by convective flows arising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

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

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

We can do the same with IL Droplets



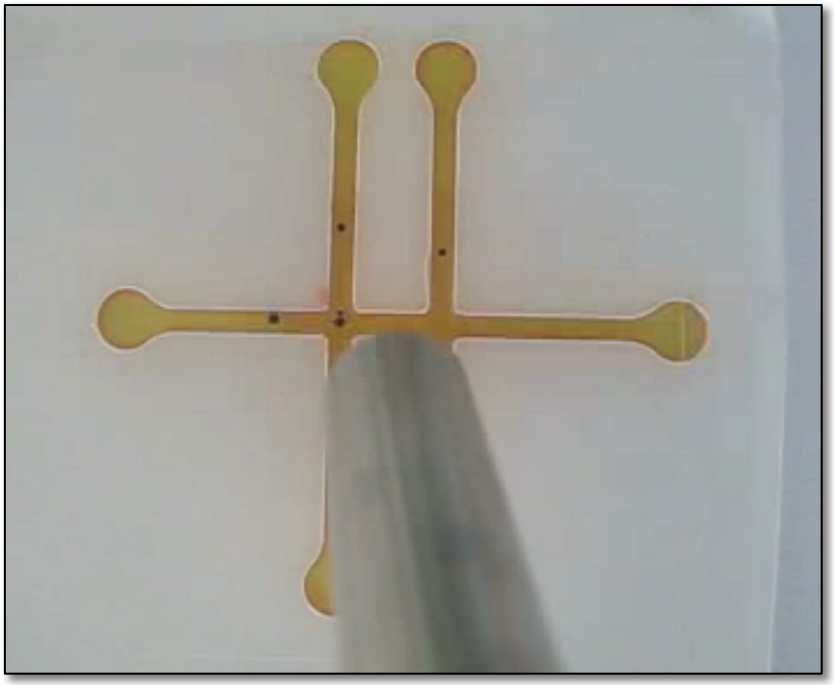


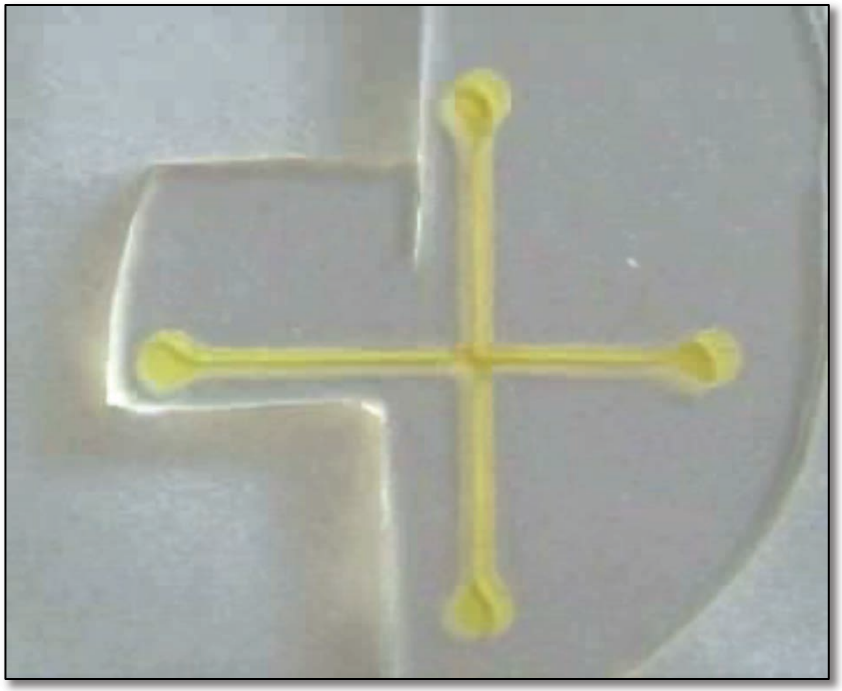
Trihexyl(tetradecyl)phosphonium chloride ($[P_{6,6,6,14}][Cl]$) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the Cl^- ion which is created using a polyacrylamide gel pad soaked in 10^{-2} M HCl; A small amount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

Self-propelled chemotactic ionic liquid droplets, W. Francis, C. Fay, L. Florea, D. Diamond, Chemical Communications, 51 (2015) 2342-2344.

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.

Controlling Droplet Movement in Channels using Light





- We use light to create a localised pH gradient via soluble photoacid
- This disrupts an ion pair at the droplet interface; Surfactant is expelled and movement of the droplet occurs
- Droplets can be used for sensing and transport & release of active components

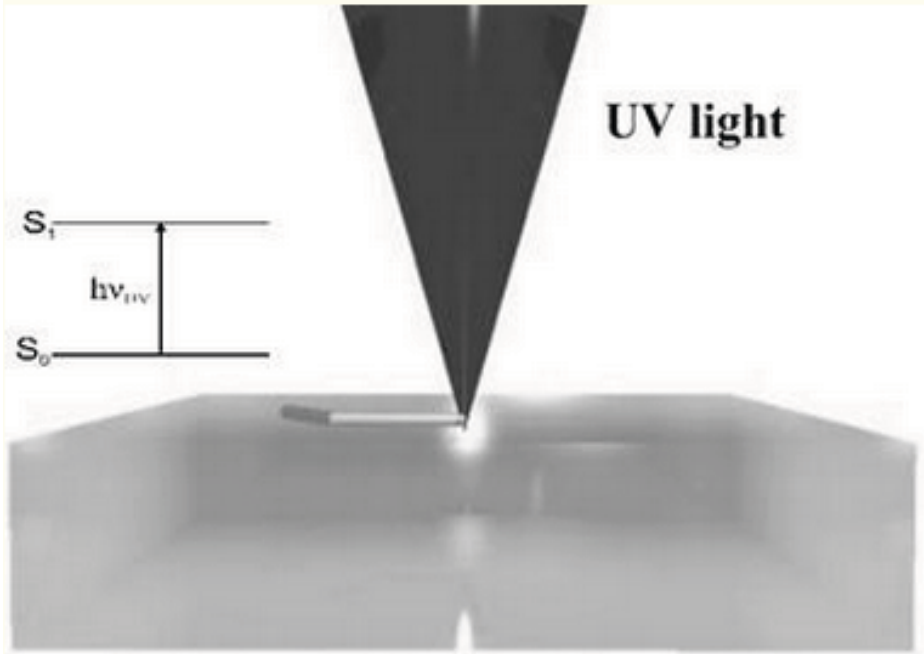
Photo-Chemopropulsion - Light-Stimulated Movement of Microdroplets, L. Florea, K. Wagner, P. Wagner, G.G. Wallace, F. Benito-Lopez, D.L. Officer, D. Diamond, Advanced Materials, 26 (2014) 7339-7345.

Multi-Functional Bio-Inspired Fluidics!

- **At present, the fluidic system's function is to;**
  - Transport reagents, samples, standards to the detector
  - Perform relatively simple (but important) tasks like cleaning, mixing
  - Switching between samples, standards, cleaning solutions
- **In the future, the fluidic system will perform much more sophisticated 'bioinspired' functions**
  - System diagnostics, leak/damage detection
  - Self-repair capability
  - Switchable behaviour (e.g. surface roughness, binding/release),
- **These functions will be inherent to the channels and integrated with circulating smart micro/nano-vehicles**
  - Spontaneously move under an external stimulus (e.g. chemical, thermal gradient) to preferred locations

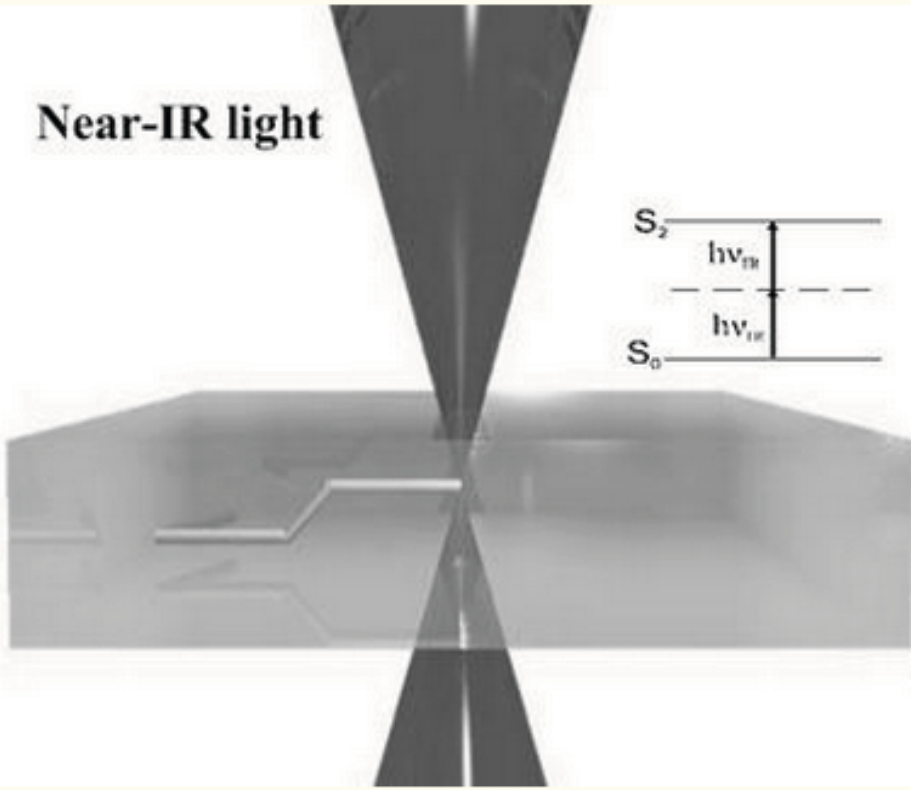
2-Photon Polymerisation

Stereolithography



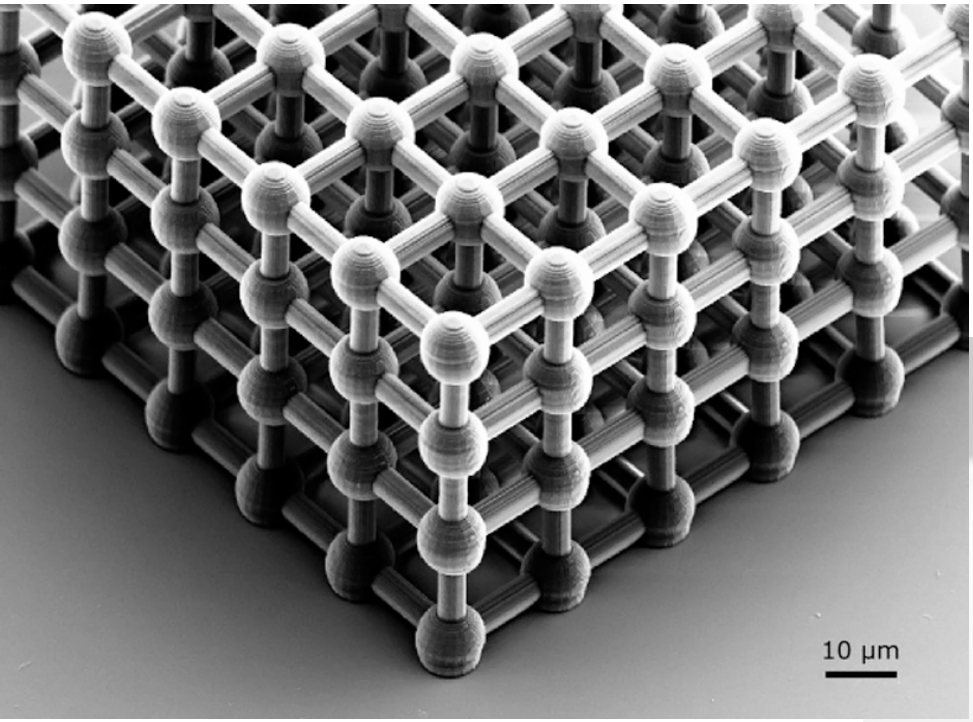
- Single photon absorption
- 2D patterns

Two-photon polymerisation



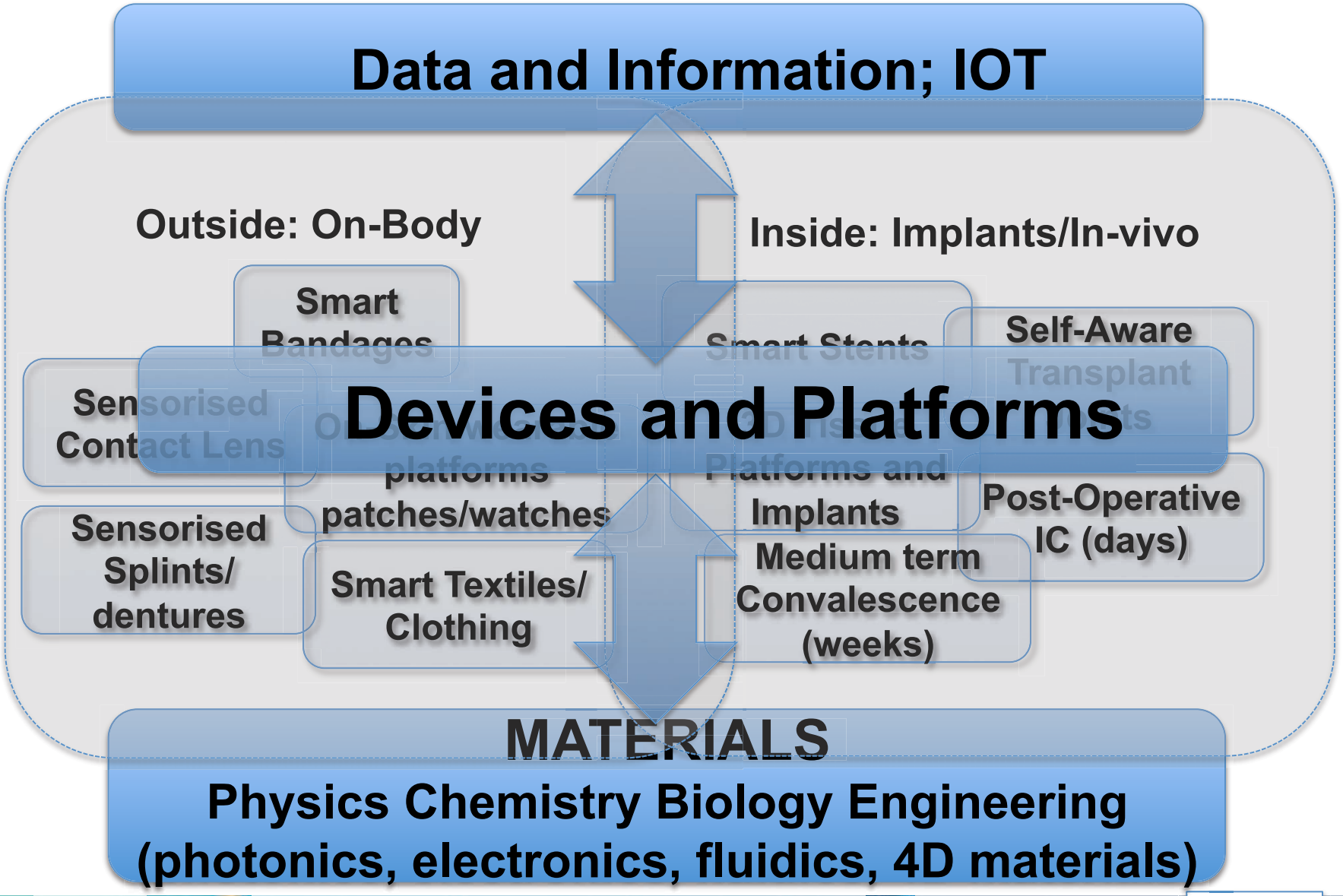
- Two photon absorption
- 3D structures

2-Photon Polymerisation



http://www.nanoscribe.de/

Near Term Goals (5Years)



Time of EXCITING OPPORTUNITY!

- 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
- Learn from nature – e.g. more sophisticated circulation systems for 'self-aware' sensing devices!

IOT will increasingly integrate chem/bio information related to health, environment, food/agri, security….

FET Programme – 2018-2020 and beyond

- **Flagships in 'Graphene' and 'The Brain'**
  - Do you think these are good topics?
  - Are they producing value for money? Is it too soon to say?
  - Are flagships needed?
  - Should there be a third flagship? If so, what should the topic be? What budget should be allocated?
  - Move towards Open Science
- **FET proactive (themed)**
  - What themes should be the focus of future calls?
  - What proportion of the budget should be allocated?
- **FETopen**
  - Very popular but hugely over-subscribed: success rates around 1%
  - How can this be improved?

See
www.graphene-flagship.eu
http://humanbrainproject.eu

Open call for input and opinions:
https://ec.europa.eu/futurium/en/content/fet-proactive
https://ec.europa.eu/futurium/en/content/fet-flagships
https://ec.europa.eu/futurium/en/blog/help-us-shape-future-horizon-2020

The European Sensor Systems Cluster (ESSC)

Information Session Europtrode Conference Tuesday 17.15

European Sensor Systems Cluster - *ESSC*

Vision, Objectives, History and Roadmap

Dermot Diamond – Chair WG1
Environmental Sensing

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Dublin City University, Ireland

Torsten Mayr – Chair WG4
Monitoring Industrial Processes

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Graz University of Technology

Thanks for the invite!

MASK
Project no: 269302
Materials and Advanced Sensor Knowledge Exchange

NAPES
NEXT GENERATION ANALYTICAL PLATFORMS FOR ENVIRONMENTAL SENSING

COMMON SENSE
MARINE SENSORS - MARINE MONITORING

aquawarn