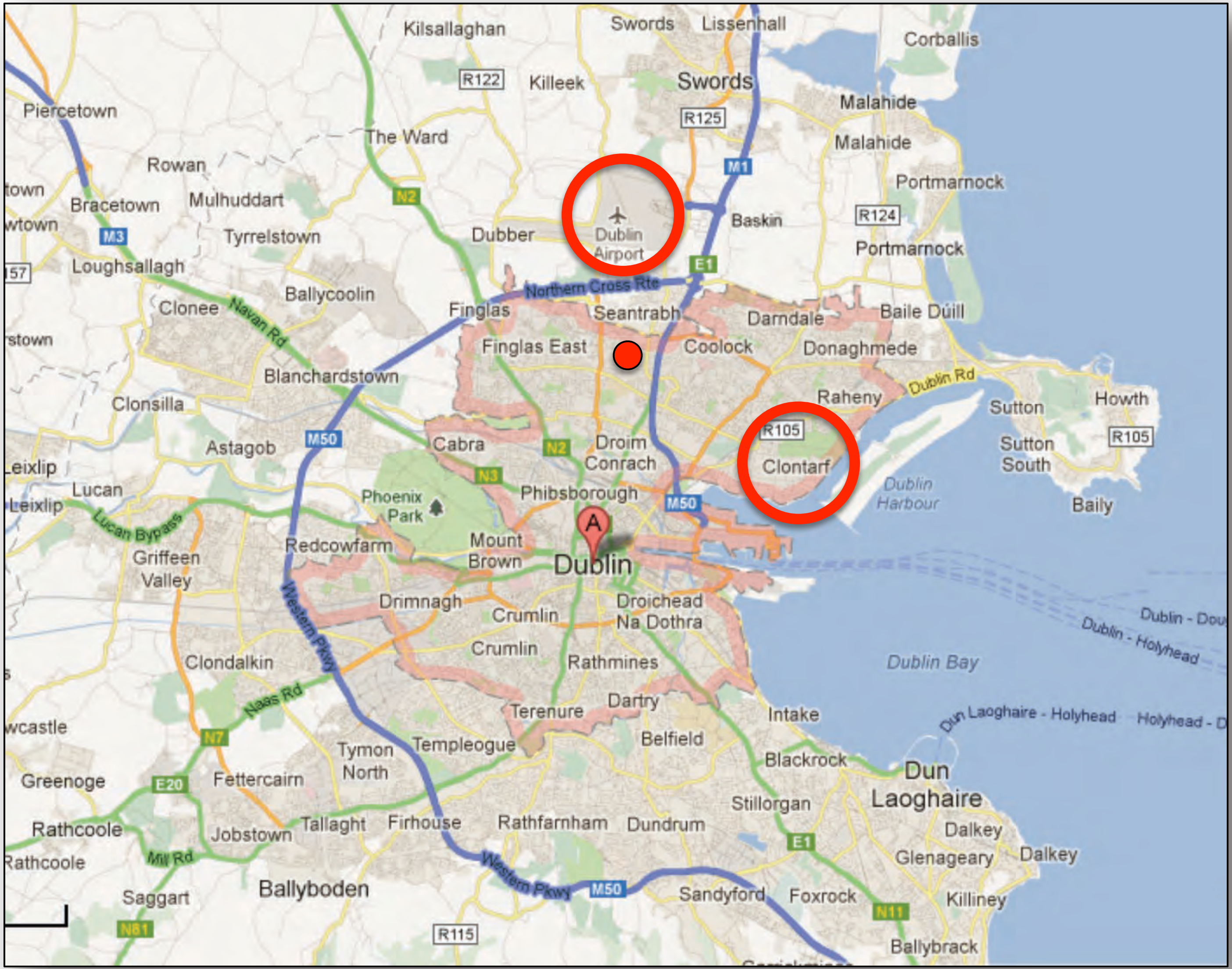
"Calixarenes as ionophores in ion-selective electrodes: The Past and The Future of Chemical Sensing"

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

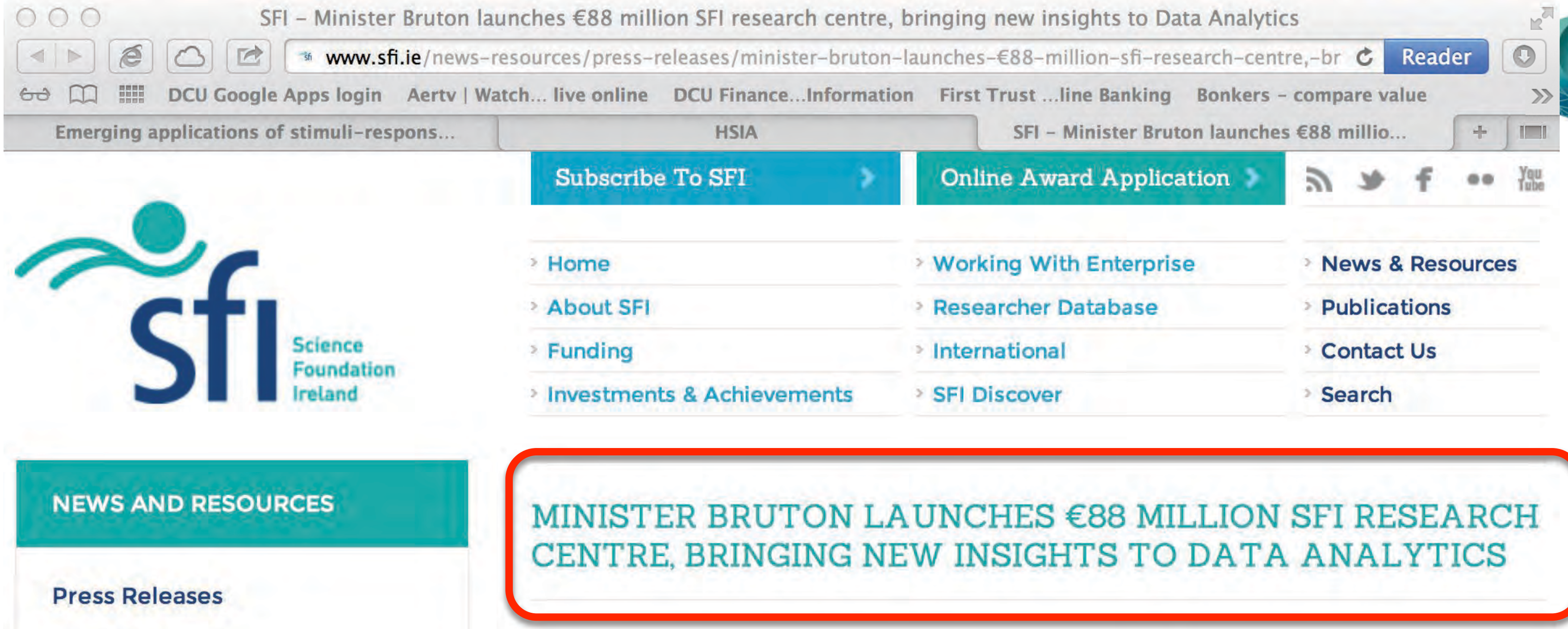
Invited Lecture presented at the

Annual Meeting of the Danish Electrochemical Society
Copenhagen, 9-10 October 2014

Dublin & DCU Location



Battle of Clontarf (1014)



Insight Centre for Data Analytics

- Biggest single research investment ever by Science Foundation
- Biggest coordinated research programme in the history of the state
- Focus is on ‘big data’ related to health informatics and pHealth
- Materials science will play a central role in the practical realisation of new concepts in chemical sensing and biosensing

Keynote Article: August 2004, Analytical Chemistry (ACS)

internet scale sensing

Dermot Diamond
Dublin City University
(Ireland)

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

Digital communications networks are at the heart of modern society. The digitization of communications, the development of the Internet, and the availability of relatively inexpensive but powerful mobile computing technologies have established a global communications network capable of linking billions of people, places, and objects. Email can instantly transmit complex documents to multiple remote locations, and websites provide a platform for instantaneous notification, dissemination, and exchange of information globally. This technology is now pervasive, and those in research and business have multiple interactions with this digital world every day. However, this technology might simply be the foundation for the next wave of development that will provide a seamless interface between the real and digital worlds.

The crucial missing part in this scenario is the gateway through which these worlds will communicate: How can the digital world sense and respond to changes in the real world? Analytical scientists—particularly those working on chemical sensors, biosensors, and compact, autonomous instruments—are

Dermot Diamond, Anal. Chem., 76 (2004) 278A-286A

(Ron Ambrosio & Alex Morrow, IBM TJ Watson)

Grand Challenge

- To develop a **scalable model** for chemical sensing in remote, hostile locations (e.g., inside the body, in the environment)
  - Completely autonomous devices
  - Must provide reliable, high quality data
  - Capable of long-term (months, years) independent operation

Surely we can do this already –can't we?

I'm afraid not. There are no examples of long-term implantable chem/bio-sensors;
In the environment (water), units cost typically €20K++

sfi DCU UCC OÉ Gaillimh NUI Galway UCD DUBLIN

Artificial Pancreas

Used a Technicon segmented flow colorimetric glucose analyser

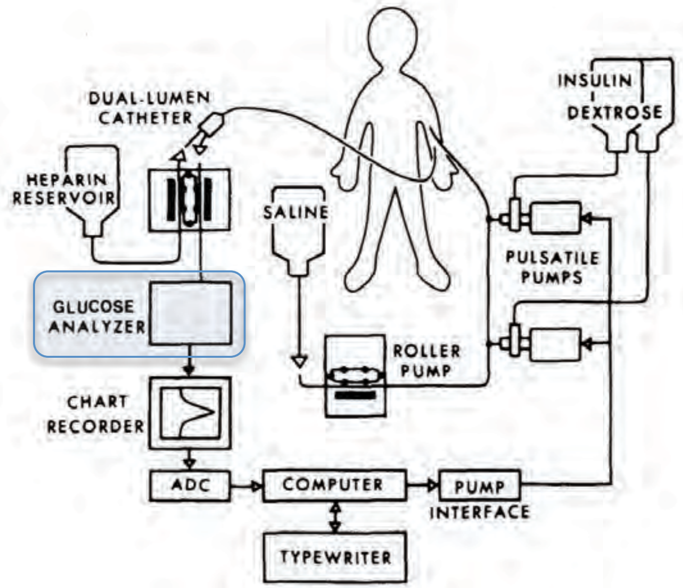
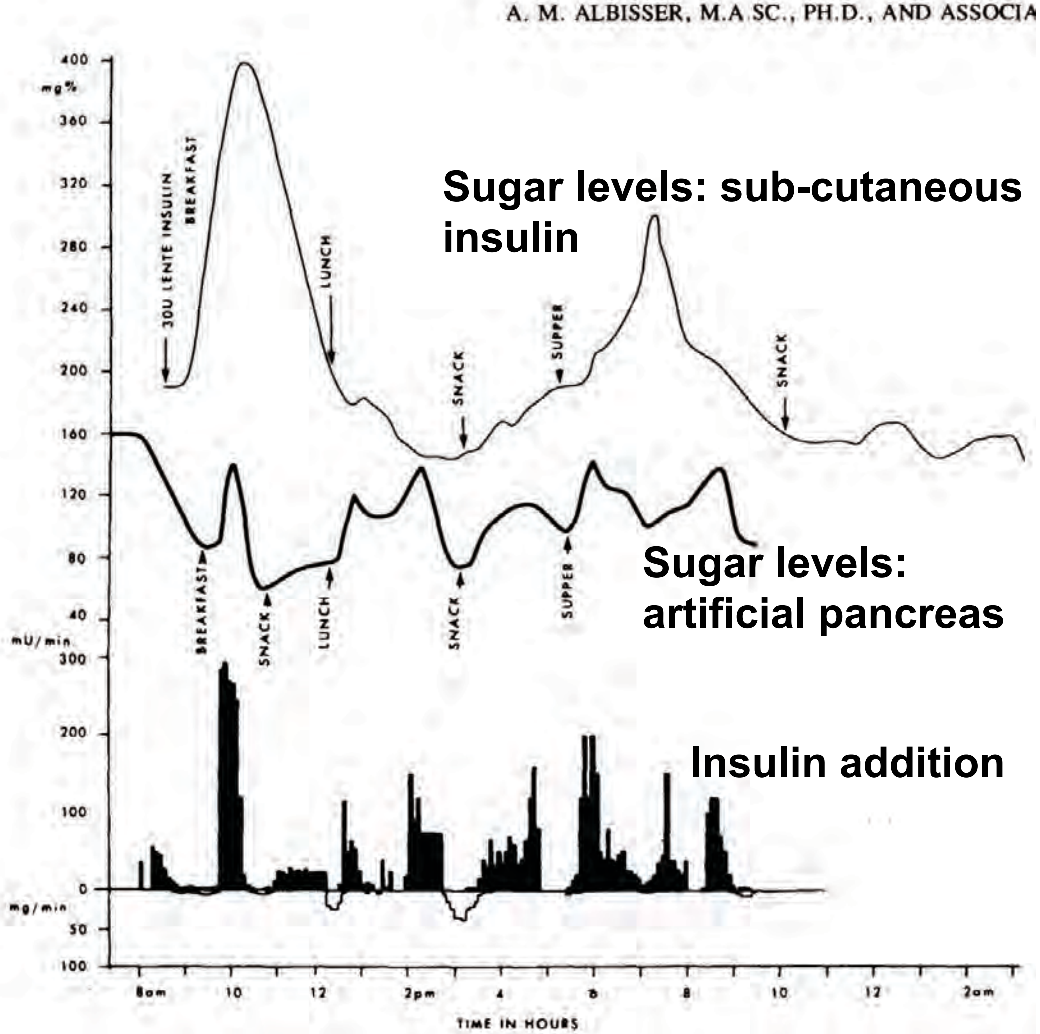


FIG. 1. Schematic diagram of apparatus used for monitoring and automatic regulation of blood sugar.



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)

Impantable Artificial Pancreas.. 1980

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. Baurschmidt, 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**'

'..several groups are working on the development of.. an implantable glucose sensor'

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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

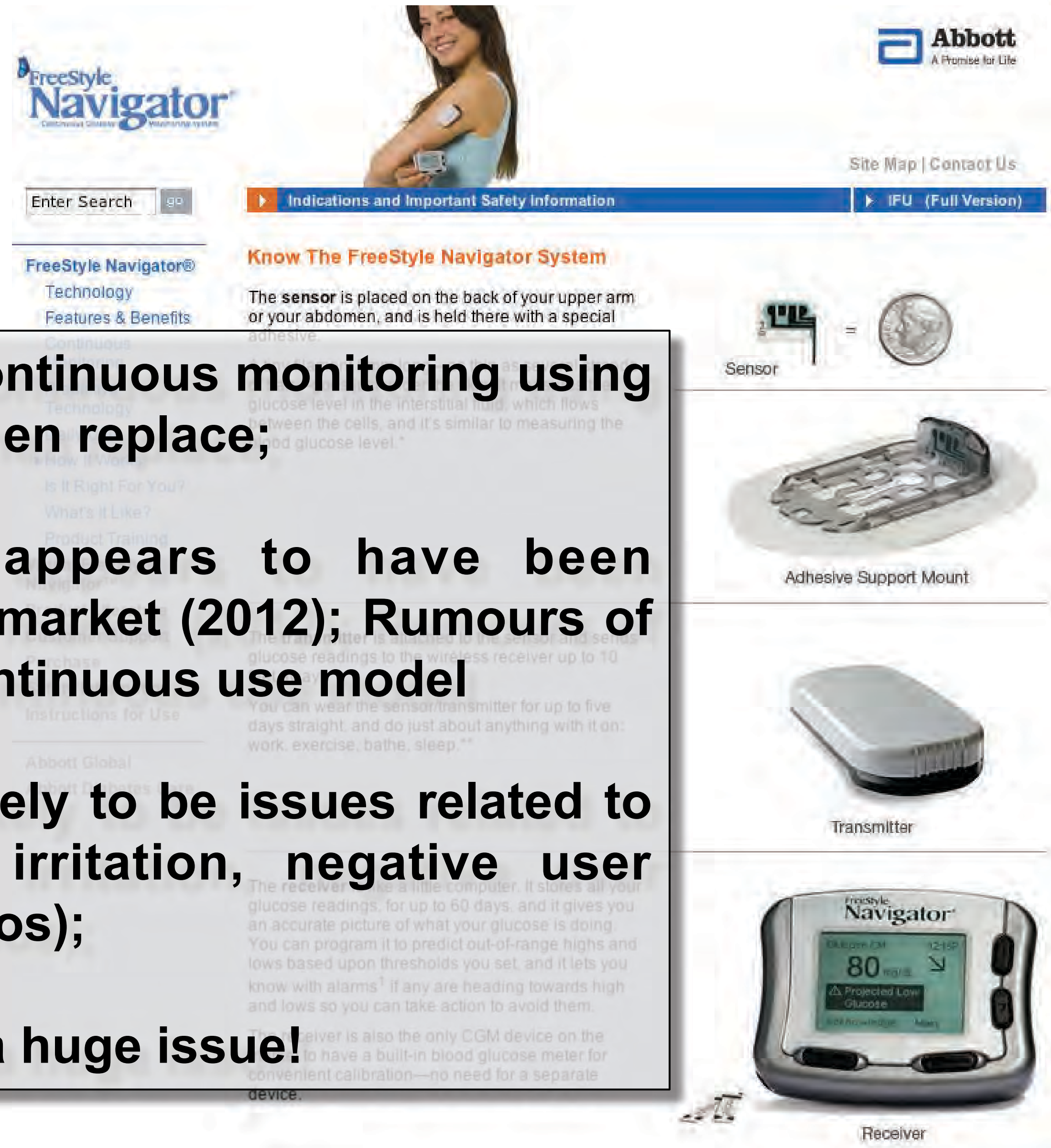
'Abbott completes TheraSense acquisition'

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

- Combines microfluidics with a micro-dimensioned filament sampling unit which is designed to minimise presence of infection (therefore can be left in place for 5 days).
- interstitial fluid (not blood) Diabetics have poor peripheral blood supply; therefore this is a major
- Wireless communications used to harvest data carers and specialists. Enables trending, aggregation, warning….



Target was for 7 days continuous monitoring using a patch-type platform, then replace;

Freestyle Navigator appears to have been withdrawn from the US market (2012); Rumours of relaunch with 14-day continuous use model

Reasons unclear but likely to be issues related to device stability, skin irritation, negative user response (YouTube videos);

Biocompatibility is still a huge issue!

Apple, iWatch & Health Monitoring

Independent.ie Wednesday 7 May 2014

News | Sport | Business | Woman | Entertainment | Lifestyle | Videos

Independent.ie > Business > Technology

Apple hiring medical device staff, shares break $600 mark

0 Comments | Recommend 7 | Tweet 89 | g+1 3 | Share

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.

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.

‘Healthkit’ personal health information platform developed in collaboration with Mayo Clinic

Google Contact Lens

United States Patent Application *20140107445*
Kind Code A1 Liu; Zenghe April 17, 2014

Microelectrodes In An Ophthalmic Electrochemical Sensor

Abstract

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

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

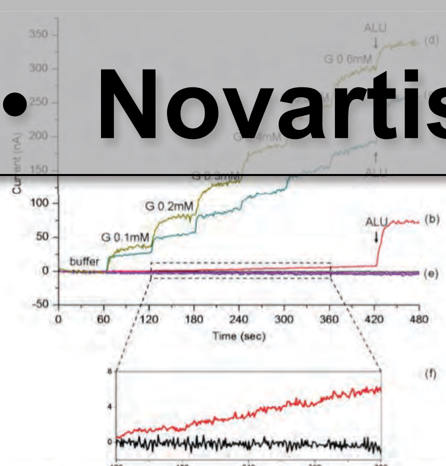


Fig. 2. Images of the sensor as it goes through surface functionalization and the related measured responses: (a) sequential images of sensor pre-treatment with GOD/titania/Nafion®; (b) measured amperometric response for the sensor just incubated with GOD; (c) measured amperometric response for the sensor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

8.6k SHARES Share on Facebook Share on Twitter

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

BY LANCE ULANOFF
1 DAY AGO

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

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

According to the patent:

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

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

pH sensing – wasn't that solved by Nikolskii in the 1930's?

EVENT	DATE
Launch (San Francisco)	September 2013
PHASE 1: Innovation Phase	
Registration opens	January 1, 2014
Early-bird Registration deadline	March 2014
OA Solutions Fair and Kick-Off Event	March 2014

Overview

Competition Guidelines

Competition Schedule

Registration Process

OVERVIEW

The Challenge: Improve Our Understanding of Ocean Acidification

The Wendy Schmidt Ocean Health XPRIZE is a $2 million global competition that challenges teams of engineers, scientists and innovators from all over the world to create pH sensor technology that will affordably, accurately and efficiently measure ocean chemistry from its shallowest waters… to its deepest depths.

There are two prize purses available (teams may compete for, and win, both purses):

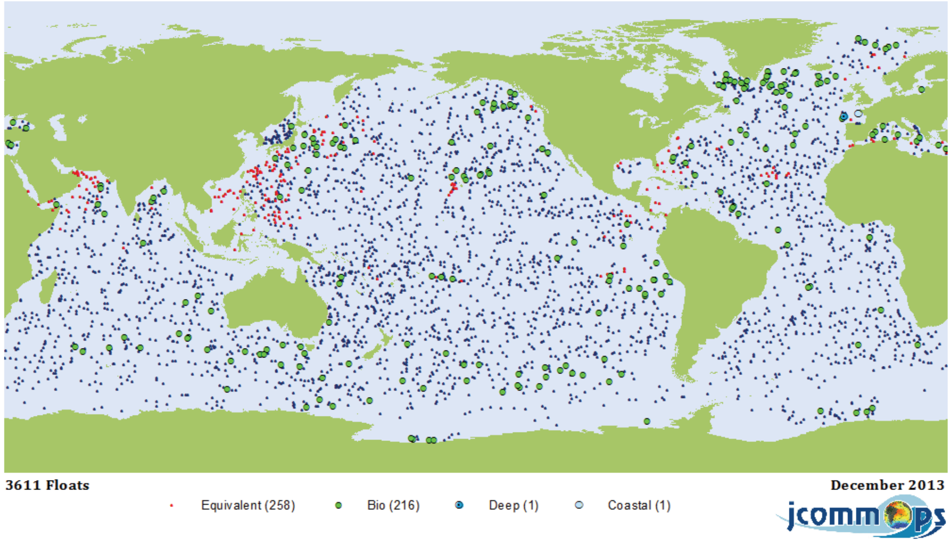
A. $1,000,000 Accuracy award – Performance focused ($750,000 First Place, $250,000 Second Place): To the teams that navigate the entire competition to produce the most accurate, stable and precise pH sensors under a variety of tests.

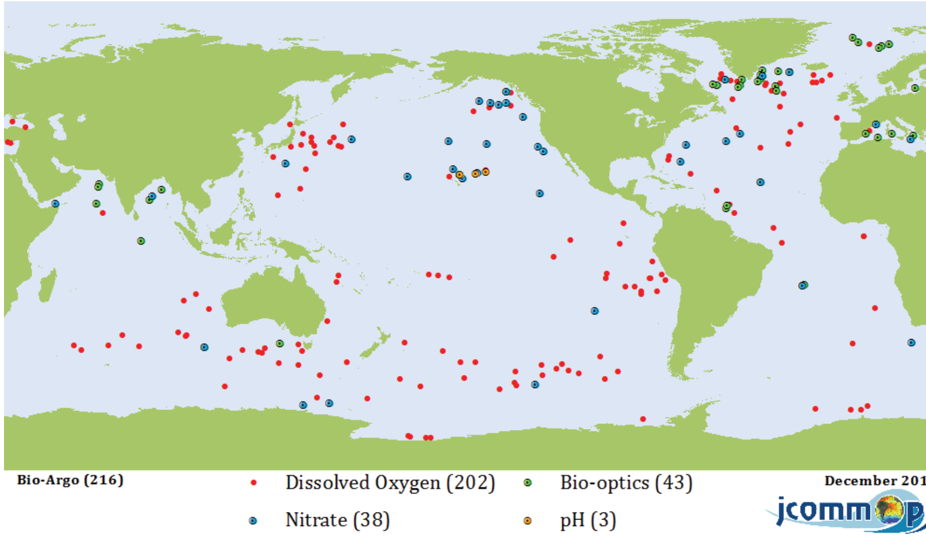
Wendy Schmidt Ocean Health XPRIZE

$2,000,000 up for grabs!
Task is to provide a way to do reliable measurements of pH in the ocean environment

The winner will almost certainly be a reagent based platform, not a conventional chemical sensor

Argo Project (accessed March 9 2014)





- **Ca. 3,600 floats: temperature and salinity**
- **Only 216 reporting chem/bio parameters (ca. 6%)**
- **Of these nitrate (38), DO (202), Bio-optics (43), pH (3)**

@€60K ea!

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

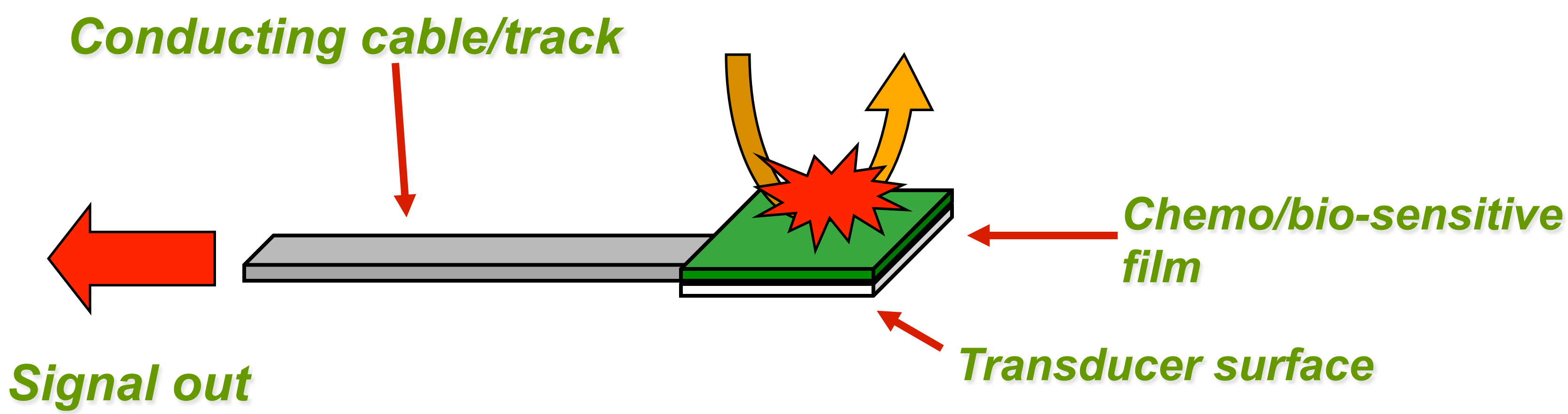
See https://picasaweb.google.com/JCOMMOPS/ArgoMaps?authuser=0&feat=embedwebsite

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

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

What is a Chemo/Bio-Sensor?

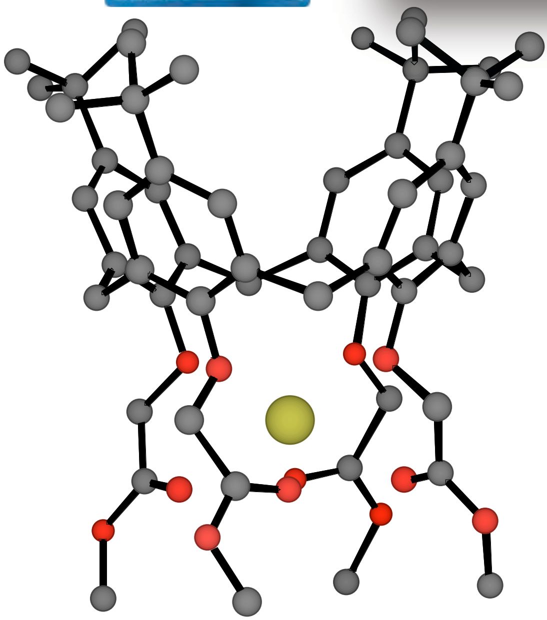
'a device, consisting of a transducer and a chemo/bio-sensitive film/membrane, that generates a signal related to the concentration of particular target analyte in a given sample'

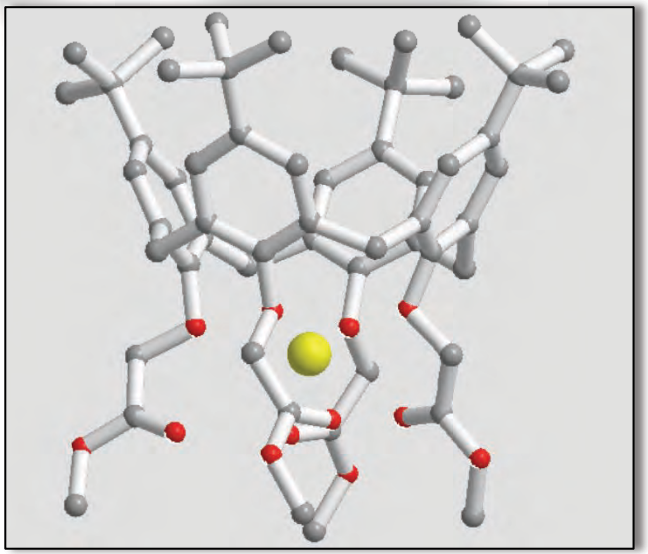


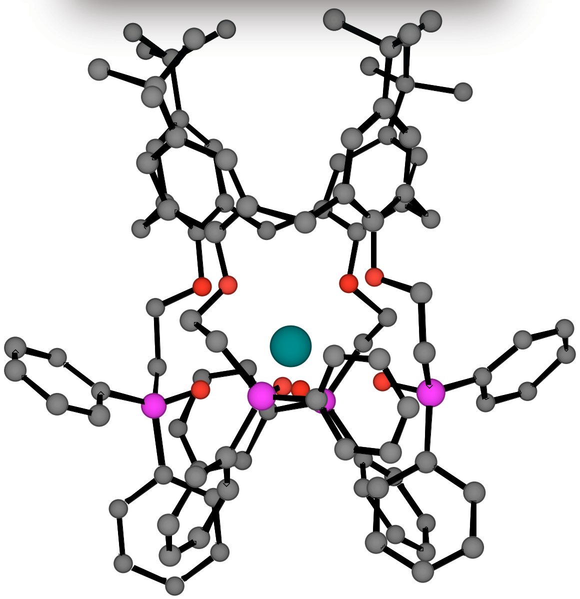
Conventionally, chem/Bio-sensors employ selective **BINDING** & **TRANSDUCTION** at the device surface, which is pre-functionalised with binding sites selective for a chosen analyte. Binding events at the surface provide a signal observable in the macroscopic world (**COMMUNICATION**)

History: Calixarenes, 1984/5

+

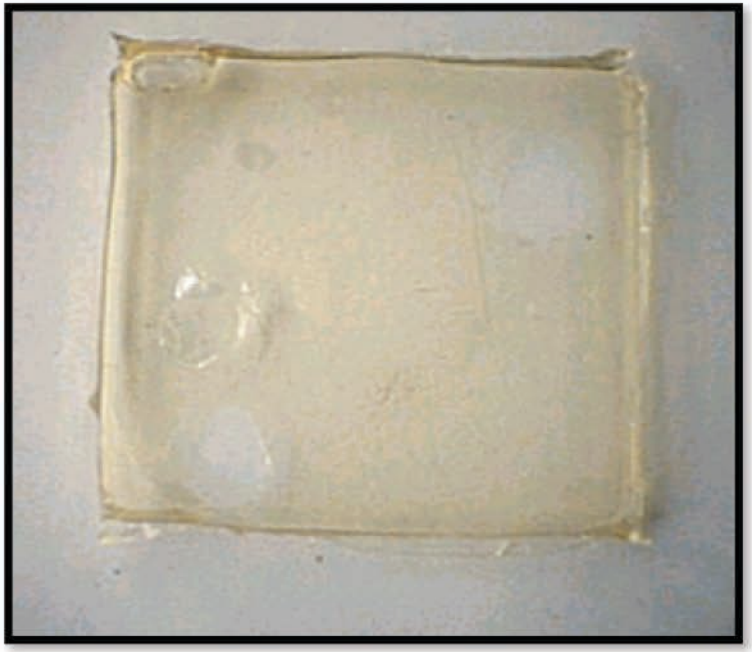


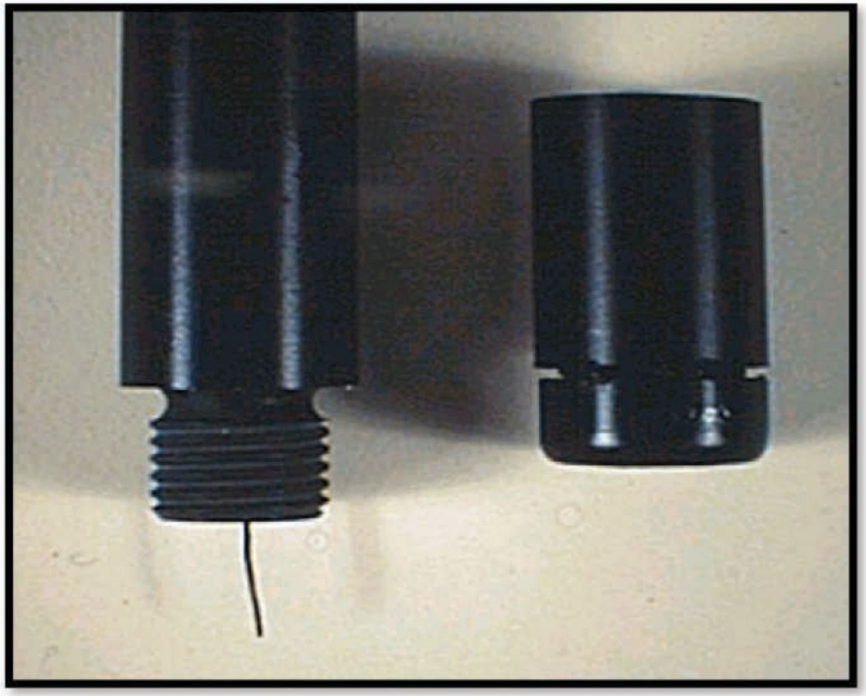




Neutral Carrier Based Ion-Selective Electrodes, D.Diamond, Anal. Chem. Symp. Ser., 25 (1986) 155.
A sodium Ion-Selective Electrode based on Methyl p-t-Butyl Calix[4]aryl Acetate as the Ionophore, D.Diamond, G.Svehla, E.Seward,and M.A.McKervey, Anal. Chim. Acta., 204 (1988) 223-231.
Sodium Selective Polymeric Membrane Electrodes based on Calix[4]arene Ionophores, A.Cadogan, D.Diamond, M.R.Smyth, M.Deasy, M.A.McKervey and S.J.Harris, Analyst 114 (1989) 1551.

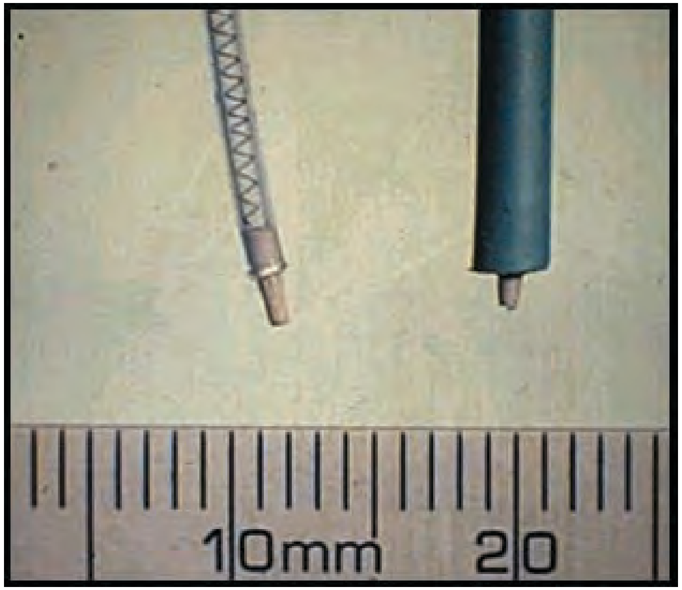
PVC - Membrane ISEs





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

Blood Analysis; Implantible Sensors



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

Dr. David Band, St Thomas's Hospital London

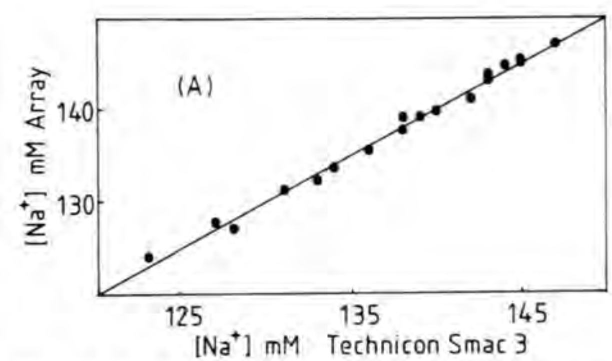
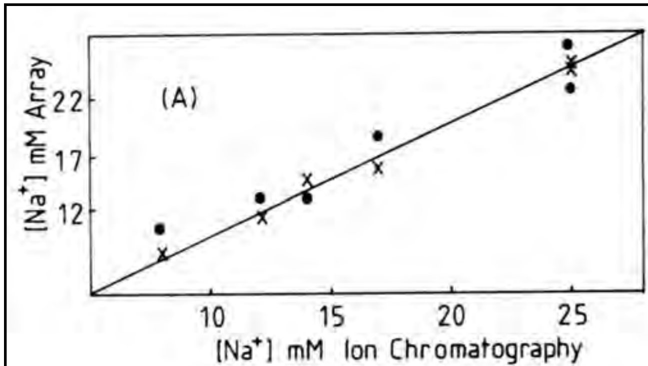


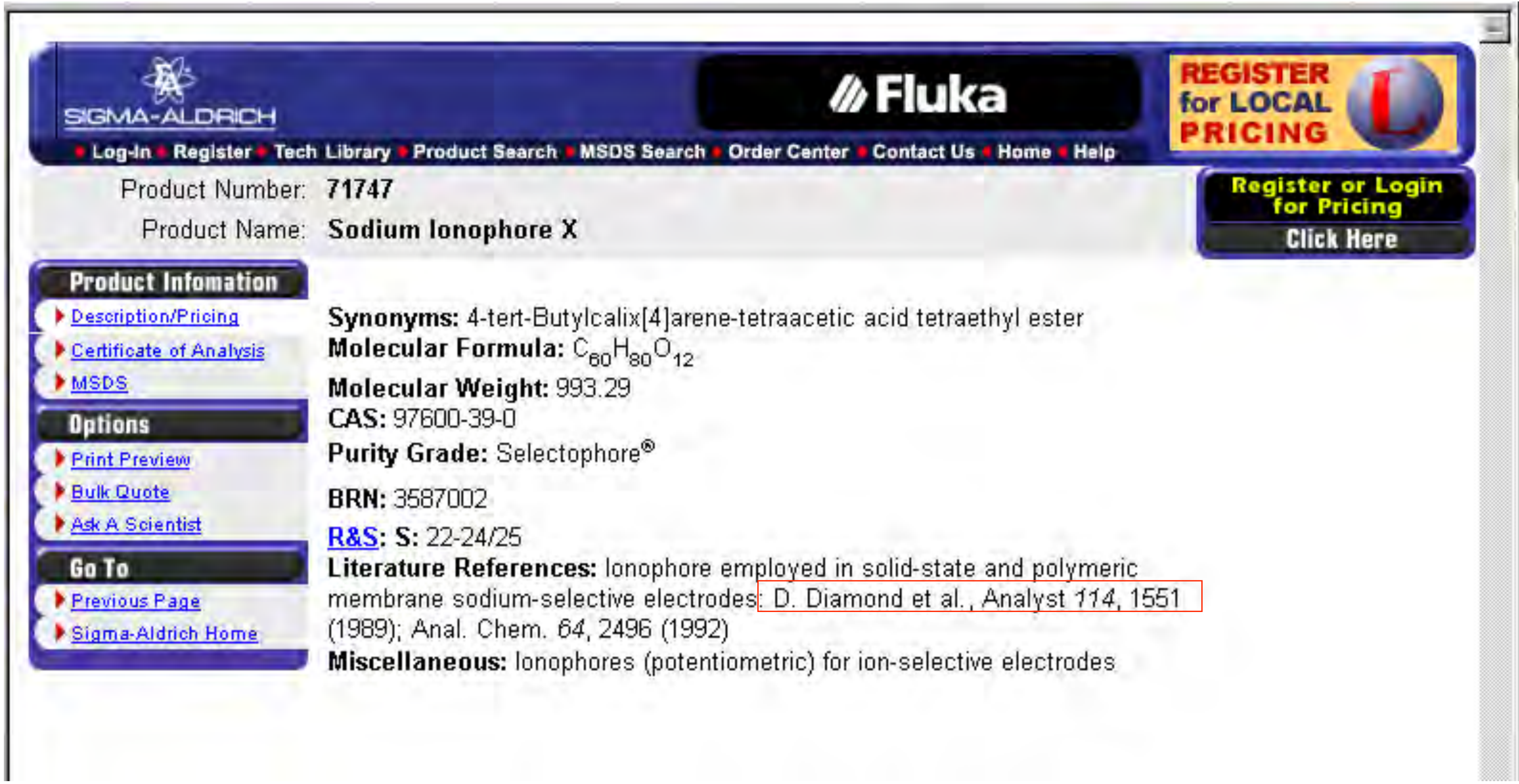
Fig. 3. Comparison of plasma sodium analysis using the array-FIA approach with a SMAC analyser. Good correlation without bias is obtained [5].



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

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

Fame at last!!

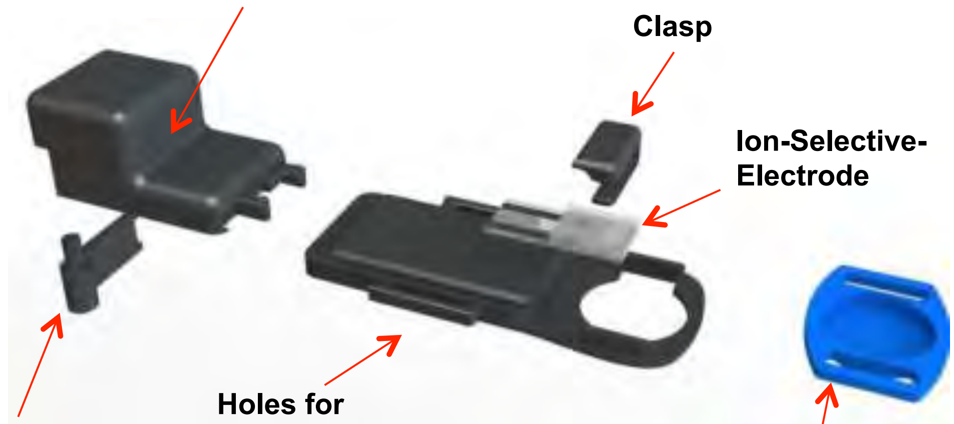


- **Best ionophore for sodium**

Na$^+$ Monitoring in Sweat

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

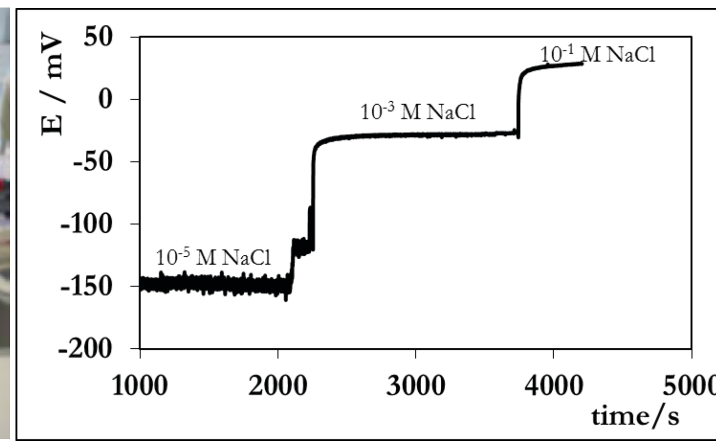
- **Monitoring of athletes during exercise**
- **Monitoring clinical conditions e.g. Cystic Fibrosis patients**



Macroduct sweat sampling unit (Wescor Corporation) Speed x4

Pilocarpine based sweat sampling

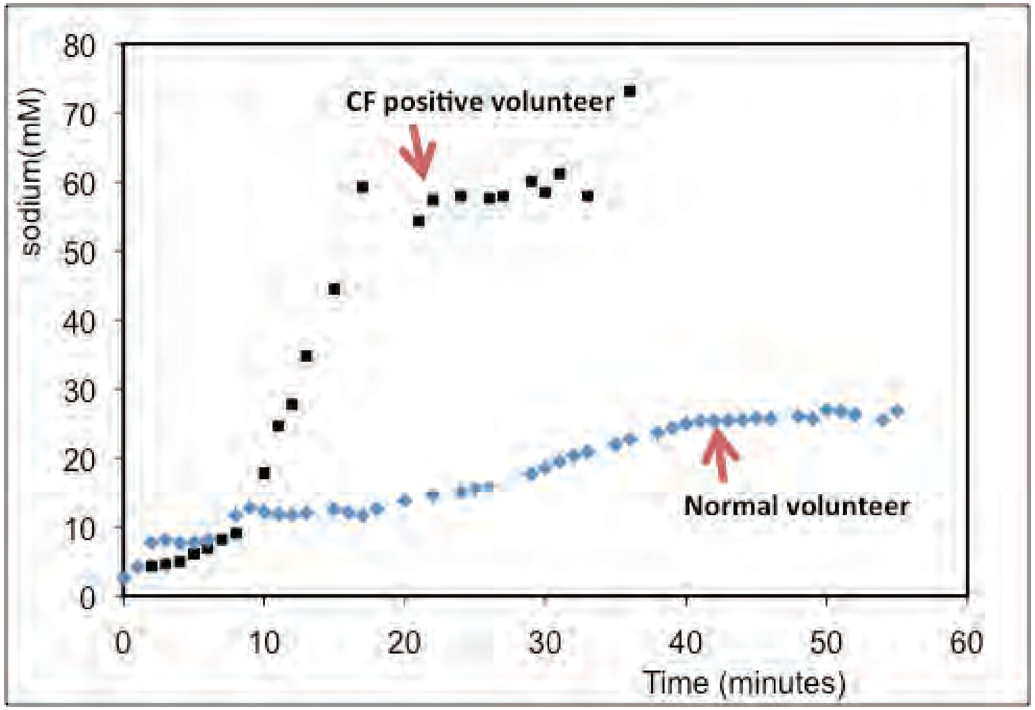
Exercise based sweat sampling



Sensor calibration

Na^+ monitoring in sweat using wearable sensor

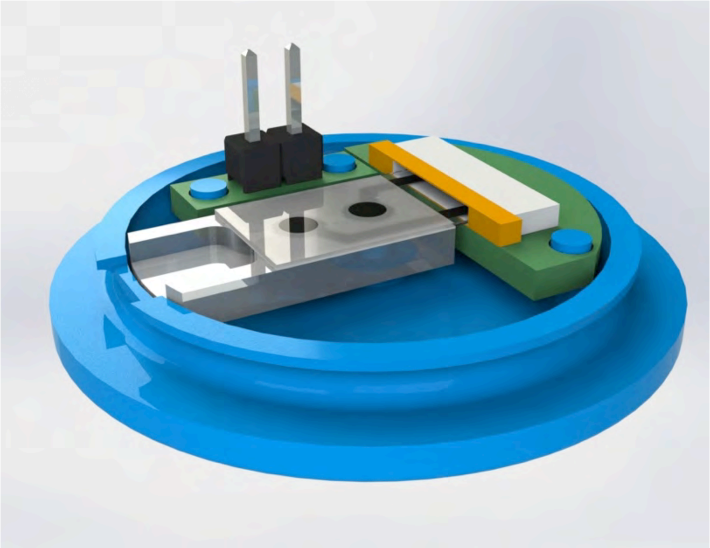
- **Measurements successfully made with CF-positive and normal volunteers**
    - clear difference between CF+ and normal levels
- **Elevated levels of Na^+ found in sweat of CF+ volunteers as expected**
- **Enables electrolyte loss to be estimated when combined with sweat rate/volume data**
- **Important 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

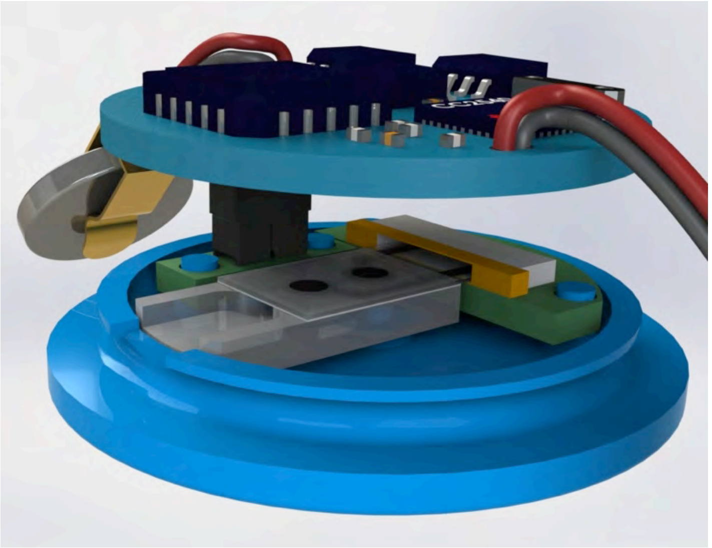


- **Diagnostic CF threshold >60mM [Na^+] reached**
- **Issue with initial delay**
    - arises from inherent delay in onset of sweating
    - contribution from device ‘dead-volume’

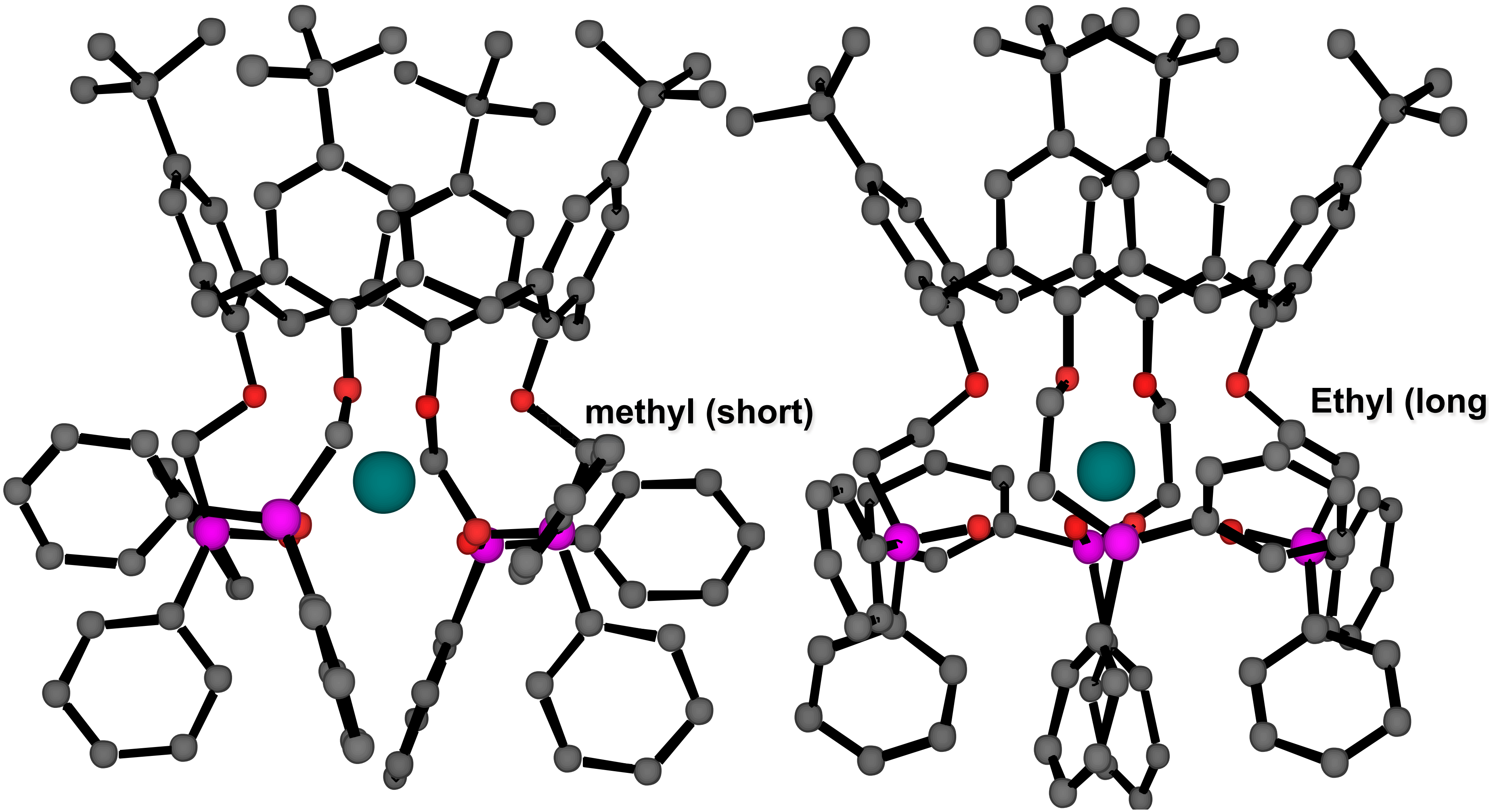
Schazmann, B., et al., Analytical Methods, 2010, 2(4): p. 342-348.

Next Generation: Watch Fluidic Sensor Concept



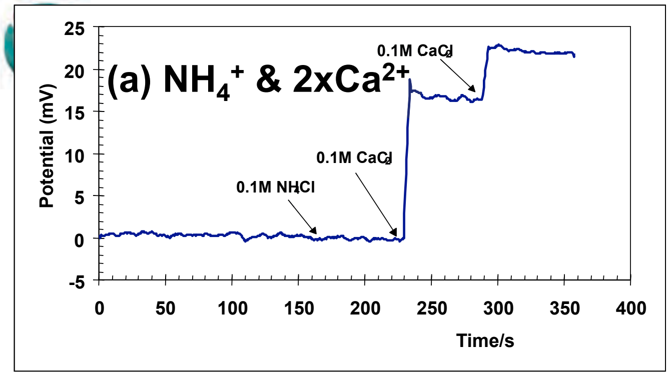


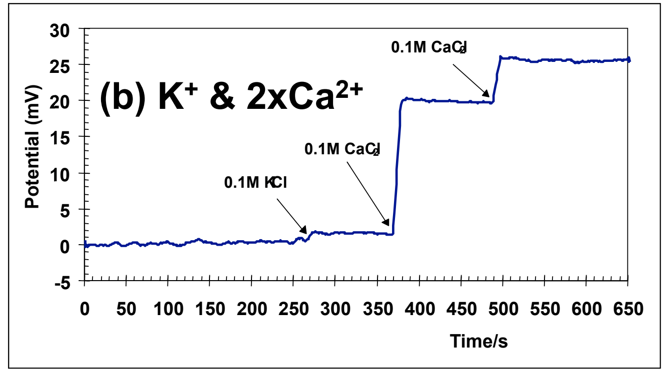
Ca^{2+} - complexes of PO tetramers

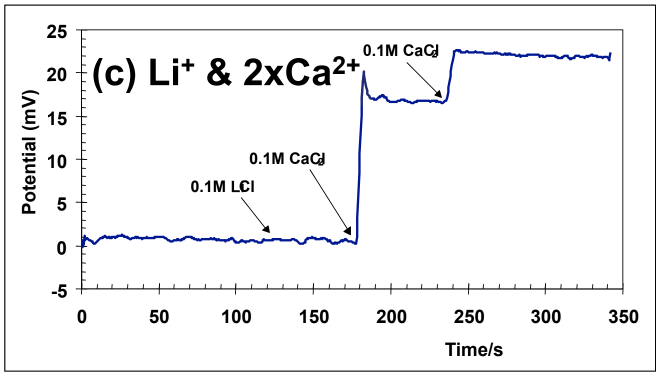


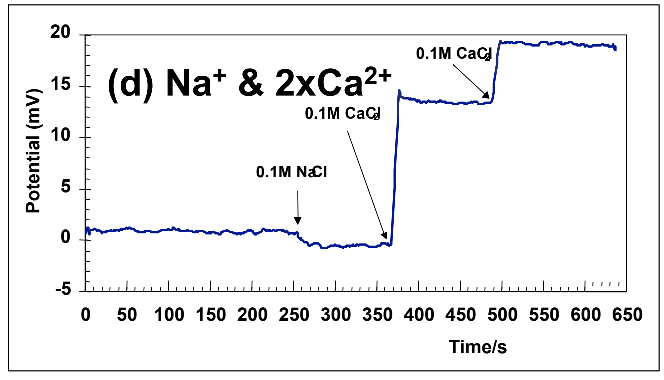
Not Ca^{2+} selective

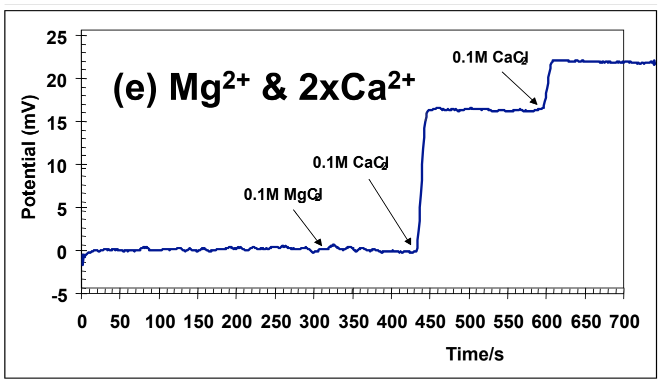
Ca^{2+} selective



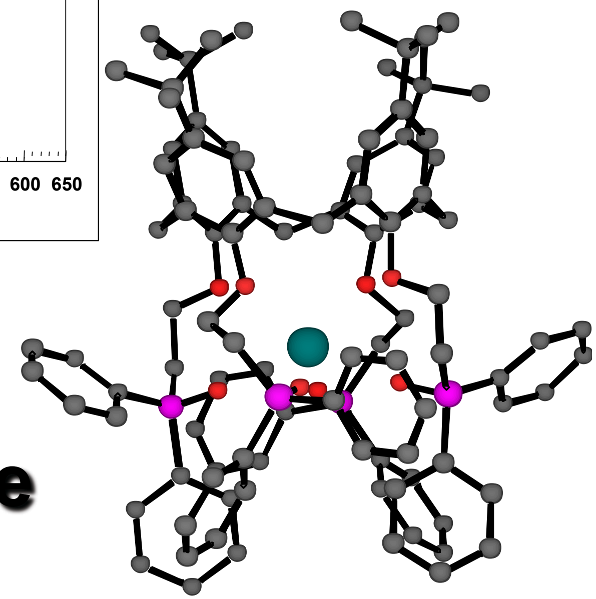








Response of TPOL Electrode



Calcium-selective Electrode based on a Calix[4]arene Tetraphosphine Oxide, Tom McKittrick, Dermot Diamond, Debbie J. Marrs, Paul O'Hagan and M.Anthony McKervey, Talanta 43 (1996) 1145-1148.

Lowering the LOD of ISEs (1999)

Anal. Chem. **1999,** *71,* 1204−1209

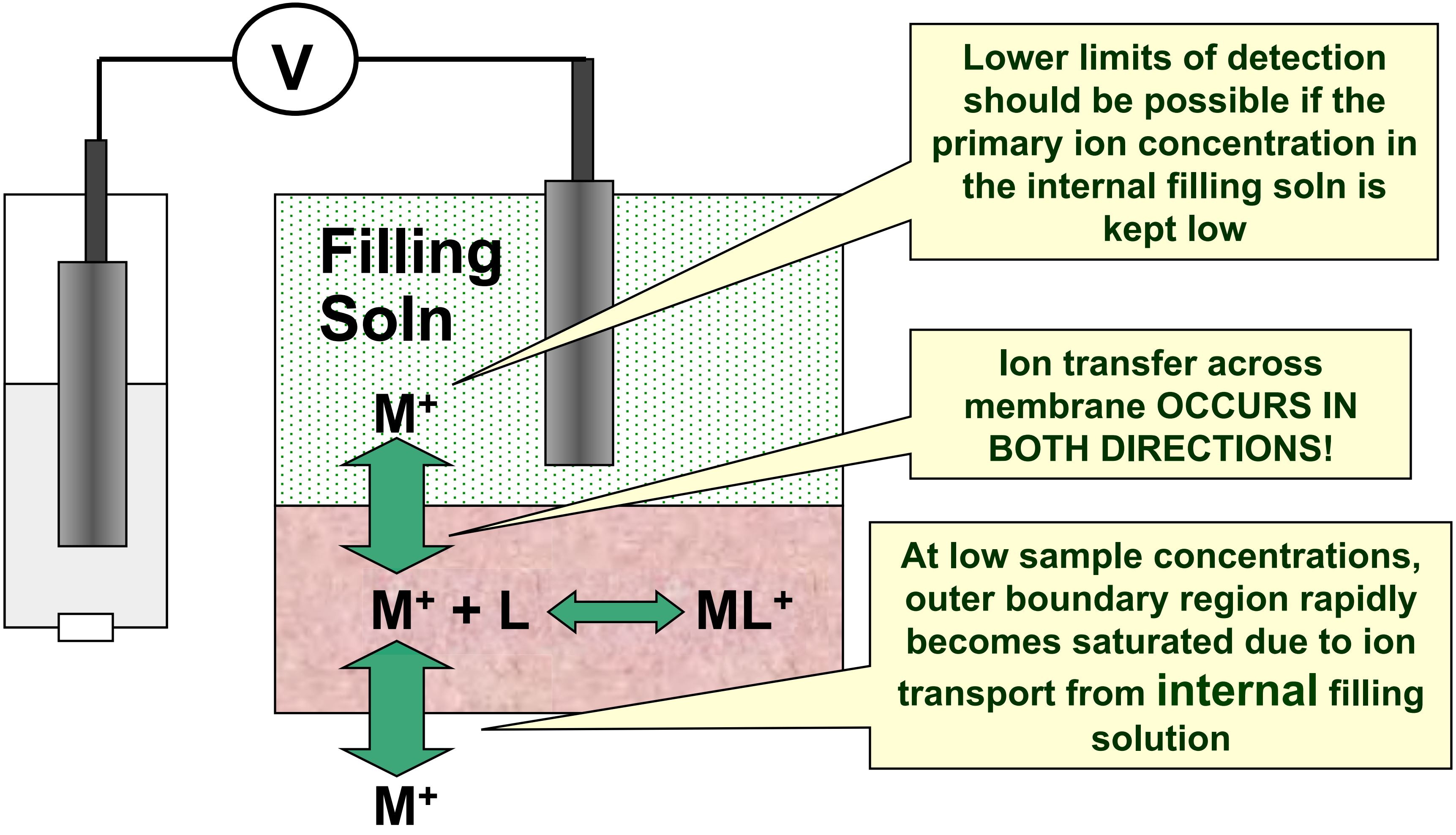
Lowering the Detection Limit of Solvent Polymeric Ion-Selective Electrodes. 1. Modeling the Influence of Steady-State Ion Fluxes

Tomasz Sokalski,[*,†,§] Titus Zwickl,[†] Eric Bakker,[*,‡] and Ernö Pretsch[*,†]

Department of Organic Chemistry, Swiss Federal Institute of Technology (ETH), Universitätstrasse 16, CH-8092 Zürich, Switzerland, and Department of Chemistry, Auburn University, Auburn, Alabama 36849

ISEs: Low Limit of Detection

- See series of papers by Pretsch, Bakker and Sokalski



Lead in Zurich Tap Water

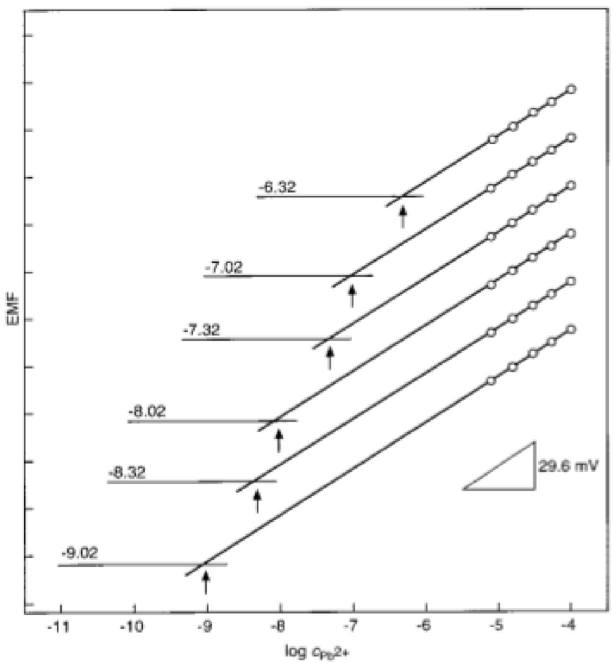


Figure 2. Measurement procedure of potentiometric trace level determinations of Pb^{2+} by calibrating with a series of lead ion solutions at higher concentration. Shown are the emf responses as a function of the sample activity for each of the separate measurements. The slopes for each of the five-point calibrations are, from top to bottom, 28.5, 28.4, 28.6, 28.6, 28.5, and 28.9 mV/decade.

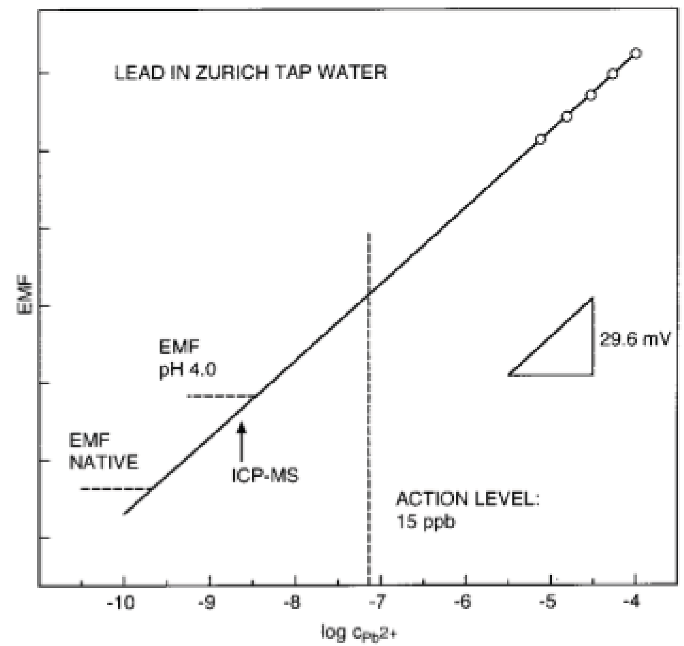
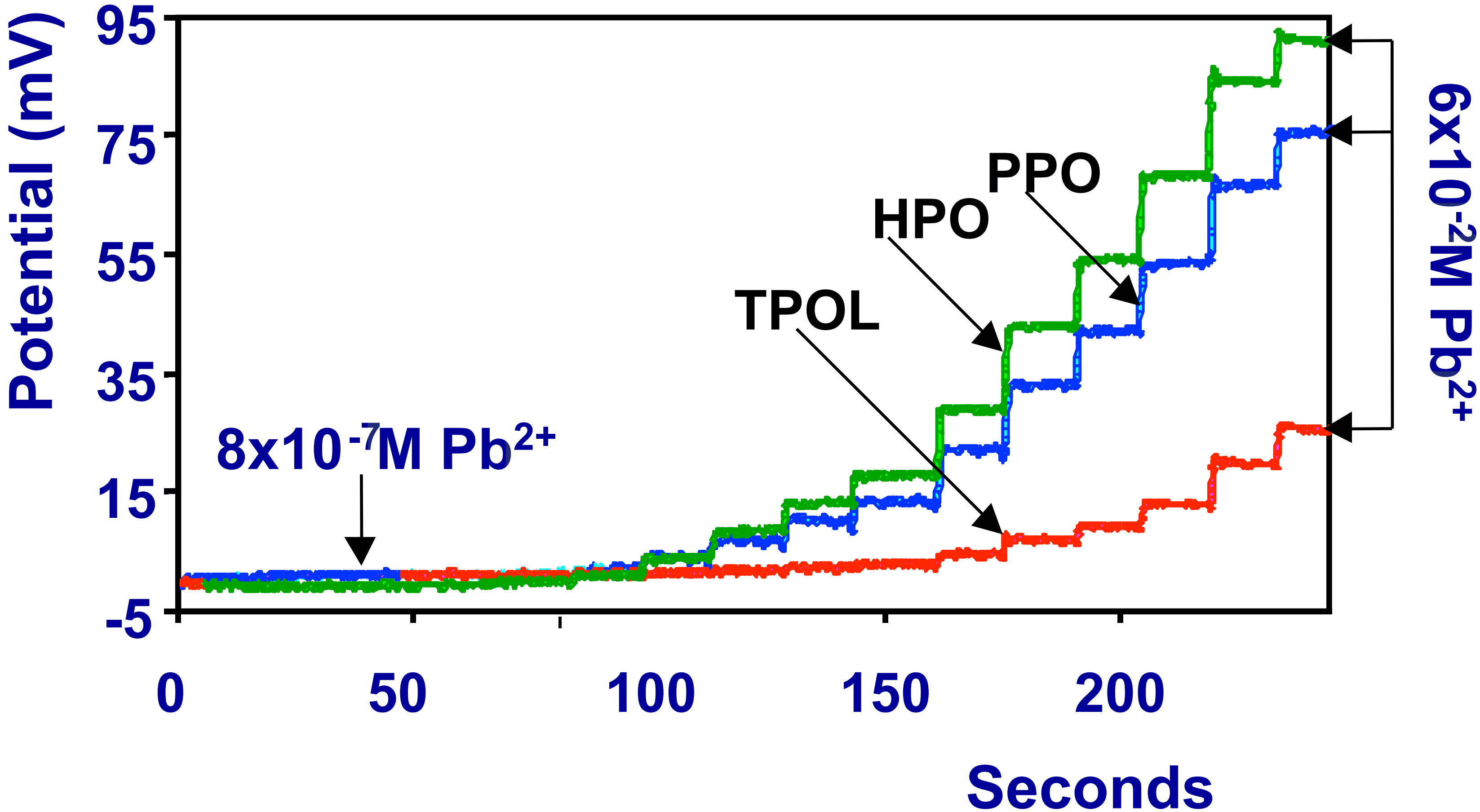


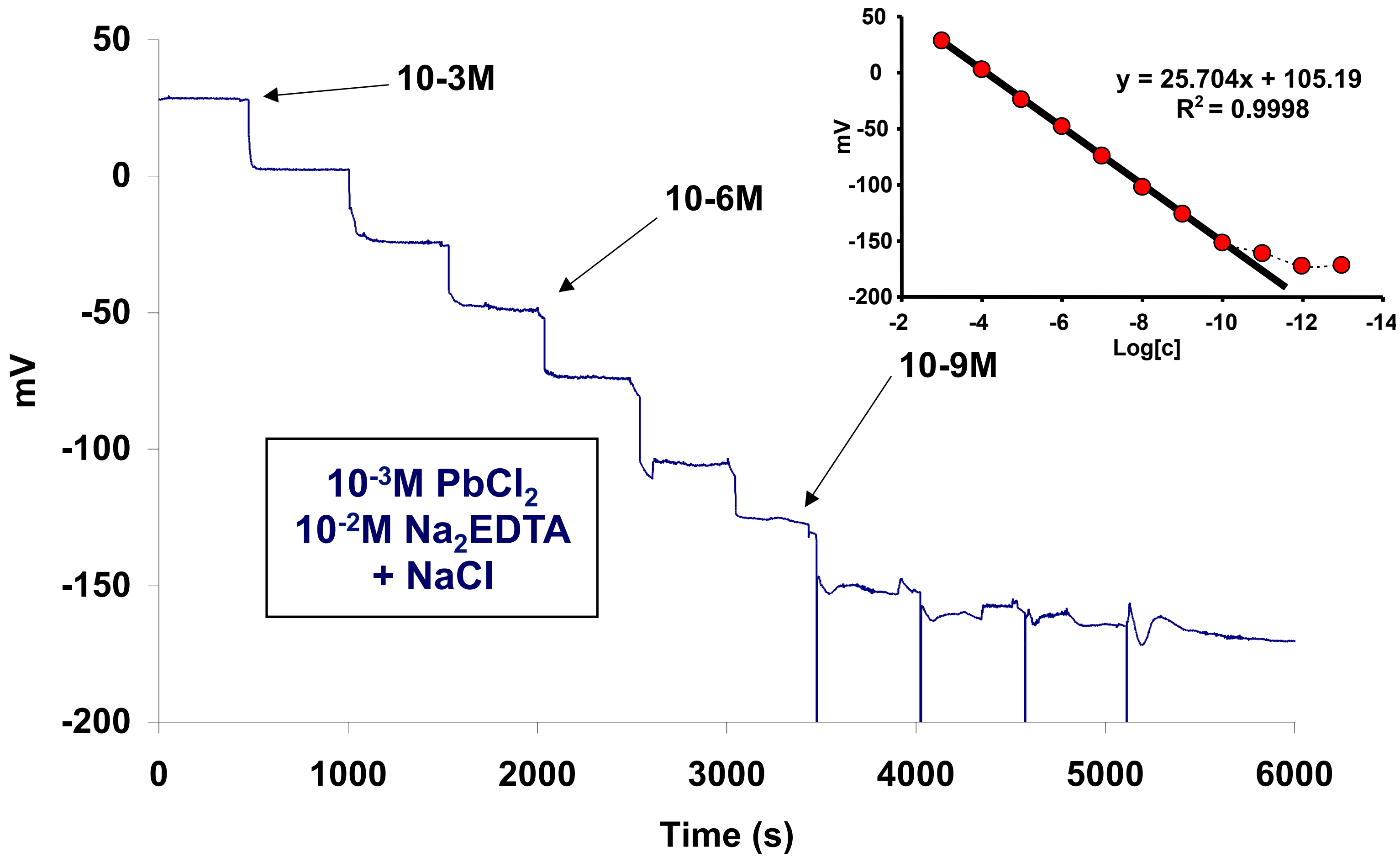
Figure 6. Potentiometric determination of Pb^{2+} in unspiked Zurich tap water at different pH values (see also Figure 5). Horizontal dotted lines: measurement of free lead in the native sample (lower value) and of total lead after buffering the pH to 4.0 (higher value). Vertical arrow: lead concentration obtained with ICPMS.

- **Anal. Chem. 2001, 73, 343-351; ‘Potentiometric Polymeric Membrane Electrodes for Measurement of Environmental Samples at Trace Levels: New Requirements for Selectivities and Measuring Protocols, and Comparison with ICPMS’, Alan Ceresa, Eric Bakker, Bodo Hattendorf, Detlef Gunther, and Erno Pretsch**

Response of electrodes based on tetra-, penta- and hexa-phosphine oxides to increasing concentration of Pb^{2+} in a background of 0.01M Ca^{2+} - evidence of 'best-fit' mechanism as response to Pb^{2+} is enhanced as the cavity size increases (size selectivity). The hexamer produces excellent ISEs for Pb^{2+}, and also Hg^{2+} (pH < 3.0).

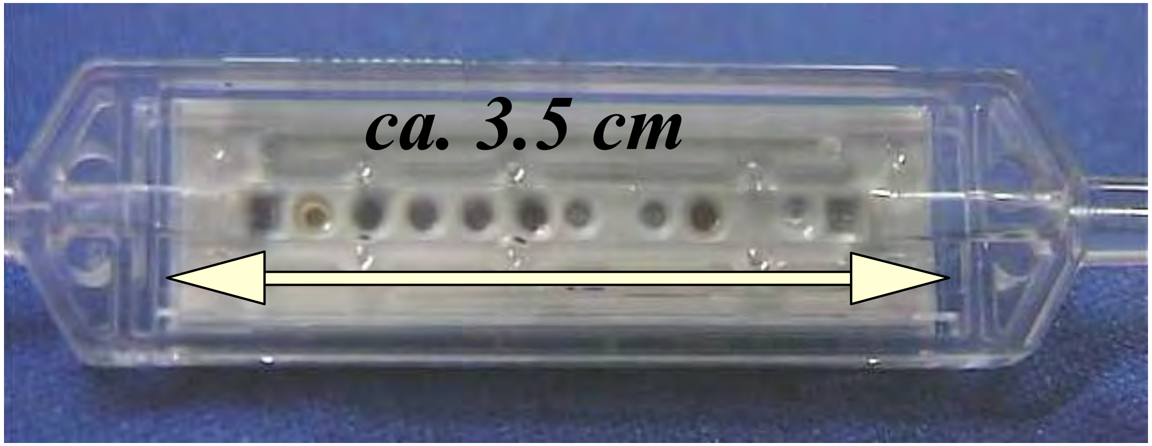


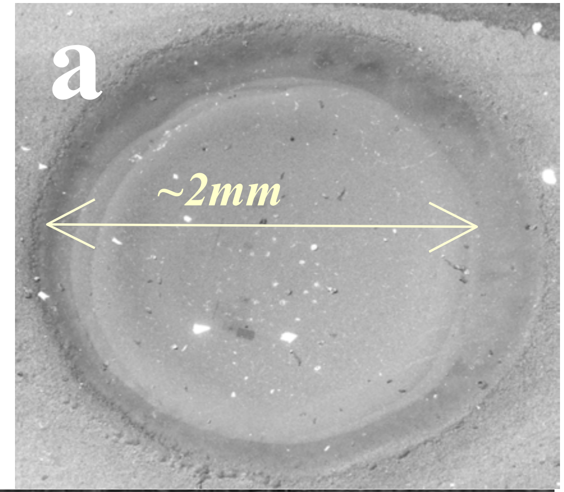
Low Limit of Detection - Control of Internal Filling Solution; Calix[6]arene Hexaphosphine Oxide

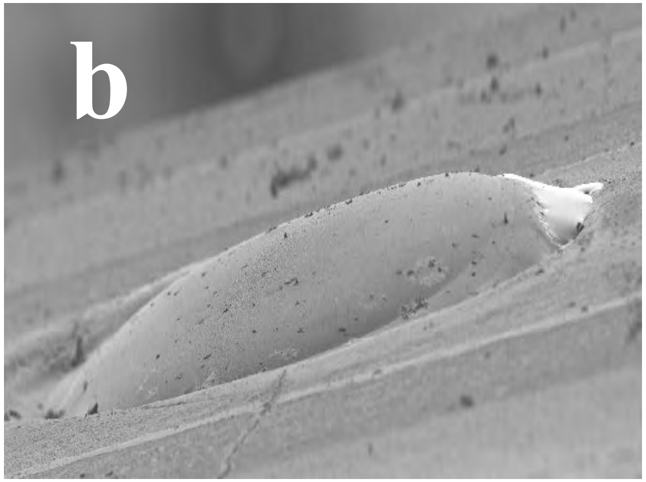


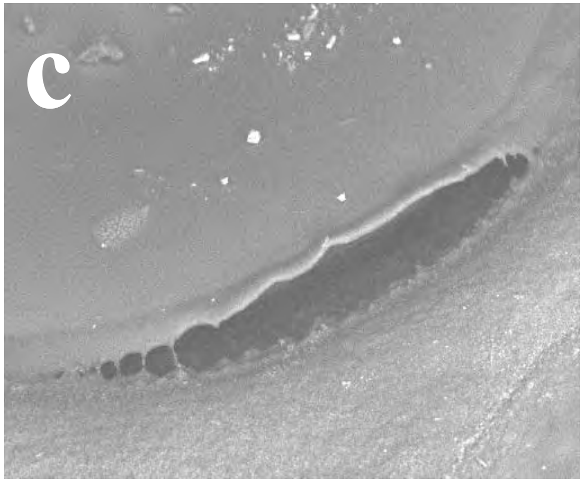
Lead-Selective Electrodes Based on Calixarene Phosphine Oxide Derivatives, Francis Cadogan, Paddy Kane, M. Anthony McKervey, and Dermot Diamond, Anal. Chem. 1999, 71, 5544-5550

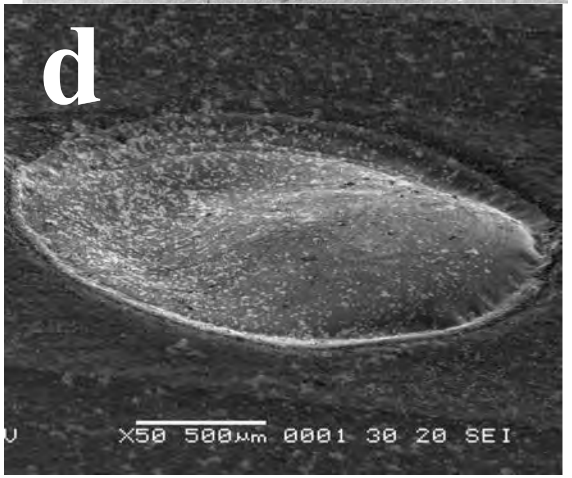
Planar ISE arrays for blood profiling *(with Matt Leader, Sendx)*









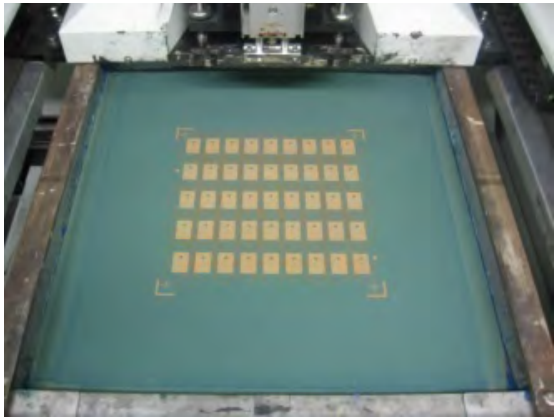


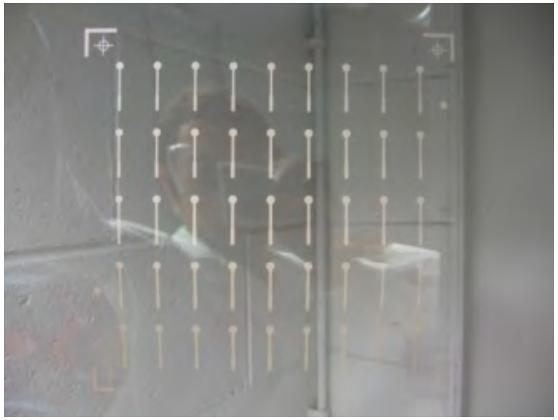
A. Lynch, D. Diamond and M. Leader, *Analyst*, 2000, 125, 2264-2267.

Mass production of SCISEs and SCREs

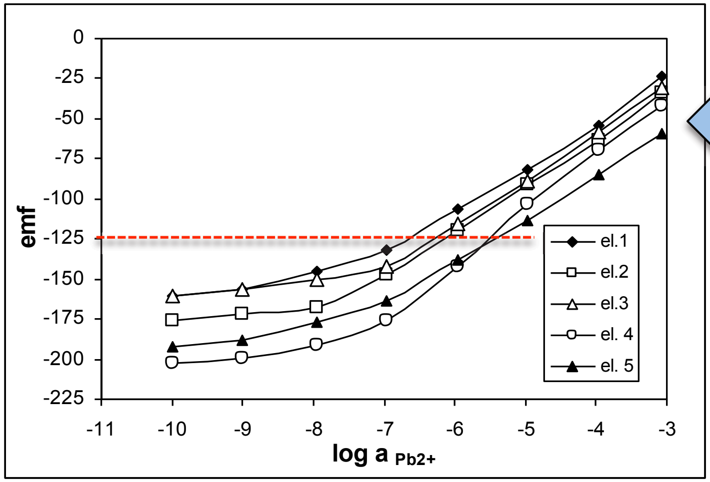
(Alek Radu and Salzitsa Anastasova)

- Using Screen Printer DEK 248 silver paste was printed on plastic sheets.
- Next, carbon was printed twice, with 15 minutes of curing in oven at 200°C between successive prints.
- After finishing carbon, the insulating layer was printed and UV-cured.
- Conducting polymer Poly (3-octylthiophene) (10^{-2} M in Chloroform) was dropcast (initially) or grown electrochemically (later) on printed platforms.
- The CP is covered with a PVC membrane cocktail containing active components for ISEs and reference electrodes (Fluka)



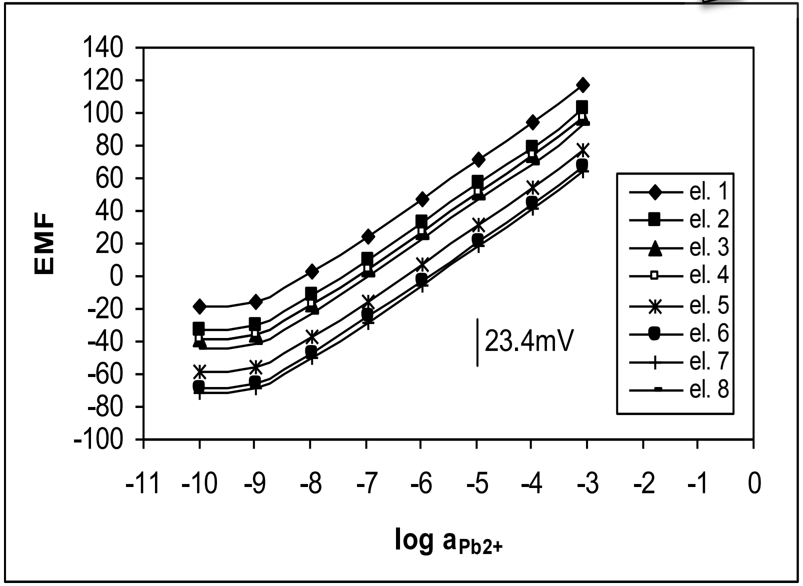


Improving sensor reproducibility

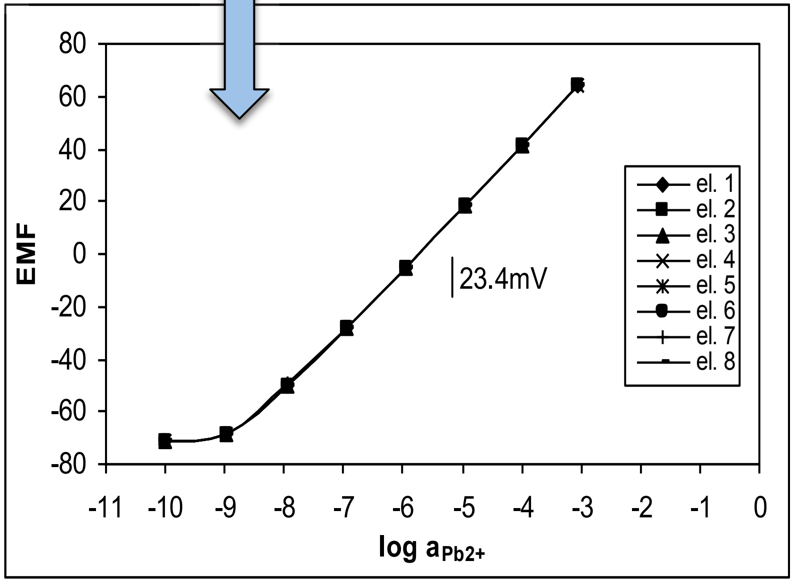


Manual fabrication, conventional design

SP fabrication, **manual deposition of CP layer (POT) and sensing layer**

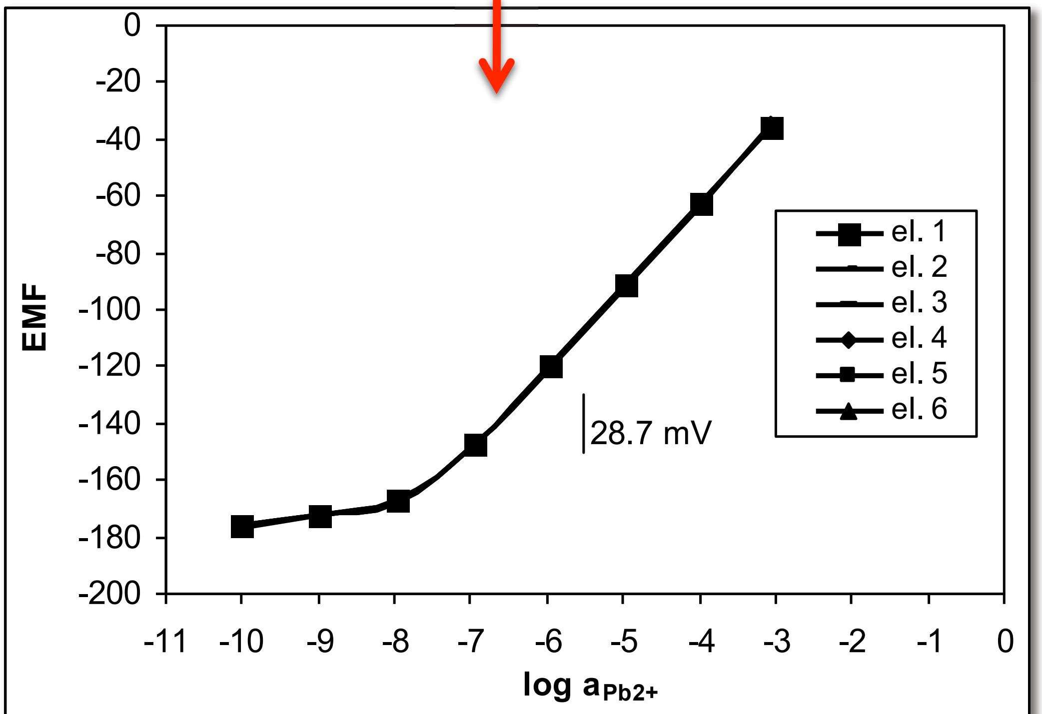


After zero point correction, slopes are virtually identical: single point calibration for each sensor



EC-deposition of CP Layer -> highly Reproducible Sensors

6 calibration curves superimposed!

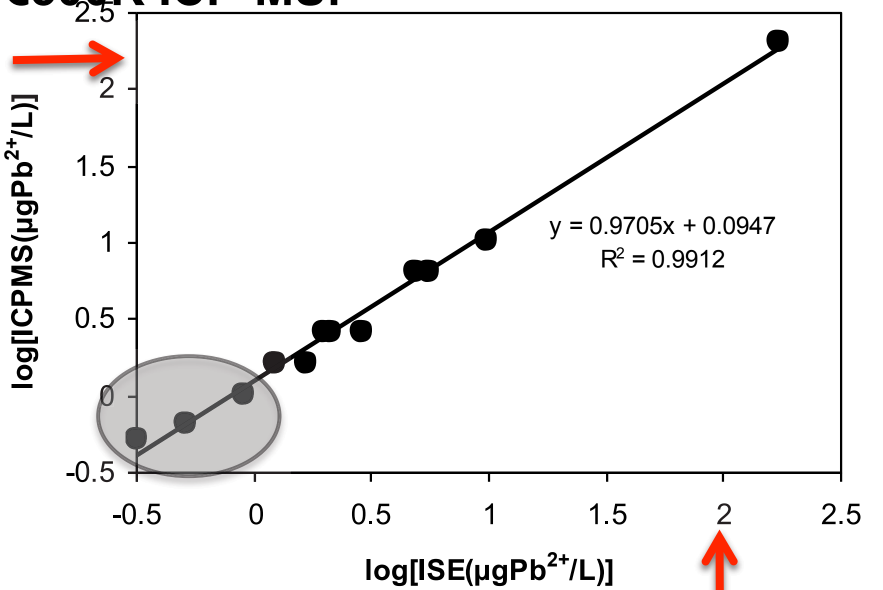


electrode number	Baseline, mV Day0	Slope, mV Day0	LOD Day0	Eo/mV Day0
1	-176.11	28.75	-8.00	53.87
2	-176.08	28.75	-8.00	53.90
3	-176.40	28.75	-7.95	52.14
4	-176.23	28.74	-7.90	50.83
5	-176.13	28.72	-7.92	51.32
6	-176.16	28.74	-8.00	53.73
Mean	-176.18	28.74	-7.96	52.63
SD	0.12	0.01	0.04	1.38

SP fabrication**, electrochemical deposition of CP (PEDOT)**, manual deposition of sensing layer;
Applied to analysis of river water samples

Disposable solid-contact ion-selective electrodes for environmental monitoring of lead with ppb limit-of-detection, S. Anastasova, A. Radu, G. Matzeu, C. Zuliani, U. Mattinen, J. Bobacka and D. Diamond, *Electrochimica Acta*, 2012, 73, 93-97.

€500K ICP-MS!



10¢ ISE vs.

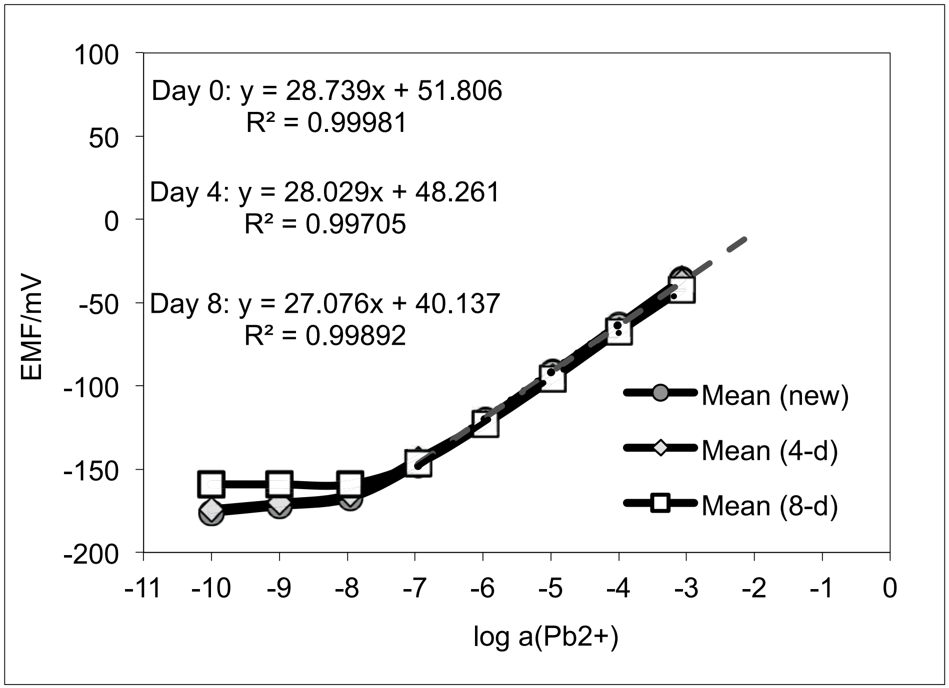
Screen Printed ISEs

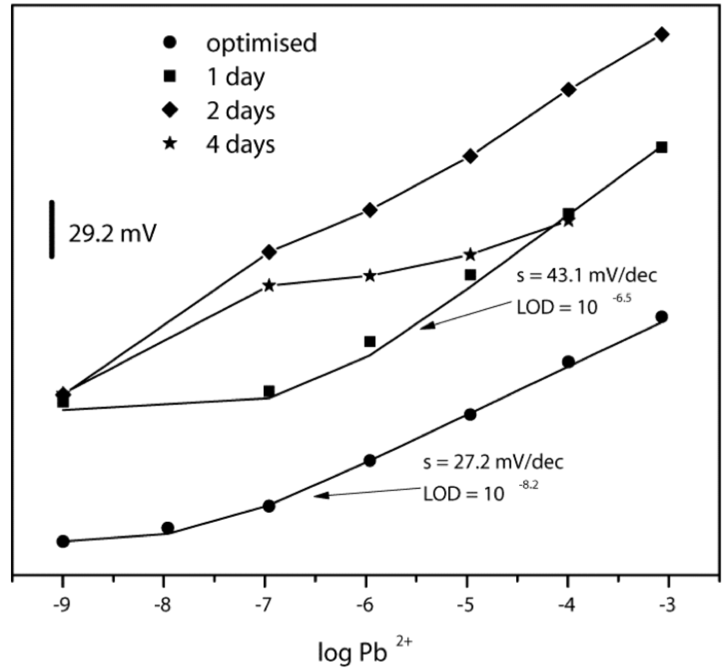
- V. low cost (cents), mass-produced
- Almost perfect reproducibility -> calibrate 1 per batch!
- V. high sensitivity -> LOD in low PPB for Pb^{2+}; better than ICP-MS!, ….. & V. selective
- Each ISE used once; unknown estimated using 4-point standard additions

Would it be possible to use these electrodes in a remote autonomous instrument?

Change in Electrode Function over Time

See Electrochimica Acta 73 (2012) 93–97



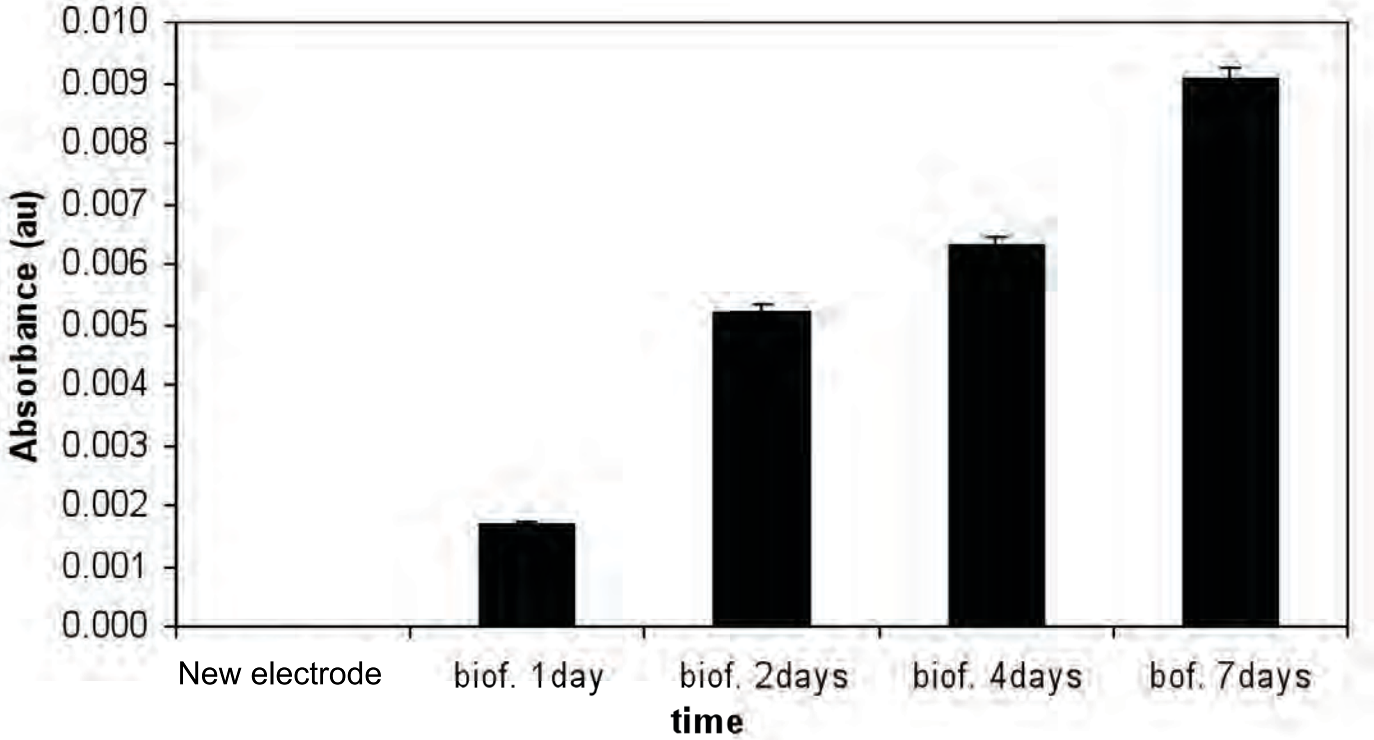


stored in 10^{-9}M Pb^{2+}, pH=4

Continuous contact with river water

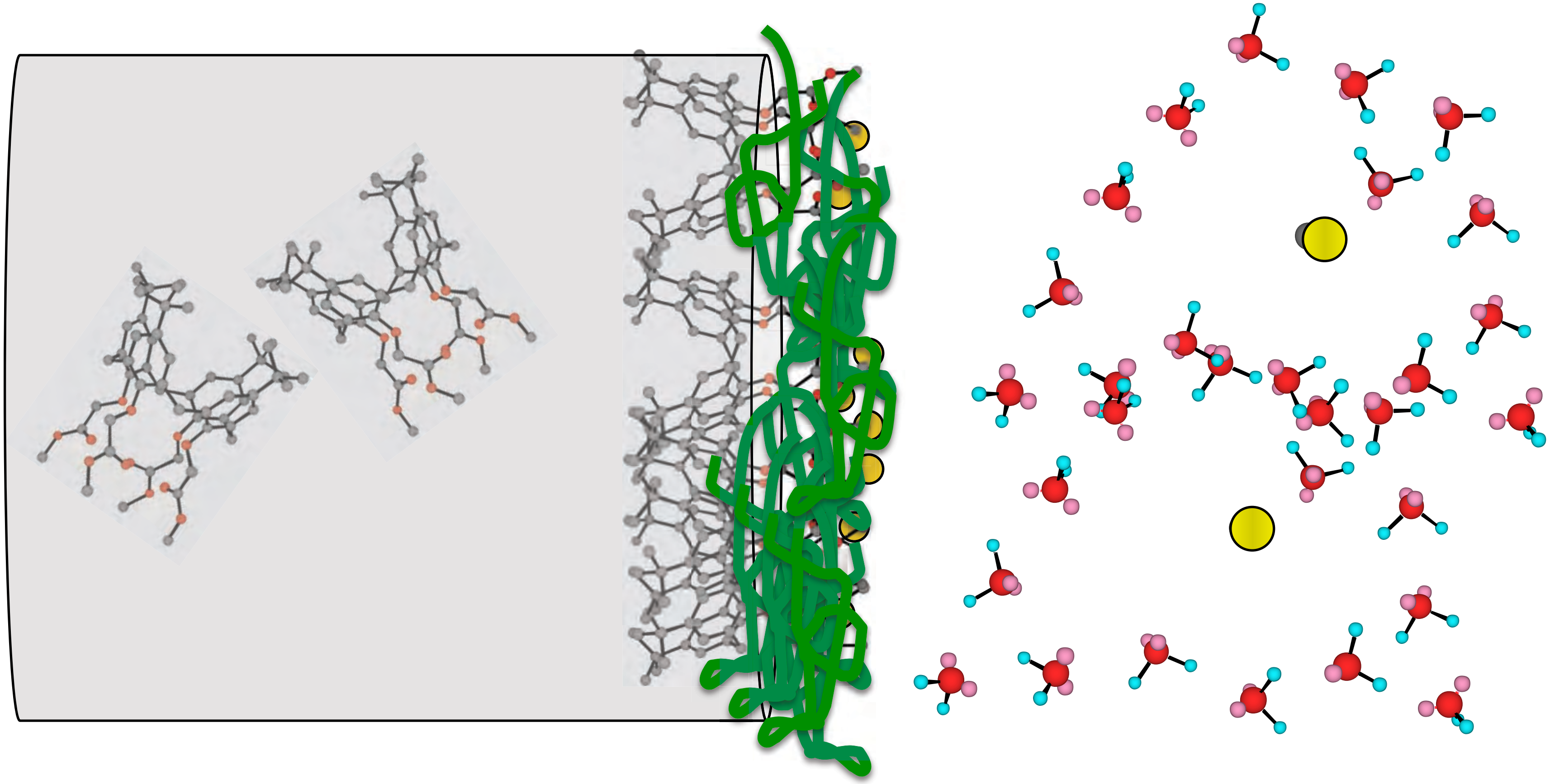
Conventional PVC-membrane based ISEs

Biofilm Formation on Sensors



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

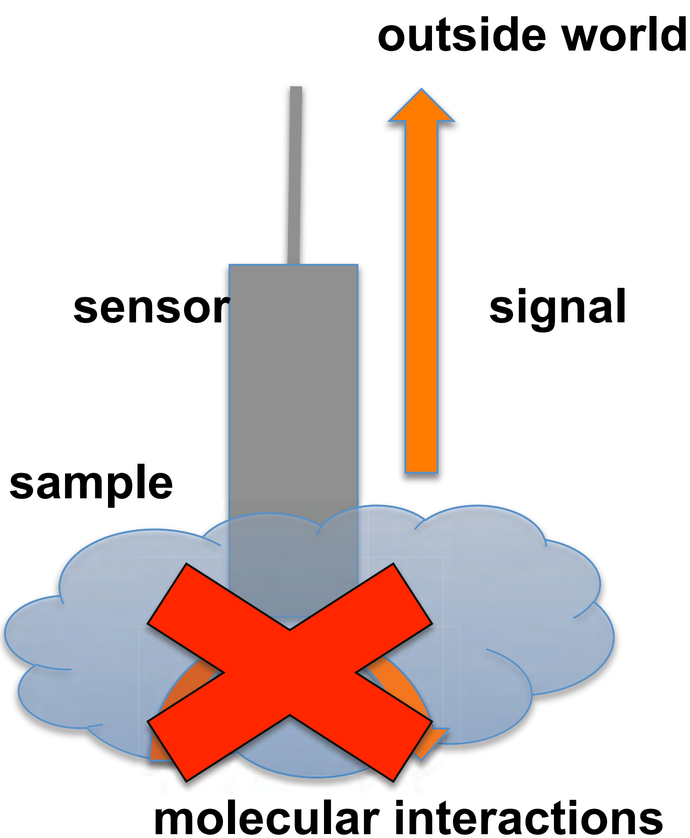
Control of membrane interfacial exchange & binding processes



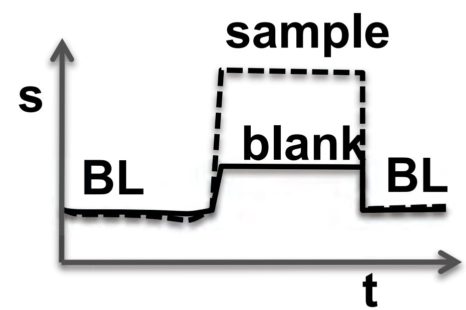
Remote, autonomous chemical sensing is a tricky business!

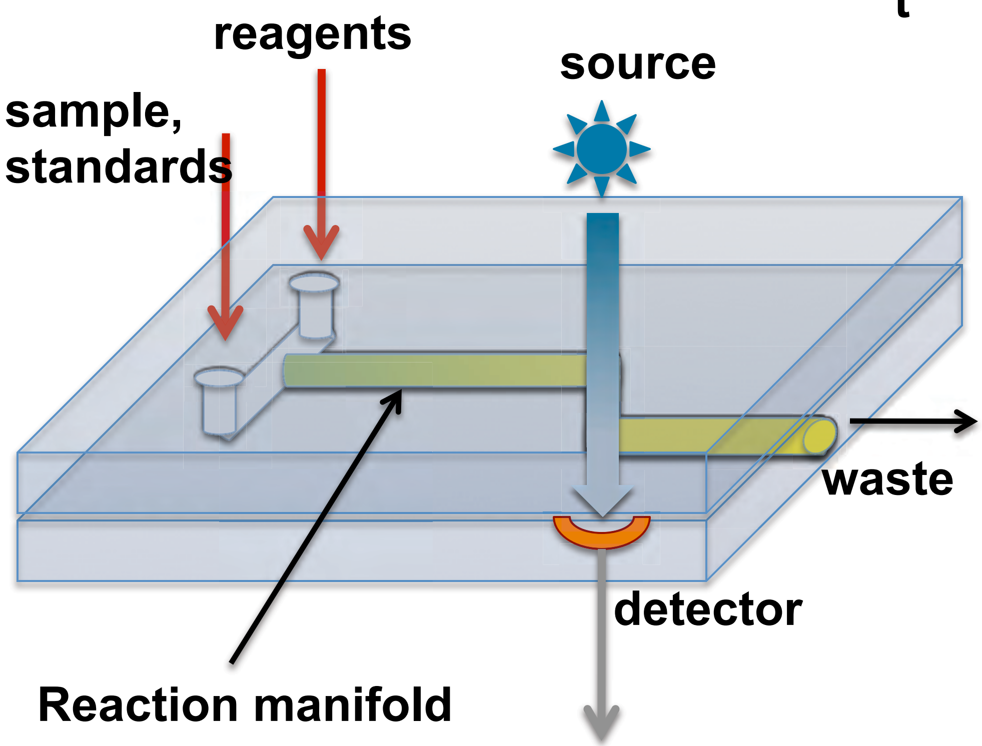
Direct Sensing vs. Reagent Based LOAC/ufluidics

Direct Sensing



LOAC Analyser





MicroTAS/Lab on a Chip/Microfluidics

Many people, myself included, expected that the ability to manipulate fluid streams, in microchannels, easily, would result in a proliferation of commercial LoC systems, and that we would see applications of these devices proliferating throughout science. In fact, it has not (yet) happened.

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

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

Autonomous platform – water Analysis

Sampling port

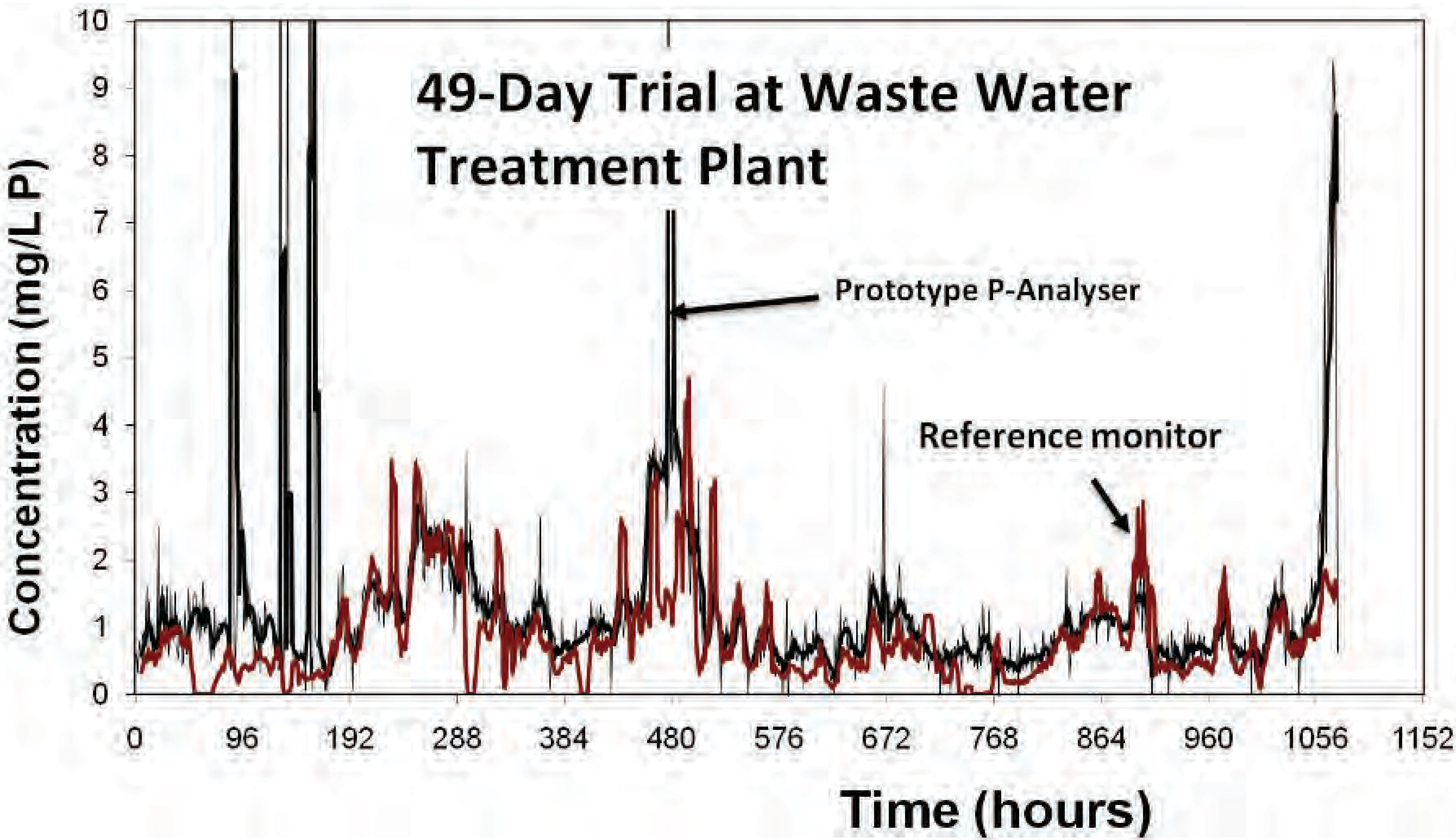
Deployment at Osberstown WWTP

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

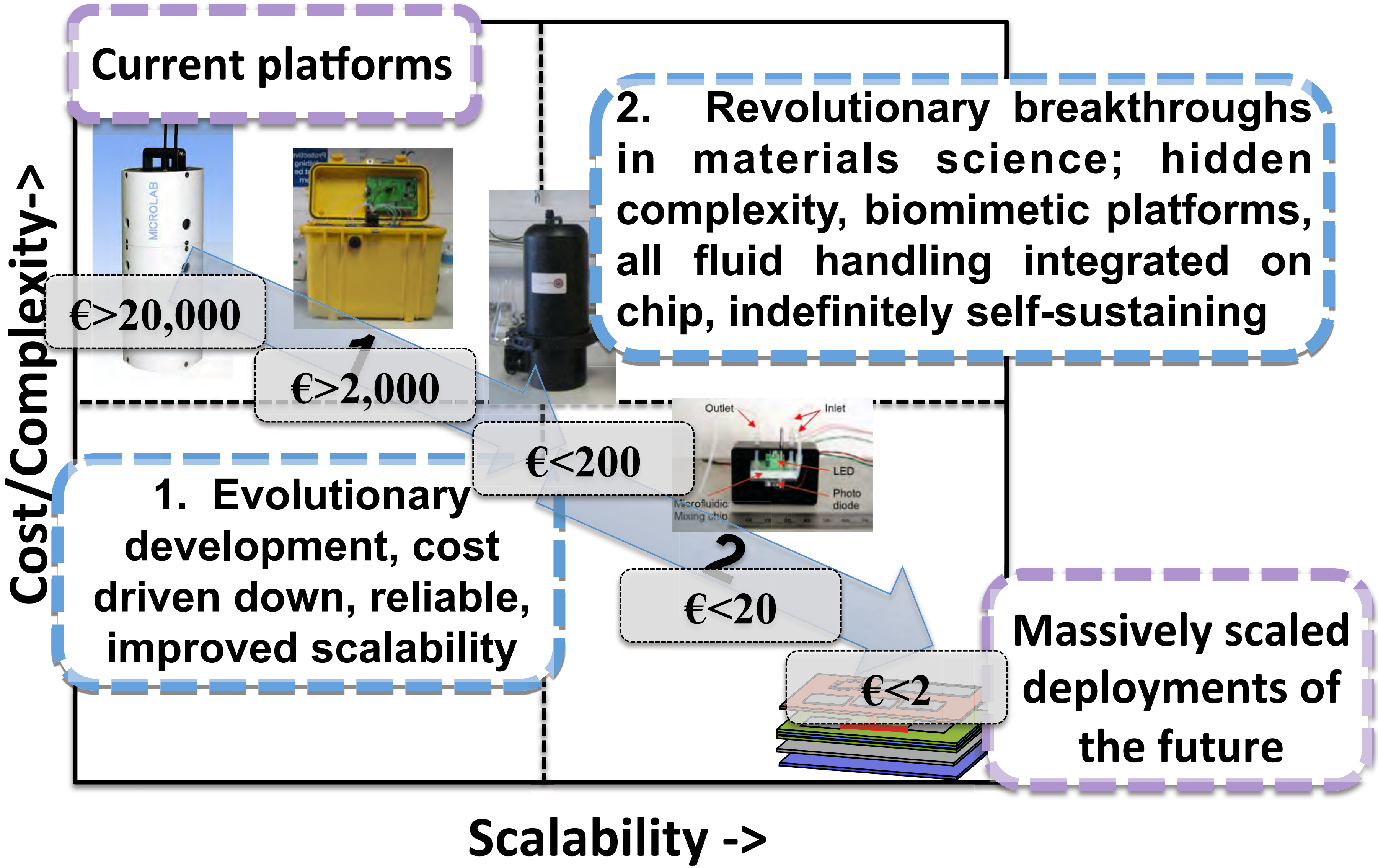
Osberstown – 3 week deployment

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

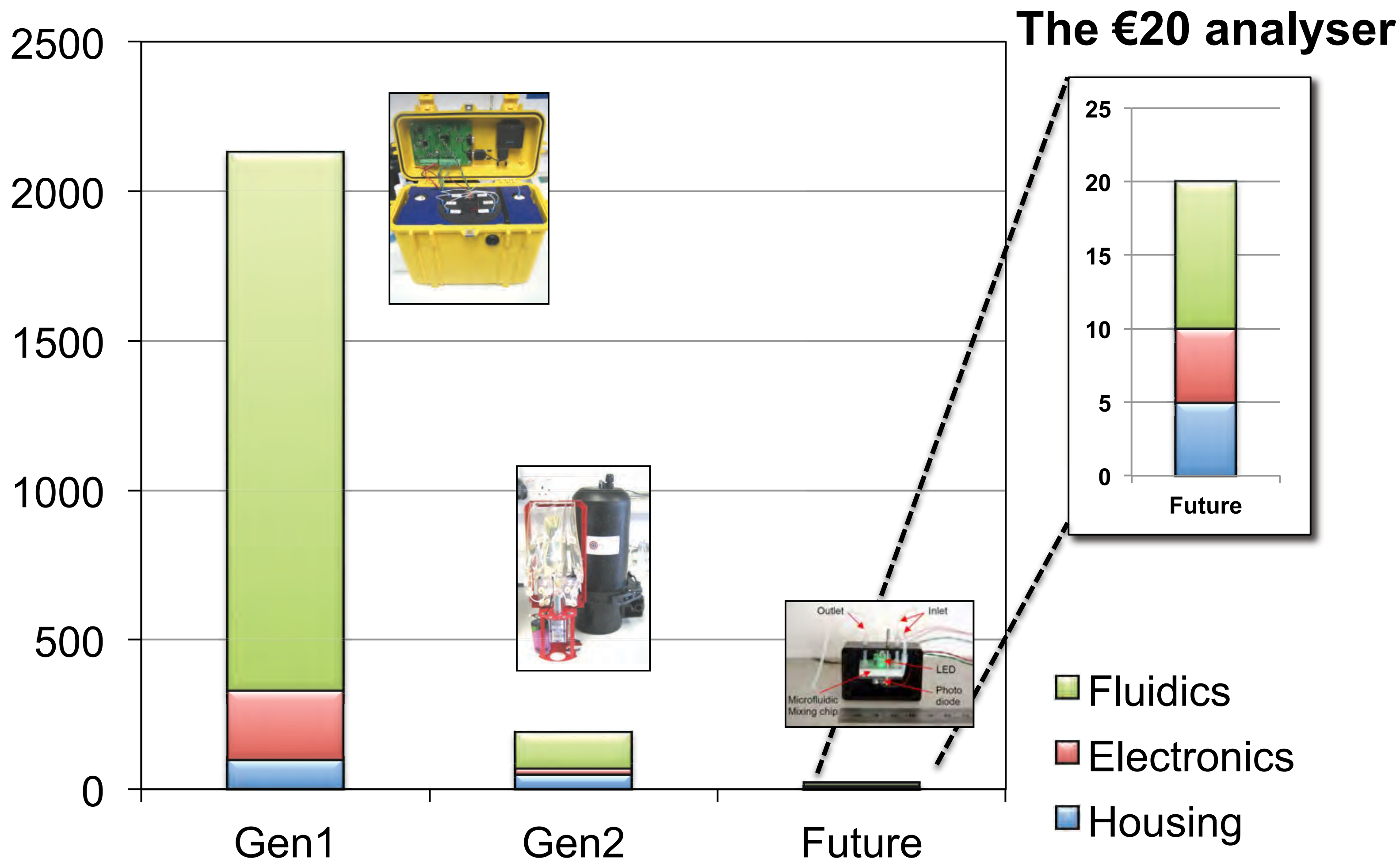
Autonomous Chemical Analyser



Achieving Scale-up

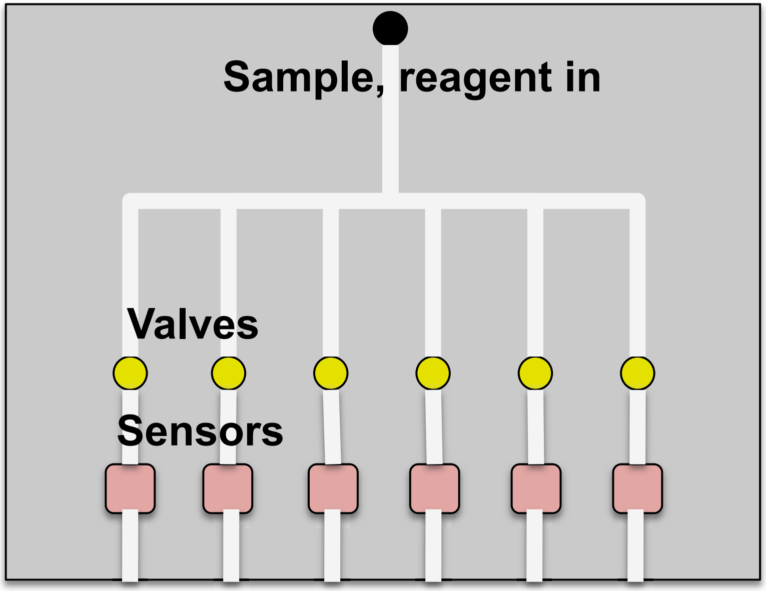


Cost Comparison Analyser (€)



Use 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)….

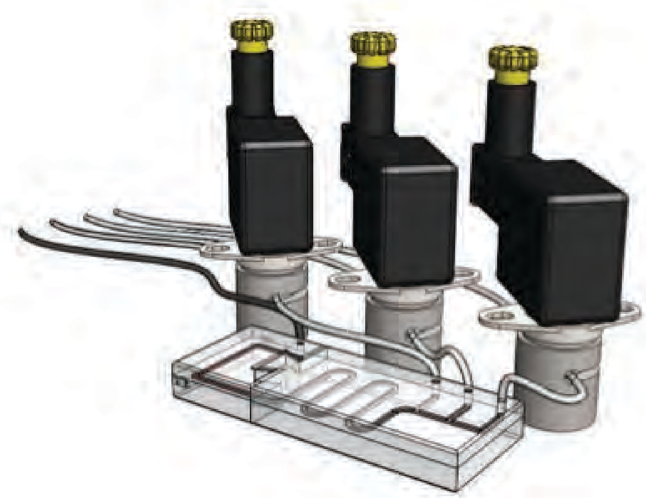


Then 50 sensors when used sequentially could provide an aggregated in-use lifetime of around 1 year

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

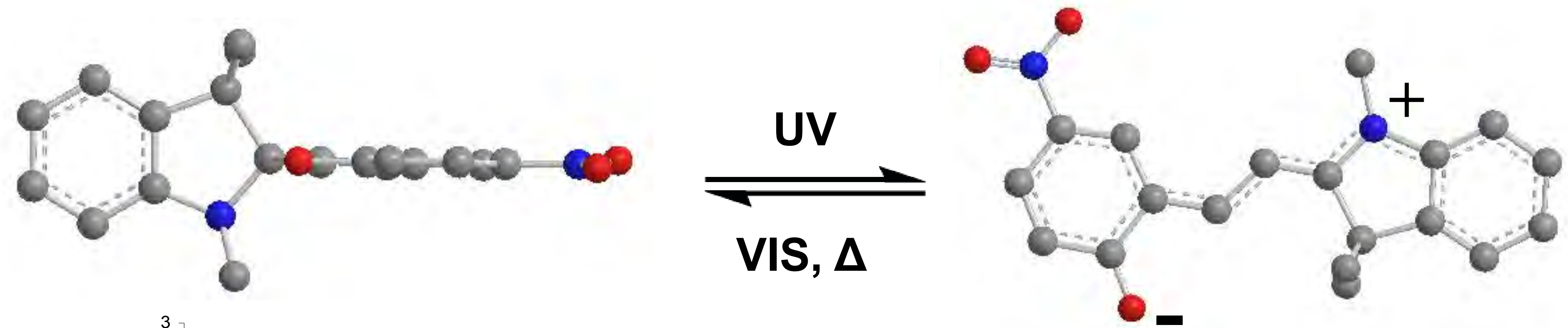
How to advance fluid handling in LOC platforms: re-invent valves (and pumps)!

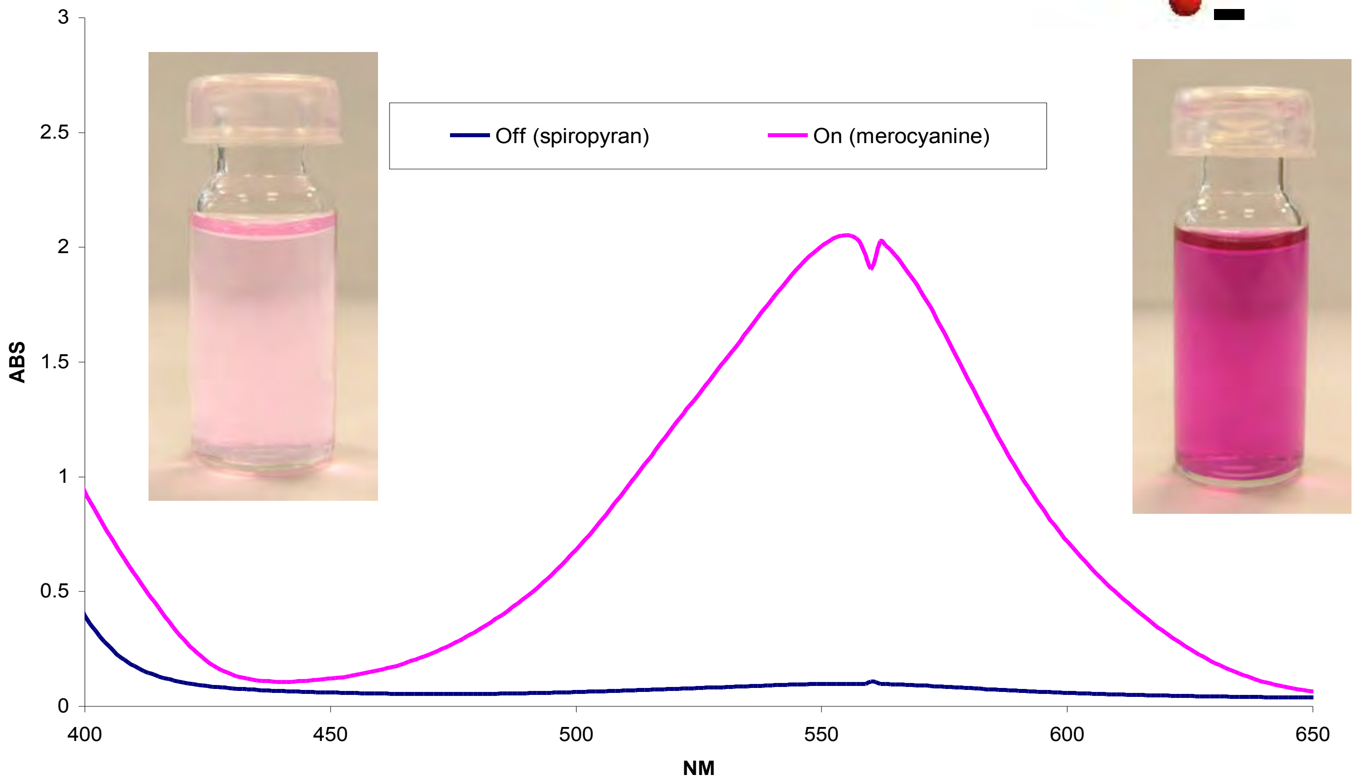
- **Conventional valves cannot be easily scaled down - Located off chip: fluidic interconnects required**
  - Complex fabrication
  - Increased dead volume
  - Mixing effects
- **Based on solenoid action**
  - Large power demand
  - Expensive



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

Photoswitchable Materials

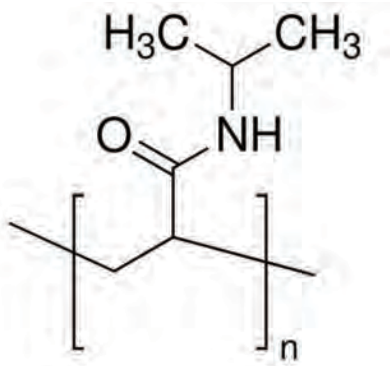




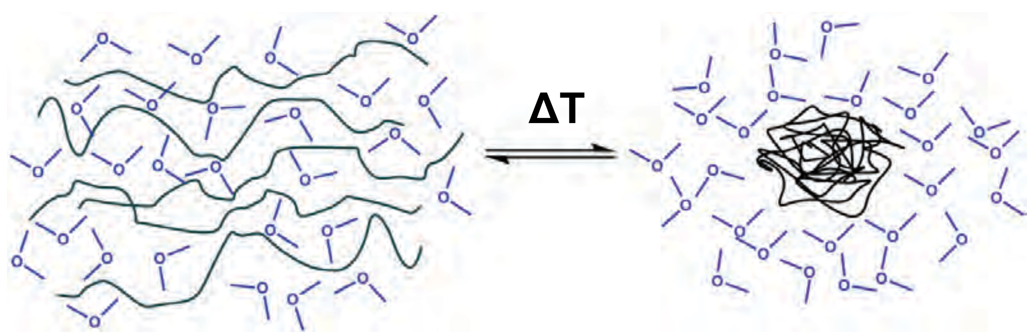
Poly(*N*-isopropylacrylamide)

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



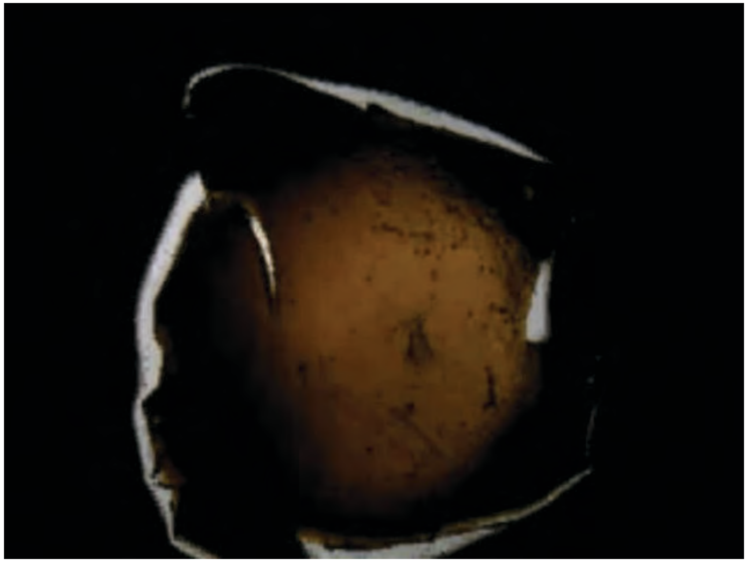
Hydrophilic **Hydrophobic**

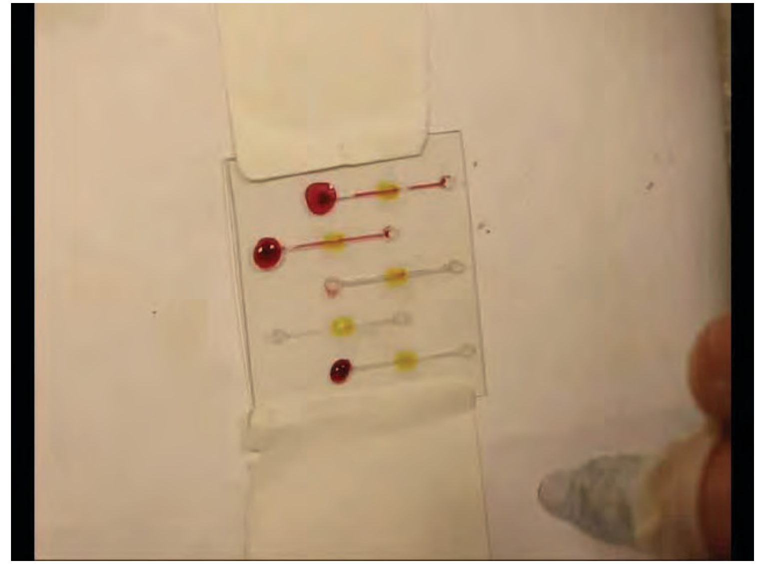


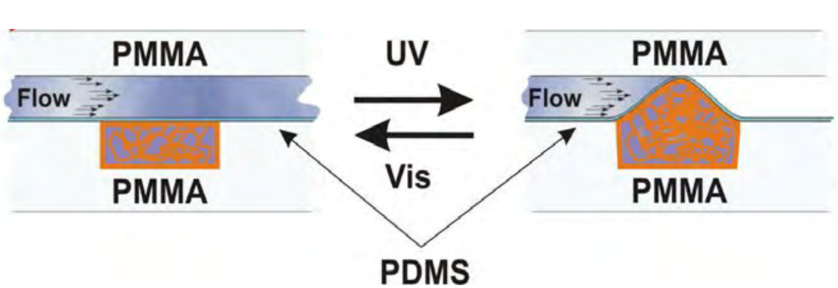
Hydrated Polymer Chains

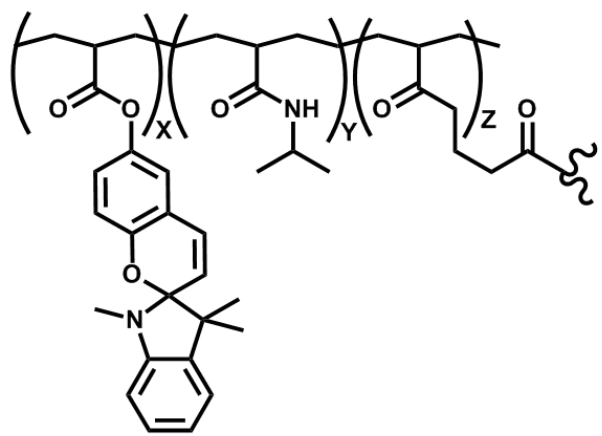
Loss of bound water -> polymer collapse

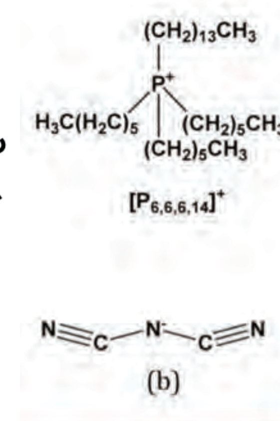
Photo-actuator polymers as microvalves in microfluidic systems







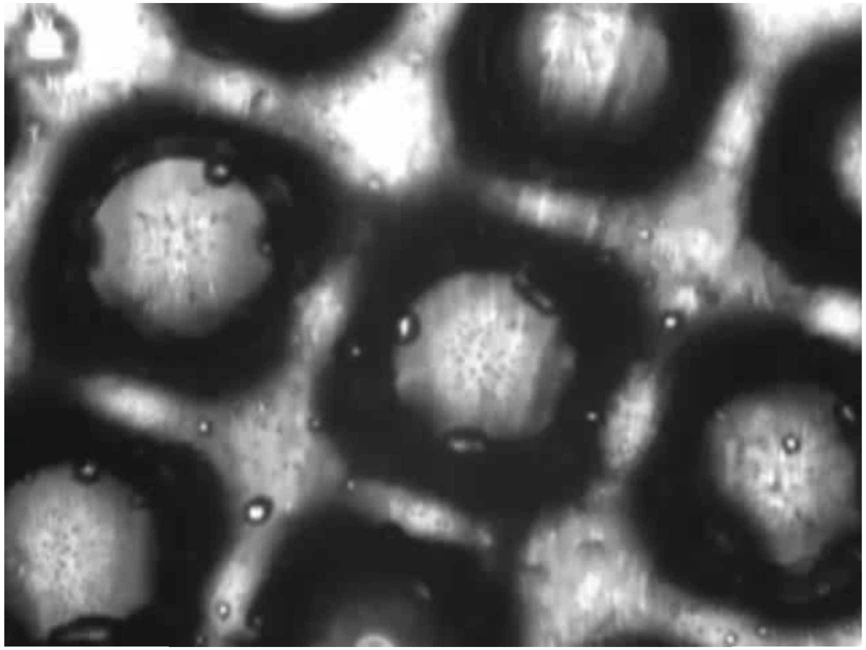




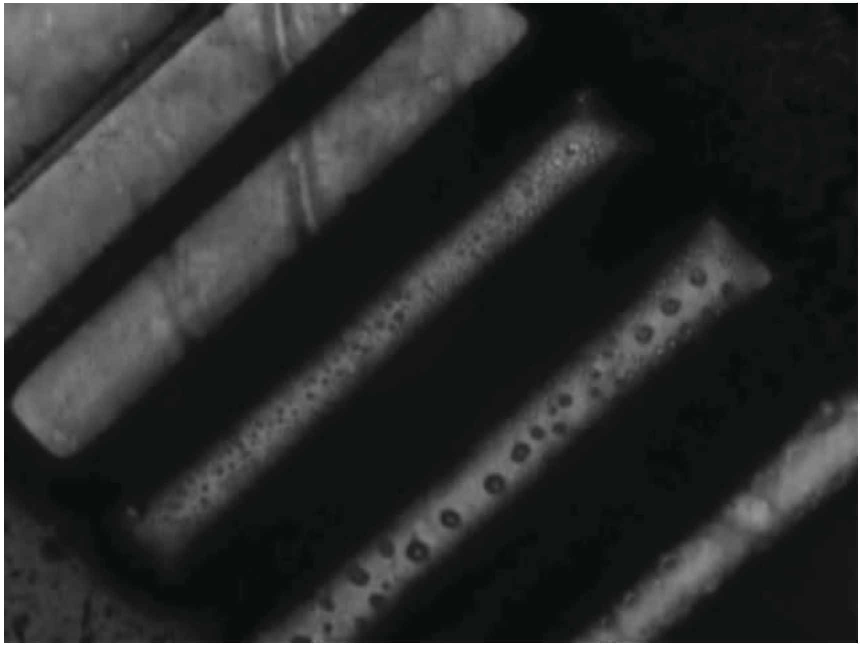
trihexyltetradecylphosphonium dicyanoamide $[P_{6,6,6,14}]^+[dca]^-$

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.

Flexible creation of μ-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

Thanks to…..

Thanks Johan for the invitation