

Bio-Inspired Systems: An Exciting Vision for Future Autonomous Sensing Platforms

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RSC Analytical Division Invited Lecture

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School of Chemistry and Chemical Engineering

Queen's University Belfast

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Fundamental Challenge: (4d!)

Can we deliver platforms (nano to macro scale) with advanced functionalities capable of long-term (months, years) autonomous operation in remote (hostile) environments (implants, environment) at a reasonable cost?

‘Deploy and Forget’ long-term use model

Functions.....

Chem/biosensing, communications, programmed uptake & release, movement, redundancy ‘death’ (biodegrade) and regeneration, self-awareness & self-maintenance...



internet
sensing

Dermot Diamond
Dublin City University
(Ireland)

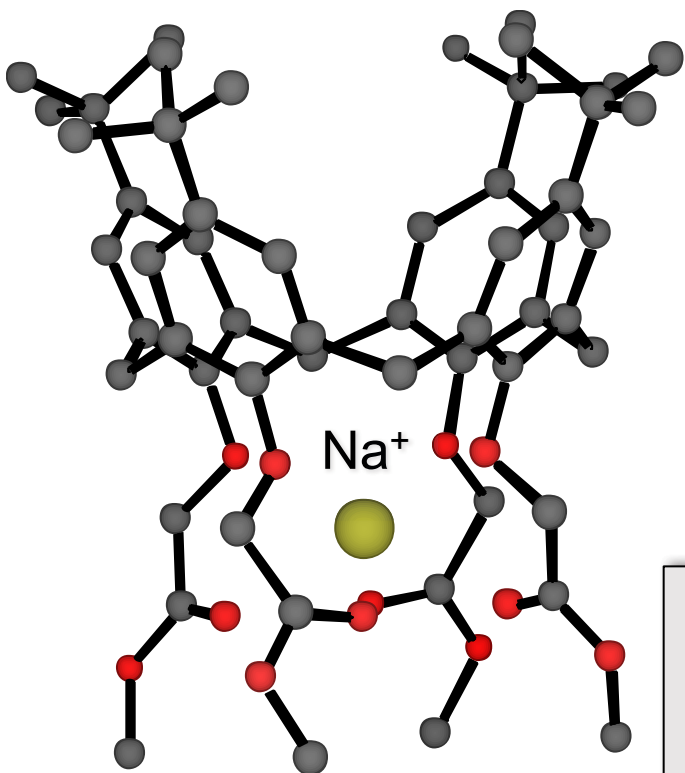
Incredible advances in digital communications and computer power have profoundly changed our lives. One chemist shares his vision of the role of analytical science in the next communications revolution.

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.

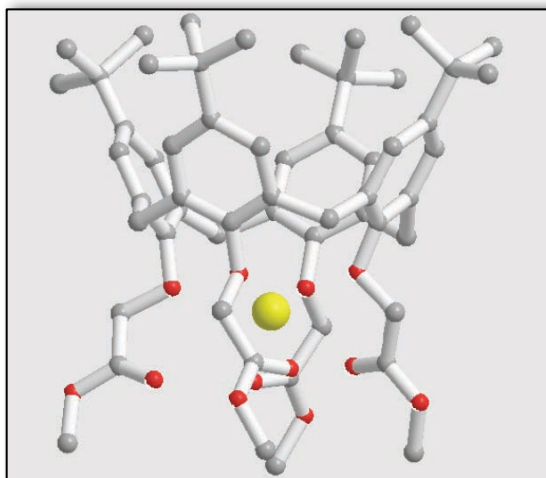
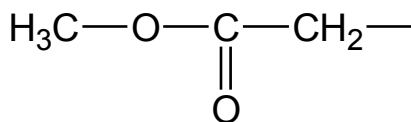
The crucial missing part in this scenario is the gateway through which these worlds will communicate: How can the digital world sense and respond to changes in the real world? Analytical scientists—particularly those working on chemical sensors, biosensors, and compact, autonomous instruments—are



Calixarene Ionophores – controlling the selectivity

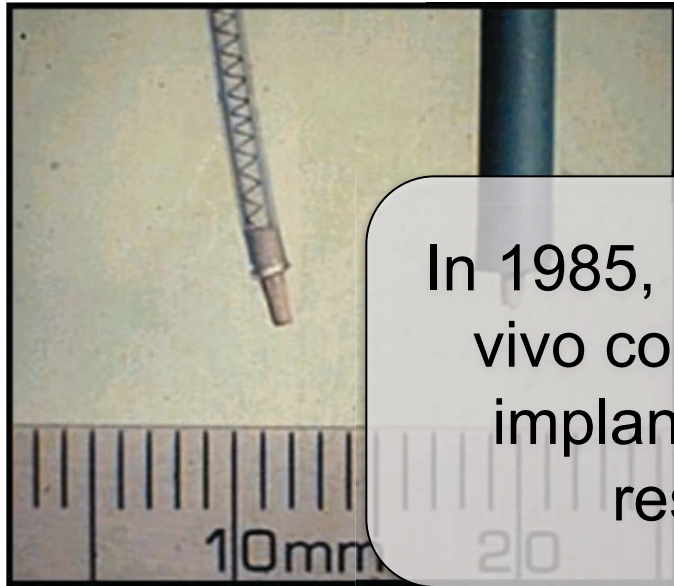


Gyula Svehla





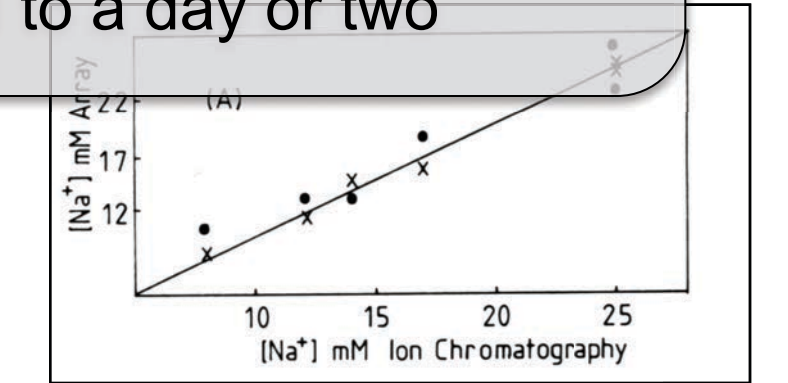
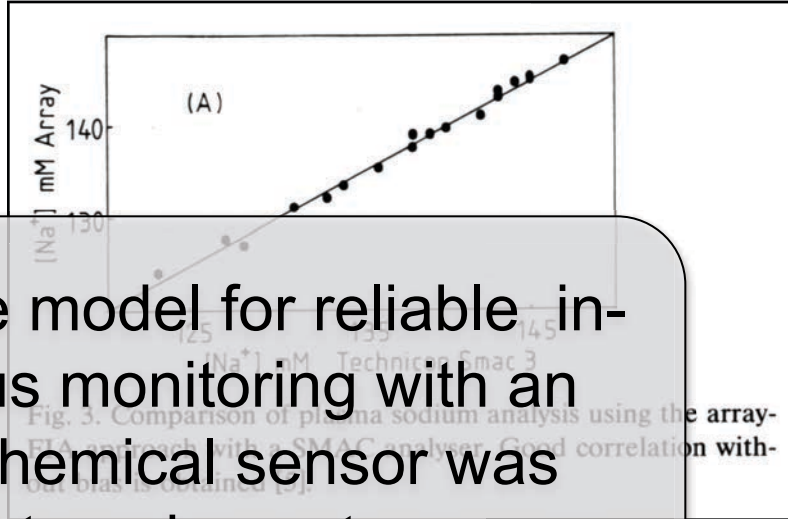
Blood Analysis; Implantable Sensors



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

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

Dr. David Band, St Thomas's Hospital London



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

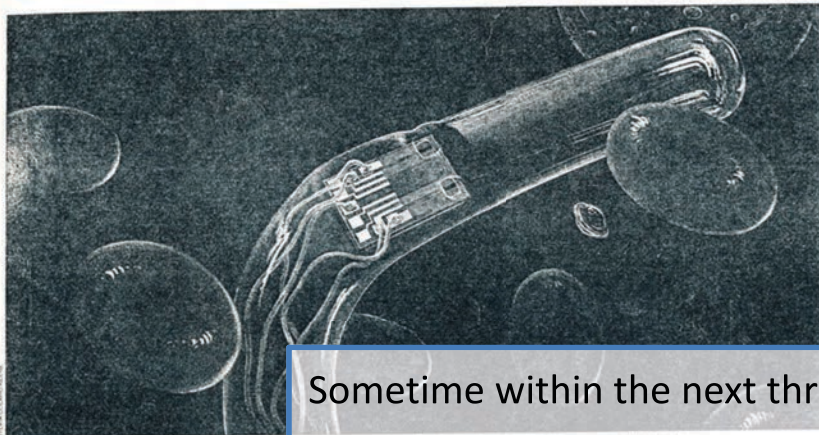
Ligand (and variations of) used in many clinical analysers for blood Na⁺ profiling



The (broken) promise of biosensors.....



BIOSENSORS THE MATING OF BIOLOGY AND ELECTRONICS

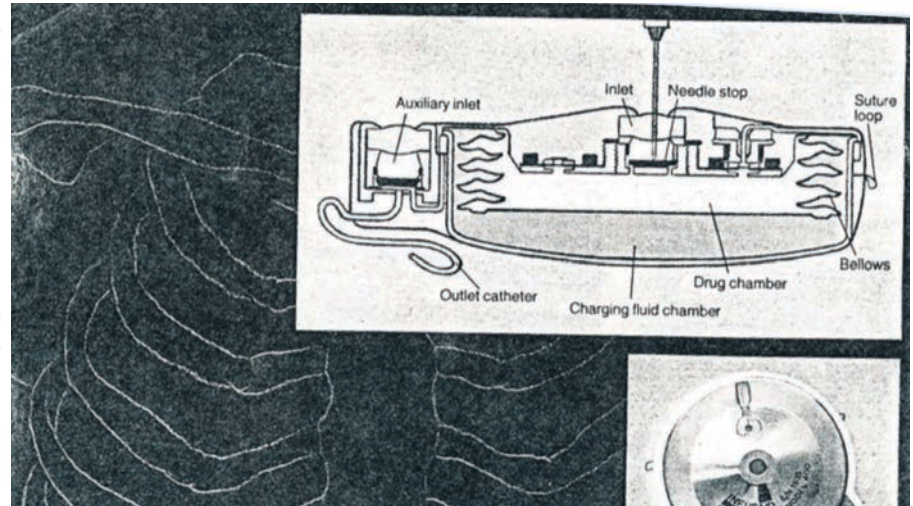


Implanted sensors connect to a computer. The Utah model is a field-effect transistor.

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 by H. Garrett DeYoung

High Technology, Nov. 1983, 41-49



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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





After Ca. 40 years – Dominant Use Model is Finger Prick Sampling

- e.g. Diabetes: ca. 7% of world population
- USA: population 300 million
- Ca. 20 million diabetics
- Personal control of condition using finger prick test => blood sample + glucose biosensor
- Say four measurements per day = 80 million/day
- Per year = ca. 30 Billion measurements/yr
- Each sensor used ONCE





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 painless⁶
- 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 exercising⁷

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

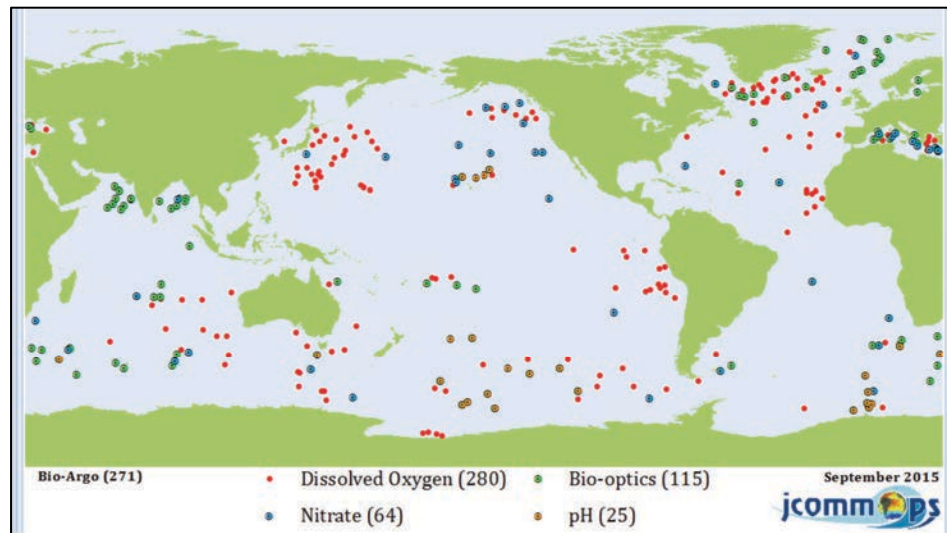
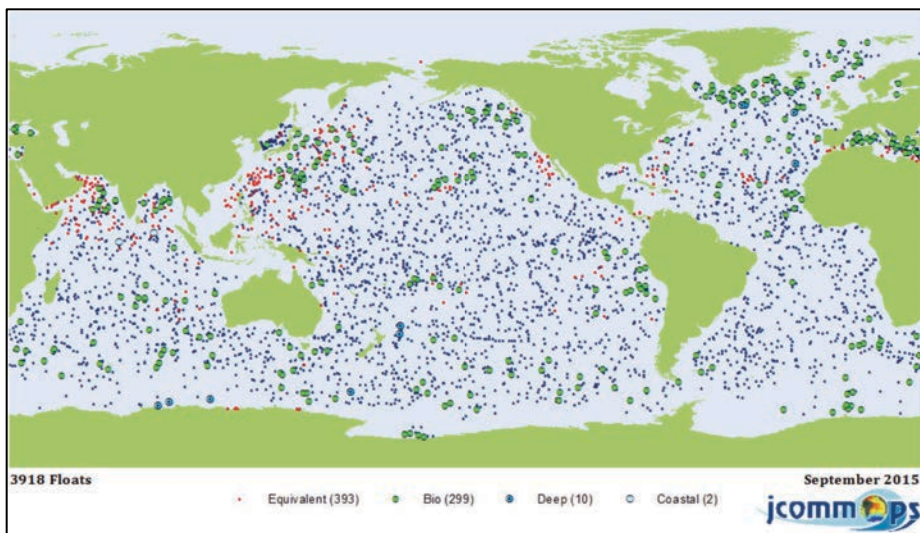


- 'Small fibre' used to access interstitial fluid
- Data downloaded at least once every 8 hr via 1s contactless scan (1-4 cm)
- Waterproof to 1 metre
- Replace every 2 weeks

Current state-of-the-art for patch based glucose sensing is 2-weeks use outside the body: Implants require 10 years inside the body



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>

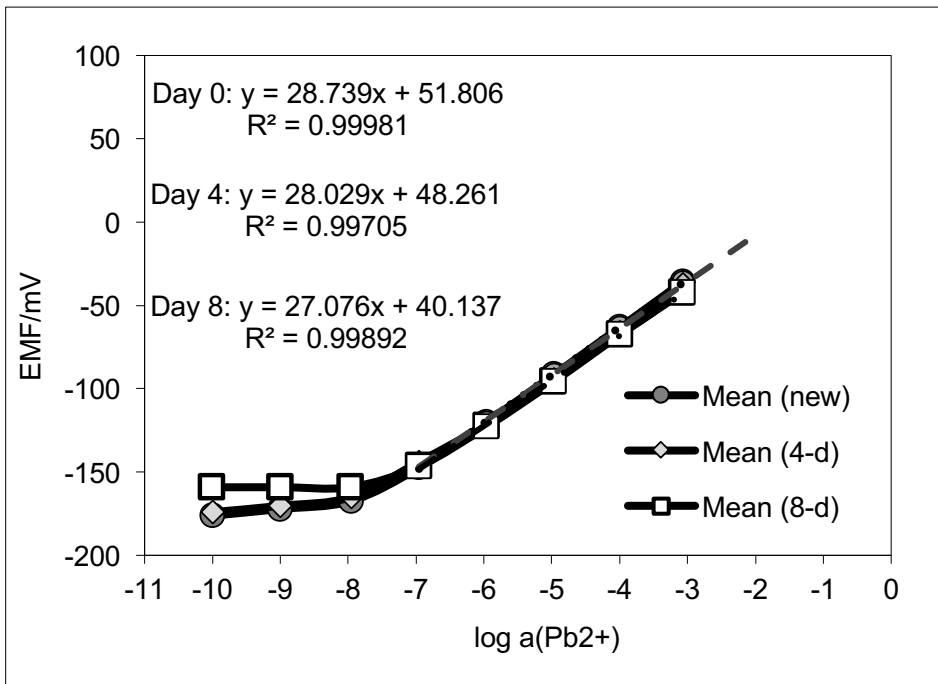
‘calibration of the DO measurements by the SBE sensor remains an important issue for the future’, Argo report ‘Processing Argo OXYGEN data at the DAC level’, September 6, 2009, V. Thierry, D. Gilbert, T. Kobayashi



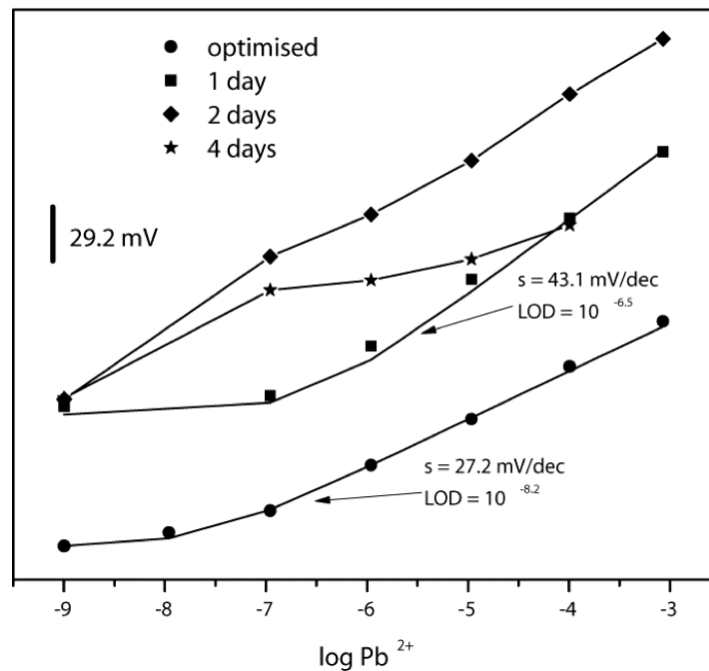


Change in Electrode Function over Time

See *Electrochimica Acta* 73 (2012) 93–97



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

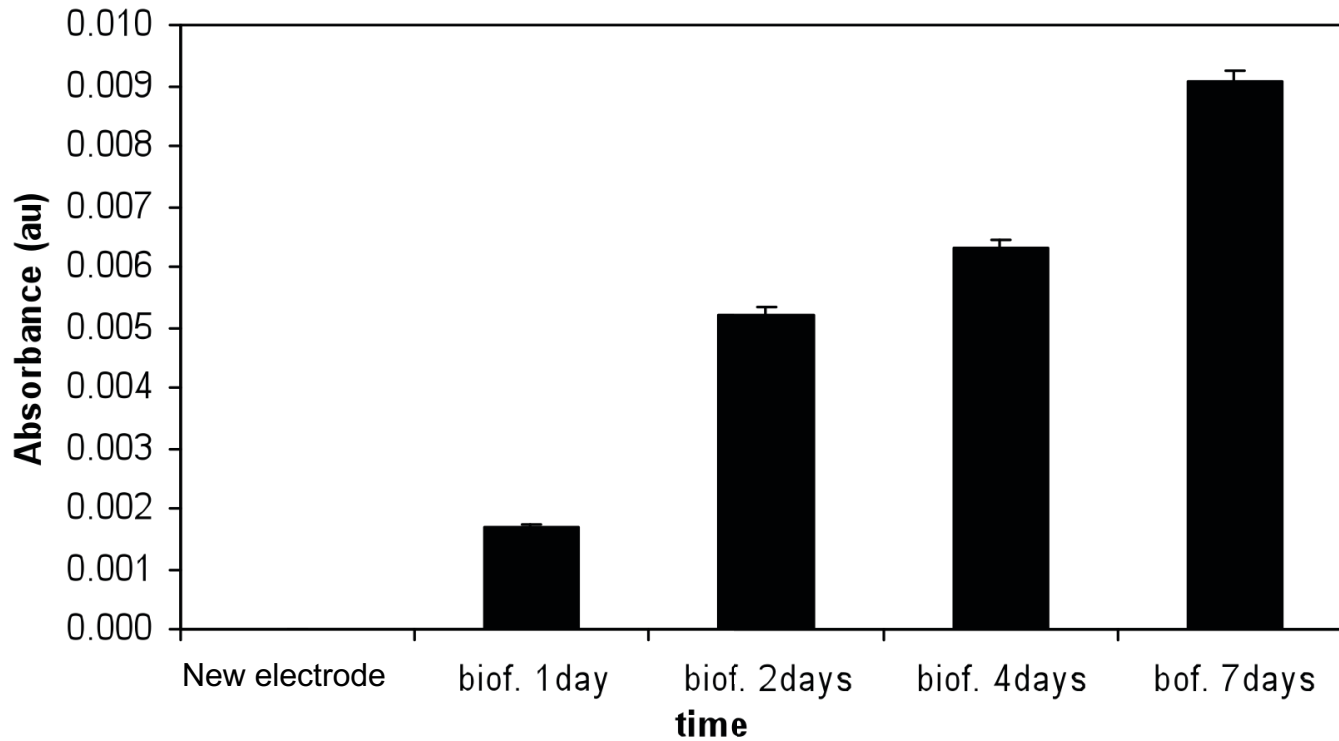


Continuous contact with river water

Conventional PVC-membrane based ISEs



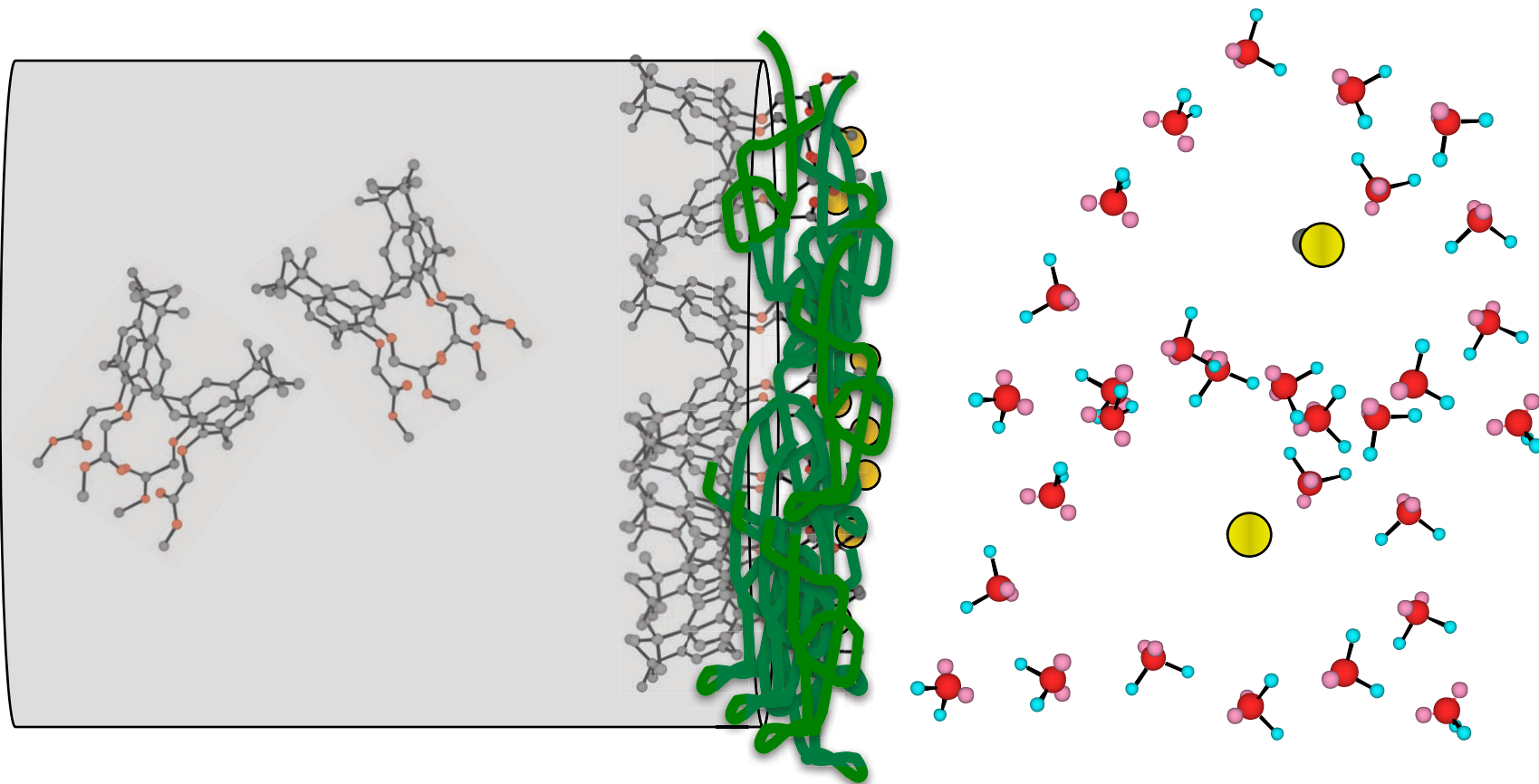
Biofilm Formation on Sensors



- **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!





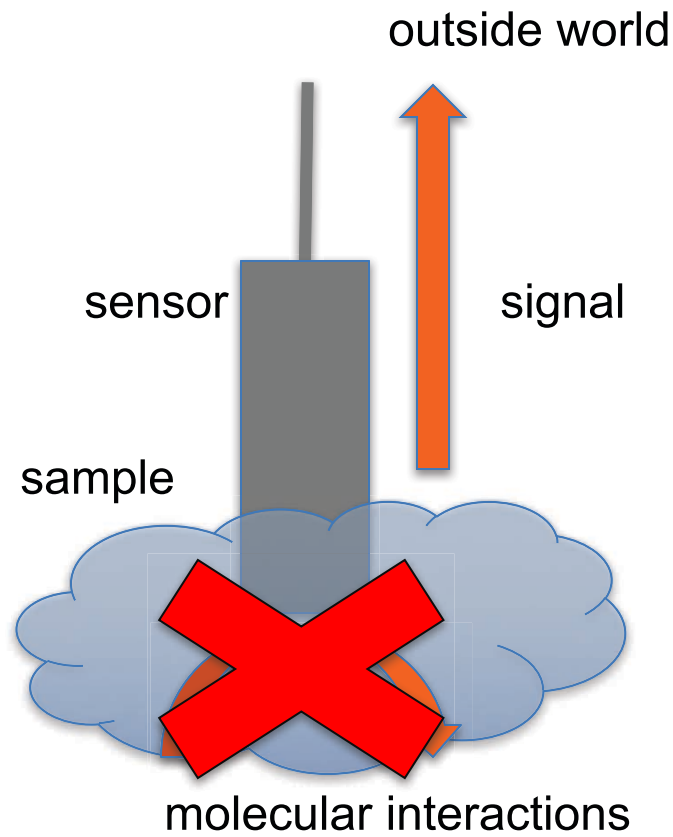
Osberstown – 3 week deployment



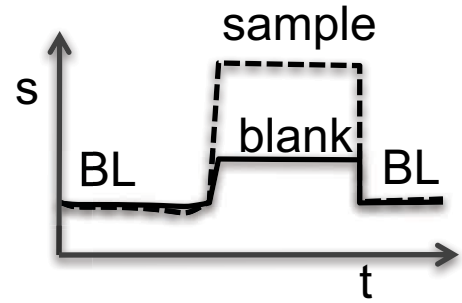
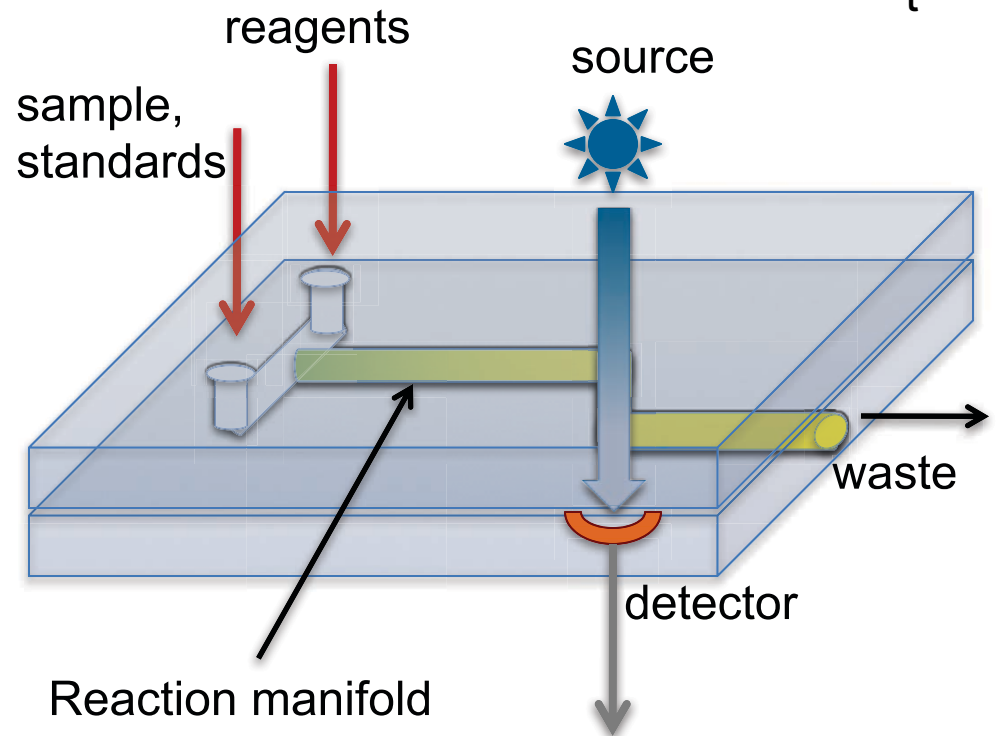


Direct Sensing vs. Reagent Based LOAC/ufluidics

Direct Sensing



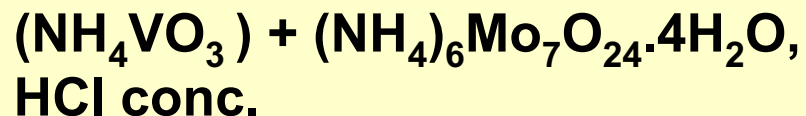
LOAC Analyser



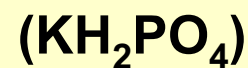


Phosphate: The Yellow Method

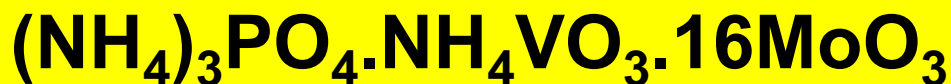
Mixture (Reagent)



Sample



+

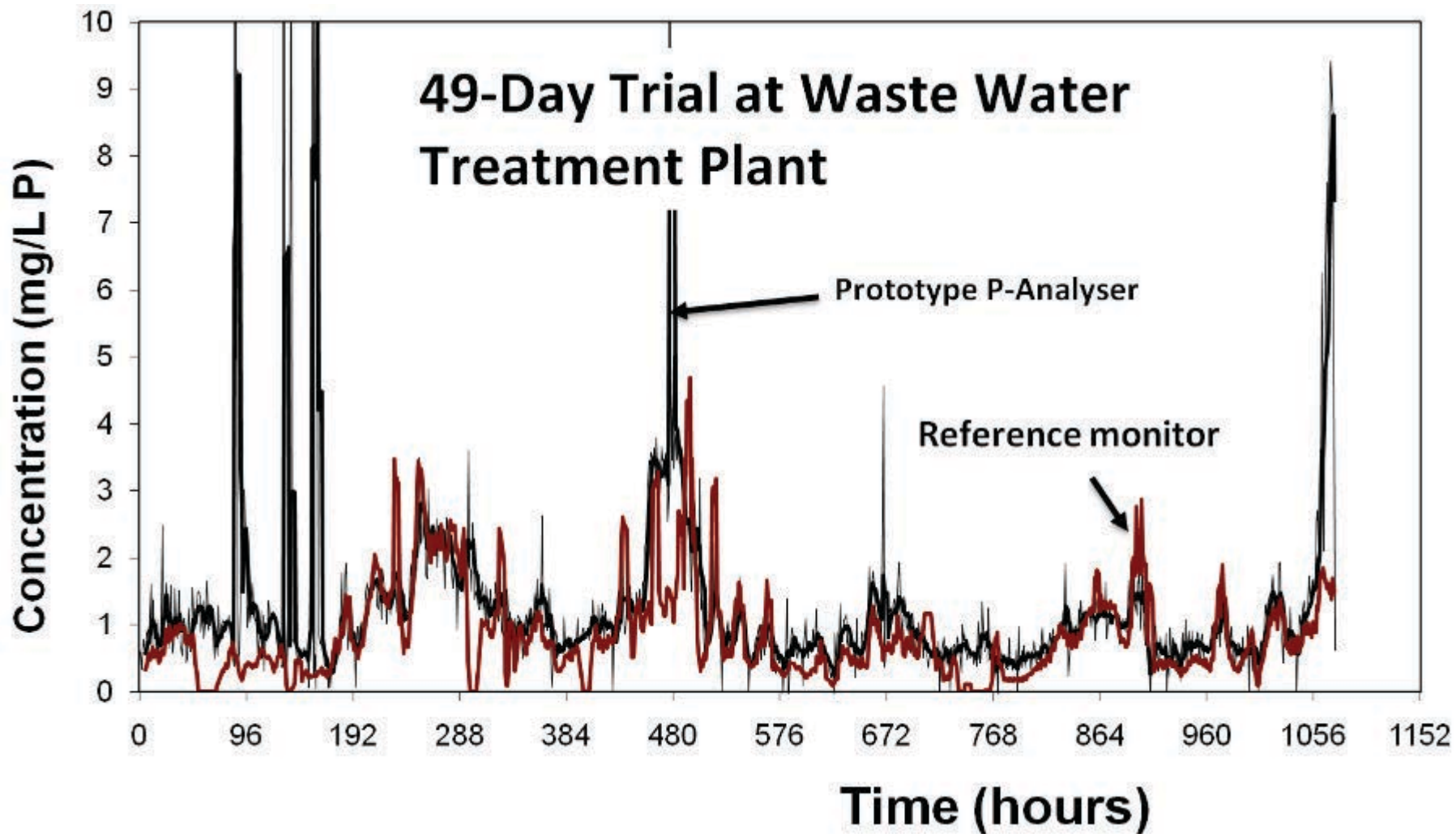


- yellow vanaomolybdophosphoric acid is formed when ammonium metavanadate and ammonium molybdate (mixture) reacts with phosphate (acidic conditions)
- In conventional (molybdate) method, **ascorbic acid** is used to generate the well-known deep blue complex (**v. fine precipitate**)
- Could not be exploited in LOAC devices until UV-LEDs became available!!!!





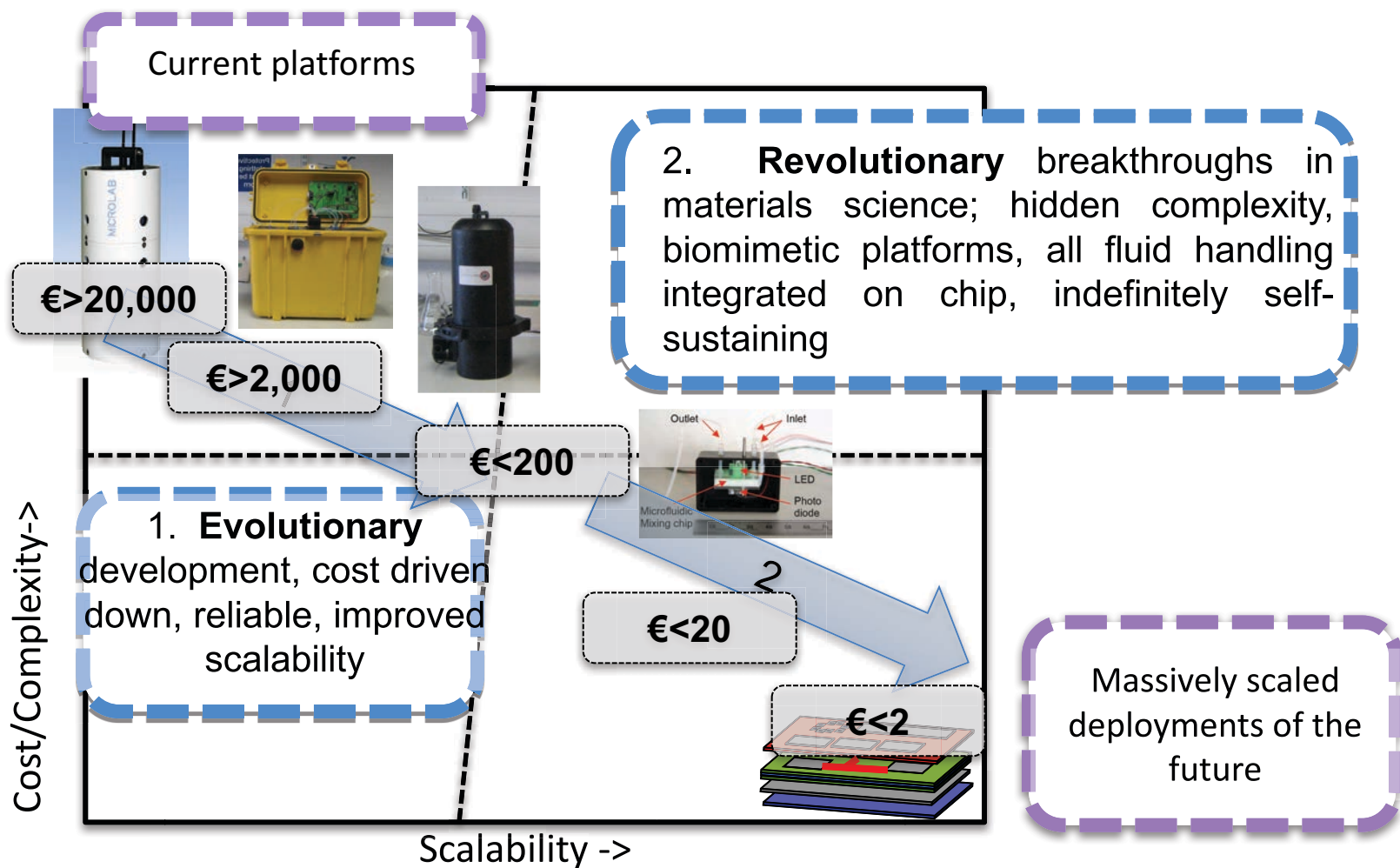
Autonomous Chemical Analyser



J. Cleary, C. Slater, D. Diamond, Analysis of phosphate in wastewater using an autonomous microfluidics-based analyser, *World Academy of Science, Engineering and Technology*. 52 (2009) 196–199.



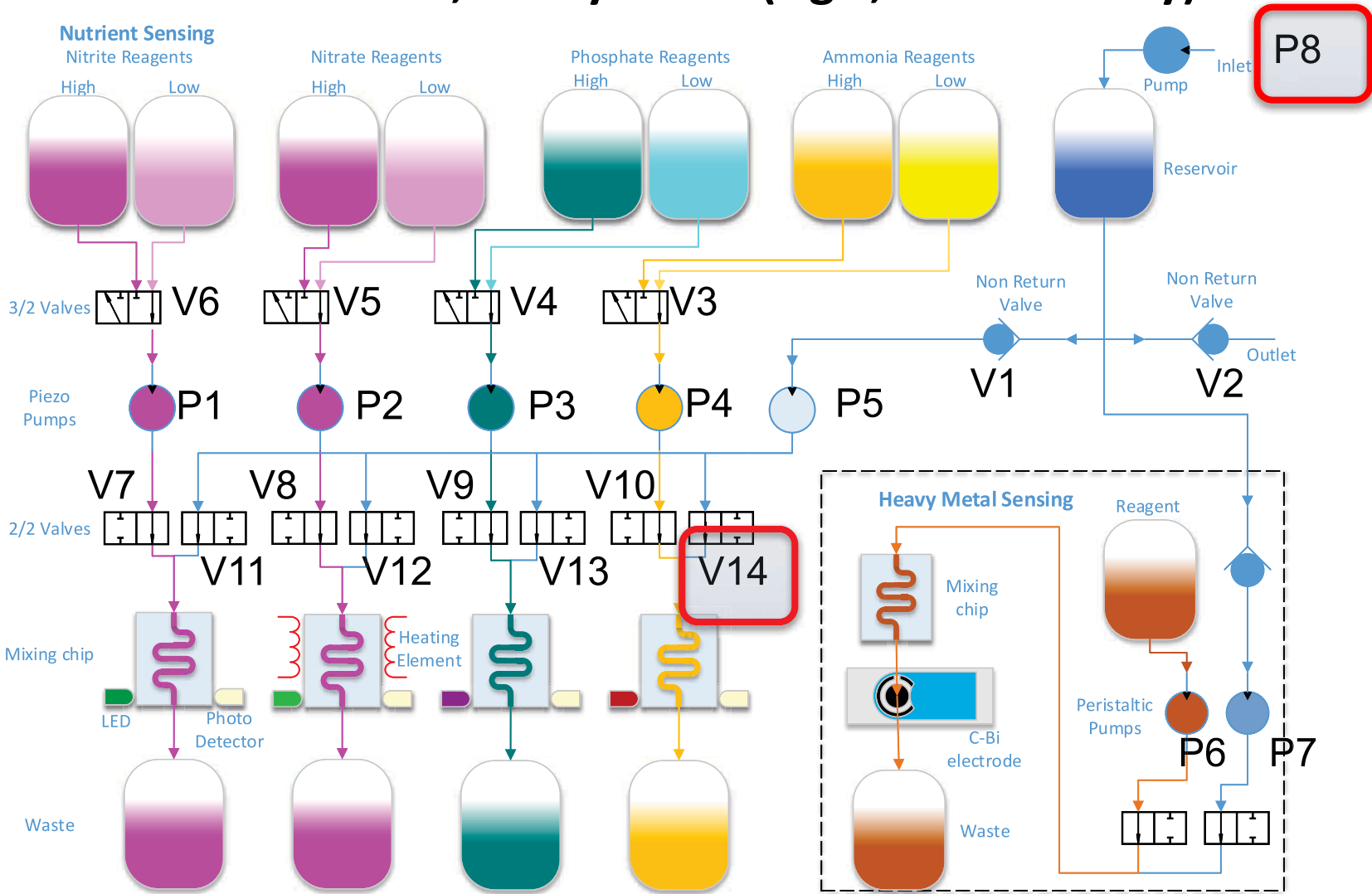
Achieving Scale-up for Environmental Sensor Networks



D. Diamond, R. Byrne, F.B. Lopez, J. Cleary, D. Maher, J. Healy, C. Fay, J. Kim, K.-T. Lau, Biomimetics and Materials with Multiple Personalities - The Foundation of Next Generation Molecular Sensing Devices, in: Proceedings IEEE Sensors Conference, Kona, Hawaii, 2010: pp. 1079–1082. doi:[10.1109/ICSENS.2010.5690729](https://doi.org/10.1109/ICSENS.2010.5690729).



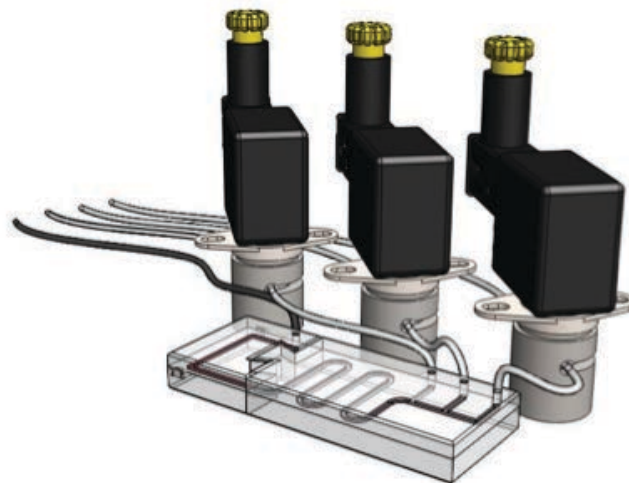
Fluidic Schematic: Multi-Analyte - Nitrite, nitrate, phosphate, ammonia, heavy metal (Hg²⁺, voltammetry)





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

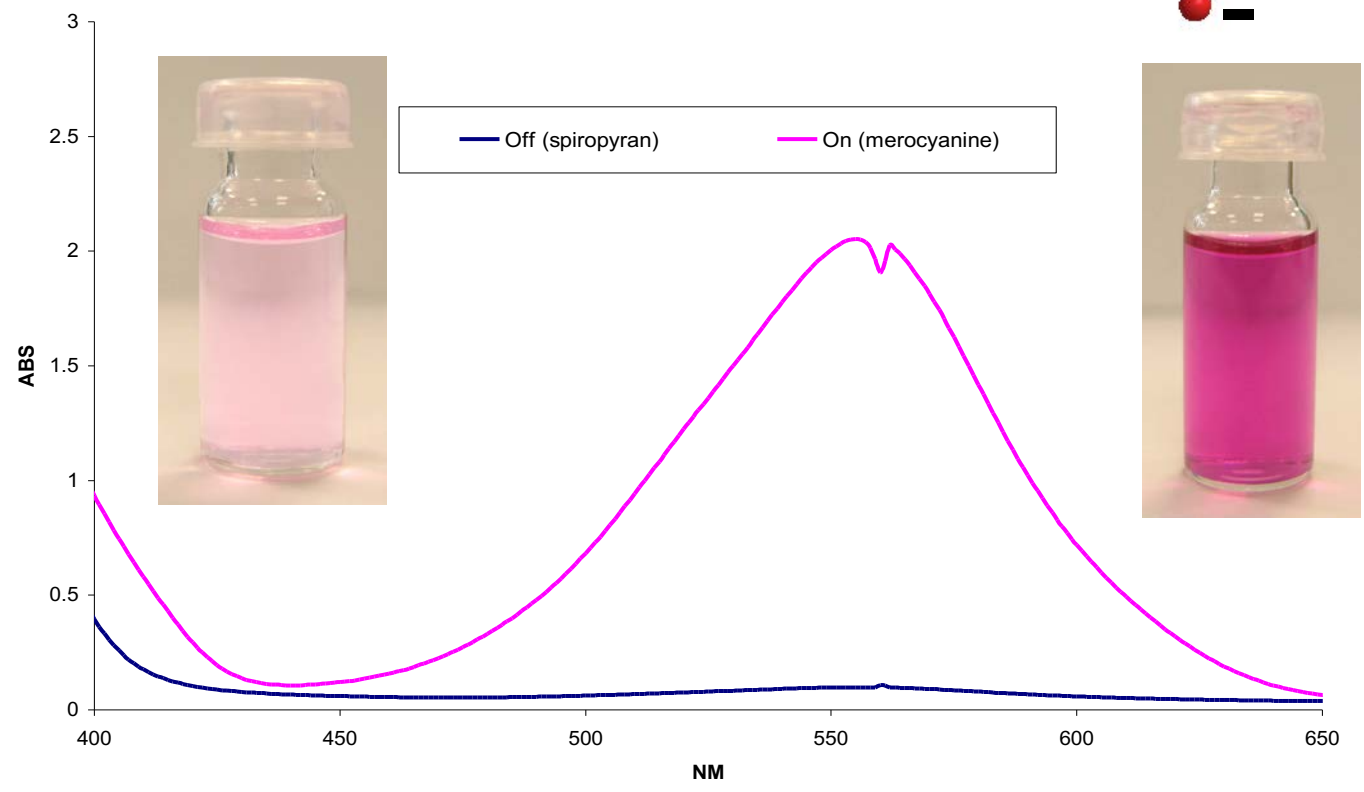
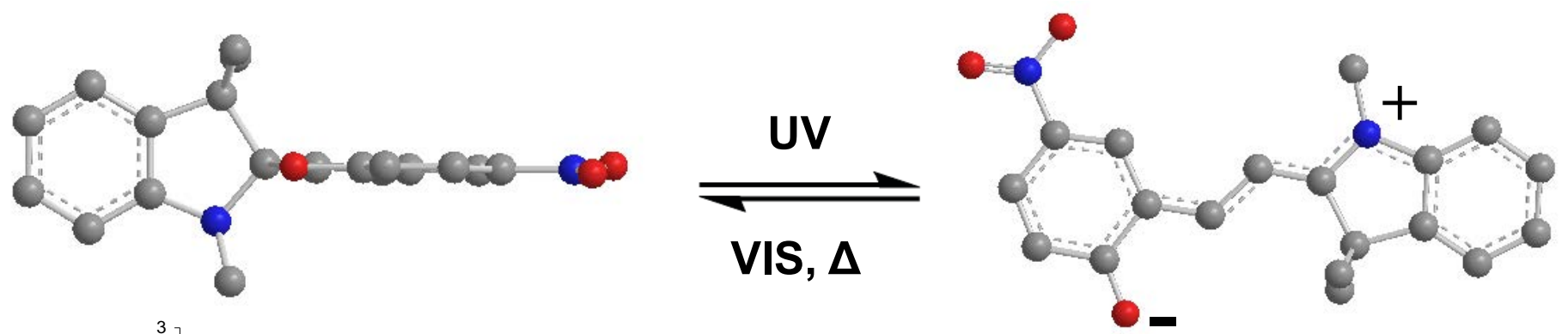


Solution: soft-polymer (biomimetic) valves fully integrated into the fluidic system





Photoswitchable Soft Actuators

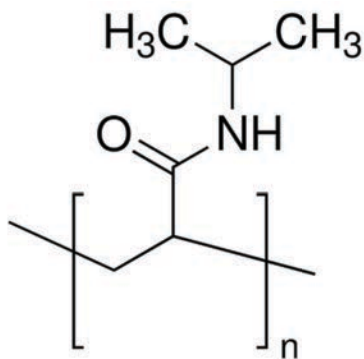




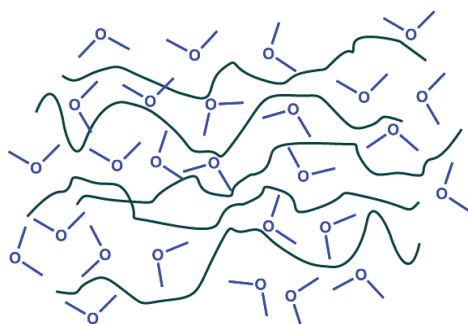
Poly(*N*-isopropylacrylamide)

- 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



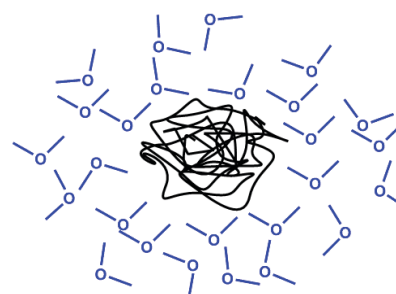
Hydrophilic



Hydrated Polymer Chains



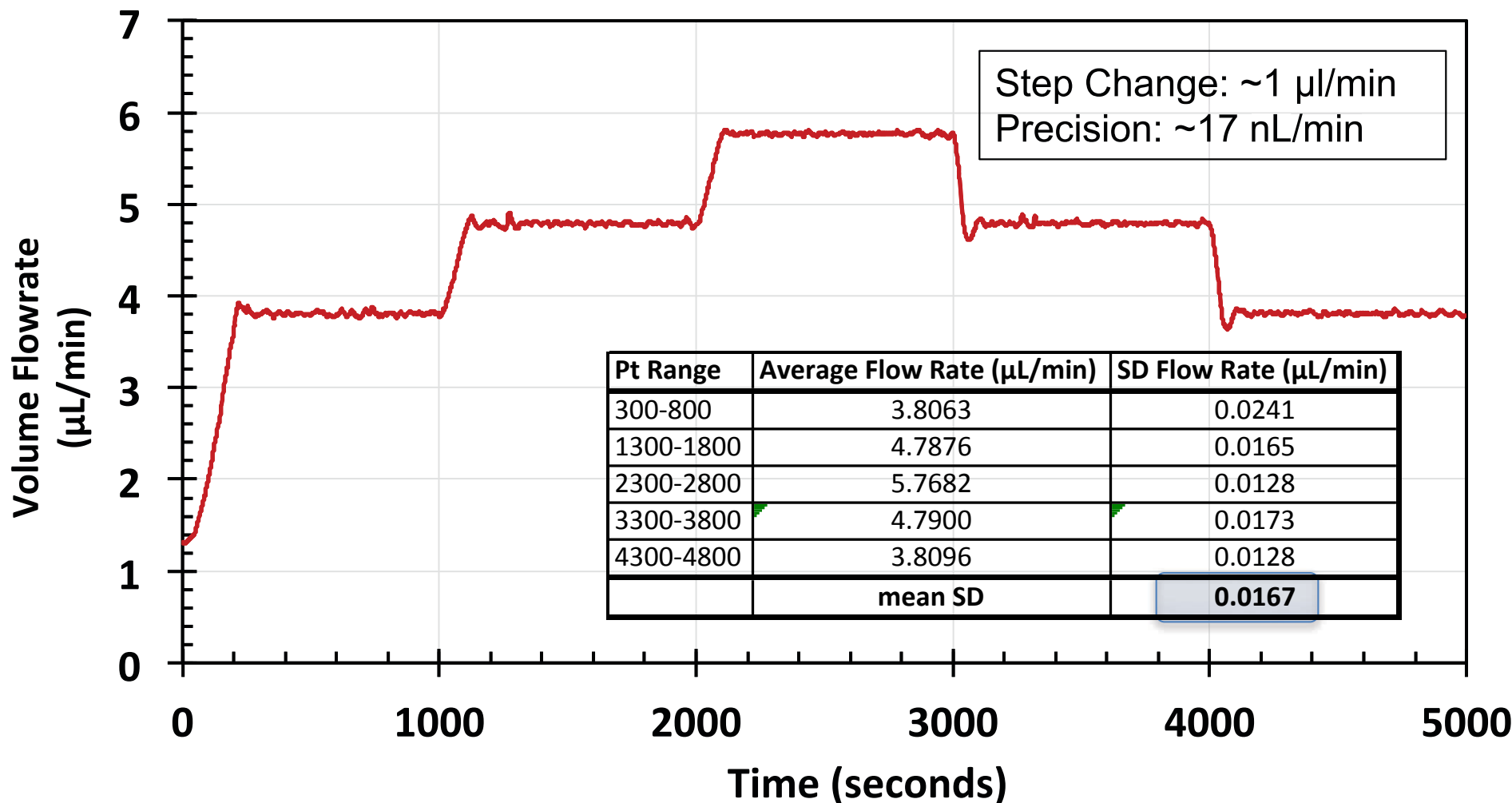
Hydrophobic



Loss of bound water
-> polymer collapse



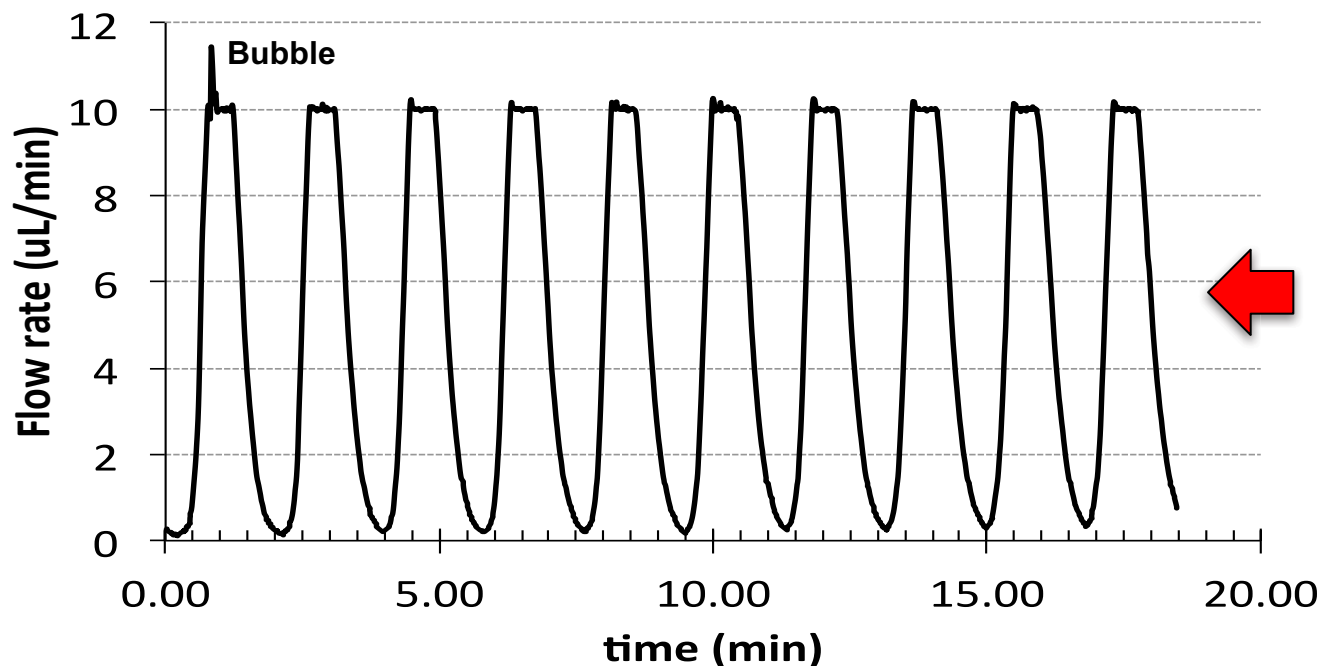
Photo-Controlled Flow Rate



C. Delaney, P. McCluskey, S. Coleman, J. Whyte, N. Kent, D. Diamond, Precision control of flow rate in microfluidic channels using photoresponsive soft polymer actuators, LAB ON A CHIP. 17 (2017) 2013–2021. doi:[10.1039/c7lc00368d](https://doi.org/10.1039/c7lc00368d).



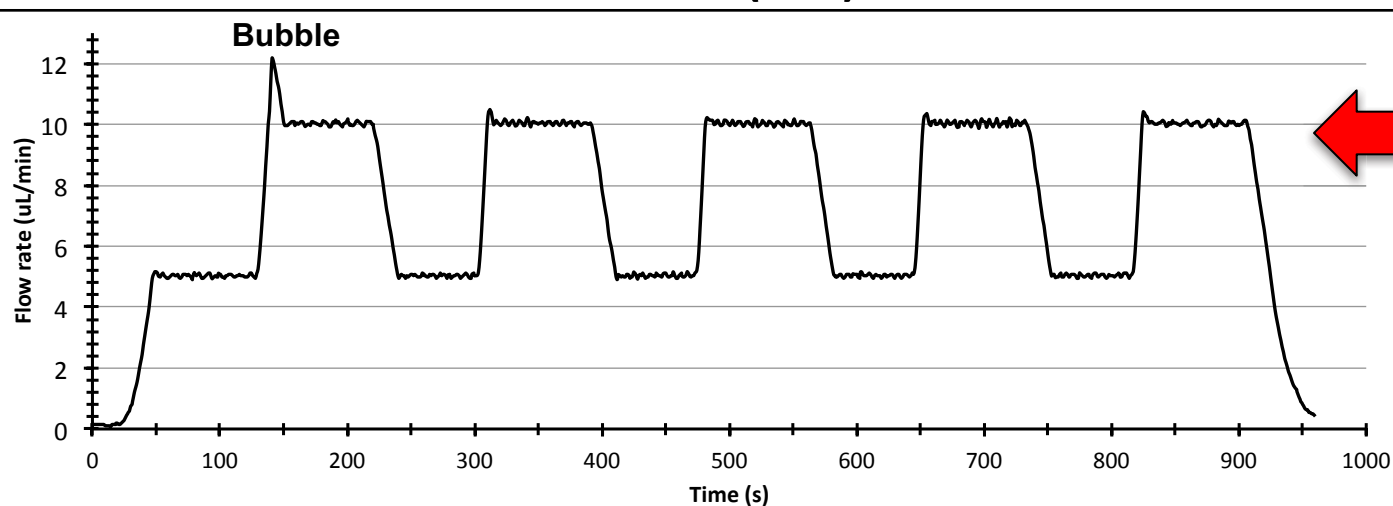
Some figures of merit



Switching 0.0-10.0 uL/min
n = 15 points sampled behind the initial small overshoot

Averages (n=10)

mean	10.0028
Mean SD	0.0323
Error Mean	0.0028
%RSD	0.3235
%RE mean	0.0279



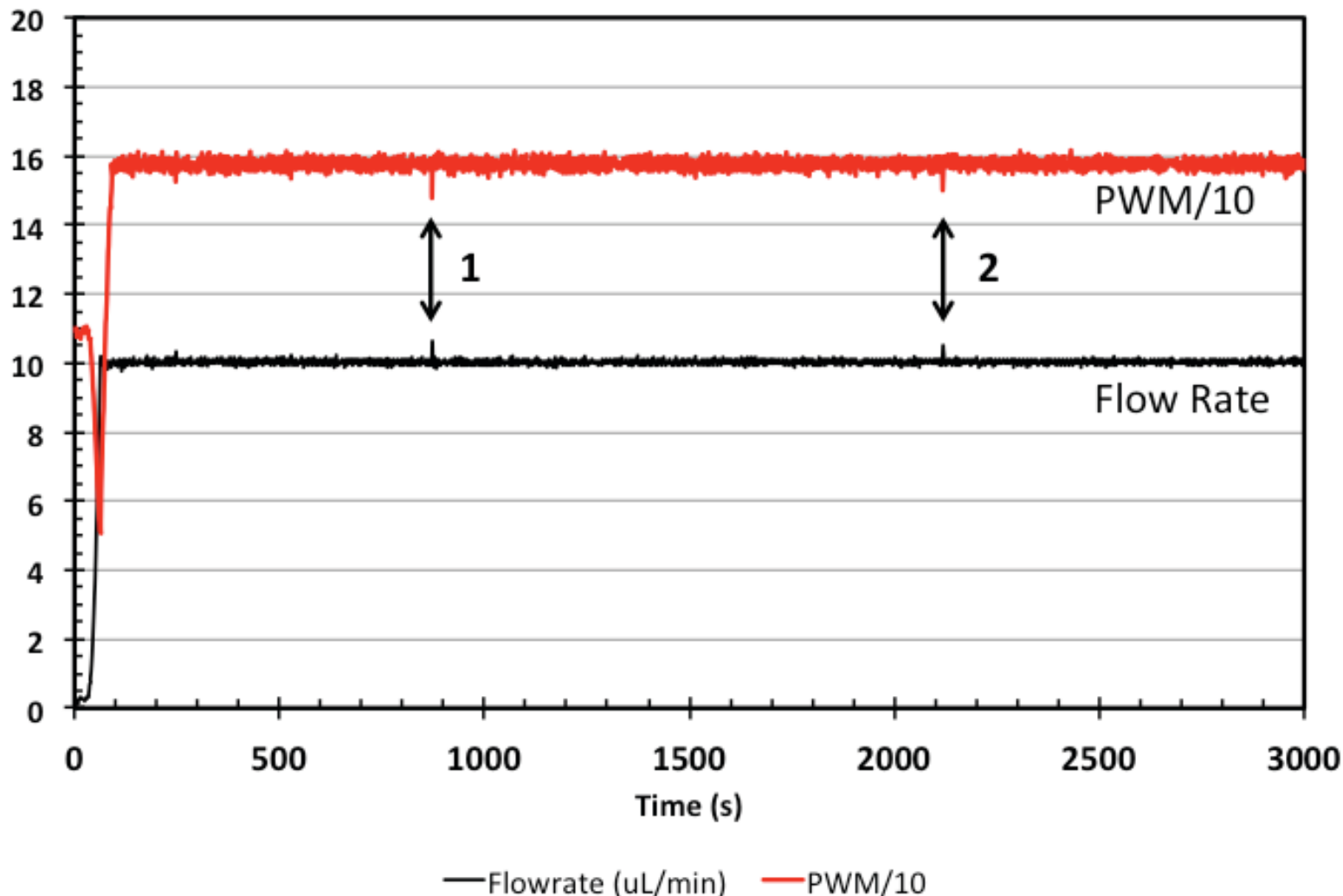
Switching 5.0-10.0 uL/min
n = 30 points sampled

Mean %RE (5=true)	0.780
Mean %RE (5.039=true)	0.098
Average of mean	5.039
SD Mean	0.006
%RSD	0.120
Mean %RE (10=true)	0.372
Mean %RE (10.037=true)	0.102
Average of mean	10.037
SD Mean	0.012
%RSD	0.124





Power Supply to LED

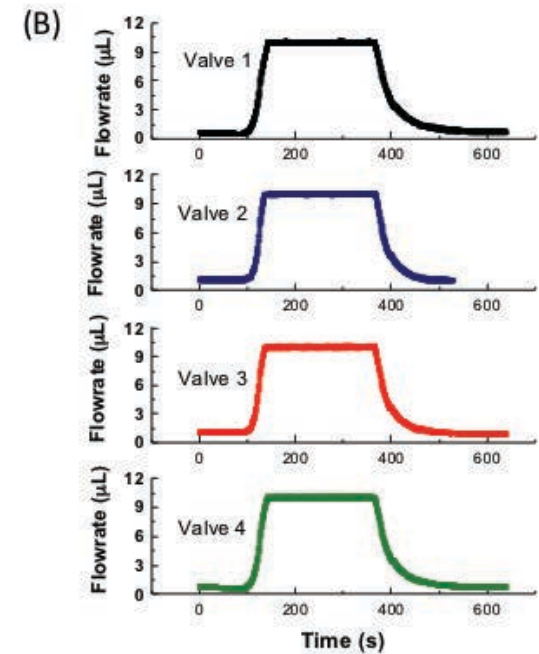
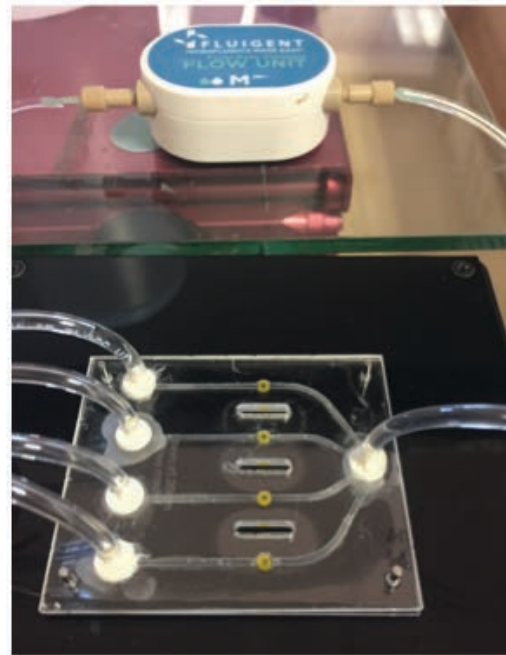
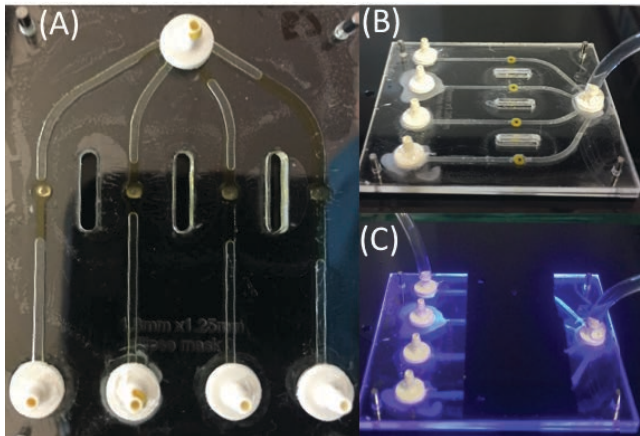
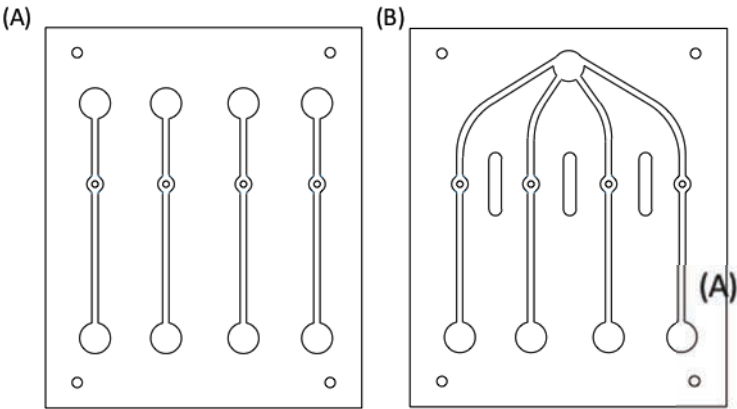
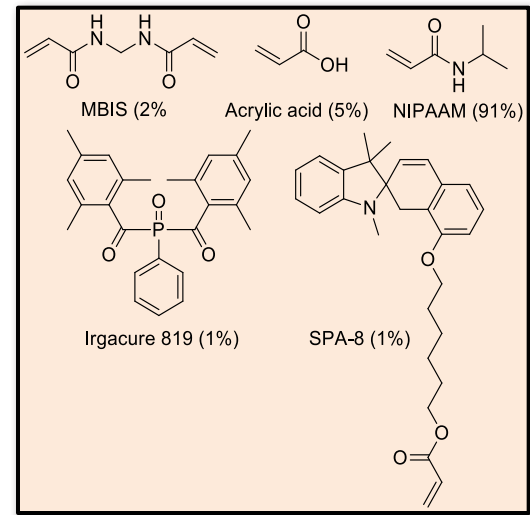


Over a period of 50 min constant maintenance of 10 $\mu\text{L}/\text{min}$ flow rate there is no discernable change in LED power \rightarrow diagnostic information





Multiplexing: Valve Arrays





Photocontrol of Assembly and Subsequent Switching of Surface Features



ACS APPLIED MATERIALS & INTERFACES

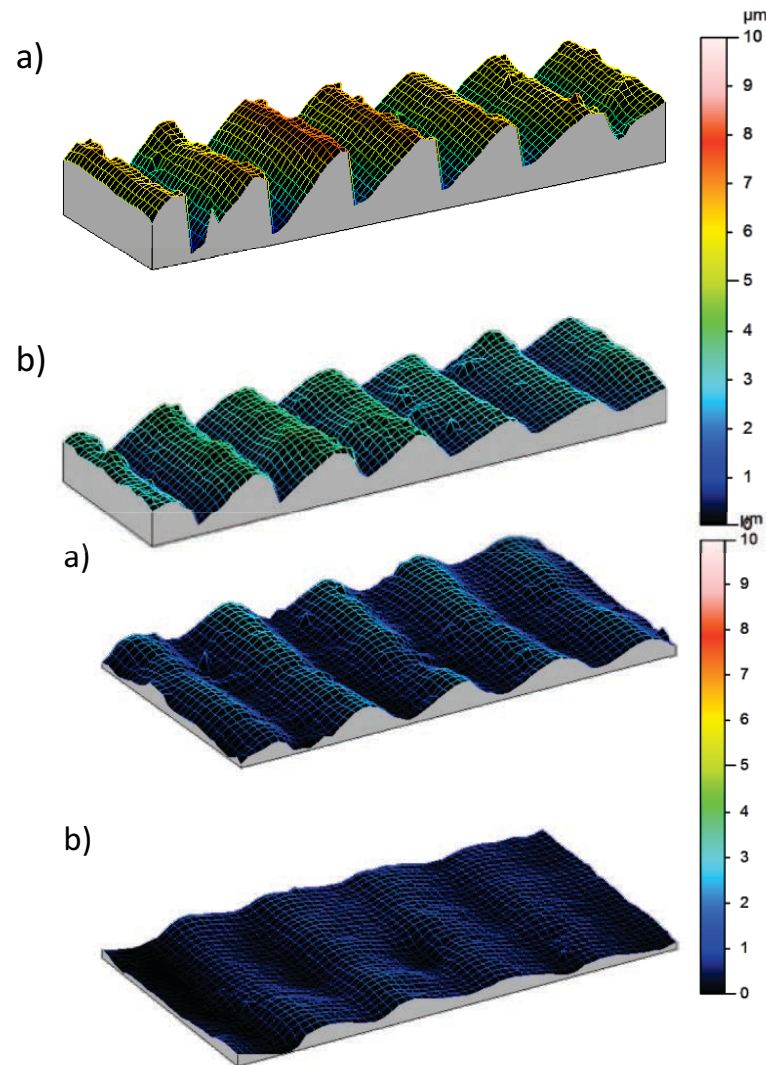
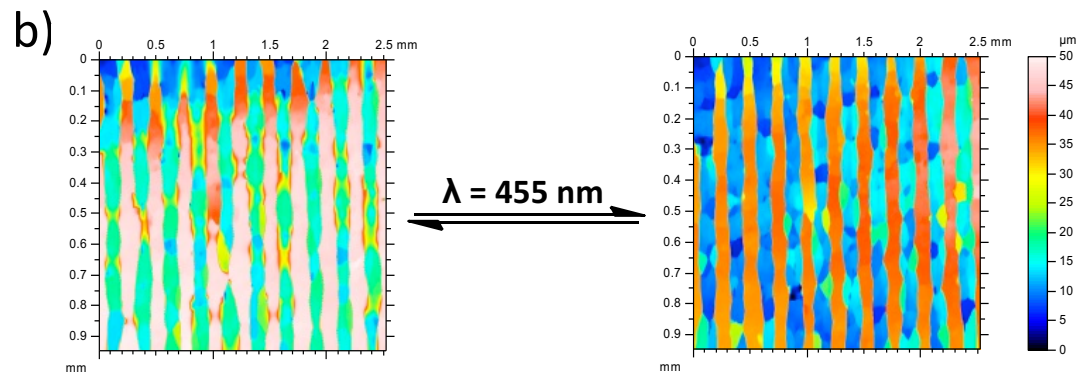
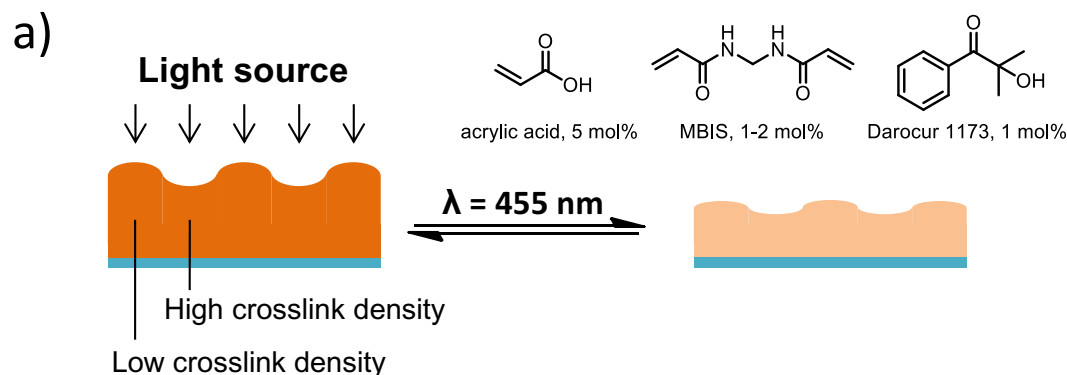
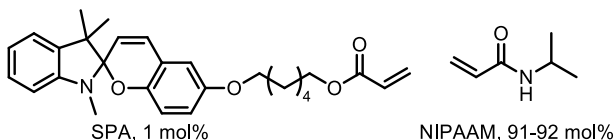
Research Article

www.acsami.org

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

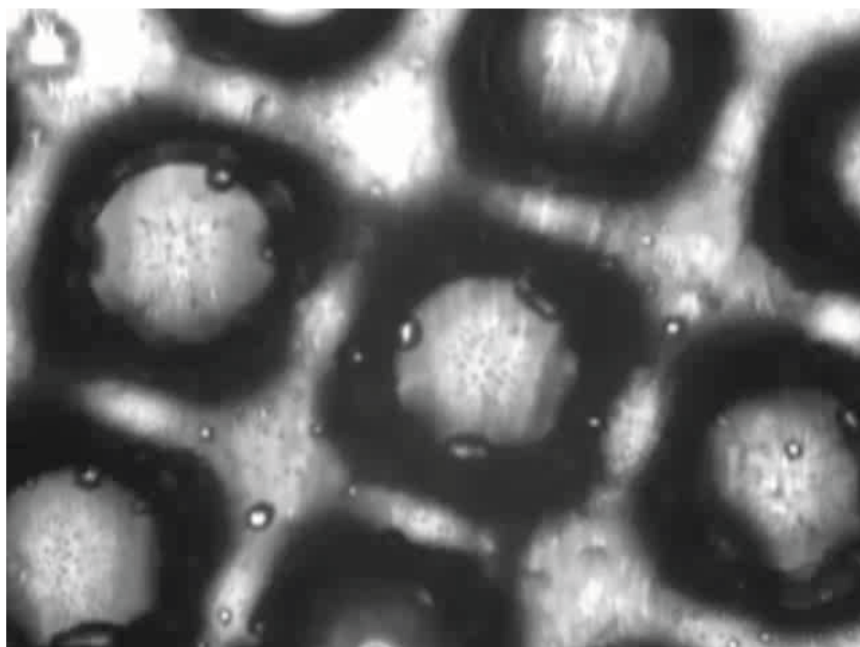
Photoswitchable Ratchet Surface Topographies Based on Self-Protonating Spiropyran–NIPAAm Hydrogels

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

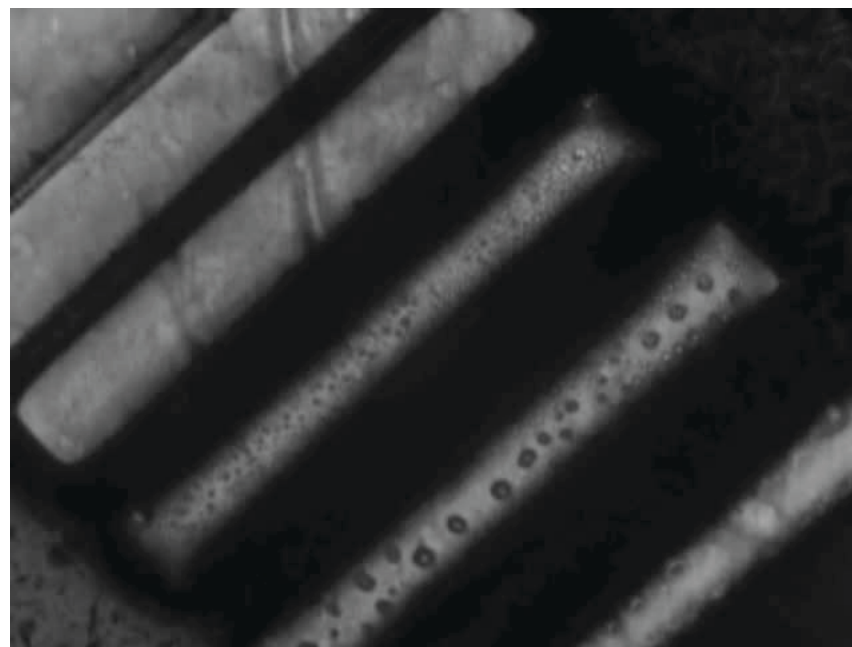




Flexible creation of μ -dimensioned features in flow channels using in-situ photo-polymerisation



Ntf2 pillars speed x3

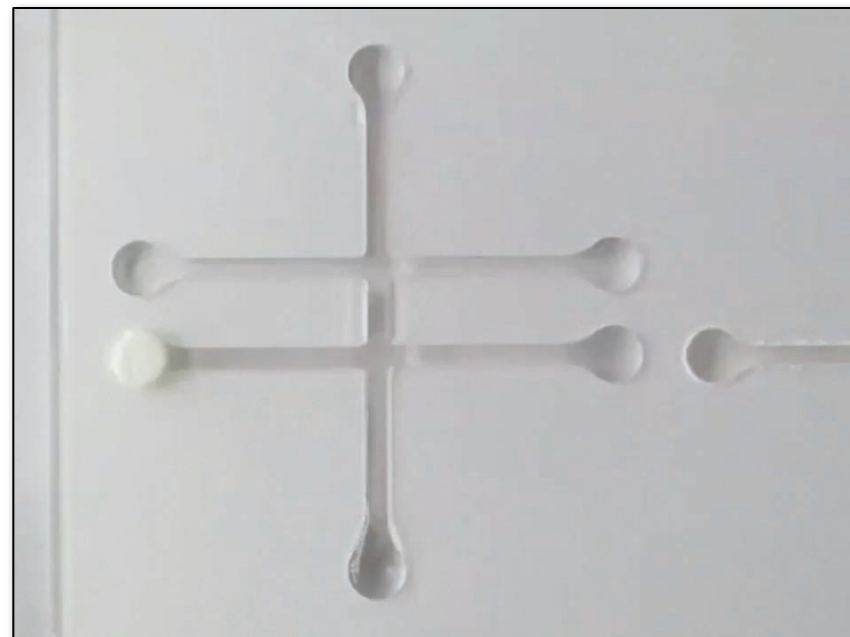
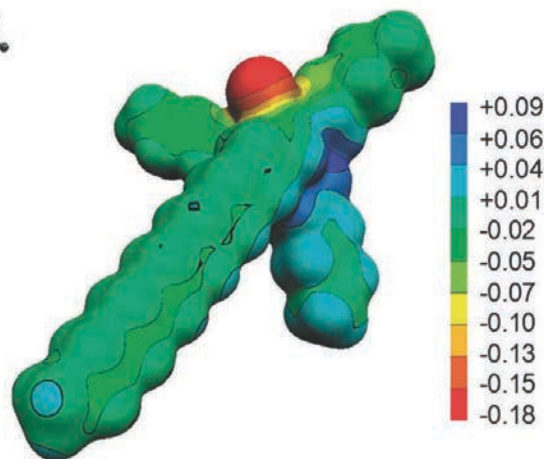
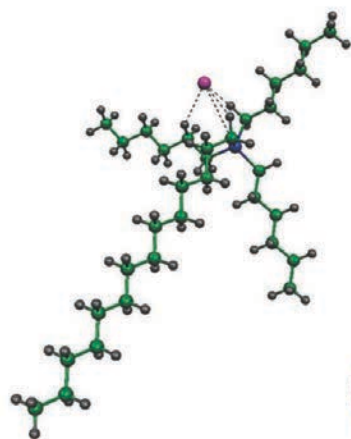


DCA lines speed x4

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



Chemotactic IL Droplets



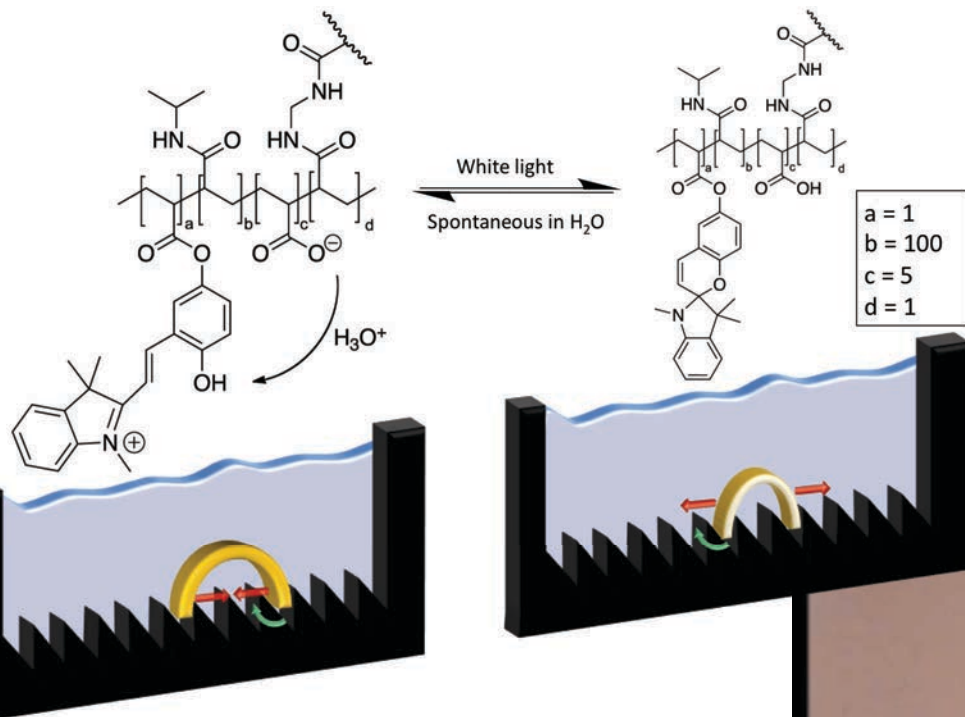
Trihexyl(tetradecyl)phosphonium chloride ($[\text{P}_{6,6,6,14}][\text{Cl}]$) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the Cl^- ion which is created using a polyacrylamide gel pad soaked in 10^{-2} M HCl;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



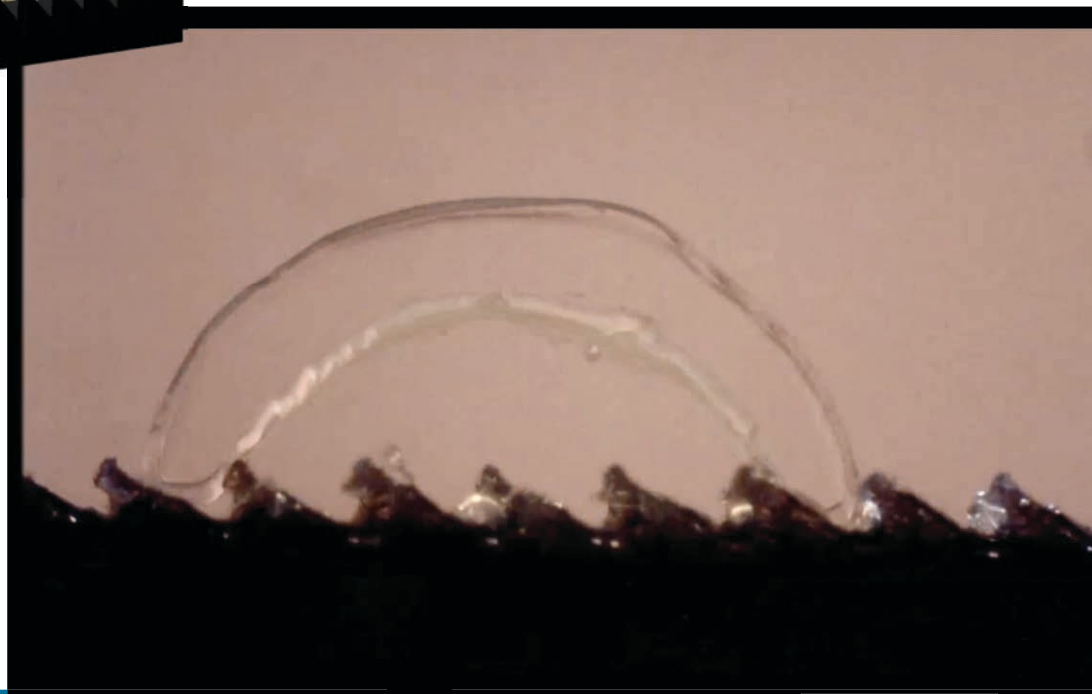


Photo-Responsive Soft Hydrogels



‘Walking towards the light’

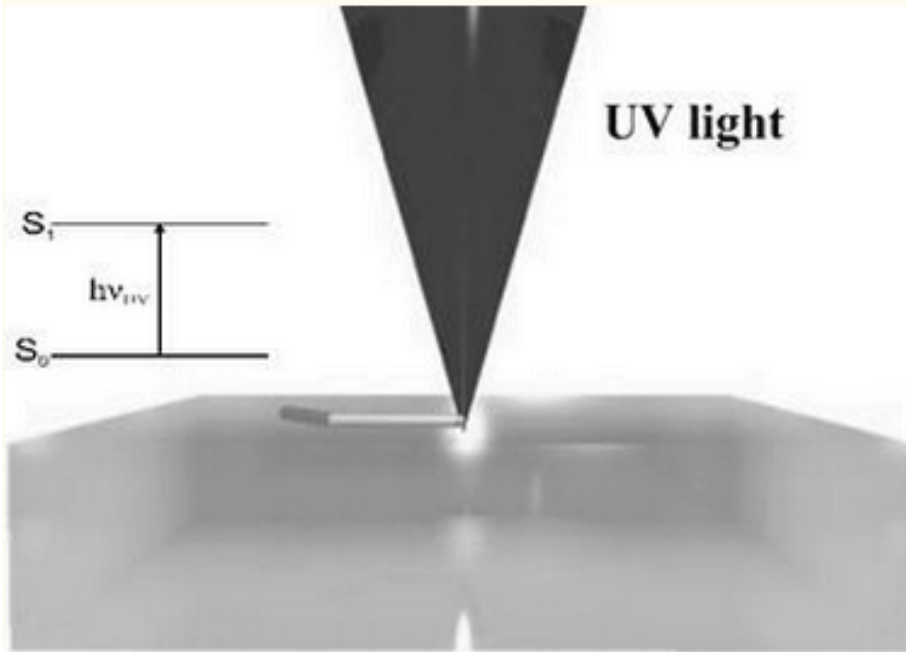
W. Francis et al. / Sensors and Actuators B 250 (2017) 608–616





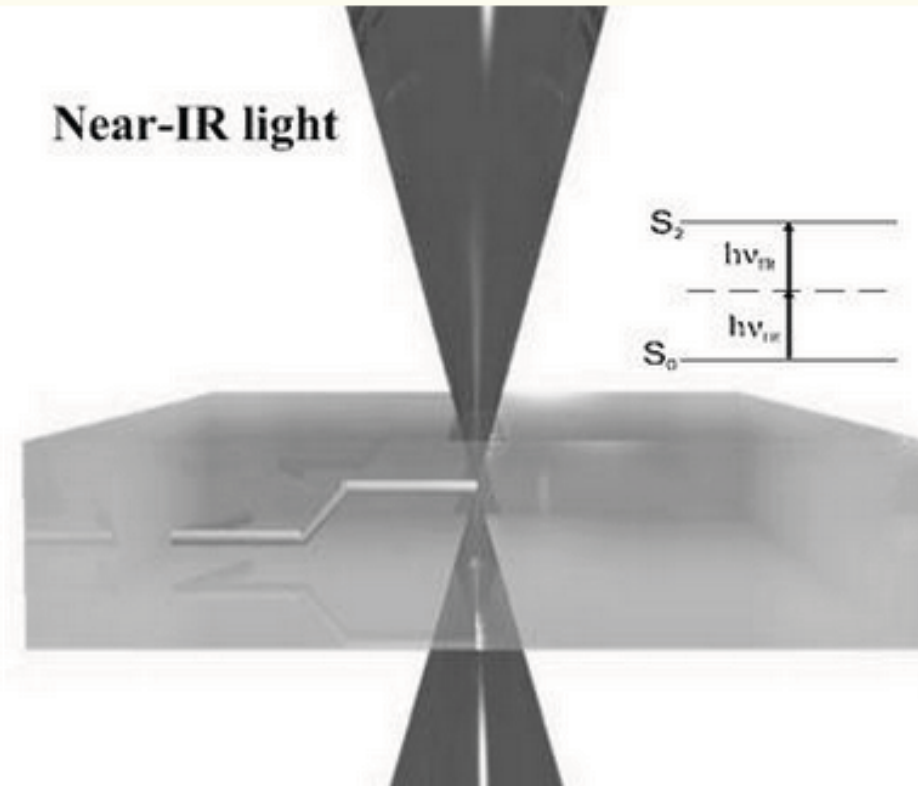
Background

Stereolithography



- Single photon absorption
- 2D patterns

Two-photon polymerisation

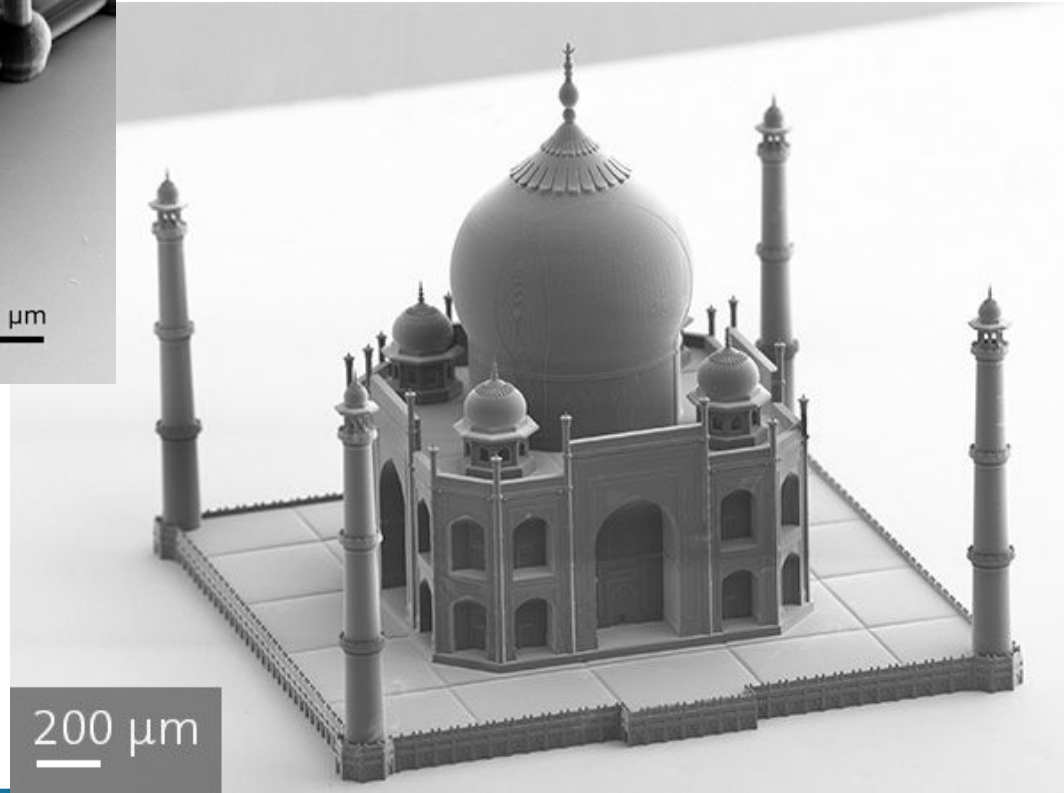
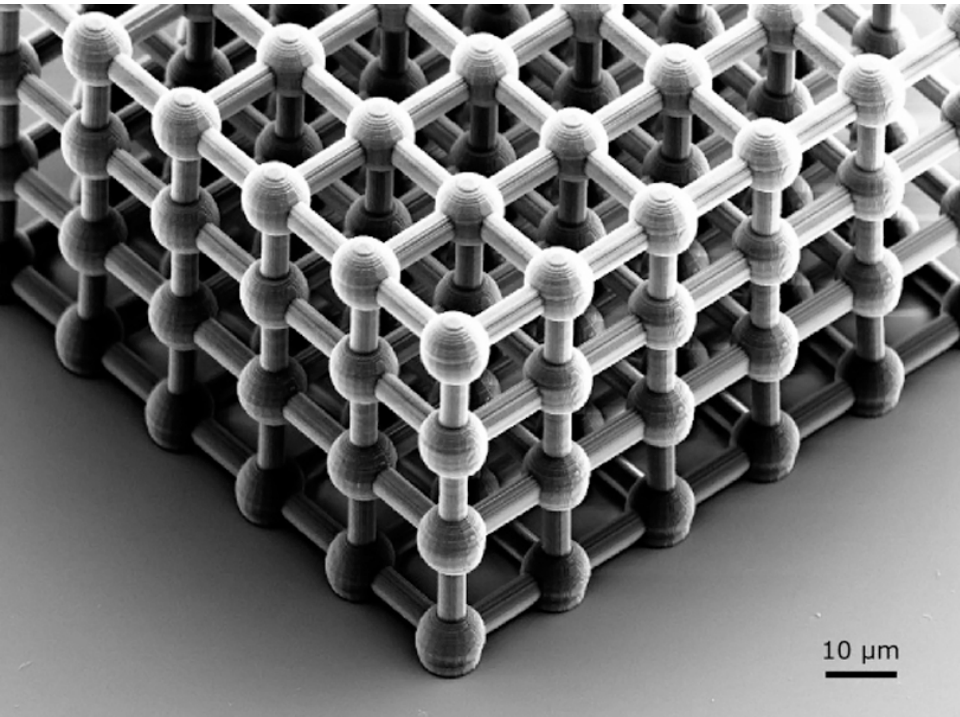


- Two photon absorption
- 3D structures





Background



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





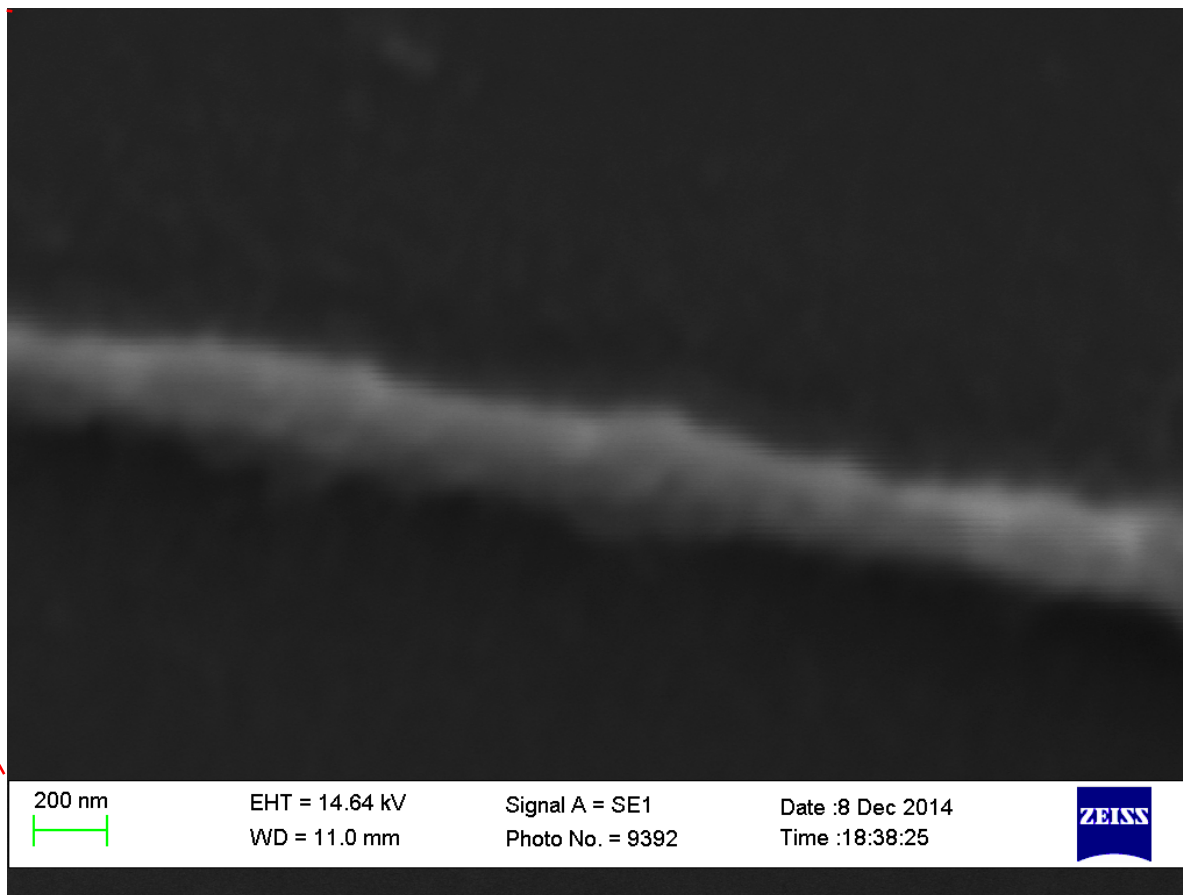
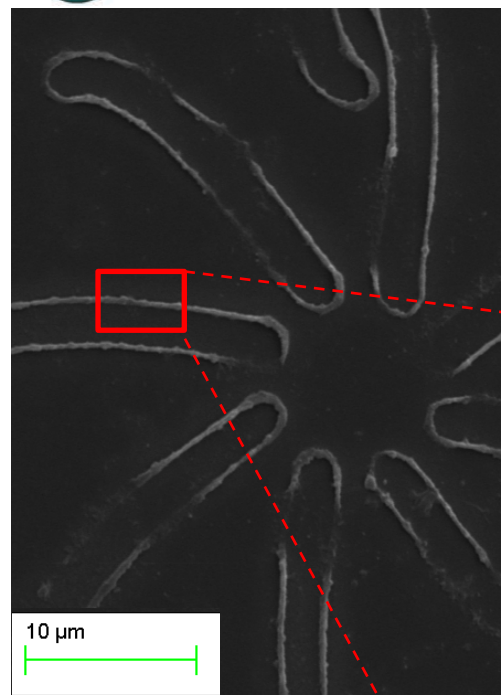
The Exciting Potential of Stimuli-responsive Materials and Biomimetic Microfluidics

Larisa Florea¹, Vincenzo Curto², Alexander J. Thompson²,
Guang-Zhong Yang², and Dermot Diamond^{1*}

¹Insight Centre for Data Analytics, NCSR, Dublin City University

²The Hamlyn Centre for Robotic Surgery, Imperial College London, London, SW7 2AZ

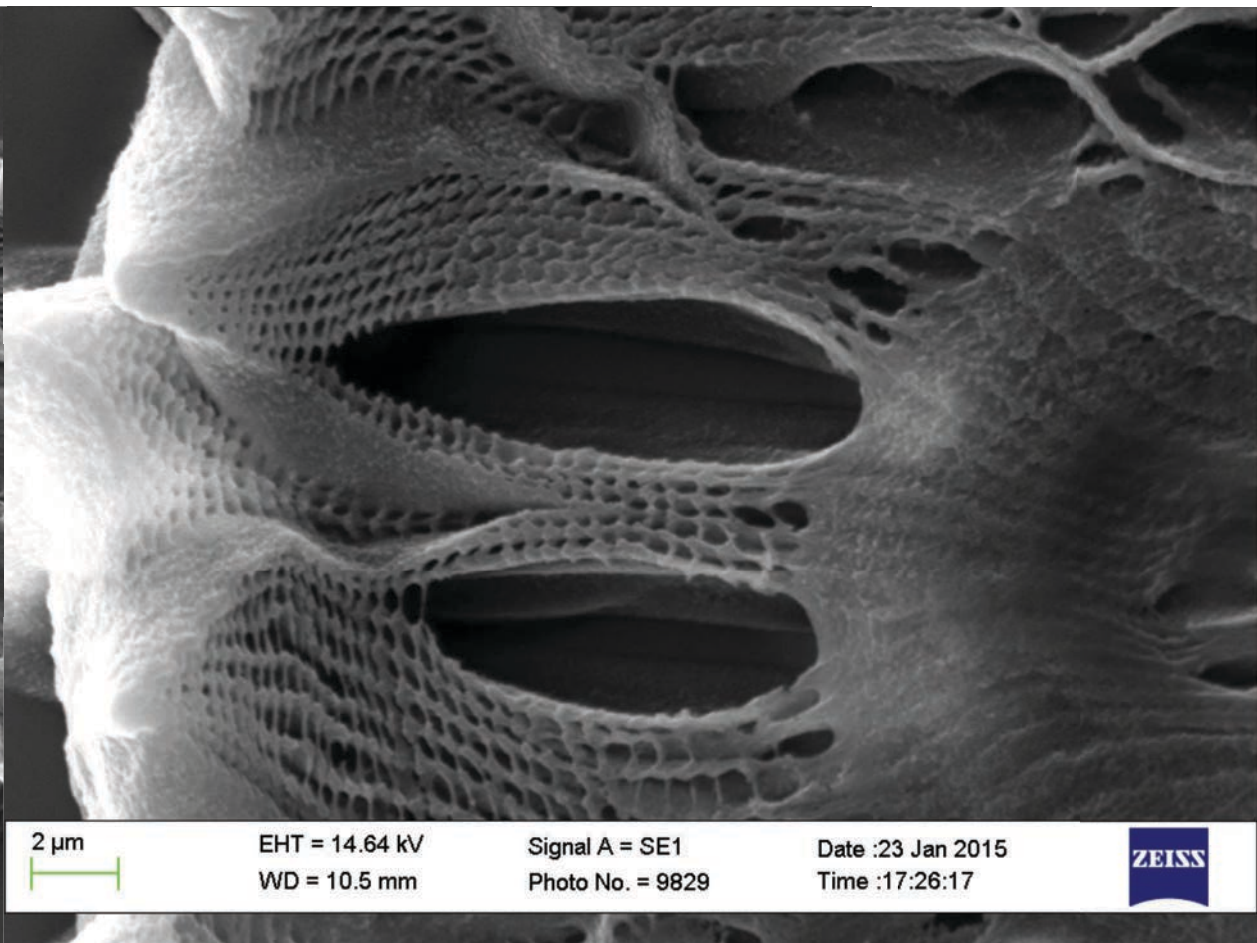
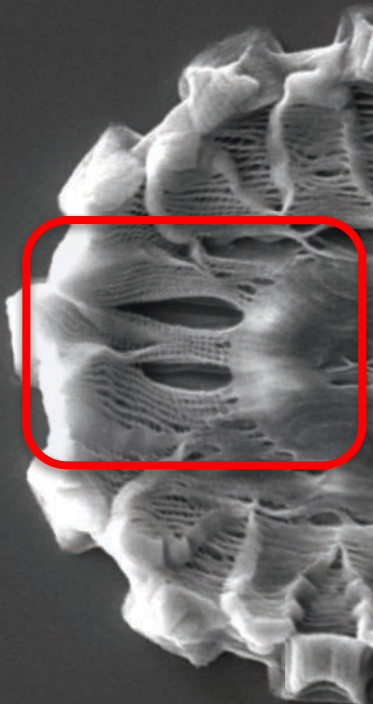
Euronanoforum, Riga, Latvia, June 2015



Creating 3D soft gel structures with a line resolution of ca. 170 nm



'Daisy' – Micro/Nano Scaled Porous Structure



2 μ m

EHT = 14.64 kV
WD = 10.5 mm

Signal A = SE1
Photo No. = 9829

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



20 μ m

EHT = 14.64 kV
WD = 10.5 mm

Signal A = SE1
Photo No. = 9826

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





Merging of Materials, Devices and Data

Data and Information; IOT

Outside: On-Body

Inside: Implants/In-vivo

Smart Bandages

Smart Stents

Self-Aware Transplant

Devices and Platforms

Sensorised Contact Lenses

Sensorised Splints/dentures

patches/watches

Smart Textiles/Clothing

Implants

Medium term Convalescence (weeks)

Post-Operative IC (days)

MATERIALS

Physics Chemistry Biology Engineering
(photonics, electronics, fluidics, 4D materials)



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