'SWEATCH' – A platform for Real-Time Monitoring of Sweat Electrolyte Composition

Tom Glennon[1], Conor O'Quigley[1], Margaret McCaul[1], Shirley Coyle[1], Giuseppina Matzeu[1], Simon Coleman[1], Aymen BenAzouz[1], Stephen Beirne[2], Gordon Wallace[2], Paddy White[3], Niamh O'Mahony[3] and Dermot Diamond[1]*

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Presented at

11th Annual International Electromaterials Science Symposium

Deakin University, Burwood Campus, Melbourne, Australia, 10–12 February **2016**

OR
Biomimetic microfluidic systems incorporating stimuli-responsive building blocks

Prof. Detonation Diamond

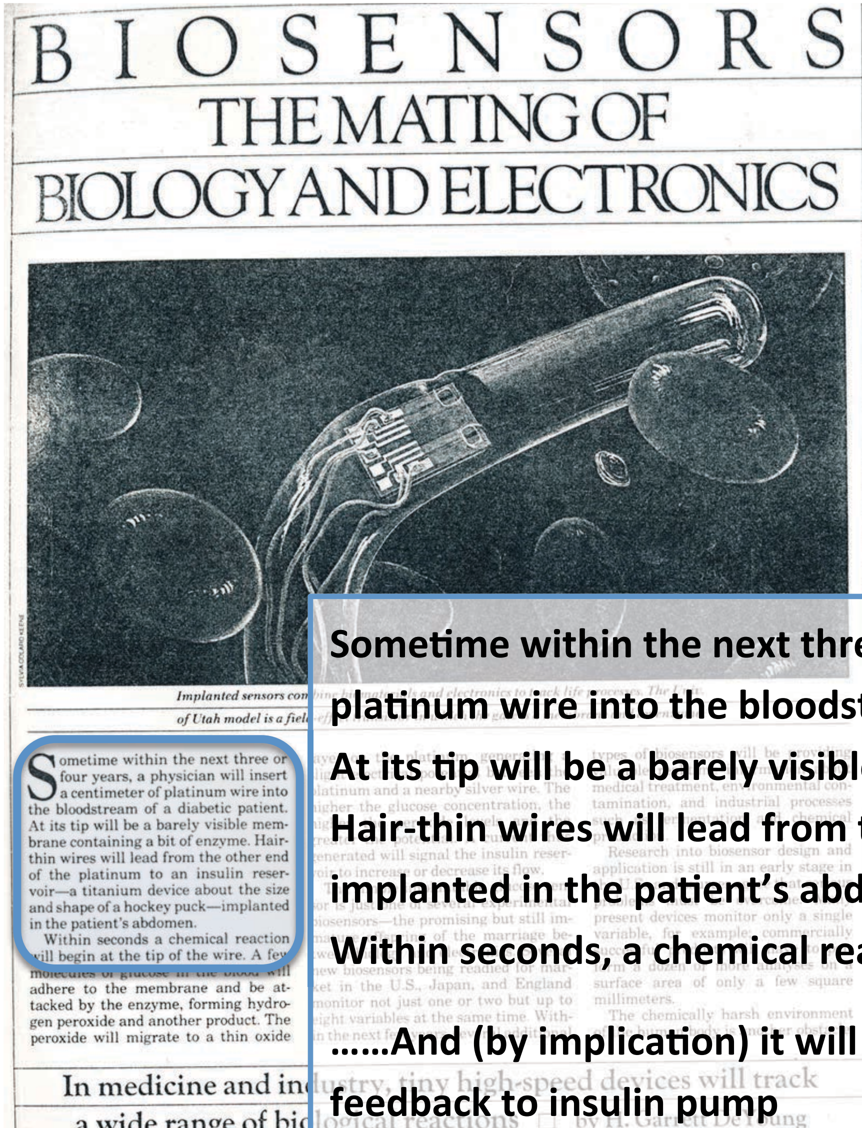
Simon Coleman, Aymen Ben Azouz, Wayne Quigley, Larisa Florea

Dublin City University, Ireland

Quang-Zhong Yang, Alex Thompson, Salzitsa Anastasova

Hamlyn Institute, Imperial College London

The (broken) promise of biosensors…..



BIOSENSORS
THE MATING OF
BIOLOGY AND ELECTRONICS

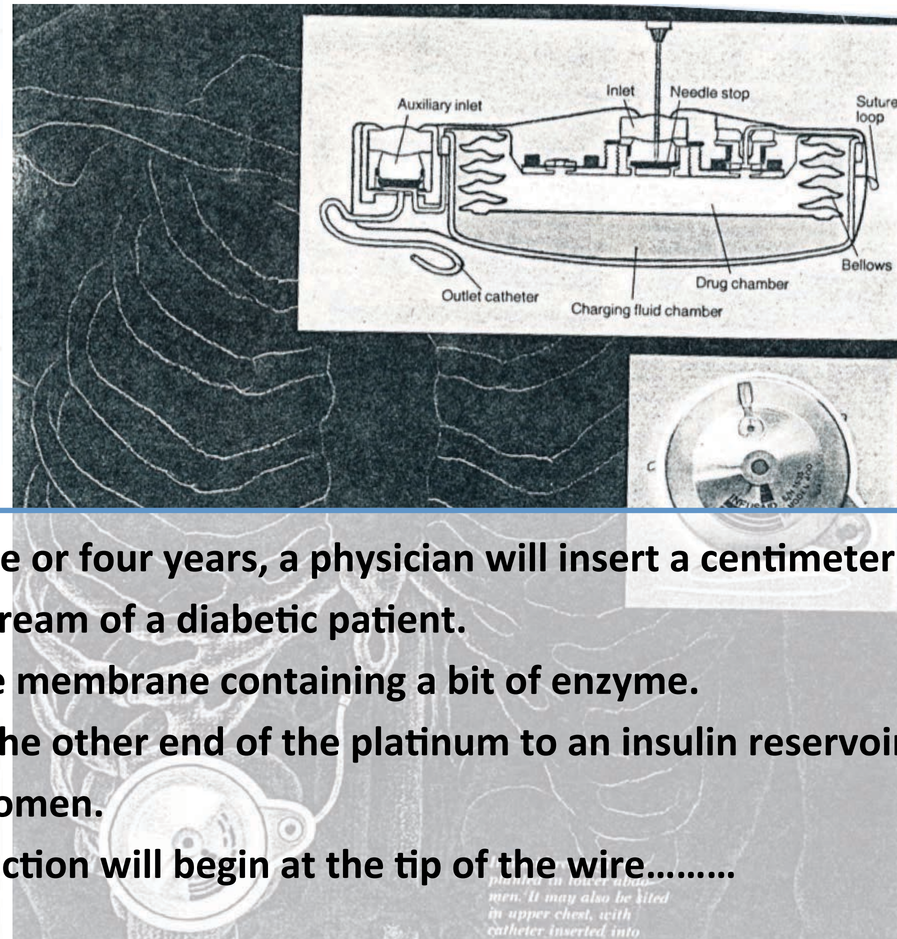
Implanted sensors com... of Utah model is a field...

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



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!

- ‘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…..?

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.

Google Contact Lens

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

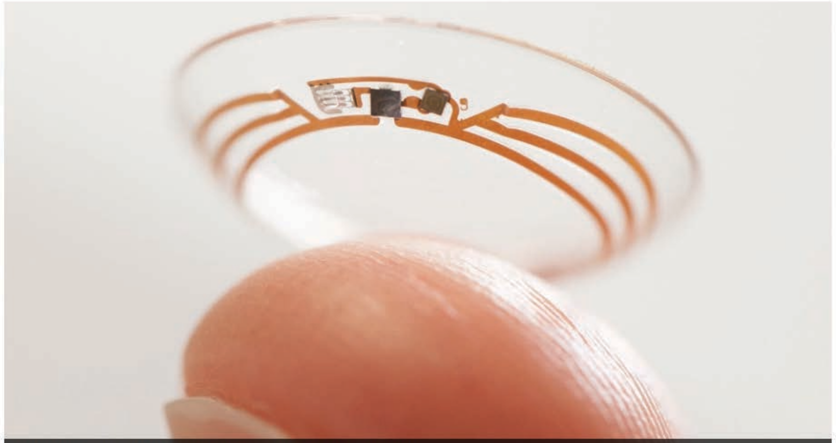
Microelectrodes In An Ophthalmic Electrochemical Sensor

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.**

Google Smart Contact Lenses Move Closer to Reality

8.6k SHARES Share on Facebook Share on Twitter + WHAT'S THIS?



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

IMAGE: GOOGLE

BY LANCE ULANOFF

1 DAY AGO

Google's plan to bring smart contact lenses to diabetes sufferers inched closer to reality as 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.

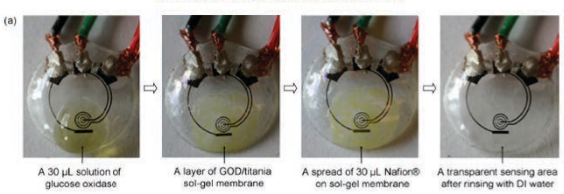
SEE ALSO: 7 Incognito Wearables You'd Never Guess Were Gadgets

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

H. Yao et al. / Biosensors and Bioelectronics 26 (2011) 3290–3296 3293



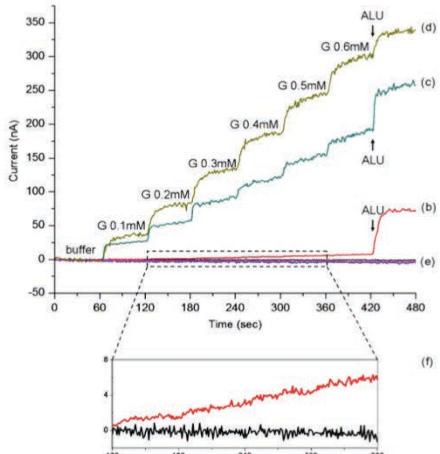


Fig. 2. Images of the sensor as it goes through surface functionalization and the related measured responses: (a) sequential images of sensor pre-treatment with GOD/titania/Nafion®; (b) measured amperometric response for the sensor just incubated with GOD; (c) measured amperometric response for the sensor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

ACS Nano Cover and Editorial

'Grand Plans for Nano', (9) 12 December 2015

EDITORIAL

Grand Plans for Nano

This year, nanoscience and nanotechnology have been called front and center to help address the grand challenges that the world faces. Our community has been asked to suggest future challenges, and the first such crowd-sourced grand challenge has been announced by the White House Office of Science and Technology Policy.[1−5] As we have said on these pages, we believe that nanoscientists and nanotechnologists around the world have special roles to play in bringing together expertise from diverse fields in order to tackle important tasks both large and small.[2] Indeed, our higher perspectives and communication across fields have great value globally in key areas such as devices, energy, health, and safety.[6−10]

As these Grand Challenge projects and other opportunities emerge, we will work with the leading and rising researchers in the relevant and potentially impacted communities to lay out the challenges and opportunities for nanoscience, nanotechnology, and other fields.[7−10] We see key roles for *ACS Nano* as a community forum to guide both nanoscience and nanoscience policy, to improve the impact of research by coordinating how it is reported,[11,12] and to showcase innovative work from around the world.

We are looking forward to an exciting year in 2016, which will mark *ACS Nano*'s tenth volume. It has already been quite an adventure, and much more is to come. We note that you will see some changes in our "look" next year. We will keep our forward-looking posture, our in-depth science and engineering, and the identifying markings that let you know right away when you are reading an article in *ACS Nano*. We have made subtle design changes that will enable us to speed up production in order to accelerate our already fast turn-around times of your work. We want to thank our production team and staff for this collaboration and all of the iterations that went into this optimization effort.

Finally, we want to thank you, our readers, authors, and referees for moving *ACS Nano* and our field to ever higher impact on our world. We wish you a safe and peaceful holiday season and look forward to hearing from you and working with you in the year and years ahead.

Disclosure: Views expressed in this editorial are those of the authors and not necessarily the views of the ACS.

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10.1021/acsnano.5b07280

Materials – great! Sensing - ????

- FET configuration (same as 1984 paper)
- Amine and hydroxy terminated surface groups respond to pH
- Attachment of GOX enables glucose sensing via pH changes due to formation of gluconic acid
- Poor kinetics
- pH response not stable
- Glucose sensor responds to pH – selectivity issue
- No integrated reference or counter electrodes

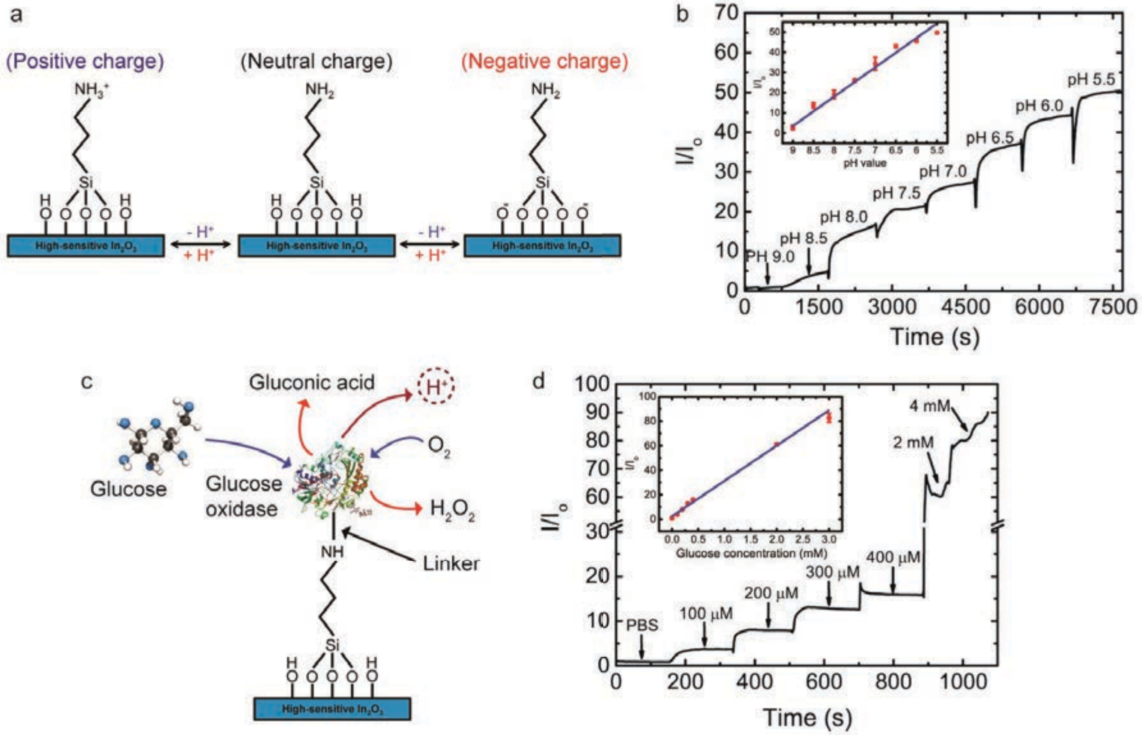
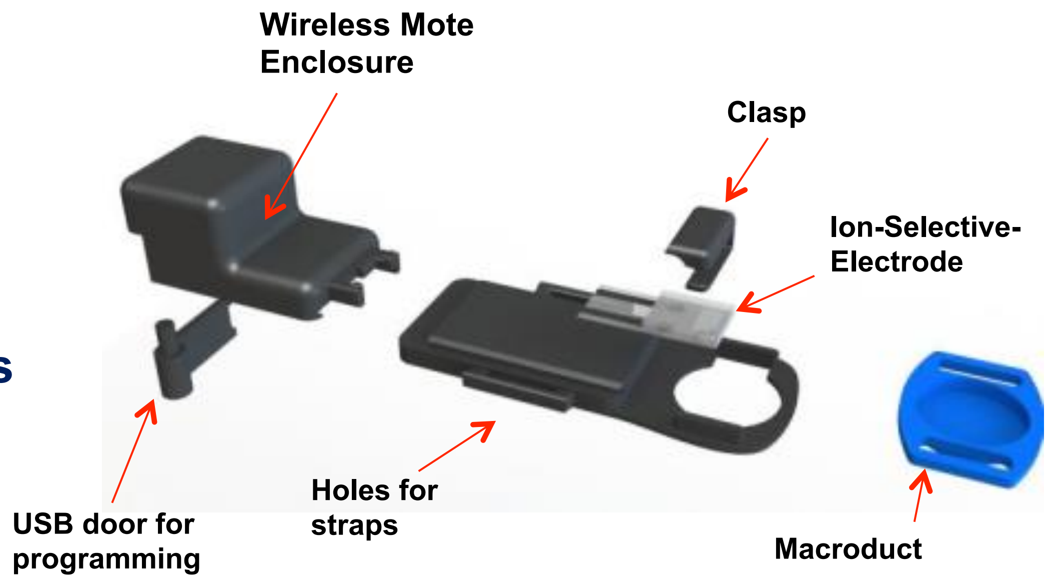


Figure 4. Chemical sensing *via* In_2O_3 FET-based conformal biosensors. (a) The pH-sensing mechanism occurs by protonation of In_2O_3 surface hydroxyl groups and primary amines of APTES at decreasing pH (increasing proton concentrations). (b) Representative responses of an In_2O_3-based FET biosensor to a biologically important pH range (pH 5.5−9). Inset shows data from five devices. (c) Enzymatic oxidation of D-glucose *via* glucose oxidase to produce gluconic acid and hydrogen peroxide. Protons are generated during this oxidation and protonation of the In_2O_3 surfaces is manifested. (d) Representative responses of In_2O_3 sensors to physiologically relevant D-glucose concentrations found in human diabetic tears (lower range) and blood (upper range). Inset shows data from five devices. Error bars represent standard deviations of the means.

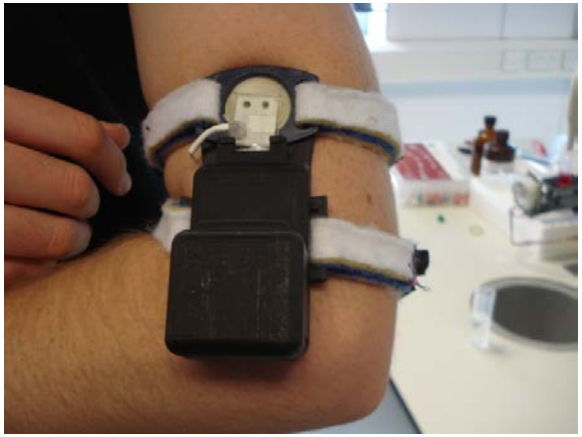
Na^+ Monitoring in Sweat

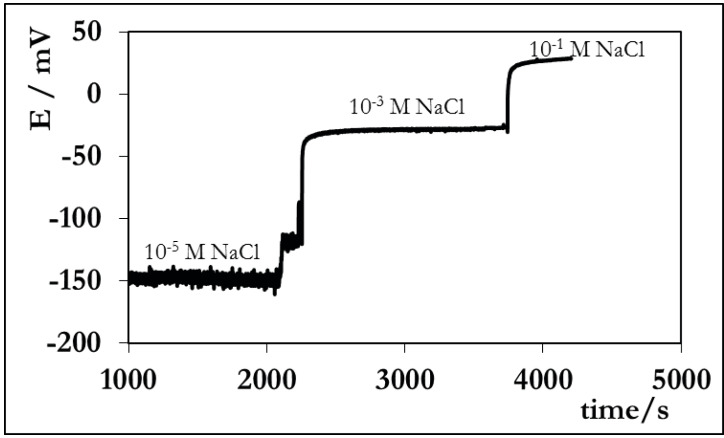
Real time monitoring of Sodium in Sweat through screen printed potentiometric strips:

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



Macroduct sweat sampling unit (Wescor Corporation) Speed x4

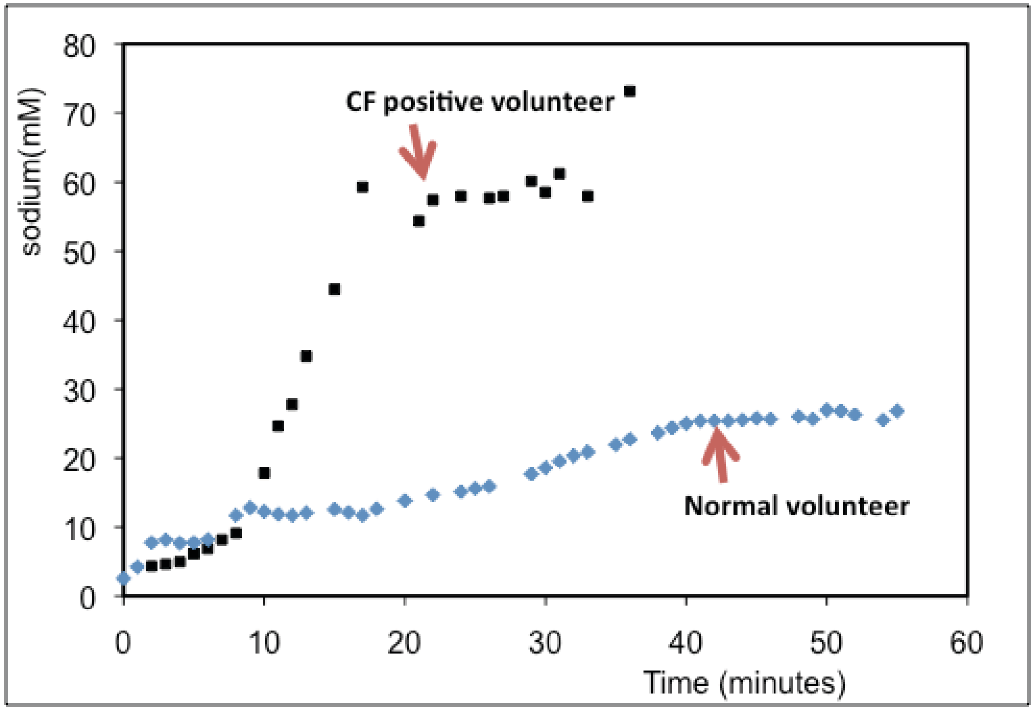




Pilocarpine based sweat sampling | **Exercise based sweat sampling** | **Sensor calibration**

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.

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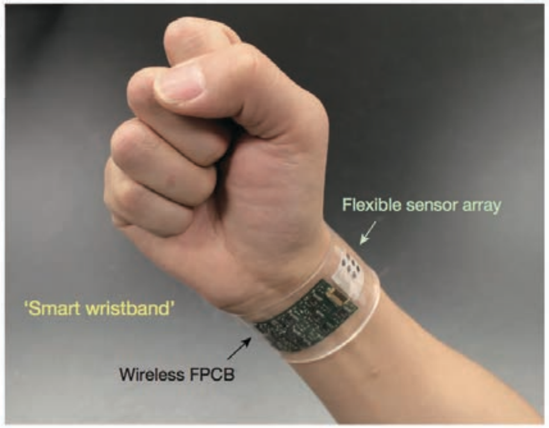


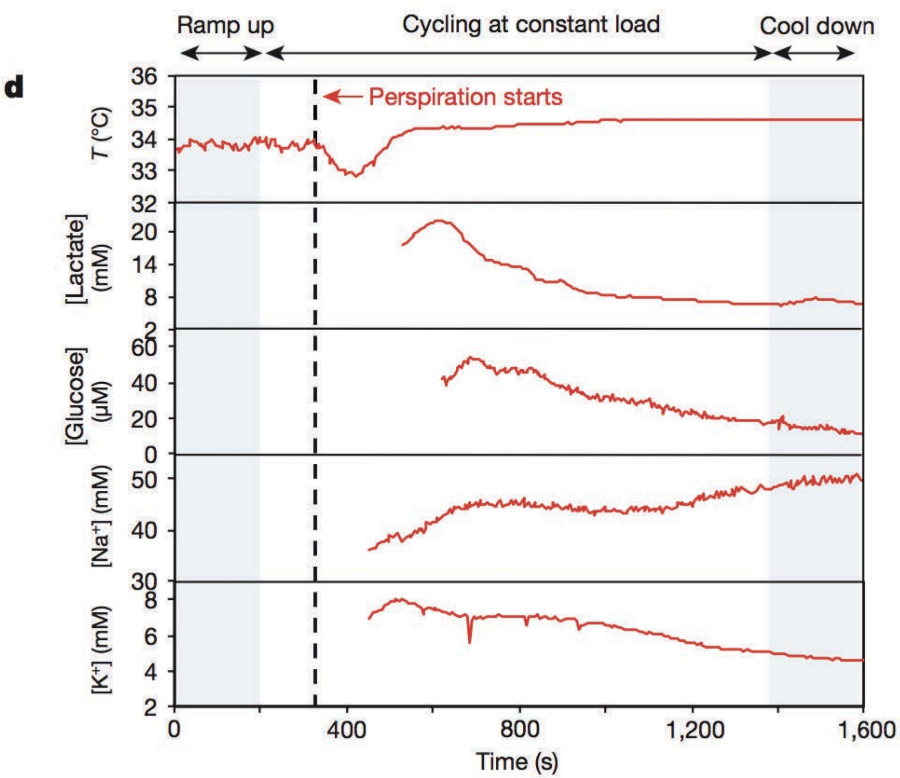
LETTER

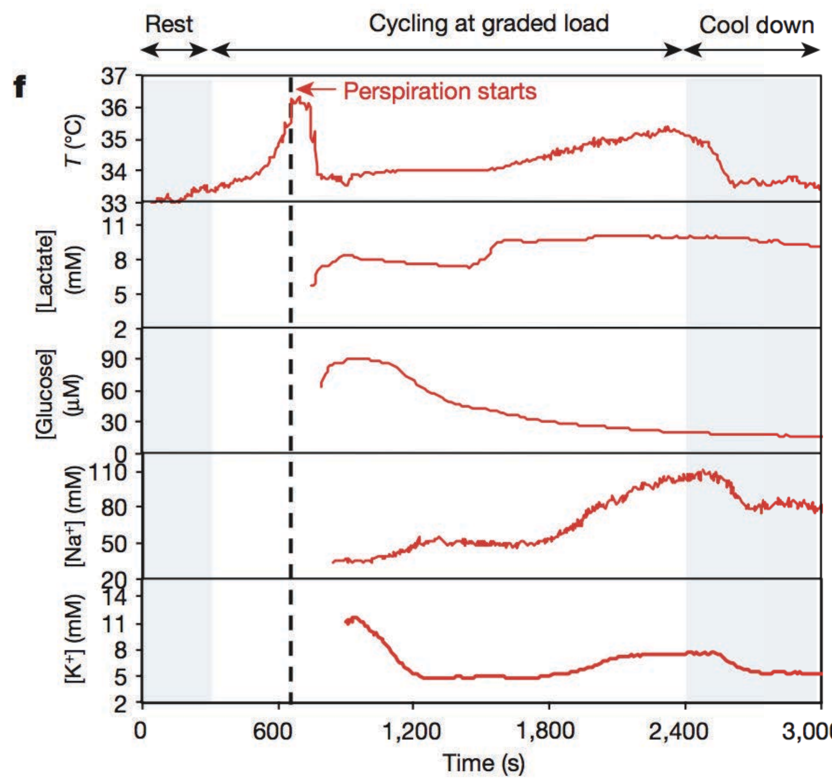
doi:10.1038/na

Fully integrated wearable sensor arrays for multiplexed *in situ* perspiration analysis

Wei Gao[1,2,3]*, Sam Emaminejad[1,2,3,4]*, Hnin Yin Yin Nyein[1,2,3], Samyuktha Challa[4], Kevin Chen[1,2,3], Austin Peck[5], Hossain M. Fahad[1,2,3], Hiroki Ota[1,2,3], Hiroshi Shiraki[1,2,3], Daisuke Kiriya[1,2,3], Der-Hsien Lien[1,2,3], George A. Brooks[5], Ronald W. Davis[4] & Ali Javey[1,2,3]

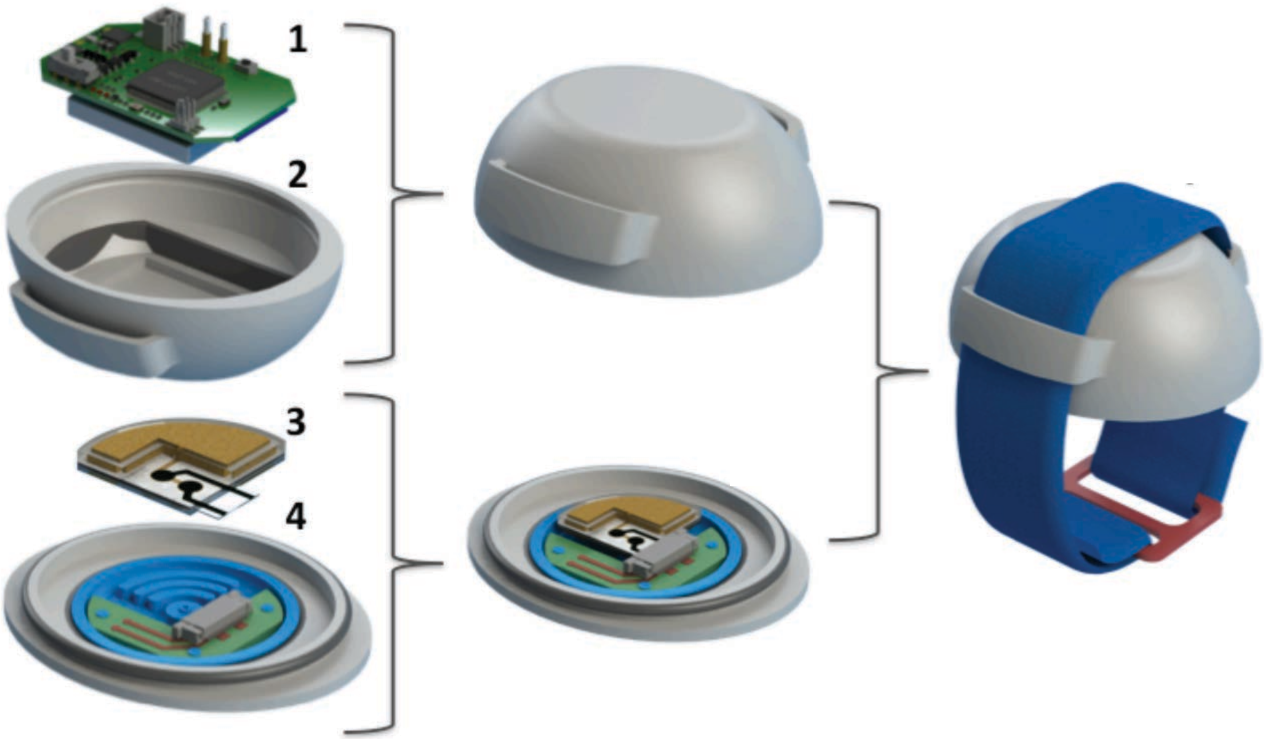
Gao, W. *et al*. *Nature* [http://dx.doi.org/10.1038/nature16521 (2016).](http://dx.doi.org/10.1038/nature16521)





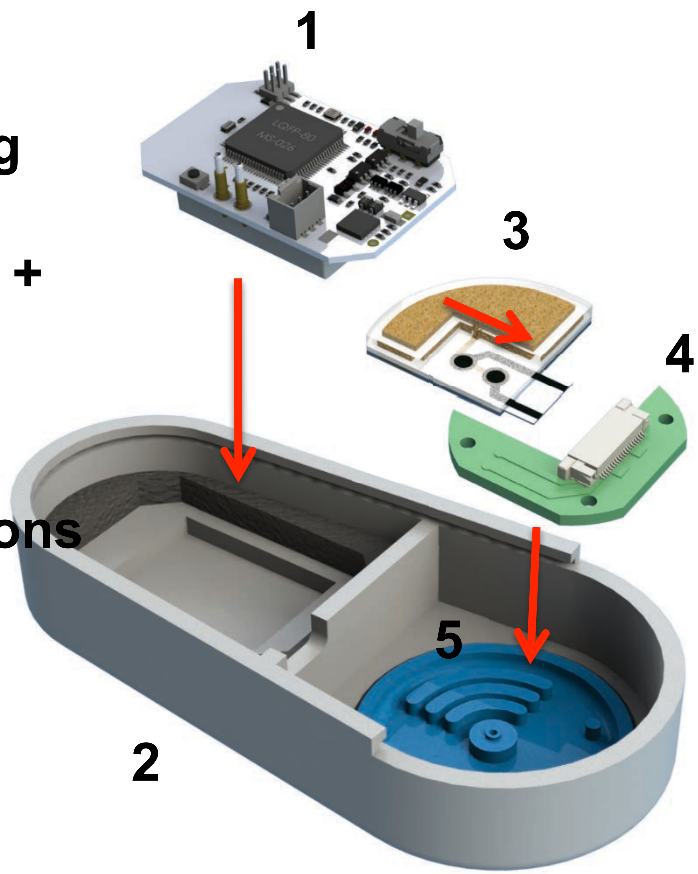
Sweatch Device (1)

1. Electronics
2. 3D printed casing
3. Microfluidic chip + ISE
4. 3D printed sweat harvester and sensor connections

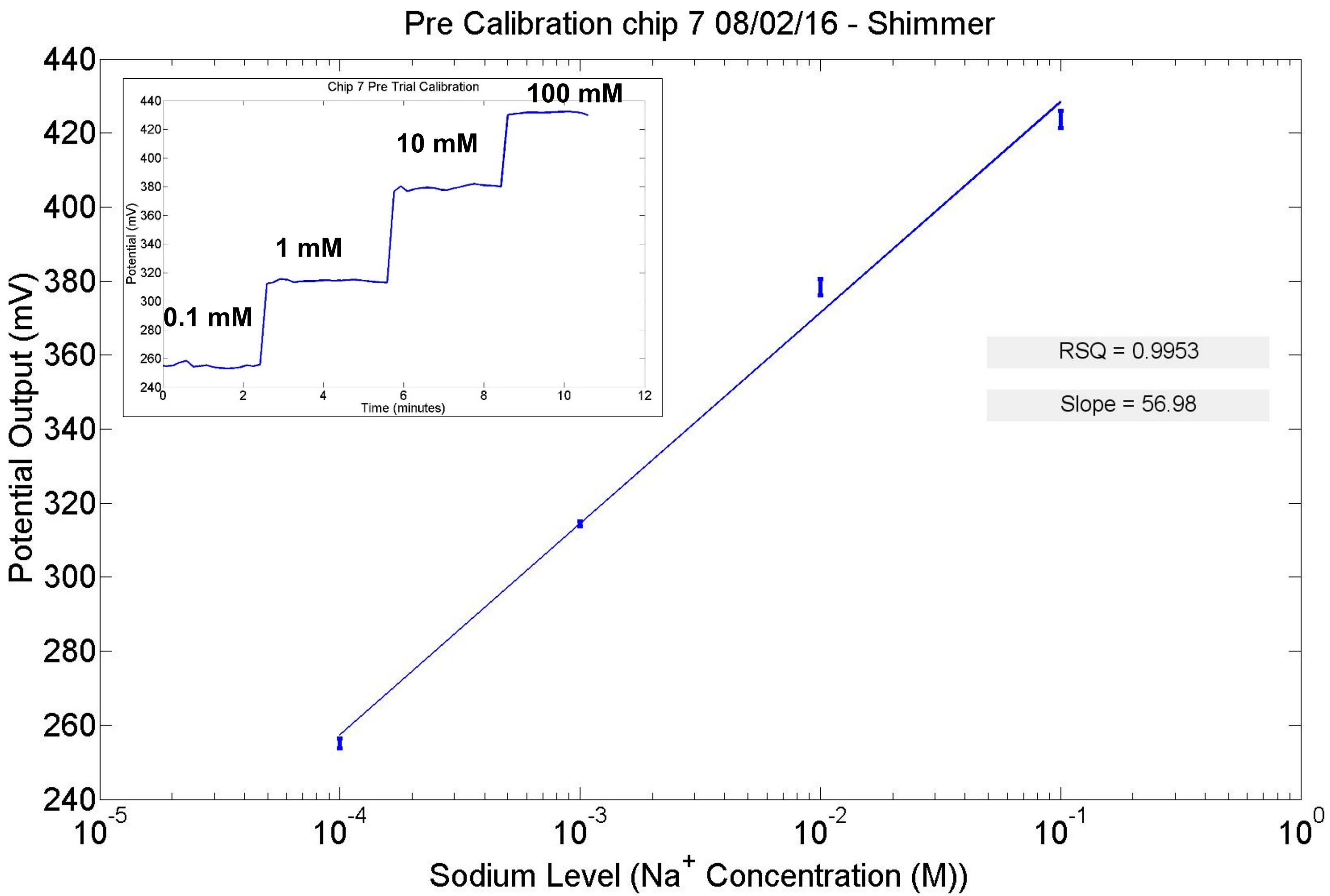


Sweatch Device (2)

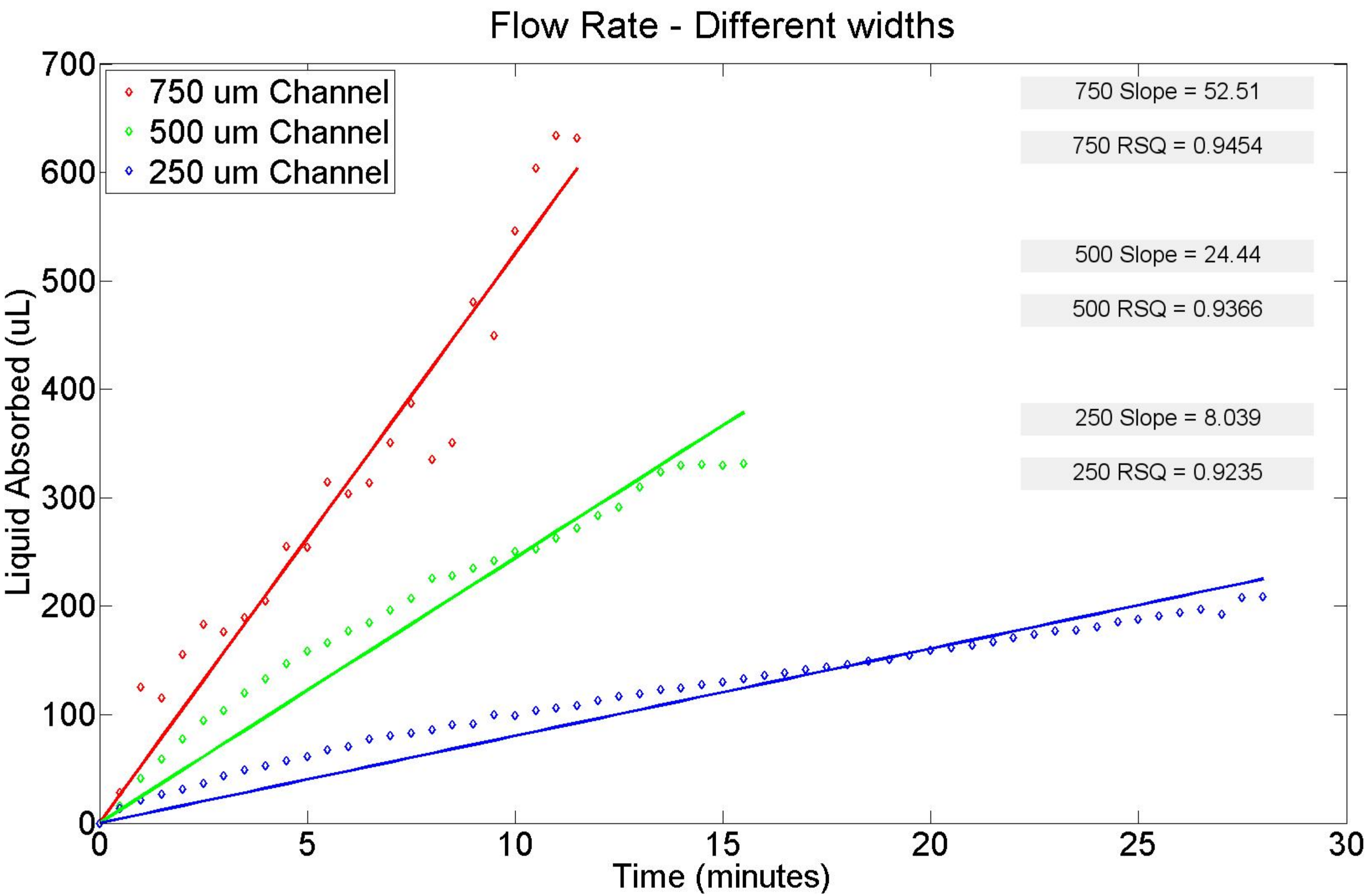
1. Electronics
2. 3D printed casing
3. Microfluidic chip + ISE
4. Sensor connections
5. 3D printed sweat harvester



Pre-Trial Calibrations

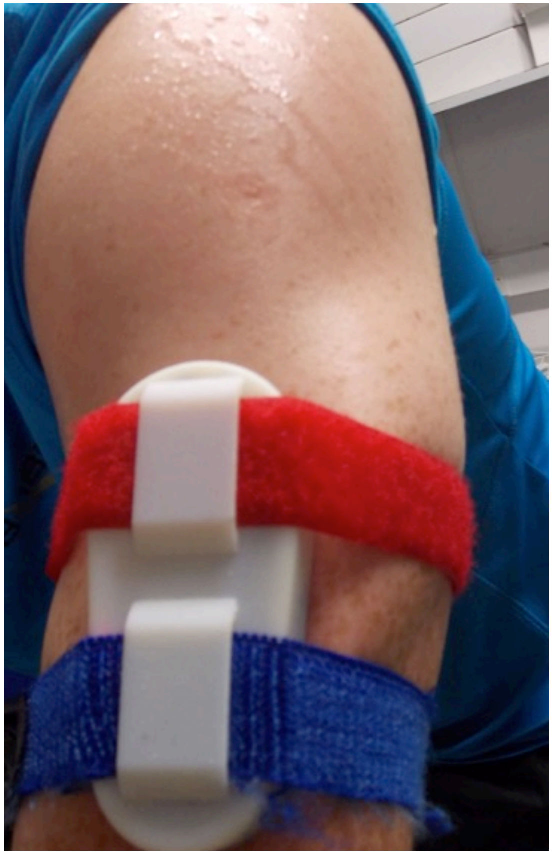


Fluidic Testing

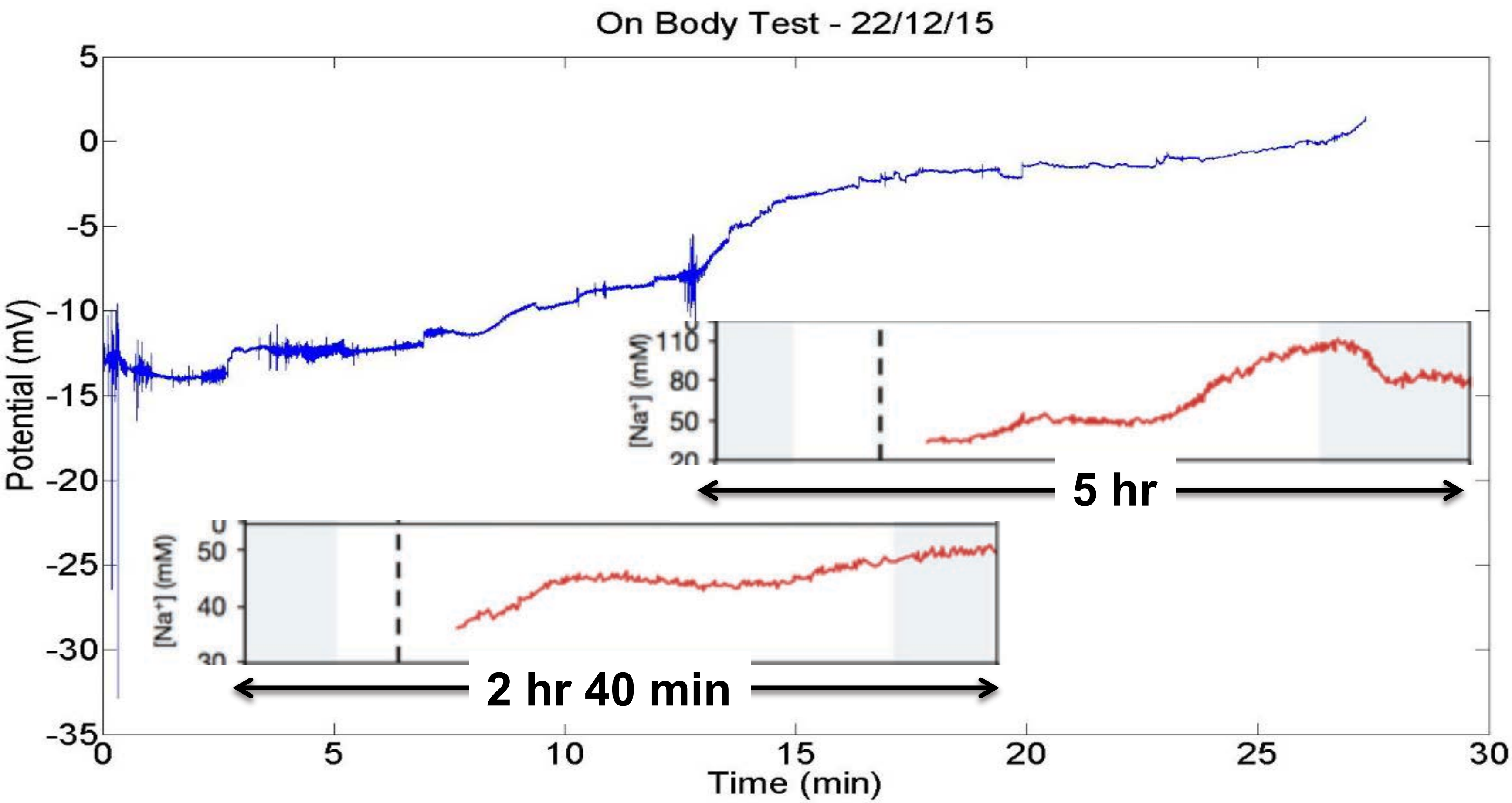


Trial 1 Sweat Sampling

- **Male volunteer cycled for 30 min on a stationary bicycle.**
- **143 ul sweat collected from arm by the POD platform during the session.**



Trial 1 Data



System might be OK for 24 hours, perhaps couple of days

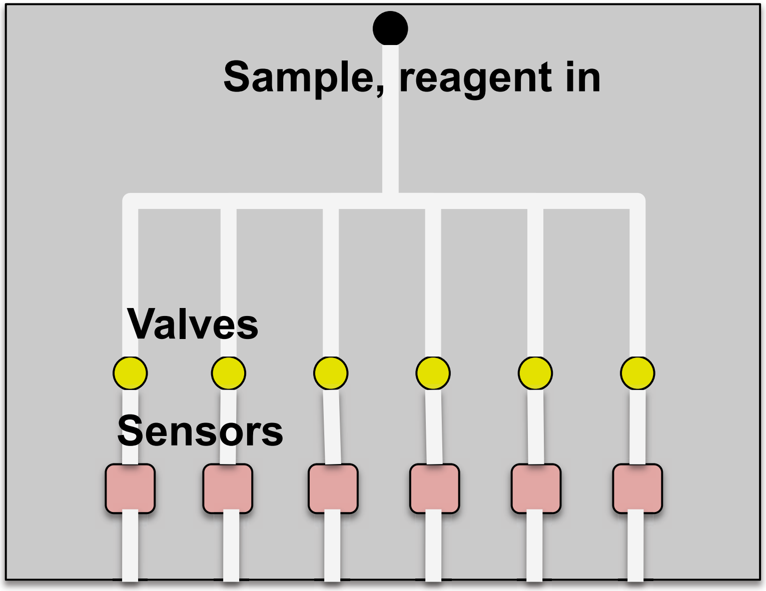
Why are Bio/Chemical Sensors so Unreliable??

- 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!

Solution: Integrate Sensing within a Microfluidic System!

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)

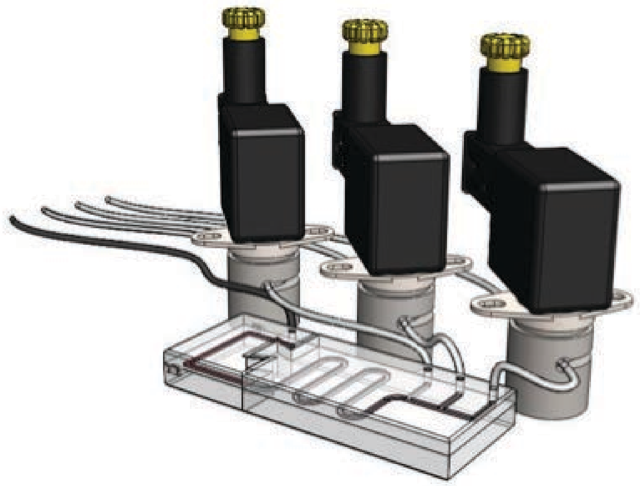


Then 50 sensors when used sequentially could provide an aggregated in-use lifetime of around 1 year

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

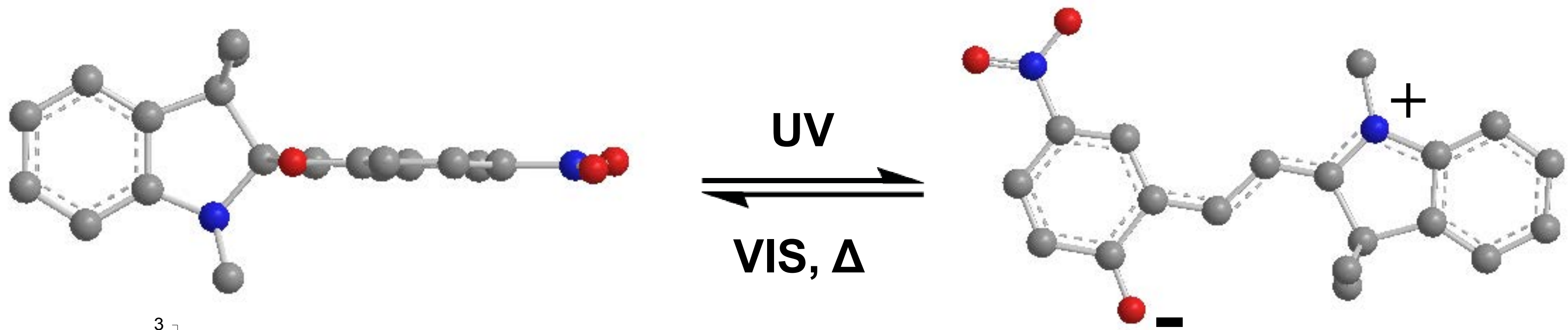
How to advance fluid handling in LOC platforms: re-invent valves (and pumps)!

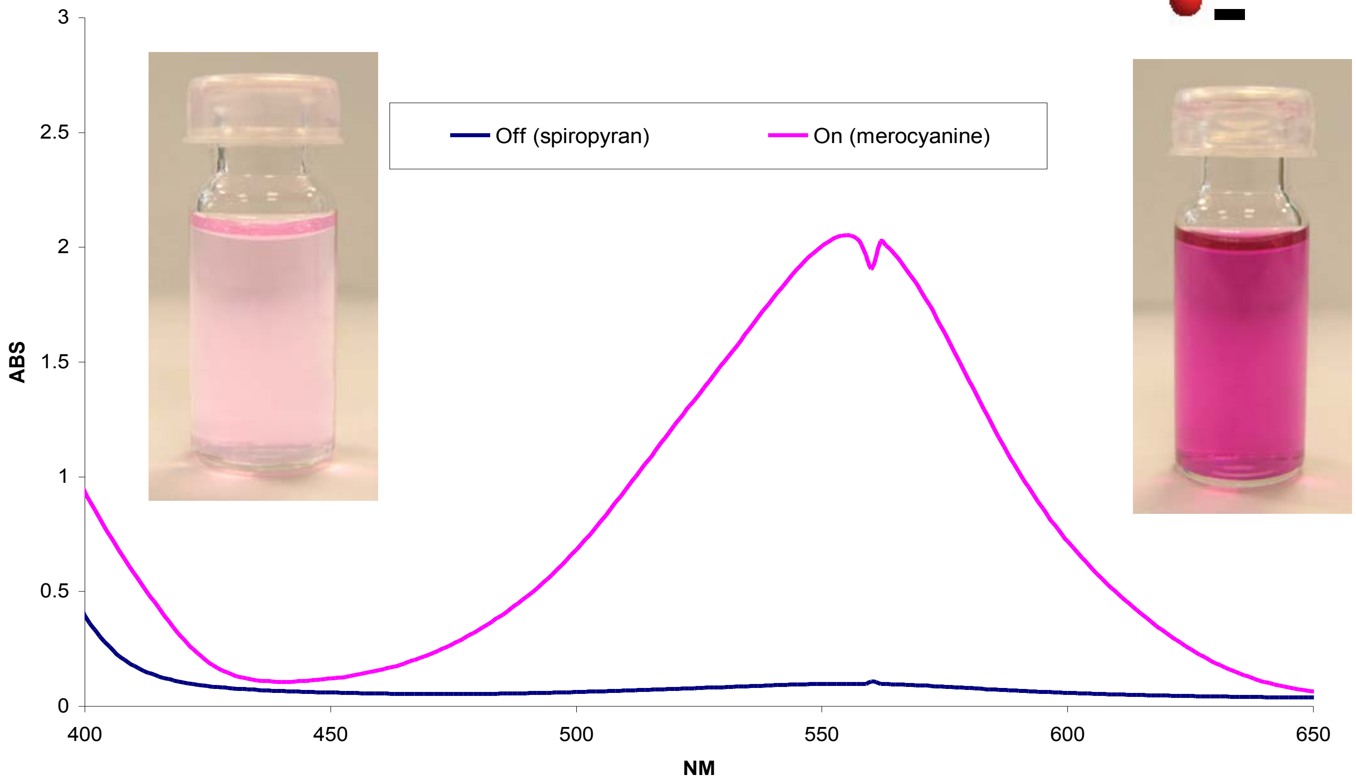
- **Conventional valves cannot be easily scaled down - Located off chip: fluidic interconnects required**
  - Complex fabrication
  - Increased dead volume
  - Mixing effects
- **Based on solenoid action**
  - Large power demand
  - Expensive



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

Photoswitchable Actuators

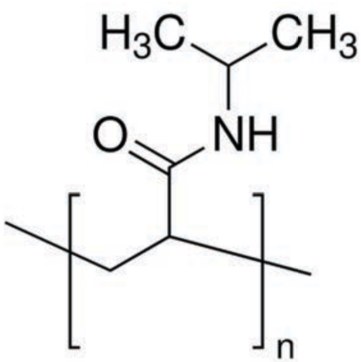




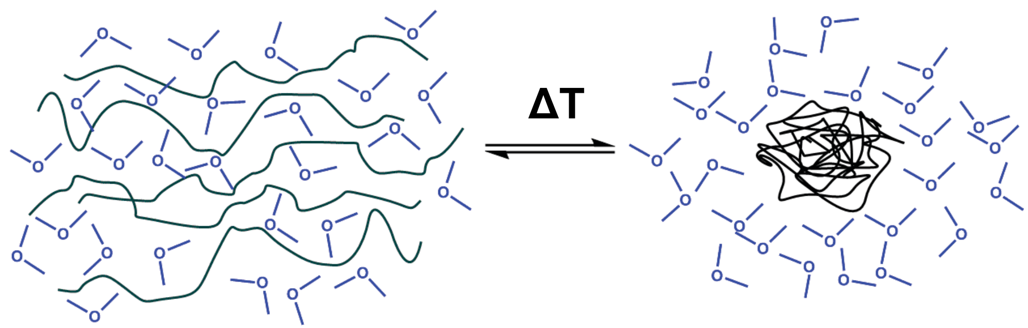
Poly(*N*-isopropylacrylamide)

- **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



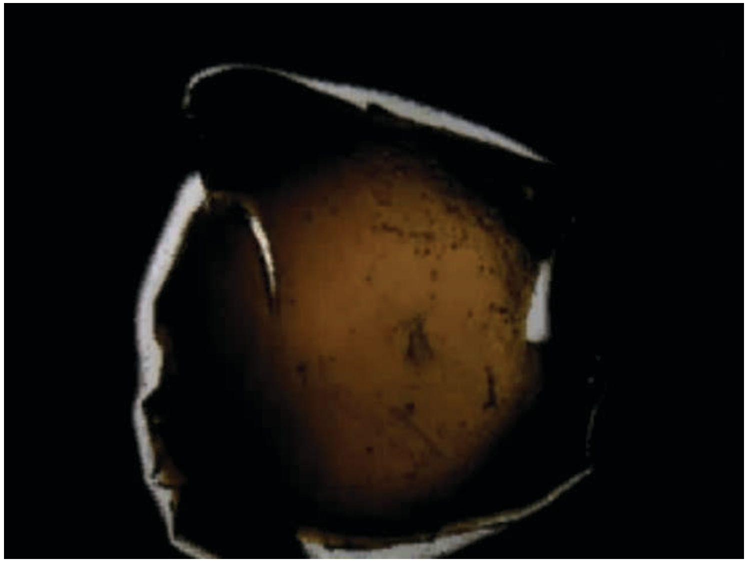
Hydrophilic **Hydrophobic**

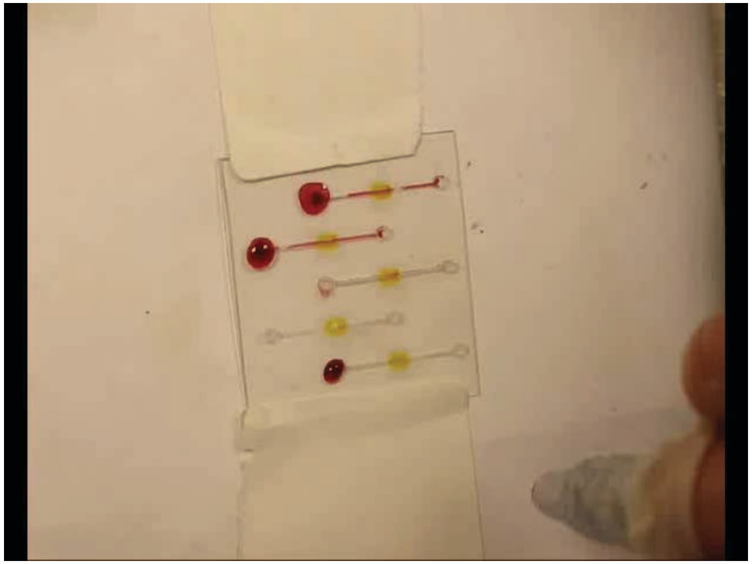


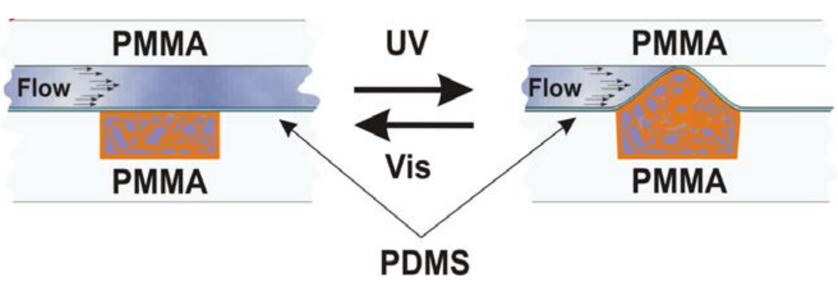
Hydrated Polymer Chains

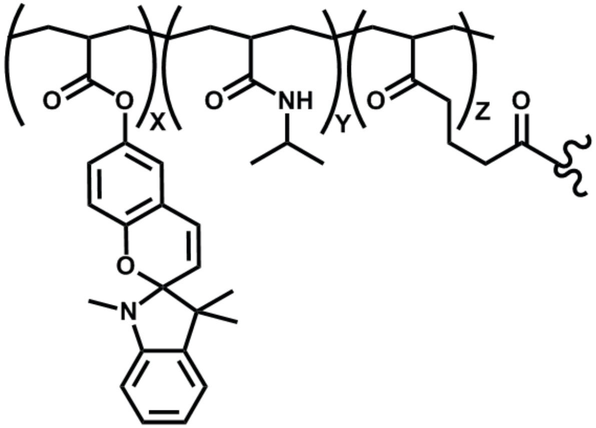
Loss of bound water -> polymer collapse

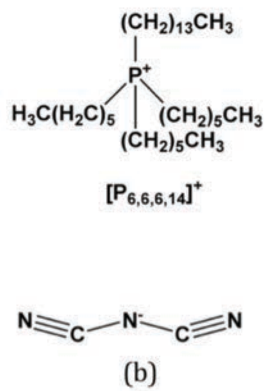
Photo-actuator polymers as microvalves in microfluidic systems









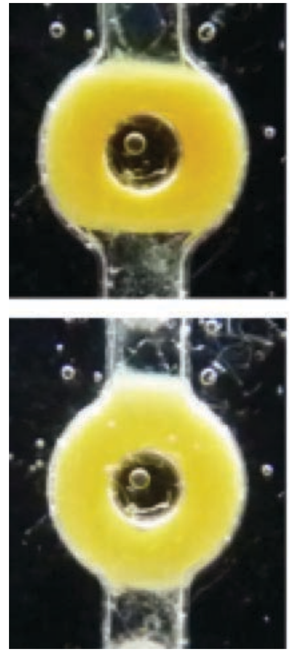


trihexyltetradecylphosphonium dicyanoamide $[P_{6,6,6,14}]^+[dca]^-$

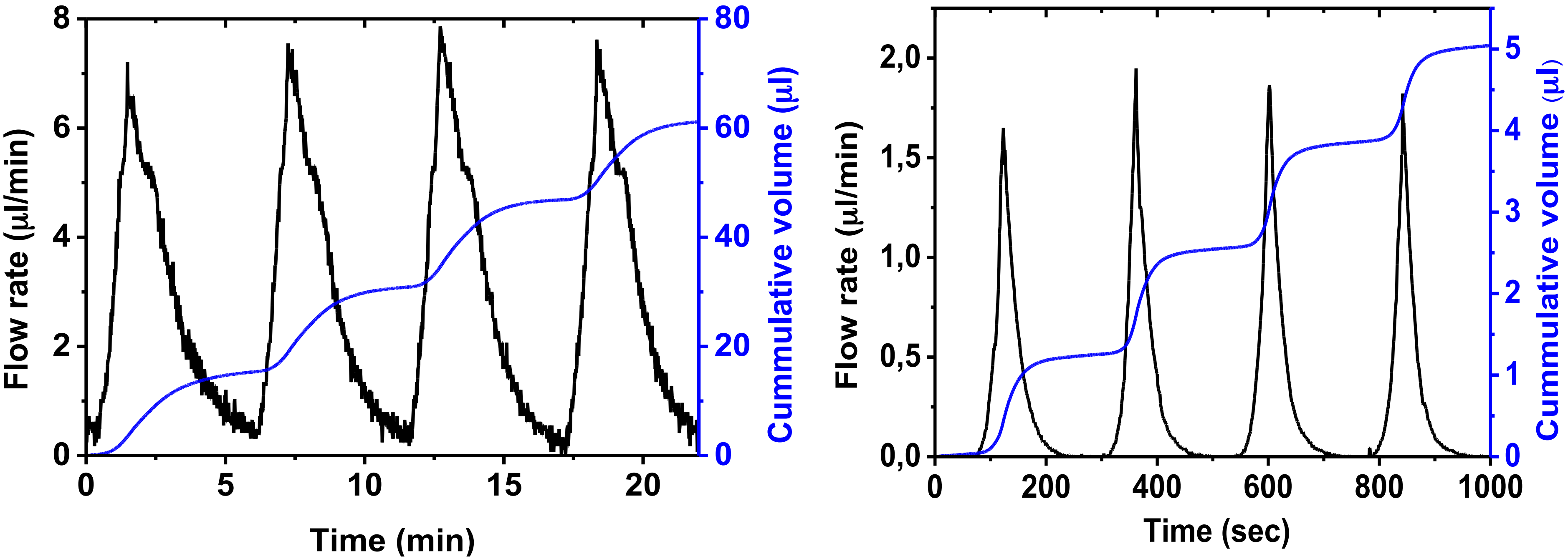
Ionogel-based light-actuated valves for controlling liquid flow in micro-fluidic manifolds, Fernando Benito-Lopez, Robert Byrne, Ana Maria Raduta, Nihal Engin Vrana, Garrett McGuinness, Dermot Diamond, Lab Chip, 10 (2010) 195-201.

Valve Polymerisation and Actuation Test Platform

- SMD 450nm Kingbright high intensity LEDs (150mA, 1.3cd) use to photopolymerise the valves in-situ
- Same valves (and mask) used to actuate the valves
- "Constant Head" method supplying stable pressure on valves using two reservoirs (R1 and R2)
- Differing water column heights to regulate pressure and flow rate.
- Flow rate measured using Fluigent "S" sensor (0-7uL/min range)



Optimisation of valve dimensions

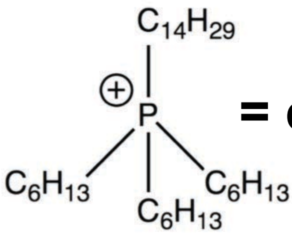


1.7 mm mask **1.6 mm mask**

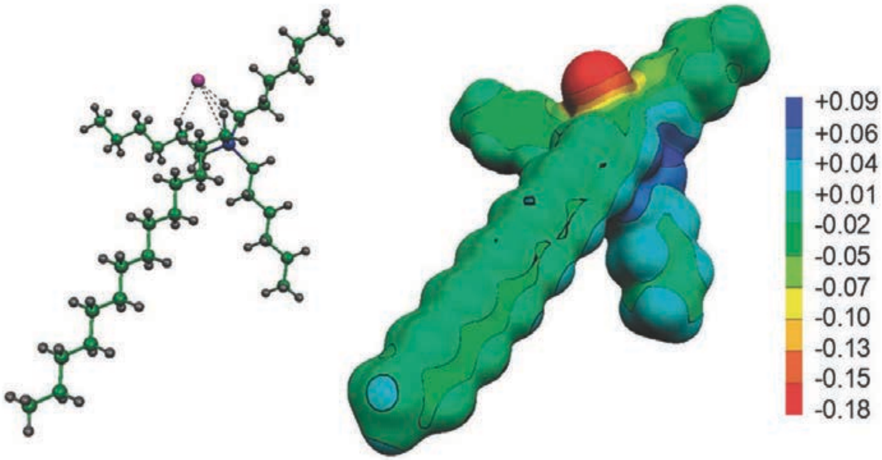
First example of actuating polymer gels as reusable valves for flow control on minute time scales (> 50 repeat actuations)

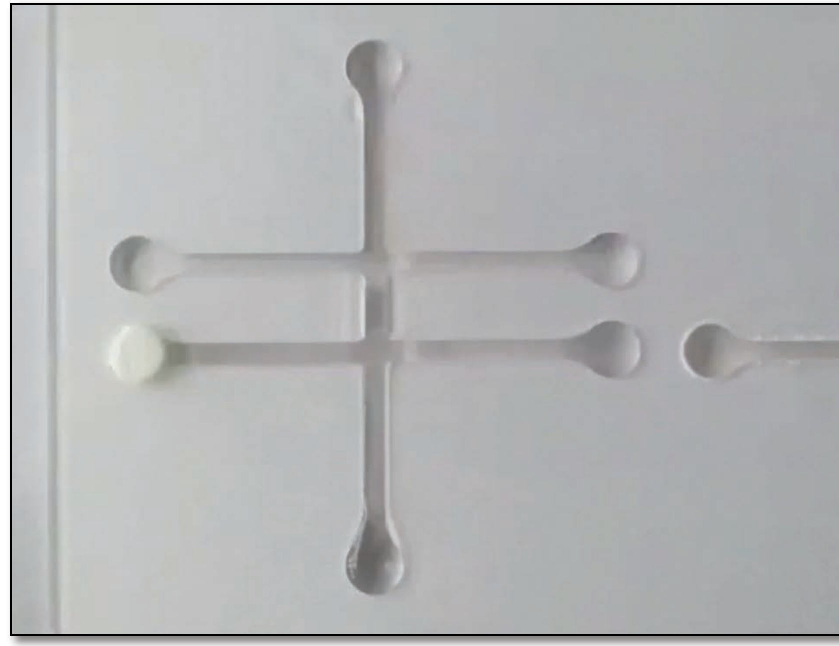
From *'Molecular Design of Light-Responsive Hydrogels, For in Situ Generation of Fast and Reversible Valves for Microfluidic Applications*', J. ter Schiphorst, S. Coleman, J.E. Stumpel, A. Ben Azouz, D. Diamond and A. P. H. J. Schenning, Chem. Mater., 27 (2015) 5925−5931. **(cover article)**

IL Droplets Respond to Cl^-



= cationic surfactant

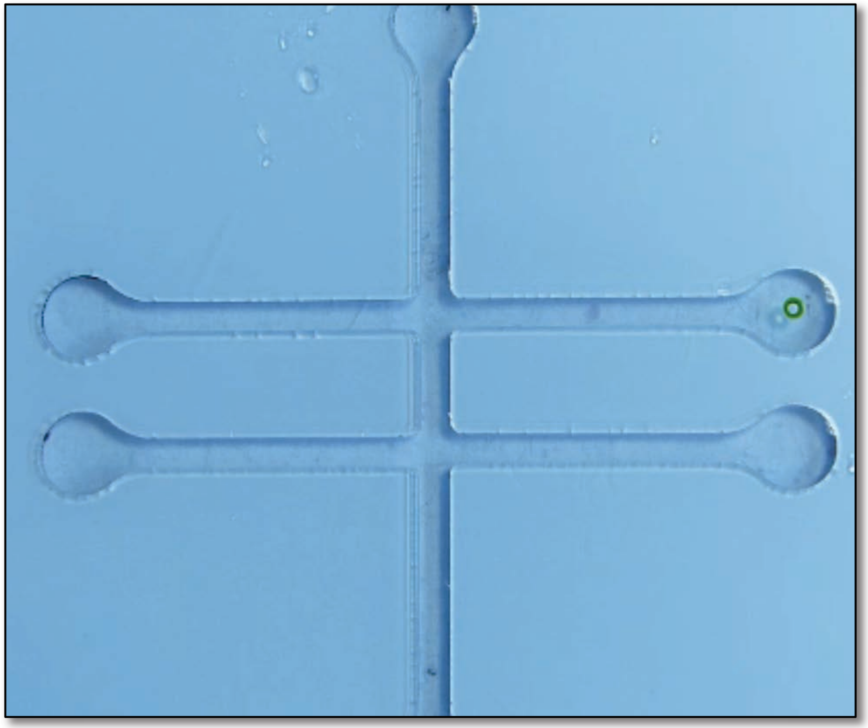


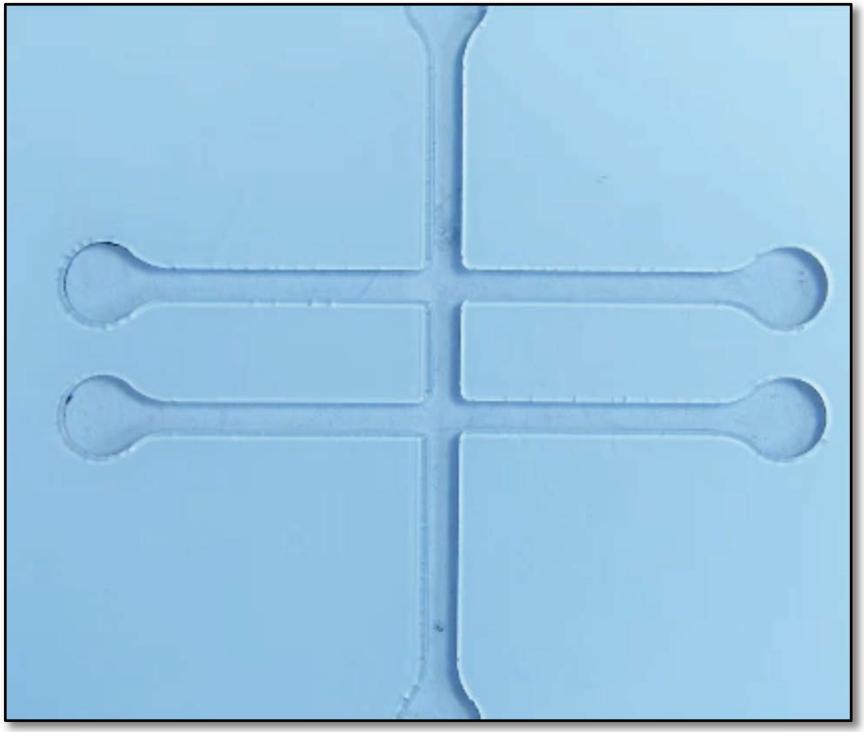


Trihexyl(tetradecyl)phosphonium chloride ($[P_{6,6,6,14}][Cl]$) droplets with a small amount of 1-(methylamino)anthraquinone red dye for visualization. The droplets spontaneously follow the gradient of the Cl^- ion which is created using a polyacrylamide gel pad soaked in 10^{-2} M HCl; A small amount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

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.

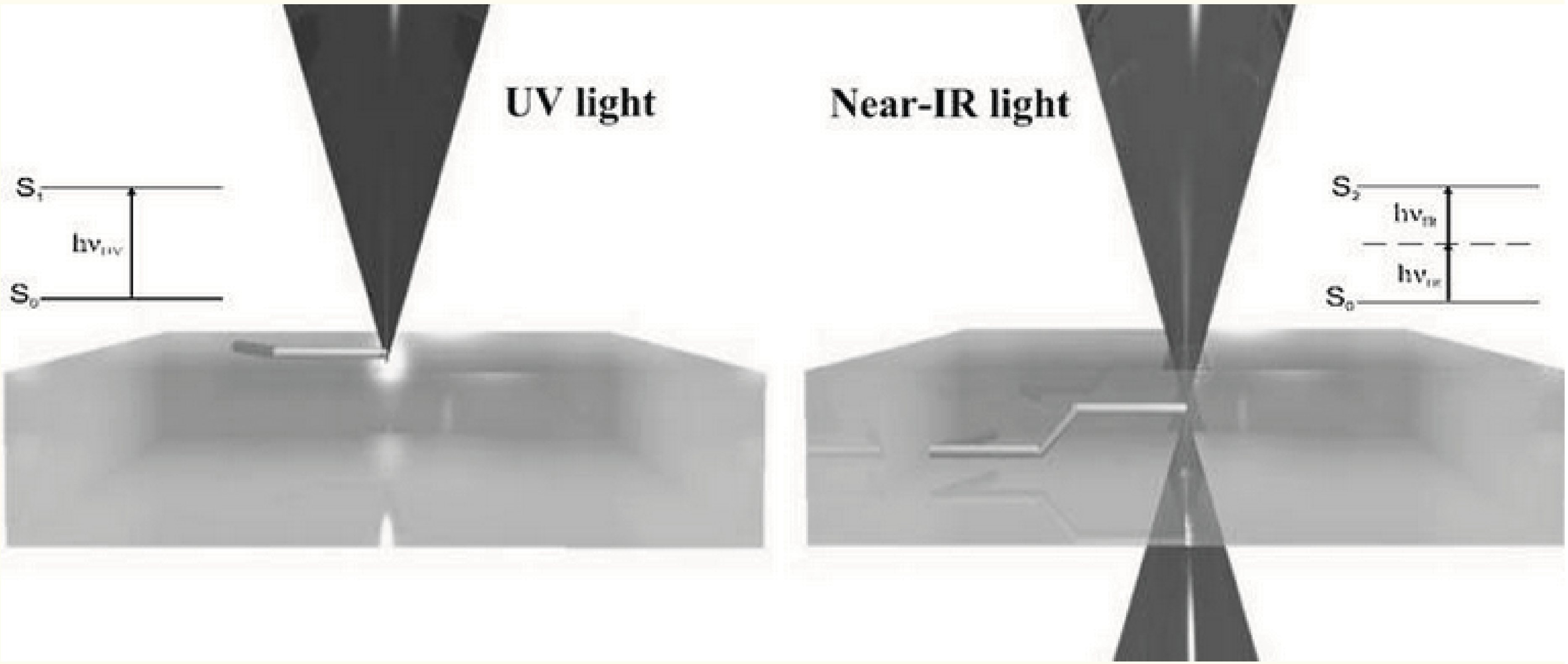
The Lonely Droplet – Valentine's Edition (speed x2)





Two Photon Polymerisation vs. Conventional 3D (Polymer) Printing

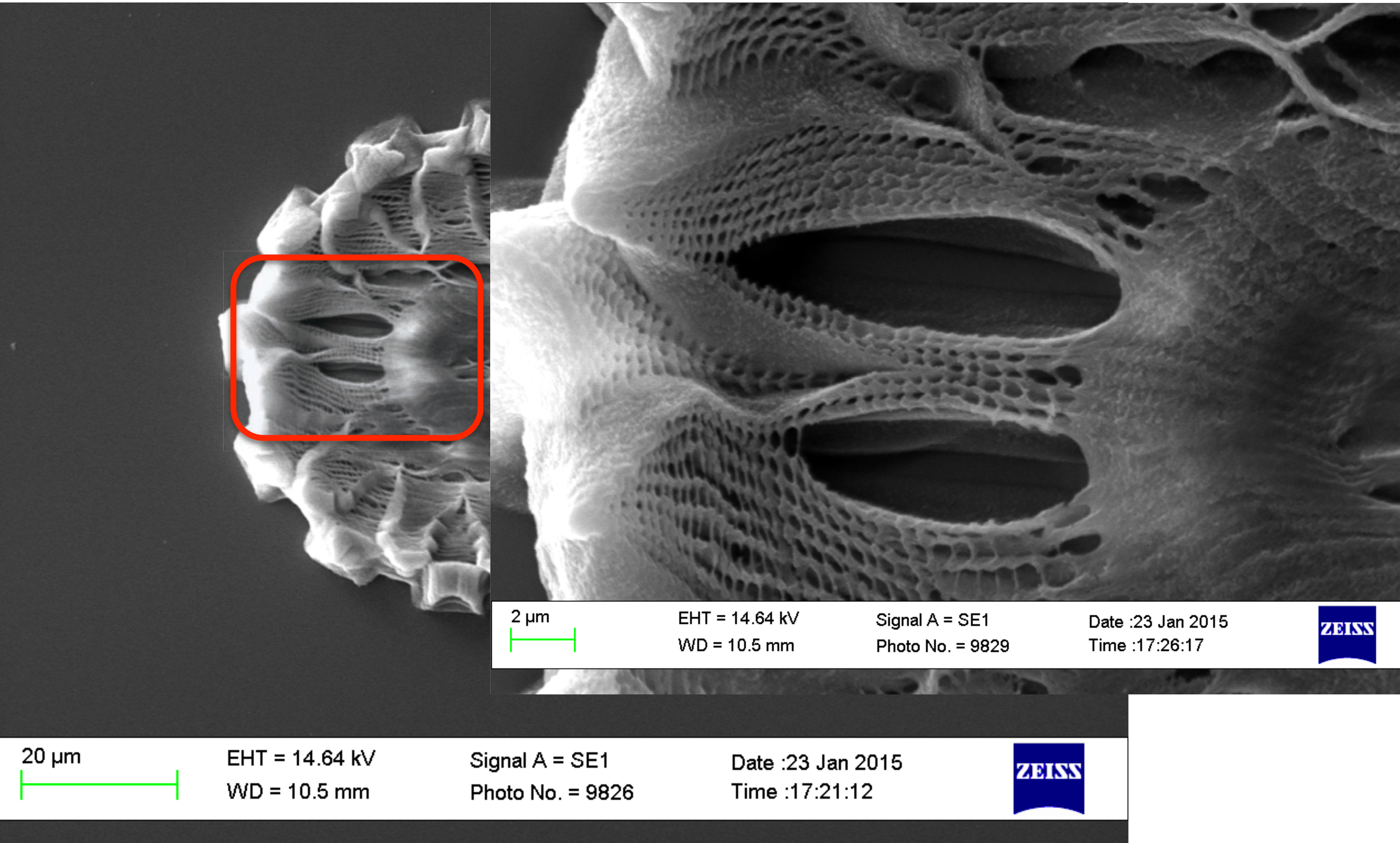
Stereolithography | **Two-photon polymerisation**



- Single photon absorption
- 2D patterns

- Two photon absorption
- 3D structures

‘Daisy’ – Micro/Nano Scaled Porous Structure



Time to re-think the game!!!

- **New materials with exciting characteristics and unsurpassed potential…**
- **Techniques for exquisite control of 3D morphology**
- **Greatly improved methods for characterisation of structure and activity**
- **Learn from nature – e.g. more sophisticated 'circulation systems'**

What is the function of the fluidic chip polymer?
Progress demands use of 'bioinspired' models: e.g. internal self-awareness, detect issues & take maintenance action
'Hierarchical cooperative' systems at multiple scales

Thanks for listening

MASK
Project no: 269302
Materials and Advanced Sensor Knowledge Exchange

SEVENTH FRAMEWORK PROGRAMME

MARIE CURIE ACTIONS

NAPES
NEXT GENERATION ANALYTICAL PLATFORMS FOR ENVIRONMENTAL SENSING

COMMON SENSE
MARINE SENSORS - MARINE MONITORING

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