Next Generation 'Wearable' Biochemical Sensors – Can Biomimetic Fluidics Help Deliver Much More Sophisticated Technologies?

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presented at

"Chemical Sensors for Wearable Devices CDWD 2021"
Technion - Israel Institute of Technology, Haifa, Israel
3rd March 2021

The Insight Centre for Data Analytics

Insight is one of the biggest data analytics centres in Europe. It undertakes high-impact research, seeks to derive value from Big Data and provides innovative technology solutions for industry and society by enabling better decision-making.

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2nd Phase funding (ca. €49 million SFI); commenced autumn 2019

Internet of (Biochemical) Things IO$_{BC}$T

- **Bridging the Molecular and Digital Worlds**
  - Emergence of 'Internet of Analytical Things', Internet of 'Molecular Things', 'Internet of Biochemical Things'
- **Long-Term "Deploy and Forget" use model**
  - Embedded 'smartness'
    - Sensing (temperature, light-level, imaging, vibration)
    - Communications (wireless)
    - Power (10-year battery life-time, energy scavenging capability)
  - Critical Need: Awareness of
    - Surrounding environment
    - Internal (functional) condition

Keynote Article: Anal. Chem., 76 (2004) 278A-286A

internet scale sensing

Dermot Diamond
Dublin City University
(Ireland)

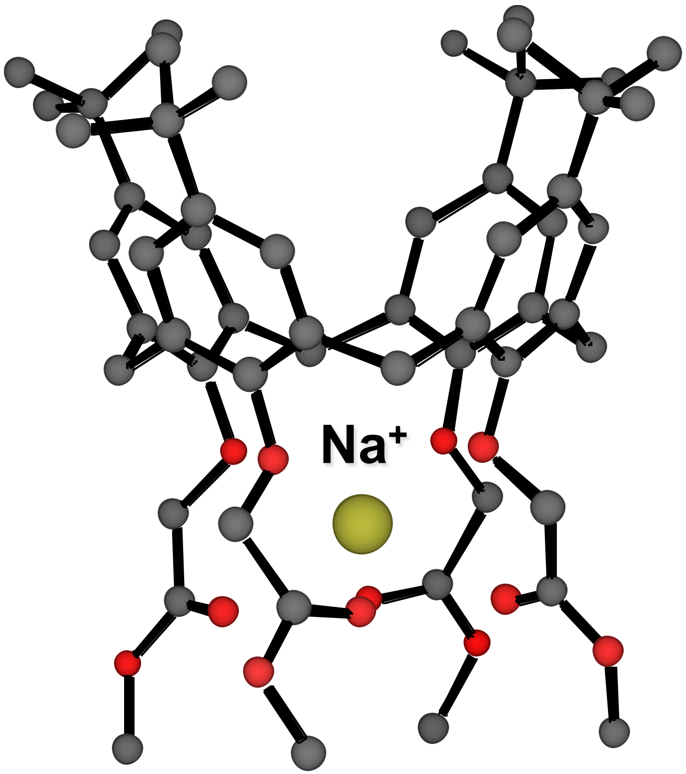
Incredible advances in digital communications and computer power have profoundly changed our lives. One chemist shares his vision of the role of analytical science in the next communications revolution.

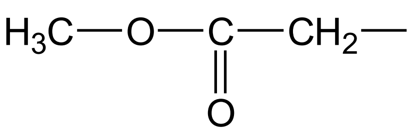
Digital communications networks are at the heart of modern society. The digitization of communications, the development of the Internet, and the availability of relatively inexpensive but powerful mobile computing technologies have established a global communications network capable of linking billions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

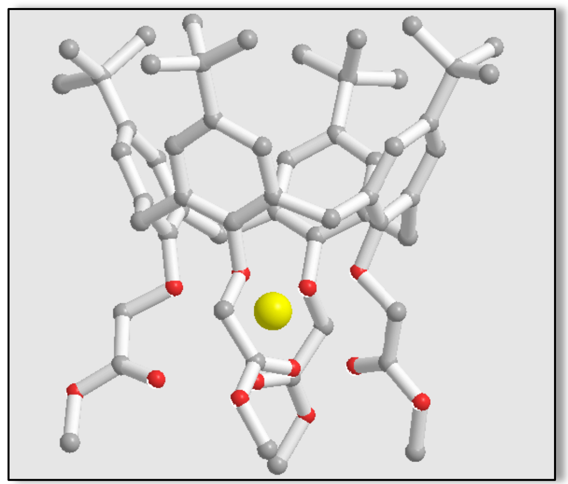
The crucial missing part in this scenario is the gateway through which these worlds will communicate: How can the digital world sense and respond to changes in the real world? Analytical scientists—particularly those working on chemical sensors, biosensors, and compact, autonomous instruments—are

Ron Ambrosio & Alex Morrow, IBM TJ Watson

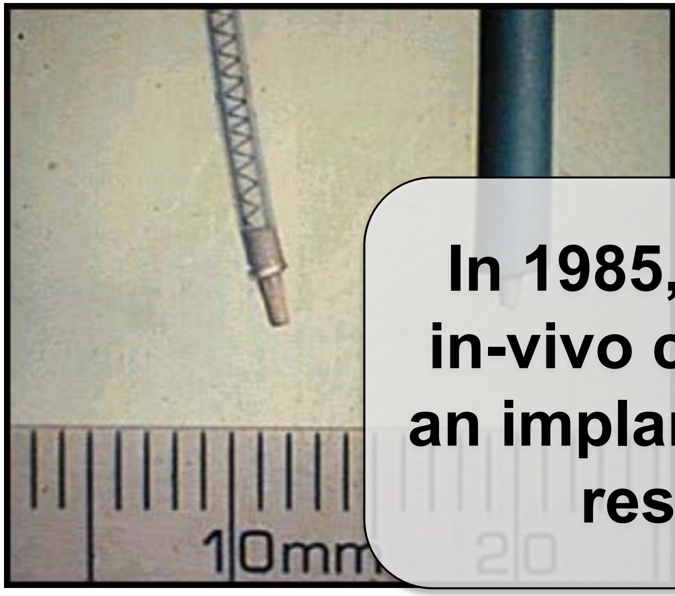
Calixarene Ionophores – controlling the selectivity



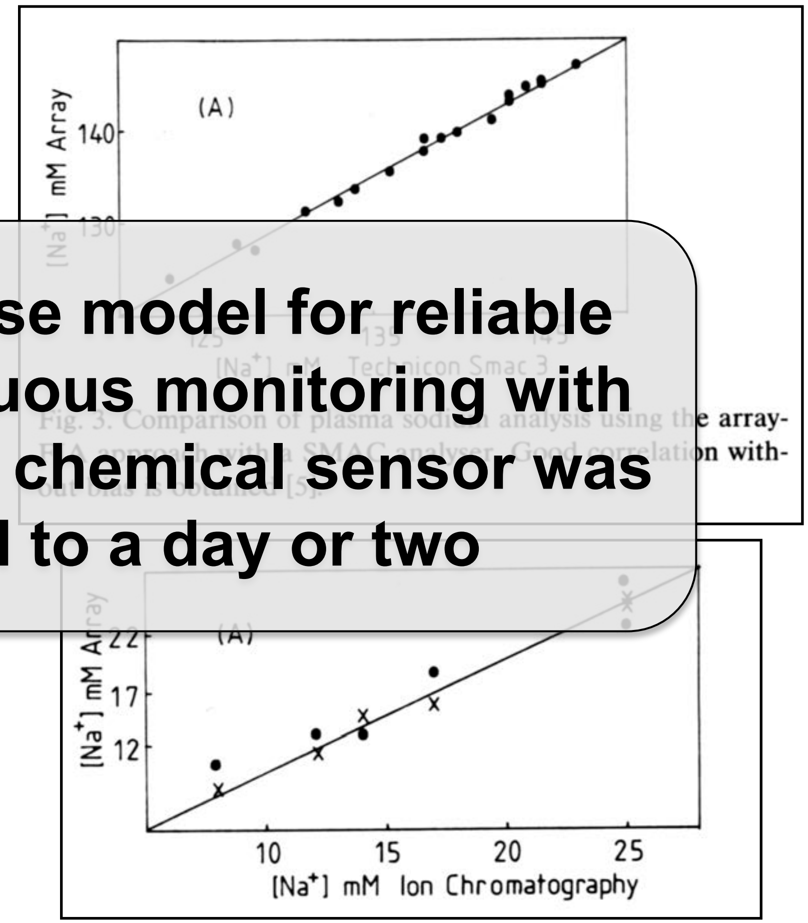




Blood Analysis; Implantible Sensors



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



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

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

Dr. David Band, St Thomas's Hospital London

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

The (broken) promise of biosensors…..

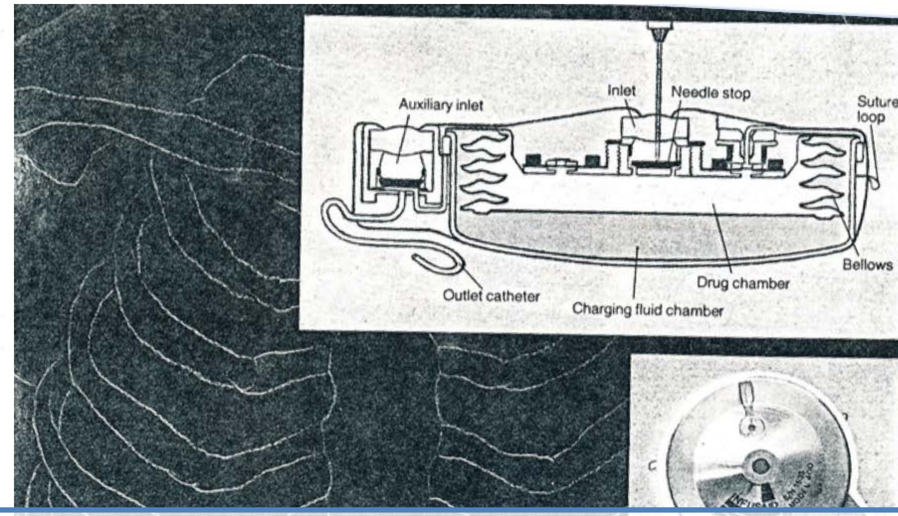
High Technology, Nov. 1983, 41-49

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 □ by H. Garrett DeYoung



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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

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 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]

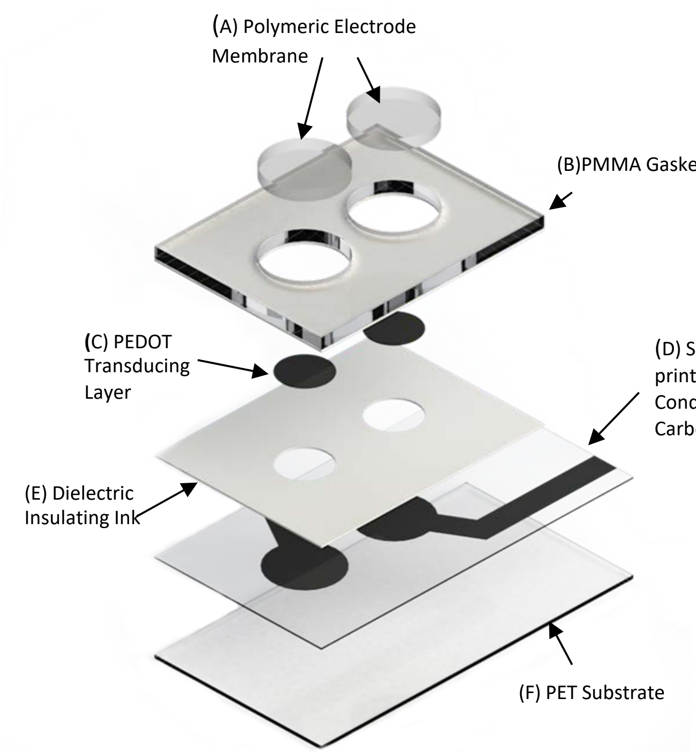
[6] Most people did not feel any discomfort under the skin while wearing the FreeStyle Libre sensor. In a study conducted by Abbott Diabetes Care, 93.4% of patients surveyed (n=30) strongly agree or agree that while wearing the sensor, they did not feel any discomfort under their skin. [29 persons have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

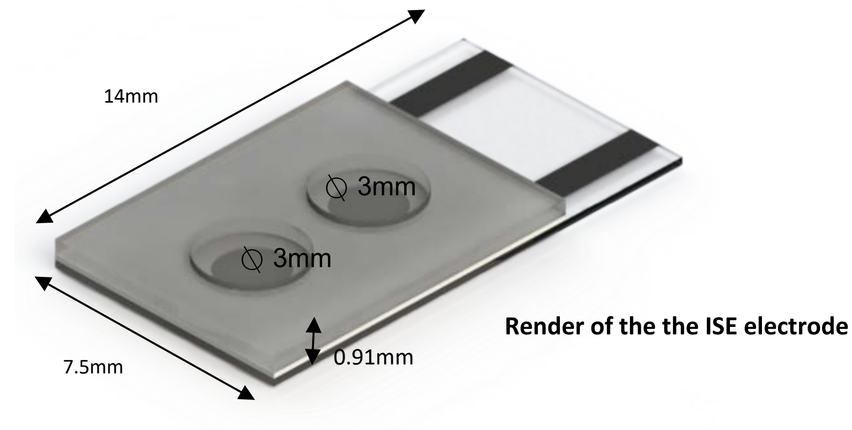
[7] Sensor is water-resistant in up to 1 metre (3 feet) of water for a maximum of 30 minutes

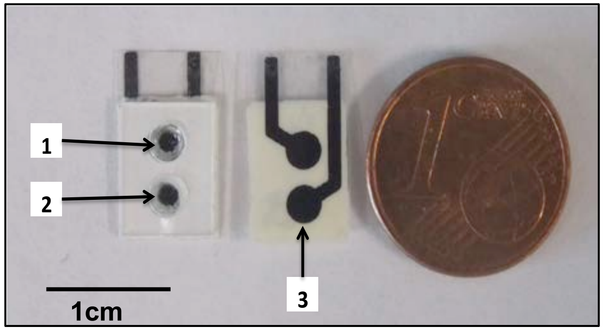
- 'Small fibre' used to access interstitial fluid
- Data downloaded at least once every 8 hr via 1s contactless scan (1-4 cm)
- Waterproof to 1 metre
- Replace every 2 weeks

Electrode Development

Design and Fabrication Na^+ Electrode







(A) Polymeric Electrode Membrane (B) PMMA Gasket (C) PEDOT transducing layer (D) Screen printed conductive carbon ink layer (E) Dielectric Insulating ink (F) PET Substrate

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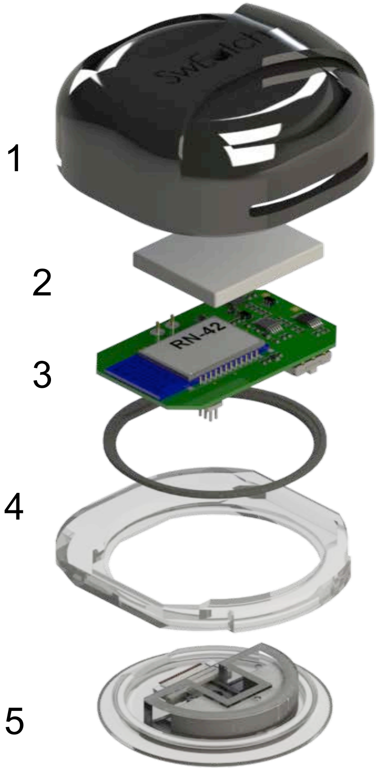
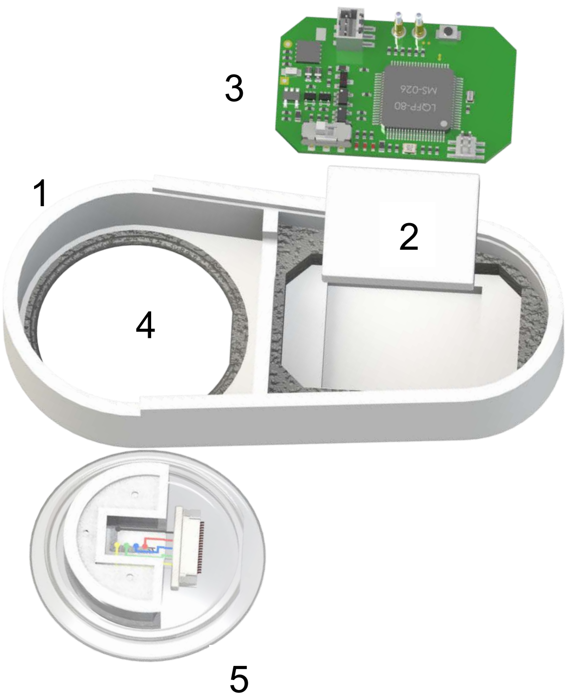
1. The Ion Selective Electrode (ISE)
2. The reference electrode (RE)
3. The screen-printed conductive carbon layer.

Wearable Platform

Watch Platform

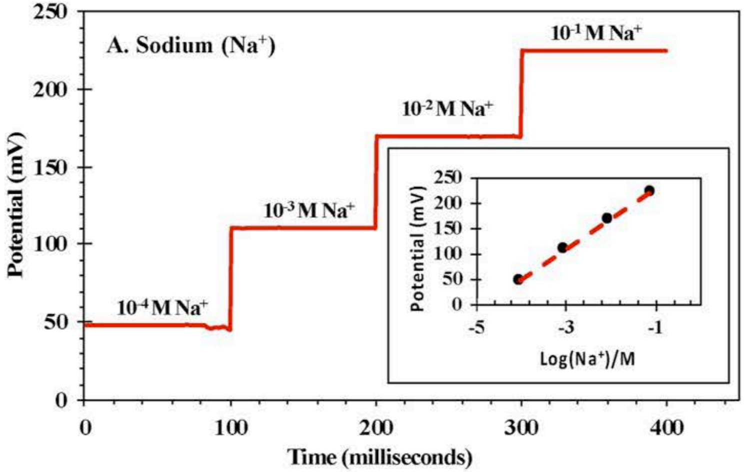


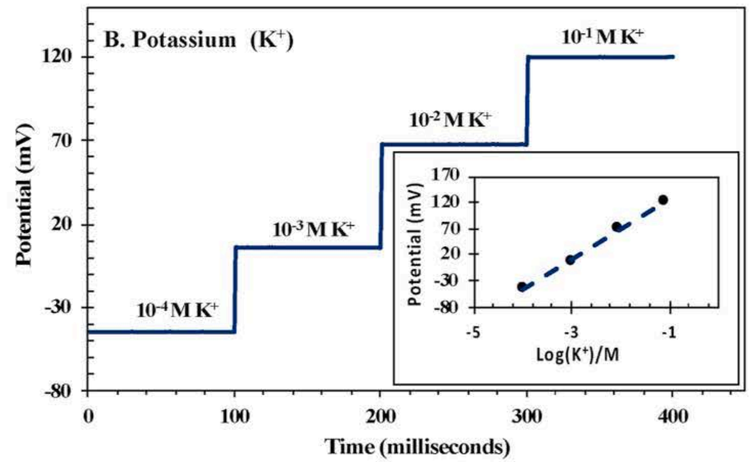
Pod Platform

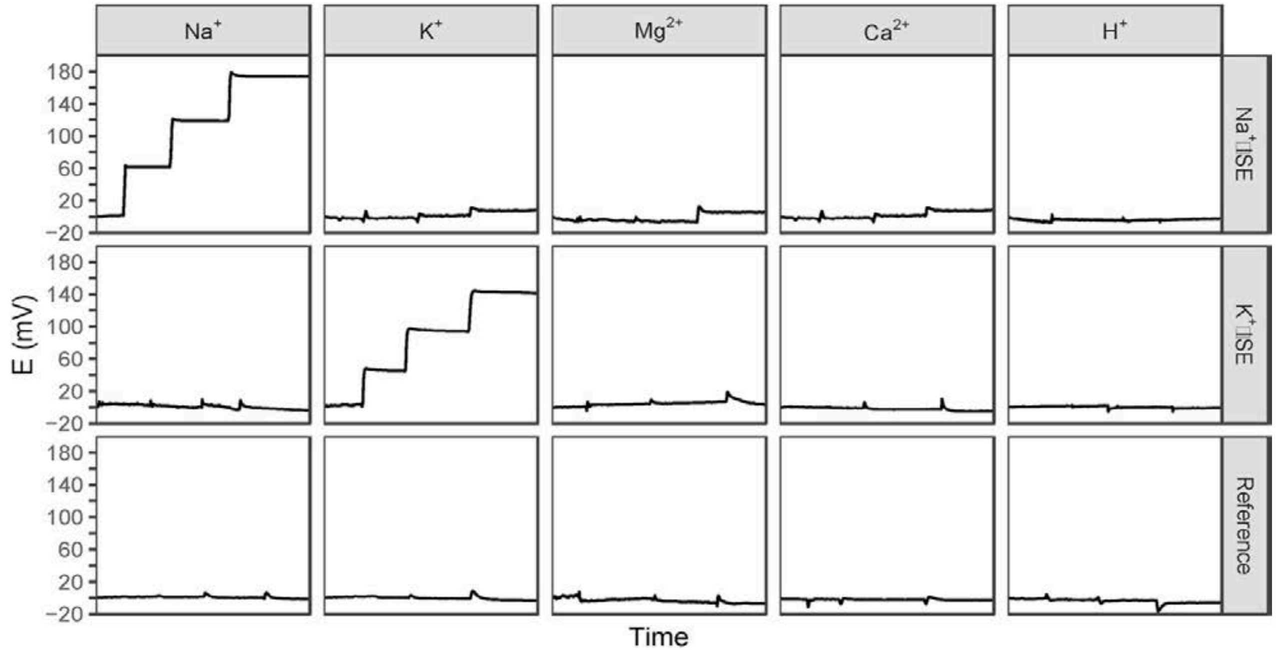


1. 3D printed housing
2. Lithium battery
3. Custom-built electronics with wireless communication (Shimmer)
4. 3D printed mount with silicon inner seal to house the sweat harvester
5. 3D printed sweat harvesting device and microfluidic chip with integrated sensor

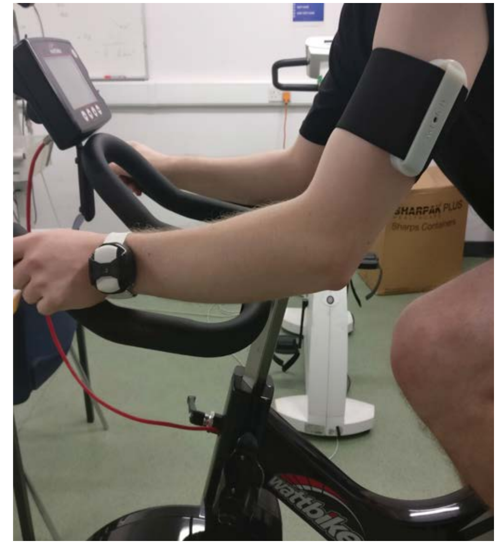
Sensor Calibration & Selectivity

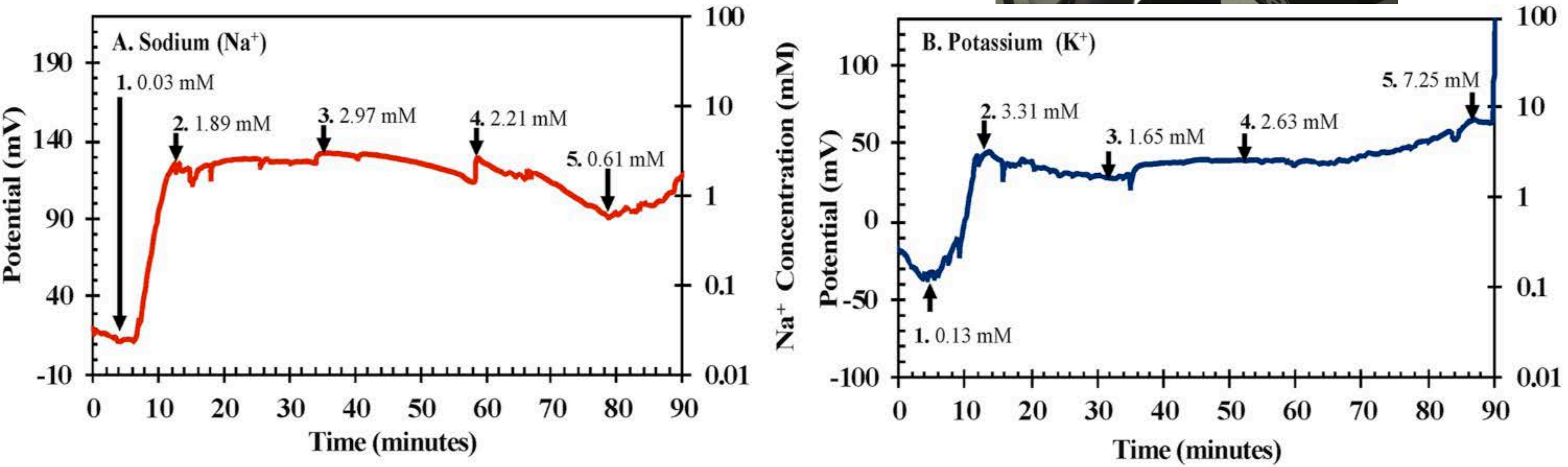






On-Body Trials





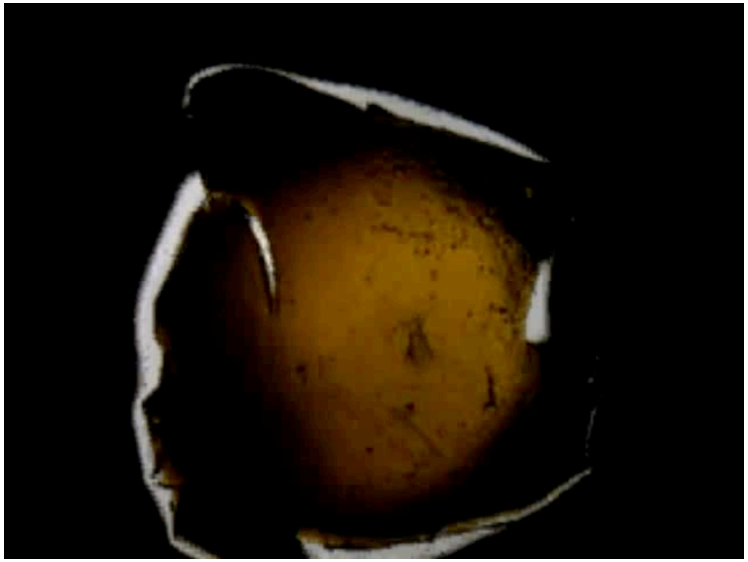
P. Pirovano, M. Dorrian, A. Shinde, A. Donohoe, A.J. Brady, N.M. Moyna, G. Wallace, D. Diamond, M. McCaul, A wearable sensor for the detection of sodium and potassium in human sweat during exercise, Talanta. 219 (2020) 121145. https://doi.org/10.1016/j.talanta.2020.121145.

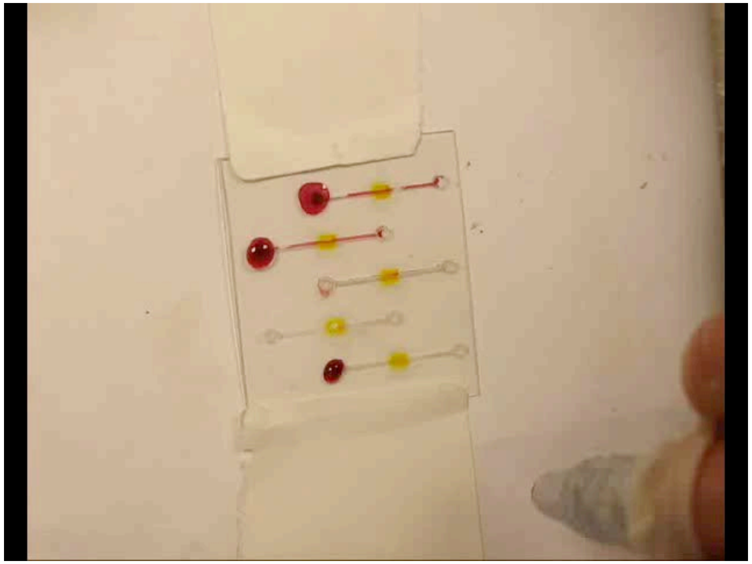
T. Glennon, C. O'Quigley, M. McCaul, G. Matzeu, S. Beirne, G.G. Wallace, F. Stroiescu, N. O'Mahoney, P. White, D. Diamond, 'SWEATCH': A Wearable Platform for Harvesting and Analysing Sweat Sodium Content, Electroanalysis. 28 (2016) 1283–1289. https://doi.org/10.1002/elan.201600106.

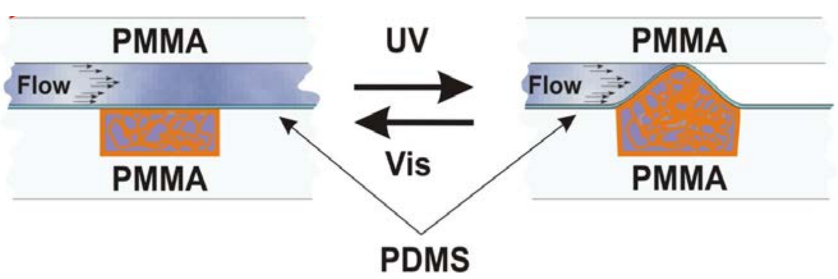
Bioinspired Devices

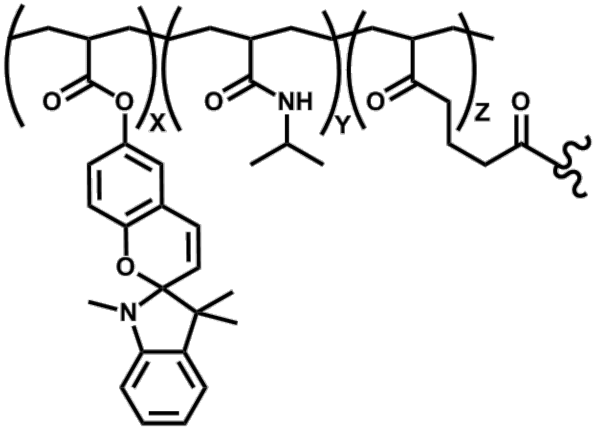
- **Functional (Bio)Materials OR Materials that can mimic characteristics of biological systems**
  - **Self-awareness of condition**
  - **Some capacity for self-maintenance/self repair**
- **Hierarchy of behaviours**
  - Routine internalized maintenance for minor issues
  - Escalation to external intervention for more serious issues (detect, report, request intervention)

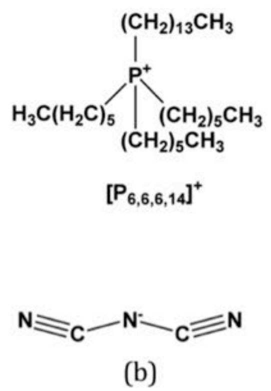
Photo-actuator polymers as microvalves in microfluidic systems







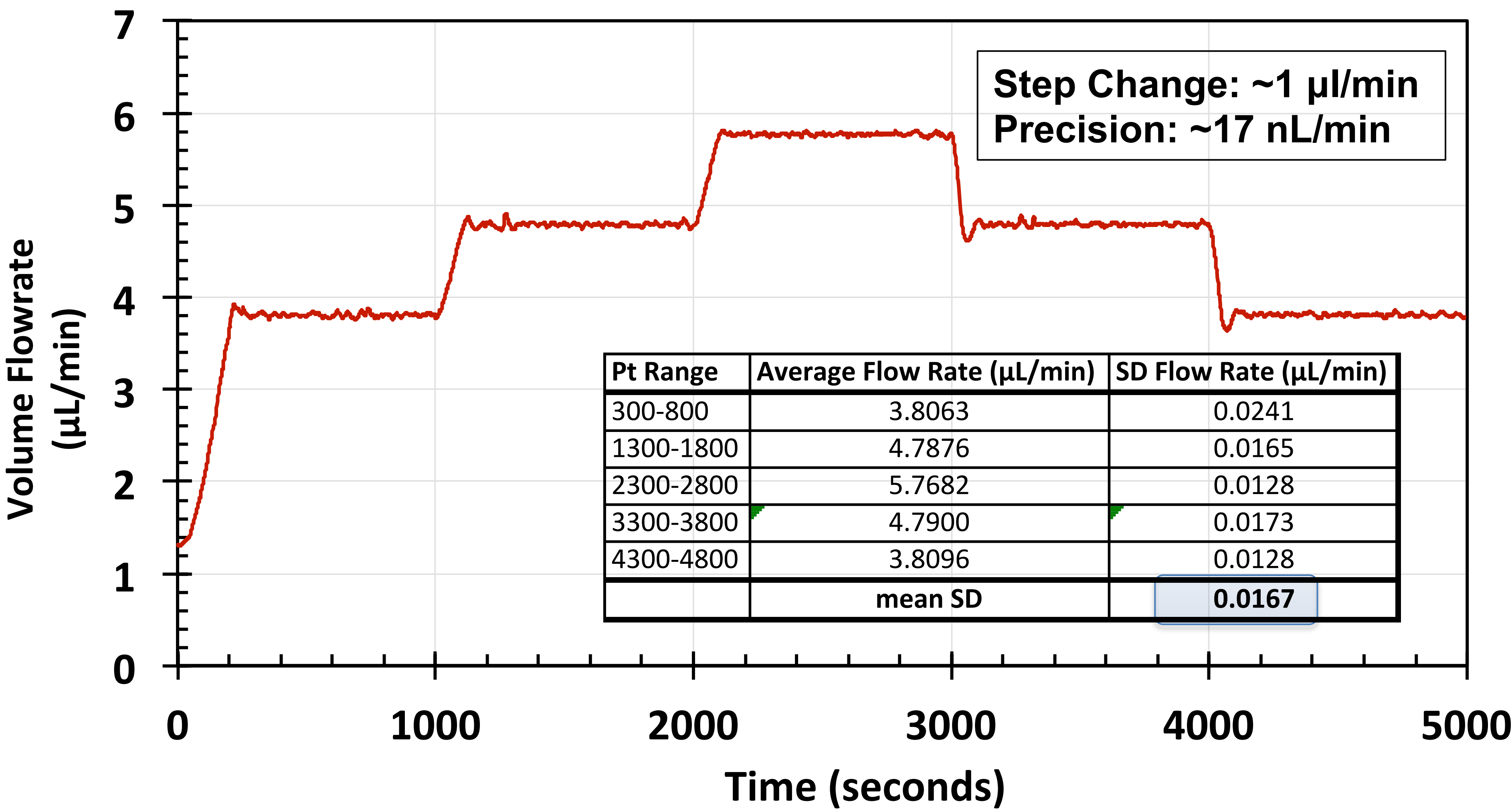




trihexyltetradecylphosphonium dicyanoamide $[P_{6,6,6,14}]^+[dca]^-$

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.

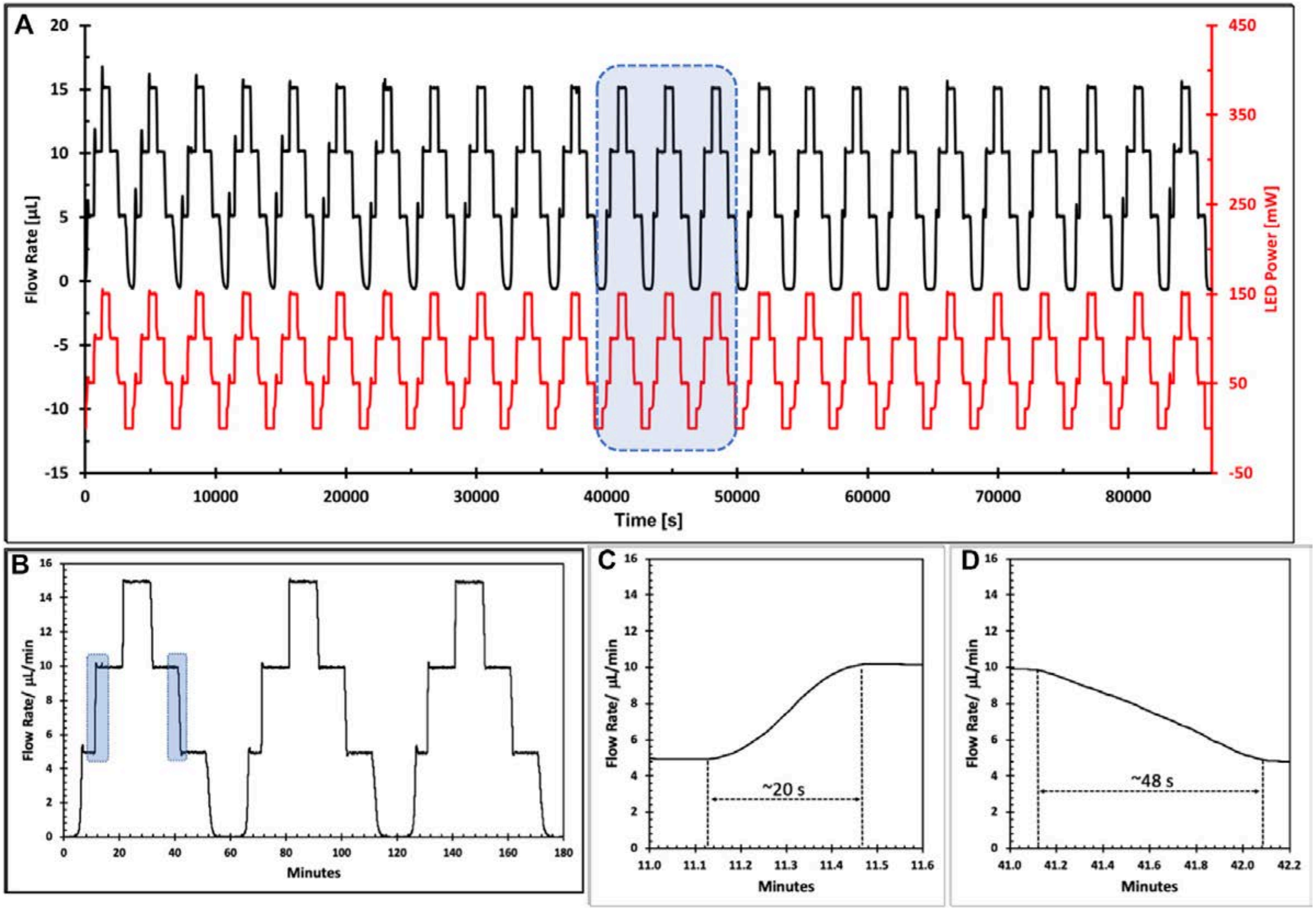
Photo-Controlled Flow Rate



Pt Range	Average Flow Rate (µL/min)	SD Flow Rate (µL/min)
300-800	3.8063	0.0241
1300-1800	4.7876	0.0165
2300-2800	5.7682	0.0128
3300-3800	4.7900	0.0173
4300-4800	3.8096	0.0128
	mean SD	**0.0167**

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.

Precision Switching of Flow rates



K. Pandurangan, R. Barrett, D. Diamond, M. McCaul, Fluidic Platforms Incorporating Photo-Responsive Soft-Polymers Based on Spiropyran: From Green Synthesis to Precision Flow Control, Frontiers in Materials. 7 (2021) 11.

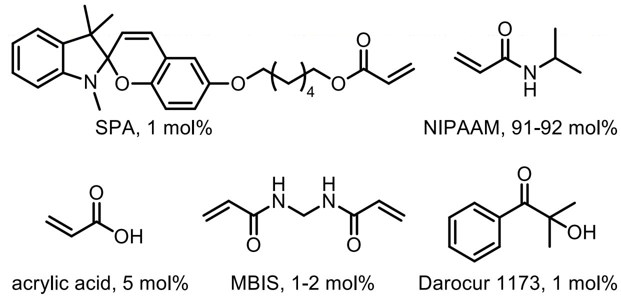
Photocontrol of Assembly and Subsequent Switching of Surface Features

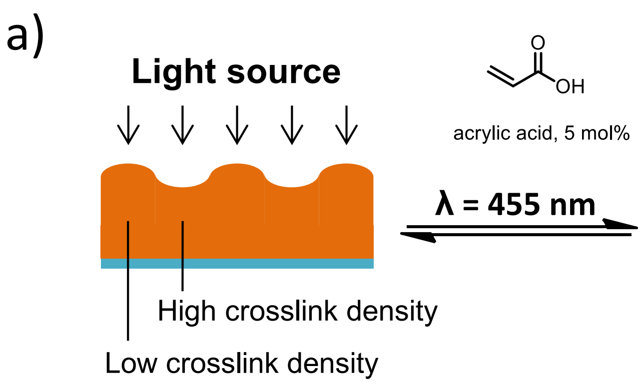
ACS APPLIED MATERIALS & INTERFACES
Research Article
www.acsami.org

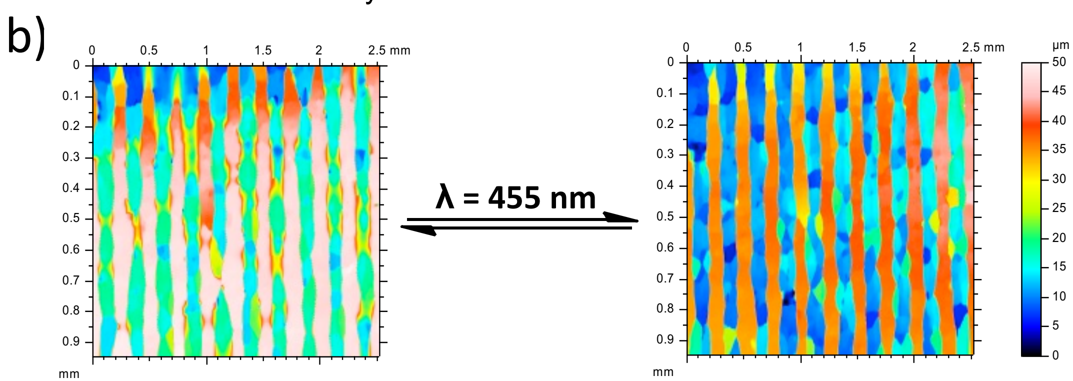
ACS applied materials & interfaces, 6 (2014) 7268-7274

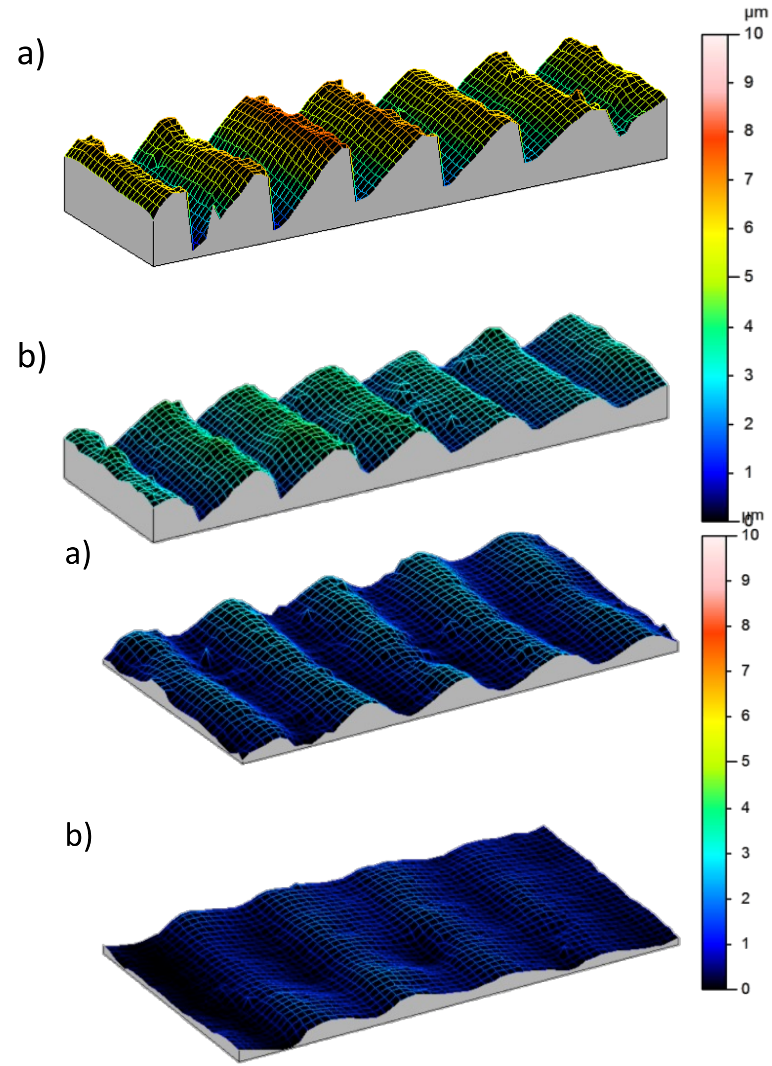
Photoswitchable Ratchet Surface Topographies Based on Self-Protonating Spiropyran–NIPAAM Hydrogels

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

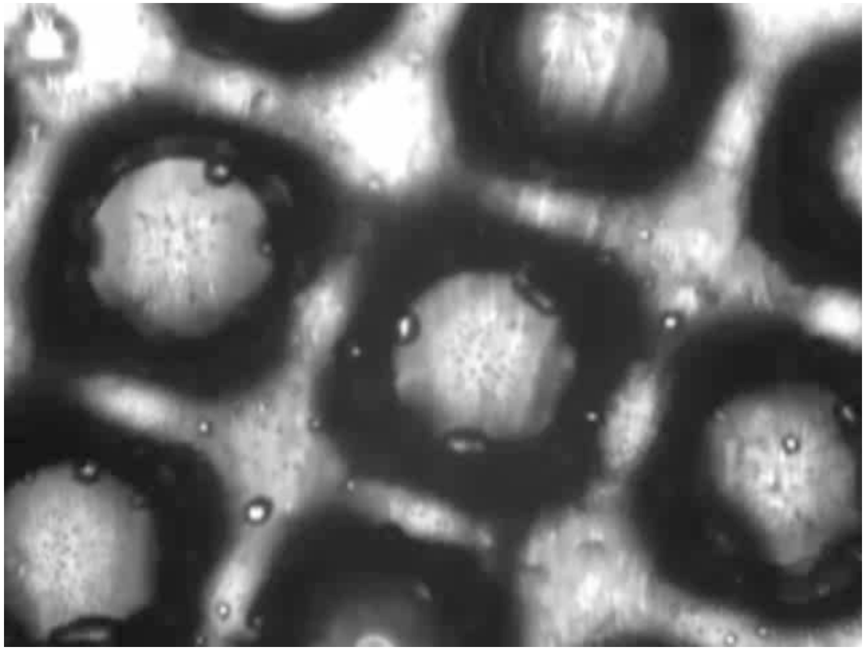




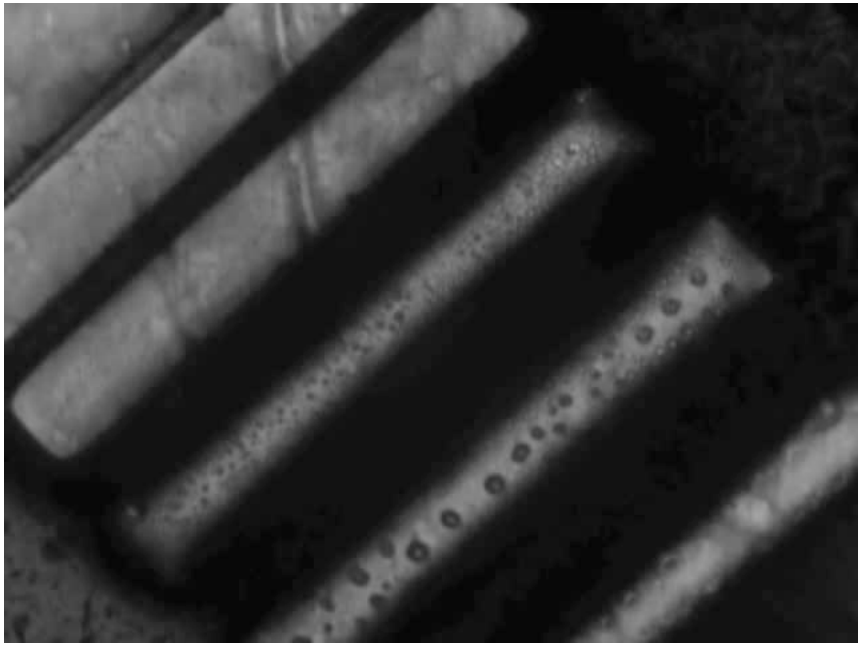




Flexible creation of μ-dimensioned features in flow channels using in-situ photo-polymerisation



Ntf2 pillars speed x3



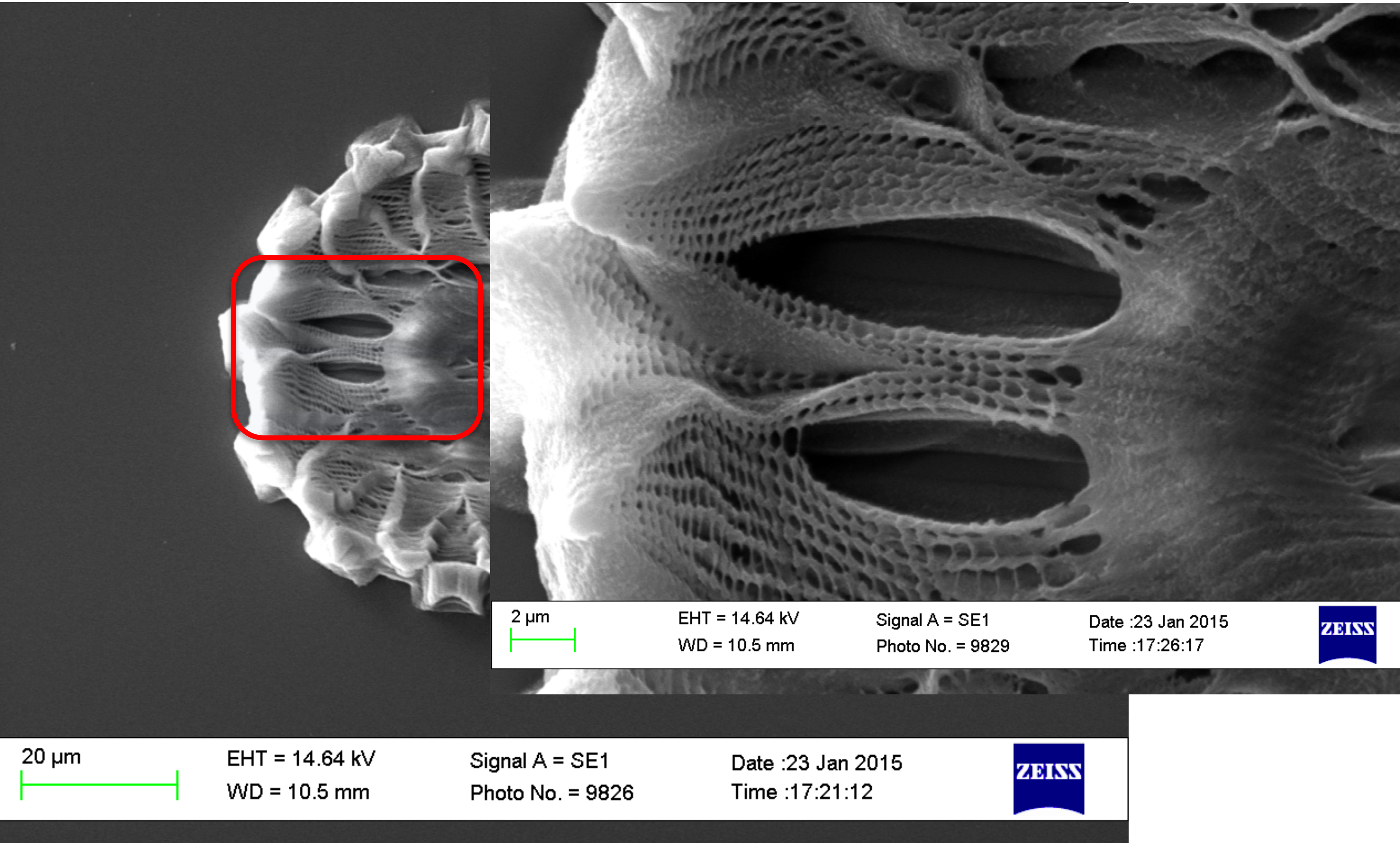
DCA lines speed x4

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

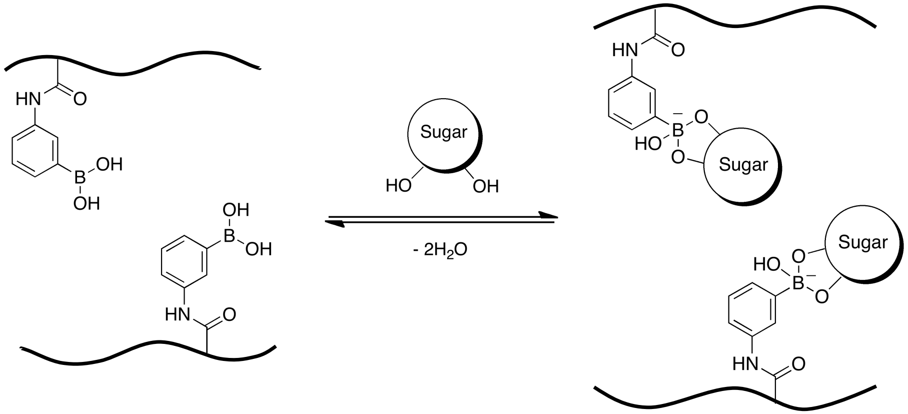
Binding behavior can also be modulated using light

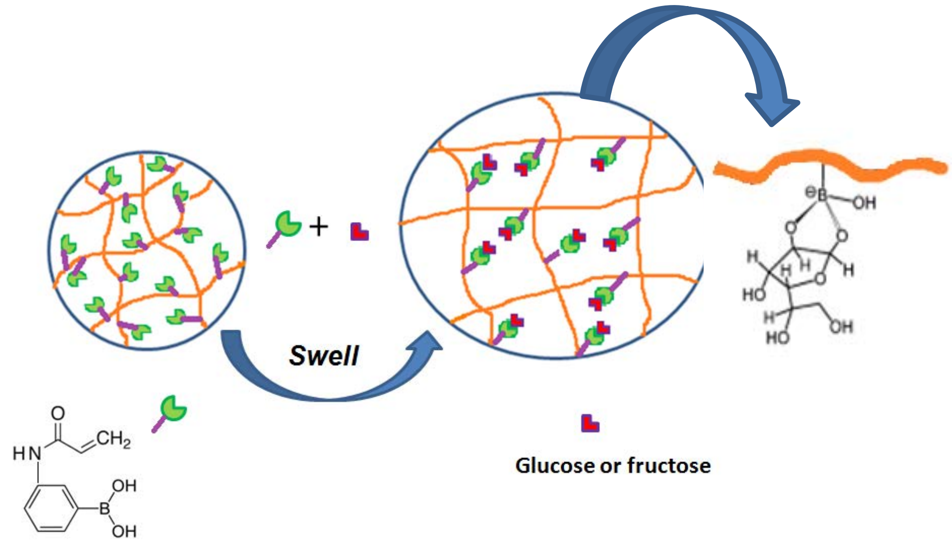
‘Daisy’ – Micro/Nano Scaled Porous Structure

(with Guang Zhong Yang, Imperial College London)

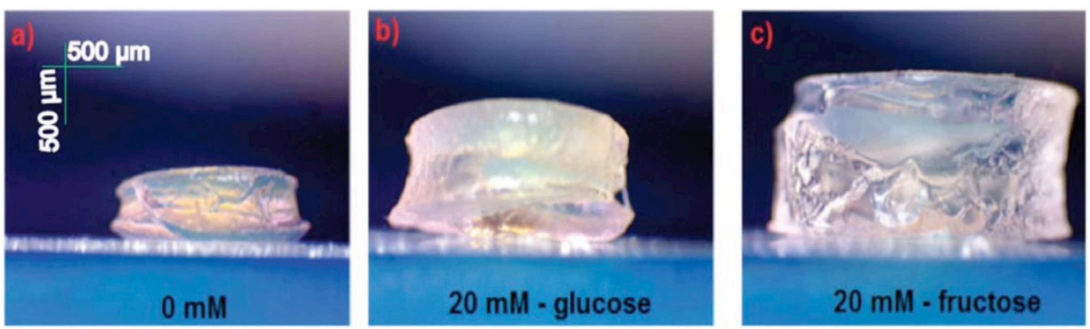


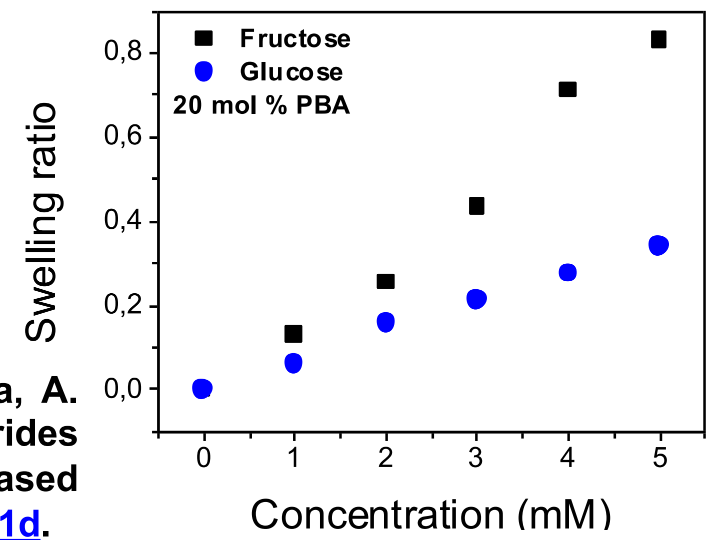
Sugar-Responsive Soft Hydrogels





Acrylamide-*co*-PBA Polymer





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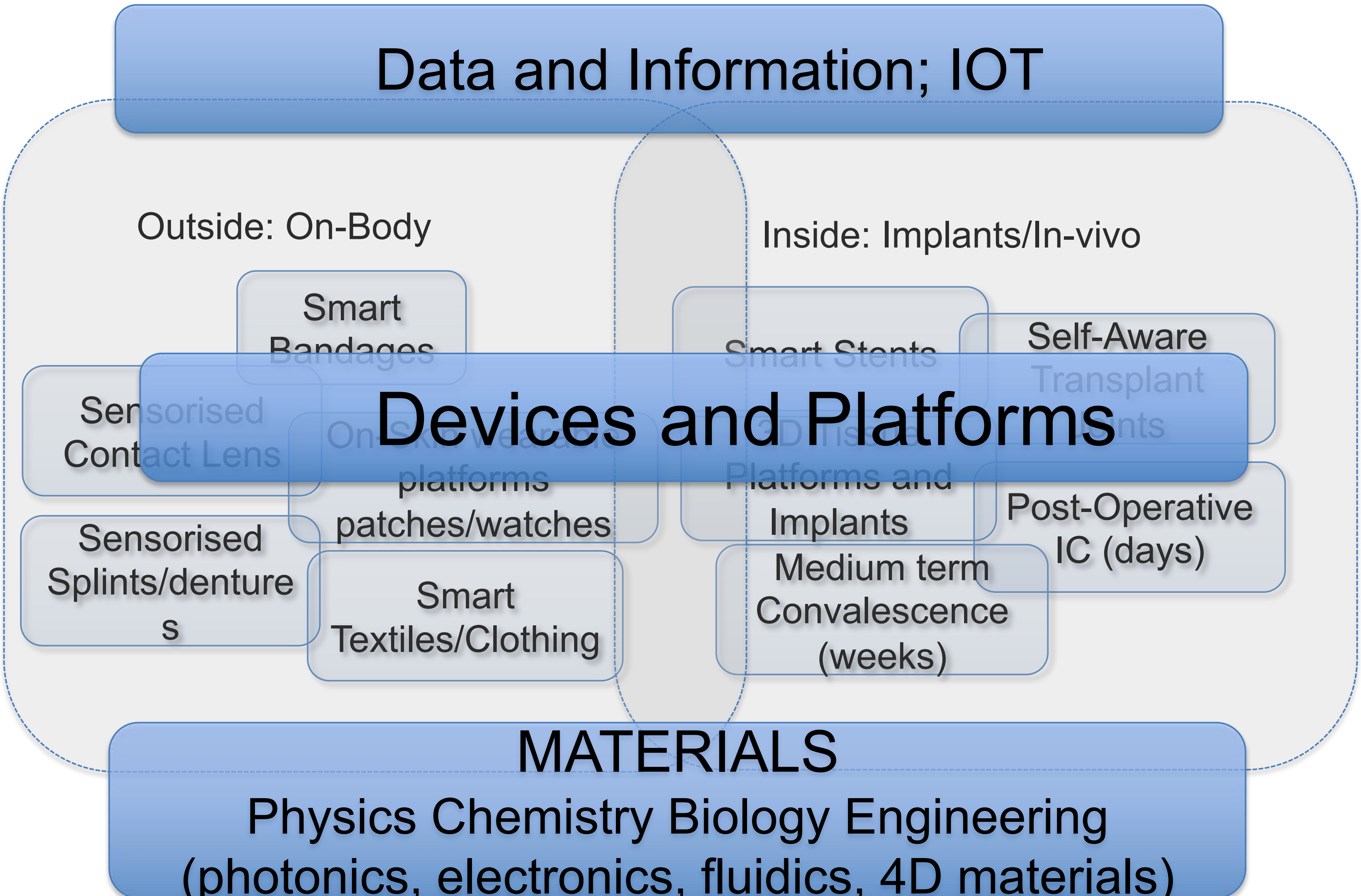
Merging of Materials, Devices and Data



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- Enterprise Ireland
- Research Partners – academic and industry
- H2020: Holifab Project

Jean Louis Viovy (Fluigent) , Mark Bowkett (TE Laboratories), Laurent Malaquin (LAAS)

THE FRAMEWORK PROGRAMME FOR RESEARCH AND INNOVATION
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Thanks for the invitation!