‘Sensing the Molecular World - Challenges and Opportunities’

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Invited Seminar Presented at GE Global Research
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Calixarene Ionophores – controlling the selectivity

H₃C—O—C—CH₂—

Na⁺
Blood Analysis; Implantable Sensors

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
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.
Microdialysis sampling via arterio-venus shunt


Real Time Blood Glucose and Lactate

System functioned continuously for up to three hours!
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. E-mail 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...
Accuracy in use depends on:
• Very reproducible manufacturing with stable, reliable materials
• Testing of representative sub-populations of sensors
• Single shot use model

Abbott Diabetes (Ireland) manufactures 100,000’s of electrodes per week using high volume printing to deposit highly accurate amounts of materials in precise locations; (carbon tracks and substrate layer, glucose oxidase enzyme layer, mediator layer..)
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.
- 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.²

² Most people did not feel any discomfort under the skin while wearing the Freestyle Libre sensor. In a study conducted by Abbott Diabetes Care, 82.4% of patients surveyed (n=323) strongly agreed or agreed 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.]

² Sensor is water-resistant in up to 1 metre (3 feet) of water for a maximum of 30 minutes

See [http://diatribe.org/drugdevice-name/freestyle-libre](http://diatribe.org/drugdevice-name/freestyle-libre)

- ‘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
But not everything is integrated…..

- Many components are located off-chip
- Detectors, pumps, valves….
- Hard Materials

- Fluidic Interconnects can get very messy
- Most of the ‘Chip’ has no function

Photoswitchable Actuators

- UV
- VIS
- Δ

**Merocyanine Spiropyran**

**ABSORPTION**

- Off (spiropyran)
- On (merocyanine)

**Absorbance (ABS)**

- 400 450 500 550 600 650

**NM**

- 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°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

\[ \text{pNIPAAm} \]

Hydrophilic | Hydrophobic
---|---

Hydrated Polymer Chains  $\xrightarrow{\Delta T}$ Loss of bound water $\rightarrow$ polymer collapse
Photo-actuator polymers as microvalves in microfluidic systems

Optimisation of valve dimensions

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

1.6 mm mask


Functional Organic Materials and Devices, Department of Chemical Engineering and Chemistry, and Institute for Complex Molecular Systems, Eindhoven University of Technology
INSIGHT Centre for Data Analytics, National Center of Sensor Research, Dublin City University, Dublin 9, Ireland
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
Photocontrol of Assembly and Subsequent Switching of Surface Features

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

High crosslink density

Low crosslink density

Light source

\[ \lambda = 455 \text{ nm} \]

acrylic acid, 5 mol%  MBIS, 1-2 mol%  Darocur 1173, 1 mol%

\[ \text{SPA, 1 mol\%} \]

NIPAAm, 91-92 mol%
Spiropyran and Metal Ions

The binding of many metals, such as Cu$^{2+}$ and Co$^{2+}$, to the phenolate of the MC form has been demonstrated.

Increase in absorbance below ~460 nm due to formation of MC-Cu$^{2+}$ complex

Decrease at 540 nm as free MC concentration decreases
Detection of switching between SP/MC/MC-Cu$^{2+}$ states using the ‘Discophotometer’

Polymethacrylic acid surface

PMMA

PMMA

EDC

PMMA

Various diamino alkyl linkers

Intermediates (carboimide, carboxylate)

Each –CH2- link is ca. 1.5 Å

Can be immobilised on polymer or silica surfaces, or within bulk materials, e.g. using SP-modified monomers

<table>
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<th>Tether Length (n=)</th>
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<tr>
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Switching SP-Doped Films

UV LED 380 nm

Green LED 523 nm
LED-Based Device for Switching and Monitoring SP-MC: The Discophotometer
Multiple Switching of SP-MC using LEDs

- Take measurements R,G,B (flash <1s)
- UV LED ‘on’ 10 s; wait 10 s; repeat measurements
- Green LED ‘on’ 10 s; wait 10 s; repeat measurements
- Green channel more sensitive as expected
- >2,000 repeat switches performed on a single surface
ROMP Chemistry – thick SP polymer ‘brush’ films

Switchable Uptake and Release – ‘Post Column’ Detection

\[ \text{Co}^{2+} + \text{PAR} \rightarrow \text{PAR-Co}^{2+} \]

410 nm

510 nm

UV

ACN

Injection Loop

Co\(^{2+}\) sol.

SP-modified micro-capillary

Non-modified micro-capillaries

Post-column reagent (PAR)

Micro-syringe pump

USB4000 Spectrometer

Halogen Lamp

410 nm

510 nm

A(410) - A(445)

10 per. Mov. Avg.(A(410) - A(445))

10 per. Mov. Avg.(A(430) - A(445))

PAR-Co\(^{2+}\)
Chemotaxis – Autonomous Movement to a Plume Source with IL Droplets

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

Electronic structure calculations and physicochemical experiments quantify the competitive liquid ion association and probe stabilisation effects for nitrobenzospirropyran in phosphonium-based ionic liquids, D. Thompson et al., Physical Chemistry Chemical Physics, 2011, 13, 6156-6168.
Channels that can sense...

- PANi deposited on channel walls - Channels are now inherently responsive e.g. pH sensitive
- Status can be determined at any location within the channels using low cost digital imaging
- Presented at: μTAS 2011 (MicroTAS) Conference, Seattle, October 2-6, 2011
Background

Stereolithography

- Single photon absorption
- 2D patterns

Two-photon polymerisation

- Two photon absorption
- 3D structures
Near Term Applications (5Years)

Data and Information; IOT

Outside: On-Body
- Smart Bandages
- Sensorised Contact Lens
- Sensorised Splints/dentures
- Smart Textiles/Clothing

Inside: Implants/In-vivo
- Smart Stents
- Platforms and Implants
- Medium term Convalescence (weeks)
- Post-Operative IC (days)
- Self-Aware Transplant Joints

Devices and Platforms

MATERIALS
- Physics Chemistry Biology Engineering (photonics, electronics, fluidics, 4D materials)
SWEATCH Device

1. Custom-built electronics with wireless communication (Shimmer)
2. 3D printed casing
3. Microfluidic chip + ISE
4. 3D printed sweat harvester and sensor connections

- Rapid prototyping techniques such as laser ablation and 3D printing are utilised to custom build various components including casing and sweat harvesting device (the Australian National Nanofabrication Facility – Materials node and the Nano-Bioanalytical Research Facility (NRF) in Dublin City University)
• Calibration of a Na\(^+\) SS-ISE and SS-RE output signal using the Shimmer board, giving a slope of 56.98mV and an R2 value of 0.99.
On Body Trials

Time to re-think the game!!!

- New materials with exciting characteristics and unsurpassed potential…
- Combine with emerging technologies and techniques for exquisite control of 3D morphology
- And greatly improved methods for characterisation of structure and activity
- Learn from nature – e.g. more sophisticated circulation systems for ‘self-aware’ sensing devices!
- Integrate flexible electronics, fluidics, photonics

Develop disruptive ‘revolutionary’ solutions
In parallel to ‘evolutionary’ improvements
Thanks to:

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Thanks to &