“Stimuli-Responsive Polymers: The Key to Revolutionary Developments in Chemical Sensing”

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Dublin City University

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INSIGHT

- €45 million SFI + ca. €30 million industry
- July 2013-June 2019; >200 researchers
- Focused on ‘Big Data’; Sensor Networks; Cloud based data
- Clinical/Personal Health and Environmental Applications
- Big emphasis on ‘citizen scientist’ (quadruple helix of research’)

INSIGHT 2013-2019
>300 researchers
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’

Chemo/Bio-sensing involves selective BINDING & TRANSDUCTION on the device surface; this also implies the target analyte MUST meet the device surface (LOCATION & MOVEMENT). It provides a signal observable in the macroscopic world (COMMUNICATION).
Calixarene Ionophores – controlling the selectivity

Blood Analysis; Implantable Sensors

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

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

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

Planar ISE arrays for blood profiling: VP-SEM (SenDx Corporation, Laguna, California ca. 2000)

Use for up to 200 assays -> replace
The dominant model for success (outside specialised laboratories) for clinical applications of chemical sensors and biosensors is primary based on short-term use, disposable devices.

Forget about long-term implants.

Lets try environmental monitoring…..
- Ca. 3,600 floats: temperature and salinity
- Only 194 reporting chem/bio parameters (ca. 5%)
- Of these nitrate (27), DO (193), Bio-optics (18), pH (2)

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

‘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
pH sensing – wasn’t that solved by Nikolskii in 1935?

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
After decades of intensive research, our capacity to deliver successful long-term deployments of chemo/bio-sensors in remote locations (e.g. environmental, in-vivo clinical) is very limited.
Direct Sensing vs. Reagent Based LOAC/ufluidics

Direct Sensing

- Outside world
- Sensor
- Sample
- Molecular interactions

LOAC Analyser

- Sample, standards
- Reagents
- Reaction manifold
- Detector
- Source
- Waste
- BL
- s
- t

Sample Blank
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.

Achieving Scale-up

1. Evolutionary development, cost driven down, reliable, improved scalability

2. Revolutionary breakthroughs in materials science; hidden complexity, biomimetic platforms, all fluid handling integrated on chip, indefinitely self-sustaining

Current platforms

<table>
<thead>
<tr>
<th>Cost/Complexity</th>
<th>Current Platforms</th>
</tr>
</thead>
<tbody>
<tr>
<td>€ &gt; 2,000</td>
<td></td>
</tr>
<tr>
<td>€ &gt; 20,000</td>
<td></td>
</tr>
<tr>
<td>€ &lt; 200</td>
<td></td>
</tr>
<tr>
<td>€ &lt; 20</td>
<td></td>
</tr>
<tr>
<td>€ &lt; 2</td>
<td></td>
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</tbody>
</table>

Massively scaled deployments of the future
Cost Comparison Analyser (€)

The €20 analyser

Graph showing cost comparison of Gen1, Gen2, and Future. The cost breakdown includes Fluidics, Electronics, and Housing.
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
(Takuzo Aida)

UV

VIS, Δ

Slide 16
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

![Polymer Structures Diagram](image-url)
Controlling gel properties using Ionic Liquids (phosphonium $[P_{6,6,6,14}]$ based)

<table>
<thead>
<tr>
<th>Ionogel</th>
<th>Axial stiffness/N mm$^{-1}$</th>
<th>UTS/MPa</th>
<th>Elongation at break (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>[dbsa]$^-$</td>
<td>0.1713</td>
<td>0.12</td>
<td>187.19</td>
</tr>
<tr>
<td>No I.L.</td>
<td>0.0493</td>
<td>0.08</td>
<td>65.910</td>
</tr>
<tr>
<td>[tos]$^-$</td>
<td>0.0187</td>
<td>0.02</td>
<td>545.48</td>
</tr>
<tr>
<td>[dca]$^-$</td>
<td>0.0149</td>
<td>0.02</td>
<td>131.53</td>
</tr>
<tr>
<td>[NTf$_2$]$^-$</td>
<td>2.9340</td>
<td>0.22</td>
<td>68.210</td>
</tr>
</tbody>
</table>

Fig. 3  (a) Photo-responsive polymer gels after immersion of the mould in a 1 mM HCl solution for 2 h. Right: [dca]$^-\$ ionogel shrinking process; (b) ionogel before illumination and (c) the same sample after 2 s illumination with a white light LED, size decrease is ca. 30% by volume.

Fig. 6  Response kinetics of ionogels upon irradiation with white light (ionogel height error: ±5 μm).
Photo-actuator polymers as microvalves in microfluidic systems

Actuation Mechanism

SPIRO (contracted)

H⁺, X⁻, solvent → acidic solution → H⁺, X⁻, solvent

white light

MERO-H⁺ (expanded)

Mechanism involves diffusion of protons, counter ions & solvent out/in of the bulk gel to/from the external solution.

X:Y:Z = 1:99:5
So far, so good: but what are the limitations?

- Response time for re-swelling is slow - 10’s of minutes due to diffusion mechanism
- Swelling requires protonation of the MC to MC-H\(^+\) within the ionogel by the external bathing solution
- These issues more or less limit the applicability of the valves to single use
Self protonating photoresponsive gel

Ziolkowski et al., Soft Matter, 2013, 9, 8754–8760

Previously proton source was external (acidic soln. required)
Protons, counter ions & solvent diffuse into/out of the gel

Now the proton exchange is ‘internalised’
The proton population is essentially conserved
Improved Extent and Rate of Contraction

![Graph showing relative gel swelling over white light irradiation time for different gels and conditions.](image)
Actuation Cycling without External Acidification

Ziolkowski et al., Soft Matter, 2013, 9, 8754–8760
Actuation Cycling without External Acidification

Samples have been recycled repeatedly over a period of 2 months

Ziolkowski et al., Soft Matter, 2013, 9, 8754–8760
Spontaneous Reformation of Acidified Merocyanine during Actuation Cycling in non-acidified water

Ziolkowski et al., Soft Matter, 2013, 9, 8754–8760

<table>
<thead>
<tr>
<th>Gel with 0 % AA</th>
<th>Gel with 5 % AA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Colour gradually changing from yellow to purple as H⁺ leaves the gel on each cycle.</td>
<td>Colour remains essentially the same, as H⁺ stays in the gel during cycling.</td>
</tr>
<tr>
<td>Switching changes from primarily MC-H⁺ -&gt; SP+H⁺ to MC -&gt; SP</td>
<td>Switching stays primarily as MC-H⁺ -&gt; SP+H⁺</td>
</tr>
<tr>
<td>Gel actuation stops.</td>
<td>Gel actuation continues.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>A</th>
<th>In the dark</th>
<th>After light irradiation</th>
<th>B</th>
<th>In the dark</th>
<th>After light irradiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>MC-H⁺</td>
<td>SP</td>
<td>2</td>
<td>MC-H⁺</td>
<td>SP</td>
</tr>
<tr>
<td>2</td>
<td>MC-H⁺</td>
<td>SP</td>
<td>3</td>
<td>MC-H⁺</td>
<td>SP</td>
</tr>
<tr>
<td>3</td>
<td>MC</td>
<td>SP</td>
<td>4</td>
<td>MC-H⁺</td>
<td>SP</td>
</tr>
<tr>
<td>4</td>
<td>MC</td>
<td>SP</td>
<td></td>
<td></td>
<td></td>
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</tbody>
</table>
Photoactuator Summary

- Need to optimise
  - Response kinetics
  - Extent of effect
  - Repeatability over time
  - Physical Ruggedness
  - Effective lifetime
  - Ease of fabrication; in-situ, spatial control/resolution
  - Cost per unit
  - ............

Lots of opportunity for materials science!
Can we go from this:
• Fluidic handling completely integrated into the microfluidic chip
• Valves actuated remotely using light (LEDs)
• Detection is via LED colorimetric measurements
Conclusions

• Linking ‘Applied’ and ‘Fundamental’ Research is critical

• Build micro/nano-scaled platforms capable of
  – Movement/intelligent location
  – Controlled binding and release of molecular pay-loads
  – Integrated communications capability

Disruptive approaches to remote chemo/bio-sensing will emerge from fundamental research in Materials Science!
Thanks for Listening!

- NCSRU, DCU
- CLARITY/INSIGHT
- Research Partners – academic and industry
- Funding sources – SFI, HEA, EI, MI, EPA, ARC, EU-FP7, IRCSET...

Thanks for the invitation