From Finger Prick Sampling to On-Body and Ultimately Implantable Chem/Bio-Sensors: The Key Role of Active Fluidics in Realising the Long-Term Functional Platforms of the Future

Dermot Diamond
INSIGHT Centre for Data Analytics, National Centre for Sensor Research, Dublin City University, Dublin 9, Ireland

Invited Lecture presented at
ACES 2017
Innovation Campus, University of Wollongong, 9th February 2016
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. A ferroxidase will attach to the membrane and be attacked by the enzyme, forming hydrogen peroxide and another product. The peroxide will migrate to a thin oxide membrane. In medicine and industrial settings, this reaction will track a wide range of biological reactions. And (by implication) it will work for years reliably and regulate glucose through feedback to insulin pump.
Current Approach: 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

Apply sensor with applicator

1. A thin flexible sterile fibre (5mm long) is inserted just below the skin. Most people reported that applying the sensor was painless

2. The 14-day sensor stays on the back of your upper arm and automatically captures glucose readings day and night.

3. The sensor is water resistant and can be worn while bathing, swimming and exercising³

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, 92% of patients surveyed (n=32) 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 5 days due to skin irritation in the area where the sensor touched the skin.

³ 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.
Sweatch......

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

See Poster Margaret mccaul, et al...
Remote, autonomous chemical sensing is a tricky business!
Direct Sensing vs. Reagent Based LOAC/ufluidics

Direct Sensing

outside world

sensor

signal

sample

molecular interactions

LOAC Analyser

reagents

sample, standards

source

Reaction manifold

detector

waste

s

BL

sample

blank

BL

t
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

Microfluidiccs – Evolution…

Engineering Inspired  →  BioInspired
But not everything is integrated.....
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
Bioinspired Fluidics
Photoswitchable Soft Actuators

UV ↔ VIS, Δ

Merocyanine Spiropyran

UV

Vis, Δ

ABS

Off (spiropyran)
On (merocyanine)

nm
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
Photo-actuator polymers as microvalves in microfluidic systems

Valve Optimisation

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

Photovalve Operation
Photocontrolled Flow rate

- 60s LED on
- 180s pulsed LED (1s on, 2s off)
- 180s LED off

Levels out ca. 4.0 µl/min

(1) Overshoot, and (2) Steady-state flow rate for this pulse sequence is ca.4.0 µL/min

Endo-Skeleton Controlled Actuation

Microscope images of micro-scale pillar array fabricated in PIL hydrogels by 2-PP showing the collapsed pillars before hydration (left) and after hydration (middle and right). The concentric contour slicing pattern used to create the microstructure is visible in the swollen hydrated structures and are very clear in the high resolution STED image (right) of rodamine modified hydrogels. The hydration process is fully reversible and shows shape-memory behaviour. (DCU unpublished results)
Flexible Conformable Displays… Flexible, Conformable Fluidics

But ultimately
3D ‘Soft’ Self-Aware Fluidics….
Thanks to…..

• Members of my research group: Simon Coleman, Peter McCluskey, Colm Delaney, Nigel Kent, Jeff Whyte, Aymen Ben Azouz, Jeroen ter Schiphorst, Albert Schenning

• NCSR, DCU

• Science Foundation Ireland & INSIGHT Centre*

• Enterprise Ireland

• Research Partners – academic and industry

• EU Projects: NAPES*, CommonSense, Aquawarn, MASK-IRSES, OrgBio