Printable Bio-Sensors for Healthcare and Other Applications

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Why Point of Care Biosensors?

- POC biosensors for disease diagnosis and condition monitoring is a large and growing market
  - Also growing markets in animal care, agriculture and food monitoring
- POC devices on the market can only test a limited number of analytes at the same time
  - Separate tests can be required to obtain the diagnosis,
  - Additional needs are
    - Wide dynamic range
    - Rapid (< 10 minutes)
    - Portable but accurate and sensitive
    - Cost effective
- We are developing together with Abingdon Health a printable organic electronics biosensor platform for healthcare and other applications
CDT Introduction

- CDT is a Cambridge University spin-out company to develop printable organic LEDs.
- Since 2007, has been part of Sumitomo Chemical Group
- More recently it's become an European based technology research centre for the group.
- Examples of current R&D projects
  - FlexOLED – low cost printed OLED
  - Organic Photodiodes (OPD) for x-ray and other applications
  - Flexible energy storage and capture solutions
  - Bio-sensors for medical, agricultural and environmental applications
    - Utilises CDT printed electronics technologies
    - In partnership with Abingdon Health
Abingdon Health Introduction

- Abingdon Health (AH) is focused on providing rapid multiplexed and near-patient medical diagnostics testing solutions.
- Developing a range of lateral flow immunoassays to allow diagnosis and monitoring of haematology-oncology conditions.

2016 Products

- Seralite© Serum, Seralite© Urine, ADxLR5 Reader, Seralite© Elisa
- Focused on Myeloma, both Seralite© assays (FLC-\(\kappa\) and FLC-\(\lambda\)) have robust analytical performance
  - Wide dynamic range (2.5 to 200 \(\mu\)g/ml)
  - Excellent linearity
  - Study of 395 samples \(\kappa/\lambda\) ratio to clinical diagnosis
    - Sensitivity = 99%. Specificity = 100%. Accuracy = 99%

ADxLR5 reader CE marked & Class I device (FDA) registered

Note: Sebia is the global distributor for Seralite© Serum
Biosensor Vision

- Integrate arrays of printed organic electronic components with a lateral flow device (LFD) to make a disposable, single use quantitative biosensor. i.e. FlexOLED and OPD technology

- Cost effective printable multi-channel system for multiplexed assays
  - Multi-biomarker panels
  - Extended dynamic range
  - Redundancy and repeats

- Thin, light-weight elements with planar emitters and detectors have potential for low coefficient of variation
  - Proximity integration of optical & fluidic elements
  - Reduced alignment errors
  - Area average over test & control lines
  - Compensate for LFD non-uniformity
Biosensor Vision

Build POC a cartridge with 18 parallel tests

Working Prototype Cartridge

FlexOLED

OPD

Working Prototype Cartridge Reader
Biosensor Performance

Biosensor/Desktop Reader Comparison

- Benchtop: Reflection Mode
- Biosensor: Transmission Mode

Same Strip Used in Both Devices

Wide Dynamic Range

- Desensitised
- Normal
- Low - Sensitivity
- Mid - Sensitivity
- High Sensitivity

Achieve wide dynamic range from one sample

Very high sensitivities less than 1 µg/ml demonstrated

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Optical Technology Options

- Absorption/Reflection
  - Measured response is due to a change in light intensity at the photodiode due to capture of the target molecule.
    - Simple architecture
    - Limited sensitivity

- Fluorescence
  - Molecule irradiated with a colour which is then re-emitted as a different colour of lower energy
    - Requires a filter to stop the excitation light impinging on the photodetector.
    - Potential for maximum sensitivity
Fluid Handling Options

- Two key fluid handling technologies
  - Lateral Flow Devices as shown before and used in pregnancy tests
    - Simple, very low cost
    - Sensitivity limited due to reduced range of bio-chemistry options
  - Micro-fluidic devices; patterned channels in plastic to allow more complex bio-chemistry to occur
    - More complexity therefore higher cost
    - Potential for higher sensitivity
Troponin Tests

- Troponin (cardiac I and T) are sensitive indicators for damage to heart muscle
  - Blood measurements can discriminate between angina and myocardial infarction (heart attack)
    - Post heart attack the troponin levels increase and peak at about 24 hours after the event
    - NICE (UK) recommends two tests 10 hours apart to monitor changes in troponin levels
      - However they recognise that with the availability of more sensitive tests this time can be reduced substantially.
  - Also Troponin increases, can be an indication of infections such as sepsis
- Troponin test has also become a gold standard for evaluating diagnostic tool capability.
**Troponin Assay**

- **Glass**
- Biotinylated-Ab
- AP-Ab
- Antigen (Troponin I)
- Blocking reagent (BSA)
- Streptavidin

**Enzyme Amplification**

**Optimised Assay**

- LOD of ~ 10 pg/ml

**Limit of detection potentially 1pg/ml = ~ 45 fM using microfluidic system**
Troponin Tests (~ 10% IVD market)

- **Troponin LOD**
  - 1pg/ml
  - 10pg/ml
  - 100pg/ml

- **μ-fluidic fluorescent system**
- **LFD absorption system**
- **Quantitative, objective, accurate**
- **Qualitative/subjective**

**Troponin Tests**

- **Troponin Trop T**
  - No reader, no capex, $10-20

- **Portable reader, capex**
  - $2-9K, ≤ $20

- **Desktop reader, capex**
  - $20-25K, ≤ $20

- **Laboratory equipment**
  - Capex $150-225K

**Troponin LOD**

- Siemens stratus
- Radiometer AQT
- Biomerieux minividas
- LOD 10-30 pg/ml

- Beckman coulter access
- Siemens advia centaur
- LOD 1-10 pg/ml

**Size and Cost**

- Troponin Tests (~ 10% IVD market)
  - µ-fluidic fluorescent system
  - LFD absorption system
Current Status (Fluorescent Platform)

Biomarker Class

- **Ions**
  - Na, K
  - Ca: 0.4-60 µg/ml

- **Small molecules**
  - Nitrate

- **Proteins**
  - Glucose: <10 µg/ml
  - C-reactive Protein: 300 pg/ml
  - Troponin: 10 pg/ml
  - DNA: 1 µg/ml

- **DNA/RNA**
  - DNA

Limit of Detection

- Fluorescence
- Organic Transistor

Developed a 4 channel Ion sensor
Where Next?

- With bench top sensitivity and wide dynamic range in a hand held device
- We are exploring additional applications where array diagnosis makes sense
  - Medical: i.e. Drugs of Abuse
  - Agriculture: fungal disease identification
  - Animal welfare
  - Food safety: contamination
- If this resonates with your needs please contact us!
Summary

- Printable organic electronic devices can be used to make very sensitive bio-assays
  - Using integrated FlexOLED and OPD commercially useful performance can be demonstrated.
- Working with Abingdon Health on the absorption/LFD based system
  - Large arrays of sensors can be used to test a wide range of conditions or to achieve a wide dynamic range from only one sample
  - CDT and Abingdon Health are scaling up the manufacturing process focused on the haematology-Oncology market
    - Myeloma (Diagnosis and Monitoring)
- We have also demonstrated using a fluorescent platform with a wide range of biologically relevant analytes
  - Achieving LOD for Troponin of 10 pg/ml
If you are interested to discuss applications please contact us

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