Laser-direct-write fabrication of paper-based point-of-care diagnostics

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Outline

- Paper-based microfluidics – POC diagnostics
- Our patterning approach – Laser-direct-write
- Patterning flow-paths and enabling flow-control in them
- Patterning for multiplexed detection on LFDs
- Patterning for improved sensitivity and limit-of-detection of LFDs
- Conclusion
Introduction - Paper-based devices

Low-cost alternatives to conventional POC diagnostic tools

- Inexpensive
- Biocompatible
- Wicks naturally
- Disposable
- Range of forms
- Easily stored and transported

Initial target application – POC diagnostic sensors that satisfy

- WHO defined ‘ASSURED’ criteria – Affordable, User-friendly, Equipment-free and Deliverable
- Aimed at requirements in countries with low-resourced settings
Introduction - Paper-based fluidics

Requirements for creating such devices on paper

- **Pattern paper** to form fluidic patterns
- **Deposit reagents** for implementing the assay
Our LDW patterning approach

Technique that allows *creation of fluid-flow channels/patterns in paper*

1. A local-deposition assisted laser-direct write procedure
2. Relies on the concept of light-induced polymerisation

Lasers used
Few mW of 405 nm c. w. lasers

Polymers used
Desolite 3471-3-14

Porous materials patterned
Cellulose, Nitrocellulose membranes, glass-fibre filters, and fabrics

Patterning speeds
> Metre per second
Patterning of porous materials

Results – patterning of user-defined devices

Device allows simultaneous detection of four different bio-markers from within a common fluidic ‘sample’.

- Yellow-green indicates the presence of BSA in the sample
- Purple-red indicated the presence of nitrite in the sample

- Example of a device which will enable multiplexed detection or semi-quantitative detection
- Can be a compact device, small footprint, but can be scaled-up, very easy
Patterning of Lateral-flow Devices (LFDs)

Lateral Flow Devices (LFDs) or Dip-Sticks

Their advantages -
✓ Used at point-of-care
✓ Provide rapid results (~few min.)
✓ Are easy-to-use
✓ Are affordable (~ few £s)

Their disadvantages -
✗ Detect a single condition or disease only
✗ Give a yes/no answer only
✗ Have low sensitivities

Hence have minimal clinical use
Introduction to multiplexed detection on LFDs

Current method – multiplexing in a single flow path

Results for multiplexed detection of CRP and SAA1 in a single LFD with multiple detection sites in the same flow path.

Drawbacks - undesired interference between different detection.
Detection of multiple inflammation markers on a single LFD

Results for detection of CRP and SAA1 using LFDs with multiple flow paths.

Advantages:
- No interference of multiple test sites positioned in the same flow path
- No need for increased device dimension
- No need for addition sample volume
Multiplexed detection of Leishmaniasis

Samples used – Serum and Whole blood
Healthy negative controls, Visceral Leishmaniasis, Chaga’s disease, Leprosy, Tegumentary Leishmaniasis
Introduction to improved sensitivity and limit-of-detection on LFDs

Example – sensitivity and limit-of-detection increase for a CRP assay

A clear signal enhancement can be observed with the decrease of the constriction widths for each concentrations.

- Improve the sensitivity of the assay by 62x;
- Improve the limit of detection by 32x.
Confinement of bacteria cultures using paper-based wells

Detection of MRSA Grown on Oxacillin Resistance Screening Agar

Detection of E. Coli Grown on Brilliance Coliform Selective Agar
Testing resistance of MRSA and MSSA to Oxacillin on paper-based mini petri dishes
Conclusion and Collaborations

Fabrication & preparation of paper-based devices by Laser-based direct-write (LDW) methodologies

- No need for specialist environment
- Flexible – changes to laser parameters
- Reducing of feature dimensions
- Rapid prototyping or even large-scale manufacture

✓ Offers a mature solution for multiplexing and enhanced sensitivity and limit of detection on LFDs.

Platform which can be adapted according to the needs
(our) platform + (your) assay = Device as per the user’s needs
Enabling point-of-care diagnostics of the future

LaserWrite™ - patented technology

Business Statement:

A spin-out company from The University of Southampton to commercialise novel technology that enables the research, development and manufacture of multiplexed and quantitative point-of-care diagnostic devices by creating fluidic structures within materials used in lateral flow devices.

Visit us on: http://highfielddiagnostics.co.uk/
Thank you!

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Fellowship - Institute for Life Sciences and the Faculty of Medicine
LDW for fabrication of paper-based devices

Polymer barriers compatibility

1. The following table shows the compatibility of various solvents and reagents with the photopolymer barriers;

<table>
<thead>
<tr>
<th>Aqueous Solvent</th>
<th>Compatibility</th>
<th>Polar Organic Solvent</th>
<th>Compatibility</th>
<th>Non Polar Organic Solvent</th>
<th>Compatibility</th>
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</thead>
<tbody>
<tr>
<td>BSA</td>
<td>Yes</td>
<td>Acetone</td>
<td>Yes</td>
<td>Hexane</td>
<td>Yes</td>
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<tr>
<td>Buffers pH 3 to 10</td>
<td>Yes</td>
<td>Isopropanol</td>
<td>Yes</td>
<td>Toluene</td>
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<tr>
<td>PBS/TBS</td>
<td>Yes</td>
<td>Ethanol</td>
<td>Yes</td>
<td>Xylene</td>
<td>Yes</td>
</tr>
<tr>
<td>Surfactants</td>
<td>Yes</td>
<td>Methanol</td>
<td>Yes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td>Yes</td>
<td></td>
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</tr>
</tbody>
</table>

2. No degradation with time (6 months) and temperature (RT – 120 °C);
Single-step colorimetric assay on cellulose

- Patterned cellulose paper used for detection of BSA and Glucose
- Semi-quantitative detection using a mobile phone camera
Requirements for creating such devices on paper

- Pattern paper to form fluidic patterns
- Deposit reagents for implementing the assay