IFSA - A microfluidic chip-platform for frit-based immunoassay protocols

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Opportunities

Microfluidic device market - Value and forecast
(Emerging Markets for Microfluidic Applications report, Yole Développement, 2011)

Total market growth 2011-2016 CAGR 24%

Total market growth 2008-2010 CAGR 18%

- Clinical & veterinary diagnostics
- Industrial and environmental
- Point of Care diagnostics
- Drug delivery (inhalers, micropumps, microneedles)
- Pharmaceutical and life science research
- Micro Reaction Technology
- Analytical devices

Microfluidic Device market in $M

Motivation

Currently main interest in molecular diagnostic assays due to value proposition and complexity

Source: www.biocartis.com
Source: www.cepheid.com
Motivation

However, mainly standard clinical tests are much simpler and based on immunoassays.

Assay steps:
1. Primary antibody bound to substrate
2. Add target analyte (antigen), incubate and wash
3. Add secondary antibody, labelled with fluorescent dye
4. Alternatively add secondary antibody bound to nanoparticle cluster
Methods

Achievable sensitivities of immunological POC tests for a typical 100 kDa protein
Methods

Signal enhancement methods to improve sensitivity:

1. Using frits instead of blank surfaces to increase number of binding sites

2. Using a signal amplifying label such as polymerized horseradish peroxidase (Poly-HRP)

3. For colorimetric detection (optical density), use self-assembling colored nanoparticles as labels (higher OD)
Chip Concept

1. The microfluidic cartridge should be able to contain all required reagents in dried or liquid form
2. The fluidic architecture should be as simple as possible and allow for multiple tests per cartridge
3. All manufacturing steps should be scaleable for volume production
4. The detection method should be as simple as possible yet yielding quantitative results

1: 2 x 120 µl reagent reservoir
2: Sample inlet port, geometry optimized for pipette tips
3: 3 lanes with 4 immunofiltration frits (diameter 2.5 mm, height 2 mm)
4: 300 µl waste reservoirs
5: Venting channel
Actual chips

- Microscopy slide size
- Injection molded COP
- Optimized for operation with pipetting robots
Instrumentation

Liquid handling
Resolubilized reagents are flown over frits

Optical readout of the chip for the colorimetric assay using two optical sensor
Results

Calibration of the chip with respect to conventional immunofiltration tubes (ABICAP) using C-reactive protein (CRP) and the poly-HRP assay
Results

Calibration of the chip with respect to conventional immunofiltration tubes (ABICAP) using C-reactive protein (CRP) and the nanoparticle agglomeration method.
Conclusions

• Microfluidics can play a role in improving immunoassays (ELISA) in handling as well as performance

• The microfluidic device for such applications has to be optimized for simplicity, multiplexing and production cost

• Methods to improve assay sensitivity (frits, poly-HRP and nanoparticle agglomeration) have been successfully proven
ACKNOWLEDGEMENTS

IFSA consortium:

Part of the work was funded within the frame of the BMBF project IFSA, FKZ: 16SV5417

We thank all partners in the projects for their support and collaboration