Microfluidics as an enabler for Medical Diagnostics

Henne van Heeren, enablingMNT

"Microfluidics: The ability to create complex channel manifolds on a single substrate with no dead volume between connecting channels which allows to integrate a variety of chemical handling operations without significant dilution or band spreading."

PoC-ID

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PoC-ID project

The aim of the PoC-ID project is to develop new micro- and nanoelectronic-based sensing and integration concepts for advanced miniaturised in vitro diagnostic devices.

The project addresses the increasing demand for rapid and ultra-sensitive point-of-care diagnostics to reduce healthcare costs and increase the quality of life with a focus on infectious diseases, one of the world's leading causes of morbidity and death.

Interdisciplinary collaboration using the technology and expertise of the consortium members will help to develop and test a breakthrough PoC prototype for the diagnosis of respiratory syncytial virus infections and host responses in the paediatric context.

Why microfluidic-based systems?

Diagnostics & analytical:

- speed of delivery testing results,
- technology platforms that can be reused for other test assays,
- customisation to optimize for specific applications,
- size of system, i.e. portable device for point of care applications, and
- specialization for small volume /smaller sample sizes.

(Chemical) processing:

- safety,
- higher yield,
- ease of up and down scaling.

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Flowrate examples

~10 µl/min

~5 ml/min

~100 ml/min

"Microfluidics"

Medical devices

Drug delivery

Point of Care diagnostics

Analytical instruments

(Bio) chemistry

Factory automation

Semiconductor industry

1 nl/min

1 µl/min

1 ml/min

1 l/min

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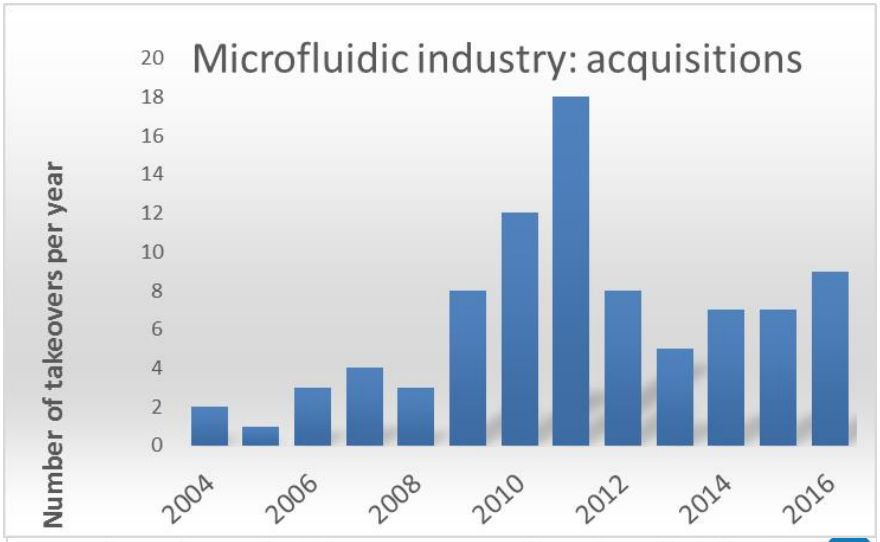
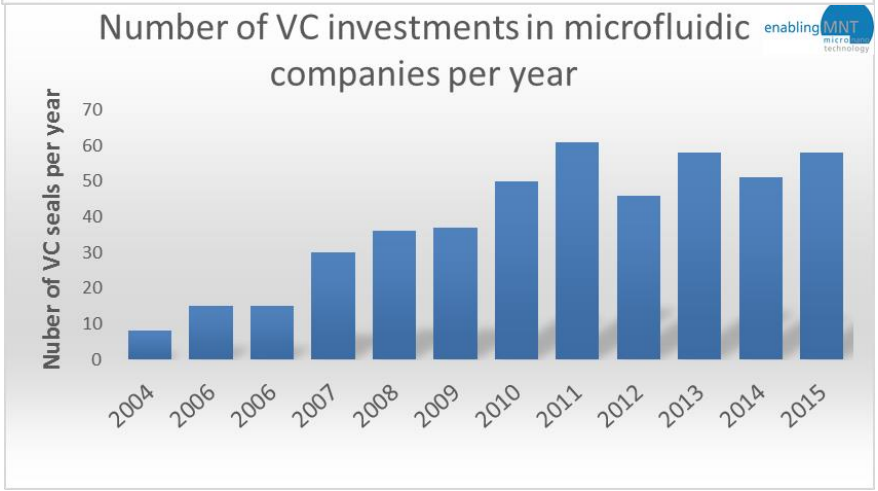
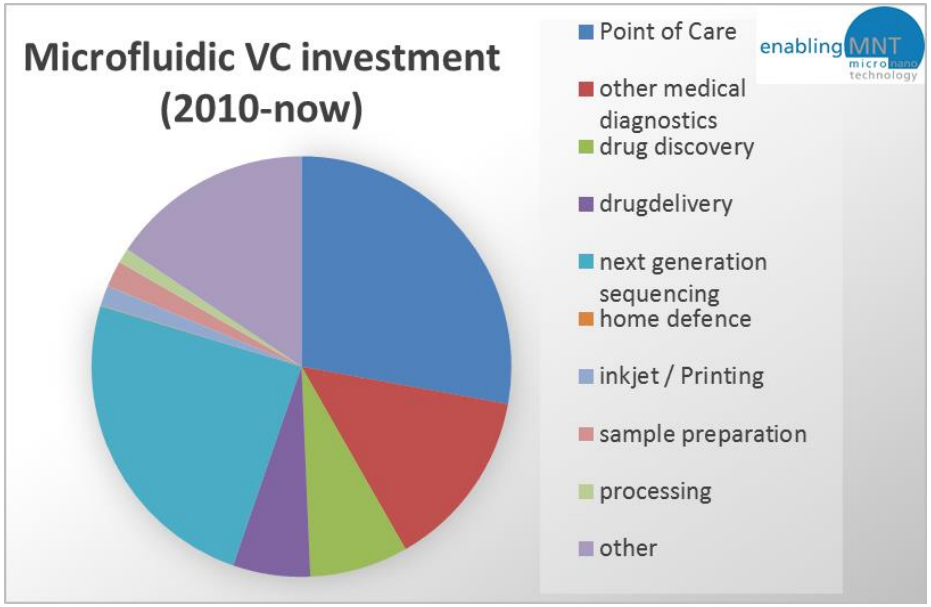
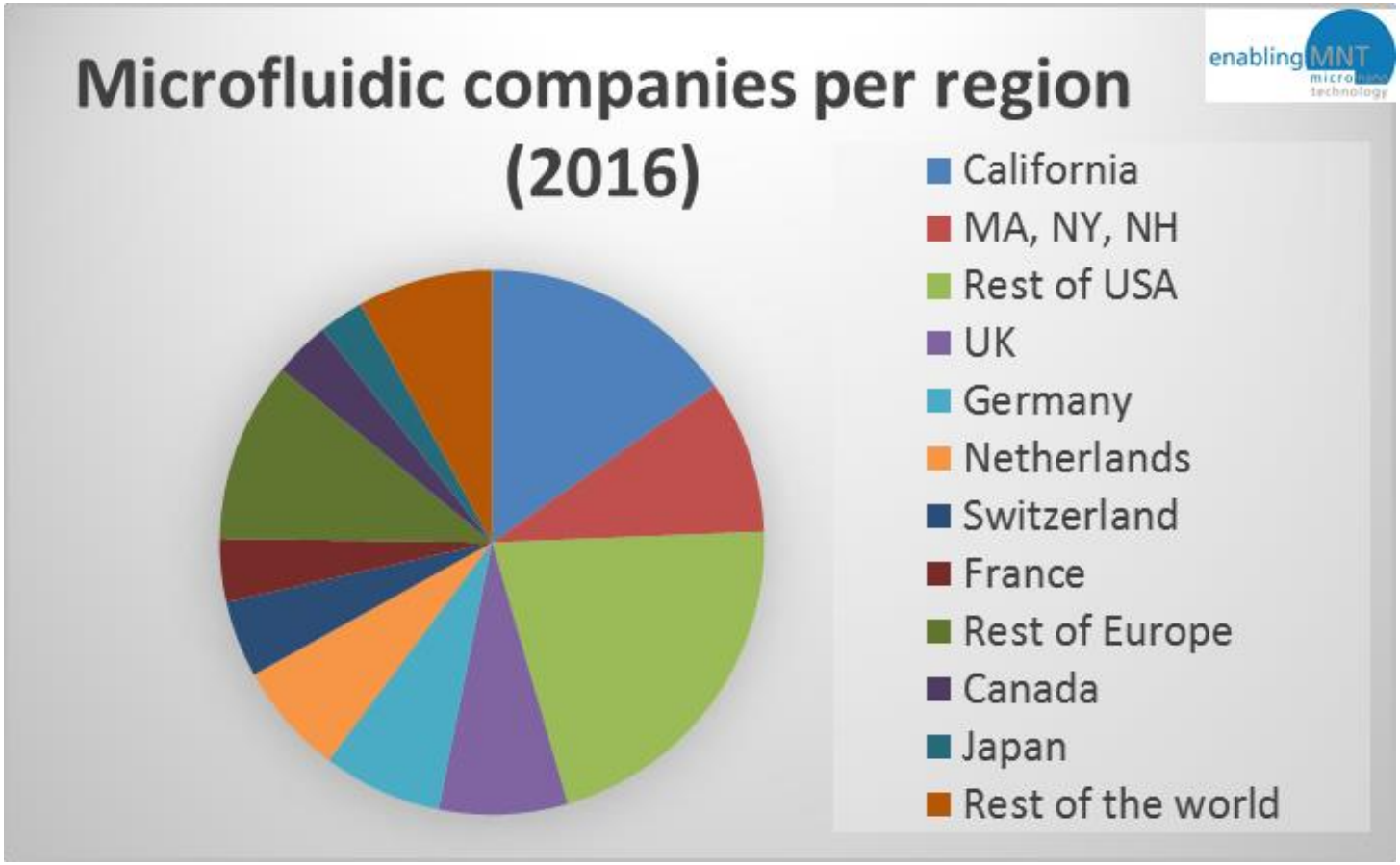
Continuing interest from investors





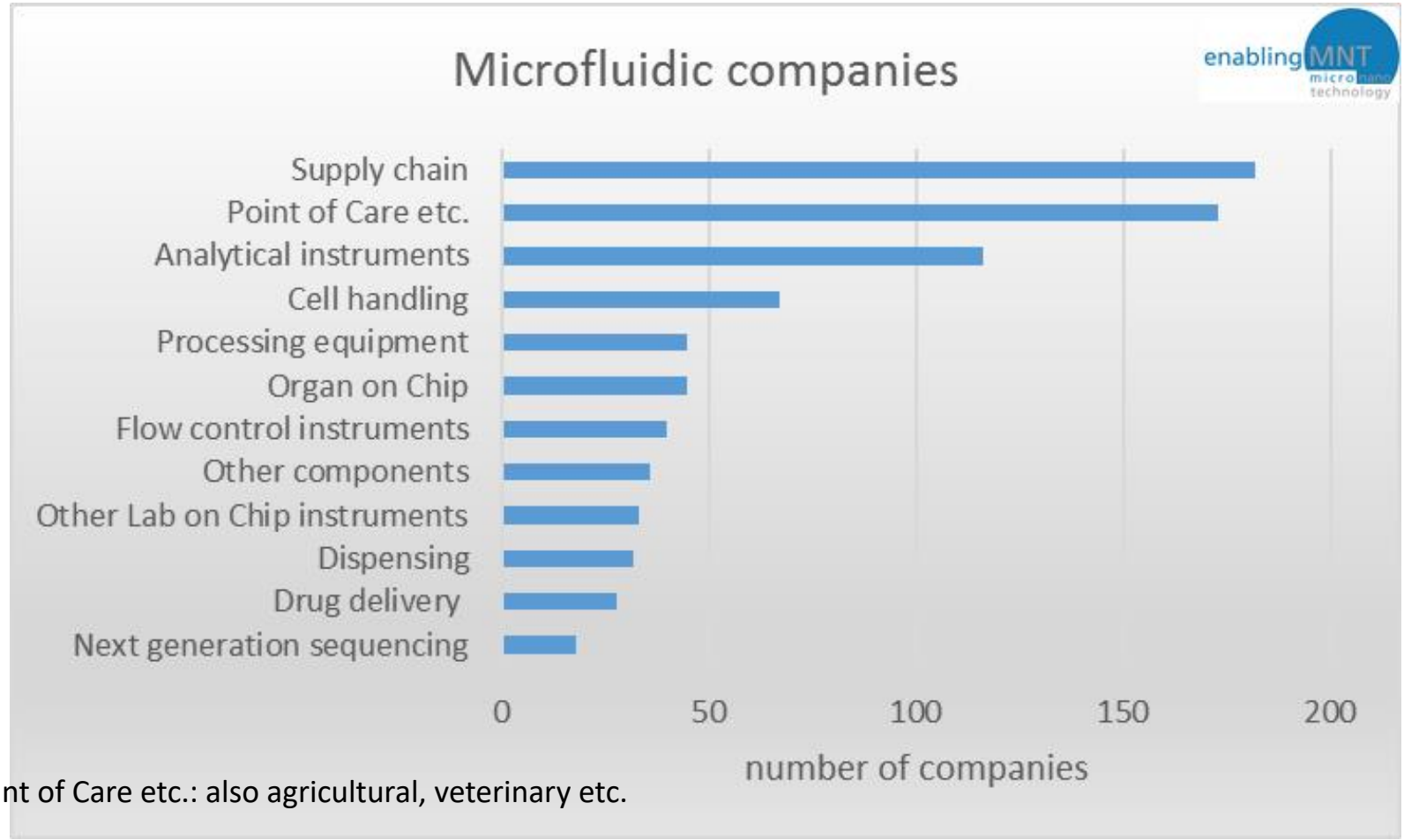


Hotspots
(based on list of 746 companies)



Microfluidic companies, orientation

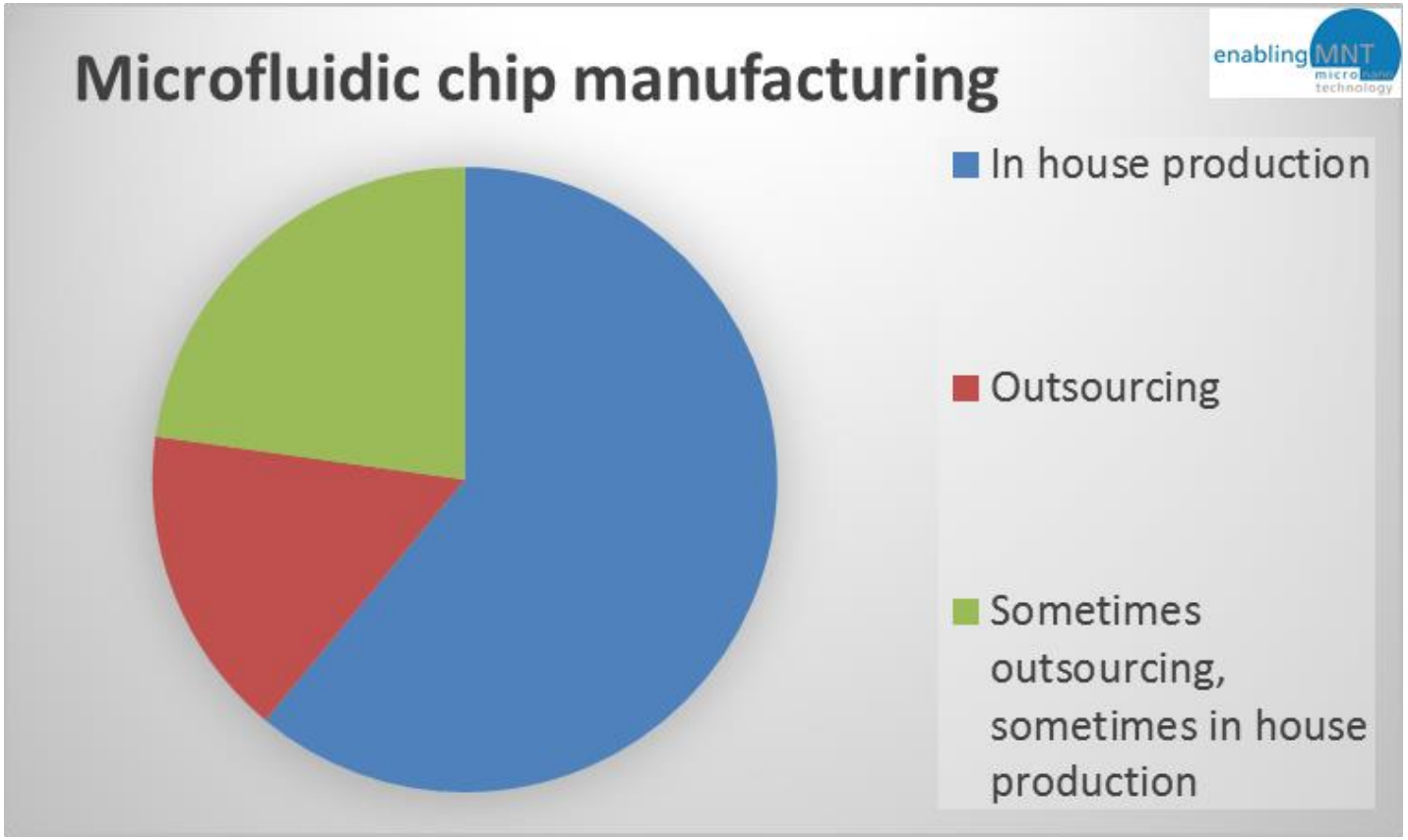
(based on list of 746 companies)



Point of Care etc.: also agricultural, veterinary etc.

“Do it yourself” is marketleader!

(based on a survey among microfluidic experts)



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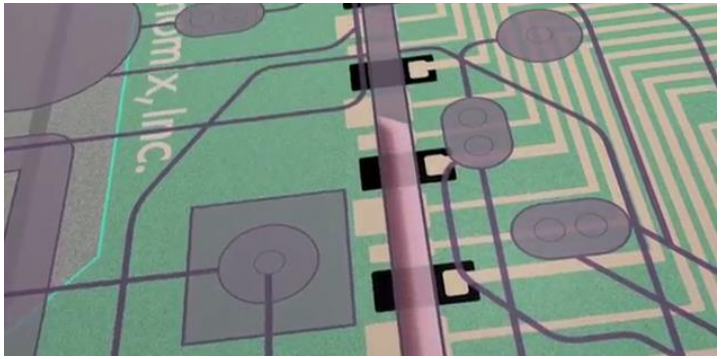
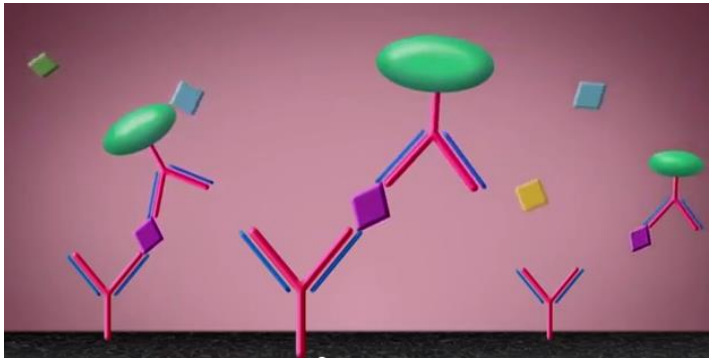
Point of care medical diagnostics

Minimal amount of liquid

Portable, fast and easy to use



Detection of many biomarkers in parallel



High specificity

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Success story Abaxis:

Spent $100 million and almost 20 years to get the product to market. Runs a full chemistry analysis (several panels available) from just five drops of blood in about 10 minutes.

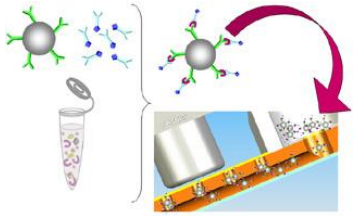
7.9 cm disk made of molded 2 cm PMMD containing a series of interlinked internal chambers and passages. Chemicals on board.

Fifteen cuvettes are reserved to analyze the patient´s sample and further ten are used as internal quality control.

Fluid control by varying the spinning speed.

In 2013 7.4 M disks sold and 28000 systems, 142 M$ TO, operating revenue 45 M$.

Bewildering number of technologies and concepts



Bionas.

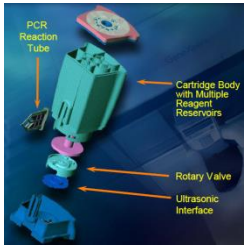
Simultaneous measurements of:

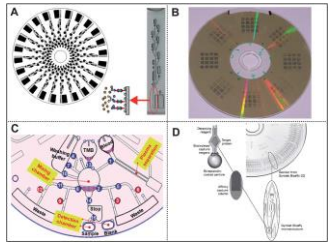
-pH

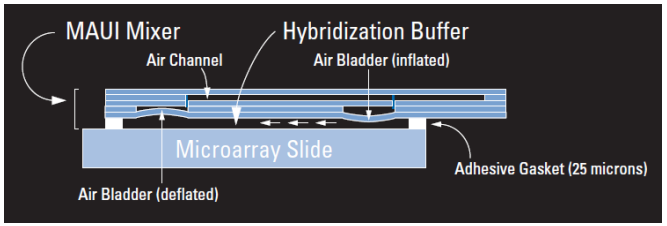
-O_2 consumption

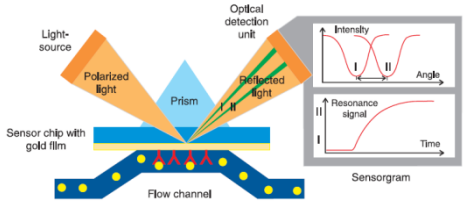
-Adhesion/confluency

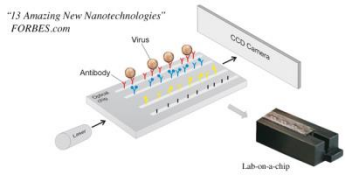
Online/real time measurements.

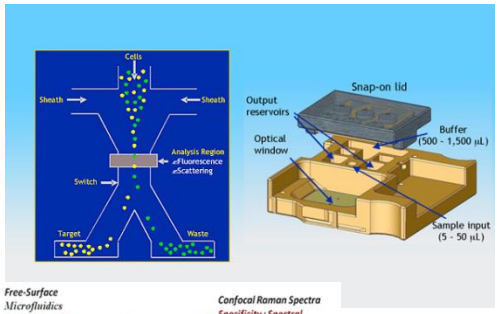


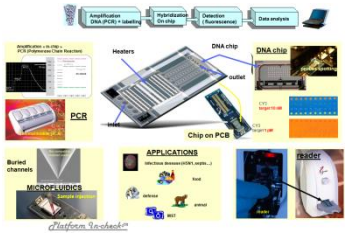


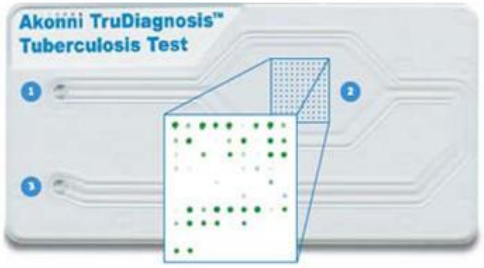


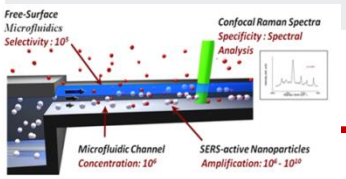


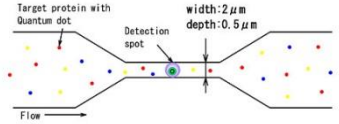


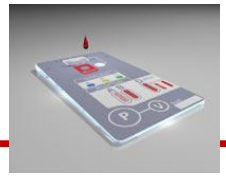


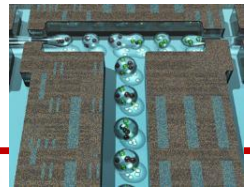












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PoC applications

Application	Medical diagnostics	Emergency care	Companion diagnostics
Goal of testing	Estimate what disease causes the complaint.	Confirm the disease or determine the specific variant.	Progress of the disease, effectiveness of treatment or check of recurrence after treatment.
Frequency	Incidental.	Incidental.	On a regular base.
Biomarker	Often test for a range of diseases. i.e. several markers simultaneously.	Optimized for one specific (set of) marker(s).	Optimized for one specific (or a very limited number of) marker(s).
Point of use	In a GP's office or in a hospital.	In or near an ambulance, in a hospital.	In a GP's office or at the patient's home.
Indication of allowable cost / disposable	<10 $.	<100 $.	<1 $.
Prefered time to result	<5 minutes for GP, <20 minutes other settings.	<20 minutes.	<5 minutes in the GP's office, in a home setting up to one hr is acceptable.

Where is the technology going to?
(example HIV diagnostics)

Status now:	Portability:	Staff training:	Instrument cost:	Disposable cost:	Time to result (min):	Technology:
State of the art	Benchtop	Moderately trained	10 K$	4 $	20	Labeling / Fluorescence
In development	Benchtop / portable	Moderately trained	1 k$	< 8 $	< 10	Diversity
In early development	Portable	Basic training	< 1 k$	< 2 $	< 10	Direct detection, on board chemicals
Ultimate goal	Handheld	Minimally trained	<100$ (or without a system)	< 0.5 $	< 5	?

Point of Care: drivers versus barriers

Drivers / benefits

Aging population

Personalized medicine

Need for fast decisions

Tuning medication

Enabling patient centred healthcare / selfcare

Cost reduction

Barriers

Reimbursement

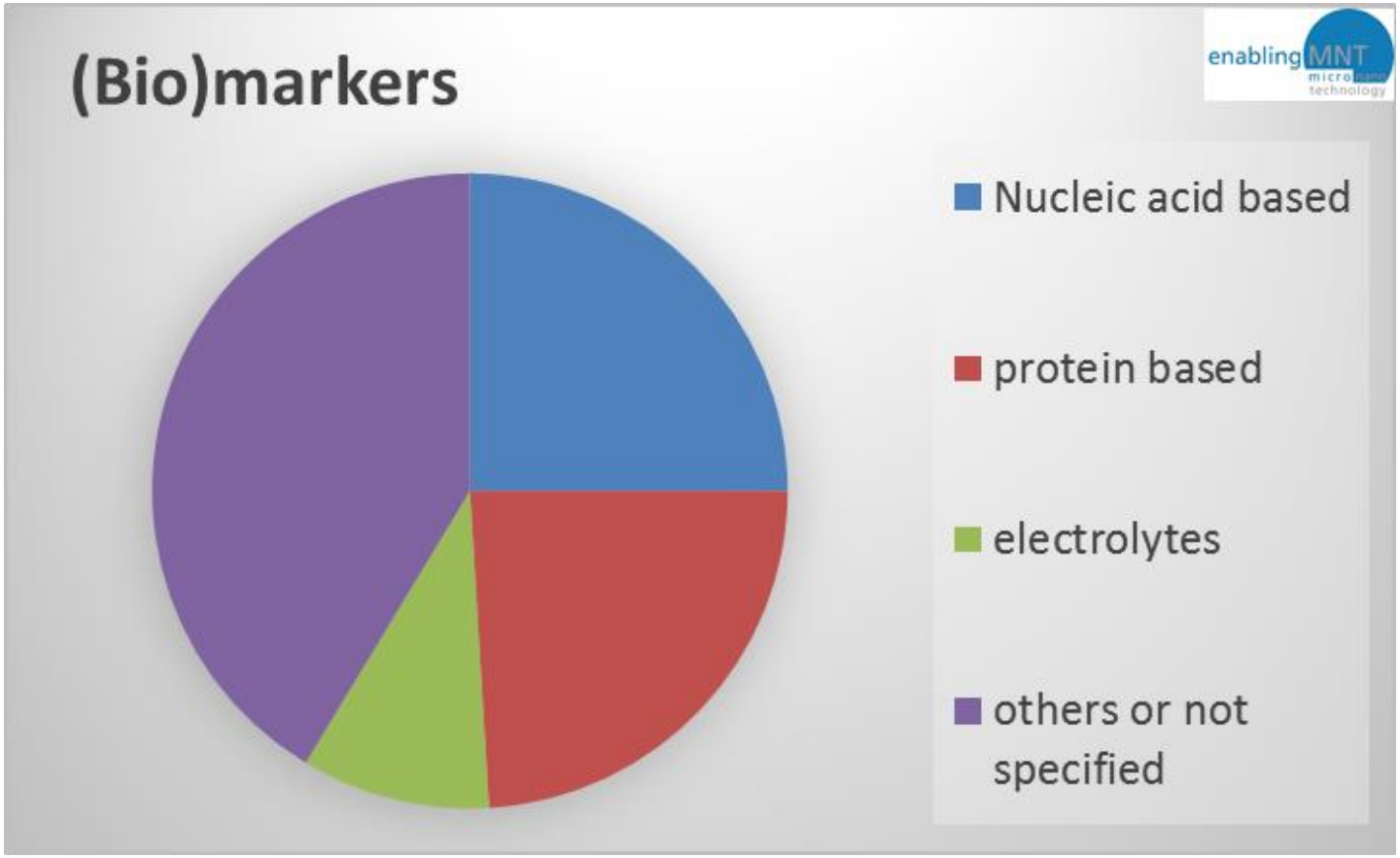
Upstream cost versus downstream benefits

Meeting the gold standard

Development cost

Which biomarkers are of interest?

(based on an analysis of 98 Lab on Chip systems)



Microfluidic based medical diagnostics, hot applications

Blood gasses / electrolytes

Cardiac markers

Coagulation monitoring

Infectious diseases

Cancer markers

Molecular Diagnostics

- Molecular diagnostic techniques, are used to analyse biomarkers based on nucleic acids, that help to diagnose diseases, prognose the likelihood of a disease in the patient and determine the most effective therapies.
- Intensive use of nano- and microfluidic technologies to enable integrated sample preparation, DNA amplification and sensing.
- Many of the technologies developed for this have found other applications in for instance food safety, home defence etc.

Challenges and opportunities for Molecular Diagnostics

- The Molecular Diagnostics industry is characterised by:
  - rapidly and continuously changing technology,
  - evolving market standards,
  - changes in customer needs,
  - intense competition (new product launches, also emerging companies)
  - long product life cycles

In the context of infectious diseases > genomic variation of pathogens and antigen drift demands for regular adjustment of diagnostic assays.

Differentiators for automated Molecular Diagnostic systems

- clinical performance,
- cost effectiveness,
- ease of use,
- multiplexing capability,
- range of tests offered,
- time to result,
- reliability.

- Barriers:
  - installed base of traditional molecular diagnostic procedures
  - Reimbursement

Medical Diagnostic market, from Point of care to centralized lab:

At home

Doctor's office

Ambulance

Beside hospital

Decentralized lab

Centralized lab

(Research lab)

Balancing speed, accuracy and cost

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It isn’t an easy task; the Biocartis case

Launched company 2007

Launched first product 2014

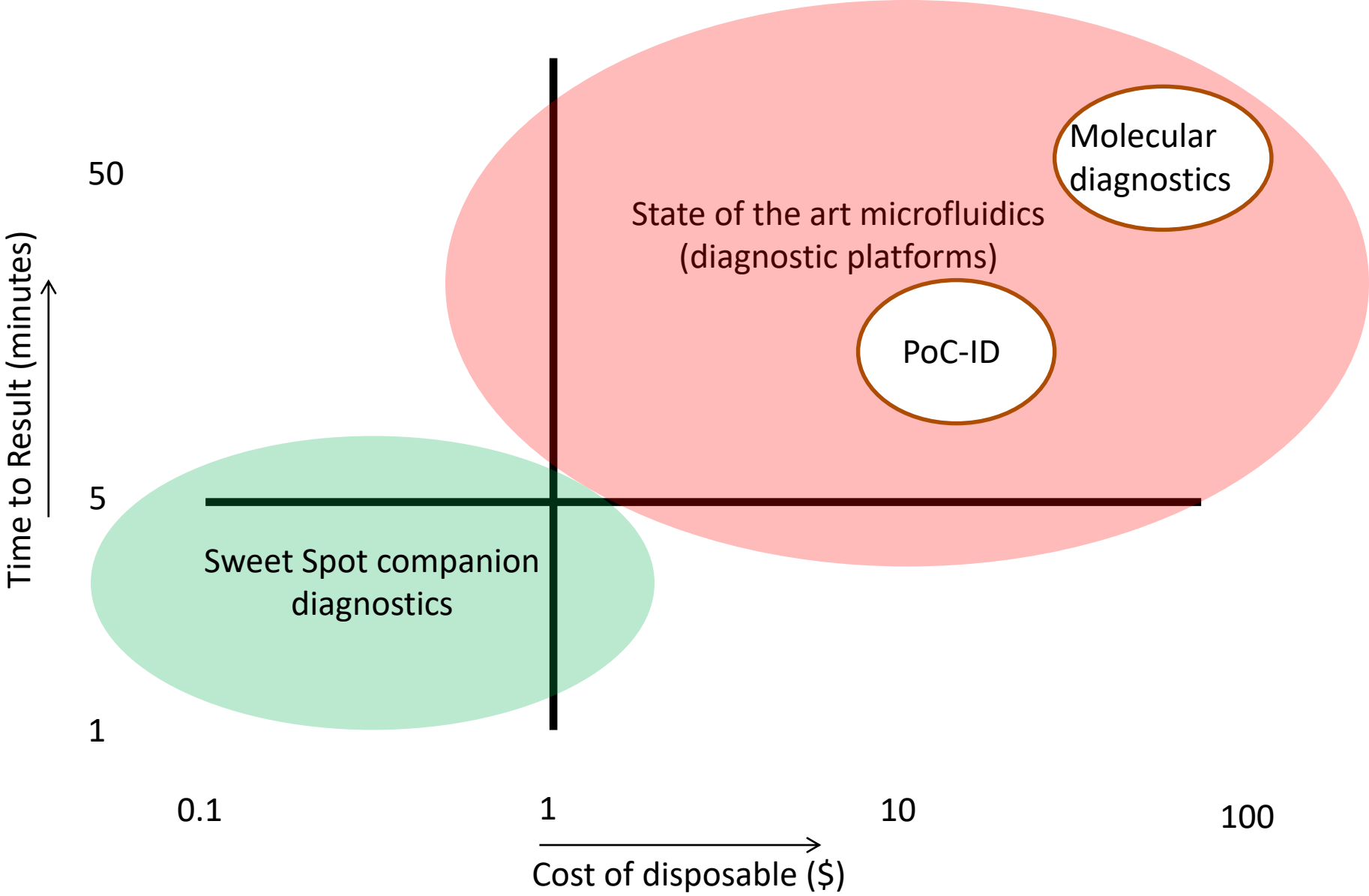
Cumulative investment >250 M€ (and more is needed soon)

Expecting profitability 2019

2015 figures: Turnover 15M €, expenses R&D: 36.6M €, loss 38.9M € , staff: 270 of which 32 in sales and about 160 in R&D.

In 2015, Biocartis added a total of 83 instruments to its installed base. Based on the 82 instruments sold in 2014, the installed base of instruments amounted to 165 as per 31 December 2015.

Their initial focus is high volume labs, thereafter low volume labs are targeted


Molecular diagnostics
State of the art microfluidics (diagnostic platforms)
PoC-ID
Sweet Spot companion diagnostics
50
5
1
Time to Result (minutes)
0.1
1
10
100
Cost of disposable ($)

PoC-ID: Platform for ultra-sensitive PoC diagnostics for Infectious Diseases based on direct detection of proteins

PoC-ID is a Research & Innovation Project, funded within the EU Horizon2020 Programme, Grant Agreement: 634415

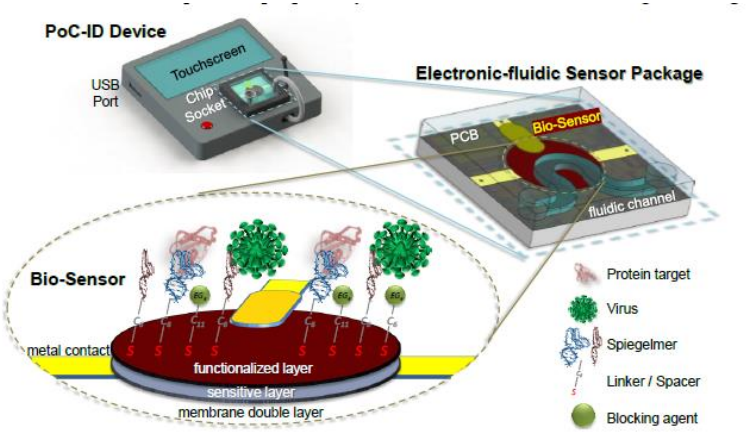
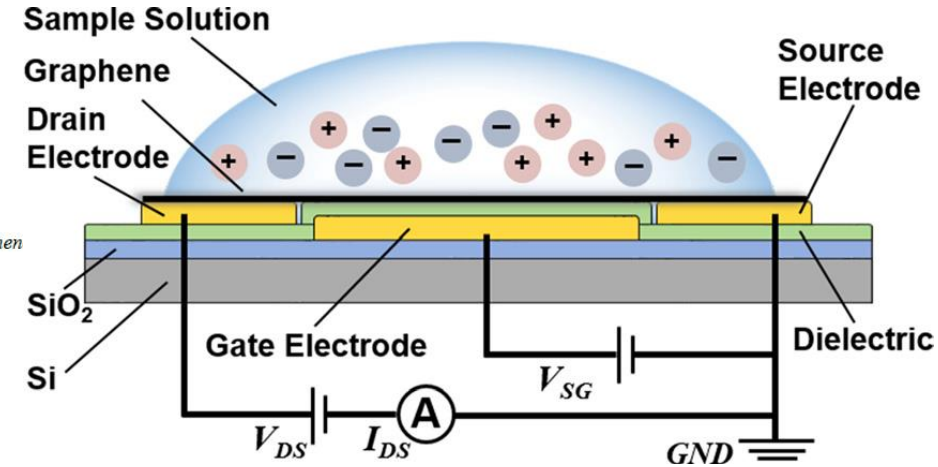


Figure 3: *Concept of the point-of-care device from macro to nano scale; device setup is applicable for graphen FET- and MEMS-based biosensing as well as other electronic sensing concepts with similar chip size*



- electrical conductivity of graphene field effect transistors (GFETs) modulated by gate voltage and target molecule concentration

Thank you for your attention!

For further information visit:

www.PoC-ID.eu or send an Email to henne@enablingMNT.com