

# Trends and Challenges in the Microfluidic Industry

Henne van Heeren, enablingMNT

SYSTEMS INTEGRATION '19

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# Flowrate examples



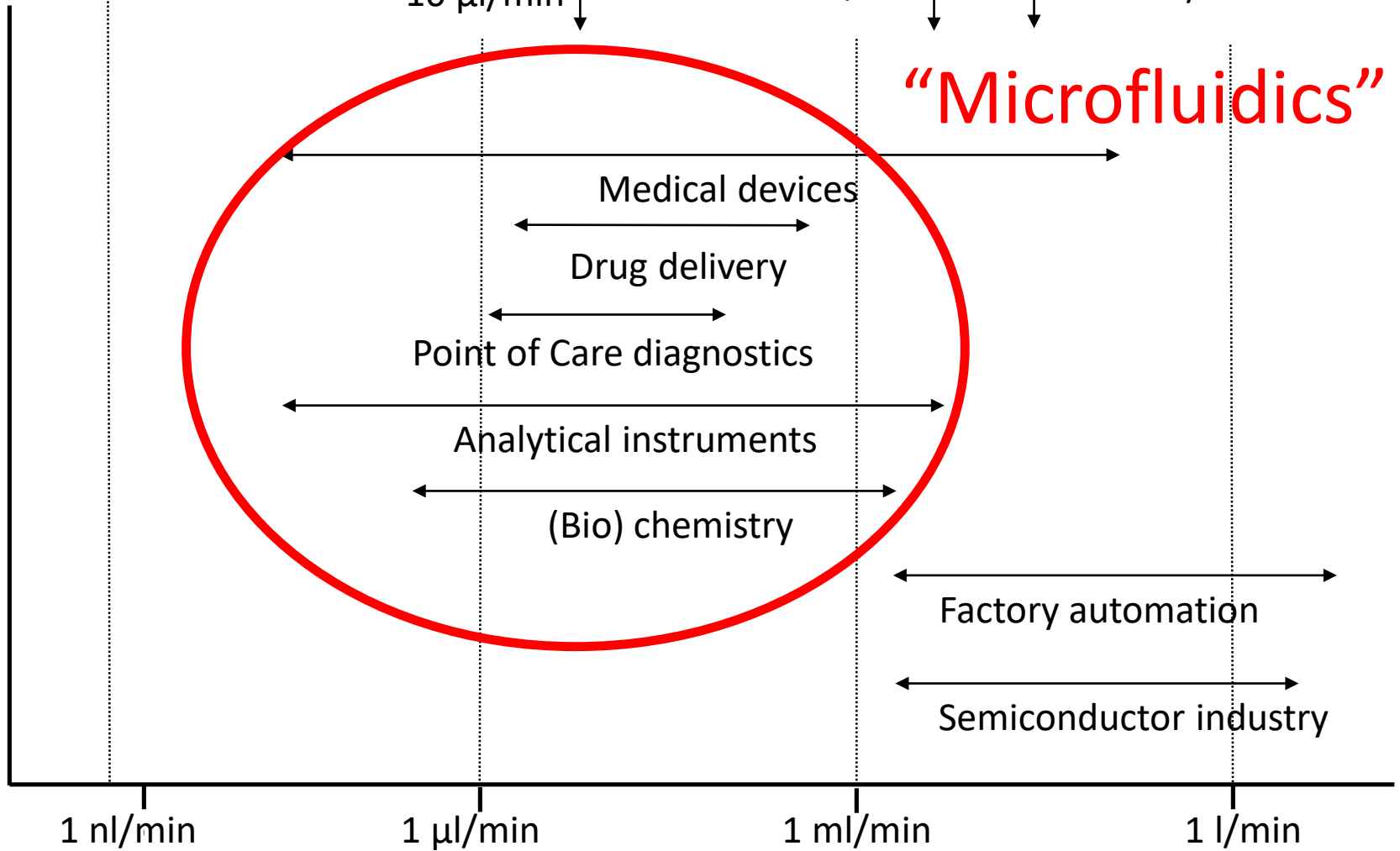
~10  $\mu\text{l}/\text{min}$



~5  $\text{ml}/\text{min}$



~100  $\text{ml}/\text{min}$





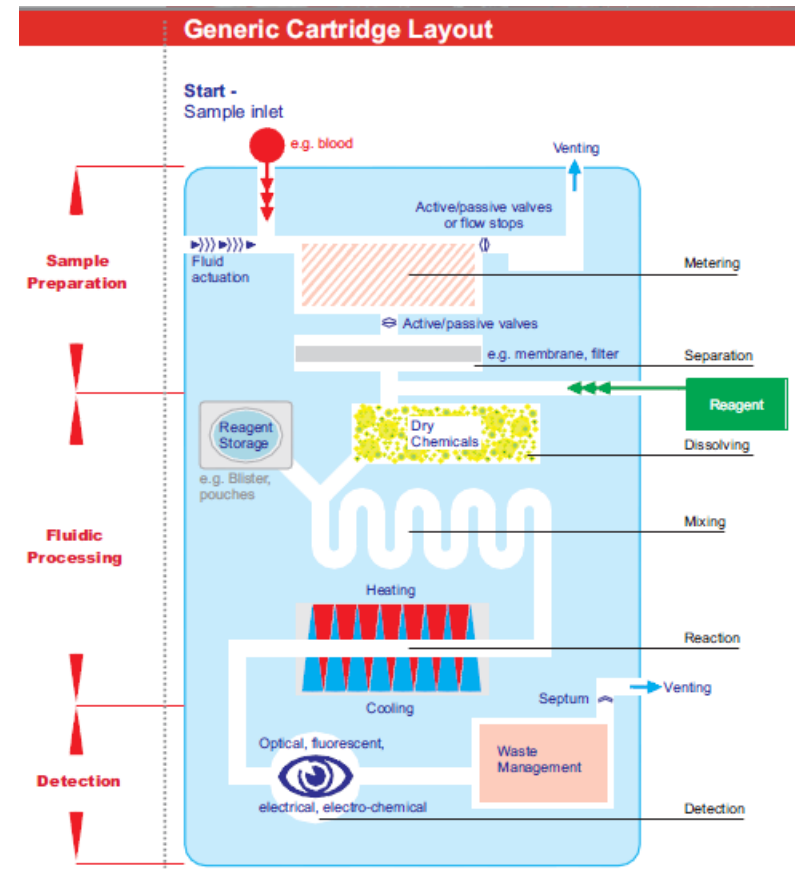
# Lab on Chip devices



- Lab Chip devices: benchtop or stand alone instruments for the (laboratory) testing market.
- Medical diagnostics is by far the largest segment, interest fuelled by potentially high speed, efficiency, and sensitivity of results with accuracy. Related to the interest in personalized medicine, drug discovery and general life science research.
- The main challenge is to develop technologies, with the ability to operate reliable and accurately on a small-scale and fabricated at low cost.
- Key players: Merck (2015 combination of Merck Millipore and Sigma-Aldric); Thermo Fisher Scientific (bought Life Technologies in 2014), Abbott Laboratories (bought Alere Technologies in 2017), Roche Diagnostics, Bio-Rad Laboratories.

# Microfluidic based diagnostic instruments

- Complex chemical factories intended to speedily, reliably, and inexpensively perform biochemical procedures that together constitute a medical test.
- Replacing the far slower, more cumbersome, more expensive laboratory equipment.
- Barriers: cost of development, qualification (and yet immature fabrication technologies.)



Courtesy  
thinXXS

# General trends for pharma and medical diagnostics.

- Pharma
  - Drugs and diagnostics for oncology biggest subsegment and growing fast.
  - Growth of orphan drugs and diagnostics market.
  - Cost of drug development rising fast. Organ on Chip might help.
  - Will pharma companies change from product supply to a service industry?
- Medical diagnostics
  - Increasing interest of the consumers to manage their own health in partnership with the doctor.
  - The number of devices connected to the internet runs in to the billions and is increasing. Increasing worry about internet safety, especially for health related devices.

# DNA diagnostics market

- Evolution of DNA diagnostic platforms and transforming from a research activity into a commercial activity with very substantial growth potential.
- Aiming at the identification of disease-causing genes and identifying patients at high risk of acquiring a disease, determining the effectiveness of the treatment and the patient's response to the treatment.
- Oncology is one of the major application areas of the DNA diagnostics.
- High costs involved in the development of the tests and reimbursement concerns of these tests are slowing the growth of the market.
- Some of the major players competing in this market are Abbott Laboratories, Thermo Fisher Scientific, Affymetrix, Inc., Illumina, Inc., and F. Hoffmann La Roche Ltd.

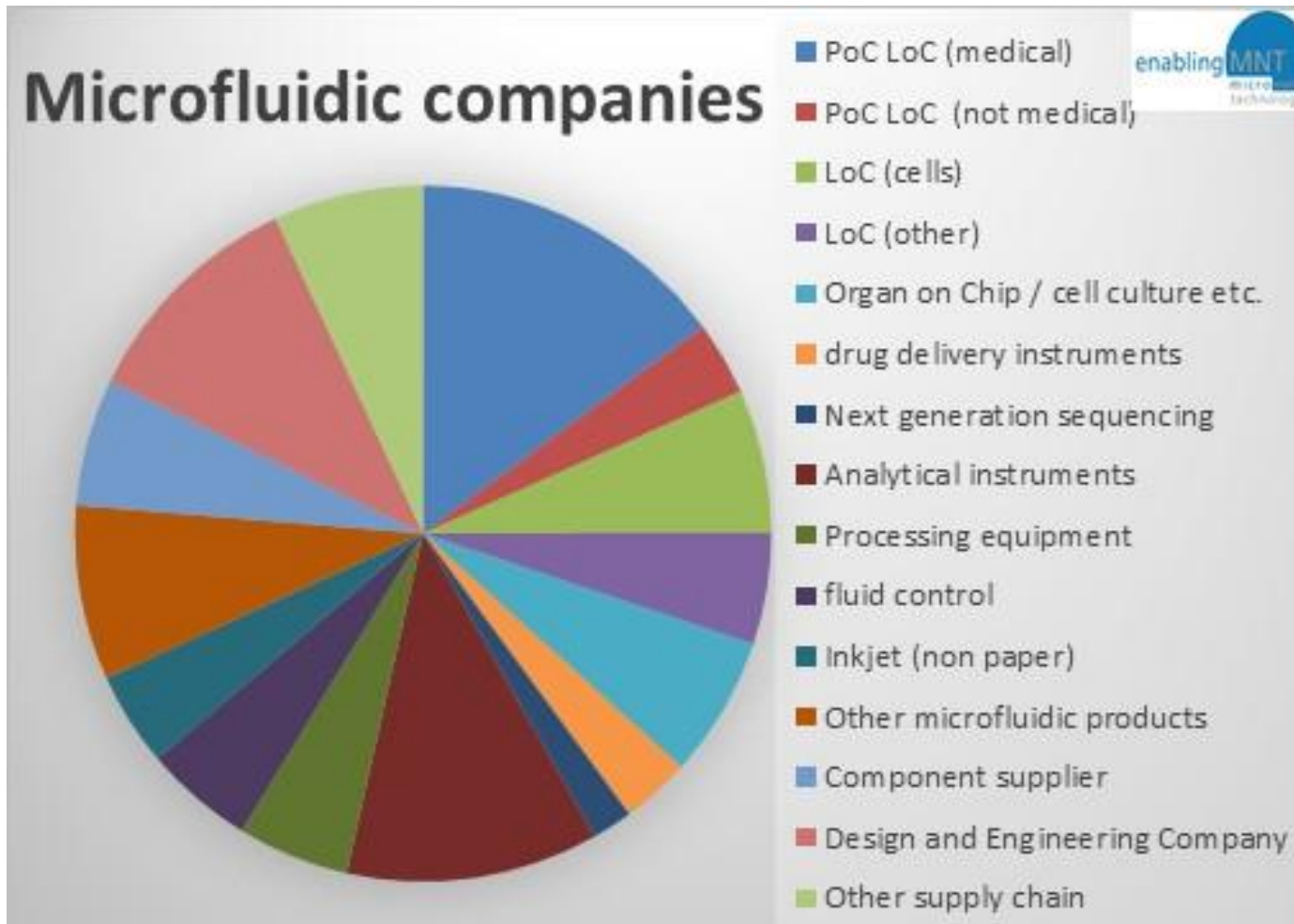
# Microfluidics is driven by the diversity of the medical diagnostic market.

- We have different DNA, therefore might react different to medication; this drives the quest for personal medicine and tests to link specific medicines to specific patient groups.
- Diagnostics and treatment options are generally linked to specific (mutating) viruses.
- There is an increasing attention for rare diseases: 6-7 k are known, ~1 in 17 people in the western world will be affected by them.
- Biomarkers range from small particles to electrolytes.
- Different biomarkers need different detection technologies and often more than one biomarker needs to be measured for a complete picture of a certain disease.

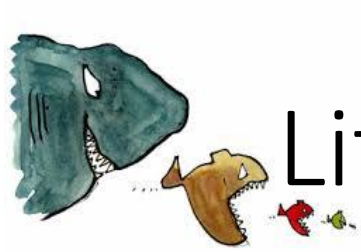
All these considerations point towards:

1. Multiplexed diagnostic testing.
2. Room for specialist medical diagnostic suppliers.

# Diversity in application







# Life science giants are buying successful microfluidic start-ups.

- Agilent: 2010 Varian, 2011 Biocius & lab901, 2012 DAKO, 2018 ACEA Bioscience & Lasergen
- Illumina: 2010 Helixis, 2013 All, 2018 Edico Genome & Pacific Bioscience
- Bio-Rad: 2011 QuantaLife, 2014 Gnubio, 2017 Raindance
- IDEX: 2011 Microfluidics International, 2015 Cidra, 2017 ThinXXs
- Life Technologies: 2009 Biotrove, 2010 Ion Torrent & Stokes Bio
- Thermo Fisher Scientific: 2009 C2V, 2012 Dionex, 2014 Life Technologies, 2019 IntegenX
- Roche: 2007: 454, 2010 BioMicro Systems & Medigon, 2014 Iquum & Genia, 2015 Geneweave
- Pall Life Sciences: 2009 GeneSystems, 2010 Microreactor Technologies
- Danaher: 2004 Radiometer, 2009 MDS, 2010 Sciex and Molecular devices, 2011 Beckman Coulter, 2015 Pall Life Sciences, 2016 Cepheid

# Partnerships (active and past, small selection only)

- J&J: Sphere Medical, Emulate, HiFiBiO, Cue, Biocartis
- Roche: DNAE, Emulate, TissUse, Pacific Biosciences, Berkeley Lights, SQZ Biotech, ACEA Biosciences, CapitalBio
- AstraZeneca: Emulate, Cellectricon, TissUse, Agplus Diagnostics, CN Bio Innovations,
- Takeda: HiFiBiO, Portal Instruments, Emulate
- And many many more

# Organ on Chip

- Research
- Testing of efficacy and safety of new therapeutics and combination of therapies, leading to:
  - New insights into disease mechanisms.
  - Earlier and better prediction of safety and efficacy of new drug candidates.
  - Expansion of innovation in the drug discovery process.
  - Prediction which disease treatments would be most effective based on a patient's genetic makeup and disease variant.
  - Prediction of the potential human response of therapeutic candidates.
- Toxicology of foods, dietary supplements, cosmetics and tattoo ink.

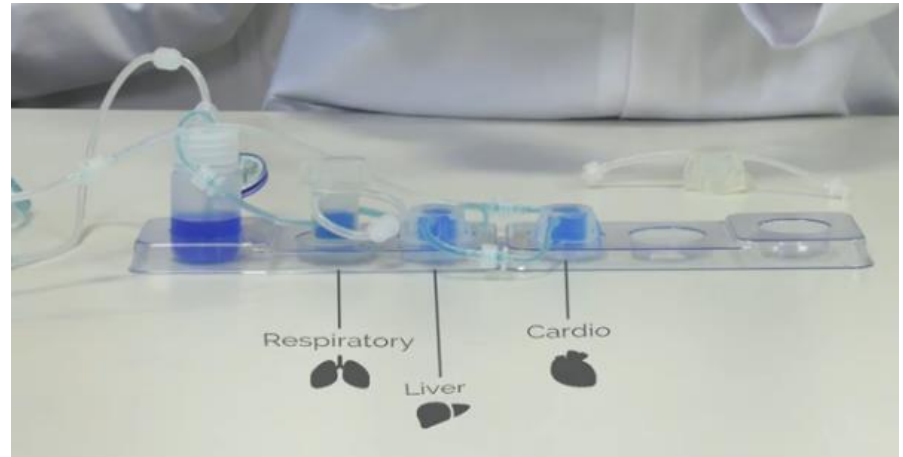
# Technical challenges for Organ on Chip

- Maintaining and culturing miniaturized organ equivalents emulating the biological function of their respective full-size counterparts over long period.
- Create and customized (and preferable flexible) combination of different tissue constructs or organ equivalents on a disposable chip-based microphysiological system.

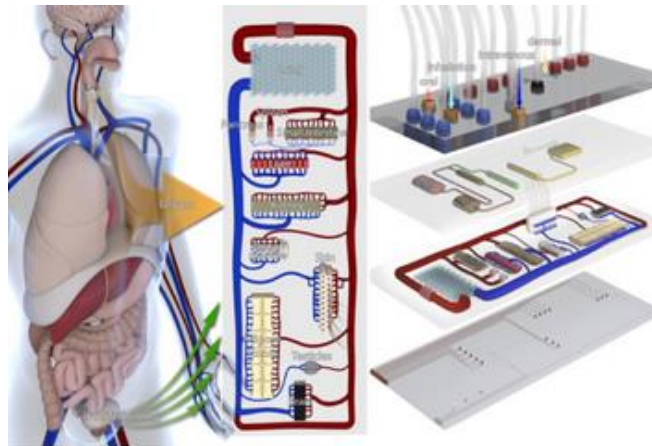
# Examples of Organ on Chip technologies



Mimetas (NL)

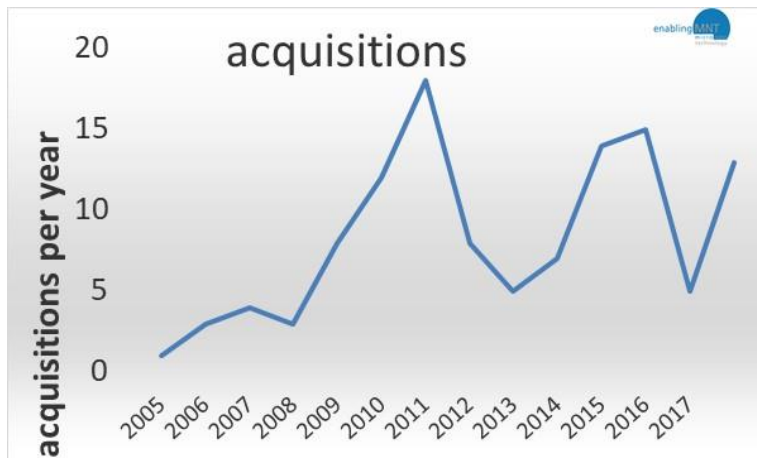
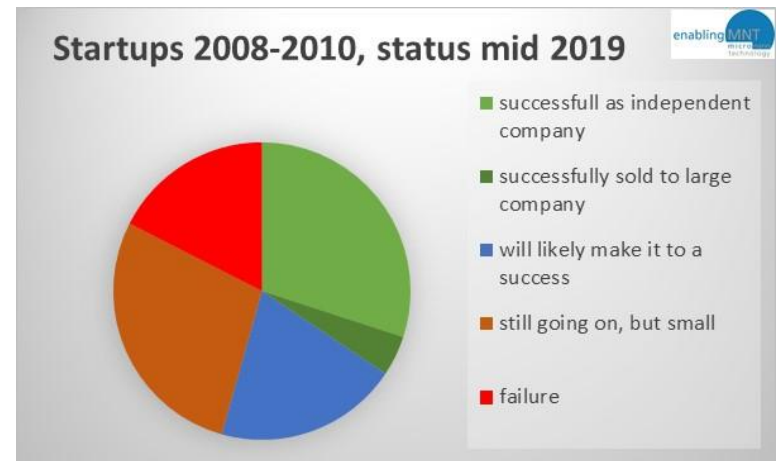
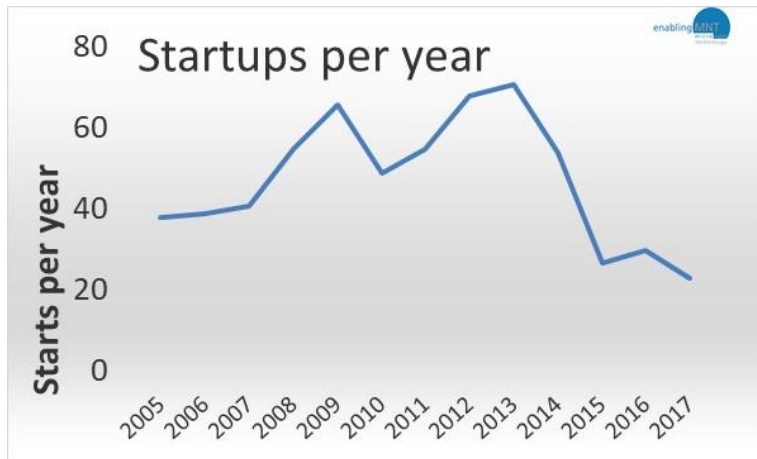


Kirkstall (UK)



TissUse (G)

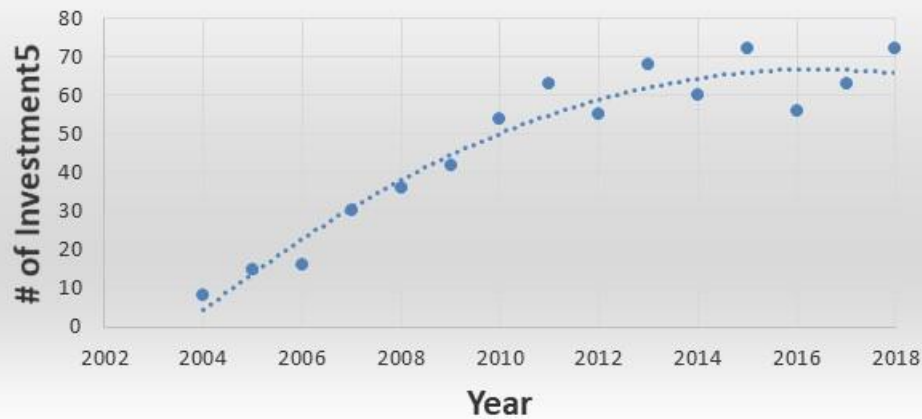
# Microfluidics start-ups



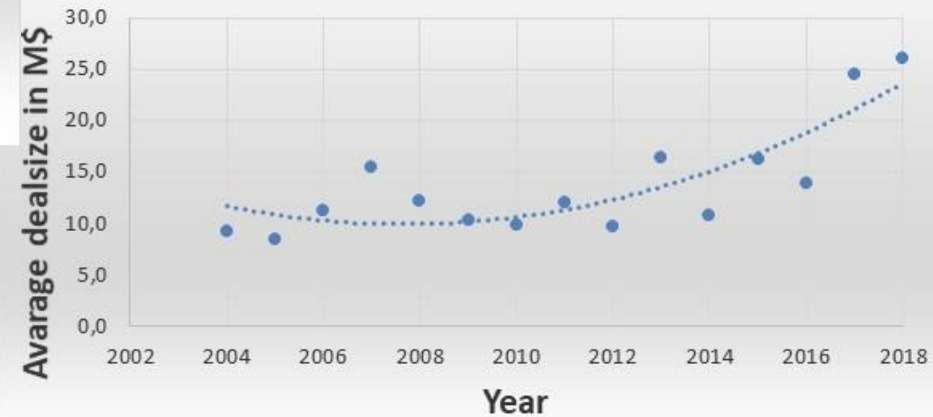
Average time to success about 8 years  
 Average time to failure about 9 years  
 Getting a foothold in the medical diagnostic market needs 50-200 M\$ and 10-15 years. (At least)  
 10 year survival rate about 75%

# VC investments in microfluidic companies

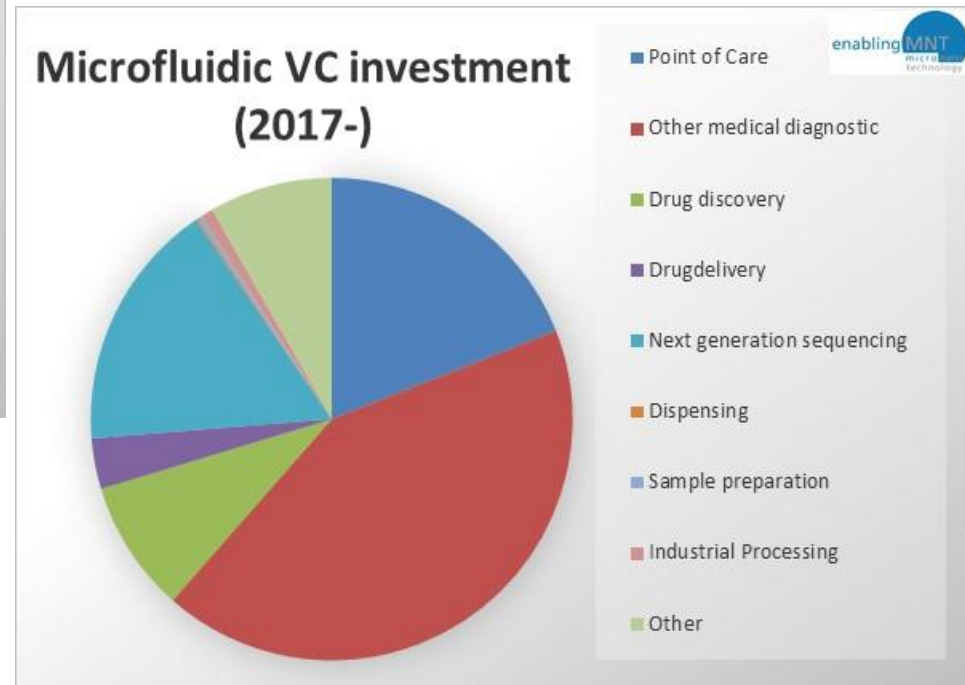
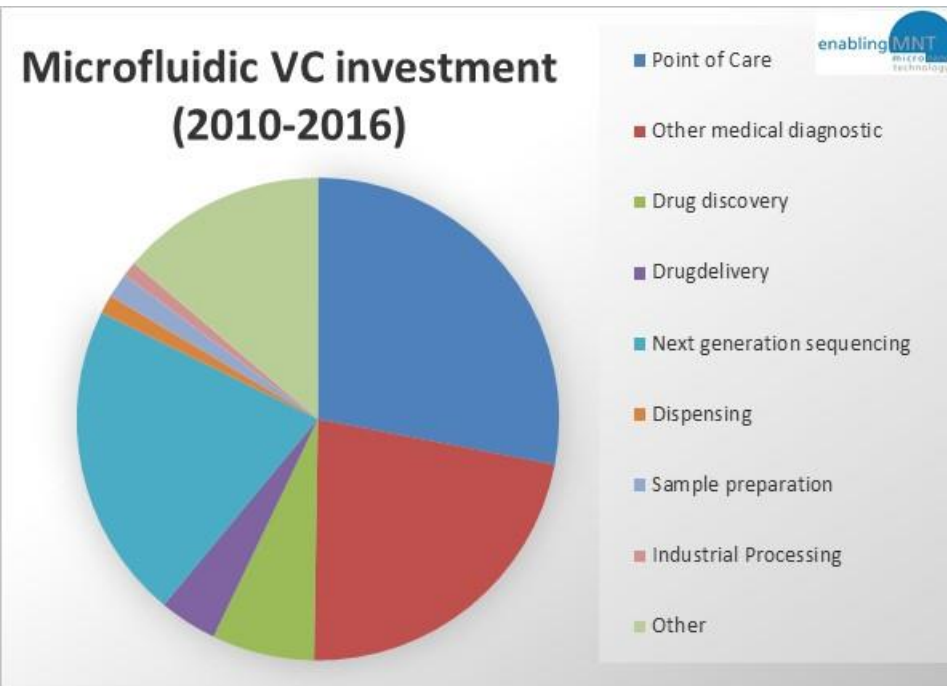
number of VC investments in microfluidics per year



average deal size VC investments in microfluidics



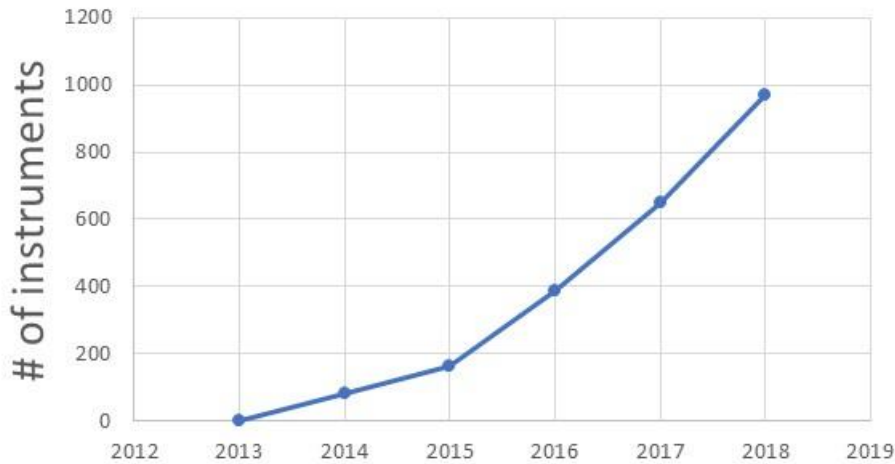
# Investors are losing interest in Point of Care



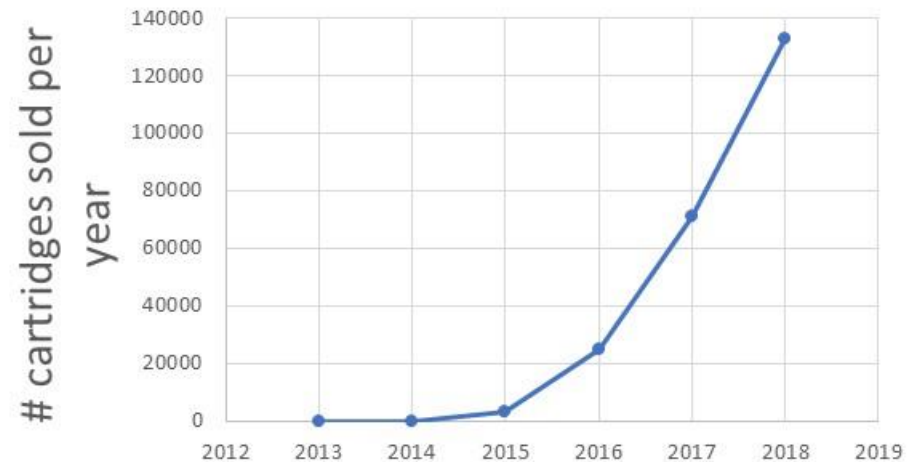


# Building up a market position

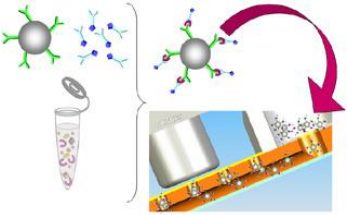
Installed base



Cartridges sold

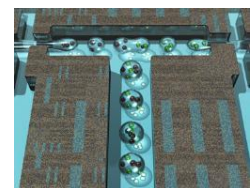
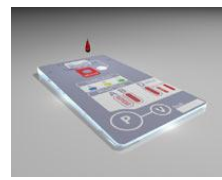
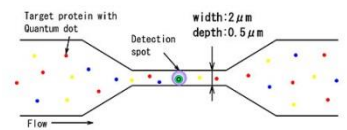
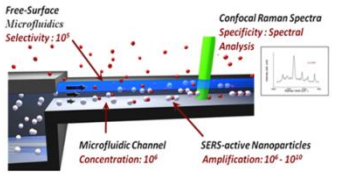
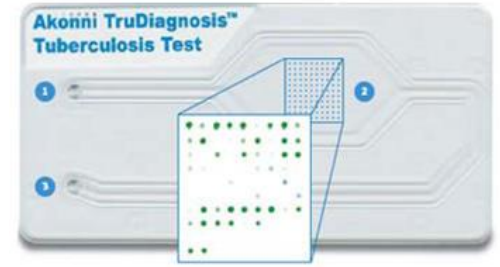
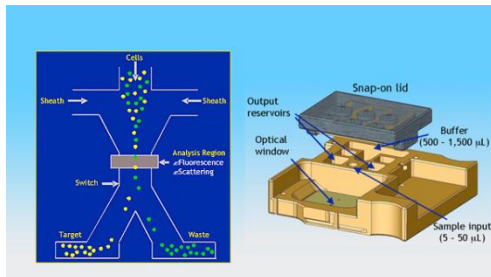
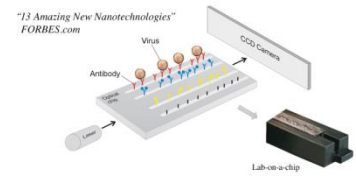
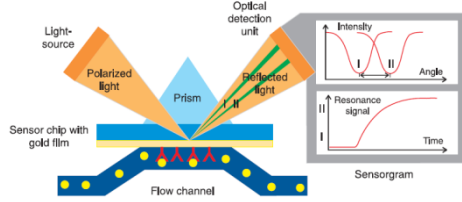
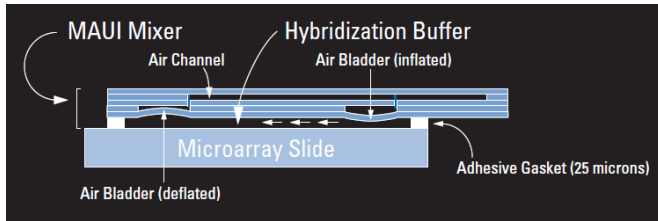
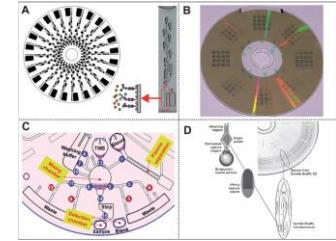
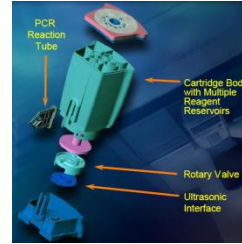


# Bewildering number of concepts, technologies, and materials



### Bionas.

Simultaneous measurements of:  
 -pH  
 -O<sub>2</sub> consumption  
 -Adhesion/confluency  
 Online/real time measurements.



# Going about the business of standardization in microfluidics



2010-2013

Initial discussions resulting in:  
1 whitepaper  
Article in Lab on Chip Journal.



2014-2017

21 partners  
5 surveys  
4 whitepapers



ISO IWA23 (International Workshop Agreement)  
ISO New Work Item Proposal

Project leader Nicolas Verplanck, CEA

2 International workshops:

- NIST, USA, June '17
- Imec, Belgium, October '17

Charta of the Microfluidics Association (MFA)



**Microfluidics Association**  
Since 2018



New ISO TC48/WG3  
Convenor Nicolas Verplanck, CEA

Published a microfluidic vocabulary

4 International workshops:

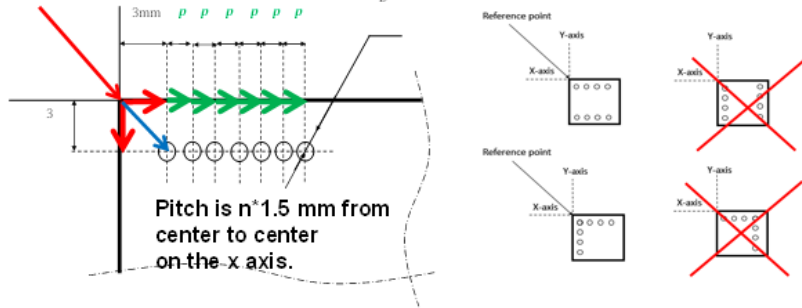
- CEA, France, March '18
- METAS, Switzerland, July '18
- Portugal, April '19
- San Diego, USA October '19

Planning for 7<sup>th</sup> workshop in Germany begin 2019

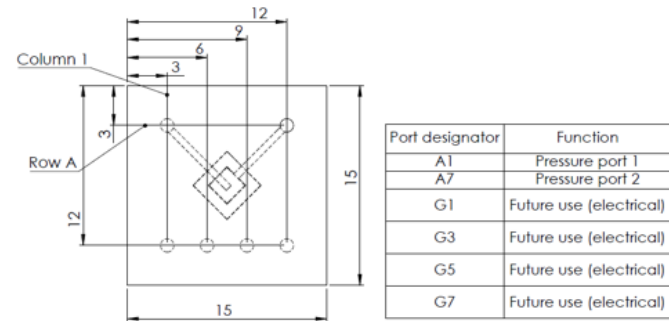
# Standardisation initiative

## Examples of industry supported microfluidic standards as of 2016

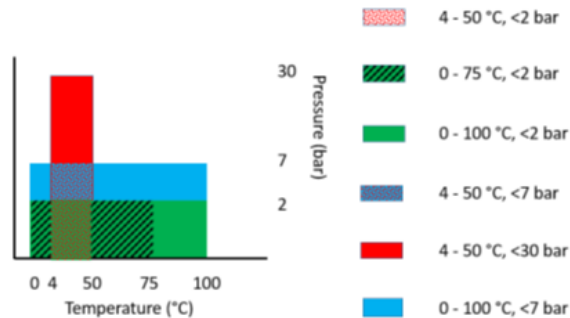
### Reference Point



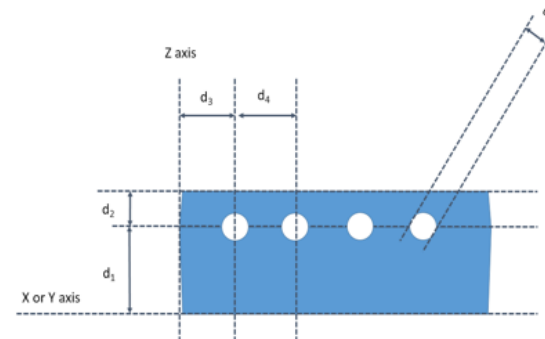
-Positions and nomenclature of microfluidic ports



-Dimensions of standard microfluidic building blocks



-Classification of microfluidic devices



-Port positions for microfluidic edge-connectors

Now being transferred to ISO

# Working on generic test protocols for microfluidic products

- There are no published generic test protocols based on proven fault modes to assist the development of more reliable microfluidic products.
- Most of the tools and techniques currently used for failure analysis are leveraged from the IC industry, and are not designed to be used with fluids. Especially not liquids.
- The microfluidic industry faces the challenge it needs to define its own testing strategies, methods and reliability models.
- Heterogenous systems need much more research to study fault modes; this is particularly true for microfluidics.

# Trends and observations about to the market for microfluidic products

- Due to the diversity in applications, figures for the microfluidic market as a whole are meaningless.
- However, they are right about the growth.
- Point of Care is less popular than it used to be, attention shifted towards lab tools for medical diagnostics.
- Organ on Chips is the current research hype, but driven by real and well defined market needs.
- Big Data: linking DNA with diseases, responses to medicine etc.

# Trends and observations in regards to fabrication (1).

- One product, one technology and often one factory.
- Major cost factor is in the assembly of microfluidic based products.
- Most of the fabrication of microfluidic based products are done in-house.
- Most of the products are heterogenous in terms of materials and technologies.
- All materials in contact with the fluid needs to be biocompatible.
- The presence of organic material in the microfluidic chip limits the temperature budget in assembly.

# Trends and observations in regards to fabrication (2)

- The industry lacks an in-depth understanding of microfluidic fault modes, how to test for them and how to prevent them.
- There is no industrial solution for combining microfluidics and electronics fitting to the scale of silicon biosensors.
- Testing of microfluidic devices is lacking standard test protocols and accepted standards
- Interest in standards and protocols for:
  - Testing,
  - flow control,
  - assembly and interconnection in general, and
  - how to combine microfluidics and electronics on a scale fitting to the scale of silicon biosensors.



Thank you for you  
attention!

[Henne@enablingMNT.com](mailto:Henne@enablingMNT.com)