

Trends in and Challenges for the Microfluidic Industry

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- What is microfluidics?
- The microfluidics industry
- The Microfluidics Association and standardisation
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Flowrate examples



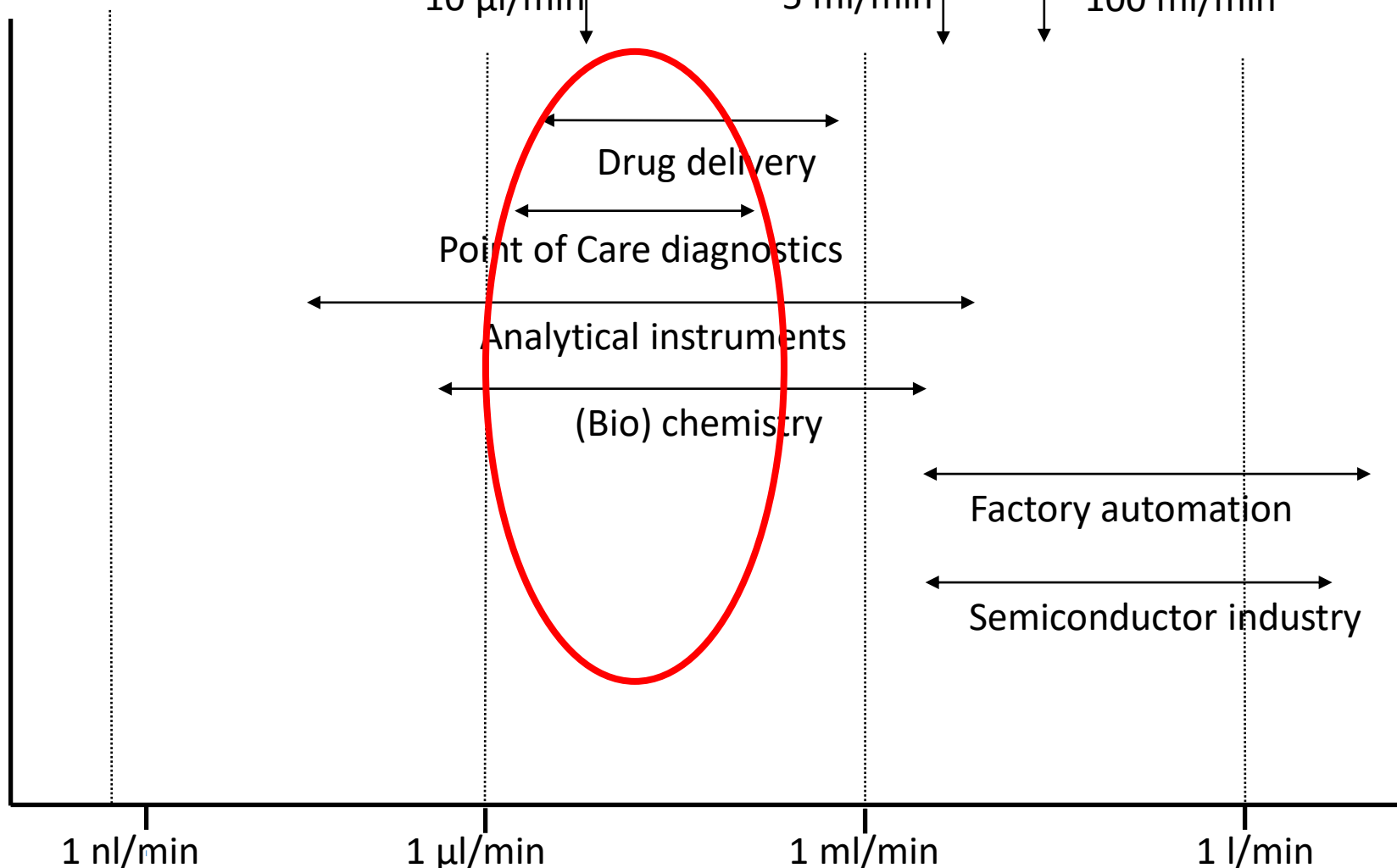
~10 µl/min



~5 ml/min



~100 ml/min

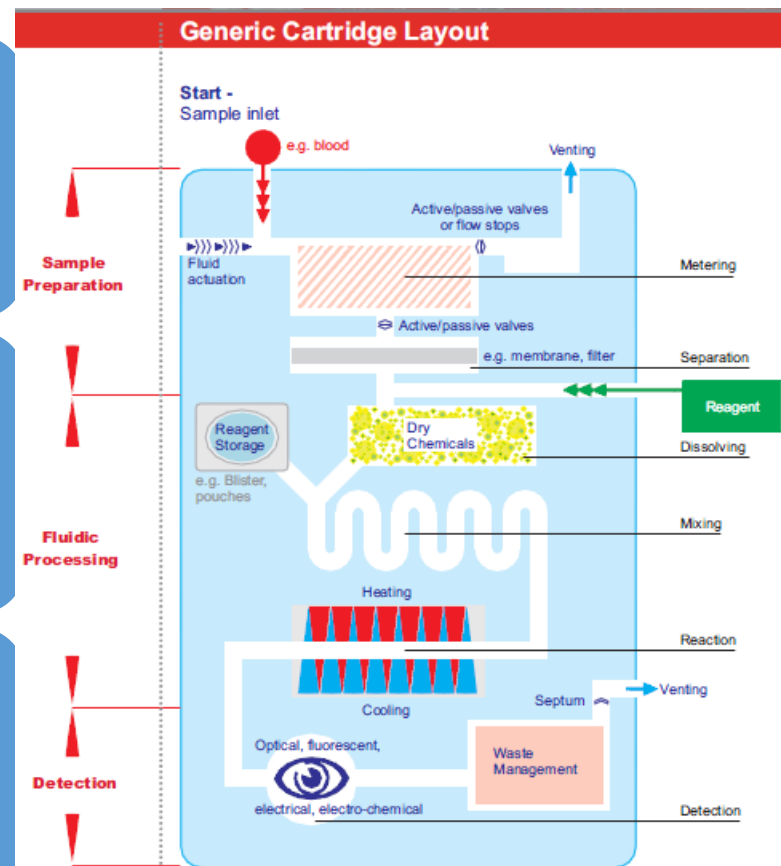


Microfluidic based diagnostic instruments

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

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\$.



Cue Health

(founded 2009)

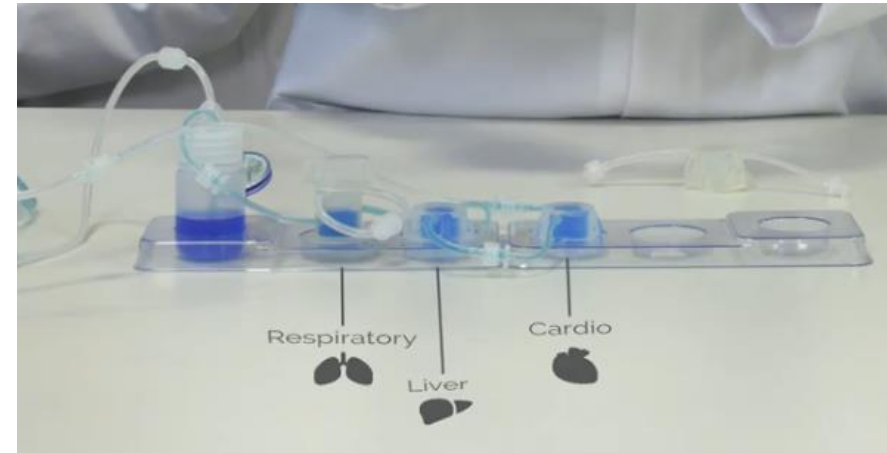
- The company's rapid molecular test, greenlighted by the FDA in June 2020, is based on a nasal swab and a cartridge-based reader, and it delivers results through a smartphone within about 20 minutes.
- After raising \$100 million earlier 2020 from VCs, Cue Health has received another \$481 million from the U.S.
- 2021 raises \$200M in IPO

Organ on Chip

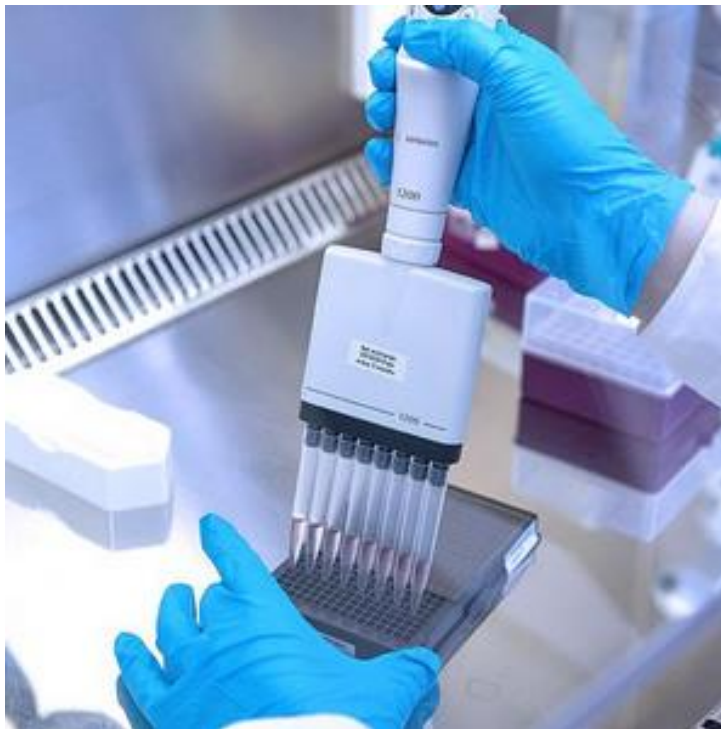
- Still mostly in research.
- Testing of efficacy and safety of new therapeutics and combination of therapies, leading to:
 - New insights into disease mechanisms.
 - Earlier and better prediction of safety and efficacy of new drug candidates.
 - Expansion of innovation in the drug discovery process.
 - 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.

Examples of Organ on Chip technologies

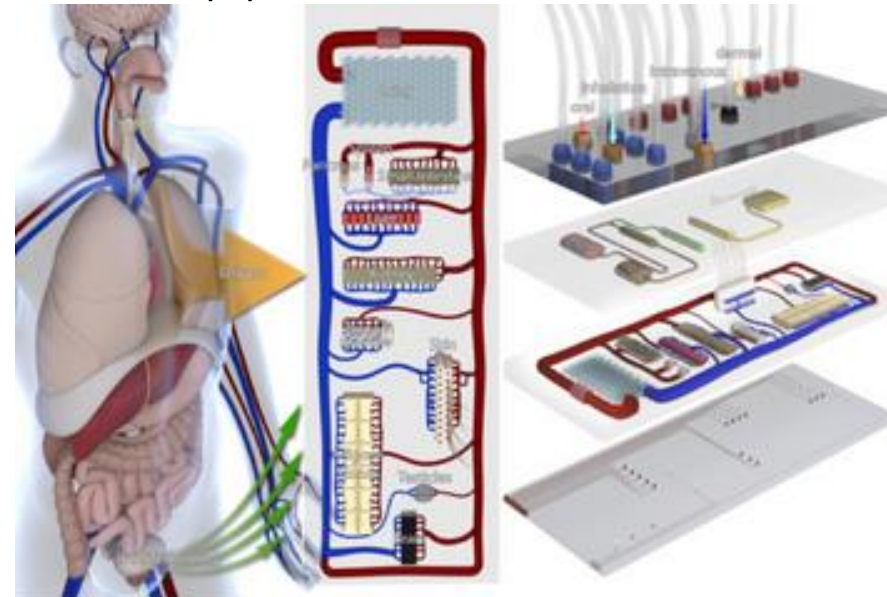
Kirkstall (UK)



Mimetas (NL)

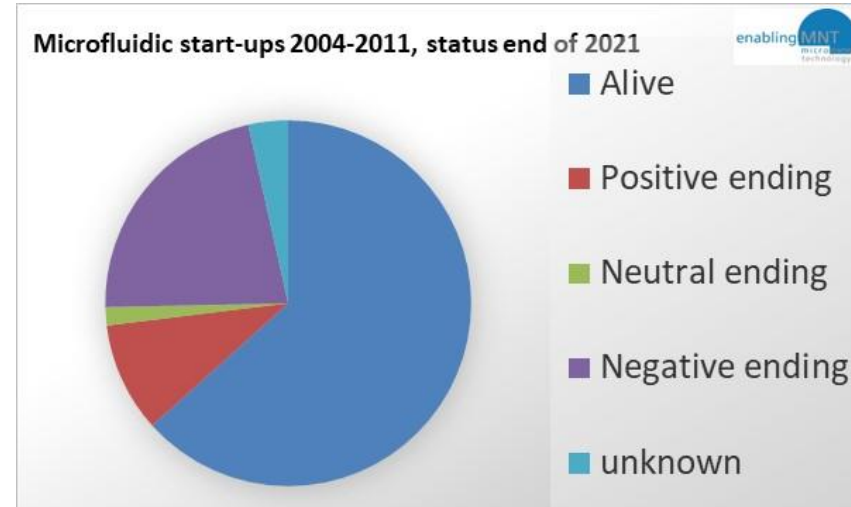
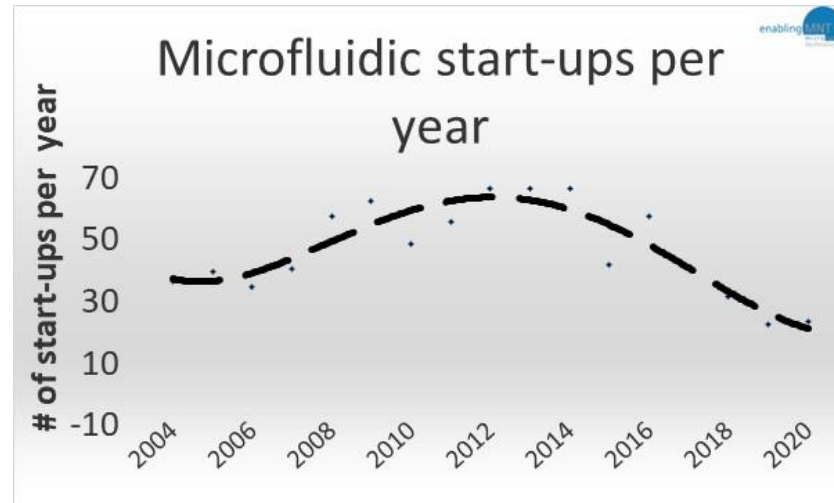


TissUse (G)

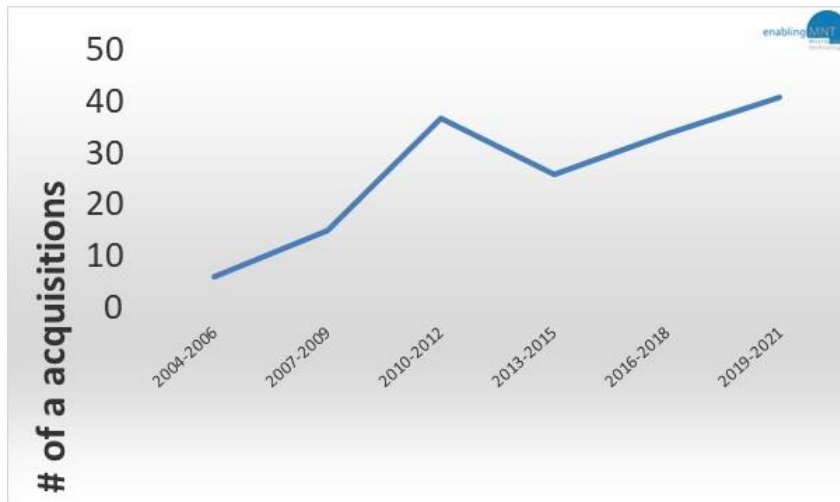


The Microfluidic Industry

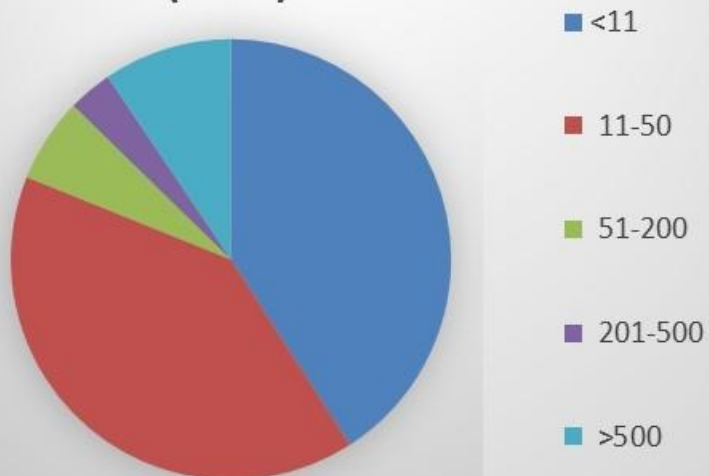
Microfluidics start-ups



- Survival rate of high-tech start-ups is about 75%.
- Most of the companies survive the first years by bootstrapping
- Only 1 in 3 of the VC supported companies end successfully.

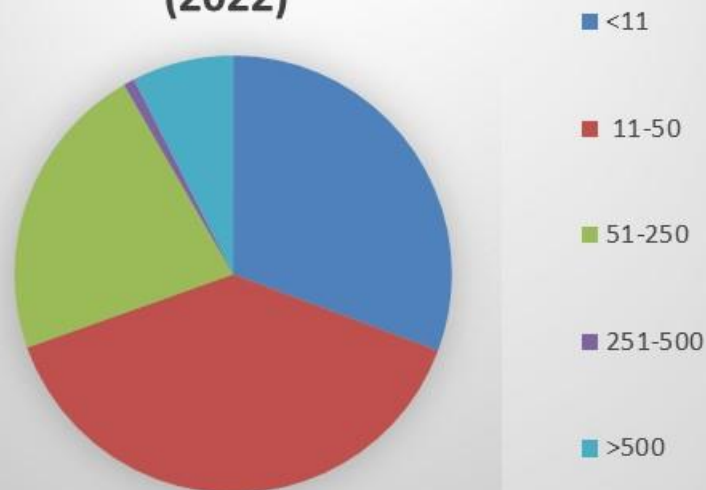


Size of the microfluidic companies
(2017)

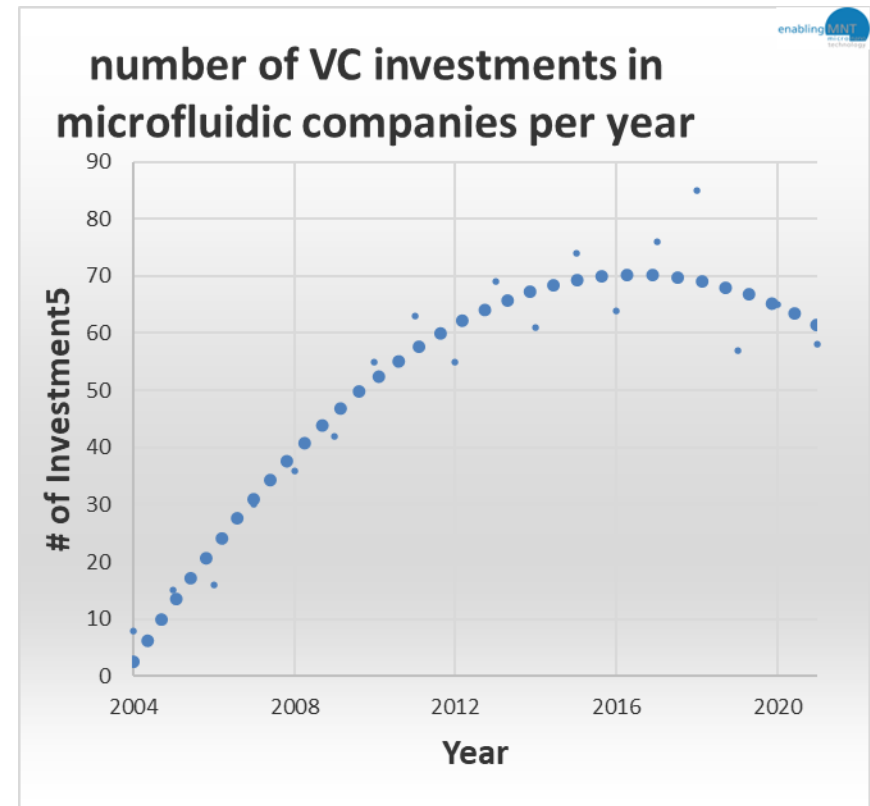
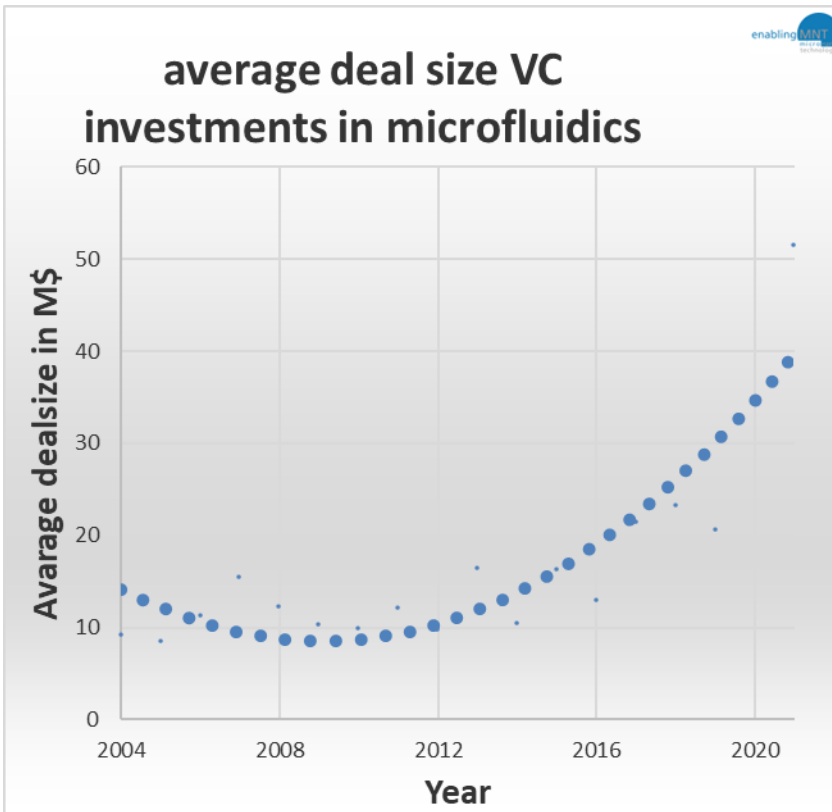


Slow but
steady
growers

Size of the microfluidics companies
(2022)

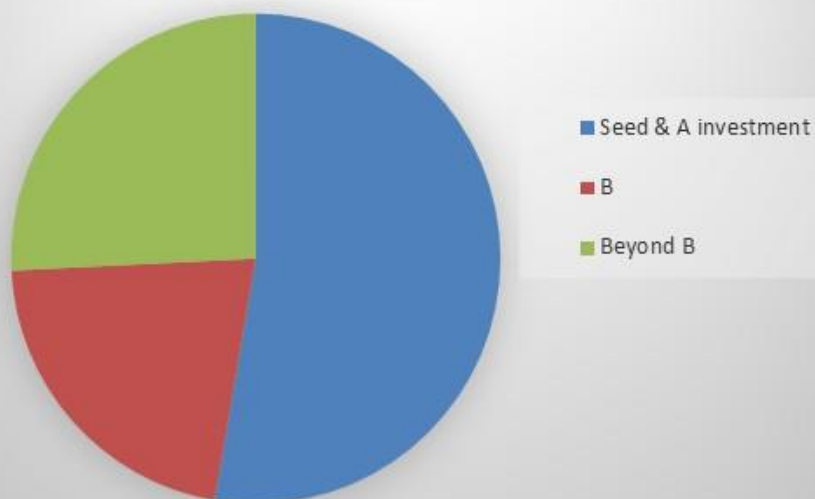


VC investments in microfluidic companies

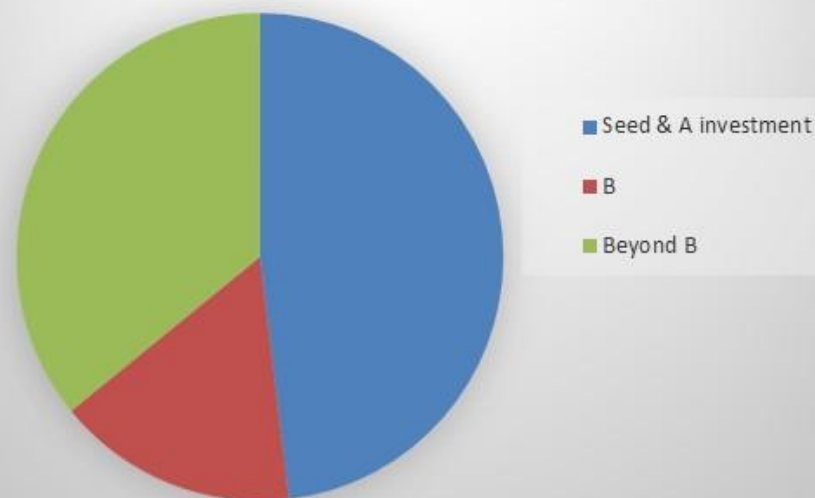


Investments (3)

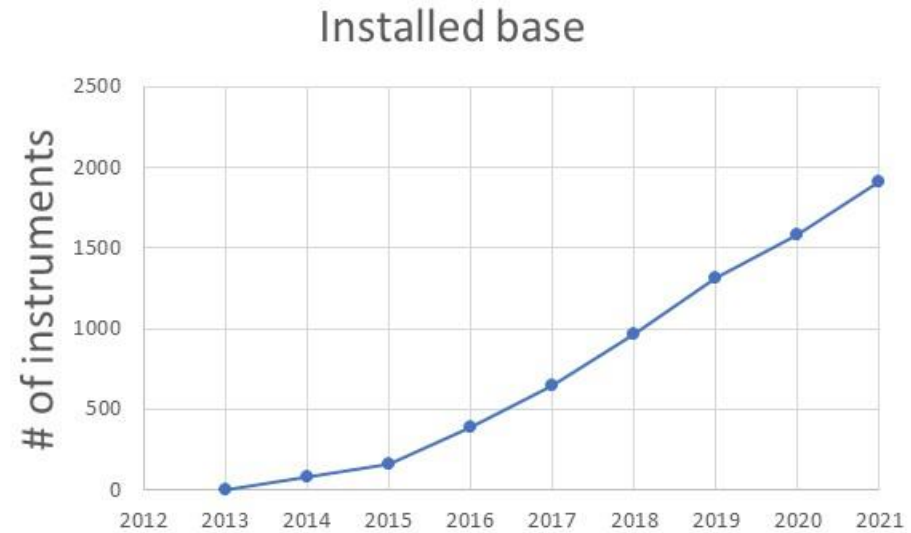
2015-2019, number of investments



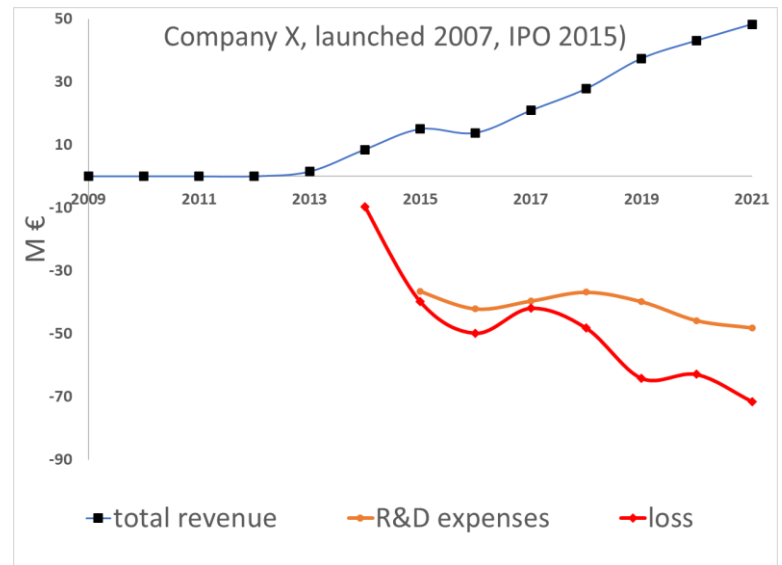
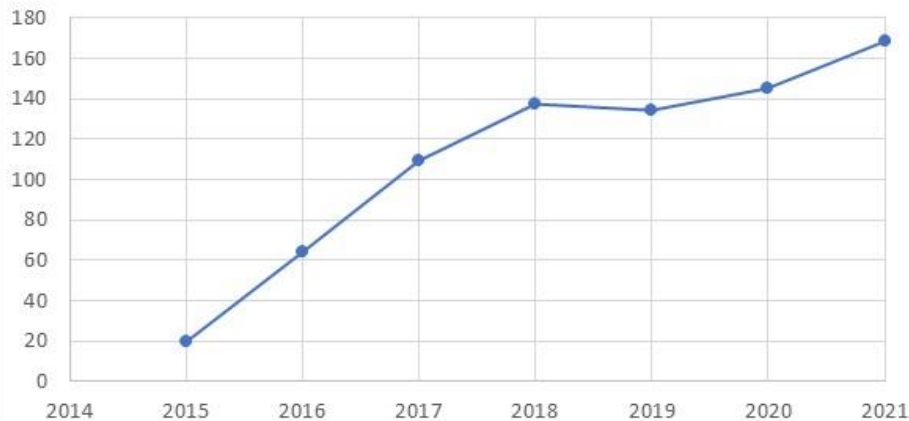
2020-, number of investments



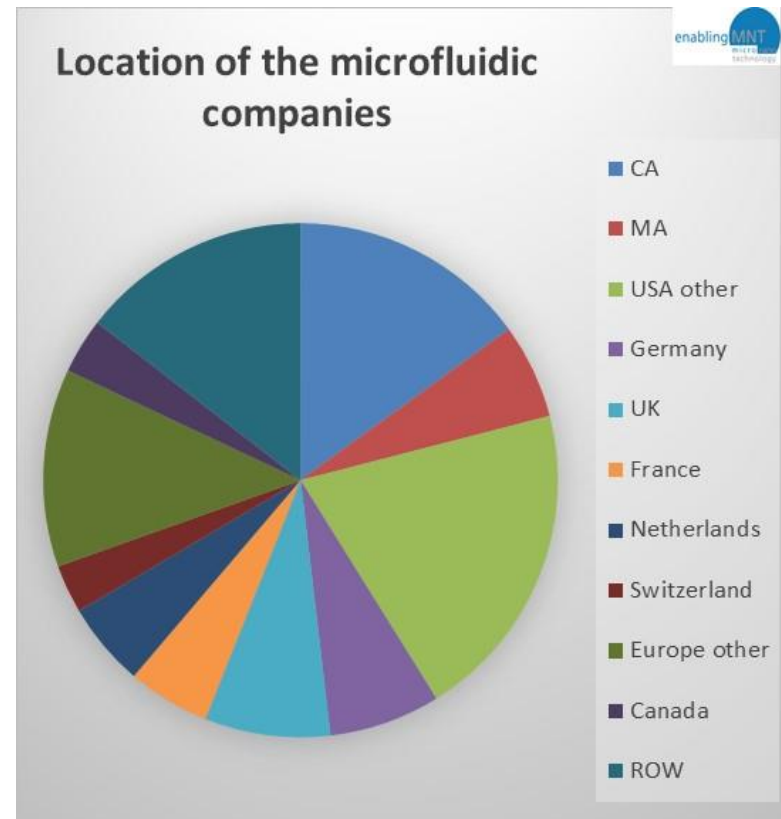
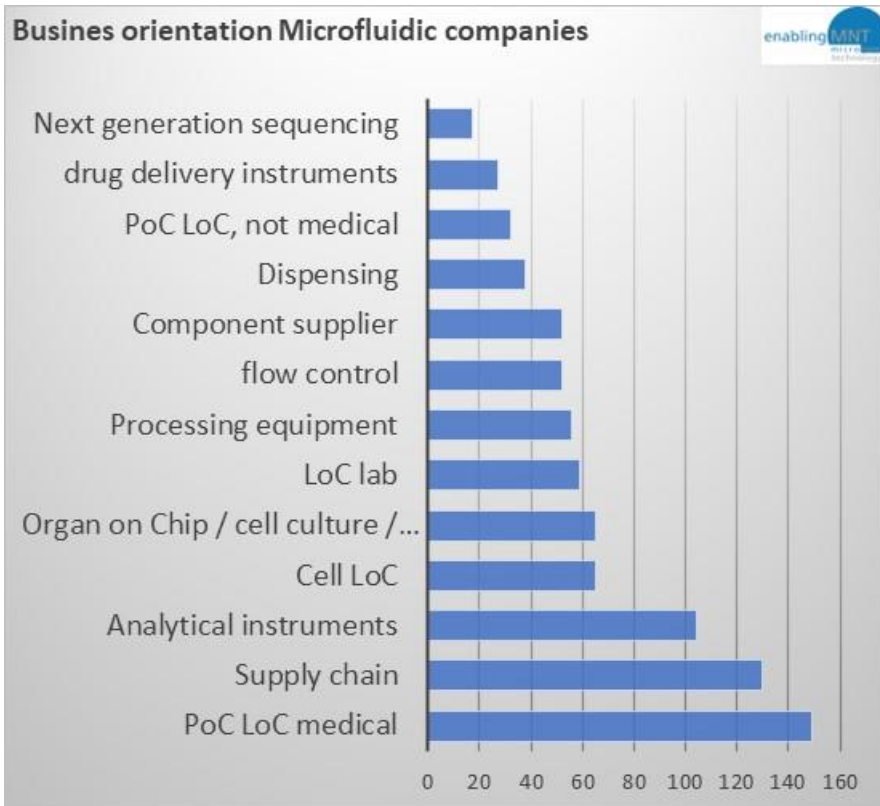
Building up a market position as a medical diagnostic company



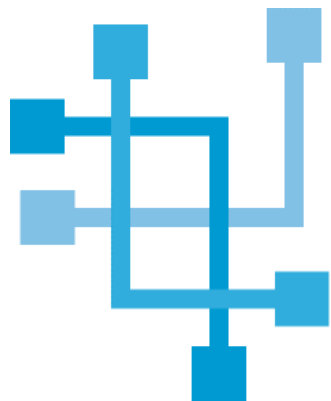
Catridges sold/year / divided by instruments installed



Business orientation and hotspots



Standardisation, guidelines and generic testing strategies



**Microfluidics
Association**



Technical challenges for the microfluidics industry

- Microfluidics is driven by the diversity of the medical diagnostic market.
- On top of that we have many other applications in research, industry, farming etc.
- The main technologies originates from universities and are as diverse as its applications.
- Most of the products are designed and often also produced inhouse.
- As a consequence:
 - It is difficult to combine components from different suppliers.
 - We lack generic test tools and protocols to guarantee quality.



To wards plug and play

- Make it easier for customers selecting microfluidic flow control components and devices, install them and use them.
- Democratisation of microfluidics or microfluidics 4.0: Components and devices to be divided in well described classes.
- Within these classes components and devices operate seamlessly with each other, can be integrated by non experts: plug and play.



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.

Measurement priorities during fabrication.

(based on interviewing industry experts)

1. Anything that affects pressure decay and flow resistivity in the device (wettability, deviation from the ideal dimensions etc.).
2. Anything that affects bonding quality of polymer devices (glass transition temperature, melting temperature, molecular weight number and distribution, ...)
3. Leakage test / burst pressure test / maximum operational pressure test.
4. Agreement about quality information of incoming materials like: optical transmission / auto fluorescence of polymer materials, thickness of glass substrates etc.
5. Measurement of fast changing flowrates.
6. Bio viability check after deposition of biomaterial on the chip / in the device.



Results

- ISO 22916 - Microfluidic devices – Interoperability requirements for dimensions, connections and initial device classification.
- Revision of the ISO microfluidic vocabulary (ISO 10991:2009) is now in progress. Basically it is the vocabulary that we created during our workshops. As the former one was created over 10 years ago and concentrated mainly on microreactors, this is a huge improvement.
- TS - Technical Specifications on Microfluidic pumps, symbols and performance communications (symbols and standard datasheets, also the work of our workshops) is also going into ballot. Such a report is not a formal standard, it is meant to be informative, although it can lead to a standard later.
- Technical

Conclusions & observations

Business trends / observations (1)

- Getting a foothold in the medical diagnostic market needs 50-200 M\$ and 10-15 years. (At least)
- Although the medical market is full of niches, many aim for a few promising area; shake-out is inevitable.
- Supply chain: Do it Yourself is market-leader, but outsourcing is increasing.
- Increasing number of companies are offering off the shelf components for R&D.
- Products based on microfluidic standards are entering the market.

Business trends / observations (2)

- Average time to success about 11 years, to failure about 8 years
- 10-year survival rate for high tech start-ups about 75%
- Growing reluctance by investors to put money in start-ups. COVID-19 changed that, Novemberbe only temporary.
- Decrease in number of microfluidic start-ups, but growth of existing ones.

Trends and observations regarding fabrication

- Most of the products are heterogenous in terms of materials and technologies and assembly is a big cost factor.
- 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!

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See: www.microfluidics-association.org