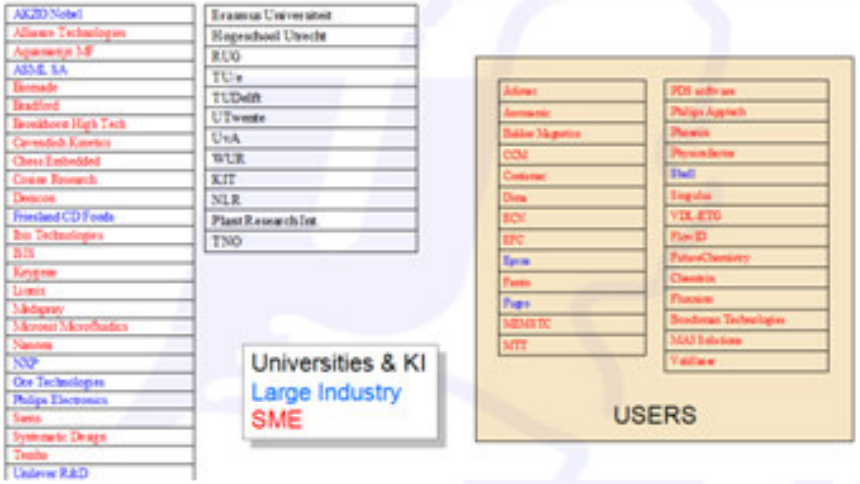
Microfluidics: Technologies and Opportunities

Henne van Heeren

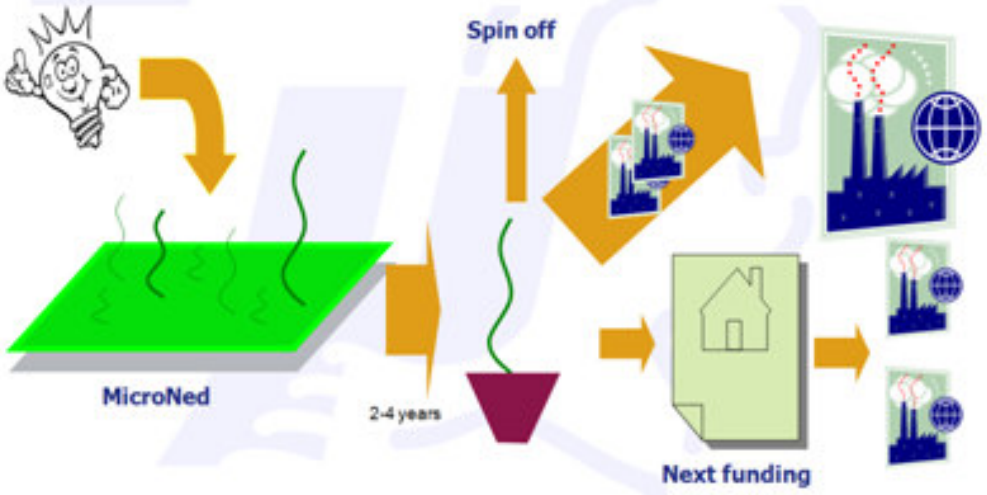
enablingMNT -the Netherlands-

MicroNed: public private cooperation

	Results
Patents	15
New products	19
New or improved processes	14
Improved products	10
Spin off companies	10
Spin off projects with industry involved	158
Spin off scientific projects	192
PhDs trained	80
New MST Professors	10
Conference contributions etc.	>600

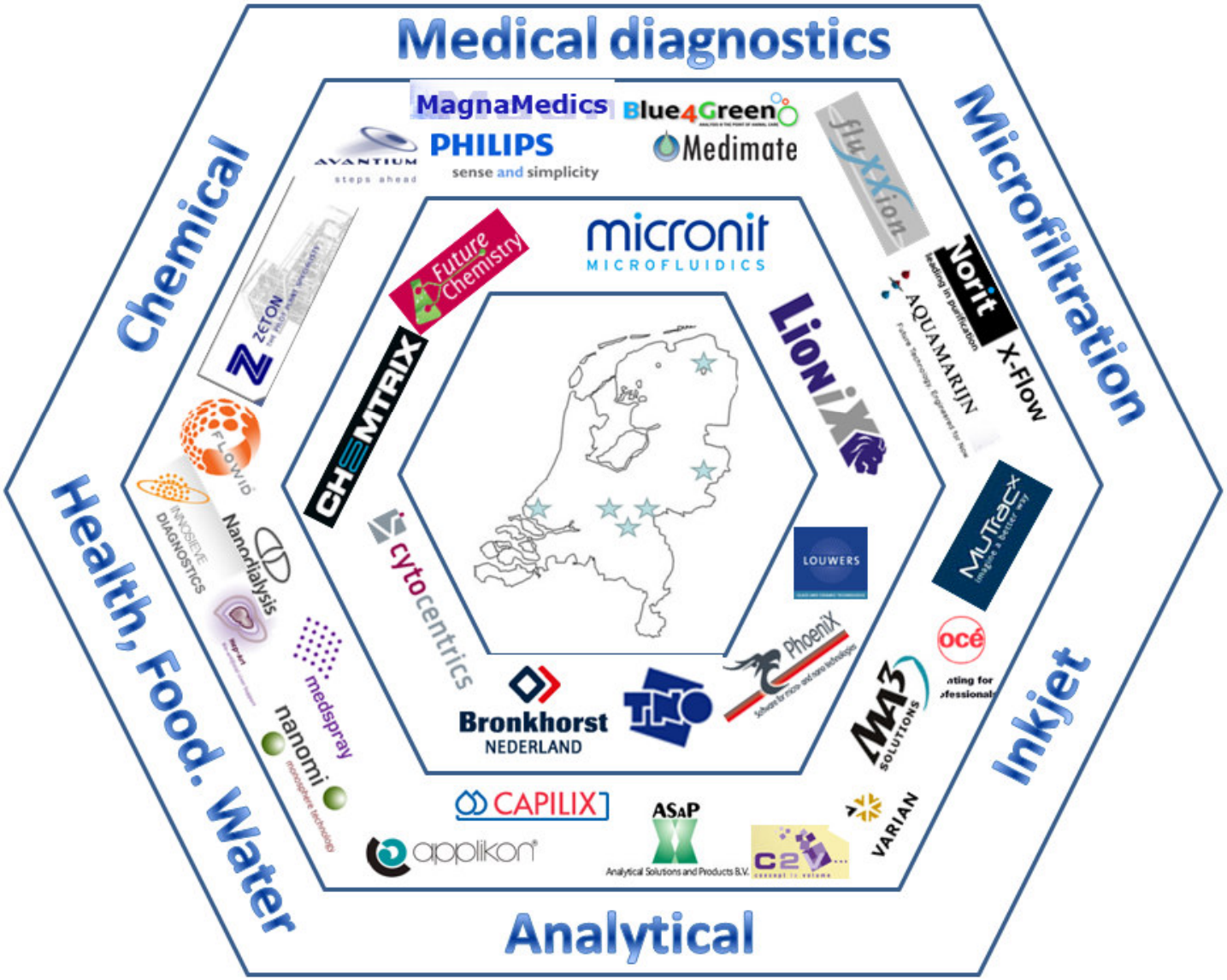


Establishing a market-oriented, dynamic and sustainable public-private MST infrastructure, which forms the basis for new product-market combinations

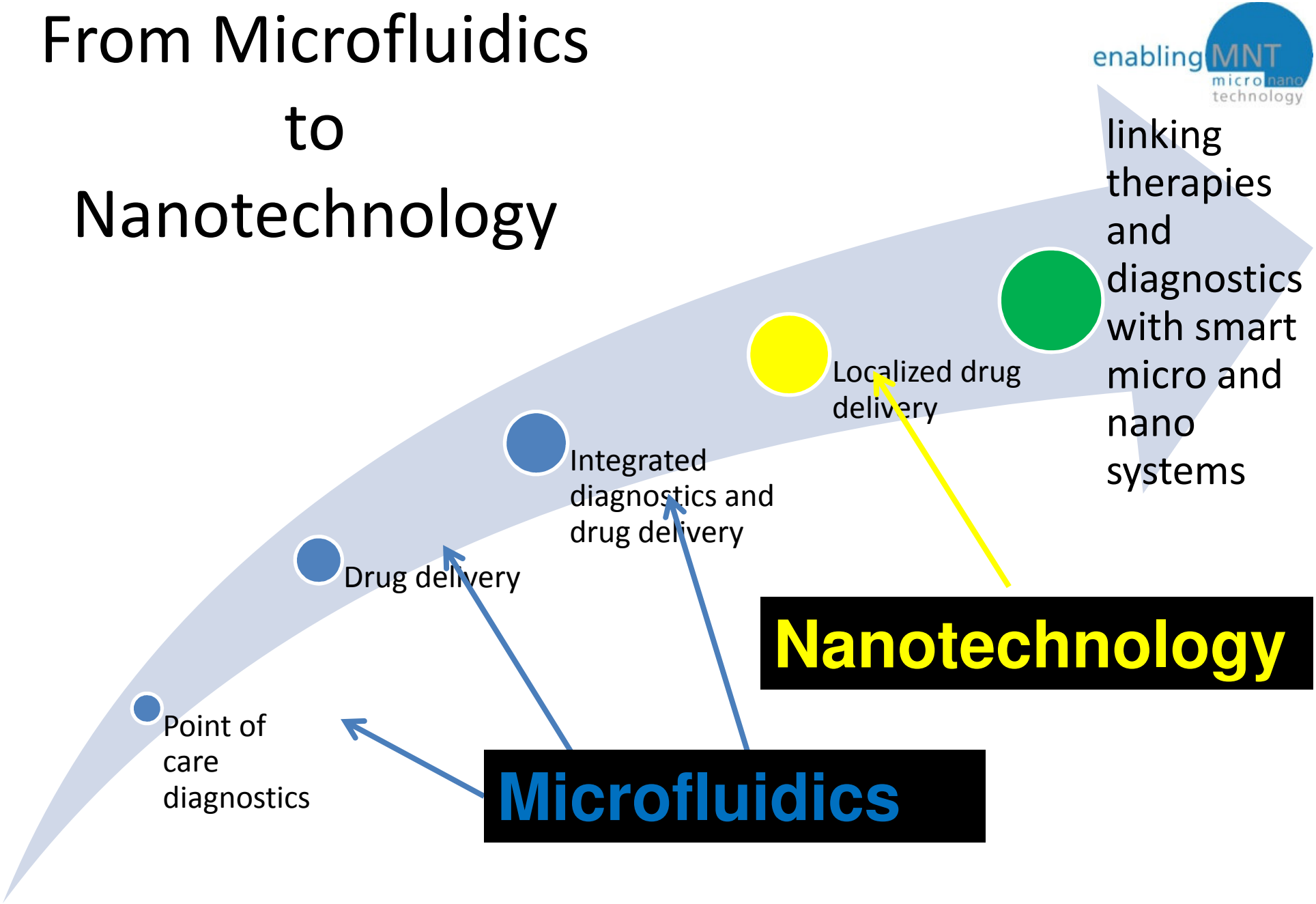


Megafluidics in the Netherlands

Dutch Microfluidic companies



From Microfluidics to Nanotechnology

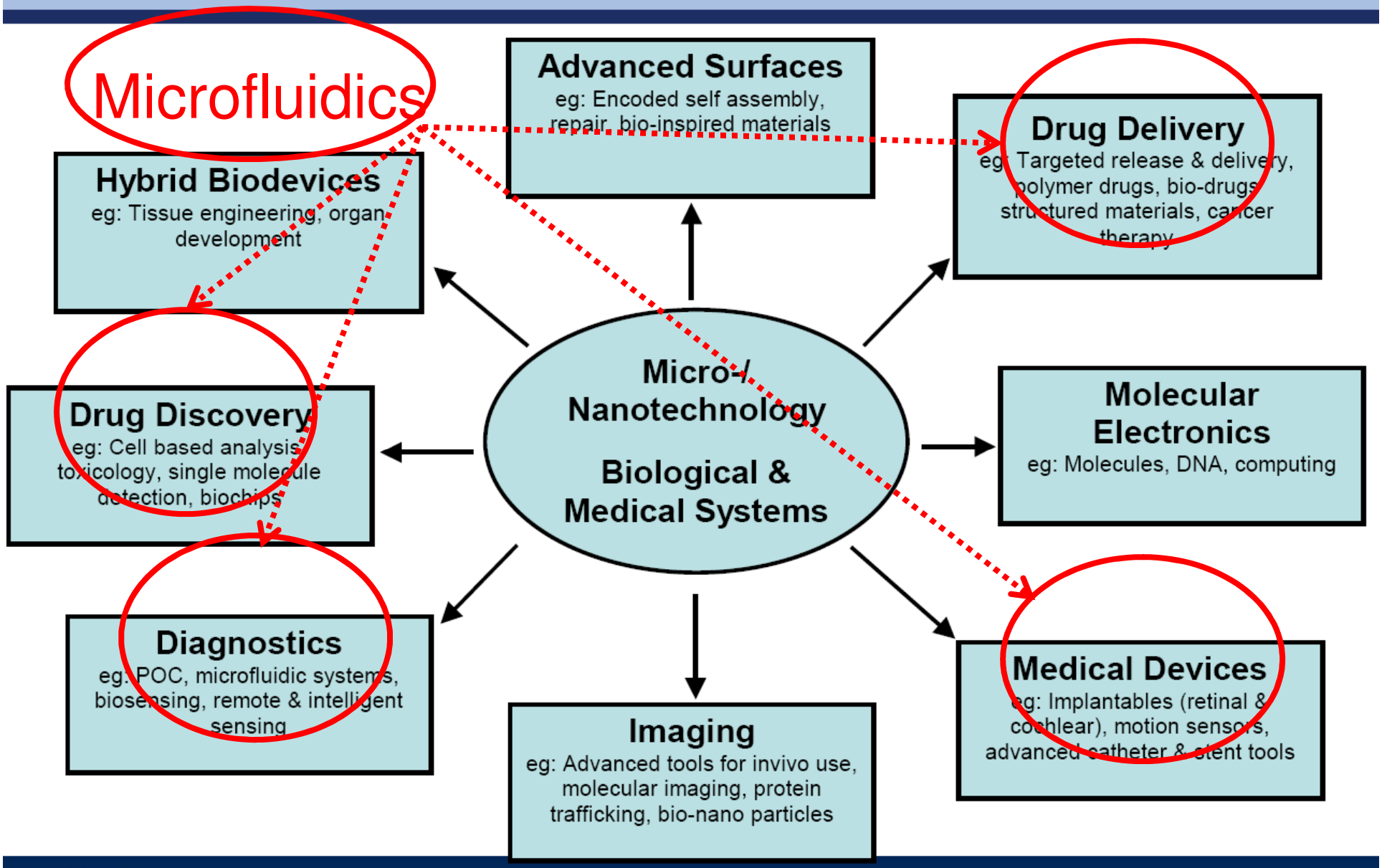


Benefits of microfluidic-based systems

- Processing:
  - safer
  - better process control
  - less energy & waste
- Diagnostics & analytical:
  - speed of delivery results,
  - generic technology platforms,
  - customisation to optimize for specific drug properties,
  - size of system, i.e. portable device for point of care applications, and
  - specialization for small volume /smaller sample sizes.

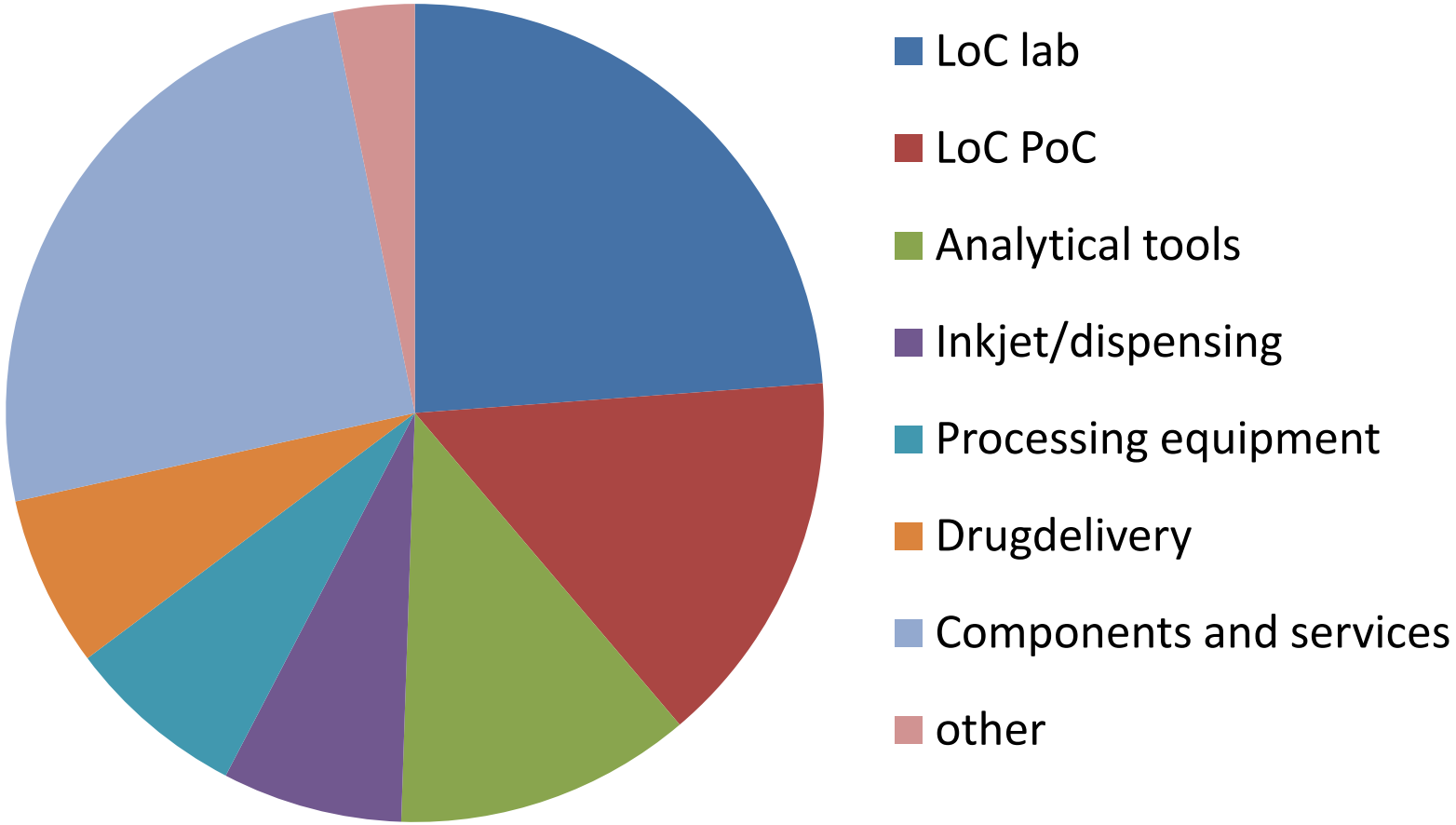
Both from batch to flow for diagnostics & processing

Nanotechnology and Healthcare: 1



Product classes

Analysis of >275 companies worldwide active in microfluidics



What problem does it solves?

Main driver: Point-of-Care Diagnostics

- Healthcare providers can deliver diagnosis and analysis:
  - faster,
  - at less cost,
  - more reliably.
- Individuals can monitor their own health.
- Individuals can bypass the conventional healthcare provider system.
- Tuning therapy to the real needs by PoC diagnostics

Functional specs

Process & system choices

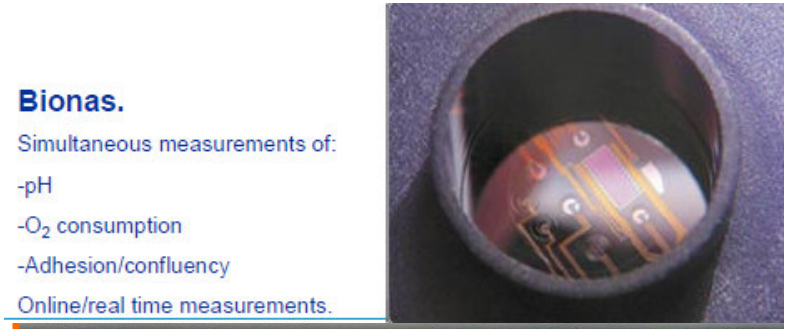
	Standard ⟷ Special
Cell sorting	FACS, filter based, dielectrophoresis, magnetic, laminar flow
Cell lysis	Thermal, chemical, mechanical
Purification	Filters, magnetic beads, silica beads & gels, micro & nano engineered surfaces
Separation	CE, dielectrophoresis, magnetic beads, laminar flow diffusion, nanochannels
Reagents	On board liquids, external liquids, onboard solid reagents
Flow control	Capillary, overpressure, membrane, centrifugal, digital, on-chip solid propellant
Target	Target, direct measurement
Target probe	(Single or multi) channel wall, magnetic beads
Detection	Fluorescence, electrical, visual, spectroscopy
Disposable	Single use, reusable

Product classes

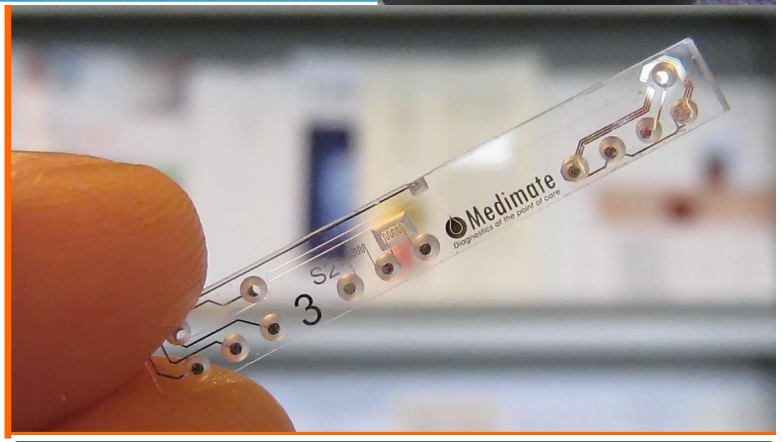
LoC main concepts

- Well array with integrated electronics and/or flow control
- Capillary flow device with electronic or optical detection
- Rigid substrate with flexible membrane for pumps & valves
- Multi flow channels with external pumping force
- *But: many more technologies are being used*

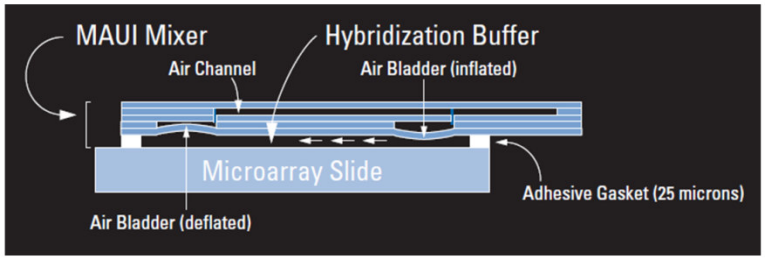
Bionas



Medimate



Biomicro



Gyros

One company, one product, one process

Product classes

LoC disposables

Fabrication costs	< 1 $	1-3 $	3-10 $	>10 $
Material for fluidic structure	Paper	plastic	Glass or plastic	Glass, plastic, PCB or silicon
Pumping	Capillary	Capillary or external pressure	Capillary, electro kinetic, integrated membrane or external pressure	Whatever
Application	PoC	PoC	PoC or lab	Central or research lab
Example	Glucose, pregnancy	?	Agilent	Agilent, Fluidign

Sweetspot?

Around the corner

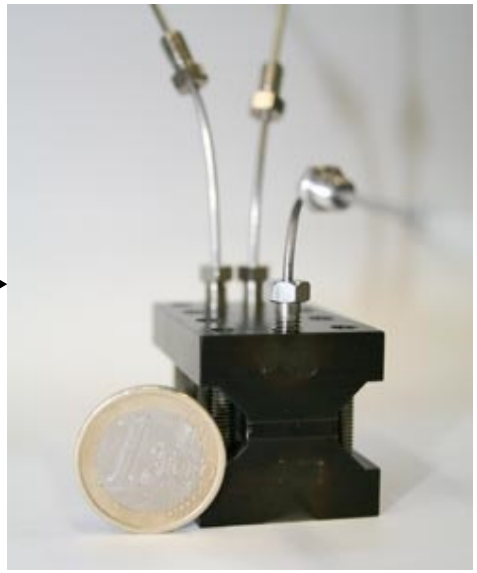
- IBM's DNA transistor technology,
- Paper microfluidics
- Nanowires for CMOS and sensing?
- Textile printed biosensors

Microreactor status

- Introduction leaders: Lonza and Sigma Aldrich, but all large chemical companies are active.
- Reactor technology leaders: Velocys, Heatric and Corning, but a number of startup companies are proposing systems (FutureChemistry, ChemtriX)
- Slow but steady introduction.
- Difficult to develop reactor and process simultaneously.

Which chemistry is suited for microreactors?

- Exothermic reactions.
- Extreme conditions difficult to realize in batch production.
- Very fast reactions.
- Reactions with safety risks (explosive or toxic).



M&A 2009 /2010

Company	Origin	Bought by	Activity
Advalytix	Germany	Beckman Coulter	single cell analysis
BioTrove	USA	Life technologies	PCR in Real Time
C2V	Netherlands	Thermo Scientific	HPLC
Handylab	USA	BD	Medical diagnostics
MDS	Canada	Danaher Corporation	mass spectrometry / bioanalytical measurement
RSIPL & Renovis	India	Evotec	Drug discovery
BioMicro Systems	USA	Roche	microfluidic microarray sample processing
Epocal	Canada	Inverness	blood diagnostic
Exigent	USA	AB SCIEX	HPLC
Stokes Bio	Ireland	Life Technologies	Identification of cancer biomarkers
Xceed	Canada	Axela	gene-expression analysis
MicroLab Diagnostics	USA	Zygem	microfluidic devices for rapid DNA testing

VC deals in microfluidics

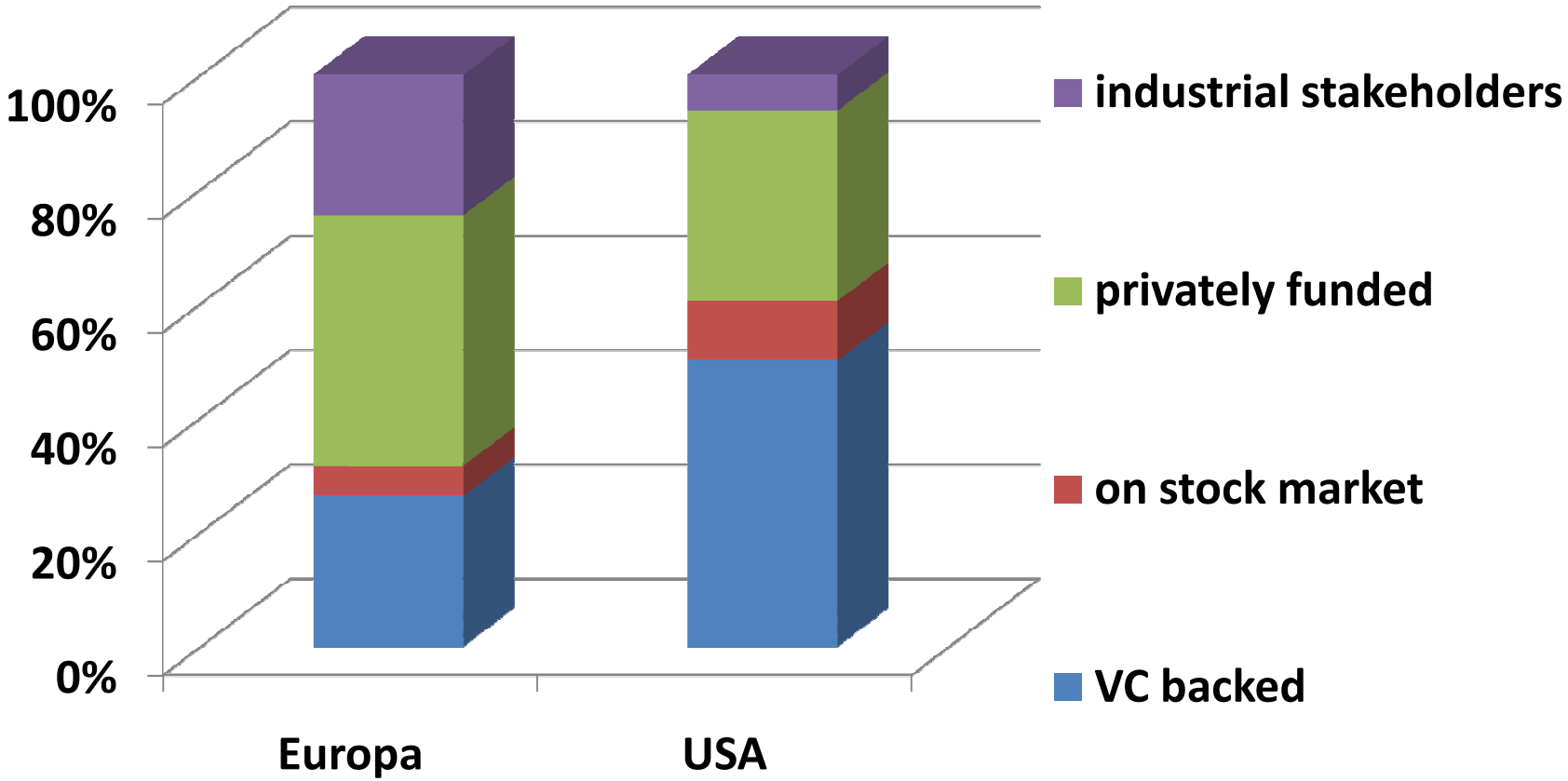
Year	Number of deals		Avarage deal size (M $)	
	USA/Canada	Europe	USA	Europe
2004/2005	4	3	12.5	8.3
2006	5	5	15.6	9.1
2007	8	6	27.2	6.2
2008	11	4	28.4	9.7
2009	12	5	20.9	9.3
2010	6	4	19.8	11.5

Over $ 1.5 B VC money in microfluidics

Typical company

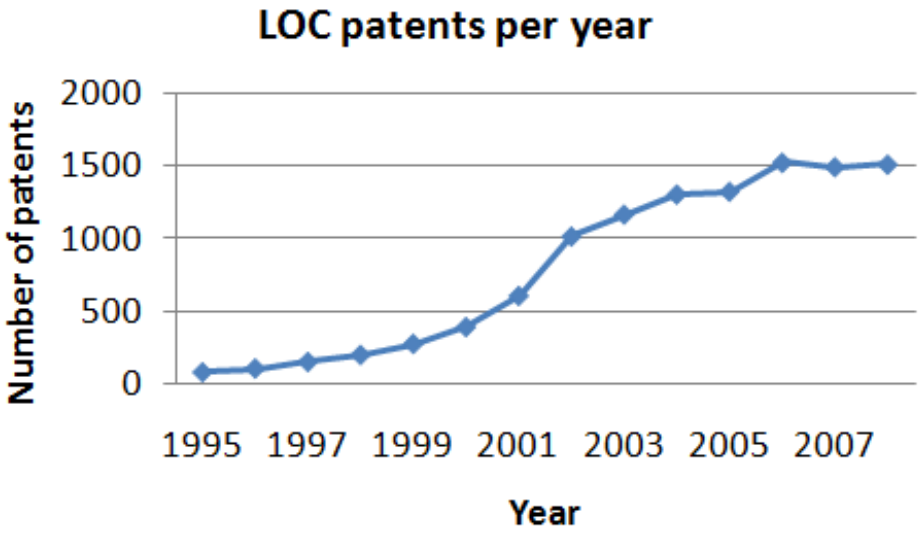
- USA 
  - Many go for DNA sequencing
  - Seed money: < 1 M $
  - Government grant: 2 – 5 M $
  - VC investment 1 – 4 M $
  - Second and third round: 10 – 20 M $ each
  - Sold to large company: 200 – 400 M$
- Europe 
  - Many go for specialized PoC
  - Seed money
  - Booth strapping for 5 – 10 years
  - VC investment < 5 M $
  - Ending up as OEM in niche application or sold to large company

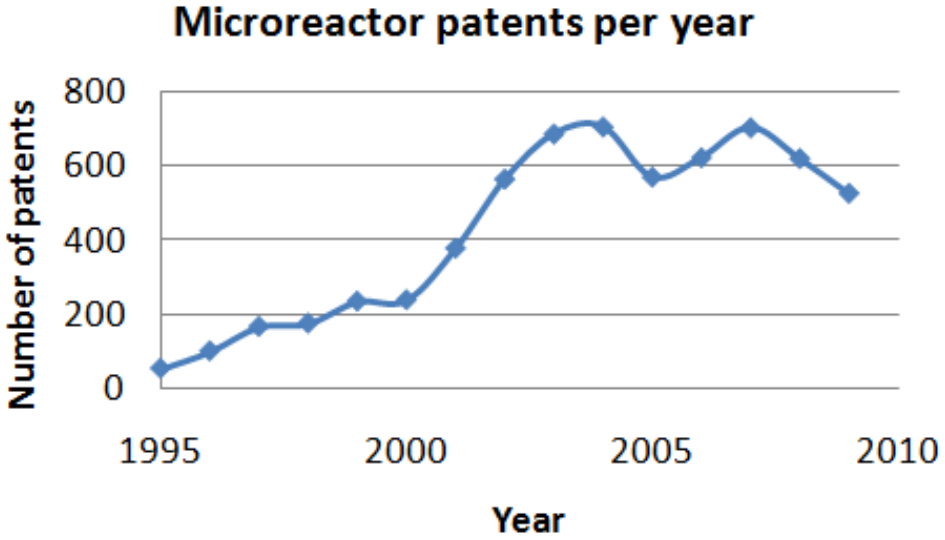
Funding of microfluidic companies



Patents/ Licences

Top patent owners?





LoC general

- Universities & Institutes: >1000
- Caliper (>500)
- >100
  - University of California, Gyros , Merck, Battelle
- 50-100
  - Agilent , Fluidigm, Micronics, Philips, Aclara, CEA ,

Microreactors

- Merck, Battelle Memorial Institute, Velocys, Forschungszentrum Karlsruhe, UDHE, Siemens, Casio, Degussa, Bayer / Ehrfeld Mikrotechnik, IMM, Clariant

Patents/
Licences

Quarrels

- Caliper against Shimadzu (CE technology): settled
- Cellectricon against Fluxion (ion channel drug screening)
- Handylab against Caliper (settled)
- Caliper against Molecular Devices (settled)
- Caliper against Aclara (settled)

Conclusions/additional remarks

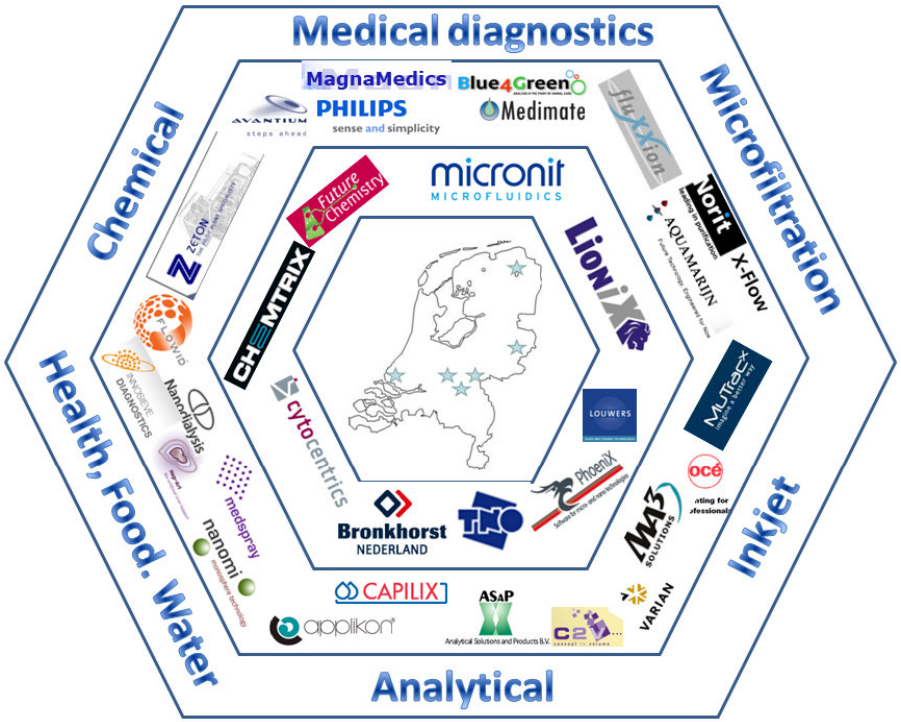
- Yes, we are going to benefit from microfluidics, but:
  - it is a long and difficult route, and will there be an attractive business case / incentive for all the players?
  - One company, one product, one process.
- And, how about all the microfluidic patents?
- The USA companies: more active in patenting & have better access to capital.
- Europeans: exploiting well defined unique segments.
- Key challenges for the microfluidic industry
  - Define business space / business case
  - Sort out your patent position
  - Design reliable products
  - Set up industrial production processes

Thank you for your attention

Henne van Heeren

henne@enablingmnt.com

0031 786300748



See you at:

Netherlands Micronanoconference 2010, November 17 & 18

www.micronanoconference.nl

MicroTAS, 3-7 October, the Netherlands,

www.microtas10.org