Commercialization of microfluidic technology based products: where is this industry heading to?

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enablingMNT

- The **enablingMNT** group provides support to new and established businesses in the Micro & Nano Technology (MNT) and System Integration sectors where the uptake of MNT offers enhanced performance and potential market advantage.
- Its partners each have over 20 years of experience in business development, marketing, and technology related services delivered to both private and public sector customers.
- The group have maintained a leading position in the field through strong participation in European projects in the MNT and System Integration areas and collaboration with international support organisations including MEMS Industry Group, NEXUS, MANCEF, IVAM, etc.

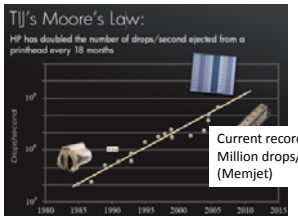
Megafluidics in the Netherlands



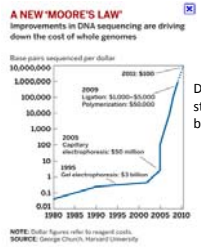




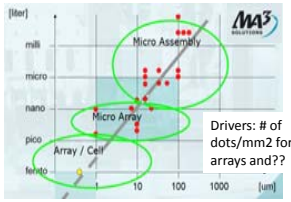
Microfluidic revolution



Current record: 750 Million drops/second (Memjet)



Development stalling? Needs breakthrough?

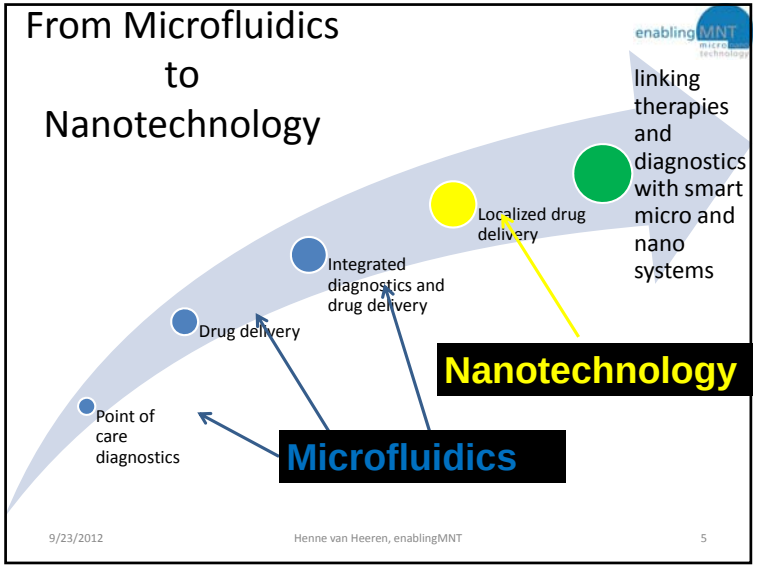


Drivers: # of dots/mm2 for arrays and??

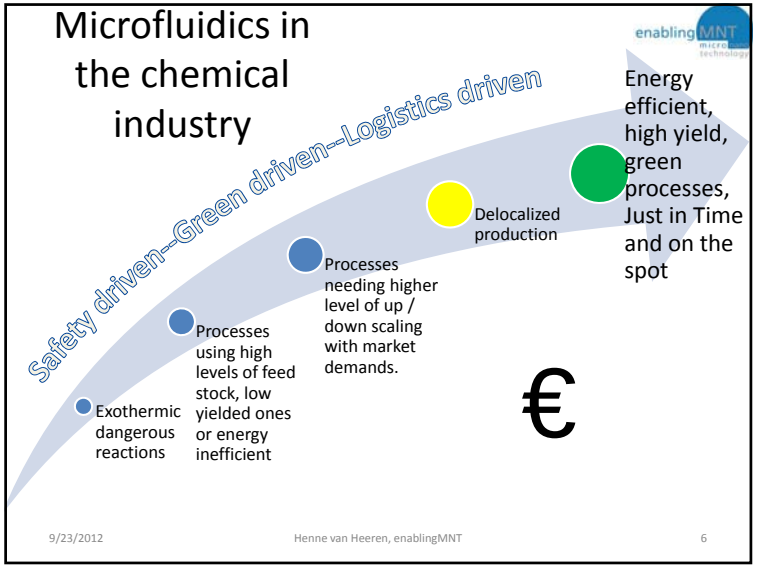
And microreactors, and diagnostics and ……

Over 400 companies worldwide active in microfluidics! (and increasing)

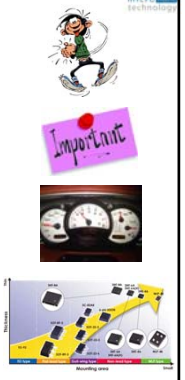
From Microfluidics to Nanotechnology



Microfluidics in the chemical industry



- New industries go from
  - Hype
  - Trends (agreement about what is important and what not)
  - Application roadmaps (agreement about product performance criteria)
  - Technology roadmaps (agreement about technology drivers and trends)
- The microfluidic industry is still in the hype phase, but are there trends?

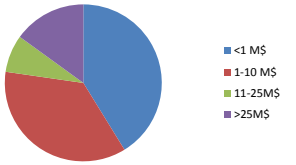


Microfluidic scene

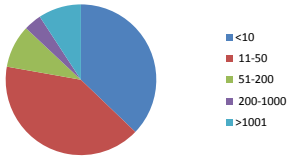
- >450 companies active in microfluidics
- 336 OEMs or would be OEMs (174 of them from the USA)
- >100 companies offering services and components
- Dominated by many start ups and a few multinationals.

The microfluidic industry

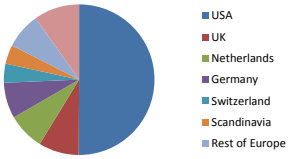
Investment in the companies



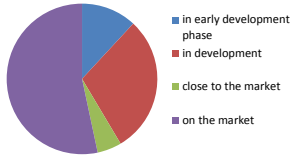
Size of the companies



Microfluidic companies



Company status



What application?

- Inkjet deposition on paper, PCB, foil, array etc.
- Sample pretreatment for analytical instruments
- Digital microfluidics
- Microreactors
- Point of care
- Bioreactors
- Lab on chip
- Micro cooling
- Drug delivery
- Drug discovery / screening
- Patch clamp
- Veterinary & agricultural
- HPLC, MS, GC
- Emulsification
- Spray drying
- DNA/RNA screening /PCR
- Molecular diagnostics

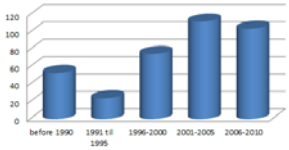
TREND 1: Chips suppliers are becoming component suppliers.
TREND 2: Would be medical diagnostic companies divert into other diagnostic applications.

University spin off hot spots (microfluidics)

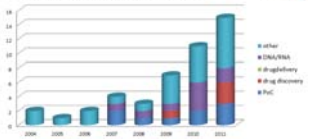
- **Havard** (Claros, Vista Therapeutics, gnubio, DFA, Nano Terra)
- **MIT** (Bostonms, Firefly BioWorks, Netbio, Pharyx, Biosscale, Hepregen, Microchips)
- **University of California Berkeley** (Cellasic, Nanomix, IntegenX)
- **University of California San Diego** (Celula, Nanosort, Biological Dynamics)
- **University of Texas (**Resonant Sensors, Nanomedical systems, Leonardo Biosystems)
- **Cornell University** (HμREL, Pacific Biosciences, Advion)
- **Caltech** (Labsmith, LeukoDx, Fluidigm)
- **EPFL** (Spinomix, Diagnoswiss, Biocartis, Ayanda, Abionic)
- **Imperial College London** (DNAE, Microsaic, Molecular Vision, Deltadot
- **Cambridge University** (Cambridge Biomagnetics, Sphere Fluidics)
- **A*STAR / National University of Singapore** (Micropoint Technologies, Veredus, Cellsievo, Curiox, Clearbridge, CE Resource)
- **IMM** (Ehrfeld, Mikroglas, ThinXXS)
- **University Twente** (U-needle, Aquamarijn, Ibis Technologies, Kryoz, Medimate, mylife technologies, Medimate, Ostendum, Opisense, Senzair)

State of the industry Happy ending for university spin offs?

Launch of the company



Number of Microfluidic Takeovers per year



Survival of the fittest	Survival rate
R&D project	200
Start up company	10
Some funding	9
Acquired	8
Market introduction	5
"Big" market success	1-2?

Staying power needed:

- Time to "success": average 9 years
- Time to failure: average 7 years
- Time to market: average >10 years

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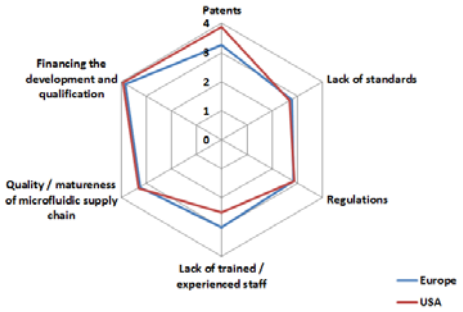
Biggest challenges facing the microfluidic industry



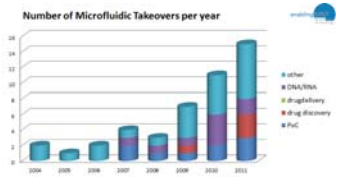
Business??

- Protea "The Company has experienced negative cash flows from operations since inception (in 2005) and had an accumulated deficit at December 31, 2011 of approximately $37 million …… The Company will continue to require substantial funds to advance the research and development of its core technologies, …."
- Cepheid: "Prior to our fiscal year ended 2011, we had incurred operating losses in each annual fiscal year since our inception (in 1996). We experienced net losses of approximately $22.5 million in 2009, $5.9 million in 2010 and we achieved profitability for the first time for the fiscal year ended 2011. As of December 31, 2011, we had an accumulated deficit of approximately $205.6 million."

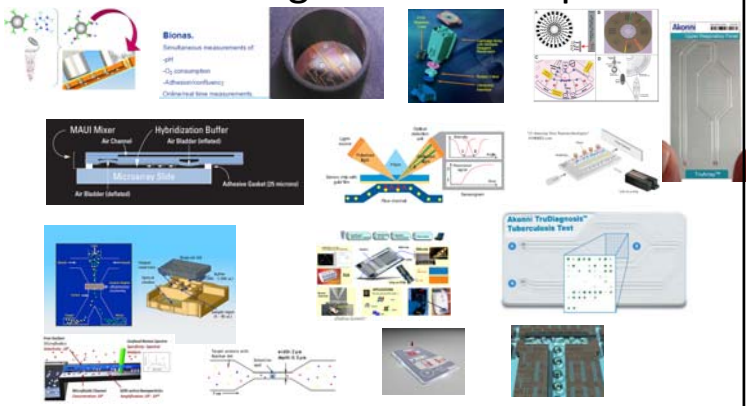
Buyers

Abott (i-Stat, IBIS)
Agilent (Biotrove, lab901, Biocos)
Beckman Coulter (Advalytix, Blue Ocean Biomedical)
Inverness Medical Innovations (Biosite, Epocal)
Johnson & Johnson (Veridex, Amic)
Life Technologies (Cytonix, StokeBio, Ion Torrent, Biotrove)
Pall (Genesystems, MicroReactor Technologies)
Roche (454, Biomicrosystems, Medingo)
Sony (iCyt, Miconic)
PerkinElmer (Caliper, Evotec Technologies)
Bio-Rad (Quantalife, Digital PCR Technology)
Becton & Dickinson (Handlylab)
GE Healthcare (Biacore)
And many others

TREND 3: Universities are actively generating microfluidic start ups.
TREND 4: Electronic and pharmaceutical companies are buying them. (When having a successful product or technology).

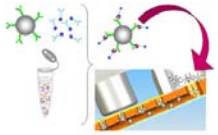


Bewildering number of technologies and concepts



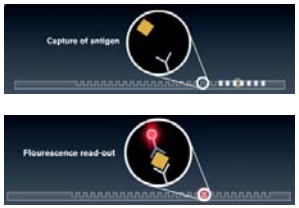
Core technologies

Magnetic beads



- The most efficient way to separate the target material from the sample.

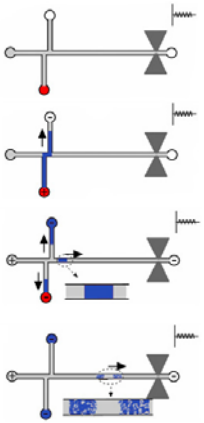
Fluorescence based immunoassay



- Workhorse of microfluidic based detection. Well known and reliable, but add complexity and needs large amounts of target material

Core technologies

Capillary electrophorese (Courtesy Medimate)

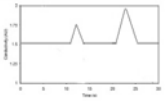


One drop of blood is placed on the sample reservoir at the end of the sample channel.

An electric field over the sample channel. causes the positive particles in the blood to migrate to the other end of the sample channel.

An electric field over the separation channel causes the positive ions at the intersection of the two channels to migrate to the end of the separation channel.

In a long channel the ions are completely separated by the different speeds of migration.



Core technologies

PCR

- Workhorse of target enrichment, but time and chemical cosumming.

- Can we do direct sequencing?
  - Digital microfluidics: Gnubio, Raindance, Gigagen.
  - Nanopore/channel: Pacific Bioscience, Stratos Genomics, Nabsys, Nanopore.
  - Micro well and direct detection of H+ release: Ion Torrent.

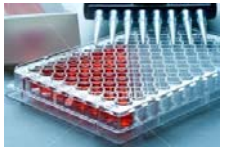
Challenge PCR based systems:

- A small device with a disposable microfluidic chip that integrates:
  - sample preparation,
  - amplification reaction,
  - concentration,
  - detection
- This device can be used at home, the doctor's office, as well as the field for applications from food safety to pathogen detection.
- Performance:
  - Price (<1 $) per disposable,
  - time to results < 7 minutes,
  - Multiple tests in parallel per disposable.

TREND 5: The industry is looking for technologies that don't need labeling, i.e. specific sensors
TREND 6: The industry is looking for technologies that don't need time consuming PCR, i.e. hyper sensitive sensors.

Core technologies

Microplate array



- Well array technology: the most used technology in diagnostic testing, but difficult to automate and miniaturize further; typical laboratory technology

TREND 7: Digital microfluidics is seen as a way to miniaturize well array testing further.
TREND 8: Well array testing is developing into more complex testing more akin to real life situations.

Integration levels:

- the whole process from input sample to result (detected electrically or optically) is in a:
  - chip: glass, polymer or silicon chip,
  - CD,
  - card: microfluidic plate with additional components like a biochip mounted on top of the plate, the fluidic does not leave the microfluidic plate,
  - cartridge: the fluid is transferred from one component to another in plane or in 3D,
  - not integrated.

Integration level

	Interconnection	Applications	Main user community	Examples	Complexity of tests and preprocessing	Typical time to result	Weakness	Comments
Not integrated	Fluidic interconnects to instruments	Standardized low cost medical diagnostic testing or R&D experiments	Central labs, R&D	Many available	High	Several hours	Labor intensive	Fitting to the standard array based workflow
Modular approach	No commercial successful examples known, except microreactors, but they are delivered as complete units.							
Chip level integration	Only electrical or optical	Point of Care/Use	Medical professionals etc.	Medimate, Capilix	low	few minutes	Only limited preprocessing possible	Mostly for small ions
Card level integration	Only electrical or free field optical	Point of Care/Use	Medical professionals etc.	Micronics	limited	15-60 minutes		
CD level integration	Only free field optical	Sample treatment, PoC	Central and smaller labs (Medical professionals)	Gyros	medium	10-15 minutes	Difficult finding the right application niche?	Excellent for multiple sample or multiple target testing
Cartridge level integrated	Not for PoC, sometimes for lab applications	All	From PoC to central labs	Many available	High	15-30	Difficult to achieve price targets	Far out the most popular approach, (but costly and slow?)

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Development priorities per segment:

- Processing industry: integration of microfluidic components
- Analytical equipment suppliers: component development + design and modeling
- Supply chain: test & measurement
- Research community: application development
- ALL: RELIABILITY

State of the industry

Business strategy

Organic growth

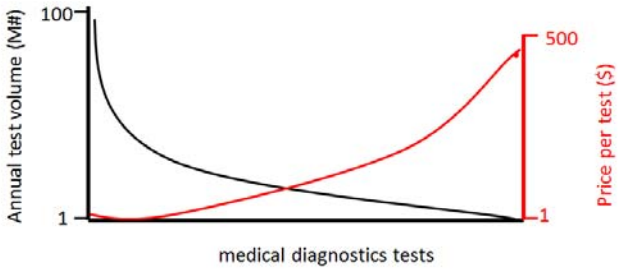
- Formulatrix (protein crystallization automation solutions) started in 2002 with 2 people; they managed to survive the first two years with services and introduced their first product during the second year. After 8 year they had 204 employees and an installed base of 237 pieces of equipment at 17 sites.

VC backed

- Oxford Nanopore founded in 2005, secured over 100 M$ for the direct, electronic analysis of single molecules. Intends to commercialize DNA strand sequencing products, directly to customers within 2012.

Long tail market: Medical Diagnostics

TREND 9: platform technology is seen as a solution for the many niche markets



State of the industry

Not always a straightforward business case

- There are about 10 high volume diagnostic opportunities, like for instance diabetes, TB, HIV, etc., but also hundreds of tests were the volumes are less, often substantial less than 1 million tests per year.
- Several chronic diseases, the (sometimes costly) measurement can show a substantial added value in another part of the health care chain.
- Tools like implantable pumps or microneedles reduce side effects / optimize the working of a drug (and extend the patent protection period). But they are also making the microfluidic instrument part of the drug sales. Those coupled sales will result in an intertwining of markets and companies.

State of the industry

Examples of complex business cases

- Medspray inhaler:
  - The big money is in the drug, the microfluidic component is an enabler.
  - Launching customer is paying the development bill; each device is developed in relation to a certain drug.
- Medimate:
  - Big saving is related to the patient's risk of side effects of the drugs
  - the insurance company benefit financially when the products becomes a success.
  - Guess who is investing in the company and who is launching customer?

Are we getting closer to the market with microfluidics?

	R&D	Pre-development	Development trials	Entering the market	On the market
Patchclamp					R&D
Micro dispensing			High volume electronics		Medical diagnostics
Lab on chip				Medical diagnostics	
MS and LC instruments				Industrial, R&D	
Sample preparation devices				Medical diagnostics, R&D	
Array with flow control and /or electronics integrated				Medical diagnostics	
Electronic coolers		Sensors & Telecom		Electronics	
Microreactors			Chemical Industry		
Emulsification		Pharma			
Drug development			Pharma		
Microneedle		Drug delivery	Drug delivery		
CE (stand alone)			Medical/ veterinary		
Artificial organs	Medical				

STATUS 2009

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Emulsification		Pharma			
Drug development			Pharma		
Microneedle		Drug delivery	Drug delivery		
CE (stand alone)				Medical/ veterinary	
Artificial organs	Medical				

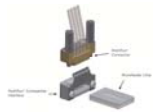
STATUS 2012

State of the industry

Examples of new products and products coming soon (1)

- Industrial equipment:
  - Sono-Tek ultrasonic coating device,
  - Cetoni & Corning microreactors,
  - Microfluidic interconnects by Dolomite,
  - Micrux chipholder and the “plug and play” chipholder from Micronit ,
  - Advanced MicroLabs: online process analyzer based on CE.

TREND 10: plug and play microfluidic instruments



State of the industry

Examples of new products and products coming soon (2)

- Point of Care
  - Epocal FDA clearance for its Point of Care Lactate test, now being sold by Alere
  - Lingvitae: low cost generic diagnostic test platform, launched 2011
  - Samsung 19 different blood tests in just 12 minutes
  - Medimate hopes to also see commercial turnover in 2012 with its lithium home test for patients suffering from Bipolar Disorder.
  - Microvisk is gearing up for market introduction in 2012 with its device to monitor the blood clotting.

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Standards, or no standards?

- The general answer can be best described as “perhaps”.
- The likelihood is rated highest for suppliers of analytical instruments and chemical reactors followed, surprisingly, by PoC instrumentation.
- But opinions are divided: over 25% will not participate in any standard discussion.




Why are standards needed?

- Select for the best available.
- Second sourcing.
- Ease of use.
- Limit the number of instruments in labs.

Specification for Industry to develop integrated Point of Care tests to support pathways of care
(NHS East of England Planned Care Clinical Programme Board)

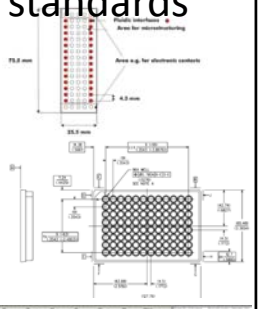
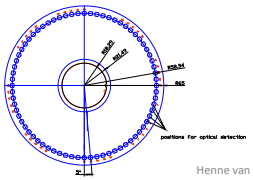
The POC unit must provide assays for

Assay	Diabetes	Hypertension	Chronic Kidney Disease
HcA1C	✓	✗	✗
Creatinine	✓	✓	✓
Thyroid function	✗	✓	✗
Total Cholesterol & HDL	✓	✓	✓
LDL	✓/✗	✓/✗	✓/✗
Triglycerides	✓/✗	✓/✗	✓/✗
Electrolytes (Na+ & K+)	✗	✓/✗	✓/✗
AST	✓/✗	✓/✗	✓/✗
Hb	✗	✗	✓
Ferritin	✗	✗	✓/✗

Key: ✓ Required
✓/✗ Desirable
✗ Not Required

ro/forma microfluidic standards

- Microscope slide
- Microtiterplate:
- 45*15 mm glass chip
- Optical disk


Trends summarized:

1. Chips suppliers are becoming component suppliers.
2. Would be medical diagnostic companies divert into other diagnostic applications.
3. Universities are actively generating microfluidic start ups.
4. Electronic and pharmaceutical companies are buying them. (When having a successful product or technology).
5. The industry is looking for technologies that don't need labeling, i.e. specific sensors.
6. The industry is looking for technologies that don't need time consuming PCR, i.e. hyper sensitive sensors.
7. Digital microfluidics as a way to miniaturize well array testing further.
8. Well array testing is developing into more complex testing more akin to real life situations.
9. Platform technology is seen as a solution for the many niche markets.
10. Plug and play microfluidic instruments.

General observations

- The products are there, but are not reliable enough, too expensive and the quality of the components is not good enough. Giving more attention to standards might help.
- The community worries very much about how to finance the development and how to survive the IP situation.
- We see signs of matureness
  - Consolidations
  - License deals
  - Better formulated business proposals
  - Standard discussions
  - Availability of training / easy to use tools etc.
  - Microfluidic Industry Consortiums: MinacNed, FMMC, MF3

Your chance to meet us all: