Interoperability of microfluidic components

(status discussions June 2015)

Henne van Heeren

enablingMNT

henne@enablingMNT.com

Ongoing standardization discussions

- Chip sizes
- Microfluidic interconnections:
  - Chip to tube
  - Micropump / microsensor to tube
  - (Bio)sensor to chip
  - Combining with electrical or optical connections
- Classes of applications
- Qualification of / tests for microfluidic components / systems
- Flow control
- Sample preparation
- The “White Box”; one instrument / many different specific disposables for different suppliers

Introduction standards

- Real operability needs standards or at least industry wide supported design rules.
- “Markets make standards, not committees”
- Therefore identify:
  - the barriers and drivers for interoperability and standards,
  - accepted (de facto) standards,
  - technology trends,
  - dominant players and their products.

Barriers & Drivers for standards in microfluidics

Barriers:

- Market position of companies dominant in the market or are expecting to achieve such dominance.
- Investment in current products might become worthless.
- Diversity in the existing products already on the market.
- Lack of uniformity in our vocabulary.
- Existing standards in established industries.

Drivers:

- Health care: to enable diversity in testing, there are hundreds of specific tests needed, but the user wants to limit the number of instruments in the lab.
- Analytical instruments / processing equipment / R&D: to enable the selection of the best components and the ability to compare / qualify those components and the systems.
- Plug & play microfluidics.

Established standards and ongoing discussions

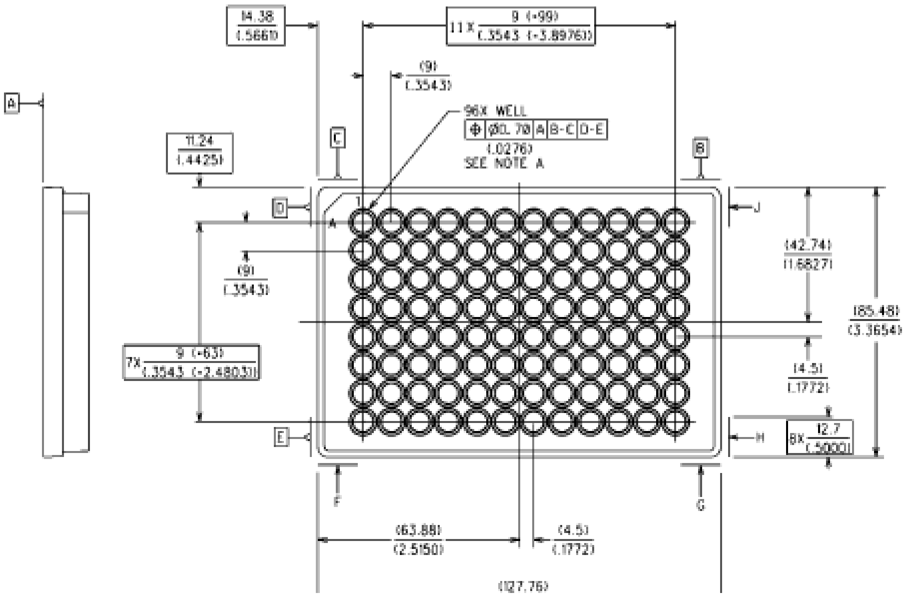
- Established:
  - Microplate Well Positions: ANSI/SBS 4-2004
  - Standard microscope slide: ISO 8037-1:1986 Optics and optical instruments -- Microscopes -- Slides -- Part 1: Dimensions, optical properties and marking
  - Luer interface (ISO 594:1986)
- In discussion:
  - Semi
    - SEMI Draft Document 3951 Proposed Guide for Standard Performance, Practices, and Assembly for Ultra High Purity Microscale Fluidic Systems for use in Scalable Process Environments
    - Semi: proposal for multi port interconnect in discussion. (8 parallel fluidic tubes with a center to center spacing of 0.500 mm and an ID of 0.250 mm)
    - SEMI Draft Document 4691, New standard: specification for high density permanent connections between microfluidic devices
    - SEMI MS7-0708 - Specification for Microfluidic Interfaces to Electronic Device Packages
    - SEMI MS6-0308 - Guide for design and materials for interfacing microfluidic Systems
  - Nessi: mainly about sampling for process control
    - ISA-SP76, Composition Analyzers?
  - DIN standardization group on microreaction technology:
    - ISO 10991 Micro process engineering - vocabulary
    - Characterization processes for microreactors.
  - Microfluidics Consortium:
    - Multi port interconnects / chipsizes & design manufacturing guide
  - Mfmanufacturing project:
    - European initiative for the standardization and manufacturability of complex micro-fluidic devices

VDMA

- VDMA has proposed a standard “Einheitsblatt” for micro fluidic technologies. Mainly for chemical process technologies. The VDMA 66305 defines the interfaces between so-called Match-X building blocks developed by Fraunhofer (IZM and IPA), both geometric as well as functional interfaces are described.
- Producers of Match-X building blocks that follow the VDMA-66305 standard, make the building block interoperable between other building blocks produced by other parties.

De facto standards for microfluidic designers

Length l	Width b
$45^{\ 0}_{-1}$	$26^{\ 0}_{-1}$
$76^{\ 0}_{-1}$	
$76^{\ 0}_{-1}$	$39^{\ 0}_{-1}$
$76^{\ 0}_{-1}$	$52^{\ 0}_{-1}$

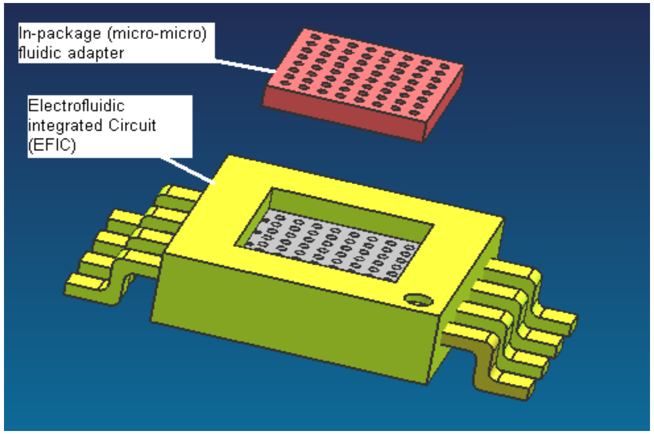


microscopy slide format

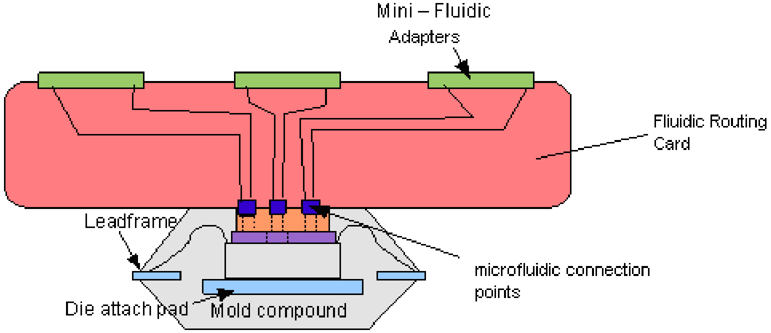
microtiter plate format, layouts with 96, 384 or 1536 wells.

Luer (ISO 594:1986)

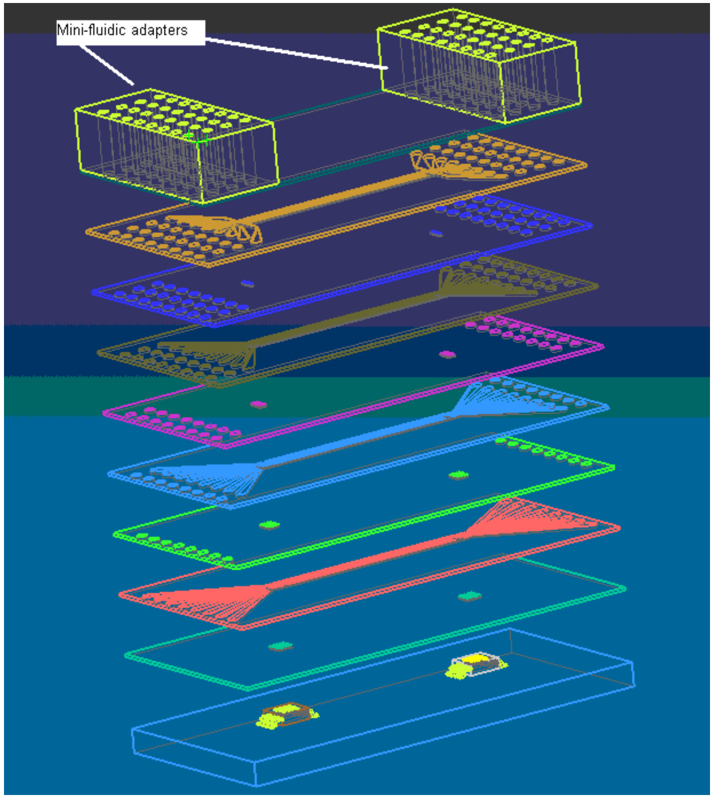
SEMI MS7-0708: Specification for microfluidic interfaces to electronic device packages



Exploded 3-D View of EFIC Package

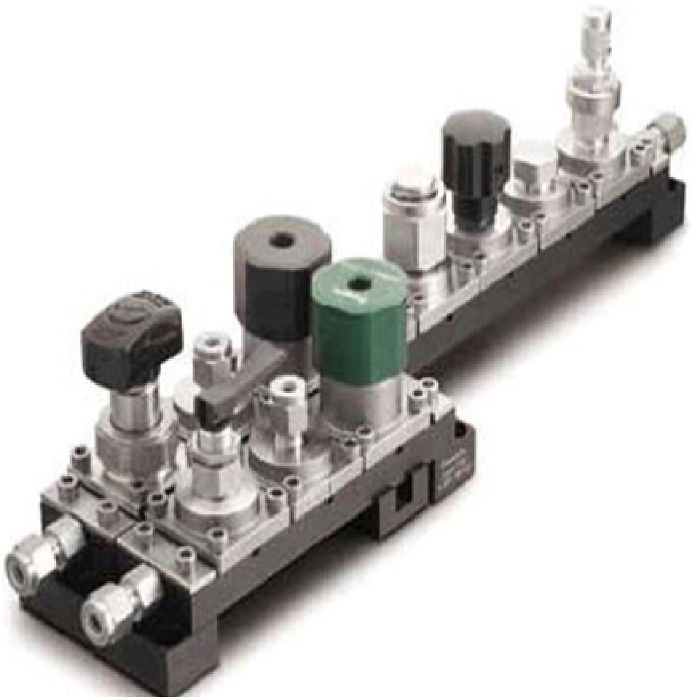


Functional Description of Assembled Parts



EFIC Fluidic Routing Card & Adapters

NeSSI™ Modular Sampling Systems



NeSSI generation III systems: microanalytical devices such as lab on chip for process and water control.

- New Sampling/Sensor Initiative
- Surface-mount modular component based gas and fluid handling and conditioning systems
  - ISA SP76 interface specification
  - Elastomeric o-ring seals
- Offer flexibility in design and implementation
- Allows for optimal positioning of analyzers in a process stream

Standardization activities in Germany

working on standardization for micro fluidic components:

- DECHEMA Fachgruppe Mikroverfahrenstechnik
  Board Members: Dietrich (mikroglas), Stenger (Evonik), Dittmeyer (KIT)
- DIN Arbeitsausschuss Mikroverfahrenstechnik
  Chairman: Dietrich (mikroglas)

activities:

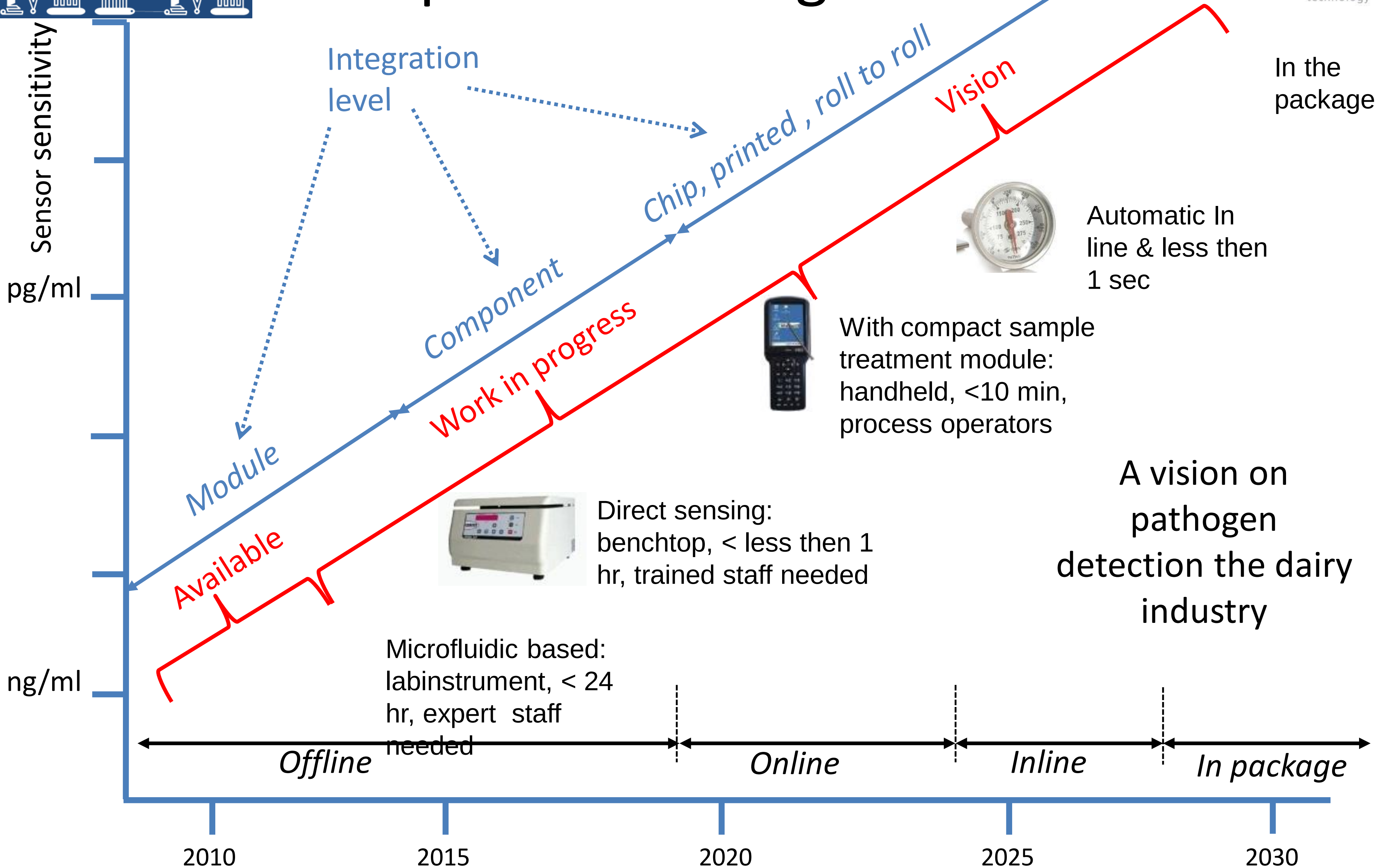
- standard of fluidic interfaces proposed by Micro ChemTec Modulare Mikroverfahrenstechnik
- terminology norm ISO 10991 already in place
- DIN norm on explosion protection with micro fluidic components in preparation
  will be published in approx. 2 months
- research project on standardization of residence time measurement approved
  will start in July 2012 for 1 year --> standard equipment and measurement procedure

De facto standard in fittings (for instance chromatography)

- Fittings:
  - low pressure fluid transfer: thread ¼-28; flat bottom configuration
  - high pressure fluid transfer: 10-32: coned configuration of port
- Tubing: 1.6 and 3.2 mm

Where are we heading to as an industry?

Roadmap for food diagnostics



Integration: a key driver for smaller and faster diagnostic devices.

- Drivers:
  - Need for small sample sizes.
  - Ease of use / robustness.
  - Need for low cost disposables.
  - Short time to measurement result.
- Challenges:
  - Microfluidics doesn't scale as easy as electronics (or even as mechanics) & electrons are electrons, but in microfluidics…………..!
  - Combining electronic, mechanical, fluidic and optical components or structures.
  - Technology and business environment are immature.

Always integrate microfluidics?

	PoC third world	PoC (home)	PoC (other)	Central Lab	Research
Acceptable time to result	Seconds to minutes	Seconds to minutes	< 6 minutes	Up till half an hour	Up till several hours
Cost of instruments	Up to a few 100's of $	Up to a few k$	Up to a few k$	Up to 100's of k$	Up to a few M$
Staff	Untrained	Untrained	Semi trained	Trained	Highly specialized
Cost of disposables	< 0.5 $	Preferable < 1 $	Preferable <3 $	Up to 10's of $	Less relevant
Number of tests running in parallel	1	1	1-10	Typical 10 -20	Less relevant, but flexibility needed
Level of integration to be expected	Very high	Very high	High	low	Very low

Identified integration concepts:

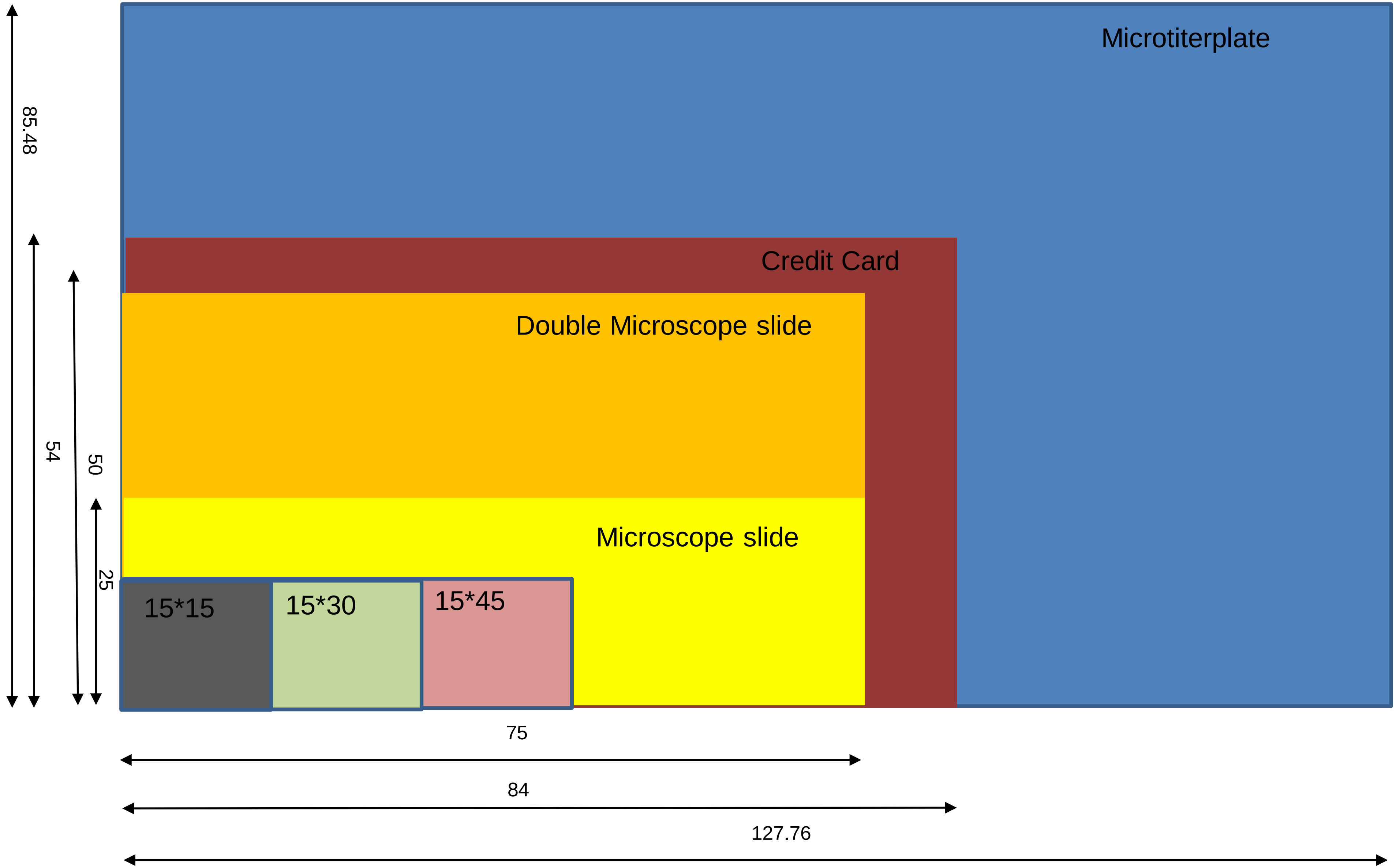
- The whole process from input sample to result (detected electrically or optically):
  - Chip: all microfluidic functions in one chip.
    - on the market: glass, polymer, silicon chip.
    - In development: paper, roll to roll manufactures films etc..
  - "CD": centrifugal driven microfluidic flow
  - 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 a plane or in a 3D configuration.
  - Not integrated: connections by tubing and wires.

Technology trends in microfluidics

1. Chips suppliers are becoming component suppliers.
2. Well array testing is developing into more complex testing more akin to real life situations.
3. Digital microfluidics is seen as a way to miniaturize well array testing further.
4. More efficient and faster sample preparation units (PCR in a few minutes).
5. The industry is looking for technologies that don't need labeling, i.e. biomarker specific sensors.
6. The industry is looking for technologies that don't need time consuming PCR, i.e. hyper sensitive sensors.
7. Plug and play microfluidic instruments, cartridges, chip holders, connectors etc. are emerging.

Agreed specifications

Chips and multiport connectors


Microtiterplate
Credit Card
Double Microscope slide
Microscope slide
15*15
15*30
15*45
85.48
54
50
25
75
84
127.76

Tolerance on chip dimensions

We have defined an asymmetrical chips tolerance for limiting oversize chips which will not fit in holders and connectors:

• Maximum / desired oversize is	+ 0.05 mm
• Maximum undersize is	- 0.15 mm
• Preferred undersize is	- 0.05 mm

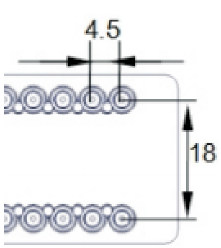
From MF5 design guide for microfluidics

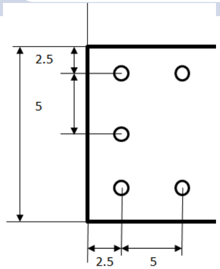
Design guide for chip layout & connections: Microfluidics

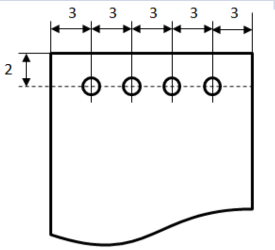
Material: Polymer | Glass

Chipsize:
- Polymer → Microtiterplate 127.76 * 85.48 mm
- Polymer → Microscope slide 75*25 mm
- Glass → Microscope slide 75*25 mm
- Glass → 45*45; 45*15; 30*30; 30*15 ; 15*15 mm

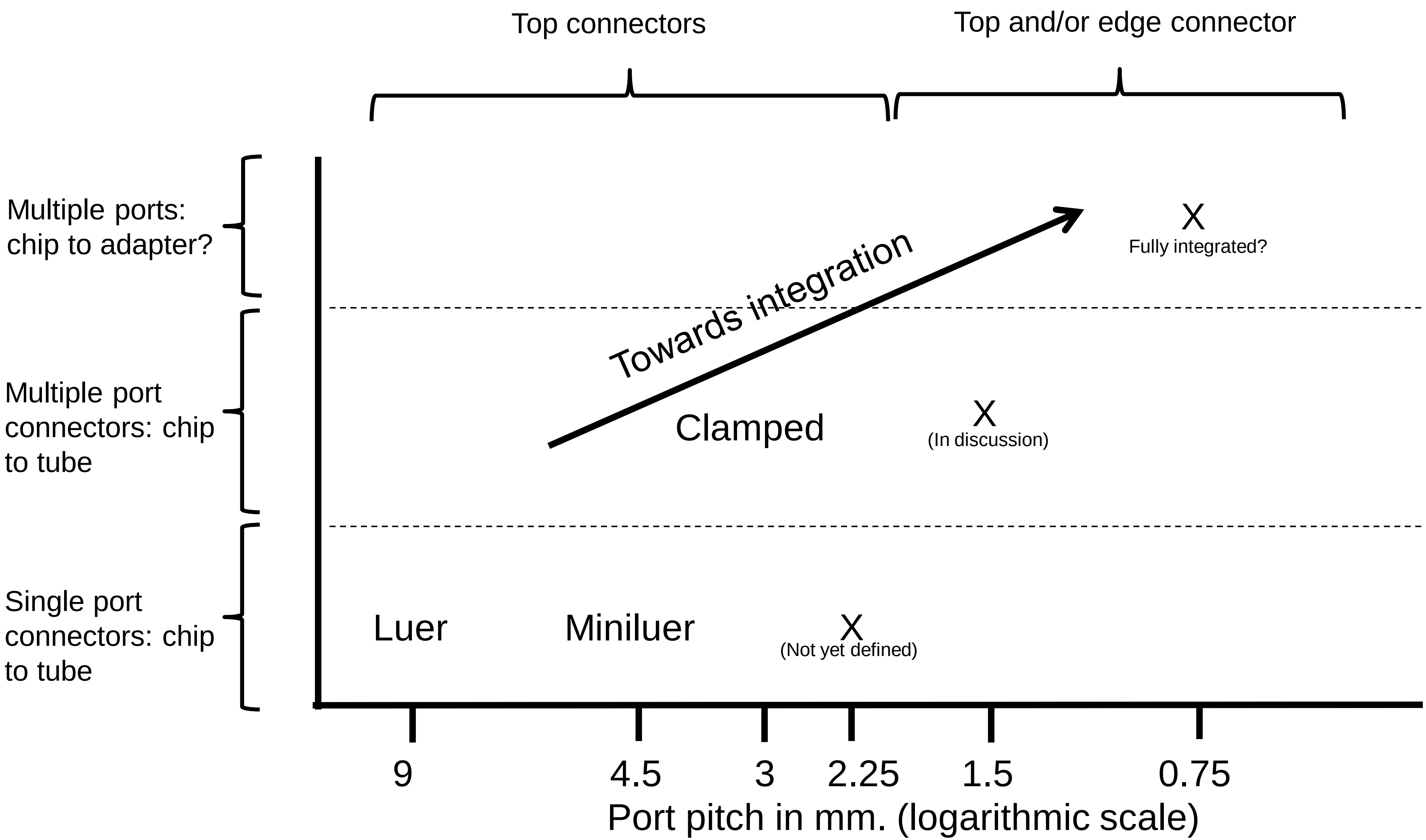
Connection:
- Microtiterplate → Miniluer
- Microscope slide (Polymer) → Miniluer
- Microscope slide (Glass) → Clamped
- 45*45 … 15*15 mm → Clamped





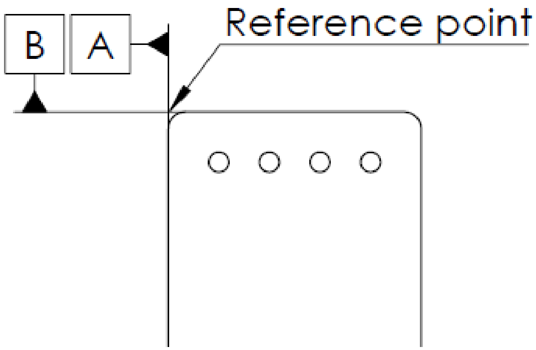


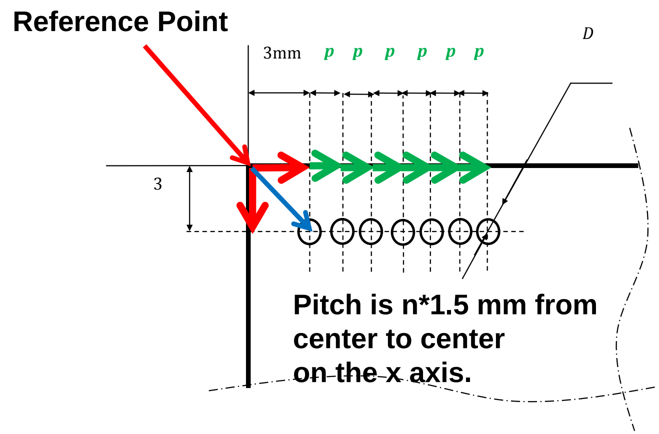
Port pitches for microfluidic interconnections



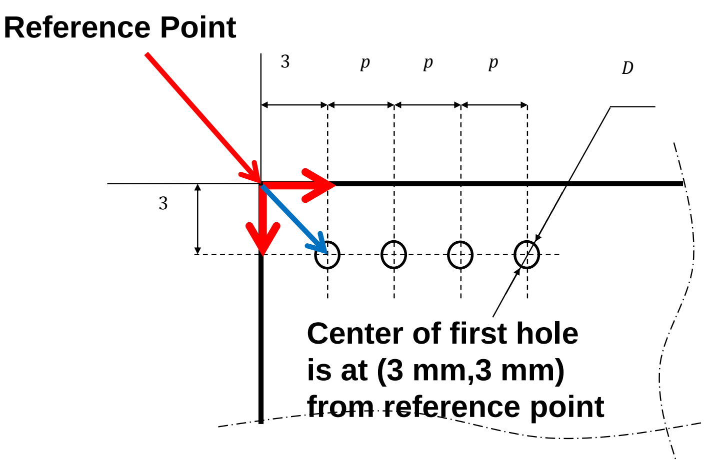
Connections to top of the chip (multiport) 1

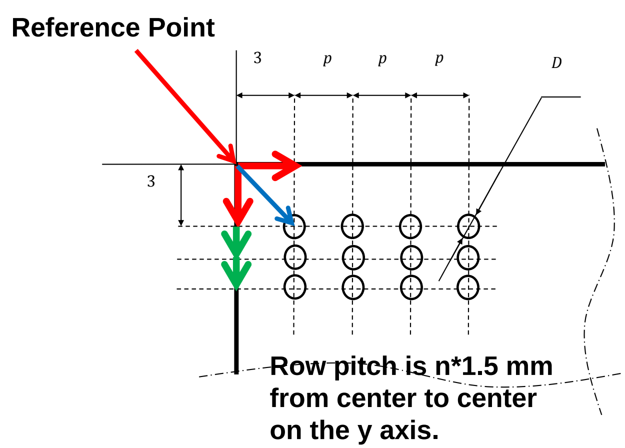
Pitches are : 1.5 mm or multiples of that



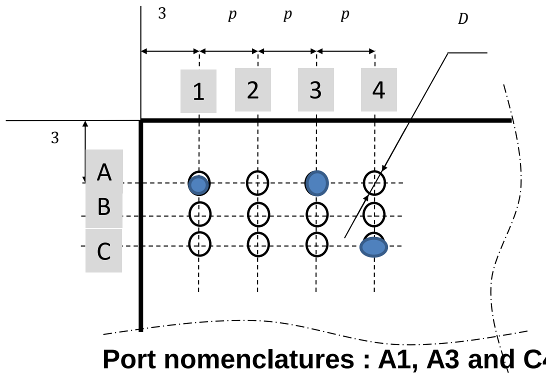


Always keep a distance of 3 mm to sides of the chip





Connections to top of the chip (multiport) 2



Port nomenclatures : A1, A3 and C4.
On a 1,5mm Fluidic port grid.

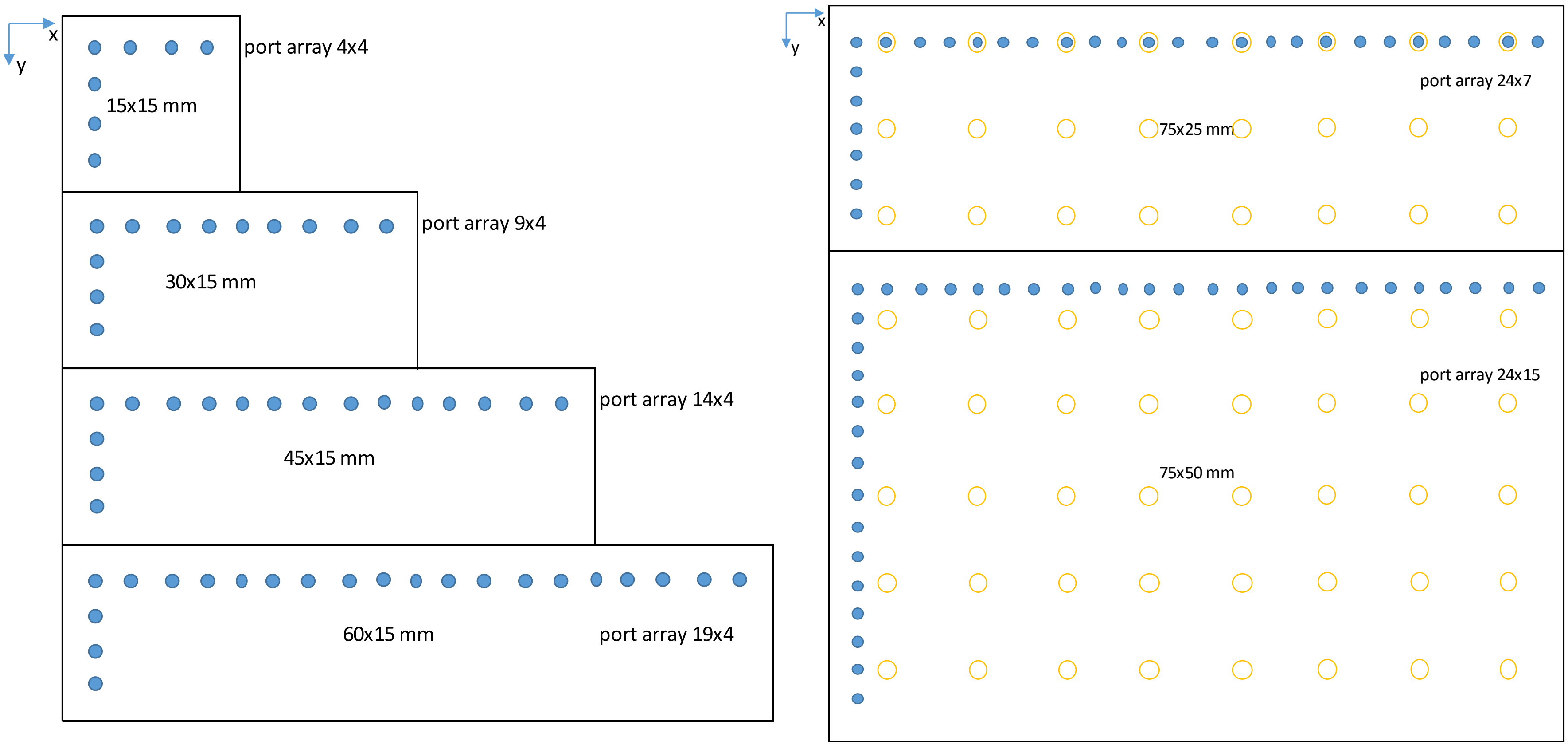
Hole diameters are not standardized however there is a minimum and maximum recommended diameter which is:

1.5 mm pitch 0.4 < D < 0.7
3.0 mm pitch 0.4 < D < 2.0
4.5 mm pitch 0.4 < D < 3.5

Summary Table of all the guideline dimensions and tolerances

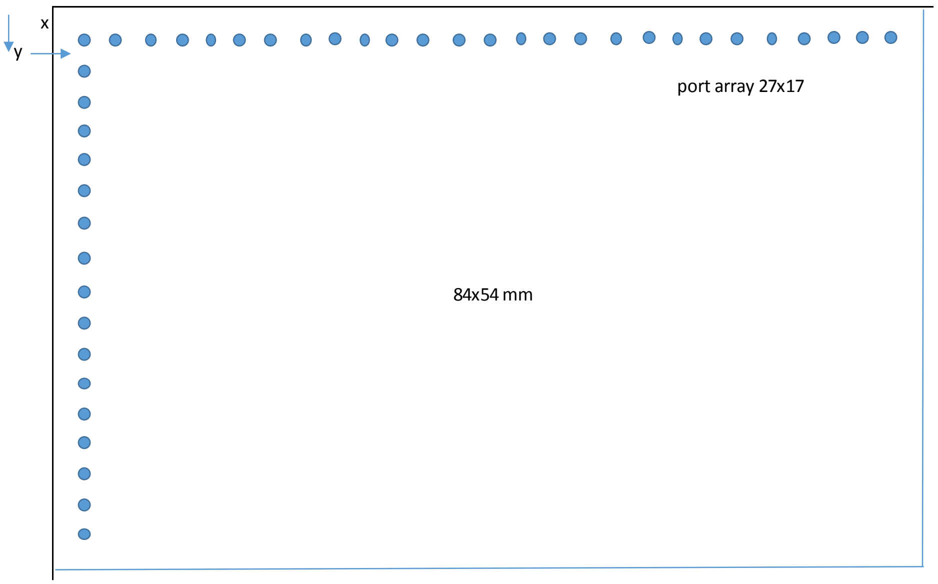
Parameter	Nominal value	Minimal value	Maximal value	Tolerance
Reference point : left chip corner				0 mm
Distance of the first hole from the reference point (3 mm, 3mm) (corner edge to hole center)	(3,3mm)			+/- 0.15 mm
Minimal distance of any hole from any side of the chip		3mm		
Distance between holes or Port pitch (center to center) from ref. point	n*1.5 mm	1.5 mm		+/- 0.15 mm
Rows are parallel to the chip's x axis at a distance from ref. point of n*1.5	n*1.5	1.5 mm		+/- 0.15 mm
Hole diameter for 1.5 mm grid		0.4 mm	0,7 mm	
Hole diameter for 3 mm grid		0.4 mm	2.0 mm	
Hole diameter for 4.5 mm grid		0.4 mm	3.5 mm	
Total Chip Thickness	1mm	0.85 mm	1.15 mm	+/- 0.15 mm
Total Chip Thickness	1.8 mm	1.65 mm	1.95 mm	+/- 0.15 mm
Total Chip Thickness	2 mm	1.80 mm	2.20 mm	+/- 0.2 mm
Total Chip Thickness	4mm	3.60 mm	4.40 mm	+/- 0.4 mm
Tight Tolerance of outer chip dimension (desired)				+/- 0.05 mm
Lower Tolerance of outer chip dimension (when tight tolerance not achievable)				+ 0.05 / - 0.15 mm

Layouts (1)



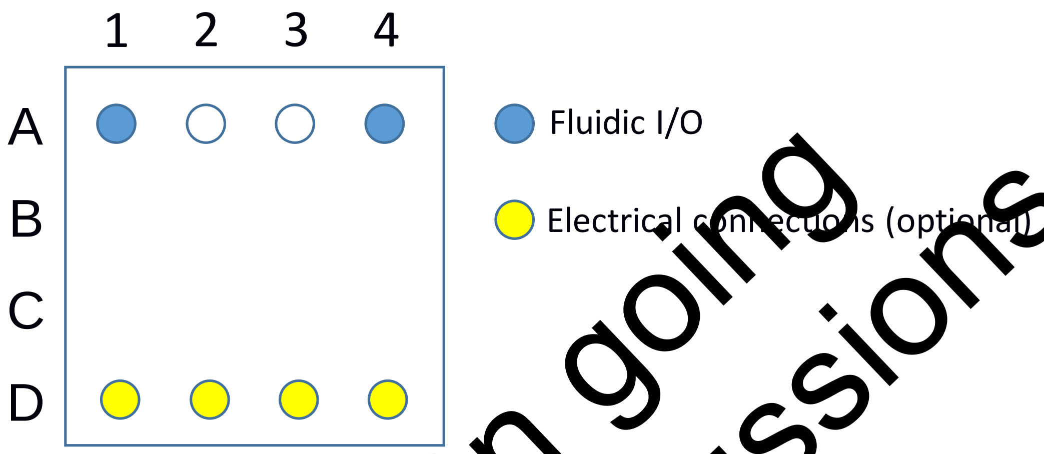
x
y
port array 4x4
15x15 mm
port array 9x4
30x15 mm
port array 14x4
45x15 mm
60x15 mm
port array 19x4
x
y
port array 24x7
75x25 mm
port array 24x15
75x50 mm

Layouts (2)



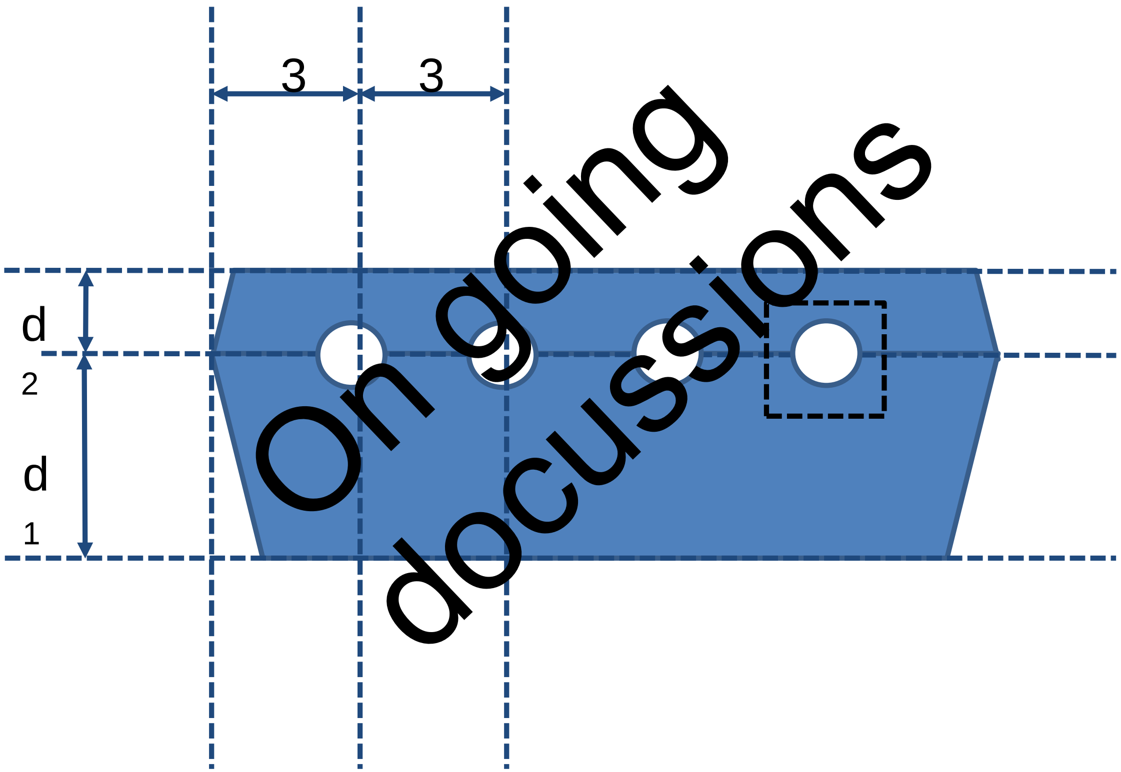
On going discussions

Sensor interface



On going docussions

Edge connector



Microfluidic device classification proposed

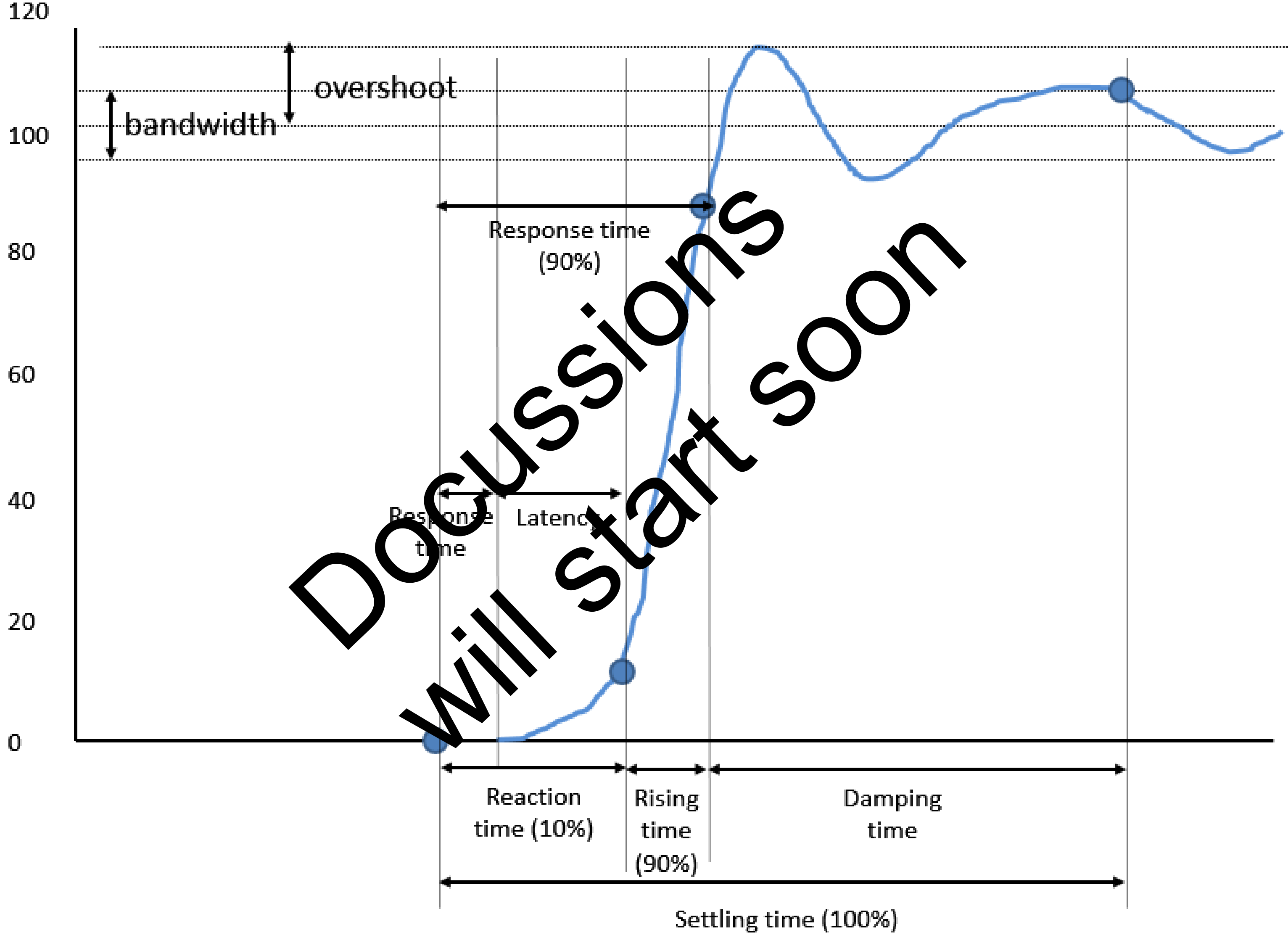
Classes	Minimum temperature (°C)	Maximum Temperature (°C)	Maximum pressure (bar)
A	4	50	2
B	0	75	2
C	0	100	2
D	4	50	7
E	0	100	7
F	4	50	30

Qualification tests for microfluidic components and devices

- For getting true standard tests, the first steps would be the definition of the basic (minimal) requirements that should fulfill the microfluidic component/system in each application.
- Taking clear this basic requirements, it is possible to start thinking about what kind of tests (the simplest possible) can be performed to ensure those requirements.
- E.g. for an application it is defined that the microfluidic component have to support temperatures of -15ºC, so you can bring the component under nitrogen bath. So, you can check that your component supports such temperatures, even the time that can support the temperature.

On going discussions

Definitions needed



Discussion to be continued

See www.mf-manufacturing.eu

Reactions to:

henne@enablingmnt.com

Acknowledgements

- Ali Tinzali, Gottfried Reiter, Harald Kraushaar (Sony DADC)
- Ronny van 't Oever, Marko Blom (Micronit)
- Mark Giligan, Andrew Lovatt (Dolomite)
- Marco Bianchessi, Roberto Brioschi (ST Microelectronics)
- Peter Hewkins (CfBI)
- Mark Tondra (Diagnostics Biosensors)
- Holger Becker (MFCS)
- Richard Bijlard (Invenios)
- Thomas Dietrich (IVAM)
- Twan Korthorst (PhoeniX)
- Paul Wright (DIBA)
- Thomas Henkel (IPHT)
- Joost Lotters (Bronkhorst)
- Gerald Kreindl (EV Group)
- Thomas Hessler (Axetris)
- Mark Crockett (Memsmart)
- Nicolas Szita (University College London)
- Peter van Stiphout (Cytocentrics)
- Ray Filteau (CMC Microsystems)
- Vincent Spiering (Qmicro)
- Alexios Tzannis (IMTag)
- Gary Ng Sum Huan (SIMTech Microfluidics Foundry)
- Daniel Mark (IMTEK)
- Juan G. Santiago (Stanford University)
- Malcolm Wilkinson (TFI)
- Thomas Hessler (Axetris)
- Mario Castaño-Álvarez (Micrux)
- Gabor Szirbik (Thalesnano)
- Francois Leblanc (Fluigent)
- Pu Chen (Stanford University)

- And many others