Design for Microfluidic Device Manufacture Guidelines

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Contents

Context:

The Mission of the Microfluidics Consortium (http://www.cfbi.com/microfluidics.htm) is to grow the market for microfluidics enabled products and services. With members from all parts of the value chain from materials to end users and covering Europe and the USA the consortium has deep insight into the challenges and opportunities which the 'microfluidics industry' faces.

One challenge is that the process of moving from a research prototype device to a production device takes too long and is too expensive. This is the case for a wide variety of materials and manufacturing processes. An important part of the challenge is that often researchers are designing devices for the first time and stumble over multiple problems that an experienced designer might be able to avoid. The flip side of the same argument is that potential manufacturers are often frustrated when prototype designs presented to them which are difficult, inappropriate or even impossible to manufacture in large volumes at low cost.

Objectives of this paper:

This White Paper is an attempt initiated by the Microfluidics Consortium to improve the situation. It is made available for free to researchers and developers around the world who are contemplating the creation of prototype devices containing microfluidics. Its purpose is to make developers aware of some of the "design for manufacture" issues which, if dealt with early, can improve the chances of their device being manufacturable, economically and reliability wise.

Positioning of this paper:

This paper is "application agnostic" – it should be relevant to people working in: Diagnostics, High Throughput Screening, Sample Preparation, Genomics, PCR, Circulating Tumour Cells, Regenerative Medicine, Flow Chemistry, Environmental, Food and Homeland Security Sensing .. and beyond!

This paper is also "materials agnostic" – we recognise that microfluidic devices can be realised in PDMA, Polycarbonate, Flexible web, Glass, Silicon, Metal and paper. Different members of the consortium specialize in different materials and have contributed "boxes" representing design for manufacture with different materials. We do, however, see that certain materials, processes are better suited to particular classes of product and application. With this in mind the "Decision Tree" in diagram 1 is designed to guide new developers to choices which suit their plans, time-scales, budgets as well as technical needs.

Furthermore this paper is "manufacturing process agnostic" – recognising again that processes such as: etching, lithography, injection moulding, hot embossing, 3D printing and even modified Xerography are valid routes to manufacture of microfluidics devices. Again, members of the consortium have contributed "boxes" highlighting design for manufacture needs associated with different processes and links to further reading.

Our vision is that newcomers to research and development using microfluidics – probably wishing to use PDMS for rapid prototyping – will spend a little time considering with what material and with what manufacturing process their prototype device might be realised. They will then look at the relevant boxes and take the design guidelines into account as they are choosing formats, geometries etc. for their devices.

While members of the consortium are always interested in talking with players wishing to scale up manufacturing of their devices, it is helpful for both sides if the "basics" are already covered so that expensive learning and re-design processes can be avoided.

It is intended that this will be a "living document" .. updated as new materials and manufacturing techniques emerge. Members of the Microfluidics consortium manage the editorial and are keen on feedback regarding how the document might be improved.

Note: This document does not guarantee IP freedom to operate! There is a complex landscape of patents around microfluidics devices so it is up to you to check whether you need a licence!

Material selection:

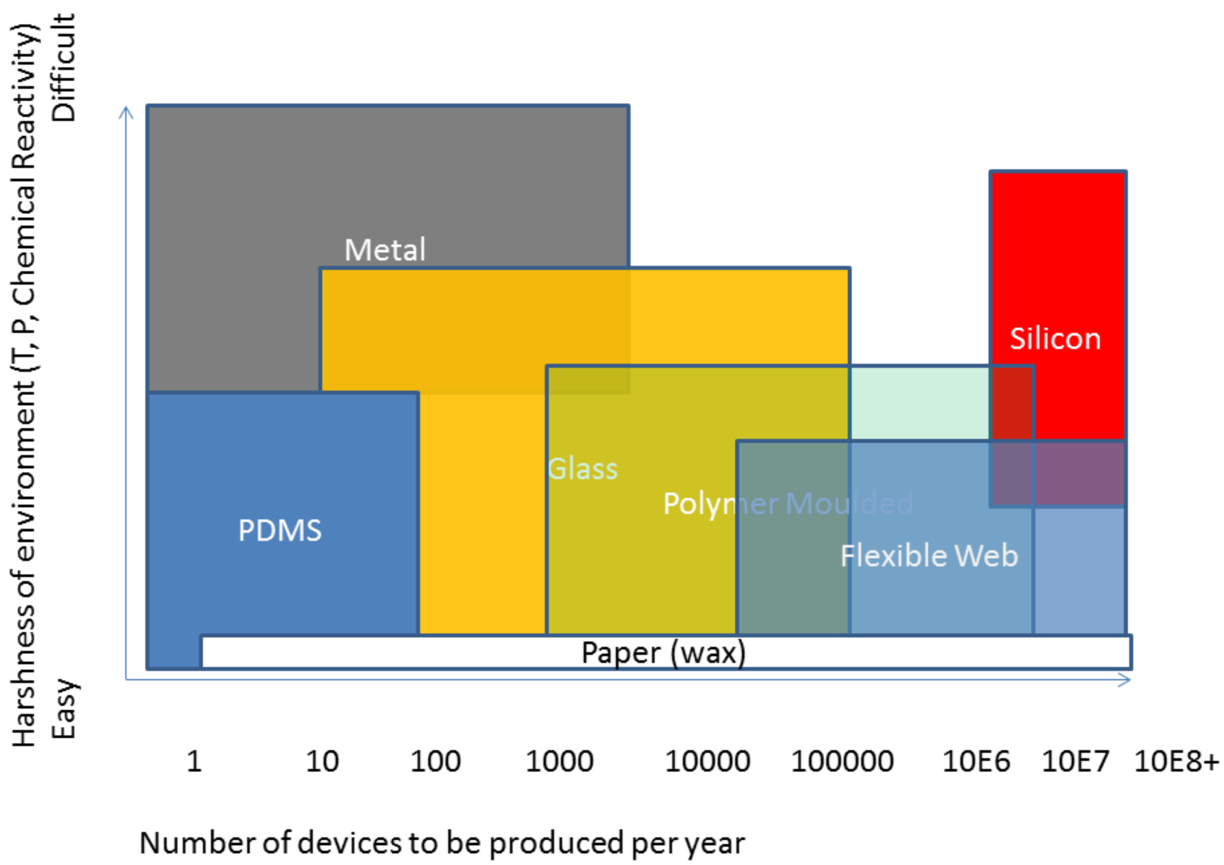
It is possible that readers know exactly what material or process they are interested in or forced to use – in which case they should "fast forward" to the boxes below which interest them. For those who are less clear (or have more operational freedom) the table below is designed to guide readers towards appropriate fundamental choices. This is intended as rough guidance – there will be special cases which need to be looked at more closely before decisions are made!

Be aware, preferably the material chosen to do your prototyping should be the same as the one intended to be the material used in the final product. Otherwise a costly and time consuming redesign is likely.

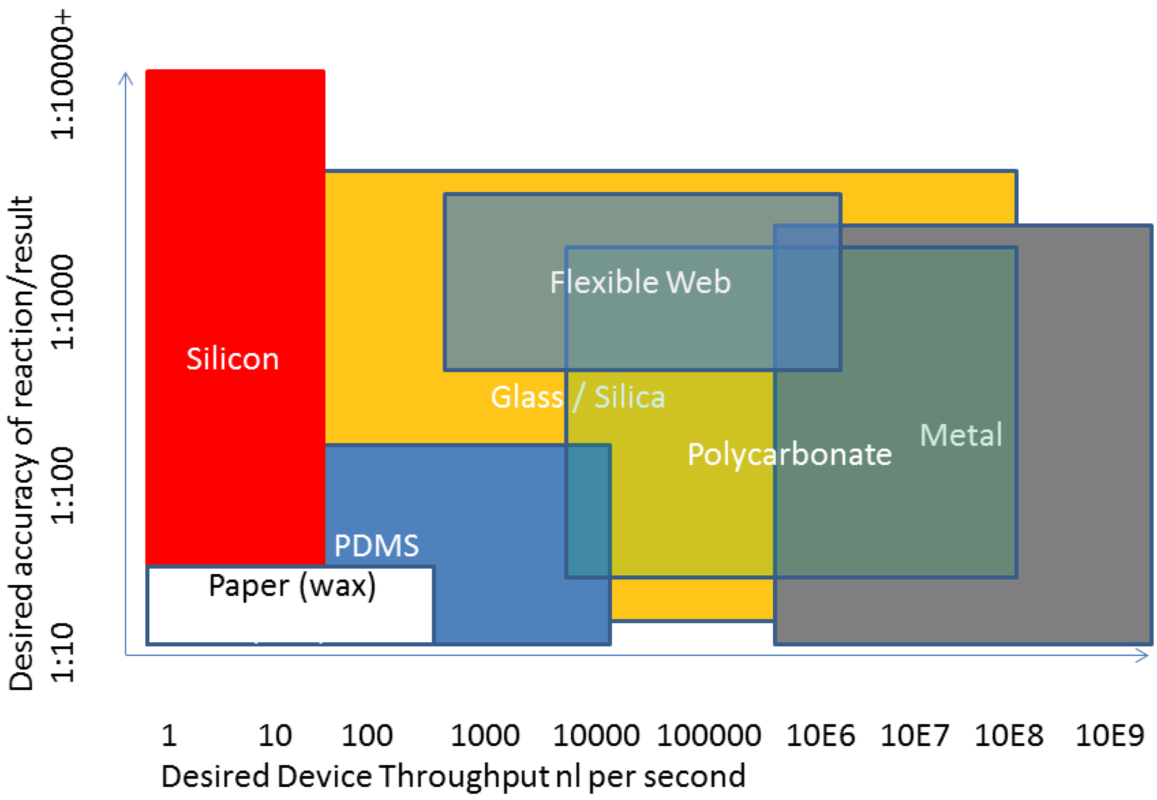
The different candidate construction materials for microfluidics differ widely in properties. Endless discussions are possible about their relative strengths and weaknesses.

The decision support charts A and B give a first pass indication of the relative merits of different materials for microfluidics applications. Further detail of materials properties is provided in Tables 1-3 in Appendix 1.

Material Selection Decision Support Chart 'A'



Material Selection Decision Support Chart 'B'



Manufacturing process selection:

In addition to material choice the aspiring product development engineer needs to consider manufacturing process.

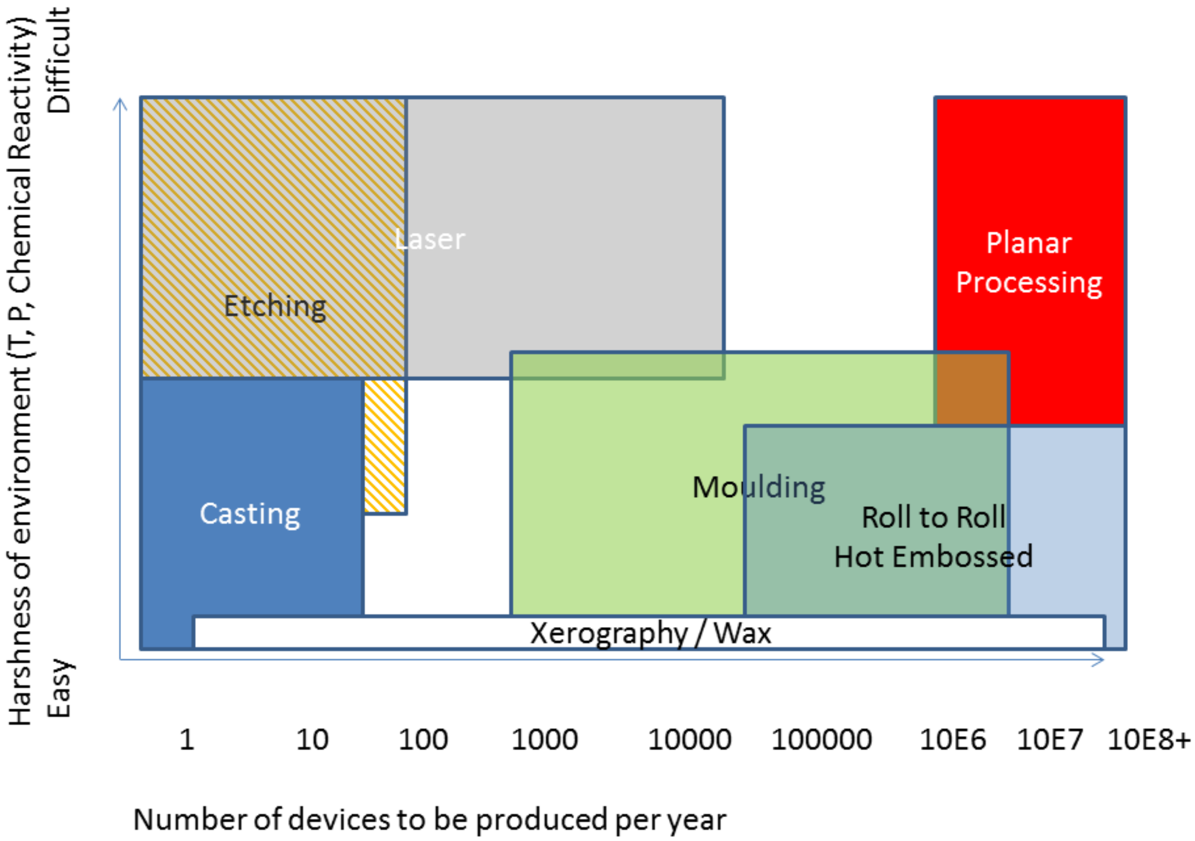
The nature of these manufacturing processes influences the type and geometry of structures/tolerances which can be achieved, the use of device 'real estate' as well as the economics of manufacture.

The following process options are currently available on an industrial scale:

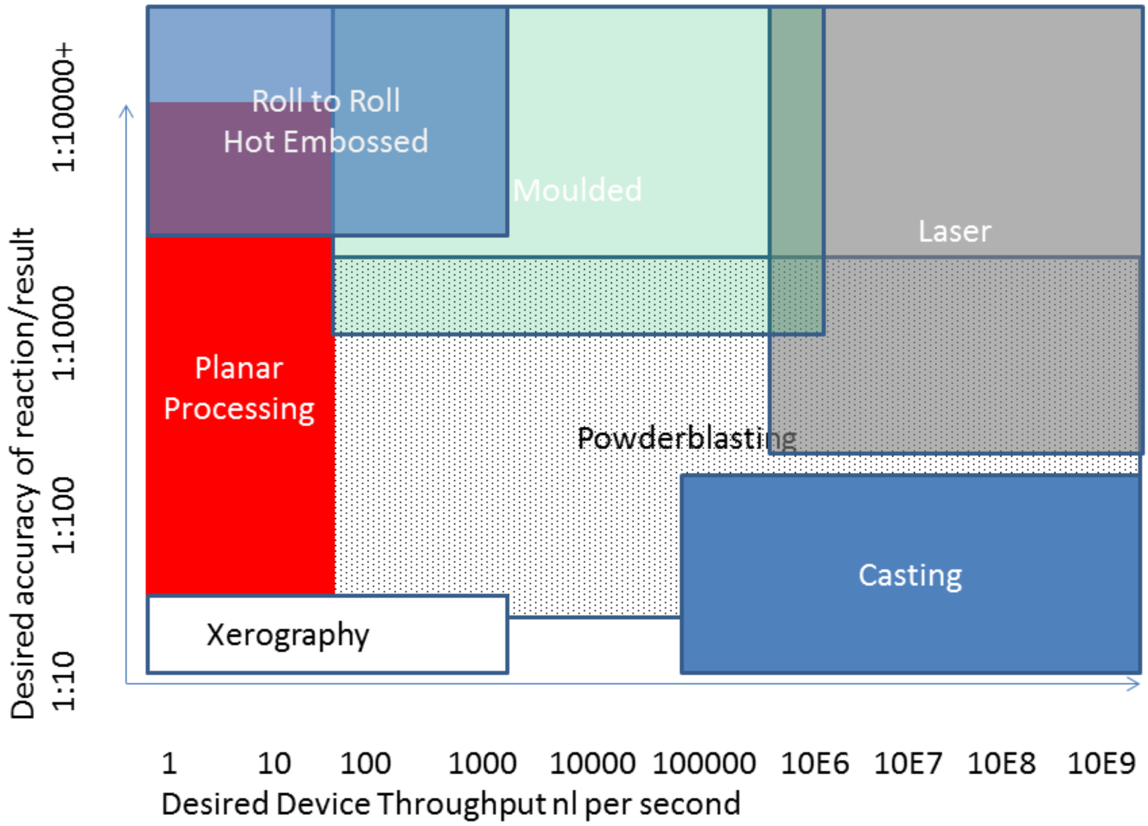
Micromachining (usually for metal)	Key Characteristics
• Precision mechanical machining	Low volumes possible; very low set up cost
• Laser machining	Slow process, limited in feature sizes
• Electro Discharge machining	Steepest draft angles/ any channel shape (except overhangs)
Planar processing (of silicon or glass)	
• Wet chemical etching	Very large volumes; medium set up cost; medium lateral feature sizes, small to medium channel depths
• Dry etching (DRIE, (Fused Silica only)	Slow process, medium setup cost, small feature sizes, high aspect ratio
• Powderblasting (Glass only)	Medium setup cost, large feature sizes, deep channels
• Photostructuring	medium set up cost; medium feature sizes
Casting (of elastomers)	High set up cost, low volume
Injection moulding	High setup cost, medium batch sizes, medium aspect ratio
Hot embossing	Medium set up cost, high batch sizes (especially if roll-to-roll). High aspect ratio possible, shallow depth of channels.

See also next two pictures and Table 4 in Appendix 2.

Process Selection Decision Support Chart ‘C’



Process Selection Decision Support Chart 'D'



Device Design Guidelines

So now you have a feeling for what material your device might be made of and what manufacturing process it might be made by when it finally gets to market! These decisions have an impact on the physical format of the device itself because of issues like: feedstock, cost of materials and the limits and capabilities of the manufacturing process. The following sections will explain in more detail for the most common materials and processes.

Microfluidic chips typically are composed of a set of different basic structures in order to realize the required functionality and the basic microfluidic operations (e.g. mixing, separation, transport, splitting, etc.), respectively. In the following, some basic microfluidic structures are listed:

Channels

Chambers / Wells / Cavities

Pillars

T- or Y-Junctions

Holes

The design guidelines below address issues such as: profile of channels, aspect ratio (height: width) of features, spacing of features (to each other and to edge of device), as well as provision for connectors.

Condensed version of the design guidelines for glass/planar processing

We are grateful to Dolomite Microfluidics, IMT Masken und Teilungen and Micronit Microfluidics for providing the information below. A more extensive version of their design guidelines can be found at:
www.microfluidicsinfo.com/glassmanufacturedolomite.pdf or by contacting directly the suppliers on: www.dolomite-microfluidics.com, www.imtag.ch or on: www.micronit.com

Wafer and chip sizes

100*100 mm: containing for example 12 chips with dimension of 45*15 mm each[1]

150*150 mm: containing for example 100 chips with dimension of 15*15 mm each

Glass layer thicknesses"

Standard thicknesses 0.7, 1.1 and 2 mm; minimum thickness 30 µm; thicker is also possible

Structures made by wet isotropic etching:

Resulting surface roughness: < 5 nm

Channel width: mask width + 2 * channel depth; minimum mask width 5 µm, 1 µm on special request

Etch depth range 0.010-500 µm

Structures made by powder blasting

Feature size accuracy is about 25µm

Channel depth: 100 µm and more

Thru hole dimension: typically 0.2mm and up

Shaped wells can be round or rectangular. The sides of the wells will not be completely vertical, but sloped at an angle of 70; on request the angle can be varied between 65° and 80°.

The average roughness of the channels will be between 0.8 and 2.5 µm

Structures made by dry etching (for fused silica only)

Channel width: 0.1 to 3 µm

Chip edge to channel 750 µm (low pressure) 2 mm (high pressure)

Minimum spacing between structures: 5 µm +2.6 * etch depth

Minimum Through Glass Via (TGV) diameter: 100 µm, needed overlap area 200 µm

Minimum inside radius: minimum spacing / 2

Drilling holes:

Typical diameters between 0.2 to 10 mm

Multiple layer chips / bonding of glass cover:

Standard alignment accuracy between two bonded layer: +/- 5 µm, on special request +/- 2 µm

Thermally bonded cover can withstand pressures up to 300 bar (also depending on geometry)

Cold bonded over can withstand pressures up to 50 bar

Thinnest possible total thickness of multiple layer chips 100 µm

Dicing and breaking

Dicing standard dimension is 3mm and up, dimensional tolerance +/- 100µm

Scribing standard dimension is 5mm and up, dimensional tolerance +/- 150µm and no cooling fluids are needed which is beneficial if SideConnectors are used.

Breaking standard dimension is 10 mm and up, dimensional tolerance +/- 300µm and no cooling fluids are needed which is beneficial if SideConnectors are used.

Edge connection (4 connection ports)

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[1] 45* 15 mm is de facto standard chipsizes, other standard lengths are 15, 22, 30 or 90 mm, but the customer is free to choose his or hers own sizes, as long as it fits on a wafer.

One of the small sides of the chip contains the four connecting holes; an area of 5.5 * 15 mm is needed; the drilled fluid holes need to be spaced 2 mm from the small edge of the chip & evenly spaced 3 mm from each other.

Side connection (individual connection ports)

For single edge connectors a pitch of ≥ 2.5mm can be used

Top connector (6 or 9 connecting ports)

When more connections are needed, 30 or 45 mm wide chips can be used; an area of 5.5 * 30 resp. 45 mm is needed; the drilled fluid holes need to be spaced 2 mm from the small edge of the chip and in sets of three evenly spaced 3 mm from each other, with 6 mm between the groups.

Top connector with 2 x 5 connecting ports or more

Connection holes are spaced 5 mm center-to-center, with a center-to-chip edge distance of 2.5 mm. A standard pattern of 2 x 5 holes on either side of a chip are oriented in a U-pattern. However, with the mentioned spacing, ports all across the chip surface can be provided. Hole diameter is typically 1.6 mm with a conical shape narrowing towards the chip interior.

Circular connector (8 connection ports). The eight fluidic ports are positioned on 4.5mm radius with 45° angular spacing. Hole diameter is typically 380 µm.

Condensed version of the design guidelines for integrated electrodes

We are grateful to IMT Masken und Teilungen and Micronit Microfluidics for providing the information below. A more extensive version of their design guidelines can be found at: www.microfluidicsinfo.com/electrodesimt.pdf or by contacting directly the suppliers on:www.imtag.ch

- Preferred materials for integrated electrodes: Pt or Au
- Metal layer thickness: between 50nm and 200 nm using standard sputtering or PVD, 1 µm or more by galvanic processing
- Minimal feature size: 2 µm (depending on the layer thickness)
- Access to electrodes: through chip holes or side connectors
- Bonding of chips with electrodes within the fluidic system
  - Deform glass at elevated temperatures
  - Electrode recess
  - With intermediate layers: using intermediate polymer layers generating a hybrid chip, electrodes inside a channel on both top and bottom of the channel can be provided, thereby eg. providing a uniform electric field between both electrodes.

Condensed version of the design guidelines for polymer/injection moulding

We are grateful to Sony DADC for providing the information below. A more extensive version of their design guidelines can be found at: www.microfluidicsinfo.com/polymermanufacturesony.pdf or by contacting them on: www.sonydadc.com

Chip sizes

Maximum lateral dimension of the moulded component (length x width) = MTP format, preferably credit card or Microscope slide 25mm x 75mm, with maximum overall thickness of 5mm (preferably <1.5mm)

Minimum thickness of the base plate = 0.8mm (remaining thickness "below" structures 0.5mm) – if the moulded component is only ca. 25mm x 75mm the minimum thickness can be 0.6mm

Distance of structures to component edges = min. 2mm

Typical tolerances: According to DIN ISO 2768-1 f-fein

Design rules for structures created by high speed milling:

Minimum dimension in the plane = 50µm

Aspect ratio for structures sticking out of the base areas (smallest dimension in the plane / height of the structure) ≤ 1:1 (if the feature size is smaller than 100µm the aspect ratio should not be ≤ 1:0.5)

Aspect ratio for structures going into the base area (smallest dimension in the plane / depth of the structure) ≤ 1:2 (if the feature size is smaller than 10 µm the aspect ratio should not be ≤ 1:1.5)

Maximum height of a structure = 5mm

Minimum radius at inside corners in the plane = 5µm

Minimum radius at outside corners in the plane = 30µm

Minimum distance between two structures = same as structure height but minimum 50µm)

Stepped structures or ramp structures are possible

Minimum draft angle 3°, preferably 5°

Undercuts are not possible

Design rules for inserts created by lithography:

All structures at one side of the moulded component either sticking out of the base or going into the base

Minimum dimension in the plane = 1µm

Aspect ratio for structures sticking out of the base areas (smallest dimension in the plane / height of the structure) ≤ 1: 0.5)

Aspect ratio for structures going into the base area (smallest dimension in the plane / depth of the structure) ≤ 1:1.5)

Maximum height or depth of a structure = 70µm

Minimum radius at inside corners in the plane = 1µm

Minimum radius at outside corners in the plane = 5µm

Minimum distance between two structures = at least same as the either the height or width of the structures (whatever is larger)

Stepped structures or ramp structures are possible

Usual draft angle 10° (if there is only one structure height/depth) up to 15° (if there are more than one structure height or ramp structures)

Undercuts are not possible

Condensed version of the design guidelines for Imprint Techniques

We are grateful to EV Group for providing the information below. A more extensive version of their design guidelines can be found at: www.microfluidicsinfo.com/EVGguidelines.pdf or by contacting them on: www.EVGroup.com

General design rules in UV Nanoimprint:

UV Nanoimprint is designed as massive parallel replication process of sacrificial layers or permanent layers. Etch selectivity is comparable to standard semiconductor processes but needs to be adjusted for the underlying bulk material. Using glass in suspension, glass micro and nanostructures without costly vacuum processes such as metallization and etching can be manufactured. Furthermore UV nanoimprint lithography enables the manufacturing of 3D structures which might reduce the required steps for device manufacturing. In any case the most important aspect in imprint lithography is the master or stamp manufacturing technique. One has to be aware that certain features like nanoscale 3D structures require unconventional manufacturing techniques.

Maximum substrate size (length x width) = 300 mm x 300 mm

Manufacturing throughput: > 60 units per hour

Maximum substrate thickness = 10mm (Semi Standard)

Minimum substrate thickness = 0.05 mm on foils; 150 µm on semiconductor materials

Top to bottom alignment: possible

Minimum structure size: down to 35 nm for high volume manufacturing

Maximum structure size: geometry dependent but up to 5 mm in diameter demonstrated

Maximum aspect ratio: 1:4, for sub µm structures ideally the aspect ratio stays below 1:2

General design rules in Hot Embossing:

Hot embossing is also considered as massive parallel replication process mostly for reshaping bulk thermoplastic materials. Dependent on equipment force and temperature, materials of glass transition temperatures up to 650° on up to 300 mm round substrates can be processed. This would even allow to thermally emboss into certain glasses directly such as Borofloat glass.

Maximum substrate size (length x width) = 300 mm round

Manufacturing throughput: equipment dependent

Maximum substrate thickness = 15 mm (Semi Standard)

Minimum substrate thickness = 0.100 mm on foils

Top to bottom alignment: possible

Minimum structure size: down to 35 nm for high volume manufacturing

Maximum structure size: geometry dependent but up to several 100 µm

Maximum aspect ratio: 1:15 (w:h), for sub µm structures ideally the aspect ratio stays below 1:2

General design rules in Roll-to-Roll Hot Embossing:

Using rolls instead of plates, roll-to-roll enable continuous molding with significant advantages in operational speed and device throughput. In roll-to-roll hot embossing, a thermoplastic sheet passes between two rotating rollers. The deformation of the thermoplastic material under the pressure and elevated temperature of the mold imprints the structures into the polymer. Roll-to-Roll hot embossing is especially well suited for structuring of micron and especially sub mm structures. Furthermore the technology implies advantages over mainstream reshaping technologies such as injection moulding if structured thin films are required.

Maximum substrate size (length x width) = 300 mm web width, Continuous mode operation

Manufacturing throughput: up to 10 m/min structure dependent

Maximum substrate thickness = 0.5 mm

Minimum substrate thickness = 0.100 mm

Minimum structure size: down to 50 nm for high volume manufacturing

Maximum structure size: geometry dependent but up to several 10 µm

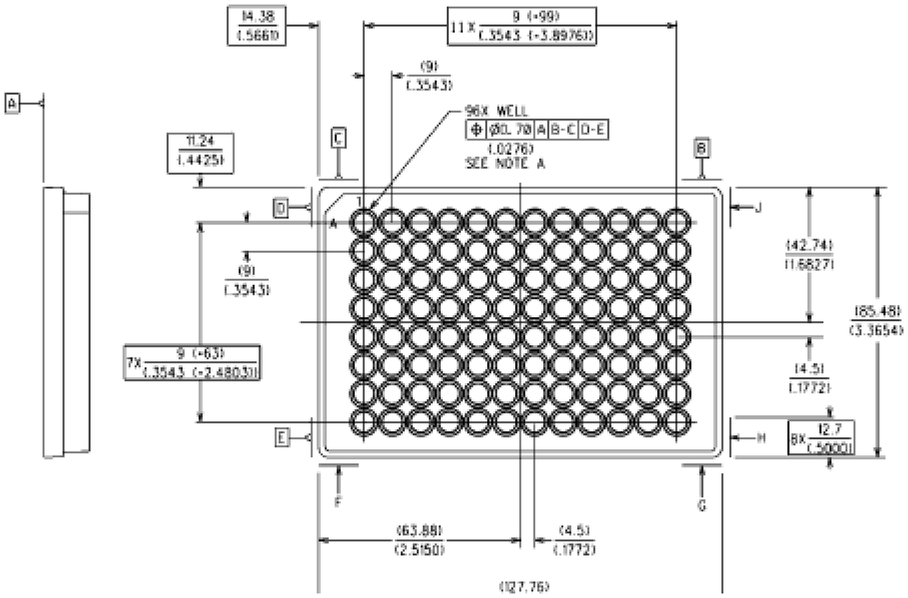
Maximum aspect ratio: 1:2 (w:h)

Preferred chipsizes and interconnections

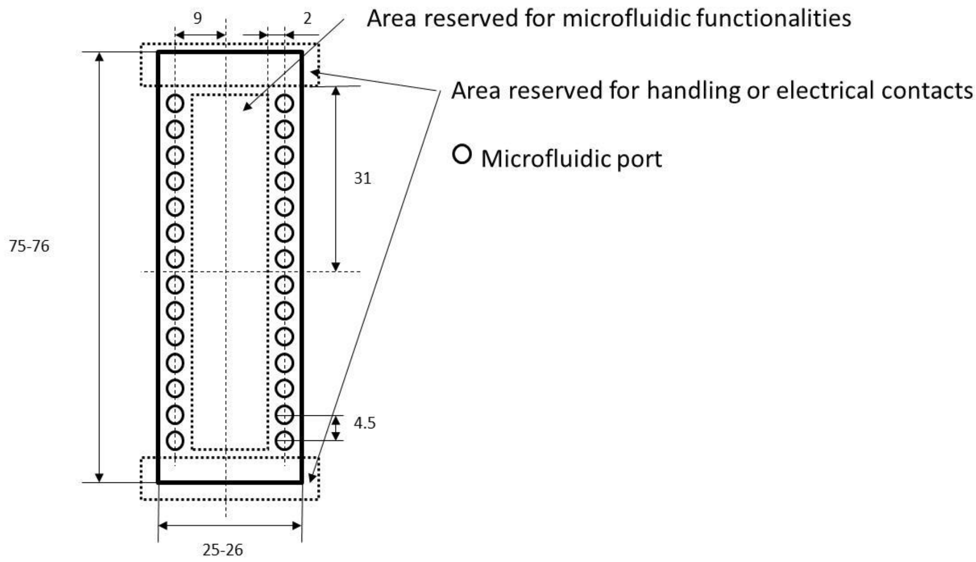
We are grateful to Dolomite Microfluidics, PhoeniX and Micronit Microfluidics for providing the information below. More information can be found at: www.dolomite-microfluidics.com or on: www.micronit.com

Although many different chipsizes are used and can be used for microfluidics, for several reasons it might be advisable to adhere to certain chipsizes that are commonly used and supported by the supply chain.

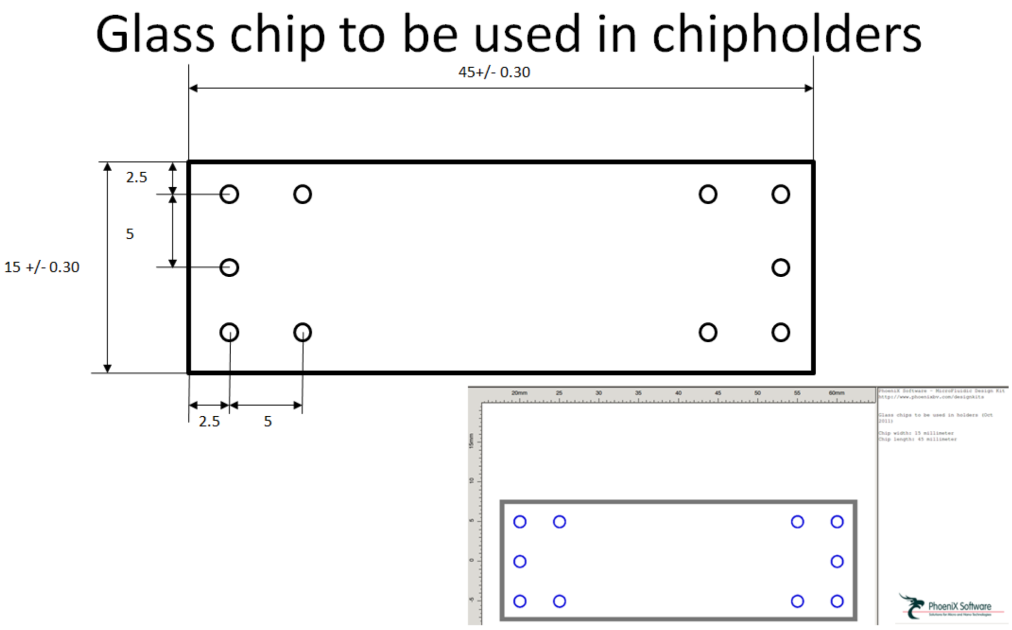
The analytical industry is using microtiterplates with standardized dimensions. (See: ANSI/SBS 4-2004). Based on this specification microfluidic chips are offered which have the same outer dimensions. The microfluidic connections are mostly miniluers, placed on the borders of the chip with a pitch of 4.5 mm according to the positions of the outer wells of the standard layout. See next figure:



Another standard chipsize often used is the microscope slide format. There is some variation in dimensions of those slides, but it seems that the industry is slowly heading towards 75 * 25 mm size, although slightly larger slides (3 * 1 inch) are still being sold. There are two options to connect tubes to these slides: In the case of micromolded chips, miniluer interconnects at one or both sides of the chip are the standard (see next figure).



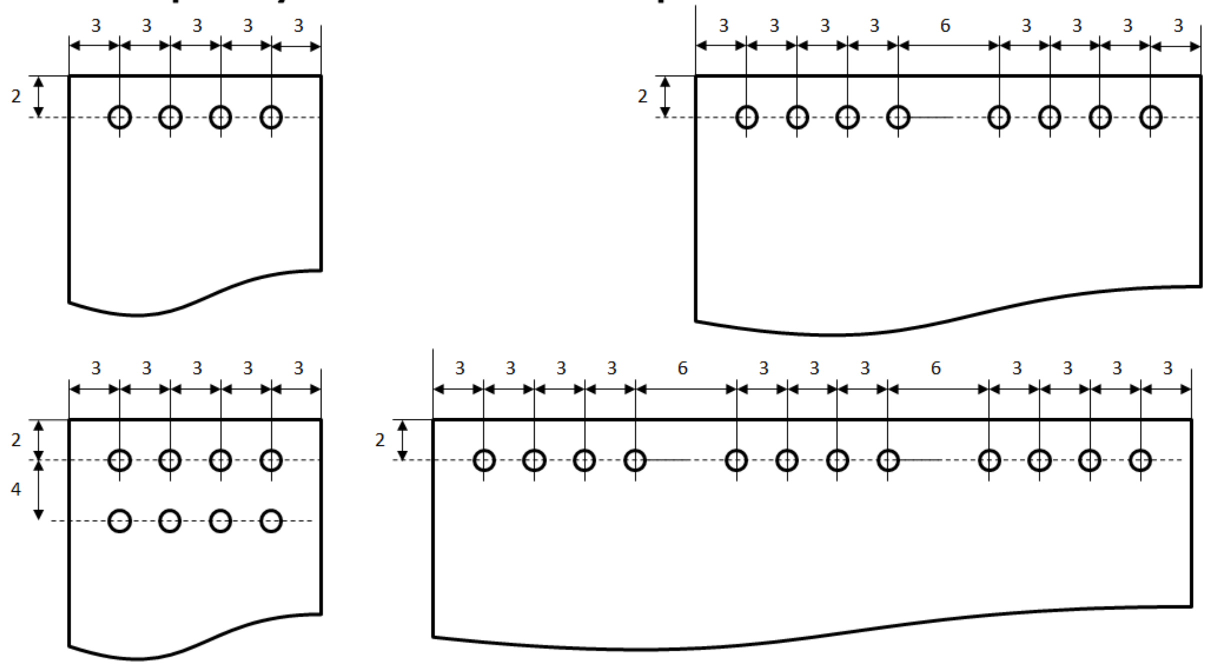
The pitch between the contacts are the same as with microtiterplate: 4.5 mm. There is however an alternative. When the microfluidic device is created by wetetching / powderblasting of a glass plate or by structuring of polymere layers on top of the plate, a clamped contact at one or both of the smaller sides is the most appropriate. (see next figure). An important advantage of clamped contacts compared to miniluers based connections is the lower dead volume of the microfluidic path and the ability to make several interconnections at the same time. For instance by using Chipholders.



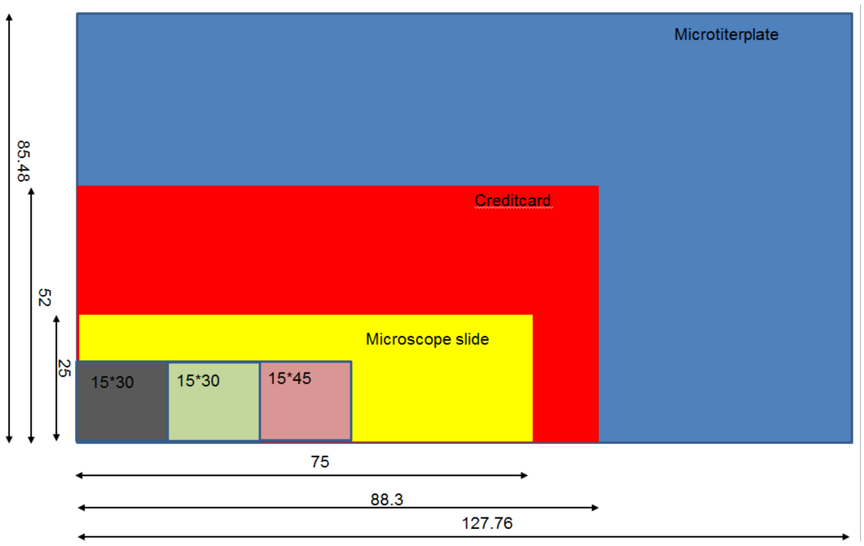
(In between those sizes the “credit card” size is proposed: 83.3 mm x 52.0 mm x 2.64 mm.)

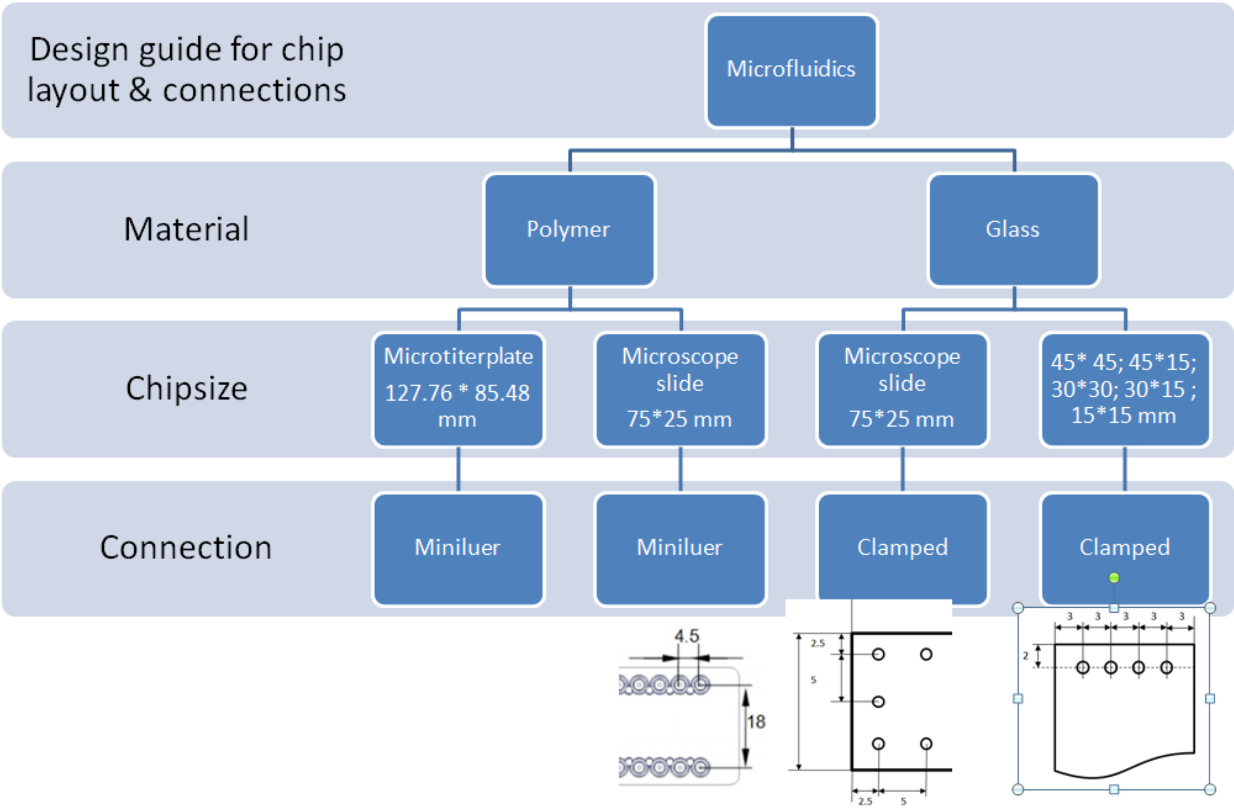
In many cases it makes sense to use smaller chipsizes. In that case a set of sizes is proposed: 15*15; 15*30 and 30*30; 15*45. The preferred interconnection layout for such chips is given in the next figures:

Chip layout for clamped interconnects



Next figures give an overview of all preferred chipsizes and their preferred interconnection methodes:




Design guide for chip layout & connections
Microfluidics
Material
Polymer
Glass
Chipsize
Microtiterplate 127.76 * 85.48 mm
Microscope slide 75*25 mm
Microscope slide 75*25 mm
45* 45; 45*15; 30*30; 30*15 ; 15*15 mm
Connection
Miniluer
Miniluer
Clamped
Clamped
4.5
18
2.5
5
2.5
5
3
3
3
3
3
2

Tailpiece

The Future

Technologies for realising microfluidic devices are changing fast. In the foreseeable future: Roll-to-roll manufacture, paper based microfluidic, 3D printing etc. might progress from being research tools, to mainstream production. Also the economics of production may well change if it becomes possible for new devices to benefit from economies of scale of other devices, possibly even in other industries.

Standards

This is a controversial subject as considerable commercial interests are at stake! At present there are a large variety of products and solutions available.

On the one hand it can be argued that upfront investment in achieving the highest possible level of integrated design for purpose will provide the lowest possible cost per unit (and for very high volume production this will be the case). On the other hand, reusing ‘platforms’ will enable the sharing of economies of scale across different products and possibly industries.

The MF5 consortium takes a pragmatic view. It is not possible to force any one solution on an unreceptive world – in particular if that would involve writing off costs already committed to particular solutions. However it is useful to encourage designs to use common formats things like: external format of devices, interconnects and certain features/functional sub-units. Contact MF5 for further information.

And Finally

This is a living document. We are interested in your feedback and involvement to improve it!

While we are grateful for help from members of the MF5 consortium, the reader should also check the supplier’s website for up to date information and contact potential suppliers with questions before committing to major development work.

We are also grateful to the members of the MF5 microfluidics consortium for their support and guidance in making this document and related initiatives possible. Please visit www.microfluidicsinfo.com and contact us on ceo@cfbi.com if you would like to join us and support initiatives like this.

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Appendix 1 More detailed comparison of material properties

Table 1: Rough guide to properties of construction materials used in microfluidic processing

		Glass	Polymer	Ceramic	Silicon	Paper
Material Properties	Optical properties	+++	+	--	--	--
	Chemical Inertness	++	+/-	+++	-	--
	Surface properties	++	+/-	--	++	--
	Thermal stability	++	+	+++	++	--
	Biocompatibility	++	++	--	++	?
	Hydrophility	+++	-	?	?	--
User Advantages	Shelf life	+	-	+++	++	-
	Reproducibility	++	+/-	?	+++	-
Application Specific	Porosity (absorption)	+++	-	?	+++	-
Functionalization	Integration of Electrodes	++	+	--	+++	--
	Coating	+	+/-	--	+++	-
	Built-in Electronics	+	--	--	+++	--
Manufacturing	3D structuring	--	++	+++	---	--
	Price	-	++	--	--	+++
	Industrial infrastructure	+	++	+	+++	---
	Set up cost	+	--	--	-	+++

There are of course many different kinds of polymers. The following two tables show the most important properties of the most commonly used ones.

Table 2: Short overview of properties of some materials

Thermoplastic Materials		
Acronym	Full name	Properties
COC, Topas	Cyclo Olefin Copolymer (COC, Topas)	High transparency, temperature stability 140°C
PP	Polypropylen	Good mechanical properties, temperature stability 110°C
PC	Polycarbonate	High transparency, temperature stability 130°C
PTFE	Polytetrafluorethylen	High chemical and temperature resistivity, temperature stability 260°C
PEEK	Polyetheretherketone	High temmperature resistivity, temperature stability 250°C
PS	Polystyrene	Transparency, temperature stability 80°C
PVDF	Polyvinylideneflouride	Chemical inert, piezo electric, temperature stability 150°C
SU8	SU8 sheets	Negative resist, quick mastering
Others: Borofloat glass, Teflon,		

Table 3: chemical resistance of glass and the most commonly used polymers

	glass	**PMMA**	**Polycarbonate (PC)**	**Polystyrene (PS)**	**COP**	**COC**
Concentrated acids	yes	No	no		yes	yes
Concentrated bases	no	No	no	yes	yes	yes
Diluted acids	yes	Yes	yes	yes	yes	yes
Diluted bases	yes	No	yes	yes	yes	
Alcohols	yes	No	yes	yes		
Esters	yes	No	no	no		
Ketones	yes	No	no	no		
Aromatics	yes	No	no			
halogenated hydrocarbons	yes	No	no	no	no	no
Aldehydes	yes	Yes	no			
Oils, fats	yes	Yes	yes	mineral oils only	no	no
Amines	yes	Yes	no			

Table 4: Other properties of glass and polymers compared

	Glass	PMMA	Polycarbonate (PC)	Polystyrene (PS)	COP	COC
Optical	++		+		--	
Ease of chemical modification of surface properties	+++	Y				
Hydrophobicity		-	Less than others	-	-	-
Permeability	nil			high	low	Very low
Melting point	Very high			low		T_g around 70° C

Appendix 2 More Detailed Comparison of Manufacturing Processes

Table 5: Indicative design rules of the different industrial processes compared

		glass/planar processing	polymer/injection moulding	Polymer/embossing
Typical chip sizes (mm)		15x15; 15 x 22.5; 15x30; 15x45	Credit card or Microscope slide: 25x75	Credit card or Microscope slide: 25x75
Chip thickness (mm)	thinnest	0.03		
	standard	0.7, 1.1, 2.0	0.6	
	thickest		5 (preferably <1.5)	
Channel width (µm)		mask width + 2 x channel depth; minimum mask width 10 µm, 1 µm on special request	>50	
Etch depth (µm)		0.010-500	<70	
Minimum spacing between structures (µm)		5 +2.6 * etch depth	Same as structure height, but at least 50	
Aspect ratio channels		<1:2	<1:2	
Electrodes (µm)	Minimal feature size	2		
	Standard feature size	5		
	thickness	0.05-1		