LAB ON CHIP

A s (LOC) is a device that integrates one or several laboratory functions on a single chip of only millimeters to a few square centimeters to achieve automation and high-throughput screening. LOCs deals with the handling of extremely small fluid volumes down to less than picoliters. Lab-on-a-chip devices are a subset of Micro-electro-mechanical systems (MEMS) devices and often indicated by "Micro Total Analysis Systems" (µTAS) as well. LOC is closely related to, and overlaps with, microfluidics which describes primarily the physics, the manipulation and study of minute amounts of fluids. However, strictly regarded "Lab-on-a-Chip" indicates generally the scaling of single or multiple lab processes down to chip-format, whereas "µTAS" is dedicated to the integration of the total sequence of lab processes to perform chemical analysis.

The first real lab-on-a-chip was created in 1979 at Stanford University for gas chromatography. However, major lab-on-a-chip research only began in the late 80s with the development of microfluidics and the adaptation of microfabrication processes for the production of polymer chips. The ability to easily fabricate polymer microchips enabled many research laboratories to start their own investigations into lab-on-a-chip technologies. Today, it is even possible to fabricate fully customized lab-on-a-chip devices in any lab without the need of a clean room

Applications

Lab-On-A-Chip And Cell Biology

Lab-on-a-chip demonstrates the ability to control cells at the single-cell level while dealing with a large amount of cells in seconds. At the microscale level flow switch can be very fast and goes down to just tens of milliseconds. Using fast optical detectors (such as the Opto Reader, for example) one can detect and isolate a given cell (such as cancerous cell made fluorescent using antibodies) with high throughput. There are several other applications for lab-on-a-chip in cell biology, including micro patch clamp, control of stem cell differentiation, high-speed flow cytometry and cell sorting.

Lab-On-A-Chip and Chemistry

The ability to perform fast heating and cooling at the microscale enables higher efficiency in some chemical reactions. Therefore, much research has been conducted on using labs-on-a-chip as microsized and highly parallelized micro chemical reactors. Lab-on-a-chip devices can also be of interest when dealing with dangerous and explosive compounds in that they contain risk by dealing with smaller volumes at a time.

Fabrication Technologies

Lab-on-a-chip uses the most common microfluidic device fabrication technologies, and depending on their applications, various polymers.

PDMS lab-on-a-chip: PDMS (polydimethylsiloxane) is a transparent and flexible elastomer. PDMS is widely used because it is very easy and cheap to fabricate PDMS labs-on-a-chip by casting .Moreover, labs-on-a-chip made of PDMS take advantage of the easy integration of quake microvalves for fast flow switch and permeability of air for cell culture and studies. Widely used for lab-on-a-chip prototyping, PDMS shows severe limitations for industrial production. Because the material is subject to ageing, and because PDMS absorbs hydrophobic molecules, it is hard to integrate electrodes into a PDMS

Thermopolymers (PMMA PS…) lab-on-a-chip: Thermoplastics are good candidates for the fabrication of labs-on-a-chip since they are transparent, compatible with micrometer-sized lithography and more chemically inert than PDMS.

Glass lab-on-a-chip: Transparent, compatible with micrometer sized machining, chemically inert, with a wide range of well-known chemical surface treatments and reproducible electrode integration, glass is a very good candidate for the industrialization of labs-on-a-chip. From a research point of view, the fabrication of glass labs-on-a-chip require clean rooms and researchers with a strong knowledge of microfabrication..

Silicon lab-on-a-chip: The first lab-on-a-chip was done in silicon, and it seems like quite a normal choice since microtechnologies are based on the micromachining of silicon. Silicon is expensive, it is not optically transparent (except for IR) and it requires a clean room as well as a strong knowledge of microfabrication. Moreover, the electrical conductivity of silicon makes it impossible to use for lab-on-a-chip operations requiring high voltage (like electrophoresis). Still, even if nowadays silicon seems like an obsolete candidate for the industrialization of lab-on-a-chip, it is not commonly used unless very necessary.

Advantages

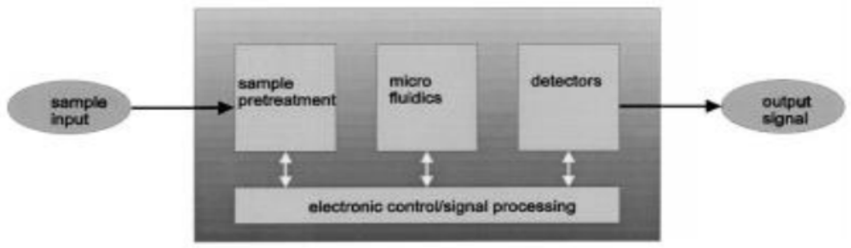
Low cost, High parallelization,Ease of use and compactness, Reduction of human error, Faster response time and diagnosis, Low volume samples, Real time process control and monitoring increase sensitivity, Expendable.

Limitations

Industrialization, Signal/noise ratio, Ethics and human behaviour, Lab-on-a-chip needs an external system to work.

SILICON AND GLASS MICROMACHINING FOR MICRO TOTAL ANALYSIS SYSTEMS (μ TAS)

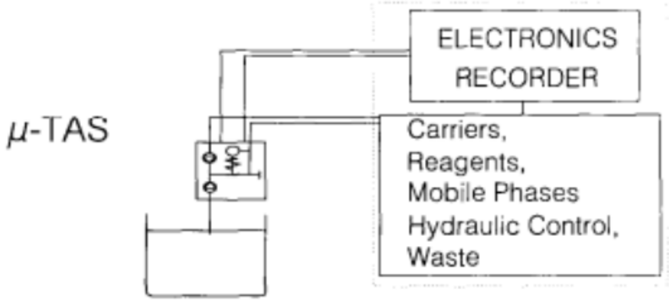
Micro total analysis system is a sub set of devices comprising the lab on the chip. It uses both hard and soft microfabrication techniques. It can be a hybrid of several chips. It is an integrated and miniaturised chemical analysis system.



Elements of a μ TAS

In general, four types of subsystems are thought to comprise a mTAS: a sampling unit, a microfluidic unit, a detector system and an electronic controller. .An important aspect is the very small size required for the sensing element operating in a microchannel of a few hundreds of microns width.

A single chip includes sample preparation, separation and detection system.



Fabrication

μTAS fabrication has matured, affording microstructure generation from a wide range of materials (e.g. glass, silicon, elastomers, plastics, thermosets, paper) and using an equally broad set of microfabrication methods (e.g. photolithography, soft lithography, injection molding, hot embossing, laser micromachining).

Recent innovations in fabrication explored unconventional materials and fabrication strategies. Corn protein (zein) was processed by soft lithography and bonded to both a glass slide and another zein film by ethanol vapor deposition to form green microfluidic devices.

An origami (paper folding) method was developed to fabricate three-dimensional (3D) paper devices from single sheets of flat paper in a single photolithographic step.

Curved microfluidic networks were built from the self-assembly of differentially photo-crosslinked SU-8 films, which spontaneously and reversibly curled on film de-solvation and re-solvation .

Advantages

- Limited mixing of fluids
- Portability
- Automation
- Reduction of sample
- Low cost
- Fast

Disadvantages

- Blockages due to gas bubbles
- Contamination

Silicon micromachining

Bulk Etching- Anisotropic wet chemical etching.

Surface micromachinig- Build structures on top of the substrate surface.

Wafer bonding – Direct bonding, Anodic bonding

Glass Micromachining

Glass is often considered a more desirable material for particular MEMS device applications due to its unique properties, such as optical transparency and biological compatibility.

MEMS applications where micro-machined glass is used include:

* sensors, such as those incorporating pressure, accelerometer, gyroscope transducers

* bioMEMS devices enabled by lab-on-chip and microfluidics technologies

* membranes

* spacers for cell phone cameras

Different glass micromachinig methods are powder blasting, laser, wet etching, ultrasonic and DRIE.

Powder Blasting

Powder blasting is also referred to as sandblasting, impact abrasive machining or abrasive jet machining (AJM). In this process, fine abrasive particles are propelled by compressed air at the workpiece and these particles mechanically remove material by small chipping.

Powder blasting can be used to create membranes in glass for MEMS applications. The process can be controlled to leave as thin as 75-100 um of glass material with a depth uniformity within 15 microns.

Advantages

- It can quickly create through-holes in brittle materials without creating burrs on the surface.
- process is anisotropic
- All surfaces are fully protected throughout the manufacturing process

Disadvantages

- The machined surface finish is slightly rough unless is it is wet etched after powder blasting.

Laser Machining

With the laser machining process, glass material removal is from thermal shock or ablation by directed optical energy. There are several sources of lasers for machining glass and their selection is based on the type of application. The laser systems that are available for glass include CO2, Nd:YAG and excimer. The wavelength of the laser needs to be such that it does not pass through the glass without etching it. Computer-controlled equipment (most commonly an X-Y table) directs the beam to the desired location.

Advantages

- Easy to create a pattern from a CAD drawing and there is no mask, tooling or tool wear.
- The process can be easily automated.
- This process has a low taper angle and can be used on large pieces.

Disadvantages

- Laser machining creates subsurface micro-cracks and also creates a HAZ (Heat Affected Zone) which results in a kerf or damaged area at the top surface of the hole.
- Laser machining can crack or break thin glass pieces.

Ultrasonic Machining

This is a non-impact process in which a mechanical tool oscillates above the workpiece at a high frequency, roughly 20,000 cycles per second. The tool end (horn) is formed in the shape of the desired feature. The tool end (horn) and workpiece are submerged in abrasive slurry. The majority of the machining occurs by the tool end and abrasive particles hitting the workpiece.

Advantages

- Ability to drill straight sidewalls and produce very fine features.
- High aspect ratios that can be achieved.
- It is also easily repeatable until tool wear.
- Also, multiple depths and contoured surfaces (2-1/2 D) can be achieved.

Disadvantages

- A slow process with a large capital investment.
- The tooling needs to be redressed for every 25-50 pieces to avoid feature degradation.
- It is more difficult to engrave contoured and interior surfaces.

Wet Etch

Wet etching involves the creation of a pattern in glass by immersing the wafer in an acid, most commonly hydrofluoric. An acid-resistant mask material can be used for selective material removal and the part can be etched to multiple levels. Common mask materials are Cr-Au and/or an acid resistant photoresist.

Advantages

- Wet etching can create very high detailed features and works well for removing thin films
- The shape and size of the part is not usually limited.
- Produced features have a low surface roughness and therefore this process can be used with applications where near optical clarity is desired.

Disadvantages

- The wet etch process is isotropic and there is undercutting of the photoresist that is equal in distance to the etch depth. This gives the process a low aspect ratio.

- The acid material is extremely hazardous to humans and the environment.

Deep Reactive Ion Etching (DRIE)

A dry etch micro-machining method is Deep Reactive Ion Etching, or DRIE. The process uses directional plasma ions to hit the glass causing erosion. A metal mask can be used to direct the ions and create the desired features. The process can be used on glass, but the gas chemistry is geared more toward silicon etching.

Advantages

- The process can be extremely accurate with feature creation and can achieve very small features.
- There is a low amount of surface roughness and it is a highly anisotropic process.

Disadvantages

- Depending on the number and type of features, the DRIE process can be very slow and because of this, it is not good for removing material across a wide area.
- Ion etching works well for etching silicon, but the process is extremely slow for etching glass. In fact, since it etches so slowly, glass is often used as a mask for etching silicon.

SURFACE CHEMISTRY IN POLYMER MICRO FLUIDIC SYSTEM

Polymers exhibit comparatively low material cost and feature a wide range of (customizable) material characteristics. Furthermore, their thermally induced castability makes polymers amenable to commercially very well-established, high-fidelity replication schemes such as hot embossing and injection molding, thus covering the full scope for upscale from small-series to mass production.

Materials

The most frequently used polymers include poly(methyl methacrylate) (PMMA), polycarbonate (PC), cyclic olefin materials, SU-8 and poly(dimethylsiloxane) (PDMS) which is commonly processed by the so-called ‘soft lithography’ fabrication scheme.

PMMA has been one of the most widely used polymers formicrofluidics. It is particularly useful for microfluidic chips due to its comparatively low cost, high optical transparency, and well definable electric and mechanical properties.PMMA is the least hydrophobic polymer, and can directly generate stable EOF in the microchannels . Owing to its unique absorption characteristics in the infrared regime, PMMA is also amenable to direct-write microstructuring by common CO2 laser ablation systems. These favorable physicochemical properties frequently make PMMA the material of choice for the fabrication of microfluidic devices.

PC is a widely used thermoplastic polymer which is,for instance, used for the fabrication of optical data storage media such as compact disks. Its high durability, strength, temperature resistance, lowdensity and good optical properties have also made PC a popular material for the fabrication of microfluidic devices.

Cyclic olefin polymer (COP) and cyclic olefin copolymer (COC) high optical clarity, even into the deep-UV range , low water absorption and, compared to other polymers, an exceptionally high resistance to organic solvents.

SU-8 is a UV-sensitive epoxy-based negative photoresist known from surface micromachining which can be obtained with range of viscosities for forming high thickness films (~100 µm) by spin coating. It has also been shown that the SU-8 native resin itself or through suitable functionalization procedures is compatible with a range of chemical and biological assays

PDMS, an elastomeric material, has been widely used for the fabrication of microfluidic devices by ‘soft lithography. Features on the micron scale can be replicated with high fidelity in PDMS using replica molding from a microstructured, e.g. SU-8,master. The replica can be sealed reversibly or irreversibly without disfeaturing of the microchannels. PDMS substrates have been utilized with biological samples because of their low toxicity and their rather high optical transparency down to 280 nm, making PDMS compatible to a number of detection methods.

Processing

There is a variety of machining techniques used for the fabrication of polymeric microfluidic devices, which can be coarsely categorized into direct/serial writing and replication schemes Often used direct structuring methods comprise (ultra-)precision milling, laser ablation photolithography, hot embossing, and injection molding,

Surface Modification

Several coating techniques are available.

Common techniques include vapor-, plasma- and liquid-phase techniques. These techniques result in different levels of process control, layer thickness uniformities, and bring about certain restrains about the topology of surfaces to be coated. Surface treatments can lead to deposition of new and/or conversion of native surface layers.

Techniques include- Chemical vapour deposition, plasma activation, UV irradiation, sol gel chemistry, dynamic coatings, serial writing, mask based techniques