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Application and Manufacturing of Microfluidic Devices: Review

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Abstract:*Micro fluidic devices are gaining increasingly popularity owing to their many advantages. Microfluidics varies in terms of forces operating from other domains as well as from macro-scale fluidic devices. Effects which can be omitted on a macro scale are dominant when fluid dynamic faces the issue of scale. With the recent achievement in the biotechnology, microfluidic devices promise to be a big commercial success. To have a better understanding of the various types of microfluidic devices, their application areas, basic design and manufacturing issues, a brief review is carried out and reported in this paper. Few devices and their applications are discussed.*

Keywords: *Microfluidics, Design, Micro-Machining, Bonding, Interfacing.*

I. Introduction

Microfluidics deals with the behavior, precise control and manipulation of fluids that are geometrically constrained to a small, typically sub-millimeter scale. Typically, micro means one of the following features,

- small volumes (nL, pL, fF)
- small size
- low energy consumption

The behavior of fluids at the microscale can differ from 'macrofluidic' behavior in many aspects such as surface tension, energy dissipation and fluidic resistance dominating the system. Microfluidics studies how these behaviors change and how they can be worked around or exploited for new uses. In particular, the Reynolds number (which compares the effect of momentum of a fluid to the effect of viscosity) can become very low. A key consequence of this is that fluids, when side-by-side, do not necessarily mix in the traditional sense; molecular transport between them must often be through diffusion. High specificity of chemical and physical properties (concentration, pH, temperature, shear force, etc.) can also be ensured resulting in more uniform reaction conditions and higher grade products in single and multi-step reactions. [1, 2,3, 9] Micro domain varies not only from the macro domain but also from each other in basic characteristics. The microfluidic domain differs from other domains in terms of area, which is indicated by difference in the whole design process, as well as in design support and manufacturing. Effects which can be omitted on a macro scale are dominant when fluid dynamic faces the issue of scale. Lack of proper understanding of this area creates difficulties and causes error prone designs. In comparison to the macro-domain, where precision in many cases is required and tolerances can be tight, in the micro-scale, dimensions are in the scale of macro-scale tolerances. Due to this, the majority of manufacturing methods start to be costly and the selection of materials for new devices is constrained. Fig.1. shows the macro and micro scales and devices for some application areas. Since, the application of microfluidic devices are continuously increasing, to have a better insight about this area, a brief review about the application areas and applicable manufacturing process and various issues is carried-out and presented in this paper.[6,7,8]

With the recent achievement in the biotechnology, microfluidic devices promise to be a big commercial success. Microfluidic devices are tools that enable novel applications unrealizable with conventional equipment. The apparent interest and participation of the industry in microfluidic research and development show the commercial values of microfluidic devices for practical applications. [10,11]

In response to the commercial potential and better funding environments, microfluidics quickly attracted the interest of the scientific community. Peoples from almost all traditional engineering and science disciplines have begun pursuing microfluidic research, making it a truly multidisciplinary field representative of the new economy of the twenty-first century. The classification of microfluidic devices based on the application areas such as pharmaceutical, biotechnology, chemical energy, cosmetics etc., is shown in Table.1 [12, 13, 17, 22]

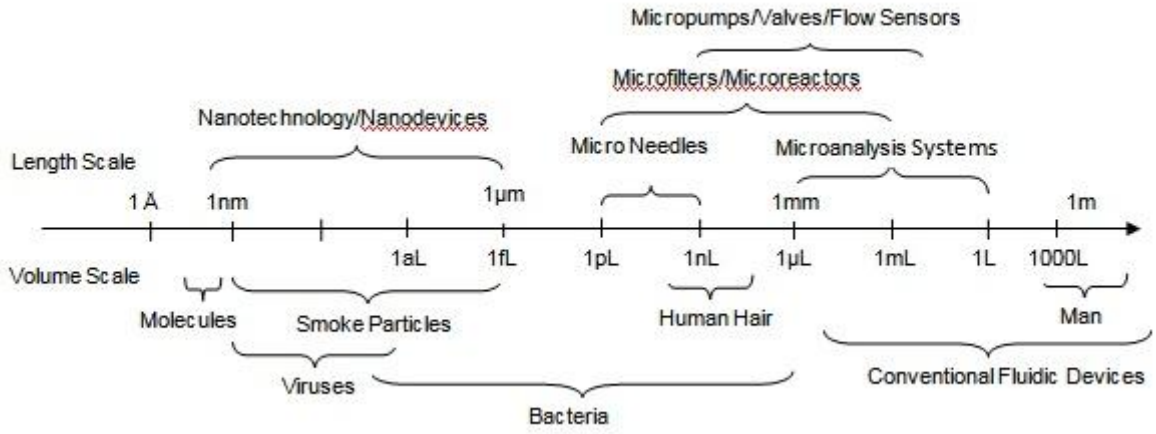

Fig.1 Macro and Micro Domain and Application Areas[11]

Table.1 Application Areas of Microfluidic Devices [10, 17, 18, 20]

Application Area	Benefits	Application
Pharmaceutical	High shear particle size reduction, uniform particle size distribution, Reliable scaleup	Vaccines, Cancer, Antibiotics, Injectables, Inhalables, Steroids
Biotechnology	High shear particle size reduction, Uniform shear rates, Rapid cell rupturing, Ease of use	Quantification of E. coli, Yeast, Algae, Bacteria, Plant, Insect, Fungi
Chemical Energy	Reduces particle size to a submicron level to create stable nanoemulsions and suspensions	Inkjet inks, conductive inks, toners, Carbon nanotubes, Resins
Cosmetics	Precisely controlling particle size reduction to the optimal level with a uniform distribution	Sunscreens, makeup's and mascaras, waxes and lipsticks
Nutraceuticals	Utilize chemistry to deliver benefits and nutrients from plants, fish oils and other natural sources	Vitamins, weight loss powders, oral vitamin sprays and functional foods
Energy	Reduce reliance on fossil fuels, never degrade, and emit minimal greenhouse gases.	Fuel cells, batteries, photovoltaics, biodiesel

II. Applications

Microfluidics has large number of applications. In the following sections, some of the extensively used devices are discussed here.

1.1. Rapid Quantification of Bacterial Cells (Cytometer)

A simplified microfluidic device for quantification of bacteria in potable water by the microfluidic system and by epifluorescence microscopy is shown in Fig.2. [1] Bacteria in natural mineral water and in purified household tap water were accurately enumerated by using this system within 15 min after fluorescent staining.The dimensions are the channels with Long & short lengths, width & depth of the channels are 28.5mm & 14mm and 60µm & 25µm, respectively. Samples are injected at inlet A, and sheath fluid at inlets B and C. sample flow: 0.5µl/min; sheath flow: 2.5µl/min. The Critical features of the systems are biocompatibility of material, surface finish, length, width and depth of channels.[1,2]

1.2. Particle Size Reduction (Microfluidizer)

There are several ways to reduce large particles into smaller ones - but Microfluidizer high shear fluid processors stand alone in their ability to achieve uniform target particle sizes on the nano-scale. Some of the reliable features are small particle sizes, narrowest particle size distribution, repeatable and consistent results and improved processing efficiencies. As depicted in Fig.3, product is input into a reservoir which supports high solid content. A high pressure pump generates forces up to 40,000 psi (2578 bar) in order to force the product stream intoprecisely engineered microchannels within the unique interaction chamber. Inside the chamber, product is exposed to consistent and intense impact and shears forces and then is immediately cooled. This repeatable process results in tiny particles with a uniform distribution. The critical features of the systems are pressure and cross section of channels.[5,23]

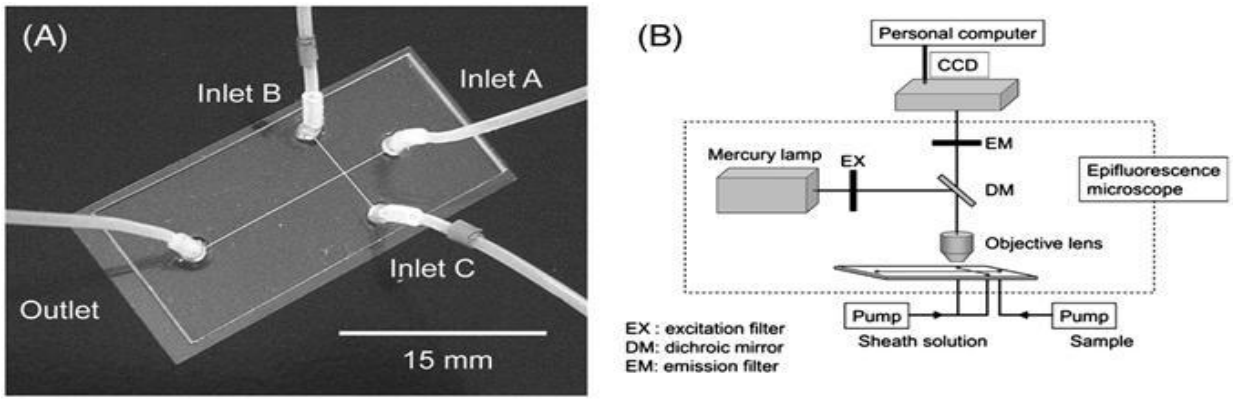

Fig.2. Design of the on-chip flow cytometer. (A) Microfluidic device with simple cross microchannels. (B) Schematic representation of the on-chip flow cytometer

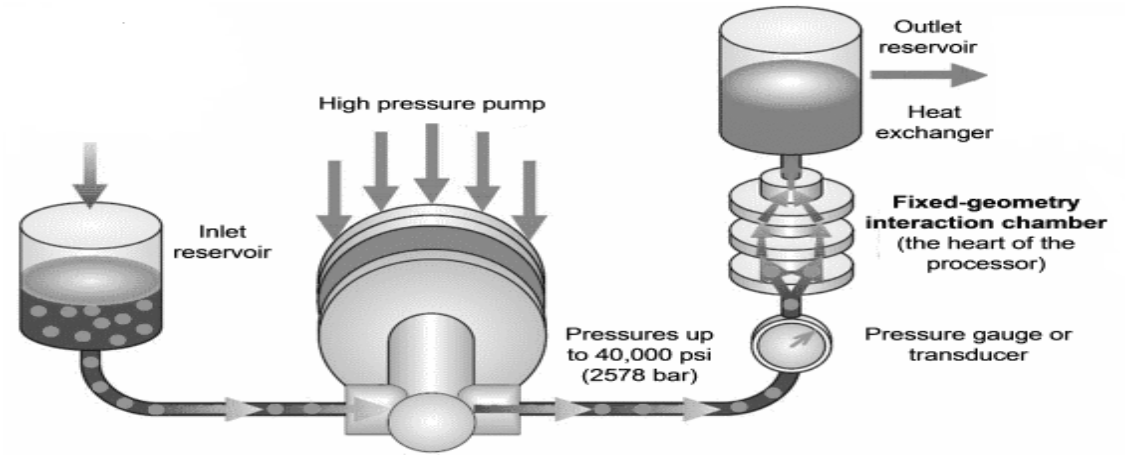

Fig: 3 Schematic of particle size reduction

1.3. Fuel Cells

The operation of a fuel cell involves the chemical interaction between hydrogen and oxygen to produce water, heat and electrical energy. Typically, a fuel cell consists of a pair of electrodes (the 'anode' and the 'cathode') separated by a membrane that allows protons (hydrogen ions) to pass through the membrane but does not allow an electric current to pass. A main objective of current research is the application of micro scale fuel cells to portable electronic devices such as cell phones and computers. The main problem with applying fuel cell concepts to mobile devices is that the power source (battery or fuel cell) must be able to deliver around 300mA of current at 3.6V. [4, 25, 26] The critical features of the fuel cell are compact size, operating temperature and electrolyte substance.

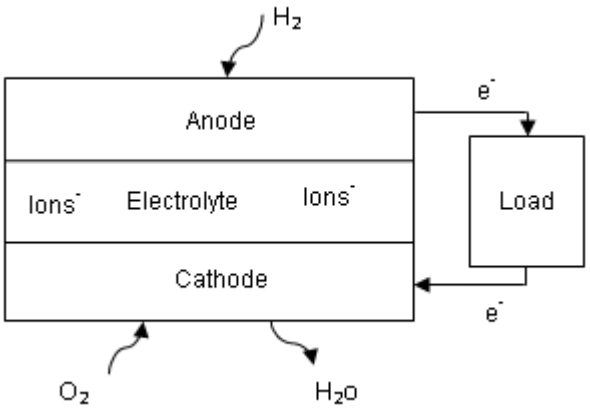

Fig: 4 Block Diagram of Fuel Cell

III. Design of Microfluidic Devices

The obvious discerning characteristics of micro-reactors are compact size, light weight, and lower material and energy consumption. Secondly, smaller linear dimensions lead to increased species gradients which are particularly important for chemical reactor processing. This results in rapid heat and mass transport, and short diffusion lengths. Faster

system response gives better process control and high product yields. Besides these, the attractive feature of micro-reactors is their high surface to volume ratio compared to conventional chemical reactors. Because of smaller passage size, flow through micro-reactors usually remains laminar. Thus, the heat/mass transfer coefficients become inversely proportional to the channel hydraulic diameter; however there is an increase in pressure drop. [11, 13, 29, 30]

The higher heat and mass transfer characteristics of micro heat exchangers are an added advantage for utilizing the full potential of catalysts used, especially during endothermic/exothermic reactions. Thus, local hot-spot formations are avoided because of high heat removal capacity. Additionally, because of higher reaction temperature, catalysis can be utilized effectively, thus requiring a smaller volume. Finally, because of smaller reactants and products inventories, high level of safety is achieved. In the following sections, the importances of the critical design features are discussed with two types of microfluidic devices.[27, 28]

1.4. Micromixer

In micromixers, diffusion or mixing time depends upon square of the mixing path. Because of their small size, micromixer decreases the diffusion time significantly. In general, fast mixing can be achieved with small mixing path and large surface area. Design considerations of micromixers are fast mixing time, small device area, integration ability in a more complex system. Mixing time is proportional to the square of the channel width and the velocity is inversely proportional to the channel width. The residence time is determined by flow velocity and channel length as given in Eq. (1). [20, 31,32,33]

$$\boldsymbol{L = \frac{(\mathrm{Qw} + \mathrm{QE}) * w}{2 * A * D}} \ldots\ldots\ldots\ldots\ldots\ldots\ldots \boldsymbol{equation1}$$

Where, Q=flow rate, A=cross sectional area, D=diffusion coefficient, w=width of channel. Hence, the smallest cross-section and longest channel length are desired. Fig.6 shows typical geometry of micromixer in which width of micro-channel is 300µm, depth is 90µm and length is 3m.

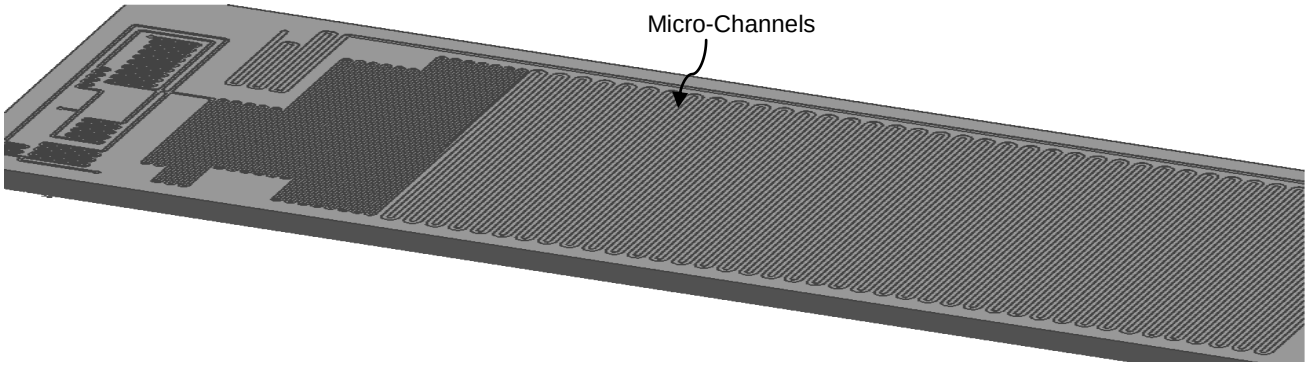

Fig.6 Typical geometry of micromixer (90^{x} 30^{x} 5mm)

1.5. Heat Exchangers

The heat exchanger are of two types 1) The high temperature heat exchanger takes high temperature gas and uses that gas to boil and superheat working fluid. 2) The second type of heat exchanger uses ambient air to cool down and condense the working fluid. The parasitic pump power required to flow the air through the heat exchangers is taken directly from the power turbine and is proportional to the product of the air volumetric flow rate and the pressure drop across the heat exchanger. [19, 34]

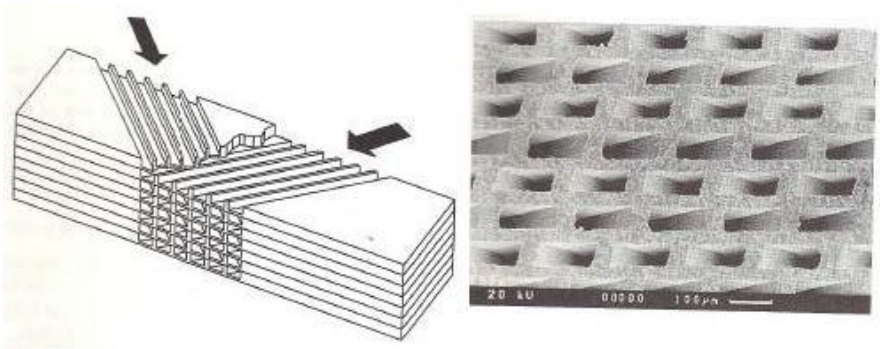

Fig.5 Multi-stack heat exchanger

There are eight sets of parameters that must be determined to establish the design of a specific heat exchanger, air inlet and outlet conditions namely pressure, temperature and mass flow, the working fluid inlet and outlet conditions, heat exchanger channel width, channel depth, channel length, total number of channels, heat exchanger fin thickness, number of stacks. [19, 43, 46] The most critical futures are smallest cross-section and longest possible length.

IV. Manufacturing

1.6. Manufacturing Methods

The manufacturing capability of device depends upon material selection.Following materials are generally used for manufacturing of microfluidic devices. Table.2 shows the different manufacturing processes and material capabilities. [7, 11, 13]

Table.2. Microfluidic Channel Manufacturing Methods

Manufacturing Methods	Principle	Materials	Features
Wet silicon etching	Chemically removal of layer	Silicon,Silicon Dioxide, Silicon Nitride	Low cost, High surface area, low aspect ratio
Dry silicon etching	Plasma assisted etching	Silicon, Silicon Dioxide, Silicon Nitride	High surface area, minimum feature size, High aspect ratio
Lithography	Series of Chemical Reactions	Aluminium , Steel, Glass	Minimum feature size, Maximum surface area, Choice of geometry
Laser Ablation	Bond-Breakage by Pulsed UV Source	Copper, Steel	High aspect ratio, Choice of geometry, Minimum feature size
LIGA	Uses X-ray or UV Light	Silicon wafer, PMMA, SU-8	Minimum feature size, High aspect ratio, Choice of geometry
Micromachining	Cutting of materials with tool	Steel, Copper, Aluminium	Maximum lifetime, Choice of geometry, maximum surface area
µ-EDM	Melting and evaporation of material	Aluminium, Copper	Maximum life time High aspect ratio

1.7. Materials

Commonly used materials for the microfluidic chip manufacturing are Low fluorescence Schott Borofloat glass, Corning 0211 borosilicate glass Fused silica, Quartz Silicon, PMMA, SU-8, PDMS, Steel, Aluminum, copper, etc. [7, 14, 35, 36]

1.8. Effect of Surface Roughness

Pressure drop during internal flow is one of the most important considerations in designing a fluid flow system. Surface roughness was identified as an important parameter in fluid flow as early as in the nineteenth century by Darcy,[21,37,38,39] who carefully conducted experiments with pipes of varying roughness. The Darcy friction factor for laminar flow (Reynolds number less than 2000) is given by the following Eq. (2).

$$f = \frac{64}{R_e} \dots\dots\dots\dots\dots equation\ 2$$

Where, 'f' is the Darcy friction factor and 'R_e' is the Reynolds number. [21]

Wall roughness can be increased to promote mixing of the fluid, or reduced to eliminate flow disturbances. Recently, the effects of surface roughness became of interest from the point of view of passive/active flow control strategies, where one is interested in determining the smallest possible surface modification that may induce the largest possible changes in flow field.[40,41,49,50]

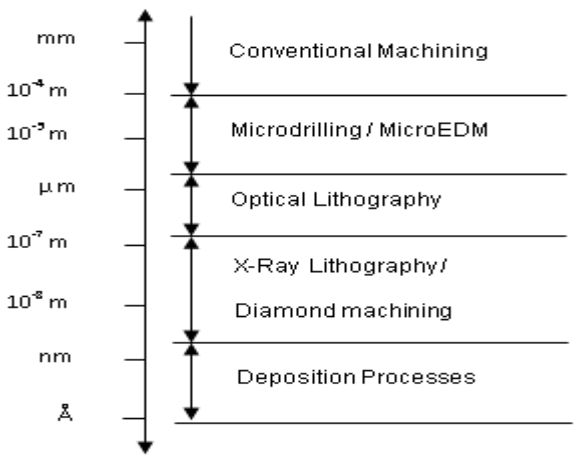

Fig:6 Comparison of surface roughness of different micro-manufacturing processes

V. Bonding Techniques

Bonding methods can be divided into mainly two categories: direct wafer bonding or bonding with intermediate layers. As shown in table.3 [8,15,16] "Wafer bonding" refers to the phenomenon that mirror polished, flat, and clean wafers of almost any material, when brought into contact at room temperature, are locally attracted to each other by van der walls forces and adhere or "bonds" to each Other. [15, 16] ''Wafer bonding'' refers to the phenomenon that mirror polished, flat, and clean wafers of almost any material, when brought into contact at room temperature, are locally attracted to each other by van der Waals forces and adhere or ''bond'' to each other. [41,42,44]

Table.3 Bonding Techniques

Direct Wafer Bonding (Without Intermediate layer)	**Fusion Bonding (same materials)**	• Surfaces must be flat and clean • Substrate washed with piranha solution and immersed in ammonium hydroxide (500C, For 30 min) • Two wafers pressed together for few hours
	Anodic Bonding (Different Materials)	• Use of electric field • surface topologies greater than about 500 Å • 300 to 450 °C and high DC voltage (500-1000V)
Indirect Wafer Bonding(With intermediate layer)	**PDMS Bonding**	• irreversible PDMS bond with an O2 plasma treatment before bonding • siloxane bond created between two wafers
	SU-8 Bonding	• Substrate is cleaned using piranha solution. • Layer of SU-8 photoresist is spun onto the substrate • The cross-linked SU-8 structures are sealed by a second cleaned substrate.

Above bonding techniques used for silicon, glasses, polymers, ceramics, and metals. Ceramic green taps and metal sheets structured by serial techniques can be directly bonded together at high pressure and high temperatures. Ceramic green types are typically bonded at 138 bars, 70^0C for 10 minutes. Stainless steel sheets are typically bonded at 276 bars, 920^0C for 4 hours.[45]

"Diffusion soldering" bonding process is an advanced type of solder bond that can form high- quality hermetic seals at lower temperatures than other bonding technologies. This technique uses one thin metal layer (typically 1-10µm thick) which during a thermal process inter-diffuses with its bonding partner forming an inter-metallic compound layer with re-melting temperature higher than the bonding temperature.[47,48]

In thermo-compression bonding process the two surfaces adhere to each other due to a metal bond established between two metal surfaces pressed together under heating. The bonding mechanism is enhanced by the deformation of the two surfaces in contact in order to disrupt any intervening surface films and enable metal-to-metal contact. By heating the two metal surfaces the contact force applied for the bond process can be minimized due to metal softening. High force uniformity across the bonding area enables high bonding yield. Several metals are used for metal thermo-compression wafer bonding, as Au-Au, Cu-Cu or Al-Al. [24,51,52,53]

The important issues in bonding are, maintaining surface finish & flatness of bonding surface and bonding of metal surfaces for which bonding techniques are not well developed.[59,60,61]

VI. Interfacing with Micro-Systems

Fig.6.illustrates the use of the PDMS connector chips The connector chip self adheres to the micro fluidic component. Aligning is easy due to matching surface relief. The single lithography mask needed for mold fabrication is almost identicalto the one that defines the inlet holes on the microfluidicchip. The only difference is that additional cutting marks forseparation of individual chips have been added. Misalignmentof microfluidic chip and PDMS connector causes airbubbles to remain at the interface, but because PDMS istransparent they can be seen and realignment is easy.Whenalignment is satisfactory, the capillary tube are gently pushed tothe holes in the connector chip. Depending on pressure toleranceneeded, an additional jig can be used to compressesthe connector chip against the microfluidic chip. [17, 54, 55, 56]

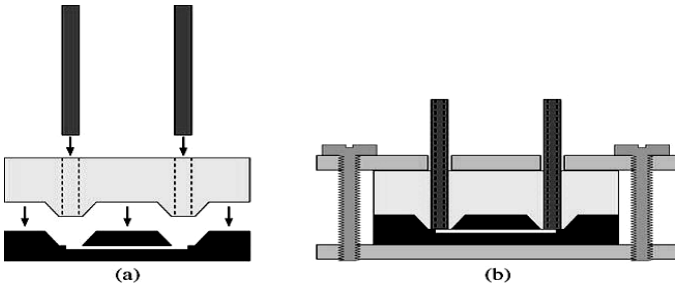

Fig.6 Connector chip usage. (a) Connector chip is aligned to matching surface relief of the microfluidic chip and capillary tubes are pushed to the holes. (b) If higher operating pressures are required, additional mechanical jig provides required tightness.

The design of connector chip mechanism include easy of assembly, reliability, chemical compatibility, minimal dead weight, minimal pressure drop.[57,58]

VII. Conclusion

Micro fluidic devices play important role in the pharmaceutical, biotechnology and chemical energy sectors. There are several issues in design & manufacturing of microfluidic devices and hence selection of material & manufacturing process are important. The material should not participate in the reaction process and hence, they should be chemically inert on the fluid flow passage. Since most of the devices undergo larger pressure, the selected material should withstand such pressures. Most of the microfluidic devices are small cross-sections and long length of channels; similarly extremely flat and high level of surface finish is required on bonding surfaces.

VIII. Acknowledgement

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