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Methodology on Scaling-down of Membrane Separation Process into Microfluidic Platform

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The use of membrane separation techniques in microfluidic devices has been gaining interest in many research field particularly in analytical chemistry where such a device is utilised to selectively remove impurities and/or unwanted components for a better detection of analyte of interest. Many different strategies have been reported to combine membranes and microfluidics. In this paper, details on how to fabricate such a micro scale filtration device are discussed. Topics covered include size and operation mode, materials and fabrication methods, strategy to integrate membrane on chip, fluidics (and electrical) interconnects, online measurement and process automation. Each design parameters were reviewed and discussed in accordance to the steps (or methodology) needed to fabricate a microfluidic membrane filtration unit. A low cost fabrication solution using polymers as materials for fabrication and the use of Arduino board for process automation have been suggested to realise a fully automated microfluidic membrane filtration unit.

1. Introduction

Microfluidic in general is regarded as a research area that involves manipulation, control and analysing of fluid behaviour at micro scale i.e. by using a microfluidic chip. A microfluidic chip is a miniaturised device containing series of micro-channels at sub-millimetre dimensions (Whitesides, 2006). The micro-channels (fluidic structures) forming the microfluidic chip are typically linked together in order to achieve specific features in mind such as mixing, pumping, sorting, and/or control of the biochemical process (Whitesides, 2006). Microfluidic platform offer so many advantages. These include the capacity to utilise small volumes of samples and reagents to facilitate specific biological analyses/reactions (lower running cost per experiment), low materials cost as most of the chip is made of disposable polymer materials (Streets and Huang, 2013), shorter analysis time and have small footprints for analytical devices (Sarghini et al., 2015). In such a micro scale operation, mass and heat transfer rates are also significantly increased by the large surface-to-volume ratio of the device (usually in the range of about 3,000 m^2/m^3) and leading to a more efficient and improved performance (Schäpper et al., 2009).
In recent years, the numbers of microfluidic chip prototypes in the area of medical diagnostics, pharmaceutical and specific biological studies have increased exponentially. Considerable advances have been made on the development of a high-speed, high-throughput DNA sequencing method on microfluidic platform for clinical molecular diagnostics, especially mutation detection and genetic screening (Taparia et al., 2017). An obvious example is the establishment of a miniaturised polymerase chain reaction (PCR) platform. Microfluidic technology also results in the development of a microscale bioreactor system for cultivation of microorganisms and animal cell cultures. Such a microbioreactor platform often integrated with sensors and actuators to support the reactor operation. It offers the capacity to perform fermentation experiments or investigation biocatalysis process at a cost much lower than utilising the shake flask (or microtitre plates) but produces results similarly to any lab scale bioreactor systems performance (Schäpper et al., 2009).

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Miniaturisation also benefits membrane separation processes (De Jong et al., 2006). Membranes nowadays are extensively applied in a wide range of industrial applications. These include in the area of waste water treatment, desalination, filtration, biocatalysis processes, etc. Membrane separation is a treatment process based on the physical separation of compounds from the water phase with the use of a semi-permeable membrane. In general, the types and the pore size of the membranes determines the types of compounds removable (filtered) by the membranes (Pinelo et al., 2009). Many macro scale membrane systems can be translated into microfluidic platform. The scope of the paper will only consider the possibility of downsizing a flat, horizontal membrane modular type system. Whilst majority of research projects pertaining to microfluidic membrane filtration unit focuses on the application and the performances of such device, this paper provided a detail overview on the design aspect of such microfluidic membrane filtration unit. Information on mechanical design and fabrication of such microfluidic device is lacking in present literature. Various design considerations including the size and operation mode of the micro membrane filtration unit, materials and fabrication methods, strategy to integrate membrane on chip, fluidics (and electrical) interconnects, online measurement and process automation were discussed. Each design parameters were reviewed and discussed in accordance to the steps (or methodology) needed to fabricate a microfluidic membrane filtration unit.

2. Size and operation mode

In a first step of development, it is important to determine the desired size of the microfluidic filtration unit in mind. Microfluidic chips usually consisted of fluidic channels with dimensions between 100 nm and 100 microns. The same characteristics also applied for microscale filtration device where the width and the depth of the micro-channels are no larger than 1 mm scale (Di et al., 2017). In the simplest chip configuration, microfluidic filtration unit can be fabricated containing a single inlet and outlet fluidic ports joined together with a microchannel that is about 30 mm (length) x 1,000 µm (width) x 500 µm (depth). This would have resulted in a microfluidic chip with working volume of approximately 15 µL (Figure 1). Excluding the dead-volume in the fluidic interconnects, the working volume is indeed very low and often operated under a bubble-free condition. This means that, during operation, the chip will be completely filled with liquid without any headspace. Bubbles are not desirable as their relatively large size (Ø ~ 1 - 2 mm) – would easily clog the micro-channels or even block fluidic ports. Fluids behaviour in such a micro scale platform exhibit physical behaviour that is not observed in larger structures. At these scales, the Reynolds number is low (N_{RE} < 10) and liquid flow is normally in laminar condition. Laminar flows limit the benefits of fluid mixing in microfluidic devices however, the Peclet number is often large, producing a device with a rapid heat transfer (Whitesides, 2006).

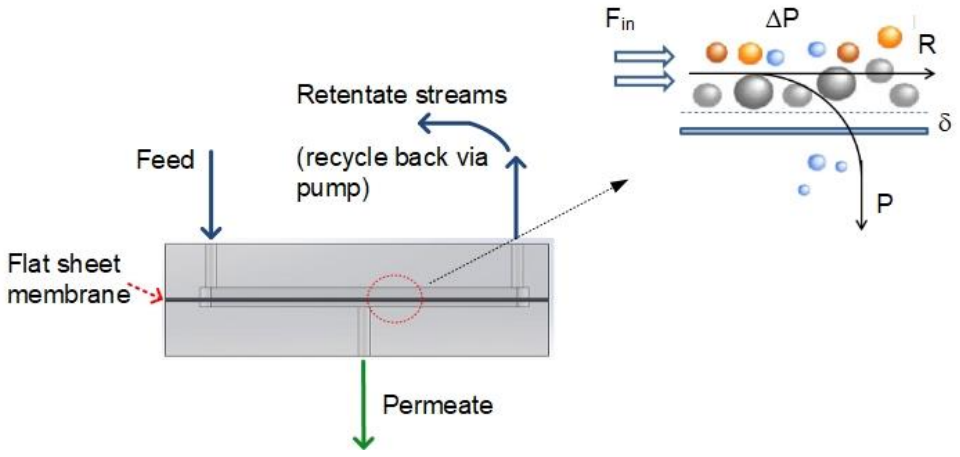

Figure 1: Basic mechanism of microfluidic membrane separation process that occurs due to pressure difference, ΔP across the membrane

There are two distinct modes of operation for a membrane system; i.e. a dead-end or a cross-flow filtration and one ought to decide which one of these modes of operation best suits the specific application. In a dead-end filtration, feed solution is pumped directly towards the membrane and forced through the membrane by the applied pressure. In micro scale, pressure for separation to occur is created using pumps (Zainal Alam et al., 2011). Contrary to the dead-end filtration mode, the concentration polarisation problem is reduced in a cross-flow system because the bulk liquid phase flows parallel to the membrane surface and sweeps any

retained particles. During every pass across the membrane surface, the applied pressure pushes a portion of the bulk phase through the membrane into the permeate stream (Di et al., 2017).

3. Membrane Integration on chip

It is crucial to apply a membrane (i.e. material and type) that best fits the targeted application. Membrane properties differ from one membrane to another and they greatly affect the overall membrane separation efficiency. The membrane can either be directly purchased from a commercial supplier (e.g. Millipore, Sigma, etc.) or prepared in-house (De Jong et al., 2006). The typical selection criteria include membrane hydrophobicity, operation variables e.g. allowable pH, temperature or pressure, MWCO, and finally the type of membrane used (i.e. flat sheet or hollow-fiber) (De Jong et al., 2006). Membrane pore-size or molecular weight cut-off is also a key factor in separation where it may influence the selectivity of the separation process (Pinelo et al., 2009). A rule of thumb for a good membrane rejection is that the membrane pore size should be in the order of one-third or one-fifth of the size of the compound to be retained. This is not entirely true because in practice, the rejection characteristic of a membrane is often a function of concentration polarisation, heteroporosity of the membrane, and system operating variables (pH, temperature and pressure or flux).

Different approaches have been used to integrate a membrane into microfluidic devices. Thus far, direct incorporation of a flat sheet membrane is the most commonly employed method for fabrication of microfluidic membrane filtration unit. Direct incorporation of a membrane is advantageous due to its easy-handling in terms of membrane assembly. Most importantly, it offers the 'clamp-and-play' chip design where a broad range of applications can be made possible by merely changing the type of membrane (Muller et al., 2005). A flat sheet membrane can be integrated into a microfluidics device (De Jong et al., 2006), simply by fitting or pressing it (i.e. sandwiched) in between two polymer pieces using stainless steel screws. The use of screws have the advantage of ensuring the whole unit is aligned properly. A slight mis-alignment would compromise the workability of the microfluidic device. As shown in Figure 2, a water tight seal can be realised using O-rings or by adding additional gasket layer made of polymer e.g. polydimethylsiloxane (PDMS). Once pressed, it is important to ensure that the final assembly of the microchip could withstand a certain limit of pressure because pressure within the chip will increase gradually during separation processes.

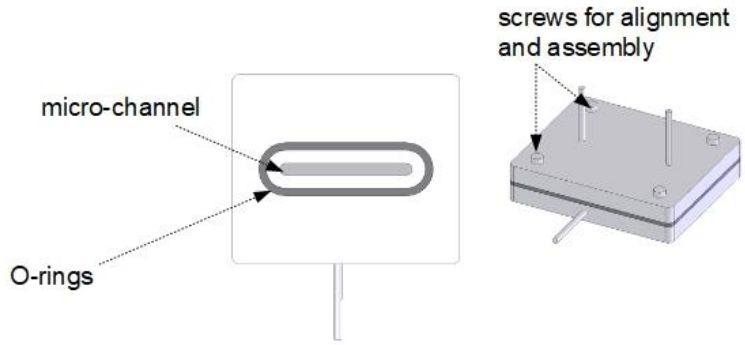

Figure 2: Basic configuration for a flat, horizontal microfluidic membrane filtration unit

4. Materials and fabrication

Contrary to many classical microfluidic chips that utilised PDMS polymer as materials for fabrication, in designing microfluidic membrane filtration unit, thermoplastics polymers are preferable. Thermoplastic polymers are not elastic neither permeable like PDMS polymers. In general, these types of polymers have good chemical and stress resistance as well as a combination of toughness, rigidity and creep resistance (Becker and Gärtner 2008). Examples of thermoplastic polymers include Polyether ether ketone (PEEK), Poly(methyl methacrylates) (PMMA), High-density polyethylene (HPE), etc. All thermoplastic polymers can be subjected to micro-milling and the resolution of the microfluidic structure is govern by the size of the cutting tools applied. Two- or three-dimensional (2D or 3D) microfluidics geometries can be easily realised through such micro-machining procedure. The final product from a micro milling fabrication step is almost a duplicate to the design of the unit produced using a 3D computer-aided-design (CAD) software e.g. SolidWorks™. Fabrication time per chip vary from chip to another depending on the complexity of the design. It is predicted that for a microfluidic membrane filtration unit with a simple configuration i.e. a 'clamp-and-play' chip design would take no longer than a couple of hours to fabricate using the micro-milling procedure (Christ et al. 2010).

Another viable option would be the use of 3D printing technology. 3D printing technology has the capacity to fabricate a complete 3D microfluidic structures in a single step literally from a computer model. Four most frequently used printing approaches include the inkjet (i3DP), stereolithography (SLA), two photon polymerisation (2PP) and extrusion printing (focusing on fused deposition modeling). 3D printing fabrication strategy could truly change the field of fabrication of microfluidic devices and its potential do not limited only for rapid prototyping of a single device but also feasible for mass production of microfluidic chips (Wardrip and Arnusch, 2016).

5. Fluidic connections and pumps

Another essential requirement of a microfluidic membrane filtration device is the establishment of a fluidic and electrical interface for the microfluidic chip. The fluidic and the electrical interconnects are both equally important to allow for easy interfacing with surrounding hardware such pumps, sensors and/or valves which usually required for operating the chip. Many underestimated the need for such interfacing solution, but it significantly contributed to the performance, operation consistency and the total cost of a microfluidic platform. Connecting the microfluidic chip to the outer world is not as straight forward as many would have thought especially considering that the chip may consisted of various fluidic, optical, electrical and/or mechanical components. These on-board features vary from one chip to another (Snakenborg et al., 2007). Since the propose microfluidic membrane filtration unit is likely to be fabricated out of thermoplastic polymers, they require fluidic interconnectors different than those typically used for PDMS chips. For simplicity and low cost, a rigid tube or stainless-steel ferrules can be directly connected into fluidic ports that have been machined on a chip interface. Such fluidic ports usually are linked directly to the internal fluidic structure of the microfluidic chip. As a rule of thumb, it is important to design the fluidic ports such that the inner diameter of the fluidic ports is at least one-tenth smaller than the outer diameter of the tube to ensure a tight connection. A certain minimum depth is also required for a steady connection and preventing the tube from disconnecting during an experiment. In order to further ensure a water-tight sealing, adhesives (glue or epoxy) can be carefully applied around the fluidic interconnects to close-up any gap or mismatch resulted from the micro milling step (Figure 3). Alternatively, one could opt for a commercial chromatography fitting (Zainal Alam et al., 2011). A threaded port can be fabricated on the microfluidic chip interface to fit these specialised connectors (Muller et al., 2005). Although these commercial fittings are relatively expensive and occupy a large area when mounted to the chip, it offers a plug ‘n’ play solution for the system. Such connections are also reversible, inert, have a low dead volume and leak-proof over a broad pressure range. To further emphasise on the plug ‘n’ play feature of the system, fluidic interconnects can be made on a chip holder rather than on the chip itself. This would allow one to optimise the design of the chip without the need to alter the fluidic interconnects.

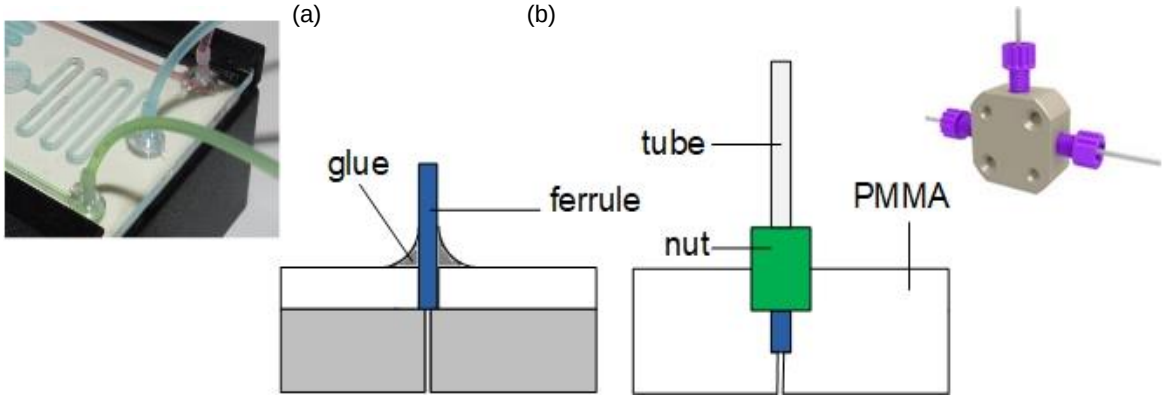

Figure 3: Typical fluidics interconnects to establish macro-to-micro fluidics interface for microfluidic membrane filtration unit (a) by gluing a tube or a metal ferrule into fluidic ports or (b) a standard tube-nut assembly

Pumps are very important components for a continuous microfluidic operation. In the context of micro membrane filtration unit, pumps are needed not only for the control of the feed flow rate and direction but also for recirculation of the retentate stream back into the feed line. It is also important to take note that in microfluidic membrane filtration unit, the necessary pressure for separation is created by the feeding pump. The feeding pump may be exploited as an actuator to regulate the system pressure. However, tuning of the feeding rate to meet the desired operating pressure is difficult as pressure might also increase due to accumulation of residues that are retained in the system during continuous operation. This type of accumulation is uncontrollable. A compact miniature size (30.0 x 12.0 x 14.0 mm, i.e. pump foot print as small

as human finger tips) peristaltic pumps are now commercially available at affordable price (e.g. Takasago fluidic system). These pumps are easy-to-use and can easily interface with a flat and horizontal membrane modular type system. There is no need to utilise bulky syringe pumps that are normally costly and not suitable to be applied as recirculation pumps for the membrane system.

6. On line measurement and process automation

In a microporous membrane system (micro- and ultrafiltration membranes), separation occurs under the influence of pressure where the pressure difference across the membrane is called the transmembrane pressure (TMP) (Zainal Alam et al., 2011). It is an important process parameter for such a membrane system and often used to characterise the membrane operation. Changes in the pressure within the system can of course be measured using a miniature light weight package pressure transducer. Such sensing device normally produces a voltage output signal ranging between 0 and 5 V. The voltage output signal of these miniature pressure sensors can be correlated to standard pressure readings (e.g. bar, Pa, psi, etc.), and often a linear relation is obtained. Measurement could be attained either as an absolute pressure or as relative pressure values. Miniaturised pressure transducers can be mounted on a T junction connector, or connected in line with any of the inlet/outlet streams (no dead volume) – depending on the type of sensor used. The flow rate of the feeding and the recirculation pumps applied for the membrane unit can also be controlled. For pumps driven by a small DC (or geared) motor, there are numbers of ways to control the speed of the motor of the pump. The easiest and the simplest method is to regulate the amount of voltage across the DC motor terminals by using the pulse width modulation (PWM) signal.

Similarly to other types of microfluidic devices, sampling is not possible due to the small working volumes of the device and monitoring of the kinetics of the process carried out in microfluidic platform often relies on online measurements. For microfluidic membrane filtration unit, this would not be the case. This is because the device has the capacity to filter out the components/products of interest continuously. Such ability allows for collection and/or fractionation of a clean samples that are free of contaminants/impurities. This opens up the possibility to perform various type off-line analysis or assays to monitor the progress of the separation process. Nevertheless, if one would prefer a fully automated microfluidic platform, the permeate stream can also be interfaced with another microfluidic chip (Fleger and Neyer, 2006) to enable on-line detection of the product concentration via optical probes. This approach offers the possibility to facilitate various types of on-line optical measurement systems such as ultra-violet (UV) absorption, Near-infrared (NIR) spectroscopy, Raman spectroscopy, etc. for measuring the product concentration (Ulber et al., 2003). Each of these measurement systems has its own merits and limitations and one must first carefully evaluate them before implementation. It requires a feasible signal processing in combination with the use of chemometric models to estimate the desired analyte concentrations.

Finally, with the establishment of the unit mechanics, fluidics and control, it is worth looking at the method on how to operate the entire system automatically. This is normally done using a customised software i.e. to create the computer interface for the operation of the microfluidic device and link it to a data acquisition (DAQ) device for input and output of signals. In this regard, there are two possible options. Firstly, is to use a commercial setup. The most commonly applied is the National Instruments (NI) DAQ device/card (National Instruments, Austin, TX). Program codes for measurement and control can be written in LabVIEW (National Instruments) software and implemented by interfacing the LabVIEW software with a suitable NI DAQ device. Secondly, is to establish a microcontroller platform (Husain et al., 2016). The latter is a more cost-effective solution especially considering microfluidic membrane filtration unit only requires few analogs in- and output ports for process automation (mainly for pressure transducer and pumps). The easiest way to accomplish this is to utilise an Arduino board. Arduino board is relatively easy to program, and it runs on an advantageous open-source platform. With the ATMEL microcontroller running as its core, it has all the digital I/Os with pulse-width-modulation (PWM) outputs that are necessary for acquisition and control purposes. A fully automated system is handy as it offers the possibility to obtain a real-time data (which can be saved for further analysis) automatically without or with very minimal intervention from human operator.

7. Conclusions

General methodology for the establishment of microfluidic membrane filtration unit is discussed. Focus was on the fabrication of a flat, horizontal microfluidic membrane modular type where overview has been given on the device mechanics (size, operating mode, membrane integration, and materials), fluidics (fluidic interconnect and pumps) and process control. Whilst development of each of the individual chip components is important for the construction of the device, the real challenge lies in combining all these components together in order to obtain a complete workable microfluidic membrane filtration system. Due to technical differences as well as the need to integrate them on a very small footprint (i.e. working volume < 1 mL), these individual components

may not easily fit together, and a compromise might be necessary to resolve the mismatch. Even though the microfluidic filtration devices are simple in working principle and rather straight forward to fabricate, such devices have yet to be widely used in industry or academia. This is probably due to system limitations and maybe lack of scale-up studies to compare the performance of such micro scale filtration unit with a lab scale unit.

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References

Becker H., Gärtner C., 2008, Polymer microfabrication technologies for microfluidic systems, Analytical and Bioanalytical Chemistry, 390, 89-111.

Christ K.V., Smith B.B., Pfefferkorn F.E., Turner K.T., 2010, Micro end milling polystyrene for microfluidic applications, 5th International Conference on Micro Manufacturing ICOMM, 5th-8th April, Wisconsin, United States, 423-430.

De Jong J., Lammertink G.H., Wessling M., 2006, Membranes and microfluidics: A review, Lab on a Chip, 6, 1125-1139

Di H., Martin G.J.O., Dunstan D.E., 2017, A microfluidic system for studying particle deposition during ultrafiltration, Journal of Membrane Science, 532, 68-75.

Fleger M., Neyer A., 2006, PDMS microfluidic chip with integrated waveguides for optical detection, Microelectronic Engineering, 83, 1291-1293.

Husain A.R., Hadad Y., Alam M.N.H.Z., 2016, Development of low-cost microcontroller-based interface for data acquisition and control of microbioreactor operation, Journal of Laboratory Automation, 21, 660-670.

Pinelo M., Jonsson G., Meyer A.S., 2009, Membrane technology for purification of enzymatically produced oligosaccharides: Molecular and operational features affecting performance, Separation and Purification Technology, 70, 1-11.

Sarghini F., Davalos-Saucedo A.A., Rossi-Marquez G., Romano A., Di Pierro P., 2015, Production of Protein/Pectin complexes using a microfluidic device, Chemical Engineering Transactions, 43, 85-90.

Schäpper D., Zainal Alam M.N.H., Szita N., Lantz A.E., Gernaey K.V., 2009, Application of microbioreactors in fermentation process development: A review, Analytical and Bioanalytical Chemistry, 395, 679-695.

Snakenborg D., Perozziello G., Geschke O., Kutter J.P., 2007, A fast and reliable way to establish fluidic connections to planar microchips, Micromechanics and Microengineering, 17, 98-103.

Streets A.M., Huang Y., 2013, Chip in a lab: Microfluidics for next generation life science research, Biomicrofluidic, 7, 11302.

Taparia N., Platten K.C., Anderson K.B., Sniadecki N.J., 2017, A microfluidic approach for hemoglobin detection in whole blood, AIP Advances, 7, 105102.

Ulber R., Frerichs J.G., Beutel S., 2003, Optical sensor systems for bioprocess monitoring, Analytical and Bioanalytical Chemistry, 376, 342-348.

Wardrip, N.C. and Arnusch, C.J., 2016, Three-dimensionally printed microfluidic cross-flow system for ultrafiltration/nanofiltration membrane performance testing, Journal of Visualised Experiments, 108, 53556.

Whitesides G.M., 2006, The origins and the future of microfluidics, Nature, 442, 368-373.

Zainal Alam M.N.H., Pinelo M., Samantha K., Jonsson G., Meyer A.M., Gernaey K.V., 2010, A continuous membrane microbioreactor system for integrated pectin modification and separation processes, Chemical Engineering Journal, 167, 418-426.