Magnetic connectors for microfluidic applications†

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We present a new type of microfluidic connector that employs a ring magnet on one side of the microfluidic chip and a disc magnet on the other side to produce a sealed connection between external tubing and inlets or outlets of microfluidic devices. The connectors are low-cost, simple to use and assemble, and reusable. We used numerical (finite element) simulations in order to optimize their geometry. Configurations that achieve interfacial forces in the range of 2 N to 15 N are discussed. Several types of gasket materials were explored. Finally, we demonstrate an application of these connectors in a microfluidic device used to generate liposomes.

Introduction

Many companies offer microfluidic products,[1] microfluidic prototyping[2] and microfluidic connectors.[3] However, techniques for world-to-chip interfacing (*i.e.* syringes, vials, wells) remain active areas of research and development[4] due to the lack of a simple way to produce low-cost, reliable, simple-to-use and reversible connections.

For elastomeric chips (*e.g.* PDMS), we have recently demonstrated a vacuum manifold that allows the connection of a device to multiple lines in a fast (minutes) and non permanent way.[5] For microfluidic chips fabricated in hard substrates (*e.g.*, glass), Kortamann *et al.*[6] recently introduced a new type of press-fit connector that incorporate springs to produce the mounting force with leak-free operation. In this approach, each connector is pressed independently against a back plate to ensure proper sealing of multiple connectors. The press-fit connectors have some important advantages such as reliability, reusability and fast assembly. However, some drawbacks are (i) high cost, (ii) high complexity (each connector requires a large number of parts) and (iii) the platform and the connectors must be mounted on a fixed geometry with limited flexibility.

Here we introduce a new type of connector for hard substrates (*e.g.* glass, silicon, and plastic) that is simple to fabricate, easy to assemble, low-cost and reusable. Our concept utilizes two magnets, one on top of the chip and modified with a gasket and the other under the chip, to seal the tubing against inlets/outlets of the microfluidic device. As a simple guide to design the connectors, we characterize the maximum operating pressures without fluid leakage and simulate the force between two magnets with different geometries that are commercially available. Finally, we demonstrate the generation of liposomes with a microfluidic chip that incorporates these magnetic connectors.

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† Electronic supplementary information (ESI) available: Materials; placing the connectors; simulations of magnetic force; plastic aligner for multiple connections; leakage tests; liposome formation; video. See DOI: 10.1039/b913331c

Experimental[7]

Fabrication

Multiple material systems were investigated to characterize the seal between the chip and the magnet as described below (for additional details see ESI†).

Connector A. The connector consists of a NdFeB ring magnet (Amazing Magnets, # TJ250B), a blunt needle (Small Parts) and double-sided polyimide tape with silicone adhesive (Argon Inc., #PC500–1000) as the sealing gasket (see Fig. 1). The blunt needle was inserted and sealed in the hole of the magnet with epoxy. The liner on one side of the tape was removed and the tape was

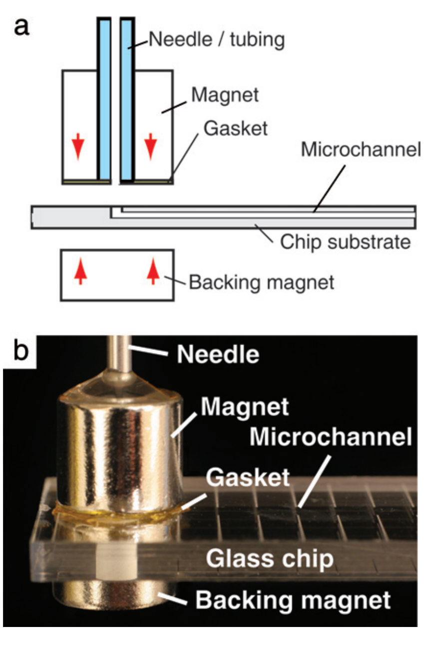

Fig. 1 Magnetic connector. The connector is made of a ring magnet with a hole that accommodates tubing or a needle. The tubing/needle is fixed to the magnet with epoxy. A gasket is attached to the bottom side of the magnet to facilitate sealing. A second magnet is placed on the back side of the microfluidic chip and provides the interfacial force to prevent leakage.

pressed manually against the bottom side of the magnet. Then the second liner was peeled off, and a hole was punched in the center of the tape with a 25-gauge needle. A razor was used to cut the excess tape around the magnet. Two stacked magnets (KJ magnetics, part D-42-N52, combined height of 6.4 mm) served as the backing magnets.

Connector B. The fabrication steps were the same as for the previous connector, except that double-sided polyester tape with acrylic adhesive 300™ (3M, #444) was used as sealing gasket. Two stacked magnets were used as backing magnets.

Connectors C and D. The fabrication steps were the same as for Connector A, with the sole difference that in addition to the polyimide tape a thin layer of PDMS was used as a sealing gasket. Briefly, a thin layer (90 μm for connector C and 200 μm for connector D) of PDMS was created by spinning PDMS on a glass slide previously silanized to produce a fluorinated surface. A magnetic connector type-A was pressed against the PDMS layer, and then the connector with the PDMS layer was cut away from the silanized glass with a razor. Two stacked magnets were used as backing magnets.

Connector E. O-rings (McMaster Carr, #9452K11) with 1.4 mm inner diameter (ID) and 4.4 mm outer diameter (OD) were used as sealing gasket. To seat the O-ring on one side of the NdFeB ring magnet (KJ magnetics, part R412), an annular groove was machined with a ball-end mill using a programmable milling machine, see ESI.† The magnet filings were cleaned from the magnet using adhesive tape. A second magnet of the same type was stacked on top of the first one to increase the total magnetic force in the assembled device and match the total height (6.4 mm) of the magnets used on connectors A, B, C and D. One terminus of clear flexible tubing (Tygon S-54-HL, 0.5 mm ID, 1.5 mm OD) was inserted through the magnet's central hole until flush with the bottom contact surface of the magnet and glued at the top of the magnet. Two stacked magnets were used as backing magnets.

Results and discussion

As proof of concept, a connector type A was fabricated and aligned above an inlet of a glass microdevice. A backing magnet was placed on the other side, see Fig. 1. The entire system was connected within seconds, see ESI.† Although, qualitatively, a backing magnet with a disc-shape provided stronger force, we found it useful to use ring-shape backing magnets, as they allow monitoring of fluid injection at the inlet after the connection has been established.

Characterization of single magnetic connectors

We first show how several configurations of magnets produce different forces based on FEM simulations. The results of the simulations and the discussion are aimed to provide a simple way to select the appropriate magnets for a given application. Sealing not only depends on the force exerted but also on the type of gasket employed. Thus, we experimentally characterized the sealing of a given magnetic connector with several different gasket materials (below).

In the simulations (for details, see ESI†), we considered the distance between magnets (s), the width (w) and height (h) of the magnets, hole size (b) and magnet grade, *e.g.* N43 (see Fig. 2a).

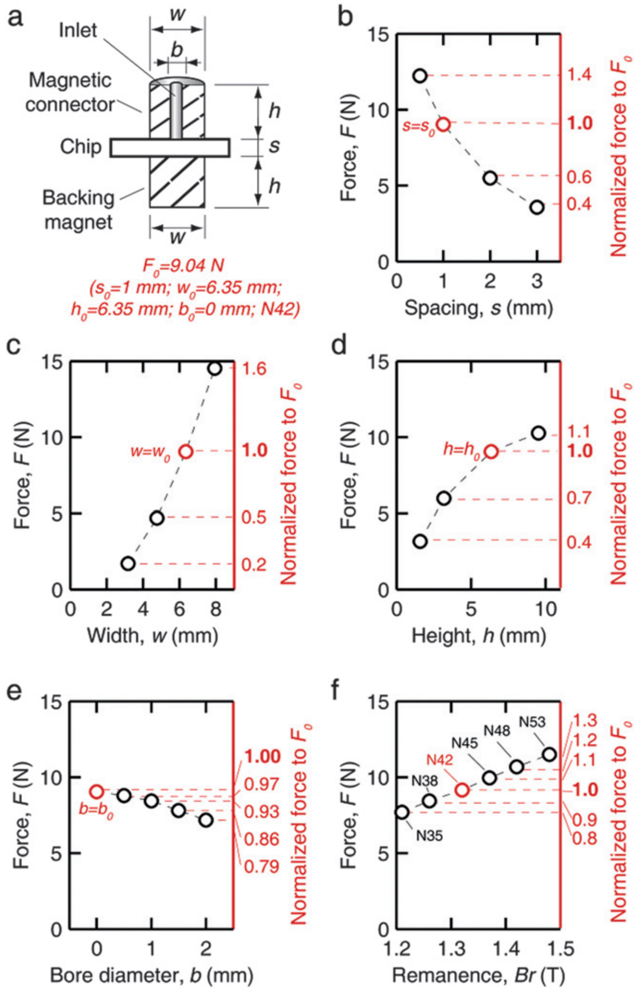

Fig. 2 Force between two magnets. (a) For simplification, we considered the case where the magnet used in the connector and the backing magnet have the same width, w, height, h, and grade. The other parameters analyzed were bore diameter, b, and spacing between magnets, s. To independently analyze the influence of each parameter on the magnetic force, an initial configuration was first simulated ($s_0 = 1$ mm, $w_0 = 6.35$ mm (1/4″), $h_0 = 6.35$ mm (1/4″), $b_0 = 0$, grade N42) and subsequently the parameters were varied one at a time. All of the results were normalized to the force between magnets with the initial configuration ($F_0 = 9.04$ N). (b) Magnetic force as a function of the distance between magnets. The distances considered were chosen to reflect the most commonly used configurations in microfluidic applications, and were 0.5 mm, 1 mm, 2 mm and 3 mm. (c) Magnetic force as a function of the width of the magnets. The widths were chosen to match those of commercially available magnets, and were 3.18 mm (1/8″), 4.76 mm (3/16″), 6.35 mm (1/4″) and 7.94 mm (5/16″). (d) Magnetic force as a function of the magnets height. The heights used for the simulations were 1.59 mm (1/16″), 3.18 mm (1/8″), 4.76 mm (3/16″), 6.35 mm (1/4″) and 9.53 mm (3/8″). (e) Magnetic force as function of hole size. The initial configuration used disc magnets without a hole. (f) Magnetic force as a function of the magnets' grade.

The initial simulated configuration was $s_0 = 1$ mm, $w_0 = 6.35$ mm, $h_0 = 6.35$ mm, $b_0 = 0$ and grading N42. The rest of the simulations were based on the initial one, with only one parameter modified at a time. According to the simulations, the attractive force between magnets for the initial configuration was $F_0 = 9.04$ N

Force *vs.* distance between magnets (*s*). The distance between magnets is typically dictated by the thickness of the microfluidic chip. Fig. 2b shows a strong dependence of magnetic force with the spacing between magnets; *e.g.*, reducing the substrate thickness from 1 mm to 0.5 mm results in an increase of the magnetic force by 40%.

Force *vs.* width of magnets (*w*). If the effects at the edges of the magnets are neglected, the magnetic force is proportional to the area of the magnet[8] (Fig. 2c). While increasing the width of the magnets results in a substantial increase of magnetic force, it also increases the footprint of each connector which may be a constraint in small chips with many inlets and outlets.

Force *vs.* height of magnets (*h*). The results shown in Fig. 2d show a strong influence of the magnet height on the magnetic force for small magnets. However, as the magnet height increases, the path for the magnetic lines to return around the edges also increases, resulting in a weaker correlation with magnetic force. Using a ferromagnetic cap around the magnet should decrease the air gap and notably increase the force between magnets, especially in the case of tall magnets, although the cap may also increase the footprint of the connector.

Force *vs.* bore diameter (*b*). The initial configuration was for bore diameter $b = 0$ mm, *i.e.* the magnet does not have a hole. Interestingly, the results in Fig. 2e show that having a hole in the magnet has a relatively small effect (<21%) on the attractive force for the five simulated hole sizes: 0 mm, 0.5 mm, 1 mm, 1.5 mm and 2 mm.

In most microfluidic applications, dead volume is a concern and needs to be minimized. According to the results, choosing a small hole not only reduces dead volume but also results in a slightly higher magnetic force. For NdFeB magnets the minimum size hole (~1 mm) is limited by the fabrication process. SmCo magnets do not have this constraint, although they display less energy density resulting in lower forces for the same size and geometry (~20% less[9]).

Force *vs.* magnetic grade. Magnets are commercially available under different grades denoted by Nxx, with xx a number that is associated with the remanent magnetic induction *Br*. While the most common grading for magnets is N43, better grades are also available at slightly higher price and produce stronger forces, see Fig. 2f. Additionally, the influence of temperature on the magnetic force depends primarily on the grade of the magnet. This information is usually available from the magnet manufacturer.

Leakage pressure. The total force between magnets is not the sole determinant of the maximum pressure the connectors can withstand before leaking. Though the force serves as a reference, leakage also depends on the type of gasket between magnetic connector and the chip substrate (*e.g.* glass or silicon). Therefore, we experimentally characterized different types of gaskets for sealing. We tested two types of double-sided adhesives, a PDMS gasket, and a commercially available O-ring.

Fig. 3 shows the results of rupture pressure tests for the different types of gaskets, see ESI.† Polyimide tape withstood higher pressures than both PDMS and O-ring gaskets ($p < 0.05$ using One-way ANOVA with Tukey Test). These experiments were performed with air and water solutions.

A commercially available O-ring withstood less pressure than polyimide tape (see Fig. 3). However, O-rings have the advantage that they do not contain adhesives that could degrade in the presence of organic solvents. With the magnets we used, the simulated force is even greater (12 N), so an optimized fabrication process could increase the upper operating pressure for magnetic connectors.[10]

Multiple connections. When different magnetic connectors are placed in close proximity they may interact and collapse together. To facilitate handling of multiple closely-spaced magnetic connectors, we developed a plastic aligner, see Fig. S1, that allows the magnets to slide vertically but not horizontally. Alternatively, a single magnet could be fabricated with multiple holes (which would need to be done by the vendor), thus requiring only one connector for multiple inlets and outlets.

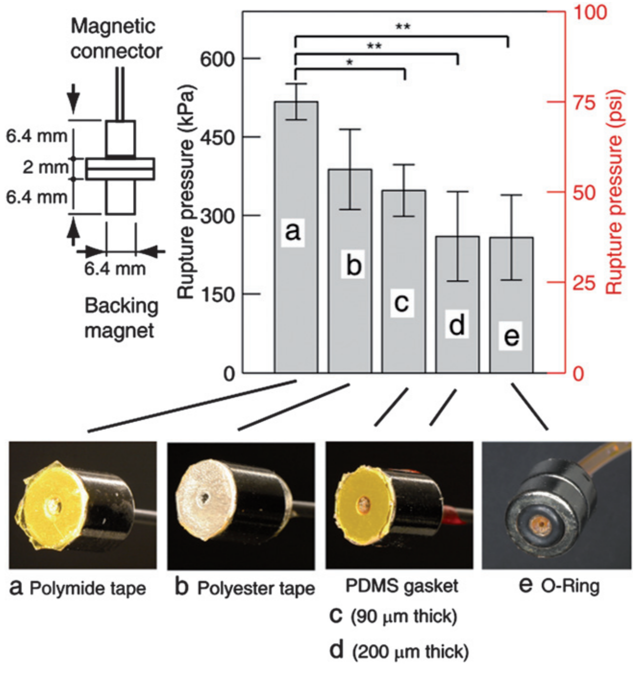

Fig. 3 Leakage experiments. Sealing depends on the magnetic force between magnets and on the material of the sealing gasket. The graph shows the results of testing the rupture pressure at which the connectors start leaking. The experiments were performed by immersing the connectors and glass wafer in a tank with water and pressurizing air through the inlet. Leakage was determined by visual inspection (bubble formation). Although the results show that the optimal performance was achieved with the polyimide tape, the O-ring configuration is best for applications requiring solvents because it does not contain adhesives susceptible to degradation. ** and * indicate that the means are significantly different with $p < 0.01$ and $p < 0.05$, respectively.

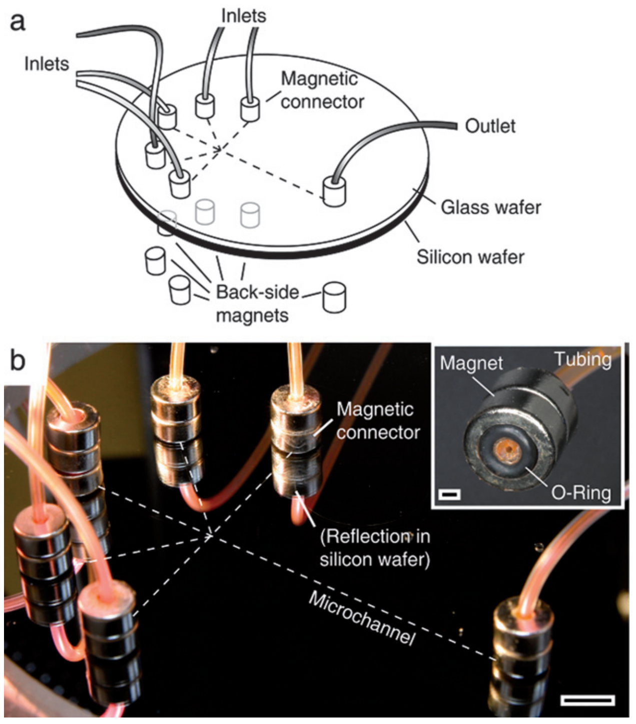

Fig. 4 Generation of liposomes in a chip using magnetic connectors. The chip has five inlets and one outlet, with all inlets connected to syringe pumps *via* tubing and magnetic connectors. The inset in (b) shows the bottom contact surface of a single connector: the first magnet has a machined semi-circular annular groove where an O-ring is placed (not glued). When the connector is placed on top of the chip, it aligns to a magnet on the other side of the wafer. The magnetic force seals the O-ring to the wafer, which prevents buffer and IPA (isopropyl alcohol) from leaking. Scale bar 5 mm.

Application: Liposomes generation

We demonstrate the generation of liposomes on a microfluidic chip connected to external fluid reservoirs *via* tubing and O-rings magnetic connectors (see Fig. 4 and Fig. S2†). This application was chosen to demonstrate the magnetic connectors' applicability for aqueous and organic solvents.

Liposomes have attracted extensive interest as vehicles for delivering drugs[11] or imaging agents to particular regions in the body, such as cancer tissues.[12] To synthesize liposomes in a microfluidic device, an isopropyl alcohol (IPA) stream containing lipids is focused to a very narrow stream by buffer streams on both sides, as shown in Fig. S2c†. Lipids self-assemble into liposomes as the buffer and IPA streams mix due to convection and diffusion that occurs in a controlled and reproducible manner. It was shown previously that the liposome size distribution can be controlled by the flow rate ratios of buffer to IPA.[13] Similar results were also obtained using magnetic connectors, as shown in Fig. S2d. The connectors were removed and reseated many times with both buffer and 100% IPA without any visible leakage, and O-rings could be easily replaced when needed. The results shown in Fig. S2 demonstrate that the magnetic connectors can be used for microfluidic liposome formation, which uses high flow rates.

Conclusions

We have introduced a new type of connector that makes fluidic connections to microfluidic chips simple, fast and reusable. The connectors are suitable for most applications except for applications using ferrofluids, superparamagnetic particles, or magnetically labeled cells, or for high temperature applications (>80 °C).

The magnetic connectors are ideal for rapid prototyping in research environments where flexibility and versatility are important. Some challenges need to be considered if these connectors are to be used as parts of commercially available microfluidic chips, such as proper confinement of magnetic interactions between connectors and external apparatus and tools.

Acknowledgements

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