A simple pneumatic setup for driving microfluidics

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We present a simple pneumatic setup for easy and precise control of pairs of inlet flows for lab on a chip applications.

Moving fluids in microchannels is at the heart of microfluidic applications. Apart from capillary effects, there are currently three main techniques that are used to generate liquid flow in microchannels: electro-osmotic flow (EOF), pressure-driven flow and flow induced by volume displacement.1–3 EOF has the great advantage of a flat velocity profile across the channel, and is thus often used in microchip-based chromatography or electrophoresis.4 However, EOF requires the presence of electrodes and strongly depends on the composition of the liquid to be moved and on the surface properties. Pressure-driven flow, on the other hand, does not require electrodes and is less dependent on the composition of the liquid.5 In its simplest configuration, gravity is used to provide the pressure, but most of the time, more flexible control of the fluids is needed. Syringe pumps and other mechanical pumps, belonging to the third category, are often used to provide the necessary control of the displaced volume. However, due to the very low-volume displacements required for microchip operation, precision becomes critical, making suitable syringe pumps very expensive because of the required precision mechanics. Even with these, flows are often found not to be sufficiently smooth for critical applications. An alternative is to use pneumatic pressure acting on liquid reservoirs located directly above the chip to control the liquid flow. Füterer et al. presented a sophisticated pressure control system for microchannels,6 with computer control. In this communication, we present a simple low-tech setup that enables the application of finely controlled pressures to liquids in reservoirs residing directly above the chip. This makes pressure-driven flows accessible to a larger community of laboratories using microfluidics. Moreover, the samples can be directly pipetted into the reservoirs above the chip, making fluid-handling simple and eliminating all dead volume associated with tubing.

The measurement setup consists of a chip holder with integrated reservoirs, and a pneumatic pressure setup used to pressurize the air above the liquids in the different reservoirs and therefore the liquids themselves (Fig. 1). The pneumatic setup is a manually controlled pneumatic-pressure supply made of HPLC tubing and pneumatic regulator valves. Its design is based on the analogy between electrical and pneumatic circuits, i.e. that Ohm’s law is valid in sufficiently narrow tubing due to laminar flow conditions. The pressure setup therefore acts as a resistive pneumatic pressure divider circuit, where tubing represents fixed-value resistances, while the regulator buttons represent variable resistances. Via air-filled tubing, the air space above the liquid in the reservoirs in the chip holder is connected to given outlets of the pressure setup. As the air space above the liquid is sealed with scotch tape, there is no escape for the air and the pressure is transmitted to the liquid. With this arrangement, liquid flow in the tubing is completely avoided, while finely controlled pneumatic pressure is directly applied to the liquid in the reservoirs, pushing it through the microchip.

One of the reasons for using a resistive pneumatic network rather than the output of a given number of pressure controllers is that the design of the network can allow for more complex functions, which otherwise would only be accessible by precise real-time computer control of the pressure controllers.6 For example, it is not practical to manually change the ratio of two inlet flows while maintaining a constant total flow.

In this communication, we detail the design of a pressure setup where turning one single button changes two pressures simultaneously (one up and one down) while the sum remains constant. This setup is generally useful when flows from two inlets need to be combined in an arbitrary ratio, but with a constant downstream flow. More specifically, two applications of the setup are switching between two flows while keeping total flow constant, and shifting the position of a hydrodynamically focused stream without changing either the flow speed or the width of the focused flow in the channel. We also use the setup for the creation of gels,7 since this requires a stable interface of two liquids.

The elementary circuit, as shown in Fig. 2A, is a resistive pressure divider consisting of two equal fixed resistances and a single variable resistance. It fulfills the basic requirement of producing two pressures, $P_1$ and $P_2$, the sum of which is constant.

Fig. 1 An example of a chip holder for microfluidic devices: the microfluidic chip is held by a plastic chip support and assembled with a PDMS cover. A fluidic interface block (PMMA) with reservoirs is mounted on top and connects the reservoirs to the pneumatic setup. The PDMS part can also be used with closed chips; alternatively, it can be replaced with O-rings. After pipetting the liquids, the reservoirs are closed with a tape in order to enable pressure build-up. The device can be observed with an inverted microscope.
and equal to the input pressure $P_0$. Indeed, the value of the variable resistance $R_v$ influences both $P_1$ and $P_2$, but the changes are opposite and equal in magnitude. In detail, $P_1$ and $P_2$ can be expressed as follows:

$$P_1 = P_0 \frac{R_s + R}{R_s + 2R}$$  \hspace{1cm} (1)$$

$$P_2 = P_0 \frac{R}{R_s + 2R}$$ \hspace{1cm} (2)$$

$$P_1 + P_2 = P_0 \frac{R_s + R}{R_s + 2R} + P_0 \frac{R}{R_s + 2R} = P_0$$  \hspace{1cm} (3)$$

$P_1$ and $P_2$ are dependent on the ratio between the fixed resistance $R$ and $R_s$, so in order to obtain a setup that can be finely regulated, $R$ and $R_s$ should be of the same order of magnitude. Moreover, when the flow-regulator button is in the fully open position, $R_s$ should be negligible compared to $R$, because otherwise $P_1$ and $P_2$ can never be equal. An implementation of this elementary circuit is shown in Fig. 2B.

The fixed resistances are made from hard plastic tubing in order to avoid changes in diameter with changes in pressure. The variable resistance is the flow-regulator button and the electrical symbol for ground simply corresponds to an open end of tubing. The exact choice of tubing dimensions and of regulator valve is not important, provided a few precautions are respected. We generally use HPLC tubing with a diameter on the order of 500 μm or less, because pressure drops of a maximum of 100 mbar through a typical total length of 10 cm of such tubing in air will still produce laminar-flow conditions, ensuring that the pressures produced are stable in time. Our current setup is as follows: The two fixed resistances $R$ are equal, and consist of ca.10 cm of polycarbonate HPLC tubing, while the variable resistance $R_v$ is a flow-regulator valve obtained from SERTO (model 462) (Aadorf, Switzerland). The connectors between these elements should have a sensibly larger diameter, in order to avoid additional pneumatic resistance. We use 4 mm inner-diameter tubing and plastic Luer fittings (World Precision Instruments, Inc., Florida, USA), and short soft plastic tubing for the connections between tubings of different diameters. Bifurcations are made by SERTO’s connection elements for the larger size tubing. Care should be taken not to put anything near the open ends, because this causes slight changes in tube resistance as the obstacle changes the gas-flow pattern. Moreover, open ends should be fixed mechanically, otherwise they may vibrate due to the gas flow, again inducing unwanted pressure variations. Once constructed, the pressure setup can be fine-tuned by measuring the pressures $P_1$ and $P_2$ with water columns or other pressure-measurement devices, and by adjusting the length of the HPLC tubing accordingly, using a scalpel. Fine-tuning is necessary for precision applications such as producing alginate gel layers in microchips.

To drive microchips with more than two inlets, a more complex pressure setup is necessary. However, as long as adjusting the ratio between two flows without altering total downstream flow is required, the elementary circuit outlined above will be part of the pneumatic network. We used two constant sum elements, each one preceded by a pressure divider for adjusting $P_0$, as shown in Fig. 3.

![Fig. 2 Model of the elementary features of the pressure setup in an equivalent electrical circuit. The elementary circuit is a resistive pressure divider consisting of two equal fixed resistances and a single variable resistance. The fixed resistances and the adjustable resistances are implemented by tubes and pneumatic regulators, respectively. Grounding is achieved by an open tube which experiences atmospheric pressure.](image1)

![Fig. 3 Model of the entire pressure setup in an equivalent electrical network, together with an example of a microfluidic chip. $P_1$ and $P_2$ correspond to the pressure in chip inlets 1 and 2. $P_1'$ and $P_2'$ correspond to the pressure in chip inlets 3 and 4. The pressure setup fulfills the basic requirement of producing two pressures $P_1$ and $P_2$, the sum of which is constant and equal to the input pressure $P_0$ (same for $P_1'$ and $P_2'$). For each pair of chip inlets, the sum of the two inlet pressures remains constant. This permits switching between the flows coming from one inlet pair without affecting the flows from the other inlet pair. A commuter S was added to each pair of chip inlets in order to select which pressure is the highest.](image2)
The pneumatic setup provides pressures for each pair of inlets where the sum of the two-inlet pressure remains constant. This permits switching between the flows coming from one inlet pair while leaving the flows from the other inlet pair unchanged. Another characteristic of the pneumatic setup is that by changing the main pressure, the pressures on all four inlets change simultaneously while their ratios remain constant. This allows for simultaneous adjustment of all four flow speeds without changing their proportion and thus the flow pattern in the chip. Moreover, at our institute, we obtain pressurized air at a pressure of 6 bar from the pressure-supply system, while we need only a maximum of 100 mbar, or more frequently 10 mbar, at the entry of the pneumatic network. We therefore used two sequential pressure reducers, the first reducing the pressure to 2 bar, while the second is a fine pressure regulator with an integrated manometer for producing pressures of up to 250 mbar (Bellofram Corp., Newell, WV). As can be seen from eqn (1) and (2), \( P_1 \) is equal to or greater than \( P_2 \) for all values of \( R_2 \). However, for switching between liquids, it should be possible to choose which pressure is the highest. We therefore added a commuter (Upchurch Scientific, Oak Harbor, WA) to each pair of outlets of the pressure setup.

Finally, we illustrate the capabilities of the setup presented above with a few micrographs (Fig. 4 and 5). The pictures in Fig. 4 are taken from the chip used to produce alginate gels (see Fig. 3), with a total of four inlets and two outlets.

The four inlets form two pairs that can be used to select one of two liquids or any ratio of the two. We show switching and adjusting of the flow ratio between the two liquids of the upper pair, while a constant flow from the lower pair is maintained despite the switching in the upper pair. The response time of the flow rates is well below the time it takes to turn the knob, making the response immediate.

Fig. 5 shows hydrodynamic focusing towards variable positions in the main channel. This chip has three inlets; the two sheath-flow inlets are connected to the constant total pressure element, while the main stream is kept at constant pressure by a separate regulator. The hydrodynamically focused flow is shifted upwards or downwards without changing the total flow speed or the ratio between sheath flow and main flow.

The pressure setup presented here is an easy but very precise way of controlling pairs of pressures in a differential fashion, i.e. increasing one pressure while decreasing the other by an identical amount. Moreover, the material used to build the pressure setup is standard and relatively inexpensive, certainly in comparison to syringe pumps, and can therefore be used in any kind of laboratory using microfluidics. As an outlook, it is also possible to control \( n \) inlets converging into a single common channel in a similar way. Passing from 2 to \( n \) inlets makes the setup slightly more complicated, but also substantially more powerful (to be published).

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