CONTROLLING THE FLOW RATE OF MANY FLUIDS WITH FLOATING VIALS IN A PRESSURIZEABLE CONTAINER

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ABSTRACT

We report a simple strategy to control the pressure-driven flow rates from fluid reservoirs to a microchip in an efficient and compact fashion. We demonstrate that using a floating reservoir, less than 1 percent change in flow rate per ml of delivered volume can be achieved with gravity-driven flow, which is more than 20-fold improvement over a non-floating reservoir. Using this principle, we fabricated a 19-reservoir system to supply fluids to a multi-inlet microfluidic device.

KEYWORDS: fluid reservoirs, high throughput, interfacing, connectivity

INTRODUCTION

Microfluidic devices are increasingly being utilized for complex chemical and biological applications, which can require connecting many different reagents, solvents, or buffers to a device.[1-3] Current methods to deliver fluids to microdevices are in many cases not suitable for controlling large numbers of fluids or for maintaining constant flow rates over large delivered volumes. For example, syringe pumps are expensive, bulky, and prone to oscillations at low flow rates;[4] integrated reservoirs[5] have limited volume, must be incorporated into every device, and experience changes in flow rate as reservoirs drain; and horizontal reservoirs[6] have limited fluid capacity and flow rates.

THEORY

An object floating in a fluid, such as a vial floating in a container (**Fig. 1a**), will float at a level such that the weight of the vial plus the liquid is equal to the weight of the fluid displaced by the vial and liquid.[7] The balance of forces in the system can be expressed as $\rho_w V_w g = \rho_v V_v g + \rho_f V_f g,$ where, ρ_w, ρ_v, and ρ_f represent the densities of water in the container, the vial, and the fluid in the vial, respectively. V_w, V_v, and V_f represent the volume of water in the container that is displaced by the vial, the volume of the round-bottom vial, and the volume of fluid in the vial, respectively, and g is the acceleration due to gravity. Since the mass of the vial, $m_v = \rho_v V_v$, the equation reduces to $\rho_w V_w = m_v + \rho_f V_f$. V_f and V_w, are calculated, respectively, from $V_f = \pi h_f r_i^2 + \frac{2}{3}\pi r_i^3$, and $V_w = \pi(h_f + h_d)(r_o^2 - r_i^2) + \frac{2}{3}\pi(r_o^3 - r_i^3)$. Solving for the drop in fluid height, h_d, as a function of the fluid height, h_f, yields

$$h_d = \frac{m_v + \pi\rho_v\left(h_f r_i^2 + \frac{2}{3}r_i^3\right) - \pi\rho_w\left(h_f r_o^2 + \frac{2}{3}r_o^3\right)}{\pi\rho_w r_o^2} \quad (1).$$

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EXPERIMENTAL

A sealable container (Savillex Corp) was modified to hold multiple floating reservoirs. Polystyrene (4.01 g, Dow Corning) and polyallomer (2.05 g, Becton Dickinson) vials were used for the reservoirs. Vial mass was reduced by sanding. A multi-vial holder was made from poly(methylmethacrylate) (PMMA) to fit in the container. Holes matching the vial positions were drilled and tapped in the container lid to insert polypropylene (PP) end fittings, PP caps (Cole Parmer #R-06471 and #ZW-06471), and 16 gauge x101.6 mm needles (Popper and Sons, Inc.). O-rings inserted between the end fittings and caps sealed around the needles. Holes for a pressurization inlet and pressure gauge were also made in the lid. Vials filled within a few mm of their tops were loaded into the container, which was then filled with water to float the vials. The lid was aligned to have needles over the appopriate reservoirs and screwed down to seal the container. Male luer hubs with were used to connect the needles in the container lid to 0.635 mm inner diameter microbore tubing. Flow rates were determined by measuring the mass of water exiting the outlet over time. Flow rates were normalized to the initial rate, plotted against the volume delivered, and fit to determine the stability of the flow as a function of the vial mass. Poly(dimethylsiloxane) PDMS (Dow Corning) devices and PMMA vacuum manifolds were made as previously reported.[2,3]

RESULTS AND DISCUSSION

We have fabricated a fluid delivery system that holds a large number of floating reservoirs in a pressurizeable container**.** This system was developed to solve the problem of how to deliver stable flow rates in the µl/ml range from many fluid reservoirs simultaneously. The performance of the reservoir system was tested by measuring fluid delivery from a single vial in the configuration shown in **Fig. 1a**. Normalized flow rates and absolute changes in flow rate as a function of the delivered volume are shown in **Fig. 1b** and **Fig. 1c,** respectively**.** We found that floating the vials inside the container considerably reduced changes in hydrostatic pressure as the reservoir drained, which greatly improved the stability of the flow rate over large delivered volumes. For example, flow rate from an 13 ml floating vial (0.82 g) dropped only 0.7 % per ml of delivered fluid compared to a 14 % change per ml from a non-floating vial (**Fig. 1c**).

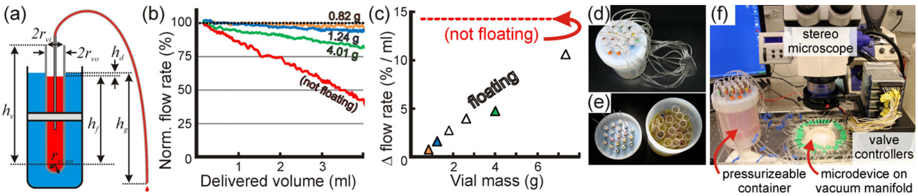

Fig. 1 ***(a)*** *Diagram of a fluid reservoir (vial) floating in a water-filled container.* ***(b)*** *Normalized flow rate as a function of delivered volume for vials with different mass.* ***(c)*** *The absolute rate of change of the flow rate, a linear fit to curves in (b), is plotted as a function of vial mass for floating and non-floating systems. Colored triangles and dotted red line (not floating) represent data from (b). Photo of the container* ***(d)*** *attached to a microfluidic device and* ***(e)*** *with the lid open.* ***(f)*** *Photo showing the container delivering fluid to a microfluidic device through a vacuum manifold.*[3]

Fluid levels dropped with respect to the container as fluid was taken from the vial, according to **Eq. 1**. Vials with different masses also behaved according to **Eq. 1**, as demonstrated by data in **Fig. 1b, c**. Because the container can be sealed and pressurized, additional control over the flow rates can be achieved. External pressure reduces the impact that hydrostatic pressure has on the total driving pressure. Thus, the flow rate becomes less dependent on the hydrostatic pressure (*e.g.* changes in h_d) as the vial drains.

We fabricated a 19-reservoir container to demonstrate flow rate stability for a system with a large number of inlets (**Fig. 1d, e**). Replicate measurements from different reservoirs had a mean flow rate of 30.2 μl/min and standard deviation of 1.34 μl/min. Over several different fluid pressures and fluidic resistances, the coefficient of variation was lower than 0.044 for replicates. These differences could perhaps be further reduced using more carefully matched tubing resistances. We also show the ability of the container, attached via a vacuum manifold, to deliver fluids to a complex microdevice (**Fig. 1f**).[3,8]

CONCLUSIONS

We have introduced a novel fluid delivery system that utilizes floating fluid reservoirs to maintain stable hydraulic pressure at the outlet even as reservoirs drain. Many reservoirs can be tightly packed inside a small, sealed container, which facilitates portability and can maintain sterility. In addition, the entire set of fluids can be exchanged by switching the lid to an alternate container. Sealing the container also facilitates external pressurization, enabling higher flow rates and further improving stability. Because each reservoir floats independently inside the container, flow rates are balanced over large volumes and flow rates from different reservoirs remain similar even when the reservoirs are drained at different rates.

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