SUB-NANOLITER PER MINUTE FLOW RATES WITH CUSTOM MICROSYRINGE PUMPS IN A MICROFLUIDIC CHIP: THE IMPORTANCE OF TEMPERATURE CONTROL

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ABSTRACT
This paper describes custom-built continuous-flow positive-displacement syringe pumps capable of delivering steady flow rates of less than 1 nL/min. The pumps described here use slow servo drives with large gear head reducers. More importantly, the pumps are thermally regulated. Without proper thermal regulation, small temperature fluctuations in the environment cause thermal expansion of components, resulting in noise and drift in the pump output. Only through rigorous thermal control of the pumps and components, can these low flow rates be achieved.

KEYWORDS: syringe pump, microfluidic, thermal control

INTRODUCTION
A wide variety of pumps are used in microfluidic systems. These include electrokinetic, acoustic, pressure, thermal, bubble, and displacement pumps, each with a broad range of implementations [1]. Electrokinetic pumps have been most widely used, owing to their precision, ease of control, and simple fabrication [2]. However, electrokinetic pumping imposes significant constraints on surface chemistries and on the composition of fluids to be pumped. Continuous-flow displacement pumps, such as microsyringe pumps, can deliver prescribed flows of many liquids, regardless of the their properties (e.g. viscosity, ionic strength, etc.). Nevertheless, microsyringe pumps have usually been restricted to prototype systems using more rapid flows (microliters per minute). Broader use is limited in part by the perceived inability of syringe pumps to generate steady flows slower than ~1 µL/min. This is widely perceived as a hard limit, arising from the inability of such mechanical systems to operate at slower speeds (many personal communications).
We demonstrate that off-chip microsyringe pumps can deliver flows much slower than 1 µL/min. We have achieved flows as slow as 1 nL/min with precision better than 0.1 nL/min and have routinely worked in the 10 to 15 nL/min range, matching flows in electrokinetic systems. These microsyringe pumps are assembled with mostly off-the-shelf components, making them easy to use in a research environment.

EXPERIMENTAL

Several novel ideas were integrated to develop these microsyringe pumps. Servo motors with large gearhead reducers (1024:1) enabled very slow rotation of a worm drive (National Aperture translation stage MM-3M-EX). Hamilton 10 µl Gastight syringes provided the smallest volume displacement per linear distance traveled (Figs 1&2). Finally, thermal control was achieved in one of two ways: (1) for control at ambient temperature, the syringes were simply mounted with good thermal contact on an aluminum block that acted as a thermal reservoir buffering the syringe from fluctuations in temperature (Fig. 1) and (2) for control at cold temperatures (4-15°C) by mounting a Peltier thermoelectric device and a thermistor to an aluminum block, using a feedback loop to maintain constant temperature, and insulating the entire system (Fig. 2). Linear gradients of fluorophores were generated in plastic microfluidic chips using two syringe pumps controlled by a custom-made LabVIEW interface (Fig. 3). Fluorescence was induced with a laser after the two solutions were completely mixed and monitored with avalanche photo diodes.

RESULTS AND DISCUSSION

In order to achieve low flow rates, thermal control of the pumps proved to be of utmost importance. The impact of even small

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Figure 2. Image of a thermally-controlled syringe pump. Up to four syringes can be thermally regulated by a thermoelectric device to within +/- 1°C.

Figure 3. (A) Schematic of two pumps attached to a microfluidic chip. (B) Experimentally measured fluorescence resulting from mixing resorufin dye with buffer using continuous linear gradients.
thermal fluctuations (+/- 3°C) can cause badly misformed gradients, as seen in Figure 4. By controlling the temperature of the pumps to within +/- 1 degree Celsius, thermal noise was significantly reduced, and extremely slow flows were achieved (Figs. 4 & 5).

CONCLUSIONS
We demonstrate a microsyringe pump using mostly off-the-shelf components that is capable of producing continuous flow rates inside microfluidic chips that are much slower than commercially available syringe pumps. By combining servo-motors with large gear-reducers, small bore, gastight syringes, and careful temperature control we achieved sub-nL/min flow rates. These pumps have been used extensively in our laboratory for drug discovery [3-4].

REFERENCES