PRECISE FLUID HANDLING SYSTEM BASED ON PRESSURE REGULATION

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ABSTRACT

We present a new algorithm which enables the flow-rate control of a microfluidic system using pressure actuators. Our algorithm combines the pressure control benefits with a direct flow-rate control of the system. Our algorithm can control a complex system with coupling effects or a mass parallel system with independent channels, whatever the number of channels.

We tested the performances of the algorithm on a coupled microsystem and compared them to the performances of a high precision syringe pumps solution on the same microsystem.

We also present the behavior of a system controlled by our algorithm and submitted to an external perturbation.

KEYWORDS

Microfluidic, pressure control, flow-rate control, algorithm, regulation, fluid handling system, coupling effects, mass parallel system.

INTRODUCTION

Conventional flow control systems, such as syringe pumps and peristaltic pumps, are not well adapted to the control of flows in microchannels. It often leads to long equilibration time, hysteresis and highly dependence on the elasticity of the system and the materials. We present here a new method to control the flows in microchannels based on pressure regulation.

PRESSURE REGULATION

The approach proposed here is based on a pneumatic pressurization of reservoirs filling with liquid to be injected in the microsystem. An original pneumatic path combined with a very fast regulation algorithm has been developed to deliver regulated pressure from a pressure source, the FASTAB™ technology.

The use of pressure regulation in microfluidic systems is explained in figure 1 and the benefits of this technology listed in table 1.

Thanks to this patented technology, the different instruments (MFCS™ series) can operate over a wide pressure range (from -800 mbar to 7000 mbar) to control flows from sub nL/min to thousands mL/min depending on the hydrodynamic resistance.

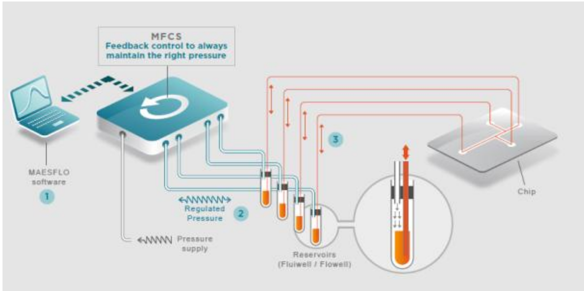

Figure 1: Principle of pressure regulation. 1: pressure values are ordered with the Maesflo software. 2: thanks to Fastab™ patented technology, the MFCS™ immediately and automatically provides the requested pressures.3: By connecting the MFCS™ pressure channels to reservoirs, Fluiwell, the pneumatic pressure allows to precisely and smoothly control the flow into the application.

Table 1: Pressure regulation benefits.

Parameter	Value	Remark
Settling time	< 1s usually between 0.1 to 0.2 s	Output volume dependent. No dependent on the elasticity of the system
Response time	< 16 ms	
Pressure stability	0.1 %	Precision of the flow. No dependent on the elasticity of the system.
Pressure resolution	0.1 % full scale	Down to 25 µbar.
Flexibility	Up to 8 independent channels. Adaptable to any kind of pressure source	Ability to control complex fluidic set-up

FLOW RATE CONTROL WITH PRESSURE REGULATION

Single flow-rate channel

Because for some applications flows need to be controlled by flow-rate, a flow-rate control was developed keeping pressure benefits. To achieve this, a precise flow sensor is implemented in the fluidic system. A feedback algorithm has been developed and integrated in the software. Thanks to this algorithm the pressure is adapted to get the target flow-rate. An autocalibration step is made in order to define the characteristics of the system and adapt the algorithm.

A first algorithm has been created to control the flow-rate on one channel. The results in terms of settling time and stability are given in figure 2 and 3 and compared to highly precise syringe pump. In the conditions of figure 2 (channel diameter 50 µm, length 50 cm), the settling time with our system is much shorter: 3 s vs 90 s with syringe pump. The stability, at low flow-rates, of the flow (figure 3) is much higher with our system, 0.2%, and not dependent of the duration of the experiment (not volume dependent). With syringe pumps, users have to find a good compromise between the volume to be injected and the precision of the flow. With our system, users do not need to make compromise as they can have very high stability (around 0.2%) even with high volumes up to 50 mL.

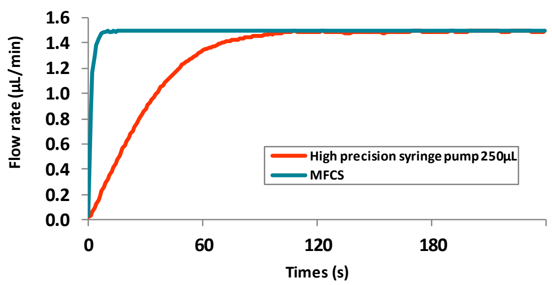

Figure 2: Comparison of the settling time at 1.5 µL/min between highly precise syringe pump (~ 90s) and our system (~ 3s).

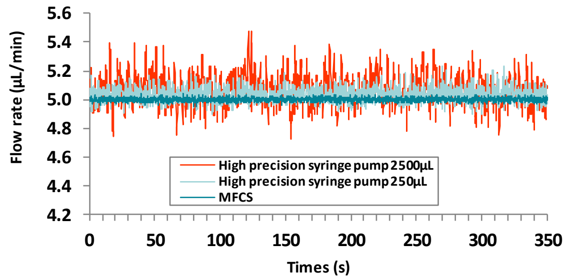

Figure 3: Comparison of the stability at 5 µL/min between highly precise syringe pump and our system. Due to the mechanical movement of the motor (to push the piston of the syringe), decreasing the volume of the syringe from 2500 µL to 250 µL increases the stability from more than 2% to 1% (CV).

New algorithm for several flow-rate channels

Usually, people need to control the flow-rate of several channels at the same time. Due to coupling effects, characteristic of the microsystem architecture, the flow-rate control of several channels using a pressure actuator could need a sharp understanding of the microsystem and the microfluidic laws. Basically, the user needs to find the right combination of pressure values which leads to the flow-rates needed. If this combination could easily be determined in basic microsystems, it could be harder for more complex systems.

The algorithm proposed here automatically calculates the pressures needed to obtain the desired flow-rate(s). It enables the flow-rate control of any microfluidic system with all the pressure control benefits (table 1).

FEATURES AND BENEFITS OF THE NEW FLOW-RATE ALGORITHM

This new flow-rate algorithm highly helps the user to precisely control its system. The user can directly control its system with flow-rate order(s) while keeping the pressure control benefits, such as very low settling time, high accuracy and stability.

Besides, the algorithm proposed here can be used on an unknown system and will help the user to empirically understand the system's behavior. For example, the algorithm is able to point-out non-reachable flow-rate order(s) to the user, meaning that the system is working on the MFCS^{TM} limits (maximum/minimum pressure reached) or meaning that the fluidic design of the system is incompatible with the requested flow-rate(s).

The algorithm proposed here is able to

control a large type and number of microfluidic systems, from a single channel with one input pressure to a mass parallel system with independent channels or single complex chip with several coupling effects between the channels. Only the relevant pressure channels will be activated to reach the flow-rate(s) wanted. This feature highly improves the flow-rate channels independence: even on a complex and coupled system, a new flow-rate order on a specific channel will not (or marginally) impact the other channels.

Besides, the algorithm handles positive or negative flow-rates and stop-flows. This feature means that a reverse-flow or a stop-flow is obtained with the responsiveness of a pressure control.

The new algorithm deals with perturbations (such as atmospheric pressure variation, fluid level variation into the tanks) and/or system modifications during the experiment (up to 20% variation of the main fluidic parameters) without consequences on the flow-rate control and accuracy. An example of a system controlled with our algorithm under perturbation is shown in figure 7.

Finally, as the algorithm always knows the pressure(s) and the flow-rate(s) used to control the microsystem, it provides an easy way to determine the microsystem main parameters such as the fluidic resistivity and the fluid viscosity or to identify any physical modifications in the device such as clogging or bubbles (volume and localization in the microsystem).

ALGORITHM PERFORMANCES

Comparison to high precision syringe pump on microchip with coupled channels

The new flow-rate algorithm, implemented with Fluigent instrumentation devices, has been tested with an IMT glass chip (ref. ICC-SY05), as shown in figure 4, and compared to high precision syringe pumps on the same chip.

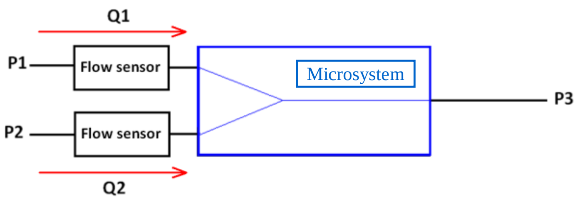

Figure 4: Scheme of the microfluidic system used to test the performances of the new flow-rate regulation. A Y microchip is connected to 3 pressure sources, 2 flow sensors are implemented on the inlets of the microchip.

The following Fluigent devices have been used for the flow-rate algorithm test: one (1) MFCS^{TM} FLEX 1000 mbar, three (3) Fluiwell 2 mL and one (1) Flowell (2 flow-rates channels, range of 7 µL/min).

The MFCS^{TM} FLEX and the three (3) Fluiwell have been replaced by two (2) high precision syringe pumps with a 250 mL syringe each for the comparative test.

The response time and the flow-rate behavior of these two experiments have been compared when a flow-rate order from -4µL/min to 4 µL/min is ordered for Q1 while the flow-rate order of Q2 stays constant at 2 µL/min.

The figure 5 shows the measured flow-rates Q1 and Q2 in the conditions described above for the two experimental conditions. The solution proposed with Fluigent devices leads to a shorter settling time compared to the high precision syringe pumps solution. The settling times are respectively 1.7s compared to 8.5s (Q1).

Besides, the solution exposed highly limits the interaction between Q1 and Q2. As shown in the figure 5, the coupling due to the chip design leads to a modification of the flow-rate Q2 when the flow-rate order of Q1 is changed. With our solution, this modification on Q2 stays punctual and limited: it leads to an over-dispensed volume of 0.01 µL. The maximal difference between flow-rate order on Q2 (2µL/min) and measured Q2 is +0.49 µL/min. With the syringe pumps solution the perturbation on Q2 leads to an under-dispensed volume of 0.07 µL. The maximal difference between flow-rate order (2µL/min) and measured Q2 is -0.87 µL/min.

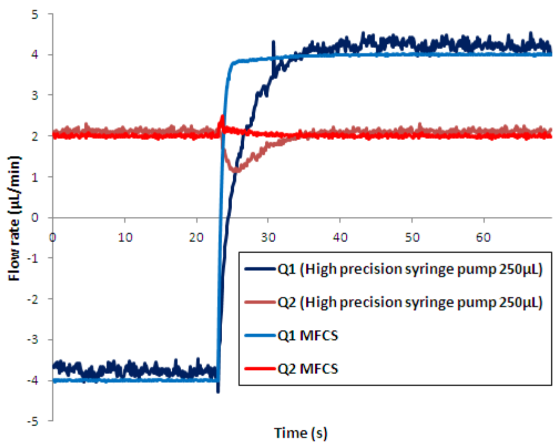

Figure 5: Flow-rates measured during the comparison test between high precision syringe pumps and our system on a Y microchip.

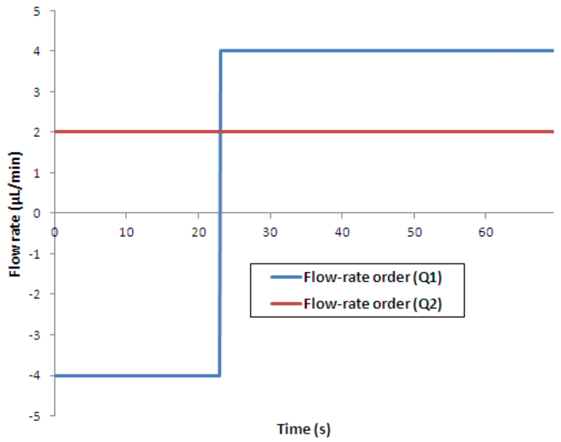

Figure 6: Flow-rate orders during the comparison test between high precision syringe pumps and our system on a Y microchip.

Performances with a system submitted to external perturbation

Flow-rate orders of 2 µL/min and -2 µL/min have been sent to the algorithm presented above to control the system presented in figure 4. Then, the system is submitted to an external perturbation: the value of the pressure channel P3 has manually been decreased and increased, respectively from 200 mbar to 50 mbar and from 50 mbar to 250 mbar. The figure 7 shows the flow-rate responses regarding to the perturbation in P3.

The table 2 quantifies the performances of the flow-rate control and shows that the algorithm presented here maintains its performances even on a system submitted to external perturbations. The maximal value of the standard deviation is 0.03µL/min.

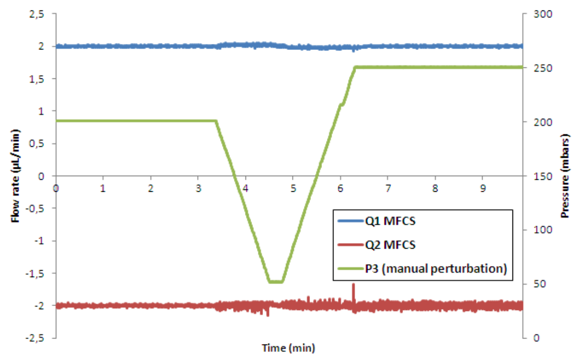

Figure 7: Flow-rates (Q1 and Q2) and output pressure (P3) measured on a Y microchip with our new flow-rate regulation. Between 3.5 minutes and 6.5 minutes, the system is submitted to an external perturbation (variation of P3).

Table 2: Flow-rates measured (Q1 and Q2) during the experiment of a Y microchip submitted to an external perturbation (variation of P3). Before perturbation: from 0 min to 3.5 min. During perturbation: from 3.5 min to 6.5 min. After perturbation: from 6.5 min to 9.5 min.

	Flow-rate Q1 (µL/min)	Flow-rate Q2 (µL/min)
Before perturbation	2,00 ± 0,01	-2,00 ± 0,01
During perturbation	1,99 ± 0,02	-1,99 ± 0,03
After perturbation	2,00 ± 0,01	-2,00 ± 0,03
Flow rate order	2	-2

CONCLUSION

We present here a new method based on pressure regulation to control flows in microfluidic systems. Thanks to the flow-rate control option we show the ability to control and monitor the relevant parameters of the flow: both pressure and flow-rate with very fast settling time, excellent stability and repeatability.

With the measurement of both pressure and flow-rate, users are able to well characterize their fluidic systems and to detect any modification (presence of bubble, clogging and/or variation of the viscosity of the system…). This benefit can't be provided with a syringe pump solution due to the fact that the only available parameter is the flow-rate order, neither the pressure nor the flow-rate are measured.

REFERENCES

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