Lab-on-a-Chip Application: Continuous Dispensing of a Solution to a Microfluidic Chip Using uProcess™ Automation

By Yolanda Fintschenko and Kirsten Pace • Labsmith, Inc., Livermore, CA 94551

In biological experiments, it is often necessary to deliver fluid at low flow rates (*eg.* ≤ 1µl/min) over experiment times of hours to days. This requires a relatively large total volume dispensed to the experiment, sometimes as much as 1-10 ml or more. In lab-on-a-chip experiments, a small overall experimental platform is often desired, challenging the researchers to use a small form factor syringe pump and valve system with the desired low flow rate accuracy and total volume. LabSmith uProcess™ automated fluid routing system now meets this challenge with the four port, two-position valve (AV202-C360). With the AV202-C360 valve, an automated uProcess™ program sequence controls the withdrawal of reagent to fill one syringe while simultaneously dispensing the fluid to the experiment from a second syringe pump, switching between full and empty syringes for uninterrupted fluid delivery at precise, low flow rates. The required components, board layout, uProcess program, operating parameters, and results are described here.

INTRODUCTION

The uninterrupted delivery of milliliter volumes of fluid at 1µl/min flow rates can be achieved using uProcess™ software to control two SPS01 syringe pumps and the four port, two-position valve (AV202-C360). By switching each syringe pump between a fill mode where one syringe pump withdraws solution from a CapTite™ breadboard reservoir (eg. BBRES-C360) while the second syringe pump dispenses solution to the experiment, continuous dispensing is achieved. The breadboard layout to control this experiment is shown in Figure 1.

EXPERIMENTAL

A detailed list of LabSmith equipment required for continuous fluid delivery using uProcess™ automation is found in Table 1.

The uProcess™ program or sequence written to control the continuous dispensing experiment is shown in Figure 2. Figure 3 illustrates the valve position during Step 1 and Step 2 of the sequence.

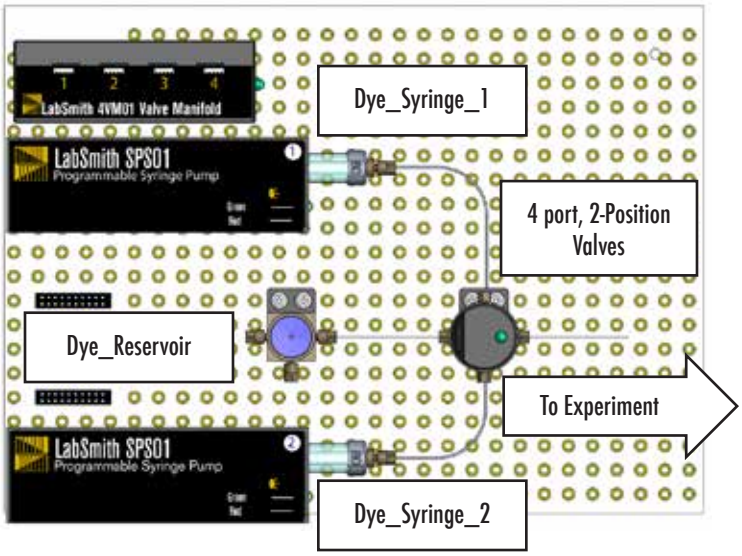

Figure 1. uProcess™ hardware, including: AV202 series automated valve, SPS01 programmable syringe pumps, 4VM01 valve manifold, and uPB-5 integrated breadboard. Not shown, the Electronic Interface Board (EIB) for communication with uProcess™ software. LabSmith's CapTite™ fluid routing components and a microfluidic chip complete this easy-to-use system for delivering micro- and nano-fluidic volumes.

uProcess Continuous Dispense Program Script

```
*Dye_Syringe_1   =        SPS01 40 ul
*Dye_Syringe_2   =        SPS01 80 ul
*LabSmith 4VM    =        4VM01
Step1
        LabSmith 4VM:    SetValves 3 0 0 0
        Dye_Syringe_1:   SetFlowRate 10.000 ul/min
        Dye_Syringe_1:   MoveTo 5 ul
        Dye_Syringe_2:   SetFlowRate 100.000 ul/min
        Dye_Syringe_2:   MoveTo 100.000 ul
        <WaitAllDone>
Step2
        LabSmith 4VM:    SetValves 1 0 0 0
        Dye_Syringe_1:   SetFlowRate 100.000 ul/min
        Dye_Syringe_1:   MoveTo 50.00ul
        Dye_Syringe_2:   SetFlowRate 10.000 ul/min
        Dye_Syringe_2:   MoveTo 55.000 ul
        <WaitAllDone>
        <Loop> Step1 25
```

Figure 2. The uProcess™ program written to control the sequence of filling one syringe with dye while dispensing dye to the microfluidic channel (experiment) then switching.

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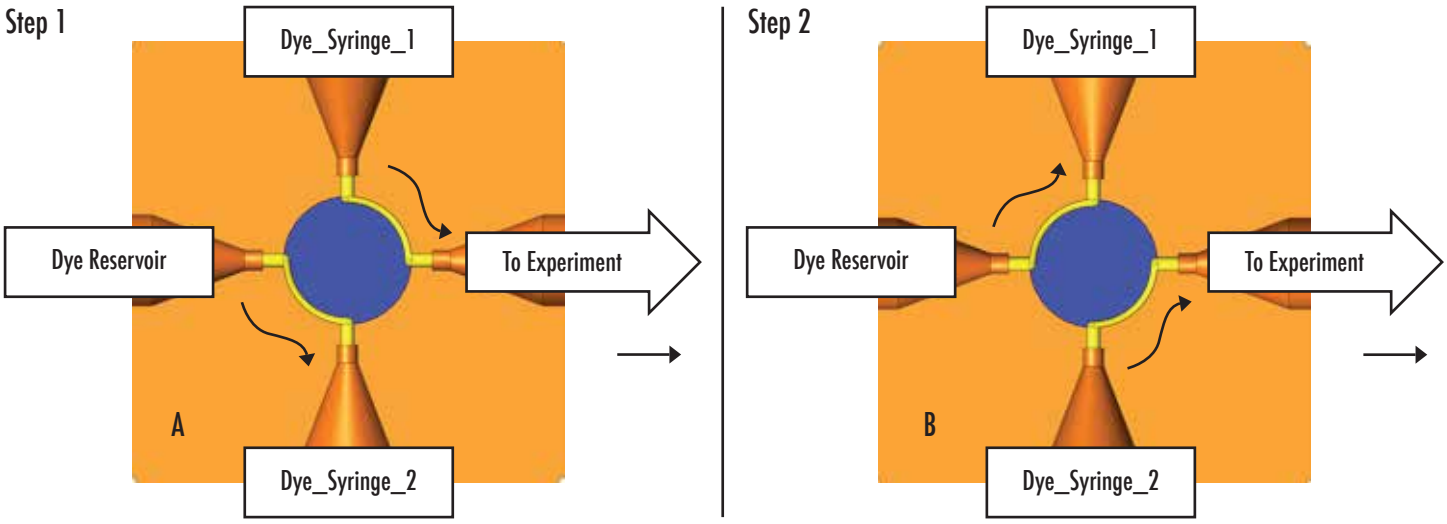

Figure 3. Operation of Continuous Dispense operation of uProcess™ Breadboard. In A, (Step 1) the valve is aligned so that dye from Dye_Syringe_1 is delivered to the experiment, while Dye_Syringe_2 is withdrawing dye from the dye reservoir, filling the syringe. In B, (Step2) the valve switches, continuously deliverying dye to the channel from Dye_Syringe_2, while pump Dye_Syringe_1 withdraws dye from the Dye Reservoir. Steps A and B are repeated for the duration of the experiment. ⟶ INDICATES FLOW DIRECTION

The intensity of the fluorescent AlexaFluor 488 dye (Life Technologies, Carlsbad, CA) delivered to a microfluidic channel on a chip was measured with the LabSmith SVM340 synchronized video microscope assembled with a blue illuminator, a 515nm Schott glass filter, and a using the Intensity Probe feature of the uScope™ software.

RESULTS AND CONCLUSION

The intensity of the dye over time is plotted in Figure 4. While intensity does vary over time, note that there is no correlation between the valve switching and any changes in intensity. The valve switch time is 0.4 seconds.

TABLE 1. Components for the uProcess™ automated continuous reagent delivery breadboard

LabSmith Part Number	Description	Number
uPB-05	uProcess Breadboard with sockets for 5 uDevices	1
EIB	Electronic Interface Board	1
4VM01	Valve Manifold	1
AV202-C360	Four port, 2-position valve connects to 360 µm o.d. tubing	1
SPS01	Syringe pump	2
BBRES-C360	Breadboard reservoir with cap and o-ring seal (1.1 ml volume). Four tubing ports.	1
C360-100	One-piece fitting for connecting 360 **µm o.d. tubing to syring pumps, reservoir and chip**	8
C360-101	One-piece plugs used to plug unused ports	3
C360-400*	Bonded port connectors to connect tubing to microfluidic chip fluid channel	4
CROSS-PMMA*	microfluidicChipShop cross channel (100 **µm x 100 µm channel, 58 mm long)**	1
LS-EPOXY*	Two-part epoxy for fixing bonded port connectors to microfluidic chip	1
LS-Tools	Hex and torx wrenches for tightening fittings ¼" screws for fixing onto breadboard	1
CAP-150P	PEEK tubing. 360 **µm o.d., 150 µm i.d. (1m)**	1
SVM340*	Synchronized video microscope with uScope™ software and B&W camera, 515 nm filter	1

* Optional

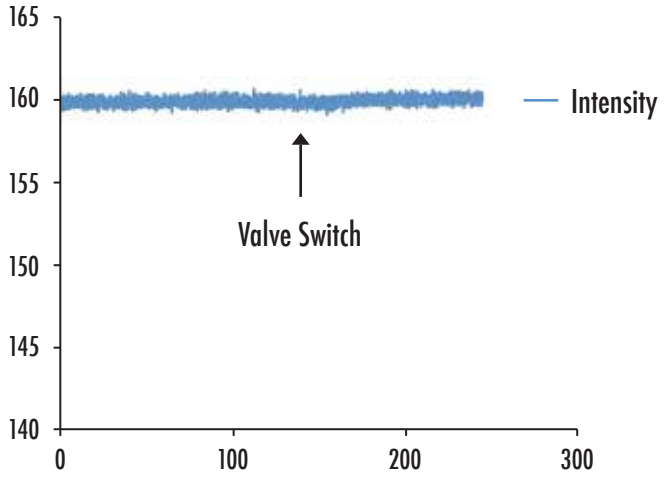

Figure 4. An intensity probe in uScope software was used to measure the brightness of AlexaFluor 488 over time. The time when the valve switched is noted in the chart.

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