Supplementary Material (ESI) for Lab on a Chip


# Microfluidic Flow-encoded Switching for Parallel Control of Dynamic Cellular Microenvironments - Supplemental Information

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### S1. Flow-encoded switching Equivalent Circuits

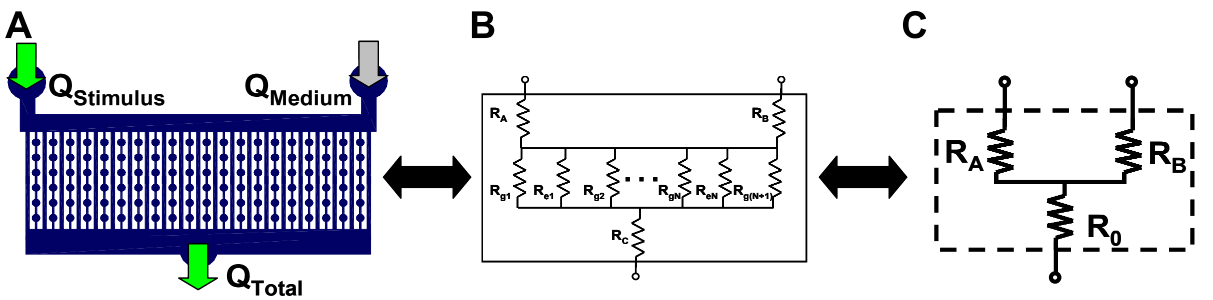
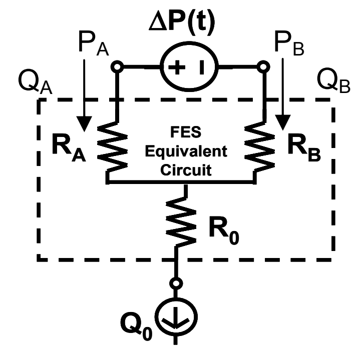



**Figure S1 –** Equivalent circuit used to derive the relationship between the linear relationship between the input pressure difference $\Delta P$ and the input flow ratio $\chi$.

The flow encoded switching network in S1A consists of two inlet channels, one outlet channel, and a series of parallel connecting channels comprised of N experimental channels and N+1 parallel gap channels, as described in the primary manuscript. Since the flow is characterized by a low Reynolds number, each channel can be treated as a linear circuit element, and represented as an electrical resistor. If the resistances of the channels connecting the inlets of experimental and gap channels are neglected (due to their short length and large width), we get the equivalent circuit shown in Figure S1B, where experimental and gap channels are in parallel. This equivalent circuit can be further simplified and represented as shown in Figure S1C, where $R_0$ represents the parallel combination of all gap and experimental channels, all in series with $R_C$.

**S2. Derivation of the linear relationship between pressure ($\Delta$P) and flow ($\chi$) control.**

Figure S2 illustrates the equivalent circuit representing pressure control of a FES network. The dotted line box represents the microfluidic device while the DC voltage source represents the applied pressure difference between the two inlets A (left) and B (right). The current source at the outlet represents the syringe pump drawing fluid from the outlet at a constant rate.




$$\chi(t) \equiv \frac{\Delta P(t)}{Q_0(R_A + R_B)} - \frac{R_B}{R_A + R_B}$$

**Figure S2 –** Equivalent circuit used to derive the relationship between the linear relationship between the input pressure difference $\Delta$P and the input flow ratio $\chi$.

We first define the inlet pressure difference to be

(S.1) $$\Delta P = P_A - P_B$$

and the constant outlet flow rate as $Q_0$, equal to the sum of the flow through inlets A ($Q_A$)and B ($Q_B$).

(S.2) $$Q_0 = Q_A + Q_B$$

The algebraic sum of the potential drops around a closed path must equal zero, giving

(S.3) $$P_A - P_B = Q_A R_A - Q_B R_B$$

Substituting from S.1 and S.2 and normalizing to $Q_0$ gives

(S.4) $$\frac{\Delta P}{Q_0} = \frac{Q_A}{Q_0} R_A - (1 - \frac{Q_A}{Q_0}) R_B$$

The inlet flow ratio is defined in the primary text as

(S.5) $$\chi = \frac{Q_A}{Q_0}$$

Substitution of S.5 in S.4 and rearrangement give a linear relationship between the inlet flow ratio and the inlet pressure difference.

(S.6) $$\chi = \frac{\Delta P}{Q_0(R_A + R_B)} + \frac{R_B}{R_A + R_B}$$

When the network is operated in pressure control mode here, it is important to avoid the situation where $\chi < 0$ or $\chi > 1$, as either will result in retrograde from one inlet to the other. In practical terms, this occurs when inlet pressure differences are too high for the fluid flow rate being drawn from the outlet. Quantitatively, the pressure ($\Delta$P) should be maintained within the following range $\Delta P(\chi=0)<\Delta P<\Delta P(\chi=1)$ where

(S.7) $$\Delta P(\chi = 0) < \Delta P < \Delta P(\chi = 1)$$

where

(S.7) $\Delta P(\chi = 0) = -R_B Q_0$

and

(S.8) $\Delta P(\chi = 1) = R_A Q_0$

So the pressure should be maintained in the following range.

(S.9) $-R_B Q_0 < \Delta P < R_A Q_0$

**S3. Pressure vs. Flow Control**

We have successfully operated the FES devices using flow control and pressure control. However, selection of the optimal control method for a given experiment requires consideration of the pros and cons for each strategy. Flow control typically involves using two syringe pumps and altering one or both flow rates to achieve the desired flow ratio and desired total flow rate. Since the syringe pumps do exhibit flow-rate dependent variability and are not stable across time, gap channels must be designed large enough to protect against these variations. The advantage of flow rate control is that many labs already have syringe pumps and do not need to build pressure control systems. Pressure control can be performed in two ways. 1) Passive hydrostatic pressure can be used (the heights of stimulus and diluent reservoirs can be adjusted to control switching). This method of pressure control is considerably more stable that the syringe pump, allowing smaller gap channels to be used without sacrificing robustness. 2) Pressure control can also be performed using a differential pressure source connected to stimulus and diluent reservoirs. Both flow and pressure control methods are effective in modulating the state of FES networks.