Behavioral Modeling of Solute Tracking in Microfluidics

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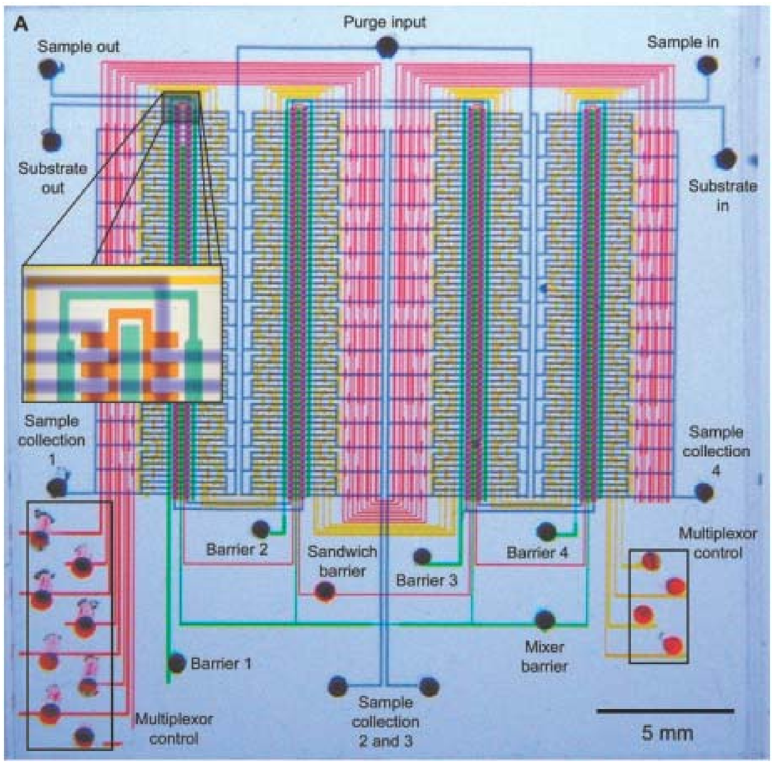
Outline

- Motivation: Simulation of transport through complex chips
- Model: Lumped Dual-Branch Model
- Modeling method: Verilog-AMS description
- Experiments and simulation results
- Summary

Motivation: Simulation of complex chips



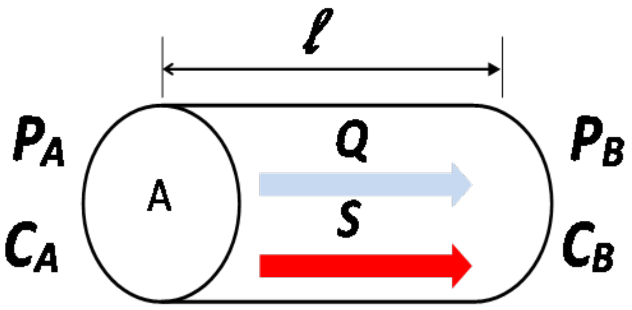
- The design of microfluidic systems with hundreds of dynamic on-chip components is a challenge
- CAD tool able to simulate time dependent transport of solvent and solutes through complex chips inclusive of dispersion and convection is desired
- Current tools are inadequate doing system-level simulation
- Analytical macromodel elements are limited with static transport problems

Todd Thorsen, et. al. Science, 2002, 298

Our Method

- A general simulation method for the approximate solution
- For pressure-driven solute and solvent transport in large microfluidic chips
- Solving linear and nonlinear, static and time-dependent transport using lumped approach
- Based on one-dimensional discretization of the Navier-Stokes and convection-diffusion equations

Lumped Transport Model



Q: solvent volumetric flow rate

S: solute current

P_A: Pressure at node A
P_B: Pressure at node B
C_A: Concentration at node A
C_B: Concentration at node B

- Consider the flow of solute and its solvent carrier through a simple capillary tube

- Four lumped nodal and branch quantities

- solvent pressure
- solvent volumetric flow rate
- solute concentration
- solute current

Solvent Transport Model

- Assume incompressible flow of uniform density

- Pressure driven and linear

- The solvent(incompressible) transport obeys the simplified Navier-Stokes equation. So we get:

$$\boxed{-\beta_f \cdot Q - A \cdot \frac{\partial P}{\partial x} = \rho \frac{\partial Q}{\partial t}}$$

ρ: solvent density; *A:* capillary area;
β_f : related to the solvent hydraulic resistance

Solute Transport Model

- Two driving forces:
  - Solvent forced convection of solute
  - Solute diffusion driven by concentration gradients

- Solute concentration $C(x,t)$ approximately obeys the simplified, lumped one-dimensional convection-diffusion equation:

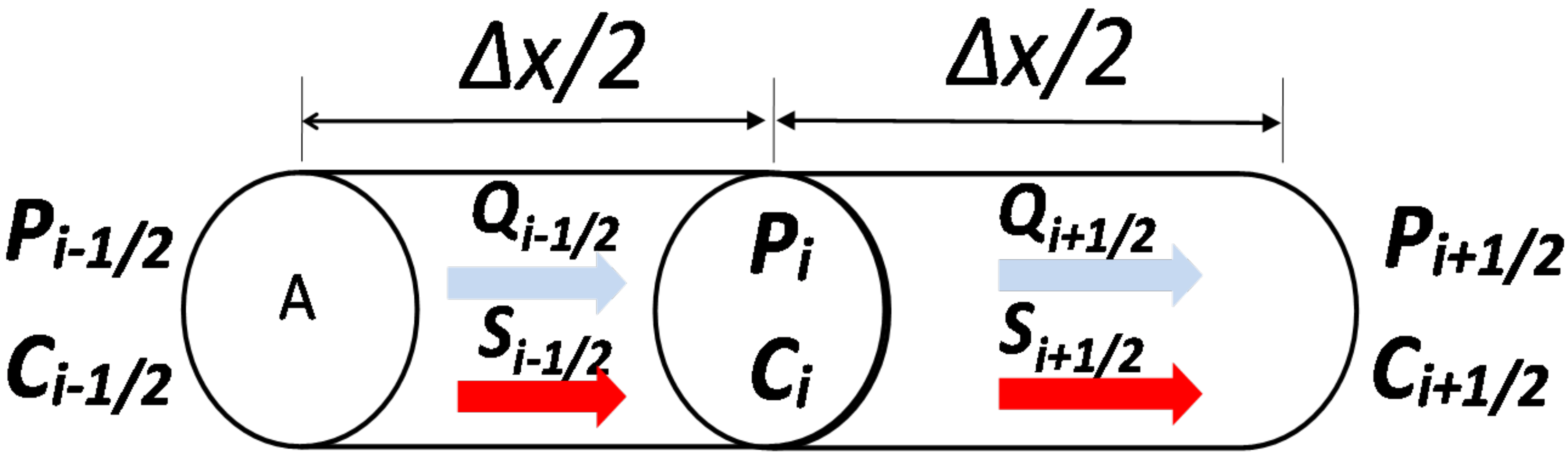
$$\boxed{D \cdot \frac{\partial^2 C}{\partial x^2} - V \cdot \frac{\partial C}{\partial x} = \frac{\partial C}{\partial t}}$$

(*D*: effective diffusion constant)

D. A. Beard, et. al. J. of Appl. Physics, 2001, 89

Dual-Branch finite difference Model

- Make finite difference discretization by slicing a capillary into smaller three-node differential elements:



length Δx with 6 nodal potential quantities and four branch flow quantities.

Lumped Dual-Branch Model

- Use following approximations:

$$\frac{\partial^2 C_i}{\partial x^2} \approx \frac{4}{(\Delta x)^2} \cdot [C_{i+1/2} + C_{i-1/2} - 2C_i]$$

$$-V_i \frac{\partial C_i}{\partial x} \approx -\frac{V_i}{\Delta x} \cdot [C_i - C_{i-1/2}]$$

- Then reach the set of discrete equations:

$$G_{st} \cdot (C_{i+1/2} - C_i) + G_{st} \cdot (C_{i-1/2} - C_i) + Q_{i-1/2} \cdot C_{i-1/2} - Q_{i+1/2} \cdot C_i = C_D \cdot \frac{dC_i}{dt}$$

$$(P_{i-1/2} - P_i) - R_f \cdot Q_{i-1/2} = L_f \frac{dQ_{i-1/2}}{dt}$$

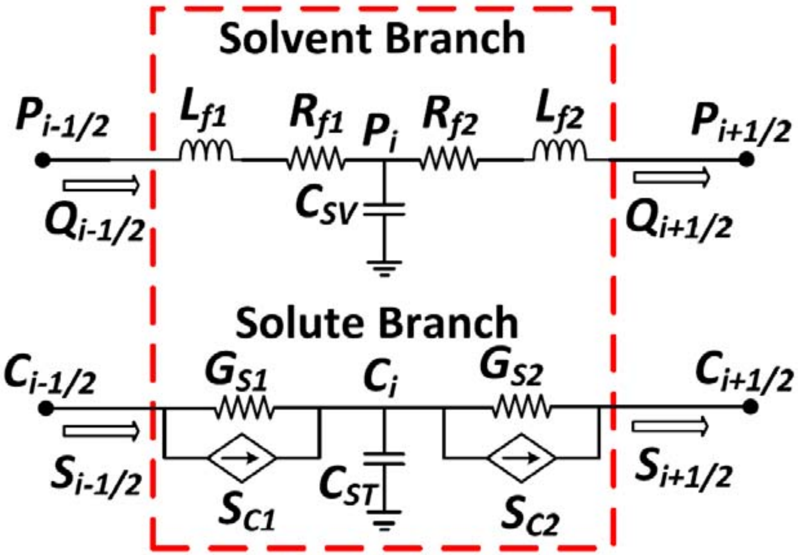
$$(P_{i+1/2} - P_i) - R_f \cdot Q_{i+1/2} = L_f \frac{dQ_{i+1/2}}{dt}$$

- If the capillary walls are flexible, the element volume:

$$Q_W = \frac{dV_{ol}}{dt} = \frac{dV}{dP_i} \cdot \frac{dP_i}{dt} = C_W \cdot \frac{dP_i}{dt}$$

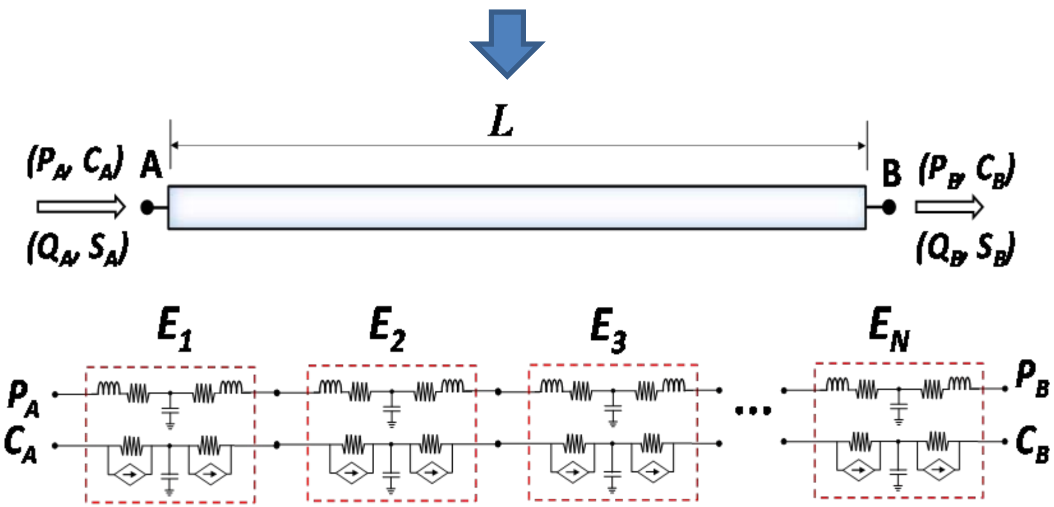
where C_W is the capillary wall compliance

Lumped Dual-Branch Model



Lumped two-branch network model

- Top branch models transport of solvent.
- Bottom branch models transport of solute.
- Capacitive elements represent storage of solvent and solute.



Equivalent network for a capillary consisting of N elements

- Each capillary in a chip is modeled as a series connection of *N* basic 4-terminal elements.

Verilog-AMS Implementation

The lumped model can be implemented in a hardware language such as Verilog-AMS.

The state variable units and their corresponding relations are first defined.

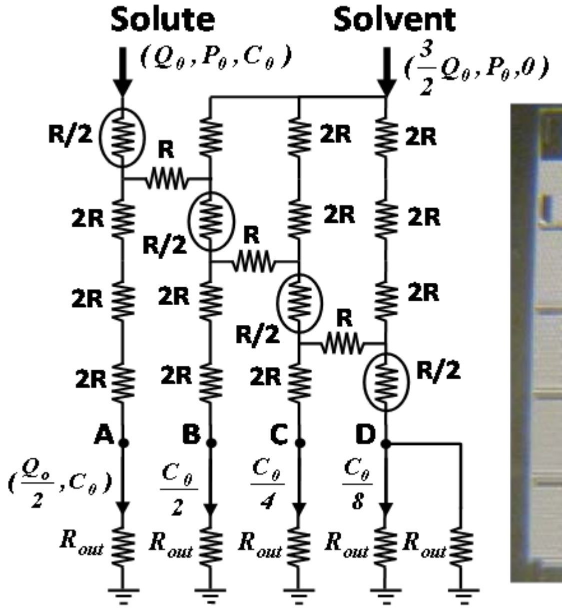
The nature of Solvent variables is shown(similar for solute):

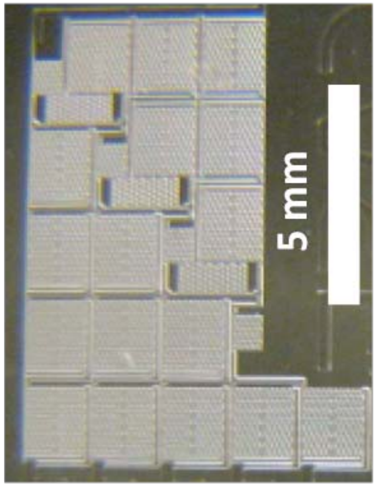
```
// Solvent quantities
nature SolventCurrent
    units = "-nL/s" ;
    access = Qsv ;
    idt_nature = SolventVolume ;
endnature
nature SolventPressure
    units = "Pa" ;
    access = Psv ;
endnature
```

Define corresponding relations(similar for solute):

```
// define discipline bindings
discipline Solvent
    domain continuous;
    potential SolventPressure ;
    flow SolventCurrent ;
enddiscipline
```

Example: Binary Dilution Network





Photograph and schematic of a PDMS binary dilution network

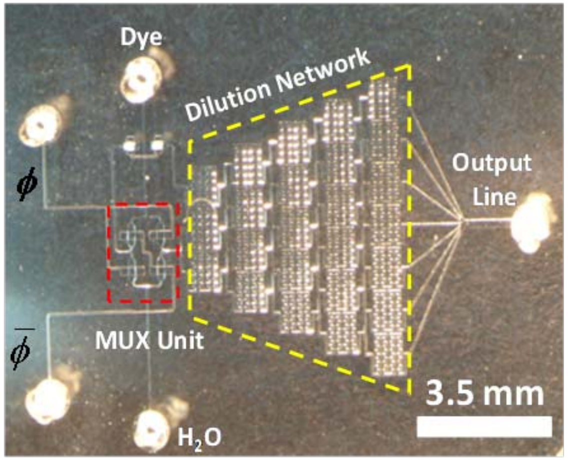
- Chip consists of a binary dilution(19-capillary) network and provides multiple static outputs.
- Capillary dimensions for the resistor *R* is 50×16×1500 μm^3
- The solute was a solution of fluorescein disodium dye in H_2O (0.1 mg/ml) and the drive pressure was about 10 PSI.

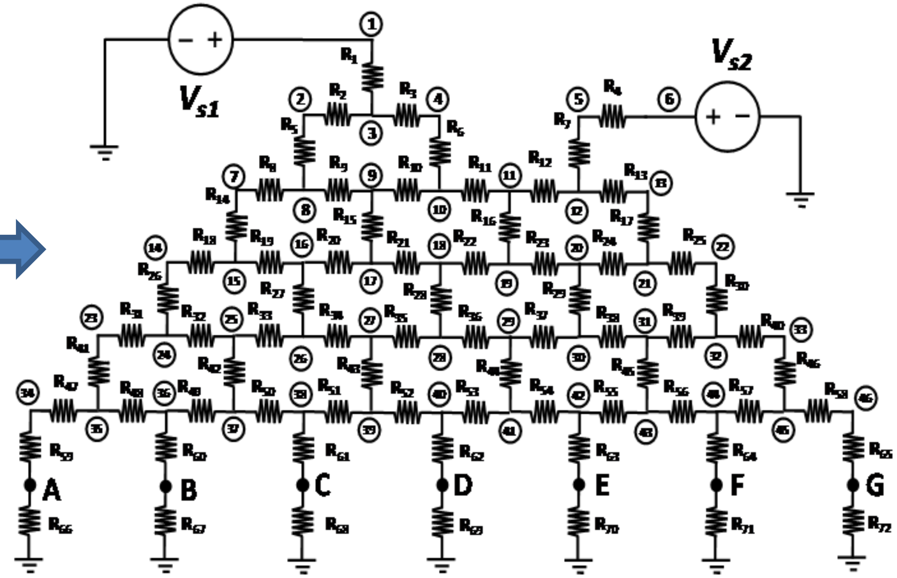
Table 1. Comparison of normalized bit concentrations

	A	B	C	D
Theory	1.0	0.5	0.25	0.125
Simulation	1.0	0.49	0.249	0.1248
Experiment	1.0	0.49	0.24	0.105

L. Chen, F. Azizi, C. H. Mastrangelo, Lab Chip, 2007, 7

Example: Switching Gradient Generator



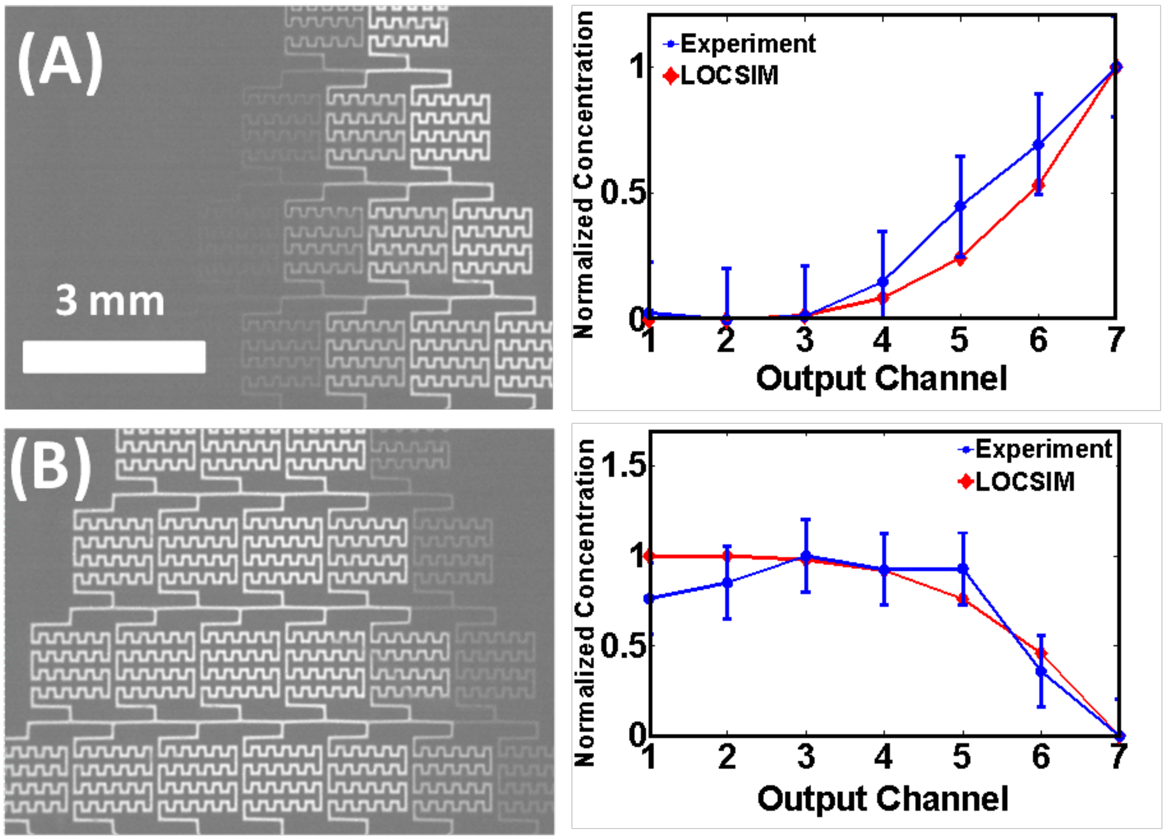


Photograph and network schematic

- 72-capillary, PDMS gradient generator.
- Equivalent 53-node, 7-output lumped network.
- Driven by alternating flows of dye and water using a four-valve multiplexer.
- Capillary dimensions: 25×16 μm^2

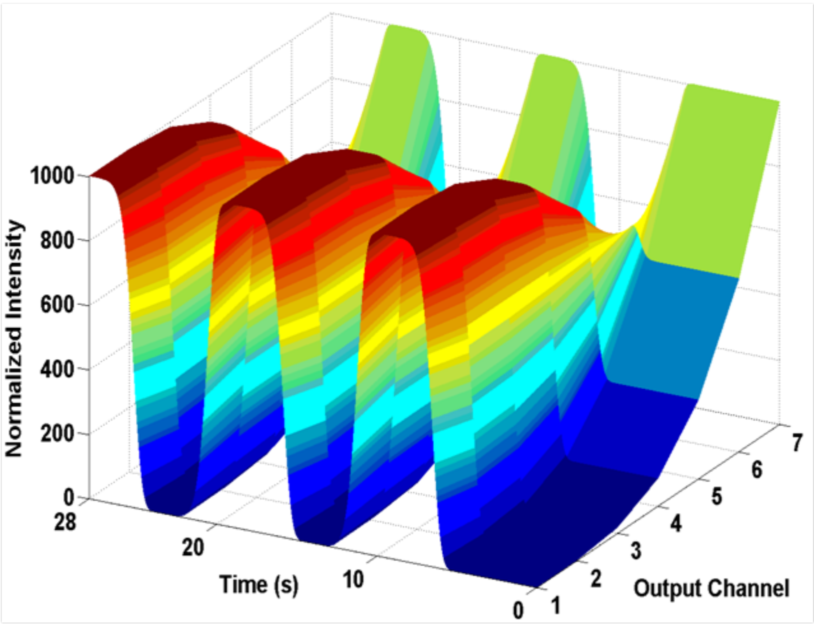
S. K. W. Dertinger, et. Al. Anal. Chem., 2001, 73

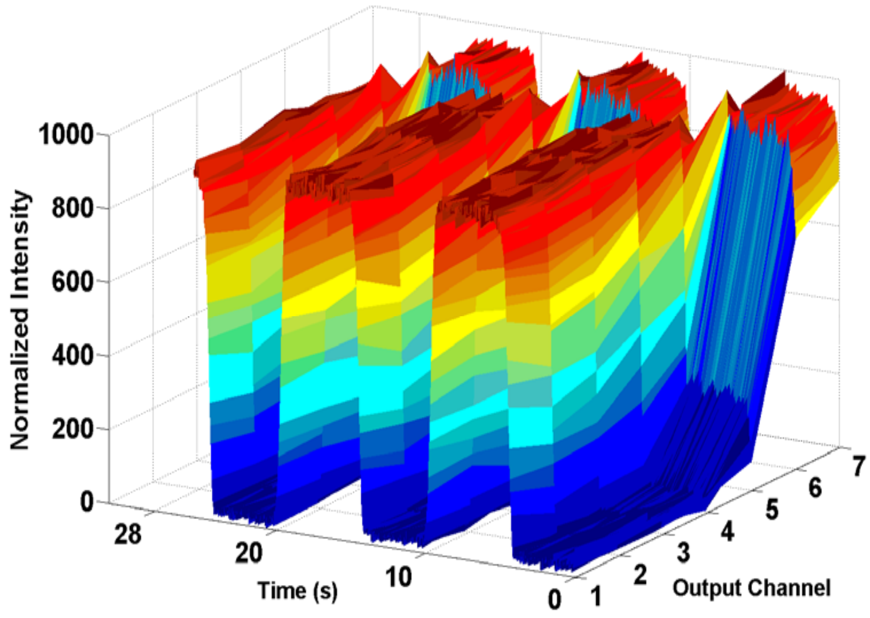
Example: Switching Gradient Generator



Comparison of experimental and simulated normalized, static dye concentration at the output channels of the gradient generator

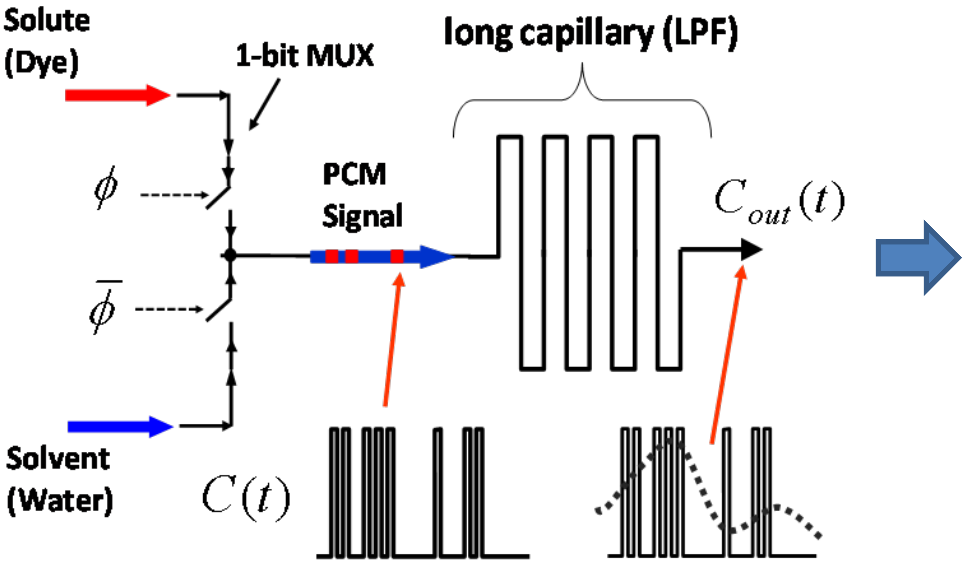
Example: Switching Gradient Generator



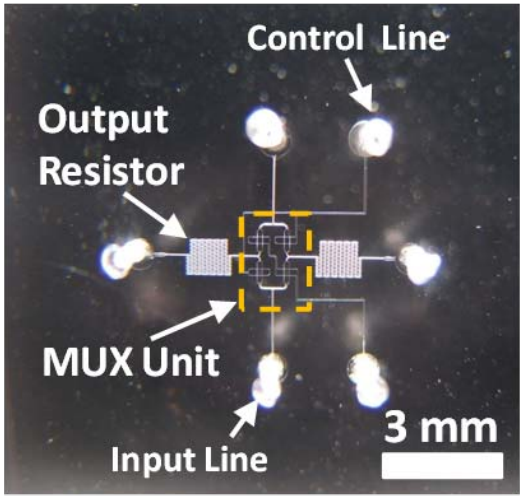


Comparison of simulation (left) of dynamic output gradients for the chip and experimental results (right). The chip solute inputs were switched at 0.1 Hz.

Example: Pulse Coded Modulators



One-bit microfluidic PCM.

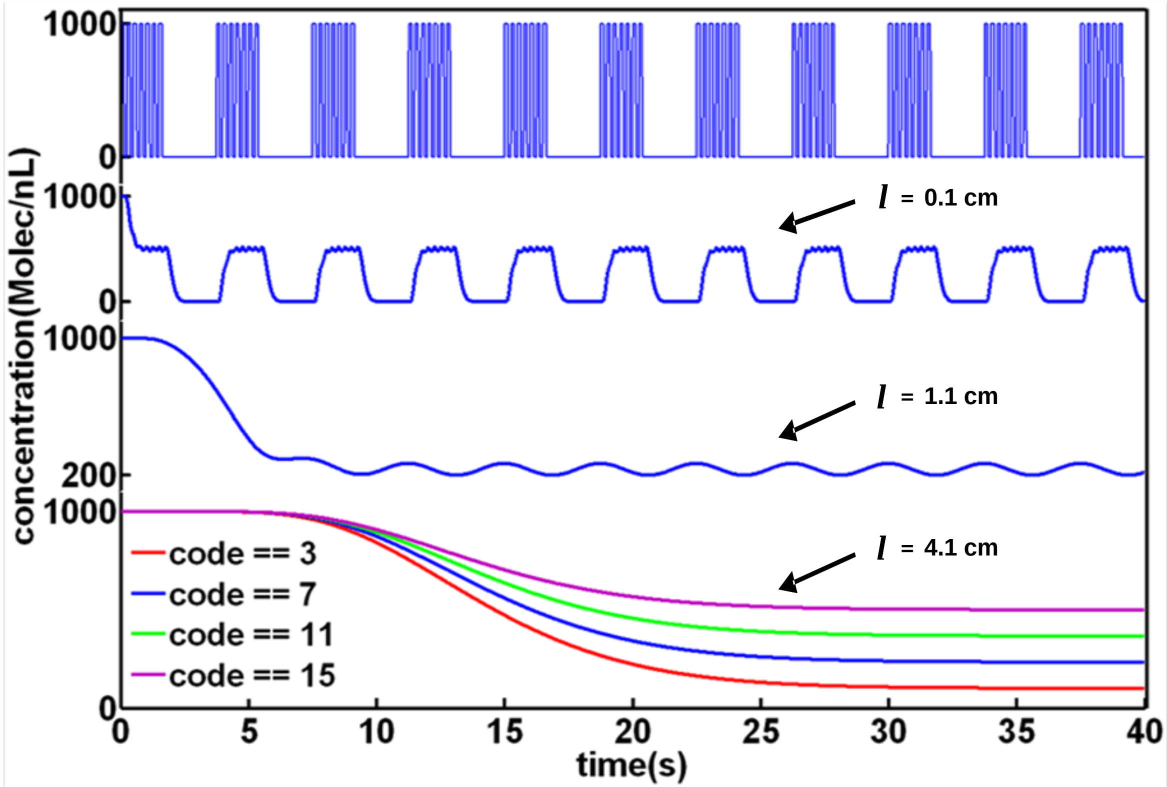


Photograph of dual one-bit PCM PDMS chip.

- Two valves are driven by digital clock to produce a series of solute plugs.
- The long capillary averages the plugs producing a smooth solute concentration signal.
- The number of plugs is determined by a digital code over a repeating cycle.
- The concentration at the output of the PCM approaches a steady value that is proportional to the PCM code.

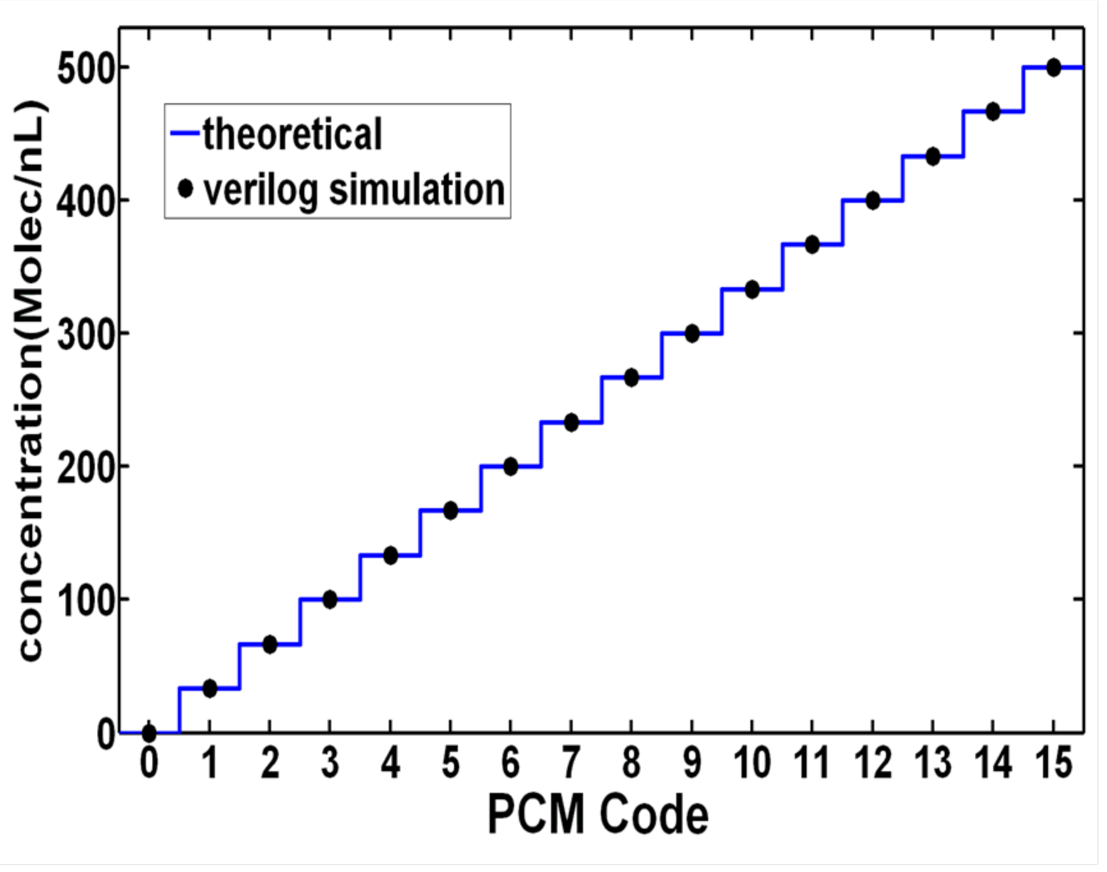
F. Azizi and C. H. Mastrangelo, Lab Chip, 2008, 6

Example: Pulse Coded Modulators



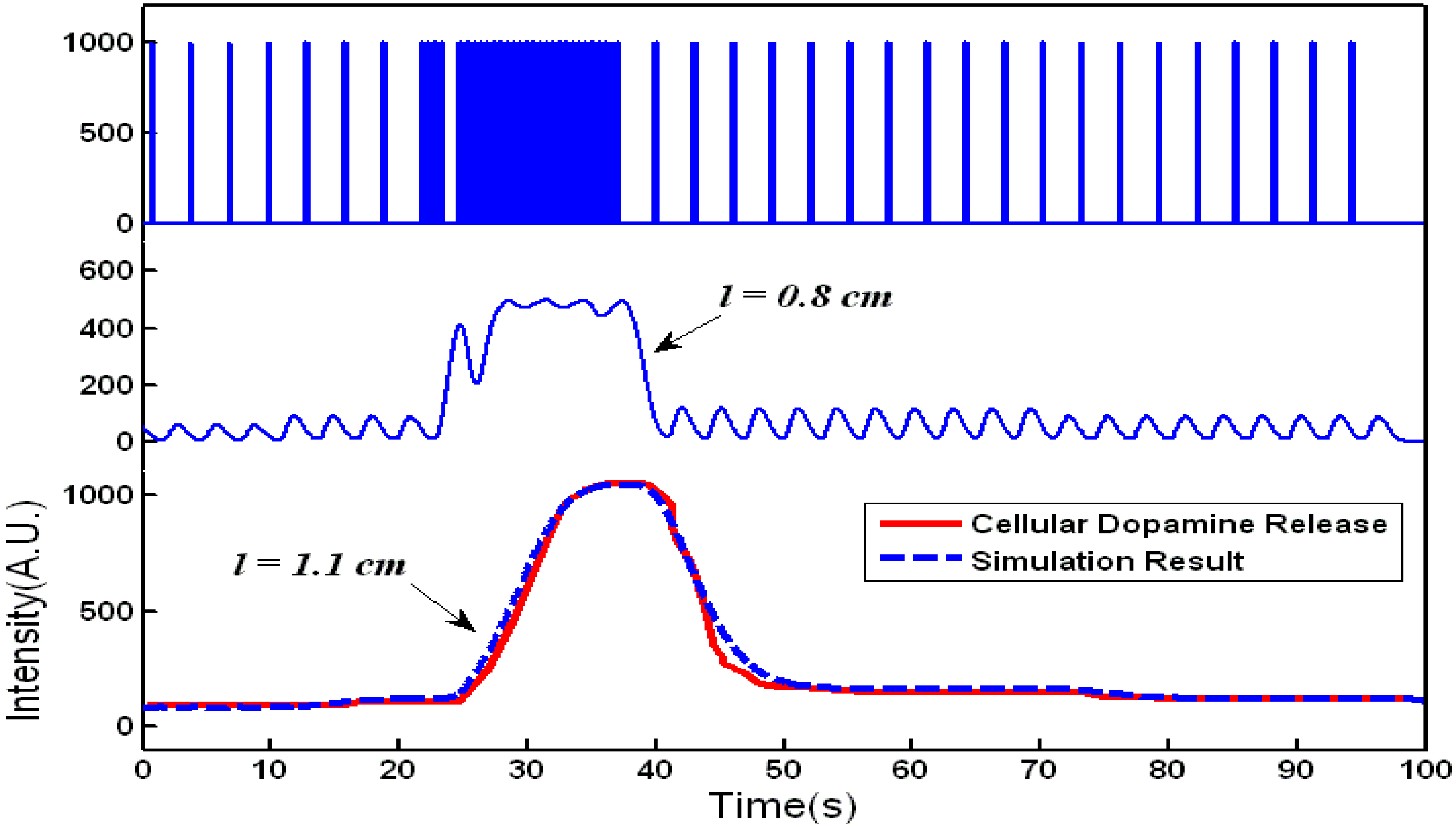
Simulated solute concentration waveforms for a 1-bit PCM chip for different codes and at different lengths from the multiplexer exit. The capillary width is 50 μm. The top three trace shows the waveforms for PCM code 7/15.

Example: Pulse Coded Modulators



Comparison of theoretical (blue) and verilog-AMS simulated PCM output solute concentration versus input code.

Example: Pulse Coded Modulators



Simulated solute concentration waveforms for a 1-bit PCM chip and at different lengths from the multiplexer exit. The capillary width is 50 μm. These trace shows the waveforms for PCM code from 2/32 to 32/32.

Summary

- Presented a general behavioral simulation method for the approximate solution of lumped pressure-driven linear and nonlinear, static and time-dependent solute and solvent transport in large microfluidic chips.
- Tracks solvent and solute transport using four dual-branch nodal and branch quantities.
- Implemented with Verilog-AMS netlist.
- Comparison of static and transient behavior of microfluidic dilution networks and a PCM signal generator.
- Simulation results are in good agreement.

Thank you!