System-level Simulation of Liquid Filling in Microfluidic Chips

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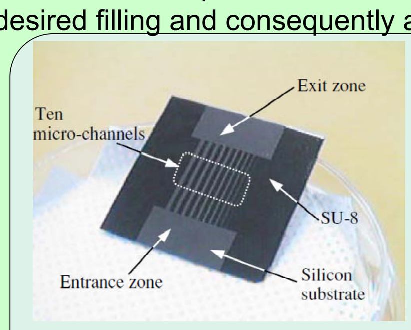
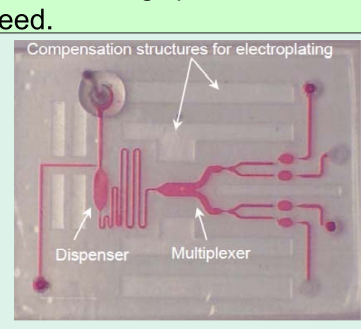
Background and Motivation

Motivation

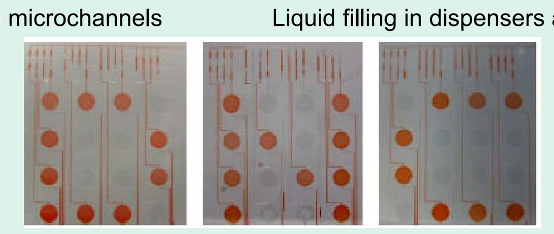
- Filling of liquid solutions into the microchannels is universally encountered in microfluidic lab-on-a-chip systems. Precise injection and delivery of the samples and reagents into the microfluidic network for programmed analysis is critical to assay performance.
- Liquid filling a complex process that depends on a variety of geometric, material, and operating parameters (e.g., flow velocity/pressure), and microchannel geometry. Variations in these parameters lead to distinctly different filling behavior in terms of filling time, air bubble trapping, and dead zone formation.
- Investigation of liquid filling process can guide the layout arrangement and protocol development to eliminate potential filling problems and achieve desired filling and consequently assay speed.



Liquid filling in microchannels



Liquid filling in dispensers and multiplexers



Selective liquid filling in complex microfluidic networks using dynamic pressure control valves

Related Work

- Single microchannel or capillary
  - **Reduced order model** for the 2D capillary filling process (*Zeng, Coventor Inc*)
  - Liquid filling into microchannels with consideration of the surface tension effect (*Kim et al , J. Micromech. Microeng., 2000*)
- Microfluidic network
  - Liquid filling in the dispenser and multiplexer (*Puntambekar, PhD. Thesis, University of Cincinnati ,2003*)
  - Selective filling in the microfluidic network using dynamic pressure control valves (*Lee et al. IEEE conference 2009*)
  - **High fidelity numerical methods** *(Yang et al. MSM, 1998)*
  - Reduced order model using a **constrained energy minimization approach** (*Treise et al. Lab chip 2005*)

Limitation of Current Numerical Methods

- High fidelity numerical methods are **prohibitively expensive**, leading to long turnaround time (several minutes to several days).
- Zeng's reduced order model only applies to a single 2D microchannel or capillary.
- The constrained energy minimization approach cannot predict the liquid filling time at each component in the network due to the lack of component-wise fluid dynamic description, which however is of more importance from the chip design perspective.

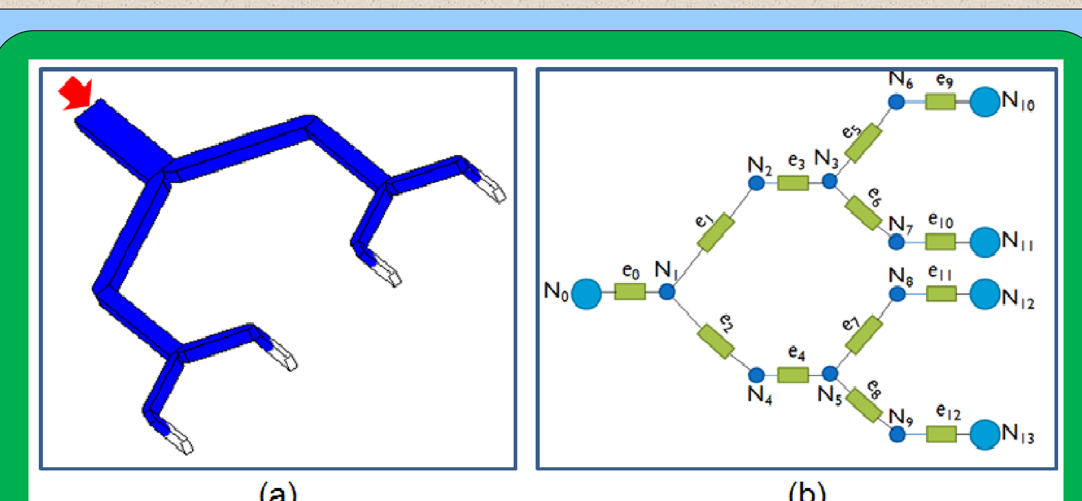
Research Objective

The overall objective of our work is to develop a system-level model and simulation framework for investigating the liquid filling process (including the filling time, filling pattern/status, flow velocity/pressure etc.) in complex microfluidic networks with order-of-magnitude speedup over the high-fidelity simulations and without appreciably compromising analysis accuracy.

Schematic Representation

Principle

- Microfluidic network is composed of a set of connected components (e.g., microchannels and junctions)
- Each individual microchannel is represented by an edge (e_i) and mathematically described by
  - Geometric parameters (such as the length, width, height)
  - Surface properties (such as the contact angle)
- Each junction is represented by a node (N_j) and treated as a point connection between the upstream and downstream edges.
- The inlet and outlet are also treated as special nodes, which are only connected to the downstream edge or the upstream edge, respectively.

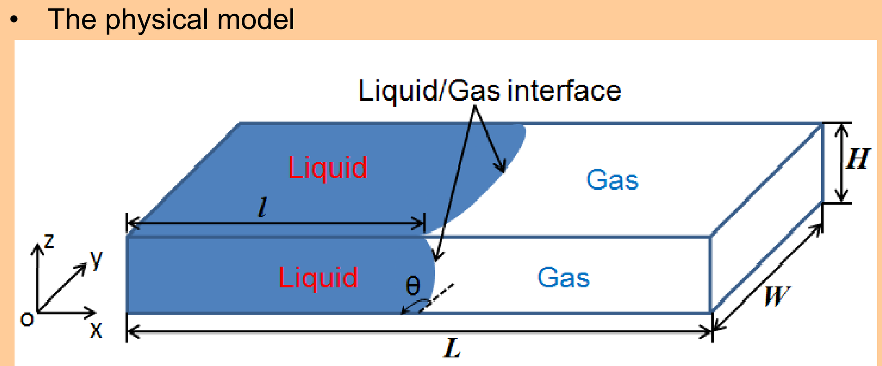


A simple microfluidic splitter : (a) the physical model (b) system-level model representation

Computational Model

Component Model

- Assumptions:
  - The flow is fully developed (the entry region at the channel inlet is neglected)
  - The model does not take into account the formation and transportation of air plug in the microfluidic networks.
- Microchannels
  - The physical model



- Liquid filling status: void, partially-filled, fully-filled
- Governing equations:

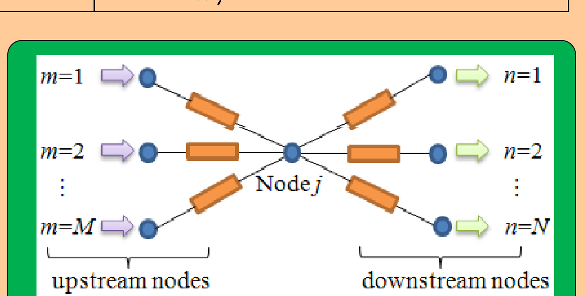
Simplified N-S Equation $$\frac{\partial^2 u}{\partial y^2}+\frac{\partial^2 u}{\partial z^2}=-\frac{1}{\mu}\frac{\partial P}{\partial x}$$

Filling status	Liquid length (l)	Balance Equation
Void	$l=0$	$P_{in}-P_{out}=0$
Partially-filled	$0<l<L$	$2\sigma\cos\theta(1+\beta)+(P_{in}-P_{out})W-\frac{12\mu l}{W\gamma}\frac{dl}{dt}=0$
Fully-filled	$l=L$	$\frac{12\mu L}{W\gamma}U-(P_{in}-P_{out})W=0$

- Junctions
  - Filling status: void, filled
  - Governing equation:

$$\sum_{m=1}^{M}Q_m^j-\sum_{n=1}^{N}Q_n^j=0$$

(at node j)



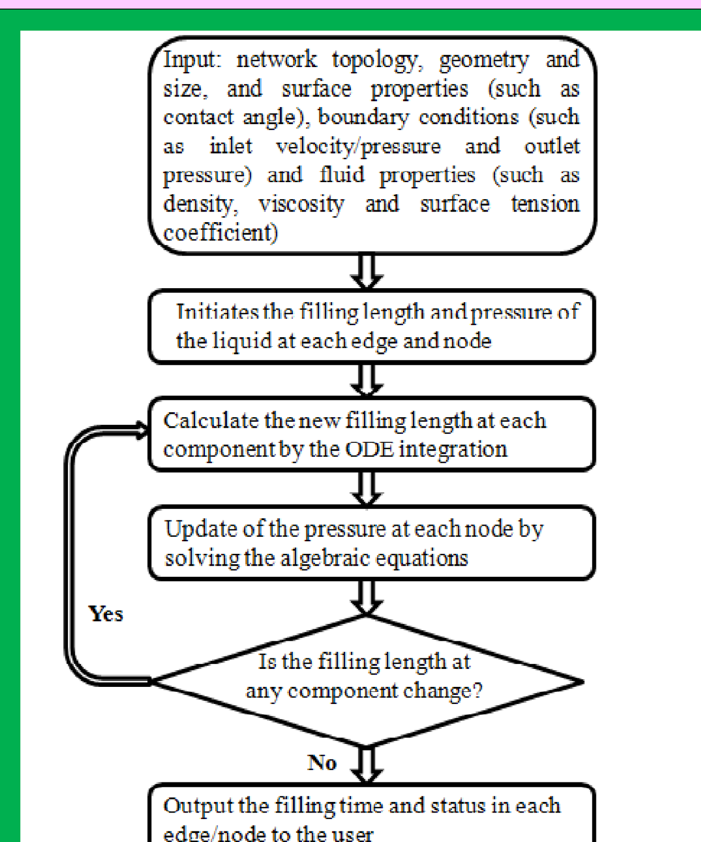
Schematic for the connection of node j

Systematic Model

- Liquid flows entering and exiting node j are a function of pressures across the surrounding edges and are linked

$$\sum_{m=1}^{M}Q_m^j\left(P_m^{in}-P_m^{out}\right)-\sum_{n=1}^{N}Q_n^j\left(P_n^{in}-P_n^{out}\right)=0$$

- Fluidic parameters and filling time at the outlet of the upstream edge is set equal to that at the inlet of the downstream edge via each node
- Equation is applied to each node yielding **a set of algebraic equations** for the network.
- Two steps are **recursively iterated** to track the propagation of the liquid front s in the edges and update pressures at the nodes



Flow chart of the system level model of liquid filling process in microfluidic network

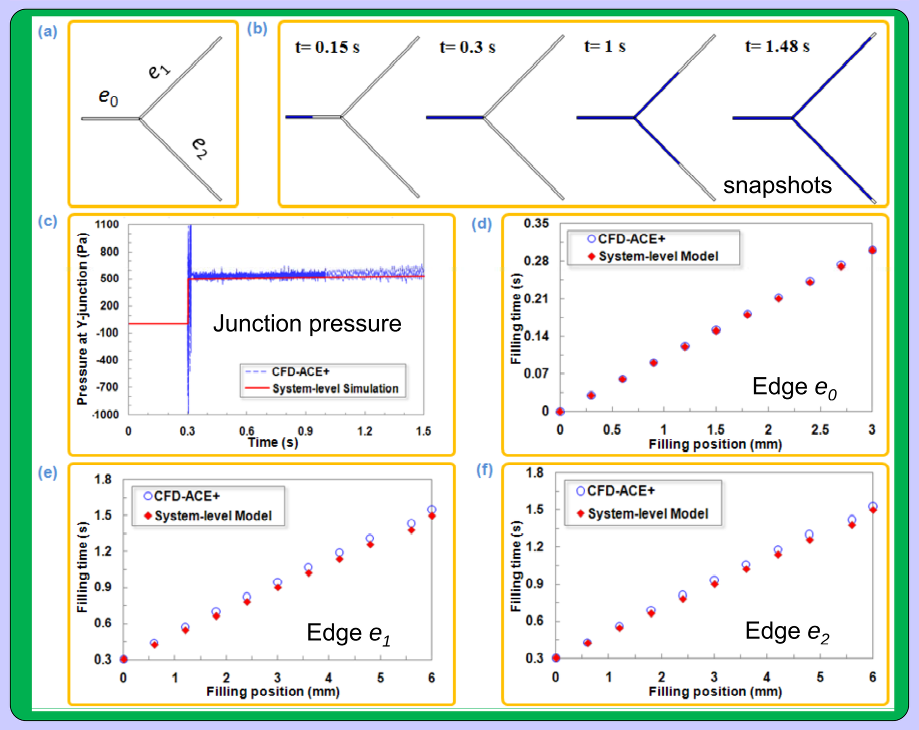
Results and Discussion

Liquid Filling in Y-Shaped Channels

Y-channel with the Same Branch Channel Width

- Excellent agreement with high fidelity model (CFD-ACE+) at all times in all the channels with a **relative error <6%.**

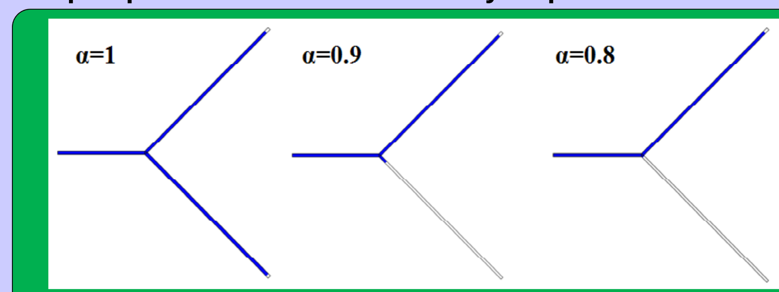
Channel Length (µm)			Channel Width (µm)	Inlet Velocity (m/s)	Contact Angle (°)
e_0	e_1	e_2			
3	6	6	100	0.01	110



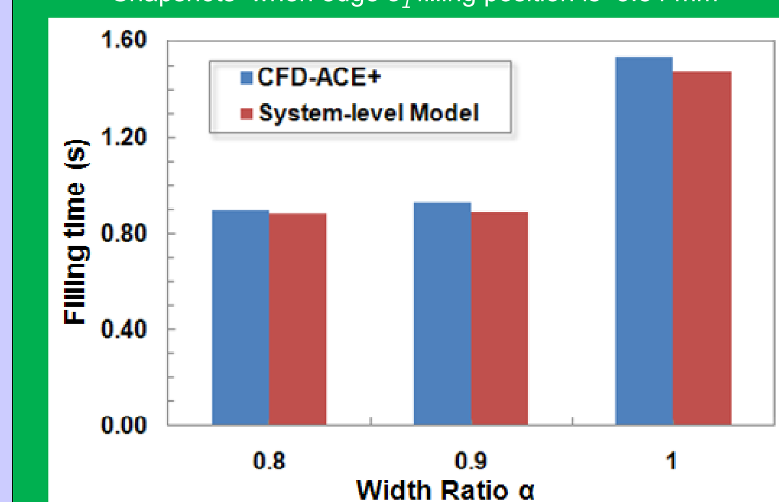
CFD-ACE+	System-level Model	Speedup	Relative error (%)
183600 sec	0.39 sec	**470,000X**	**<6**

Effect of the Width of the Branch Channel

- Define width ratio $\alpha = W_2/W_1$
- Asymmetric filling processes due to the unequal branch channel widths
- Good agreement with **relative error less than 4.1 %.**
- **Liquid prefers to enter the wide hydrophobic channels**



Snapshots when edge e_1 filling position is 5.84 mm

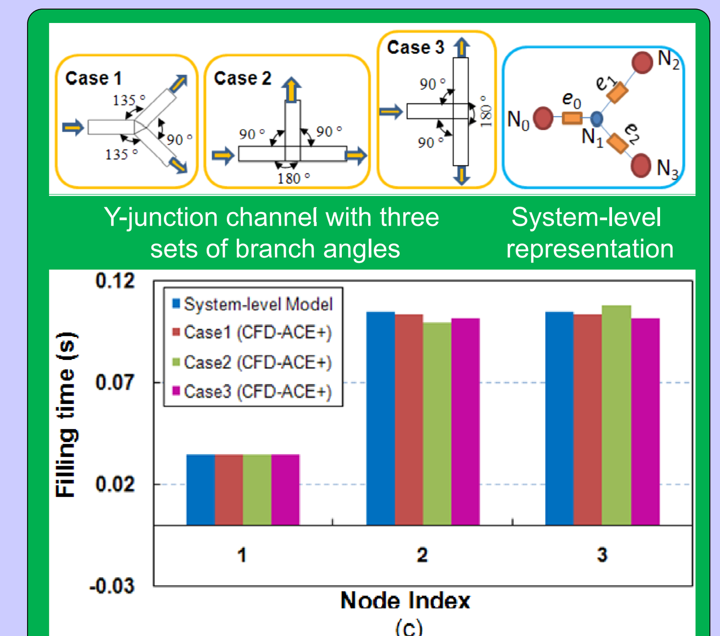


The filling time when edge e_1 is fully filled

Effect of the Branch Angles

- Case 1={135°, 90°, 135°}
  Case 2={180°, 90°, 90°}
  Case 3={90°, 180°, 90°};
- Good agreement with **relative error <5.4%**
- **Branch angle effects are negligible for liquid filling**

CFD-ACE+	System-level Model	Speedup	Relative error (%)
1200 sec	0.031 sec	**38,000X**	**<5.4**

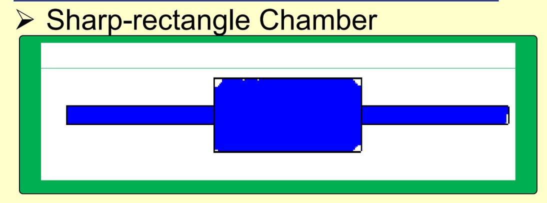


The filling time at the nodes

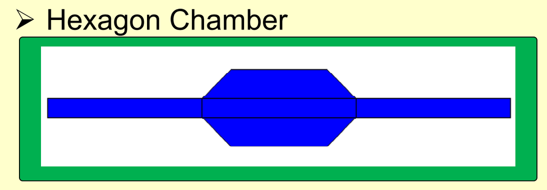
Liquid Filling in Abrupt Structures

Three different abrupt structures

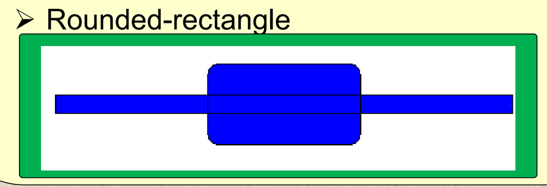
- Sharp-rectangle Chamber



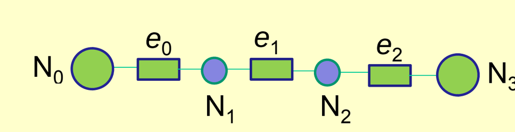
- Hexagon Chamber



- Rounded-rectangle



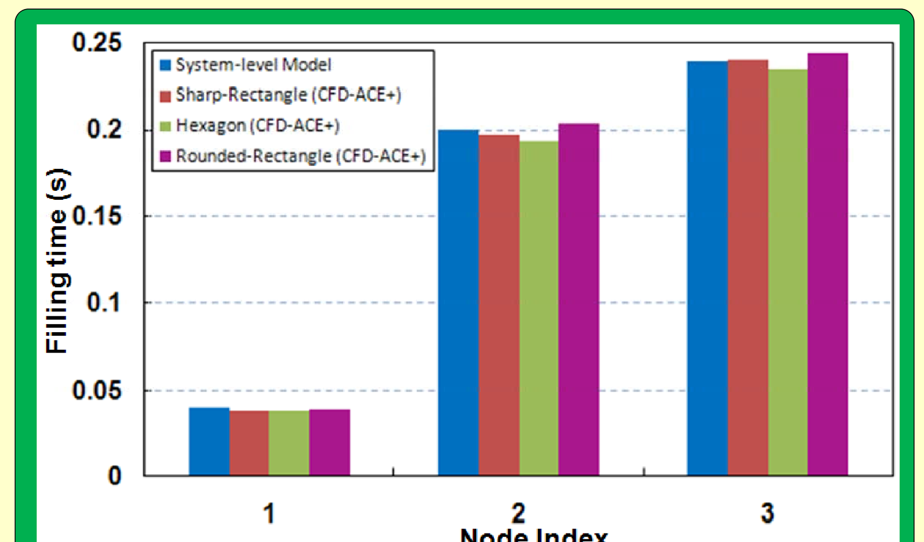
- System-level Model Representation



Parameter		Value
Channel Length (µm)		400
Channel Width (µm)	e_0	50
	e_1	200
	e_2	50
Inlet Velocity (m/s)		0.01
Contact Angle (°)		110

- Result analysis:
  - Good agreement with **the relative error <4%.**
  - **The filling times at the nodes (junctions) are almost independent of the shapes**
  - The dispenser with transitioning structures are completely filled, but **small air bubbles were trapped at the corner in the sharp-rectangle dispenser**

CFD-ACE+	System-level Model	Speedup	Relative Error (%)
7200 sec	0.047 sec	**150,000X**	**<4**

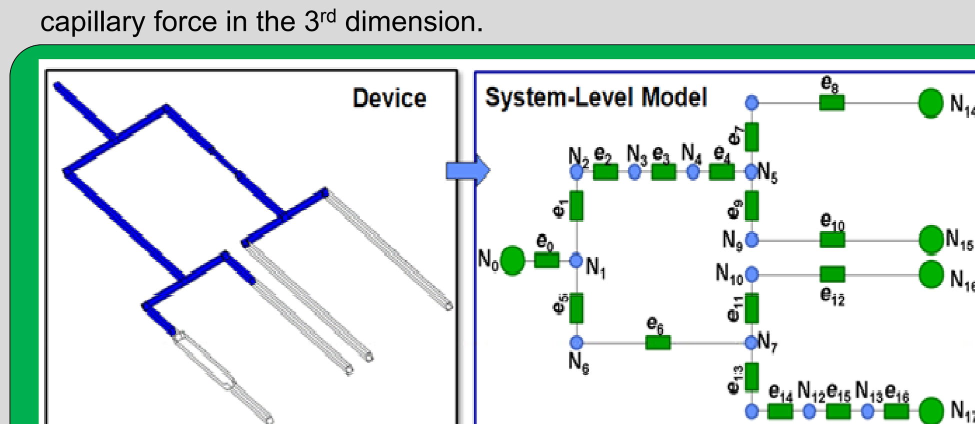


The filling time at the nodes

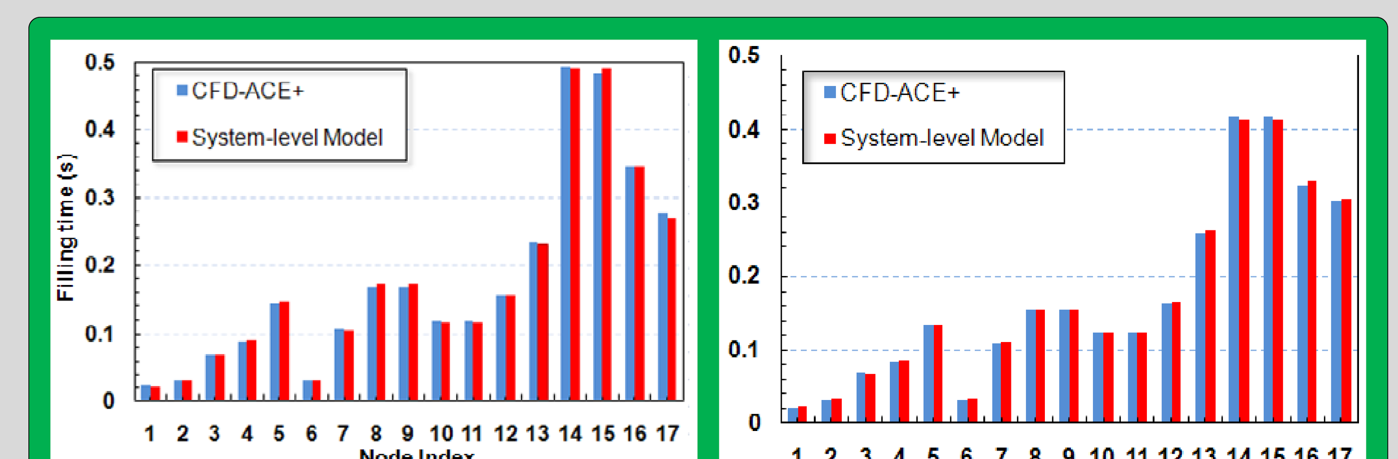
Liquid Filling in Microfluidic Multiplexers

Two-tier Microfluidic Multiplexer

- Both 2D (i.e., $H>>W$) and 3D (H = 100 µm) simulation were undertaken.
- Good agreement with the **relative error <4%** for both 2D and 3D cases
- The arrival time to the outlet node N_{14} and N_{15} are the longest, and are 30–60% more than the other two outlet nodes (N_{16} and N_{17}).
- The asymmetric liquid filling in branch channels caused by the abrupt geometries in the 2D case is more noticeable than the 3D case due to the introduction of the capillary force in the 3rd dimension.



The physical model System-level representation



2D channel network 3D channel network

	CFD-ACE+	System-level Model	Speedup	Relative Error (%)
2D	42900 sec (11 hour 55min)	0.235 sec	**180,000X**	**<4**
3D	864000 sec (about 10 days)	0.203 sec	**4200,000X**	**<4**

Conclusions

Conclusions

- Our reduced order liquid filling model is validated against high-fidelity computations in **a variety of microfluidic constructs** (including symmetric branching channels with various junction shapes, asymmetric branching channels, and abrupt cross-section channels) and complex microfluidic networks (e.g., multiplexer).
- The system-level model demonstrates **order-of-magnitude speedup (30,000X – 4,000,000X)** over the high-fidelity simulation along with good agreement (**the worst relative error less than 6%).**
- The parametric analysis in various microfluidic structures **provides several key findings** that can be exploited for practical chip design:
  - The filling process is virtually independent of the branch angles
  - The channel width has significant impact on liquid filling. Liquid tends to enter the hydrophobic (or hydrophilic) channels with small (or large) surface-to-volume ratios. Therefore, channels with distinctly different sizes should be circumvented if homogeneous liquid filling is desired.
  - Despite its minor impact on filling time, the abrupt features in microfluidic structures may trap air bubbles and jeopardize the functionality of the chip, and hence, should be minimized.
  - Depending on the application, local variations in geometry (e.g., asymmetric shapes) or surface properties can be exploited to precisely manipulate liquid filling (at desired positions and times).

Future Efforts

Model extension to account for kinematics of the isolated gas phase (such as air bubble trapping and propagation) and integration of the model with our system-level microfluidic design tool

Acknowledgements

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