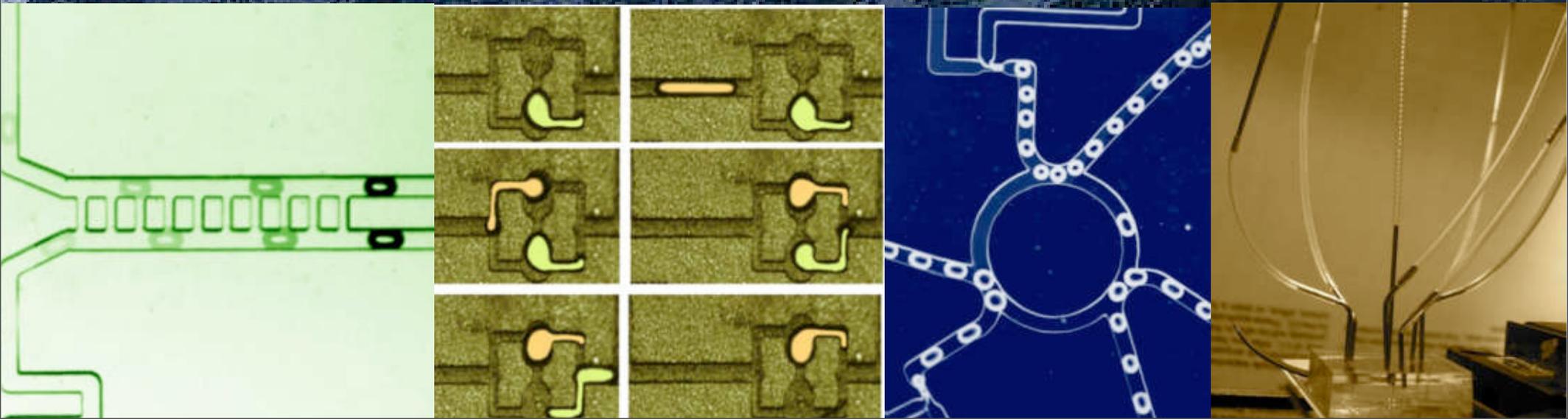
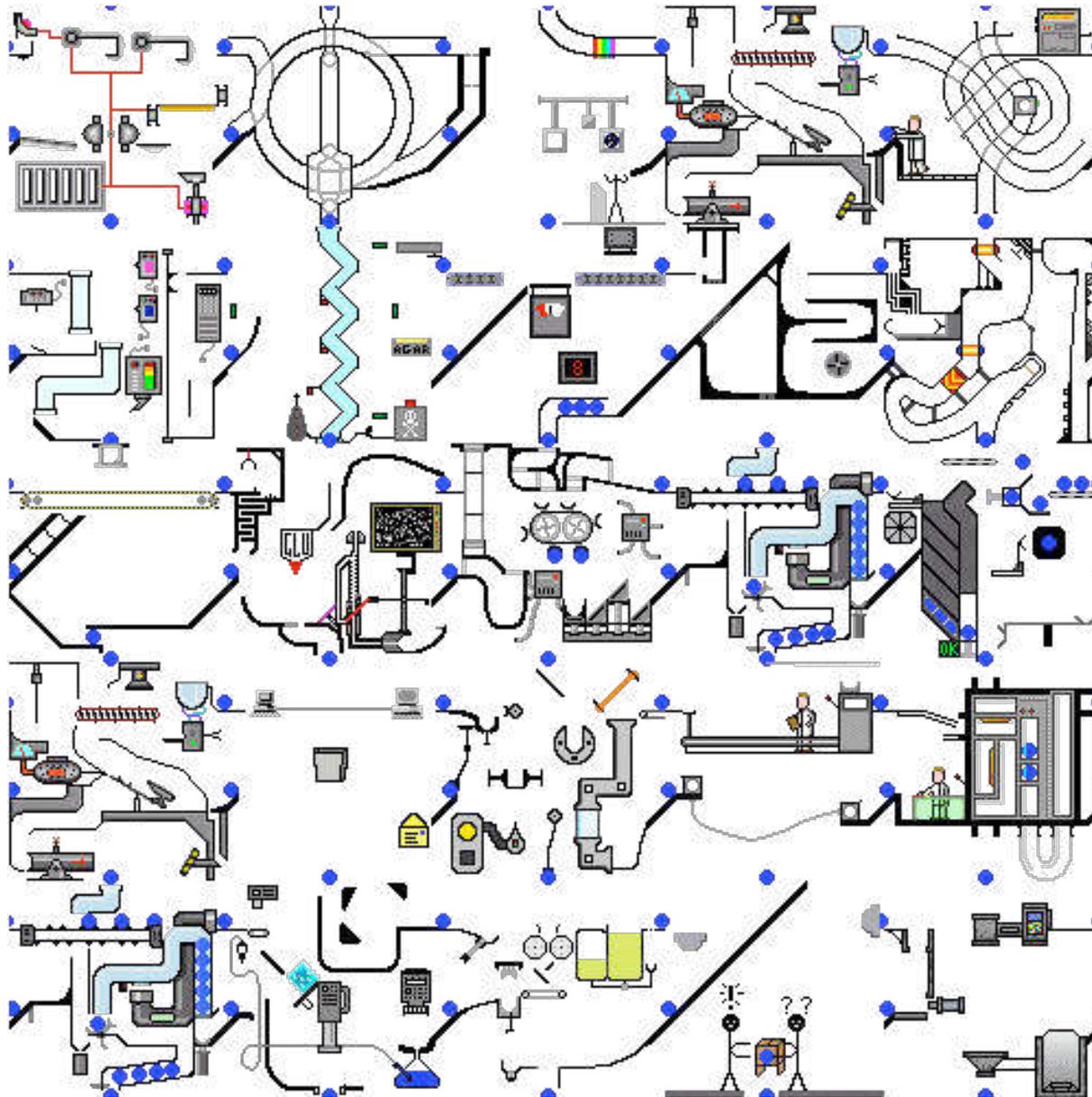


Microfluidic Bubble Logic

Manu Prakash
Massachusetts Institute of Technology



Future of materials (chemical/biological) processing



Bubble logic
Capillary ratchet
Micro-slot detector

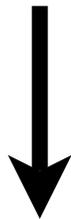
Information is Physical

“Information is inevitably tied to a physical degree of freedom through a charge, a spin, a hole in punch card or chalk marks on a blackboard”

Rolf Landauer, 93



Bits are Atoms



Information processing => Material processing

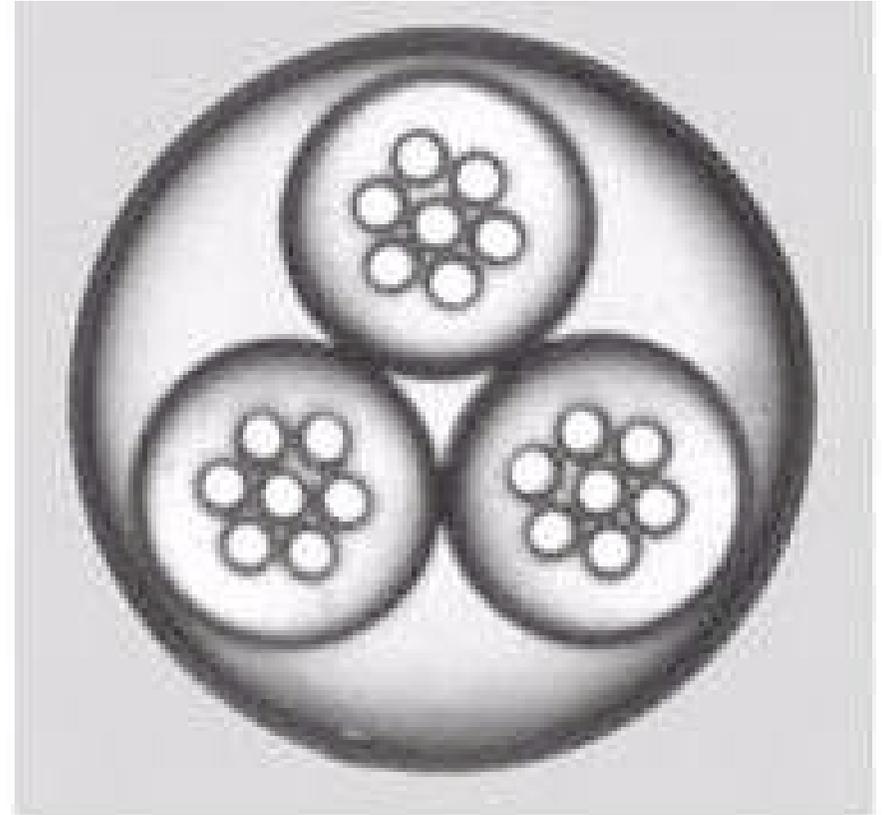
Drops and Bubbles

1737



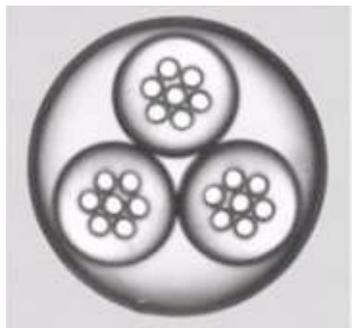
Young man blowing bubbles
Oil on canvas 61 x 63 cm
Metropolitan Museum of Art, New York

2007

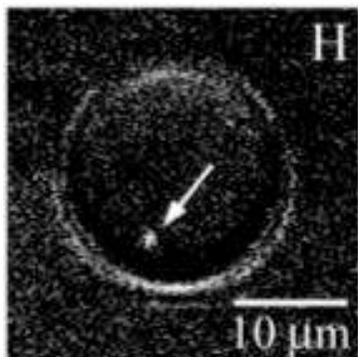


Weitz Group, Harvard

Trapping

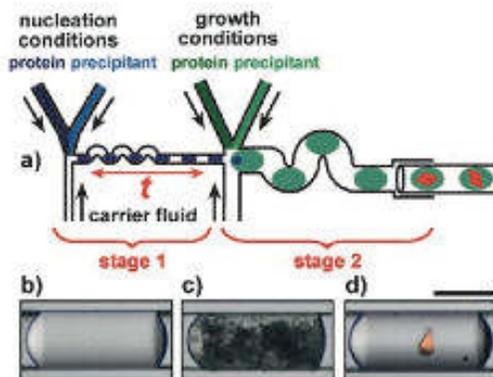


Weitz 2007 (unpublished)



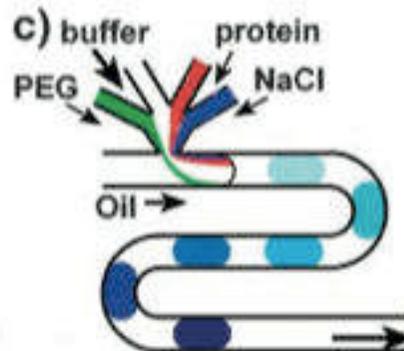
D. Chiu, Anal. Chem 2005

Reactions



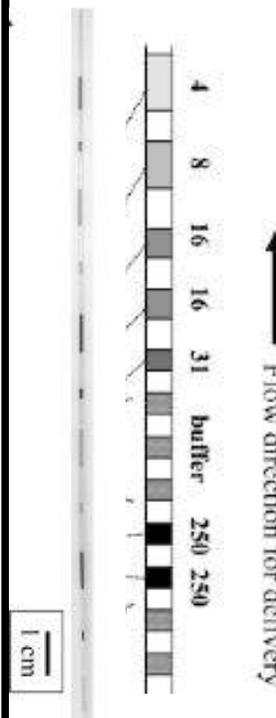
Multi-step protein (thaumatin) crystallization
Ismagilov, Angew. Chem. 2006

Optimization/ Mixing



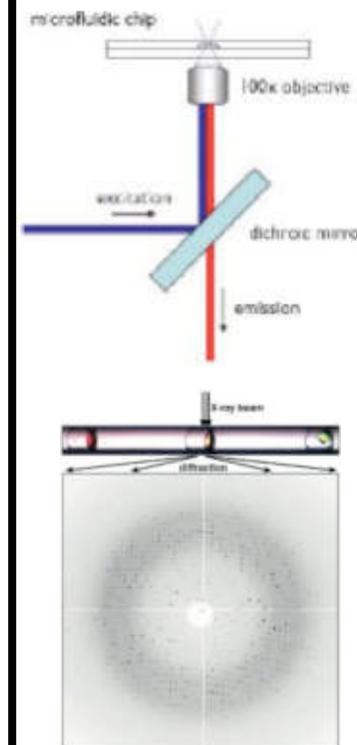
Gradient screening for crystallization conditions
Ismagilov, 04

Storage

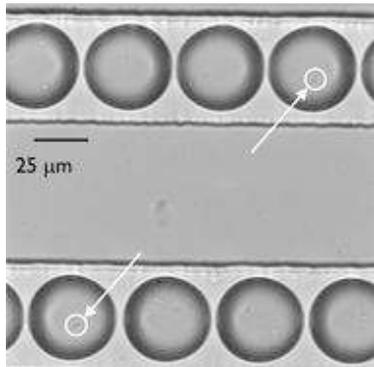


Whitesides 05

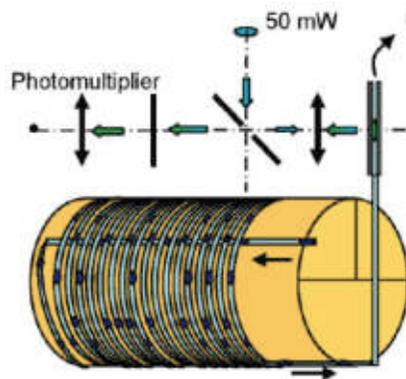
Detection



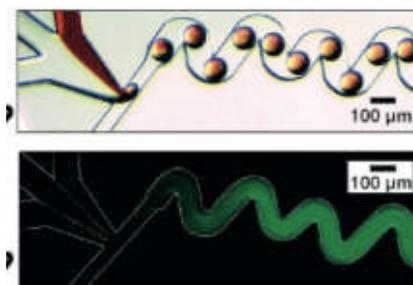
Ismagilov 2006



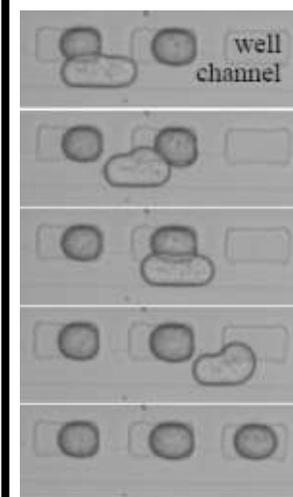
Huebner et al. ChemComm
Jan 2007



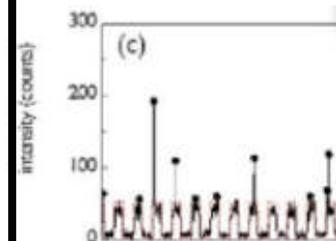
PCR in a drop (Chabert,
Nov. 06)



Milli-second time scale
mixing



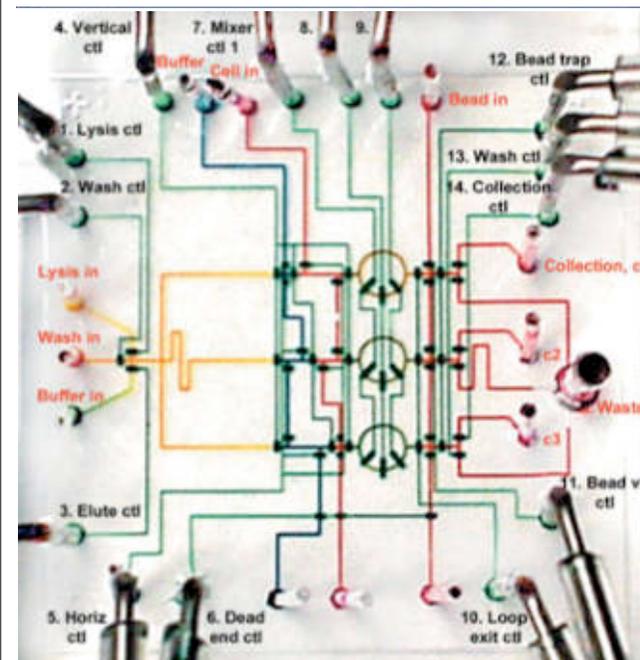
Fraden 06



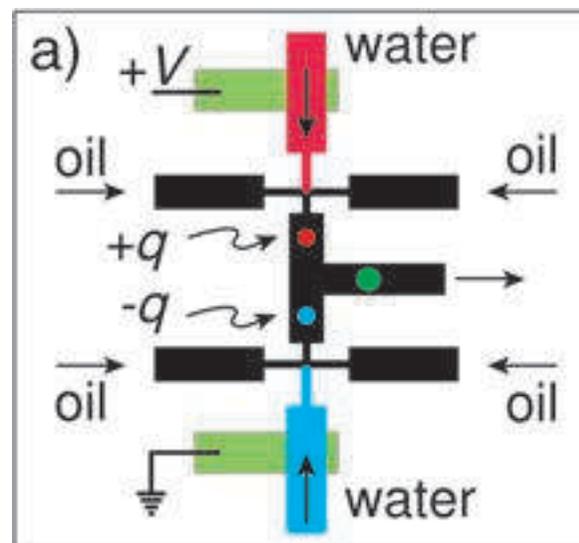
Huebner
ChemComm07

Control Strategies

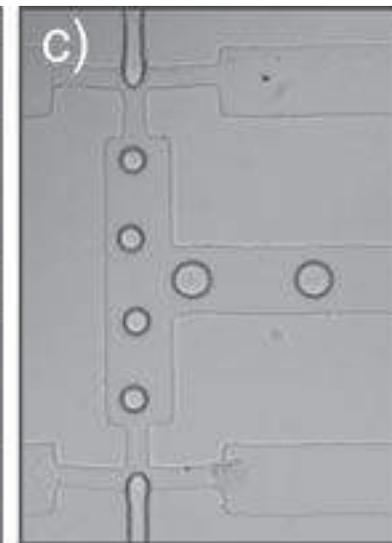
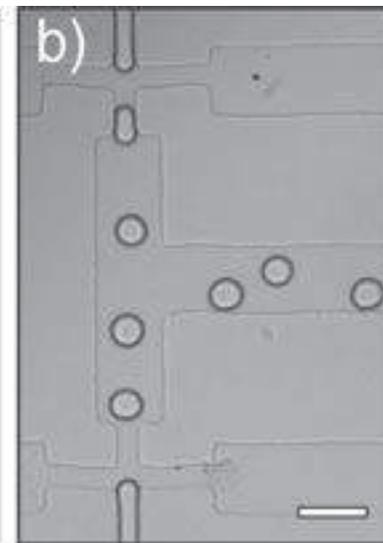
portability
scaling



Fluidigm



RainDance
Technologies



Bubble Logic

On-chip process control

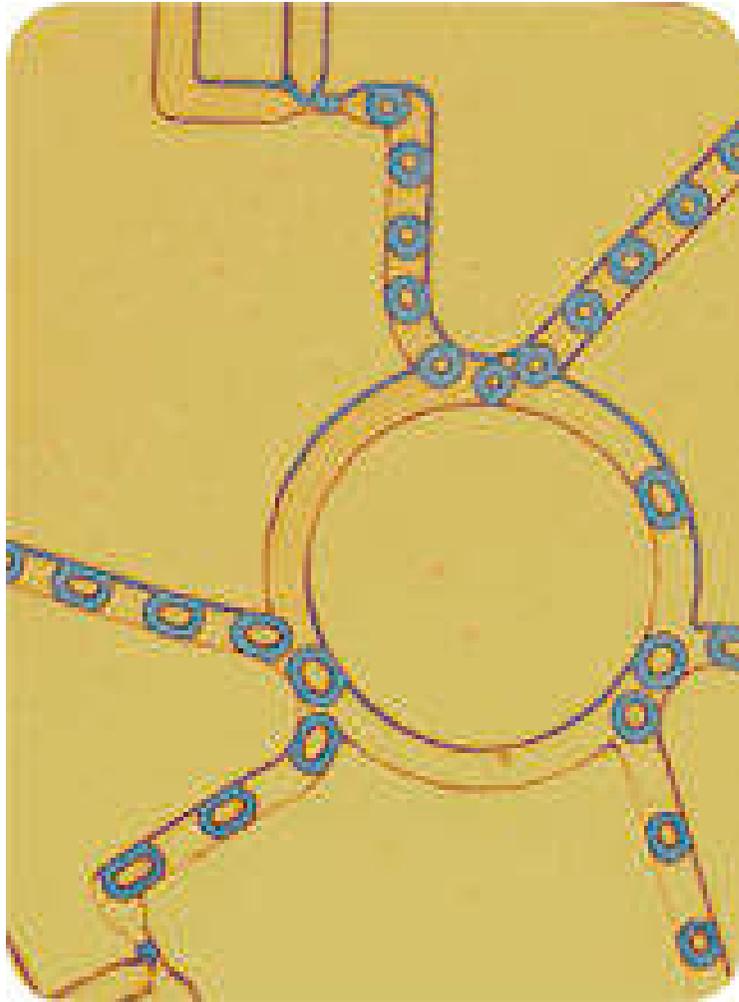
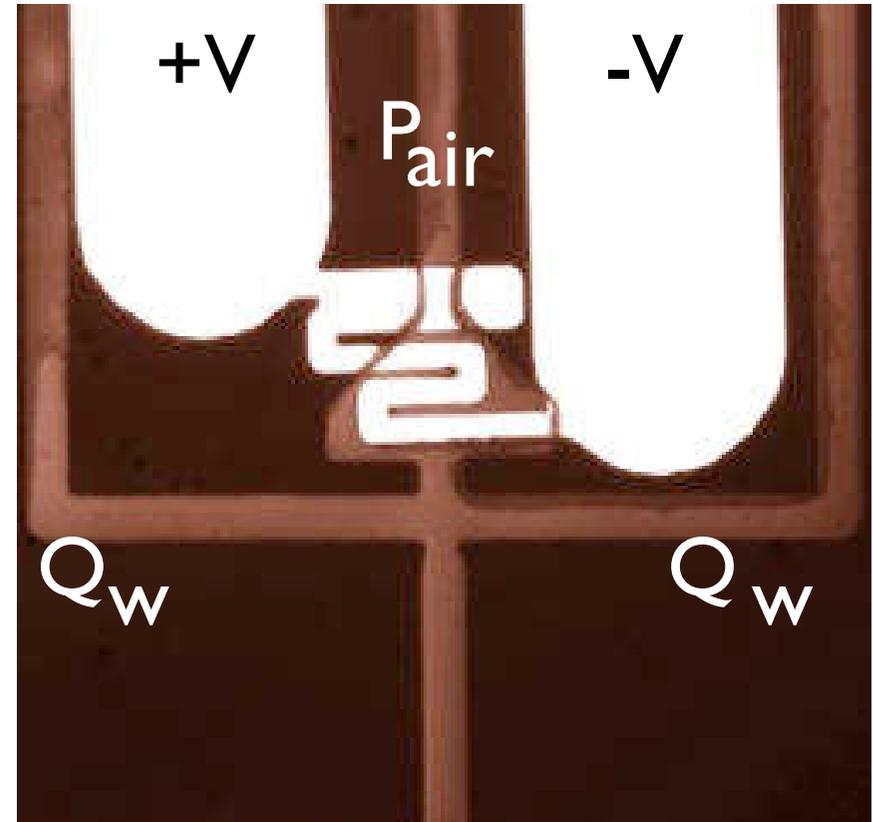
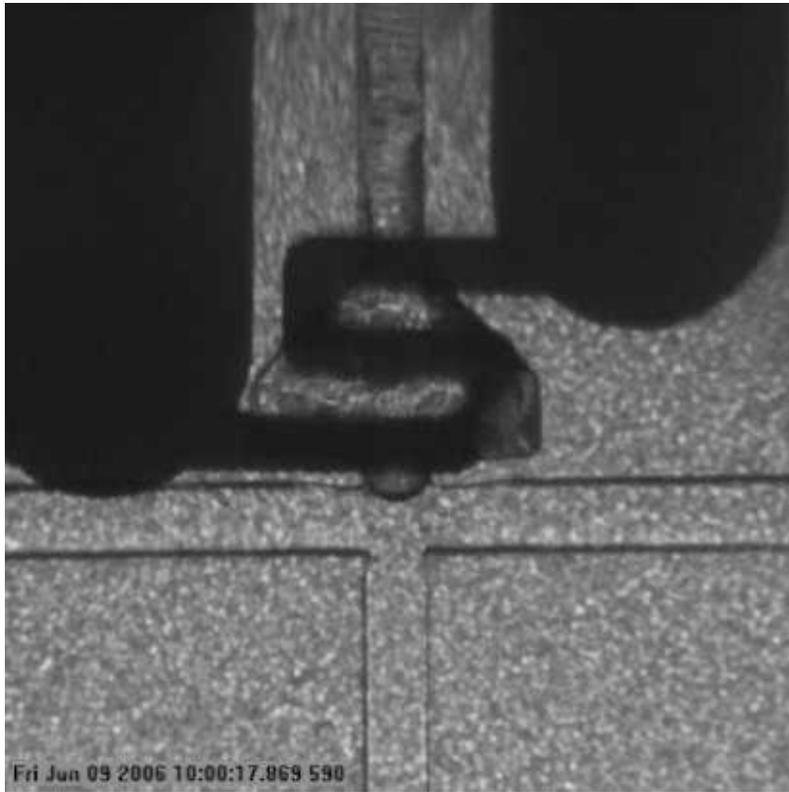


Image credit : F. Frenkel, M. Prakash

- A bubble is a bit of information, but can also carry a material payload
- Integrating chemistry and computation

[Prakash, Gershenfeld; Science Vol. 315 2007]

Programmed generation of bubbles



$$\Delta P + \tau = Ca^{-1} k$$

$$Ca = \mu U / \sigma$$

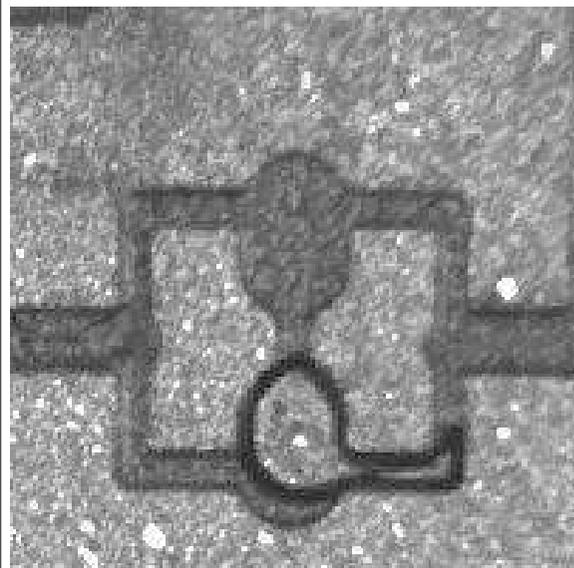
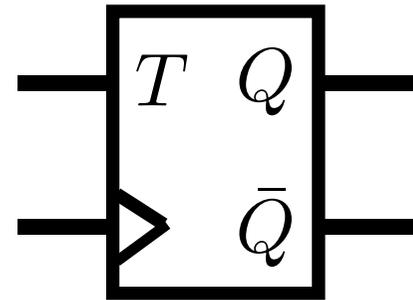
R = 95 Ω , 20V 100ms pulse

Microfluidic Toggle Flip-Flop

- One bit memory
- If T input is “high”, the flip-flop “toggles” state. If T is “low”, the flip-flop holds its state

$$Q_{next} = T \oplus Q$$

$$Q_{next} = T\bar{Q} + \bar{T}Q$$

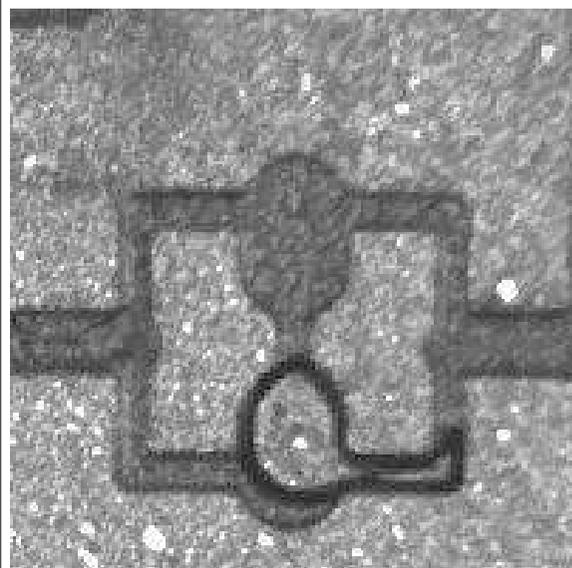
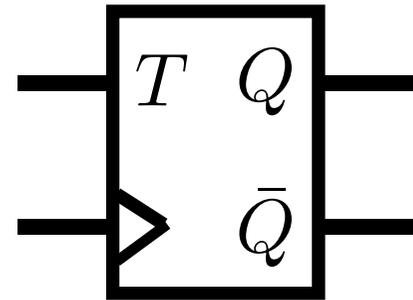


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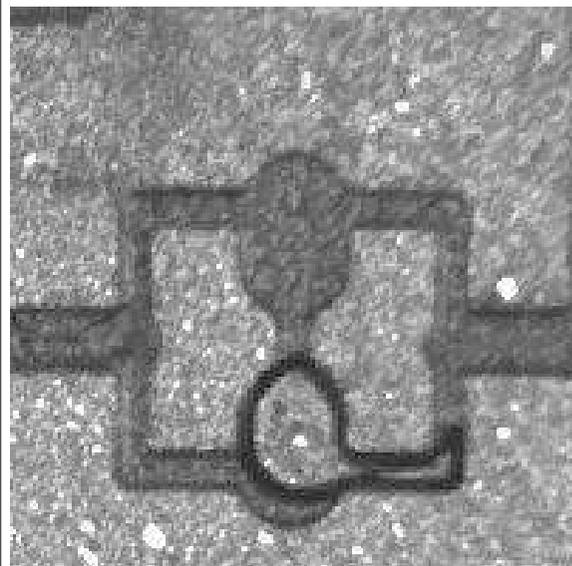
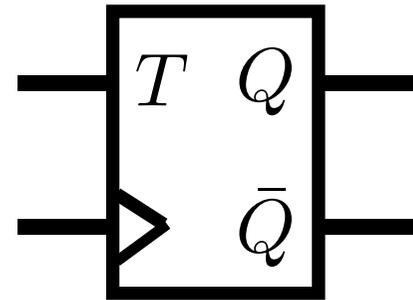


Microfluidic Toggle Flip-Flop

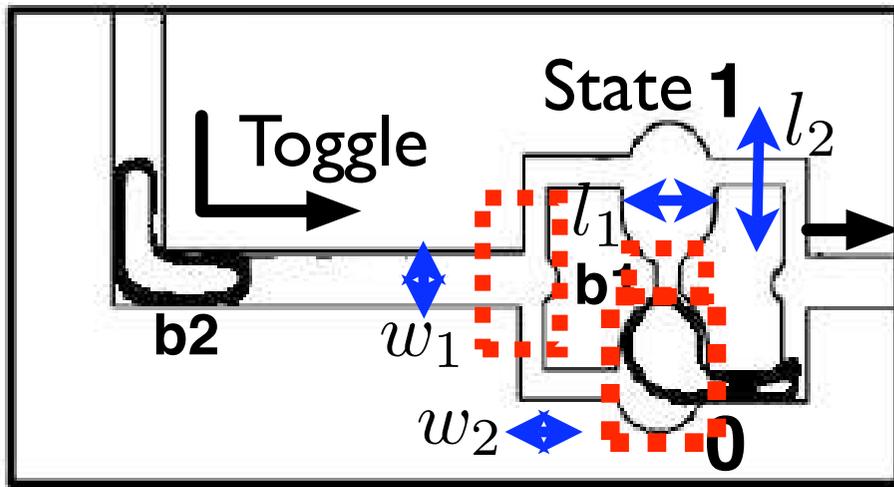
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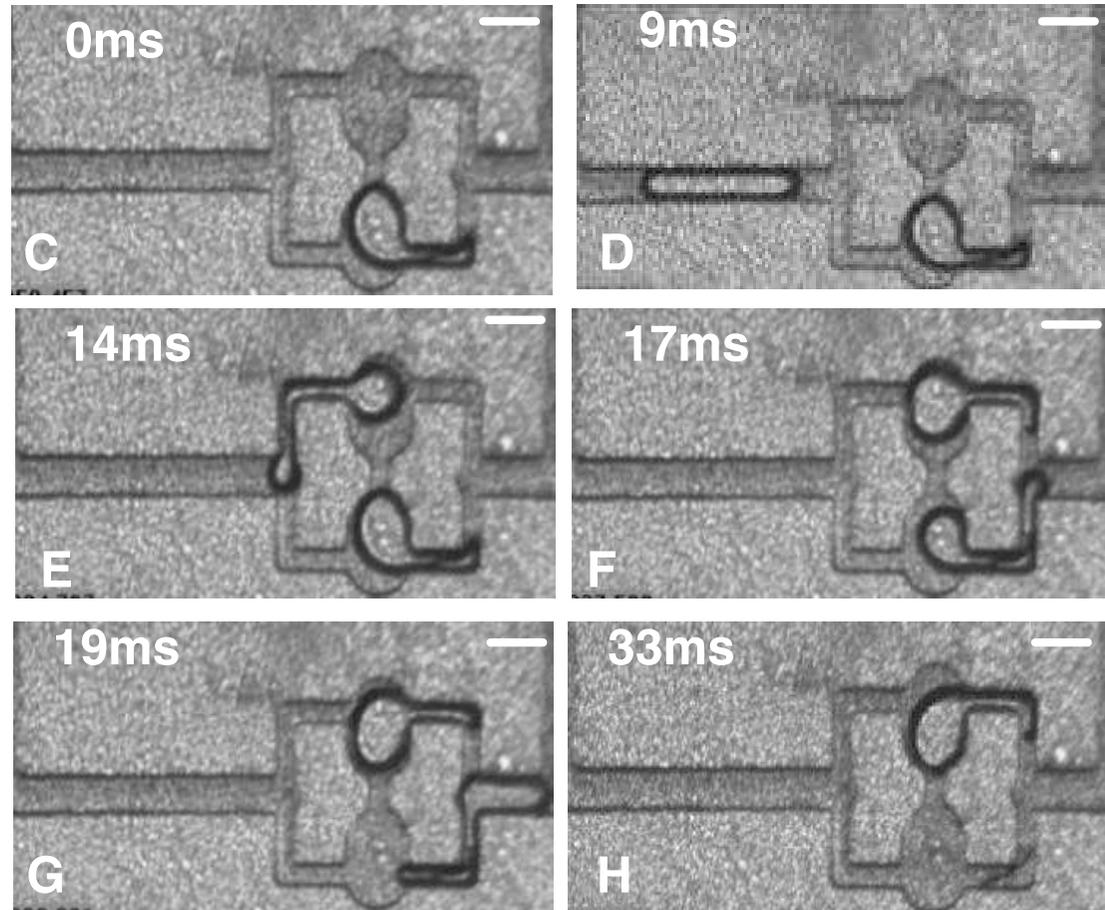


Device Physics



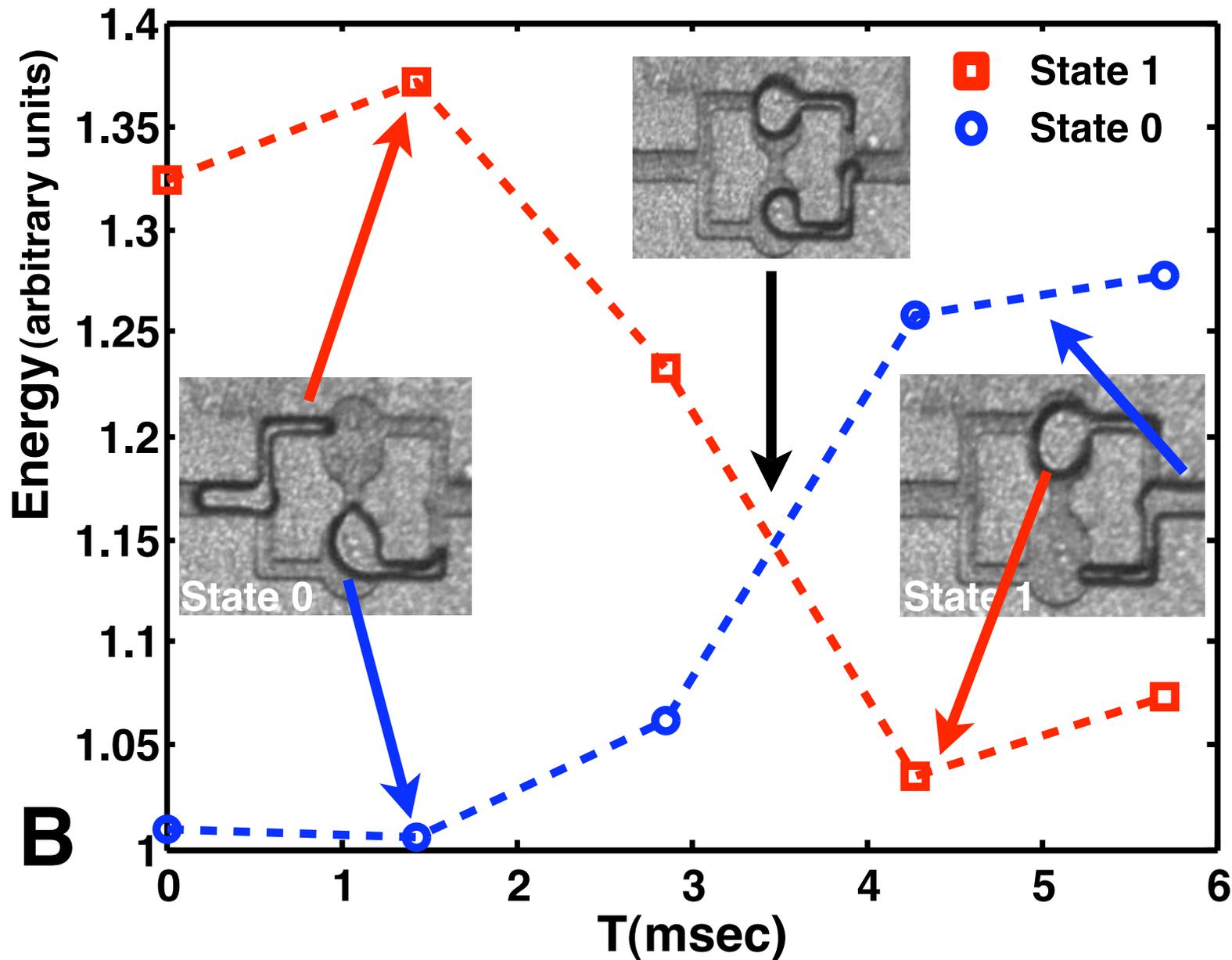
$$w_1 = 100\mu m, w_2 = 40\mu m, h = 70\mu m$$
$$l_1 = 200\mu m, l_2 = 300\mu m$$

T junction followed by two elliptical lobes, forming energy minima :
Connected via a feedback channel



Switching time $\tau = 8ms$

Surface Free Energy



$$S = \sigma l_g A$$
$$S \propto P_{\text{perimeter}}$$

Bifurcation at T junction

Rayleigh-Plateau breakup at the T junction

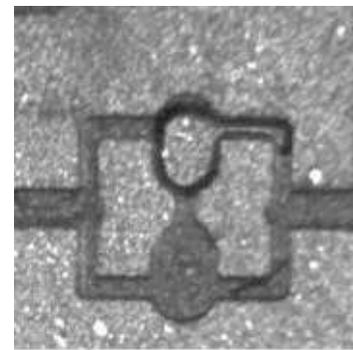
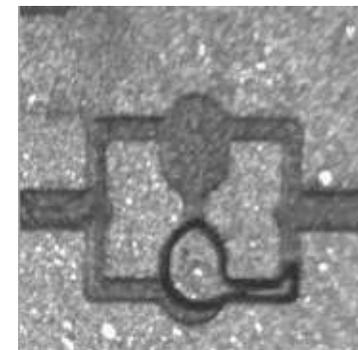
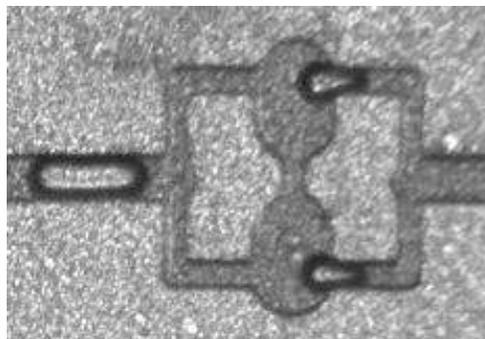
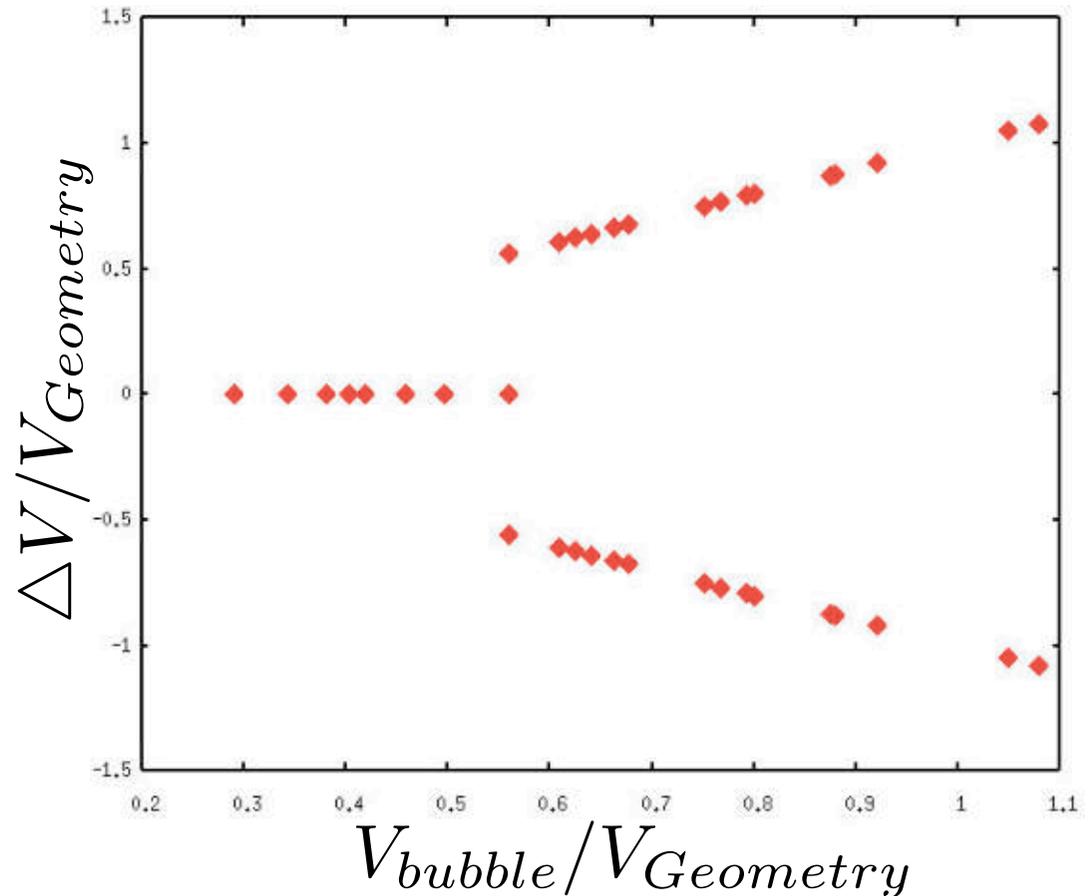
$$l/\pi w = 1$$

[H.A. Stone, PRL 2004]

Behavior independent of bubble arrival frequency

[Garstecki, PRE, 2006]

[Ajdari, PRL 2005]



Bifurcation at T junction

Rayleigh-Plateau breakup at the T junction

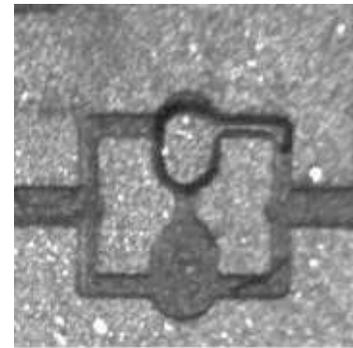
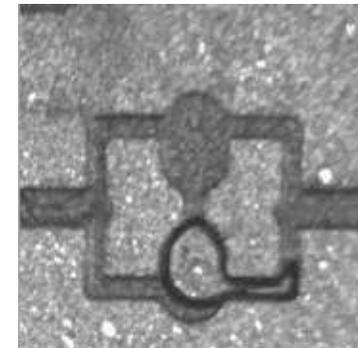
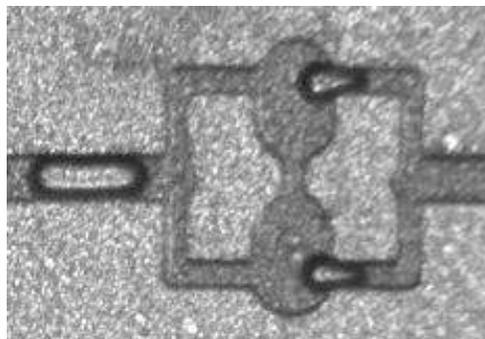
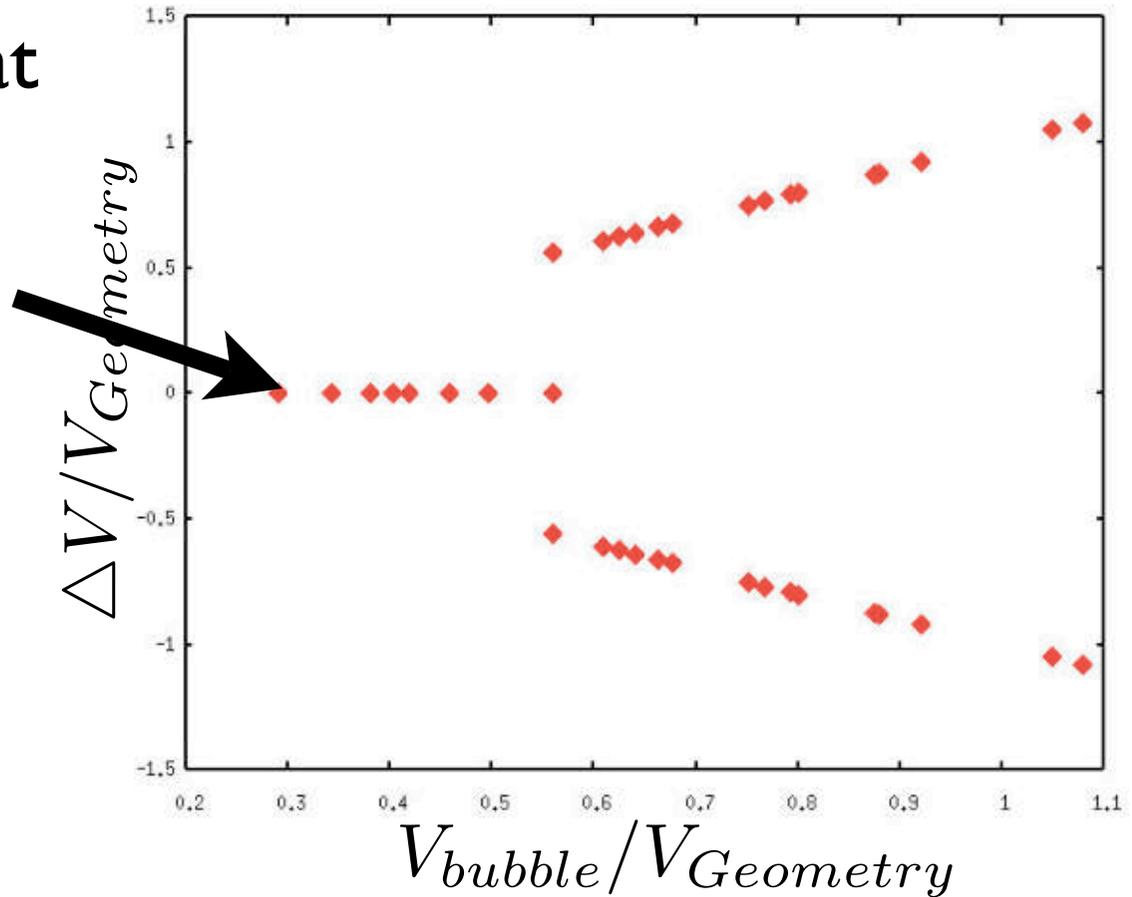
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Bifurcation at T junction

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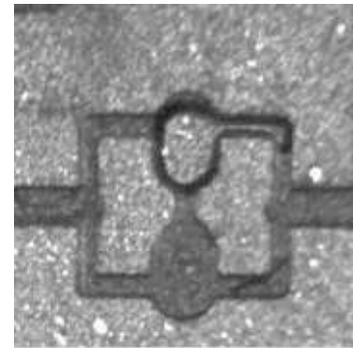
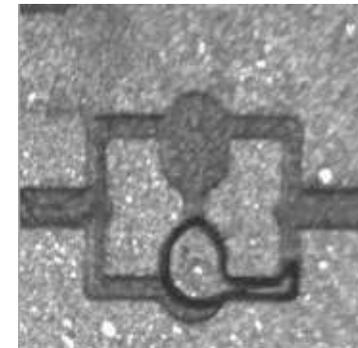
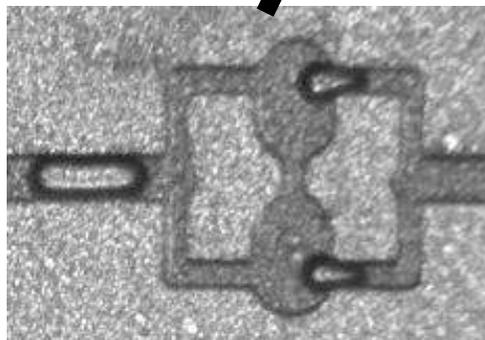
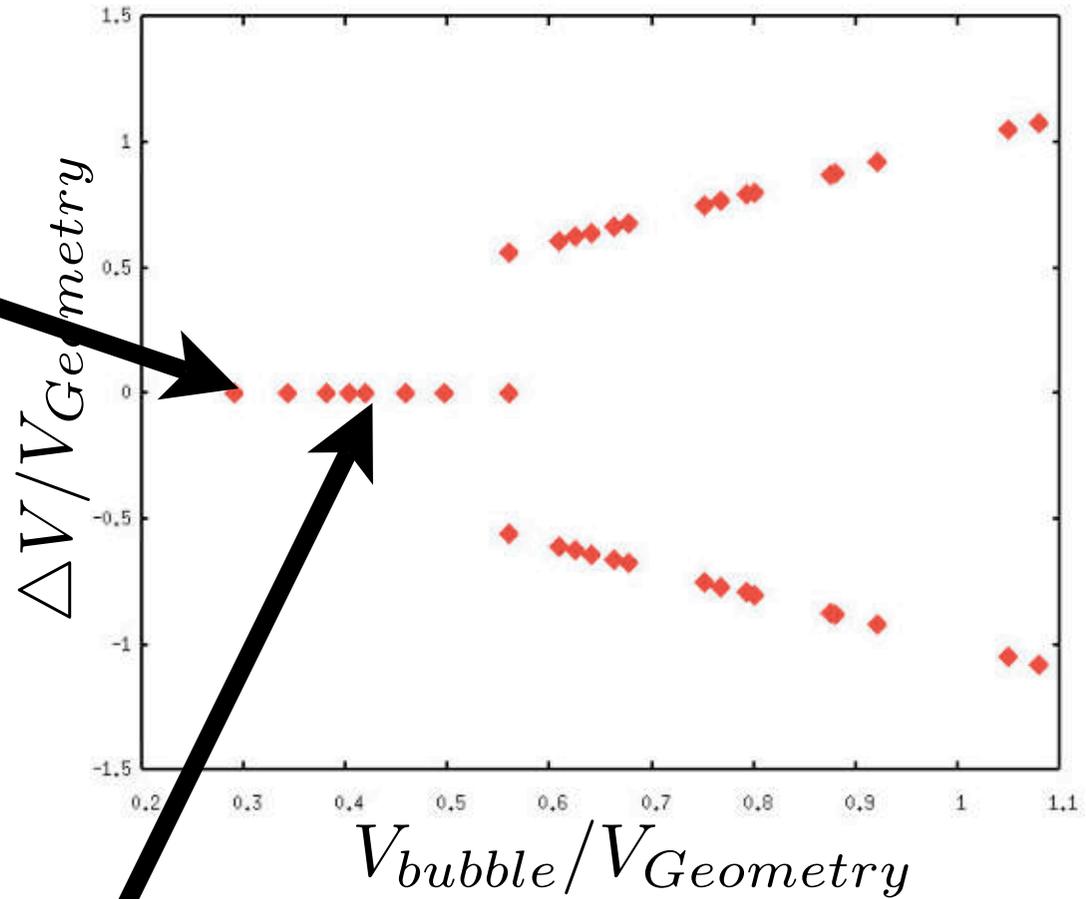
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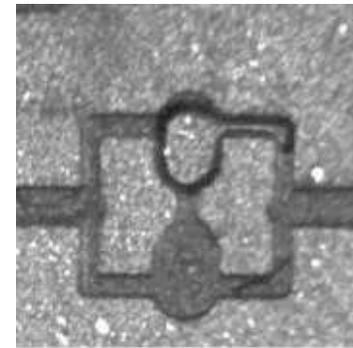
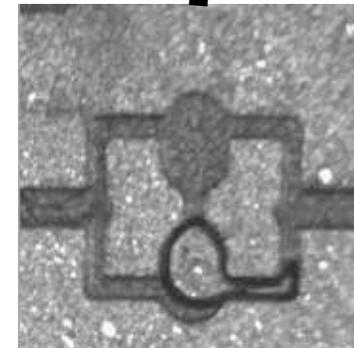
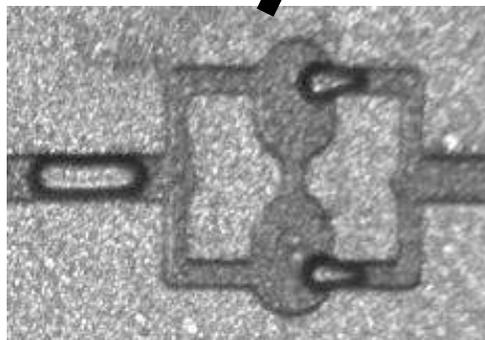
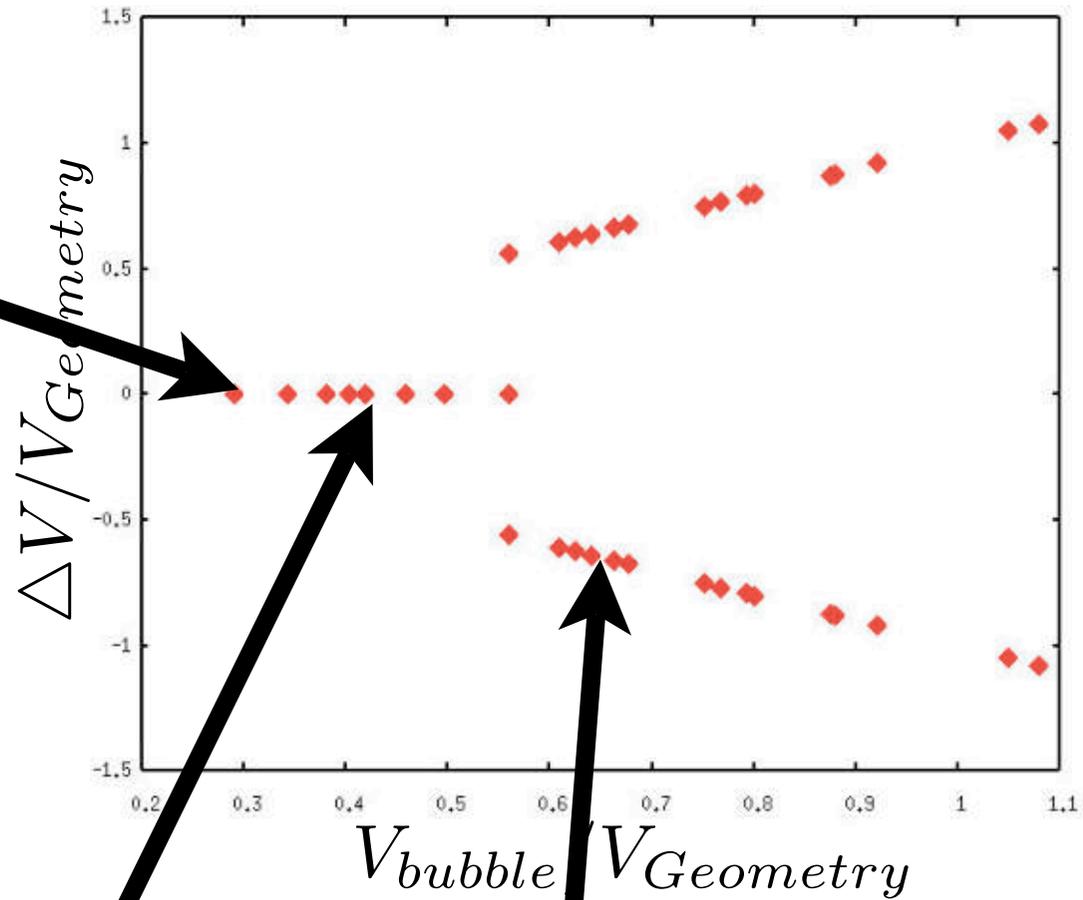
$$l/\pi w = 1$$

[H.A. Stone, PRL 2004]

Behavior independent of bubble arrival frequency

[Garstecki, PRE, 2006]

[Ajdari, PRL 2005]



Bifurcation at T junction

Rayleigh-Plateau breakup at the T junction

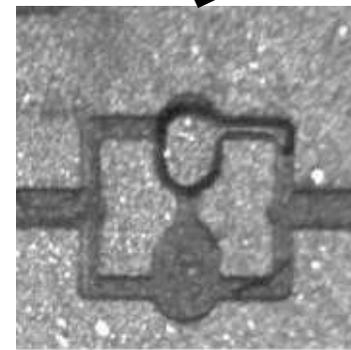
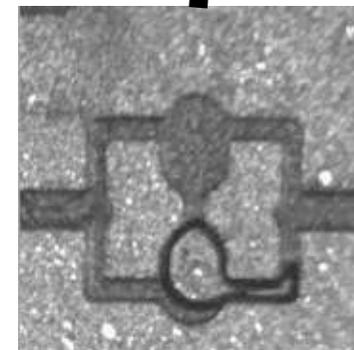
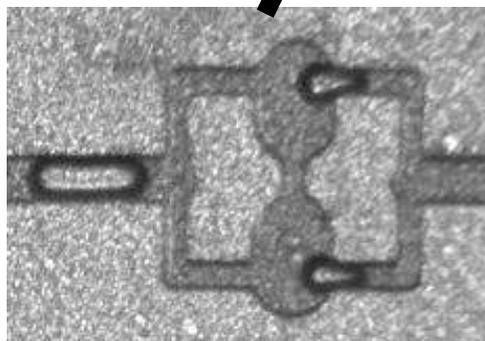
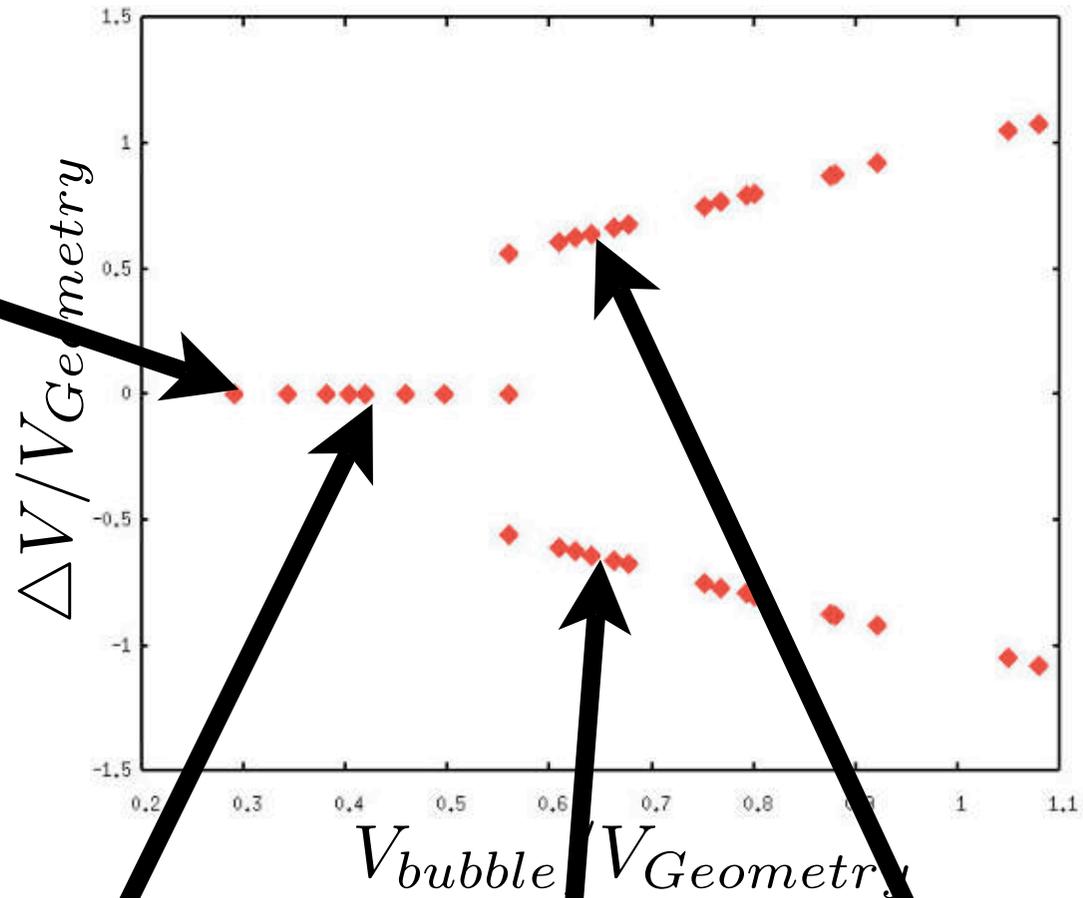
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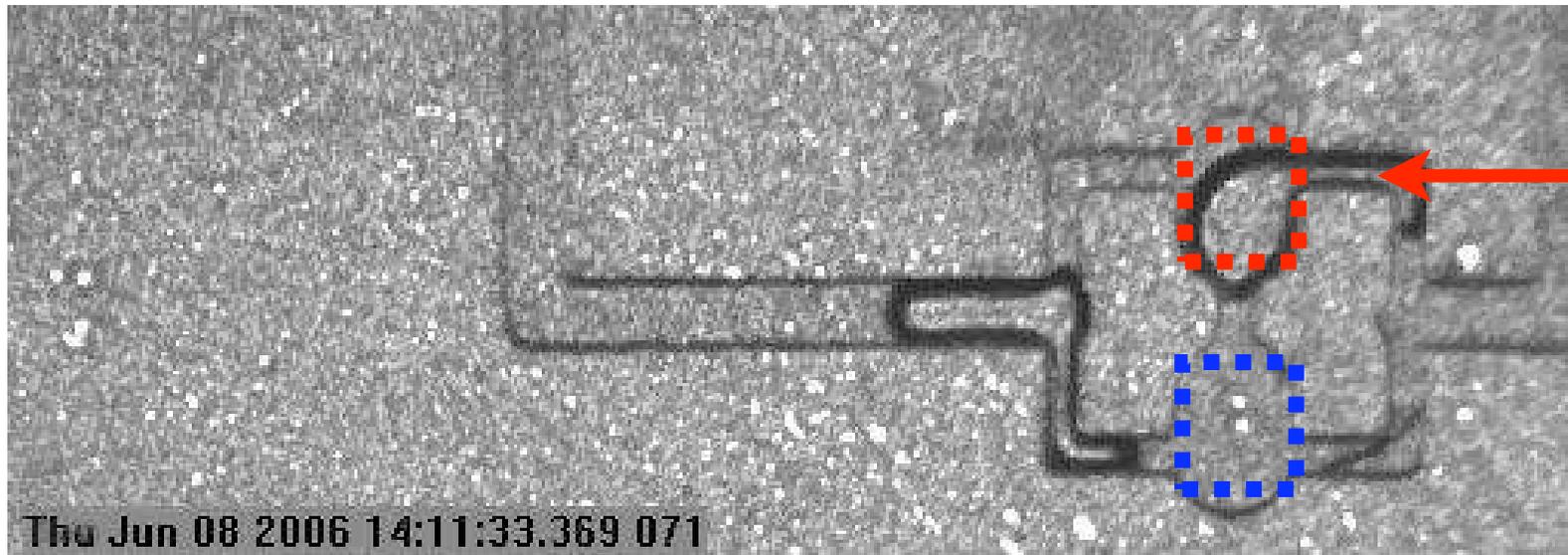
Behavior independent of bubble arrival frequency

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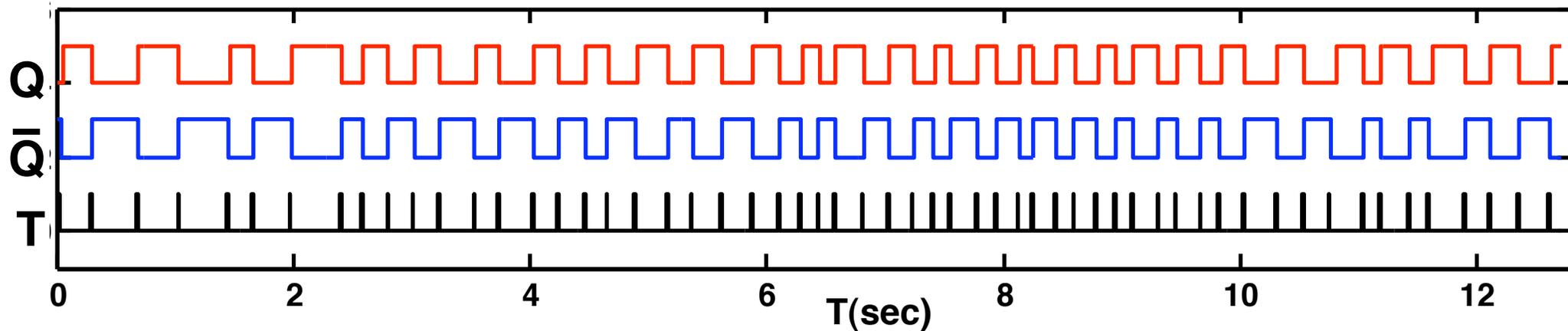


Trap repeatability

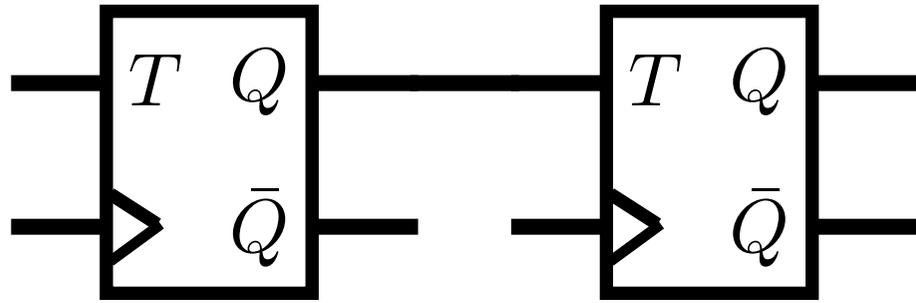


light intensity
vs
time

10Hz bistable one-bit memory

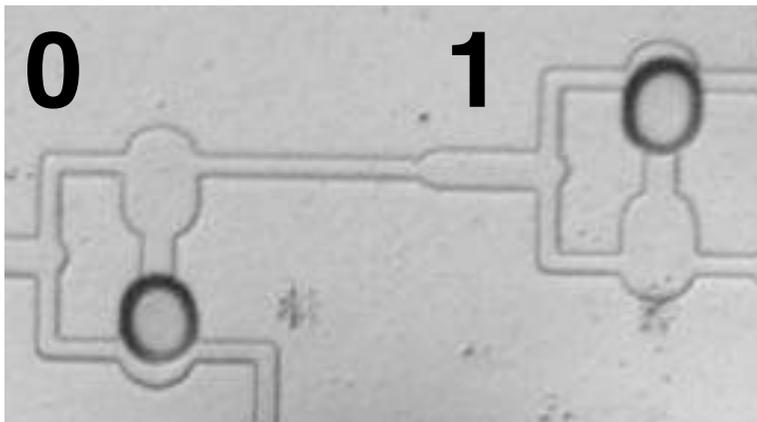
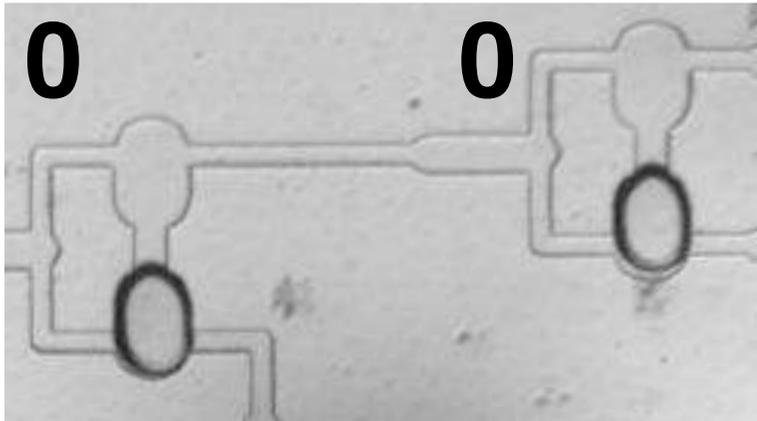


Applications



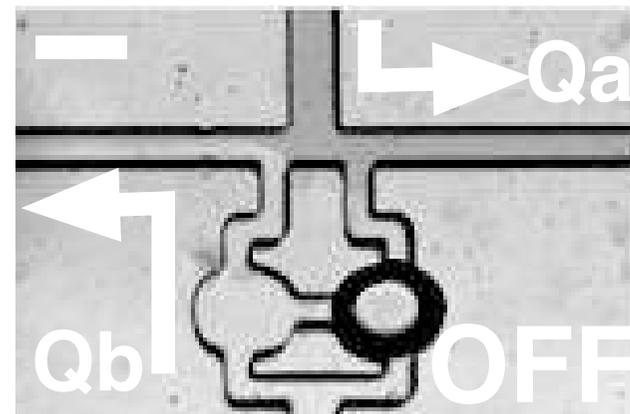
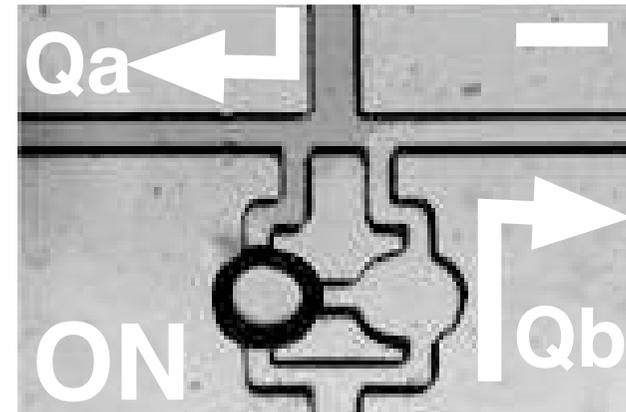
Counting drops

RIPPLE COUNTER



High speed switching valves

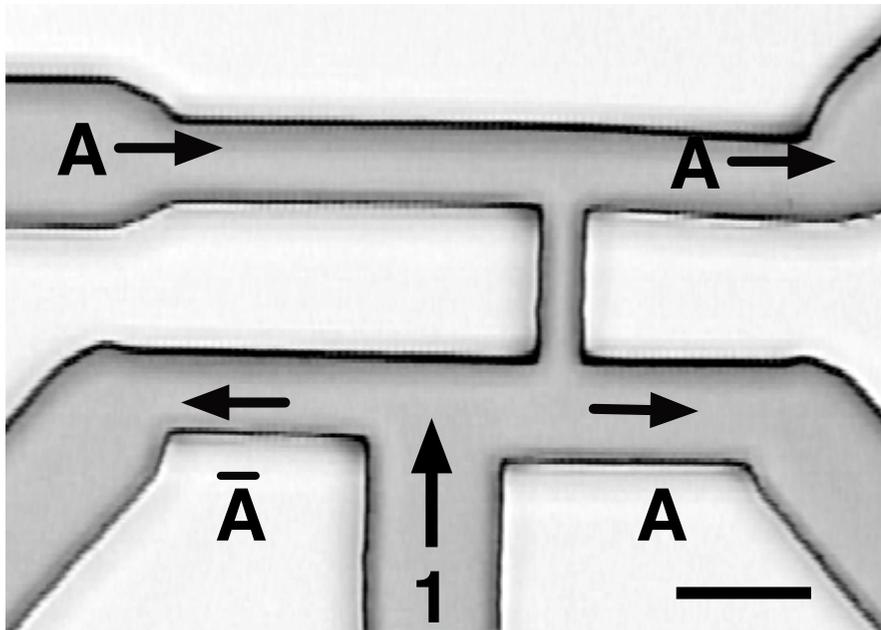
BISTABLE VALVES



Inverter

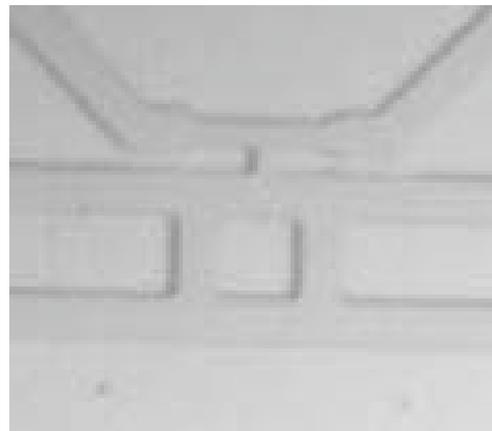
Designed as
 $\text{NOT}(A).B$ gate for $B=1$

**INVERTER
WITH GAIN**



Scale bar $100\mu m$

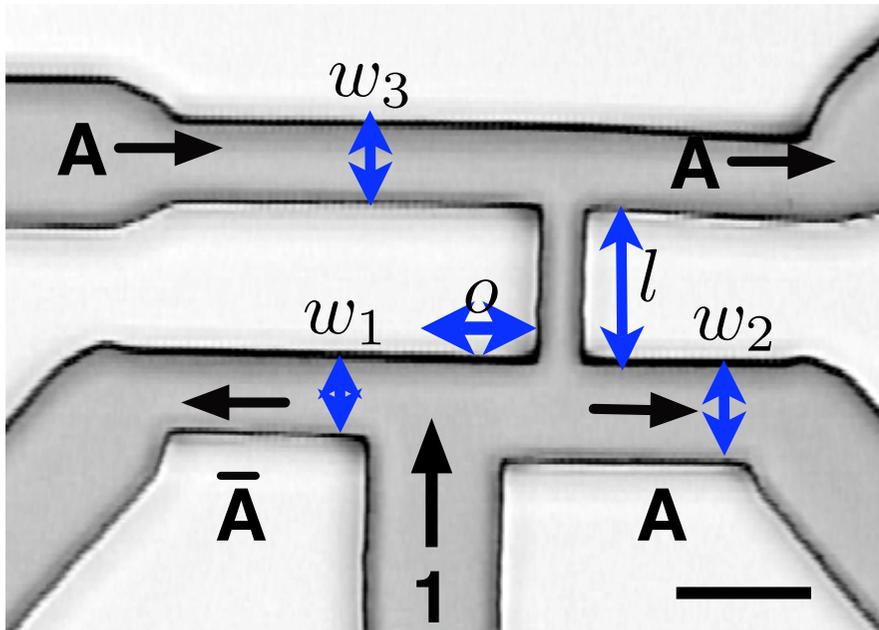
Fredkin gate
(reversible
logic)



Inverter

Designed as
NOT(A).B gate for B=1

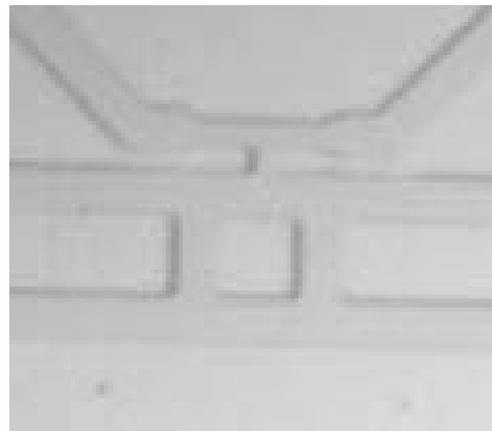
INVERTER
WITH GAIN



$$w_2 > w_1$$

Scale bar $100\mu m$

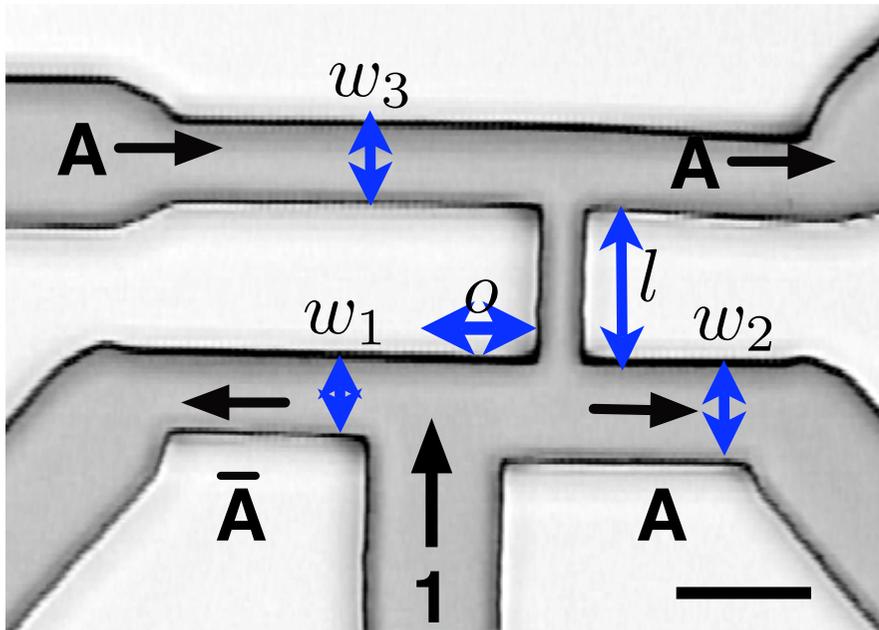
Fredkin gate
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Inverter

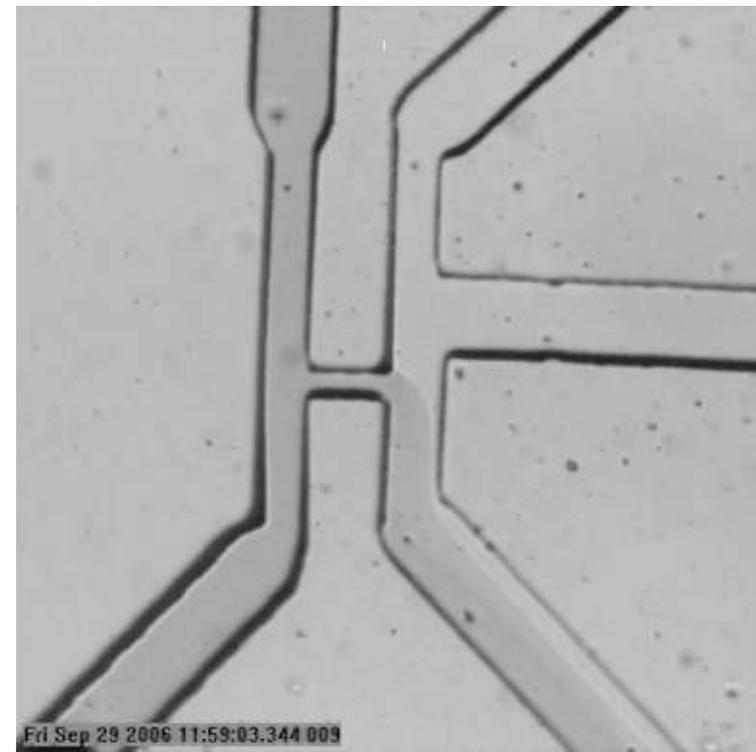
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INVERTER
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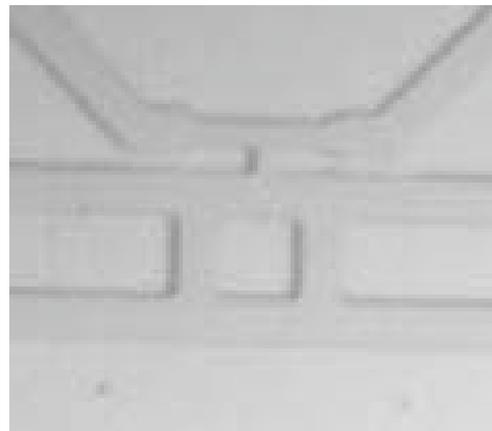


$$w_2 > w_1$$

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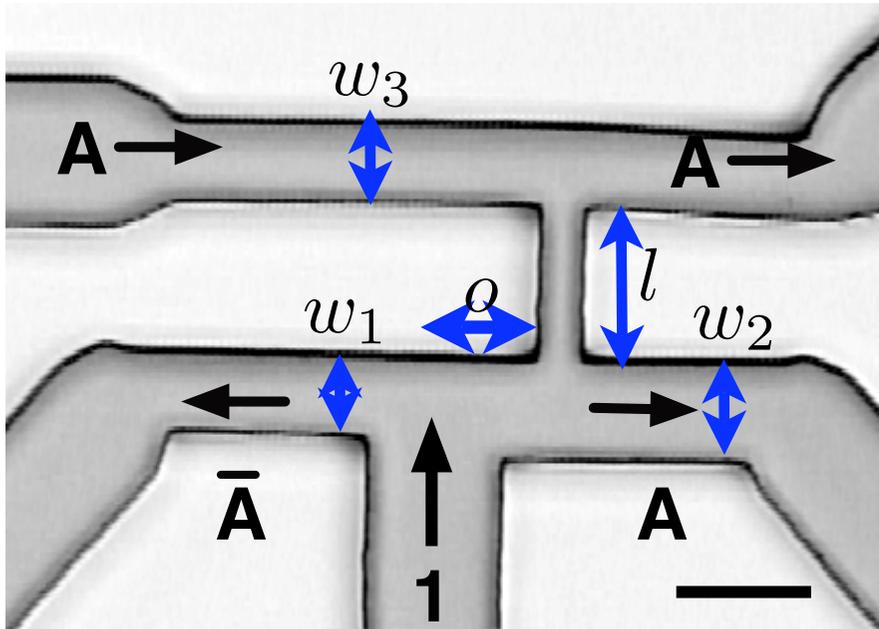


Inverter

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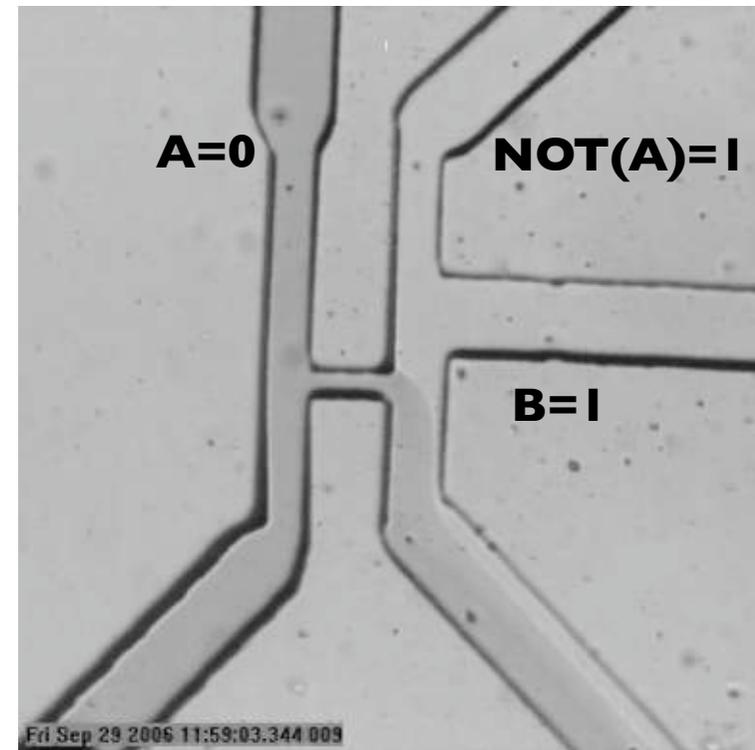
A=0
B=1
NOT(A)=1

INVERTER
WITH GAIN

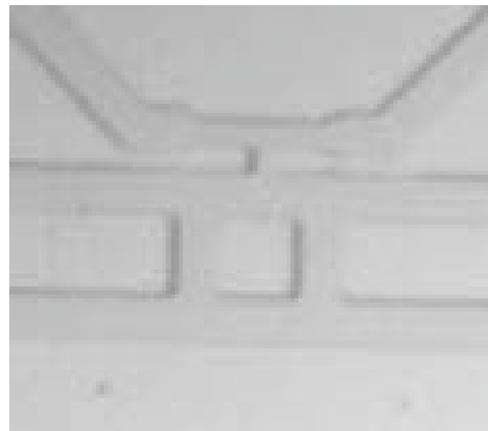


$$w_2 > w_1$$

Scale bar $100\mu m$



Fredkin gate
(reversible
logic)

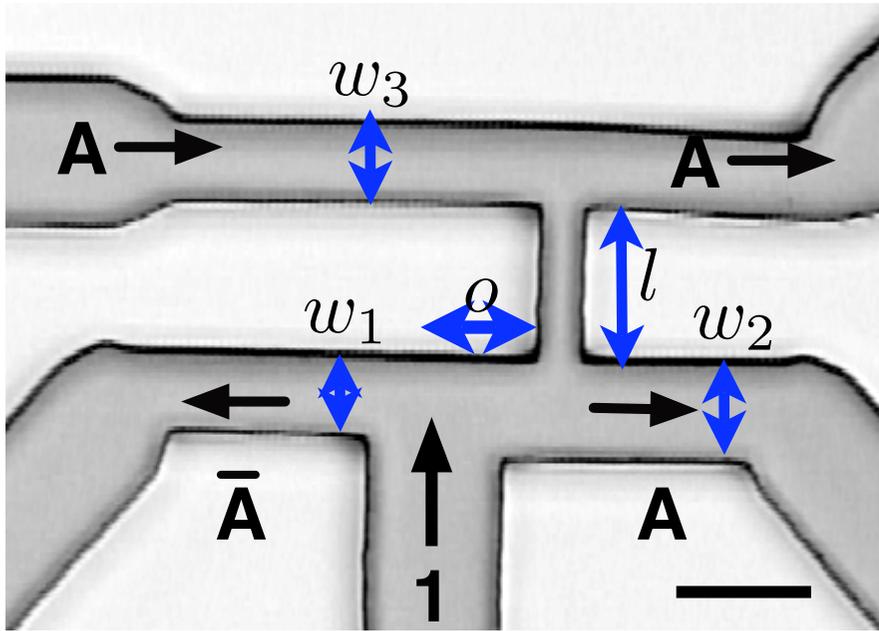


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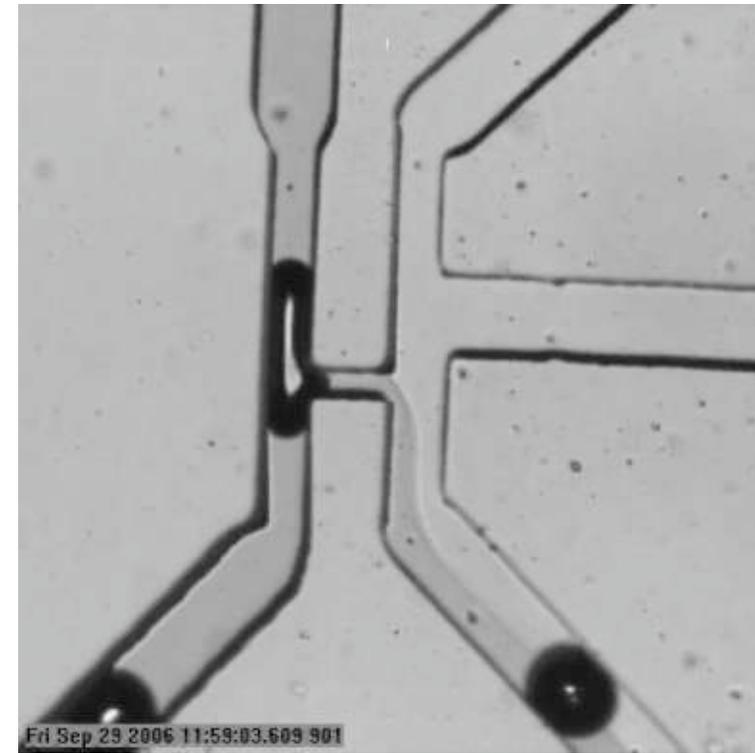
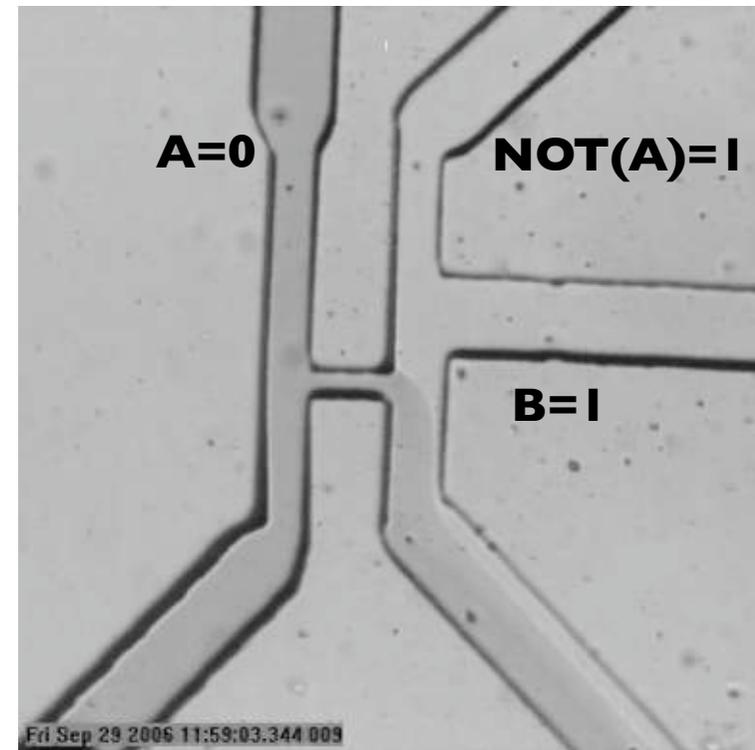
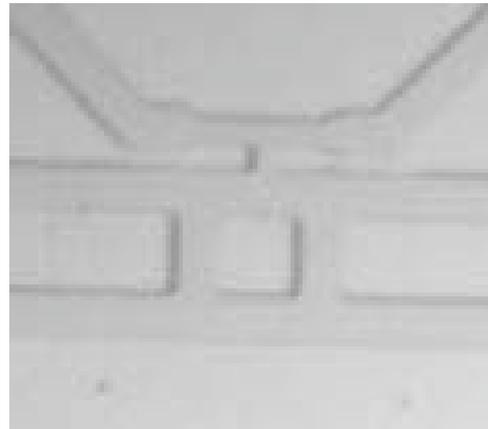
INVERTER
WITH GAIN



$$w_2 > w_1$$

Scale bar $100\mu m$

Fredkin gate
(reversible
logic)

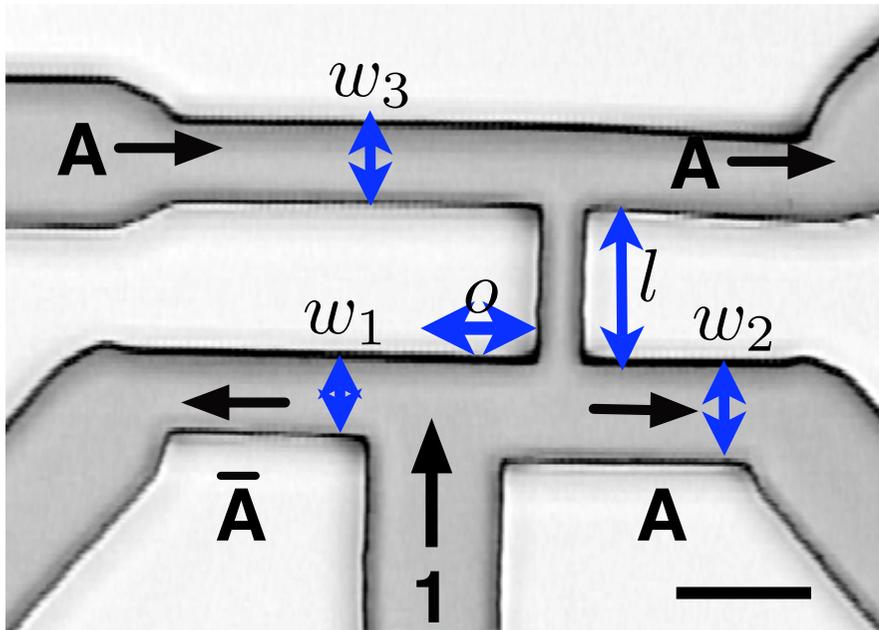


Inverter

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NOT(A).B gate for B=1

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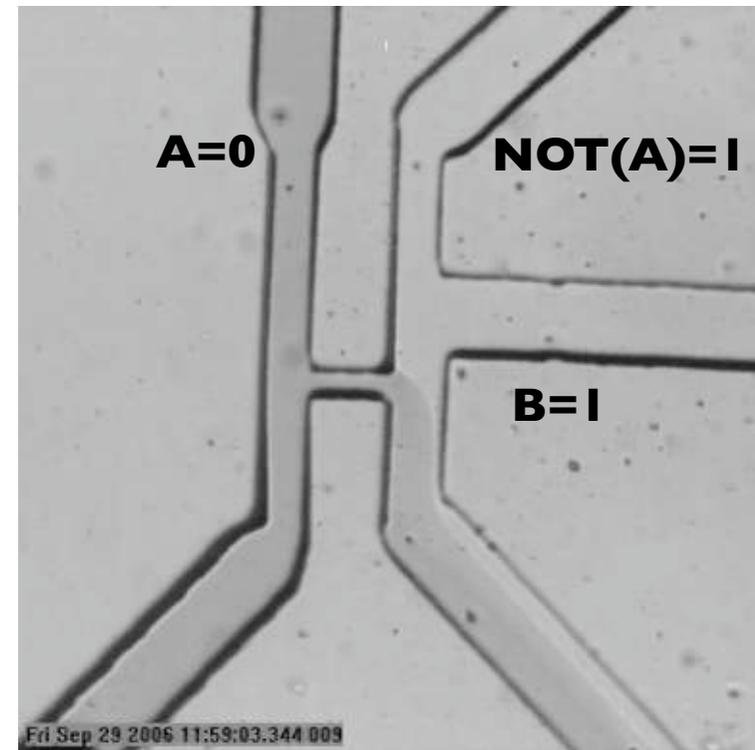
INVERTER
WITH GAIN



$$w_2 > w_1$$

Scale bar $100\mu m$

A=1
B=1
NOT(A)=0



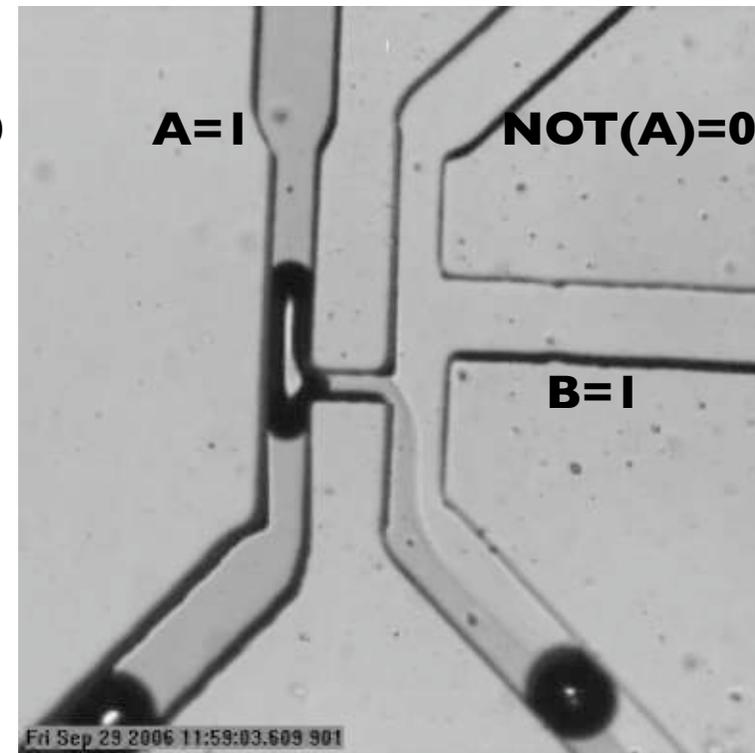
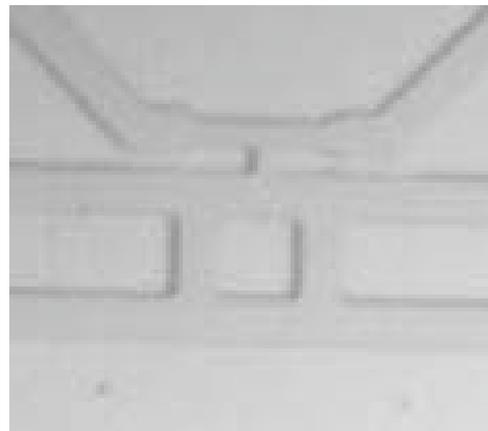
A=0

NOT(A)=1

B=1

Fri Sep 29 2006 11:59:03.344 009

Fredkin gate
(reversible
logic)



A=1

NOT(A)=0

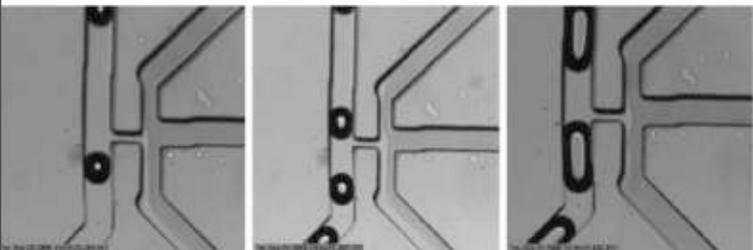
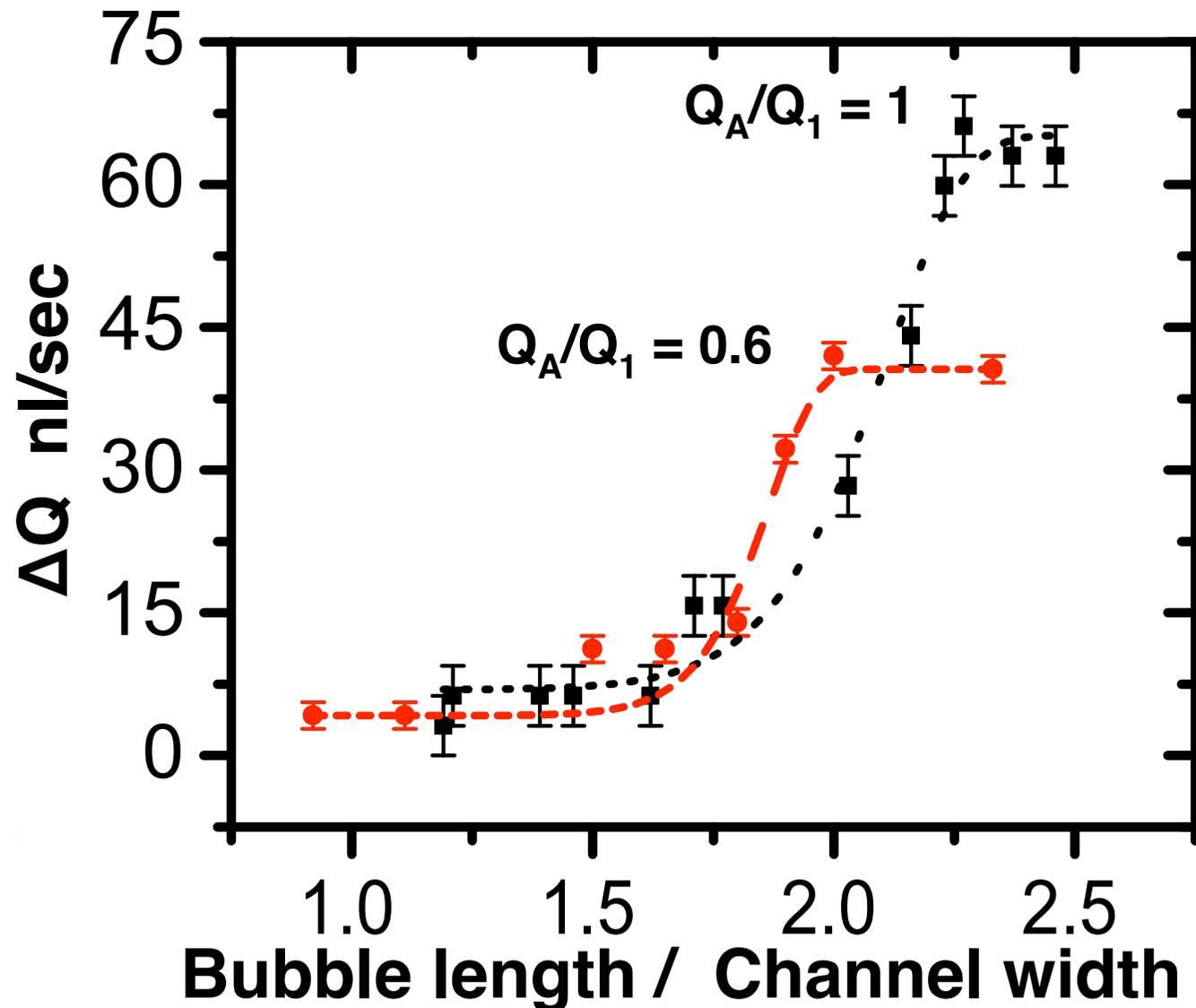
B=1

Fri Sep 29 2006 11:59:03.609 901

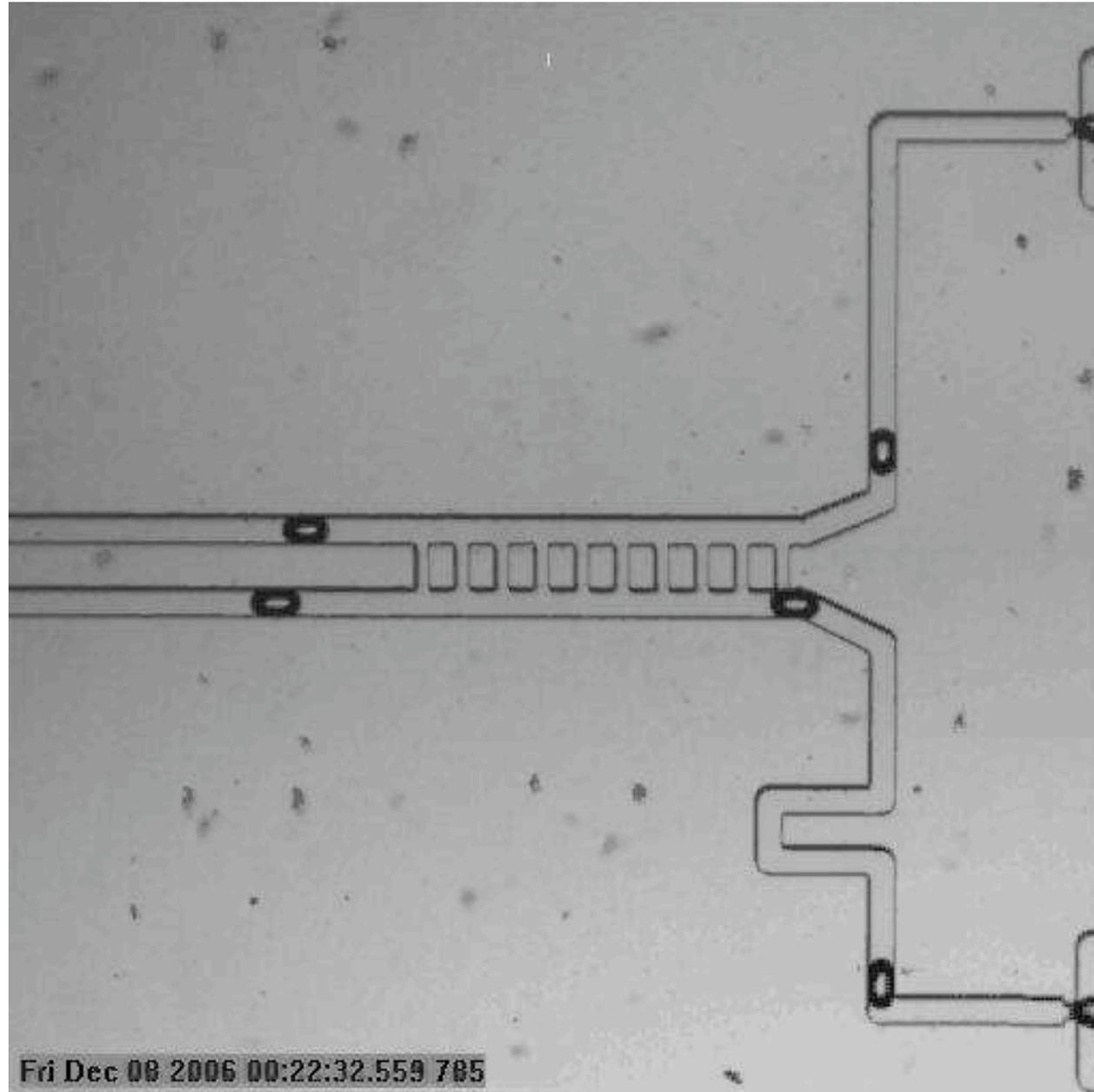
Inverter : amplification/gain

Dependence on bubble length

- Viscous dissipation in thin continuous fluid film
- Viscous dissipation in dispersed phase

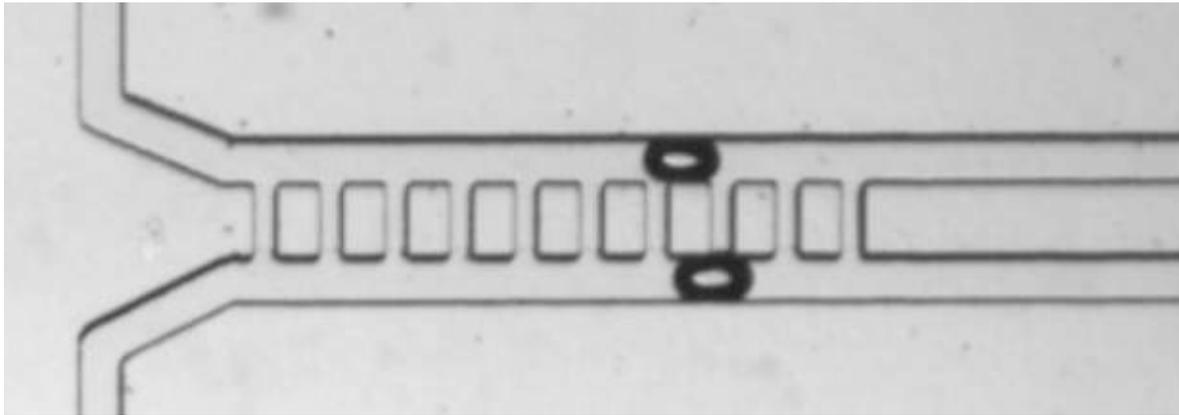


Bubble/Bit synchronizer



1000 fps
high speed
video

Non-linear ladder network



Parameters

- r/R relative flow resistance
- m, n state of the device
- k number of channels
- I constant injected flow

$$U_A - U_B = f(r/R, m, n, k, I)$$

$$I_j - \bar{I}_j = \frac{r}{R}(i_{j+1} - i_j)$$

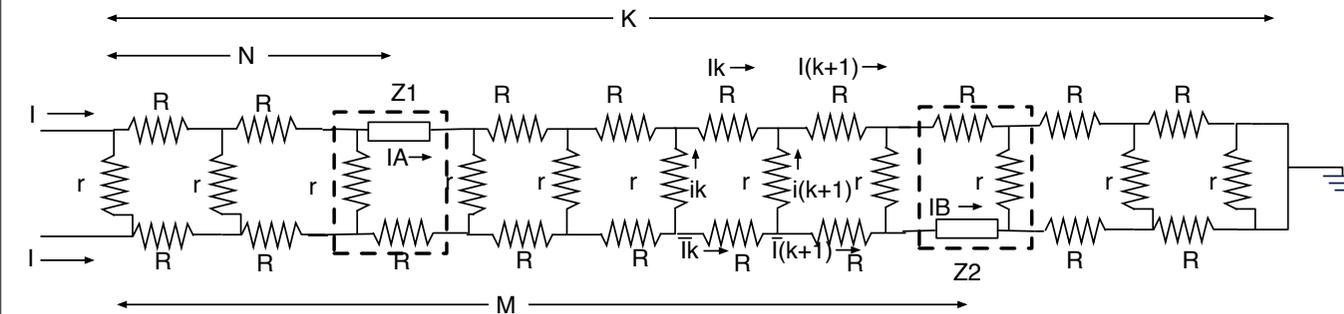
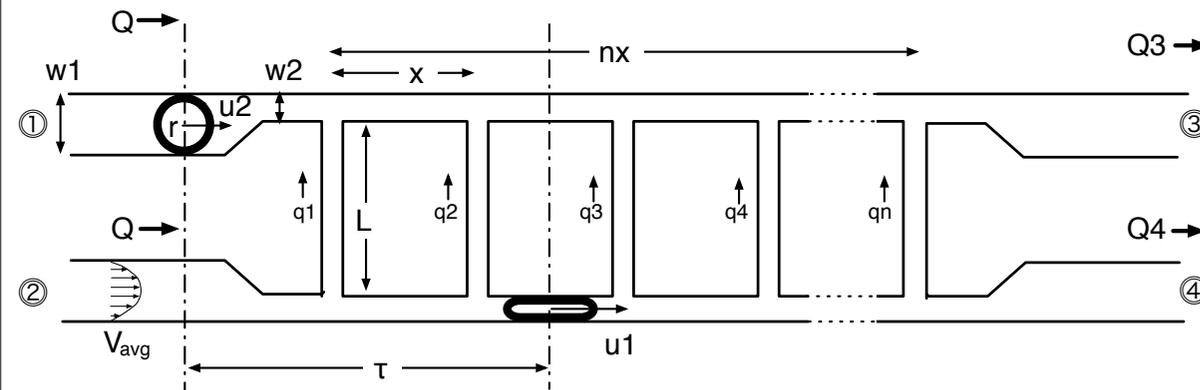
$$I_j - I_{j-1} = i_j$$

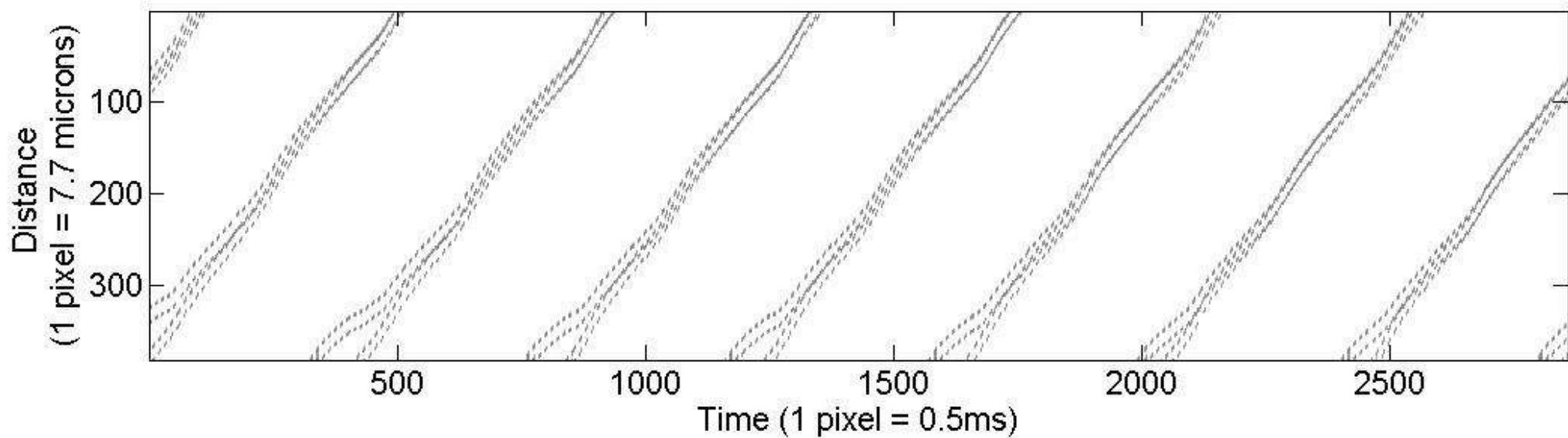
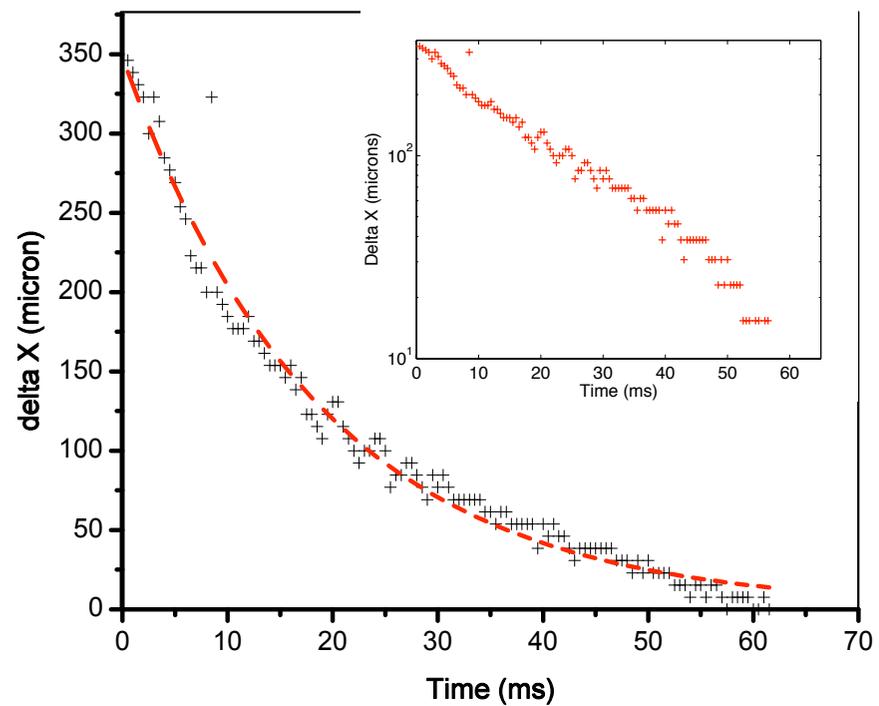
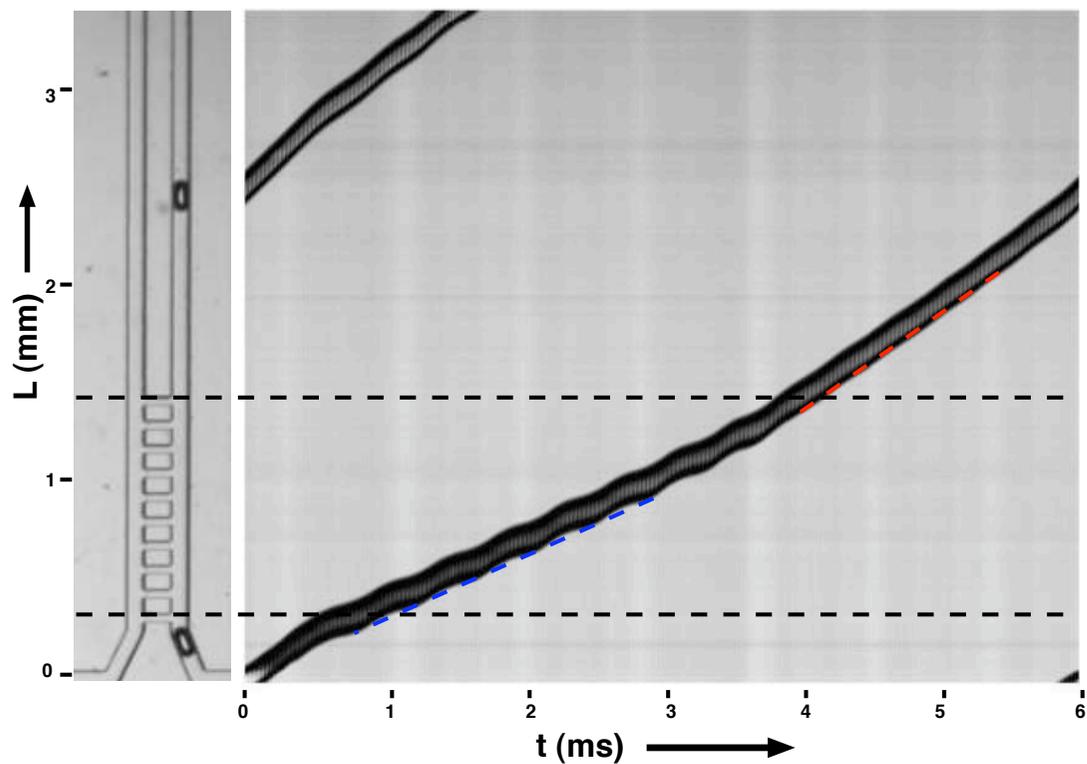
$$\bar{I}_j - \bar{I}_{j-1} = -i_j$$

$$I_j = I_{j-1} + 2\frac{R}{r}S_{j-1}$$

$$I_j = 2\frac{R+r}{r}I_{j-1} - I_{j-2}$$

$$\text{where } S_{j-1} = \sum I_{j-1}$$



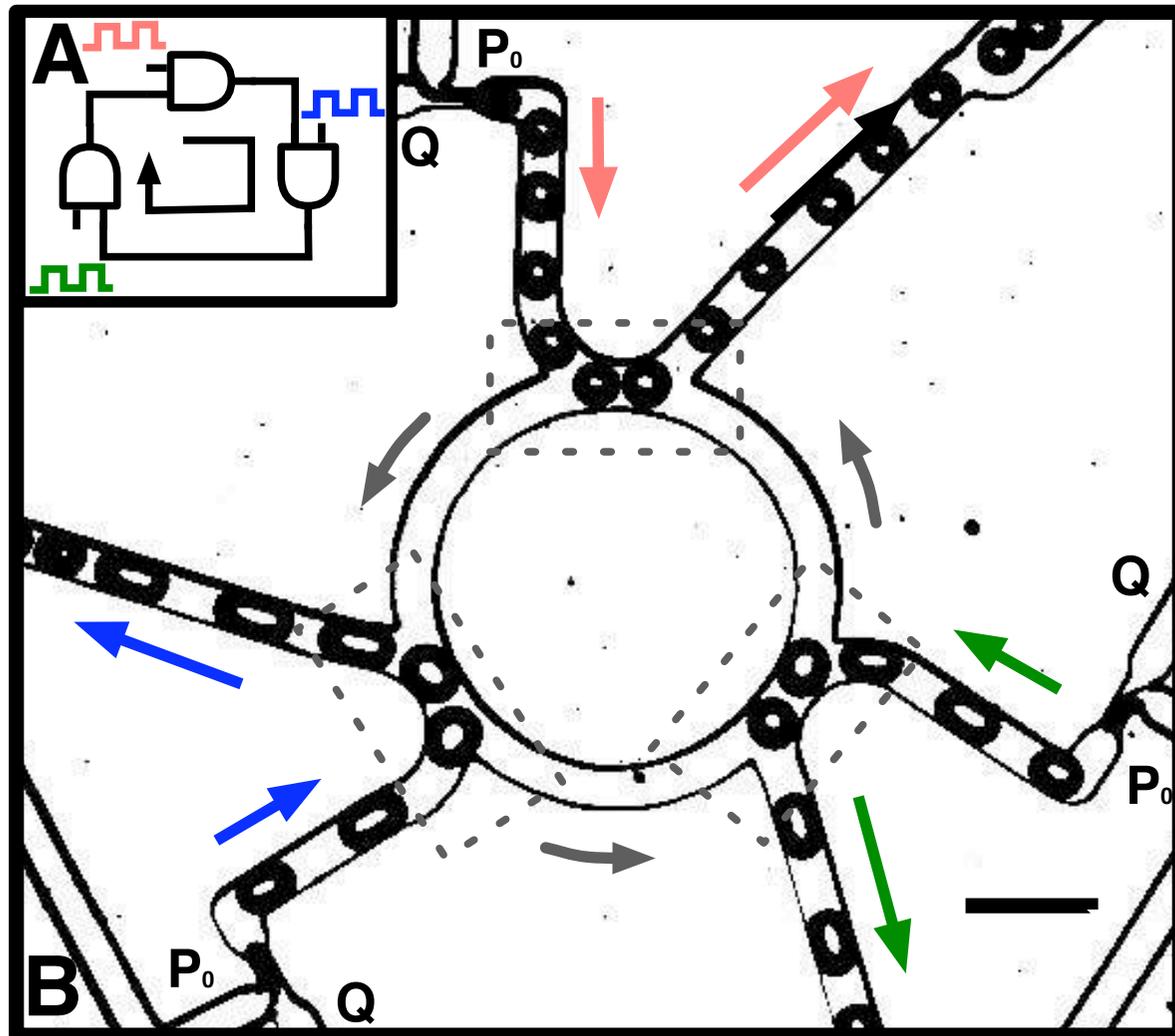


Designing microfluidic circuits

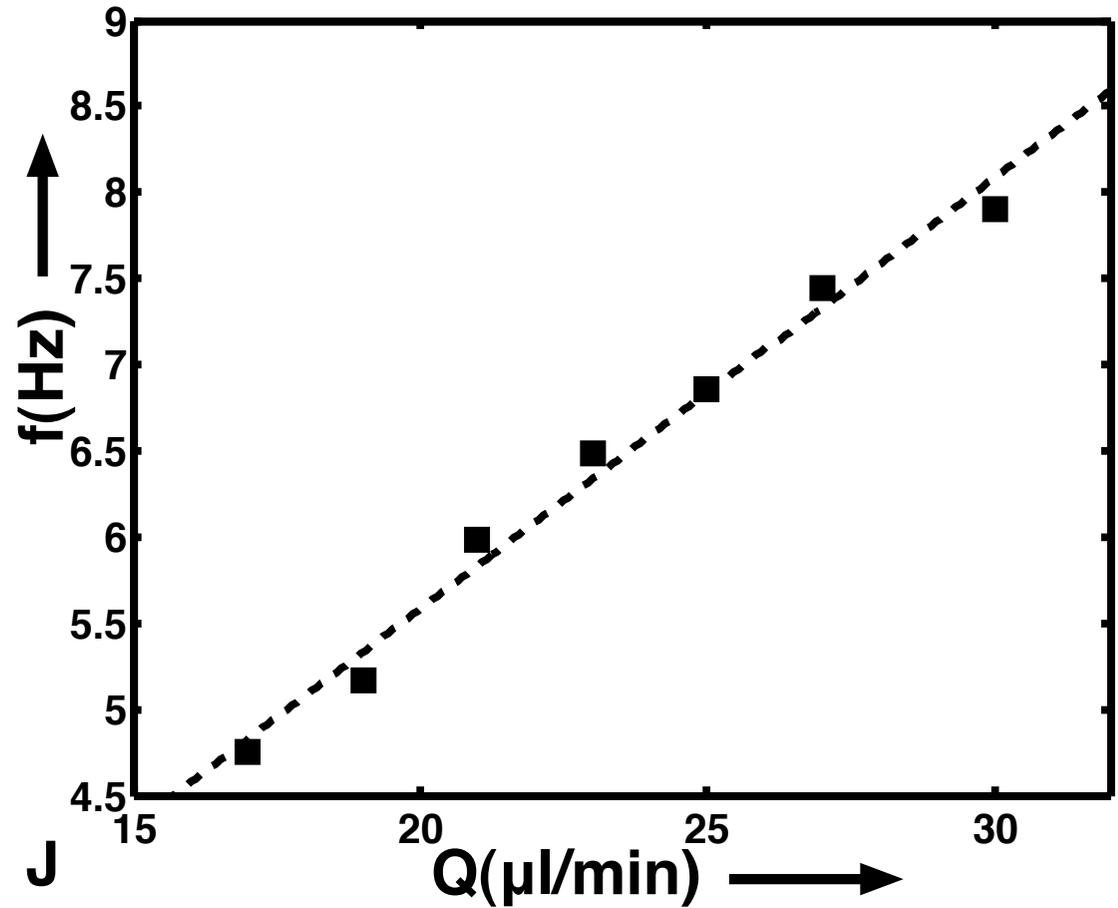
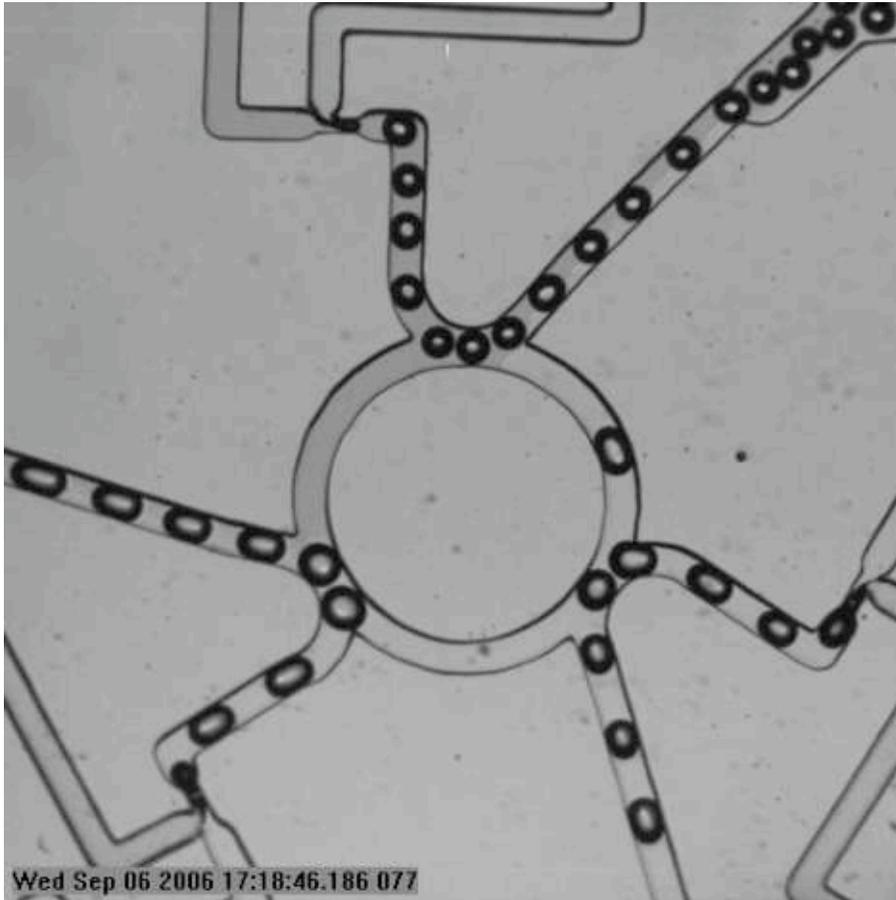
What if we connect three AND gates and three delay lines .. in a ring?

Designing microfluidic circuits

What if we connect three AND gates and three delay lines .. in a ring?



Ring Oscillator

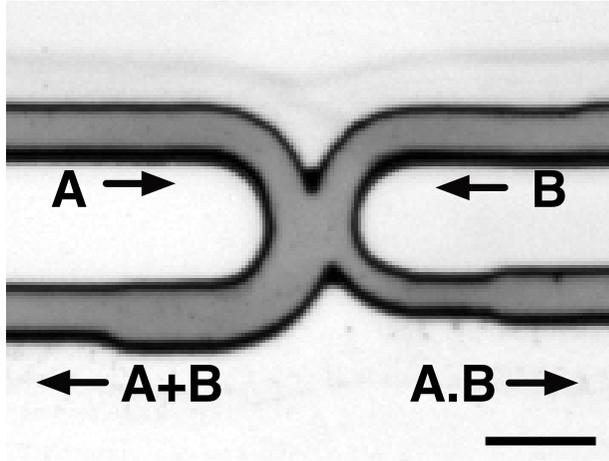


Frequency dependence

$$f \propto 1/[3(l/v + \tau_d)]$$

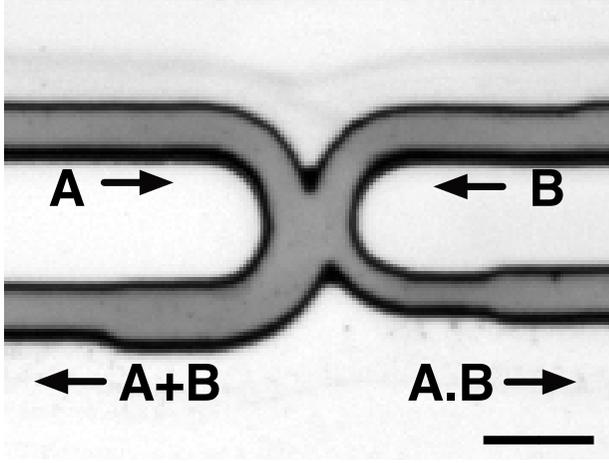
NONLINEARITY

AND/OR gate

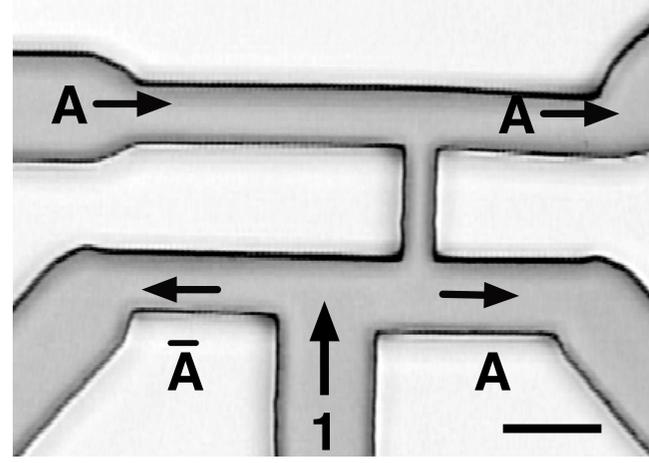


NONLINEARITY

AND/OR gate



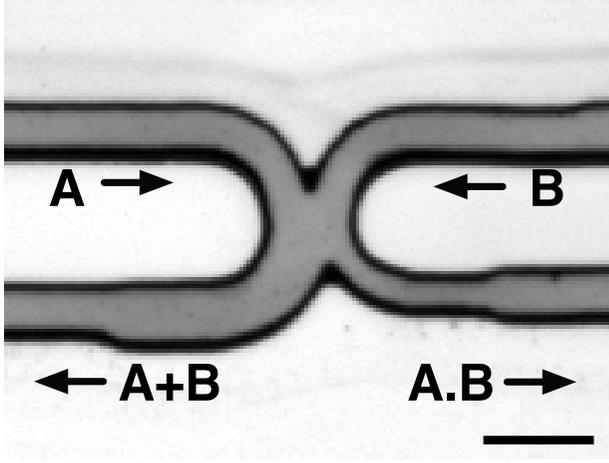
NOT gate



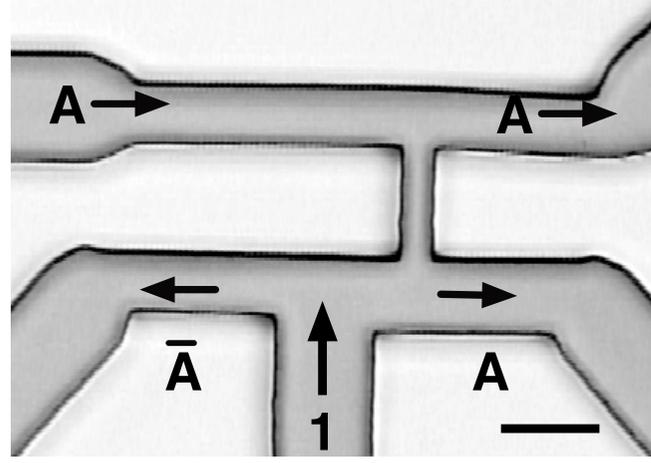
GAIN
INVERSION

BISTABILITY NONLINEARITY

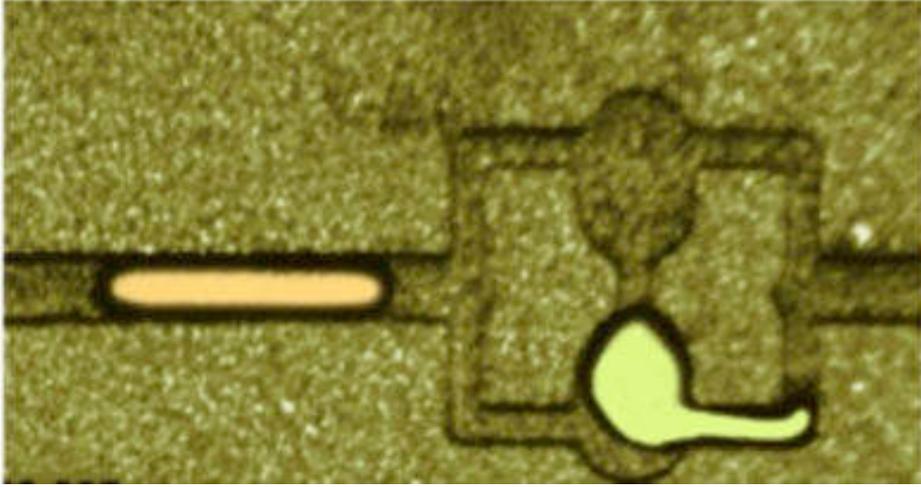
AND/OR gate



NOT gate



Toggle Flip-Flop

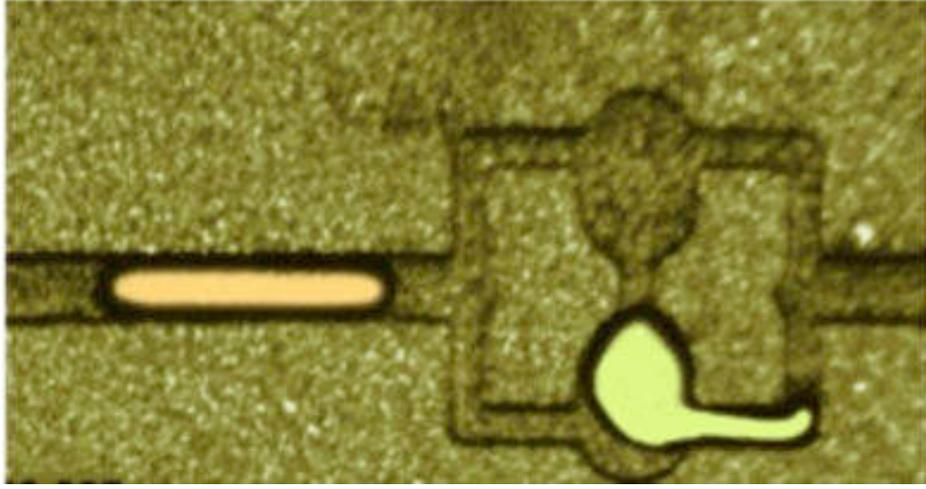


GAIN
INVERSION

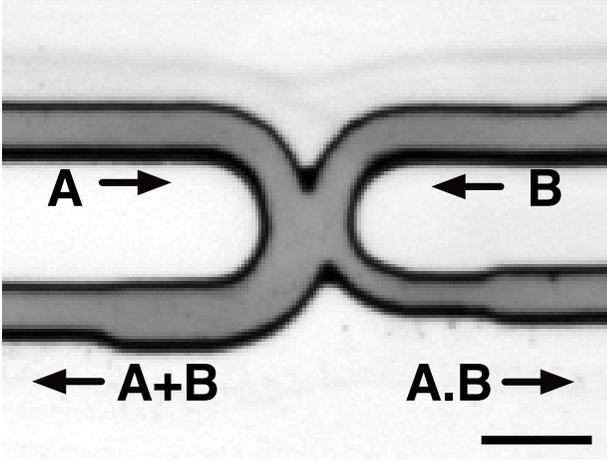
BISTABILITY

NONLINEARITY

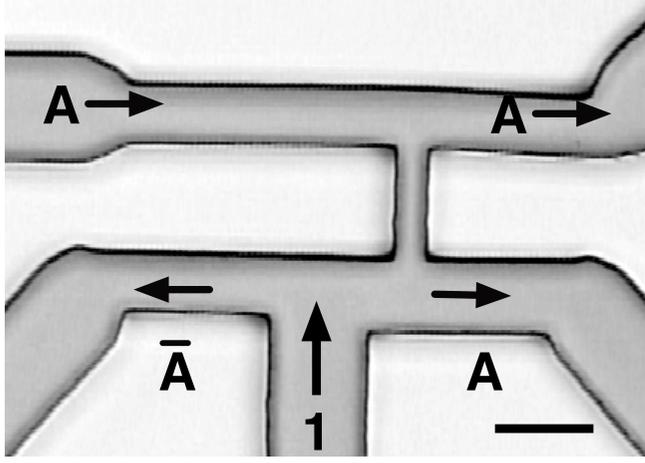
Toggle Flip-Flop



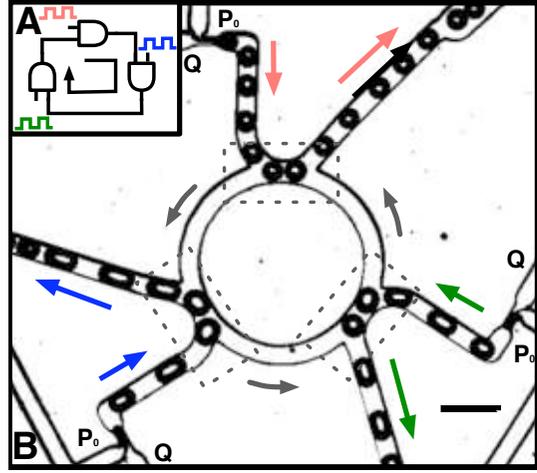
AND/OR gate



NOT gate



Ring Oscillator

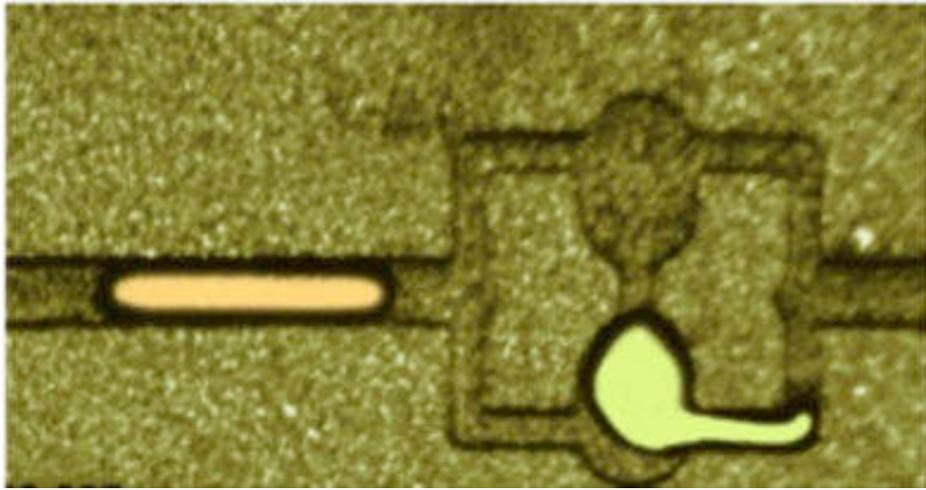
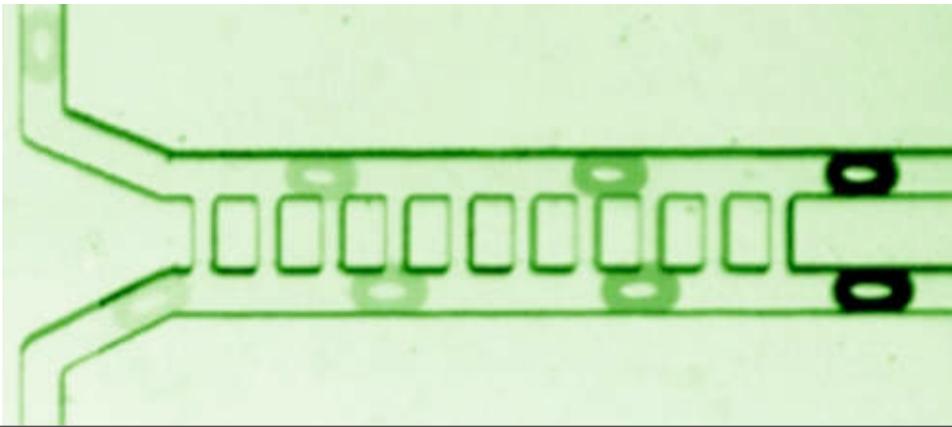


CASCADABILITY
FEEDBACK
GAIN
INVERSION

SYNC

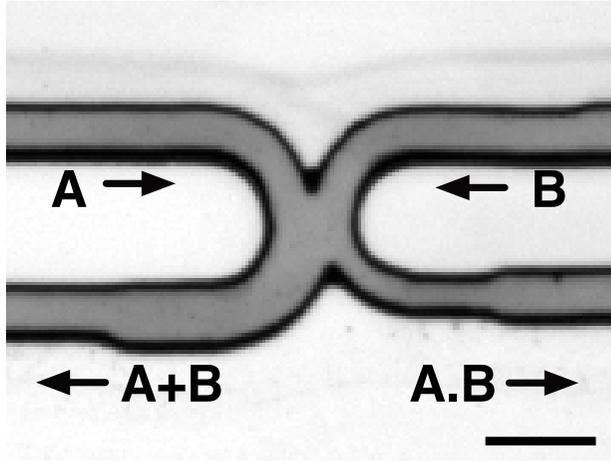
BISTABILITY

NONLINEARITY

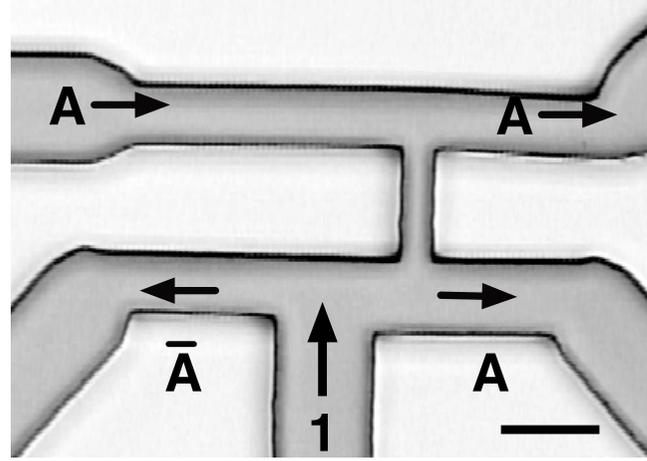


Toggle Flip-Flop

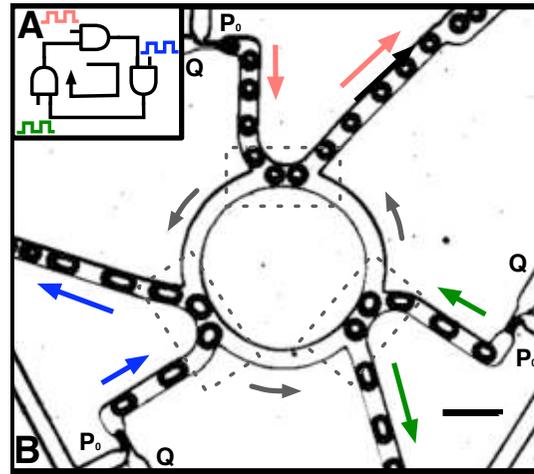
AND/OR gate



NOT gate



Ring Oscillator

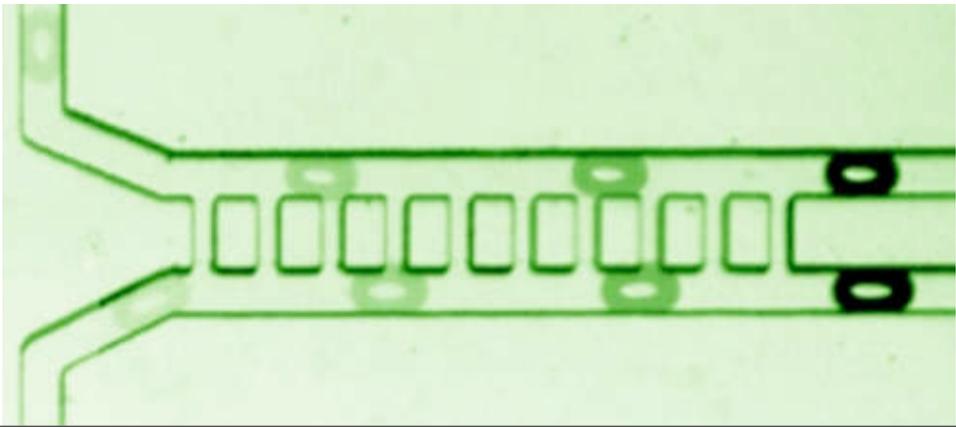


CASCADABILITY GAIN
 FEEDBACK INVERSION

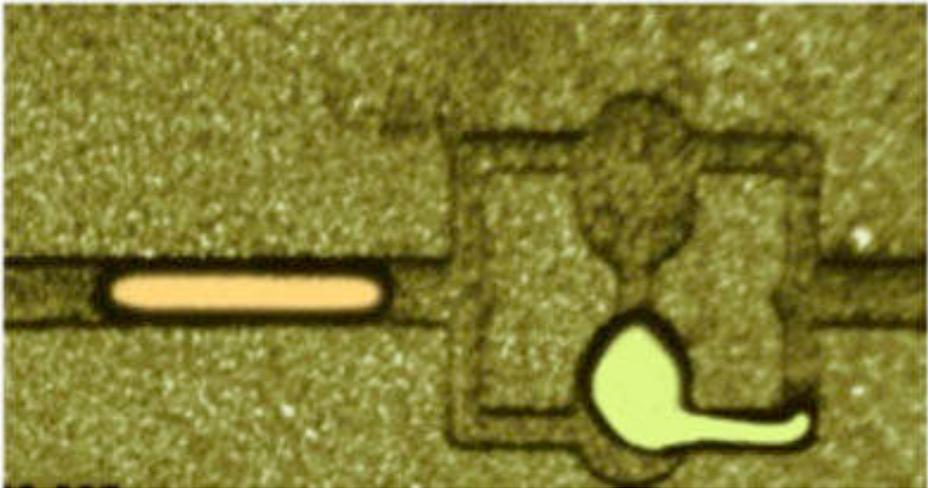
SYNC

BISTABILITY

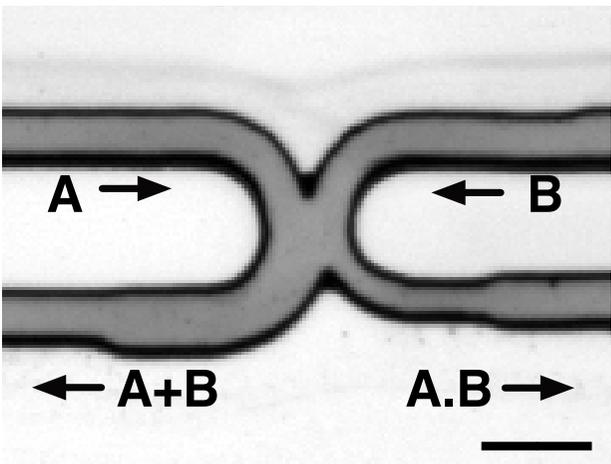
NONLINEARITY



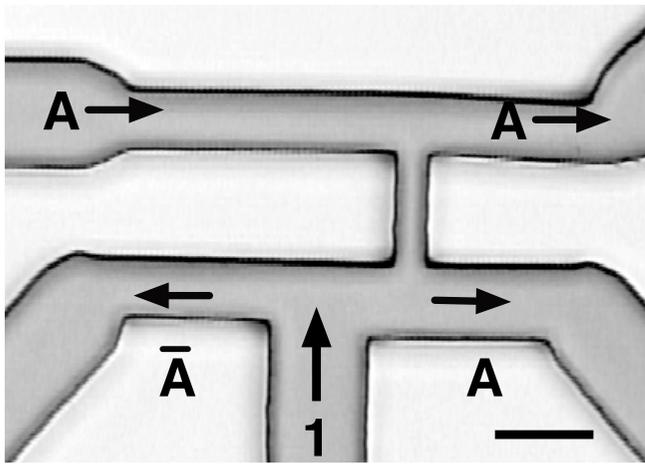
Toggle Flip-Flop



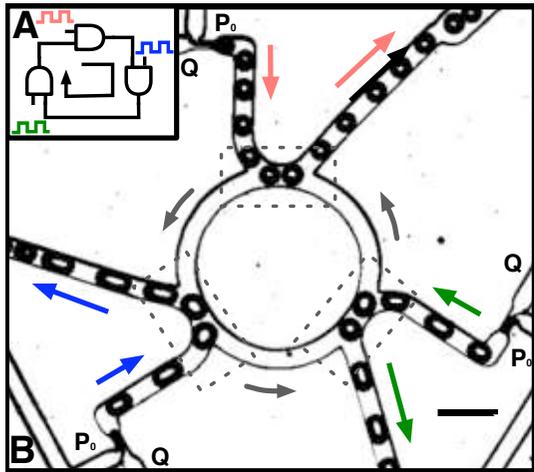
AND/OR gate



NOT gate



Ring Oscillator



GEN.

CASCADABILITY

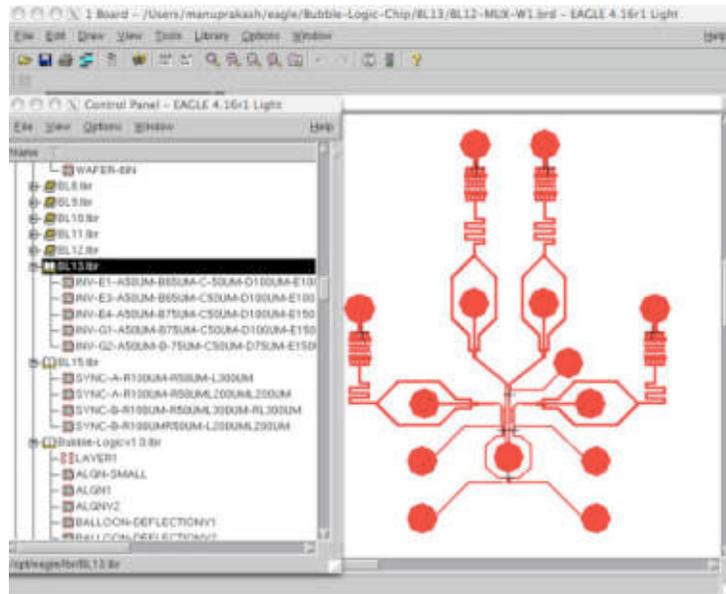
GAIN

FEEDBACK

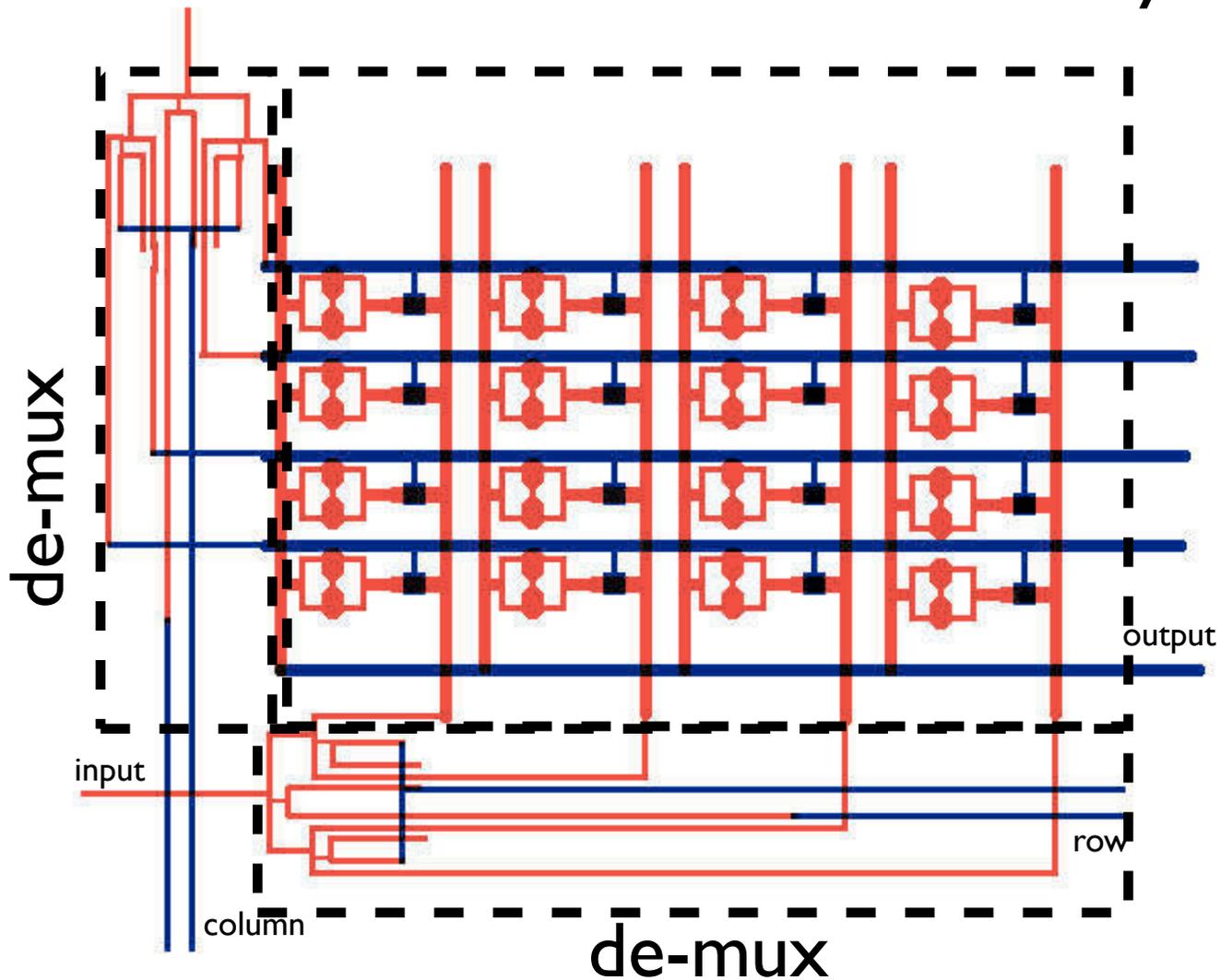
INVERSION

Integration

Modular elements
Open source CAD
Component Libraries



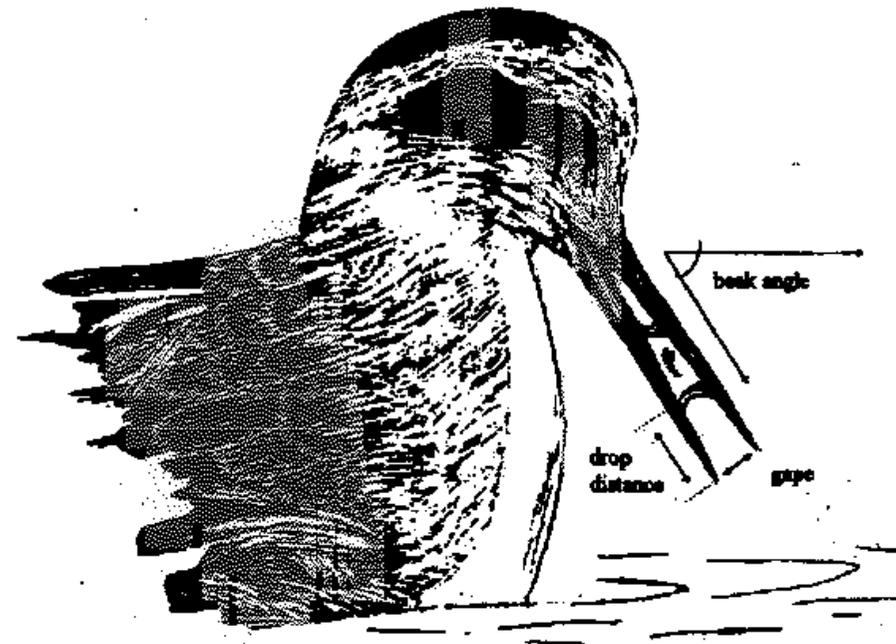
Random Access Chemical Memory



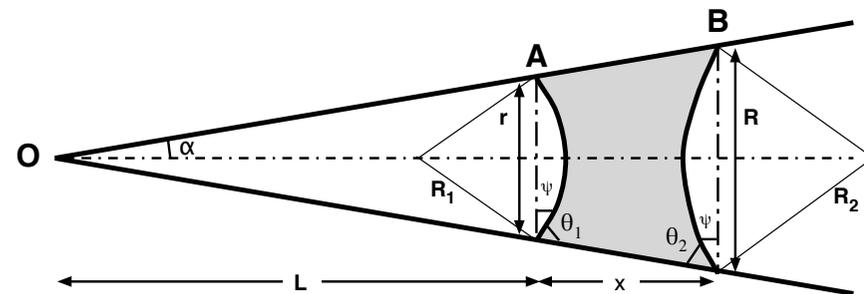
Self-clocked microfluidics?

Capillary Ratchets

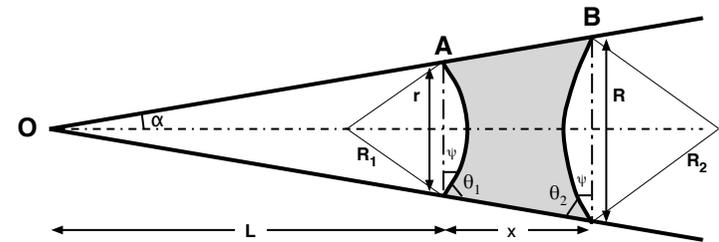
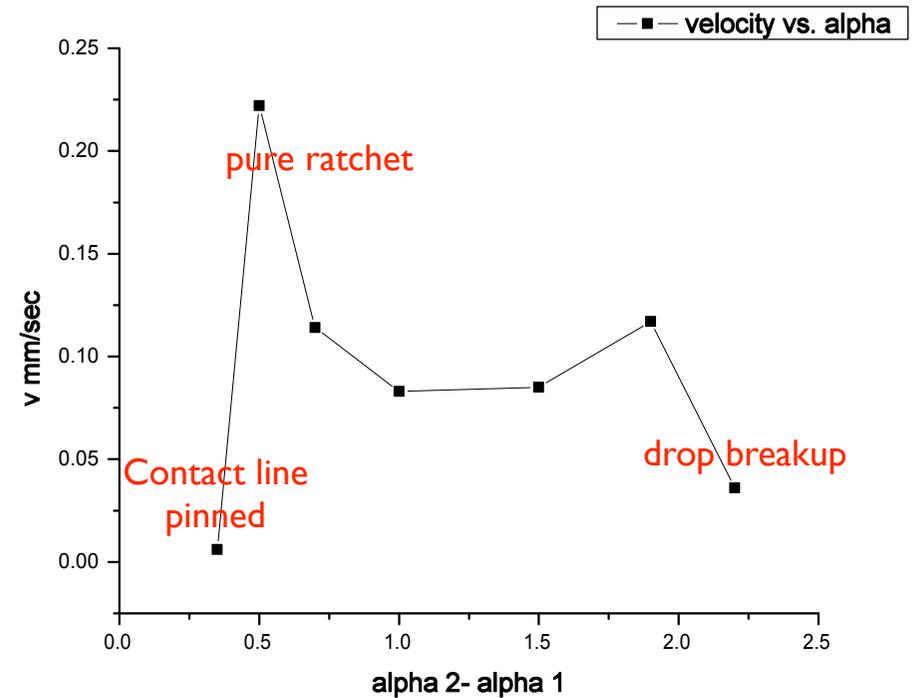
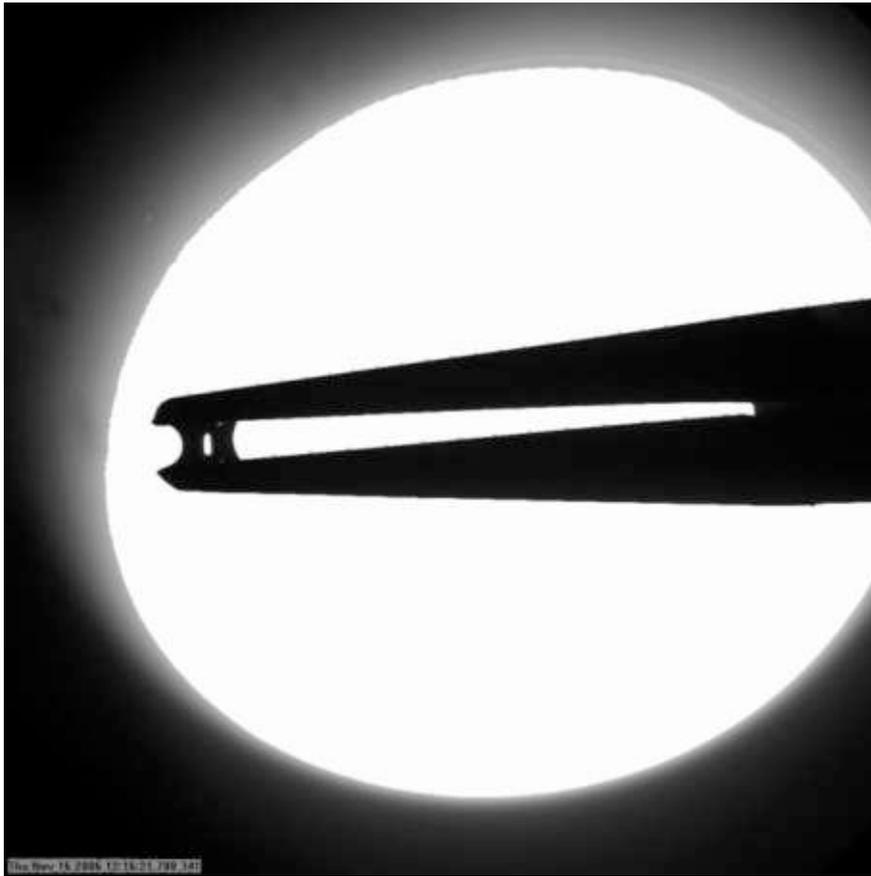
Red-neck phalarope



[Rubega et al, 93]



Capillary ratchet



$$\tan(\pi/4 - (\theta_a - \alpha_{min})/2) = \frac{3(x\alpha_{min}(x + 2L) - 2V)}{4\alpha_{min}^2(L^2 + (L + x)^2)}$$

$$\tan(\pi/4 - (\theta_r + \alpha_{max})/2) = \frac{3(x\alpha_{max}(x + 2L) - 2V)}{4\alpha_{max}^2(L^2 + (L + x)^2)}$$

Line tension balance

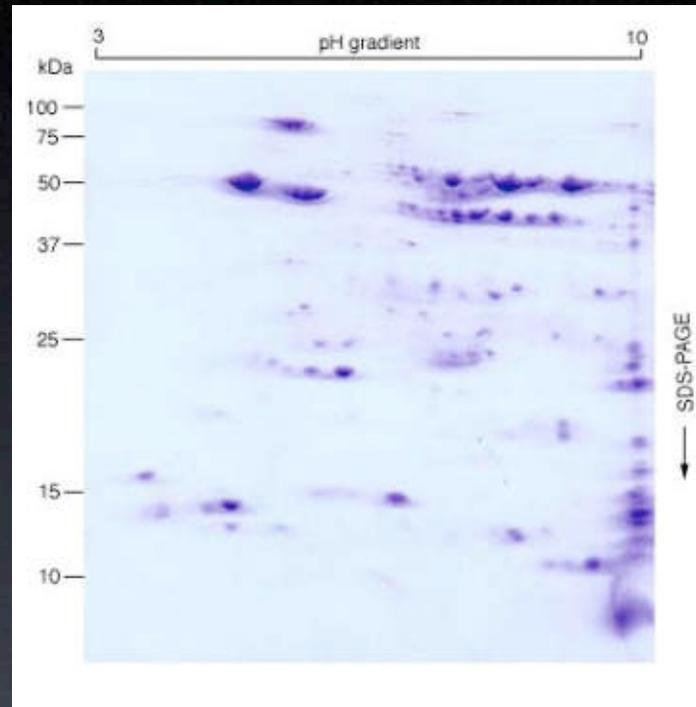
$$\theta_1 - \theta_2 = 2\alpha$$

$$d\theta_1 - d\theta_2 = 2d\alpha$$

Can be solved graphically for alpha max and min
Criteria for alpha when the drop just starts to move

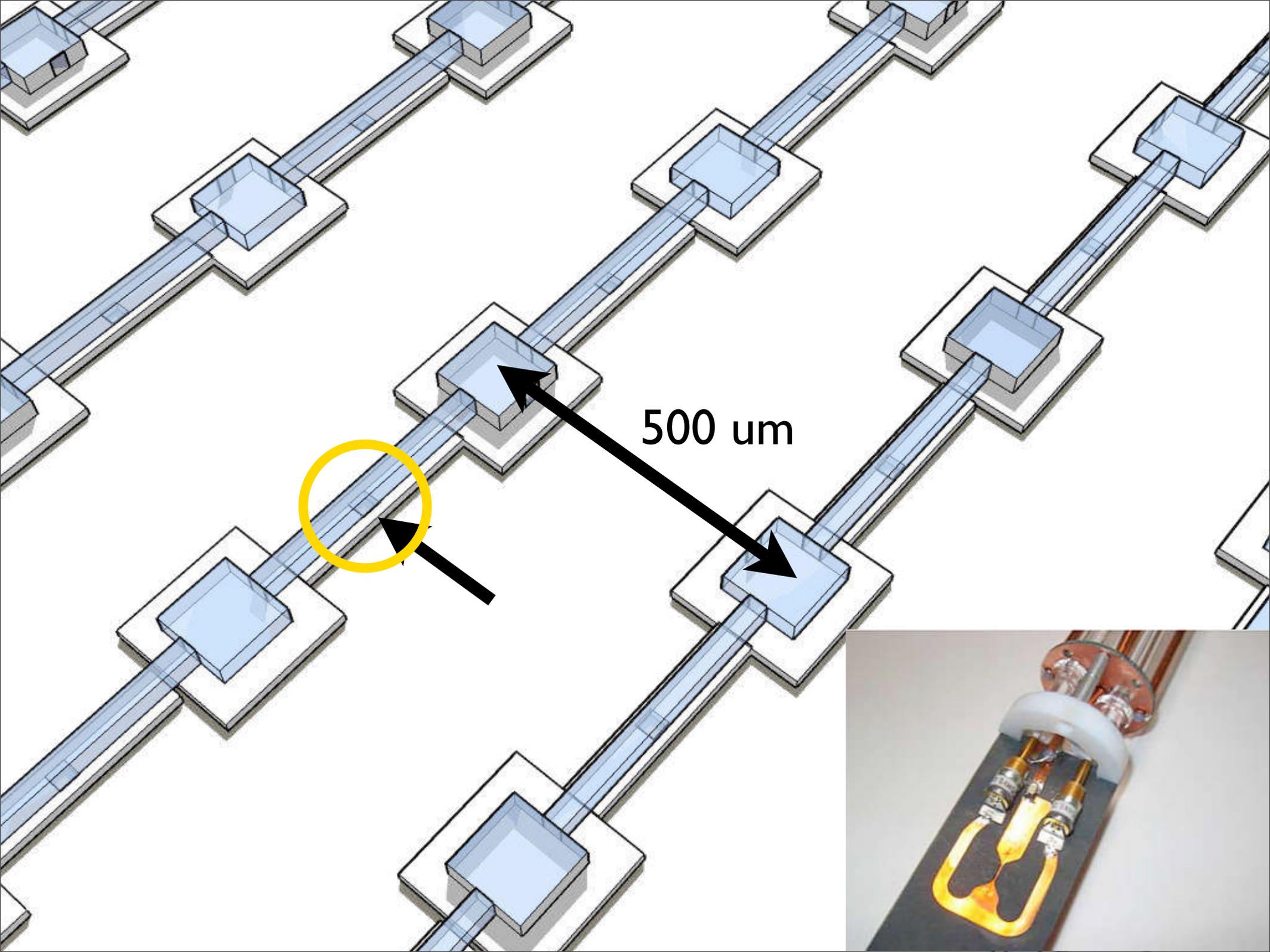
[Prakash et al. 2007 in prepration]

Ultra-Small-Sample Molecular Structure Detection Using Microslot Nuclear Spin Resonance



Yael Maguire

- To create a technology that can get structural information from 10^{13} - 10^{14} (100pmols - 1nmol) biomolecules and avoid DNA/bacteria amplification.



500 um

- highest SNR for planar detector
- demonstrated detection of $\sim 10^{14}$ biomolecules
- scalable, parallel geometry to improve SNR_{puv}

Maguire et al, PNAS v104, n22 (2007)

Ultra-small-sample molecular structure detection using microslot waveguide nuclear spin resonance

Yael Maguire^{*†}, Isaac L. Chuang^{*}, Shuguang Zhang^{*†‡}, and Neil Gershenfeld^{*}

^{*}Center for Bits and Atoms and [†]Center for Biomedical Engineering, NE47-379, Massachusetts Institute of Technology, Cambridge, MA 02139-4307

Communicated by Alexander Rich, Massachusetts Institute of Technology, Cambridge, MA, April 6, 2007 (received for review August 25, 2006)

We here report on the design of a planar microslot waveguide NMR probe with an induction element that can be fabricated at scales from centimeters to nanometers to allow analysis of biomolecules at nano- or picomole quantities, reducing the required amount of materials by several orders of magnitude. This device demonstrates the highest signal-to-noise ratio for a planar detector to date, measured by using the anomeric proton signal from a 15.6-nmol sample of sucrose. This probe had a linewidth of 1.1 Hz for pure water without susceptibility matching. Analysis of 1.57 nmol of ribonuclease-A shows high sensitivity in one- and two-

(RF) homogeneity (27). As with other miniaturized probes, a microslot has much shorter tipping times for the same power input and very little radiation damping compared with conventional probes, enabling more complex pulse sequences. Moreover, it is not only easily fabricated at a wide variety of scales, but multiple samples can be measured in parallel by an array. In realizing this design, we demonstrate the fabrication of this device and perform a set of experiments to determine the linewidth of water, measure the device's SNR, perform multiple-quantum measurements on a protein ribonuclease-A, and mea-



.4 m



~1 m



~4 m

Conclusions

Internal control scheme

Material independent

KHz operation

Digital control

Combinatorial chemistry

Chemical synthesis

High throughput screening

Large scale chemical memories

Handheld diagnostics

Printing

Physical Cryptography

Playground for fluid mechanics