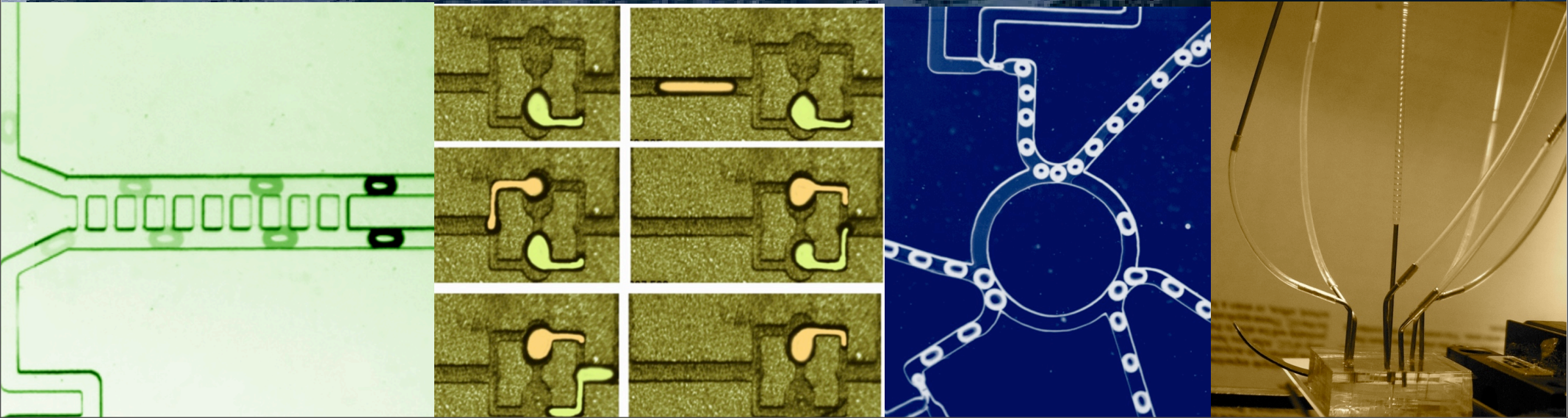
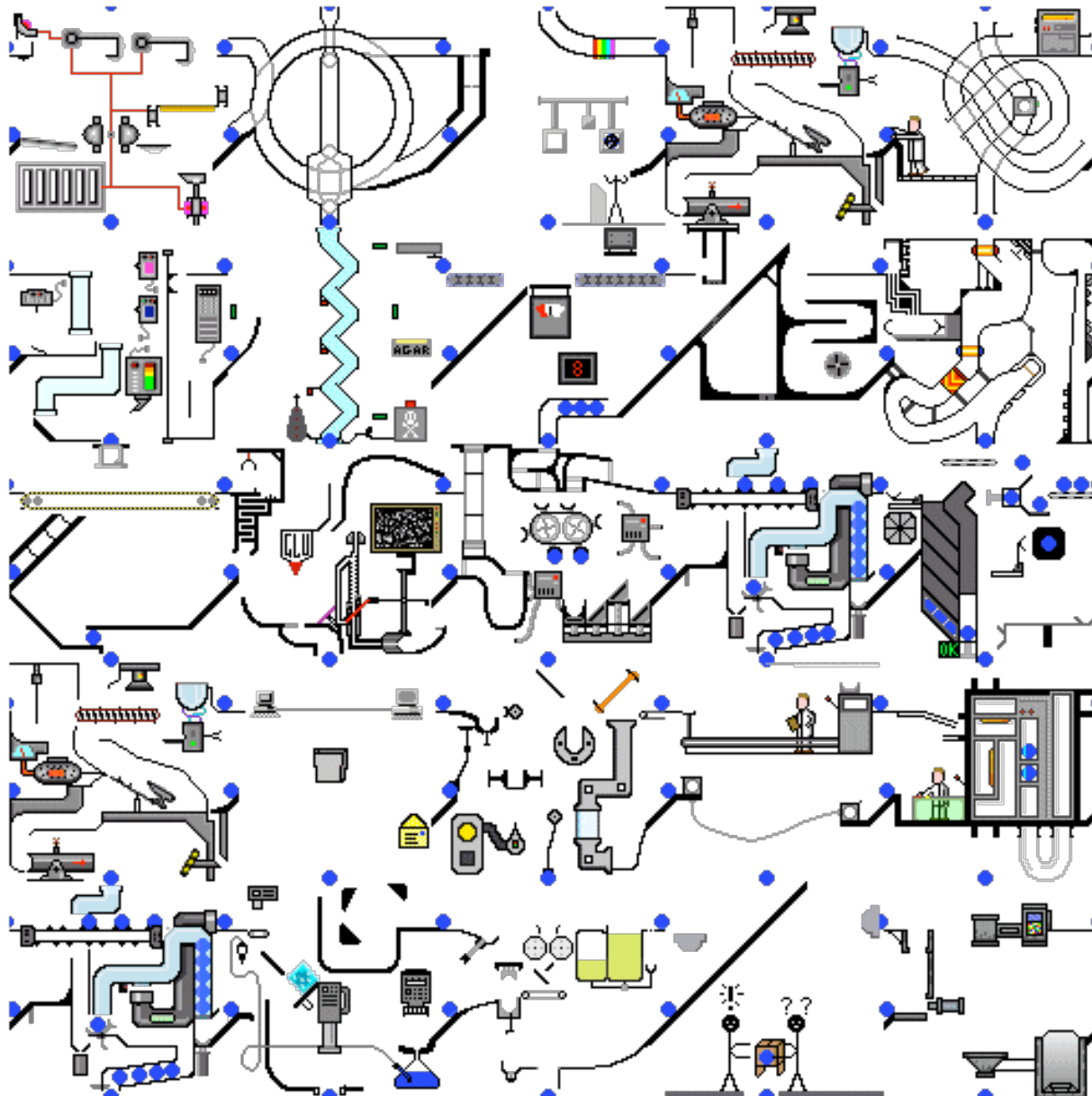


# Microfluidic Bubble Logic

Manu Prakash  
Massachusetts Institute of Technology



# Future of materials (chemical/biological) processing



Bubble logic  
Capillary ratchet  
Micro-slot detector

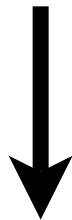
# Information is Physical

“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**

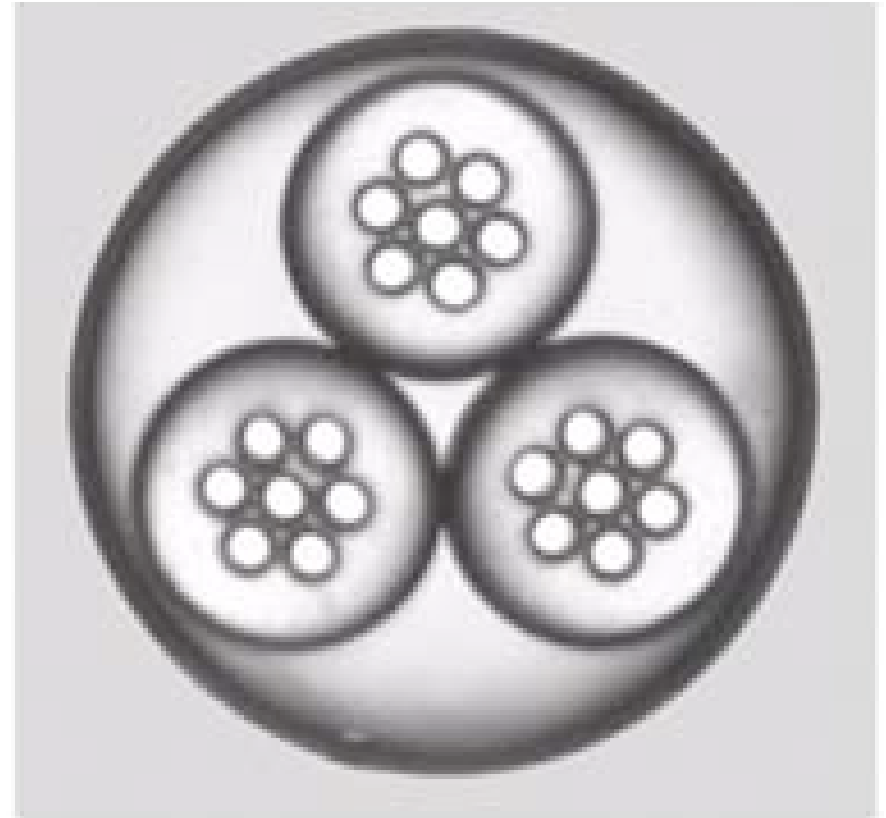
# Drops and Bubbles

1737



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

2007

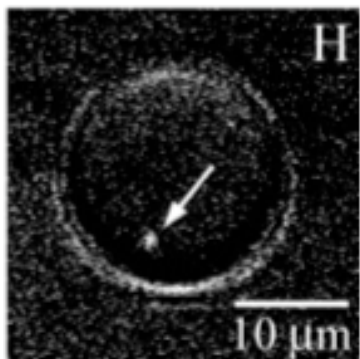


**Weitz Group, Harvard**

# Trapping

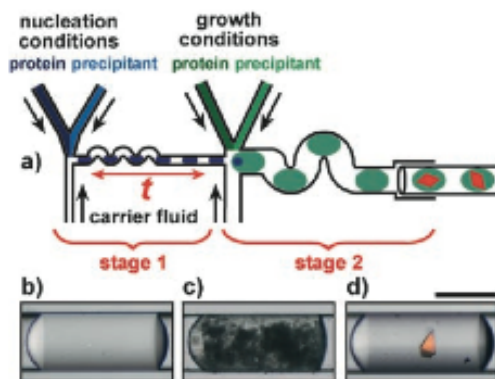


Weitz 2007 (unpublished)



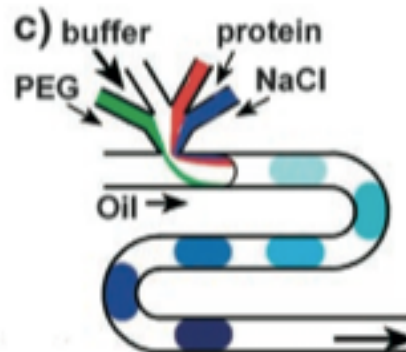
D. Chiu, Anal. Chem 2005

# Reactions



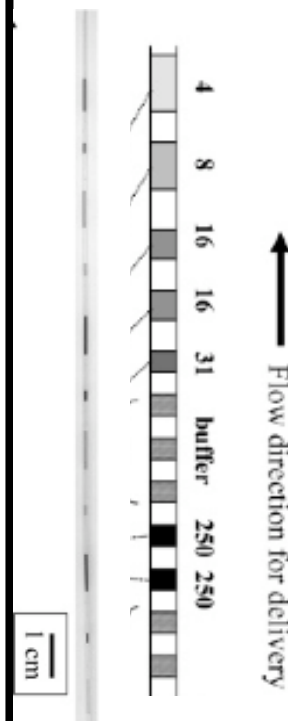
Multi-step protein (thaumatin) crystallization  
Ismagilov, Angew. Chem. 2006

# Optimization/ Mixing



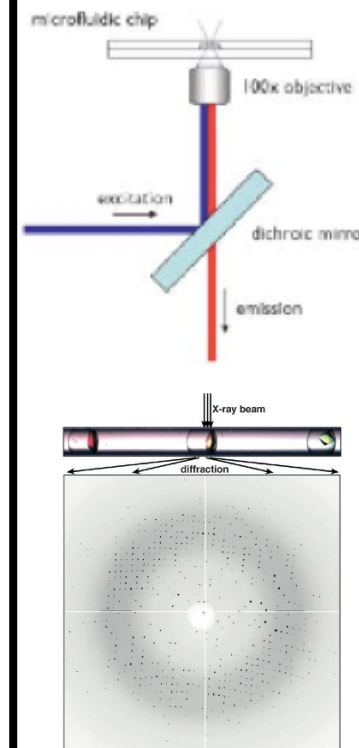
Gradient screening for crystallization conditions  
Ismagilov, 04

# Storage

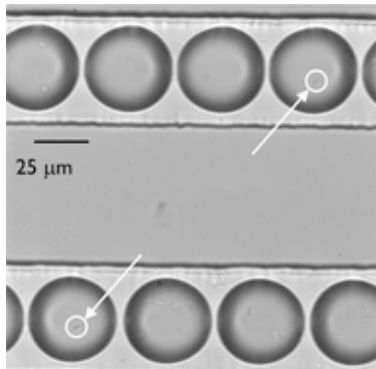


Whitesides 05

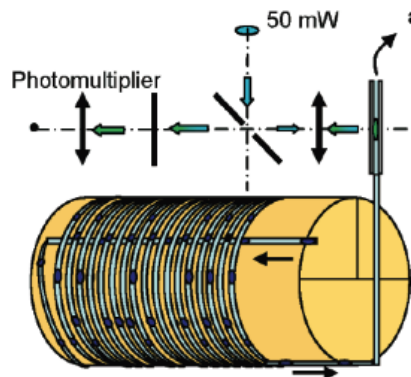
# Detection



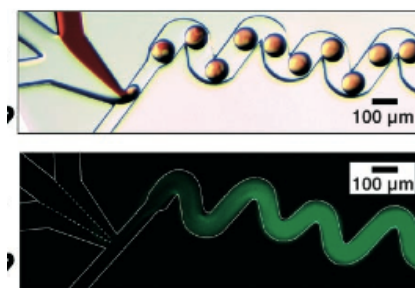
Ismagilov 2006



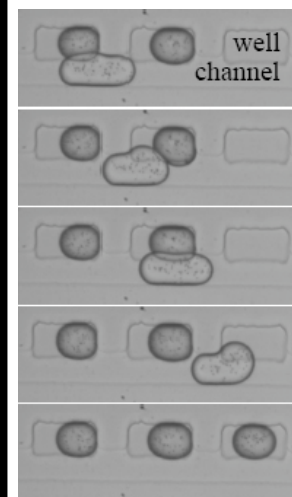
Huebner et al. ChemComm  
Jan 2007



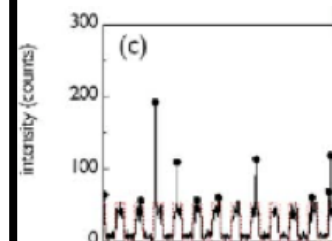
PCR in a drop (Chabert,  
Nov. 06)



Milli-second time scale  
mixing



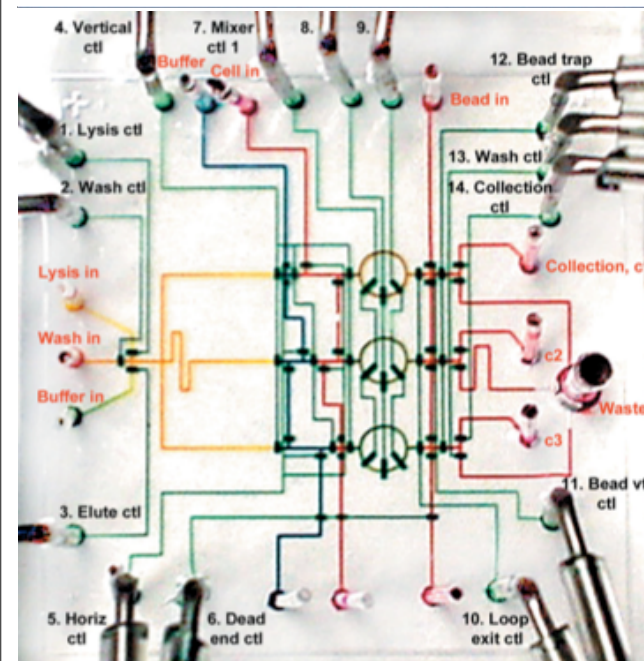
Fraden 06



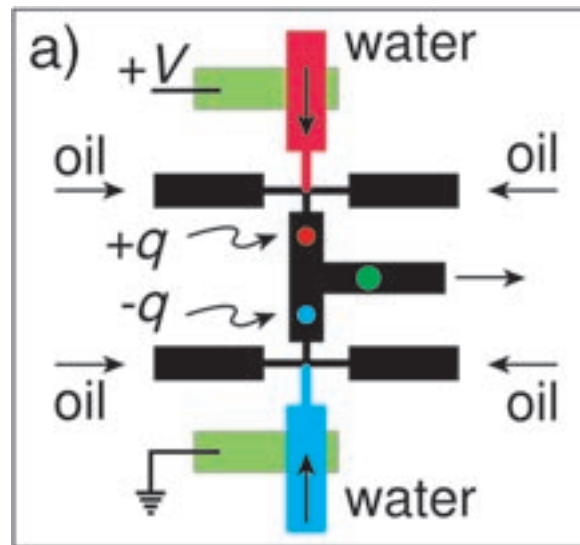
Huebner  
ChemComm07

# Control Strategies

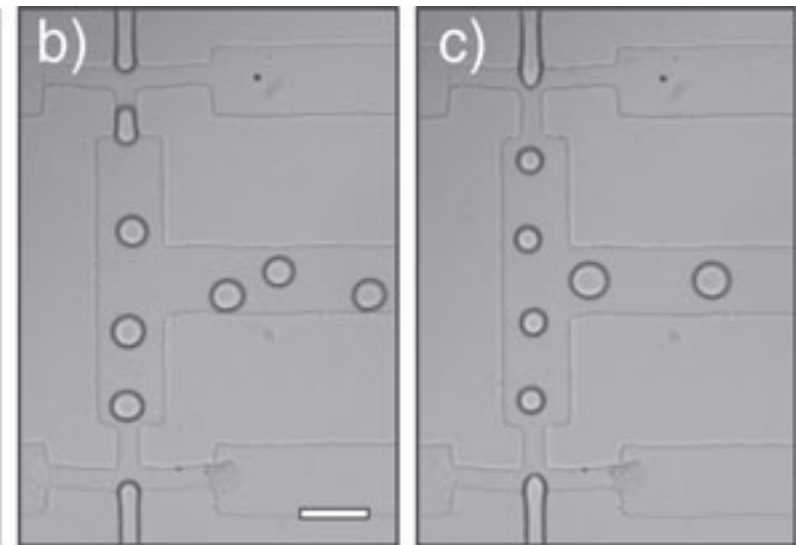
portability  
scaling



Fluidigm



RainDance  
Technologies



# Fluidic Computing

1965

2003

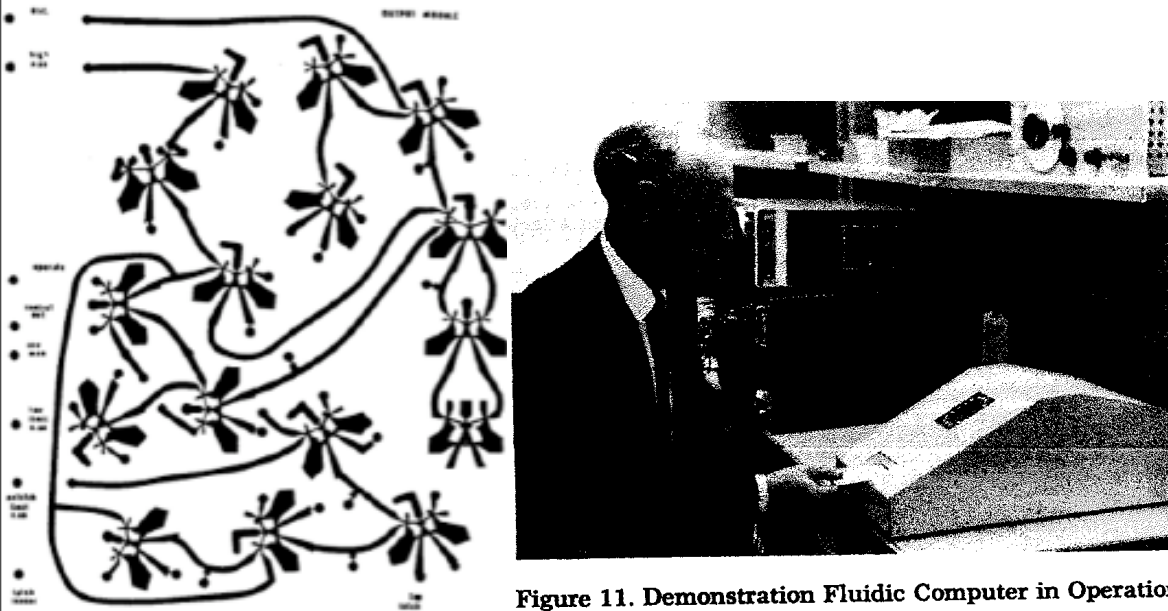
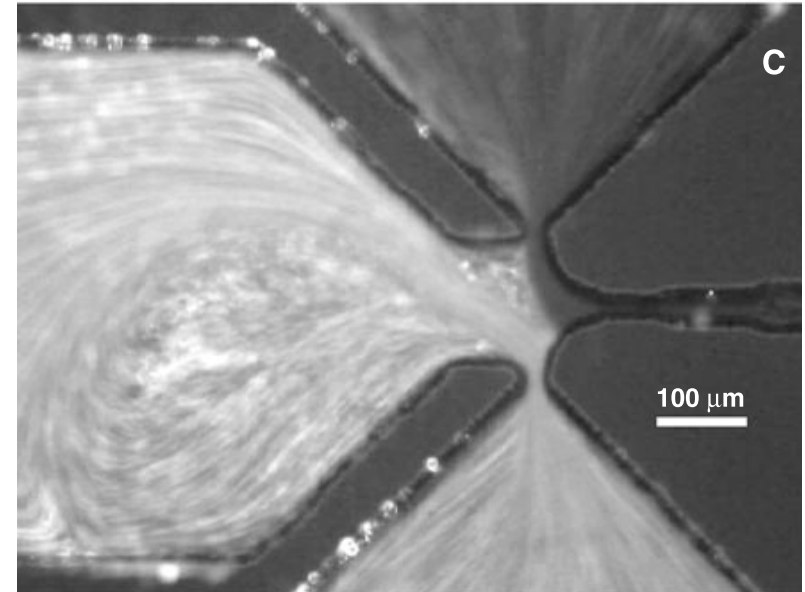


Figure 11. Demonstration Fluidic Computer in Operation



Wall attachment - Coanda effect  
Jet interaction - Inertial effects

large **Re number systems**

[Humphery et al. Fluidics 1965]

Requires non-newtonian fluids  
for operation

[Quake et al. Science 2003]

# Bubble Logic

## On-chip process control

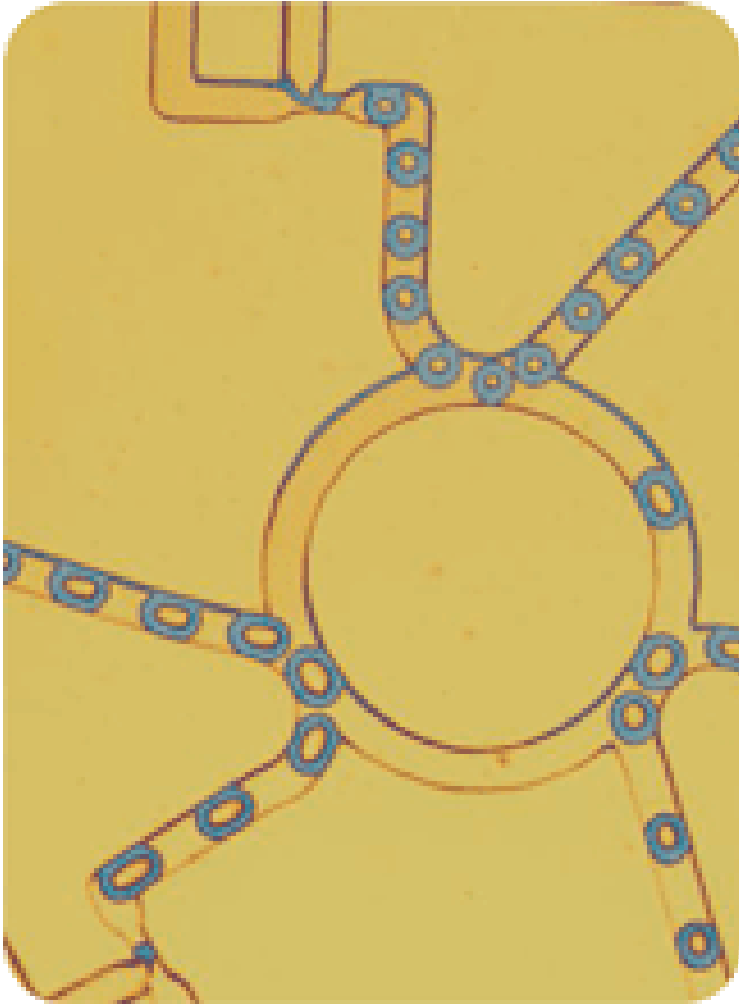


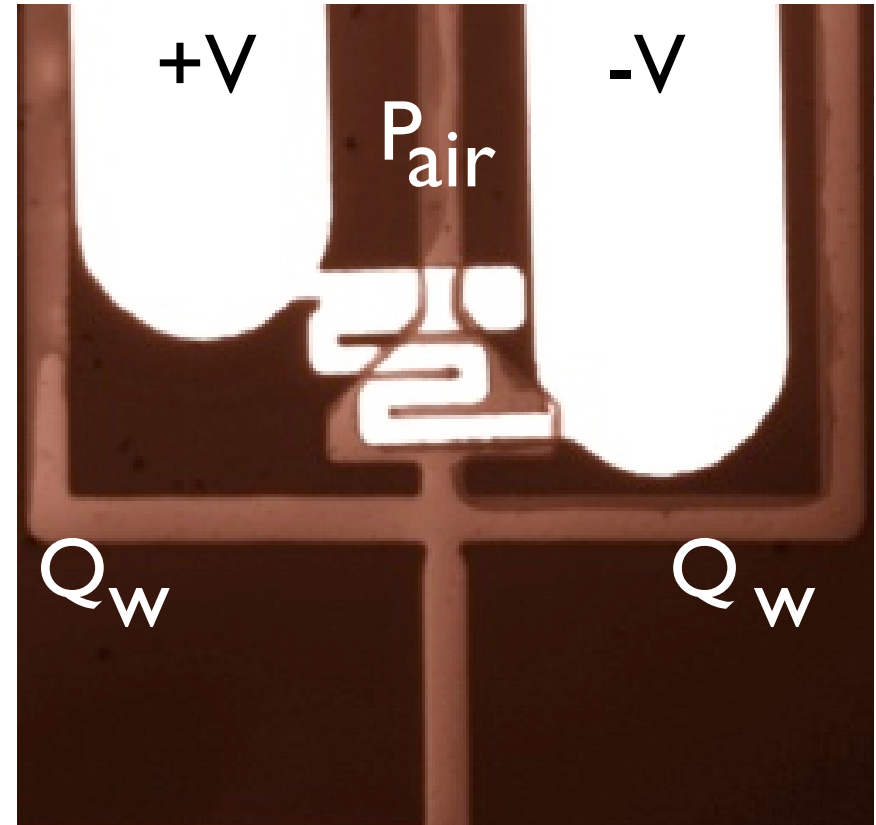
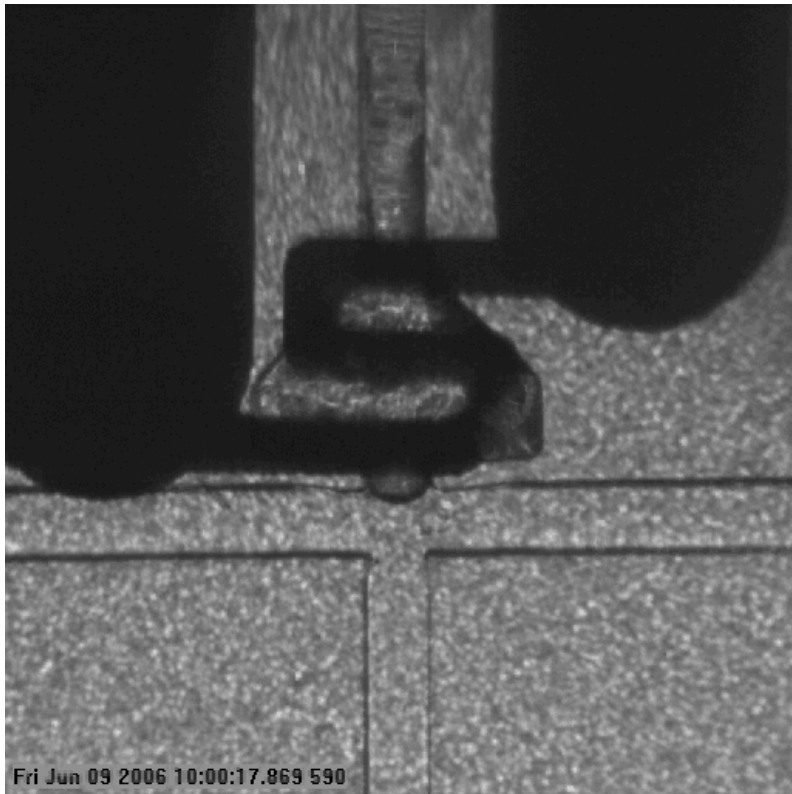
Image credit : F. Frenkel, M. Prakash

- 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



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

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

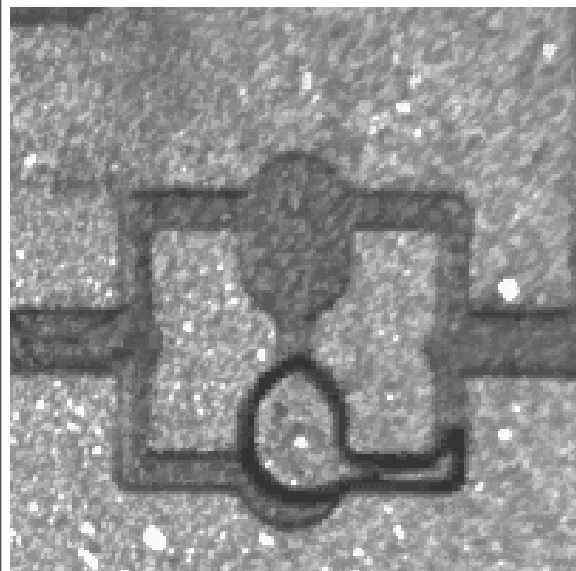
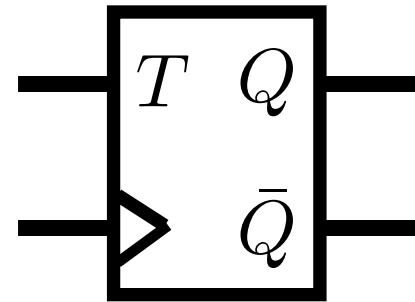
R = 95  $\Omega$ , 20V 100ms pulse

# 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

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

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

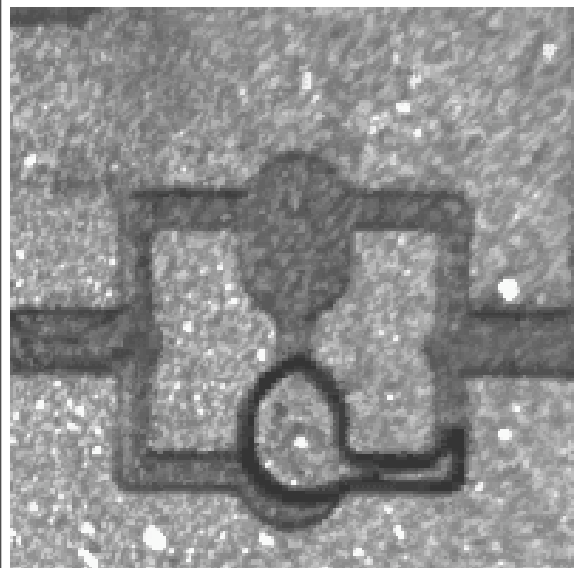
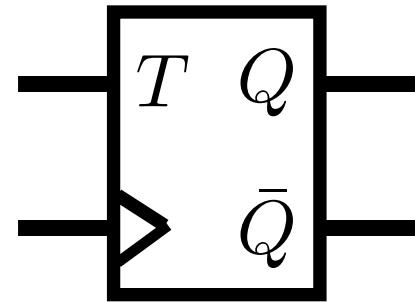


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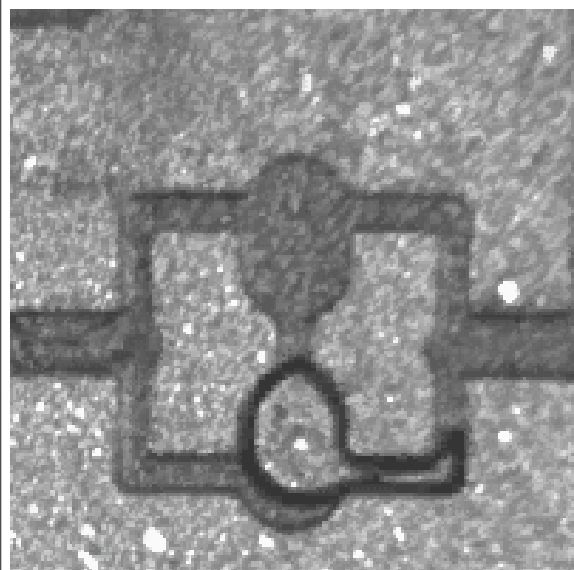
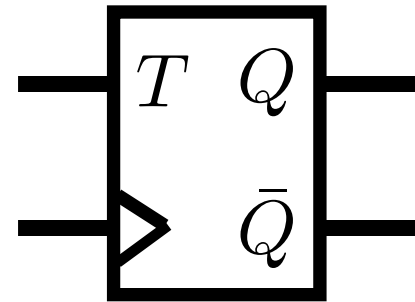


# Microfluidic Toggle Flip-Flop

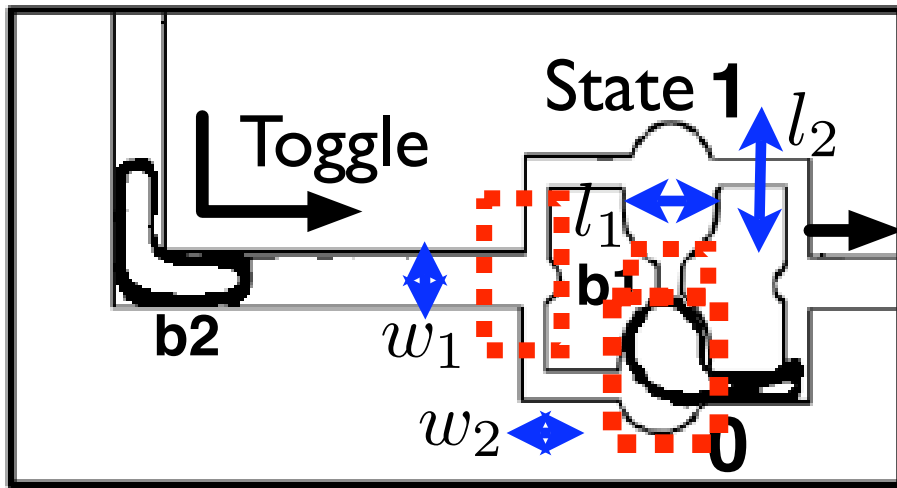
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$$Q_{next} = T \oplus Q$$

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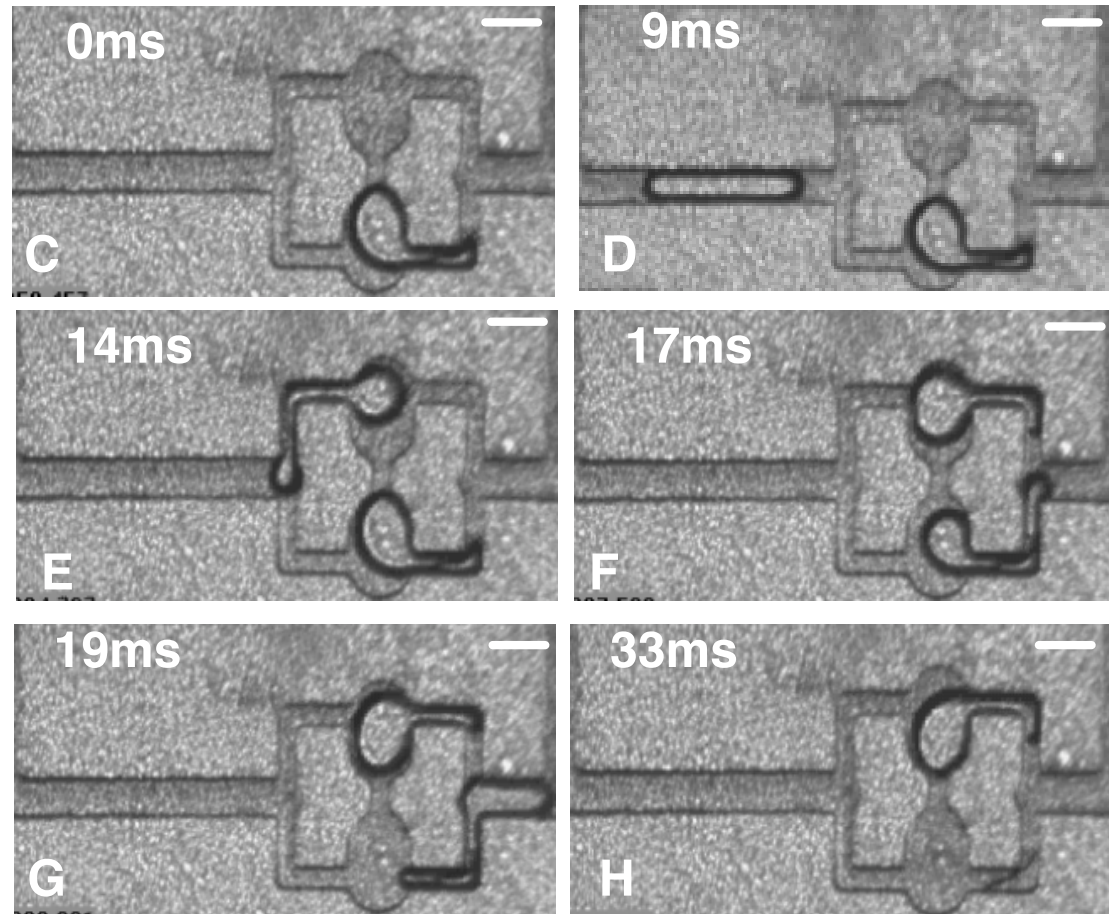


# Device Physics



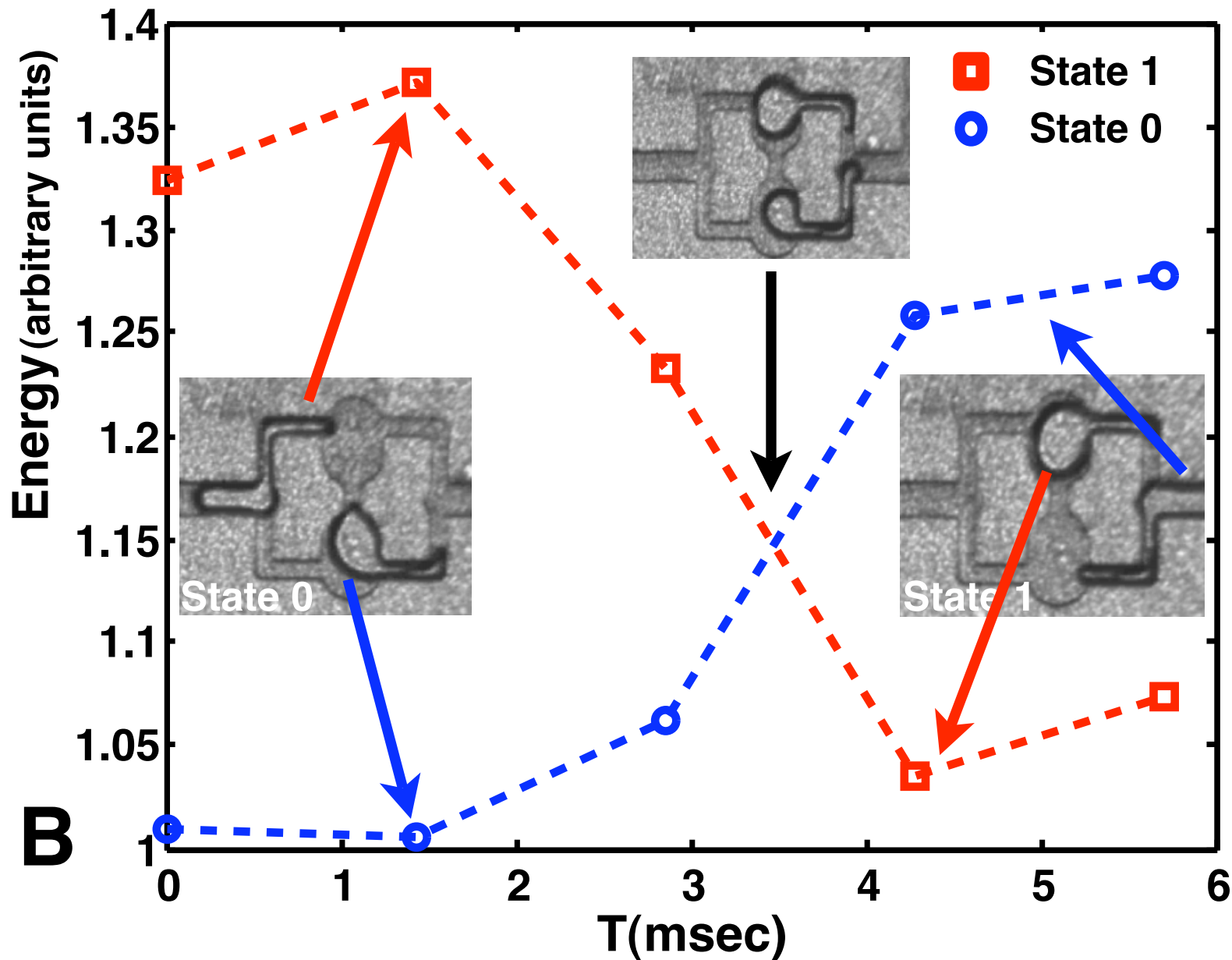
$$w_1 = 100\mu m, w_2 = 40\mu m, h = 70\mu m$$
$$l_1 = 200\mu m, l_2 = 300\mu m$$

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

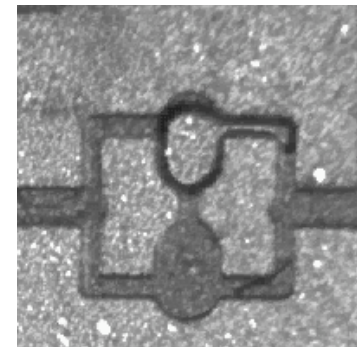
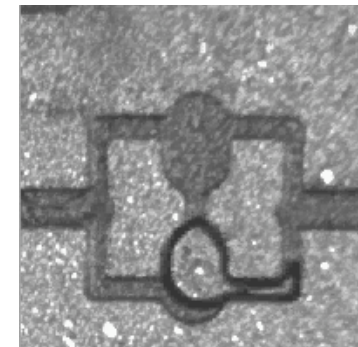
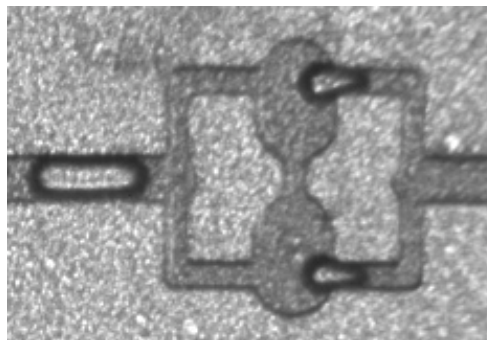
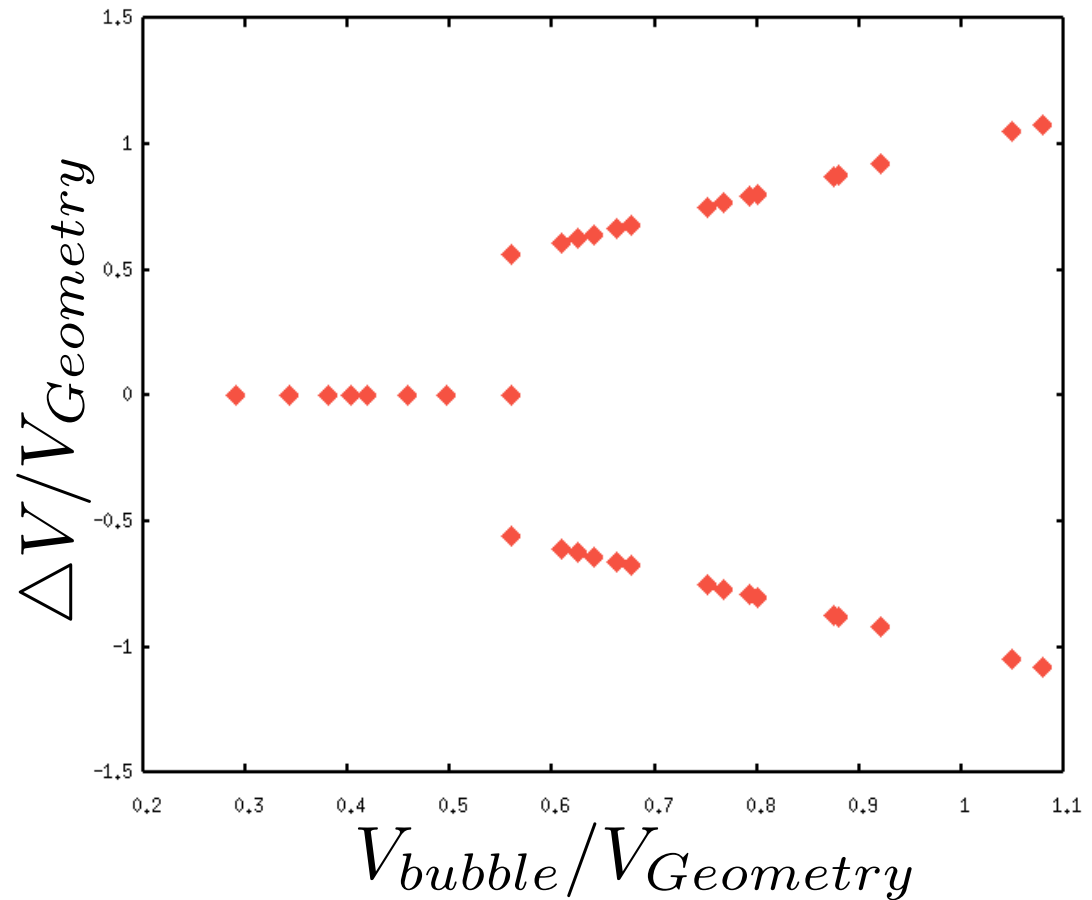
$$l/\pi w = 1$$

[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

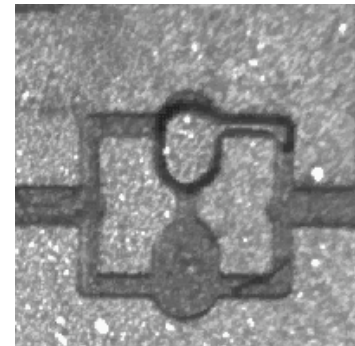
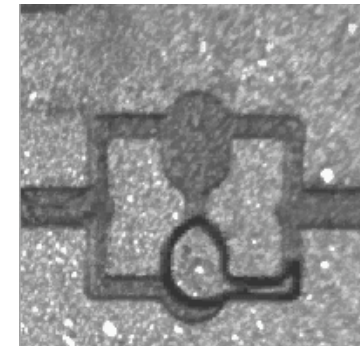
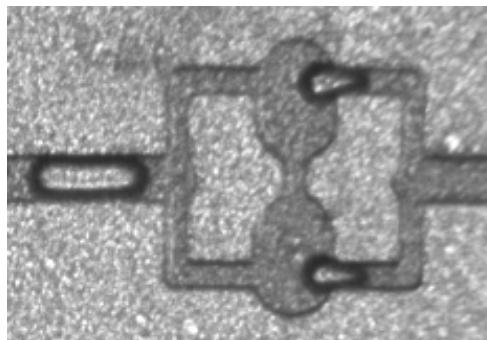
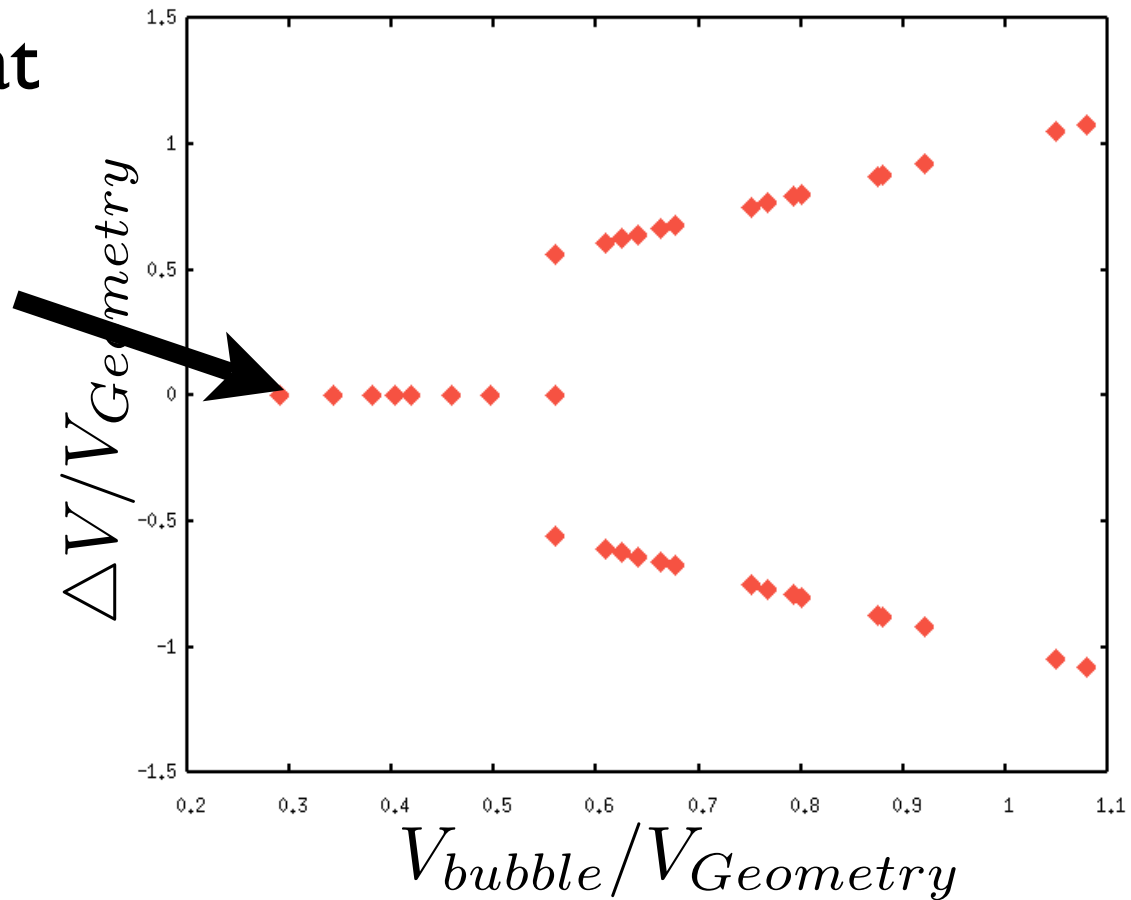
$$l/\pi w = 1$$

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Behavior independent of bubble arrival frequency

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# Bifurcation at T junction

Rayleigh-Plateau breakup at the T junction

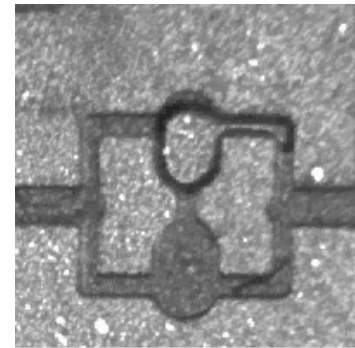
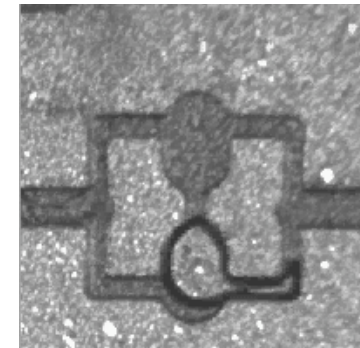
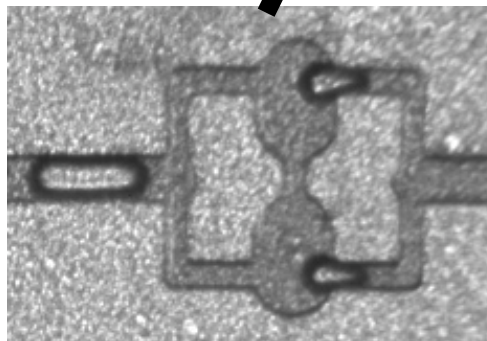
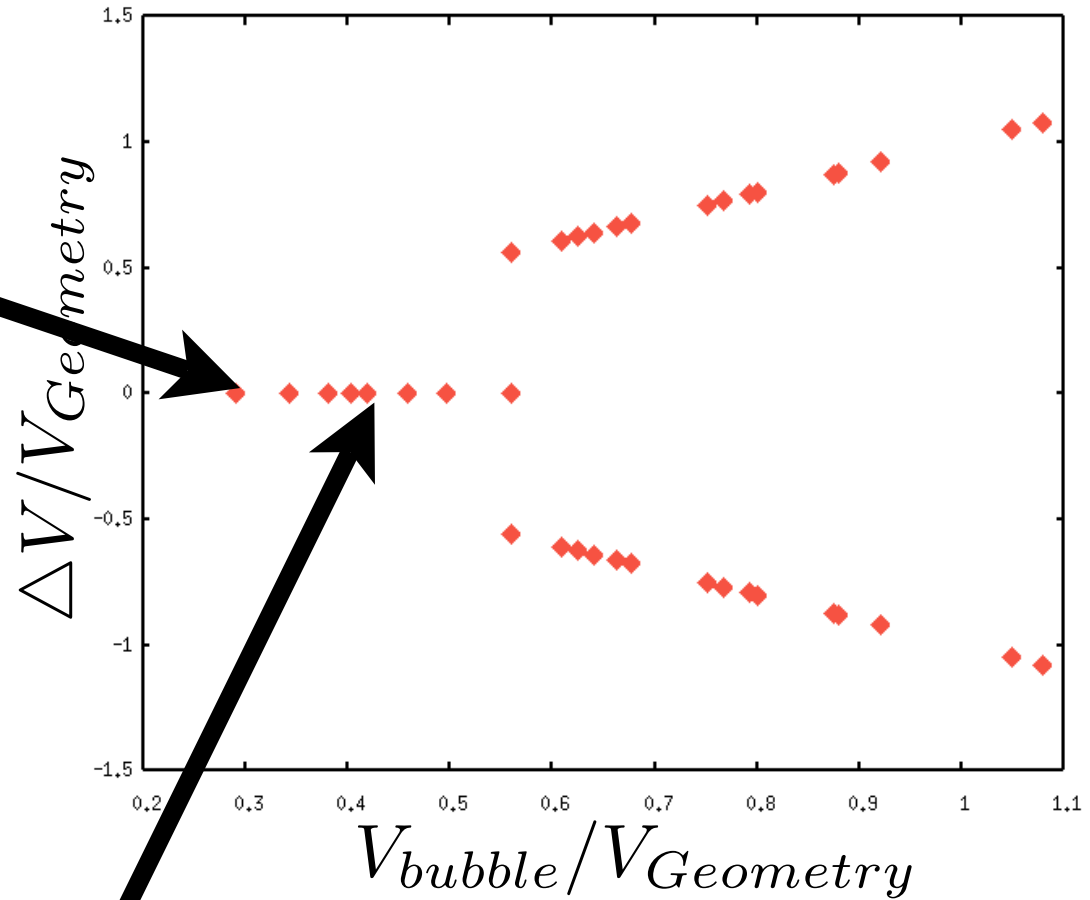
$$l/\pi w = 1$$

[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

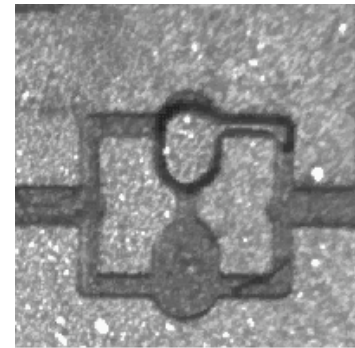
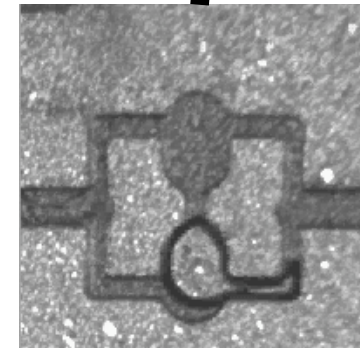
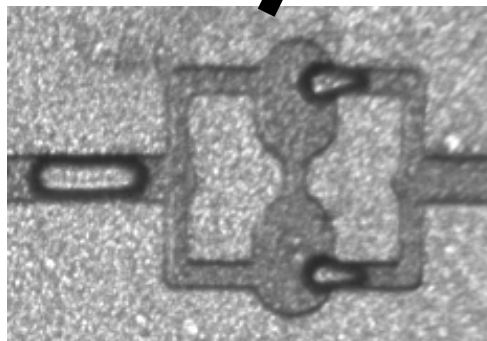
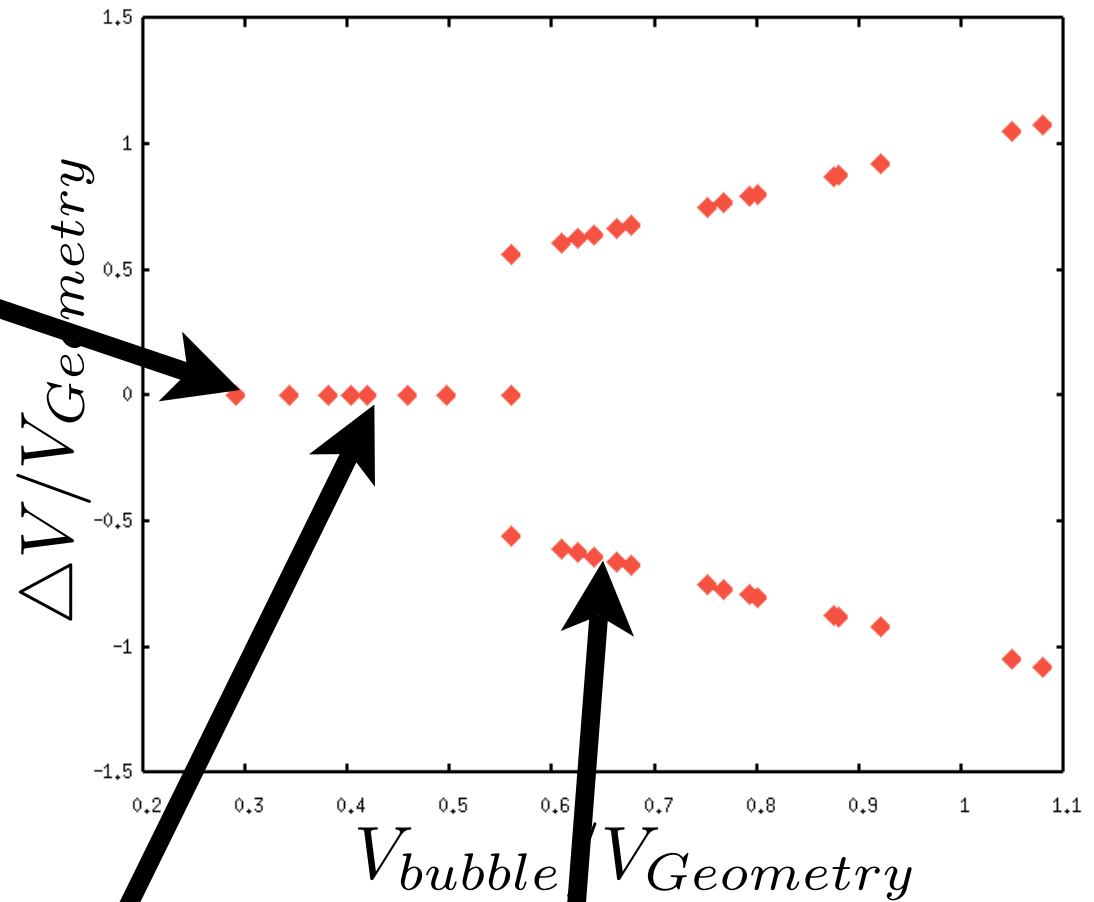
$$l/\pi w = 1$$

[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

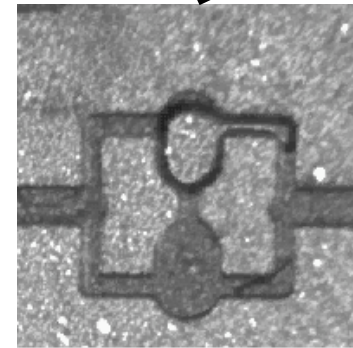
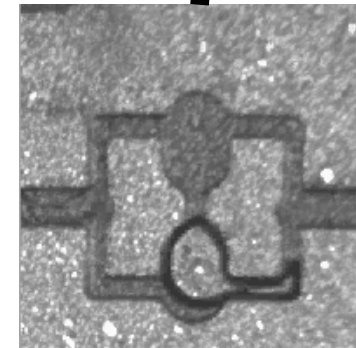
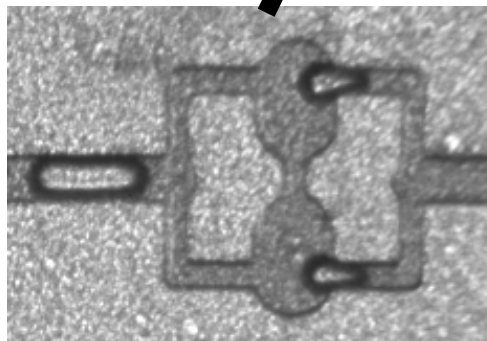
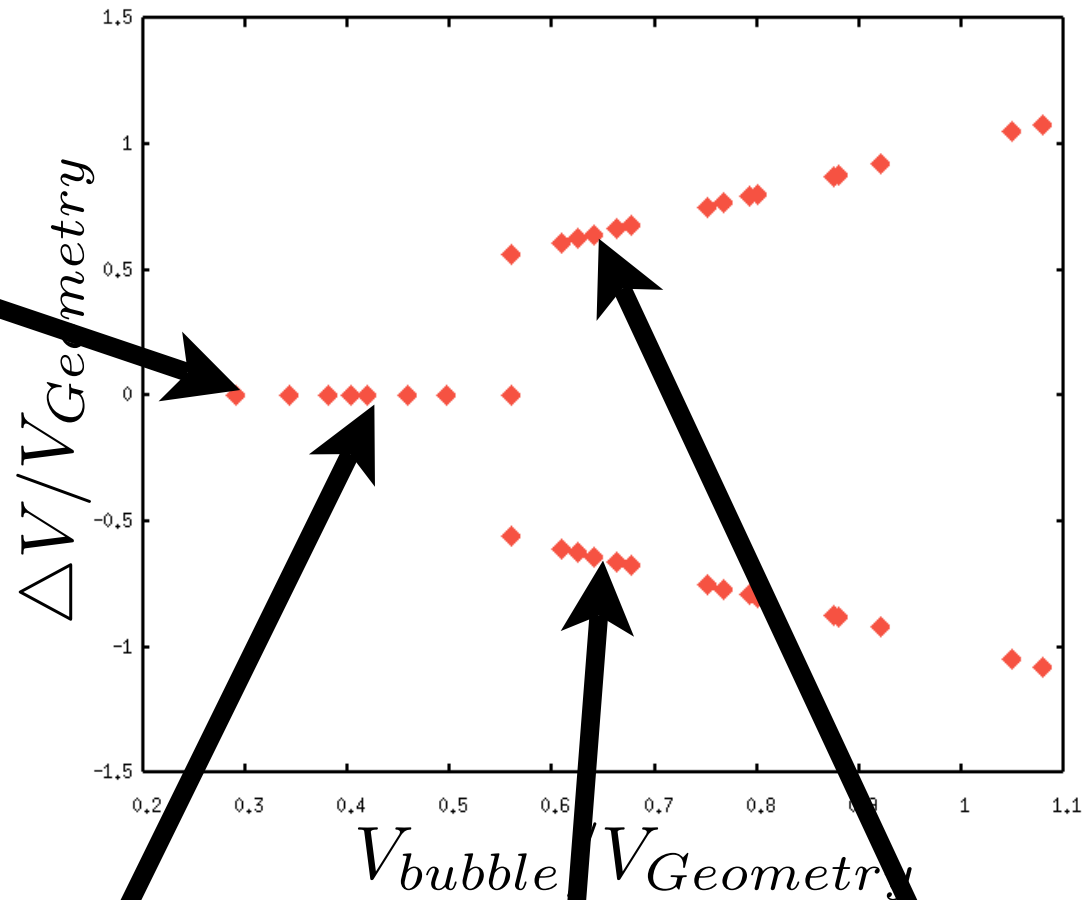
$$l/\pi w = 1$$

[H.A. Stone, PRL 2004]

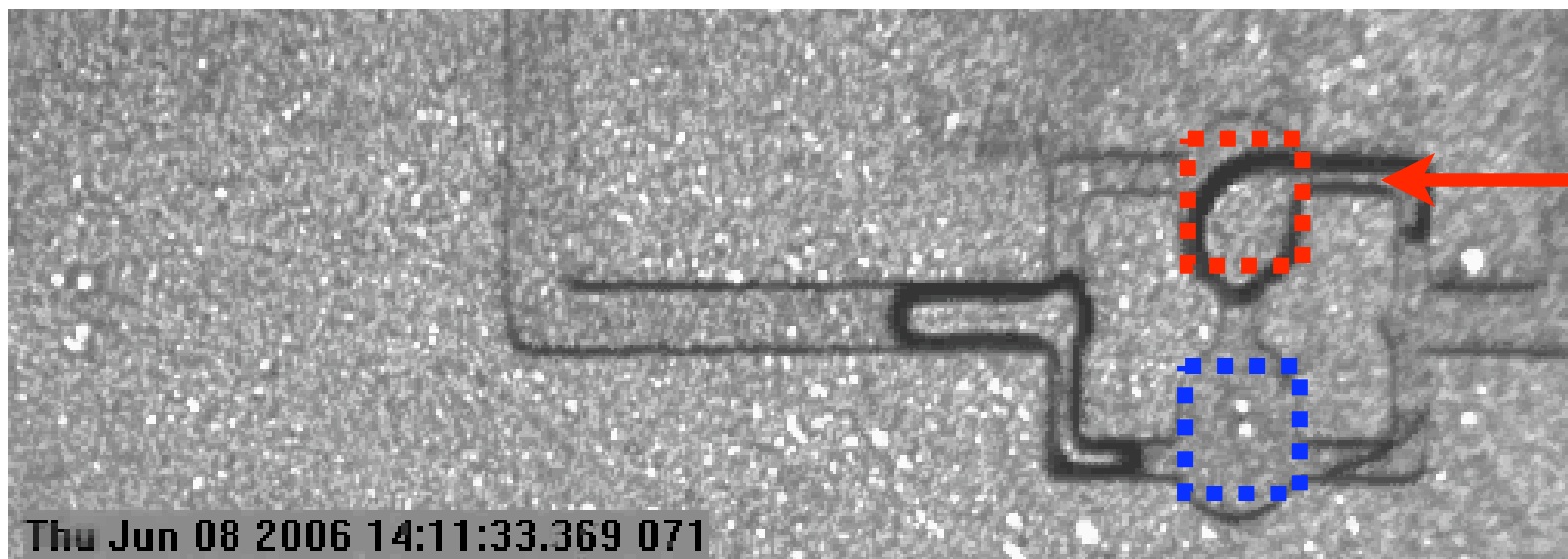
Behavior independent of bubble arrival frequency

[Garstecki, PRE, 2006]

[Ajdari, PRL 2005]

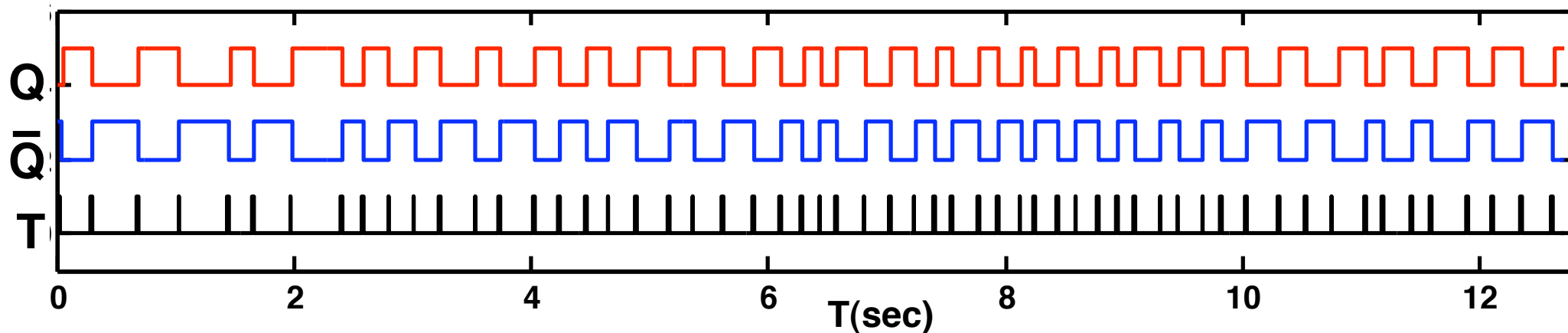


# Trap repeatability

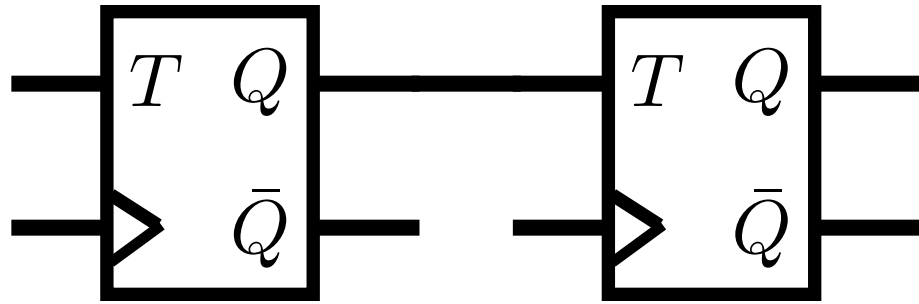


light intensity  
vs  
time

10Hz bistable one-bit memory

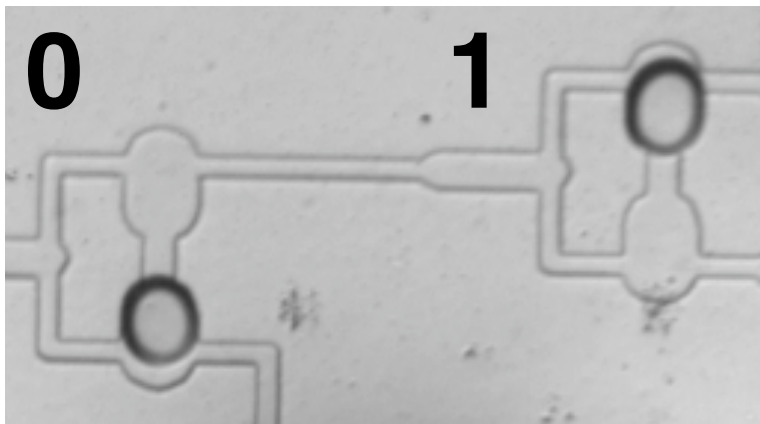
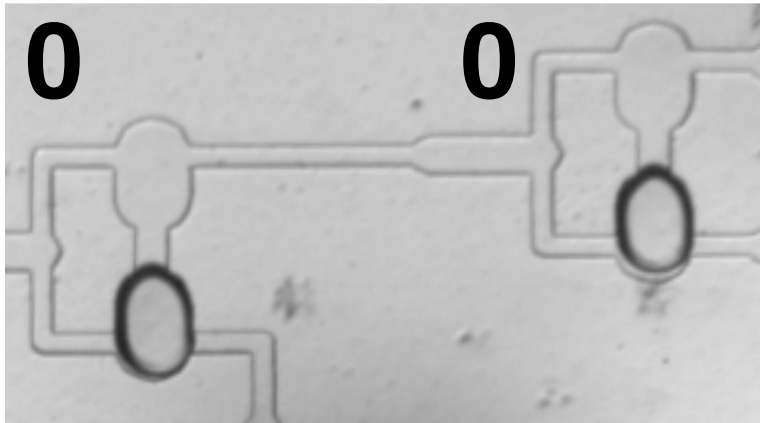


# Applications



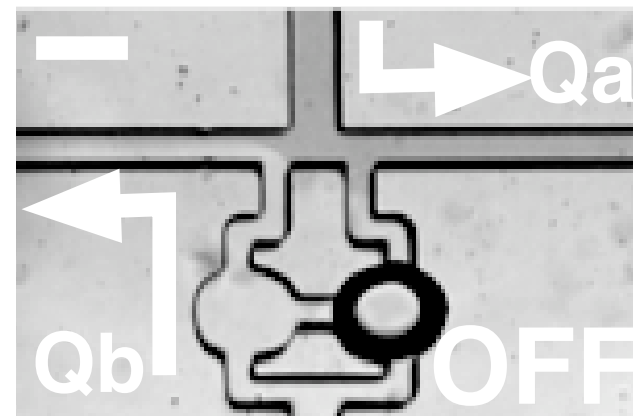
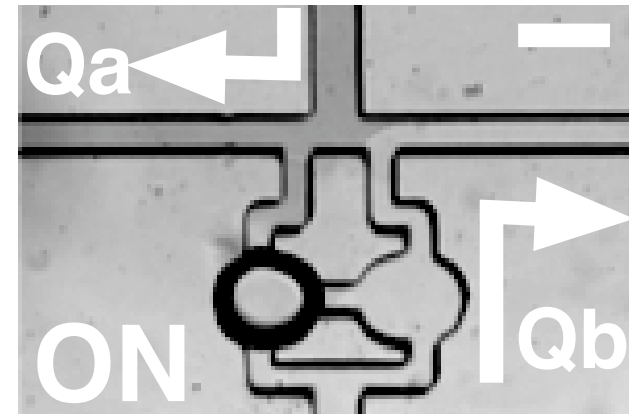
Counting drops

RIPPLE COUNTER



High speed switching valves

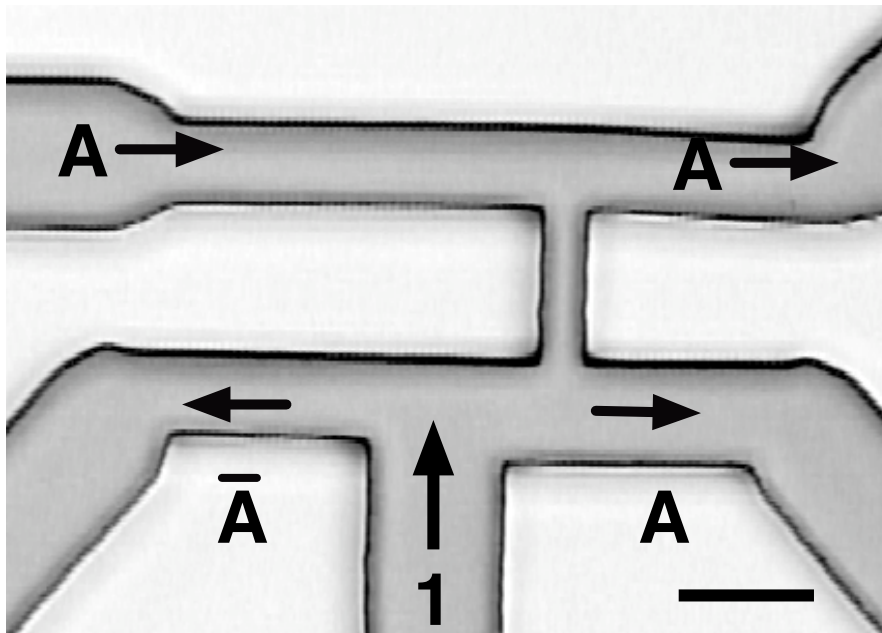
BISTABLE VALVES



# Inverter

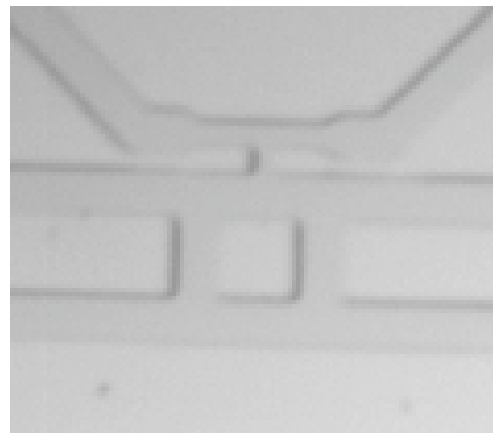
Designed as  
 $\text{NOT}(A).B$  gate for  $B=1$

**INVERTER  
WITH GAIN**



Scale bar  $100\mu m$

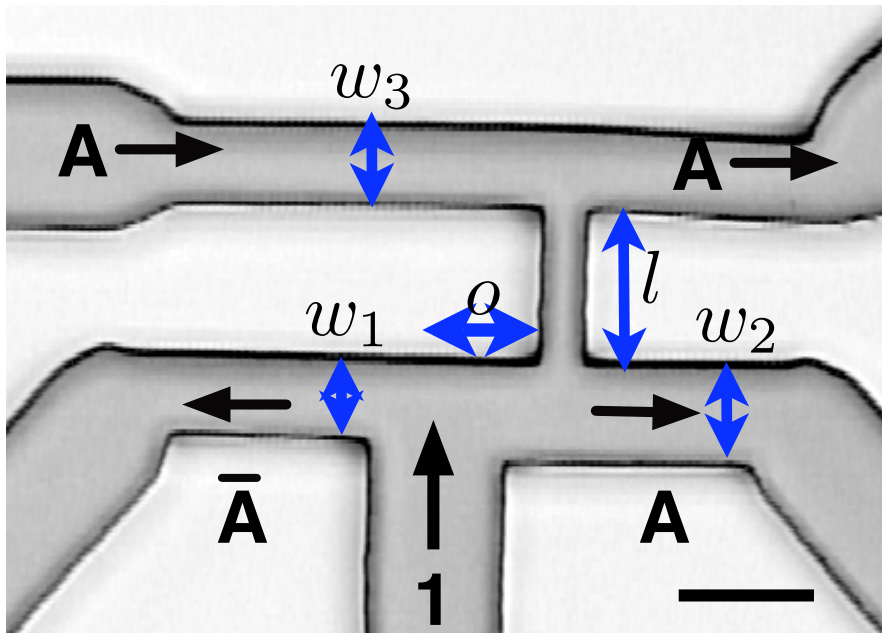
Fredkin gate  
(reversible  
logic)



# Inverter

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

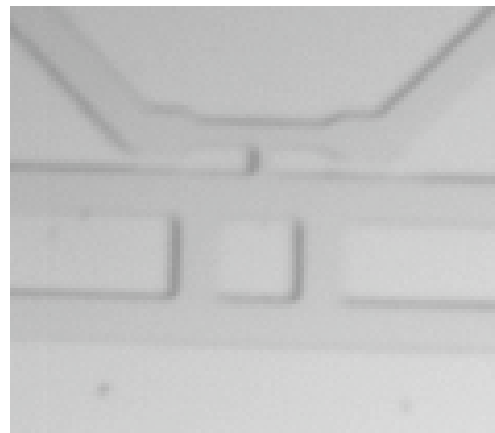
INVERTER  
WITH GAIN



$$w_2 > w_1$$

Scale bar  $100\mu m$

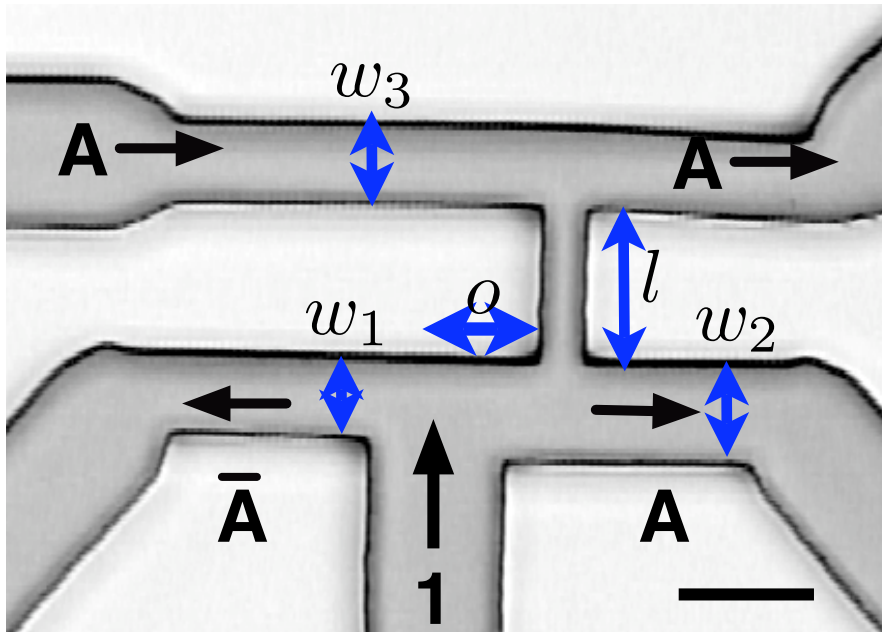
Fredkin gate  
(reversible  
logic)



# Inverter

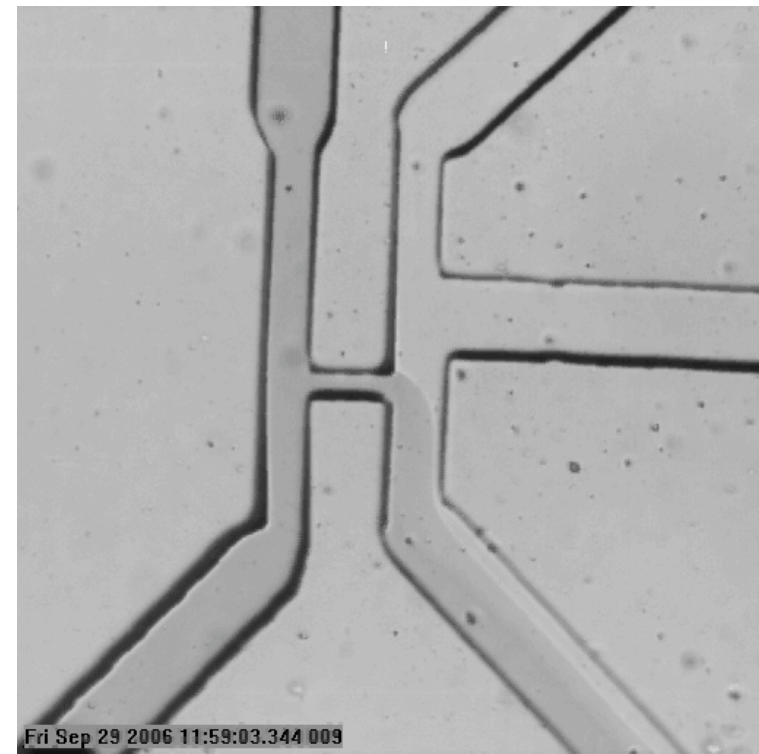
Designed as  
NOT(A).B gate for B=1

INVERTER  
WITH GAIN



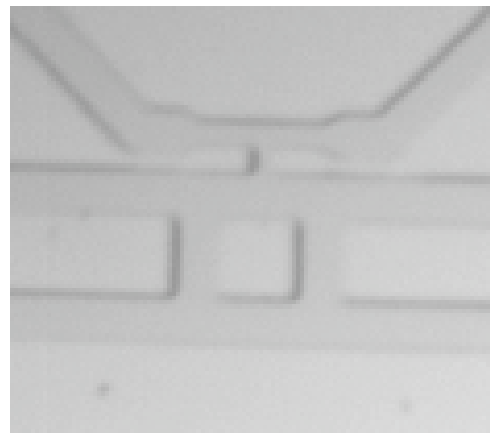
$$w_2 > w_1$$

Scale bar  $100\mu m$



Fri Sep 29 2006 11:59:03.344 009

Fredkin gate  
(reversible  
logic)



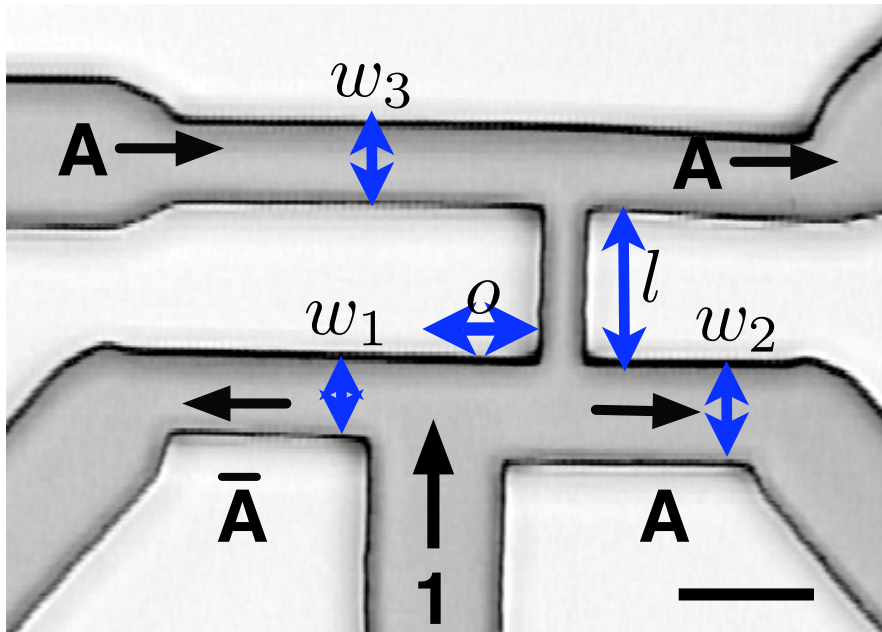


# Inverter

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

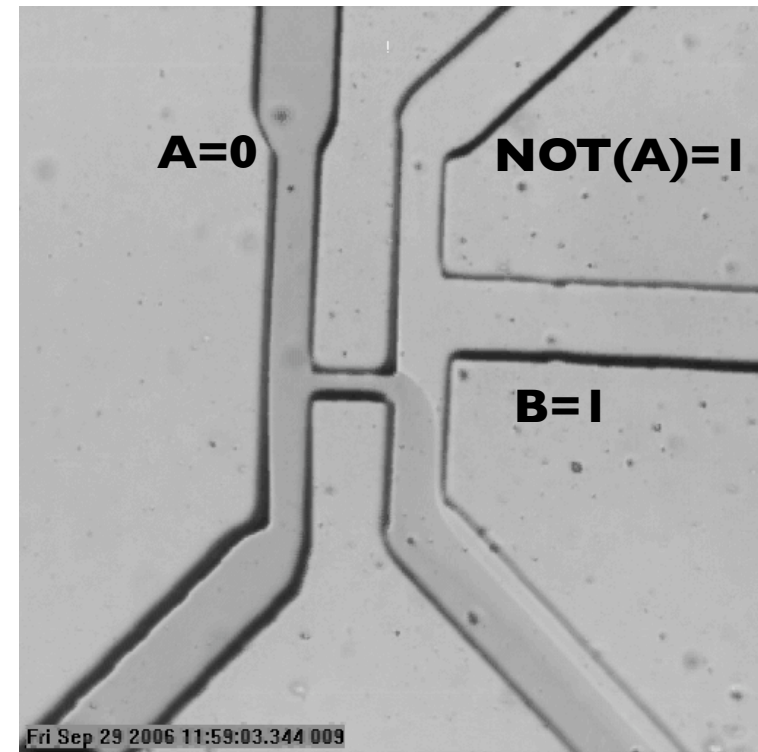
A=0  
B=1  
NOT(A)=1

INVERTER  
WITH GAIN

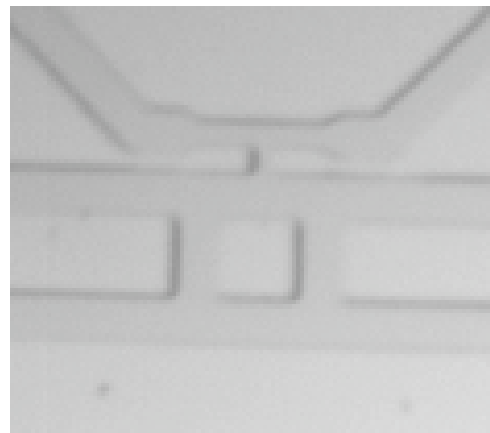


$w_2 > w_1$

Scale bar  $100\mu m$



Fredkin gate  
(reversible  
logic)

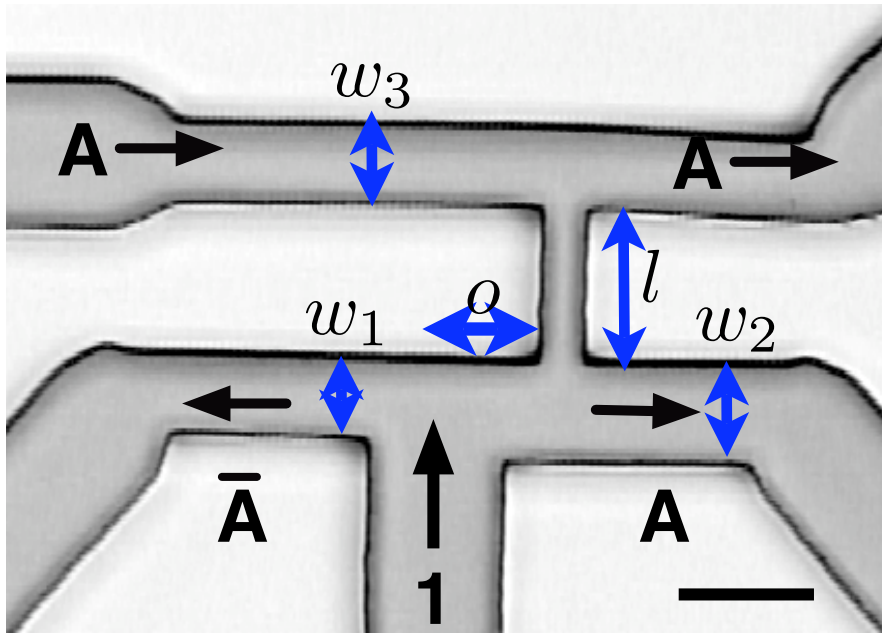


# Inverter

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

$A=0$   
 $B=1$   
 $\text{NOT}(A)=1$

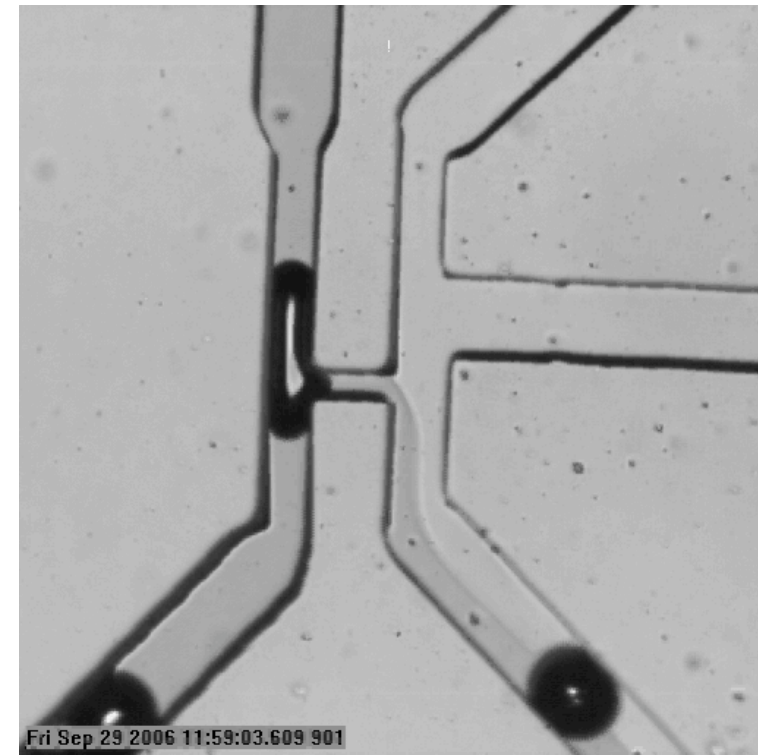
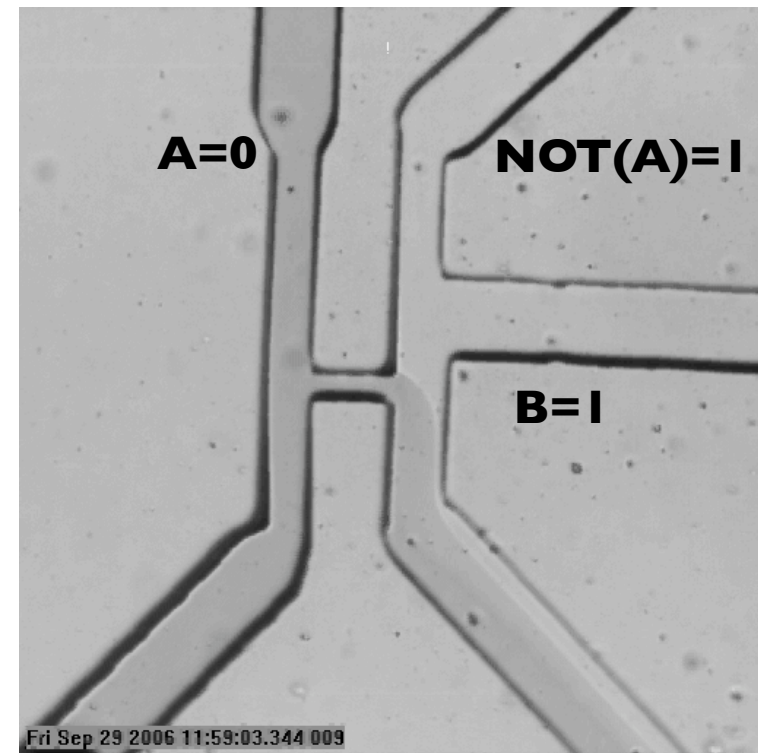
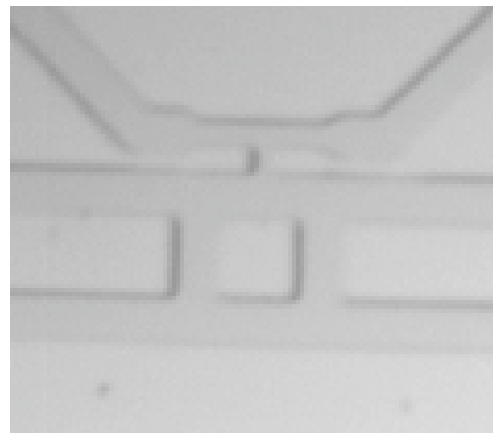
INVERTER  
WITH GAIN



$$w_2 > w_1$$

Scale bar  $100\mu m$

Fredkin gate  
(reversible  
logic)

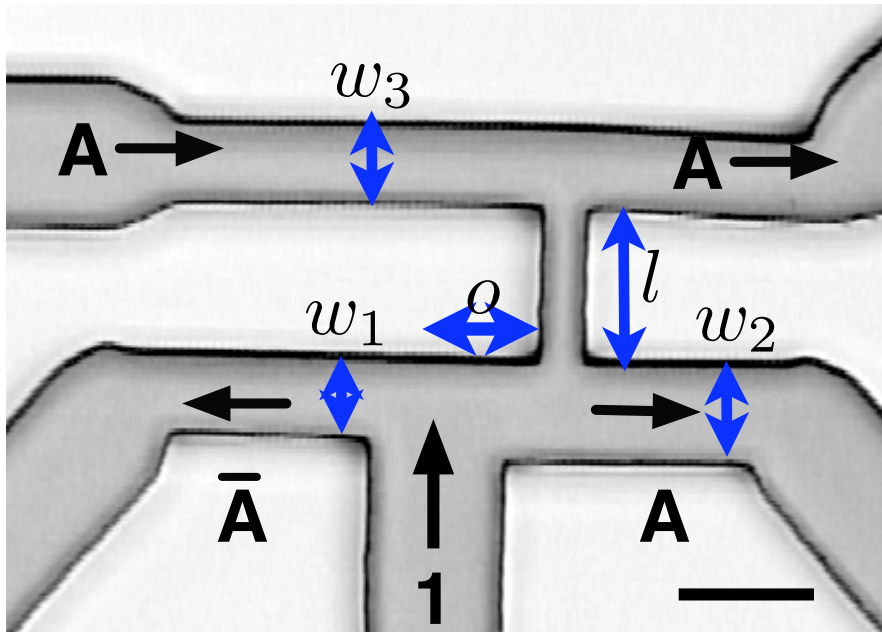


# Inverter

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

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

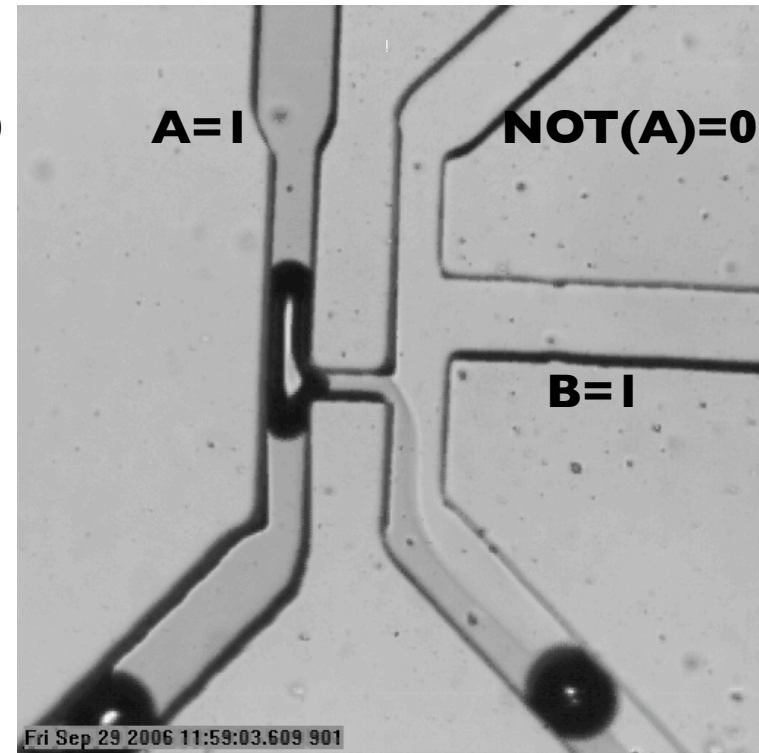
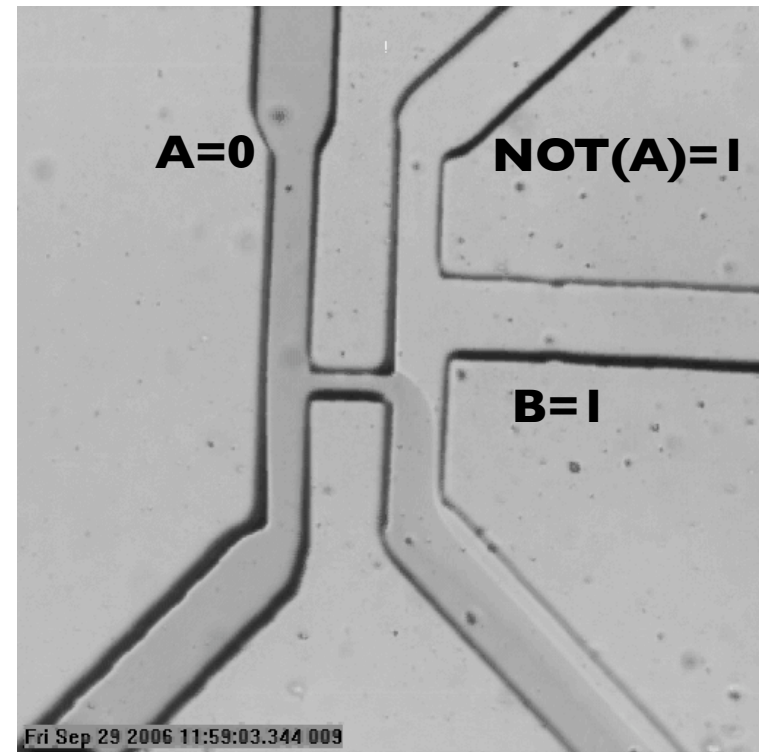
INVERTER  
WITH GAIN



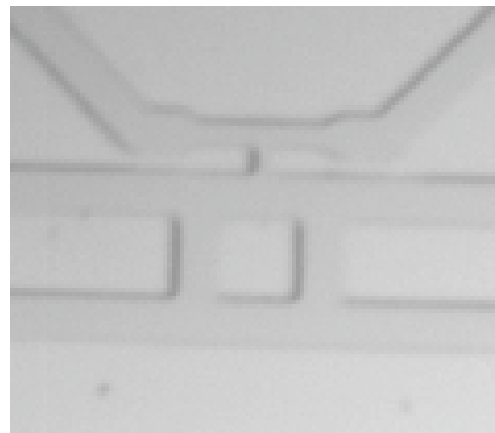
$$w_2 > w_1$$

Scale bar  $100\mu m$

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



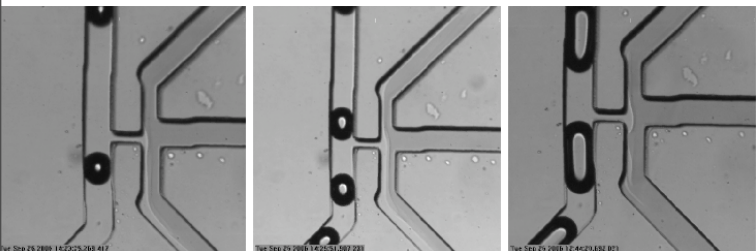
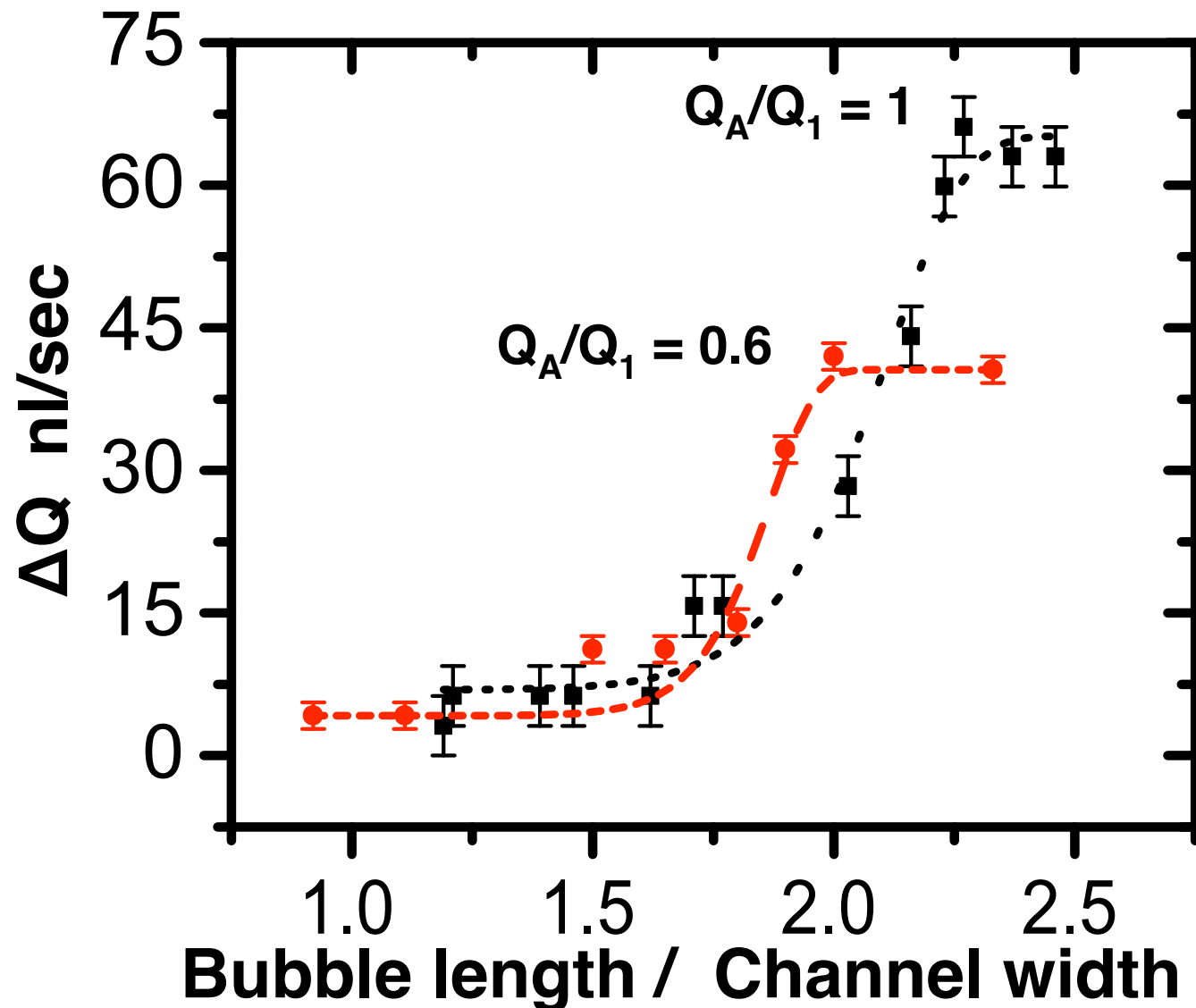
Fredkin gate  
(reversible  
logic)



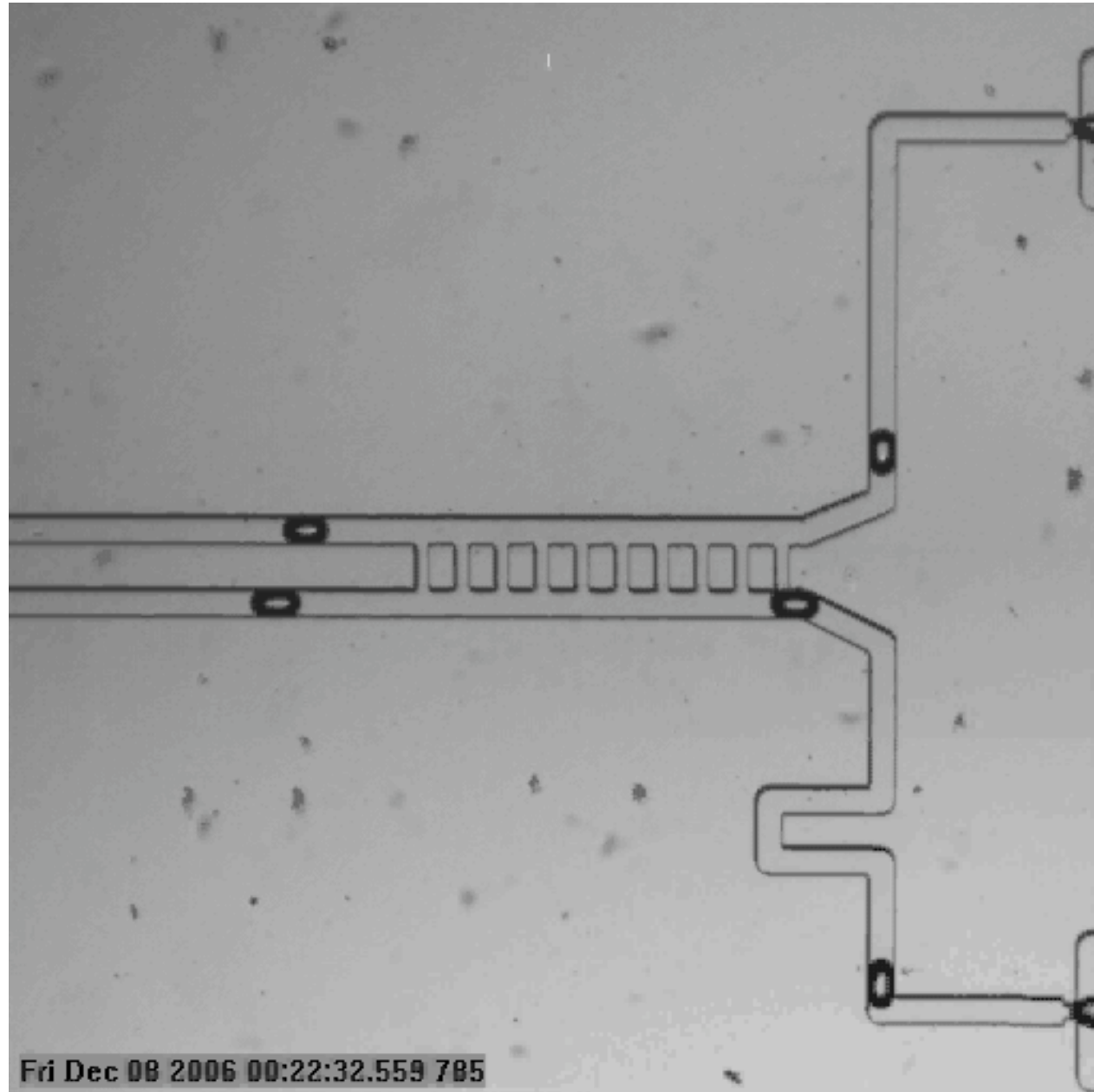
# Inverter : amplification/gain

Dependence on bubble length

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

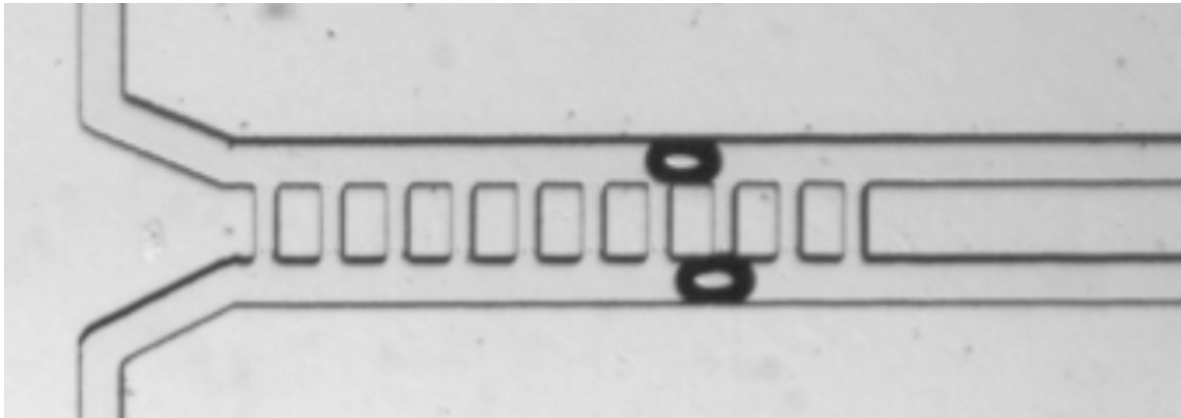


# Bubble/Bit synchronizer



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

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

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

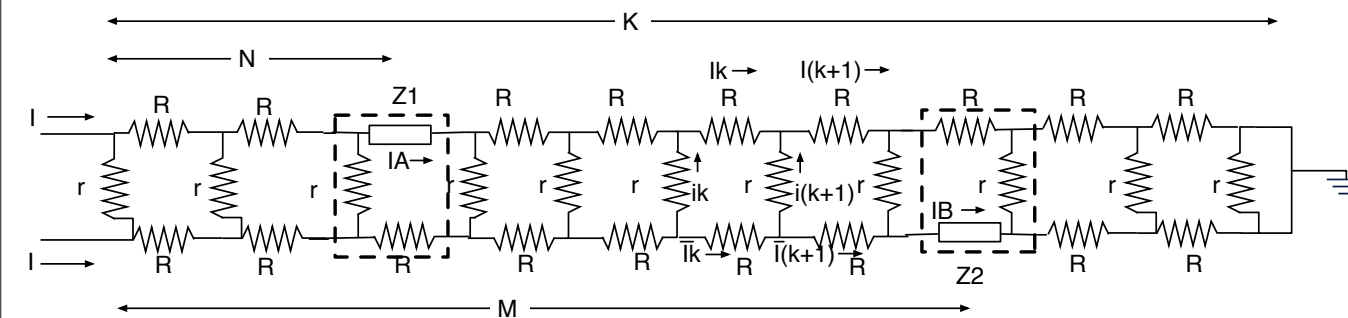
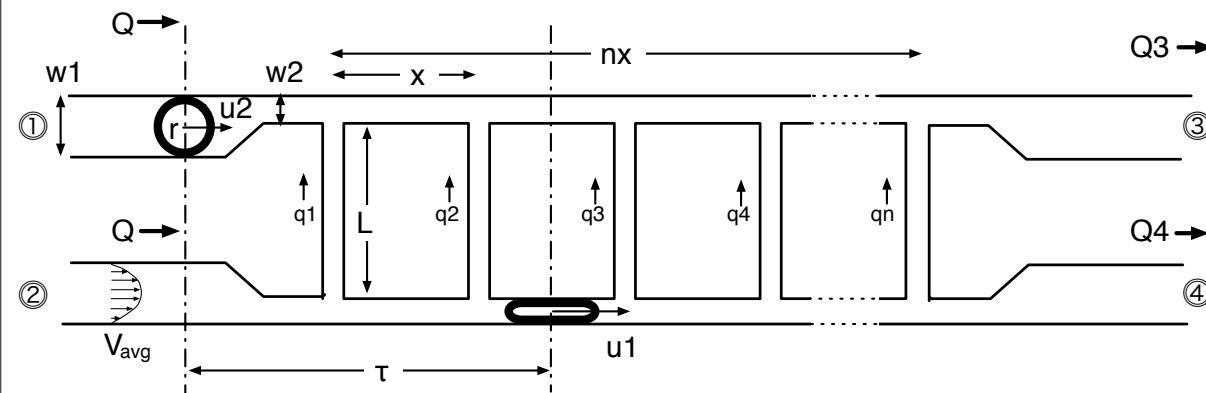
$$I_j - I_{j-1} = i_j$$

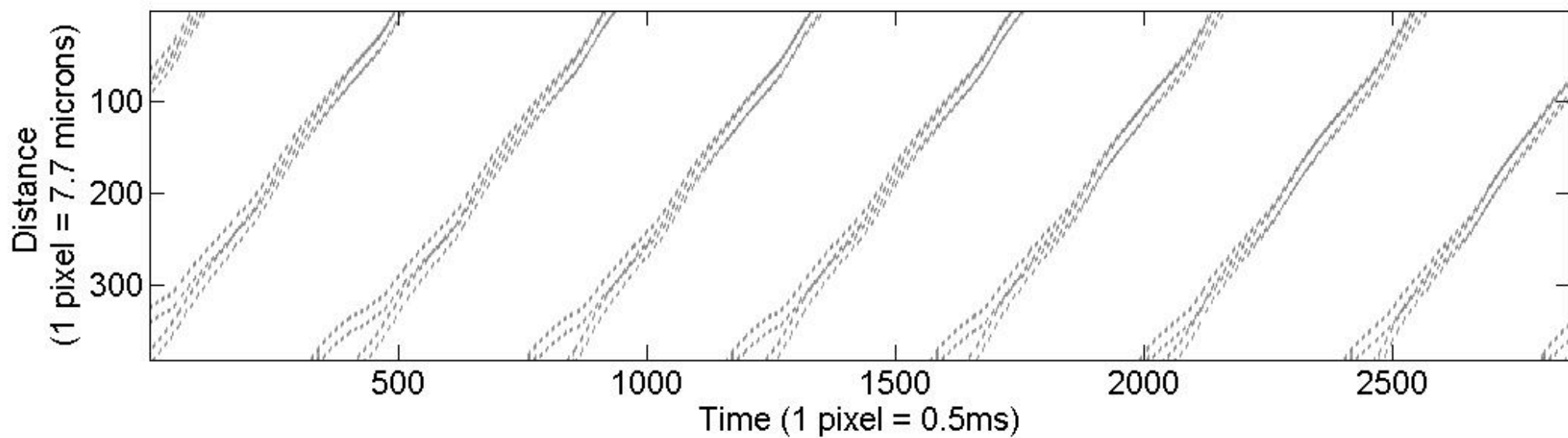
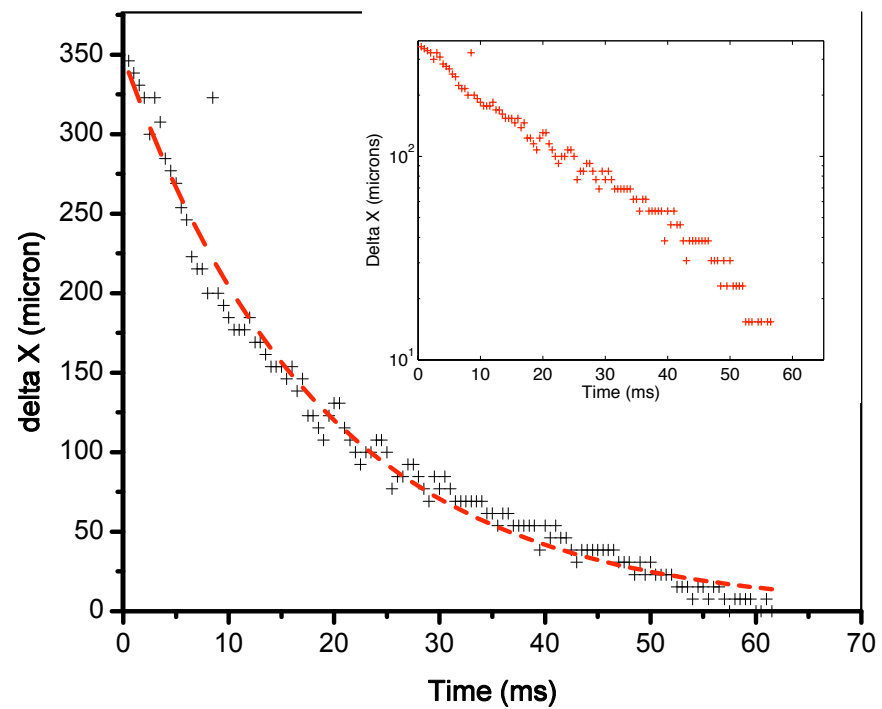
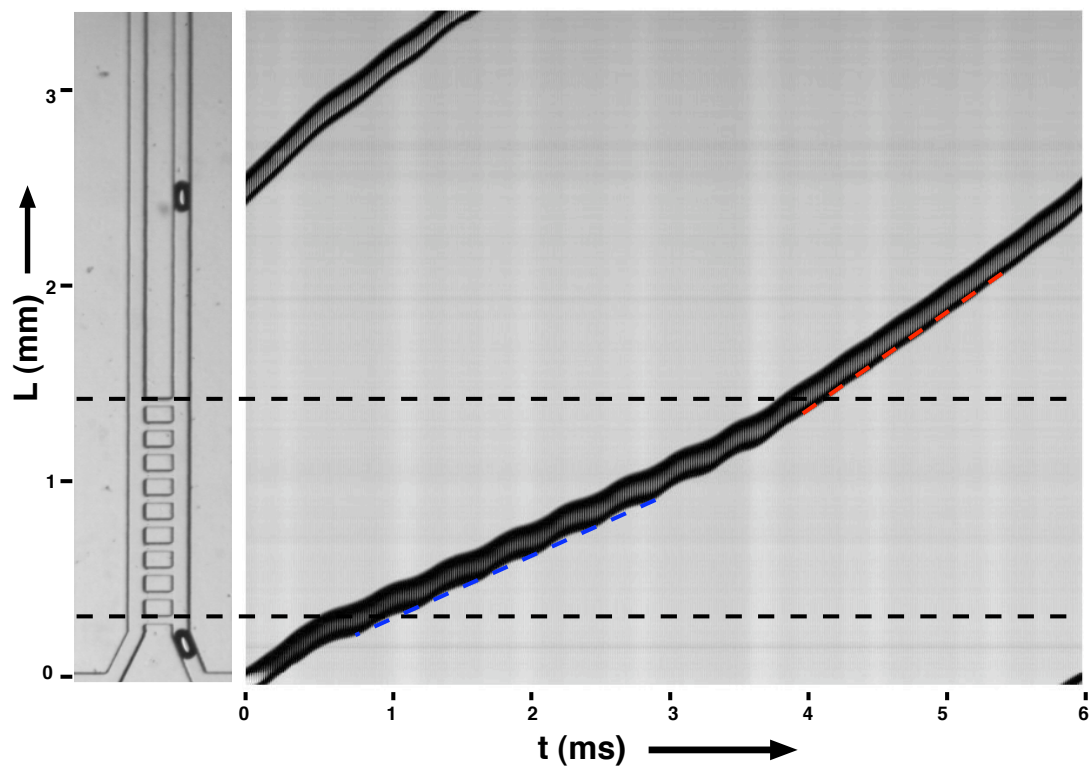
$$\bar{I}_j - \bar{I}_{j-1} = -i_j$$

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

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

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





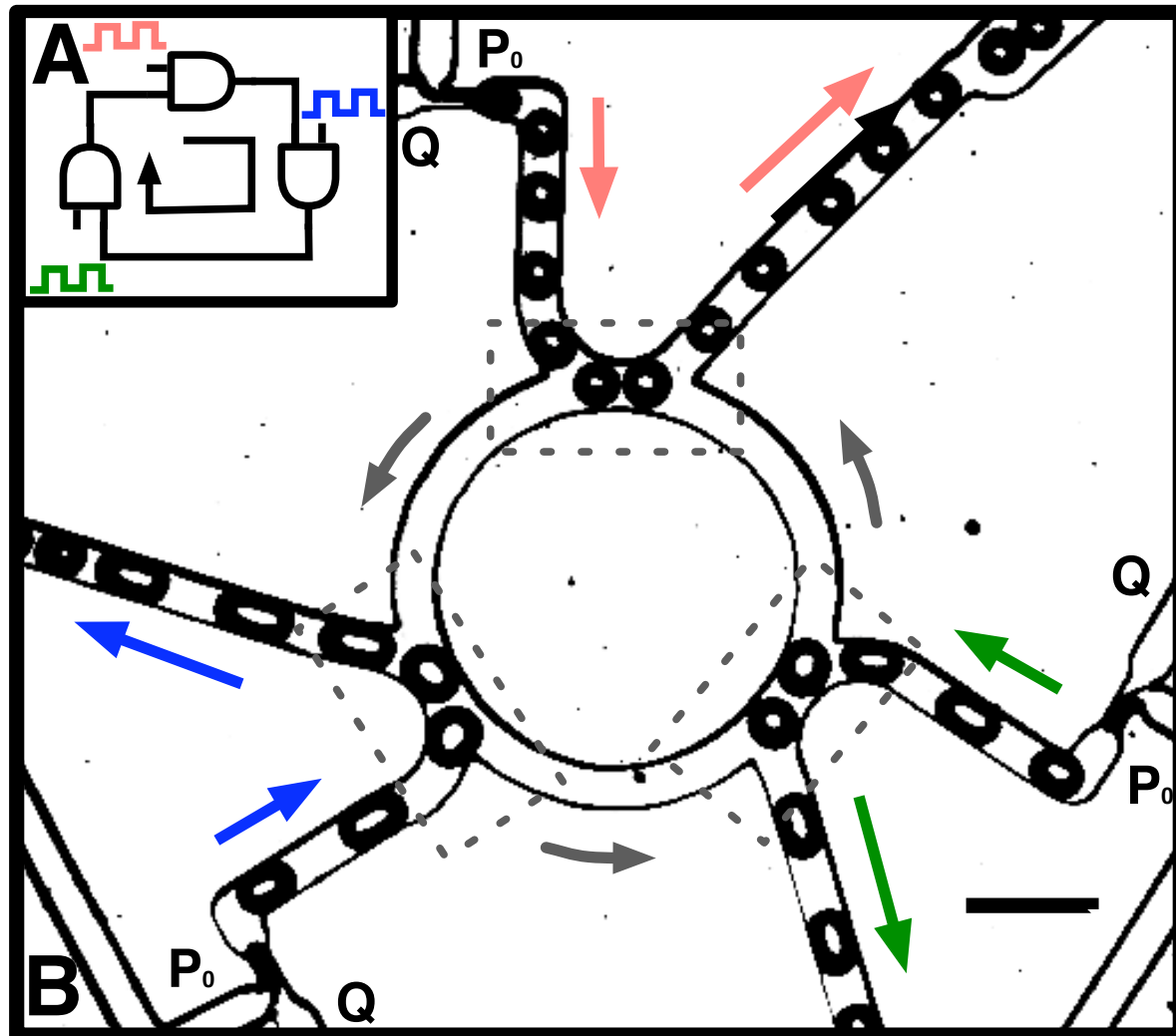
# Designing microfluidic circuits

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

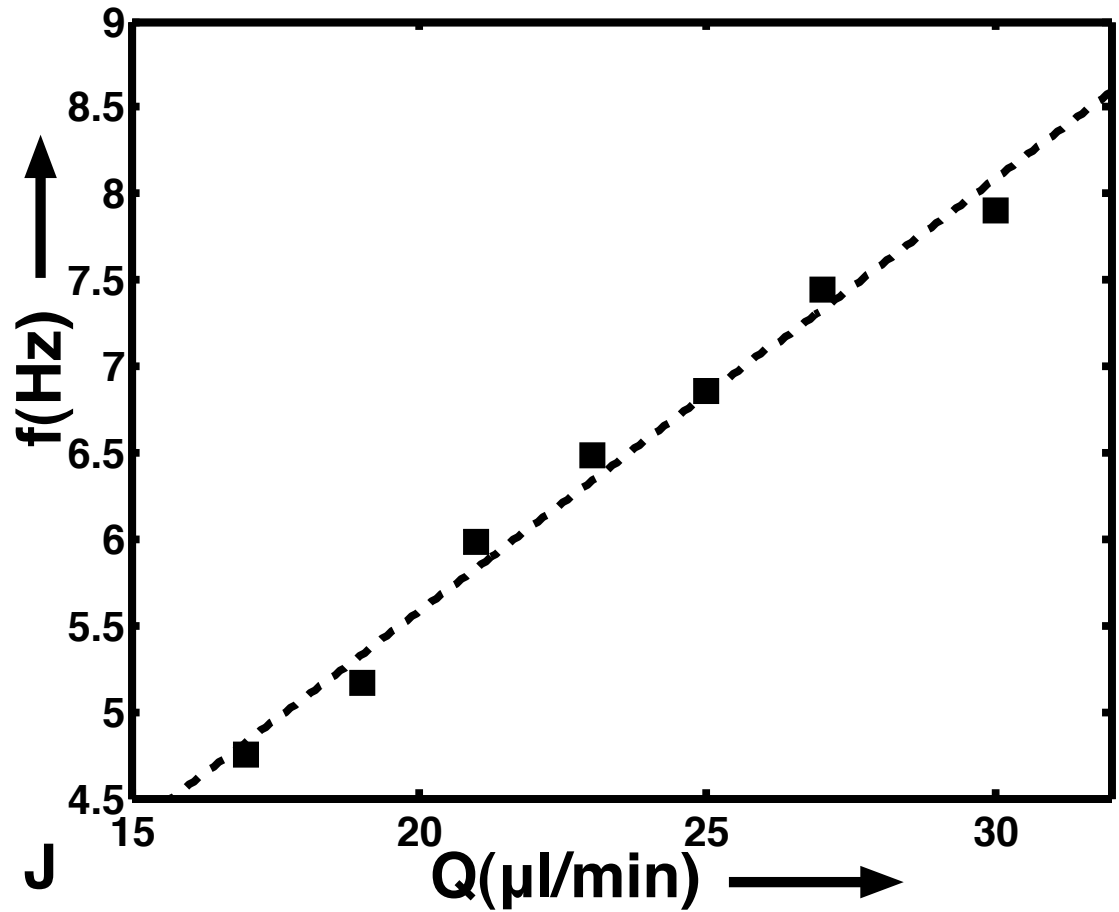
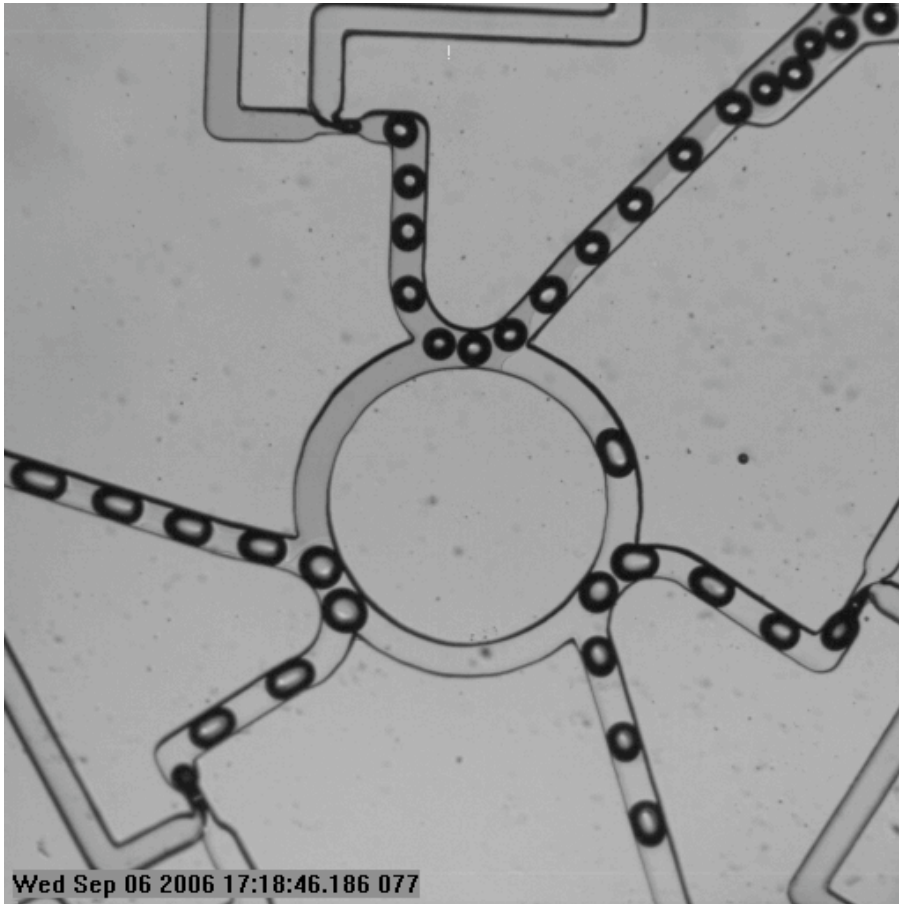


# Designing microfluidic circuits

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



# Ring Oscillator



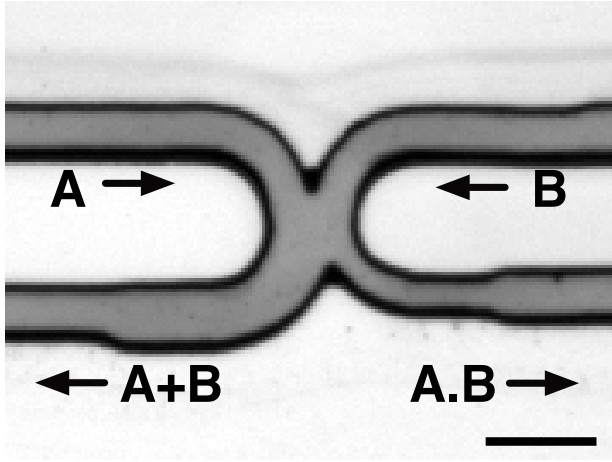
Frequency dependence

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



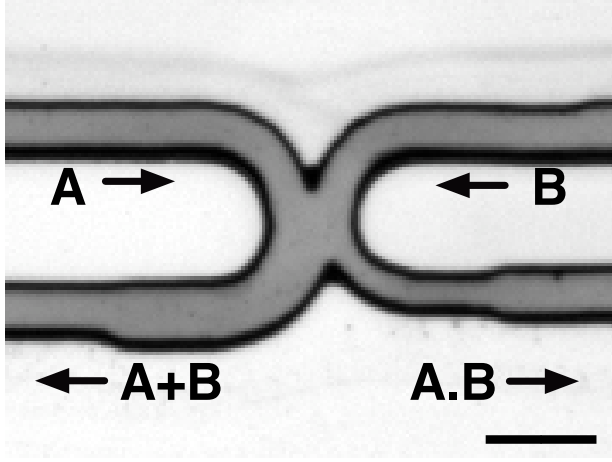
# NONLINEARITY

AND/OR gate

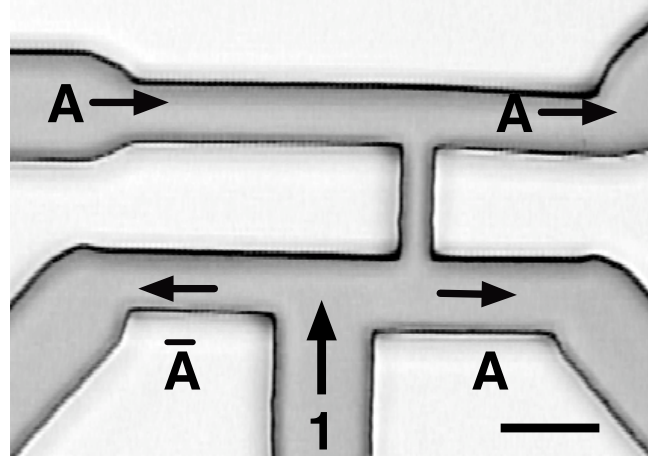


# NONLINEARITY

AND/OR gate



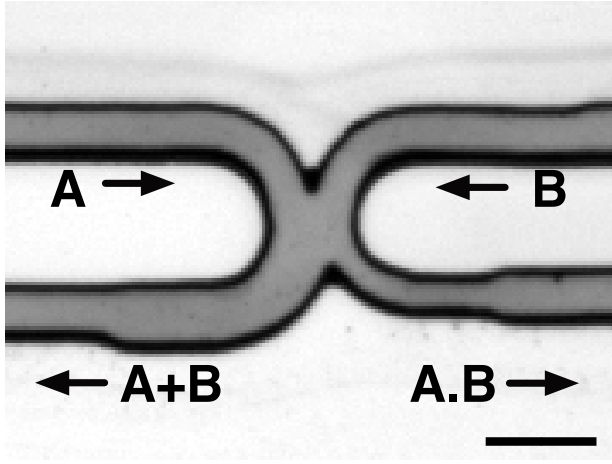
NOT gate



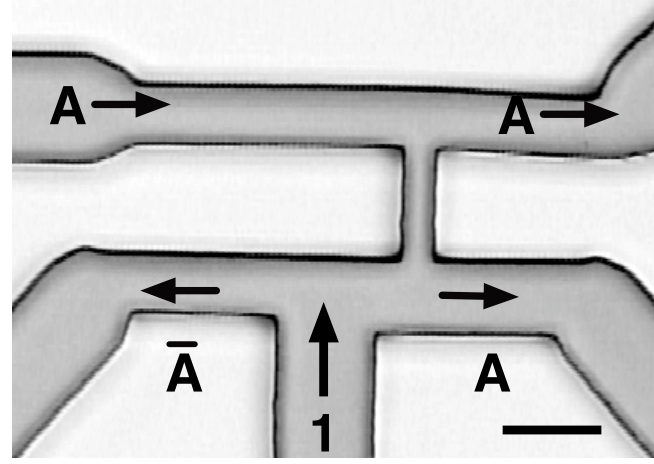
GAIN  
INVERSION

BISTABILITY NONLINEARITY

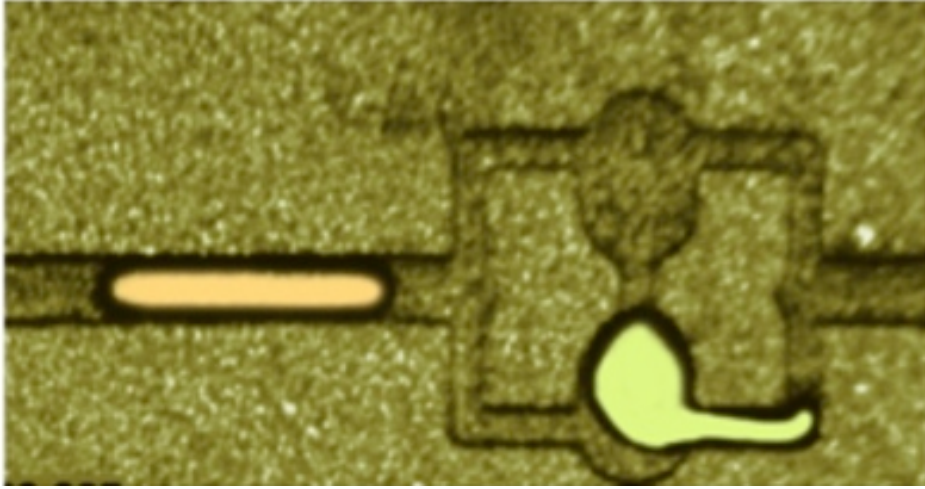
AND/OR gate



NOT gate



Toggle Flip-Flop

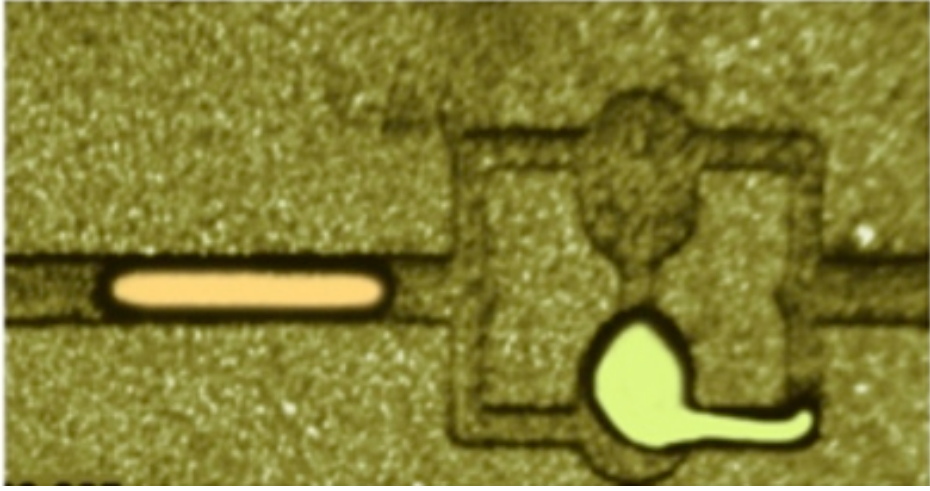


GAIN  
INVERSION

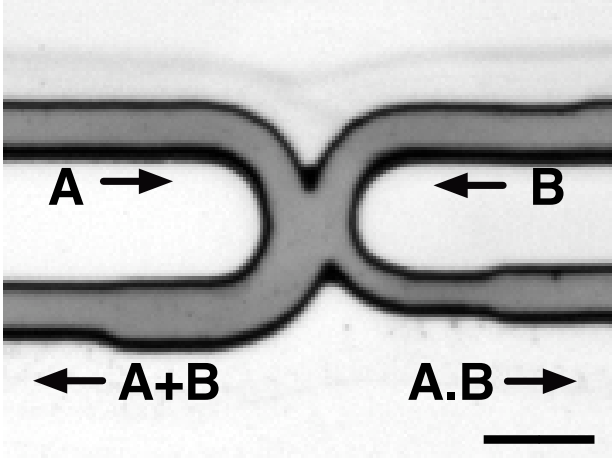
BISTABILITY

NONLINEARITY

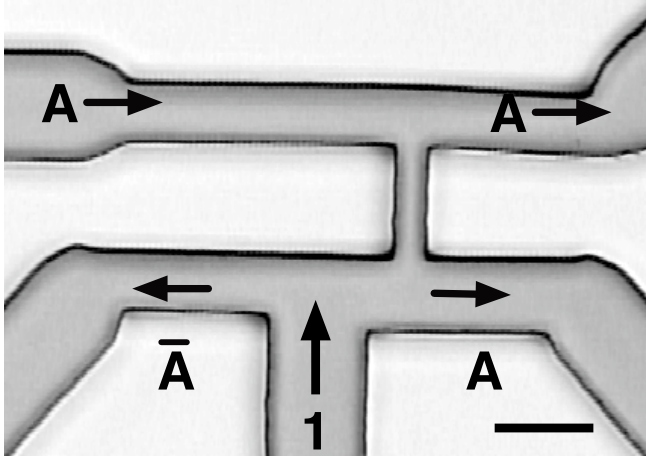
Toggle Flip-Flop



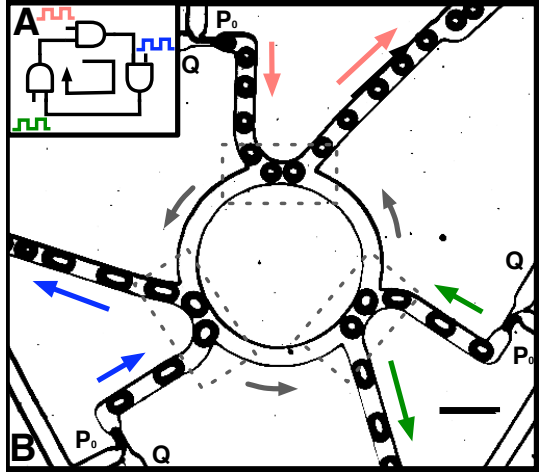
AND/OR gate



NOT gate



Ring Oscillator

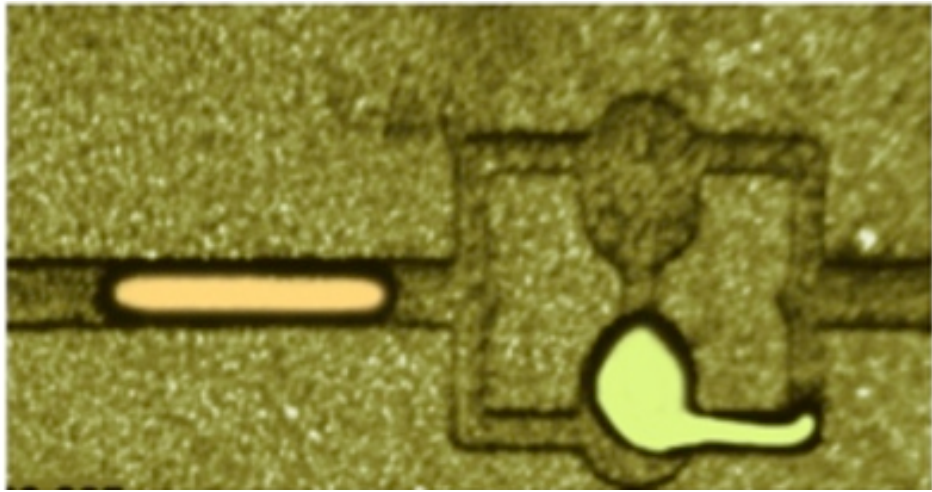
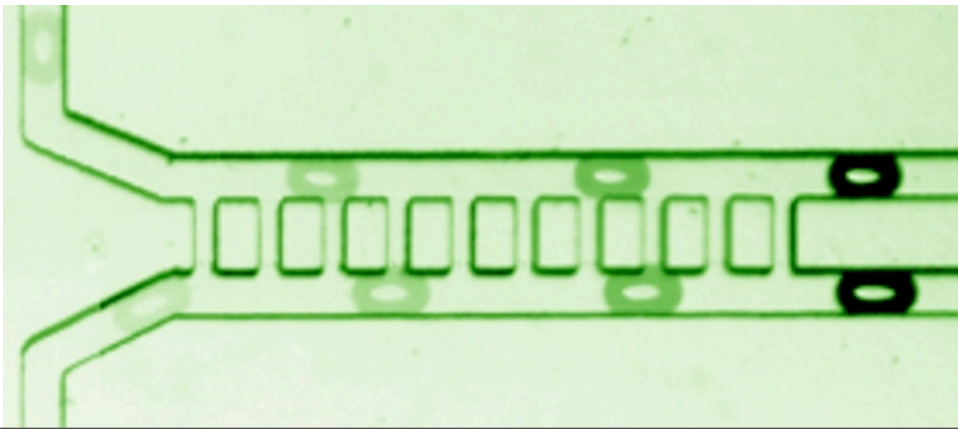


CASCADABILITY    GAIN  
FEEDBACK    INVERSION

SYNC

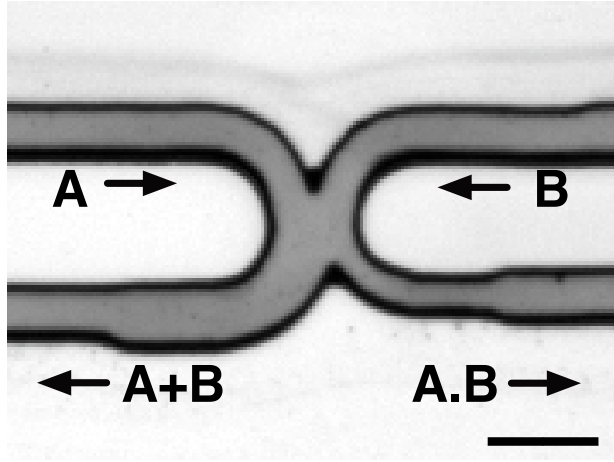
BISTABILITY

NONLINEARITY

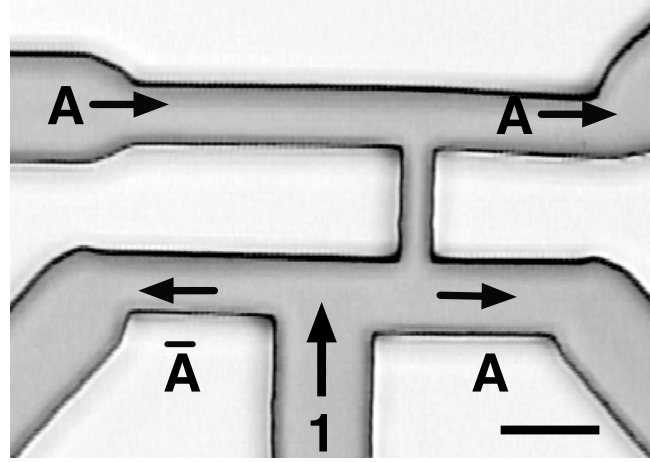


Toggle Flip-Flop

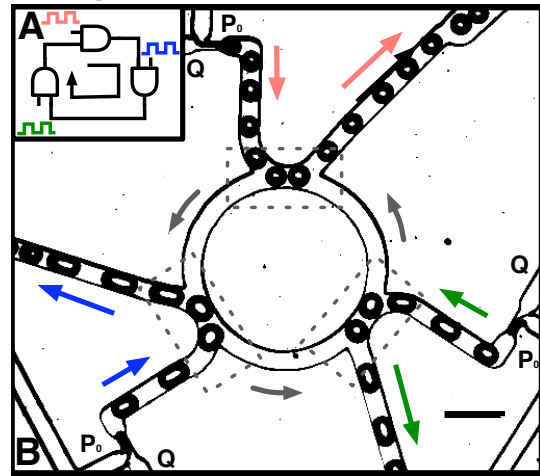
AND/OR gate



NOT gate



Ring Oscillator



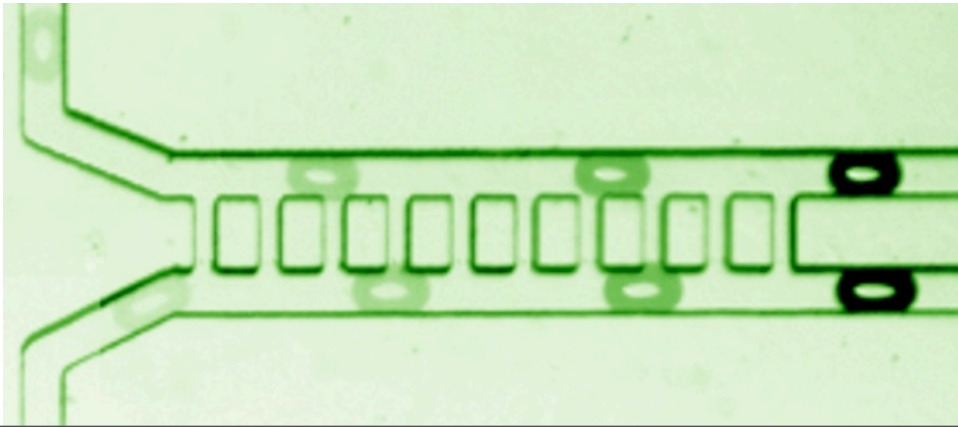
CASCADABILITY    GAIN  
 FEEDBACK        INVERSION



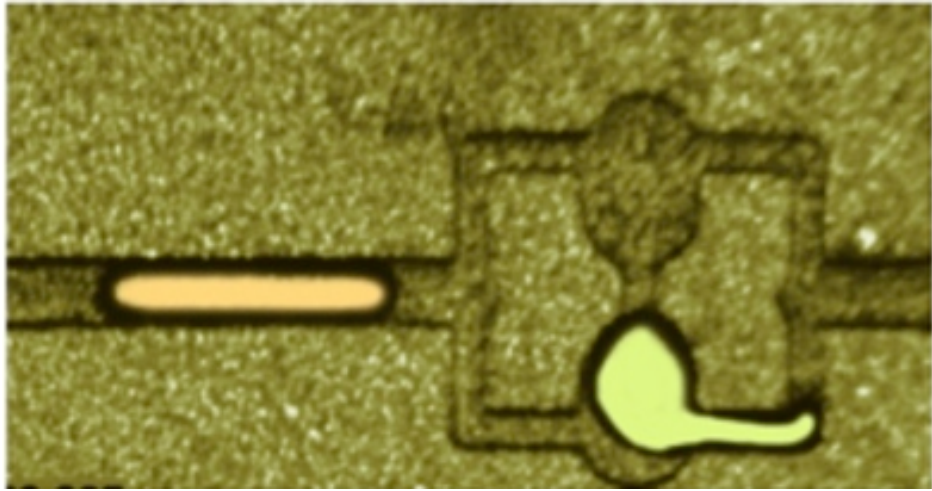
SYNC

BISTABILITY

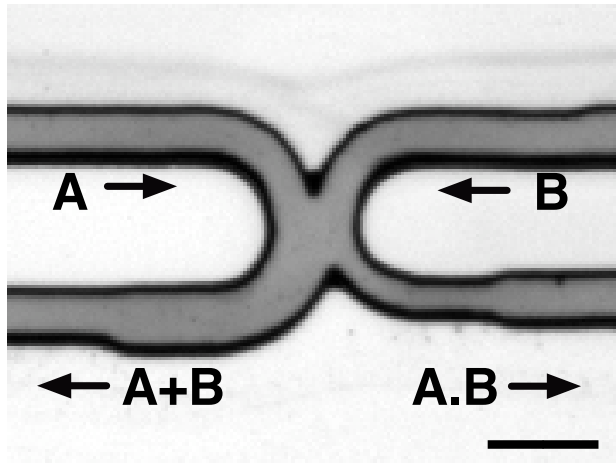
NONLINEARITY



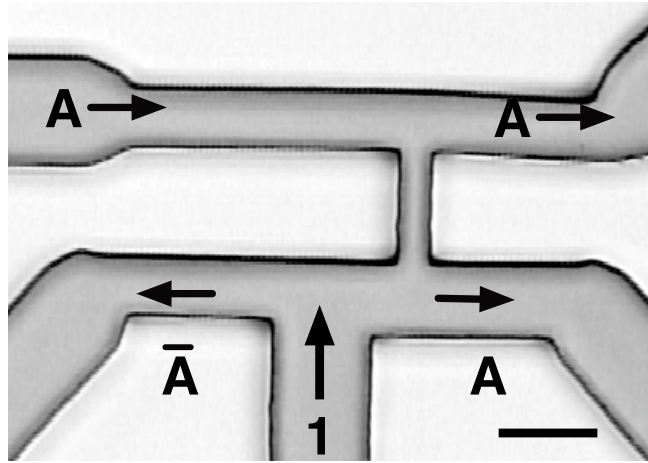
Toggle Flip-Flop



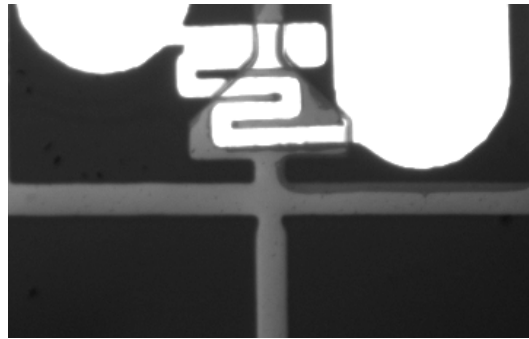
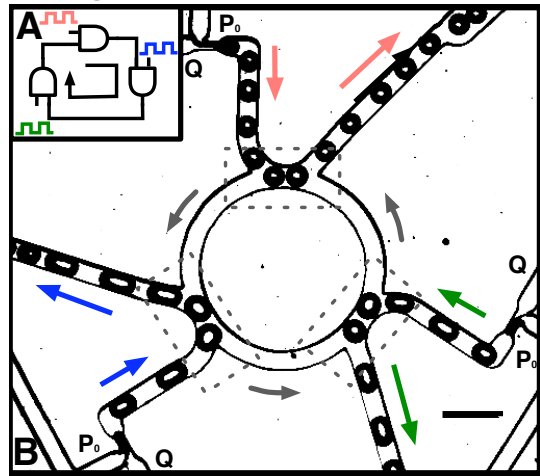
AND/OR gate



NOT gate



Ring Oscillator



GEN.

CASCADABILITY

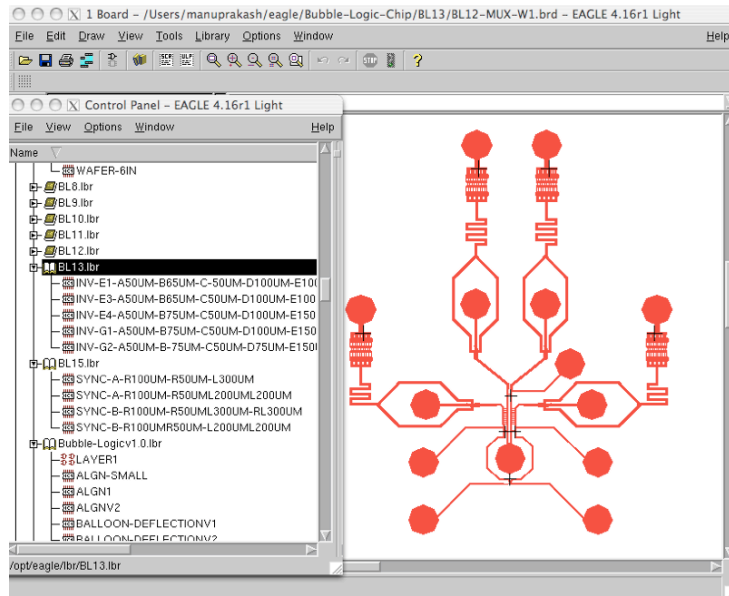
GAIN

FEEDBACK

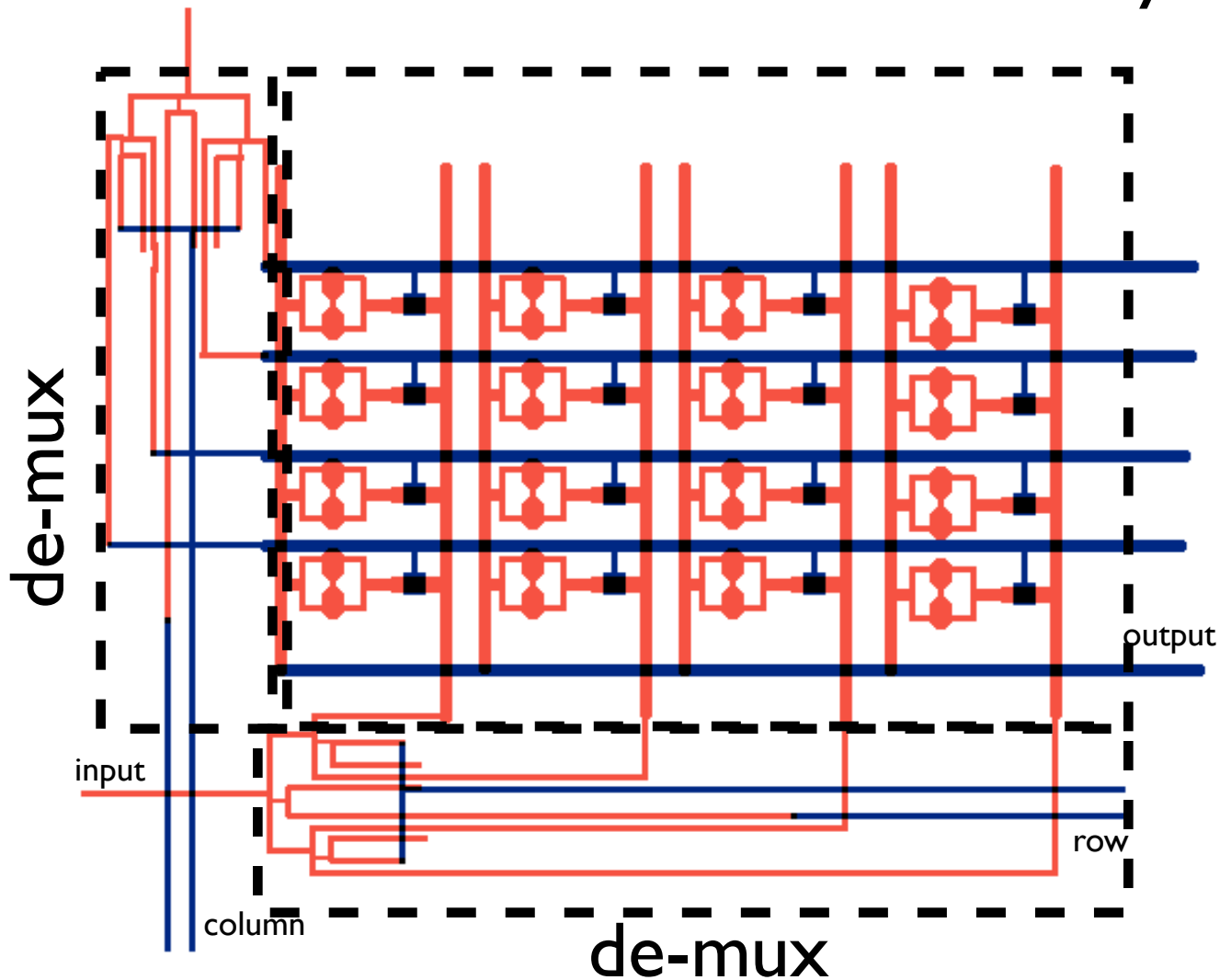
INVERSION

# Integration

Modular elements  
Open source CAD  
Component Libraries



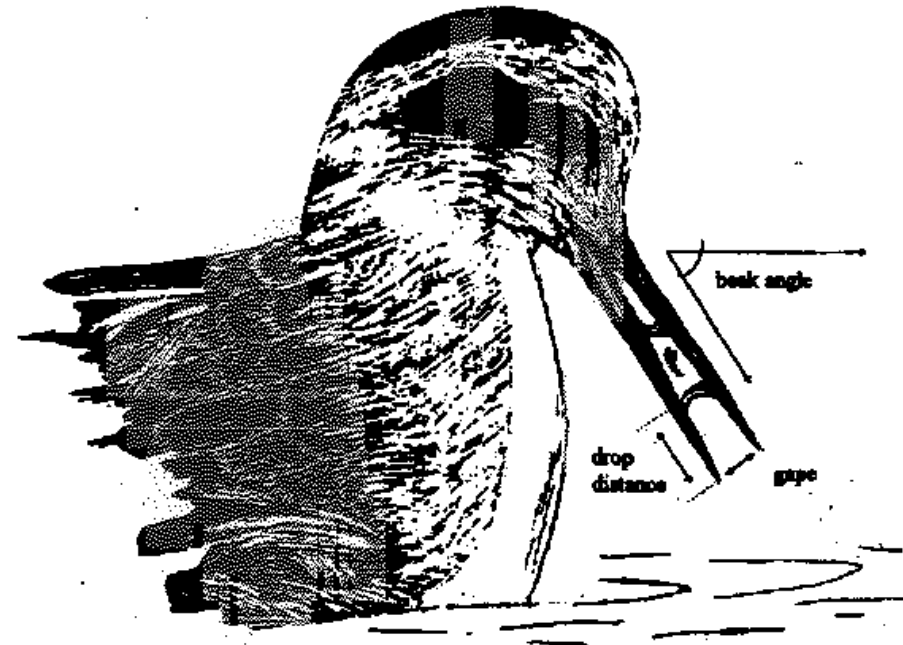
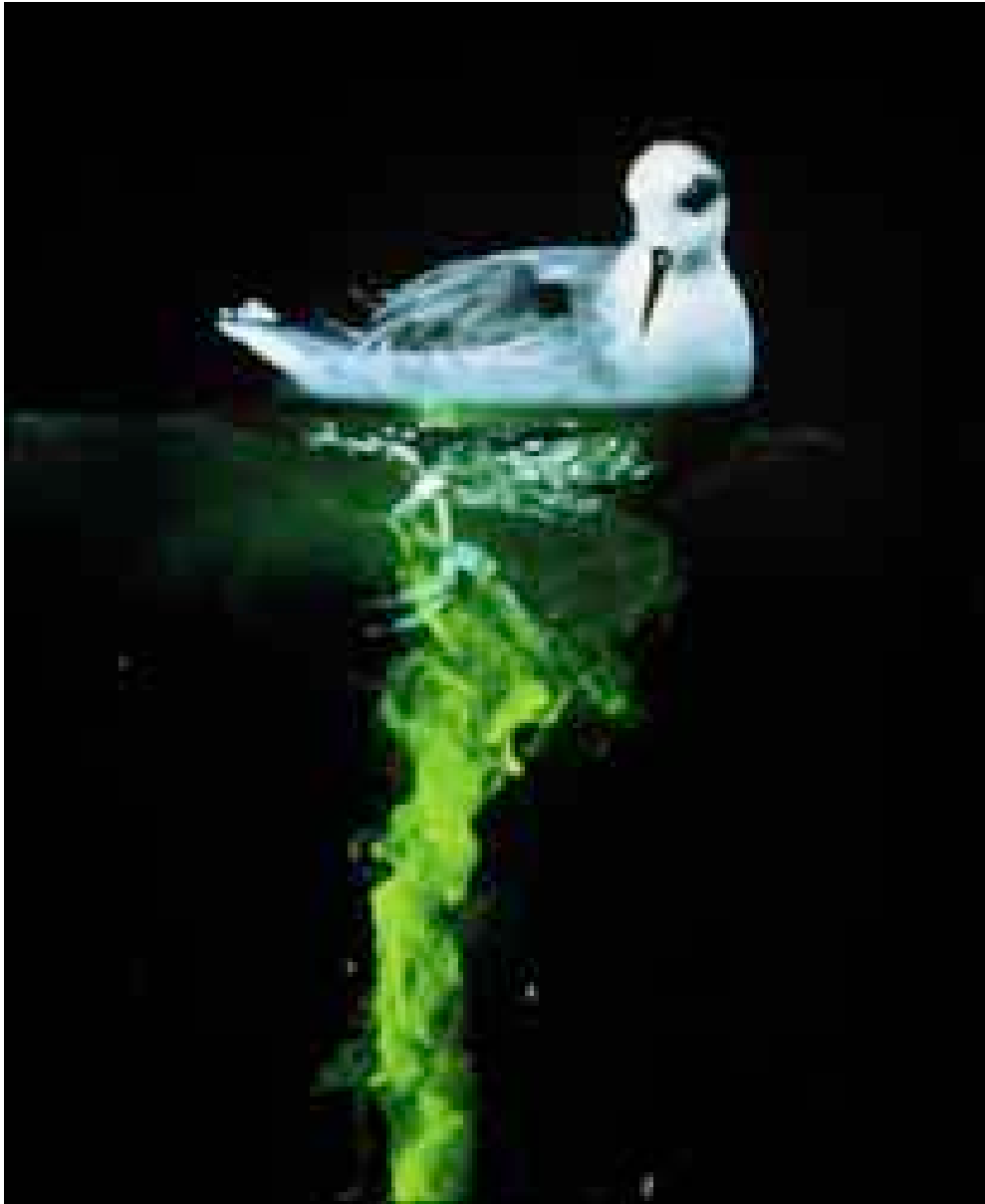
Random Access Chemical Memory



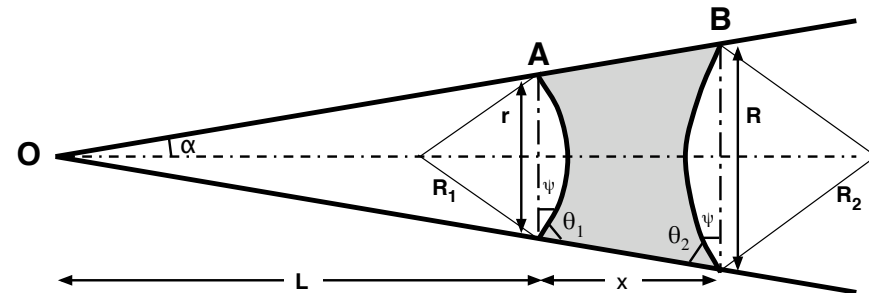
**Self-clocked microfluidics?**

# Capillary Ratchets

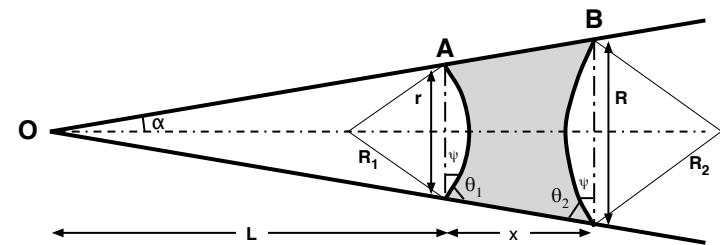
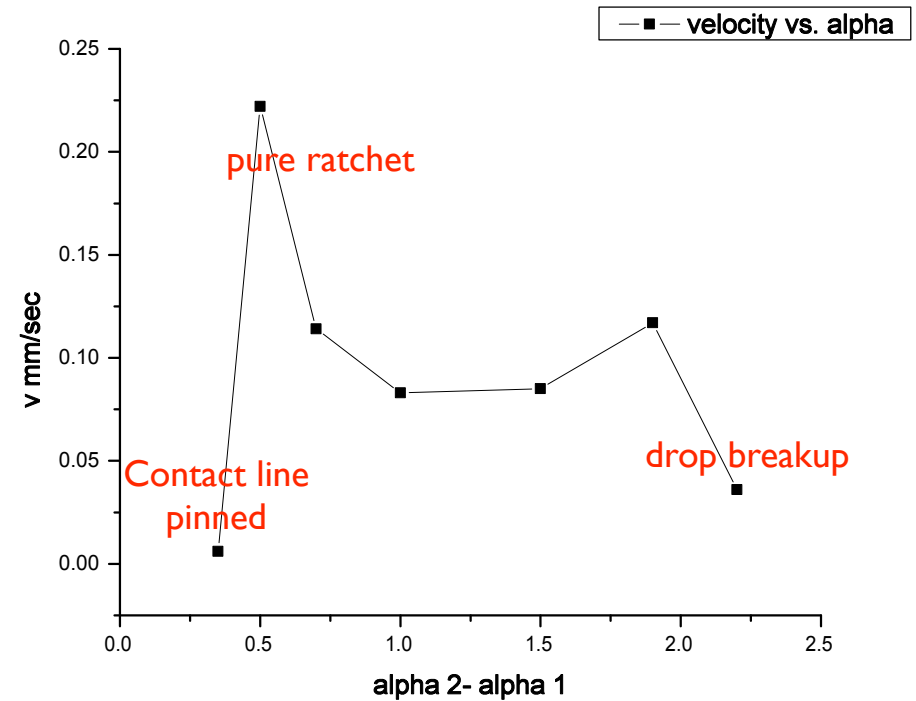
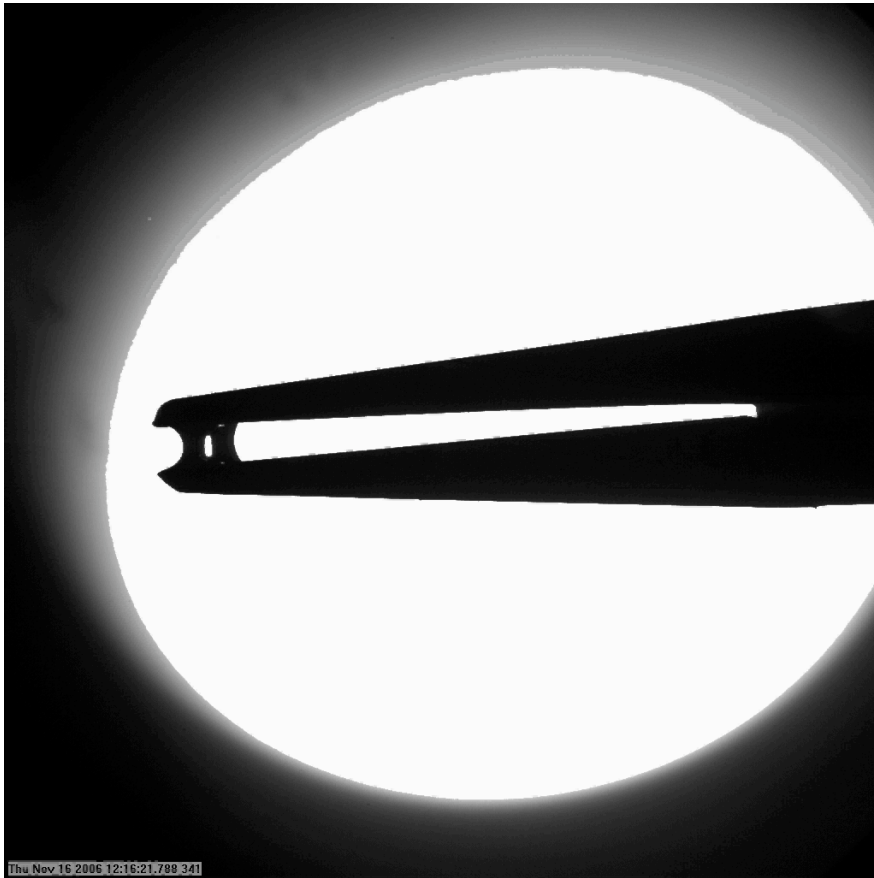
## Red-neck phalarope



[ 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

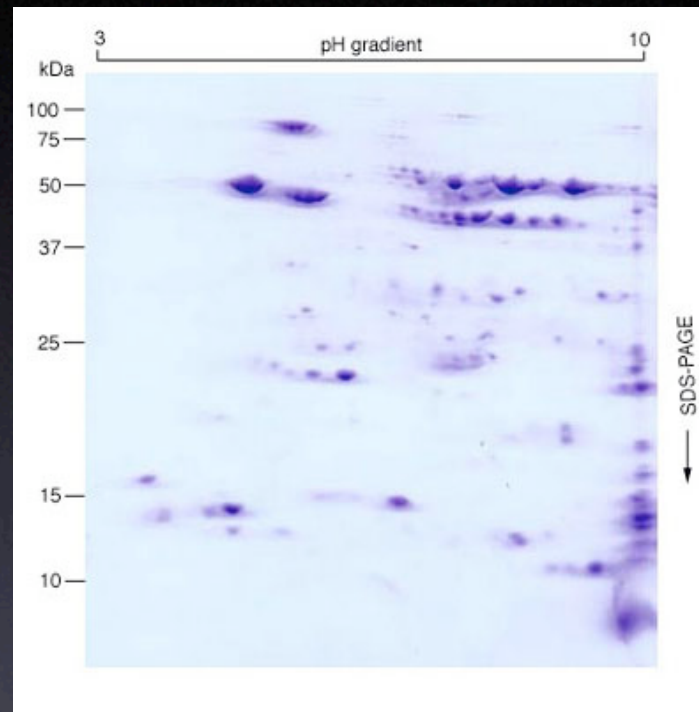
$$\theta_1 - \theta_2 = 2\alpha$$

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

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

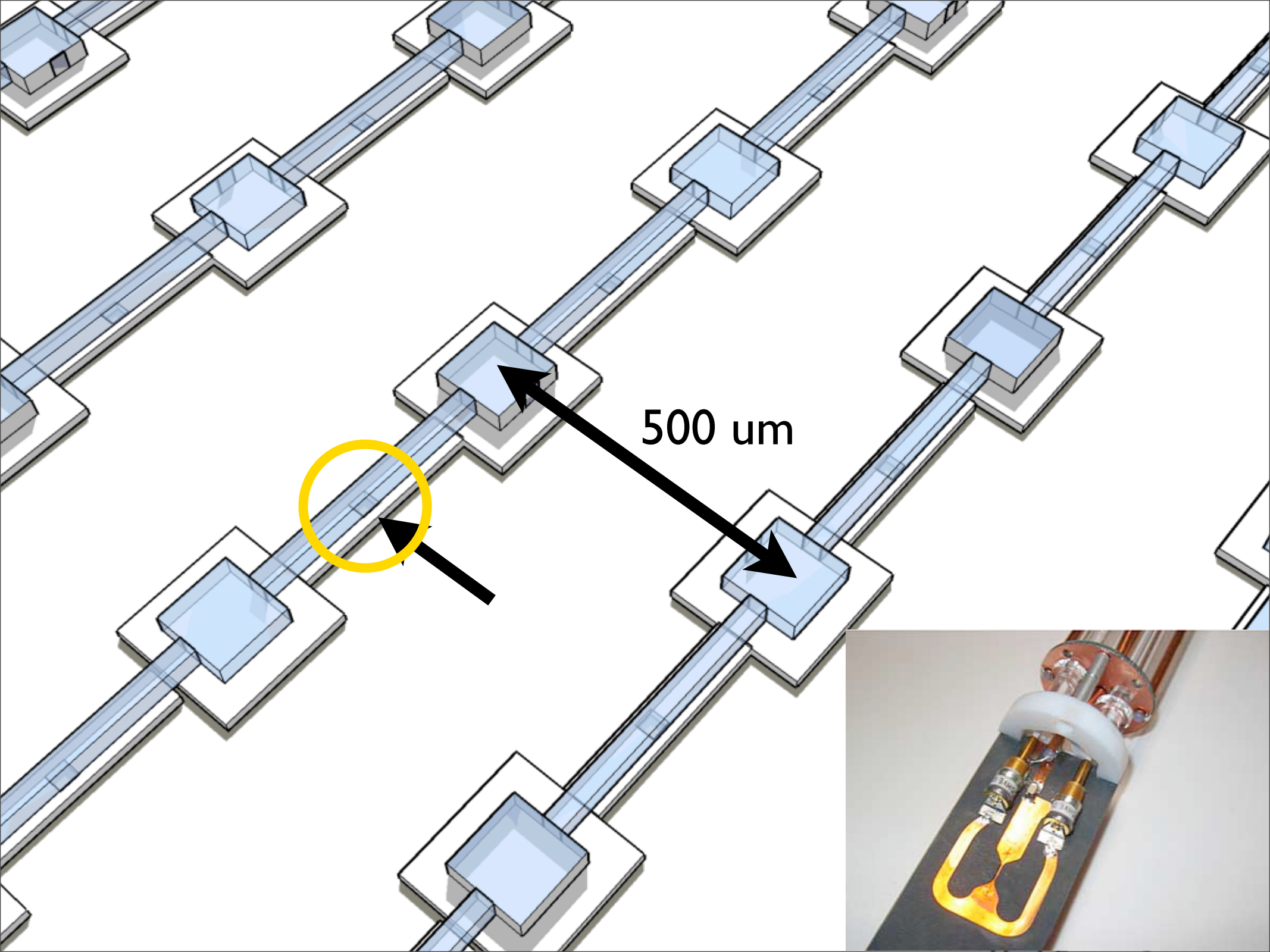
[Prakash et al. 2007 in prepration]

# 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<sub>puv</sub>

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\*

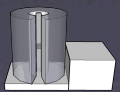
\*Center for Bits and Atoms and †Center for Biomedical Engineering, NE47-379, Massachusetts Institute of Technology, Cambridge, MA 02139-4307

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