Integrated Microfluid Systems

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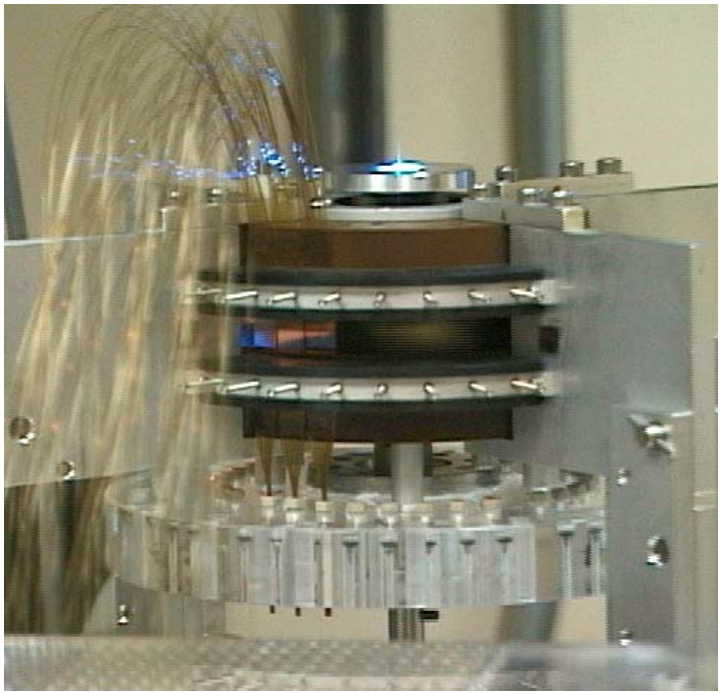
Outline

- Basic argument for microfluid systems
  - motivation
  - areas of applications for microfluidics
- Very basic fluid mechanics concepts
  - basic fluid driving mechanisms and flow profile
  - Viscosity, Reynolds number, laminar flow, viscous flow, etc.
- Microfabrication techniques
- Example of microfluid systems



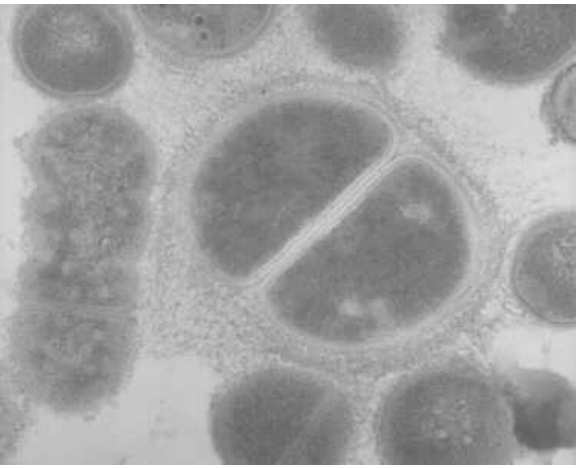
A bulk fluid system

Basic Argument for Microfluid System

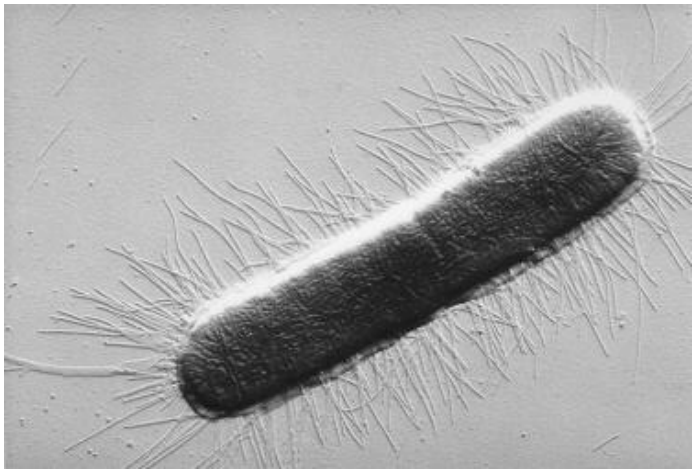
- Parallel to the argument for using the integrated circuits to replace the discrete component circuits
- Advantages
  - simplified system operations - integrated protocol and procedures
  - potentially portable systems for field use
    - www.digitalangel.net
  - potentially low-cost systems for home use
  - uses small amount of fluid rather than wasting much
    - however, be aware that some fluid reactions requires large volume and quantity
  - relieve from the *tyranny of interconnects*
    - interconnects are made while the flow systems are developed.

Basic Players in Microfluid Systems

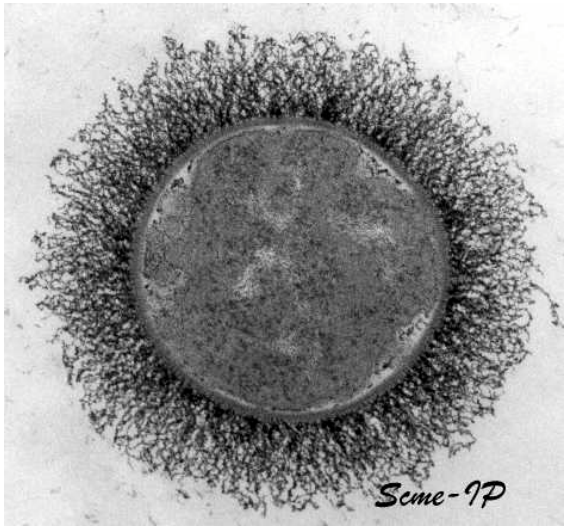
Other players:
Particles
bubbles
……



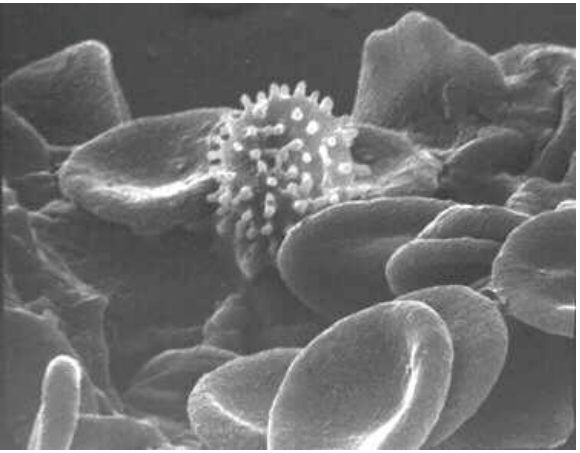
cell



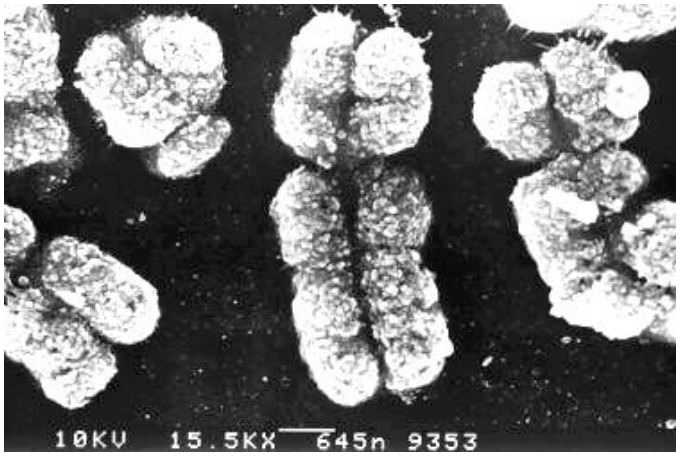
Bacteria (*E Coli*)



Pathogens
e.g. Bacillus anthracis



Blood cells



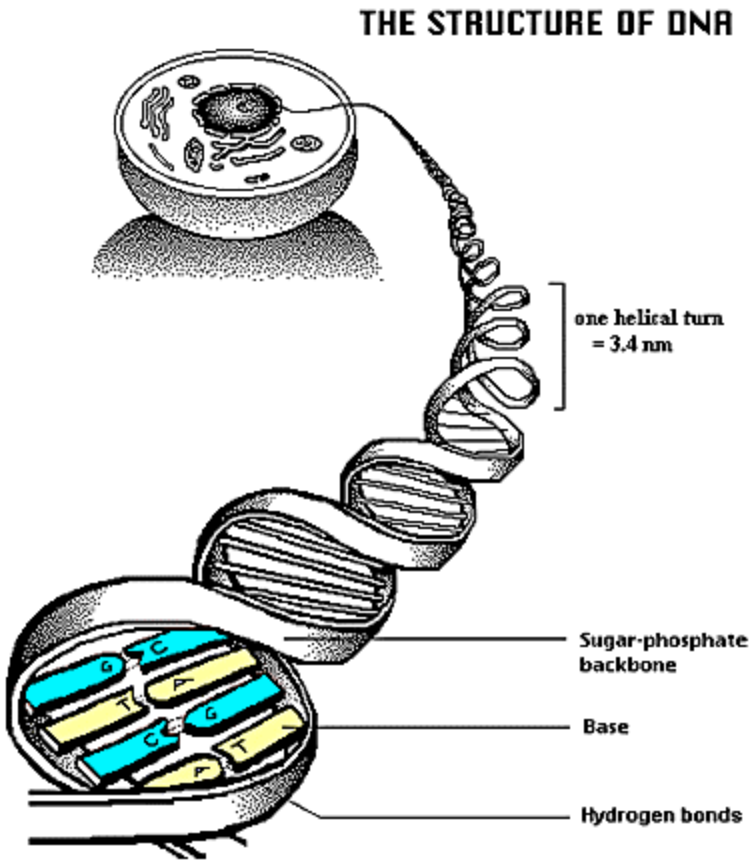
Chromosome and DNA/RNA

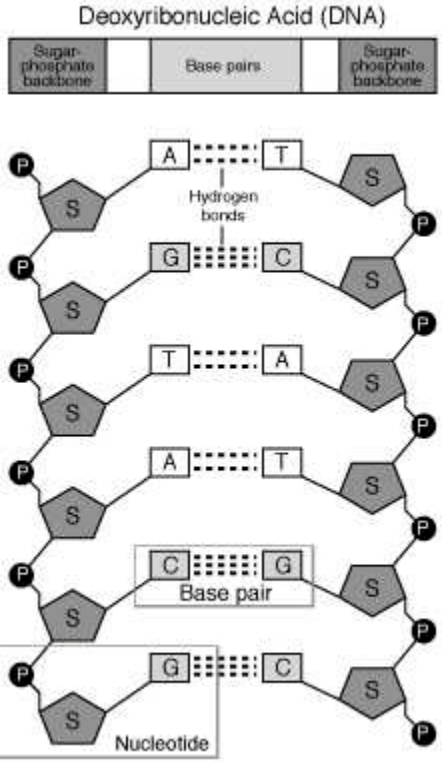
Case in Mind: Anthrax Spore detection

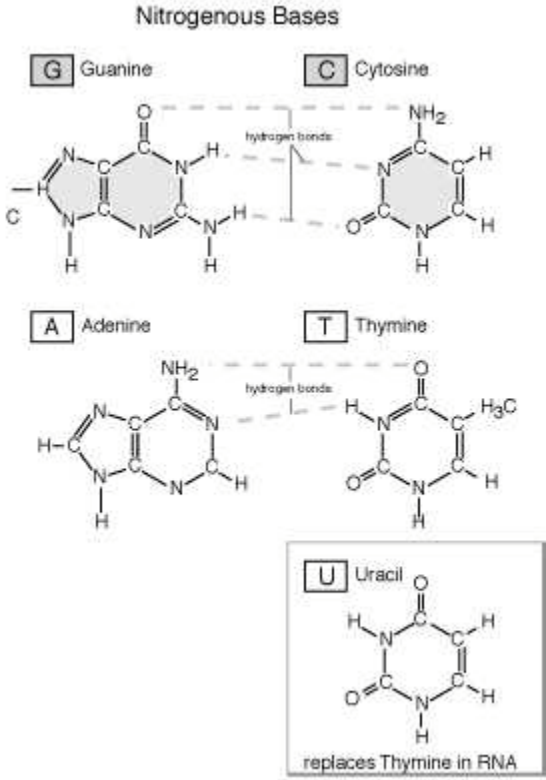
- Procedure
  - sample collection
  - mixing in vials
  - cell lysing (dissolving cell walls) to extract DNA
  - DNA/protein separation
  - DNA amplification to make more copies
  - Gel electrophoresis to separate DNA strands
  - Identify presence of anthrax DNA

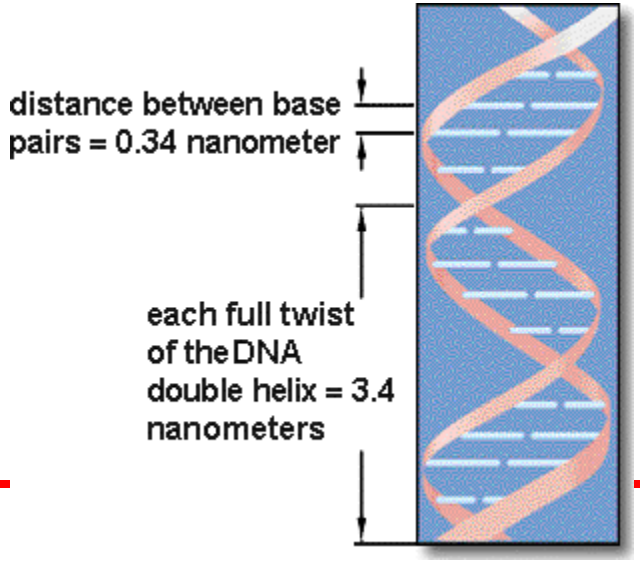
- Time: 1 day to 1 week
- Challenges
  - small amount of samples
  - needs faster turn-around time
  - need high specificity (no false positive) and sensitivity (no false negative)

DNA


THE STRUCTURE OF DNA
one helical turn
= 3.4 nm
Sugar-phosphate
backbone
Base
Hydrogen bonds


Deoxyribonucleic Acid (DNA)
Sugar-phosphate backbone
Base pairs
Sugar-phosphate backbone
Hydrogen bonds
Base pair
Nucleotide


Nitrogenous Bases
G Guanine
C Cytosine
hydrogen bonds
A Adenine
T Thymine
U Uracil
replaces Thymine in RNA

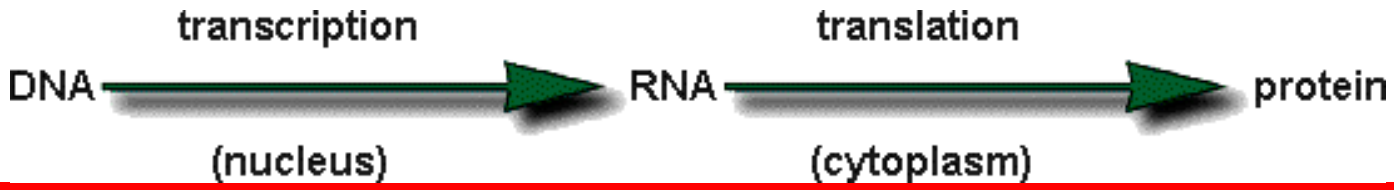

distance between base pairs = 0.34 nanometer
each full twist of the DNA double helix = 3.4 nanometers

Human Genome Project

- Informational websites
- http://www.ornl.gov/hgmis/
- http://www.nhgri.nih.gov/
- http://www.ncbi.nlm.nih.gov/genome/guide/huma

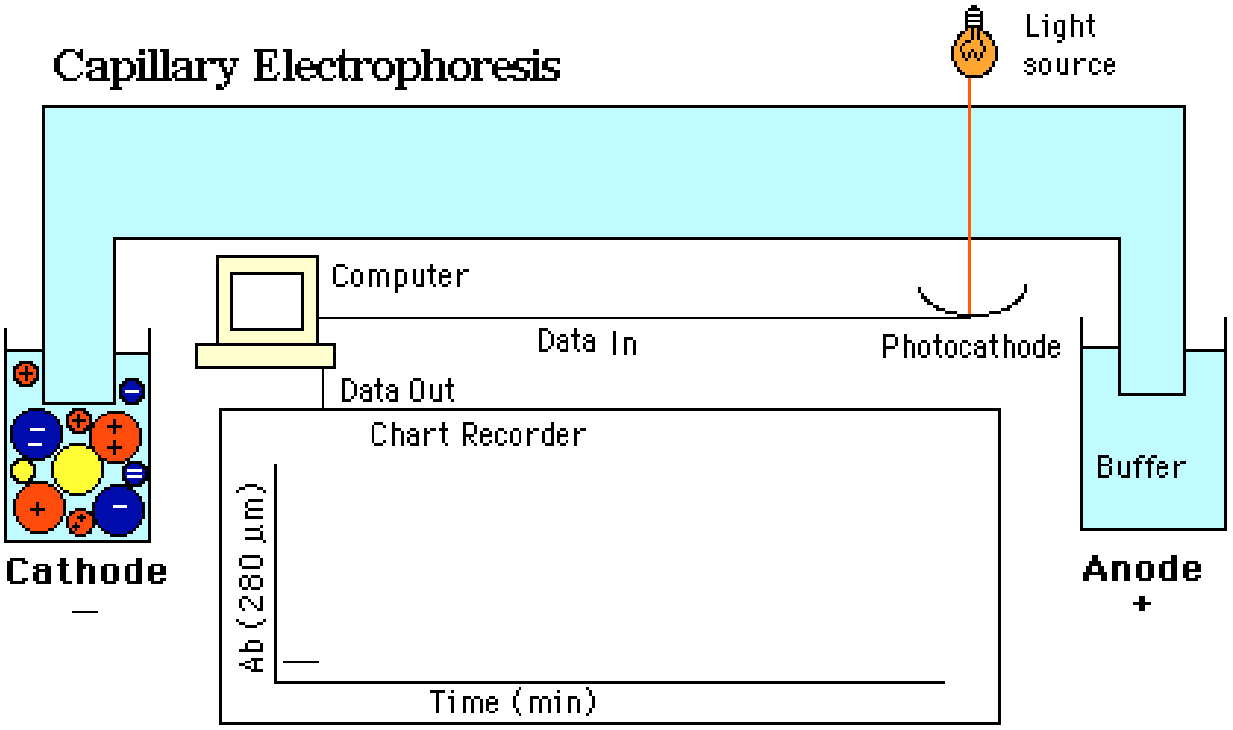
Proteins

- Most diverse and functional
  - enzymes: makes metabolic events faster
  - structural proteins: feathers, webs, bone and cartilage
  - transport proteins: move molecules and ions across cell membranes
  - nutritious proteins
  - protein hormones and regulatory proteins
- Proteins are formed out of 20 kinds of amino acids
  - http://www.sirius.com/~johnkyrk/aminoacid.html
  - three-dimensional folding determines protein constructs and functions
- Proteomics: Protein + Genomics
  - PGI: Post genomics institute



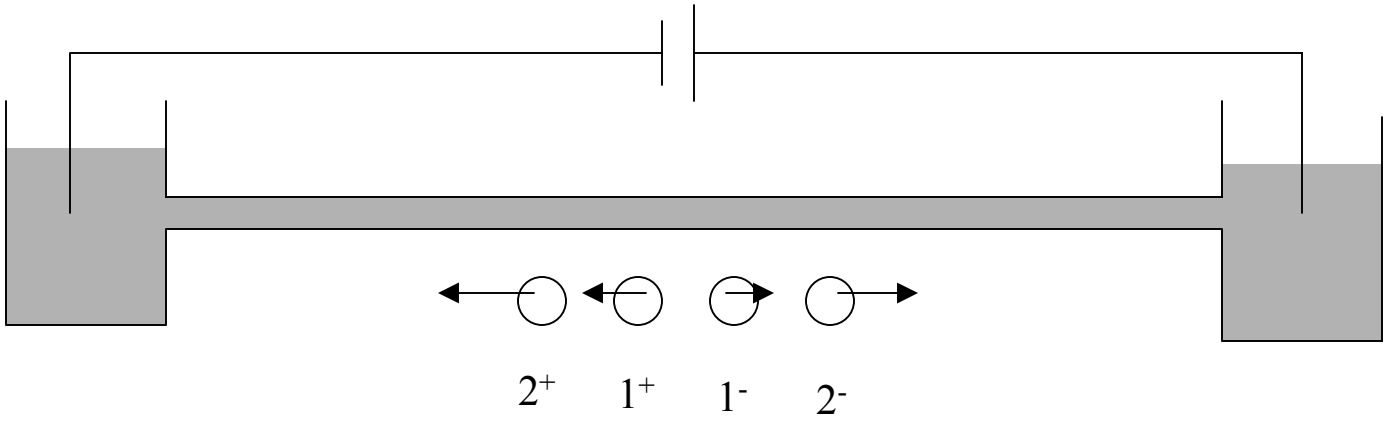
Capillary Gel Electrophoresis

- size-based separation of biological macromolecules such as oligonucleotides, DNA restriction fragments and proteins;
- gel materials: cross-linked polyacrylamide, agarose or even solutions of linear polymer



http://www.ceandcec.com/
http://ntri.tamuk.edu/ce/ce.html

Electrophoresis



- Under equilibrium, the electric force and the friction force balance.
  - F_i: friction coefficient of species *i*

$$F_{elec} = z_i eE = net - charge \times electricfield$$

$$F_{fric} = f_i v_i$$

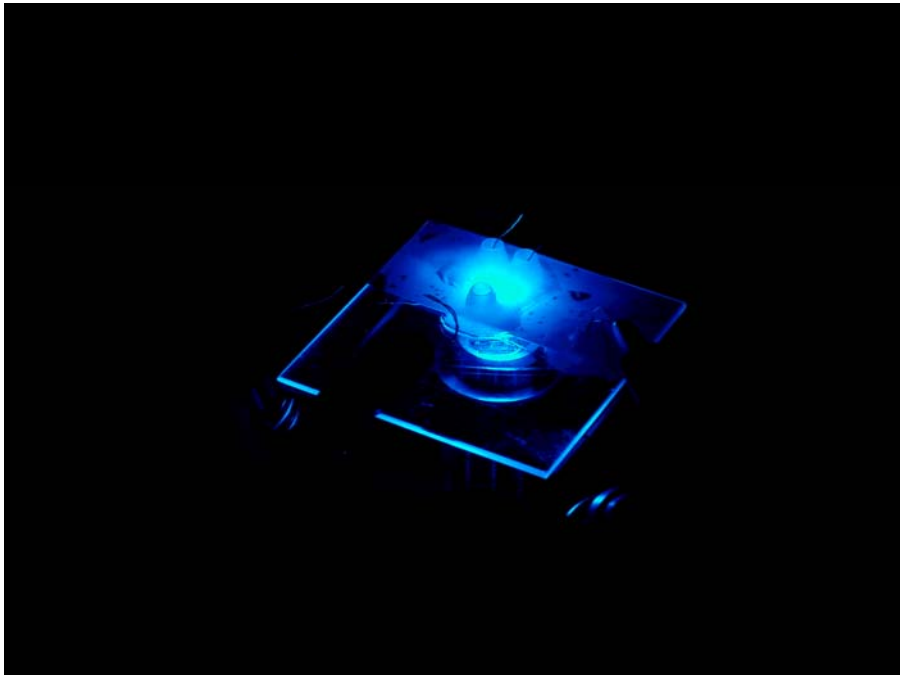
  - this yield

$$v_i = \frac{z_i e}{f_i} E = \mu_i E$$

  - the friction coefficient is a function of gel pore sizes, size of particles, and the strength of applied field.

Applications of CE

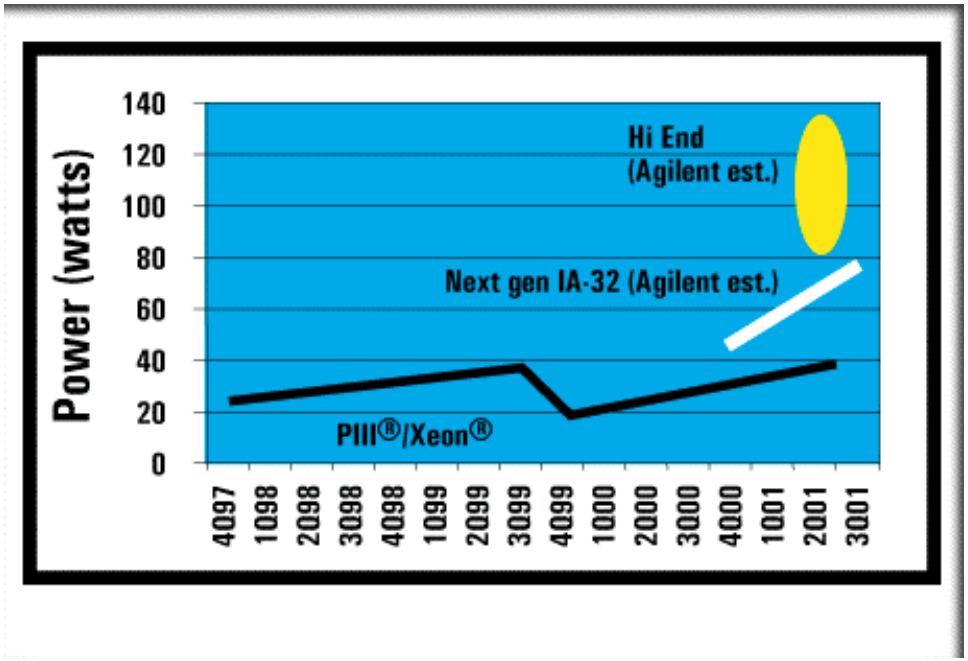
- Thousands of instruments are now in use for the analysis of pharmaceuticals, DNA, proteins, peptides, clinical and forensic samples, agrochemicals, fine chemicals and natural products.
- DNA analysis by CE using fluorescence



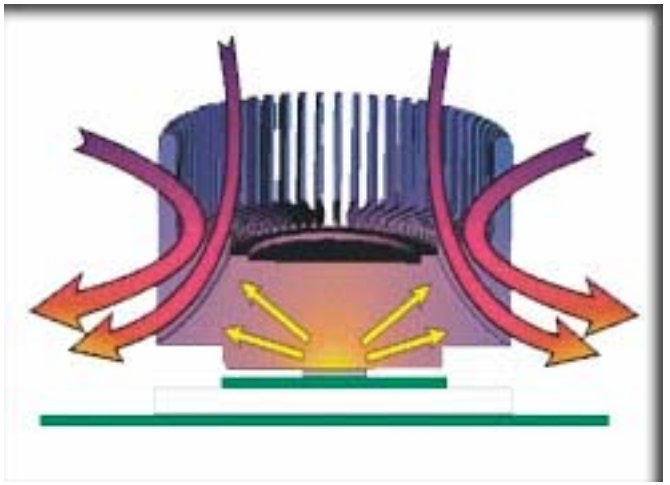
Chip Cooling is Serious Business Now

- **NATIONAL TECHNOLOGY ROADMAP for SEMICONDUCTORS (1998-2006)**
- CONSEQUENCES for 2006
- Chip Frequency: 300 to 1250 MHz
- Chip Size: 75 to 900 mm2
- Package I/O's: 400 to 2200
- Chip Power: 1 to 28 to 140 Watts
- Junction Temp: 100 to 195 C
- Ambient Temp: 45 to 170 C
- Voltage: 0.9 to 3.3V

•HP PolarLogic thermal management
•KryoTech reduces temperature to -40 degree C



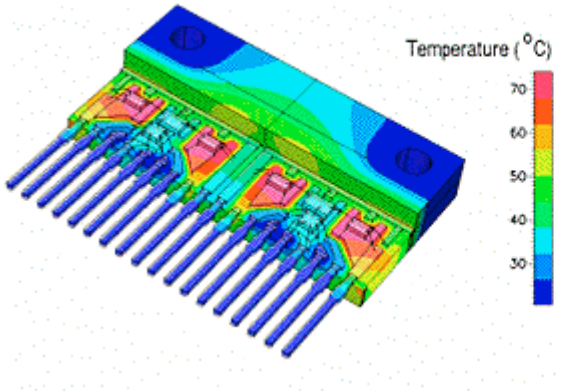
Agilent PolarLogic Arcticooler

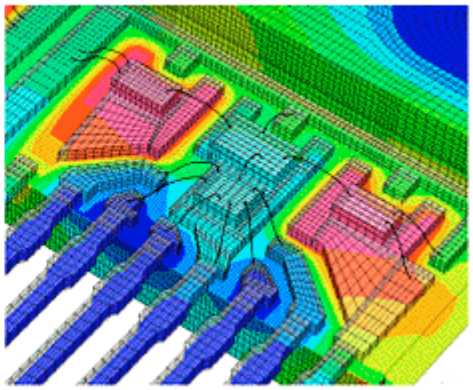


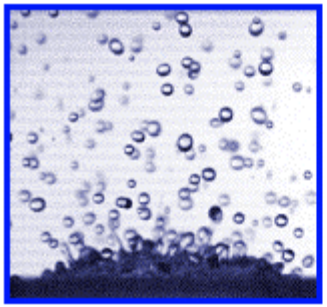
http://www.engr.orst.edu/~petersr/me442.html
http://support.intel.com/support/processors/pentium/8021.htm
http://www.me.umn.edu/divisions/tht/tme/rtour4.html

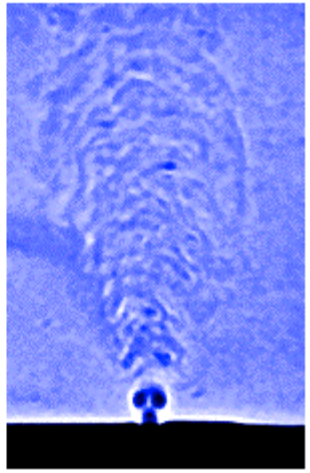
MEMS Ways for Chip Cooling

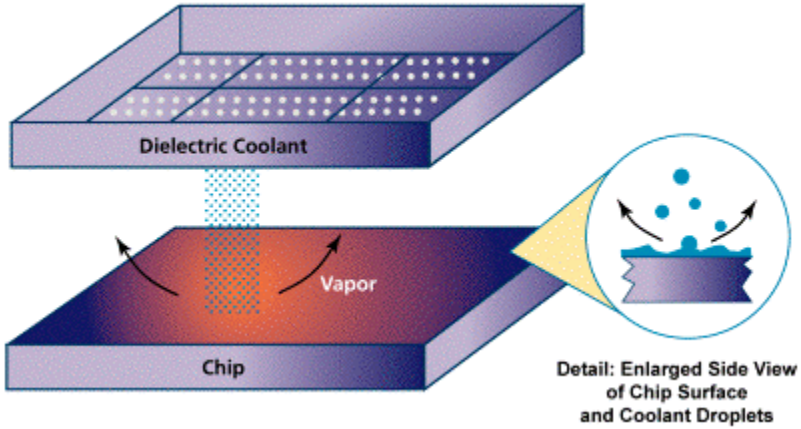
- Integrated heat exchanger for advanced IC chips



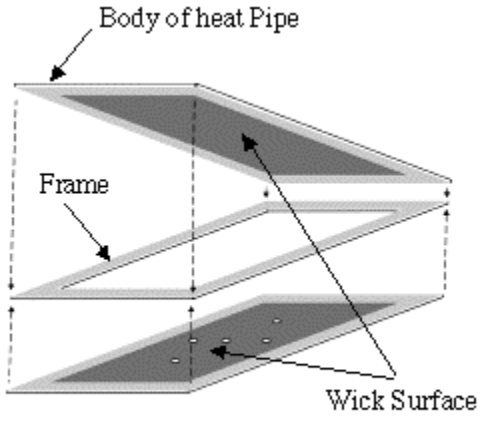




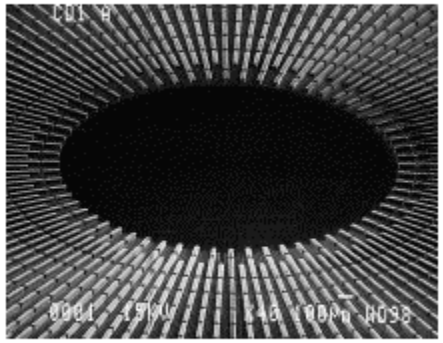




Detail: Enlarged Side View of Chip Surface and Coolant Droplets



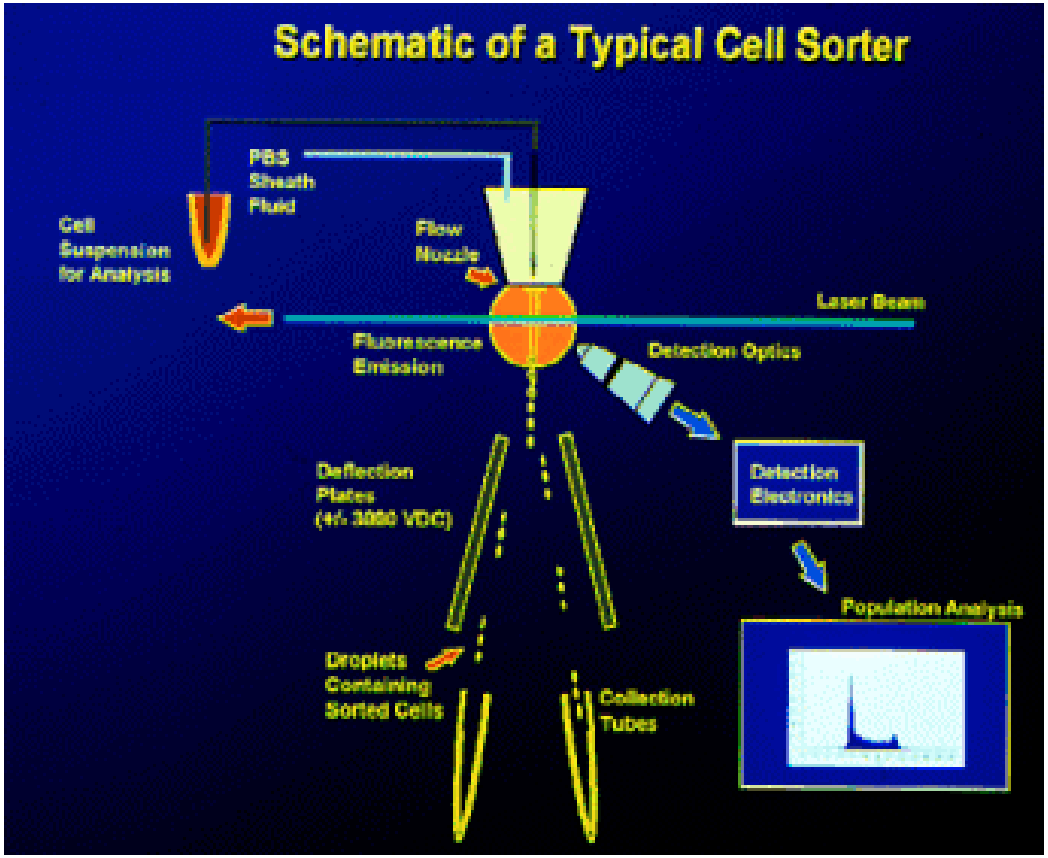
Heat Pipe Assembly



Micrograph of wick structure

Flow Cytometry

- Sorting two types of cells in a suspension fluid.



Combinatorial Chemistry

- For high-throughput screening of chemicals and pharmaceutical compounds.
- Designing chemicals with specific functions is difficult. Sometimes thousands or millions of chemicals are possible.
- MEMS fluid systems can facilitate the tasks of making many variety of chemicals efficiently.

Basic Microfluic Components

- Microfluid channels and chambers
  - for transporting and storing fluid
- Microfluid pumps
  - for moving fluid
- Microfluid valves
  - for isolation of fluid
- (micro) electrodes (metal)
  - for provide potential or current, or to detect signals
- Mixers
  - structures to prompt mixing at the micro scale
- Sensors
  - flow parameter sensors and chemical parameter sensors

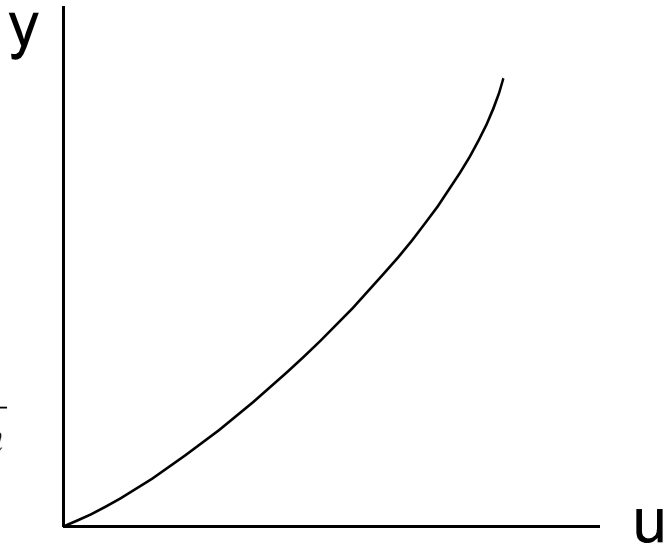
Methods for Transporting Fluid

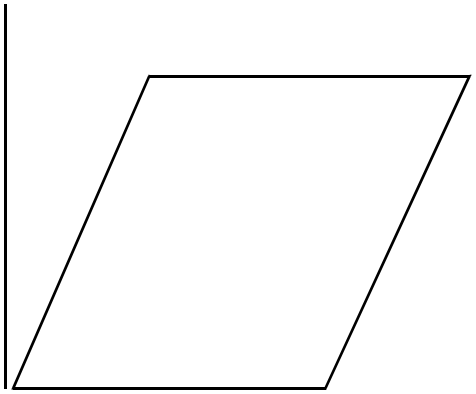
- Pressure driven flow
  - fluid flow caused by pressure differential
- Electrokinetic flow
  - fluid flow caused by movement of charged particles or molecules
- Surface acoustic wave

- **Methods for Transporting Fluid Pressure driven flow**
- electrokinetic flow
- bead-based analysis (magnetic beads)
- laser tweezer

Basic Fluid Terms

- Density of fluid (ρ)
- Viscosity (μ)
  - dynamic viscosity $\tau = \mu \frac{du}{dy}$
    - u: velocity
    - y: vertical distance
  - kinematic viscosity (ν=μ/ρ)
  - unit of dynamic viscosity: $Poise = \frac{g}{s \cdot cm}$
    - kg/(m-s) = 10 poise
  - Viscosity of water: 1.7 centipoise
- The Reynolds Number
  - V: characteristic velocity $\mathrm{Re} = \frac{\rho V L}{\mu}$
  - L: characteristic length
  - A cell swimming in water would have similar flow characteristics compared to a human swimming in a pool of honey.

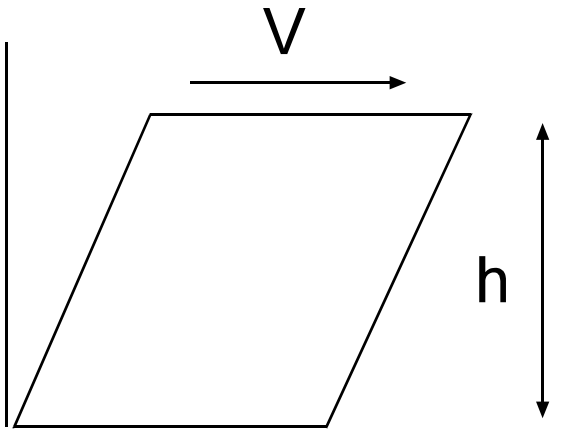




Example

- Suppose the fluid being sheared in SAW30 oil at 20°C. Computer the shear stress in the oil is V=3 m/s and h=2 cm.

$$\mu = 0.29 kg/(m \cdot s)$$



- For the given velocity and height

$$\tau = \frac{\mu dV}{dy} = \frac{\mu V}{h} = \frac{0.29 kg/(m \cdot s) 3 m/s}{0.02 m} = 43 kg/(m \cdot s^2) = 43 N/m^2$$

Definition of Characteristic Length

- Airplane
  - distance between wing tips
- A microfluid channel with circular cross-section
  - diameter
- A microfluid channel with rectangular cross-section
  - the height of the channel
- A cell moving in a fluid
  - diameter of cell

Laminar Flow and Turbulent Flow

- Laminar flow:
  - flow stream follow regular paths
- Turbulent flow:
  - unsteady flow stream
- Laminar - Turbulent transition:
  - Reynolds number 3×10^5

- For microfluid systems, because of the small channel cross-section or the small object, the *Re* is small.

Low speed

High speed

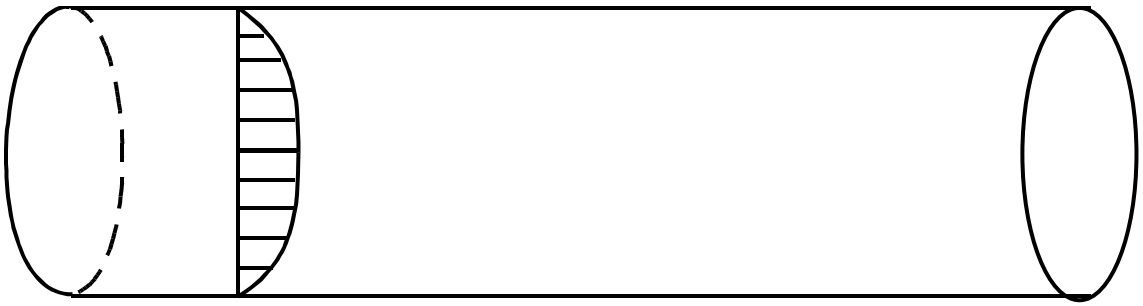
Pressure Driven Flow in A Tunnel

- Channel shown as below
- For a pipe with a circular cross section with radius r (in m) and length L (also in m)

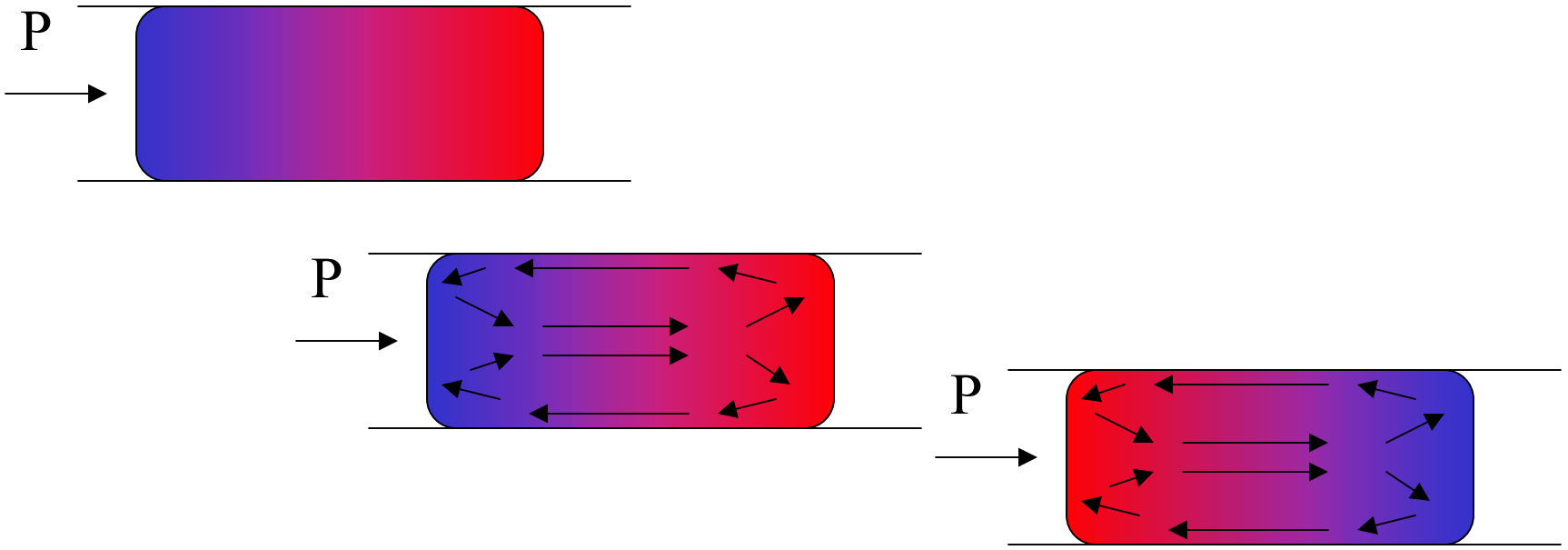
$$Q = \frac{\pi r^4}{8\mu L}\Delta P$$

- For a pipe with rectangular cross-section: width w, height h. The ratio of w/h is relatively large such that the flow is two-dimensional.

$$Q = \frac{wh^3}{12\mu L}\Delta P$$

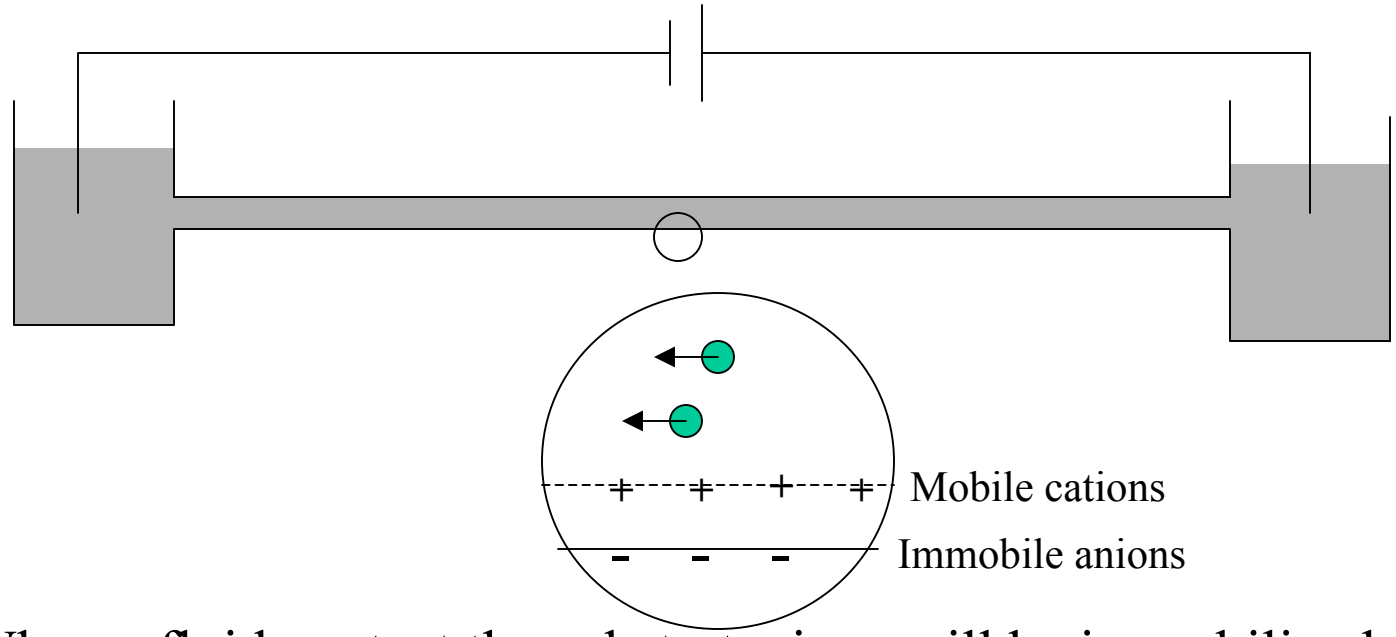


Circulatory Flow Phenomenon



- Fluid in the center moves faster than along the edge
- Circulation with the flow drop will occur as the drop is moved along the channel.

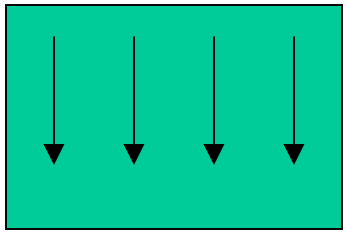
Electrokinetic Driven Flow

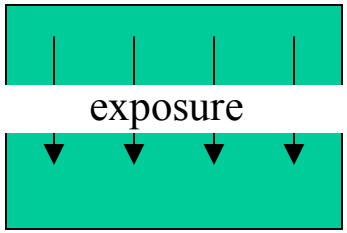


- When a fluid contact the substrate, ions will be immobilized on the substrate surface. This induces mobile counter ions in fluid near the surface, creating a surface double-layer.
- If an electric field is applied, the cations will move and therefore pull the entire fluid bulk with it.
  - ζ Is the zeta potential.

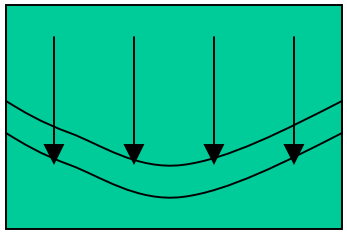
$$V = \mu E = \frac{\varepsilon \xi}{4\pi\eta}\mu$$

Parabolic flow rate profile by Fluorescence Measurement

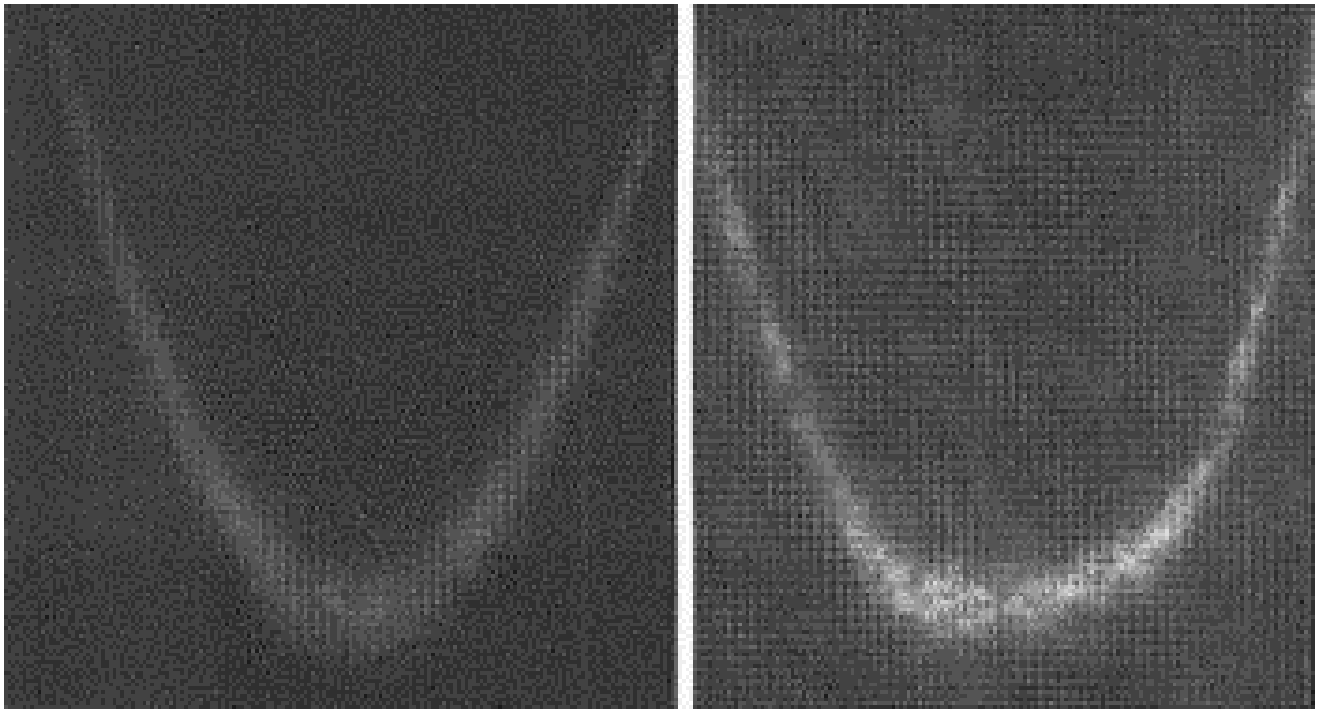




T=0
exposure

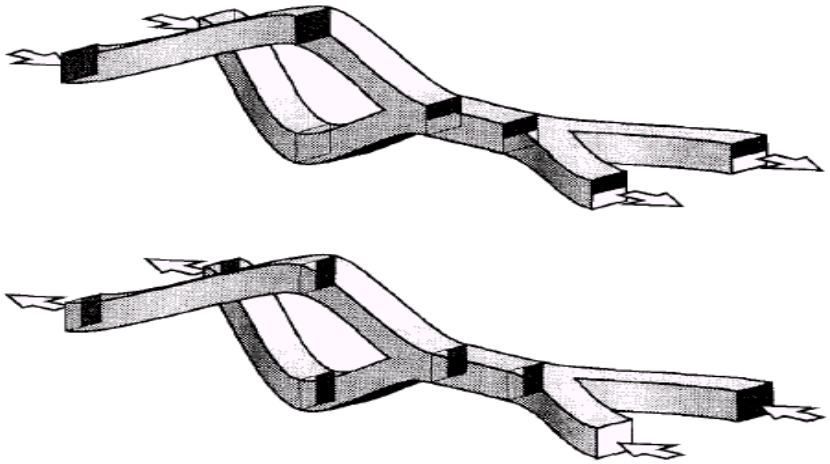


T>0
observe



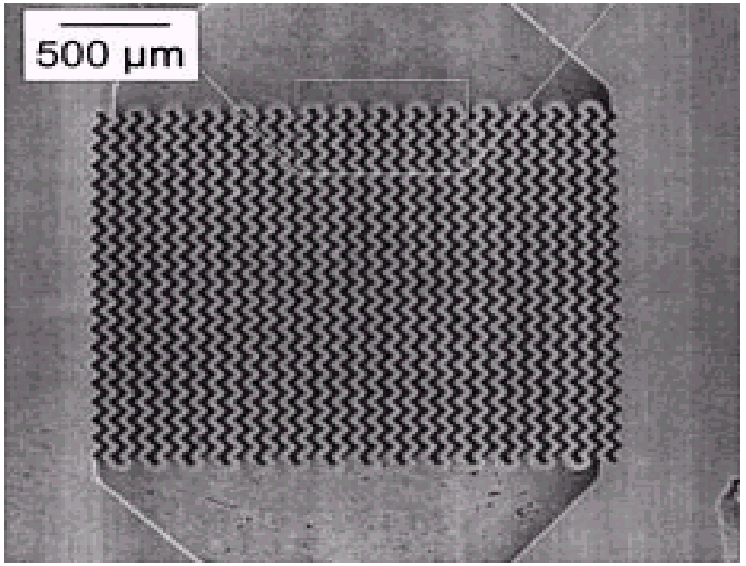
Passive Mixer

- Increase interfacial area to reduce diffusion length
  - sinusoidal, square-wave, or zigzag channels
  - divide and conquer approach
  - lamination-splitting



Lamination splitting mixer

J. Branebjerg, et al., *IEEE MEMS*, 1996, p. 442

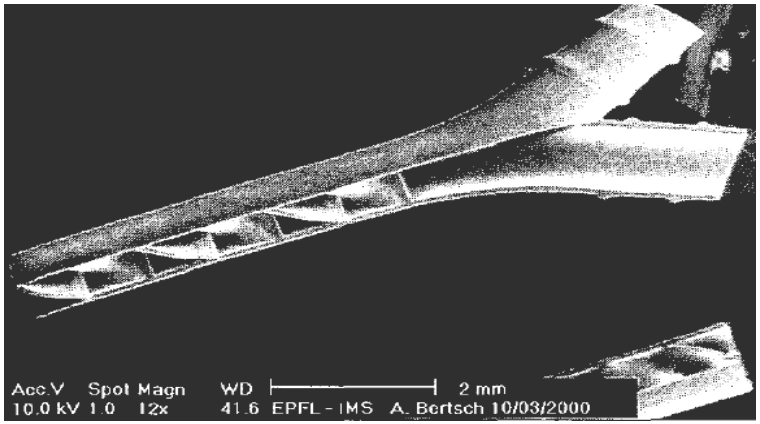


LIGA micro mixer

W. Erhfeld, et al., *Ind. Eng. Chem. Res.*, 1999, 38, p. 1077

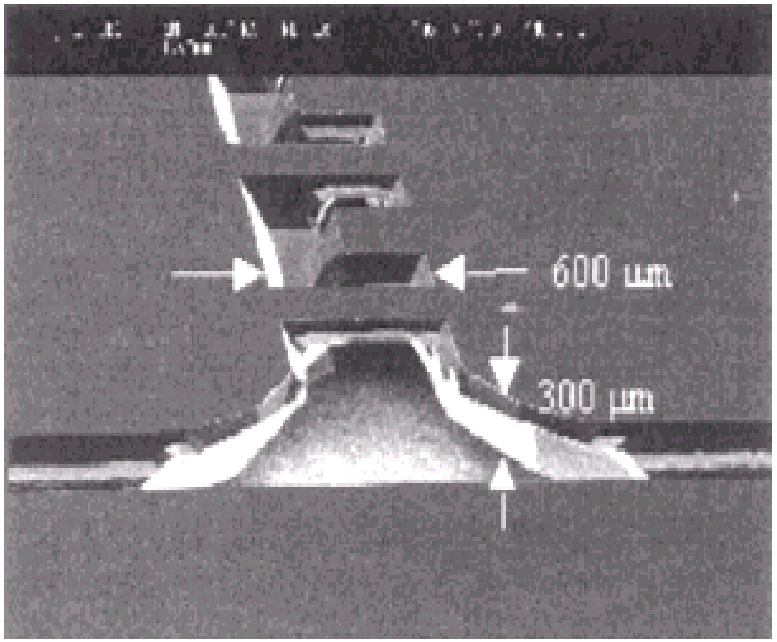
Chaotic Advection

- Chaotic pathlines can occur and disperse fluid species effectively in smooth and regular flow fields.
- Passive mixing using chaos:
  - 3D serpentine channel
  - 3D channel made by microstereolithography



3D mixer made of helical elements

A. Bertsch, et al., *IEEE MEMS*, 2001, p. 508

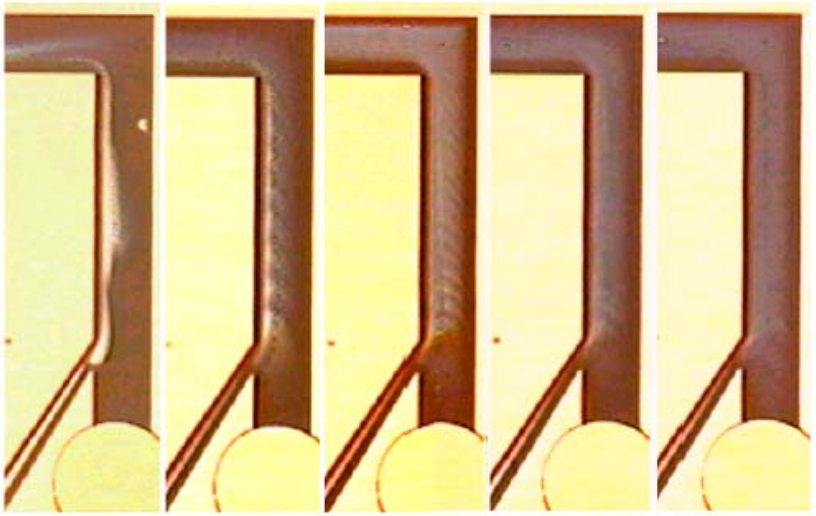


3D serpentine channel

R. H. Liu, et al., *J. MEMS*, vol. 9, No 2, June 2000, p. 191

Active Mixer

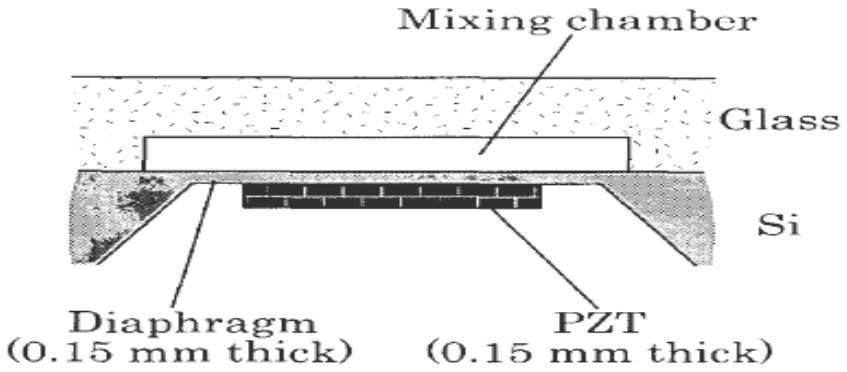
- Use active perturbation to create time-dependent 2D flows so that chaotic advection can occur
- Perturbation can be generated by different sources
  - vapor pneumatic power
  - pressure driven
  - ultrasonic/piezoelectric
  - electrohydrodynamic convection
  - electrokinetic flow
  - mechanical stirring



Thermal bubble pump mixer

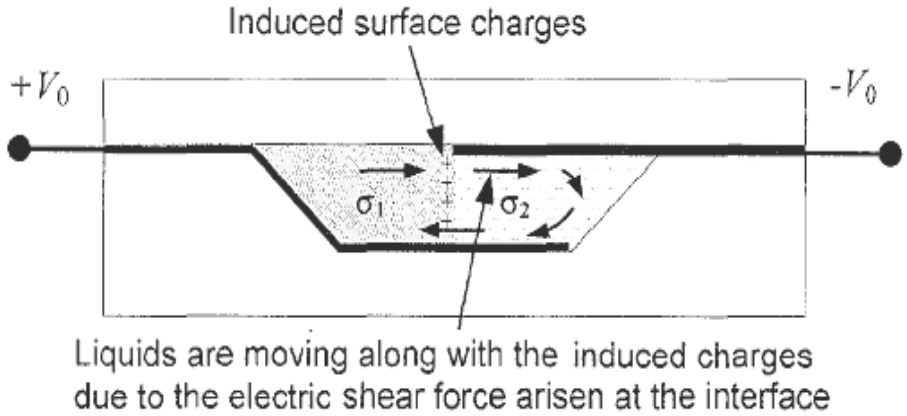
J.-H. Tsai and L. Lin, *Transducers '01*, p. 968

Active Mixing (cont'd)



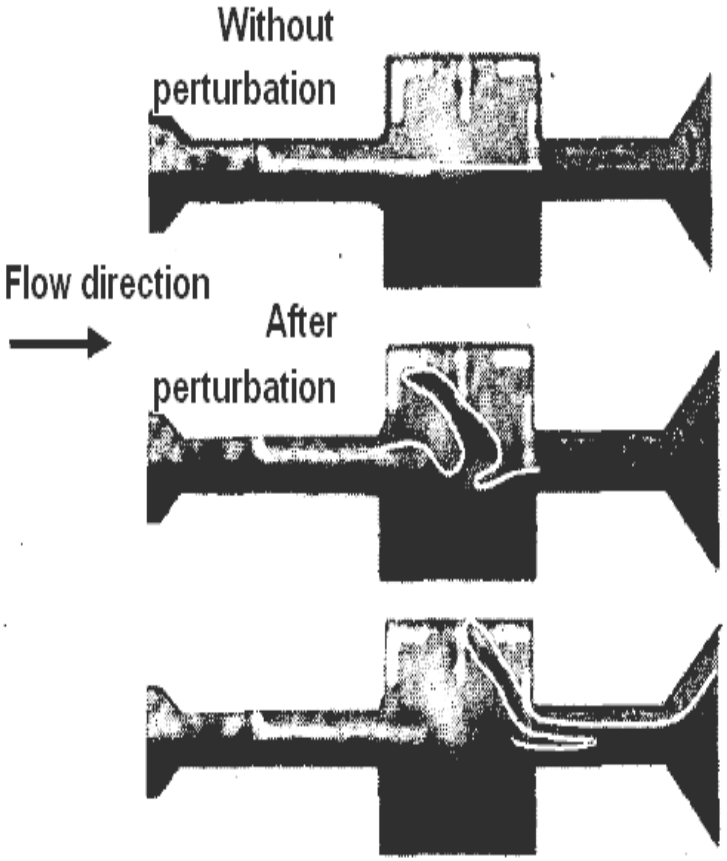
Ultrasonic mixing chamber

Z. Yang, et al., *IEEE MEMS*, 2000, p. 82



Electrohydrodynamic (EHD) convection mixer

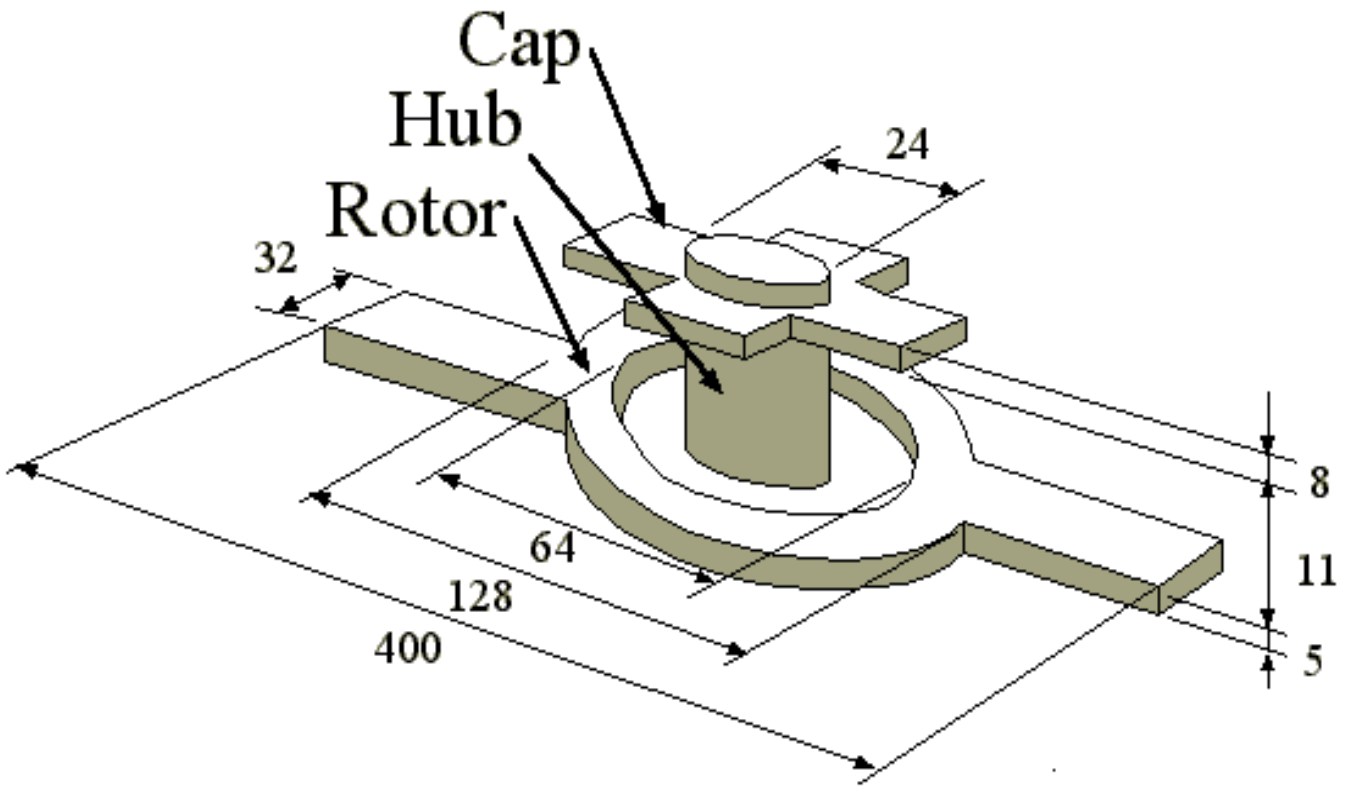
J.-W. Choi and C. H. Ahn, *Solid-State Sens. and Actuator Workshop*, 2000, p. 53



Mixing by electrokinetic perturbation

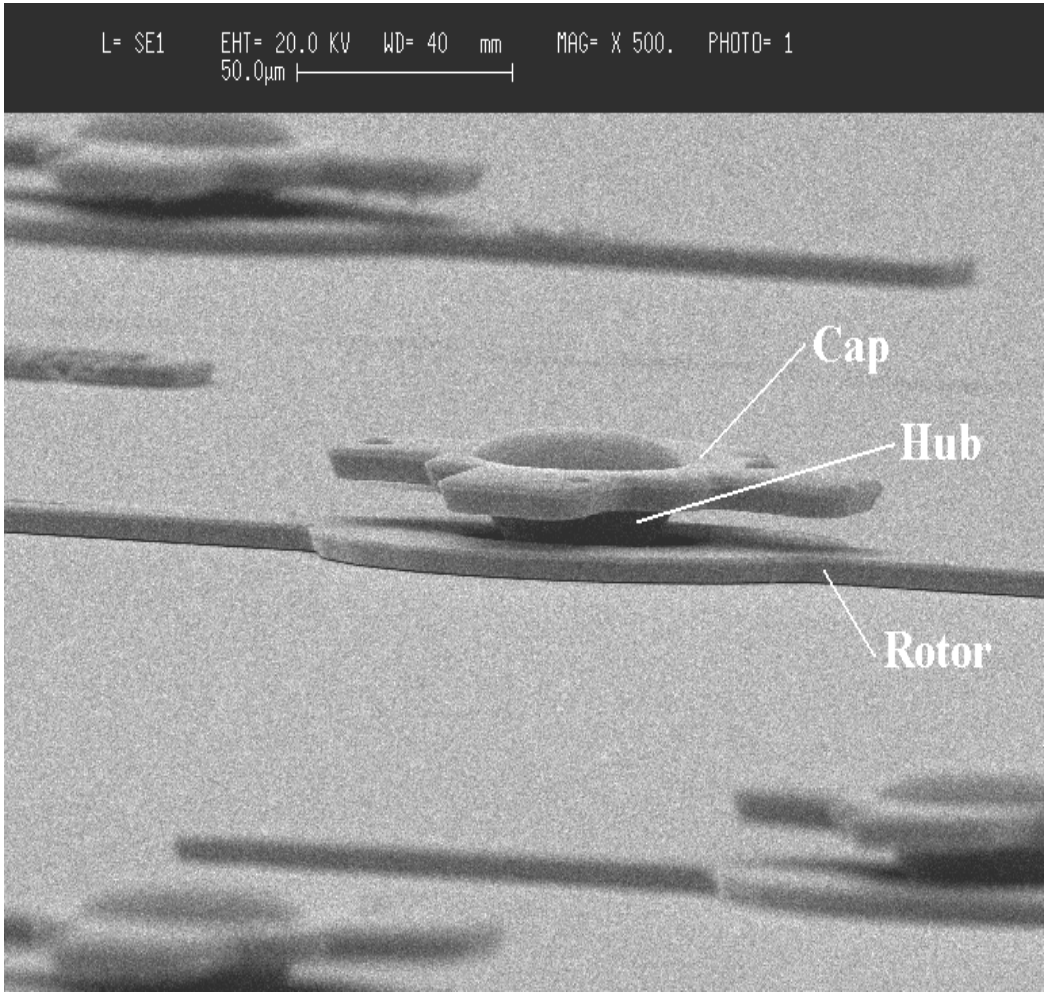
Y.-K. Lee, et al., *IEEE MEMS*, 2001, p. 486

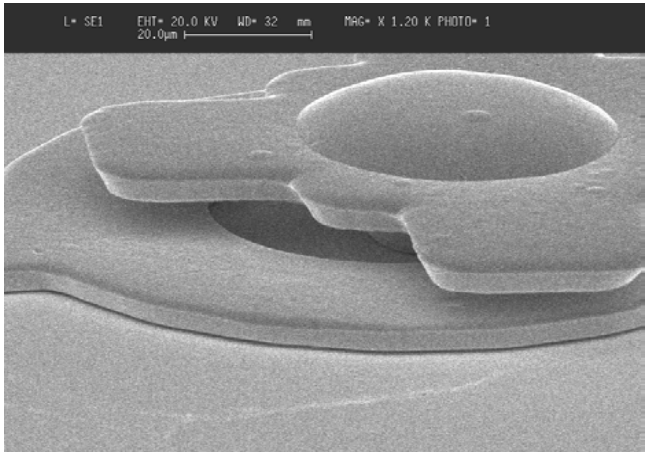
Principle of the Microstirrer

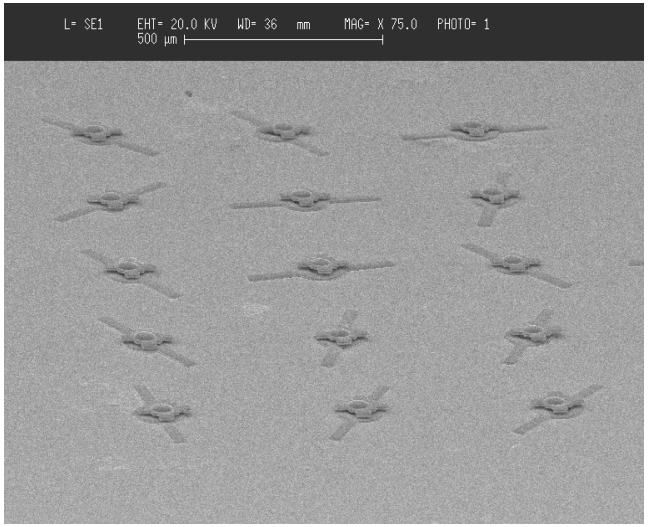


Schematic of a microstirrer

Micrographs of the Microstirrer



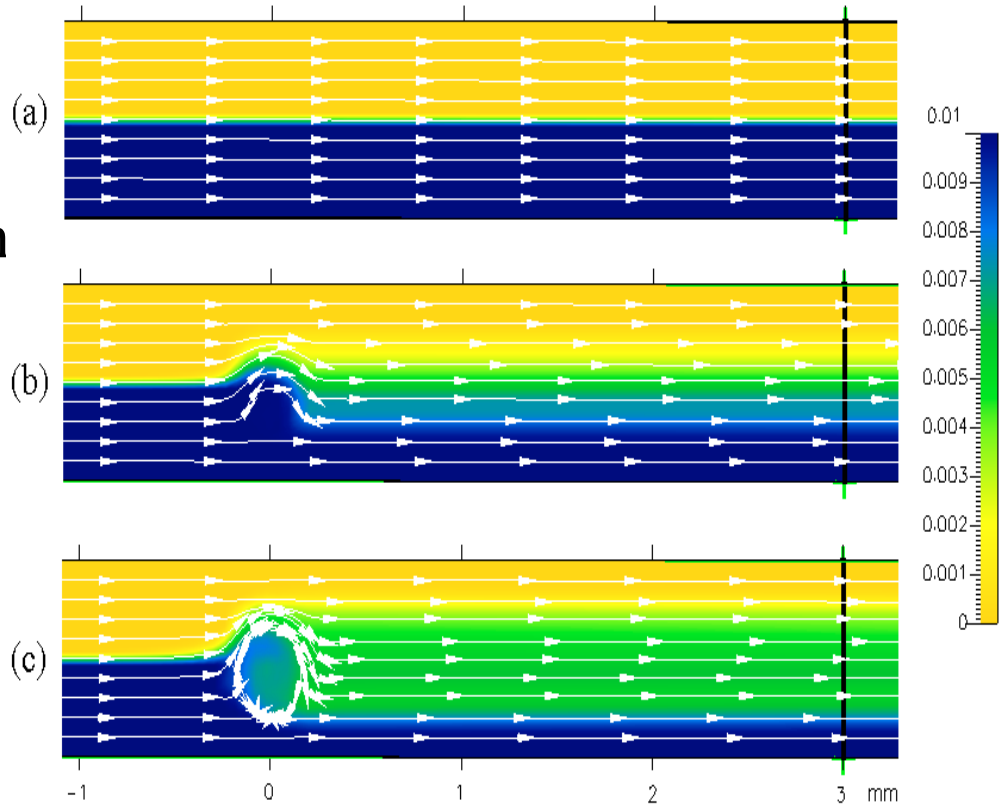




SEM pictures of a single microstirrer in a 5x3 array

Simulation of Channel Mixing

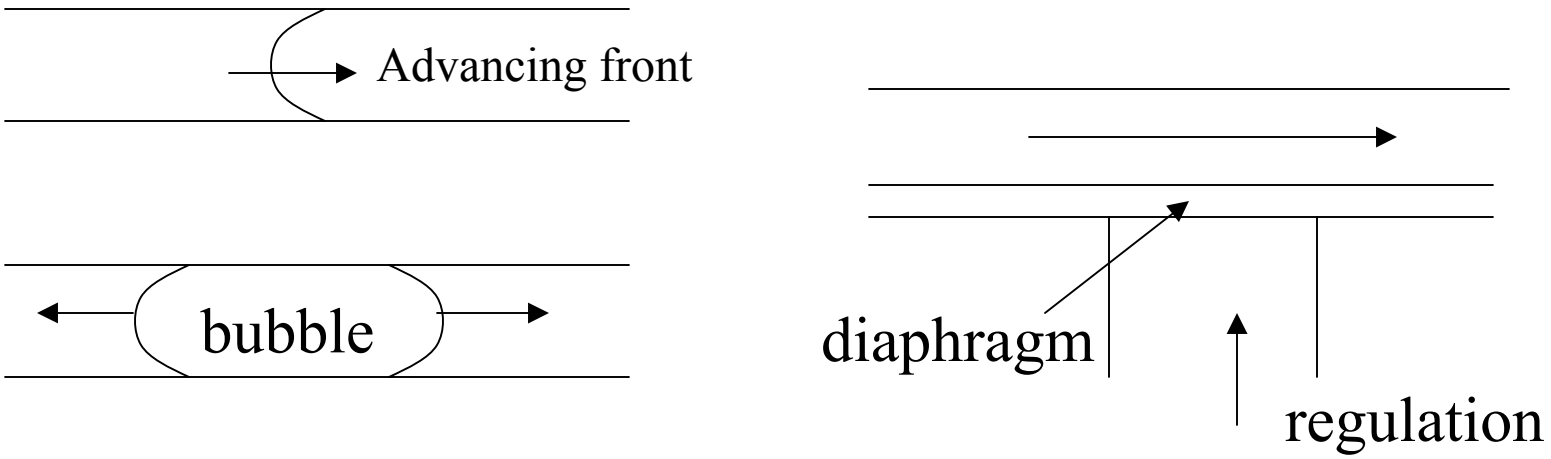
- Simulated by CFDRC fan model
- Results can provide a fast way to verify design issues
  - flow condition
  - dimension
  - rotating speed
- Mixing vs. rotating speed
  - increasing micro-stirrer speed can improve mixing



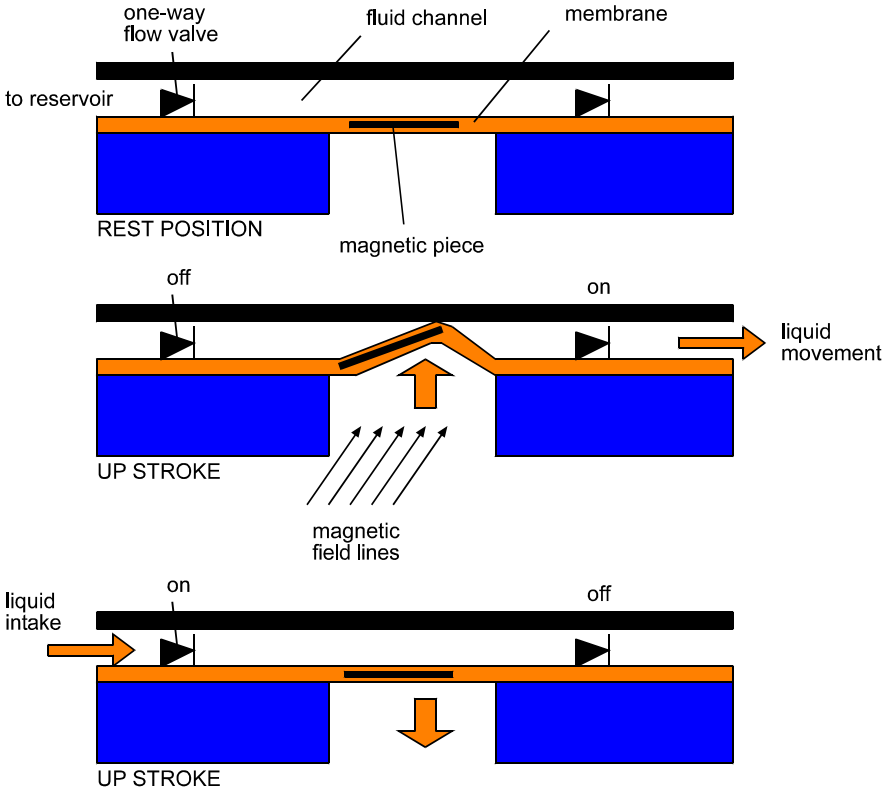
Simulation of steady-state channel mixing at (a) rest, (b) 300 rpm, (c) 600 rpm.

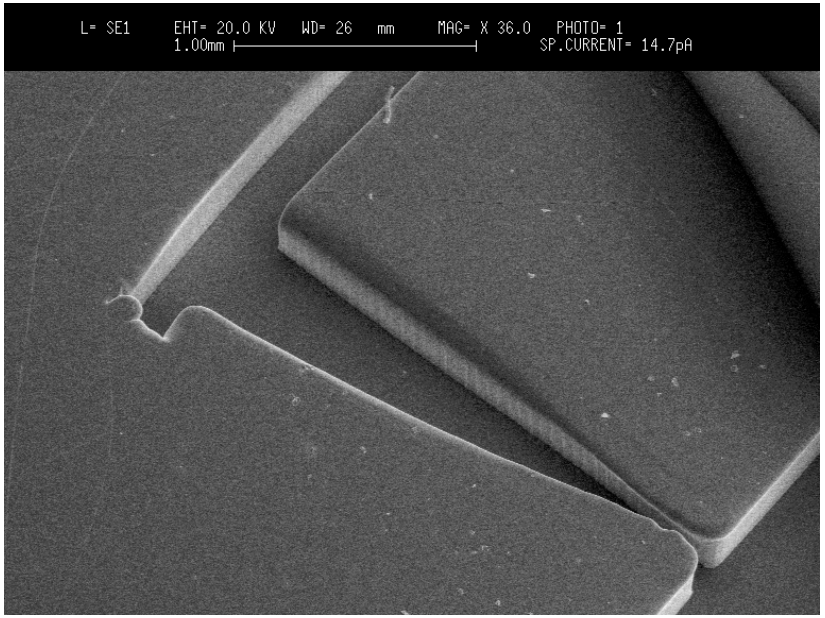
Pressure Driven Flow

- External pumps
  - fluid pumps, air pumps
  - pressure head (common in laboratory)
- Internal pumps
  - capillary force (hydrophilic surface)
  - thermal pneumatic force
  - diaphragm pumps (various ways to generate diaphragm motion)



One-way Valve





Channel Fabrication Processes

- Discrete fabrication
  - channel etch + wafer bonding
  - materials (etchants): Silicon (EDP, KOH, HNA), glass (HF), molded plastics (various molds including silicon), molded polymer
- Monolithic fabrication
  - sacrificial layer etching for channel fabrication
  - materials for sacrificial layer: photoresist, oxide
- Channel-less microsystems
  - droplet based microfluid processing

Microfluid Channel Fabrication Technology

- Criteria for processing technology
  - Simplicity of fabrication (hence yield and costs)
  - Channel material and interior material
    - compatible with fluid being transported
    - hydrophobicity
  - Optical transparency
    - optical fluid detection is predominant - optical window is required for many concurrent fluid circuits
    - transparency in visible spectrum, IR, or UV
  - Geometry constraints
    - available variety of geometry (depth, width, intersection)
  - Temperature of processing
  - Electrical conductivity

Ease of fab	Materials	Optical	Geometry	Temperature	Conductivity	Other

Bulk Micromachined Channels

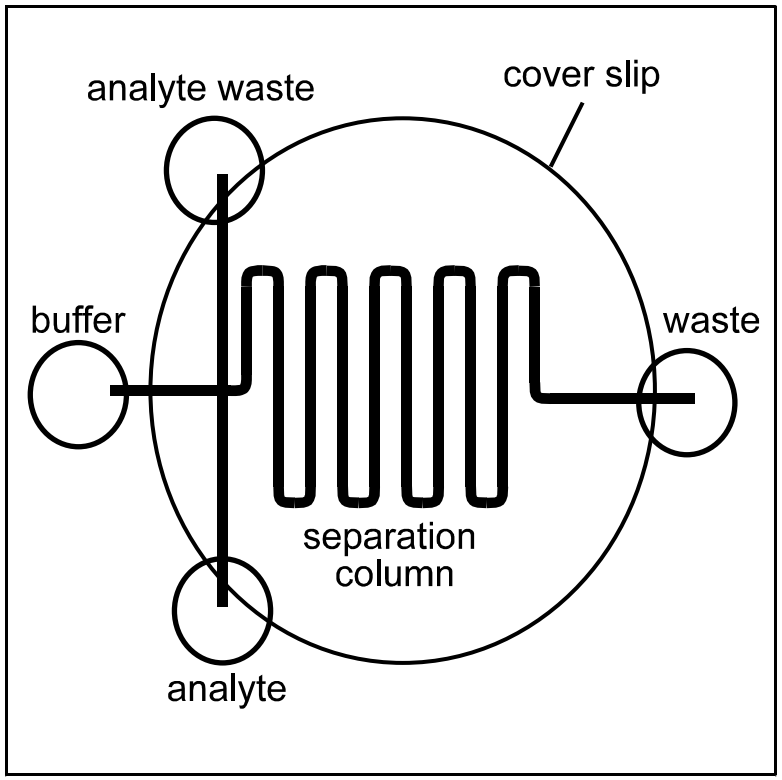
- Etch channels in glass or silicon

- silica substrate
- pyrex glass
- photosensitive Foturan glass

- * All examples can be found in the text book, chapter 9.

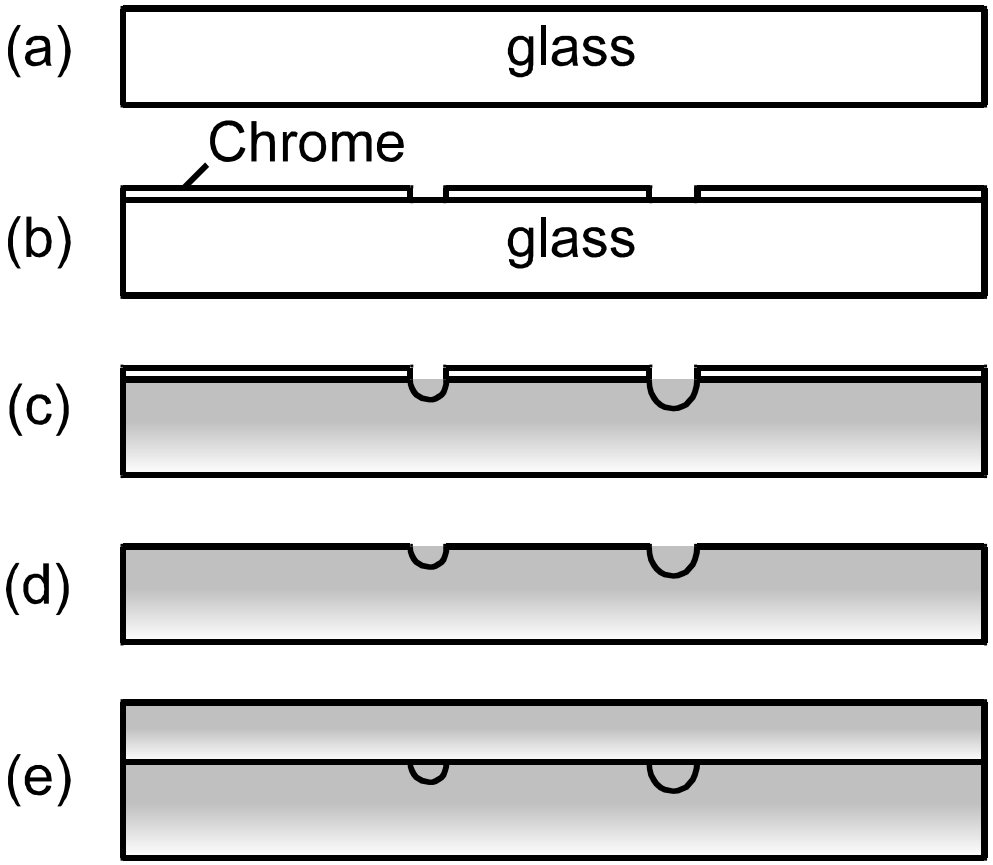
Glass Microchips

- Jacobson “electrically driven separations on a microchip”, HH’94, p. 65.
- * 796



Glass Microfabrication Process

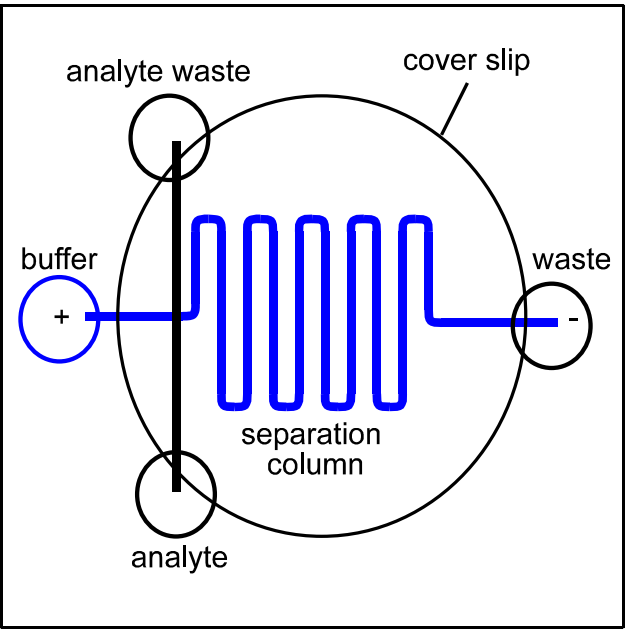
- (a) starting with glass
- (b) deposit and pattern Cr
- (c) use Cr as mask to etch the glass with HF and NH4F bath
- (d) remove Cr
- (e) bond cover slip.

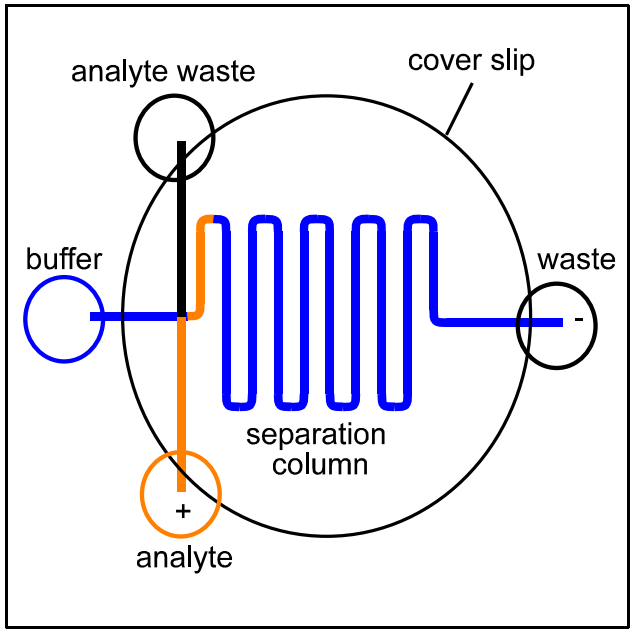


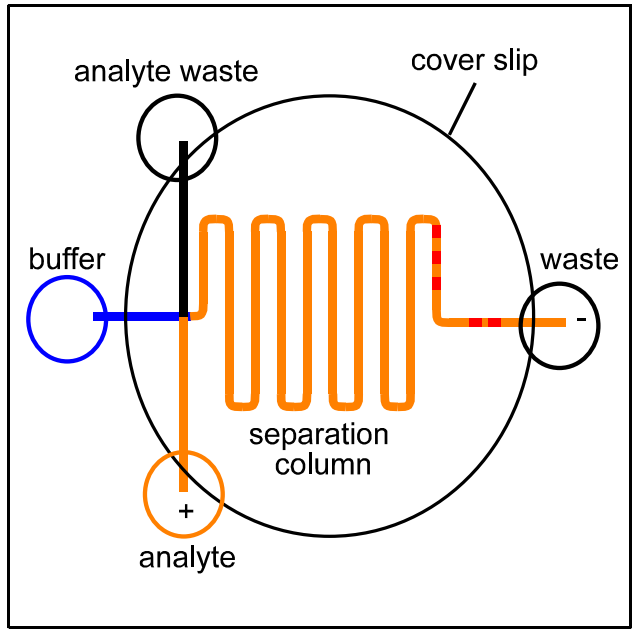
Ease of fab	Materials	Optical	Geometry	Temperature	Conductivity	Other
Simple	Low cost	yes	semicircle	High T bonding	insulator	

Operating Principle

- Buffer injection to fill in the entire channel
- Analyte injection using electrokinetic flow
- Sample introduction and analyte electrophoretic separation
- Optical detection is done near the waste port.







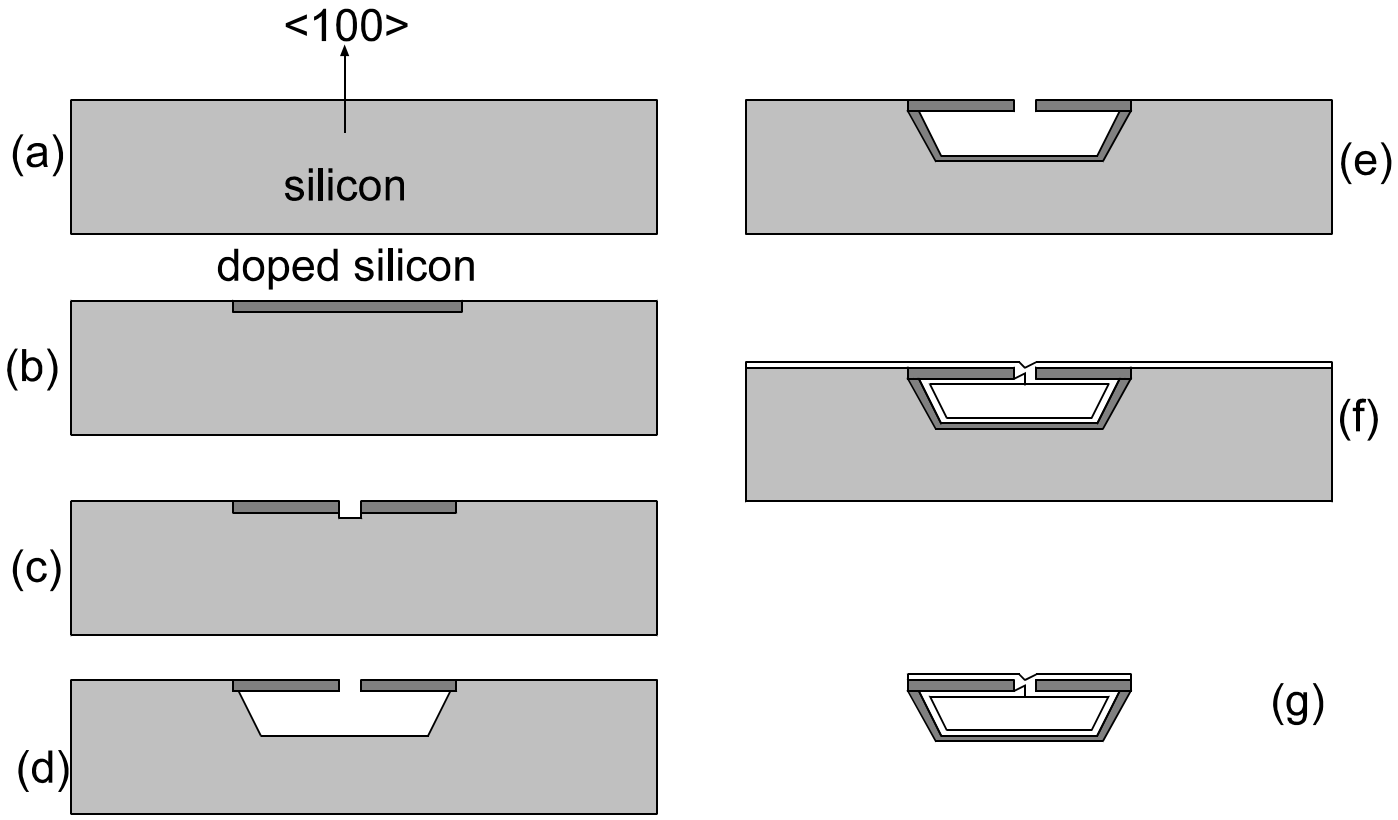
Hollow Needle
Example: Neuron Probes

- Micro needle buried in neuron probes for injection of chemicals for neuron stimulation.
- Chen and Wise, “A multichannel neural probe for selective chemical delivery at the cellular level” HH’94.
- * 798

Ease of fab	Materials	Optical	Geometry	Temperature	Conductivity	Other
difficult	moderate	no	Anisotropic etch	High temp	insulator	

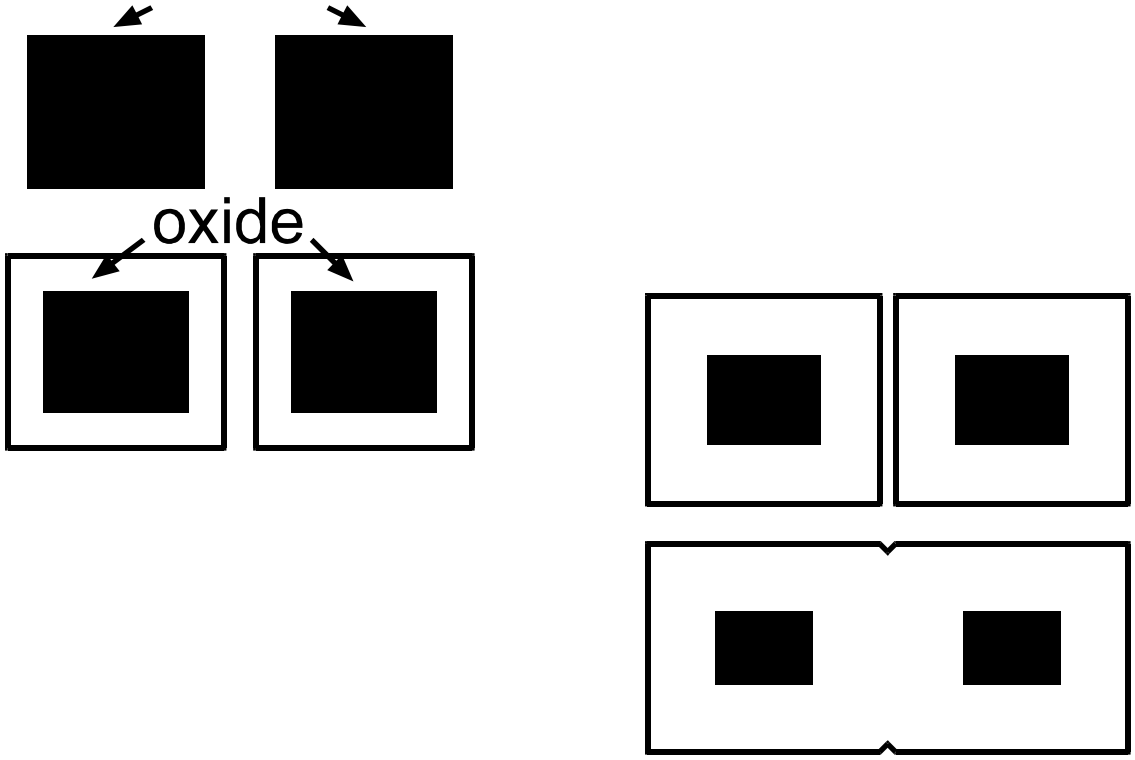
Fabrication process

- (a) starting wafer; (b) heavily dope silicon; (c) reactive ion etching; (d) anisotropic etching; (e) heavily boron diffusion; (f) oxidation sealing; (g) etching low doped silicon.



Oxidation Sealing

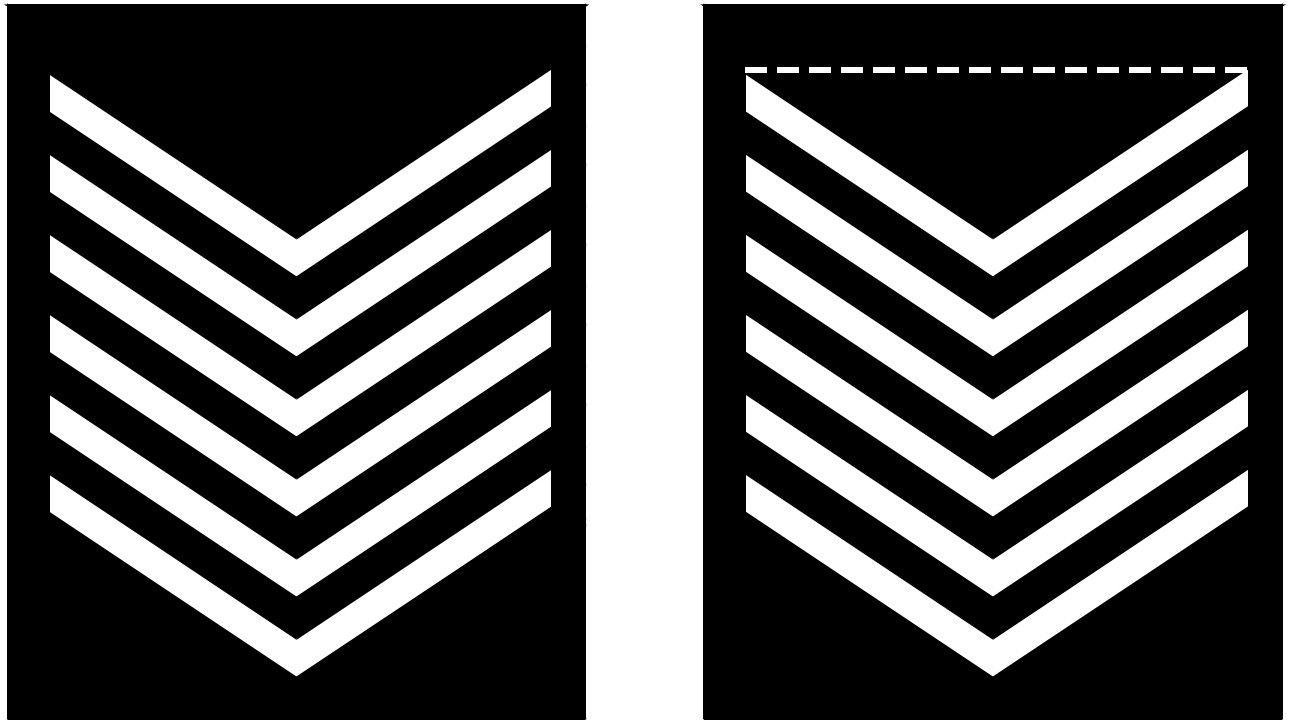
- Oxidation: oxygen reacts with silicon to form silicon dioxide.
- Silicon is consumed at the same time of oxide growth.



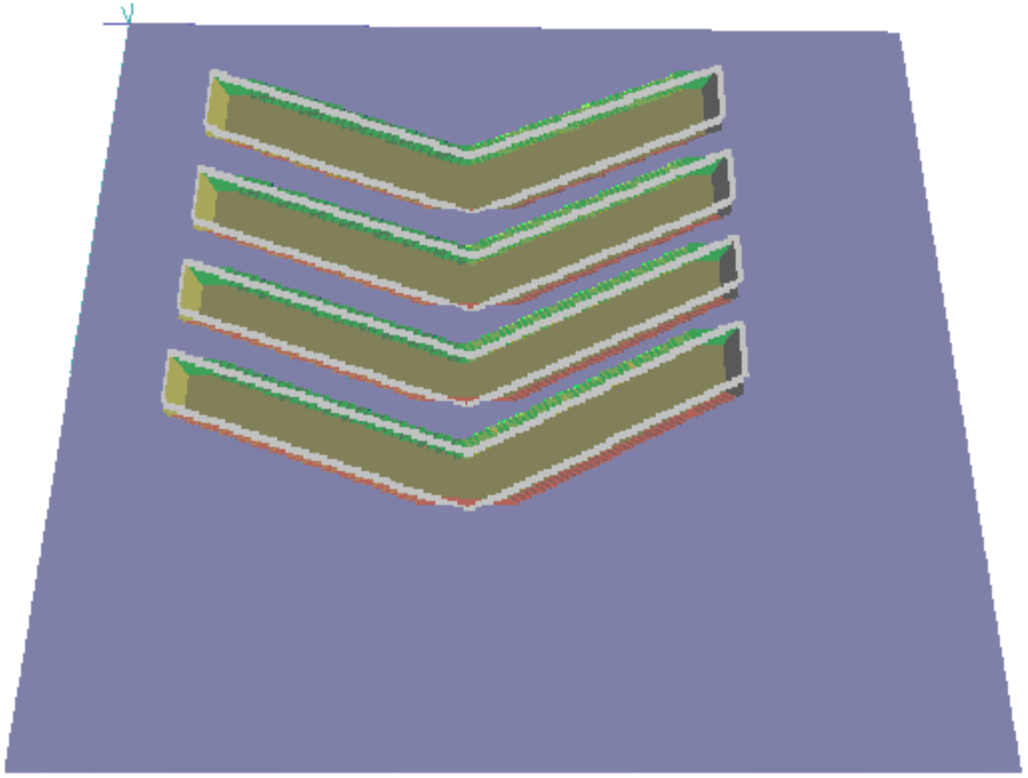
Requirement for Anisotropic etching Masks

- Capable of producing undercut channels
- The opening must be small such that oxidation can close the gap and seal the cavity.

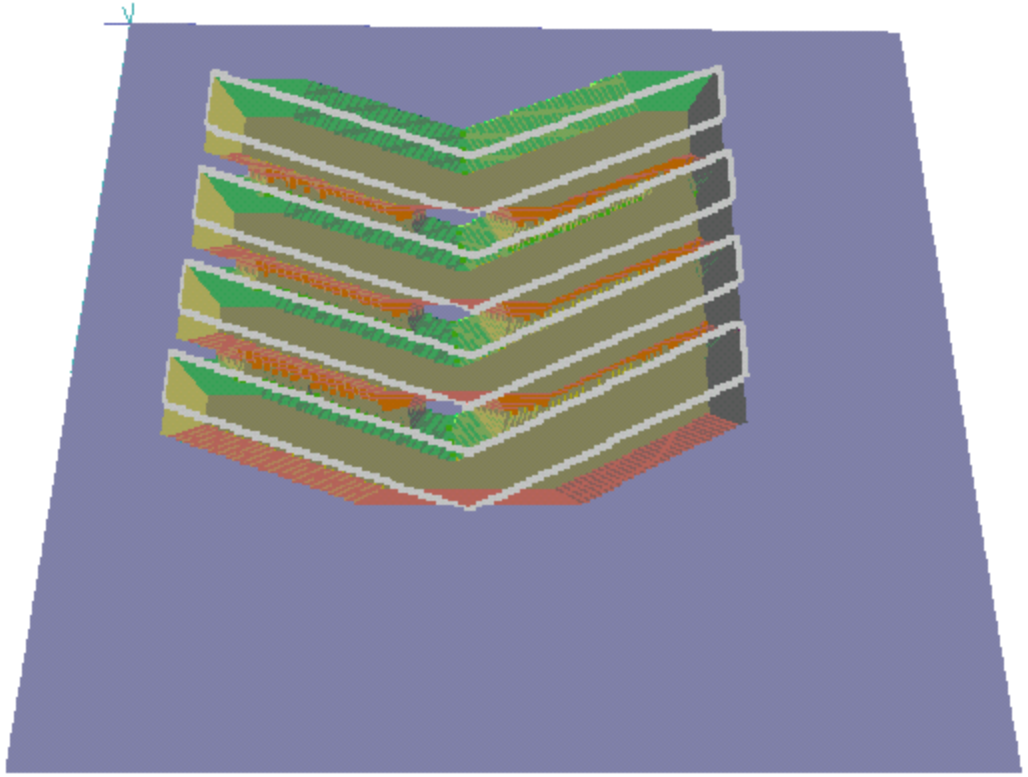
Chevron Pattern Mask



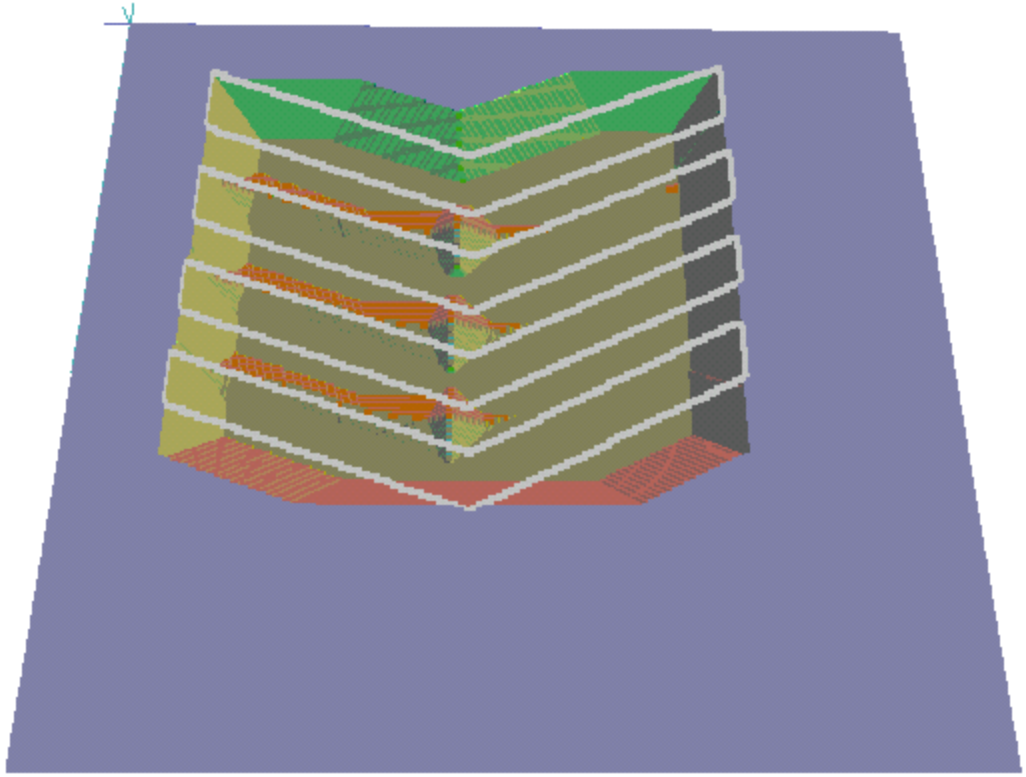
Etching Pattern Evolution - 20 Min



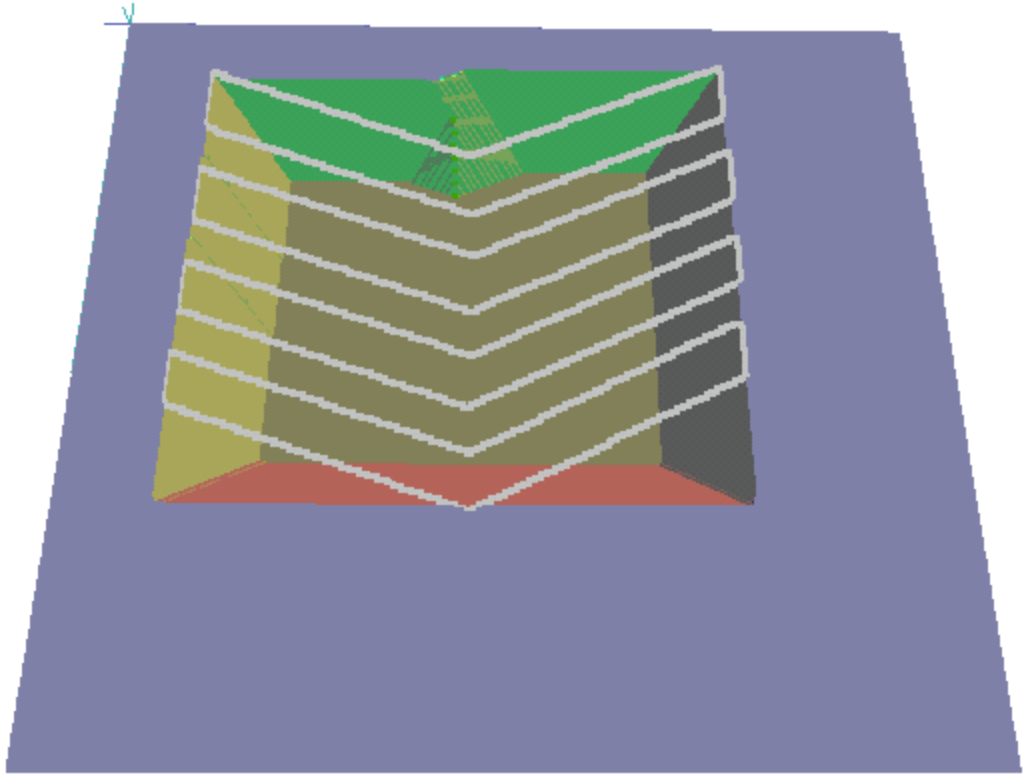
Etching Pattern Evolution - 40 Min



Etching Pattern Evolution - 60 Min



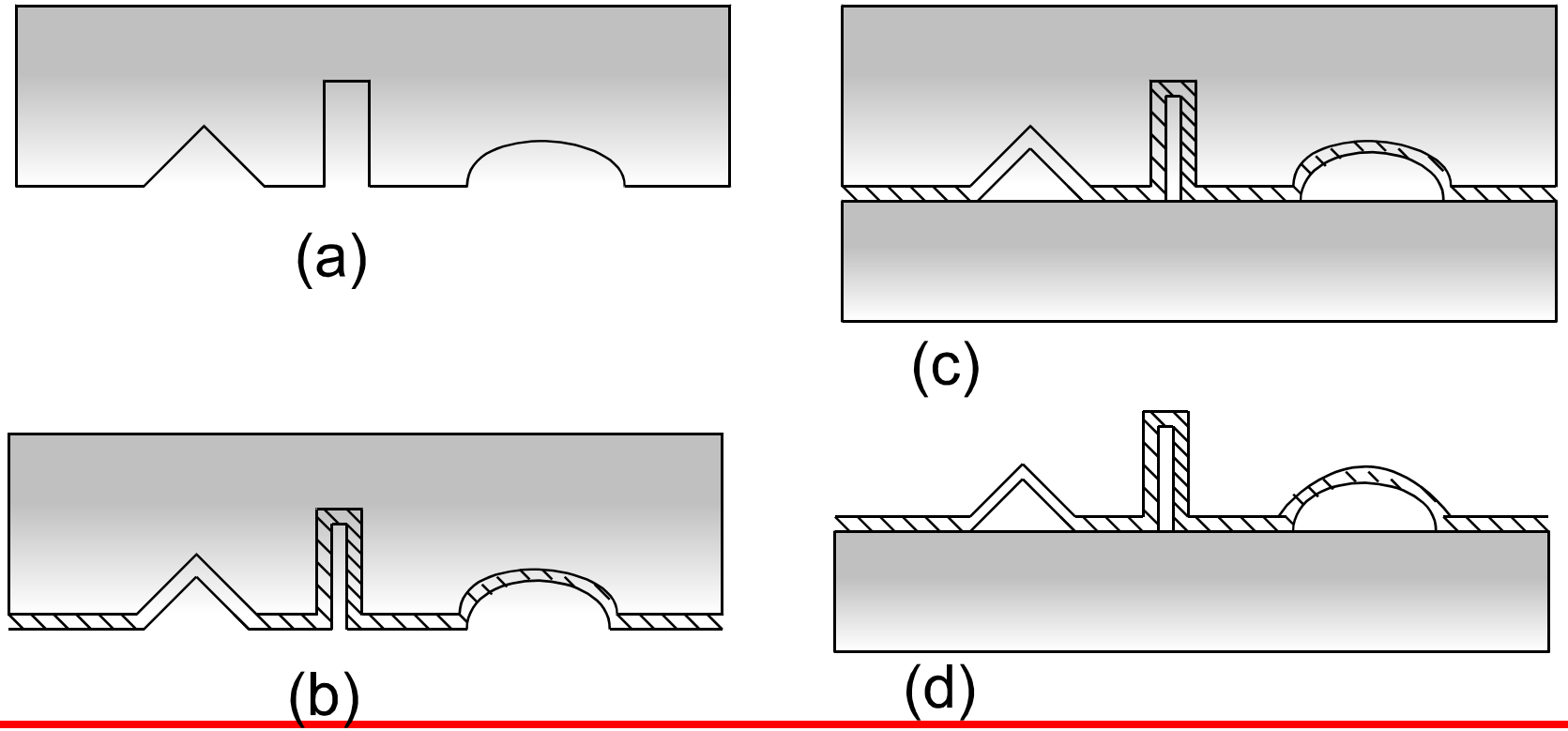
Etching Pattern Evolution - 100 Min



Silicon Nitride Channels Above Surfaces

Tjerkstra 1997 * 799

- (a) etching channels in silicon using various techniques to have different shapes; (b) conformal deposition of thin film (e.g. silicon nitride); (c) anodic bonding of two wafers; (d) etching the top silicon surface.



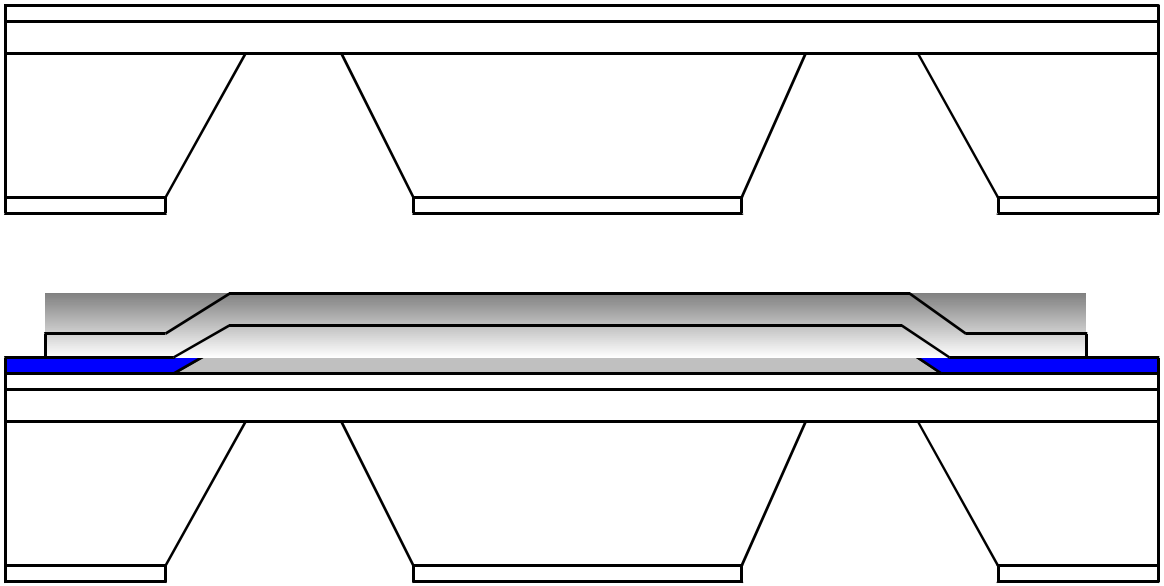
Merits

Ease of fab	Materials	Optical	Geometry	Temperature	Conductivity	Other
moderate	high	moderate	varied	moderate	yes	

Plastic Micro Channels

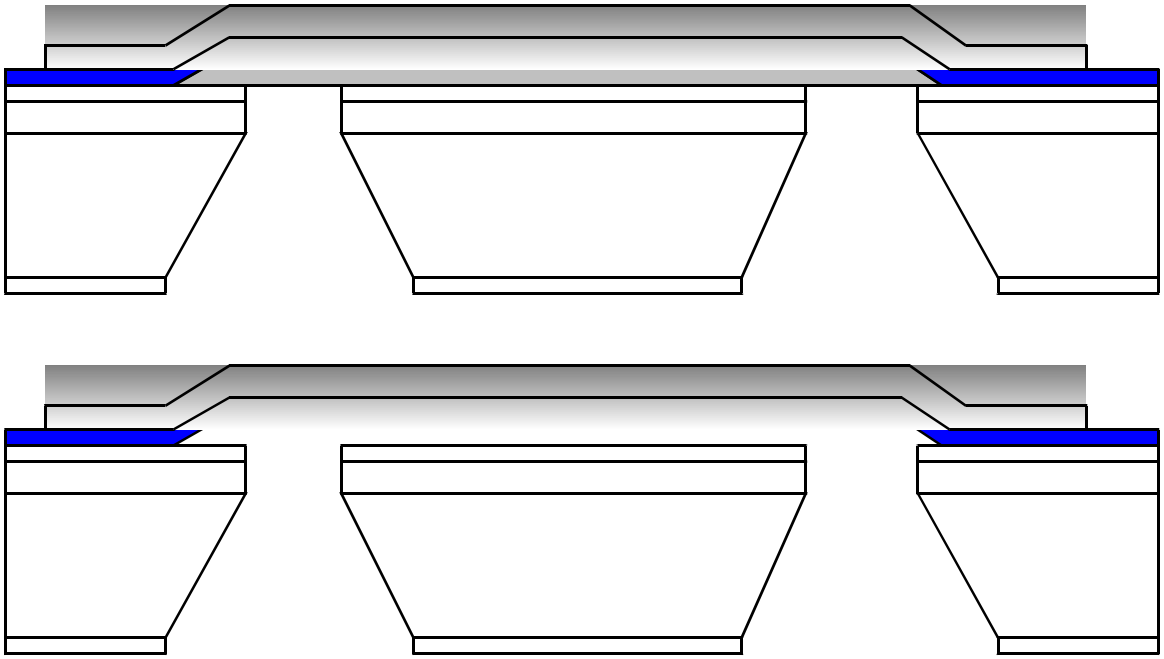
Man et al (1997) * 802

- First step: deposition of silicon oxide and parylene (first layer);
- Second step: deposition of photoresist as the sacrificial layer; deposition of Parylene layer on top of photoresist (since the deposition is done at room temperature); deposition of polyimide (photopatternable) for strengthening the top layer.



Continued….

- Step 3: Etching of silicon oxide on back side; etching first Parylene using oxygen plasma.
- Step 4: Etching of photoresist using warm acetone (40-50^{o}C)



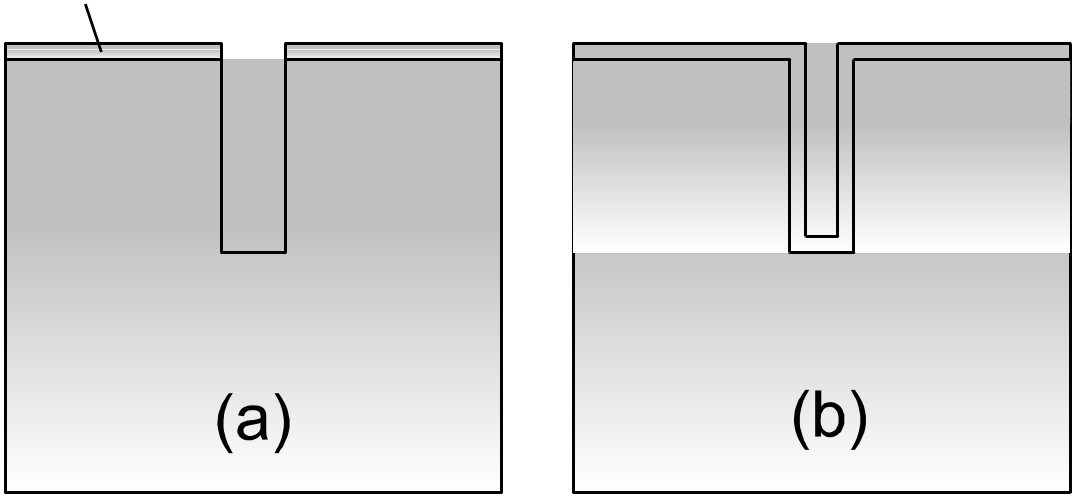
Merits

Ease of fab	Materials	Optical	Geometry	Temperature	Conductivity	Other
moderate	Low	Yes	one	Low	Low	

Fabrication of Buried Channels

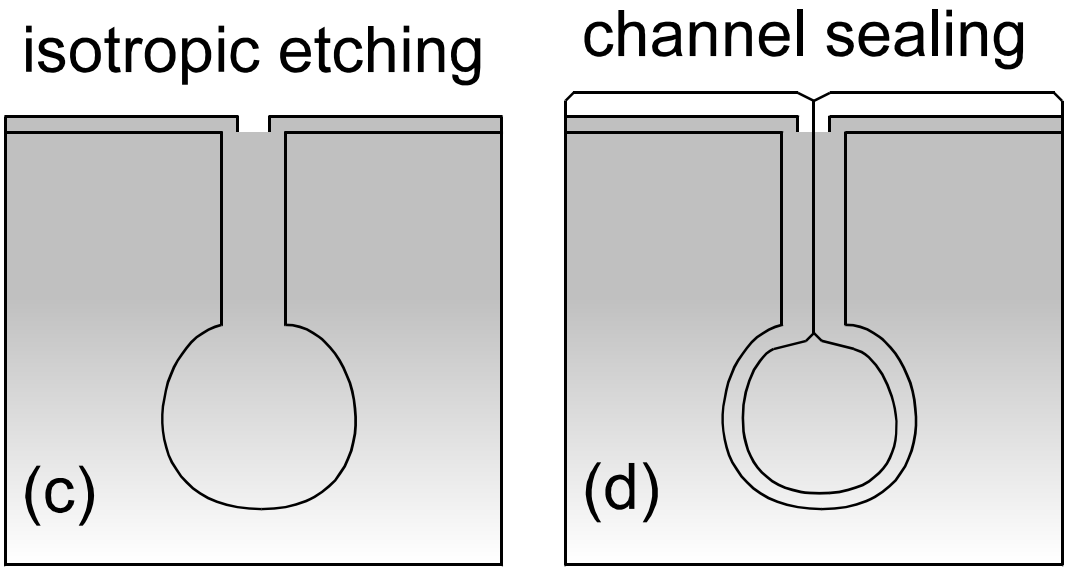
Tjerkstra 1997 * 800

- Step a: Deep reactive ion etching to form channels;
- Step b: Low pressure chemical vapor depostion.



Buried Channels (continued …)

- Step C: isotropic etching to form the channel; drying of channel solutions;
- Step D: deposition of chemical vapor deposition to seal the channels.



Micro- fludics Systems Level Applications

Integrated Chemical Analysis Systems
(* Chapter 9, Section 10)

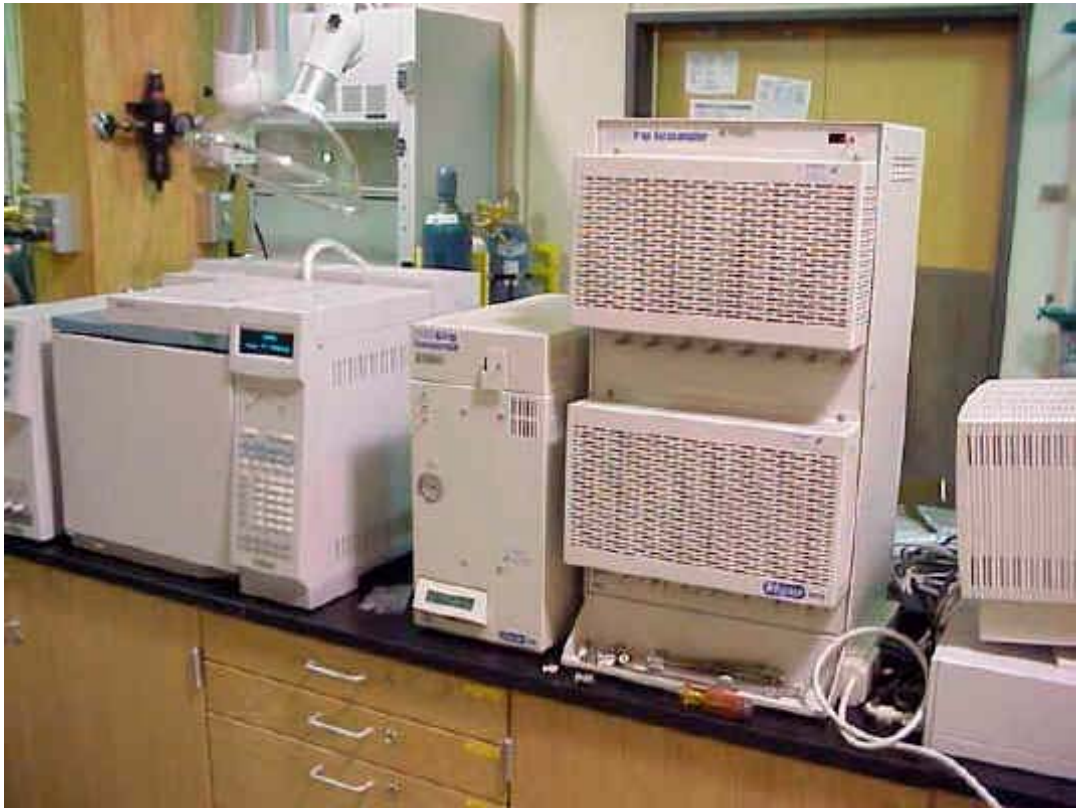
- Gas chromatography systems (*10.2)
  - separate gas components out of gas mixture
- Liquid chromatography systems (*10.3)
- Electrophoresis systems (*10.4)
- DNA amplification system (*10.6)
- Block diagram of a complete DNA sequence chip

Gas Chromatography

- Applications:
  - Sensing pollutants in real time, in-situ.
  - Sensing toxic gases in industrial environments.
  - Protective instrument for a potential chemical warfare situation.
  - Chemical trace analysis.

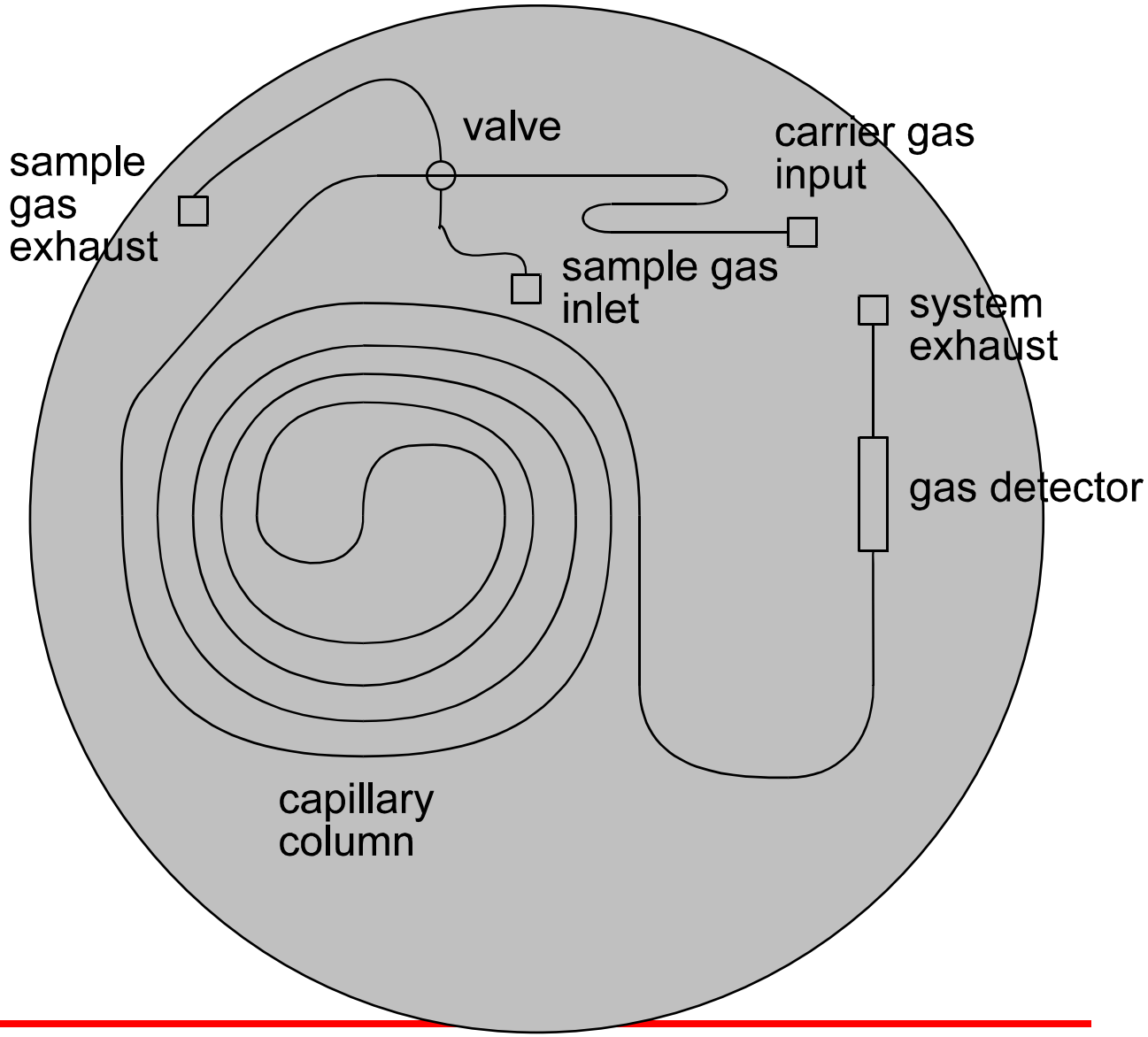
Conventional “large foot print” GC Instruments

- HP 6890 GC with Tekman thermal desorption autosampler.



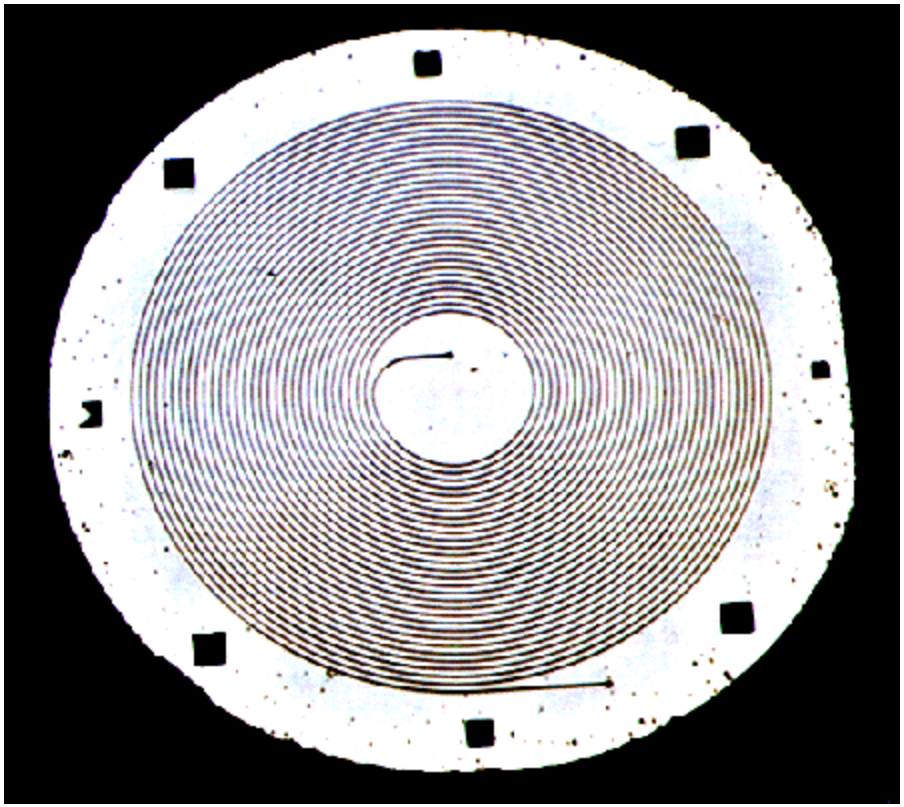
Gas Chromatography

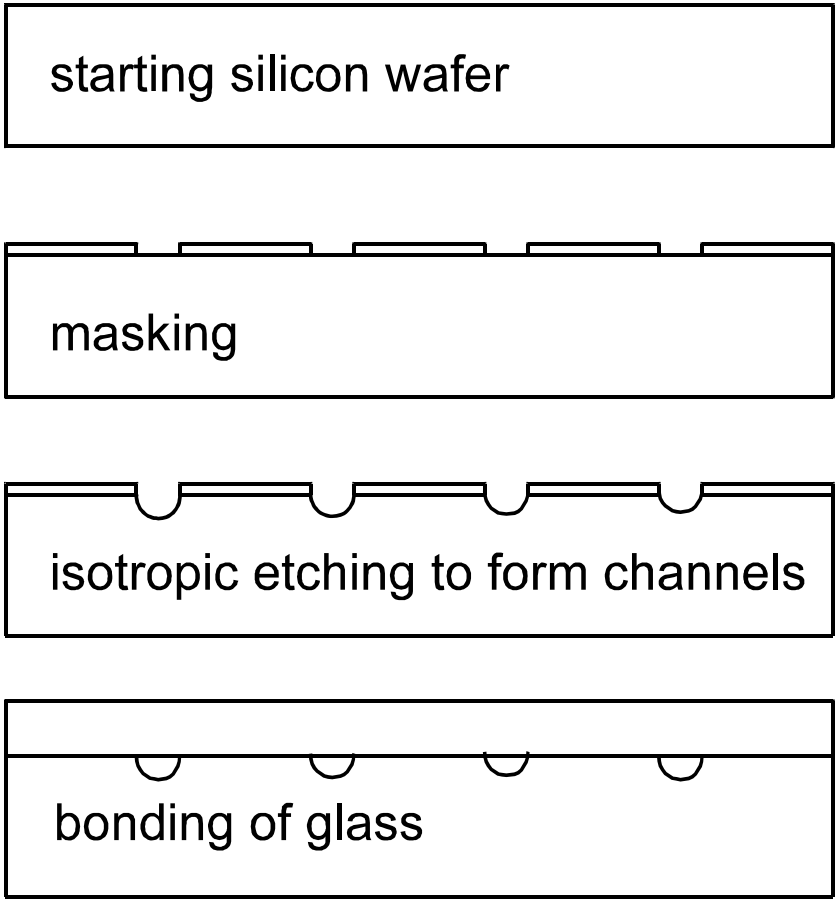
- An analytical technique for separating, identifying and measuring the quantity of each gas in a mixture.
- The inner wall is lined with silicone oil or a polymer in which different gases have different degrees of solubility.
- Component gases are repeatedly absorbed and deabsorbed, and the effective mobility is different for component gases.



Capillary Microfabrication

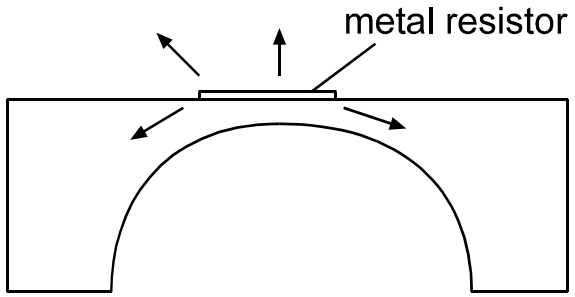
- Etch capillary channels in silicon using isotropic etching
- anodic bonding of glass to silicon substrate.





Specifications

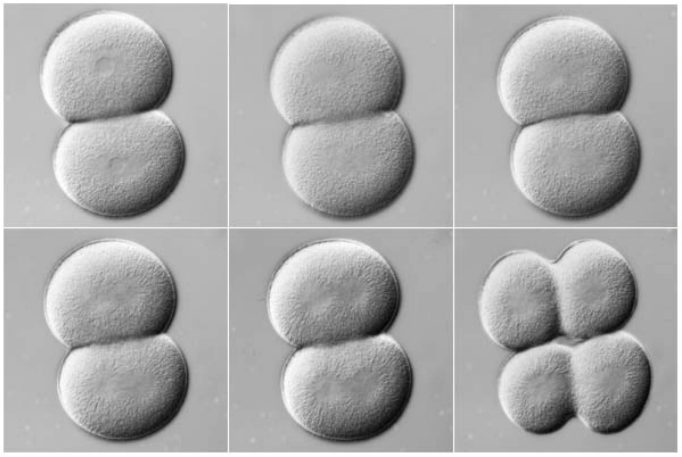
- Micro capillary channels
  - 200 μm at the interface with glass
  - 40 μm deep

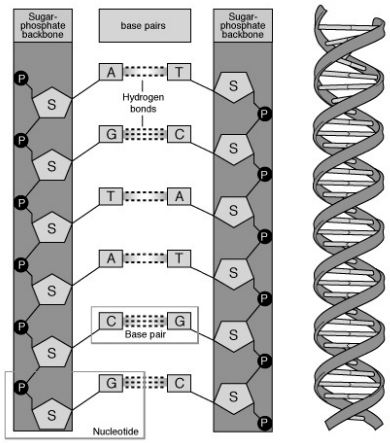


- Anodic bonding
  - 400 ^{o}C contact area heating
  - under applied voltage, sodium ions in glass move toward negative electrode, leaving behind negative image charges. When the temperature is reduced, the charges are retained due to low mobility.
- Gas sensing
  - thin film metal resistor is heated
  - different gases have different conductivity, therefore affecting the temperature of the resistor under constant power input.

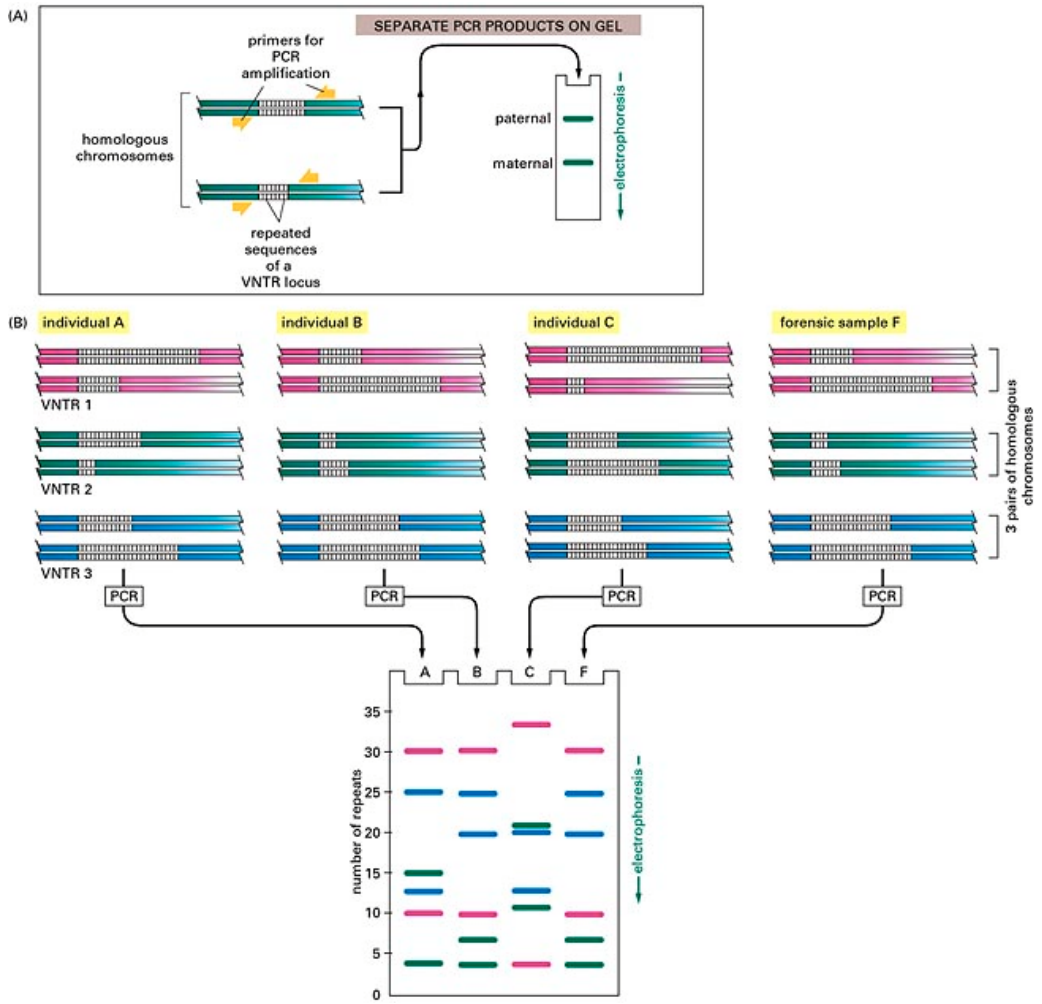
DNA PCR (* 876)

- Applications
  - amplify the amount of DNA molecules to increase the quantity and to enhance detection sensitivity
- Principle
  - PCR mimics a natural process during cell splitting. When any cell divides, enzymes called polymerases make a copy of all the DNA in each chromosome
  - The PCR technique, which was invented in 1985 by Nobel Laureate Kary Mullis, involves three basic steps





Forensic Analysis

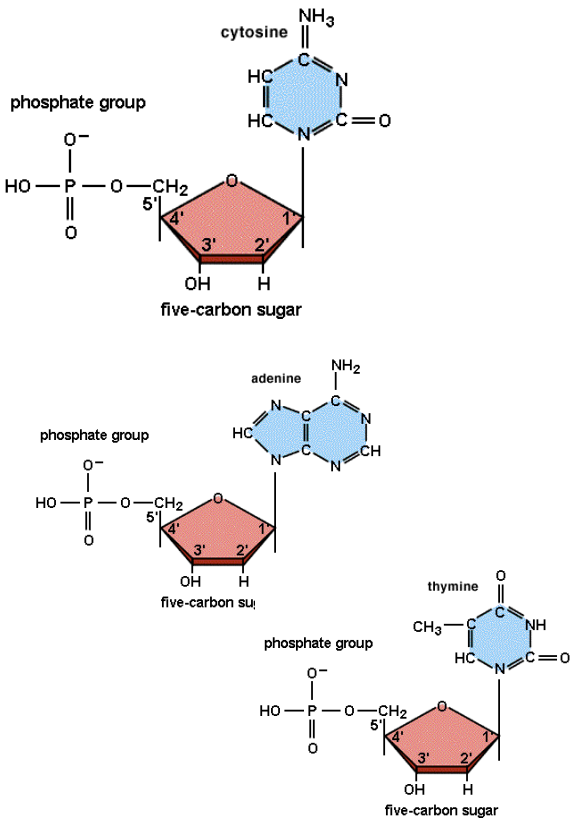


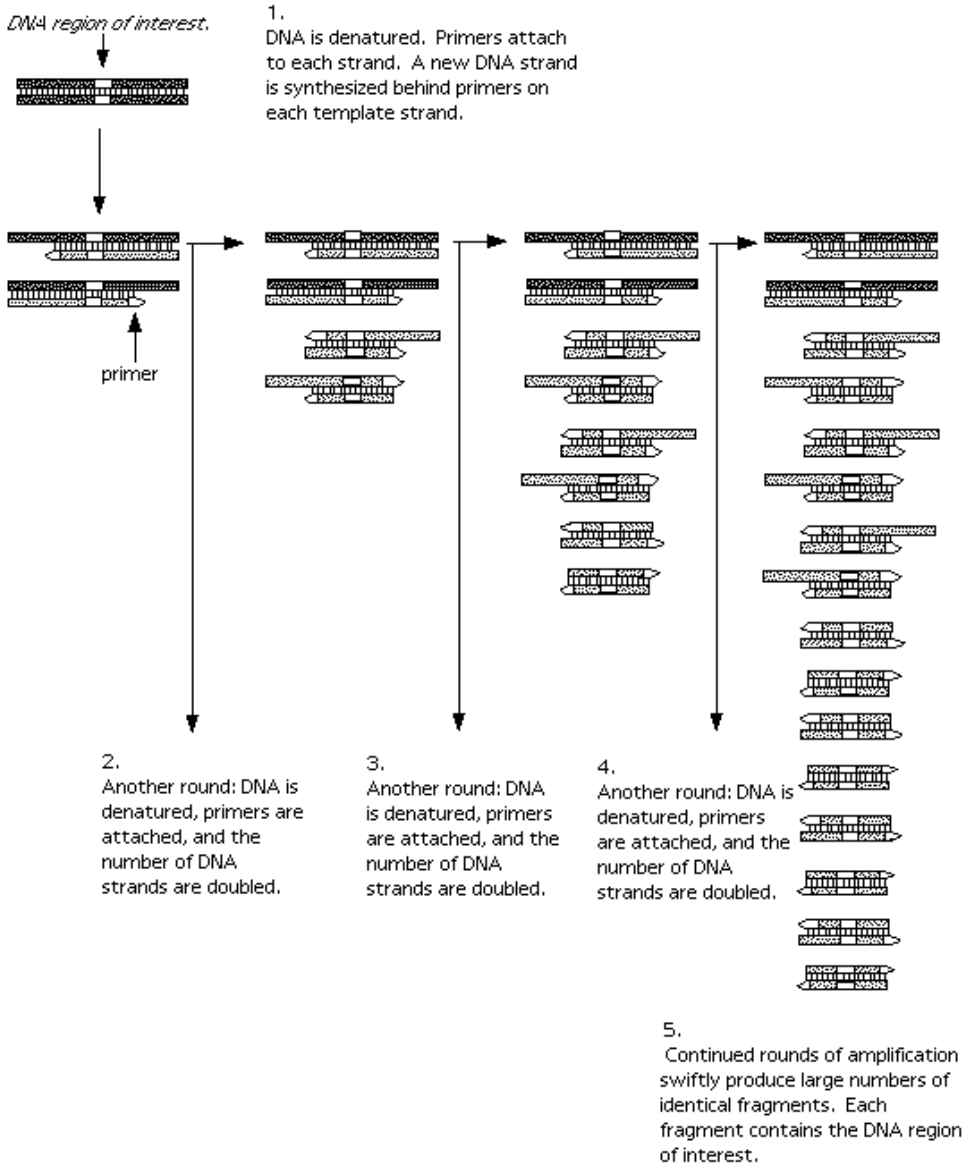
PCR Principle

- A PCR vial contains all the necessary components for DNA duplication: a piece of DNA, large quantities of the four nucleotides, large quantities of the primer sequence, and DNA polymerase. The polymerase is the Taq polymerase, named for *Thermus aquaticus*, from which it was isolated.
  - The three parts of the polymerase chain reaction are carried out in the same vial, but at different temperatures. The first part of the process separates the two DNA chains in the double helix. This is done simply by heating the vial to 90-95 degrees centigrade (about 165 degrees Fahrenheit) for 30 seconds.
  - the vial is cooled to 55 degrees C (about 100 degrees F). At this temperature, the primers bind or "anneal" to the ends of the DNA strands. This takes about 20 seconds.
  - The final step of the reaction is to make a complete copy of the templates. Since the Taq polymerase works best at around 75 degrees C (the temperature of the hot springs where the bacterium was discovered), the temperature of the vial is raised.

Thermus aquaticus is isolated from Yellowstone National Park

PCR Diagram

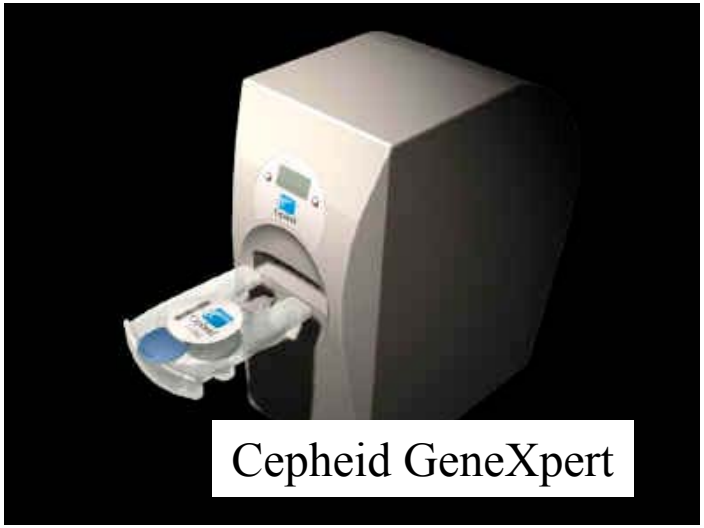

cytosine
phosphate group
five-carbon sugar
adenine
phosphate group
thymine
phosphate group
five-carbon sugar


DNA region of interest.
1.
DNA is denatured. Primers attach to each strand. A new DNA strand is synthesized behind primers on each template strand.
primer
2.
Another round: DNA is denatured, primers are attached, and the number of DNA strands are doubled.
3.
Another round: DNA is denatured, primers are attached, and the number of DNA strands are doubled.
4.
Another round: DNA is denatured, primers are attached, and the number of DNA strands are doubled.
5.
Continued rounds of amplification swiftly produce large numbers of identical fragments. Each fragment contains the DNA region of interest.

Micro PCR

- http://www.cepheid.com/
  - Cepheid microDiagnostics™ systems cover the full range of biochemical processing required to yield an analytical result - from sample collection, to nucleic acid extraction and concentration, to nucleic acid amplification, to detection. While others focus on nanoliters and picoliters of fluids, Cepheid has developed systems for processing real-life, practical biological samples, from microliters to milliliters.
  - While others are satisfied with nucleic acid amplification procedures that require several hours, Cepheid has developed systems for performing amplification in minutes.

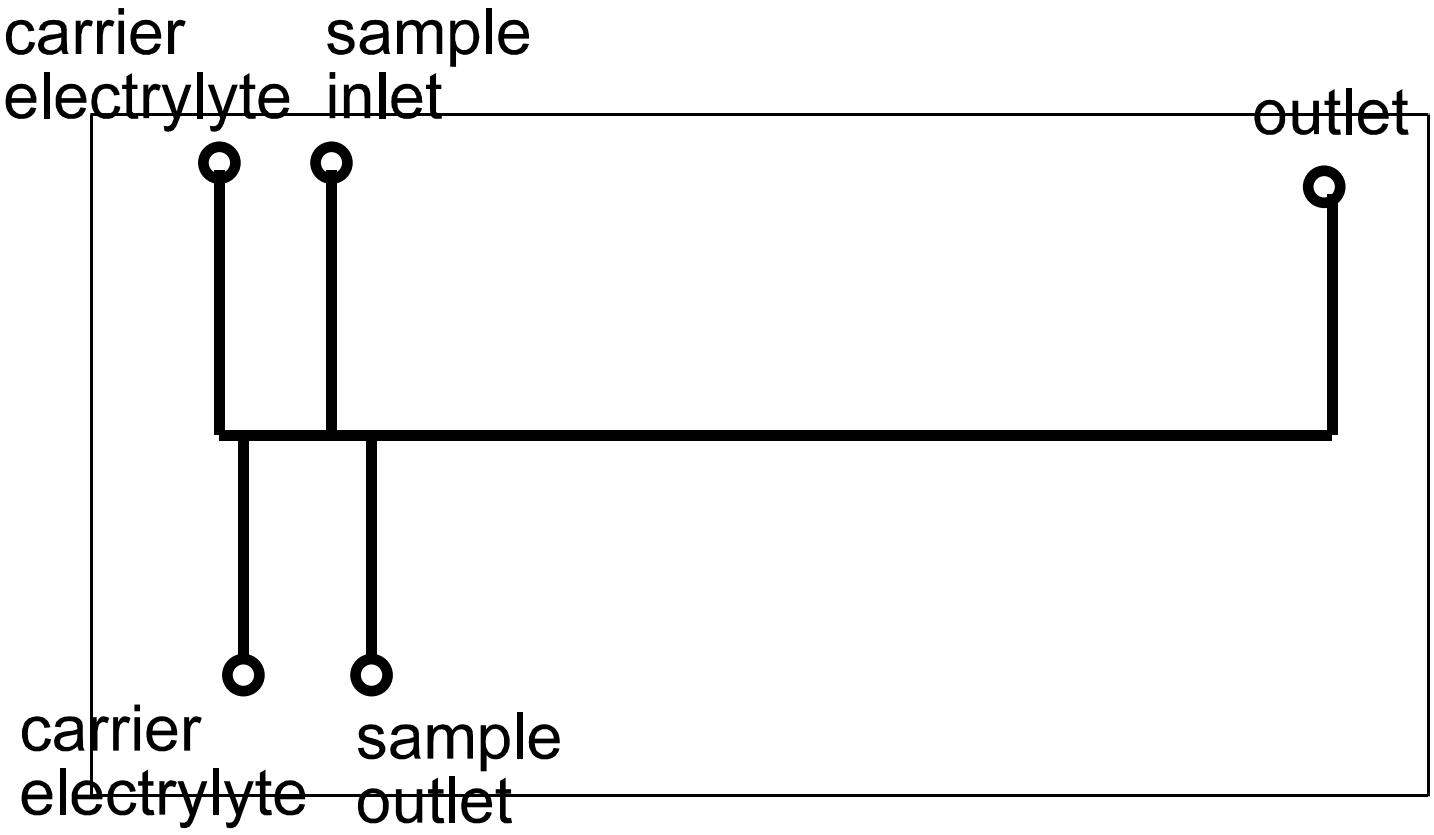
- Advantage of MEMS for fast PCR
  - low thermal mass
  - fast heating and cooling
  - greatly reduced error rate



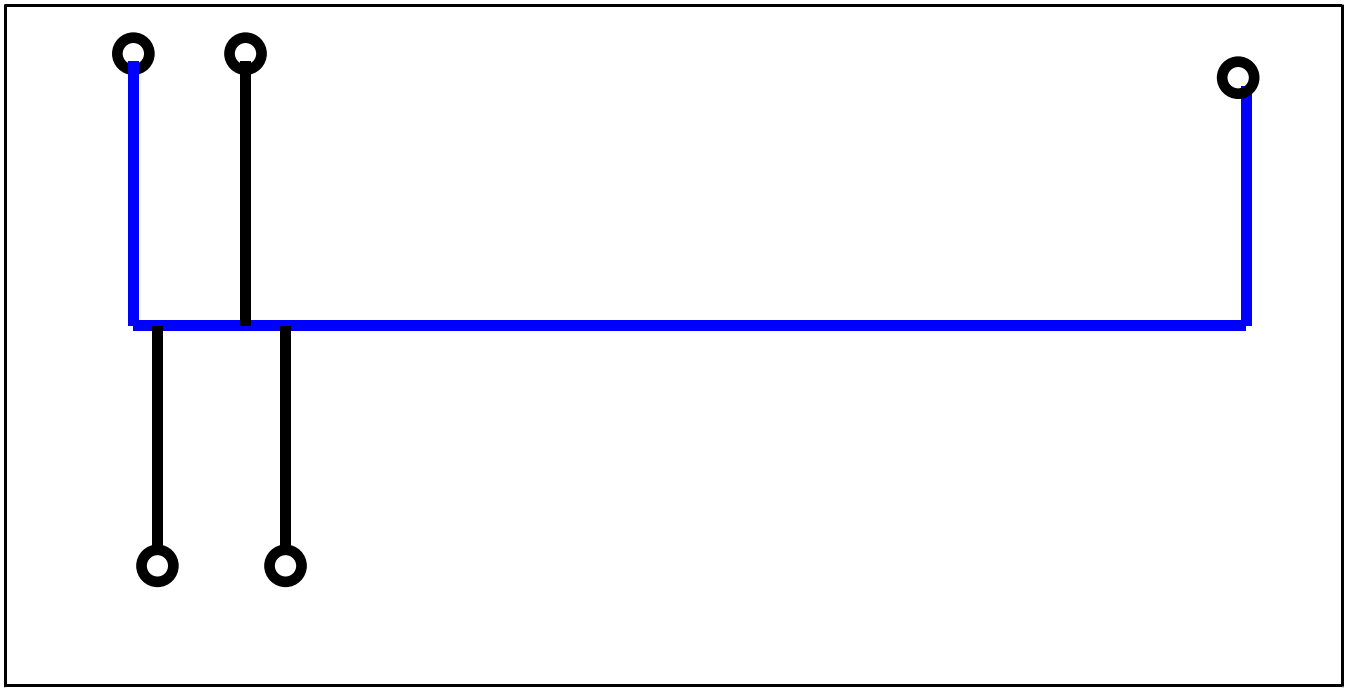
Cepheid GeneXpert

Electrophoresis of Sample Plugs

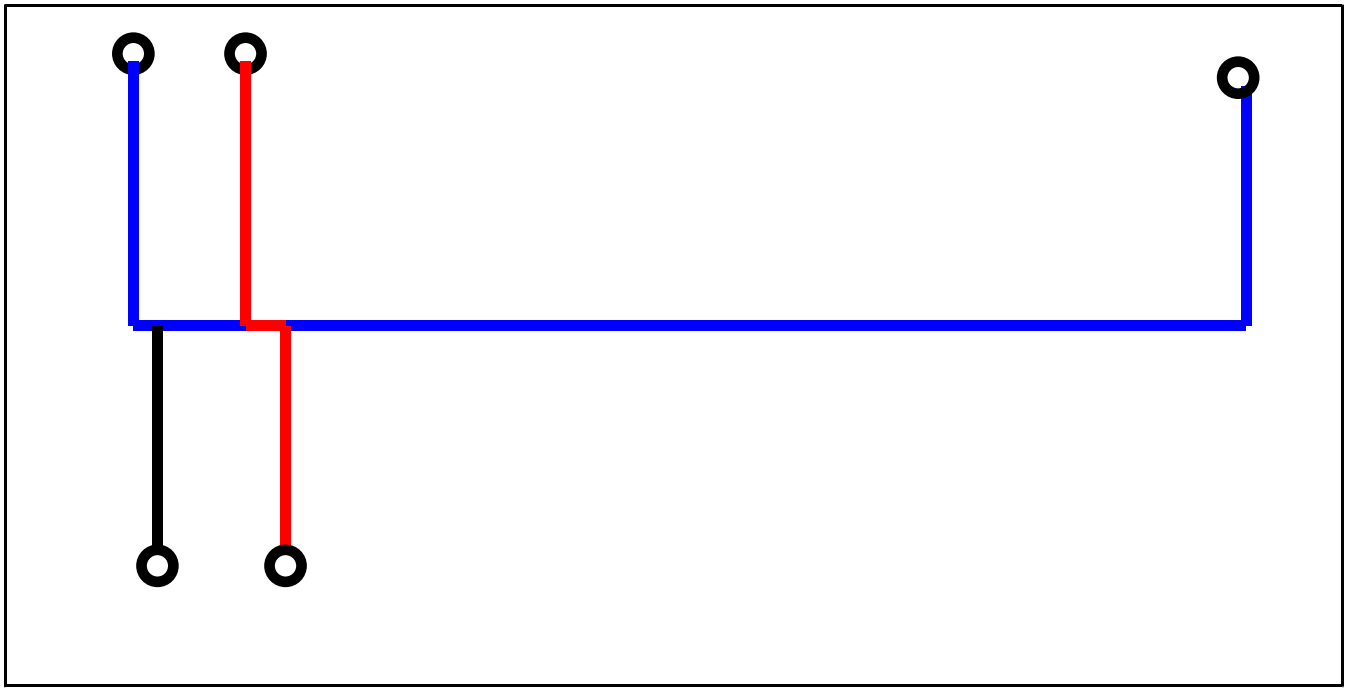
- A sampling system to analyze small and well-controlled quantity of samples using electrophoresis method.
- * 872



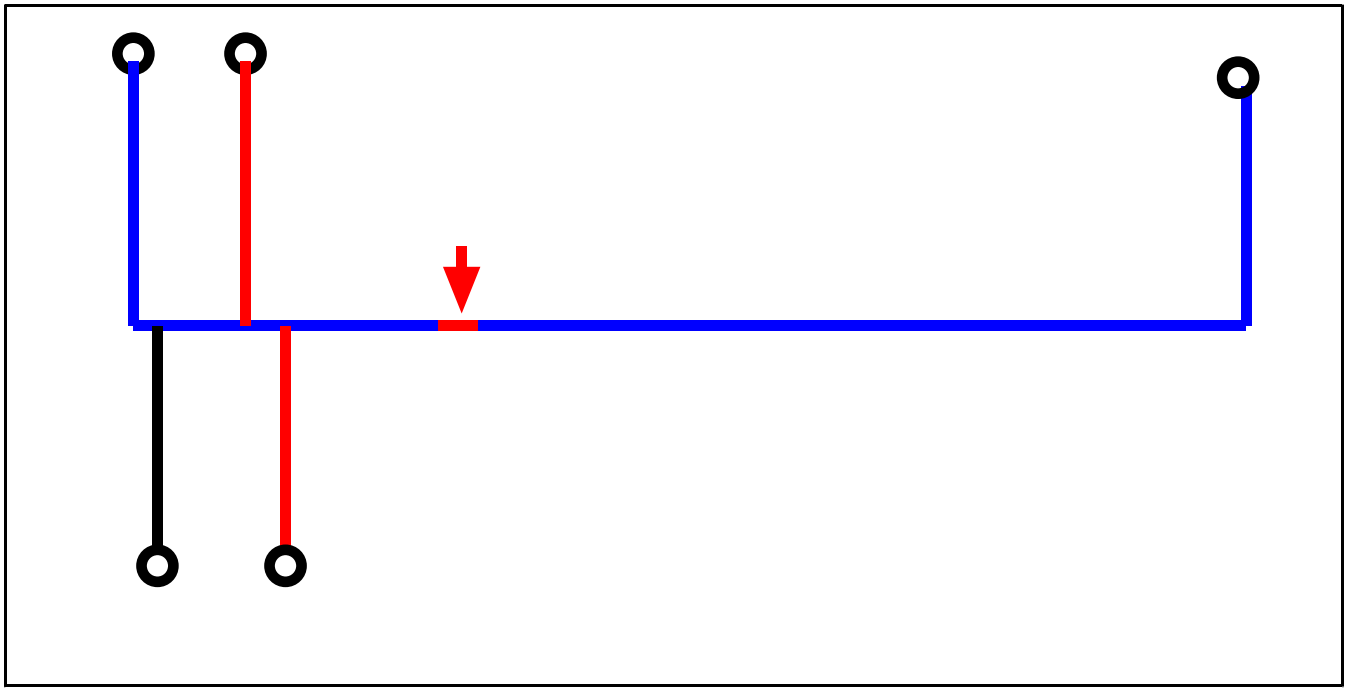
Step 1: Injection of buffer solution



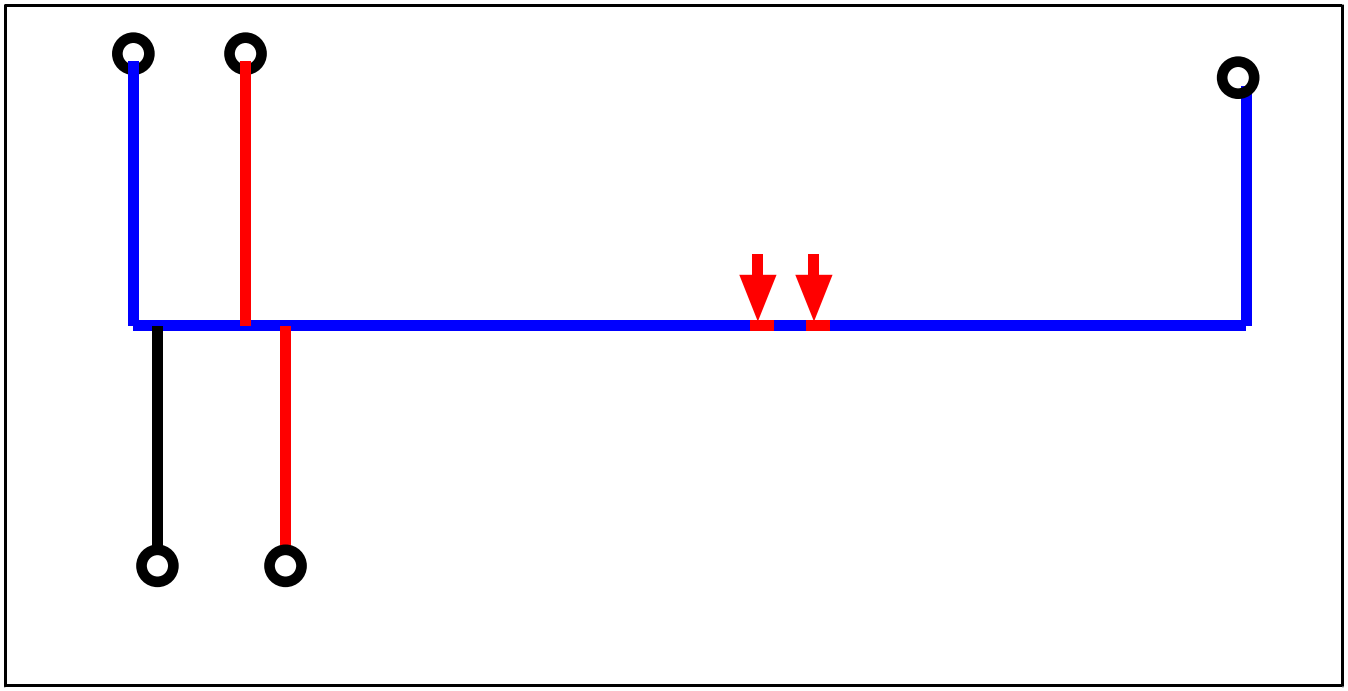
Step 2: Injection of sample solutions



Step 3: Start of electrophoresis



Step 4: EP Separation

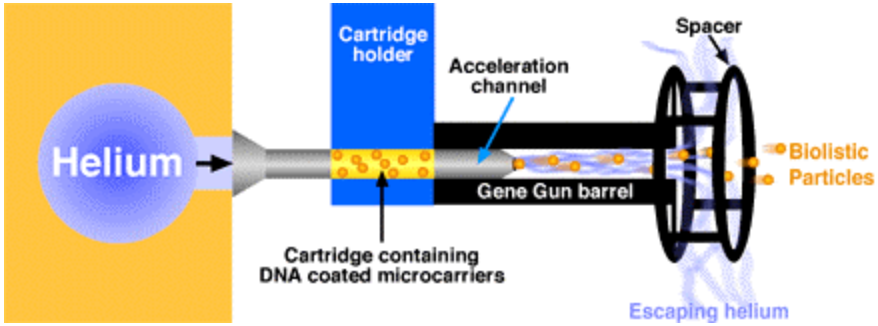


A Complete DNA Sequence Chip - Major Components

- Cell lysing -
  - extraction of DNA from cells by enzymatic dissolution of cell wall
- Protein/DNA separation
  - purification of DNA using electrophoresis flow
- DNA Amplification
  - PCR amplification
- DNA purification
  - separation of amplified DNA and DNA polymerase, a protein used in PCR reaction
- DNA electrophoresis analysis
  - EP separation of DNA
- Optoelectronics detection/mixing of DNA with DNA detection arrays

Why Gene Chips Are Useful?

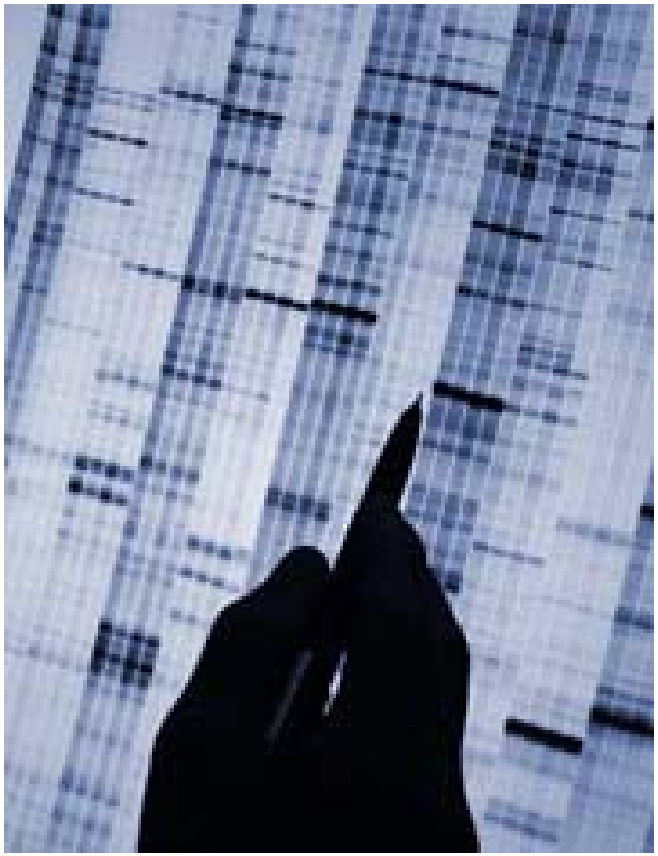
- To live life longer.
  - http://www.lifespangenetics.com/
- To get rid of cancer
  - fast identification of early cancer development
- To cure genetic diseases
  - identification of genetic traits for certain symptoms and treat early
- Advancing medical science
  - "personalized drugs" vs. broad-band drugs.

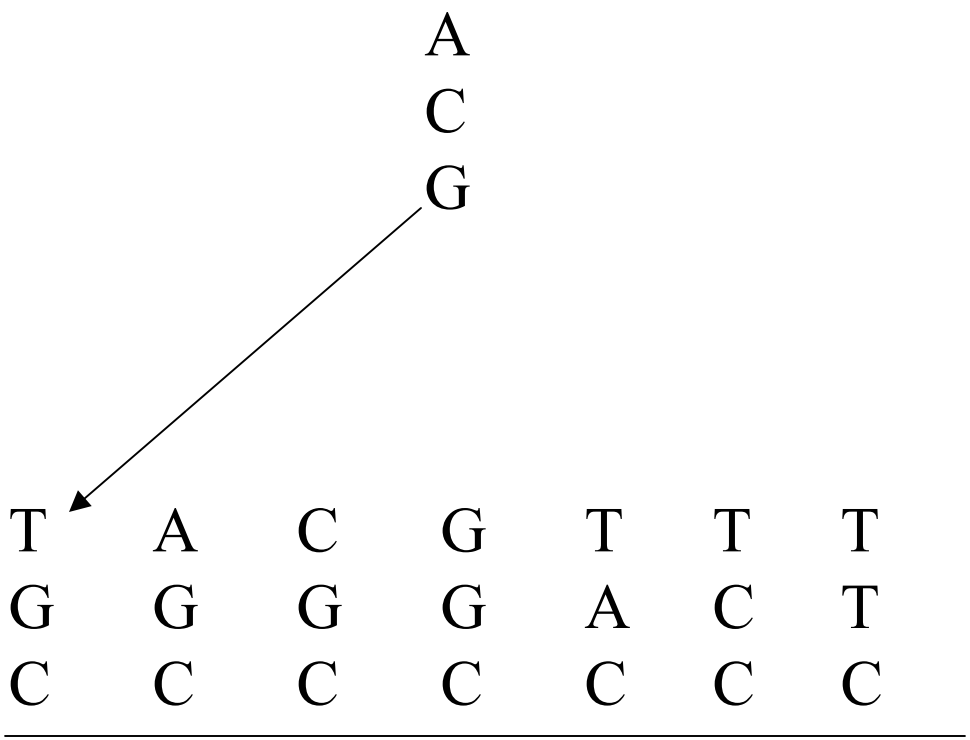


- Visit http://www.affymetrix.com/resources/genetics.html

Methods for DNA Sensing

- DNA electrophoresis
- DNA array - Gene Chips

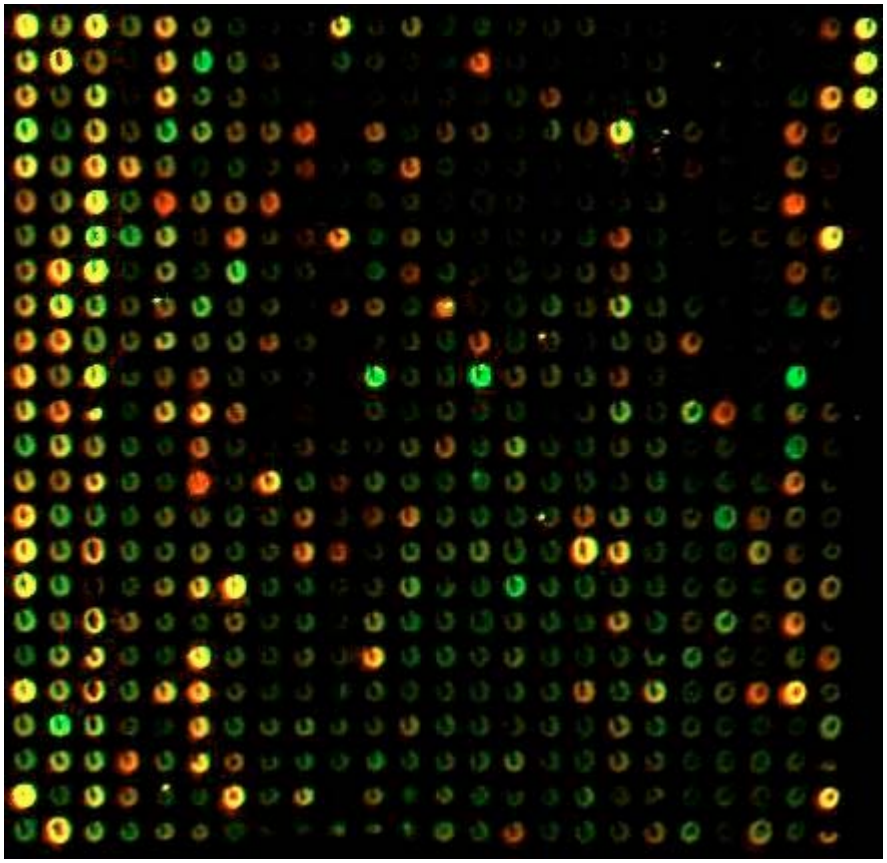


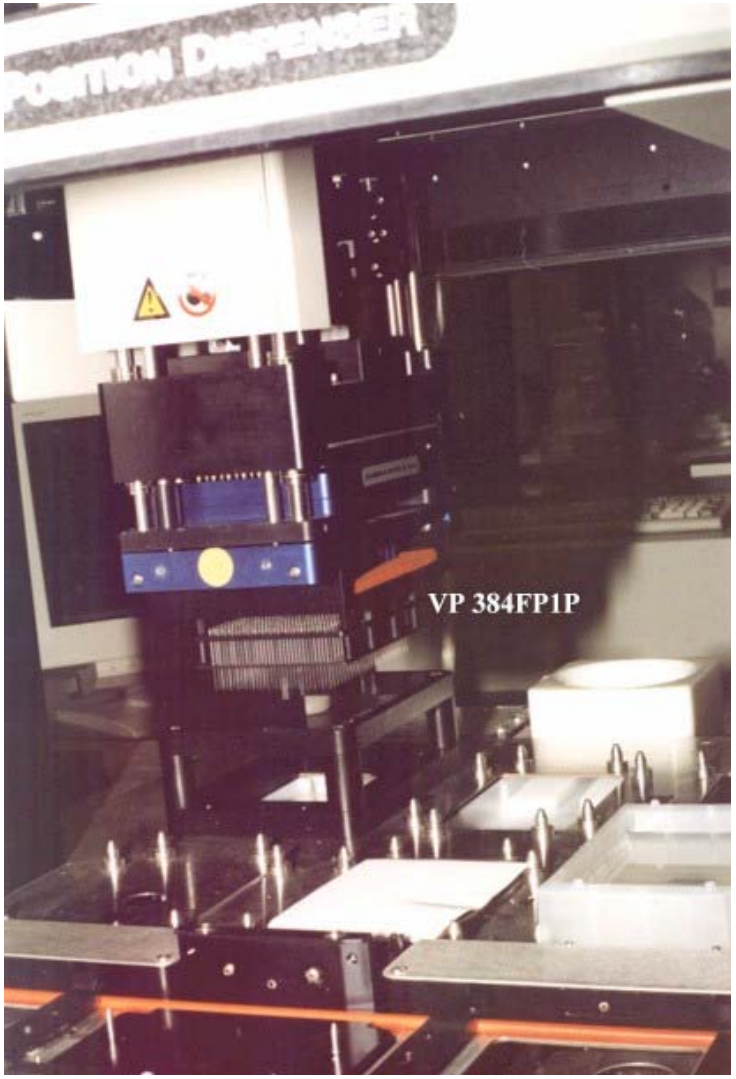


DNA segment with n-base pairs requires 4^n probe DNA arrays

DNA Sensor - Gene-Chip

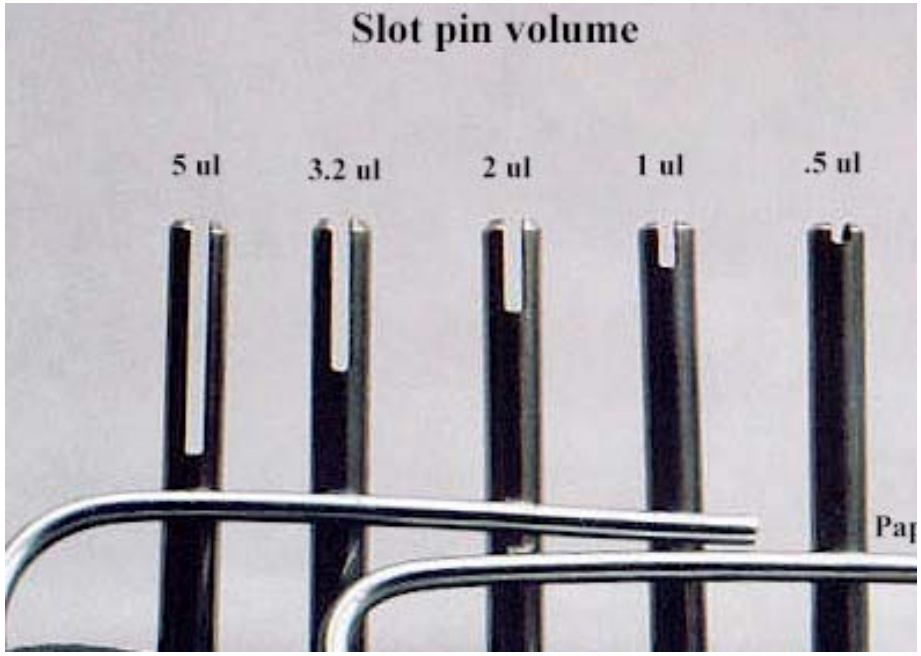
- Visit http://www.gene-chips.com/
- http://www.vp-scientific.com/web/htdocs/new_products_page.htm

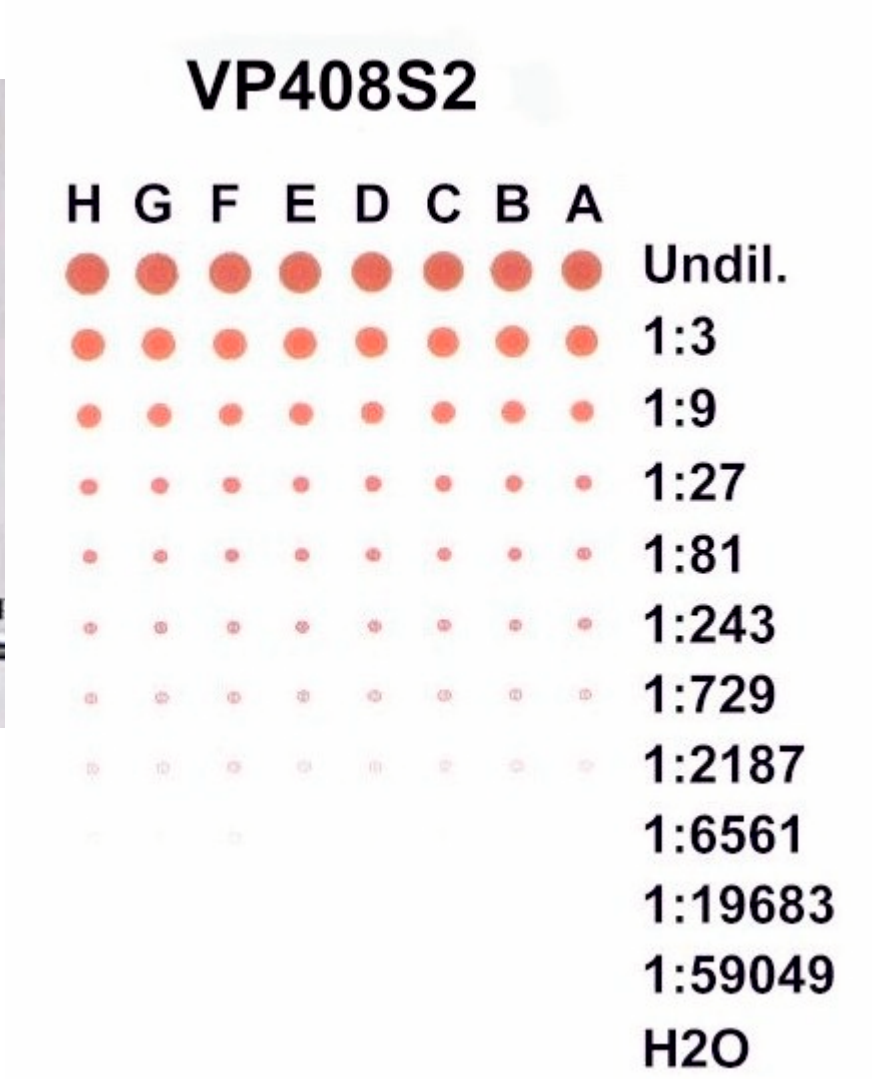



VP 384FP1P

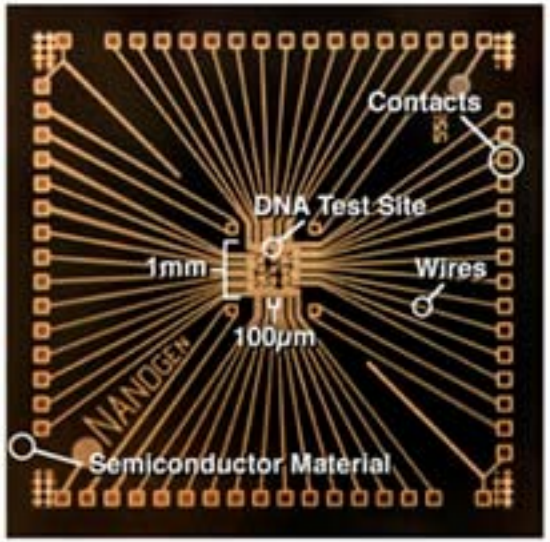

VP 384S2A
VP 381A

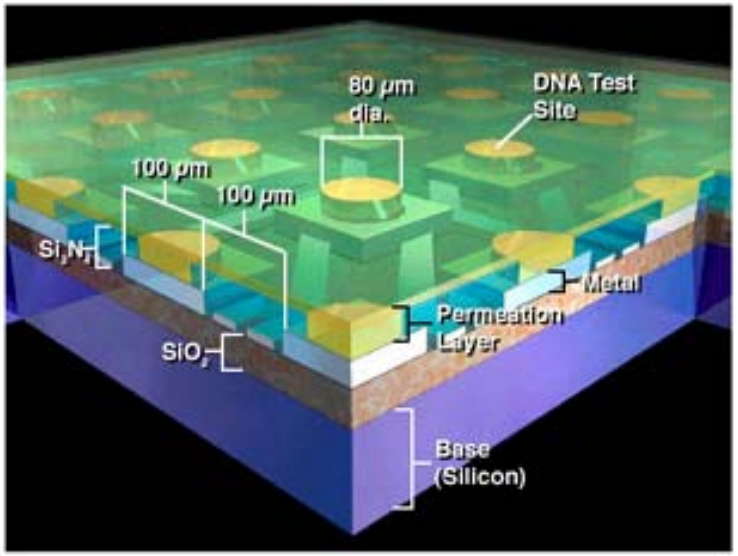

VP 460


Slot pin volume
5 ul
3.2 ul
2 ul
1 ul
.5 ul

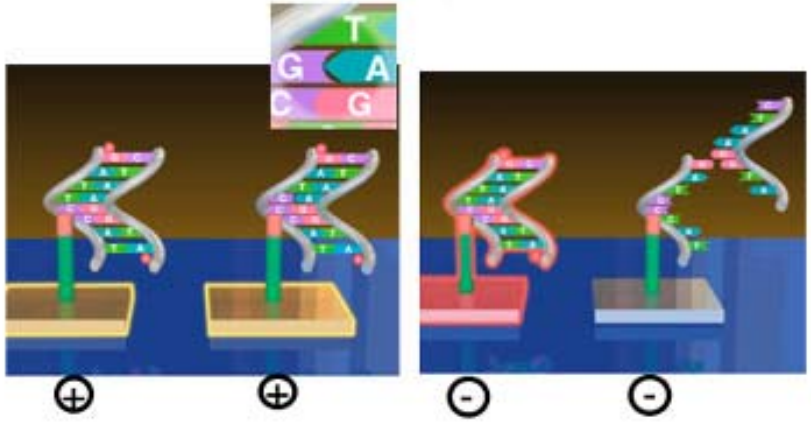

VP408S2
H G F E D C B A
Undil.
1:3
1:9
1:27
1:81
1:243
1:729
1:2187
1:6561
1:19683
1:59049
H2O

Electronics Control of Gene



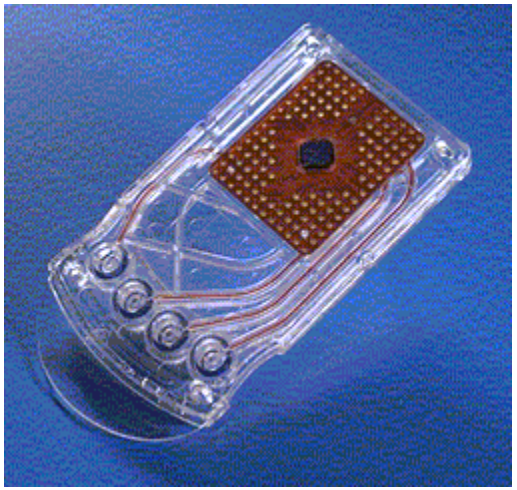


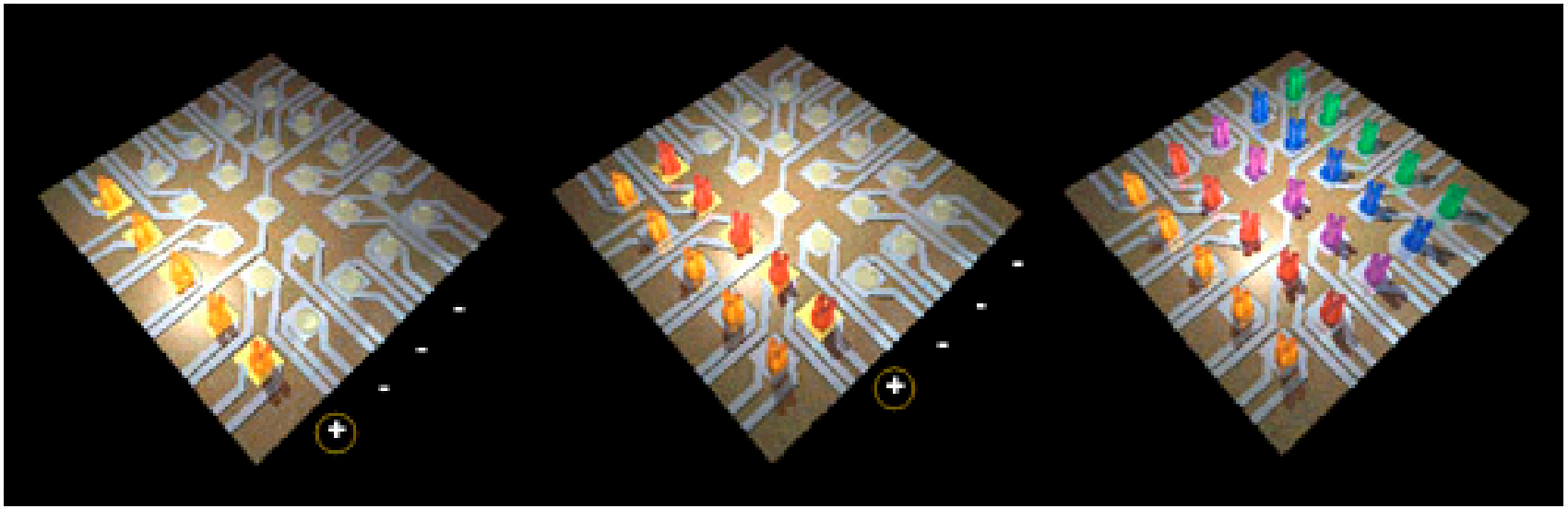
- Discriminates single base pair mismatch



Electronics Addressing

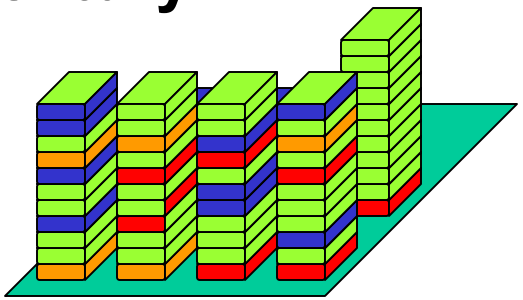
- Electronics assisted hybridization
  - faster speed than passive
- Serial probe DNA capture
- Electronics stringency control
  - removes unbound and unspecified DNA

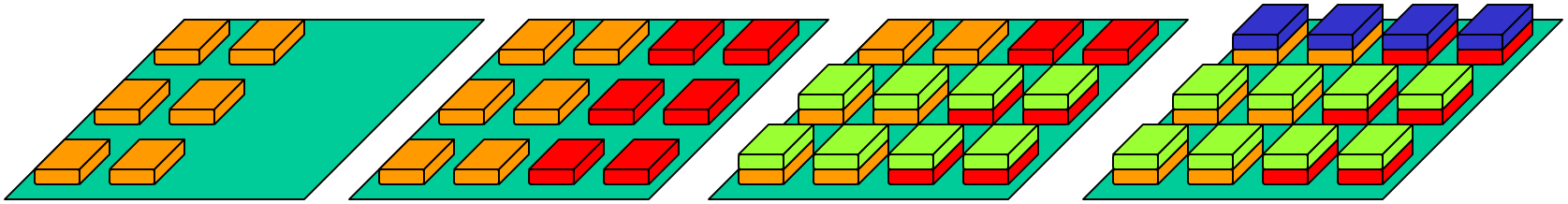




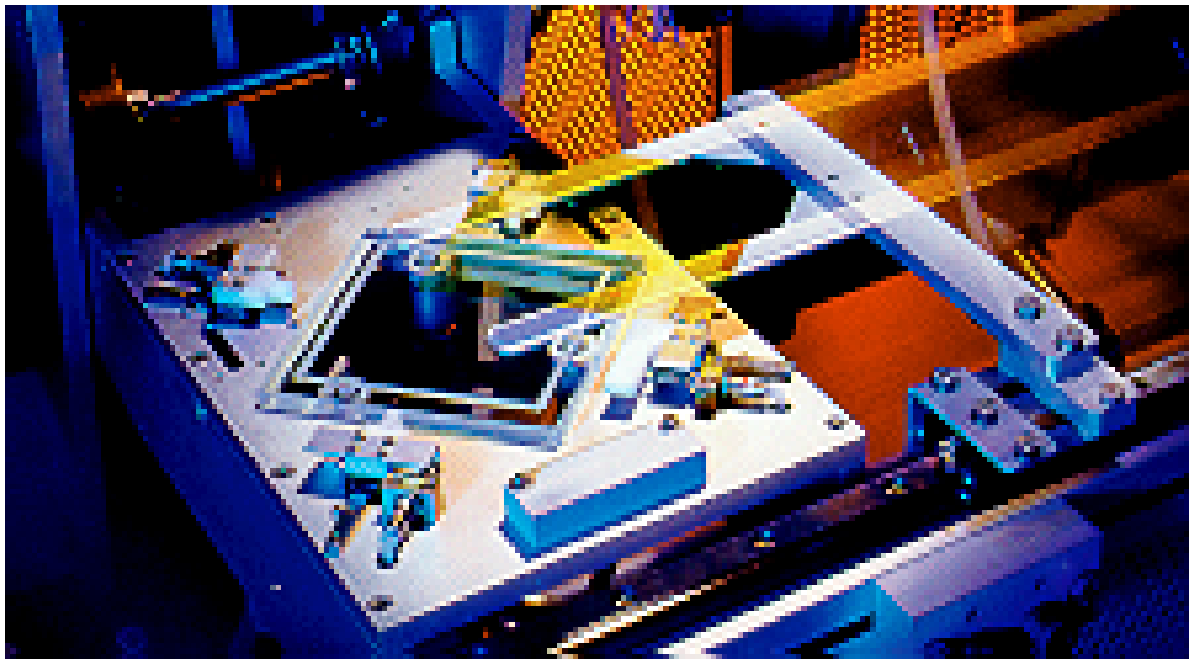
Gene.COM - Intel of the next Century?

- Gene sequence identification
- Detection of polymorphisms (variation)



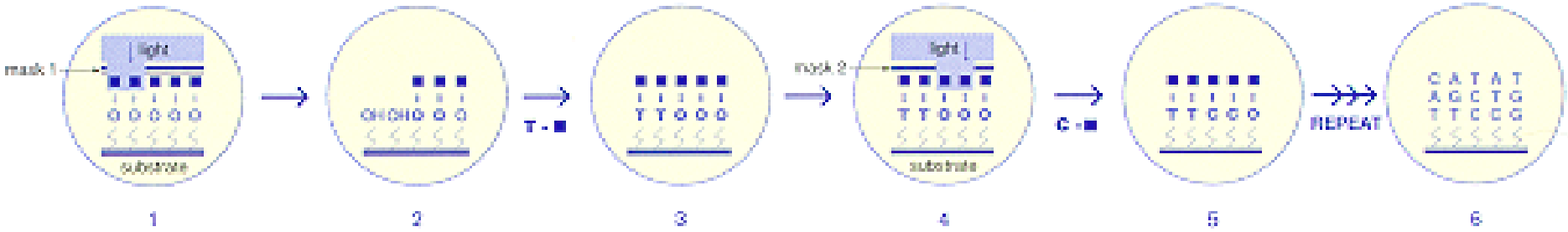


Affymetrics Gene Chip Fabrication



http://www.affymetrix.com/

http://www.affymetrix.com/technology/tech_probe.html



The Synthesis Process

1. A photo-protected glass substrate is selectively illuminated by

light passing through a photolithographic mask.

2. Deprotected areas are activated.

3. With nucleoside incubation, chemical coupling occurs at activated positions.

4. A new mask pattern is applied.

5. The coupling step is repeated.

6. This process is repeated until the desired set of probes is obtained.

Conclusions

- Applications
  - Importance of microfluid analysis systems for biomedical applications, microelectronics, and neuron physiological studies
- Fabrication techniques
  - various flow channel fabrication techniques
  - more on micro pumps, valves and mixers can be found in text book.
- Chemical analysis systems examples.