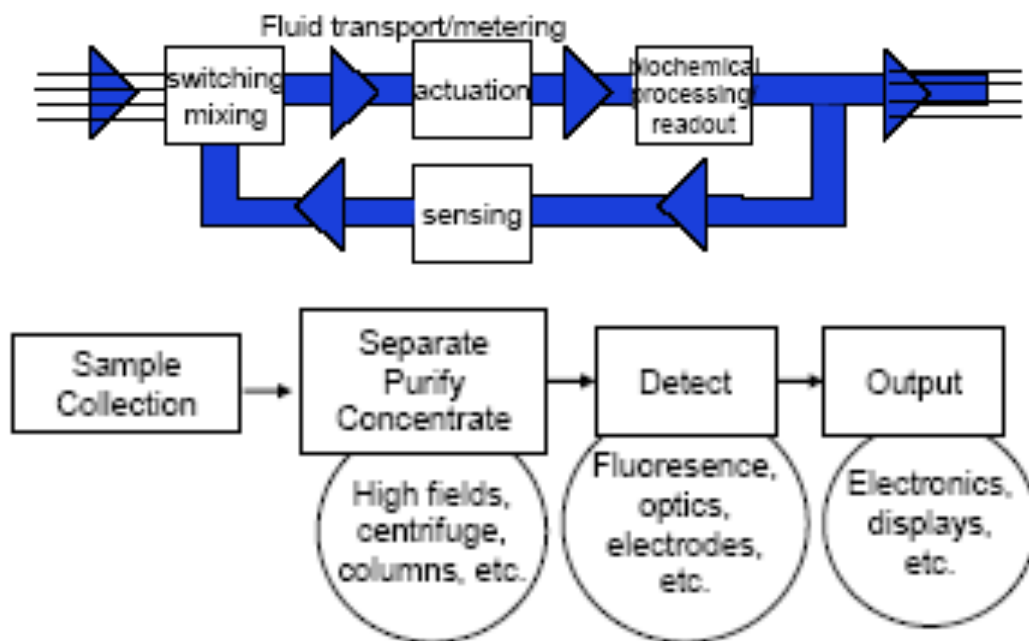


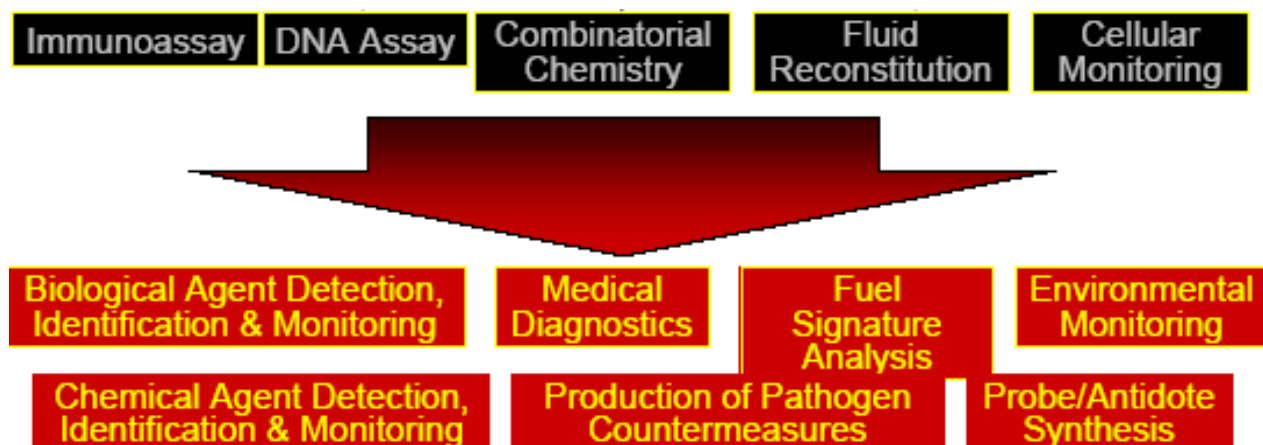
## Lecture 4 Fabrication pathways to micro/nano scale systems

### ⇒ The Potential for the Integration of Detection, Diagnostics, and Treatment in One Microsystem [1]

Totally-integrated bio-fluidic chip technologies capable of on-chip selfcalibration, reconfiguration, and local feedback control of physical/chemical parameters



### ⇒ Ultimate Goal for $\mu$ TAS: A single programmable machine that performs 100s of fluid-based process sequences for Biological Analysis & Synthesis [1]



## ⇒ Microfabrication of Lab-on-a-Chip [1]

- **Microfabrication tools: from the IC to MEMS :**
  1. most microfabrication processes came out of the IC fabrication industry, however, there are different spins to them to achieve physical shapes and mechanical properties
- **Baseline Technologies:**
  1. surface micromachining -polysilicon and other materials, baselines derived from surface  $\mu$ machining
  2. bulk silicon micromachining bonding processes - bond and etch back, packaging, fluidics
  3. deep reactive ion etching processes: HEXSIL, fusion bond
  4. high aspect ratio (HAR) processes: LIGA, LIGA-like, new photoresist technologies, laser machining, polymer solidification, porous silicon for HAR, grey-tone lithography for 3-D structure, 3-D structuring of glass
  5. packaging of MEMS
  6. Polymer MEMS
- **Generally speaking, micro fabrication is a top-down process by adding or subtracting precise amounts of material to form structures. The technologies consist of the following:**

### 1. General Microfabrication Processes/Tools

- Photolithography
- Thin film deposition
- Wet/Dry etching
- Analytical/testing equipment

### 2. Packaging issues - bonding, wire bonding (feedthroughs), dicing

- Bonding - Anodic bonding, fusion bonding, eutectic bonding, epoxy/polymeric bonding
- Packaging examples.

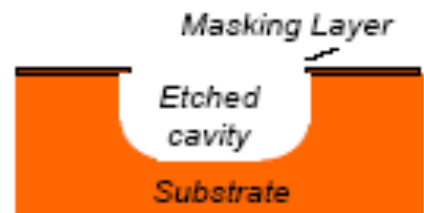
### 3. Process Design General Issues:

- Compatibility
  - temperature
  - stress
  - circuitry

- process equipment contamination
- **Alignment**
- **Characterization of Process**
  - Stress-strain measurement
  - Yield strength
  - Elastic modulus
  - Etch stop controls
- **Bulk/Surface Micromachining**

— **Bulk Micromachining**

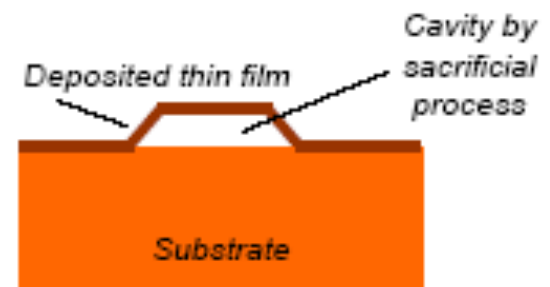
1. Removes “bulk” from the substrate
2. Typically uses materials such as Si, Glass, or polymers



**Bulk machining**

— **Surface Micromachining**

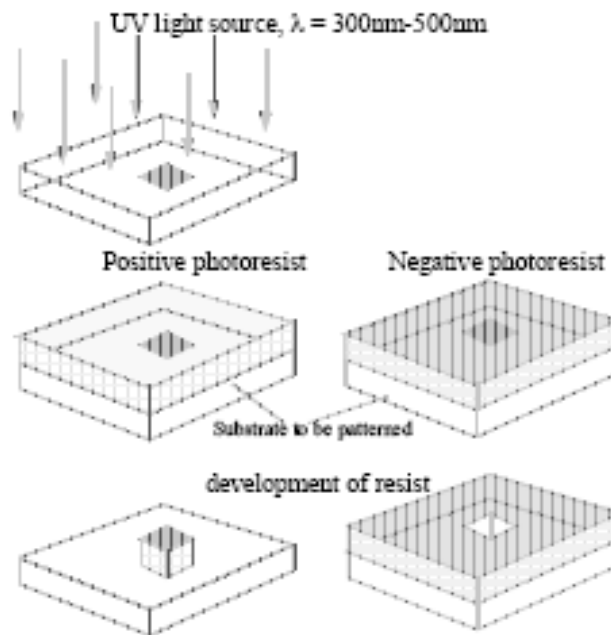
1. Deposited one (or more) layer of thin films ON a substrate
2. Films are subsequently etched / modified to define microstructures
3. Materials – Poly-Si, Silicon Dioxide, Silicon Nitride, Metals, Photoresist etc.



**Surface machining**

- **Photolithography**

The process of transferring a 2-D pattern onto a plane via exposing light sensitive coatings(photoresist, polyimide) through photomasks.



- **Thin film deposition**

**PVD (Physical vapor deposition):** most of metals, some dielectrics

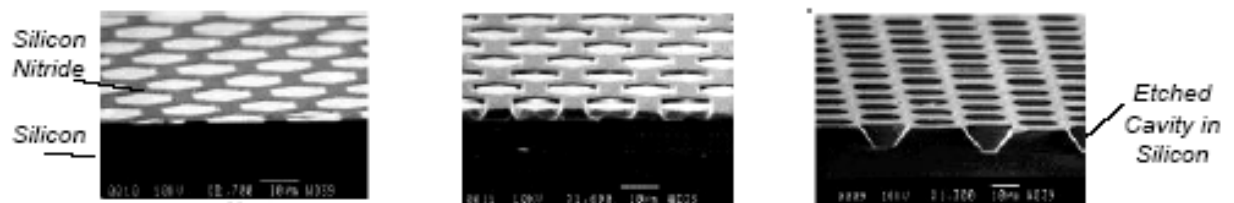
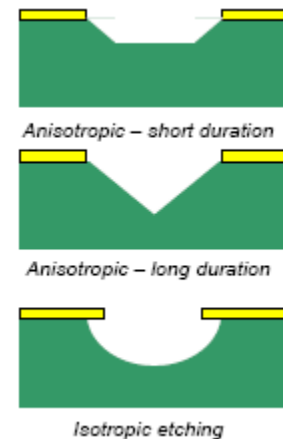
**CVD (Chemical vapor deposition):** dielectrics such as  $\text{SiO}_2$ ,  $\text{Si}_3\text{N}_4$ , polysilicon, etc.

- **Wet/Dry etching**

- **Silicon wet etching:**

- Silicon has a preferential etch direction depending on which plane is exposed to etchant
    - Etch rate is slowest in  $\langle 111 \rangle$  direction

- $\sim 100:1$  etch rate anisotropy compared for  $\langle 100 \rangle$ :  $\langle 111 \rangle$  or  $\langle 110 \rangle$ :  $\langle 111 \rangle$
- Anisotropic etchants
- KOH (pottasium hydroxide), TMAH (tetra-methyl ammonium hydroxide), EDP (ethylene diamine pyracatechol) etc.
- Isotropic etchant
- HNA ( $\text{HF} + \text{HNO}_3 + \text{Acetic Acid}$ )

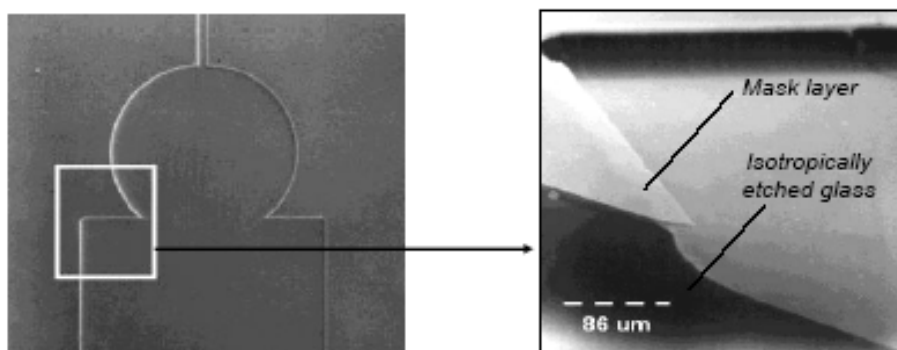


*Etch profile of Silicon As a function of etching interval  
(Etching solution: EDP; masking layer: Silicon Nitride)*

*B. Parviz, JMM 11, 277-282, 2001*

## Glass wet etching

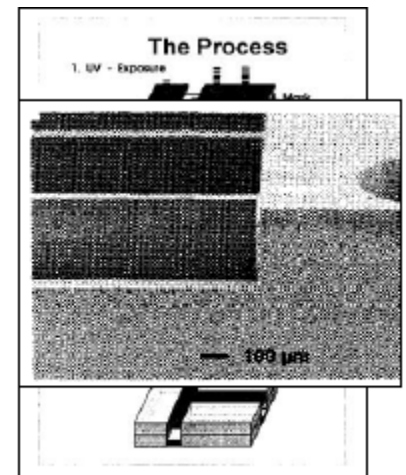
- Most commonly used etchant is HF (Hydrofluoric Acid) or buffered HF
- Gold (with a adhesion promoter layer of Chrome) is most often used as etch mask
- Only isotropic etch profiles can be realized



*C. Lin, JMM 11, 726-732, 2001*

## Photoimagable Glass (Foturan)

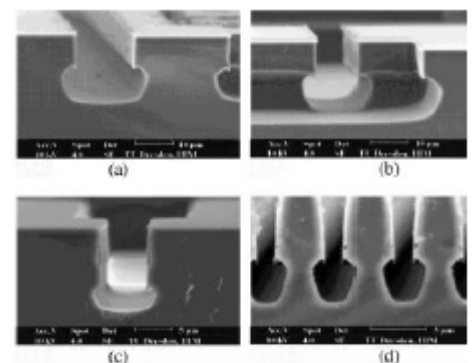
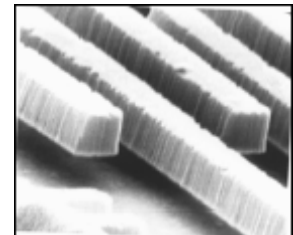
- Anisotropy introduced in GLASS by making the glass photosensitive
- FOTURAN composition: Lithium-Aluminum-Silicates
- Glass is exposed to UV light (310 nm)
- Annealed at high temperature (600°C)
- Heat treatment results in a different composition at the exposed sites
- Subsequent wet etching (with HF) removes only exposed regions while sharply delineating the edges
- Possible to generate vertical profiles of upto 1mm thickness



Microelectronic Engineering 30, 497-504, 1996

## Dry etching

- Most commonly used processes are RIE (reactive ion etching) and DRIE (deep reactive ion etching)
- RIE:  
RF energy is used to excite ions in a gas to an energetic state.  
The energized ions bombard the substrate and etch out exposed regions  
Can generate strong anisotropy (as well as isotropic) profiles



Different etch profiles possible with RIE / DRIE

## Deep Reactive Ion etching

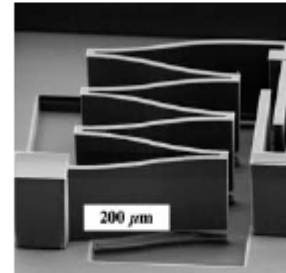
- Can etch silicon with high aspect ratios (>20:1) and deep trenches are possible (500μm)
- Alternate steps of etching and sidewall passivation using

polymer deposition

- Uses an inductively coupled high density plasma (HDP) source and fluorine etching species.
- Neutral fluorine atoms combine with silicon to form volatile silicon-fluorine ( $\text{SiF}_4$ ) complexes.
- Reference: Micromachine Devices vol.2, no.2, Feb.1997.



Source: <http://www.sea.rl.ac.uk/newsea/newpubs/i-speeder/MST2001.pdf>



Klassenn et al., Transducers '95, Stockholm, Sweden

## Other techniques:

Etching related

- **Etch Stops**
- Can use various techniques to completely stop etching at a precisely defined depth. Useful for creating precisely defined membranes in Silicon
- **Porus Silicon Formation**
- Under applied voltage and very strongly oxidizing agent in solution, Silicon will not etch uniformly but form pores

Lithography related

- **LIGA**
- Used for creating very high aspect ratio microstructures. Uses PMMA as photoresist exposed to high energy radiation for direct patterning
- **UV-LIGA**
- Avoids use of PMMA as resist, but can still deliver relatively high aspect ratio structures

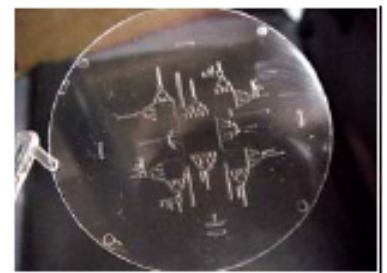
- **Polymer Microfabrication**

### **Benefits gained from polymer for $\mu$ TAS fabrication**

- Plastics offer a wide range of surface properties that can be tailored to meet specific biocompatibility requirements.
- Plastic substrates offer (usually) better qualities in terms of mechanical bulk strength and optical properties.
- Can be produced very inexpensively using processes such as injection molding / hot embossing.
- Rapid turn-around time.
- Ideally suited for disposable biochip applications.



**Installed Injection Mold Machine at UC**



**Injection molded plastic wafer**

### **Classes of Polymers**

#### **Synthetic Polymers**

1. Thermoplastics
  - Divide into crystalline or non-crystalline
  - Linear or branched
  - Melt (PS, PE)
2. Elastomers (rubbers)
  - Silicone, lightly cross-linked and soft
  - Does not melt after crosslinking
3. Thermoset
  - Epoxy, heavily cross-linked and rigid
  - Degrade rather than melt

#### **Natural Polymers**

1. Proteins
  - Polypeptide, collagen
  - Silk, wool



2. Nucleic acids
  - DNA, RNA
3. Polysaccharides
  - Cellulose, starch

### Considerations of Polymers in bioMEMS

- Biocompatibility
- Optical properties (visible and UV)
- Physical properties
- High-volume manufacture
- Bonding
- Cost

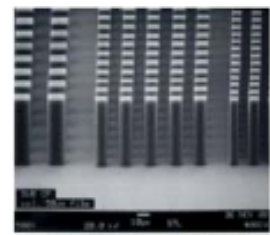
### Candidate Materials

- Polyacrylates
- Polycarbonates
- Polycyclic olefins (POC)
- Polymethylmethacrylate (PMMA)
- Polyimides (PI)
- Polyurethanes (PU)

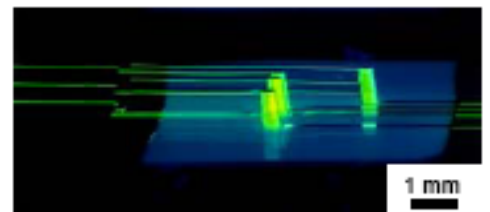
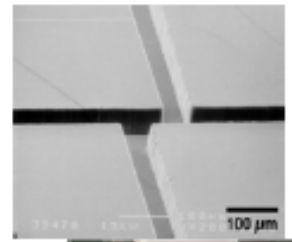
### Fabrication Processes

1. Design
2. Master fabrication
3. Replication against master
4. Sealing/bonding
5. Completed polymer
6. microfluidic device

SU-8 mold

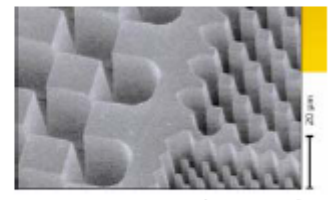


From MicroChem



## Fabrication of Master Mold

- SU-8, thick photoresist
- Si and Glass micromachining
- Electroplating
- Precision machining



From Steag Microparts

## Si Master molds by RIE

## Prototyping of Polymer Devices

1. Elastomer casting (Fluidigm, Surface Logix)
2. Injection molding
3. Compression molding/Hot embossing
4. Laser ablation (Micronics)
  - Heat tool and polymer resin beads above  $T_g$
  - Hot isostatic press
  - Holes for inlets and reservoirs
  - Seal with pressure sensitive tape, ultrasonic welding, thermal bonding, and plasma bonding

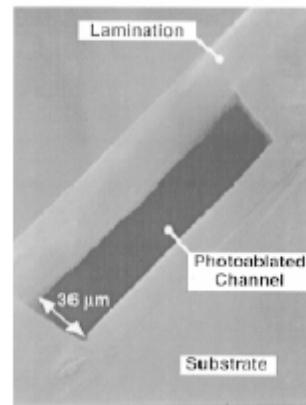
## Molding technology comparison:

Process	Materials	Tool cost	Cycle time	Geometries	Minimum Dimensions Aspect ratio
Hot embossing	Thermoplastic Thermoset	Low- medium	Medium-long (3-10 min)	Planar, wafers and plates	nm 50-small area 5-wafer scale
Injection molding	Thermoplastic Thermoset	High	Short-medium (0.3-3 min)	Bulk, spherical	Some 10 $\mu\text{m}$ , 50- small area 5- larger area
casting	Elastomers epoxy	low	Long (min-hours)	Planar	nm, about 1

- **Chip Connections**

- Lamination
- Gluing
- Thermal bonding
- Ultrasonic
- Laser

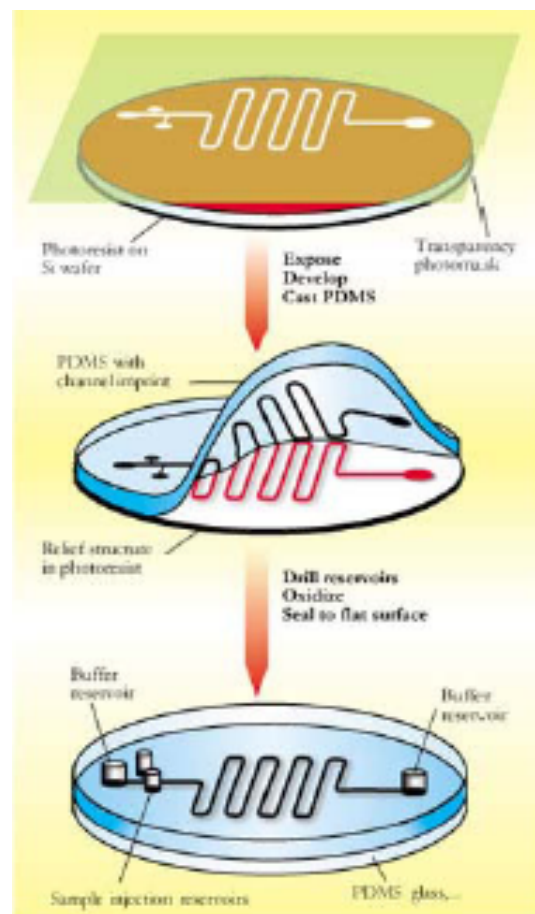
**Laser-ablated microchannel laminated with PET/PE film**



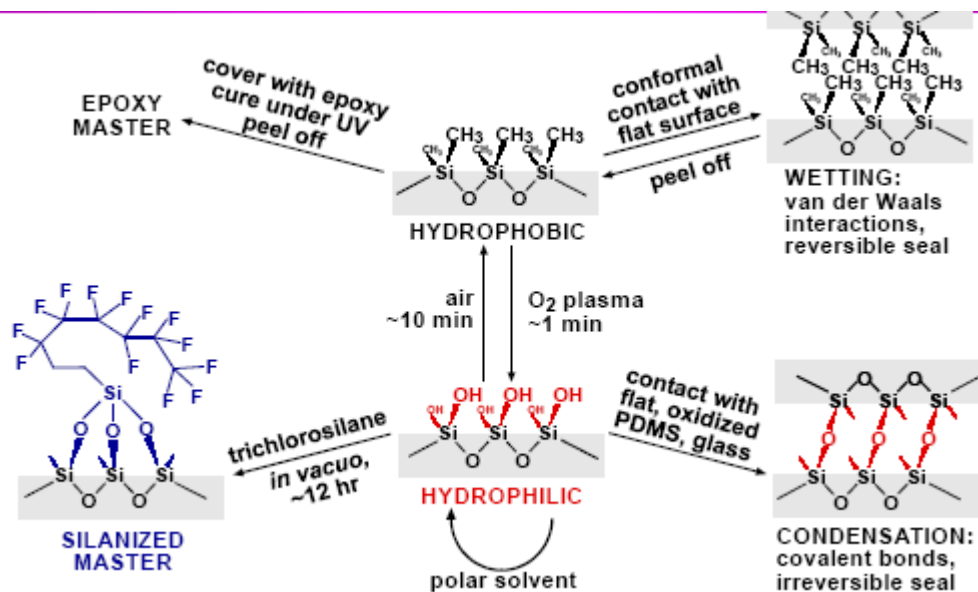
R. M. McCormick et al., *Anal. Chem.*, 1997, 69, 2828-2830.

- **Micro fluidic devices made by PDMS**

**Fabrication process**



## Surface modification for bonding



## Comparison between Si/glass and PDMS fluidic system

	Si/Glass	PDMS
Cost	• expensive	• inexpensive
Fabrication	• micromachining	• molding
Structure	• rigid	• elastomeric
Gas Permeability	• no	• yes
Optical	• opaque (Si)	• transparent
Bonding	• anodic/thermal	• oxidation
Temperature Stability	• good	• limited
Solvent Stability	• good	• limited

## ⇒ Nano fabrication techniques for biomedical applications

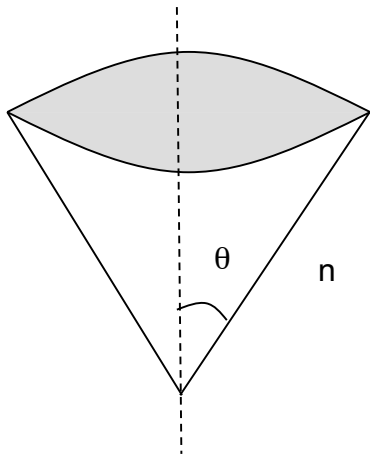
### 1. Top-down process (Nanotech 4)

- Limitation of traditional lithography

- a. Diffraction-limited resolution, Rayleigh criteria:

$$resolution = k_1 \frac{\lambda}{NA}$$

**$k_1$ : constant, near 0.6 (dependent on resist contrast, and processing condition),  $\lambda$ : exposure wave length, NA: numerical aperture of the lens (the sine of convergence semi-angle at the focal point), here is**



$$NA = n \sin \theta = n \left[ \frac{D}{2\sqrt{D^2/4 + f^2}} \right]$$

**N : index of the medium where the lens is working, D: diameter of the lens, f: focal length. NA~<0.63.**

**So for conventional optics, the resolution is approximately equal to  $\lambda$ , which limit UV optical lithography from being useful for nanolithography.**

- b. extensions and limits of optical printing technologies:

**Enhancements (optical proximity correction, phase-shifting masks, innovative off-axis illumination designs, etc.) to the optical step-and-repeat lithography method have been employed to demonstrate further extension of the resolution capability of mercury I-line UV (365 nm) and DUV (248 nm and 193 nm) reduction lithographies.**

### Table 3 p. 190 nanotech

TABLE 3. Estimated Performance of Optical Stepper Lithography Systems

Wavelength	Resolution	Depth of Focus
365 nm	0.5 $\mu\text{m}$	1.5 $\mu\text{m}$
365 nm w/ enhancements	0.35 $\mu\text{m}$	1.5 $\mu\text{m}$
248 nm	0.35 $\mu\text{m}$	1.0 $\mu\text{m}$
248 nm w/ enhancements	0.25 – 0.18 $\mu\text{m}$	1.0 $\mu\text{m}$
193 nm w/ enhancements	0.18 – 0.13 $\mu\text{m}$	0.75 $\mu\text{m}$

- **Throughput limits of serial Tools**

- Scanning focused beam (electron: 1-10 nm, or ion: 8-30 nm) systems: arbitrary patterns can be written and modified using CAD software. The number of pixels which need to be addressed increases linearly with the writing area and as the inverse square of the pixel to pixel spacing.

- Exposure time:

$$t = 4(D_0 A) / \pi d_0^2 J$$

t: exposure time (seconds),  $D_0$ : areal resist sensitivity ( $\text{C}/\text{cm}^2$ ), A: writing area ( $\text{cm}^2$ ),  $d_0$ : beam diameter at focus (cm), J: beam current density.

$$J = \pi \beta \alpha_0^2$$

$\beta$ : source brightness ( $\text{A}/\text{cm}^2$ ),  $\alpha_0$ : convergence angle.

$$\Rightarrow t = 4(D_0 A) / \pi^2 d_0^2 \beta \alpha_0^2$$

- High resolution patterns, needing high beam energy but low beam flux, require exceedingly long time.
- Comparison between FEB (Focused Electron Beam) and FIB (Focused Ion Beam) systems:
  - FEB use electrons and FIB typically uses Ga ion source, electrostatic lens can be used for both.
  - Electrons are low in mass and have a large charge-mass ratio. Ions have opposite effect.

- iii. Electrons below 250 kV do not displace atoms (damage materials), do material mixing, amorphize crystals, act as dopants, and sputter materials, but ions do.
- iv. Stopping range: electrons, 2-50  $\mu\text{m}$  for 5-100 KV. 10 nm for ion beam.
- v. electrons have low angle or “forward scattering which broadens the incident beam as passing through resist. – need proximity correction. Negligible in higher energy (above 50 keV).
- vi. Ions undergo little long range redirection due to scattering.
- vii. Electron beam: 1-10nm, ion beam: 8-30 nm.

Table 1. page 173 nanotech

TABLE 1. Dependence of electron beam writing time for a sample grating on resist sensitivity and electron source type.

System	Source	Resist	Sensitivity (nC / cm)	Current (nA)	Grating Rate (mm <sup>2</sup> /hr)
JBX5DII	$CeB_6$	PMMA	4.5	0.25	0.42
JBX5DII	$CeB_6$	ZEP320	0.7	0.25	2.75
JBX6000FS	Zr/W TFE	PMMA	4.5	10.0	16.8
JBX6000FS	Zr/W TFE	ZEP320	0.7	10.0	110

• Future high throughput lithography alternative

Mask types for nanolithography:

Membrane Supported Transmission Masks:

(for X-ray, or electron projection)

Fig. 10 pp185

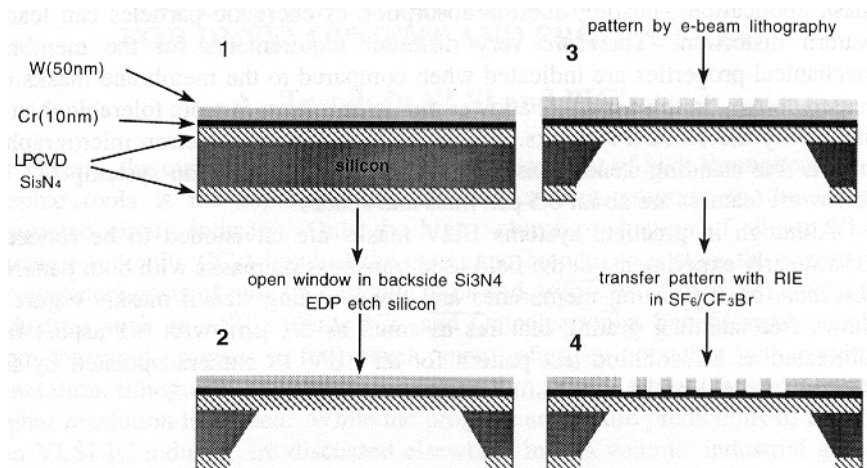


FIGURE 10. Process Steps used to prepare SCALPEL transmission masks[43].

why, and



**Fig. 11**

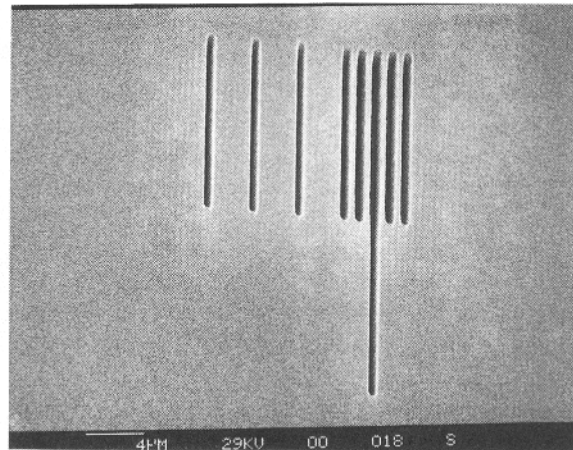


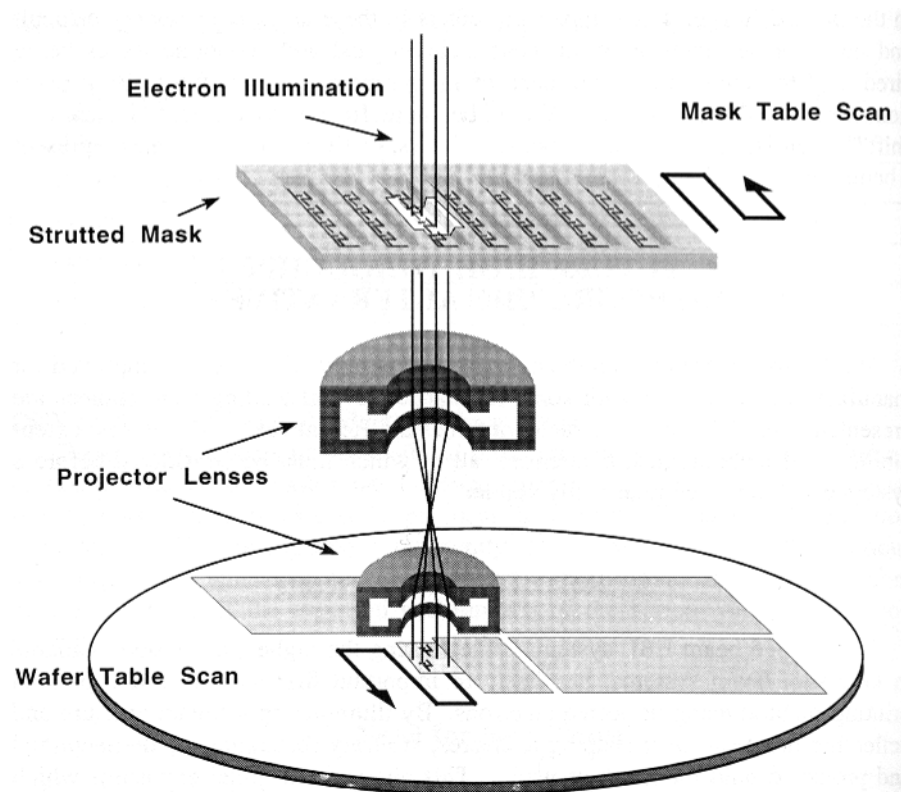
FIGURE 11. Ion beam lithography free standing stencil mask[44].

#### **A. Electrobeam writing**

- a. **Shaped beam EBL system** (compared to **direct-write-on-wafer EBL**): lacking the highest resolution available in Gaussian beam systems, has been an important first step toward a **parallel printing** method using projection electrons.
- b. By illuminating a square aperture (or characters, cells) and deflecting the beam over shaping apertures, arbitrary rectangles are de-magnified and projected onto the mask or wafer. (limit cell printing field of order  $5\text{ }\mu\text{m}$  on a side)---allows multi-pixel exposures which can significantly reduce the writing time and relax the system requirements for high speed deflection.
- c. **drawback:** less general in nature since the shaped apertures are unique to a narrow set of patterning tasks. Problems including the use of absorber masks, large field low-distortion electron optics, and electron-electron interactions.
- d. **SCALPEL:** use of scattering mask (thin membrane with a thin metallic layer 50 nm tungsten) rather than an absorptive one. Scattered electrons are sorted and absorbed by an aperture placed at the back focal plane of the magnetic lens, forming a high contrast image. **Issues:** complex control of the scanning of both the mask and the wafer.



**Fig. 14. pp192.**



**FIGURE 14.** Schematic view of SCALPEL e-beam projection system which uses a scattering mask and a back focal plane aperture to derive image contrast.

## **B. X-ray Proximity Printing (XRPP)**

**a. Simplest and most extensive development method.**

**Collimated X-rays are incident on a membrane mask with a patterned absorber (high aspect ratio structures on a supporting membrane).—controlling residual stress is especially important, thus mask material research become an active topic.**

**b. Mask is brought into contact with wafer to pursue good resolution.**

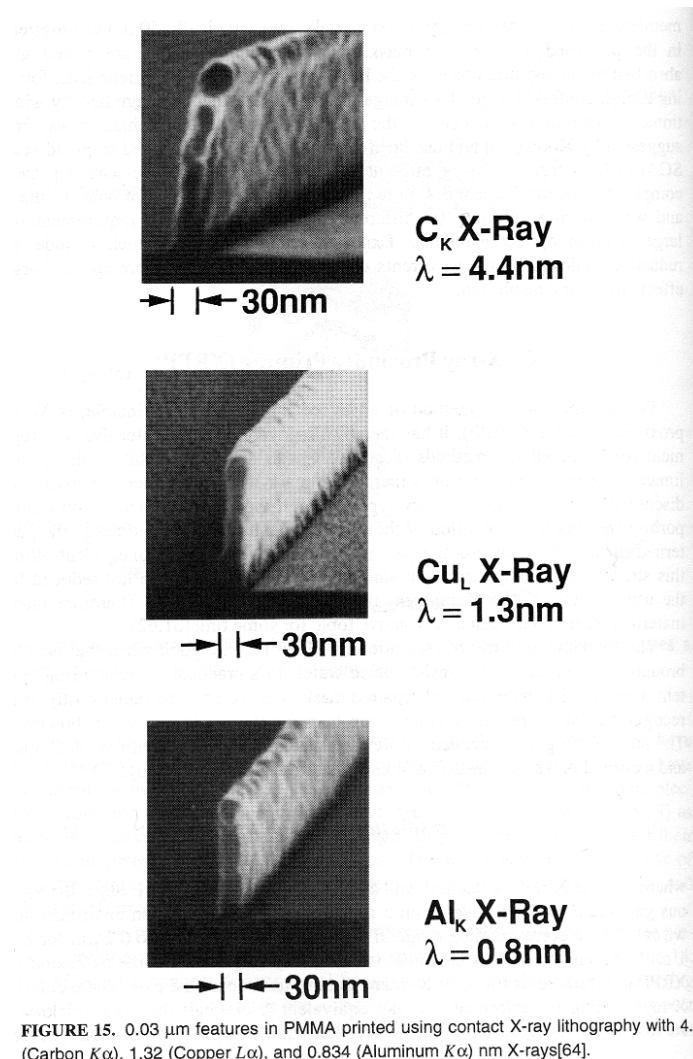
$$resolution = k(\lambda g)^{1/2}$$

**$\lambda$ : X-ray wavelength. k: constant of order. g: gap**

**for gap 5-40  $\mu\text{m}$ , corresponding resolution from 0.07 to 0.2  $\mu\text{m}$  for  $\lambda=1\text{nm}$ . (theoretically g can be as small as one half the resist thickness, but can not be too small to prevent mask damage.)**

- c. Synchrotron sources at research labs have been used as high flux X-ray soruces. IBM developed Helios, the first commercial compact synchrotron.

Fig. 15 pp. 194



### C. Ion Projection Lithography

- ALG-1000 print 20 mm×20mm fields and 3×reduction, 150 keV hydrogen ions for 0.1  $\mu\text{m}$  IC design rules. The use of high voltage and light ions allows reasonable depth penetration.
- Since ions are highly absorbed, the system needs standing stencils as masks. Full filed projection can suffer from distortions from space charge effects.

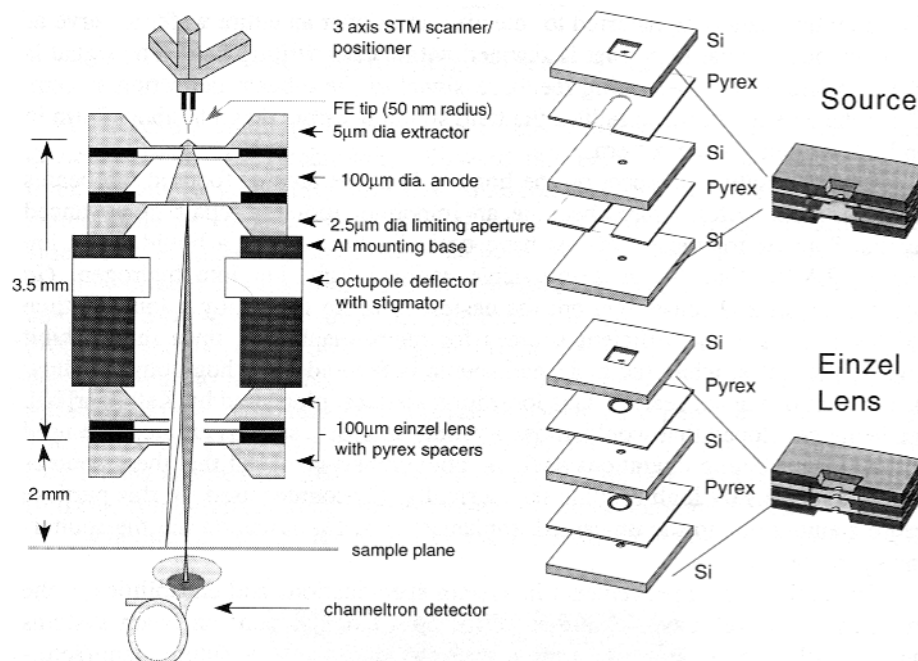
**c. Advantage: lack of long range scattering which is present in e-beam lithography.**

### **D. Extreme Ultraviolet Lithography (EUVL)**

- a. Also refereed as soft X-ray projection lithography, SXPL, most similar in concept to optical step and scan lithography. However, reflective optical systems are required since all materials are too highly absorptive to fashion refractive lenses. Multilayer reflector is required to enhance reflectivities for 13nm~20nm wave length light, resolution about 100 nm (50 nm with reduction).
- b. EUVL can use thick reflective multilayer masks instead of fragile membrane type masks in SCALPEL, IPL, XRPP. Typical masks comprise a patterned absorber or composite absorber atop a multilayer reflector.

### **E. E-beam Micro-column and Tip Array Systems (micro SEM/TEM system, 10 nm resoluton images)**

**Fig. 19 p 200 nanotech**



**FIGURE 19.** Schematic of the SAFE micro-column: a) functional diagram, b) assembly of silicon micro-machined column parts.

### **F. Soft lithography/self assembly [4]**

- a. Definition: Soft lithography, a collective name for techniques based on self-assembly and molding, as a convenient and low-cost approach to micro- and nano-fabrication.
- b. Principle: Soft lithography uses soft, organic materials (e.g., functionalized alkanes and polymeric materials) to generate patterns and structures without the use of light or other high-energy particles.
- c. Comparison between different soft lithography techniques:

Technique	dem. features (nm)	dem. Largest area
<b>1. Microcontact printing (mcp)</b>	100	50 cm <sup>2</sup>
<b>2. Replica molding</b>	30	1 cm <sup>2</sup>
<b>3. Micromaolding in capillary (MIMIC)</b>	1000	1 cm <sup>2</sup>
<b>4. Microtransfer molding (mTM)</b>	70	2 cm <sup>2</sup>

## 1. Self-assembled monolayers and microcontact printing

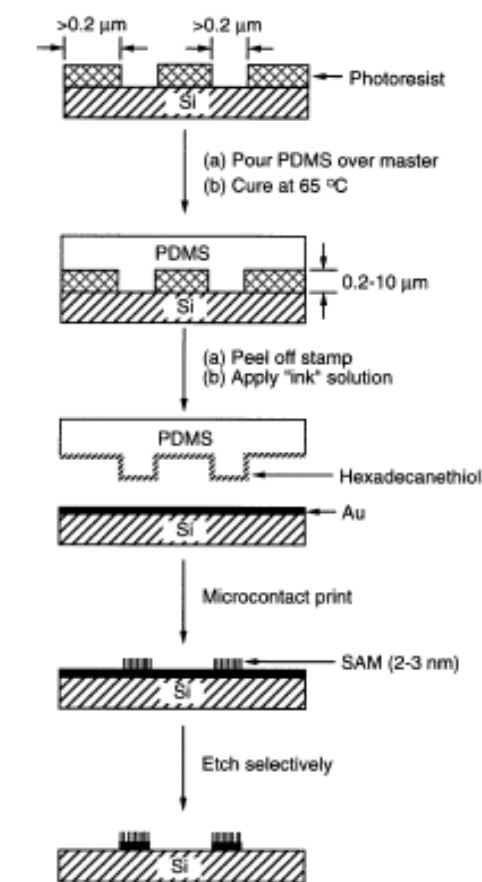


Fig. 1 Schematic illustration of the procedure for mCP. An elastomeric stamp is made by casting a prepolymer of PDMS against a master that is usually made by microlithographic techniques. The stamp is inked with a solution of hexadecanethiol in ethanol, dried in a stream of  $\text{N}_2$ , and then brought into contact with the gold surface. The patterned SAMs can be used as resists in wet chemical etching to transfer patterns to the Au film.

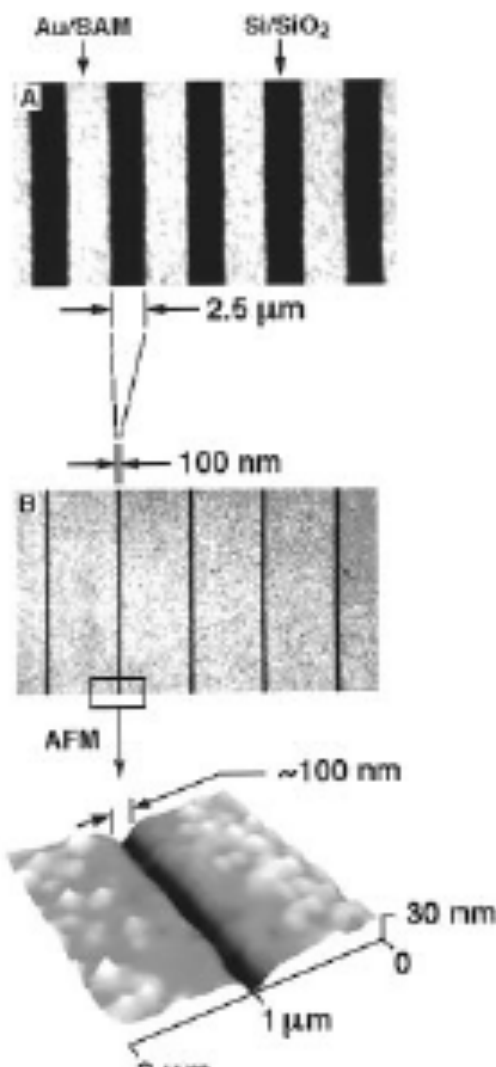


Fig. 2 (A) Scanning electron micrograph (SEM) of an array of  $2.5 \mu\text{m}$  wide lines of Au generated using the standard procedure of mCP, followed by chemical etching in a basic cyanide solution. (B) SEM of a gold pattern that was produced using mCP under water with the same PDMS stamp as in (A). The inked stamp was allowed to remain in contact with the gold surface for ca.  $5 \text{ min}$ .

## 2. Replica molding

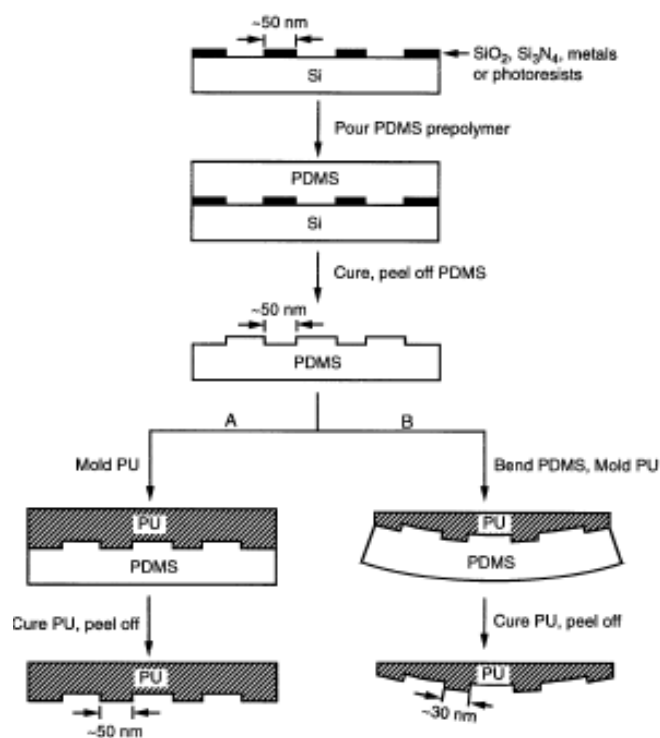
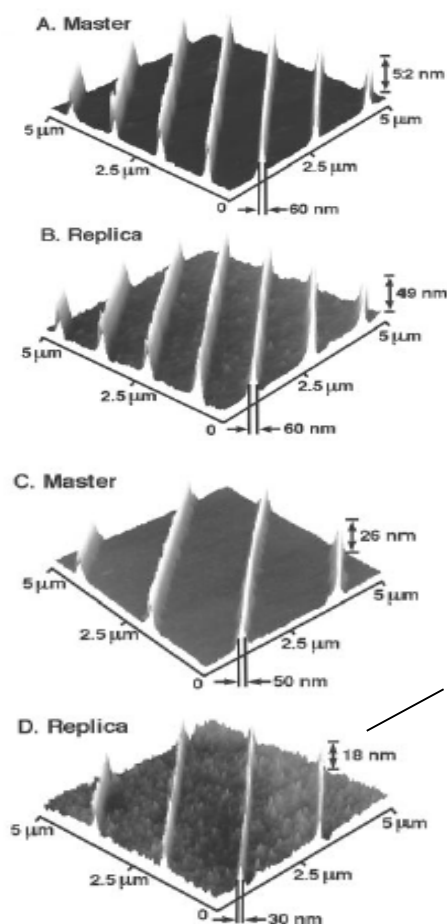


Fig.4 (A, B) AFM images of a master with an array of 60 nm wide lines of Au on Si/SiO<sub>2</sub> and a PU replica generated from the PDMS mold cast from this Au master; (C, D) AFM images of another Au master having an array of 50 nm wide lines and a PU replica generated from a bent PDMS mold cast from this Au master

Fig. 3 Schematic procedure for carrying out replica molding against an elastomeric PDMS mold. The PDMS mold is fabricated by casting against nanometre-sized relief structures fabricated using X-ray lithography or electron-beam writing. The test pattern shown here is an array of ca . **50 nm** lines. Replica molding can also be conducted while the PDMS mold is deformed, for example, by mechanical bending (B). The dimensions of the lines were reduced from ca . 50 nm to ca . **30 nm** in this process while the spacings between the lines increased slightly.



Reduced  
features  
by mold  
bending



### 3. Micromolding in capillaries

Fig.5 Schematic procedure for MIMIC. This technique relies on a conformal contact formed between a support and an elastomeric (PDMS) mold with relief features on its surface to create a network of microchannels. A low-viscosity, liquid prepolymer fills these channels by capillary action. Solidification of the precursor in situ, followed by removal of the PDMS mold, results in the formation of polymeric structures on the surface of the support.

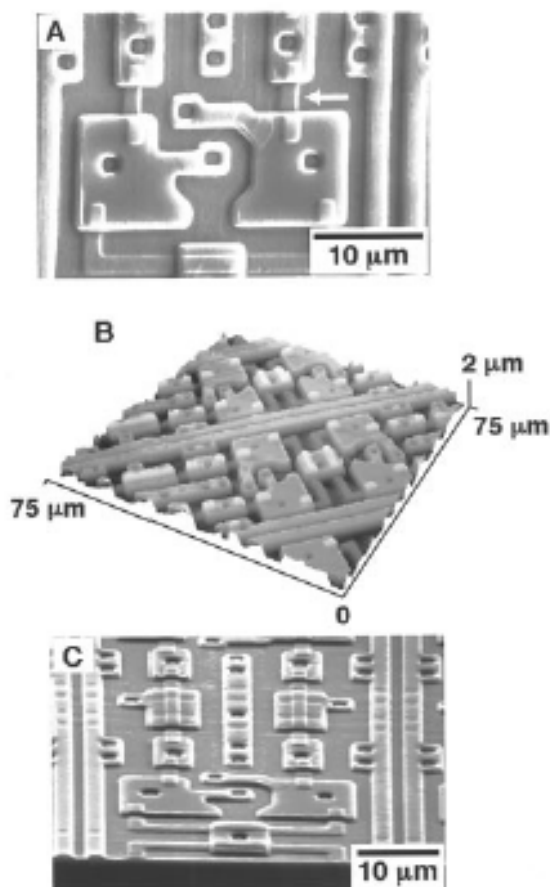
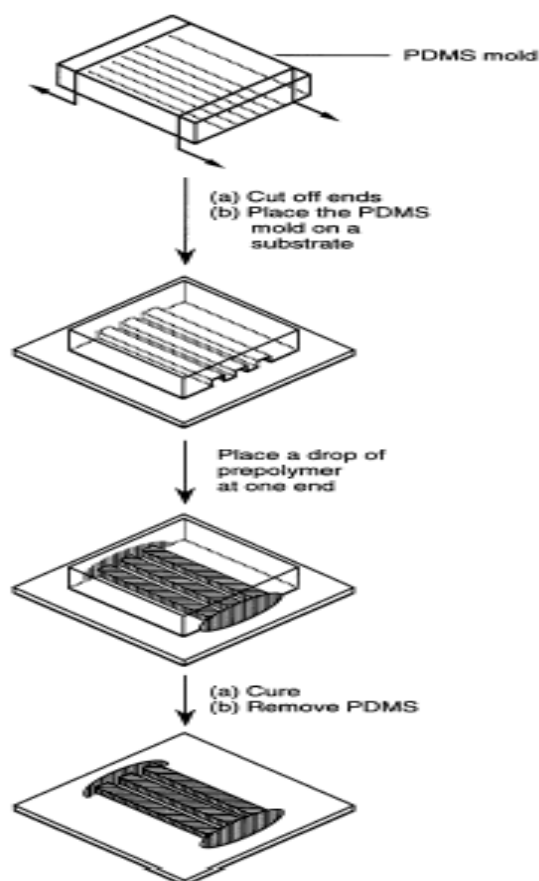


Fig. 6 SEM (A) and AFM (B) images of patterned microstructures of PU on a Si/SiO<sub>2</sub> surface generated using MIMIC. The arrow in (A) indicates a line that is <100 nm in height. (C) A cross-sectional SEM image of the fractured sample.

## 4. Microtransfer molding

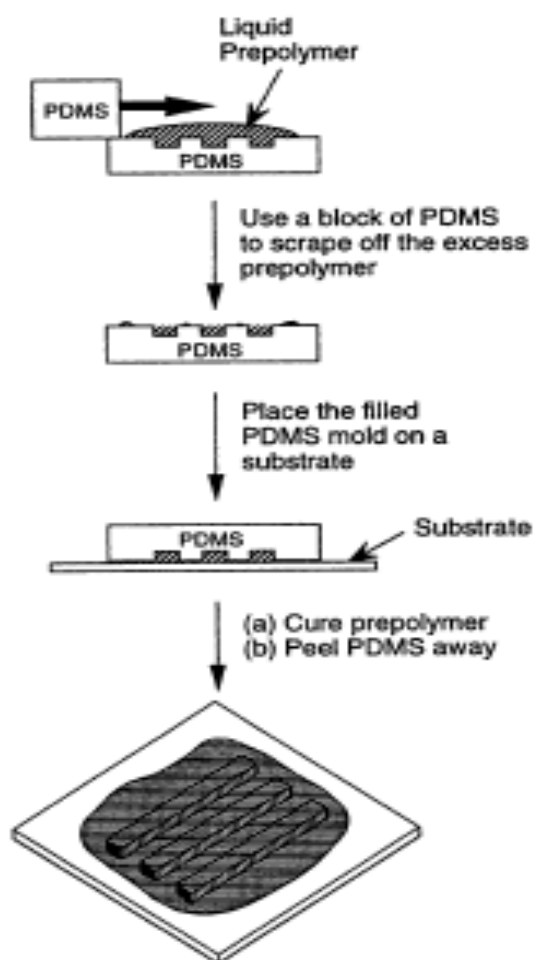
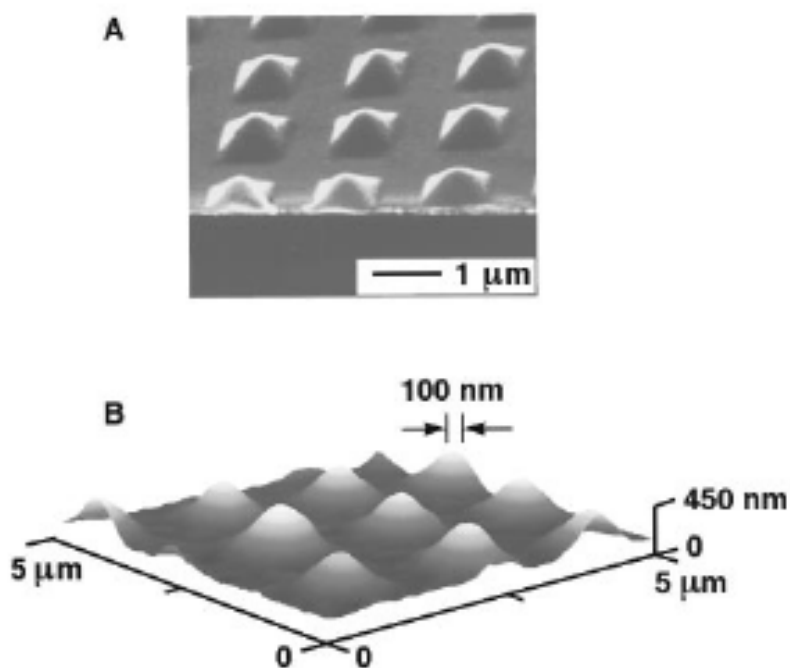


Fig. 7 Schematic diagram for mTM. A drop of prepolymer is applied on the patterned surface of a PDMS mold. The excess prepolymer is scraped away using a piece of flat PDMS, leaving a filled PDMS mold. The filled mold is then brought into contact with a substrate and the prepolymer is allowed to solidify in situ. Patterned microstructures are obtained after the PDMS mold is removed. The process can be repeated on a substrate whose surface has already been patterned with a layer (or layers) of relief structures to build multilayer structures layer by layer.

Fig. 8 SEM (A) and AFM (B) images of an array of sub-mm pyramids of PU. The tip of each pyramid, as shown in (B), is ca. 100 nm across. The original master was fabricated using anisotropic etching of a Si (100) substrate.





**d. Advantages:**

- Cost effective
- Rapid for single layer
- $>30$  nm size possible
- Batch fabrication
- Possible for pattern metals, semiconductors
- and insulating materials
- self assembly may self-heal or defect-reject

**e. Challenges:**

- Density of defects is high in current stage
- Mold deformation
- Lack of tools for registration with nanometer accuracy limits its use in multilayer fabrication

**2. bottom-up process**

**A. Biocatalytical synthesis of polymers of precisely defined structure (nanotech 9)**

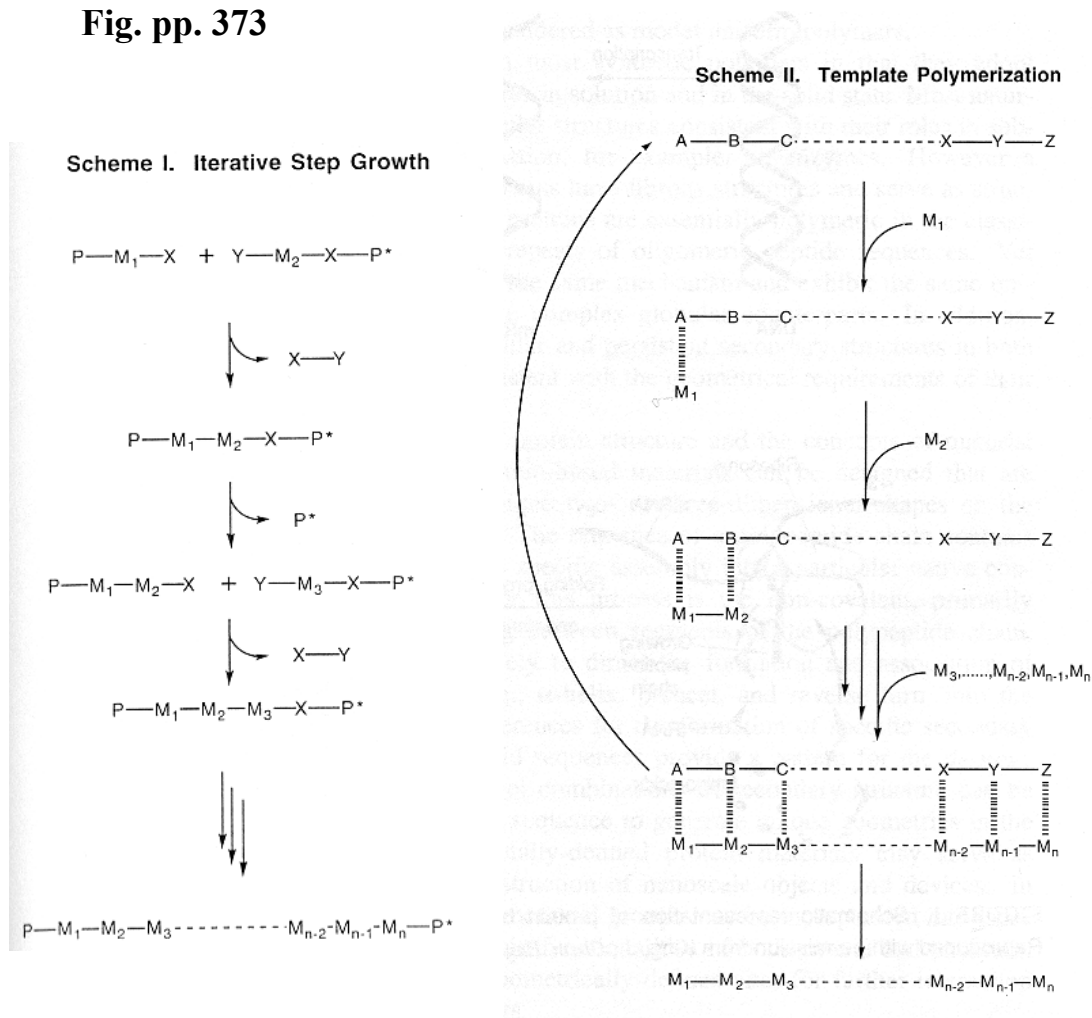
- An intriguing approach to nanoscale fabrication involves the association of individual molecular components into the desired architectures by supramolecular assembly.
- advantages of polymers: ease of synthesis and fabrication, well delineated structure-property correlations, and thermal and mechanical stability.
- four architectural variables: molecular size, composition, sequence, and stereochemistry. Conventional methods of polymer synthesis afford only statistical control of each, and are not pure substances but comprise heterogeneous populations of molecular species.
- Two techniques for polymer synthesis: iterative coupling of selectively activated monomers, or template-directed polymerization.

**Iterative coupling**: stepwise assembly of the desired material via a repetitive sequence of intermolecular coupling and activation steps. Two reactive end-groups are coupled intermolecularly, and one the the remaining end-groups is selectively deprotected.—serial process. (examples: dendritic

## (樹枝狀) macromolecules, Merrifield synthesis of polypeptides)

However, owing to the linear nature of the process, the degree of synthetic difficulty increases geometrically with the length of the sequence. This feature, coupling with the lack of an intrinsic proof-reading mechanism, limits this process to the synthesis of moderate length polymers (~60 residues for a polypeptide sequence)

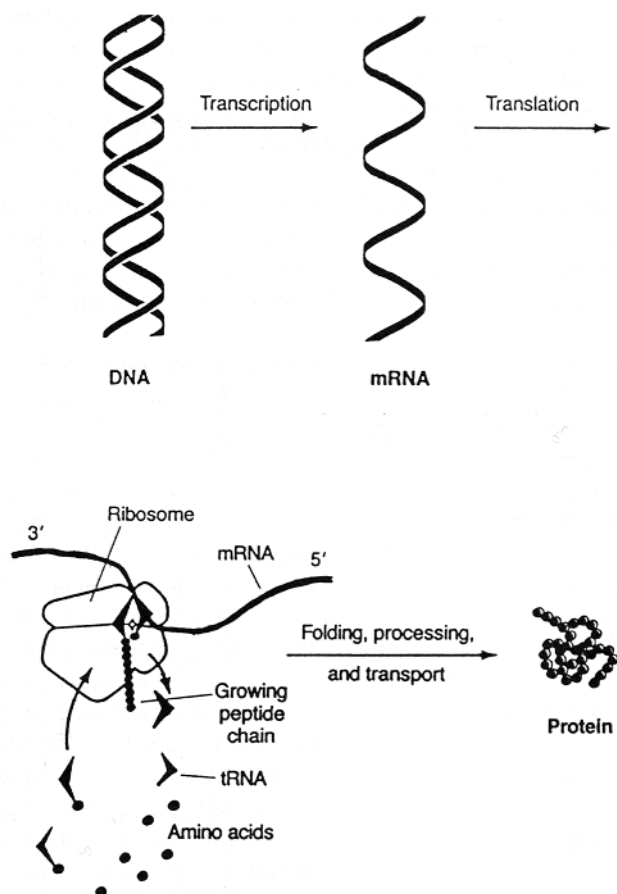
Fig. pp. 373



**Template-directed synthesis:** provide an intrinsic proof-reading capacity, and therefore a self-correction mechanism. It is also a parallel process. (For example protein

**biosynthesis, in which a DNA sequence serves as a template for the synthesis of the polypeptide chain through the intermediacy of a complementary mRNA sequence. Those polypeptides also have ordered three-dimensional structures in solution and the solid state)**

**Fig. 1 p. 374**

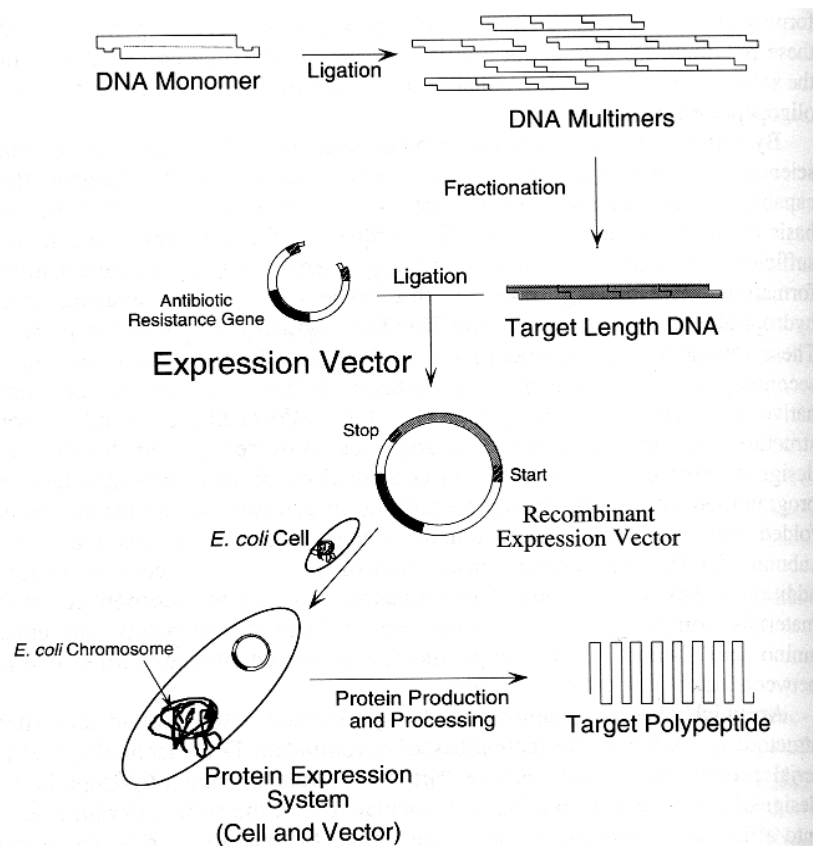


**FIGURE 1.** Schematic representation of protein biosynthesis from a DNA template. Reproduced with permission from King, J., *Chem. Eng. News* 32, April 10, 1989.

- e. By utilizing the principles of protein structure and the concepts of material science as guides, unnatural protein-based materials can be designed that are capable of self-assembly into unique two- or three-dimensional shapes on the basis of their primary structures**
- f. Artificial protein sequences can be synthesized with absolute uniformity of structure by utilizing the techniques of recombinant DNA technology and bacterial**

**protein expression.**

**Fig. 2 p. 376**

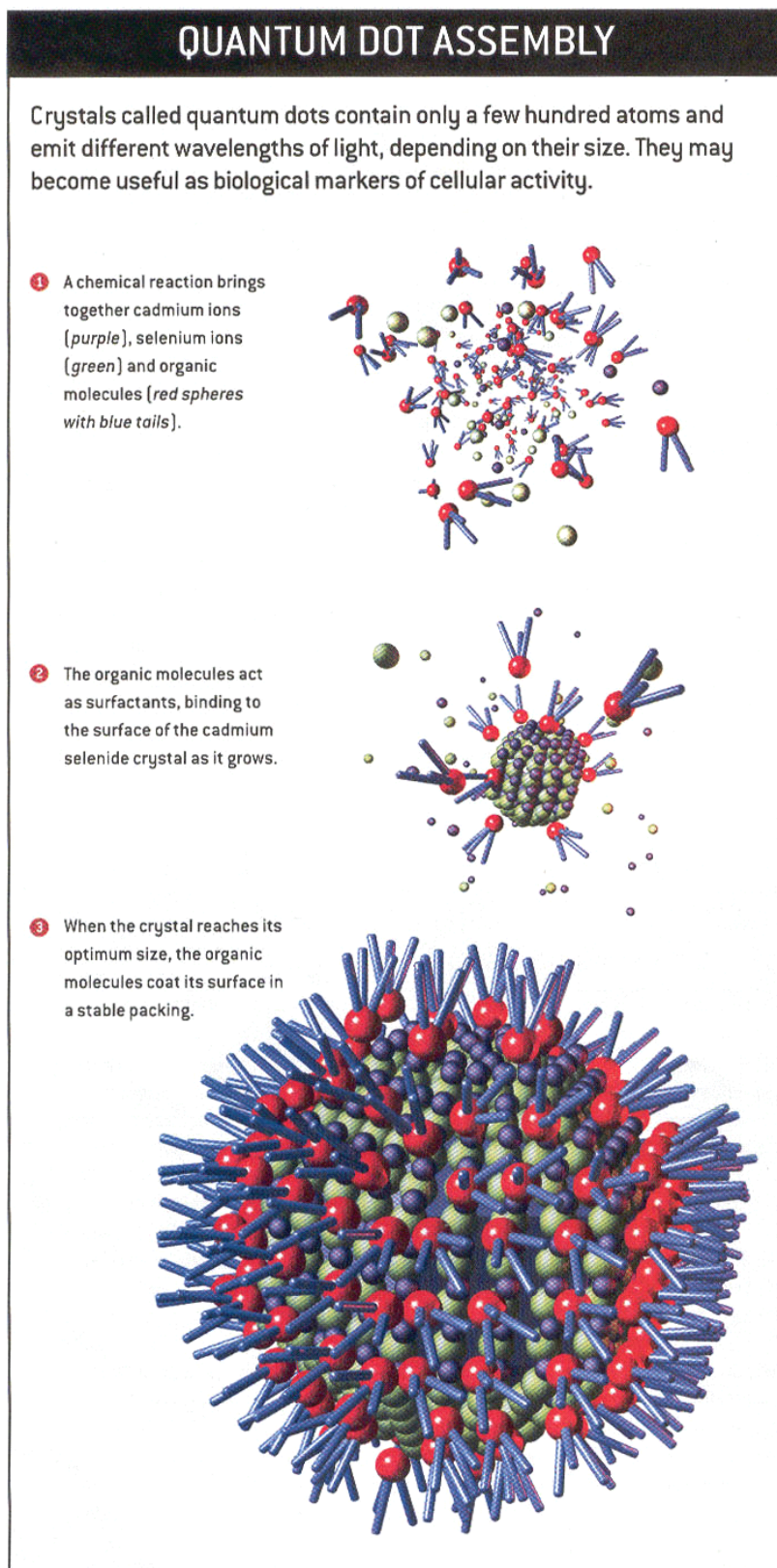


**FIGURE 2.** Synthesis, cloning, and expression of artificial genes encoding rRepetitive polypeptides.

g. examples in nature: silk, collagen, elastin (provides the elastic properties of mammalian artieries, lungs, skin and other tissue), and adhesive proteins.

## B. Molecular and Supramolecular Chemistry (nanotech 6)

### a. Quantum dot



1. The research of quantum dots started on 1970s', and the original goal was for optoelectronic industry. However, the most potential application so far is for disease diagnosis and drug screening.
2. The difference between organic dye and bulk semiconductor:

excitation emission

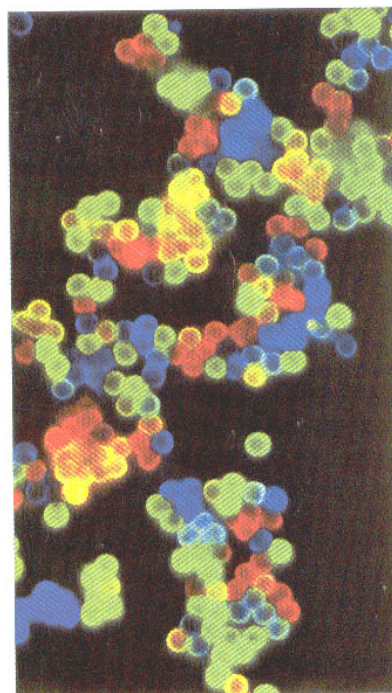
Organic dye: single single

Bulk semi. : multiple single (band gap)

Quantum dot: multiple single (size)

=>a single type of semiconducting material can yield an entire family of distinctly colored labels

3. quantum dots can be excited many times without emission degradation.
4. color can be custom designed, and there is almost no limitation.
5. color spectrum is very narrow.

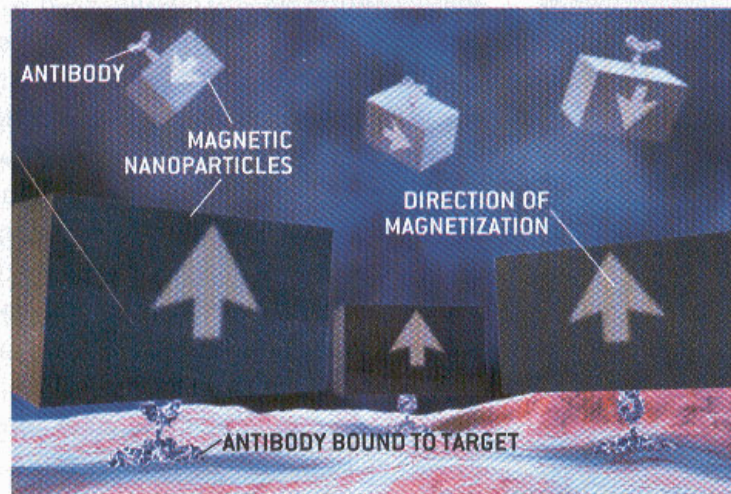


**LATEX BEADS** filled with quantum dots of single colors glow at nearly the same wavelengths as the dots themselves. Researchers have also loaded selections of different dots into single beads. Their aim is to create a huge variety of distinct labels for biological tests. (See also "Nano Bar Codes" in the box on the opposite page.)



## b. magnetic tags

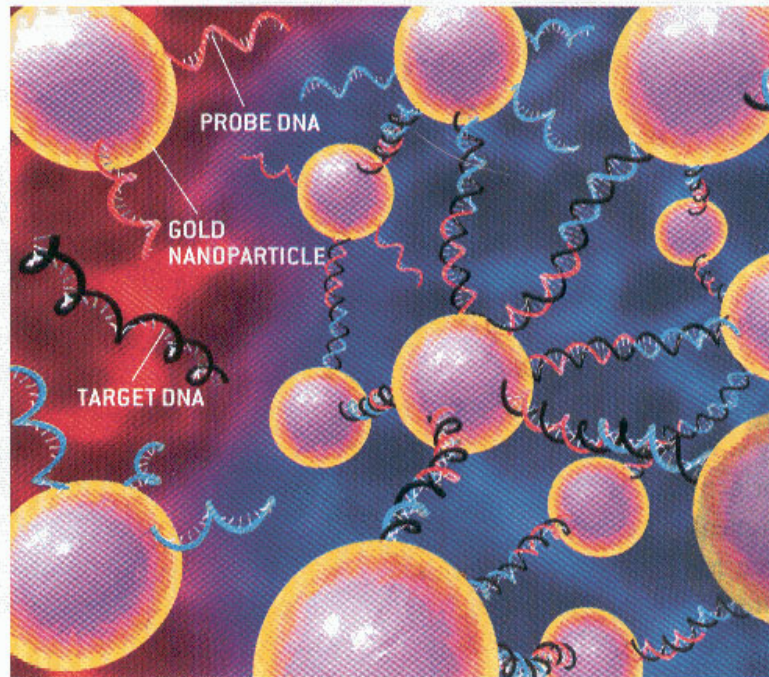
The items here could one day enhance the speed and power of biomedical tests, such as those used to screen small samples of material for the presence of particular genetic sequences. For clarity, the images have not been drawn to scale.



### MAGNETIC TAGS

Many tests reveal the presence of a molecule or disease-causing organism by detecting the binding of an antibody to that target. When antibodies labeled with magnetic nanoparticles bind to their target on a surface (*foreground*), brief exposure to a magnetic field causes these probes collectively to give off a strong magnetic signal. Meanwhile unbound antibodies tumble about in all directions, producing no net signal. This last property makes it possible to read the results without first washing away any probes that fail to find their target.

### c. Nano gold particles



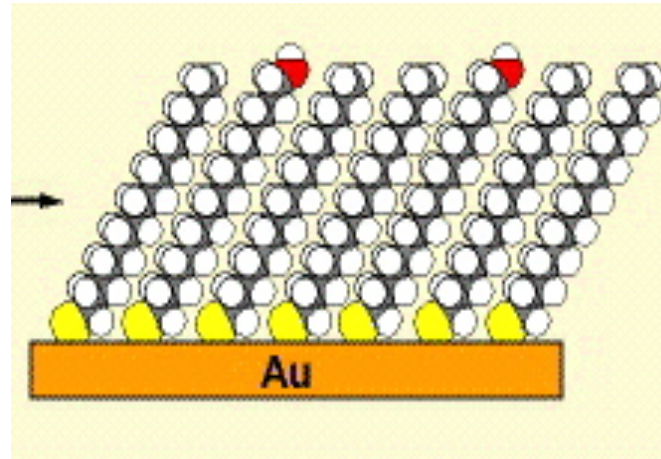
#### GOLD PARTICLES

Gold nanoparticles studded with short segments of DNA could form the basis of an easy-to-read test for the presence of a genetic sequence (*black*) in a sample under study. DNA complementary to half of such a sequence (*red*) is attached to one set of particles in solution, and DNA complementary to the other half (*blue*) is attached to a second set of particles. If the sequence of interest is present in the sample, it will bind to the DNA tentacles on both sets of spheres, trapping the balls in a dense web. This agglomeration will cause the solution to change color (*from red to blue*).

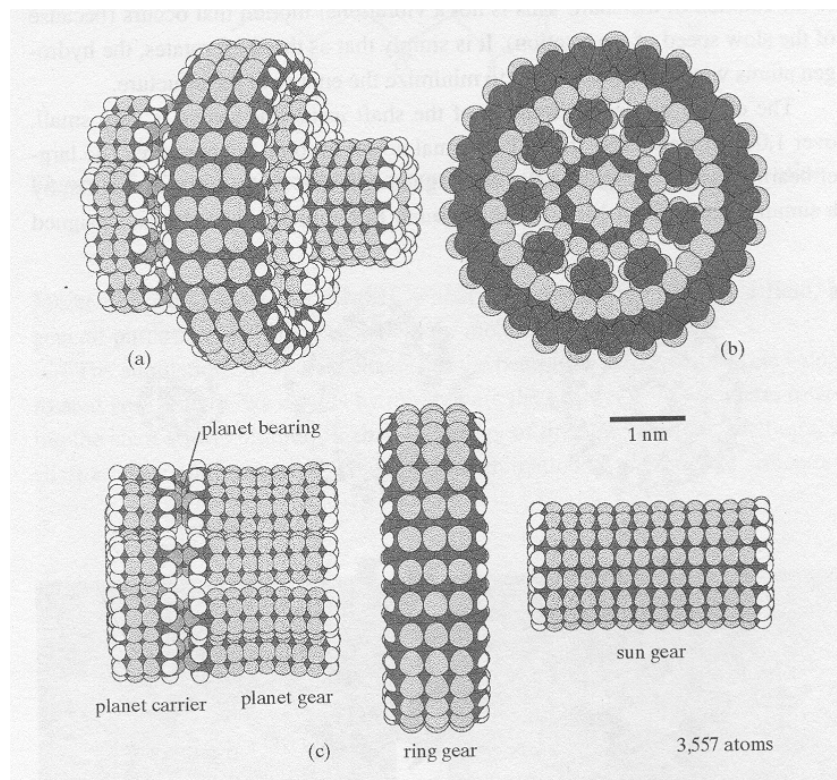


## C. Molecular Components and Molecular Assemblers (nanotech 8)

### Molecular self assembly



### Molecular device-Planetary gear.



## D. Scanning probe Technology (nanotech 10)

- Building things using individual atoms as the building blocks.
- The size of objects built up by top-down process is approaching the size of the largest molecules that chemists construct.

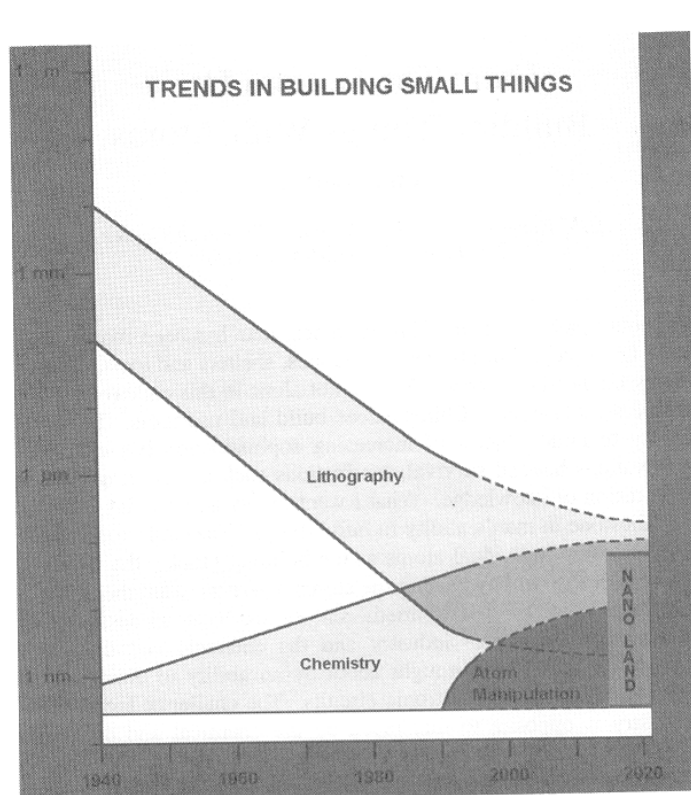
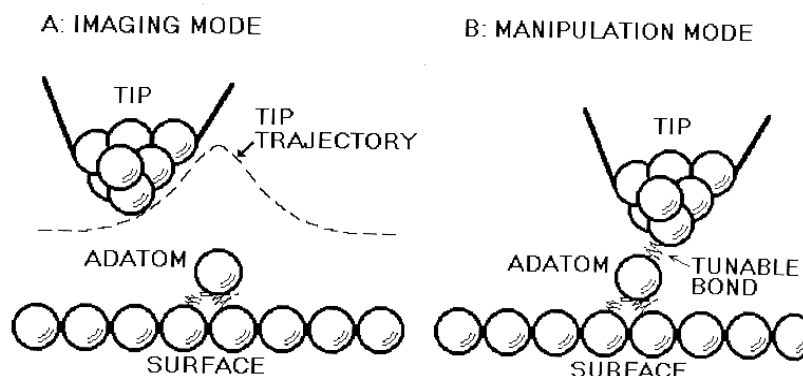
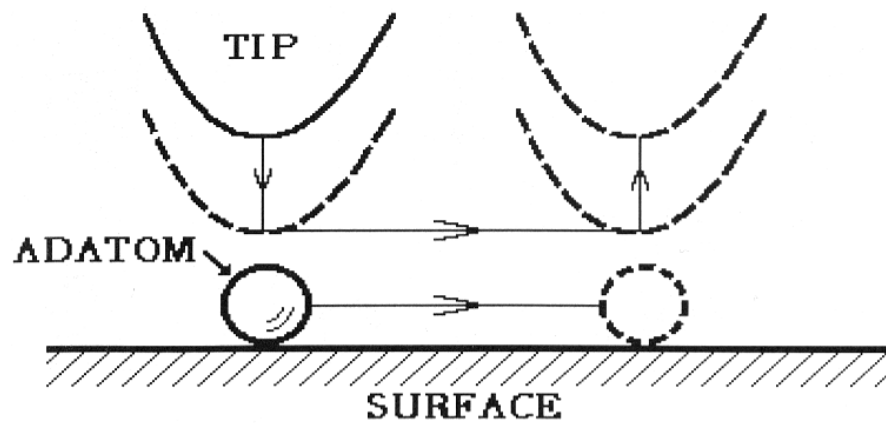


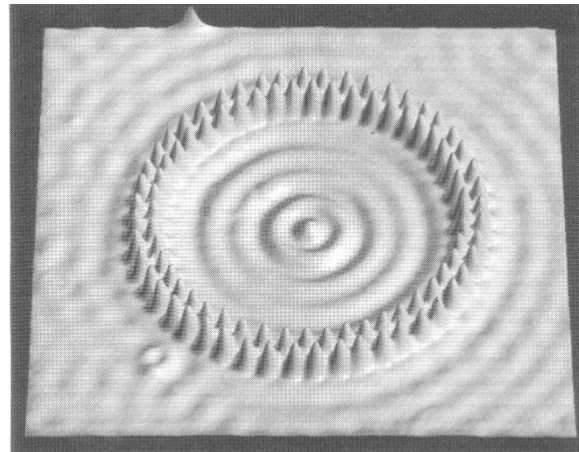
FIGURE 1. The scale of the smallest things built using the top-down approach of the electronics industry is approaching the scale of the largest molecules built by the bottom-up approach of chemistry. (See color plate.)

### c. Atom manipulation by STM (Scanning Tunneling Microscopy)

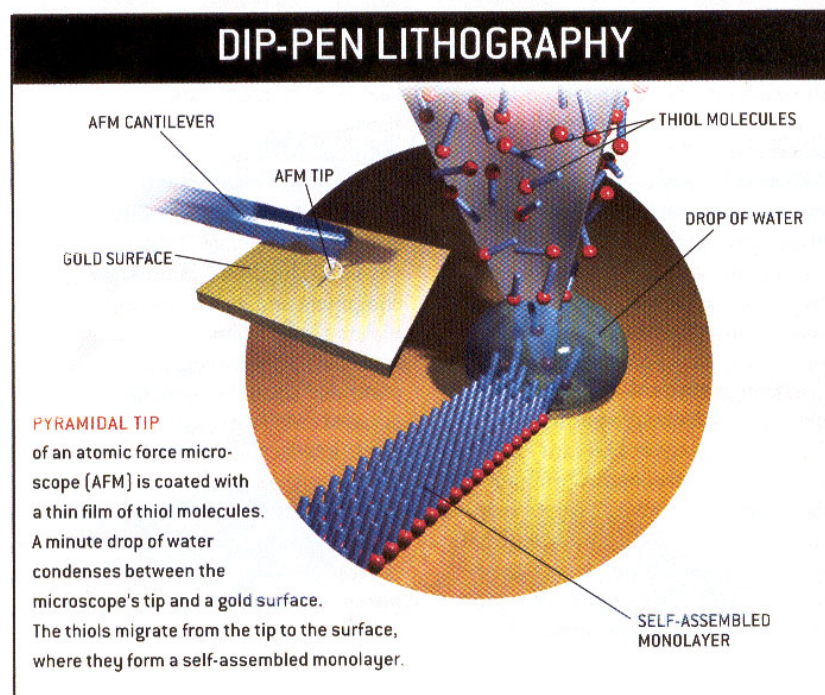




**FIGURE 3.** Schematic of the sliding process. The tip is placed above the adatom and then lowered to an empirically determined height at which the attractive interaction between the tip and the adatom is sufficient to pull the adatom along the surface. Once the adatom is moved to its final location, the tip is raised back to the height used for imaging, effectively terminating the tip-adatom interaction.



#### d. Dip Pen lithography for nanopatterning



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