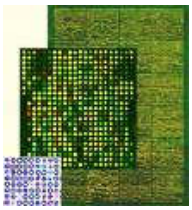
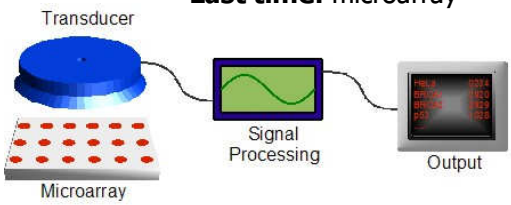
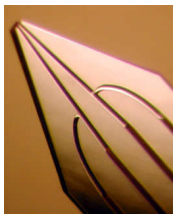
Welcome to Lecture 13

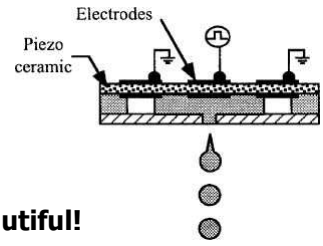




Last time: microarray

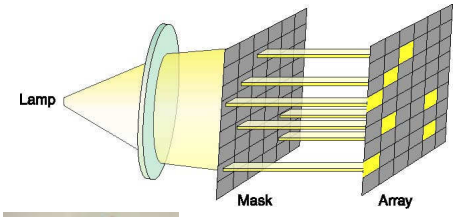


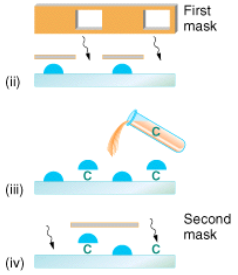
Manufacturing technologies:



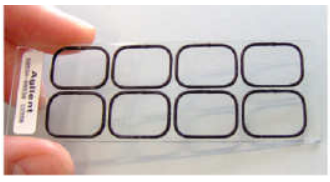
Small is beautiful!

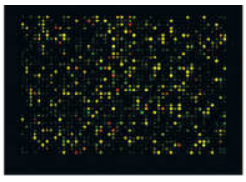
Also last time





Applications:

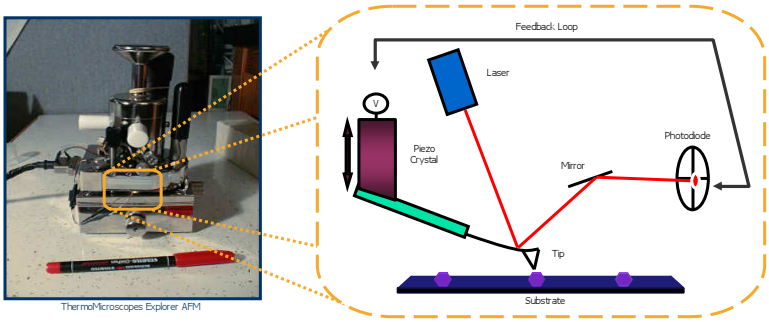




Today: We will continue the discussion of biosensors platforms and talk more about lithography

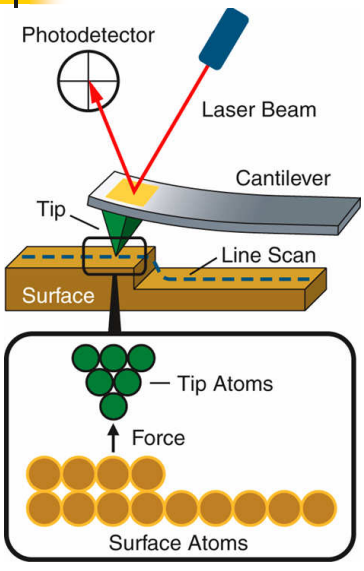
Atomic Force Microscopy

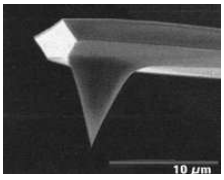
In a nutshell, AFM is scanning/imaging instrument based on measuring molecular forces - incredible resolution at atomic level

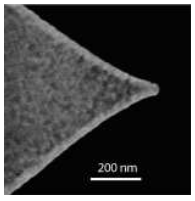


Surface is scanned with a sharp tip with a feedback mechanism enabling the piezoelectric scanner to maintain the tip at, for example, a constant force above the sample surface

Atomic Force Microscopy

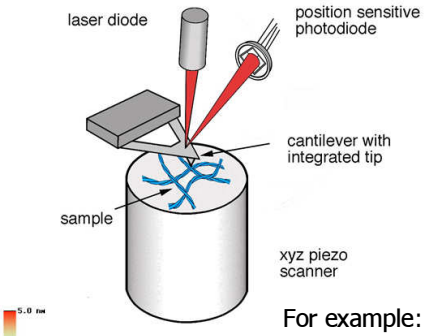




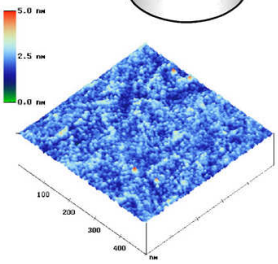


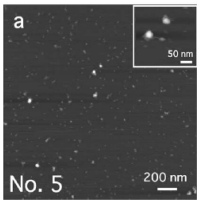
- The key element of AFM is micro-cantilever with a sharp tip or probe (silicone or silicone nitride) at the end for scanning the specimen surface
- When the tip is brought into contact with the surface, interaction between the tip and the sample leads to micro-cantilever movement to or away from the surface
- The movement of the tip is monitored

Atomic Force Microscopy



For example:





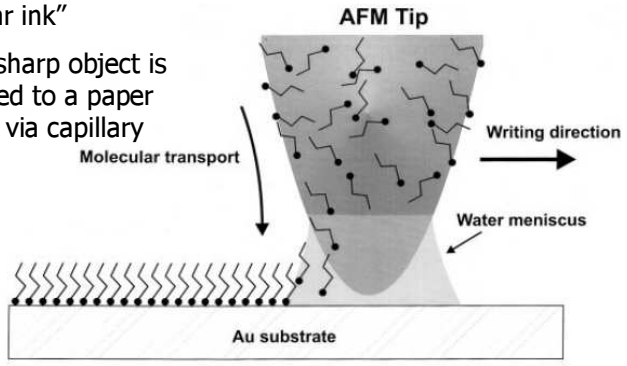
- The AFM head employs an optical detection system with a diode laser beam focused on the back of a reflective cantilever carrying the AFM tip
- As the tip scans, moving up and down with the contour of the surface, the laser light beam is reflected off the cantilever and captured by detector
- Position sensitive photo-detector measures the difference in light intensities and converts it into a signal

Nanolithography with AFM

Dip-pen lithography with "molecular ink"

Ink on a sharp object is transported to a paper substrate via capillary forces

- AFM tip is a pen
- Thiols is ink
- Gold is paper



An AFM tip is used to write alkanethiols with 30-nanometer line width resolution on a gold thin film in a manner analogous to that of a dip pen

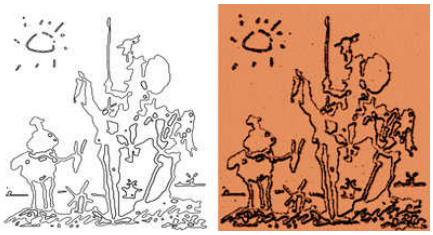
Allows to directly transport molecules to substrates of interest

Piner, et al (1999) Science 283, 661

Nanolithography

The AFM image produced at IBM: the lines are ~20 nm wide

What does it have to do with biology and biosensors?

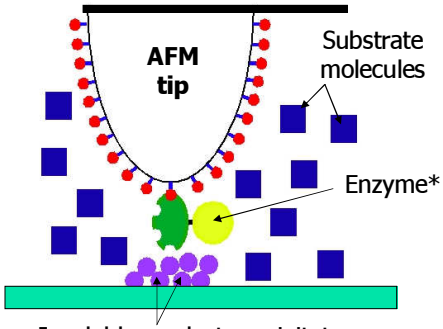


Coordinates of the imported JPEG line drawing (left) and AFM phase image (right) nanolithographically etched polycarbonate, 5μm scan

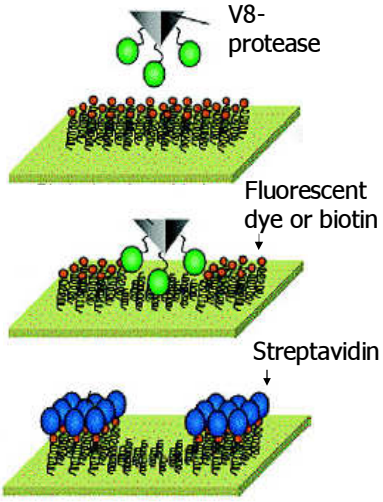
The original JPEG scan is a copy of Pablo Picasso's, "Don Quixote"

Enzymatic nanolithography

Principle: The substrate is present in the solution but the product is insoluble and precipitates on the support



*e.g. alkaline phosphatase

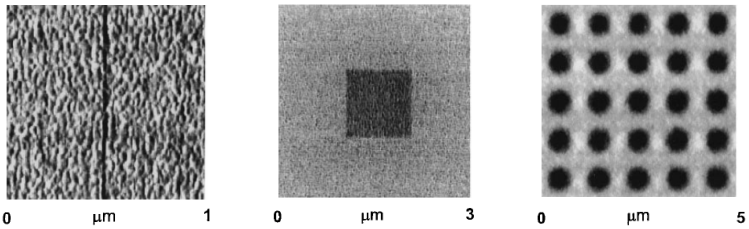


Nano Letters, 2003, 3, 1471-1474

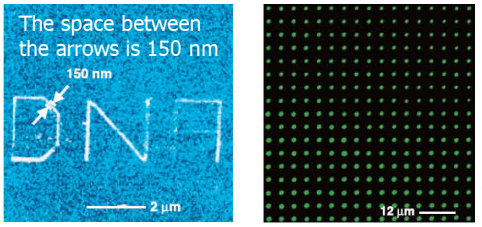
Nanolithography with AFM

A 30-nm-wide lines (3 μm long) | 1 μm by 1 μm square | Array of dots

Why?



Direct Patterning of Modified Oligonucleotides on Metals and Insulators by Dip-Pen Nanolithography



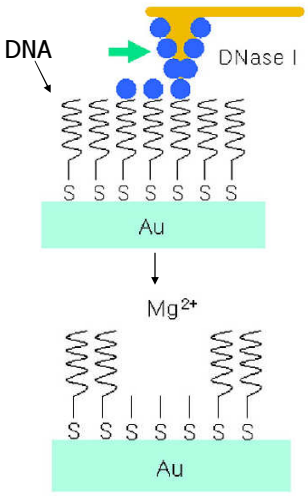
Direct DPN transfer of DNA onto a substrate: green fluorescence is DNA complementary to the probe deposited in the patterned area (~50nm)

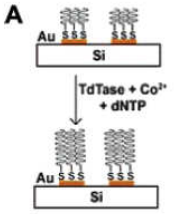
Demers (2002) Science 296, 1836

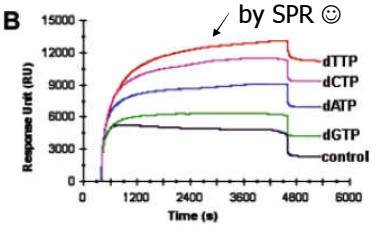
DNA manipulation

Enzymatic manipulation of surface DNA

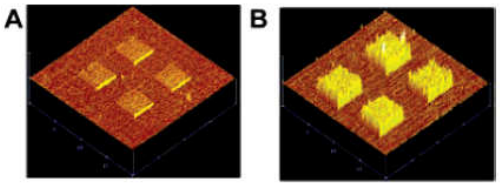
Followed by SPR ☺







TdTase can directly add dNTP to the 5/ of a short oligonucleotide template without the need for a separate DNA primer



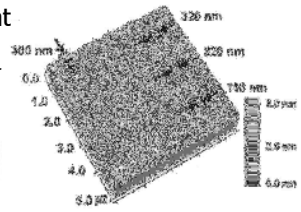
J. Am. Chem. Soc., 2004, 126, 4770-4771

J. Am. Chem. Soc., 2005, 127, 14122-14123

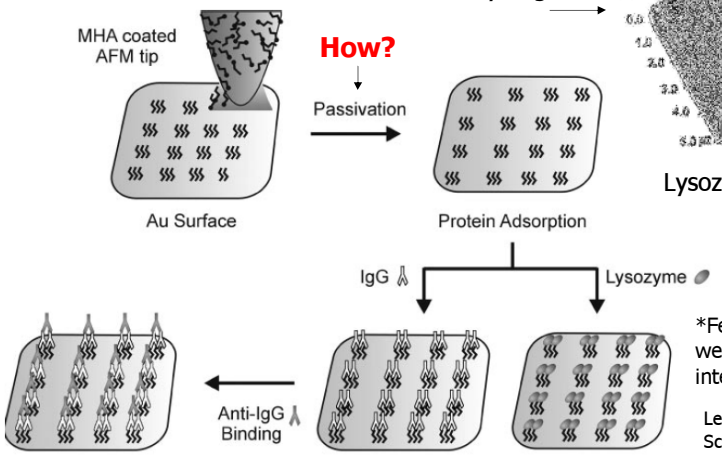
Protein arrays by DPN

Proof-of-principle:

This is what you get



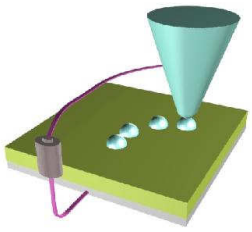
Lysozyme nanoarray*

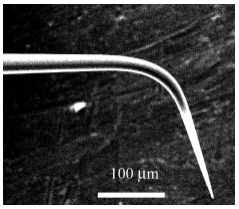


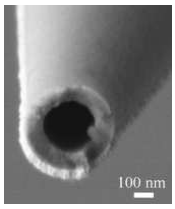
*Feature dimensions were varied intentionally

Lee, et al (2002) Science 295, 1702

Manipulation of surface proteins

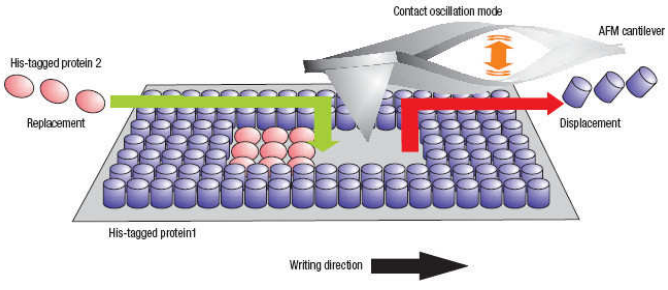






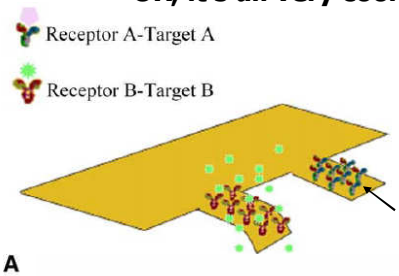
The tools: cantilever nanopipette

Deposition and displacement of his-tagged protein 1 (blue) bound to NTA SAM with His-tagged protein 2 (pink) using AFM tip



Nanocantilever sensors

OK, it's all very cool but let' make a biosensor



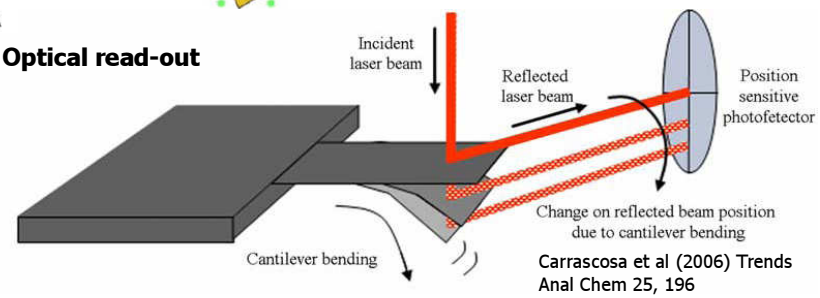
Any ideas how?

Cantilever bending resulting from biomolecular interaction between an immobilized receptor and its target

Note: ligands are immobilized on one side

A

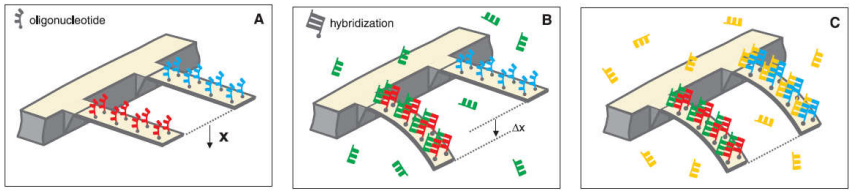
Optical read-out



Carrascosa et al (2006) Trends Anal Chem 25, 196

Nanocantilever sensors

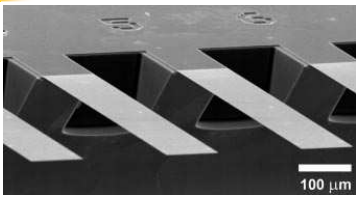
Translating Biomolecular Recognition into Nanomechanics
Fritz et al (2001) Science 288, 316
IBM Research, Zurich Research Laboratory



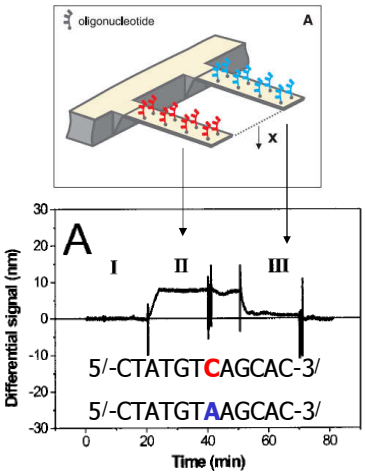
Each cantilever is functionalized on one side with a different oligonucleotide base sequence (red or blue)

(A) The differential signal is set to zero. (B) After injection of the first complementary oligonucleotide (green), hybridization occurs on the cantilever that provides the matching sequence (red), increasing the differential signal Δx. (C) Injection of the second complementary oligonucleotide (yellow) causes the cantilever functionalized with the second oligonucleotide (blue) to bend

The experiment



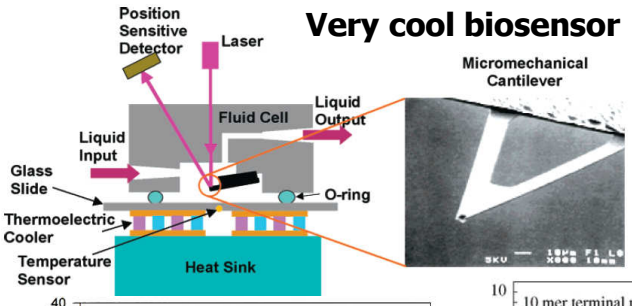
Scanning electron micrograph of a section of a microfabricated silicon cantilever array (eight cantilevers, each 1 mm thick, 500 mm long, and 100 mm wide



Differential signal in a hybridization experiment to detection of a single base mismatch in 12-mer oligo-nucleotides

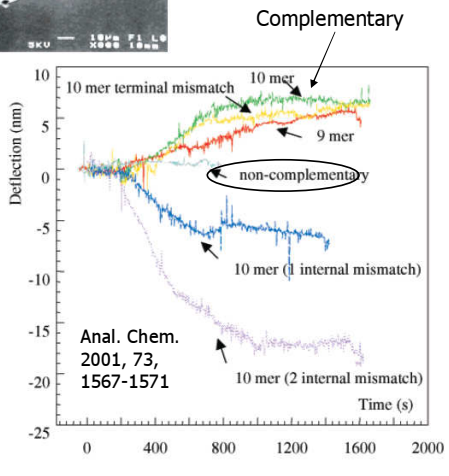
The injection of the 1st complementary oligo increases the differential signal (interval II); injection of the 2nd oligo decreases the signal (interval III)

Very cool biosensor



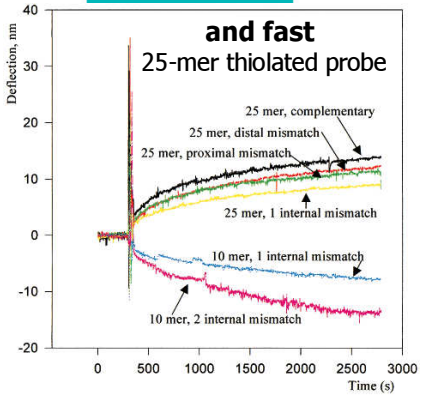
Cantilever surfaces functionalized with thiolated 20-mer probe

It's sensitive

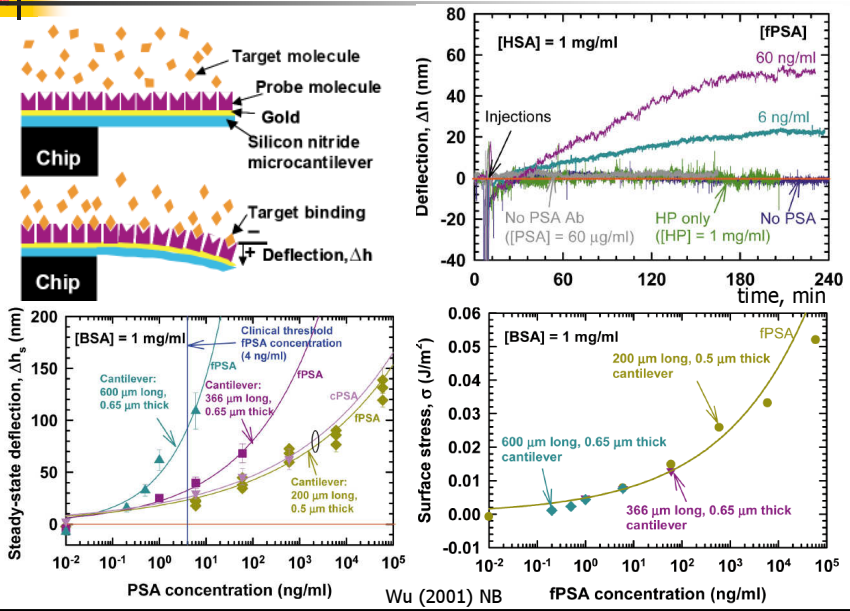


and fast

25-mer thiolated probe

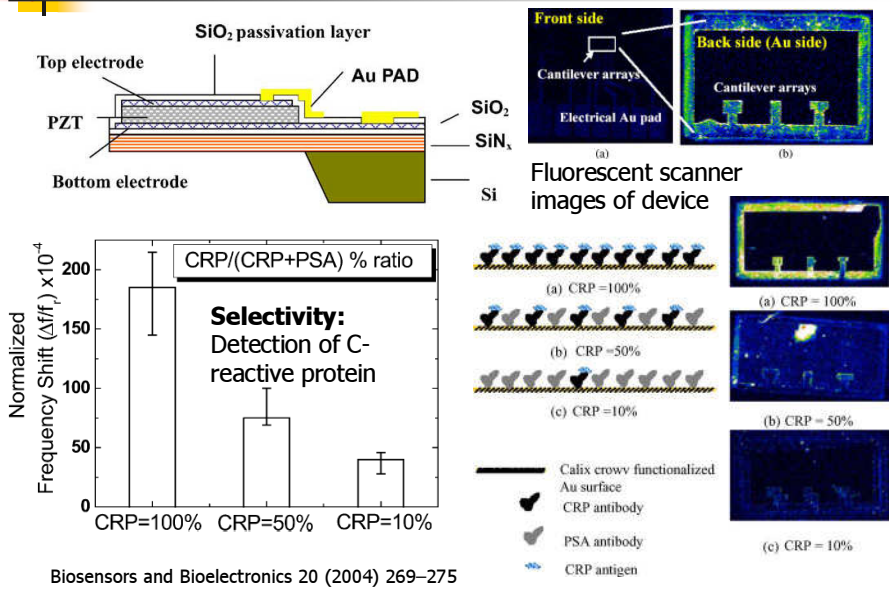


Early detection of cancer



Wu (2001) NB

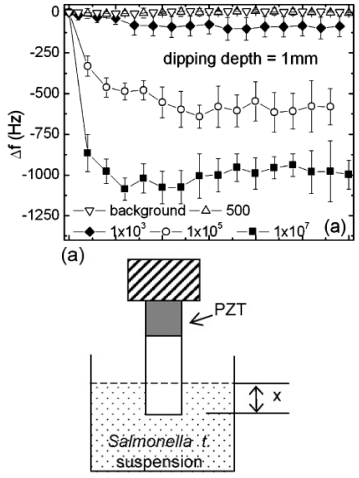
Piezoelectric detection



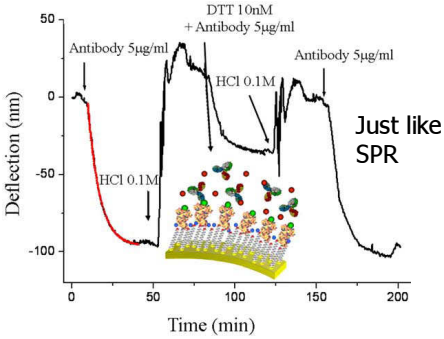
Biosensors and Bioelectronics 20 (2004) 269–275

Food and environment

Resonance frequency shift vs. time of Salmonella detection



Zhu et al (2007) Biosens. Bioelectron 22, 3132



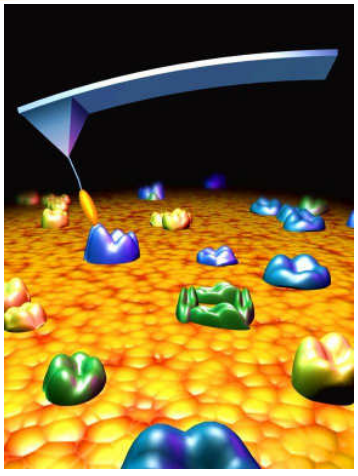
Just like SPR

DDT pesticide detection using a single microcantilever sensor by real-time competitive immunoassay

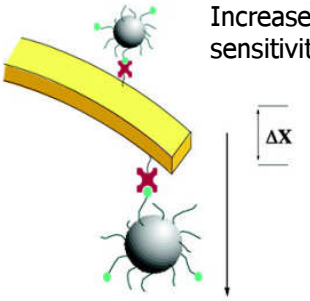
The cantilever surface was regenerated with 100 mM HCl to break the hapten/antibody complex

Alvarez et al (2003) Biosens. Bioelectron. 18, 649

And some really cool stuff



Antibody is immobilized on the tip to scan cell surface: imaging?



Increased sensitivity

J. AM. CHEM. SOC. 2004, 126, 1073-1080

Magneto-Mechanical Detection of Nucleic Acids and Telomerase Activity in Cancer Cells

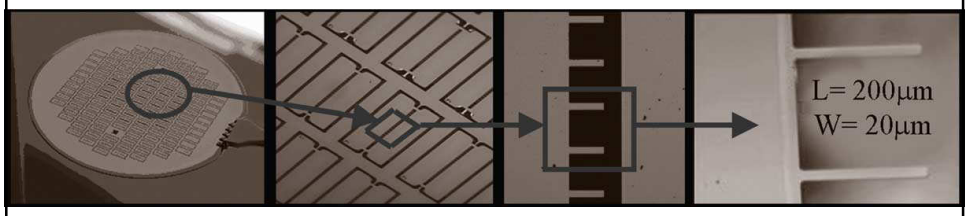
Nanolithography with AFM

Commercialized cantilever array sensors (May 2005)

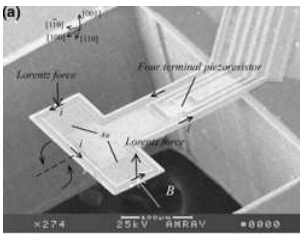
Country	Company	Products	
		On the market	Year
Basel, Switzerland	Concentris www.concentris.ch	Micromechanical silicon cantilever arrays	2003
Lyngby, Denmark	cantion www.cantion.com	Canti Chip 4 Canti Lab 4 Canti Spot	2004 2004 2004 2003 2003 2003 2003
Mannheim, Germany	Veeco www.veeco.com	Scentris cantilever sensor	–
Rockville, USA	PROTIVERIS www.protiveris.com	VeriScan 3000 System	2004 2001 2000
San Francisco, USA	Kalinex Inc.	BioCOM	–

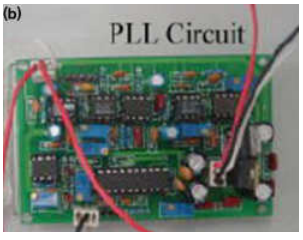
Carrascosa et al (2006) Trends Anal Chem 25, 196

Production and integration



Nanomechanical sensors based on microcantilever arrays; allow further integration in "lab-on-a-chip" microsystems



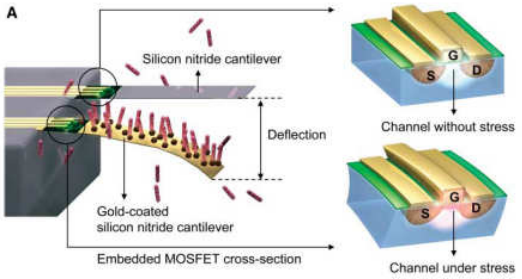


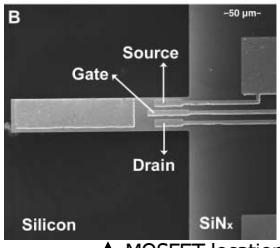
SEM image of the fabricated micro-cantilever with the integrated actuating and sensing elements and a picture of the controlling circuit board

Carrascosa et al (2006) Trends Anal Chem 25, 196

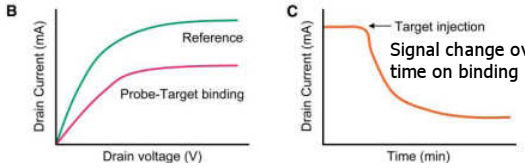
Bioelectronics

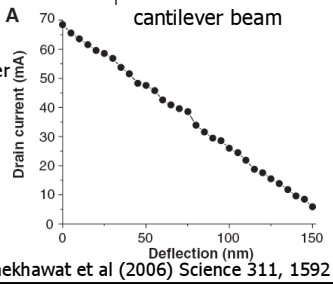
MOSFET-embedded microcantilevers with biomolecular sensors





MOSFET location on cantilever beam





Allows massively parallel on-chip sensing and signal processing, integration with RFID, etc

Shekhawat et al (2006) Science 311, 1592

MEMS Technology

MEMS: Micro-Electro-Mechanical Systems

Integration sensing and sample manipulation on a single chip

Manufacturing: There are three basic "building blocks" in MEMS technology

- Deposition of thin films of material on a substrate
- Application of a patterned mask by photolithograpic imaging
- Etching the films selectively to the mask

Typically, a MEMS process is a structured sequence of these operations to manufacture actual devices

Thin film deposition

Can be classified into two main groups:

Chemical depositions (reaction):

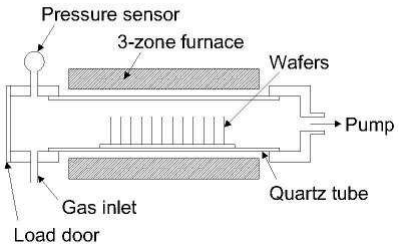
- Chemical Vapor Deposition (CVD)
- Epitaxy
- Electrodeposition
- Thermal oxidation

Physical deposition:

- Physical Vapor Deposition (VPD)
- Casting

Thin film deposition

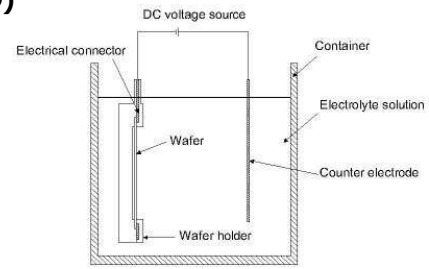
Chemical Vapor Deposition (CVD)



The principle: a chemical reaction takes place between the source gases producing a solid material, which condenses on all surfaces inside the reactor

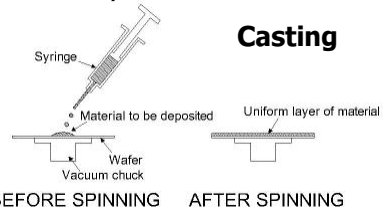
Once the material is deposited it has to be patterned

Electrodeposition



Also known as "electroplating" typically for electrically conductive materials

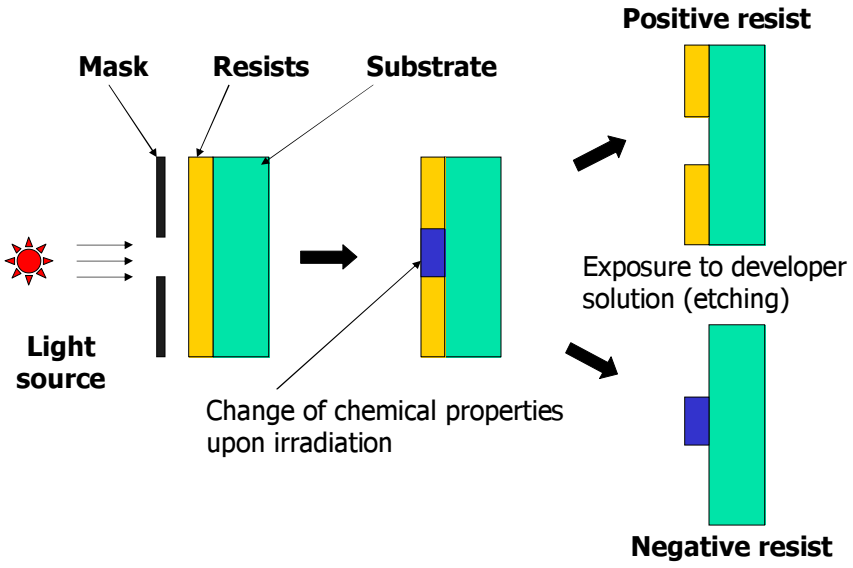
Casting



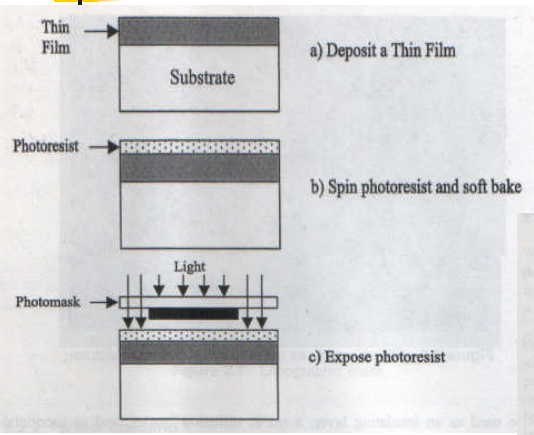
Lithography: resists

- In lithography for micromachining, the photosensitive material used is called a (photo)resist
- When resist is exposed to a radiation source, the chemical reactivity of the resist (i.e. its "resistance") to developer e.g. a solution of chemicals changes
- After selective exposure to light source, one of the two regions of the resist (exposed or unexposed) will be etched away
- The material is called a positive resist, if the exposed region is etched away and the unexposed region is resilient
- The material is called a negative resist, if the exposed resilient and the unexposed region is etched away (the other way around)

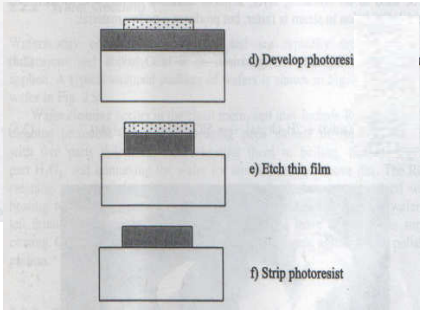
Resists



Positive resists



A typical lithographic cycle when using positive resists



Let's take a look at etching

Wet etching

In order to form a functional structure on a substrate, it is necessary to etch the deposited thin films and/or the substrate itself

- There are two main methods: wet etching and dry etching. Wet etching is the simplest – all one needs is a "bucket" with chemicals to dissolve the resists. However, mask is required for selective etching the material; some materials e.g. silicon etch anisotropically

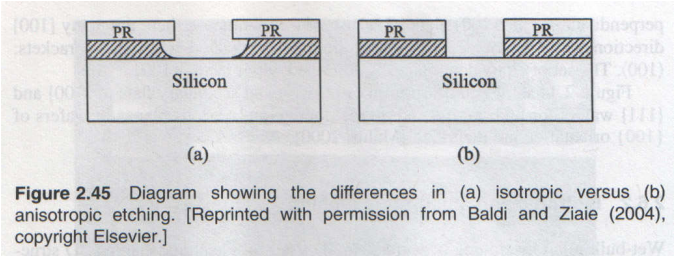
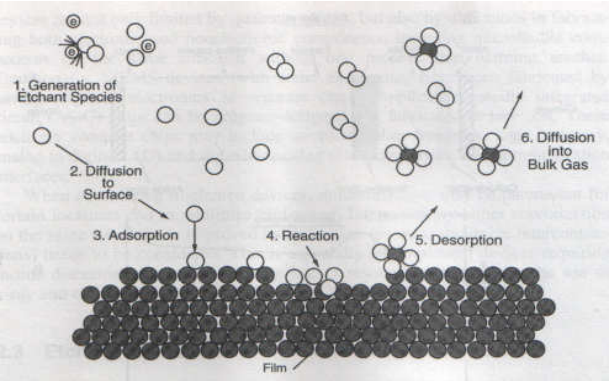


Figure 2.45 Diagram showing the differences in (a) isotropic versus (b) anisotropic etching. [Reprinted with permission from Baldi and Ziaie (2004), copyright Elsevier.]

Dry etching

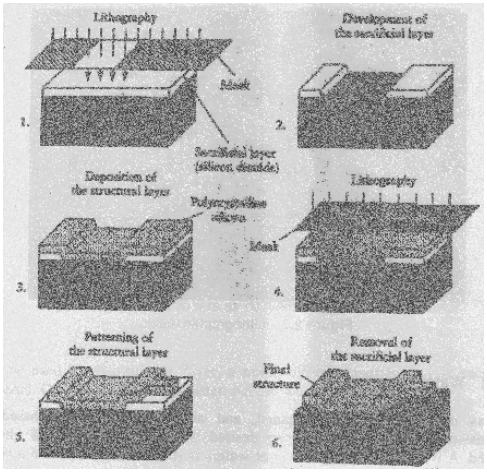
Principle methods:

- Reactive ion etching (RIE) and plasma etching (PE)
- Sputter etching
- Vapor phase etching

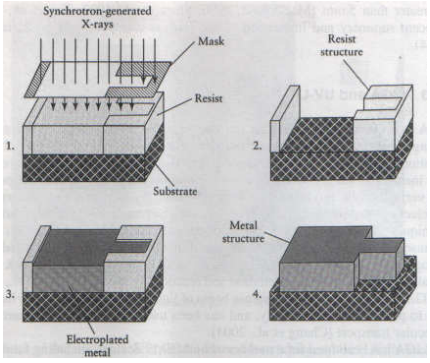


- In RIE, the substrate is placed inside a reactor in which several gases are introduced
- A plasma is struck in the gas mixture using a powerful radiation source to break the gas molecules into ions
- The ions are accelerated towards, and react at the surface of the material which is being etched, forming a gaseous product that diffuses away

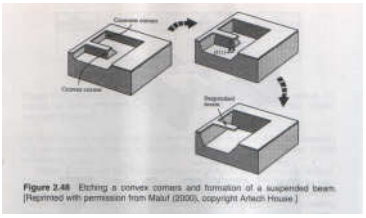
Multi-step process

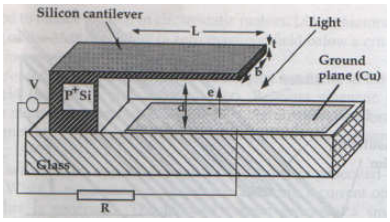


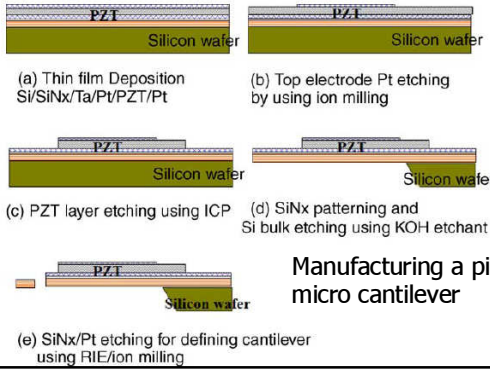
In lithographic electroplating molding a fabricated structure can then be used as a mold to inexpensively mass produce exactly the same elements



Why all the complications?







Manufacturing a piezoelectric micro cantilever

Fancy high resolution devices

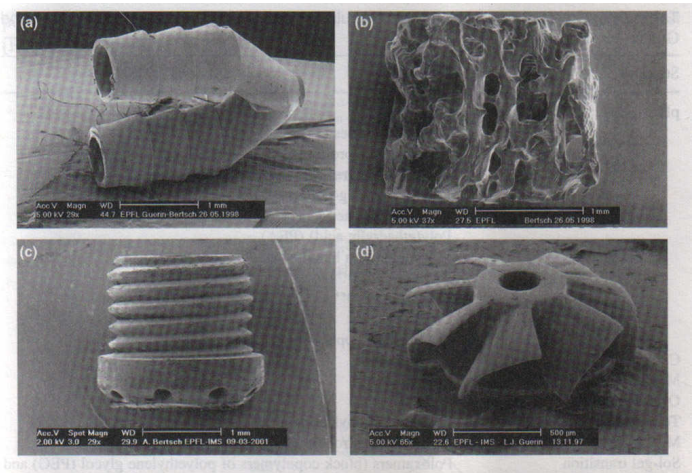
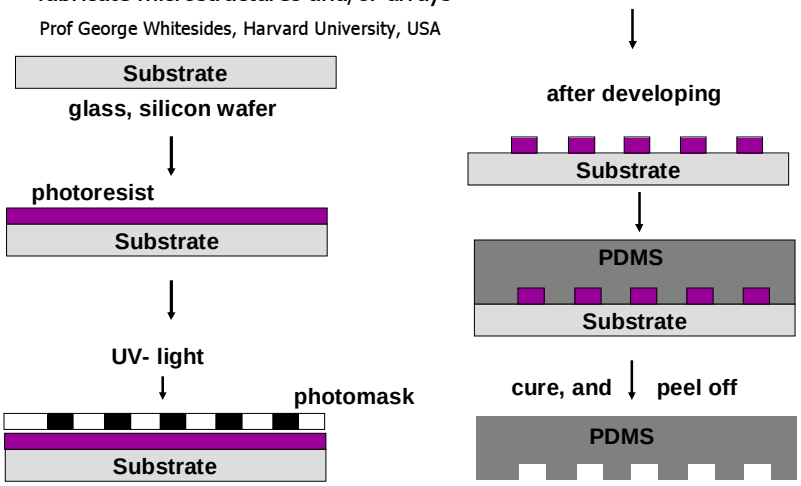


Figure 3.12 Examples of devices that may be fabricated by high resolution stereolithography (a) pipe structure; (b) bone material; (c) nozzle; and (d) turbine.

Soft lithography

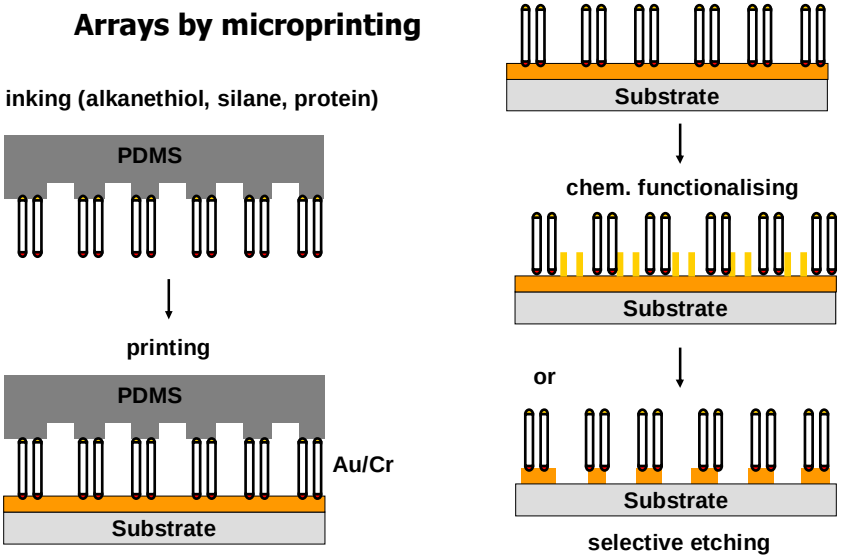
Microcontact printing: the method relies on a patterned elastomeric stamp (typically poly dimethyl siloxane) or mold to INEXPENSIVELY fabricate microstructures and/or arrays

Prof George Whitesides, Harvard University, USA



Soft lithography

Arrays by microprinting



Micro-channels, -mixers, -pumps

Micromolding in capillaries

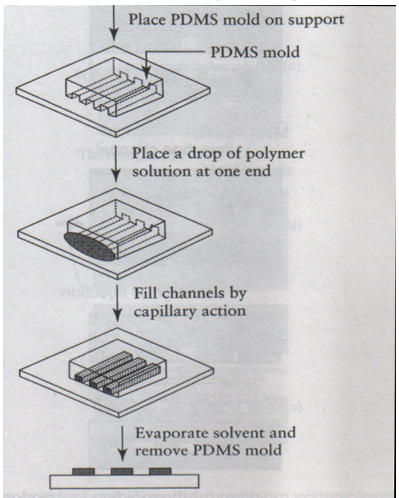


Figure 3.4 Micromolding in capillaries (MIMIC)

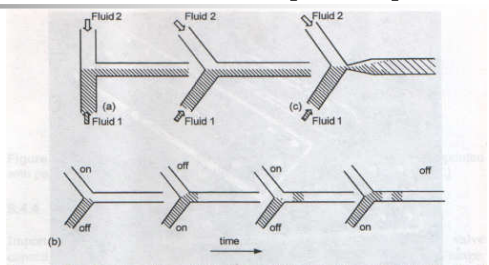


Figure 5.23 Passive mixers. (a) T-mixer and Y-mixer; (b) sequential mixing; and (c) a throttle design. [Reprinted with permission from Nguyen and Wereley (2002), copyright Artech House.]

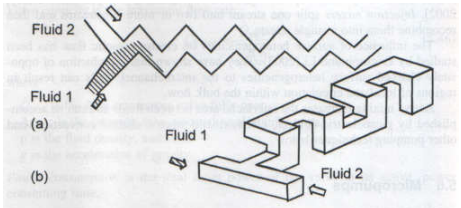


Figure 5.24 Serpentine mixers. (a) The planar serpentine structure has been found not to work in micromixers because of laminar flow in microscale [Branebjerg et al., 1994]; whereas (b) the 3D serpentine structure does provide chaotic advection to laminar flow. [Reprinted with permission from Liu et al. (1999), copyright IEEE.]

Remember insulin pumps?

Figure 7.15 Microneedle array. (Photo courtesy of Micronit, Inc.)

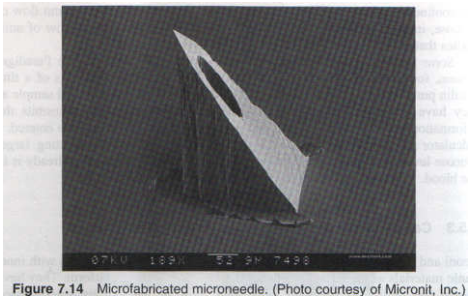
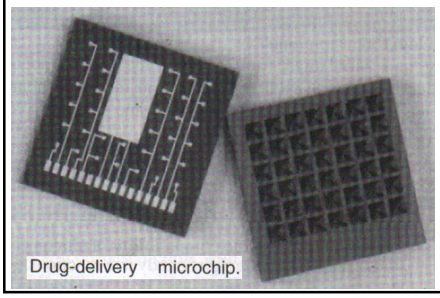


Figure 7.14 Microfabricated microneedle. (Photo courtesy of Micronit, Inc.)



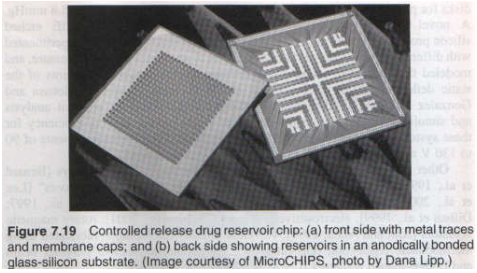


Figure 7.19 Controlled release drug reservoir chip: (a) front side with metal traces and membrane caps; and (b) back side showing reservoirs in an anodically bonded glass-silicon substrate. (Image courtesy of MicroCHIPS, photo by Dana Lipp.)

And you can do chemistry

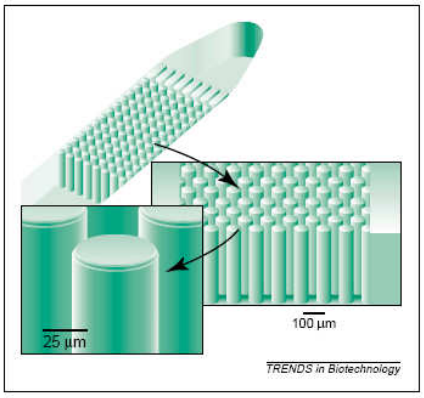


Fig. 3. Example of a microfabricated catalyst packing. The catalyst is deposited on the surface of the microfabricated poles.

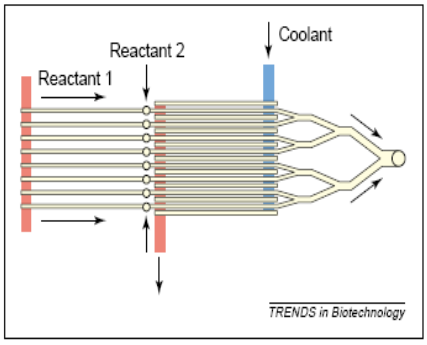


Fig. 1. Structural element of a multichannel, liquid-phase microreactor. The elements were applied in a two-stage scheme. The first reactor had short (1 second) residence time and the second reactor had a longer residence time (minutes). Reproduced, with permission, from [26].

and separations

Separations

Micro Total Analysis Systems

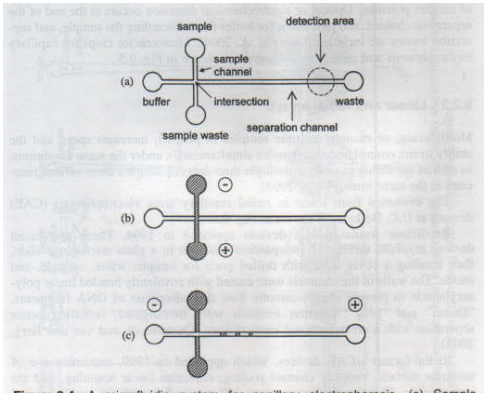
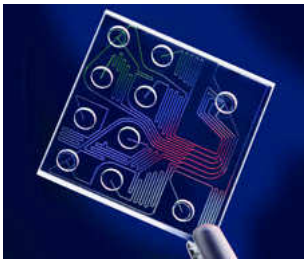


Figure 9.4 A microfluidic system for capillary electrophoresis. (a) Sample introduction and electrophoretic separation are accomplished in each of two crossing channels. (b) The sample is driven through the short sample channel across the separation channel by application of a potential, and (c) the "plug" is electrophoretically separated by application of another potential. [Reprinted with permission from Guber et al. (2004), copyright Elsevier.]



Caliper's LabChips may usher in an era of labs in miniature.

and analysis

Ab biosensor µATS sensor

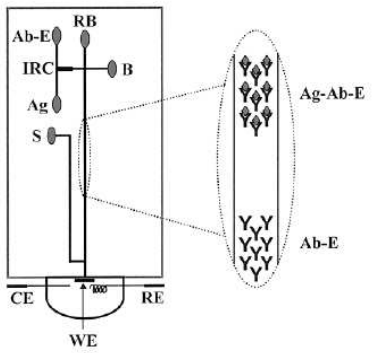
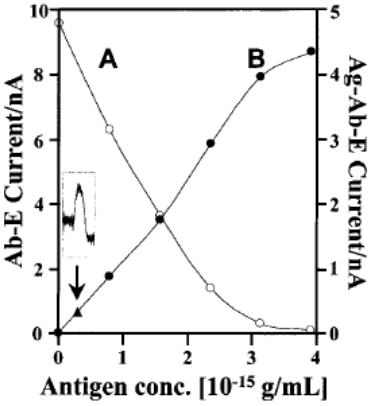


Figure 1. Schematic of the immunochip used in this study. Key: RB, running buffer; Ab-E, enzyme-labeled antibody; Ag, antigen; S, substrate; IRC, immunoreaction chamber; RE, reference electrode; CE, counter electrode; WE, working electrode; B, unused reservoir. See text for exact dimensions and details.

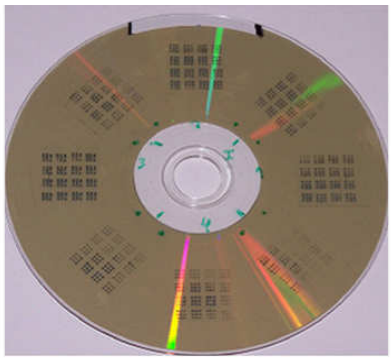


This "lab-on-a-chip" device integrates pre-column reactions of alkaline phosphatase-labeled antibody with the antigen, followed by electrophoretic separation of the free AB and the complex and post-column reaction of the enzyme with the 4-aminophenyl phosphate with amperometric detection

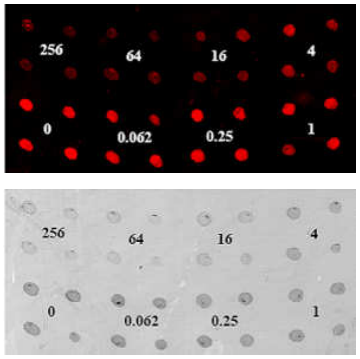
ELISA on CD?

What does this look like?

Abs microarray on a CD



We will discuss how CDs work after the break



Digital images of a parallel micro-immunoassay for chlorpyriphos developed over PS-coated L-CDs obtained from fluorescence scanner using GAR-Cy5 (top) and from CD reader detection (bottom)

Welcome to Lecture 13

Biosensor on a CD

- 3072 reaction cells on the surface of a CD have a dye or silver salt which interacts with added microdrops of pesticides. The change in dye color or plating of silver metal on the CD is detected by the CD-ROM
- Adding two extra lasers to the device enables the tracking of the individual reaction cells

How does it work?

A modified, off-the-shelf external CD-ROM drive is converted to a light sensor-based portable lab

A couple of extra light sensors turn an everyday CD drive it into a cheap, portable, chemical scanner that could replace larger, more expensive machines (Image: UPV)

Recording and playing sound

- CDs were first introduced in the early 1980s for the main purpose of storing and distributing music in a digital format; prior to that it was analog…
- The first device for recording and playing back sounds was invented by Thomas Edison
- **Phonograph** is a remarkably simple device for to dealing with analog sound waves mechanically

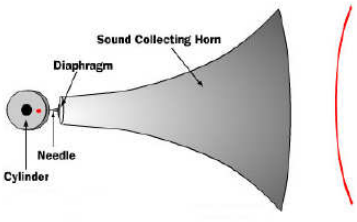
Phonograph

In the simplest mechanical recording, the air waves directly actuate a very thin membrane connected to a needle

Driven by vibrations, the needle cuts a continuous groove in the moving surface of the membrane (recording medium)

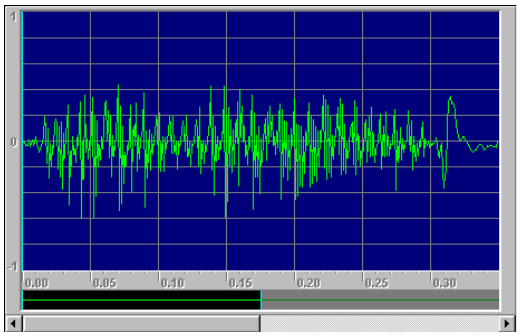
To amplify the intensity of the impact on the membrane, sound waves are let in through a horn, where the acoustic energy is concentrated on a small area

To play back a second needle traces this groove, forcing the attached diaphragm to oscillate and, thus, to produce sound



Analog sound wave

The needle in Edison's phonograph scratched an analog sound wave onto the tin the cylinder



Recorded on PC – the same principle This is the sort of wave scratched onto the tinfoil in Edison's device

In essence, this graph shows the position of the microphone's diaphragm (Y axis) over time (X axis); the diaphragm is vibrating FAST - 1,000s of oscillations per sec

Analog-digital conversion

- To produce a digital recording the analog wave must be converted into a stream of numbers
- The conversion is done by a device called an **analog-to-digital converter** (ADC)
- To play the music, the stream of numbers should be converted back to an analog wave by a **digital-to-analog converter** (DAC)
- Fortunately, this is not really required in modern biosensors, although one can imagine circumstances when this would be useful…

Any ideas?

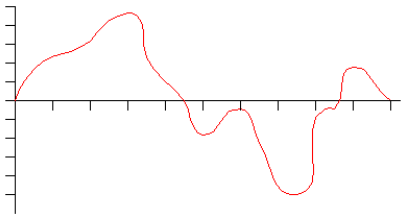
Converting digital readout into an audible signal e.g. an alarm message

Digitization

To produce digital signal two variables should be set up:

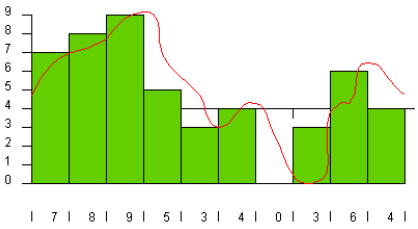
The sampling rate - how many samples are taken per second

The sampling precision - how many different gradations (quantization levels) to be used when taking the sample; for example….



Every 1/1,000 of a sec, the ADC looks at the wave and picks the closest number between 0 and 9 (bottom of diagram). These numbers are digital representation of the original wave.

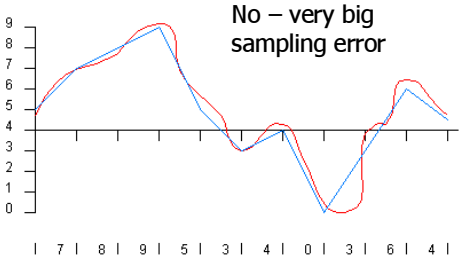
Let's assume that the sampling rate is 1,000 per second and the precision is 10



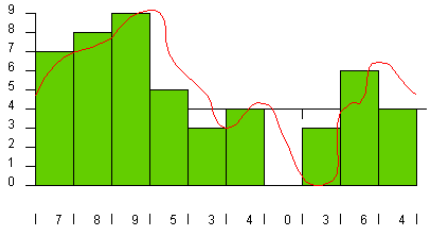
The green rectangles are samples

AD converter

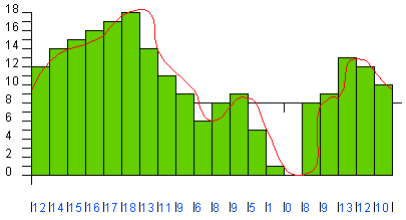
Is this good enough?



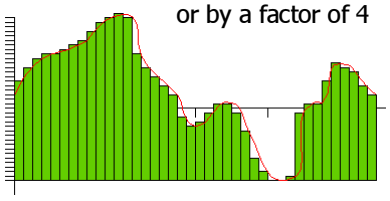
No – very big sampling error



Let's increase the sampling rate and the precision by a factor of 2



or by a factor of 4



40 gradations at 4,000 samples per second

Storing the stuff

In CD recording the sampling rate is 44,100 samples per second and the number of gradations is 65,536

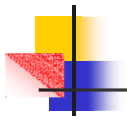
At this level, it is so closely matches the original waveform that the sound is great for most human ears

On a CD, the digital numbers produced by the ADC are stored as **bytes**; it takes 2 bytes to represent 65,536 gradations. There are two sound streams being recorded (one for each of the speakers on a stereo system) and a CD can store up to 74 minutes of music.

So, the total amount of digital data that can be stored on CD:

44,100 samples/(channel*second) * 2 bytes/sample * 2 channels * 74 minutes * 60 seconds/minute = **783,216,000 bytes**

That's a lot of bytes!



Where bits and bytes come from

A digit is a single place that can hold numerical values between 0 and 9

For example, 6,357 has four digits where

6 holds 1000s, 3 holds 100s 5 holds 10s and 7 holds 1s

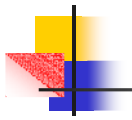
(6x1000) + (3x100) + (5x10) + (7x1) = 6000+300+50+7 = 6357

$(6x10^3) + (3x10^2) + (5x10^1) + (7x10^0)$ =6000+300+50+7 = 6357

Hence, each digit is a **placeholder** for the next higher power of 10, starting in the first digit with 10 raised to the power of zero

But why 10? Where has it come from?

Probably because we have 10 fingers; if we happened to evolve with eight fingers instead, we would probably have a system based on 8 numbers ☺



Computers like 2s

Computers happened to have "two fingers" and so they operate using the base-2 number system i.e. the **binary number system**

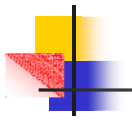
It is possible to build a computer that would operate in 10s but it would horrendously expensive (remember how diodes and transistors work? Current/no current, which is equivalent to two numbers – 0 and 1 i.e. binary

For example, what is the value of the binary number 1011?

$(1x2^3) + (0*2^2) + (1x2^1) + (1x2^0) = 8 + 0 + 2 + 1 = 11$

each digit is a **placeholder** for the next higher power of 2

In fact, the word **"Bit"** is short for "**B**inary dig**IT**"



Counting in 2s is just like in 10s

0 = 0
1 = 1
2 = 10
3 = 11
4 = 100
5 = 101
6 = 110
7 = 111
8 = 1000
9 = 1001
10= 1010
11= 1011

In computers bits are bundled into 8 bits collections, called **BYTE**s

With 8 bits in a byte, we can represent 256 values ranging from 0 to 255

or record a CD - 2 bytes (16 bits) per sample

0 =	00000000
1 =	00000001
2 =	00000010
.....	
254 =	11111110
255 =	11111111

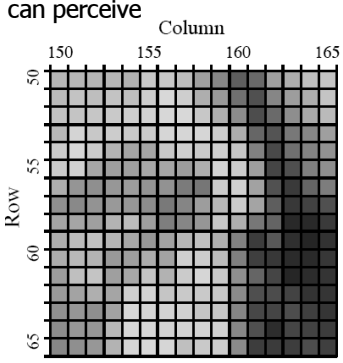
0 =	0000000000000000
1 =	0000000000000001
2 =	0000000000000010
.....	
65534 =	1111111111111110
65535 =	1111111111111111

$1x2^3 + 0x2^2 + 1x2^1 + 0x2^1 = 8 + 0 + 2 + 1 = 11$

Image processing

In image processing it is common to have 256 quantization levels (**gray levels**), corresponding to a single byte per pixel, because

- One byte is convenient in terms of data management
- A brightness step size of 1/256 (0.39%) is smaller than the eye can perceive



Row \ Column	150	155	160	165
50	183	183	181	184
	186	195	190	195
	194	196	198	201
	184	212	200	204
55	202	215	203	179
	203	208	166	159
	174	149	143	151
	143	137	147	153
60	164	165	159	179
	173	187	193	181
	172	184	179	153
	156	191	196	159
65	154	163	175	165
	144	150	143	162
	140	151	150	185
	135	143	151	179

Row \ Column	150	155	160	165
50	183	183	181	184
	186	195	190	195
	194	196	198	201
	184	212	200	204
55	202	215	203	179
	203	208	166	159
	174	149	143	151
	143	137	147	153
60	164	165	159	179
	173	187	193	181
	172	184	179	153
	156	191	196	159
65	154	163	175	165
	144	150	143	162
	140	151	150	185
	135	143	151	179

ASCII files

Text characters are also coded in bytes – ASCII files

In the **ASCII character set**, every specific character is given a binary value between 0 and 127 (one byte), so that computer can store your document in memory or save to disk

For example, the sentence "I hate Biosensors" has 17 characters including spaces (ex inverted comas!)

What would be the size of this file on PC, if I save it as ASCII?

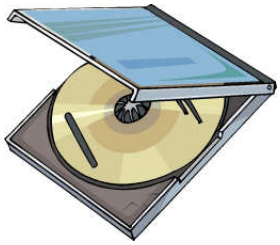
Let's check it

In notepad (ASCII file) the size of the file is exactly 17 bytes; it will be bigger in MS word (.doc) because font size, color, etc must be coded too

Compact disks

CDs and DVDs are standard media to hold music, data and software – great technology, very cheap in mass production

To fit more than 783 megabytes onto a 4.8 inches (12 cm) disk requires individual bits of info to be physically very small

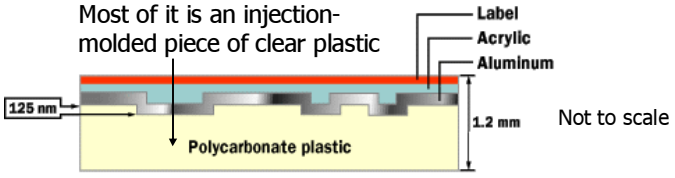


Remember what we need?

44,100 samples/channel/second x 2 bytes/sample x 2 channels x 74 minutes x 60 seconds/minute = 783,216,000 bytes

CDs

A CD is a pretty simple plastic construction ~1.2 mm thick

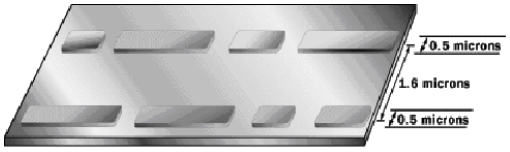


- During manufacturing, this plastic is impressed with microscopic bumps ("pits" on the aluminum side) arranged as a continuous, very long spiral track
- Once the polycarbonate mold is formed, a thin, reflective aluminum layer is sputtered onto the disc, covering the bumps
- Then a thin protective acrylic layer is sprayed over the aluminum
- Finally, the label is printed onto the acrylic

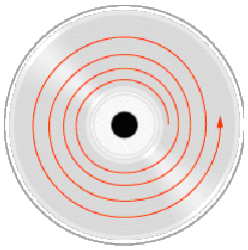
Data storage

The data is stored as a single spiral track, circling from the inside to the outside of the disc

The data track is ~0.5 µm wide, with 1.6 µm separating one track from the next; height ~ 125nm



If one could straighten this track it would be about 5 km long



Because the track runs from the inside smaller CDs can be made too

CD Drive

The CD drive has the job of finding and reading the bumps as data

The drive consists of three main components:

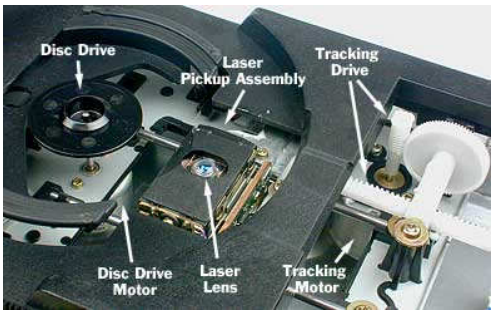
- A **drive motor** for precisely controlled spinning the disc at a rate between 200 and 500 rpm depending on which track is being read
- A **laser** and a **lens system** to focus on and read the bumps
- A **tracking mechanism** for moving the laser so that the laser's beam can follow the track; given the dimension of the bumps, the tracking system has to at micron resolutions

and you get all these for 20 bucks

Inside CD-ROM

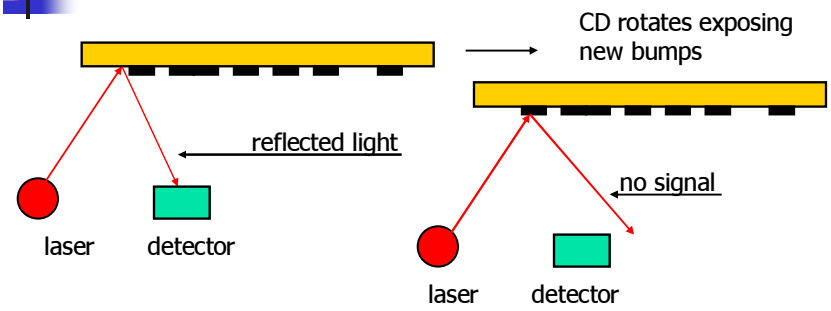
The main job of the CD player is to focus the laser on the track of bumps

- The laser beam passes through the trans-parent plastic layer, reflects off the aluminum layer and hits a sensor that detects changes in the intensity of the reflected light



- The opto-electronic sensor can see the change because the bumps reflect light differently than the rest of the aluminum layer ("lands")
- The electronics in the drive detects the changes in reflectivity and converts it into bits and bytes of information

Reading the track

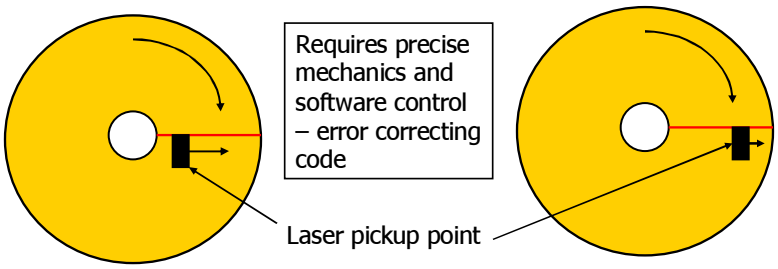


As CD track moves along you get a string of hits and misses or in binary language 0,1,1,0,0,1,0,1,1,1,etc – e.g. the digitized sound wave of recorded music

The hardest part is keeping the laser beam centered on the data track

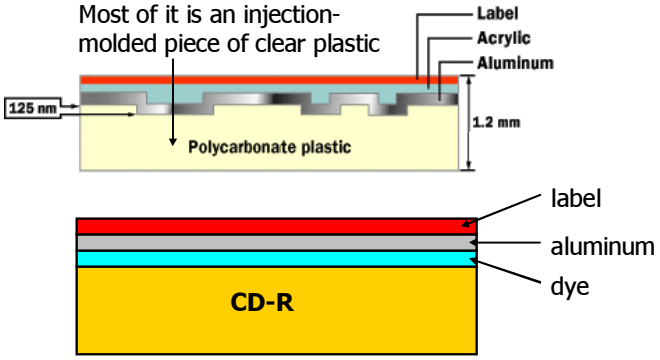
Tracking system

- As CD plays, the tracking system must continuously move the laser outward from the center of the disk
- However, the further it goes the faster the bumps fly by $v_{linear} = v_{rot} \times R$ (v_{rot} in rpm, R – radius)
- Hence, to allow the laser to read the bumps at a constant speed, the **spindle motor** must slow the speed with which it rotates the CD to provide a constant data stream



Type of disks

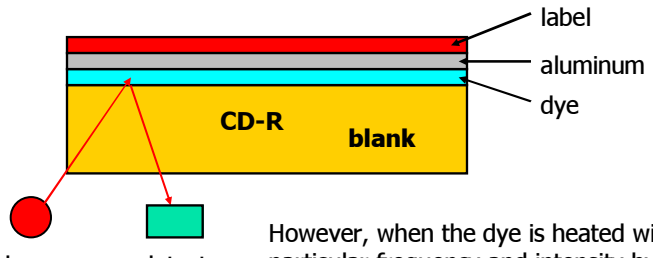
The CD fabrication machine uses a high-powered laser to etch the bump pattern into **photoresist** material coated onto a glass plate - the master. This pattern is then pressed (imprinted) onto plastic discs



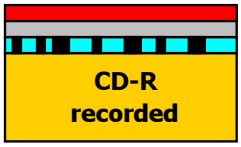
Blank CD-R disk has no data (bumps) but it can be "burnt"

Recording CD-R

When the disc is blank, the dye is **translucent**: Light can shine through and reflect off the metal surface

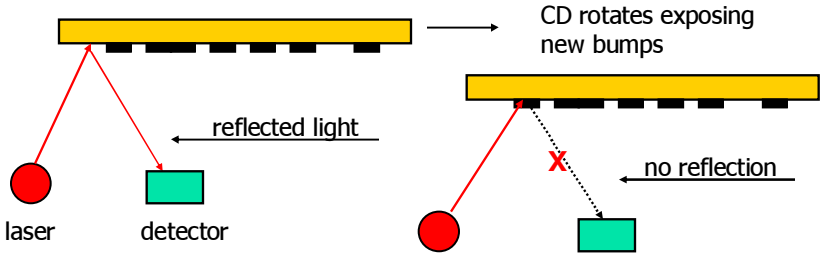


However, when the dye is heated with light of particular frequency and intensity by the **more powerful** "write laser", it turns **opaque** i.e. the light can no longer pass through

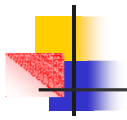


By selectively "darkening" dots along the CD track, and leaving other areas translucent, a digital pattern similar to that on a standard pressed CD is created

Reading CD-R

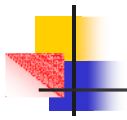


- The light from the reading laser only reflects back to the sensor from the spots, where the dye is left translucent, just like it would only bounce back from the flat areas of a pressed CD
- Hence, despite the lack of bumps on CD-R discs they behave in exactly the same way (but less durable)
- **Note:** the read and write lasers must have different power/intensity; otherwise the read laser may destroy the CD!



FYI: CD-RWs and DVDs

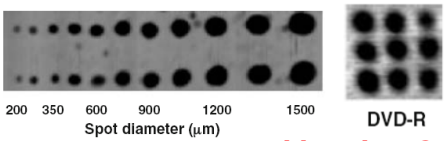
- Use **phase-change compounds**, instead of dye, which exists in the crystalline (translucent – the light is reflected) and amorphous ("dark" – adsorbs light) forms
- New disks are crystalline and to record it the write laser heats the compound to its melting temperature; it is then cooled down rapidly to create amorphous like glass state
- To erase it, the writable areas are illuminated for longer time and kept at higher temperature to allow crystallization
- These melted spots serve the same purpose as the bumps on pressed CDs and the opaque spots on CD-Rs
- **DVD disks** are very much the same technology but making features smaller, the tracks are longer – hence, higher capacity (there encoding and other differences too)



Biosensor on CD

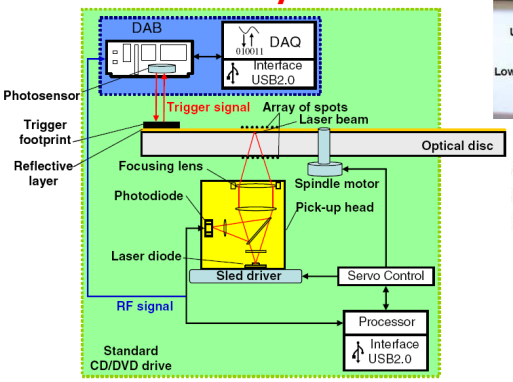
Can you tell me how it works?

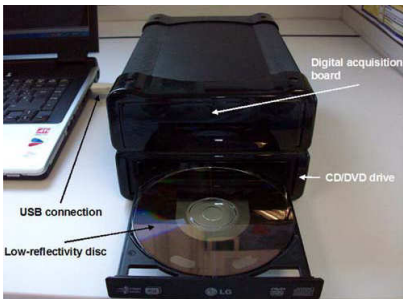
Biosensor on CD



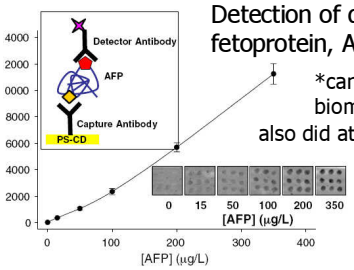
DVD-R

Any ideas how?





Detection of α-fetoprotein, AFP*



*cancer biomarker also did atrazine

Anal Bioanal Chem (2008) 391:2837–2844

Microtiter plate using a CD

Fixing additional light sensors/lasers to a normal CD drive can transform it into a highly accurate scanner for chemical or medical tests

The first sensor identifies the sector of a disk containing a sample (can be coded with black marks or spots), while the second analyses the sample, measuring how much laser light is reflected

All we need now is the right chemistry i.e. make sure that the amount of dye produced in each sample (micro-spot) is proportional to the amount of analyte being detected e.g. for herbicide atrazine (LoD ~0.02 μg/L)

Capacity: more than 10,000 per CD (should be better!?)

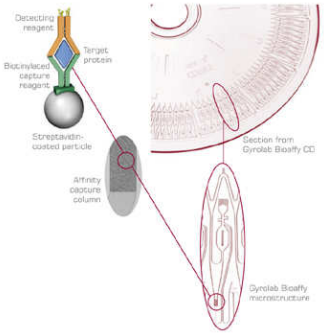
Not a rocket science after all ☺

There are other CD devices too

Gyros and Nanogen are developing microfluidics devices on CDs (left) and semiconductor microchips (right), respectively.

Each CD contains individual microstructures in which samples are analyzed in parallel. The CD microstructures are assembled in segments (each segment containing 8 microstructures connected by a common channel)

Each microstructure contains a column (15 nL) pre-packed with streptavidin-coated beads for capturing Abs, ets



In conclusion

CDs can be a great platform, if someone works out how to make money on it

Biotech students: Knowing a bit about digital processing does not hurt ☺

Have fun and
see you next week