

Life Science with you



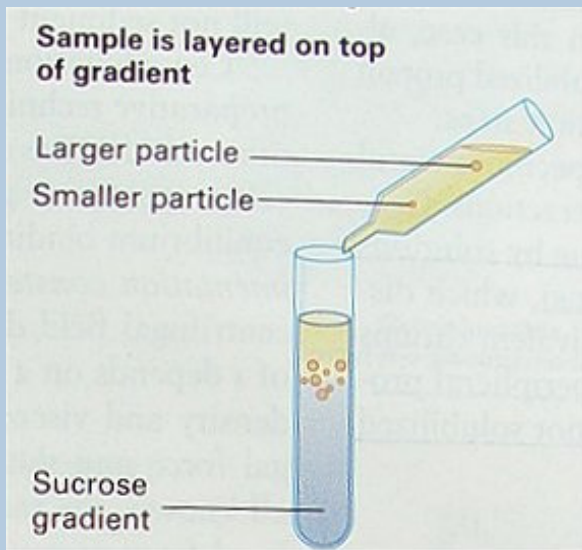
Content

- I. How tools development push Life Science progress
- II. How do fundamental knowledges be applied in biological problem study
- III. What's kind of information in Life Science you can use in your field.
- IV. Future work in Life Science

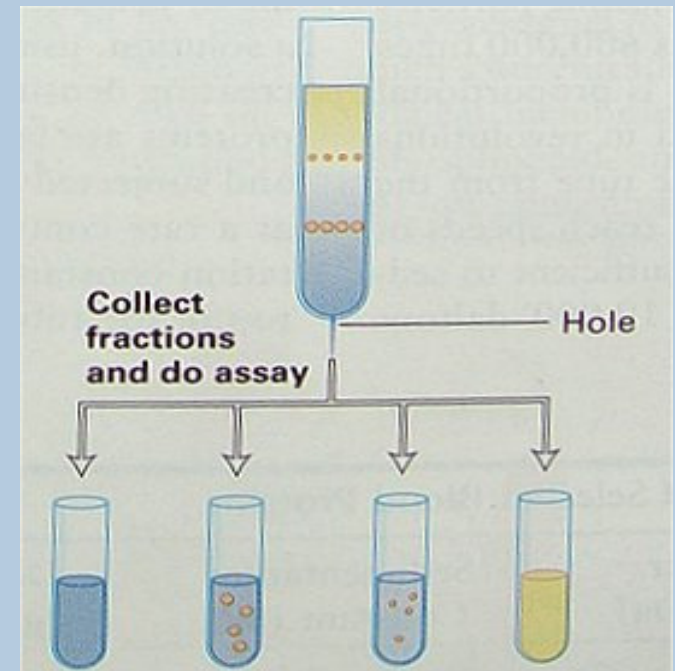
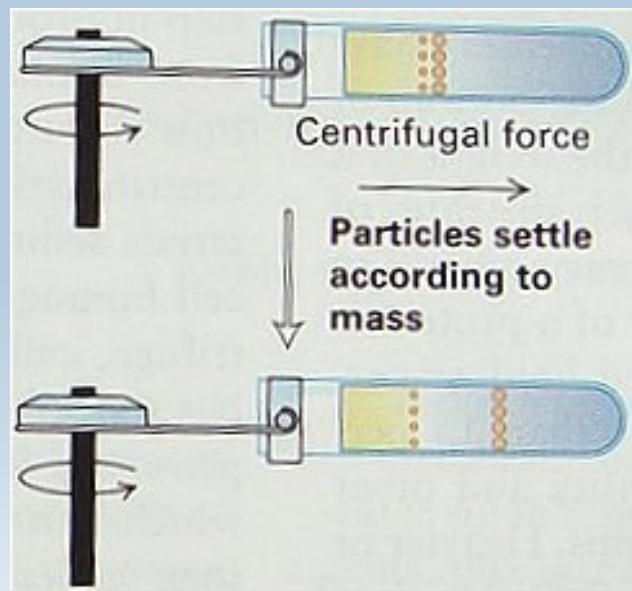
How tools development push Life Science Progress

Fundamental knowledge play a key role

Separate organelles of cells by centrifugation

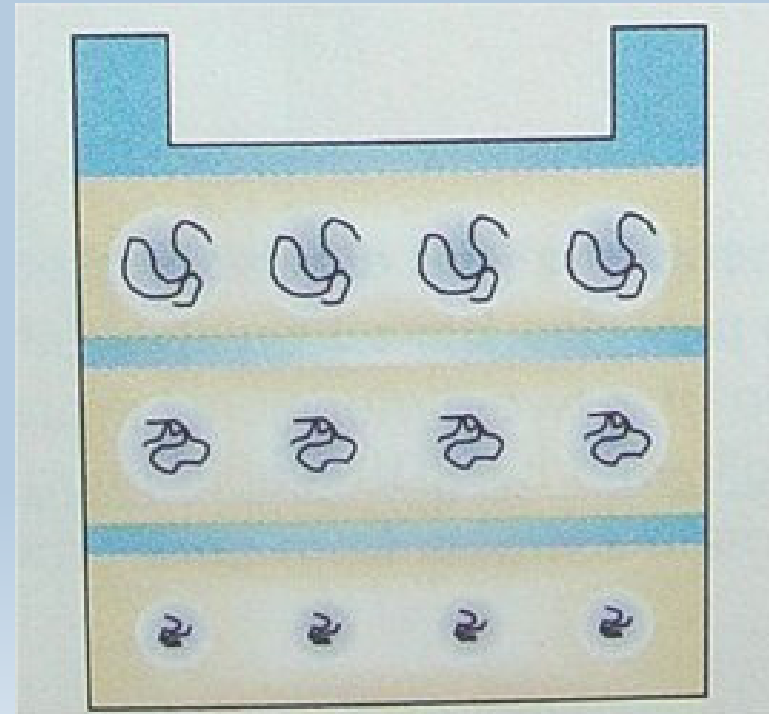
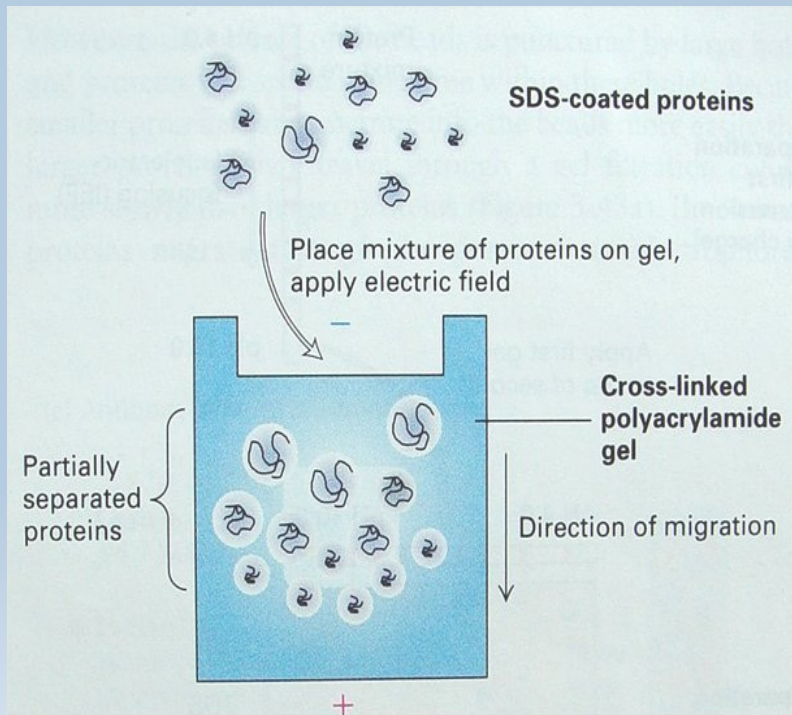


Drift velocity \sim centrifugal force



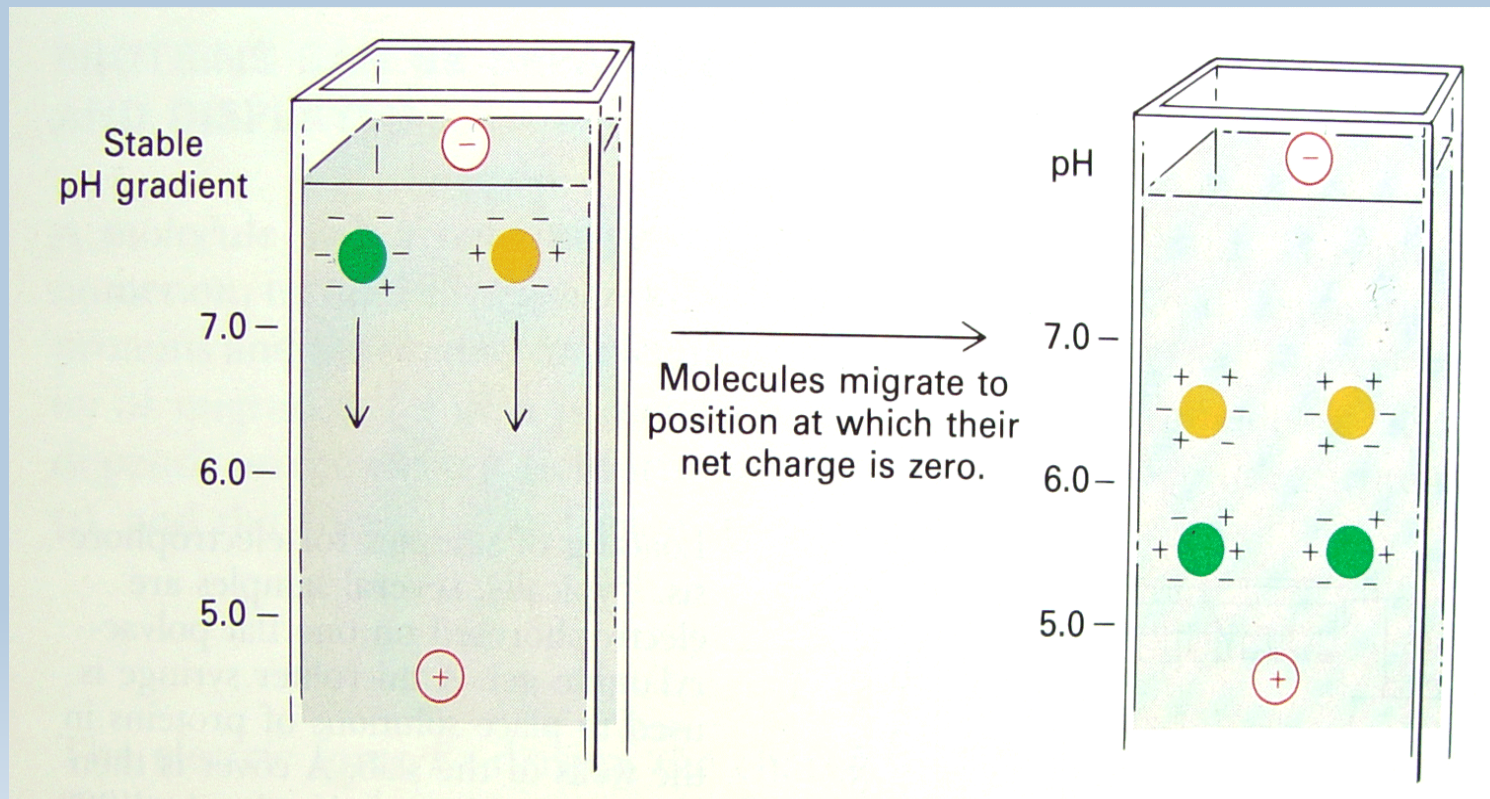
Separate Protein/DNA/RNA by gel/isoelectric point electrophoresis

Gel Electrophoresis

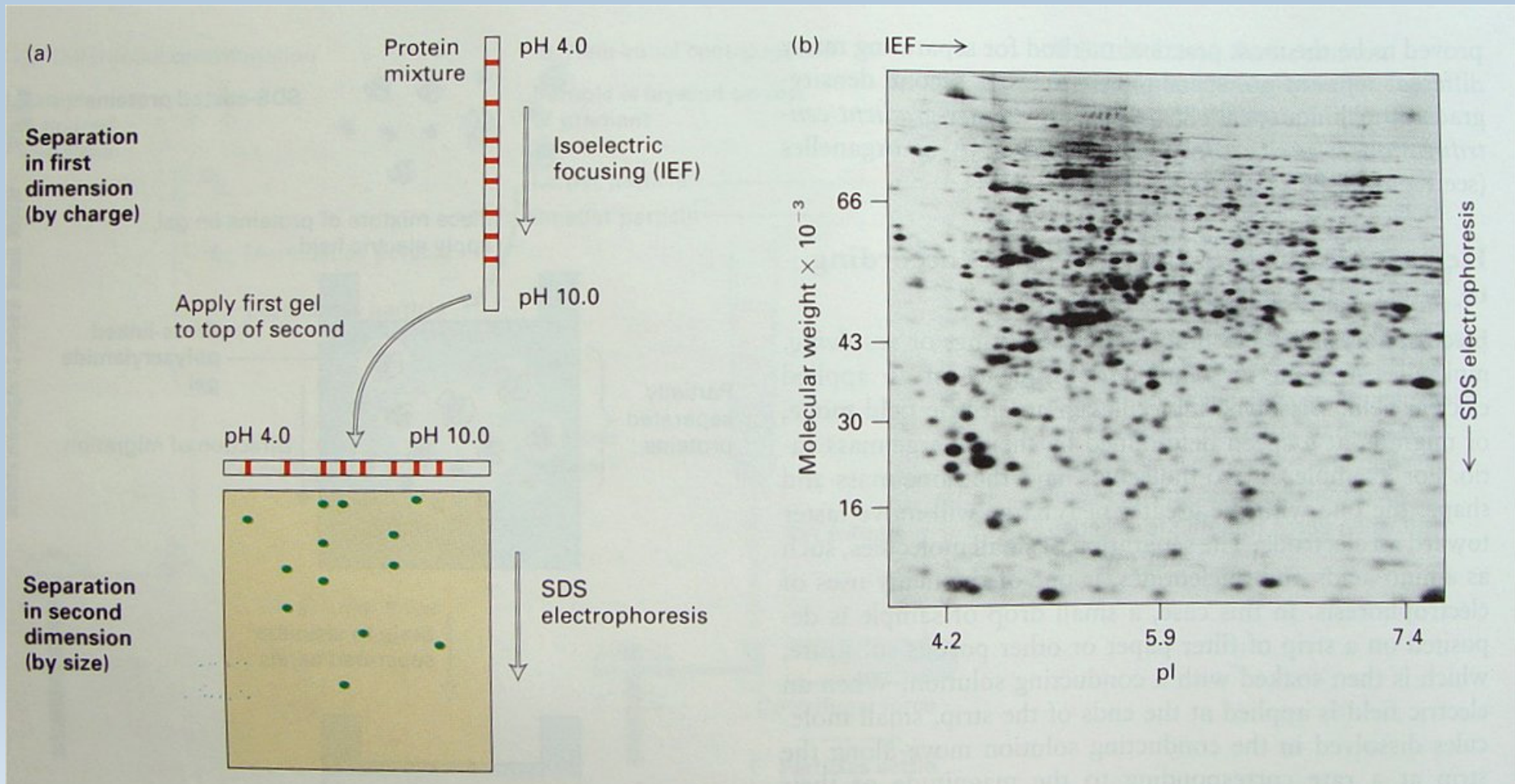


Isoelectropoint

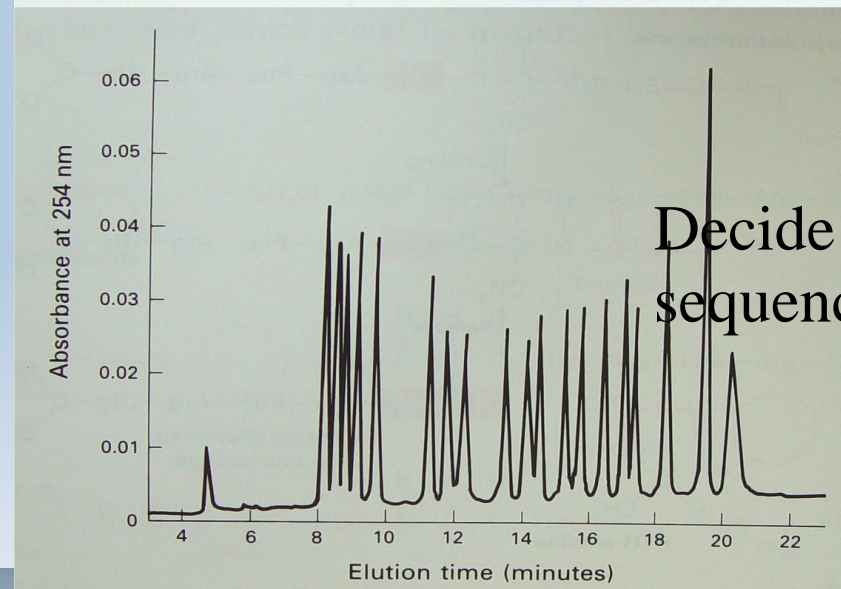
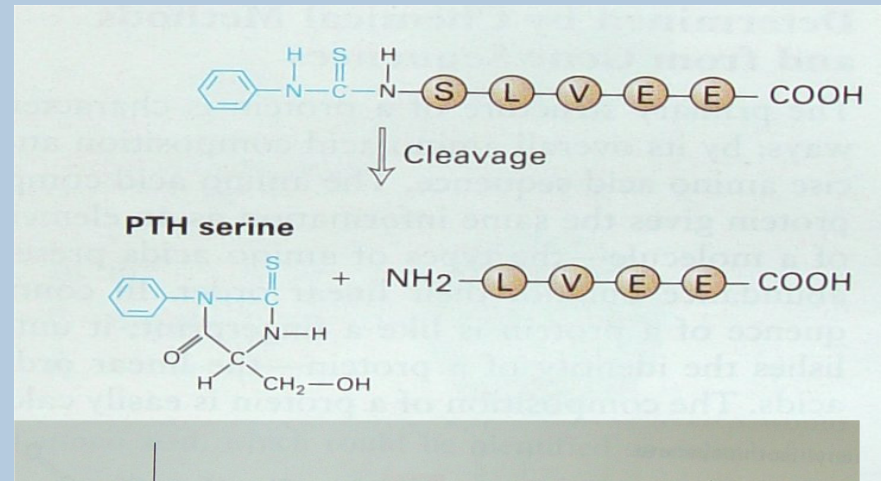
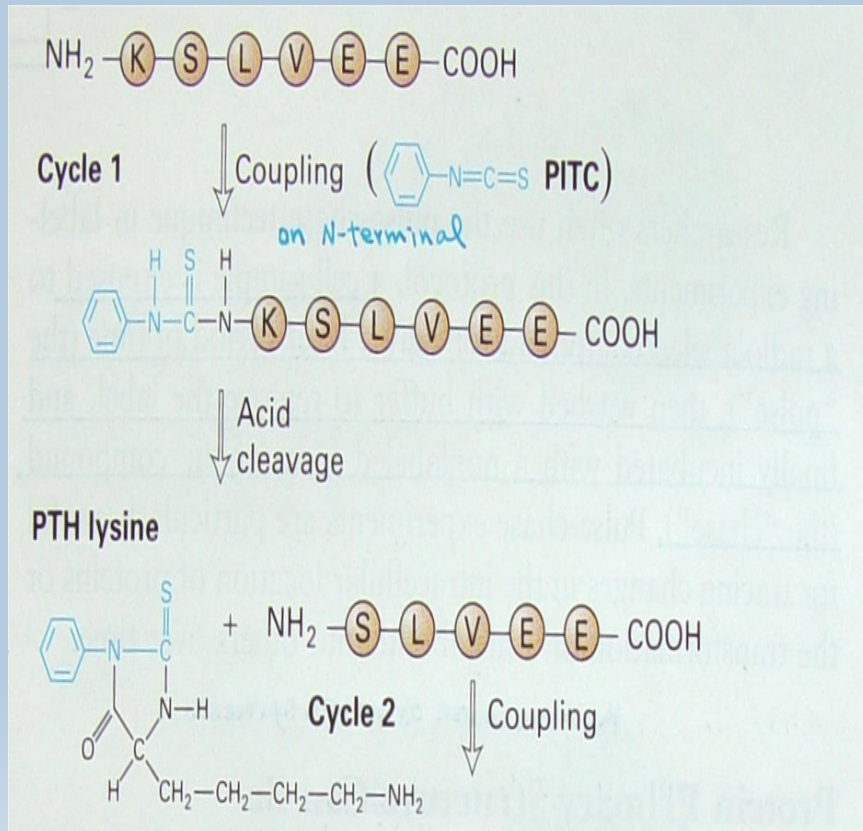
Amino acid carry different charge at different pH value



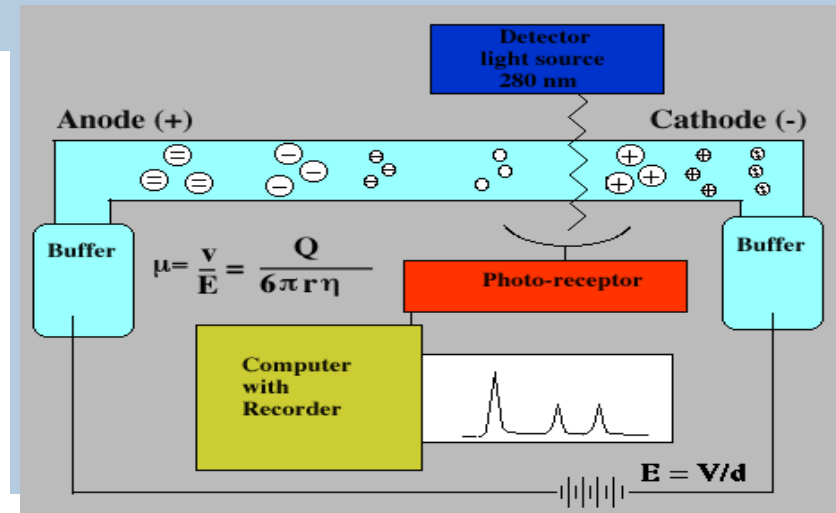
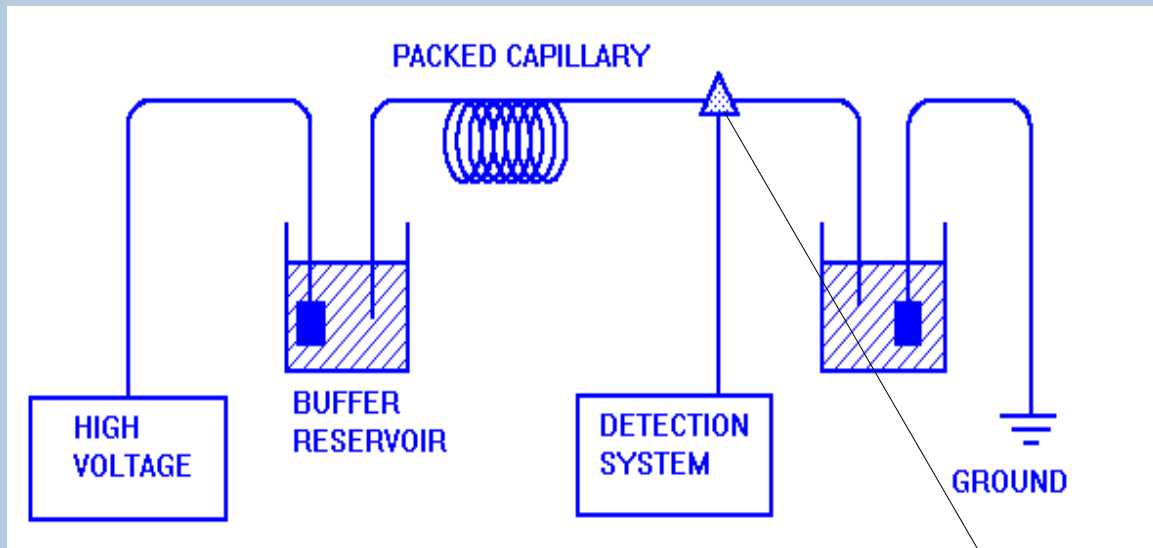
Combine gel electrophoresis and isoelectropint >> 2D electrophoresis



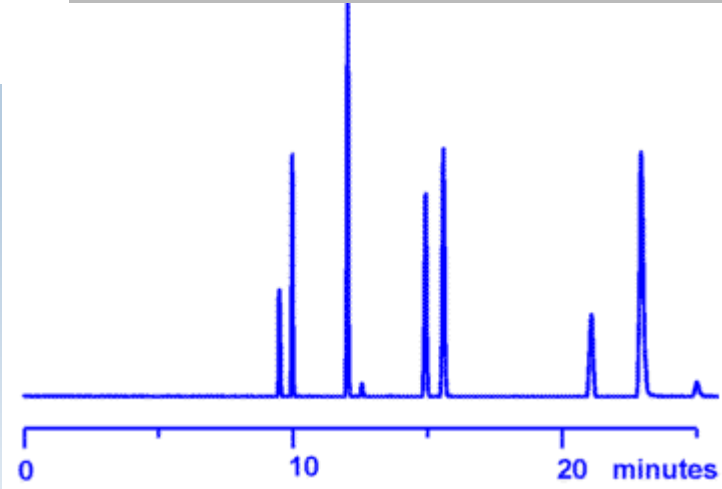
Find protein sequence by Chemical degradation and CE



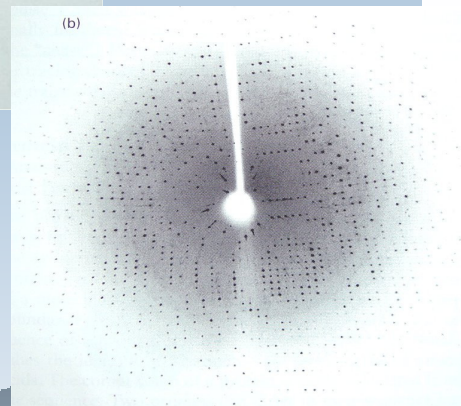
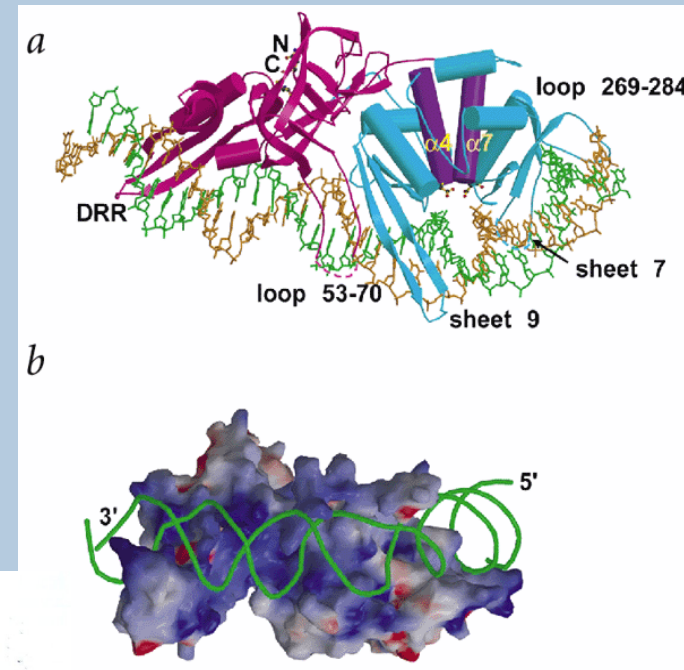
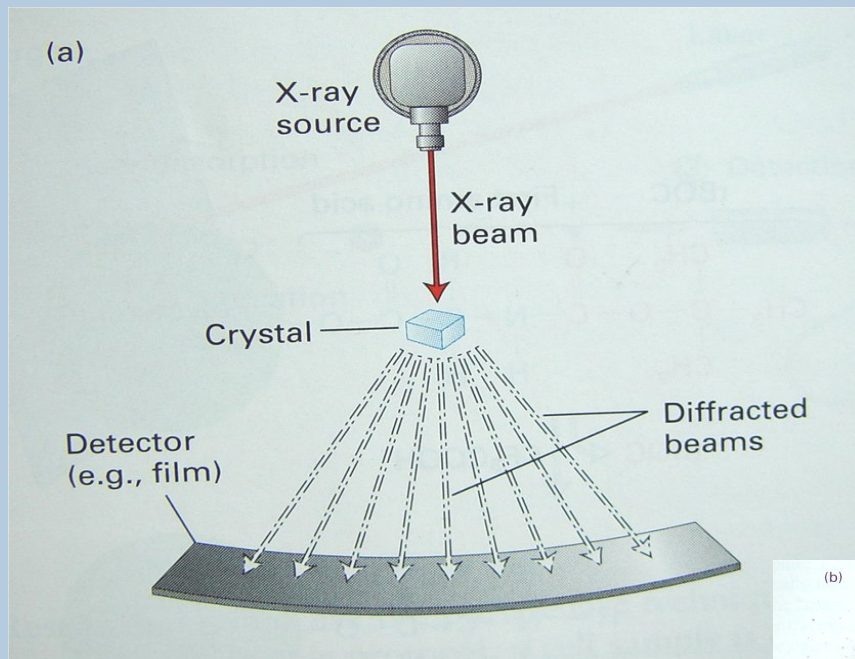
DNA/RNA/Protein separation/sequence by capillary electrophoresis



Fluid dynamics help us to design and analyze gathering data



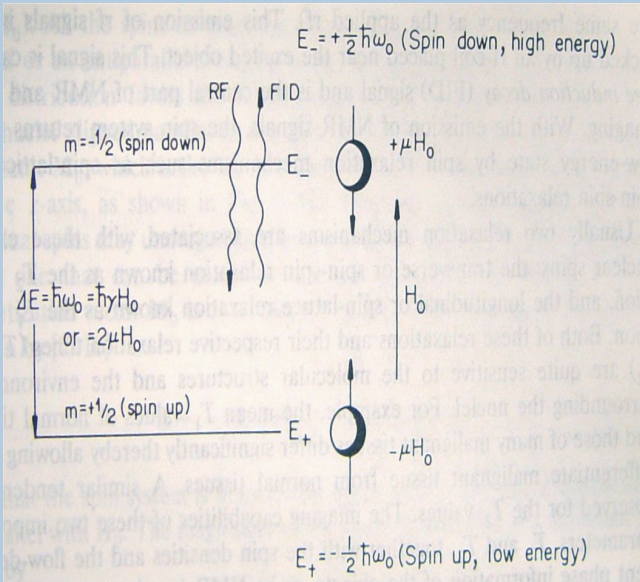
Solve DNA/Protein structure by X-Ray Crystallography



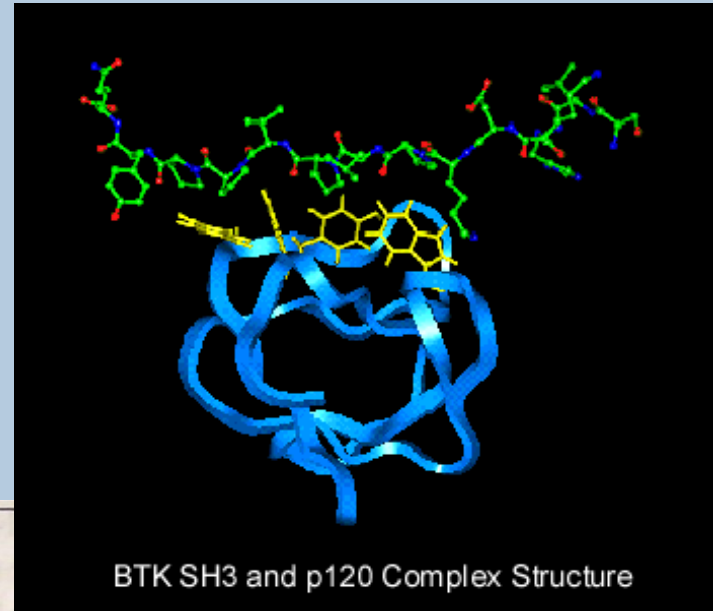
Fouriers Transform
to get structure information

Diffraction point
collection

Inspect protein structure by nuclear magnetic resonance (NMR)

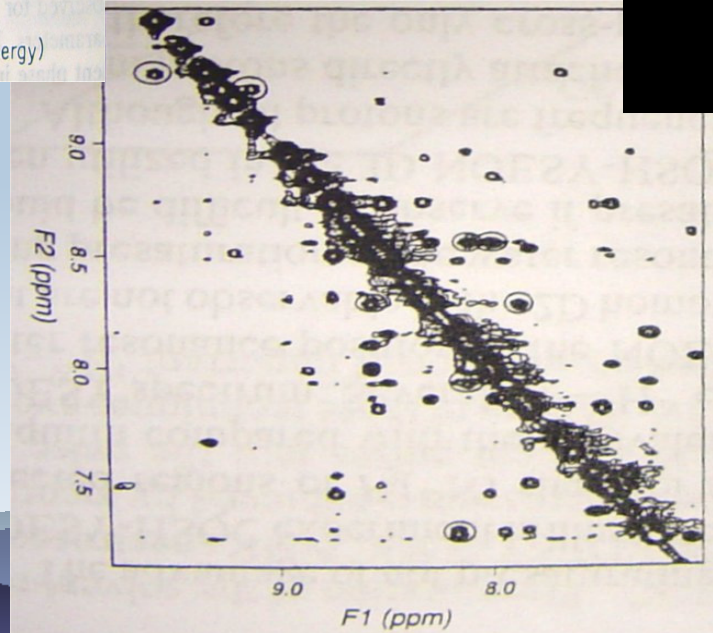


Magnetic resonance
Momentum precision



BTK SH3 and p120 Complex Structure

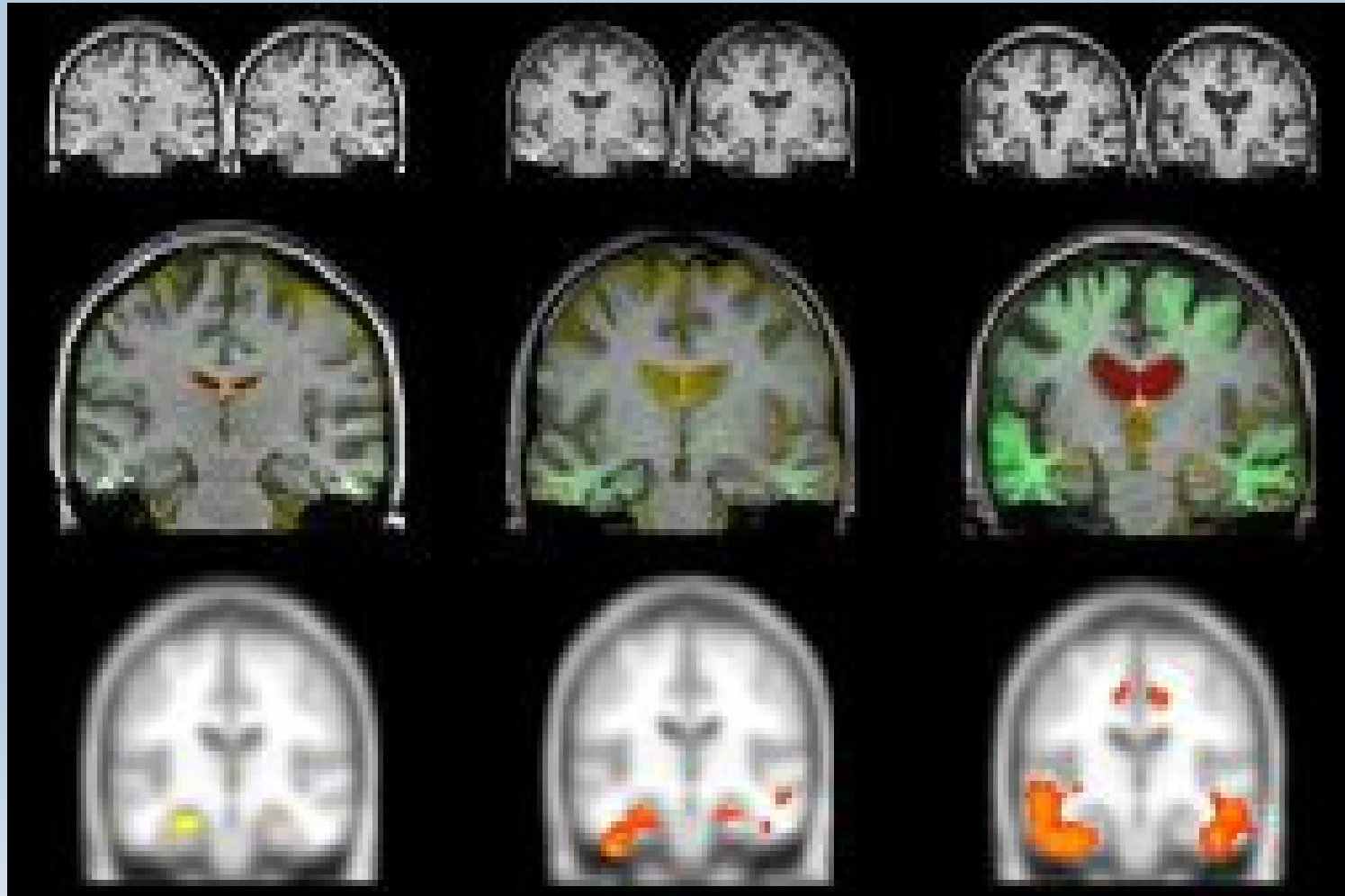
2D Fourier Transform



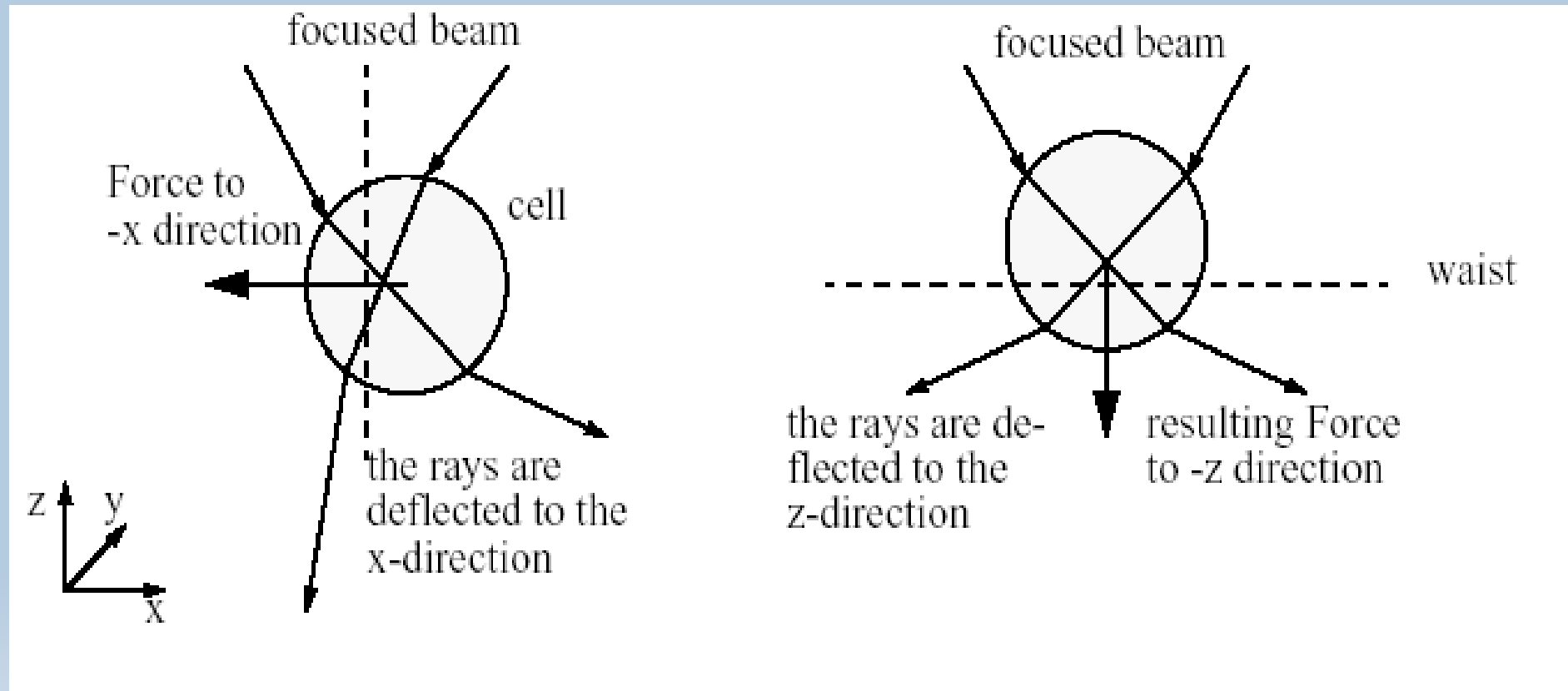
Decide molecule structure

(<http://tel.life.nthu.edu.tw/>)

Medical application

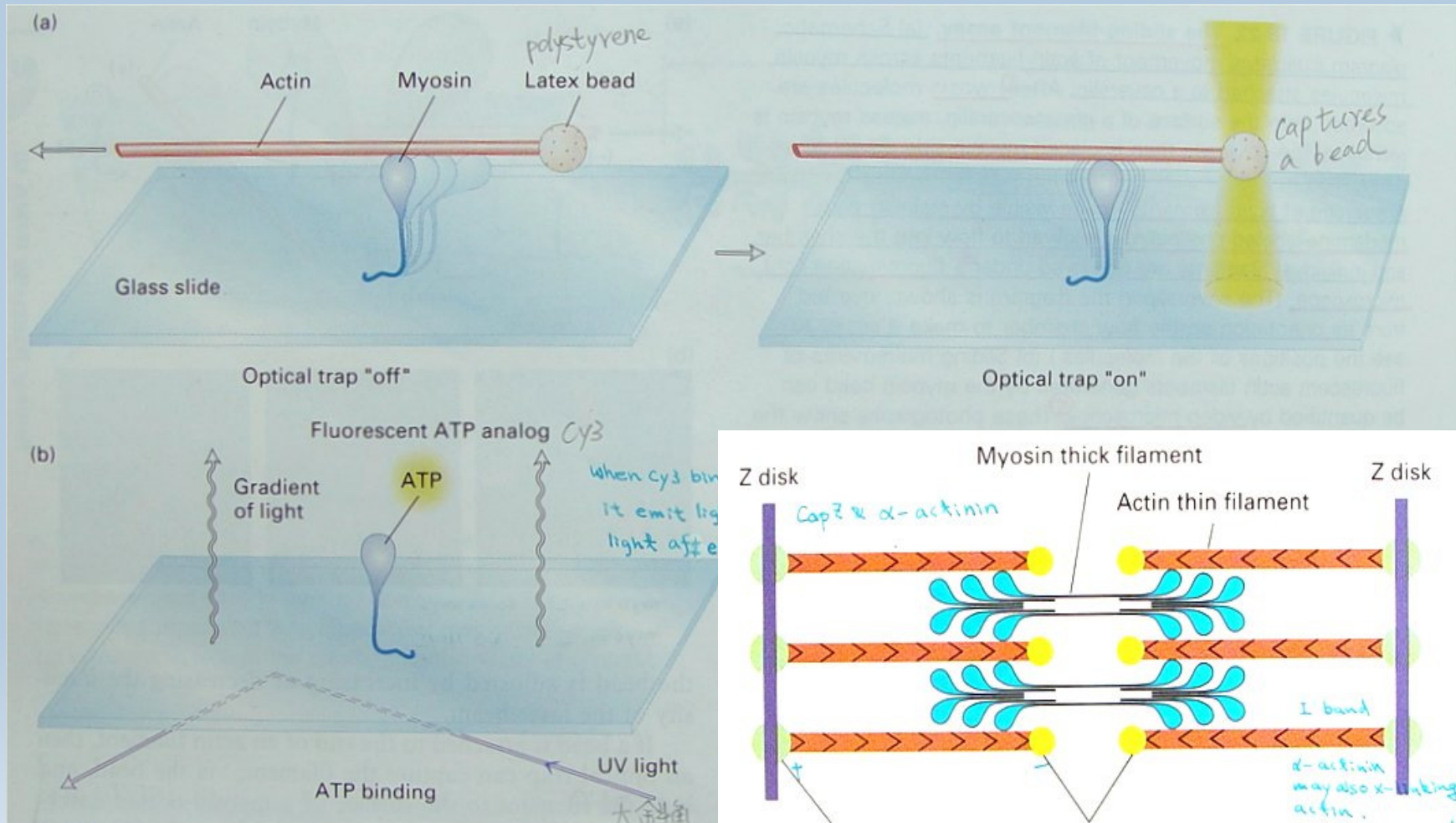


Study molecule dynamic behavior by LASER Trapping/Twizer

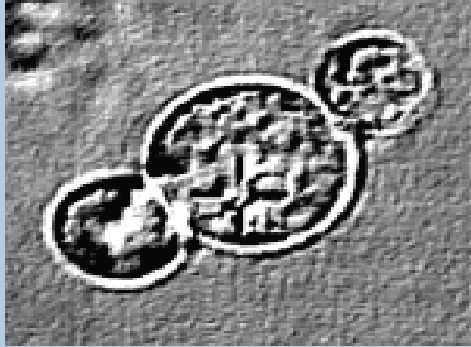


<http://www.phys.umu.se/laser/tweezer1.htm>

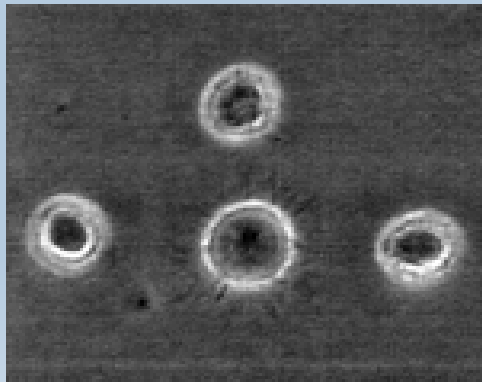
Use Laser trapping to measure kinetics



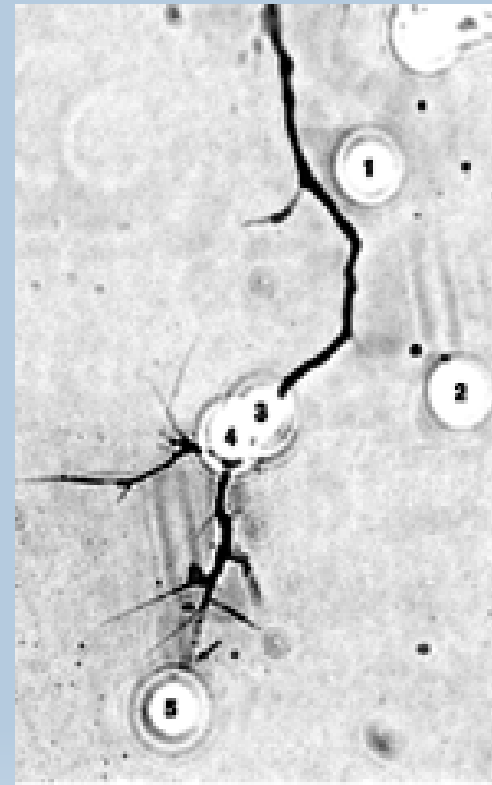
Use Laser trapping to manipulate cells



Select different cells to contact with each other

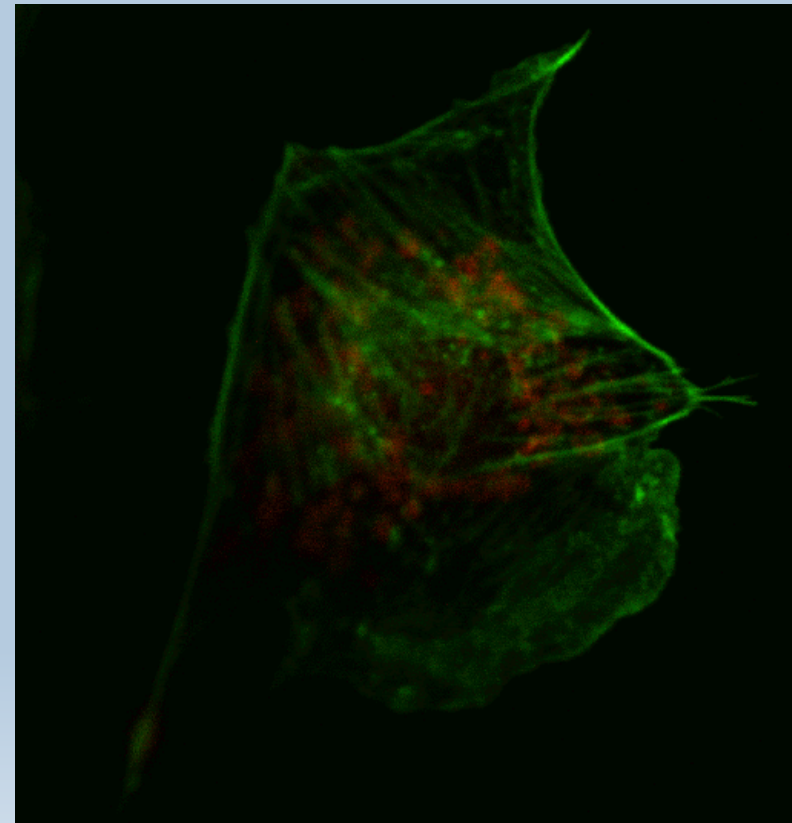
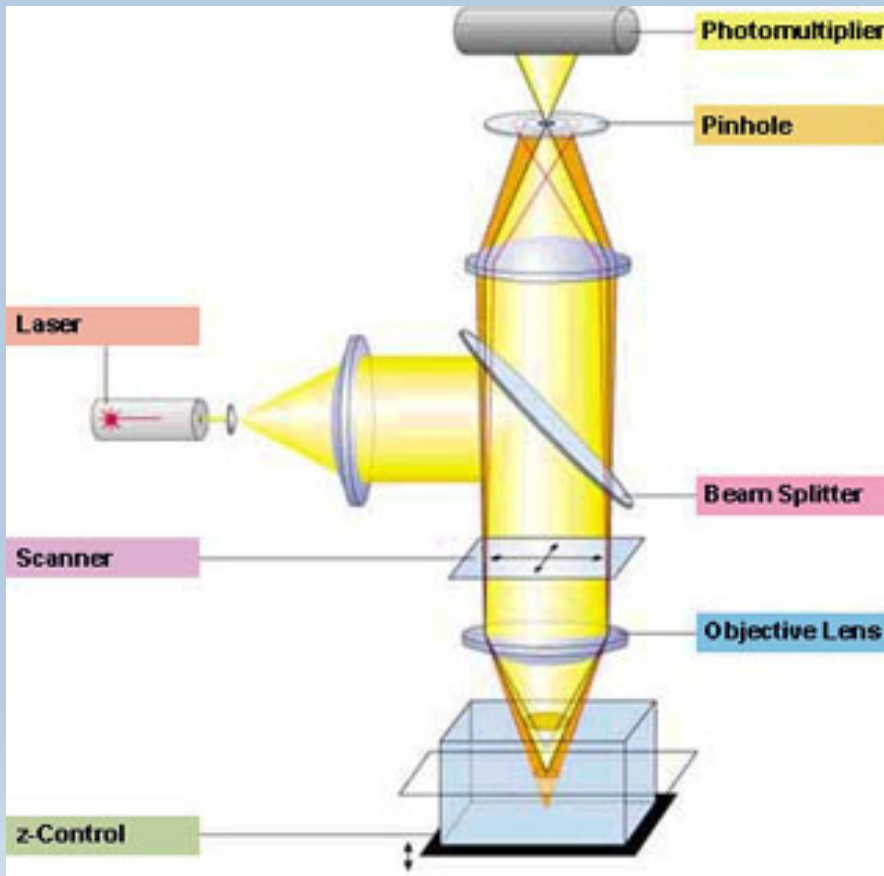


Arrange neuron in a special pattern



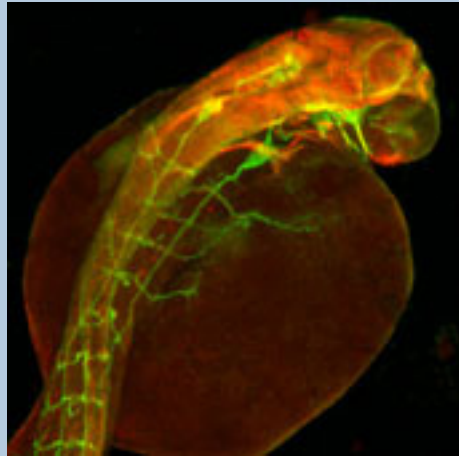
Axon growth guiding

Explore cell structure by confocal microscope

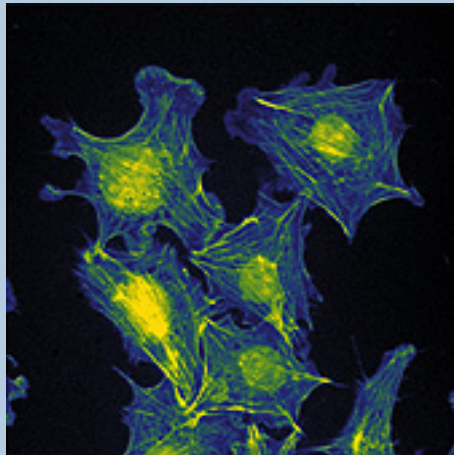


Green -- F-actin
Red -- mitochondria

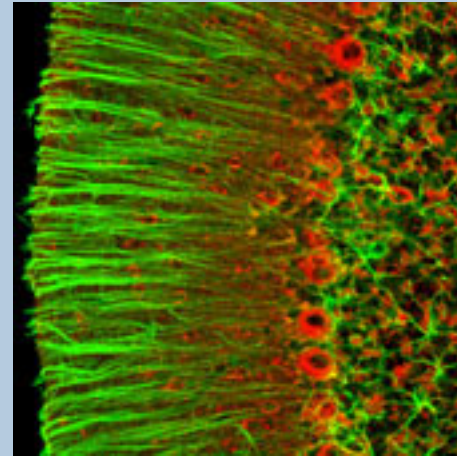
3D molecule label



Zebrafish embryo, wholemount, neurons (green), cell adhesion molecule (NCAM, red), (Monika Marks, Martin Bastmeyer, University of Konstanz)

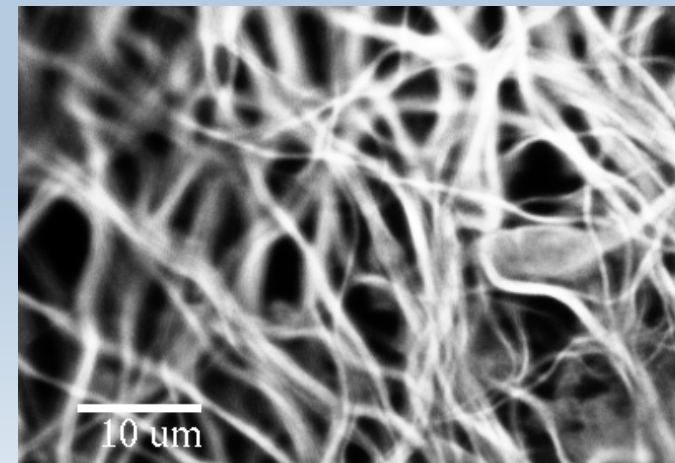
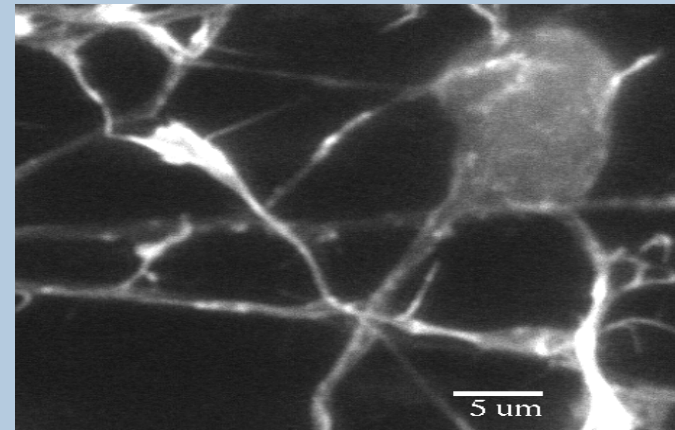
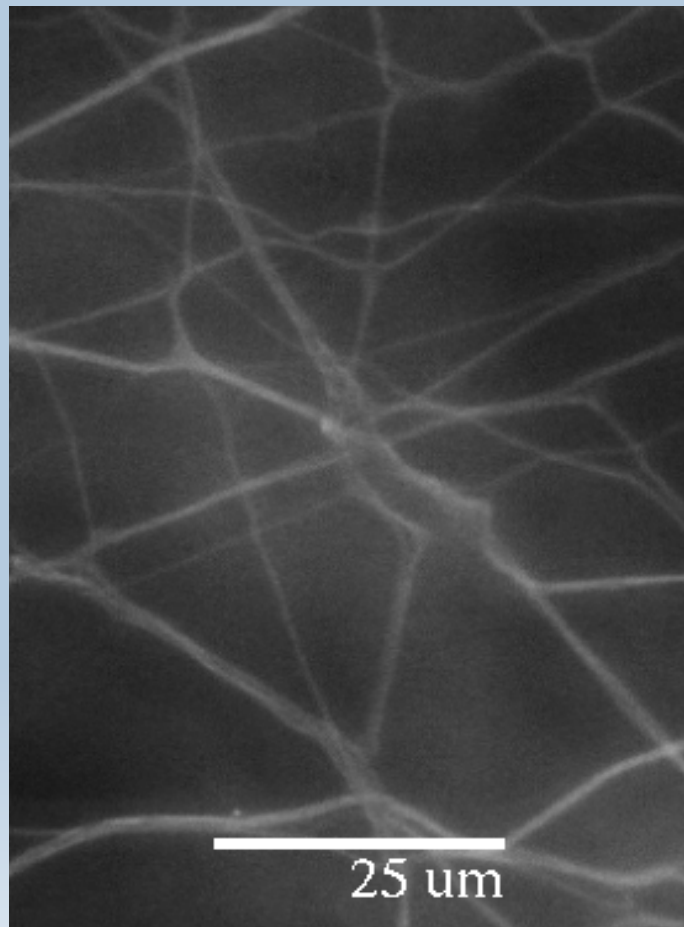


Mouse fibroblasts, cytoskeleton structures (Dr. Iwig, University of Halle)



Rat cerebellum fluorescent staining of astrocyts (green), and Mn superoxide dismutase (red), (Jörg Lindenau, University of Magdeburg)

*Understand neuronal connection
by confocal microscope*



More detailed inspection by electron optics

Transmission Electron Microscope

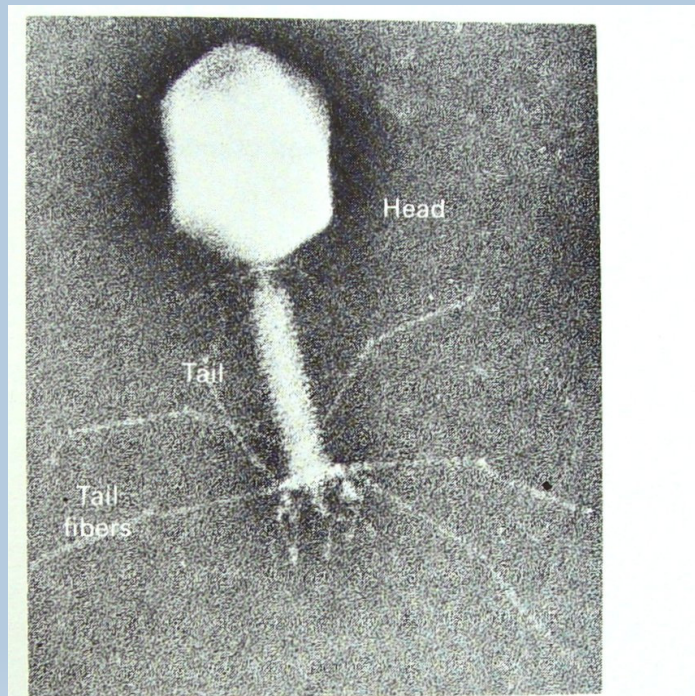
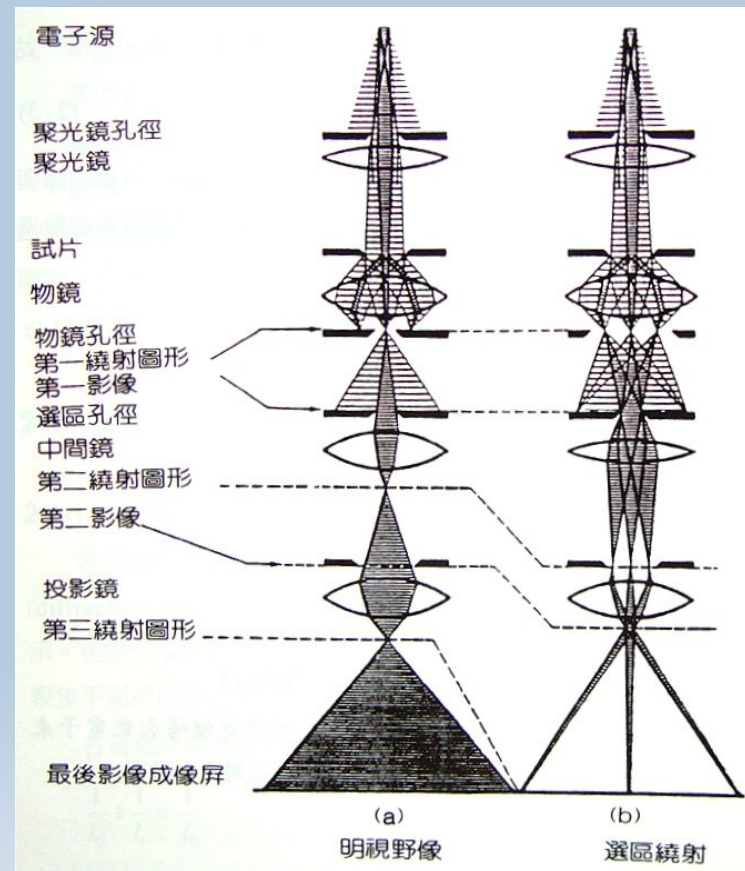


Figure 34-10
Electron micrograph of a T4 phage.



Scanning electron microscope

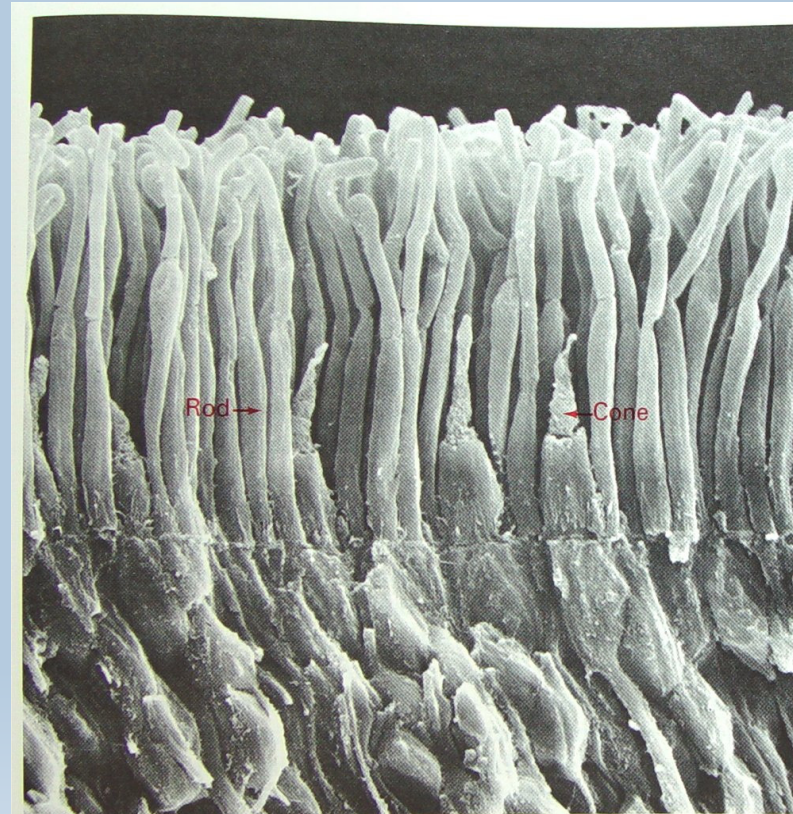
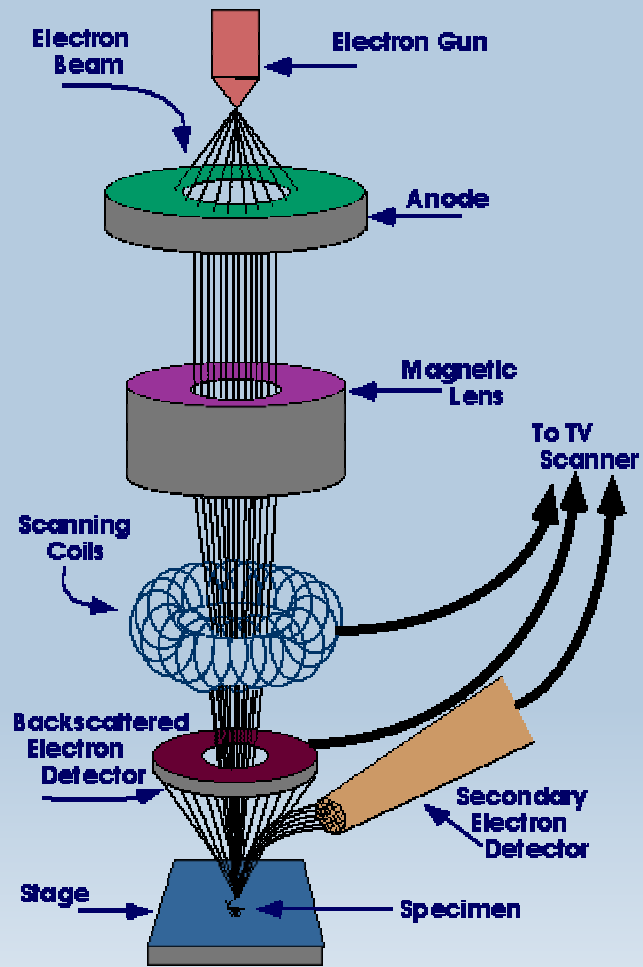
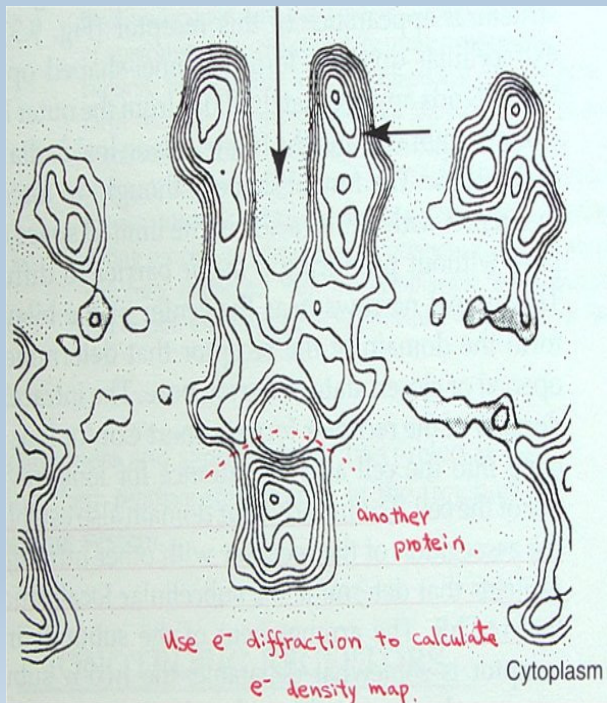
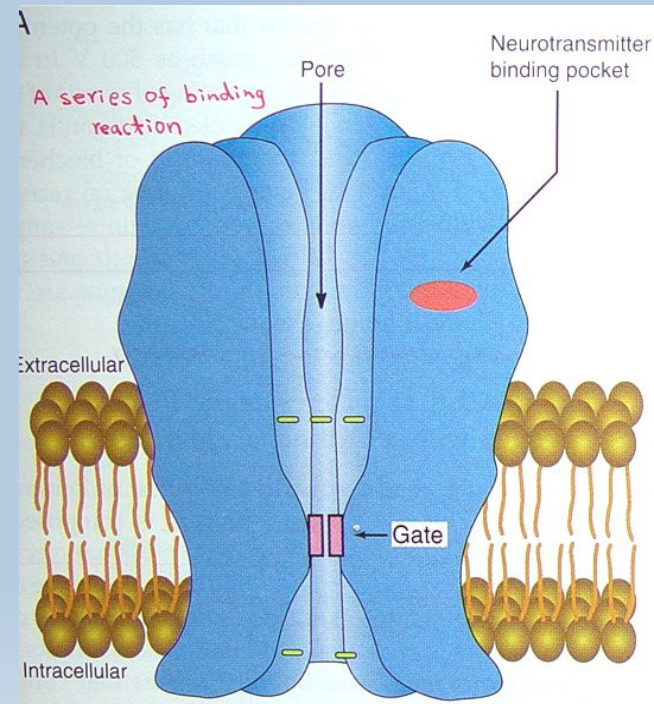


Photo receptor

Electron diffraction can solve protein structure under 2D crystal



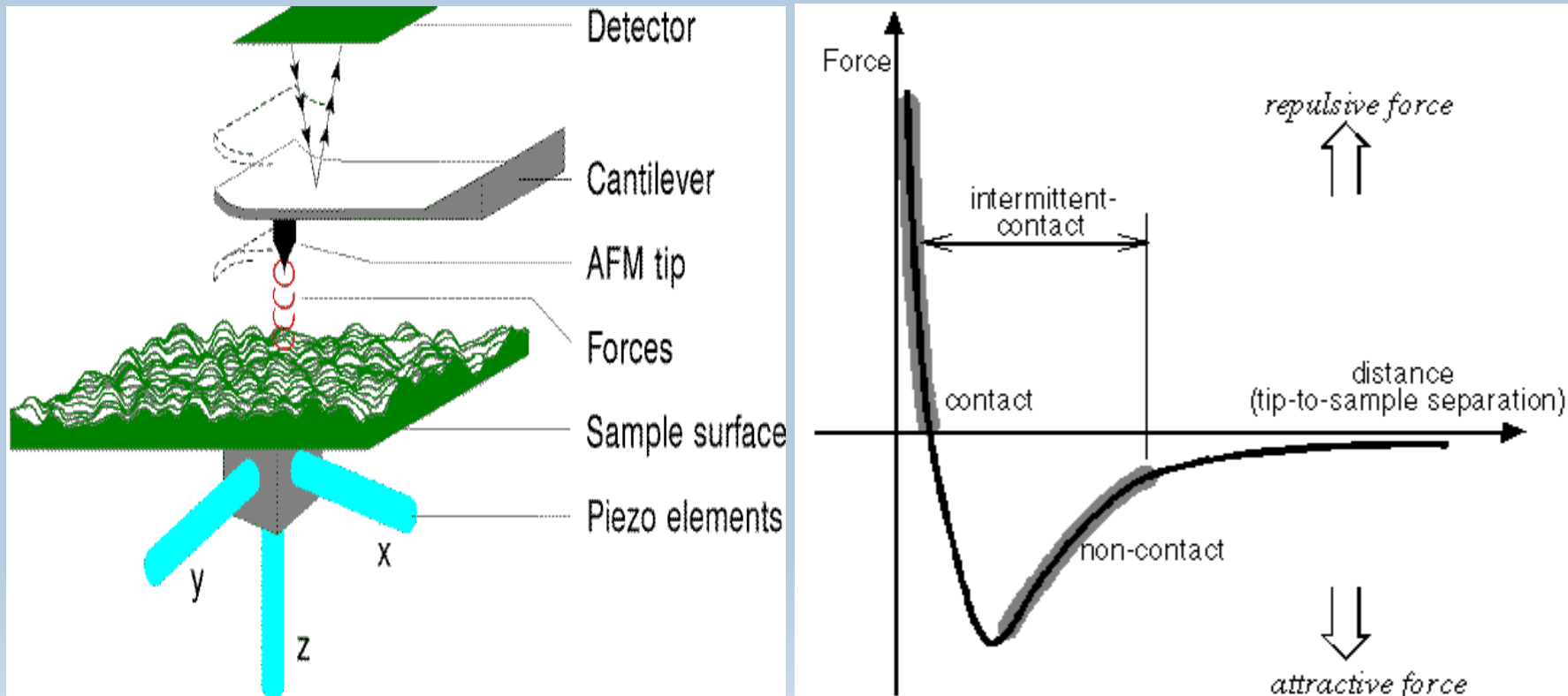
Electron density map



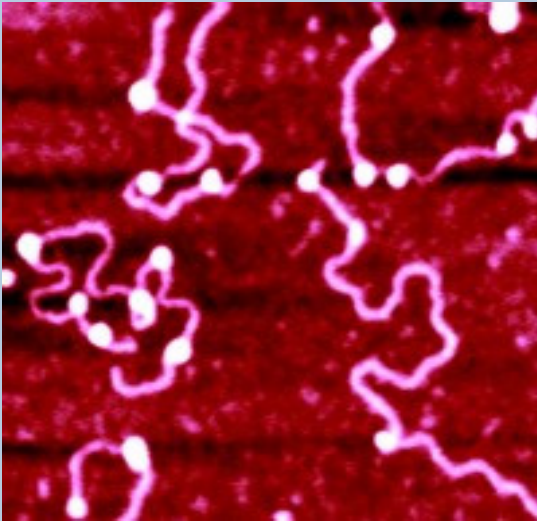
Ion channel model

Scanning Microscope

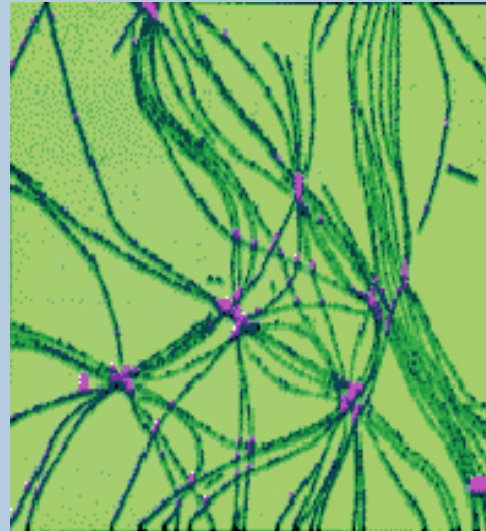
Atomic Force, Scanning Probe, Magnetic force, Scanning tunneling microscope



Use AFM to inspect from μm ~ nm scale

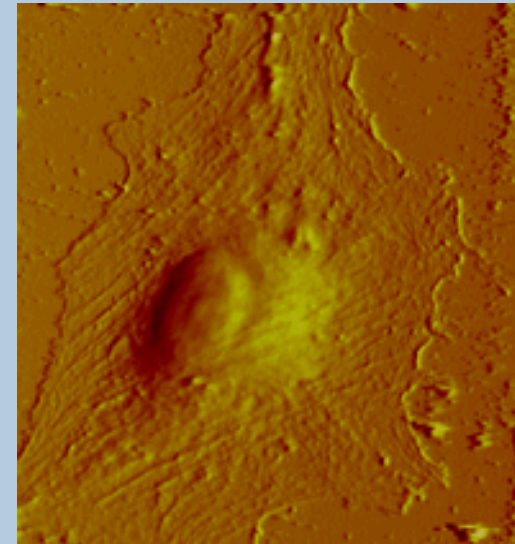


Nucleosomal DNA



Actin Filaments

Actin is an important component of contractile myofibrils in skeletal muscle and the cytoskeleton of all animal cells



Living Xenopus
Glial Cell

Fr : www.di.com

Use AFM to analyze antibody/antigen binding

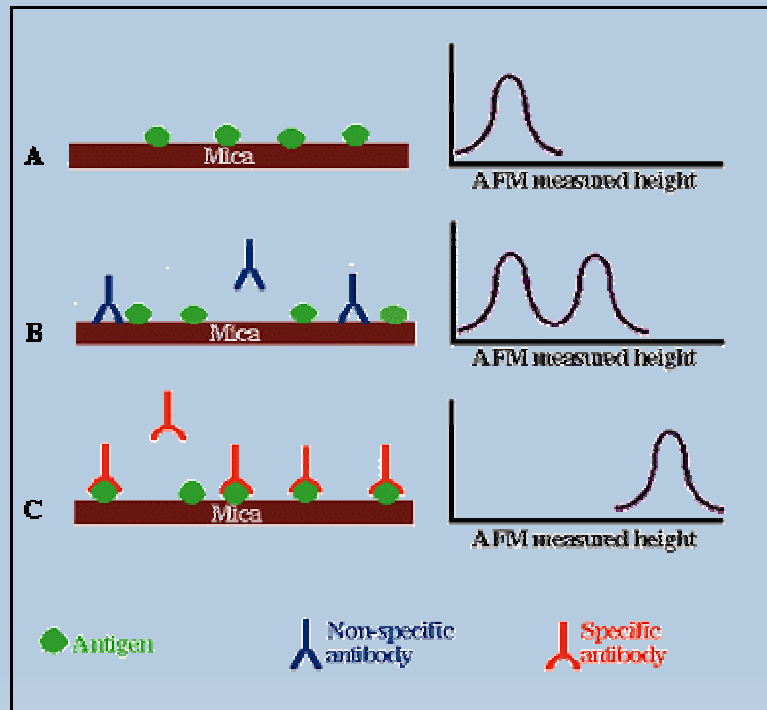
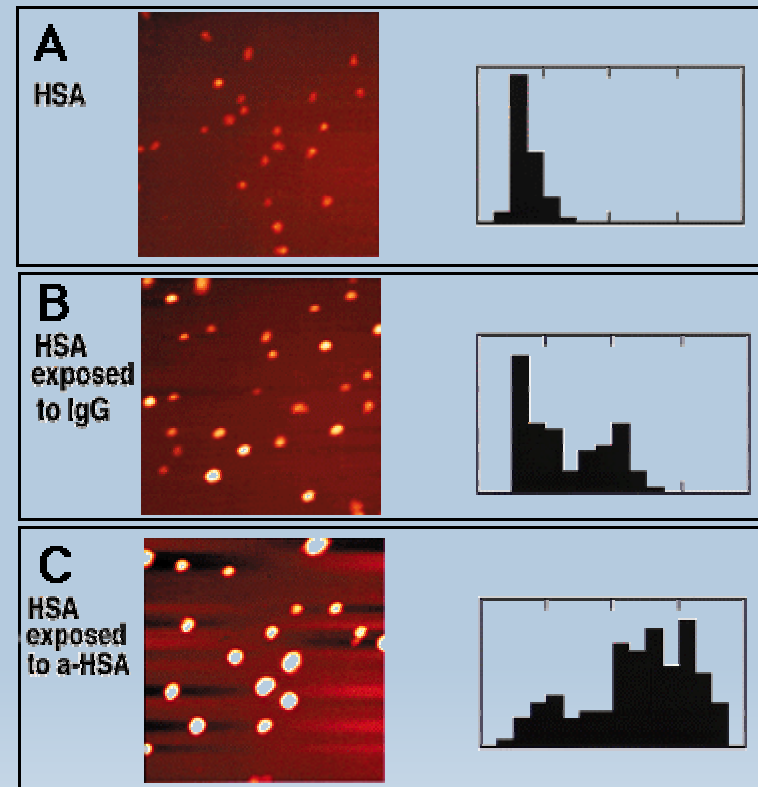
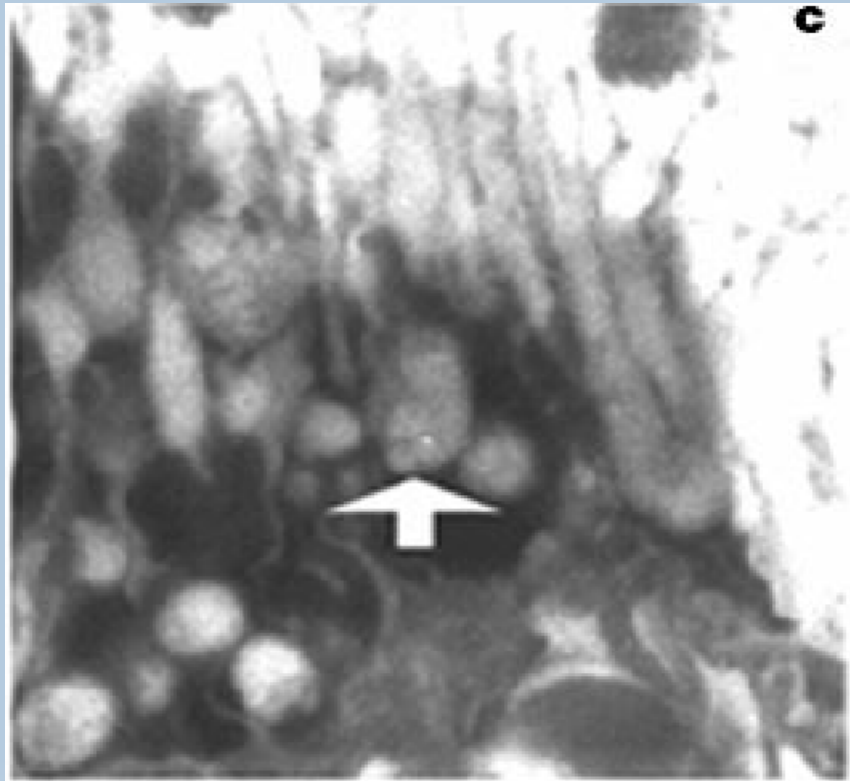


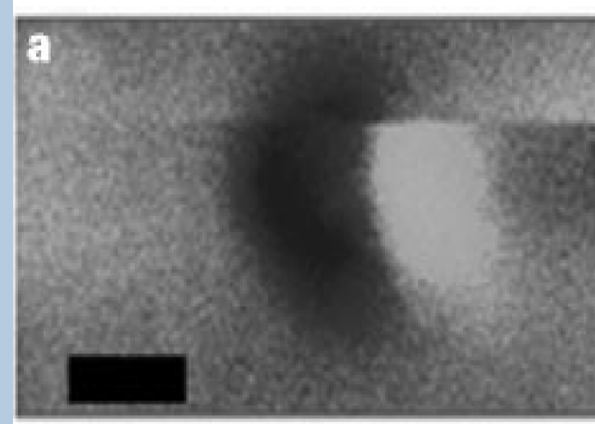
Figure 1: Experimental concept of using AFM to monitor antibody-antigen interaction. (See text for details.)



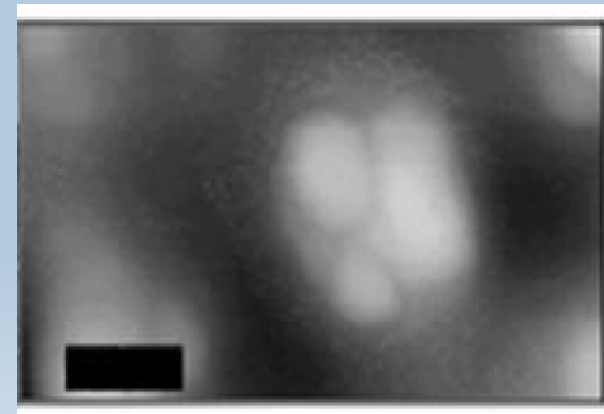
Use MFM to identify biomagnetics



CLSM image

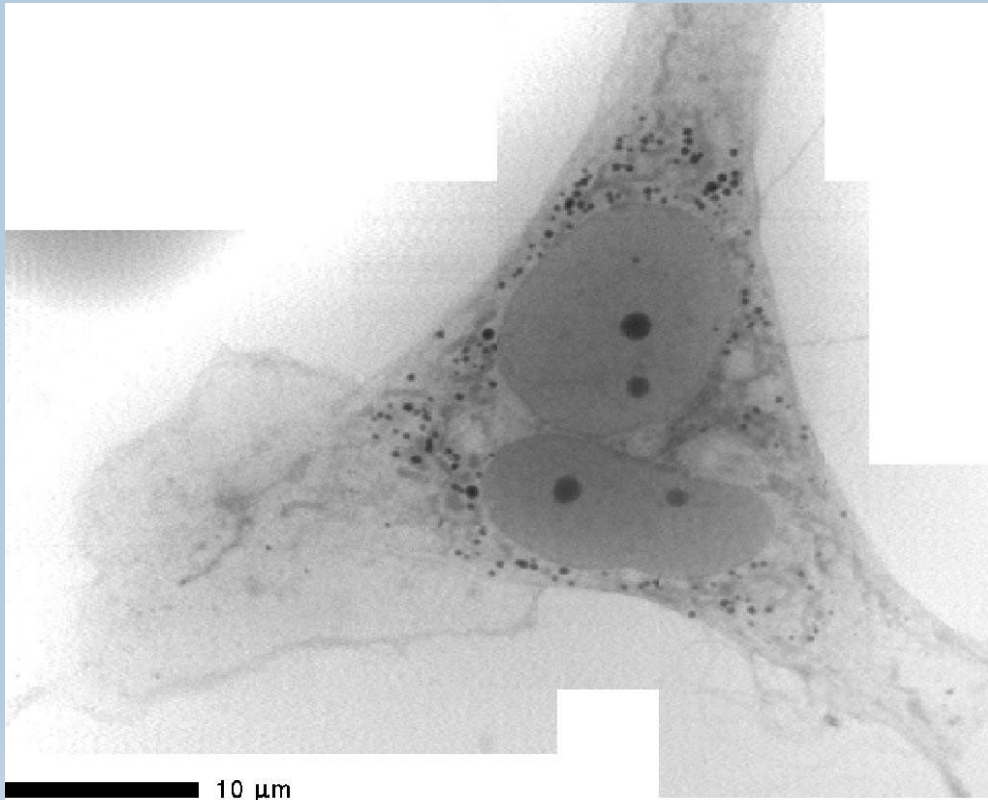


MFM image

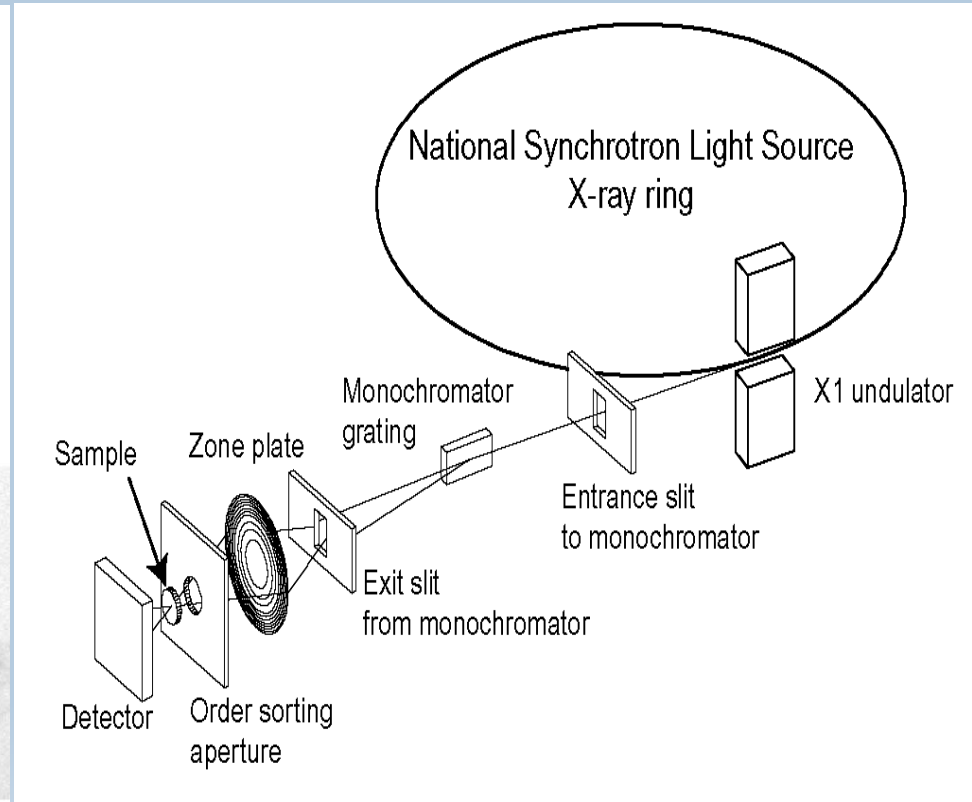


AFM image

X-Ray Microscope



wet, glutaraldehyde-fixed chick
embryo skin tissue fibroblasts



X-ray optics and microscopy
at Stony Brook

Comment

- When a new tool develop, life science then jump a step.
- All tool development strongly rely on basic physical / chemical knowledge
- You must know how life scientist play their game, their language, then you can perfound know their need.

How do fundamental knowledges be applied in biological problem study

- Mathematics and computer science
 - Statistics -- general tools in biology. Since all data need statistical process to make them meaningful.
 - Fouriers Transform – noise reduction, information extraction.
 - Differential equation & difference equation – behavior analysis, kinetic study.
 - Model simulation & numerical analysis – experimental data analysis.
 -etc

◆ Physics

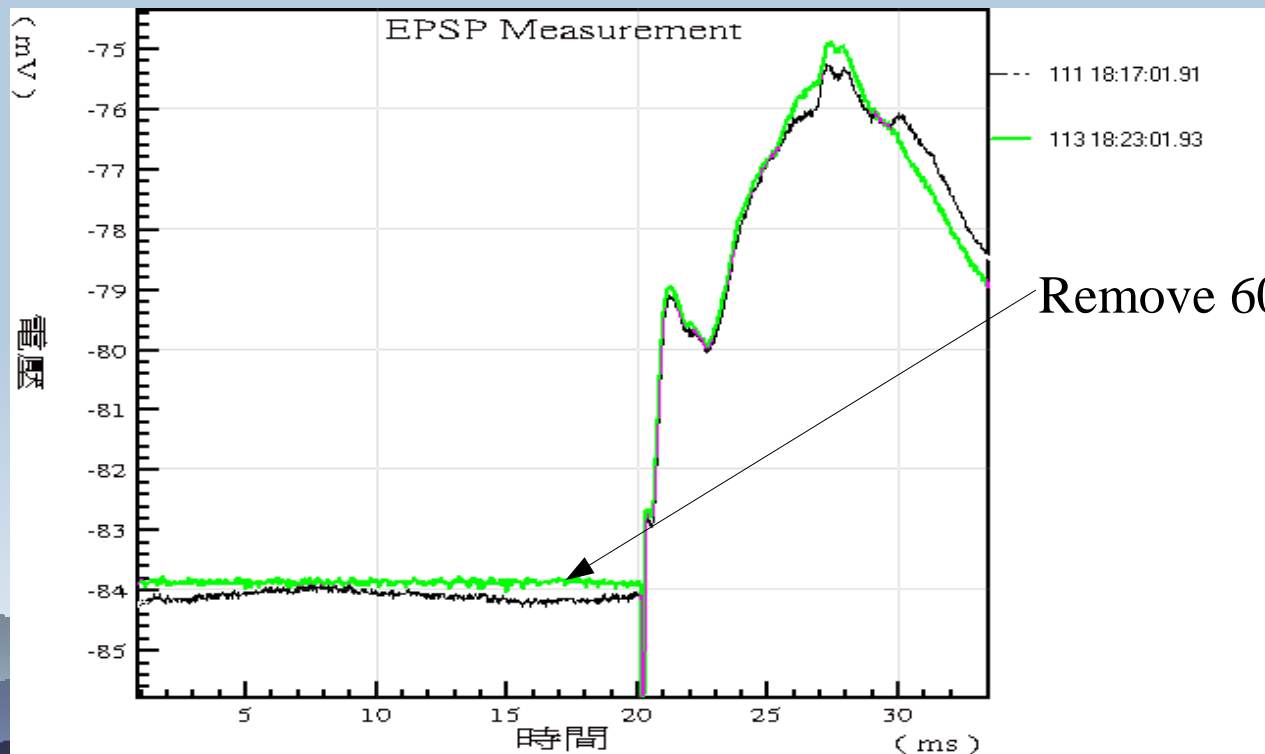
- ◆ Thermal dynamics – chemical process, transport analysis, cell behavior, tool design
- ◆ Electronics – experimental design, instrument like biosensor, MEMs
- ◆ Wave, spectrum, optics & Quantum physics – molecular structure analysis, signal transduction, cell behavior study.
- ◆ Mechanics – biological mechanics like sport training, supporting analysis.

▶ Chemistry

- ▶ Organics – molecule like DNA, protein, drug design, analysis, biosensor design.
- ▶ Instrument analysis – chemical process, protein, DNA, RNA, purification, separation.

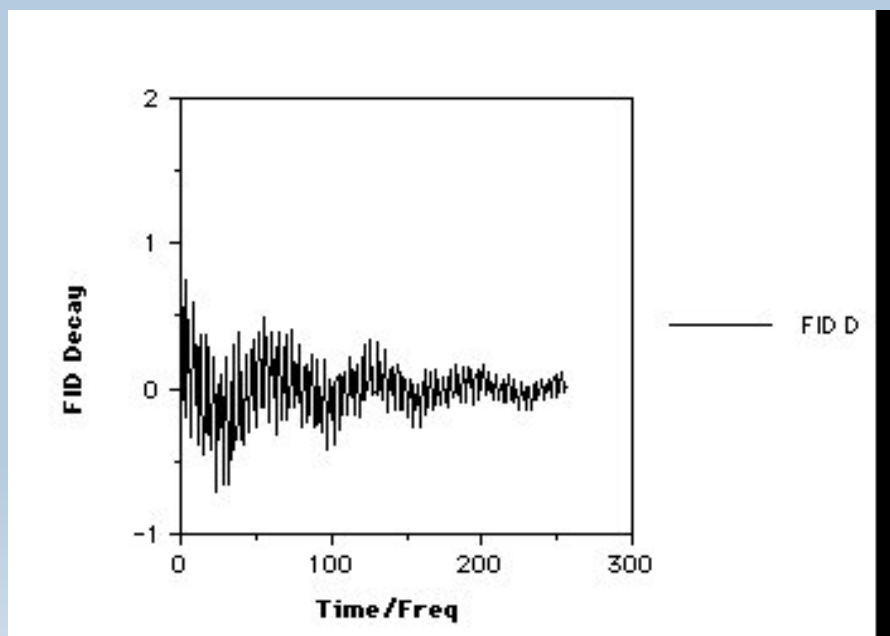
Mathematics always provide a powerful analytical tools

- Since the concept of **complete set theory**, we can reduce inspection noise, filter what's we want, or space transform with the assistance of computer, or electronic circuit.

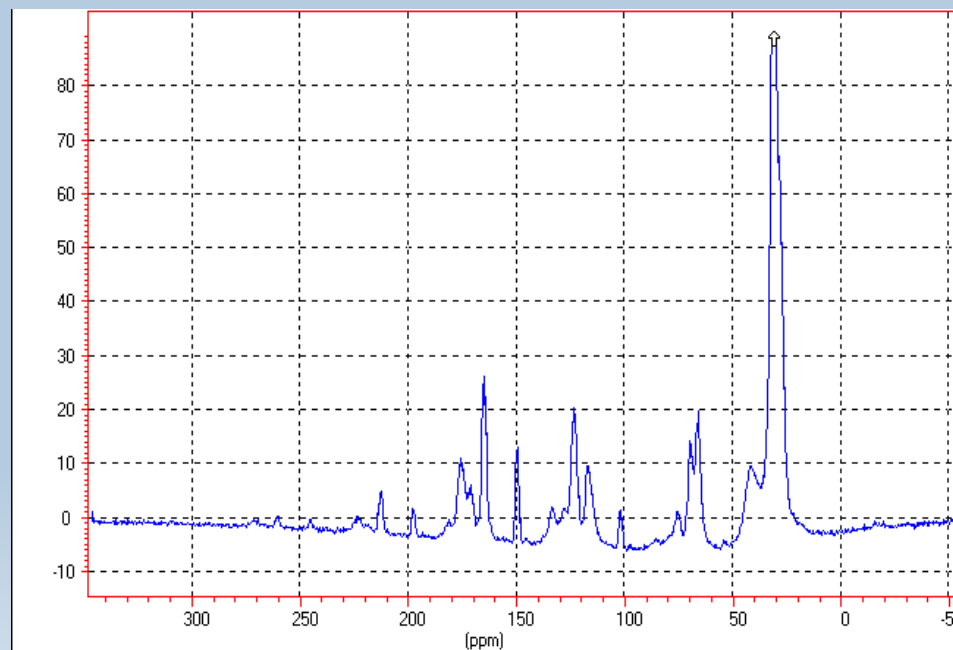


From Quantum mechanics, we know that each proton has its resonance frequency since different ambient

Use Fourier Transform, we can separate the oscillation of each proton



NMR free induction decay

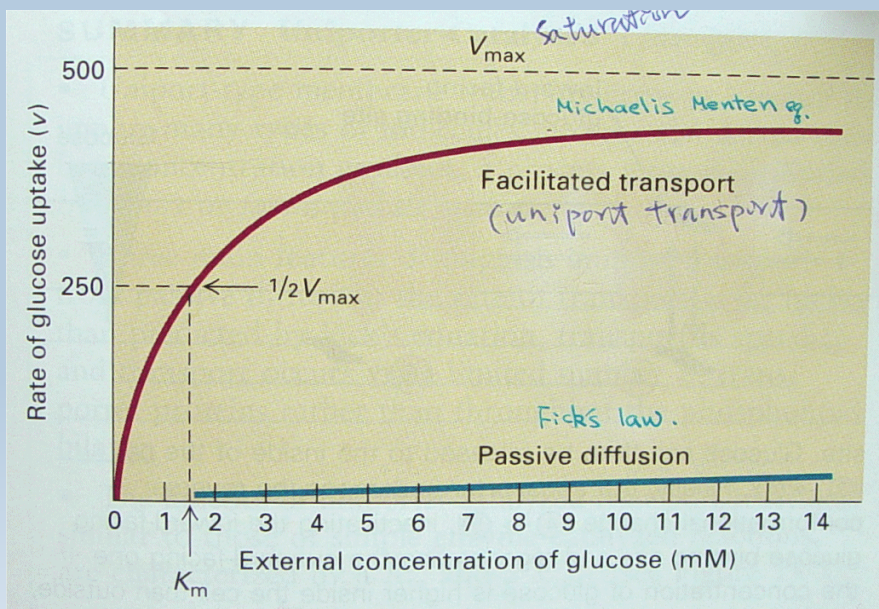


NMR 1D spectrum

Biological model base on physics / chemical kinetics

Biological model can help us to understand or explain your experimental data.

Transport across cell membrane



Passive diffusion

$$J_x = -D \frac{\partial C}{\partial x} = -D \frac{C_{outside} - C_{inside}}{\text{membrane nonpolar thickness}}$$

Facilitated transport (carrier transport)

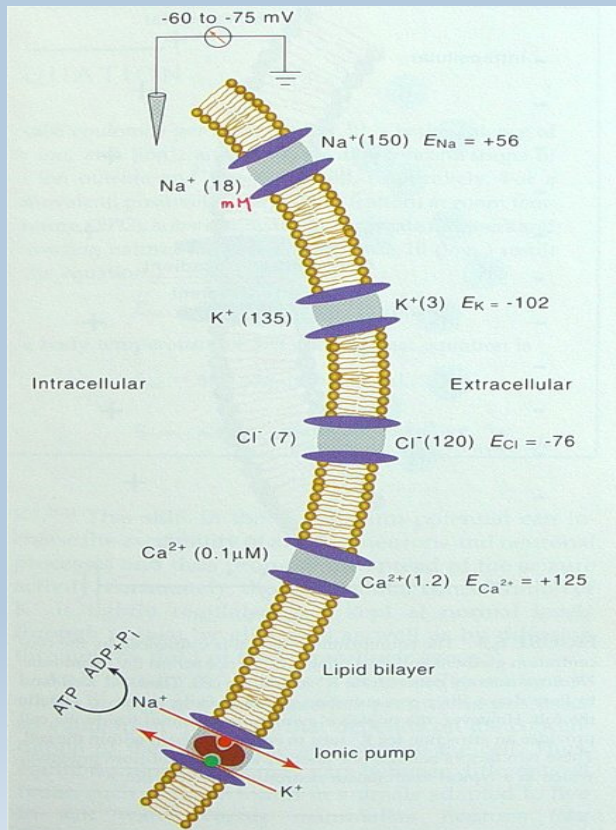
Enzyme reaction

$$J_x = \frac{V_{max}}{1 + \frac{K_m}{C}} \quad \begin{array}{l} K_m \text{ means substance-transport binding constant} \\ V_{max} \text{ means max. transport rate} \end{array}$$

Base on model analysis, and experimental data
We can judge if associated protein exist or not

How neuron send and process message

Use thermal dynamics to analyze how membrane potential create



From thermal dynamics

Diffusion force must balance with electrical field

$$E_{\text{ion}} = RT / zF \cdot \ln[\text{ion}]_o / [\text{ion}]_i.$$

When multi ions exist, the meta state is membrane potential keep constant but ion still flow with net flow charge flow = 0

$$V_m = RT / F \cdot \ln\left\{ \frac{p_K [K^+]_o + p_{Na} [Na^+]_o + p_{Cl} [Cl^-]_i}{p_K [K^+]_i + p_{Na} [Na^+]_i + p_{Cl} [Cl^-]_o} \right\}.$$

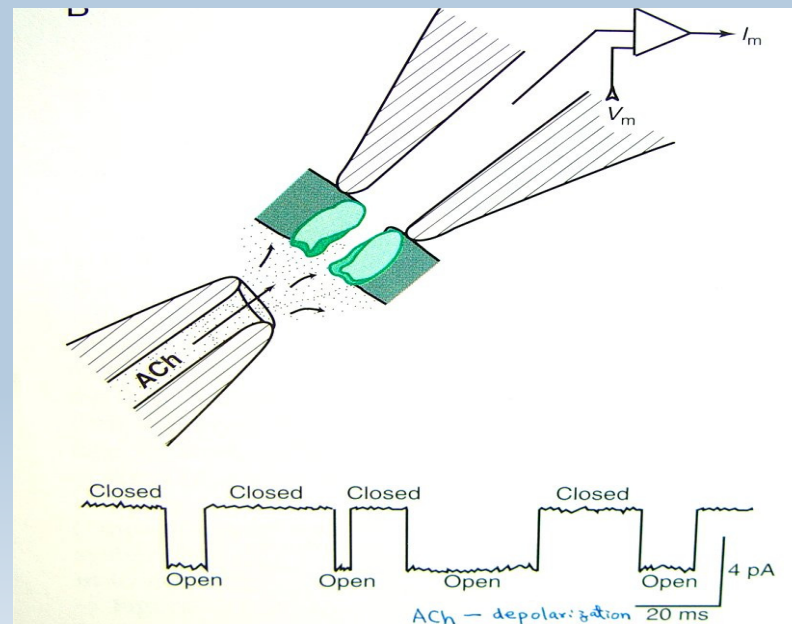
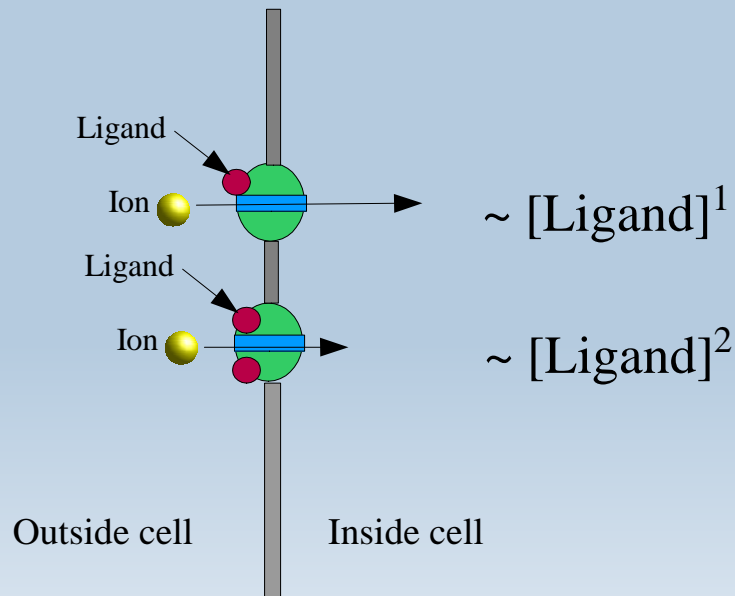
(ref. Mathematical Physiology -- James Keener & James Sneyed Springer)

This study let us realize the ion channels composition or properties on membrane

Chemical kinetics help us understand ion channel behavior with experimental data

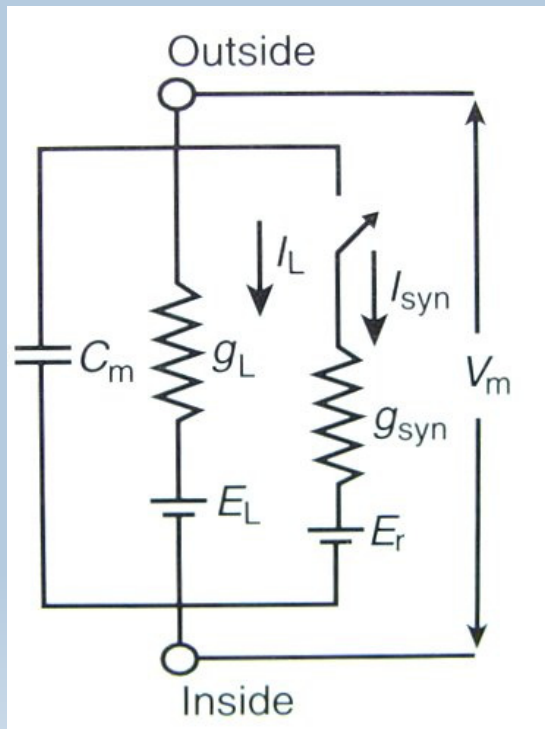
By model analysis, and current experimental data
We can predict how many subunit to form a channel

Ligand \longrightarrow Receptor \longrightarrow Ion flow into cell

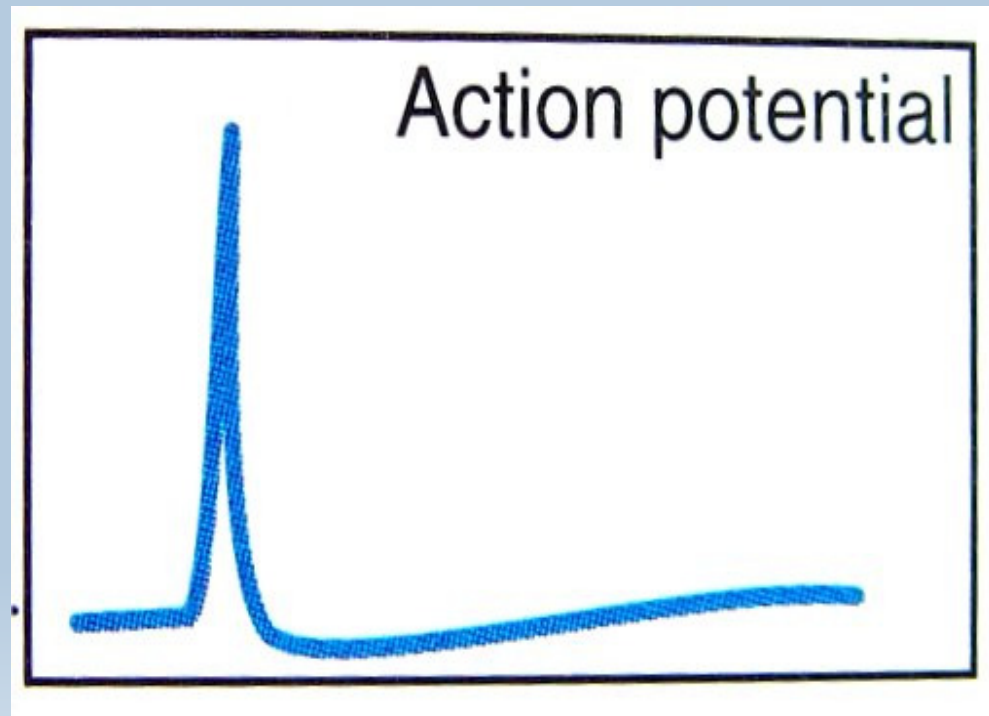


Patch clamp technique

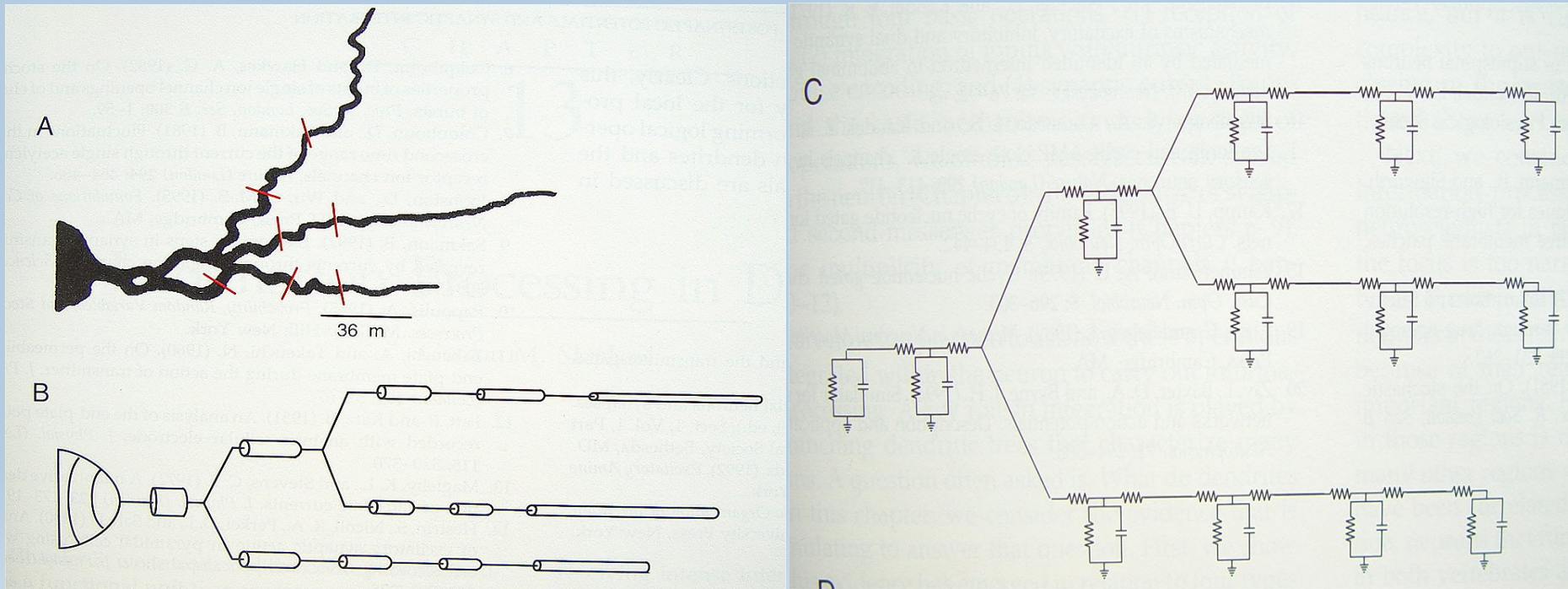
Electrical circuit theory and experimental data help us to realize how action potential create



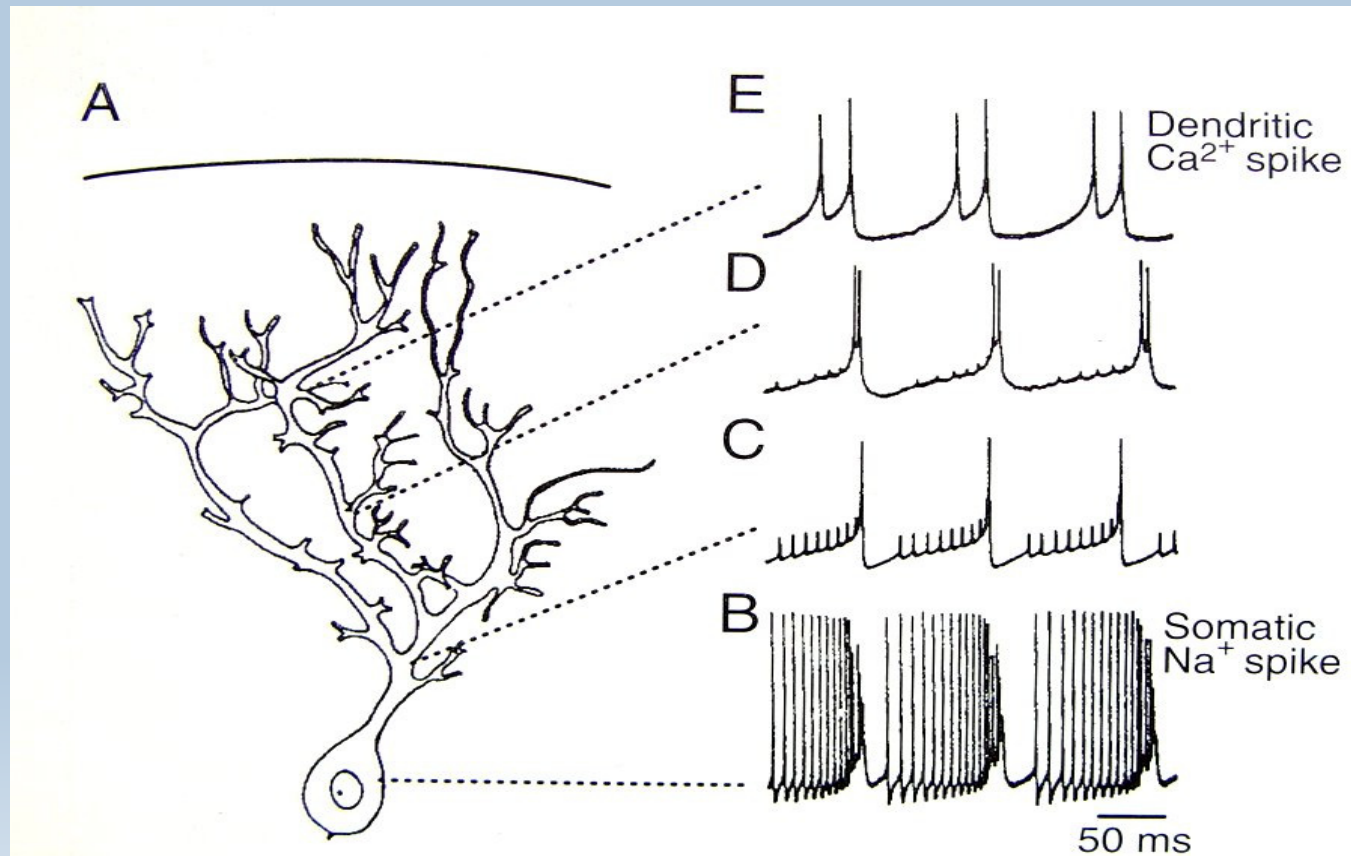
Model circuit



Electrical circuit theory and experimental data help us to realize how action propagate



Base on previous knowledge and model analysis we can explain what we found and guide our next step



Purkinje cell in cerebellar slice

Comment

- Fundamental knowledges can let you enjoy in life science.
- Some basic knowledge in life science is necessary :biology, biochemistry, molecule biology, cell biology.
- Keep in mind, don't forget what you learn when you enter this field.
- Practice is the real

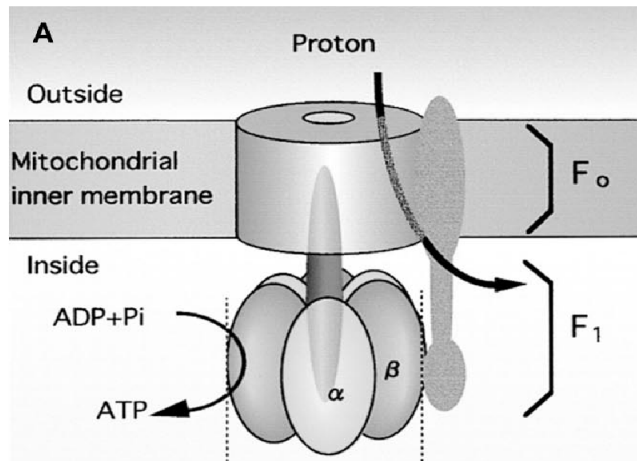
How knowledge in LS can help you?

- ▶ Science can let us convenient, keep side effect away. Those fundamental knowledge in life science can help you do some judgement.
- ▶ Can mobil phone induce any side effect ? Cancer, behavior change, headache ...or others.
- ▶ Neuroscience & behavior study can help you in your invention.
 - ▶ Simulator, game station.
 - ▶ Computer & communciation tool

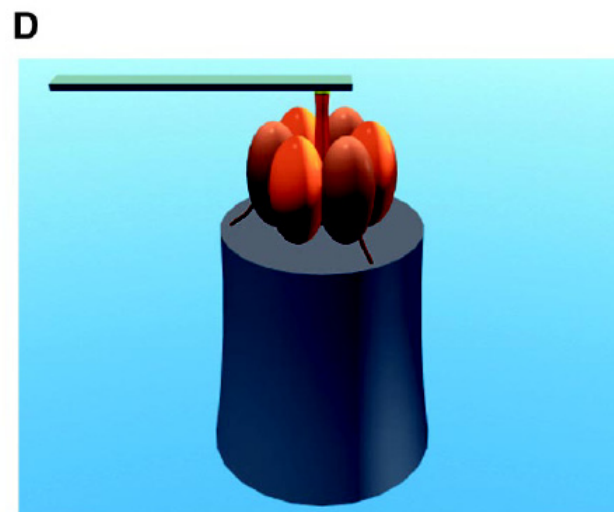
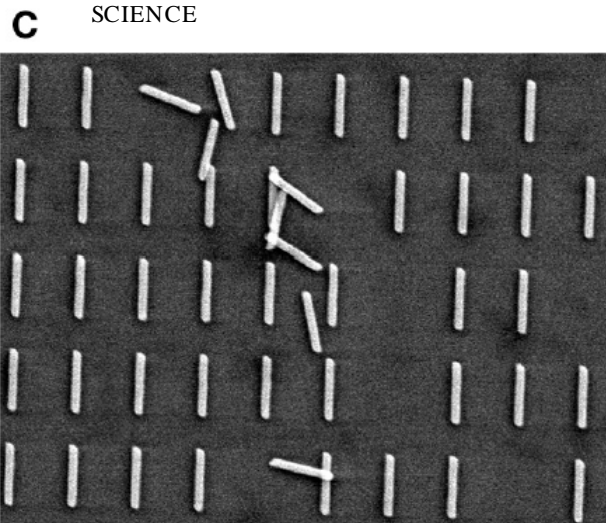
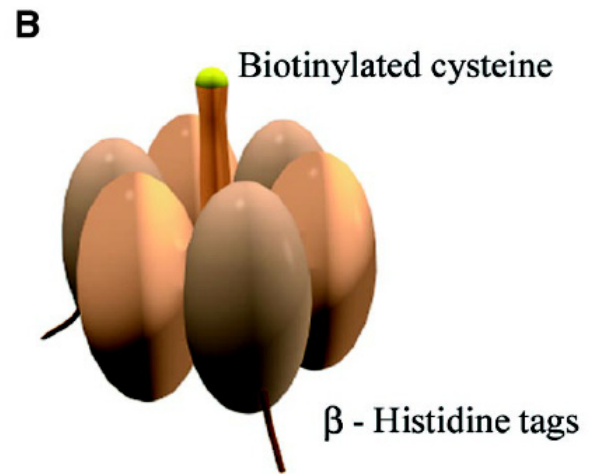
- ▶ Field of life science can expand your your working area
 - ▶ Nanostructure – Enzyme, drug, medical material like collagen, chitosan ..etc.
 - ▶ MEMs – Bio chips, bio-sensor like nose, eye, organs like liver kidney, lung, micro plant for drug, medical material fabrication, DNA , protein analysis...etc.
 - ▶ Mechanics – Heart, skeleton, robot like hand , legs.
 - ▶ Others – bio-reactor in pollution removalment
 - ▶ Complex system for dynamic study – how thousands of chemical rection co-work in keep cell living, body operation.



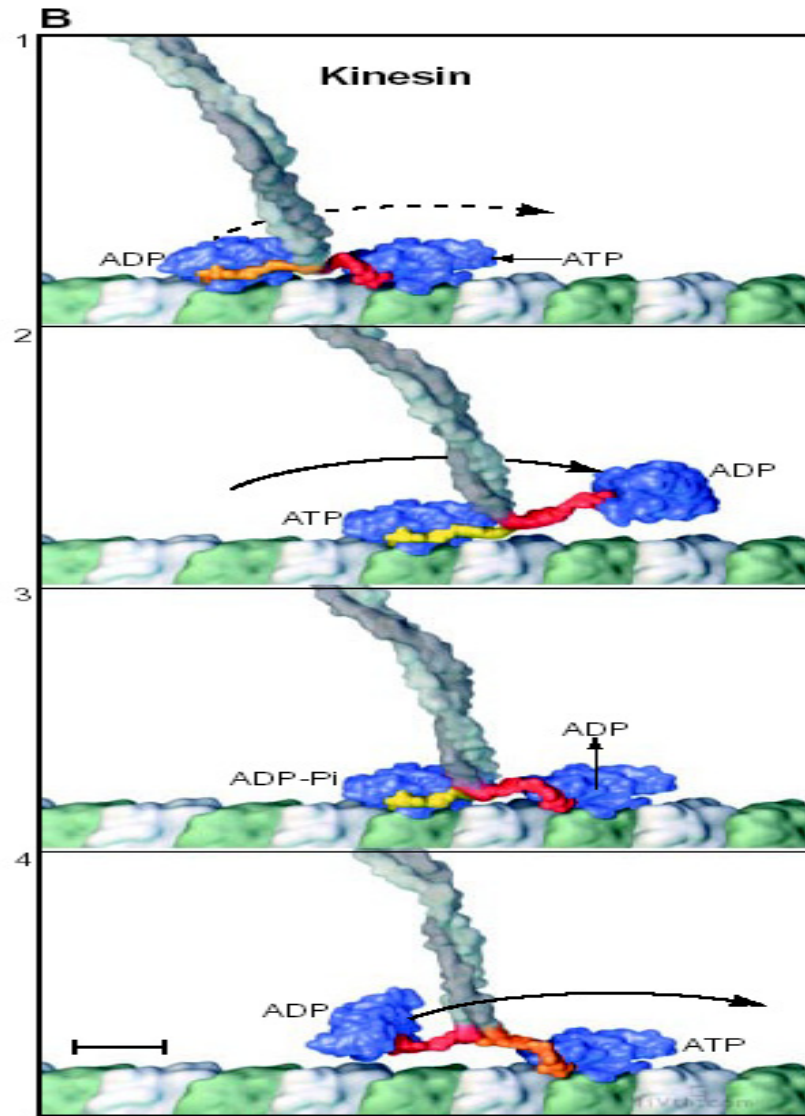
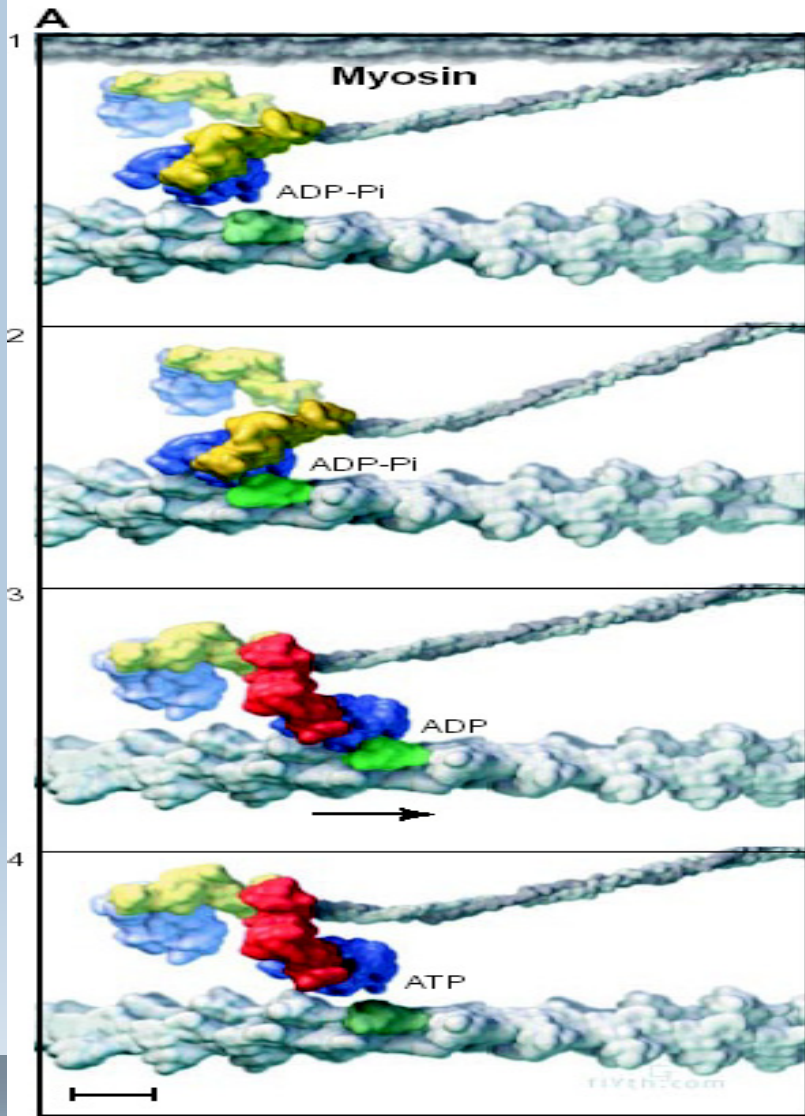
- ▶ Life science can provide some models in your area
 - ▶ Energy saving airplane, boat, navigation system
 - ▶ Bioinformation can simplify your system design
 - ▶ Nanostructure – molecule motor, molecule robot, enzyme, drug, material like silk..etc, and electrical generator.



12 MARCH 1999 VOL 283
SCIENCE



SCIENCE VOL 290 24 NOVEMBER
2000



Comment

- There are many application field in life science you can enter.
- Biological system has already provide very efficient operation process. They can provide you good models.

What 's kind of knowledge you need

- Keep basic principle of your field in mind.
- New learning and working style with current knowledge platform - network.
- Computer language and electrical knowledge – Shorten your research time and add your capability.
- Language in each field. Know how to communciate with different field.

Knowledge in life science

- Molecule manipulation – Biochemistry , molecular biology
 - The relation of DNA ... RNA ... Protein
 - Technique of DNA/RNA/Protein engineering – PCR, sequencing, purification, protein synthesis, modification, labeling or marking, protein functions.
- Cell – Cell biology, pharmacology
 - What's is the money in cell.
 - How signal communciation inside cell outside cell, their mechanism, result?

- ▶ Development concept? Living?
- ▶ Behavior – Neuroscience, Ecology
 - ▶ How neuro-circuit programming, learning, and memory.
 - ▶ Sensing, emotion, decision
 - ▶ Communication, competition, adaptation, survival

What's kind of treasure you see

