Molecular Imaging Techniques

NMR Spectroscopy

X-Ray Crystallography

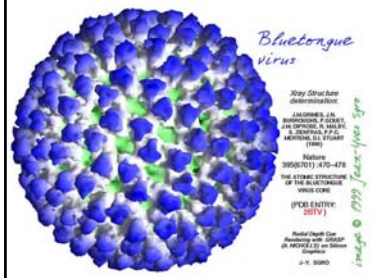
Electron Microscopy

TEM – Transmission Electron Microscopy

(Cryo EM)

SEM – Scanning Electron Microscopy

Medical Imaging Methods



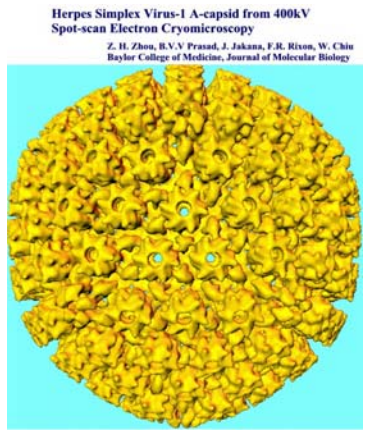
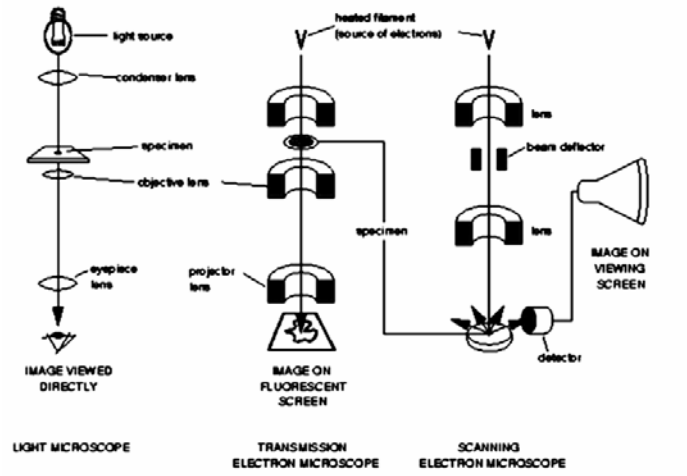
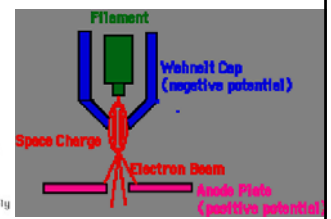


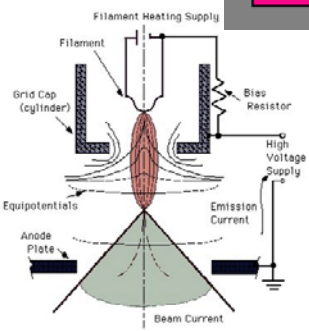
Image Formation



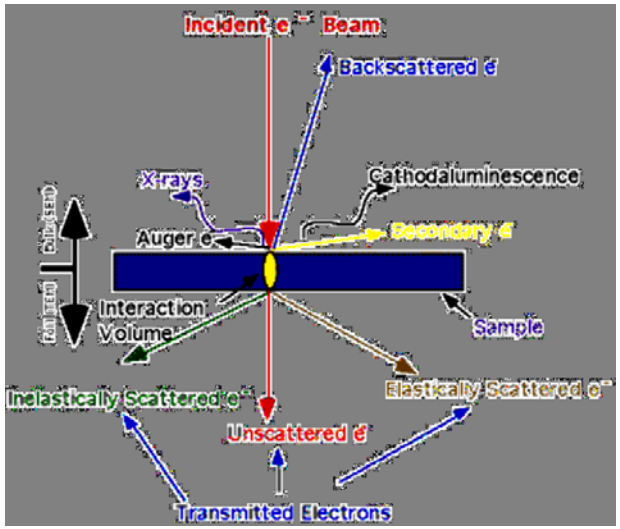
The Electron Source



The electron beam comes from a filament, made of various types of materials. The most common is the Tungsten hairpin gun. This filament is a loop of tungsten which functions as the cathode. A voltage is applied to the loop, causing it to heat up. The anode, which is positive with respect to the filament, forms powerful attractive forces for electrons. This causes electrons to accelerate toward the anode. Some accelerate right by the anode and on down the column, to the sample. Other examples of filaments are Lanthanum Hexaboride filaments and field emission guns.

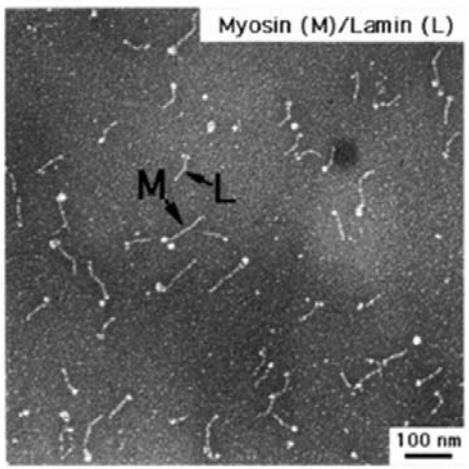


http://mse.iastate.edu/microscopy/source.html



TEM – Transmission Electron Microscope

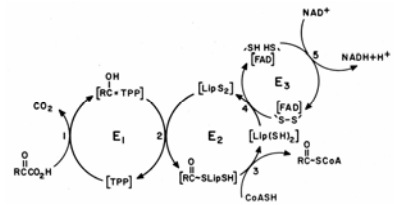
JEOL JEM-2010: 200kV high-resolution TEM with interchangeable polepieces, where one can change from an analytical version (resolution = 0.23nm, +/- 30 degrees tilt) to a high-resolution version (0.19nm, +/- 10 degrees tilt). Double-tilt and heating specimen holders are available on this TEM. http://www.tamu.edu/mic/instruments.html#jem2010

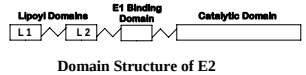


Electron micrograph of a mixture of myosin (M) and nuclear lamin (L) dimers after glycerol spraying/rotary metal shadowing with platinum. Both molecules are composed of two globular heads linked to a common rod-like tail, approximately 100 nm long in the case of myosin and 52 nm in the case of nuclear lamin.

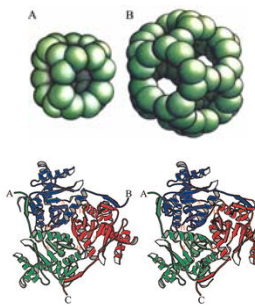
http://www.mih.unibas.ch/Booklet/Lecture/Chapter1/Chapter1.html

Multienzyme Complexes – with Professor Lester Reed

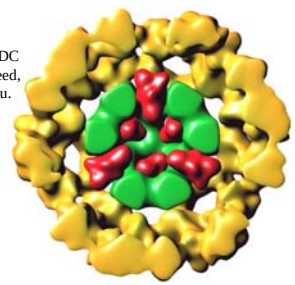




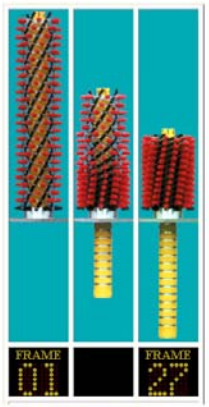
Domain Structure of E2



EM model of PDC (E1 E2 E3) - Reed, Stoops and Zhou.



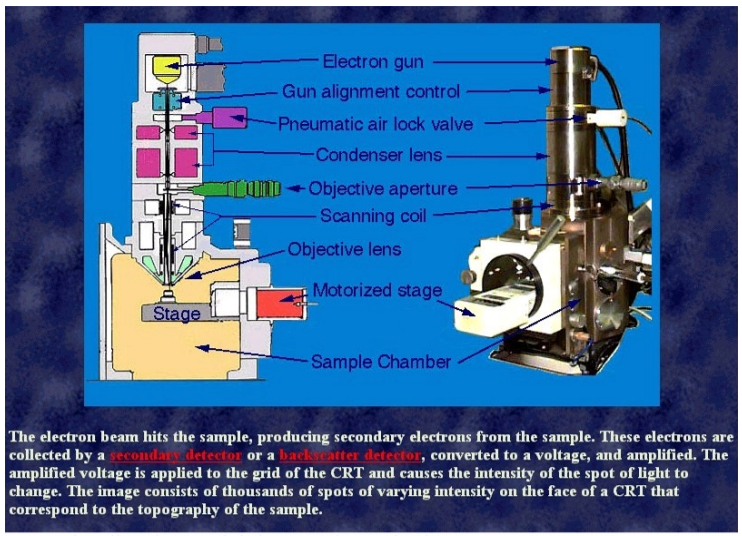
T4 bacteriophage tail sheath motility



http://www.sb.fsu.edu/~caspar/animation/anim1sm.html

SEM - Scanning Electron Microscope

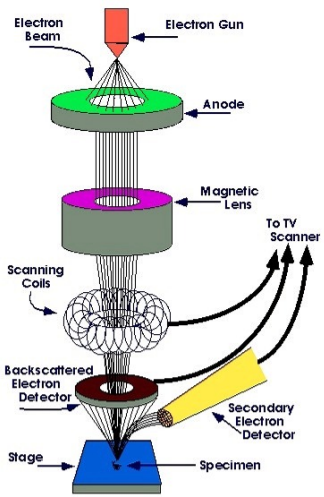
JEOL JSM-6400: This software-oriented, analytical-grade SEM, is capable of acquiring and digitizing images. Acceleration voltages from 0.2 to 40kV, a magnification range of 10 to 300,000x, and a guaranteed resolution of 3.5nm allow an operator to achieve excellent results on a wide variety of samples. http://www.tamu.edu/mic/instruments.html#jsm-6400



The electron beam hits the sample, producing secondary electrons from the sample. These electrons are collected by a secondary detector or a backscatter detector, converted to a voltage, and amplified. The amplified voltage is applied to the grid of the CRT and causes the intensity of the spot of light to change. The image consists of thousands of spots of varying intensity on the face of a CRT that correspond to the topography of the sample.

http://mse.iastate.edu/microscopy/source.html

The SEM uses electrons instead of light to form an image. A beam of electrons is produced at the top of the microscope by heating of a metallic filament. The electron beam follows a vertical path through the column of the microscope. It makes its way through electromagnetic lenses which focus and direct the beam down towards the sample. Once it hits the sample, other electrons (backscattered or secondary) are ejected from the sample. Detectors collect the secondary or backscattered electrons, and convert them to a signal that is sent to a viewing screen similiar to the one in an ordinary television, producing an image.

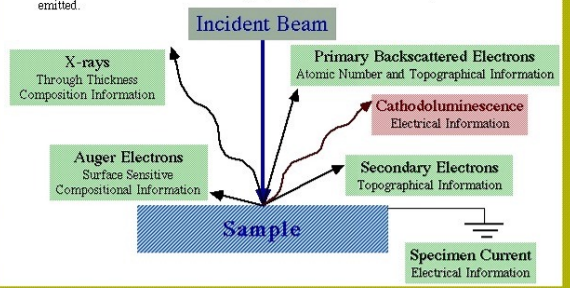


http://mse.iastate.edu/microscopy

SEM Setup

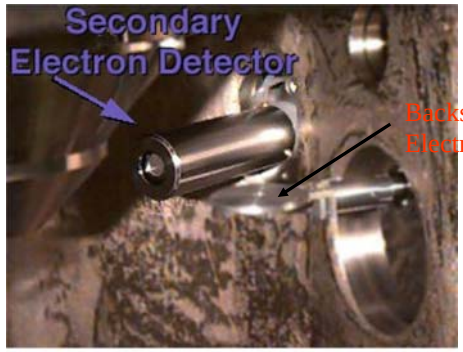
Electron/Specimen Interactions

When the electron beam strikes the sample, both **photon** and **electron** signals are emitted.



While all these signals are present in the SEM, not all of them are detected and used for information. The signals most commonly used are the Secondary Electrons, the Backscattered Electrons and X-rays.

http://mse.iastate.edu/microscopy



http://mse.iastate.edu/microscopy

Secondary electrons are specimen electrons that obtain energy by inelastic collisions with beam electrons.

Elastic scattering results in little (<1eV) or no change in energy of the scattered electron, although there is a change in momentum. Since momentum, p=mv, and m doesn't change, the direction of the velocity vector must change. The angle of scattering can range from 0-180 degrees, with a typical value being about 5 degrees. Elastic scattering occurs between the negative electron and the positive nucleus. This is essentially Rutherford scattering. Sometimes the angle is such that the electron comes back out of the sample. These are backscattered electrons.

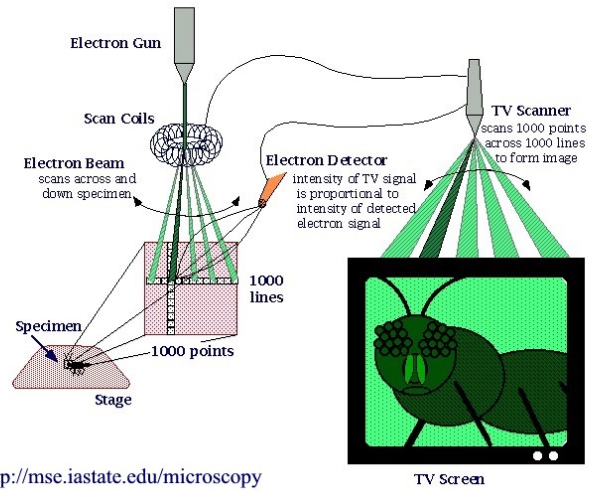
Sputter Coater

http://mse.iastate.edu/microscopy

A sputter coater coats the sample with gold atoms. The purpose is to make non-metallic samples electrically conductive.

The sputter coater uses argon gas and a small electric field. The sample is placed in a small chamber which is at vacuum. Argon gas is then introduced and an electric field is used to cause an electron to be removed from the argon atoms to make the atoms ions with a positive charge. The Ar ions are then attracted to a negatively charged piece of gold foil. The Ar ions act like sand in a sandblaster, knocking gold atoms from the surface of the foil. These gold atoms now settle onto the surface of the sample, producing a gold coating.

How an Image is Produced



http://mse.iastate.edu/microscopy

SEM Images

http://mse.iastate.edu/microscopy

Chigger Mite

Deer Tick

Pollen Grain

Pollen Mix

Medical Imaging - Radiology

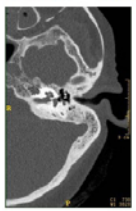
MRI (or NMRI) - Magnetic resonance imaging (MRI) is an imaging technique used primarily in medical settings to produce high quality images of the inside of the human body. MRI is based on the principles of nuclear magnetic resonance (NMR). MRI is a noninvasive imaging technique that does not use x-rays. The fluid contrast between structures in the brain can then be visualized.

CAT (or CT) - Computerized Axial Tomography or computerized tomography. A CT scan is essentially a computerized assembly of several x-ray images taken from a series of different angles. With a CT, the resolution is much better than conventional x-rays, and the detail that can be seen is much greater. As with all other typical x-rays, the procedure is radiographic and the patient's body is exposed to a small amount of radiation during the scan.

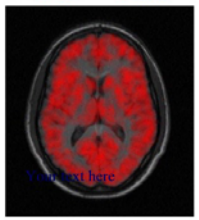
PET - positron emission tomography (PET); PET produces images of metabolic activity as opposed to images of the body's physical structures that are derived from other imaging techniques (MRI / CT). For a PET scan, a small amount of radioactivity is attached to biological substances that are similar to those already found in the body. These radioactive agents, once introduced into the body, are processed by organs and tissues as part of their normal function. The PET scanner is able to detect the location of the radiation in the body. A computer then creates a picture of the activity using colors to highlight the different levels of function.

Medical Imaging

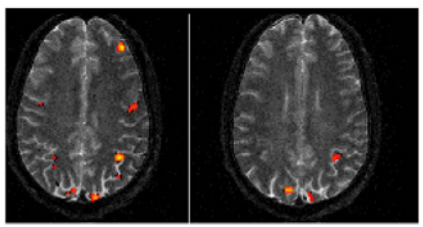
CAT scan - ear canal



PET - brain

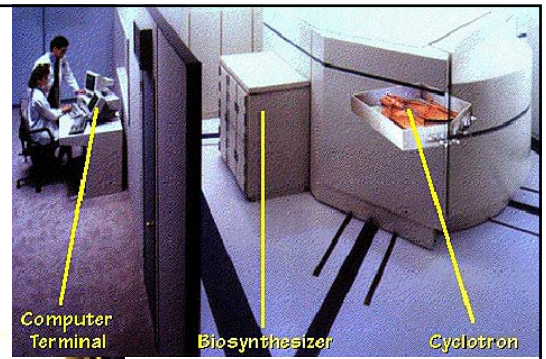


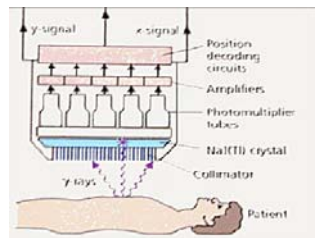
MRI - brain

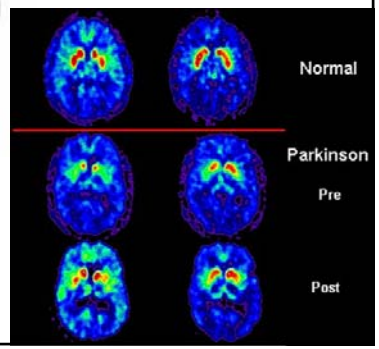


http://www.macalester.edu/~psych/whathap/UBNRP/Imaging/mri.html

PET Scans







Ultrasonography:

Introduction to Ultrasound Imaging

Ultrasound scanners - a form of 'medical' Sonar

SONAR = Sound Navigation and Ranging

RADAR = Radio Detection and Ranging

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1877 - Lord Rayleigh – "The Theory of Sound" – sound waves

1912 - Underwater navigation - submarines WWI, Titanic sank

1935 - First practical RADAR using electromagnetic waves

1940s – Ultrasound therapy: **arthritis**, **craniotomies**

1952 – John Wild – "Application of Echo-Ranging Techniques to the Determination of Structure of Biological Tissues"

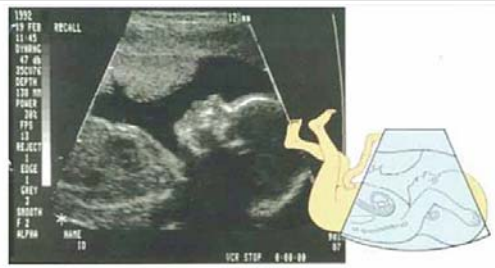
1958 – "Investigation of Abdominal Masses by Pulsed Ultrasound" (the most important paper on medical diagnostic ultrasound ever published)

What are Obstetric Ultrasound Scans?

Obstetric Ultrasound is the use of ultrasound scans in pregnancy. Since the late 1950's ultrasonography has become a very useful diagnostic tool in Obstetrics. Currently used real-time scanners using very high frequency sound waves of between 3.5 to 7.0 megahertz (i.e. 3.5 to 7 million cycles per second) can provide a continuous picture of the moving fetus can be depicted on a monitor screen. and growth in the fetus. The conducting gel is non-staining but may feel slightly cold and wet. There is no sensation at all from the ultrasound waves.

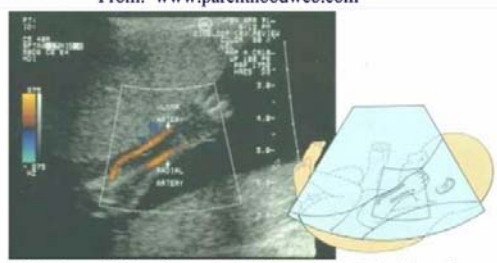
Transducer (probe) on the abdomen

3-D scan of fetal face

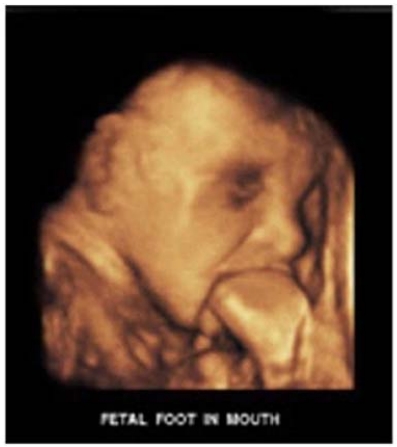


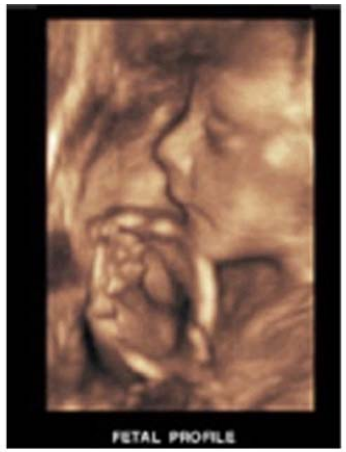
Profile of a fetus at four months. This face is approximately 1 1/2 inches (4cm) long.

From: www.parenthoodweb.com



The fetal arm with the major arteries (radial and ulnar) clearly delineated.





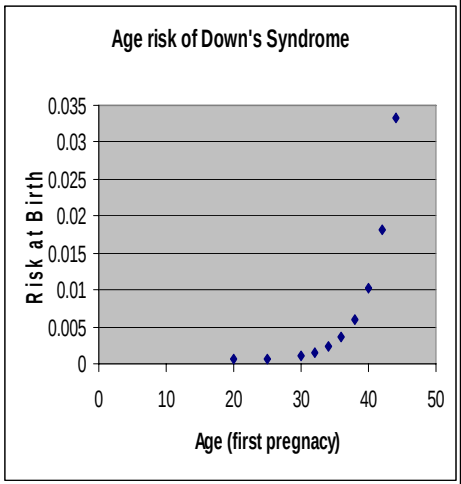
From: www.medical.philips.com/main/products/ultrasound/

Pregnancy later on in life also carries an increased risk of certain chromosomal disorders such as Down's syndrome so many older women are offered the **Nuchal translucency** scan along with the **alpha-fetoprotein blood test**. Some women may also be offered an amniocentesis to determine if their child has a chromosomal abnormality.

On the positive side many older women are often more prepared for motherhood, both emotionally and financially. More and more women are waiting until at least their mid-thirties before starting a family and are happy that their increased financial security and self-confidence have made it worth the wait.

Down's Syndrome (Trisomy 21)

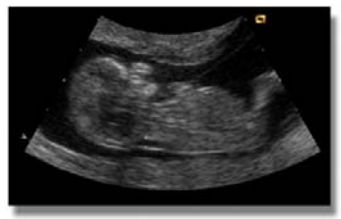
MATERNAL AGE	RISK AT BIRTH
20	1/1527
25	1/1352
30	1/895
32	1/659
34	1/446
36	1/280
38	1/167
40	1/97
42	1/55
44	1/30

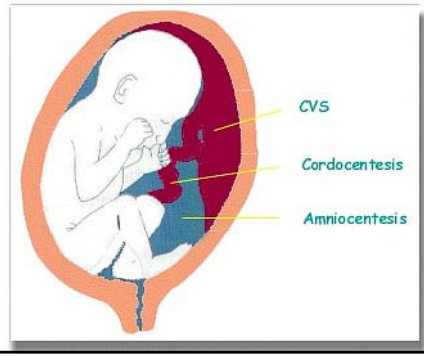


http://www.fetalmedicine.ac.uk/antenatal.htm

Non-invasive procedure

Amount of fluid behind the neck of the fetus (Nuchal translucency) scan





Three invasive procedures

chromosomal abnormality

Chorion villus (placenta) sampling (11-14 wks)

Amniocentesis (>15 wks)

Cordocentesis (>20 wks)