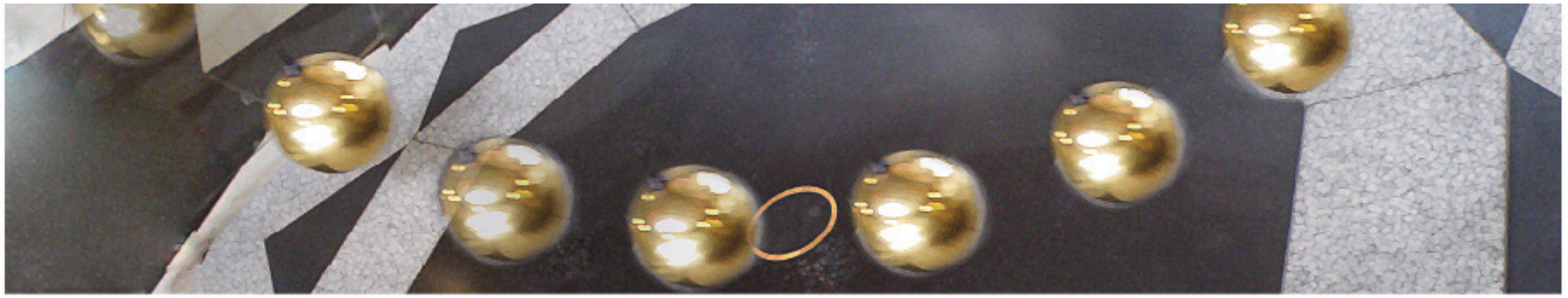

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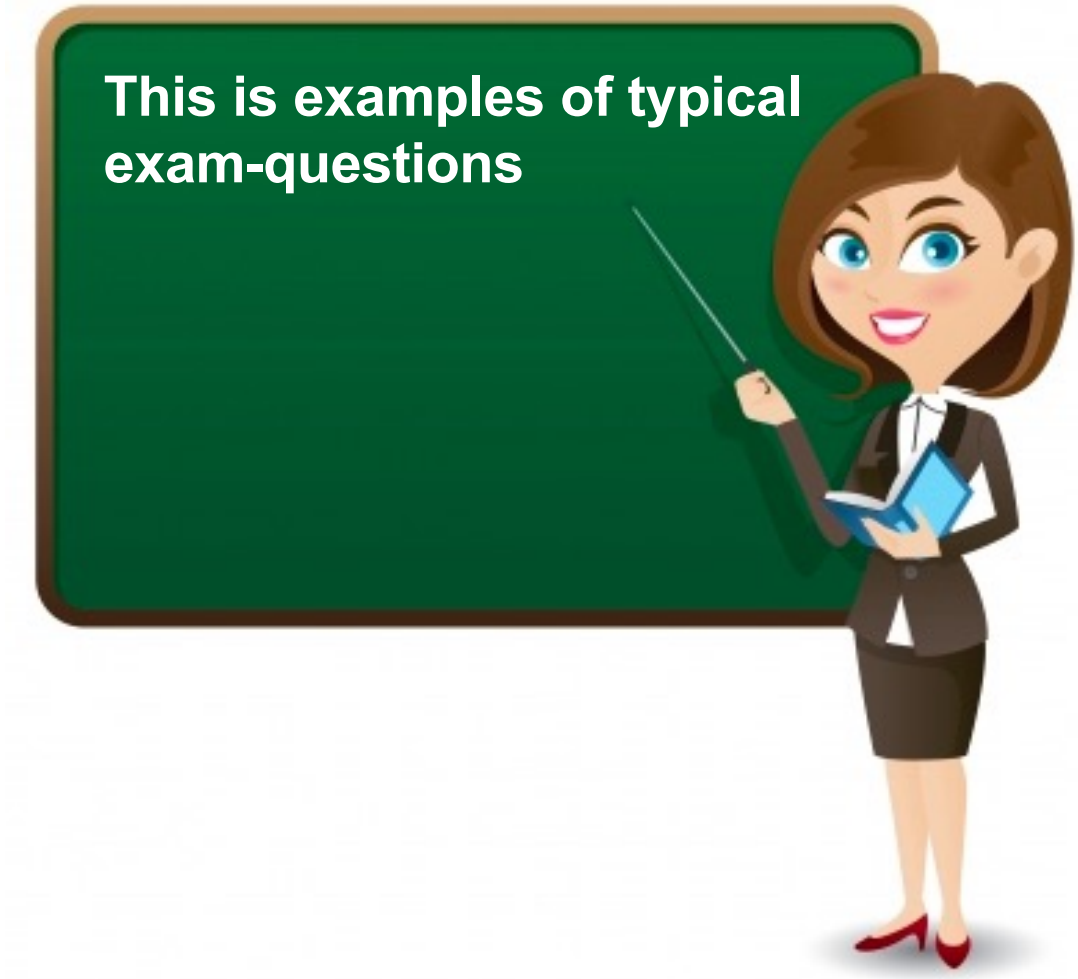
Repetition part 9-16

What is a typical question?

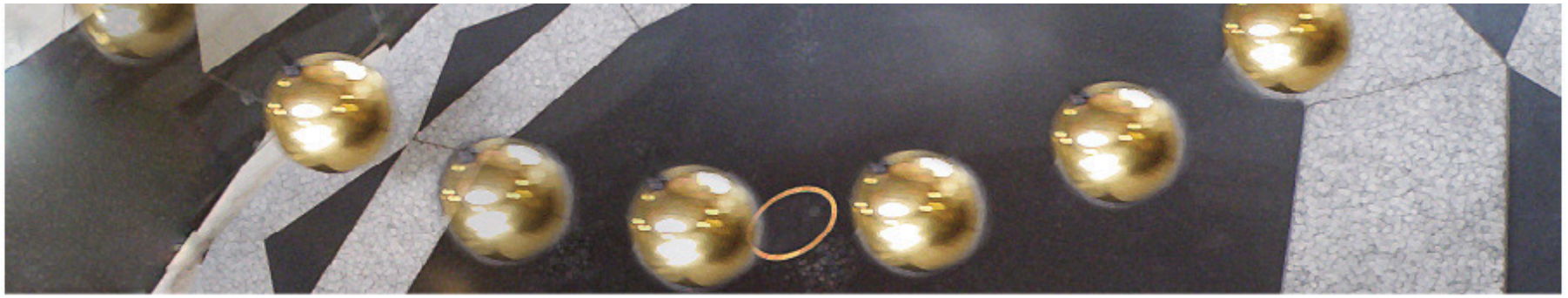
For example:

1. Mention some different methods for measuring blood pressure, explain the different advantages, disadvantages and eventual risks associated with each method
2. Blood flow is another interesting parameter. Describe how it is possible to measure the blood flow both invasive and non-invasively and explain the advantages, disadvantages for each method. What would be the proper requirements for an amplifier in such a measurement system?
3. Do you know any non-invasive methods of measuring the oxygen concentration in the blood? Give a brief description of the manner of operation, sources of error and advantages/disadvantages
4. Give a short explanation of the function of the human heart. How is it possible to detect patology in the heart function without entering the body?



This means that this slide is especially important

http://kidmechanix.com/wp-content/uploads/2017/06/ABAprinciplesforteachers.jpg



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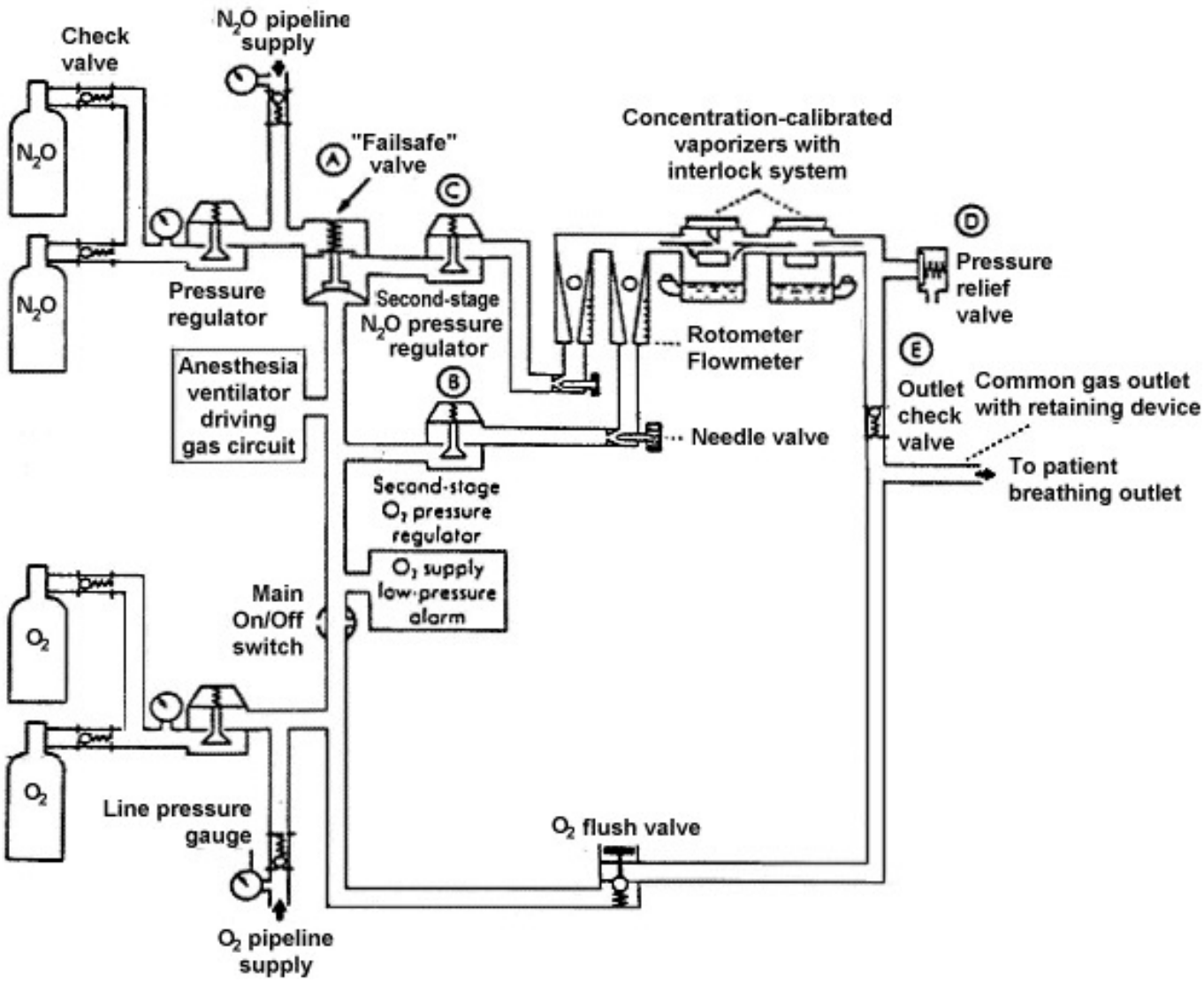
Lecture 9

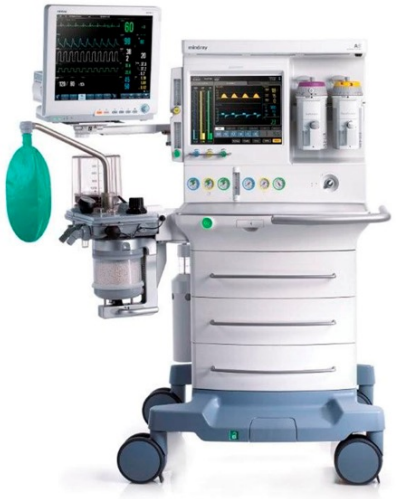
Anesthesia machine, overview



The Anesthesia Workstation

Main functions:

a. Provide anesthetic drugs in correct concentration
b. Take care of the waste
c. Ventilate the patient
d. Monitor the vital signs during anesthesia

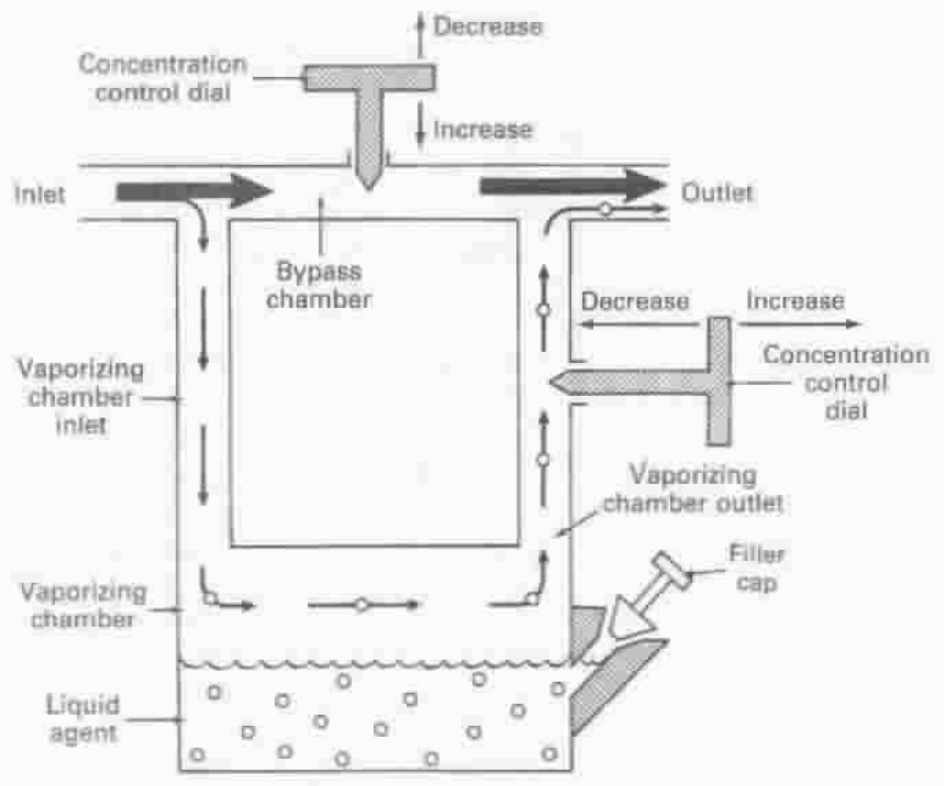


Main concerns:

1. Wrong gas concentrations
2. High pressure
3. Rebreathing
4. Leakages

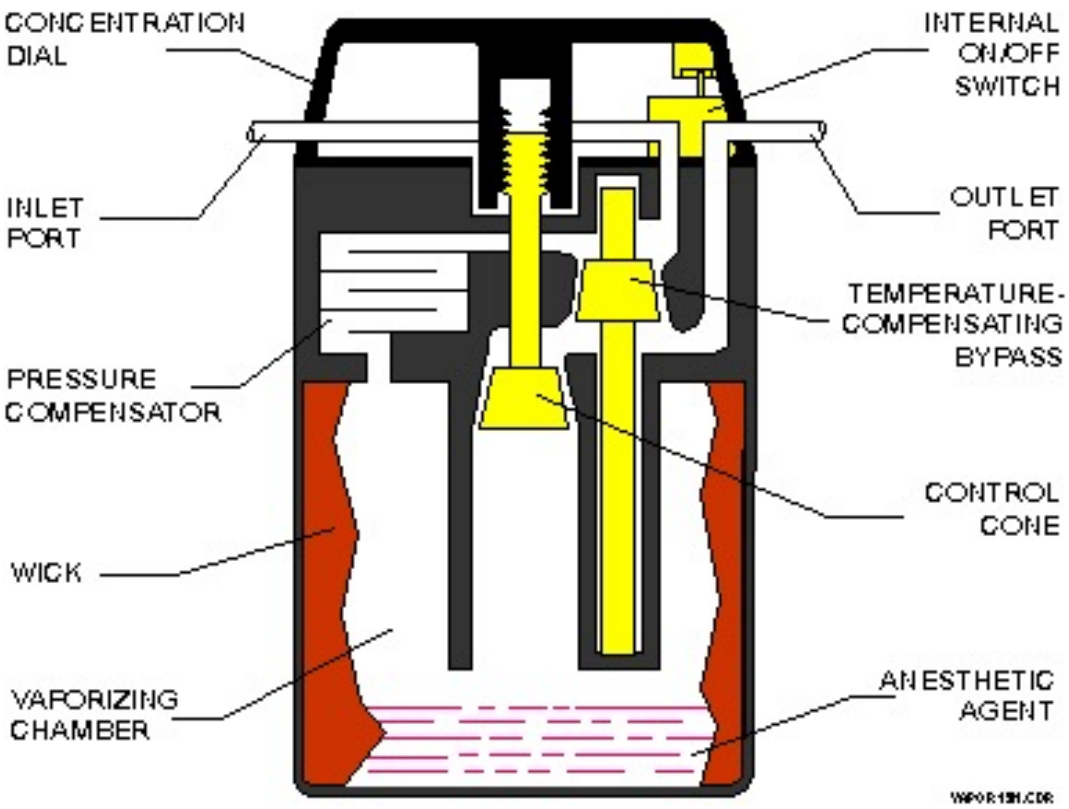
The vaporizer

A vaporizer will change the liquid anesthetic agent into a vapor and insert a certain amount of this vapor into the fresh gas flow



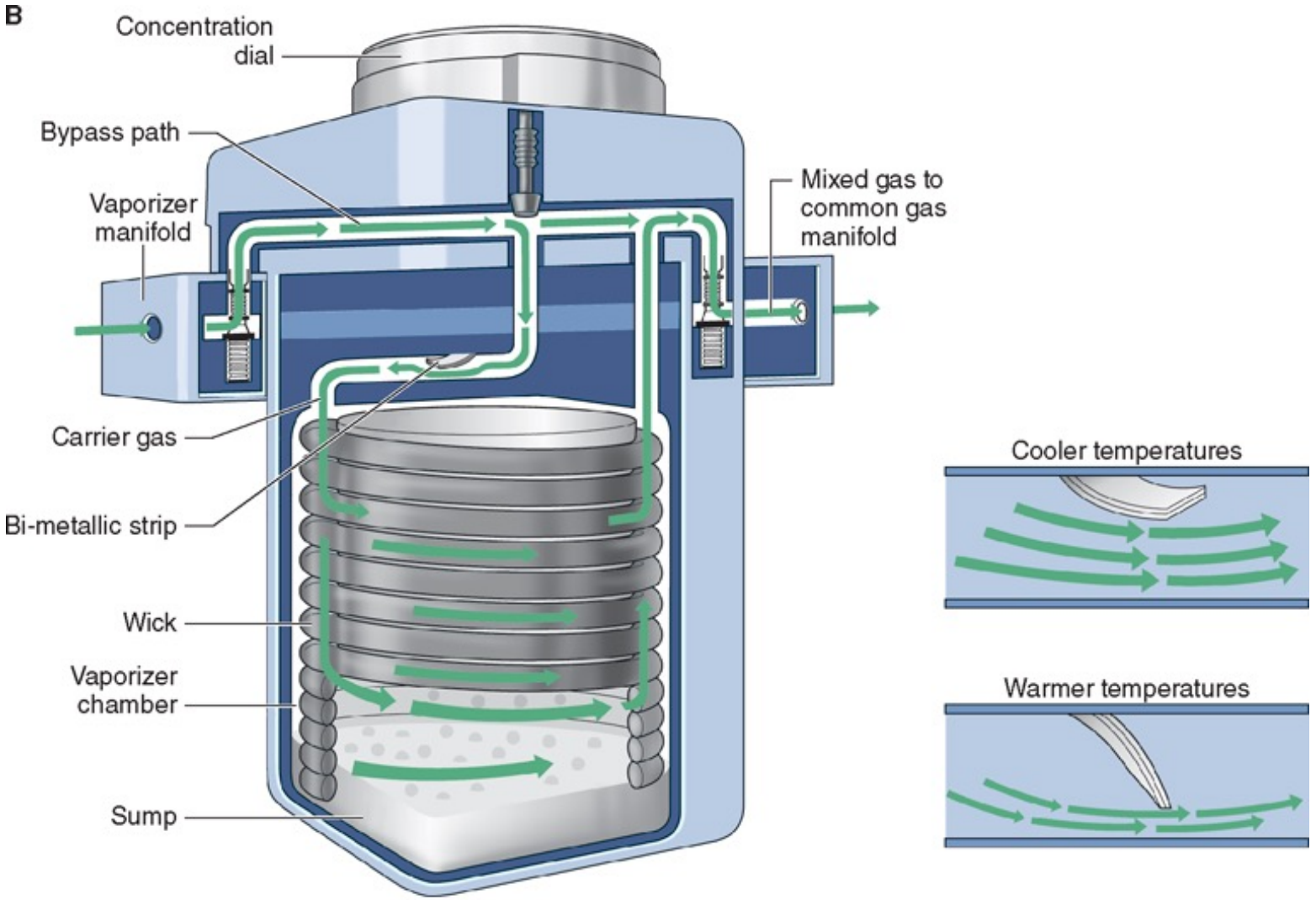
http://www.vajira.ac.th

Main source of error?



http://www.anesthesia2000.com/physics/Chemistry_Physics/physics17.htm

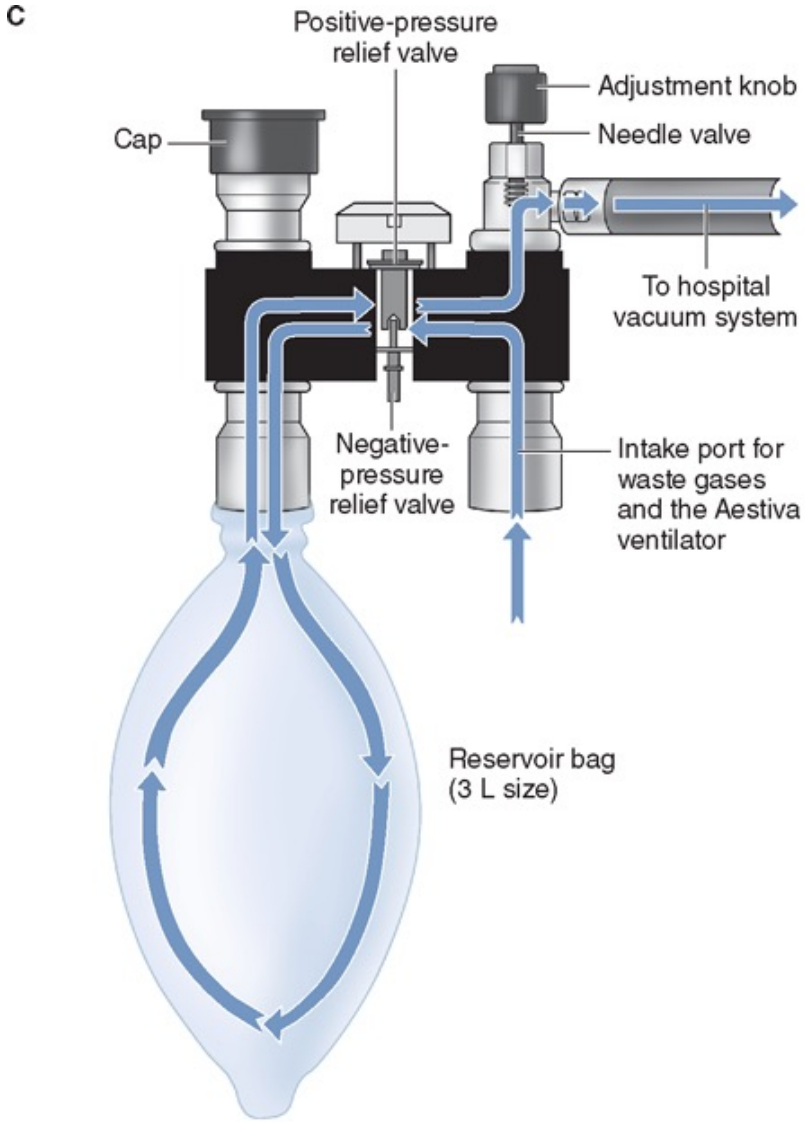
Vaporizer with temperature compensation



Source: Butterworth JF, Mackey DC, Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology*, 5th Edition: www.accessmedicine.com

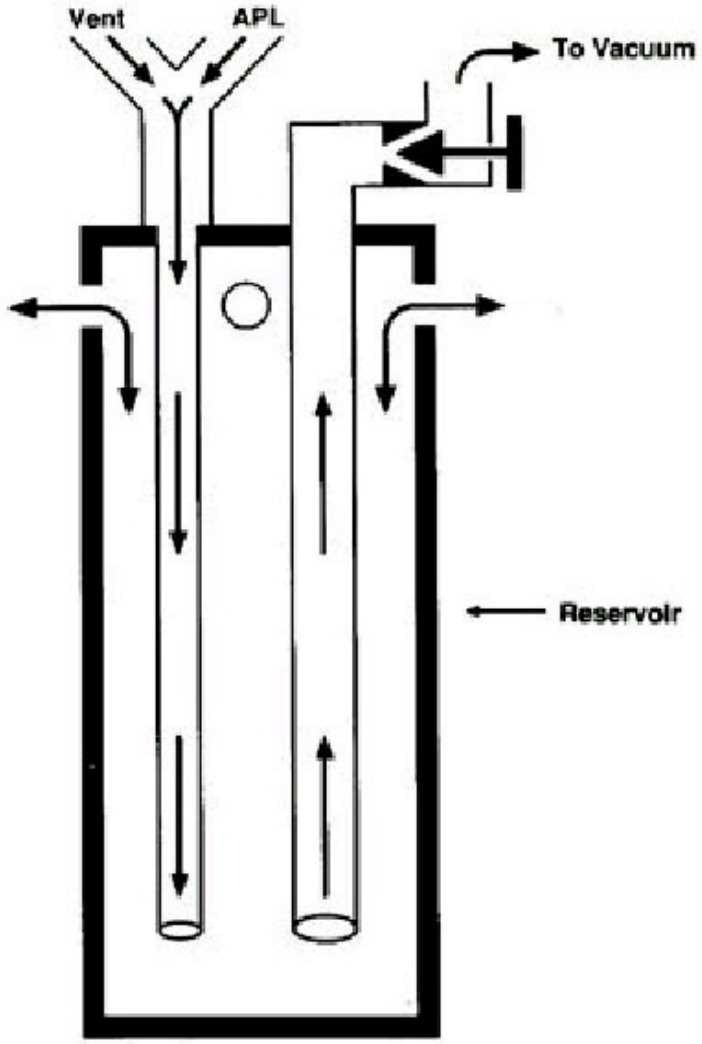
b. Scavenging system

Scavenging system



Source: Butterworth JF, Mackey DC, Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology*, 5th Edition: www.accessmedicine.com

Scavenging system

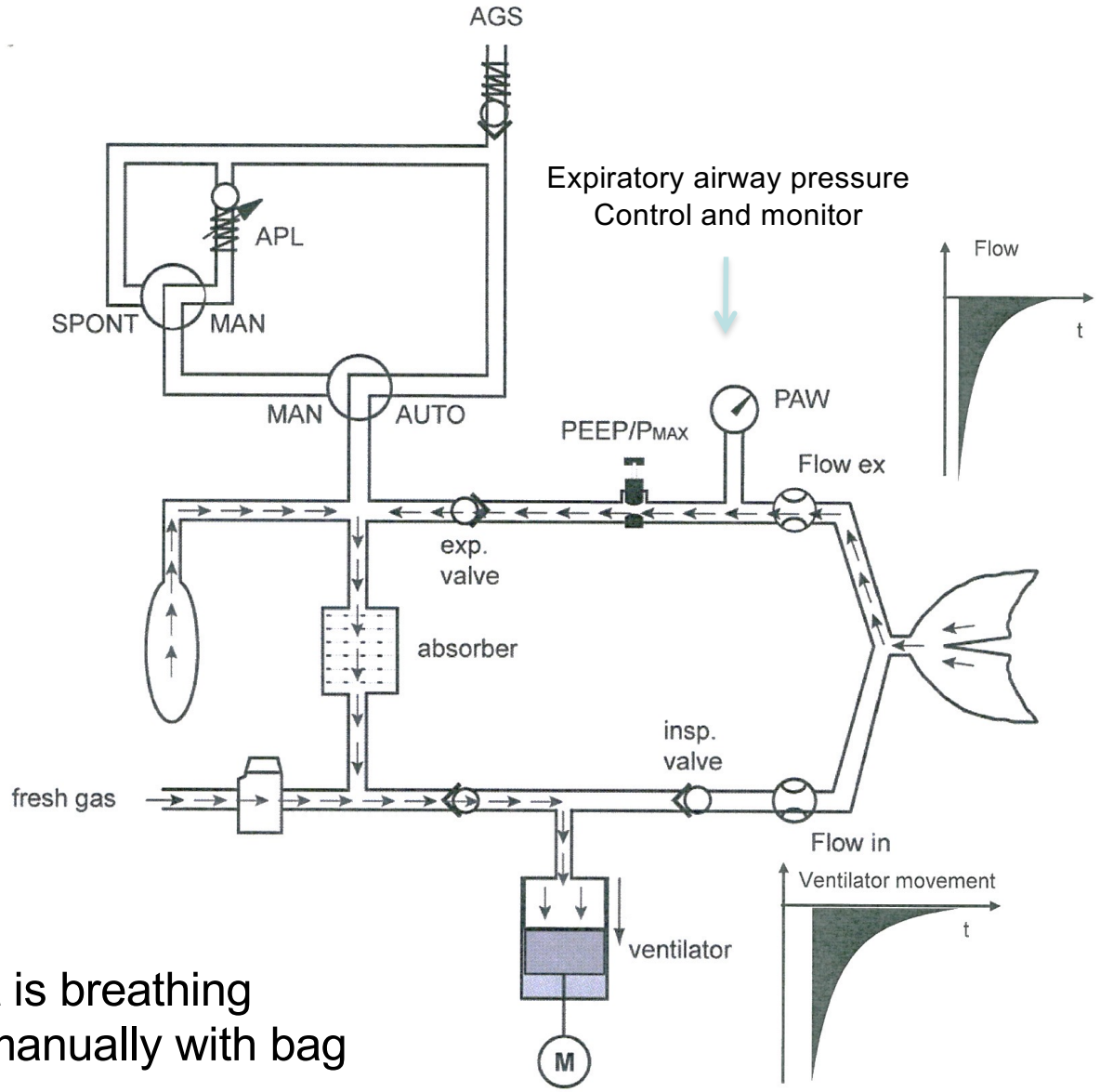


Dräger open scavenging interface

c. Ventilate the patient

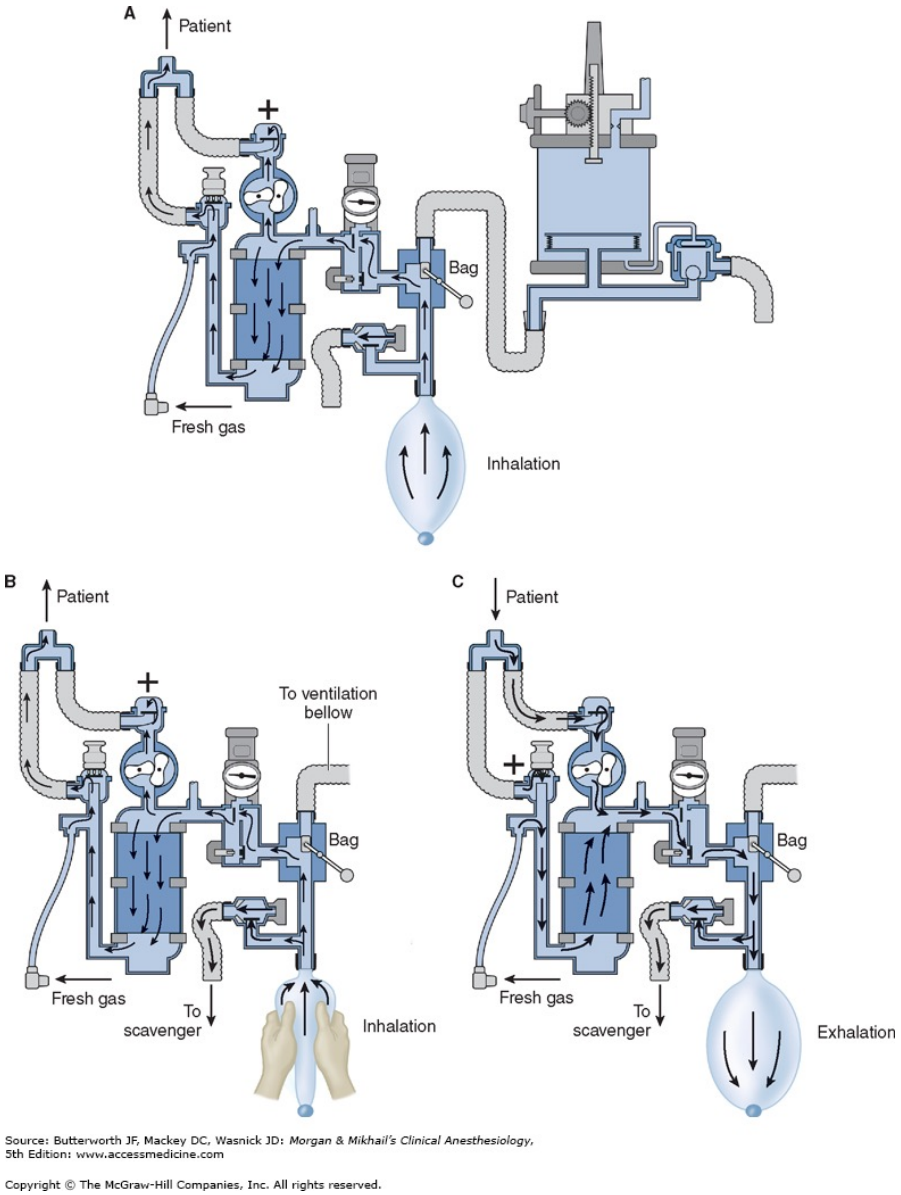
Adjustable pressure limiting valve provide control of the pressure in the breathing circle

The patient circle



Three modi:
Spontanous – Patient is breathing
Manual - Ventilating manually with bag
Auto - Ventilator

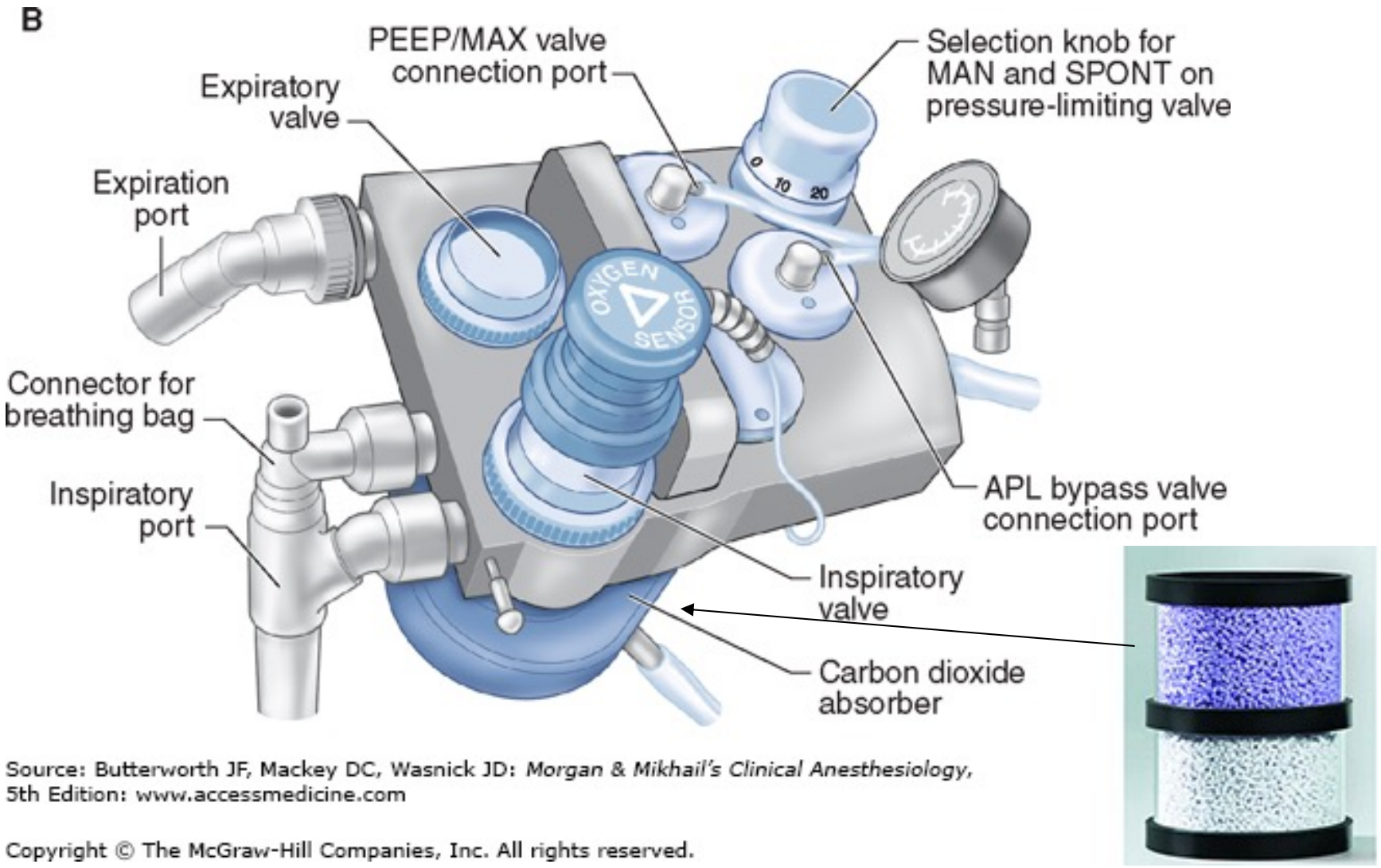
Inhalation/exhalation with bag (Manual ventilation)



Exhalation
Air from the patient together with fresh gas is filling the bag, the excess is evacuated through the APL-valve

Inhalation
The bag is squeezed and the air is pushed through the calc absorber (soda lime) into the patient. The exhalation valve makes sure that there is no backflow of air (Rebreathing)

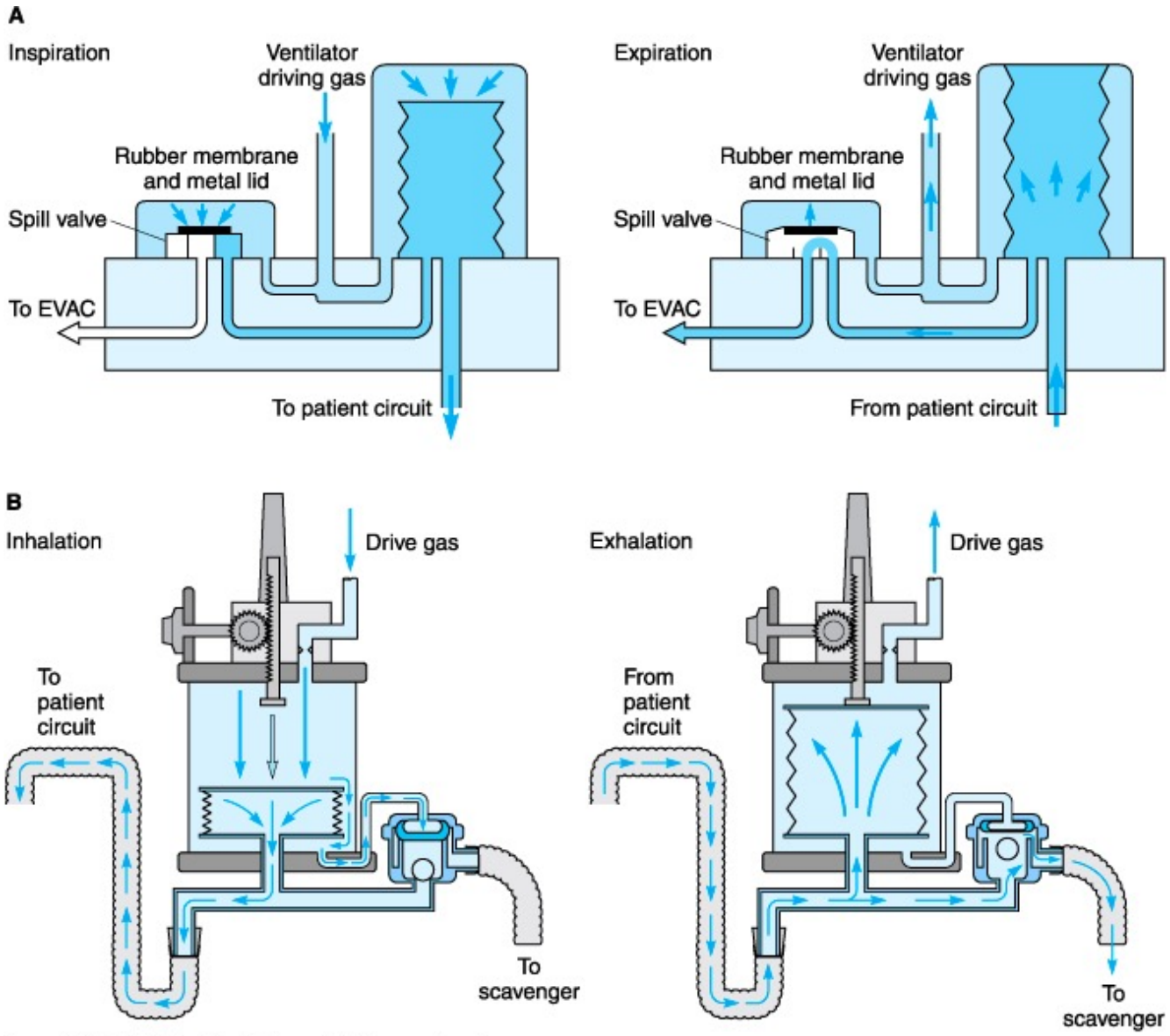
Patient casette



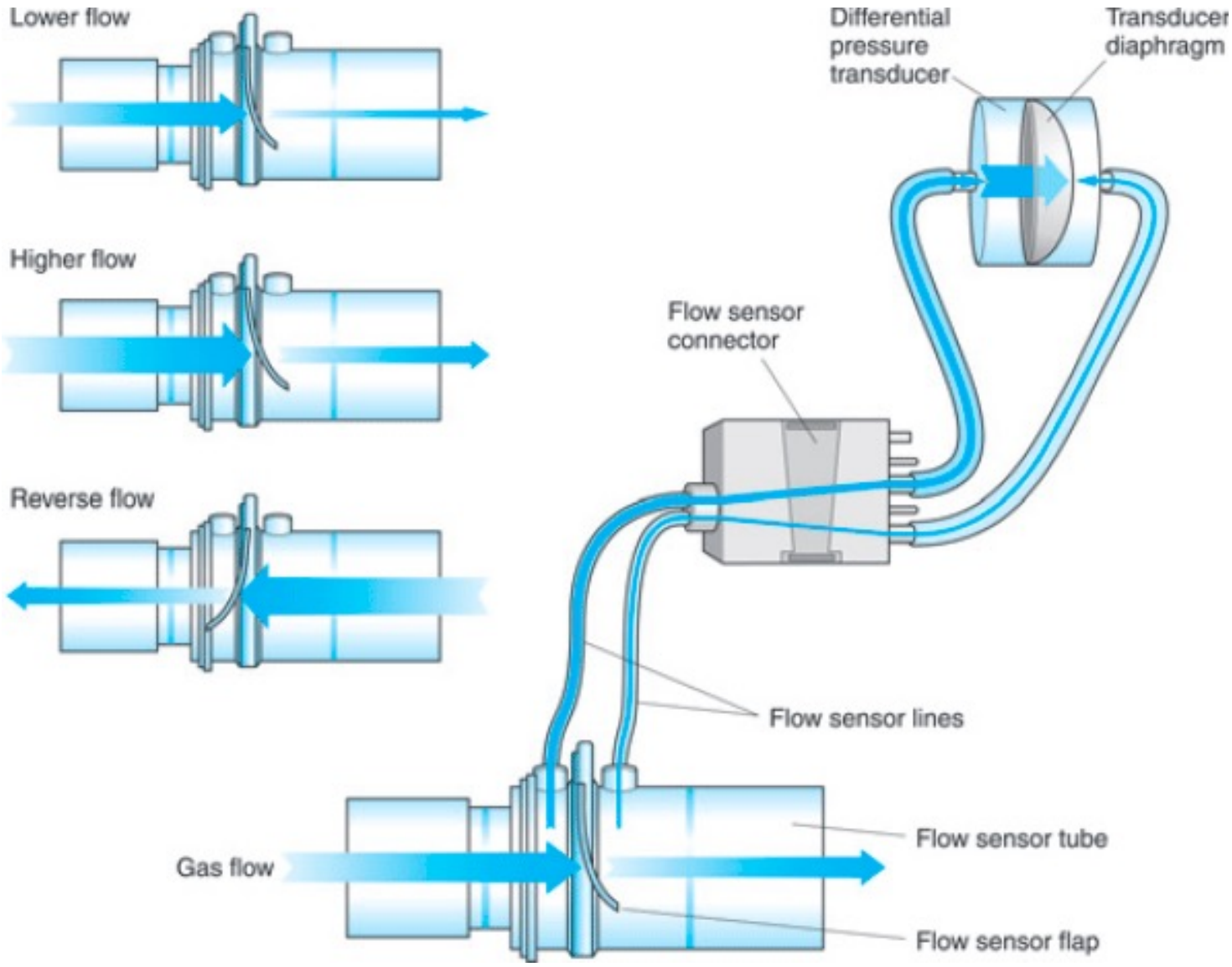
Source: AccessAnesthesiology McGrawHill medical

https://www.osha.gov/dts/osta/anestheticgases/

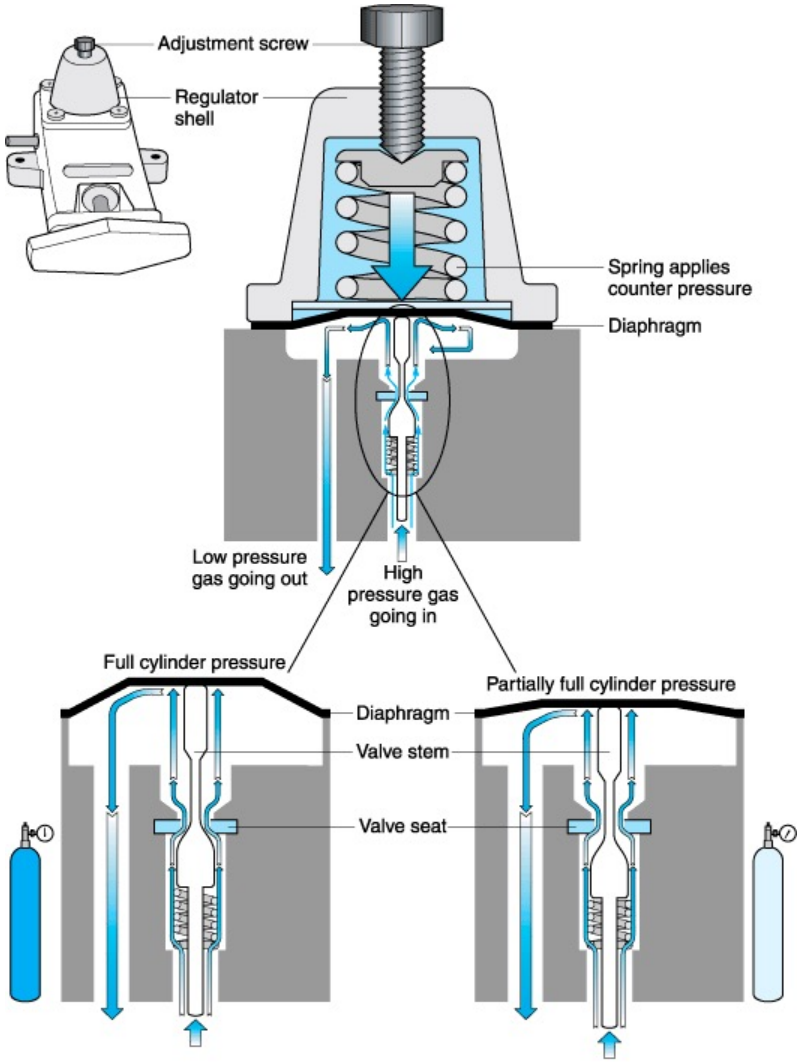
Bag in bottle



Flow sensors, vane flow and differential flow



Pressure regulator



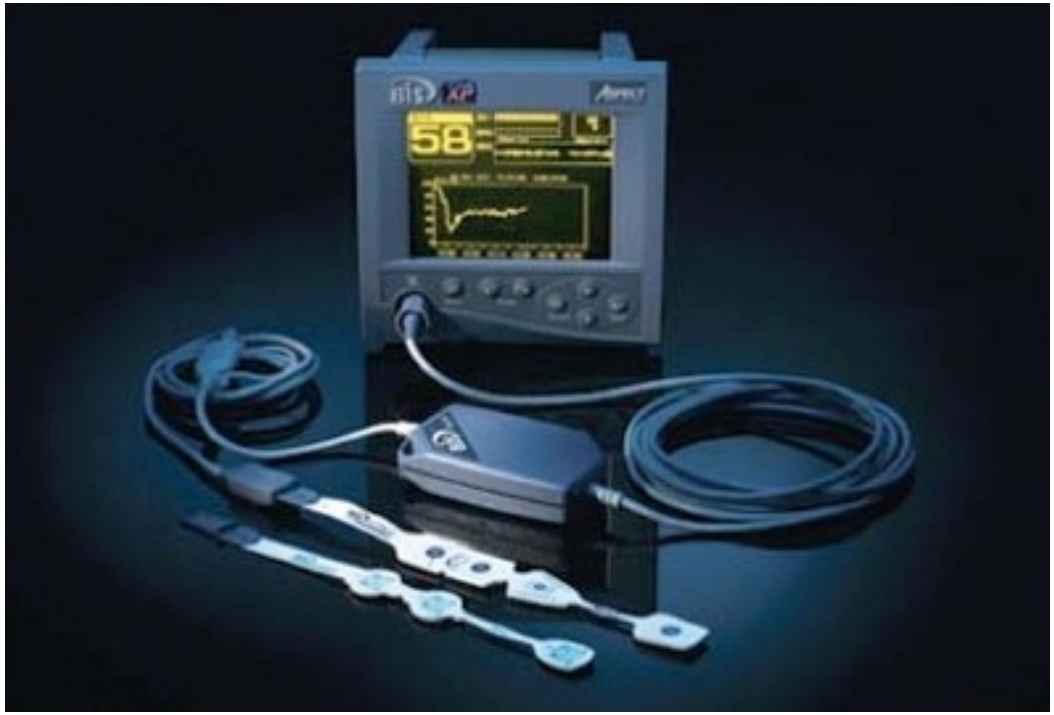
Source: Morgan GE, Mikhail MS, Murray MJ: *Clinical Anesthesiology*, 4th Edition: http://www.accessmedicine.com

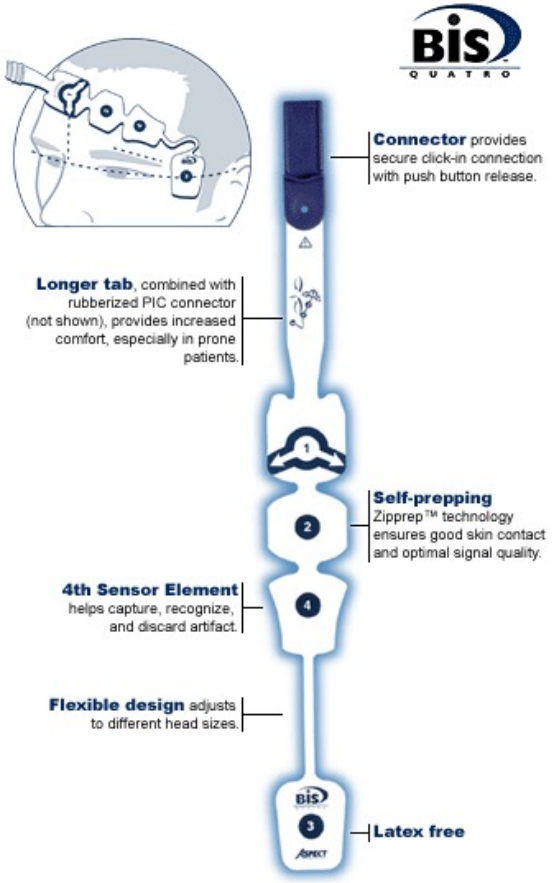
d. Monitor vital signs

Anesthetic monitoring

- Connecting it all together, what is necessary?
  - ECG
  - Blood pressure
  - End tidal CO_2
  - Sleep depth
  - Other?

Sleep depth: Bispectral index score (BIS)





http://bcrt.ca/wp-content/uploads/2009/07/bis.jpg

http://www.firesa.co.za/medical/1f65e210.gif

Bispectral index score (BIS)

- Based on EEG-measurements. A sensor placed on the forehead registers raw EEG-signals, transmits to a monitor which filters and digitalizes the EEG signal. Advanced pattern recognition calculate a value (BIS-score) from 0 (Isoelectric EEG) to 100 (completely awake)

http://bcrt.ca/wp-content/uploads/2009/07/bis.jpg

http://www.firesa.co.za/medical/1f65e210.gif

BIS Sources of error

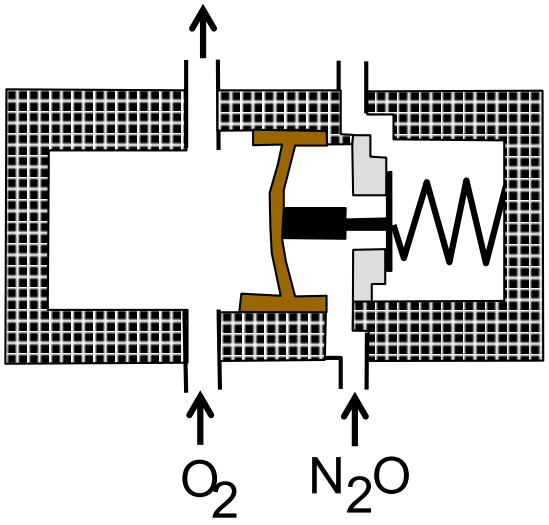
- Hypothermia: Decrease in BIS value
- Sleep: Decrease in BIS value
- Cerebral ischemia: Decrease in BIS value
- Neurological states: Decrease in BIS values
- Encephalopathic states: Decrease in BIS values
- Interference from medical devices: Increase in BIS values
- Low $PaCO_2$: Decrease in BIS values
- And what about the electrodes??

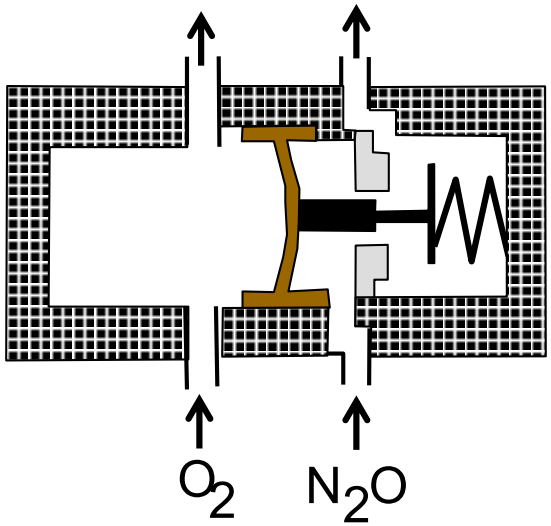
http://bcrt.ca/wp-content/uploads/2009/07/bis.jpg

http://www.firesa.co.za/medical/1f65e210.gif

Wrong gas concentrations

Accident: Leakage from O_2 to N_2O





2-room slave regulator

Wrong gas concentrations

Accident: No O2 flow

Berge Grimnes: Gassteknisk medisinsk utstyr Del 2

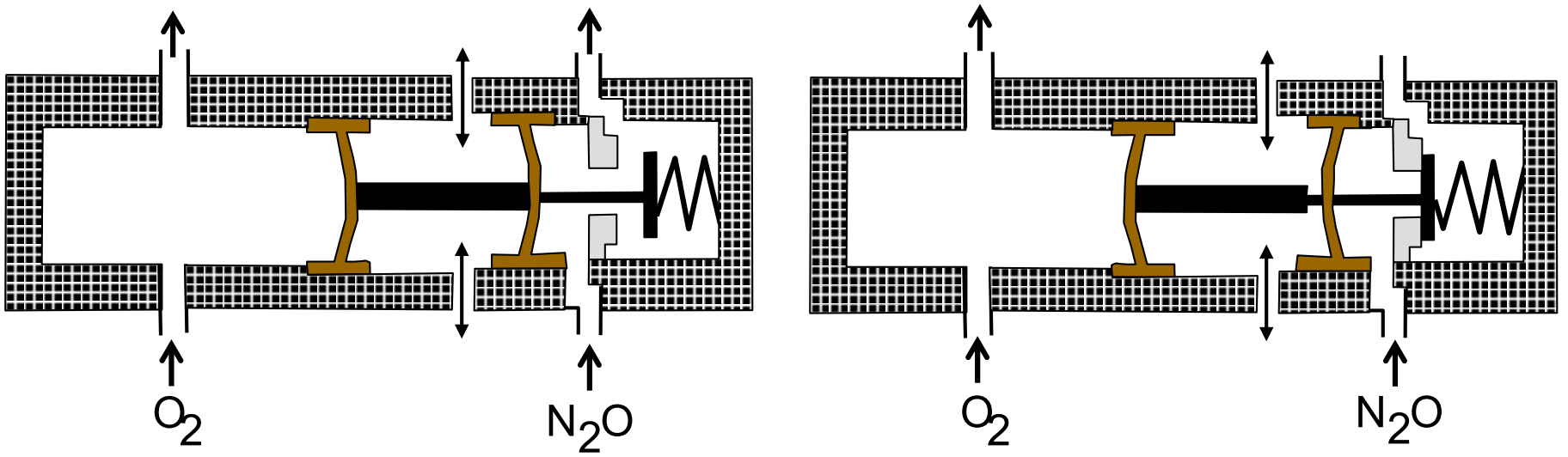
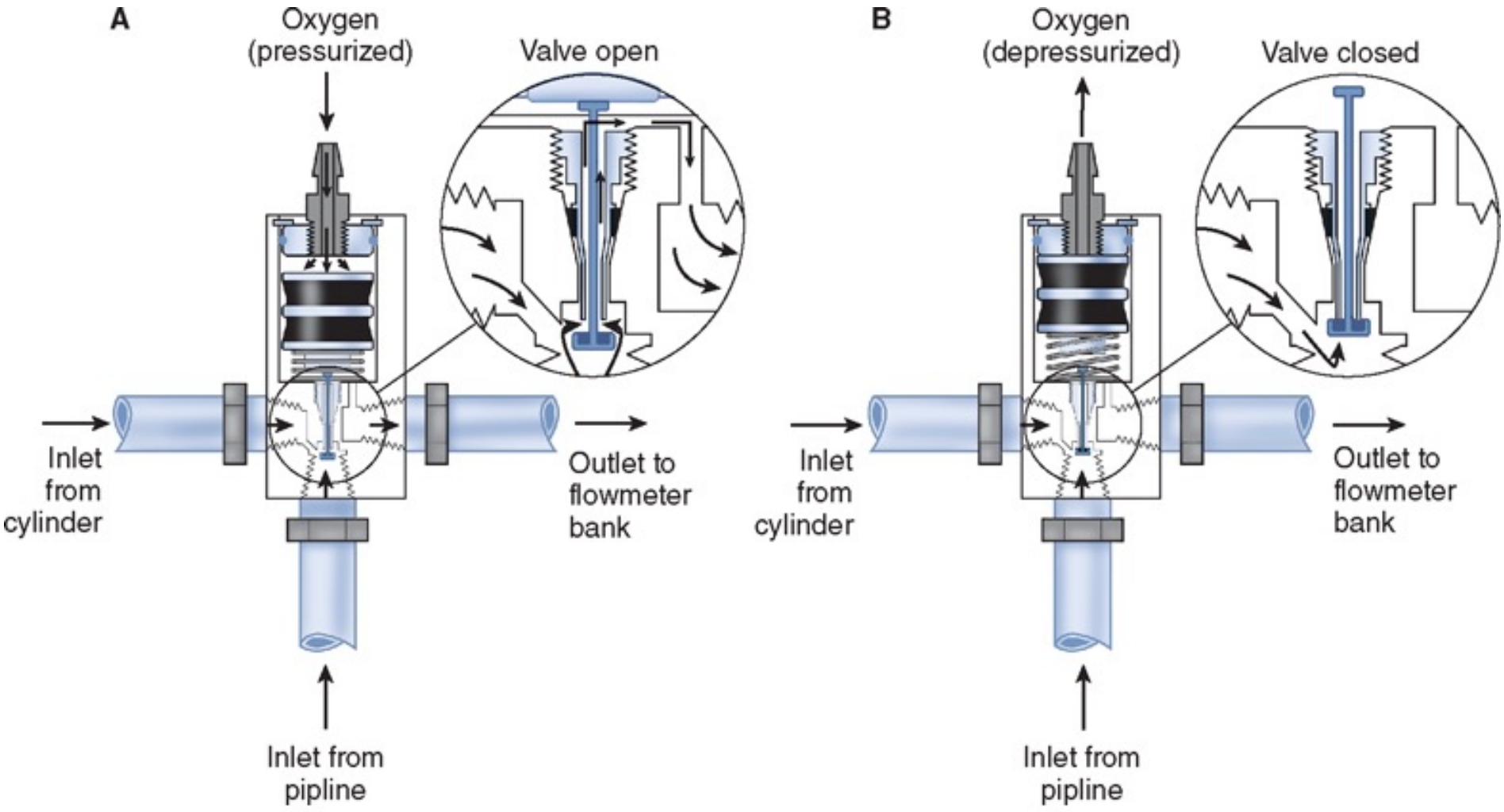
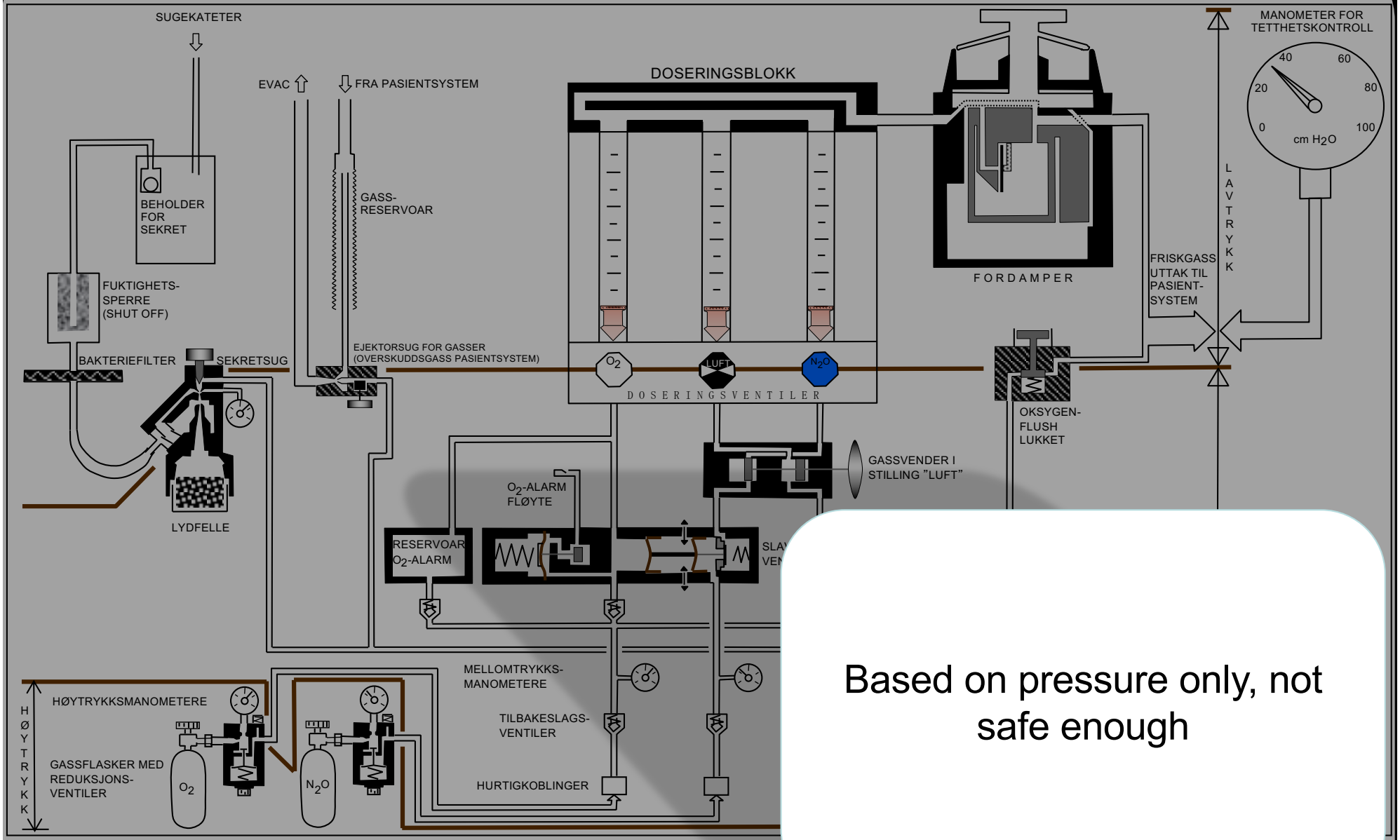


Fig. 2.F. 3-room slave regulator

Slave regulator, pressure controled



Source: Butterworth JF, Mackey DC, Wasnick JD: *Morgan & Mikhail's Clinical Anesthesiology*, 5th Edition: www.accessmedicine.com



Based on pressure only, not safe enough

Fig 2A, side 11

Redigert 2006
av TM.

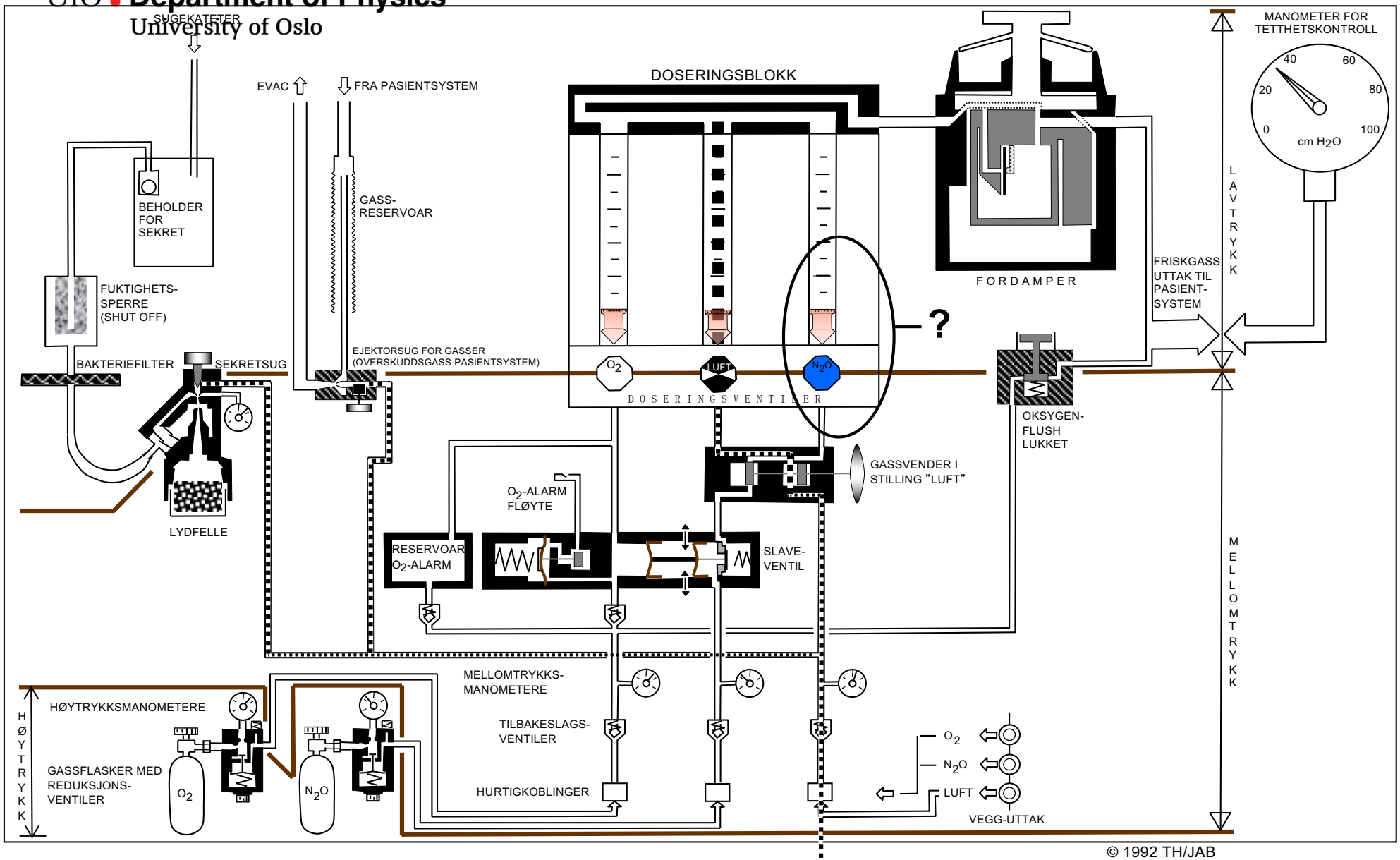


Fig 2A, side 11

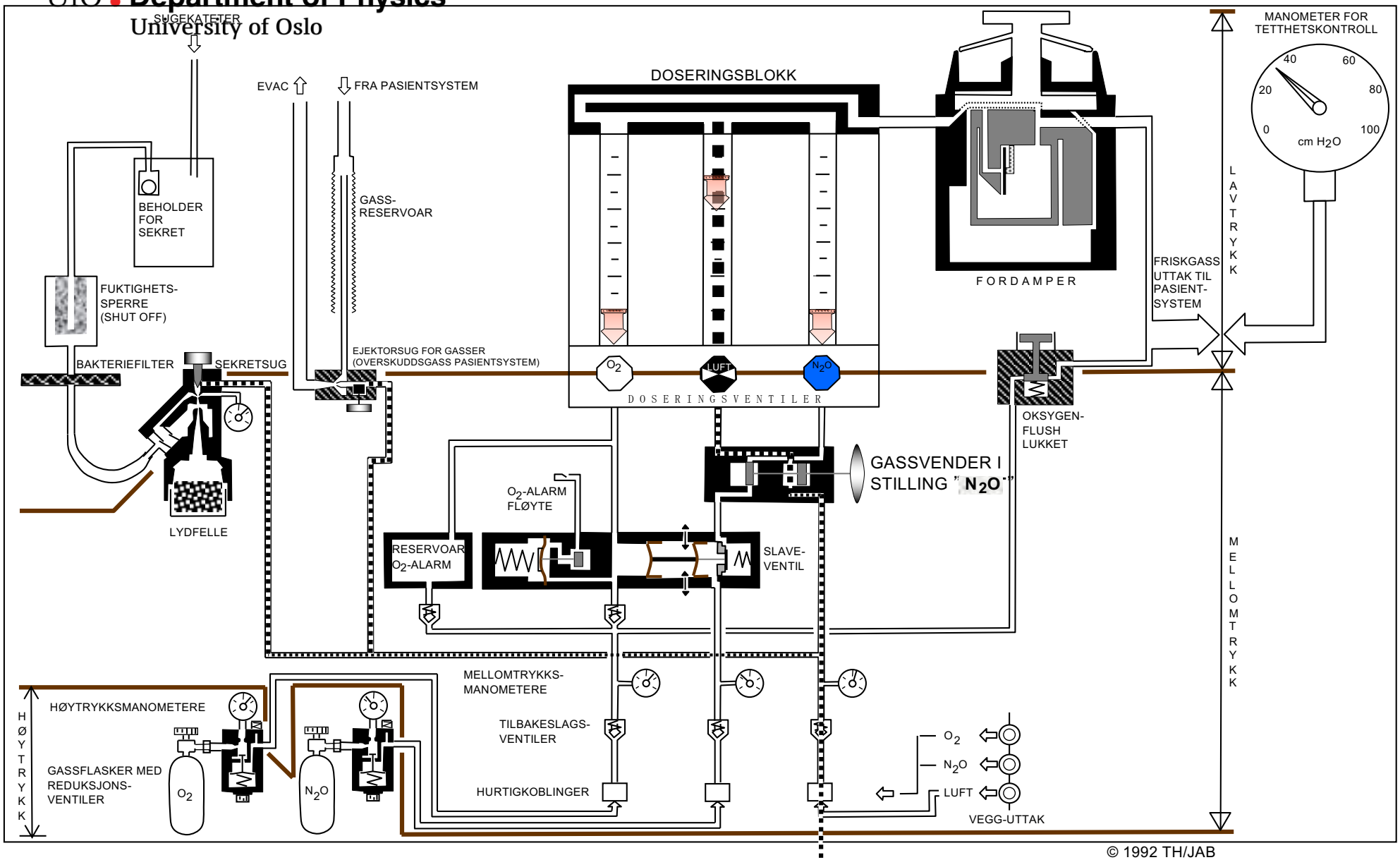


Fig 2A, side 11

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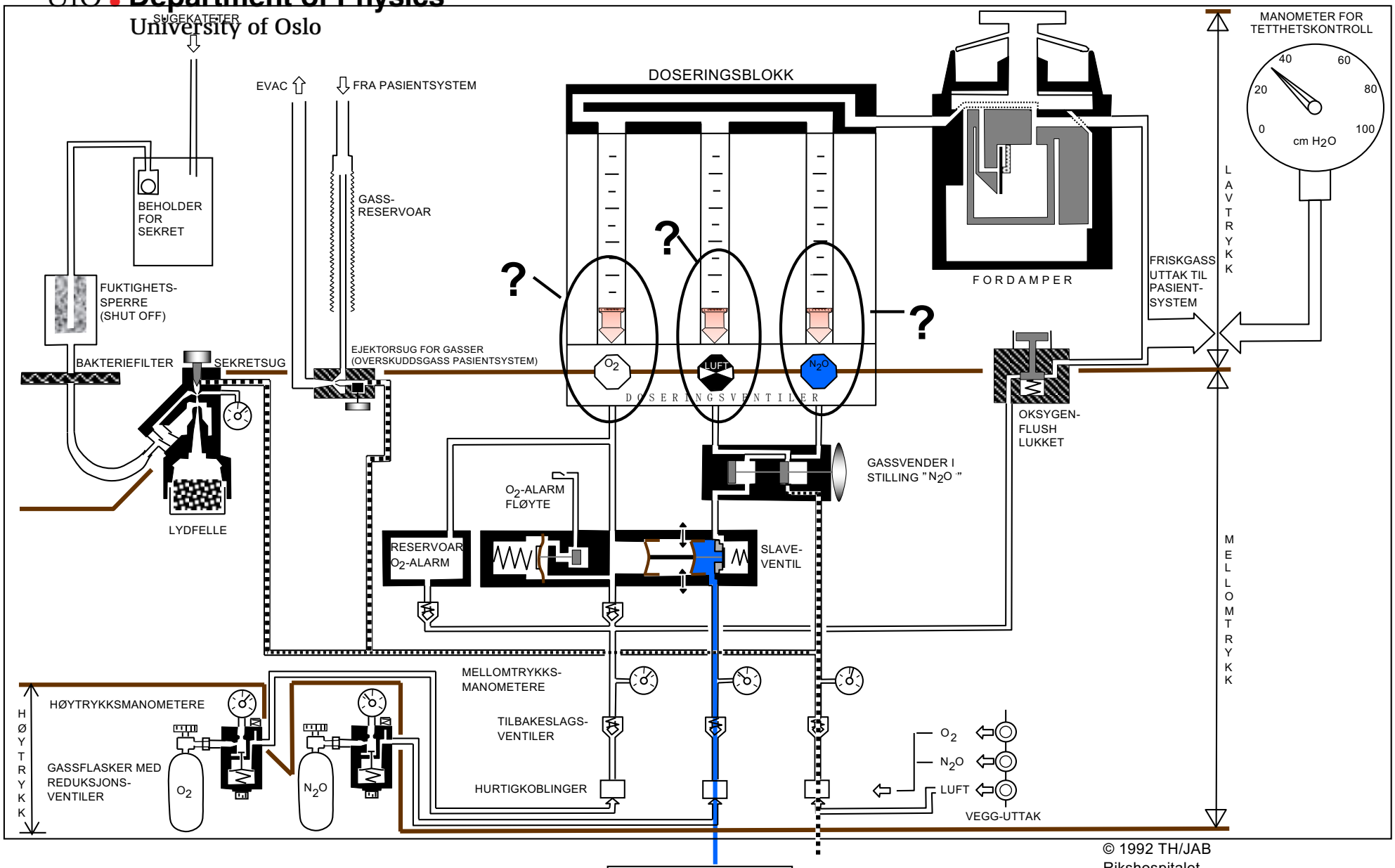

Fig 2A, side 11

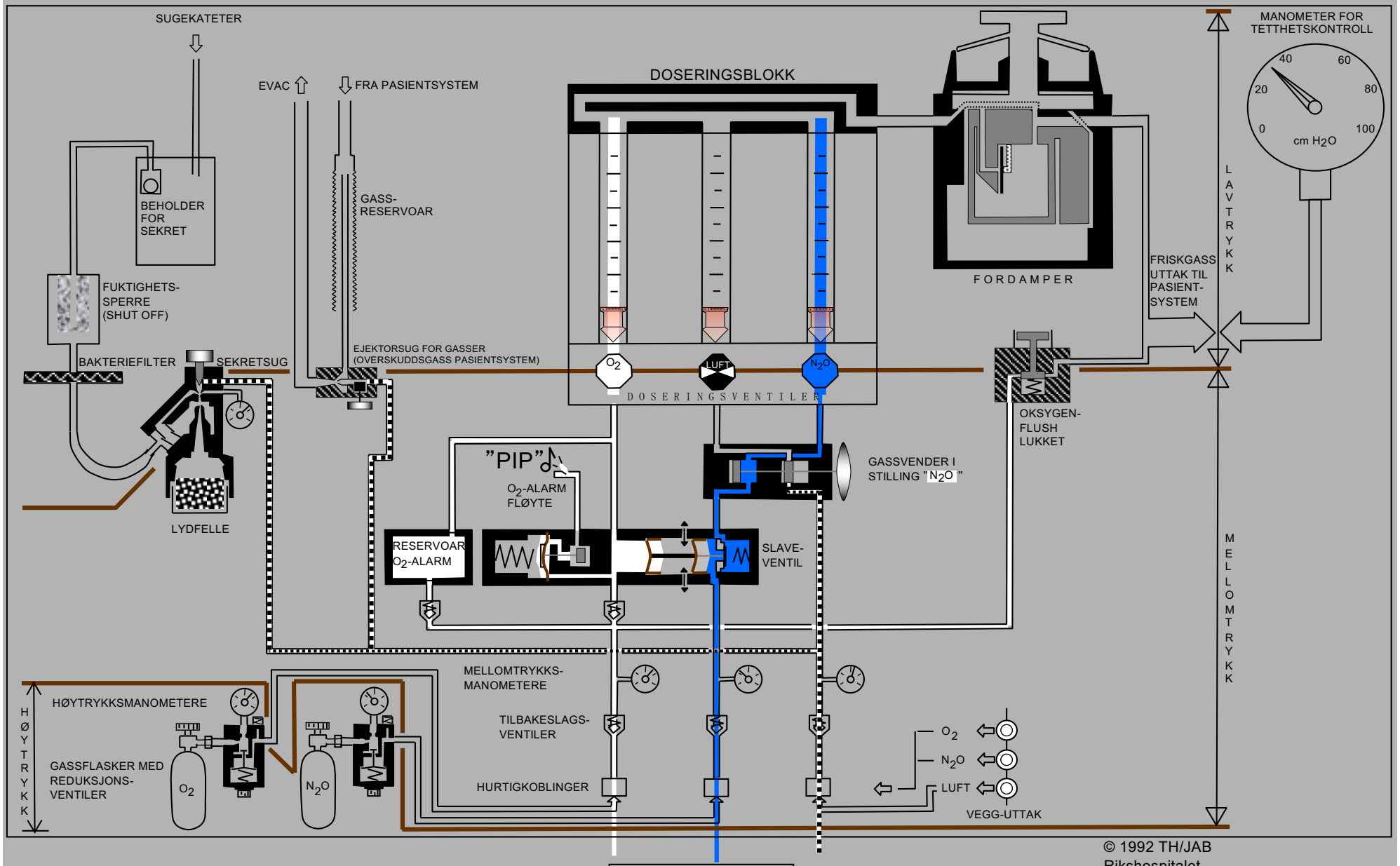

Fig 2A, side 11

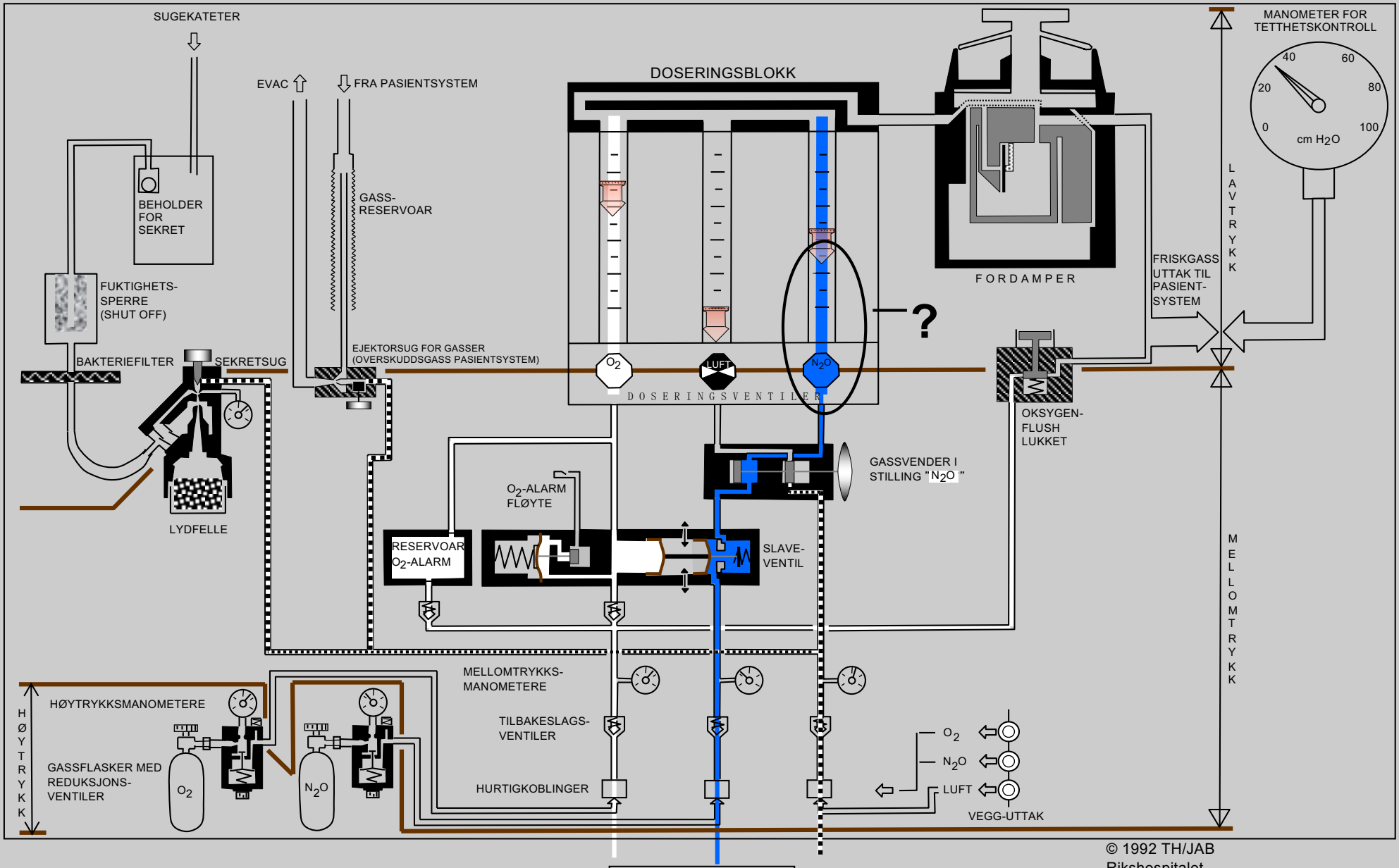

Fig 2A, side 11

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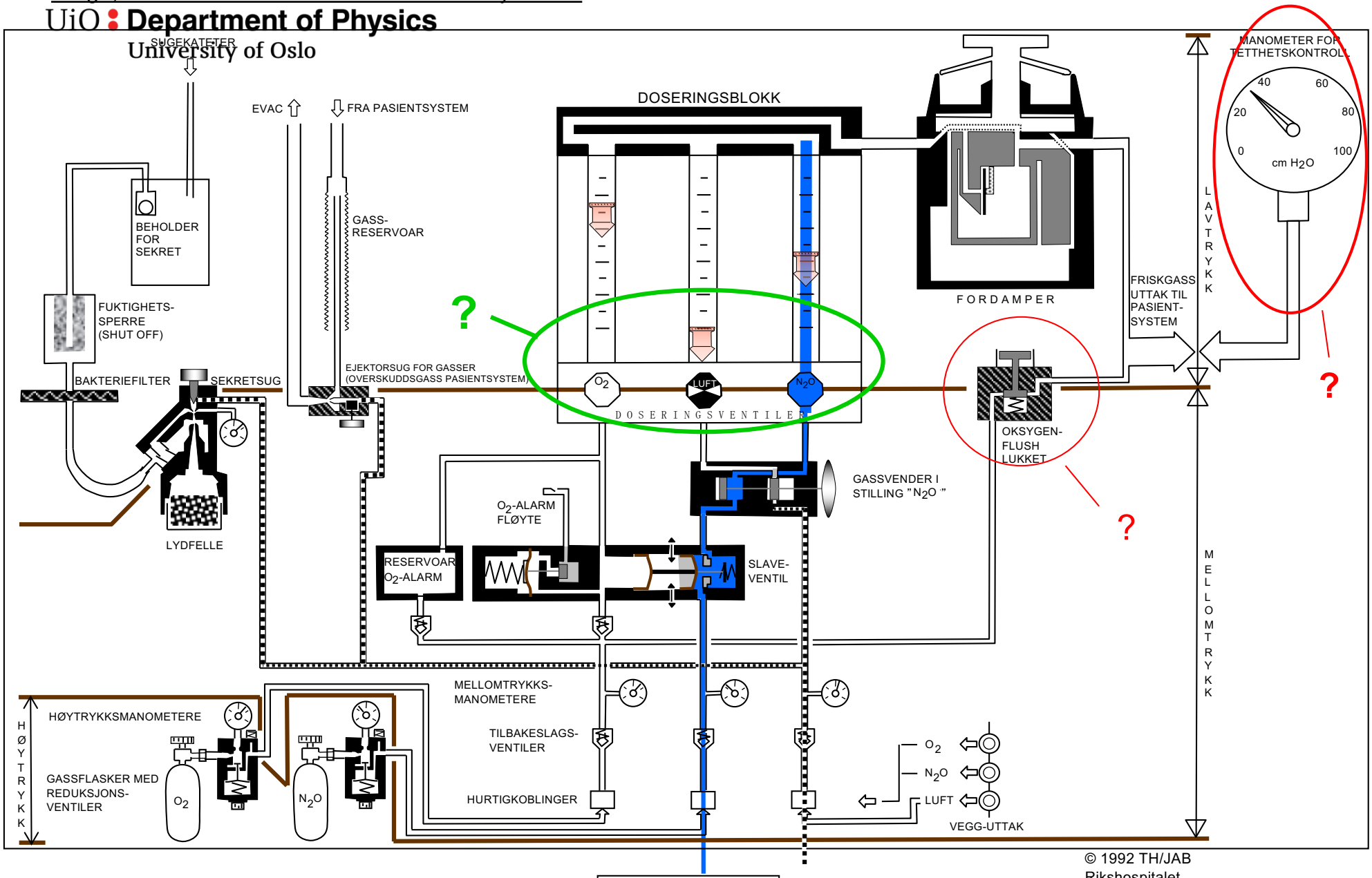

Fig 2A, side 11

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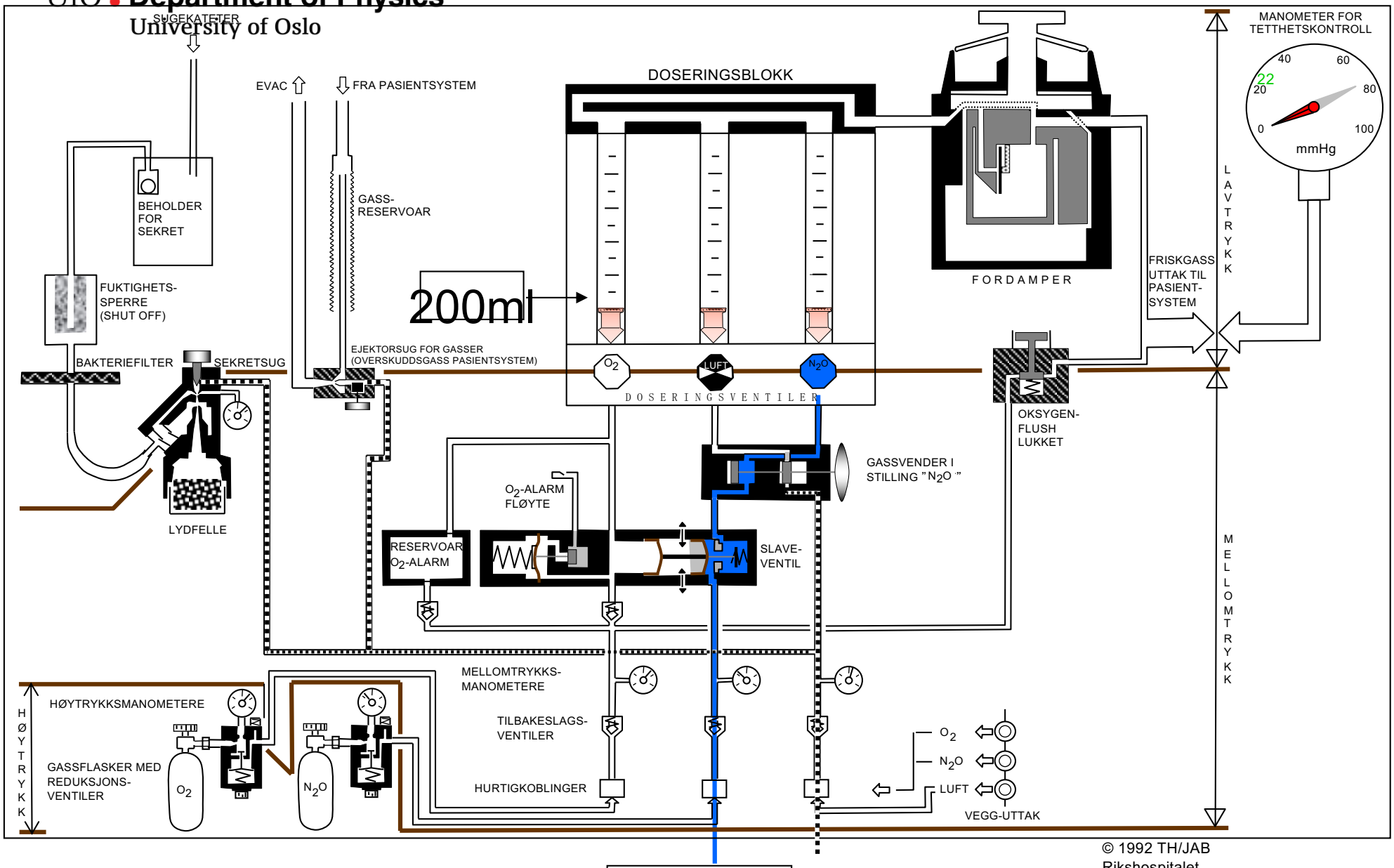
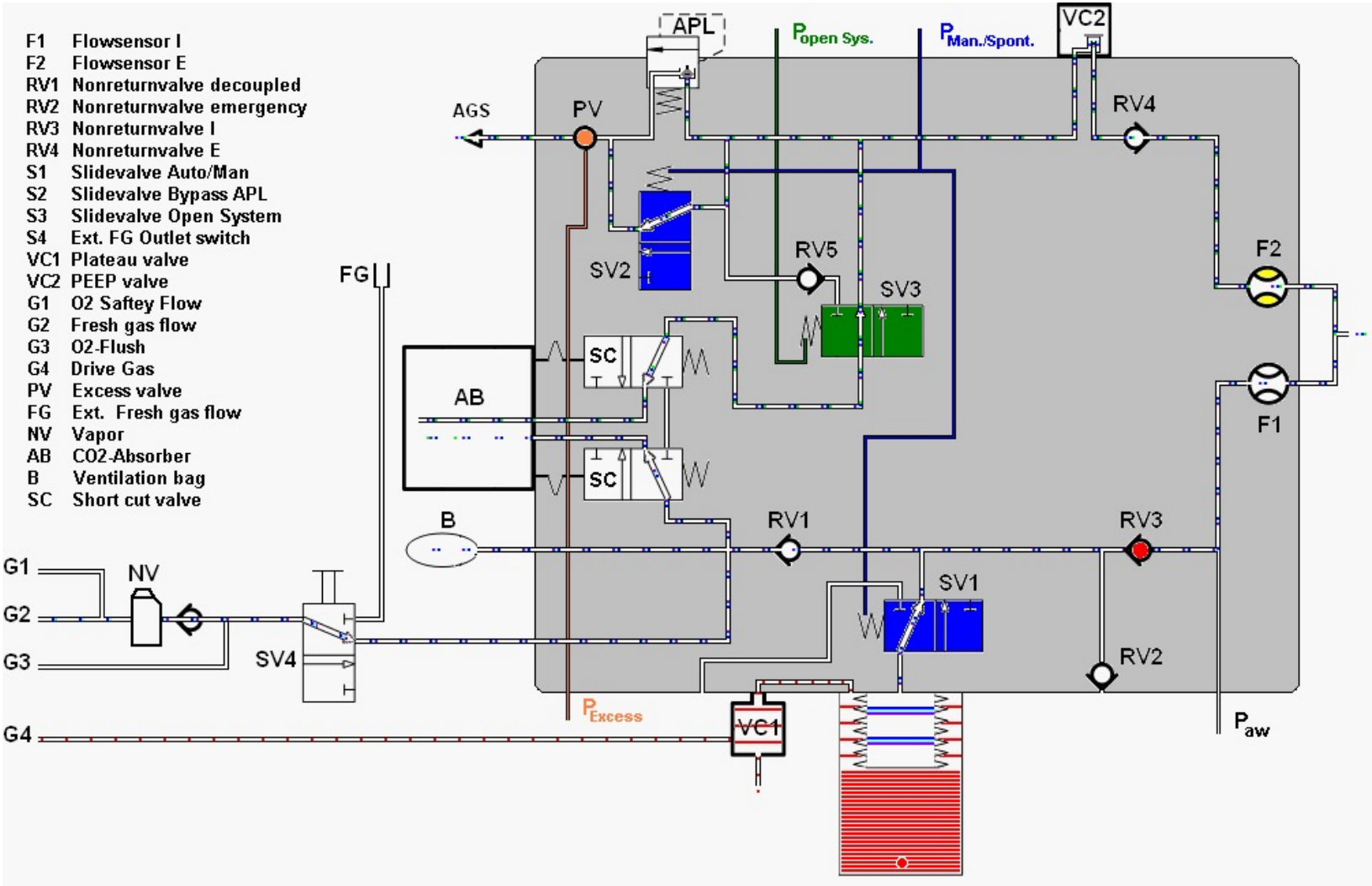
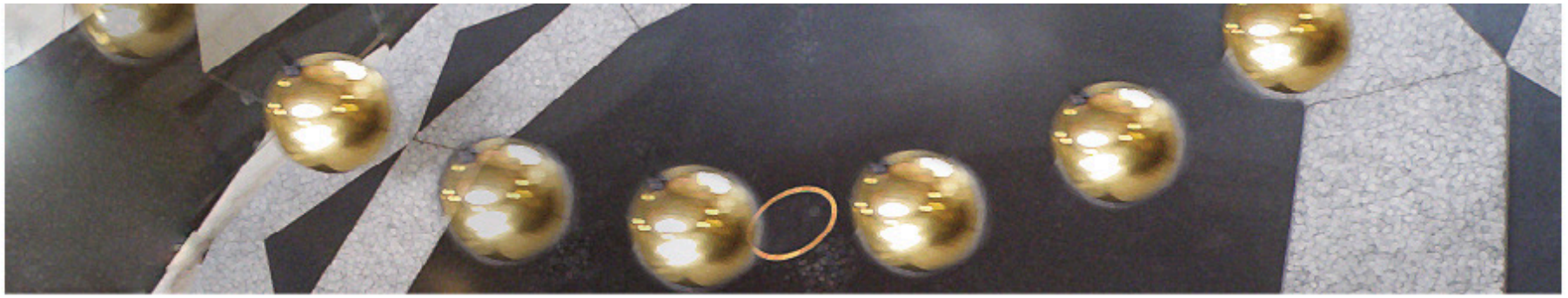


Fig 2A, side 11


Flow meter
ventilator
bellow
vaporizer
Corrugated tube
APL valve
Soda lime
Scavenging system

Block diagram





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Lecture 10

”Once a scout always a scout!”

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Spectrophotometer

$$P = P_0 10^{-aLC}$$

P0 = radiant power arrivint at the cuvette
P = radiant power leaving the cuvette
a = absorptivity of the sample
L = length of the path through the sample
C = concentration of the absorbing substance

Hydrogen and deuterium lamps produce about 90% of their power in the infrared range
Tungsten: Progressively vaporizes from the filaments and condenses unevenly on the glass envelope

Wavelength selector: Filters and monochromators. Glassfilters used in applications in which modest accuracy is required
Monochromators utilize prisms and diffraction gratings = narrow bandwiths and adjustable wavelengths

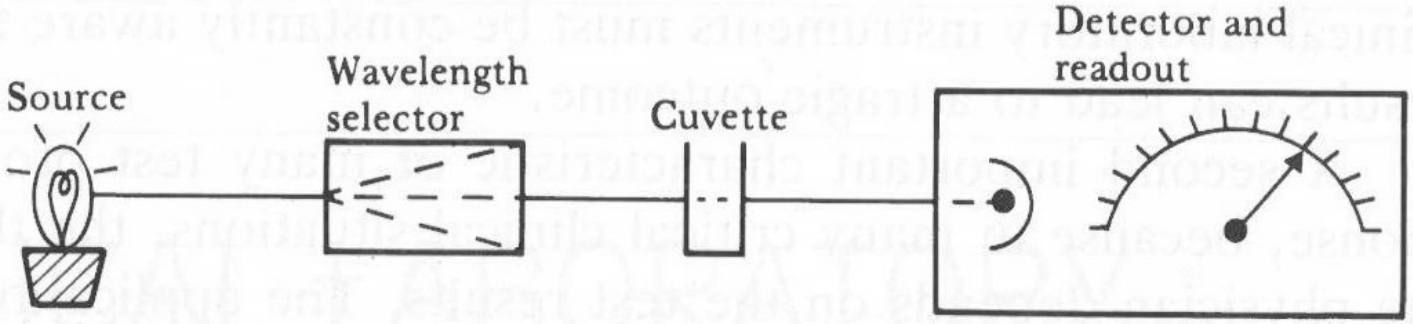
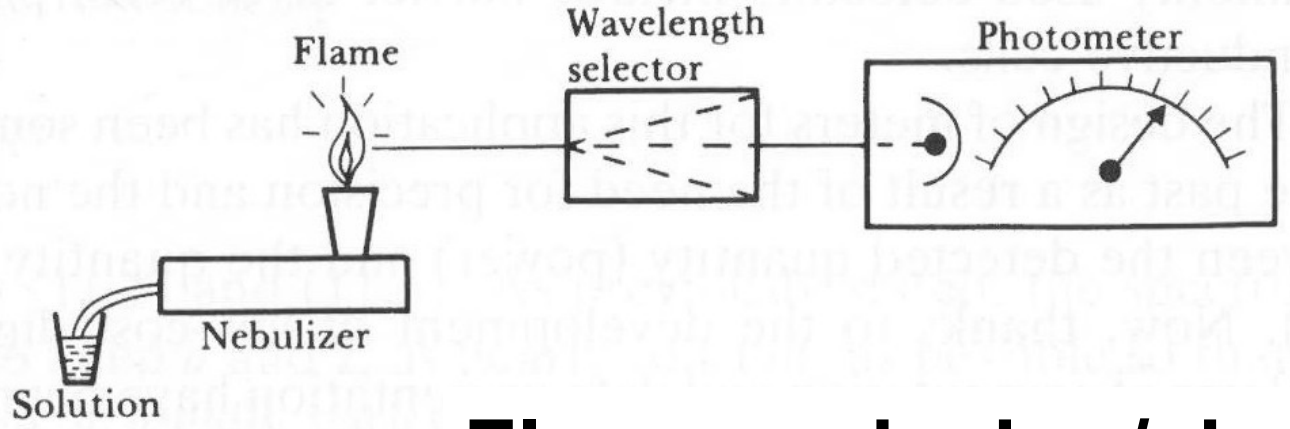
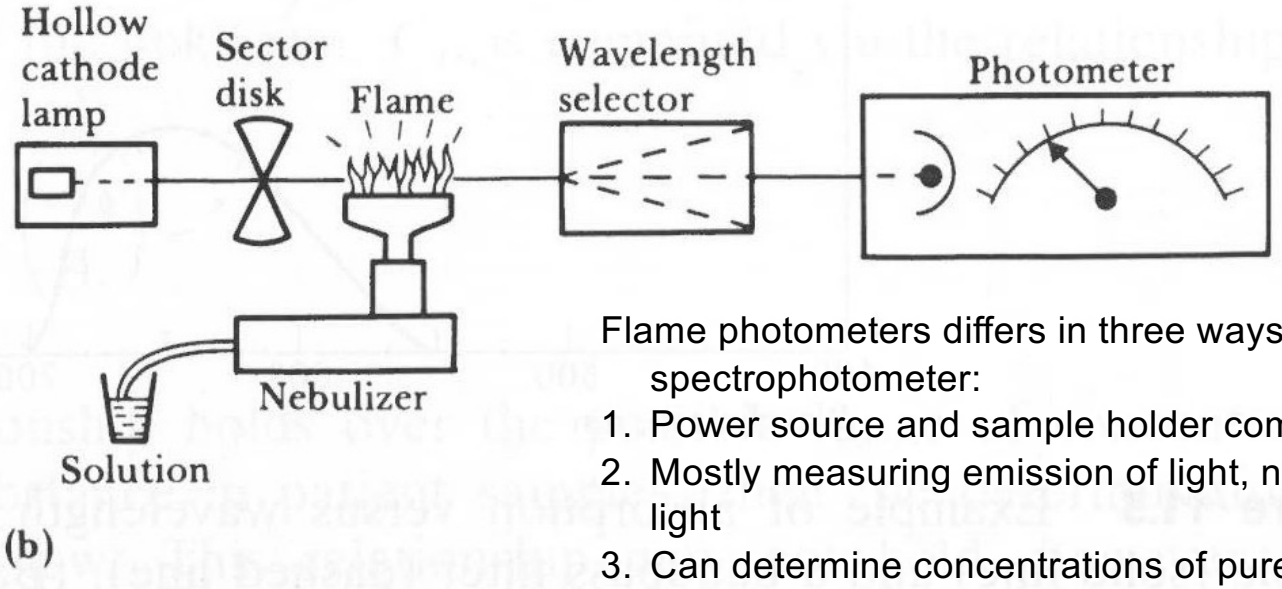


Figure 11.1 Block diagram of a spectrophotometer (Based on R. J. Henry, D. C. Cannon, and J. W. Winkelman, eds., *Clinical Chemistry*, 2nd ed. Hagerstown, MD: Harper & Row, 1974.)



Flame emission/absorption



Flame photometers differs in three ways from spectrophotometer:

1. Power source and sample holder combined in flame
2. Mostly measuring emission of light, not absorpion of light
3. Can determine concentrations of pure metal only

Figure 11.4 Block diagrams of instruments for (a) flame emission and (b) flame absorption. (Based on R. J. Henry, D. C. Cannon, and J. W. Winkelman, eds., *Clinical Chemistry*, 2nd ed. Hagerstown, MD: Harper & Row, 1974.)

Fluorometry

Advantage: High sensitivity
Disadvantage: Few substances have the property of fluroescense, Sensitivity to temperature and pH

Based on the fact that molecules emit light in a characteristic spectrum immediately after absorbing radiant energy and being raised to an excited state.

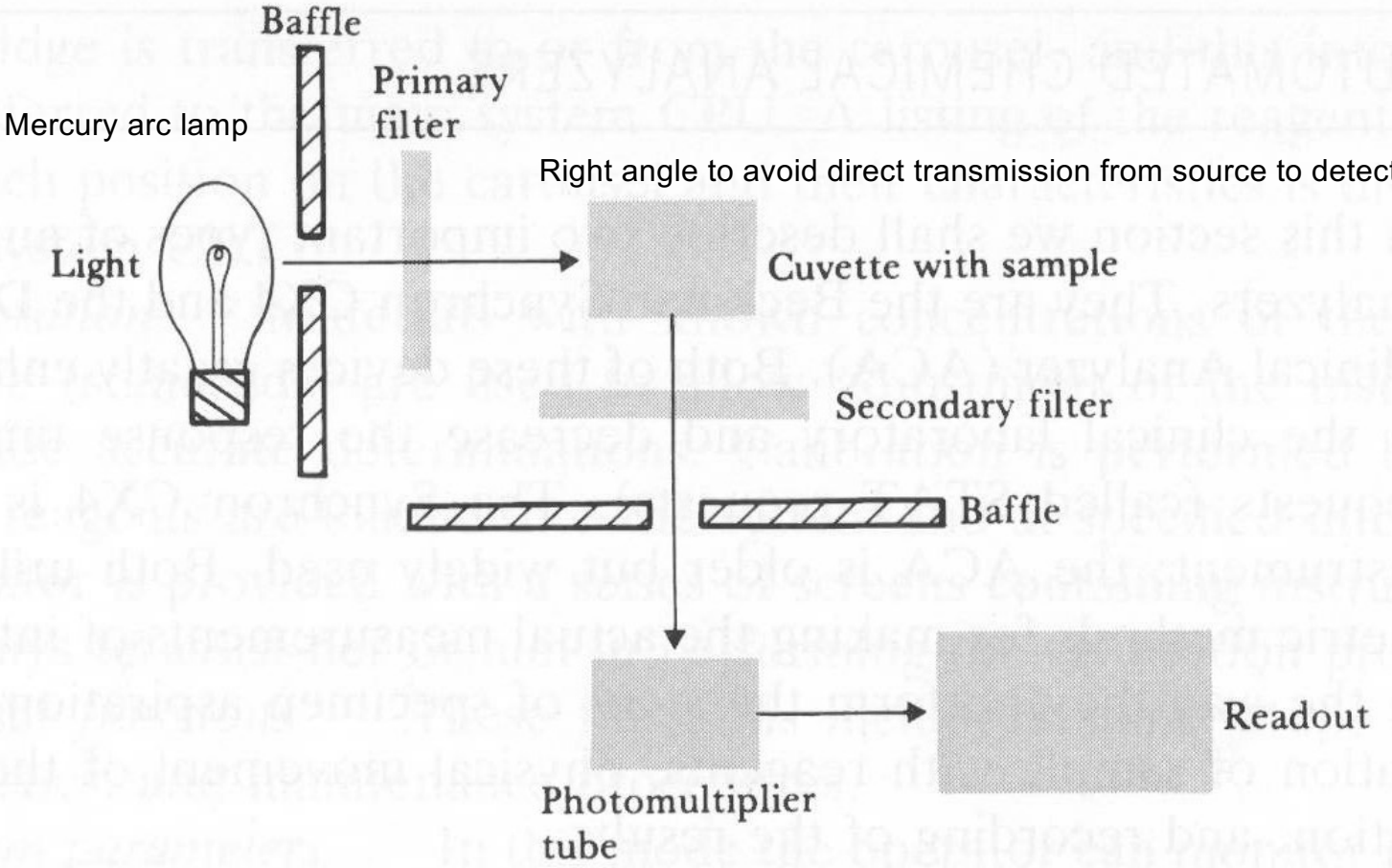
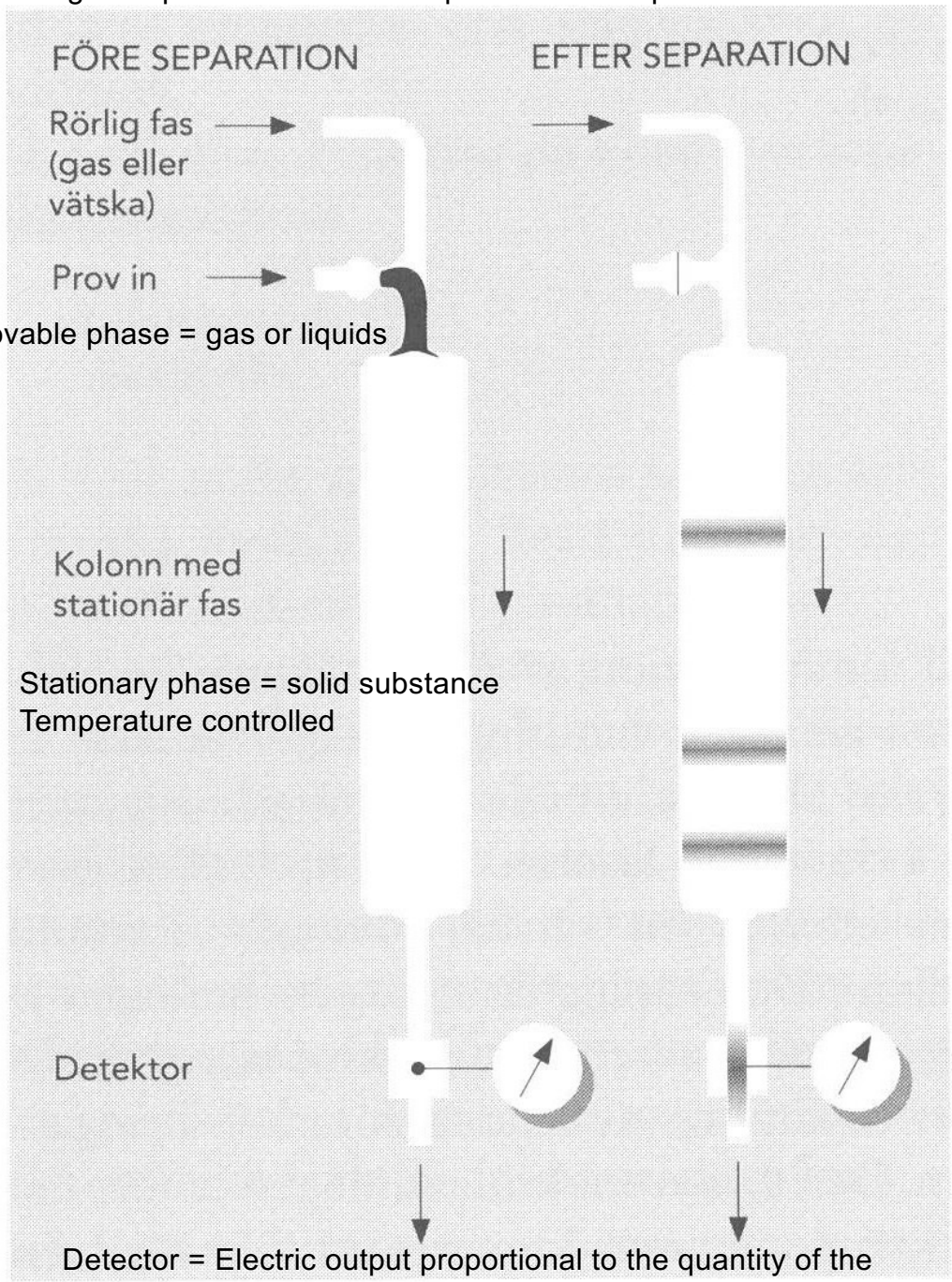


Figure 11.5 Block diagram of a fluorometer (From R. Hicks, J. R. Schenken, and M. A. Steinrauf, *Laboratory Instrumentation*. Hagerstown, MD: Harper & Row, 1974. Used with permission of C. A. McWhorter.)

High temperature to flash evaporate the sample and solvents



Movable phase = gas or liquids

Stationary phase = solid substance
Temperature controlled

Detector = Electric output proportional to the quantity of the compound in the effluent gas

Gas/liquid cromatography (GLC)

Used for separating mixture of substances into component parts

Carrier gas = inert gas, sweeps the evaporated sample and solvent gas down the column

Advantages = Speed, ability to operate with a small amount of sample and great sensitivity

Figur 5:14. Princip för kromatografi. Separation av provets komponenter sker genom utnyttjande av att de har olika vandringshastighet, då en rörlig fas flyter fram över en stationär fas.

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Electrophoresis

Charged particles migrate in response to ar electrical field

- Field strength
- Charge
- Size
- ++

Mobility = distance in centimeters a particle move in unit time per unit field strength, expressed as voltage drop per centimeter

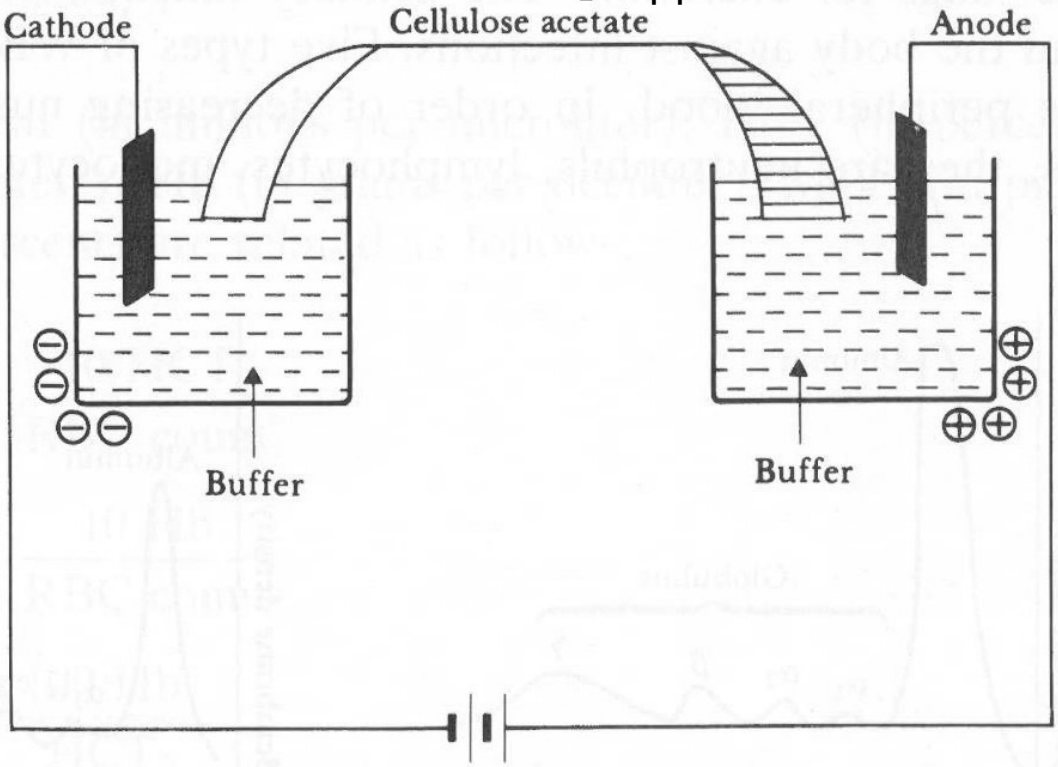


Figure 11.11 Cellulose acetate electrophoresis (From R. Hicks, J. R. Schen-

Typical = various proteins in blood and nucleic acids, csf ++
Defined as the movement of a solid phase with respect to a liquid (buffer solution).
Buffer -> carry current and keep the pH constant
Electrid field -> particles similar in charge, size and shape migrate at similar rates directly related to the net magnitude of the particle's charge
Disadvantage = temperature dependency
Advantage = Rapid and highly sensitive

Coulter counter cell counter

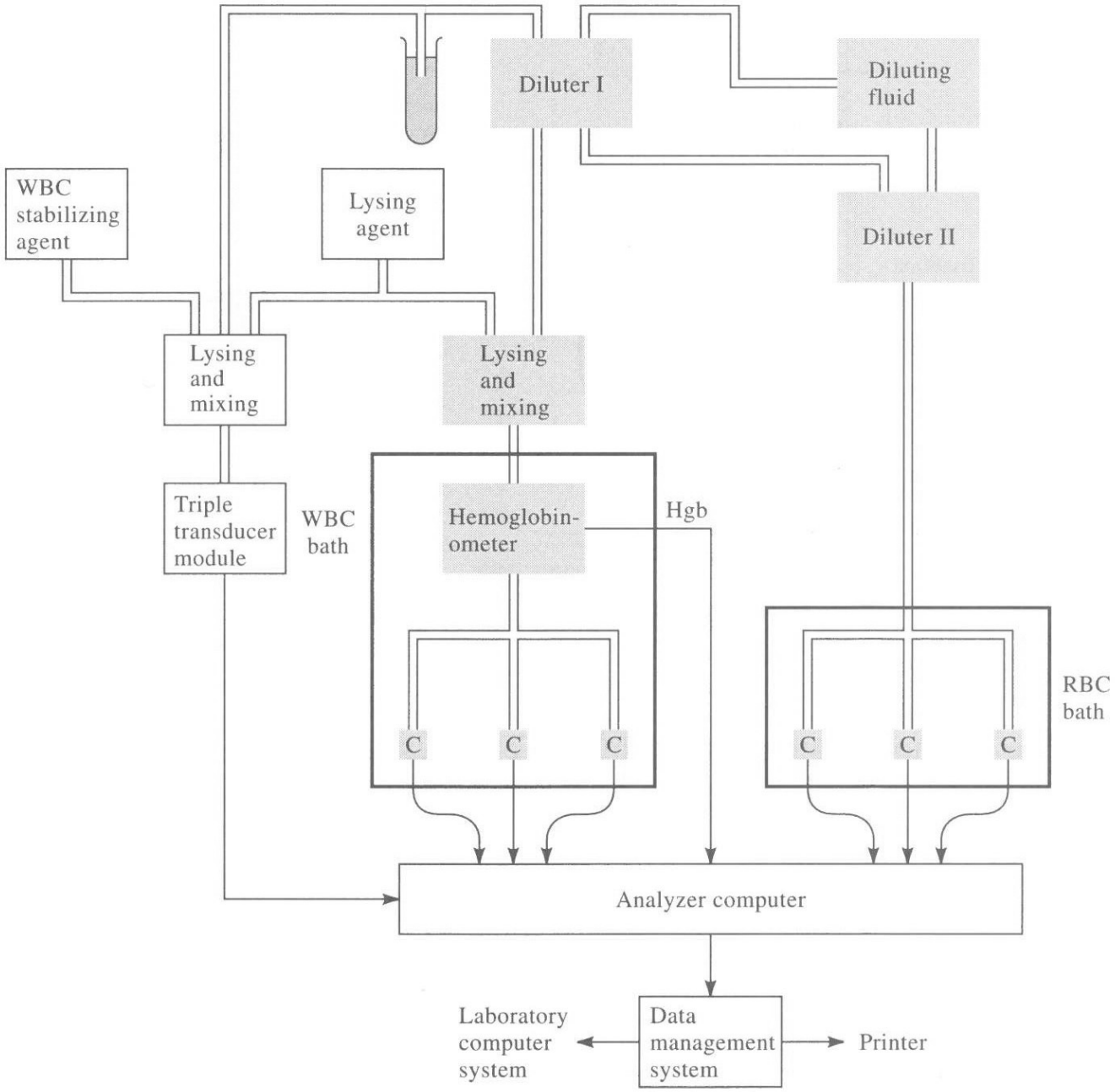


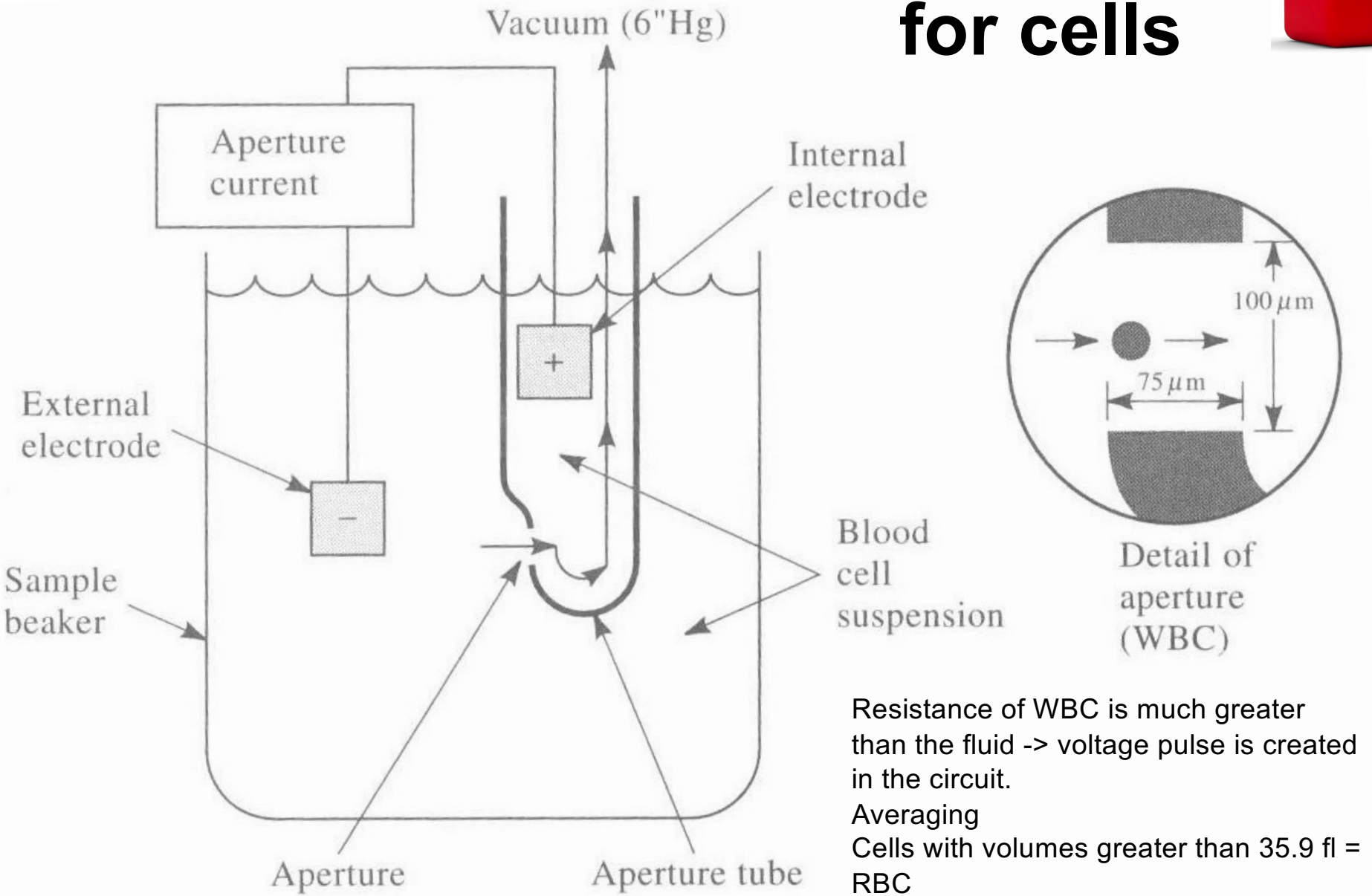
Figure 11.11 **A block diagram of a Coulter Model STKS.** (Modified from J. Davidsohn and J. B. Henry, Todd Sanford Clinical Diagnosis by Laboratory Methods, 15 ed. Philadelphia: W. B. Saunders Co.)

Hematology:
RBC, WBC and plateles
Anticoagulants

Lyzing agent causes cell membranes of RBC to rupture and release HGB

Ratio WBC vs RBC 1:600
1% of the blood vs 36-50% of the blood

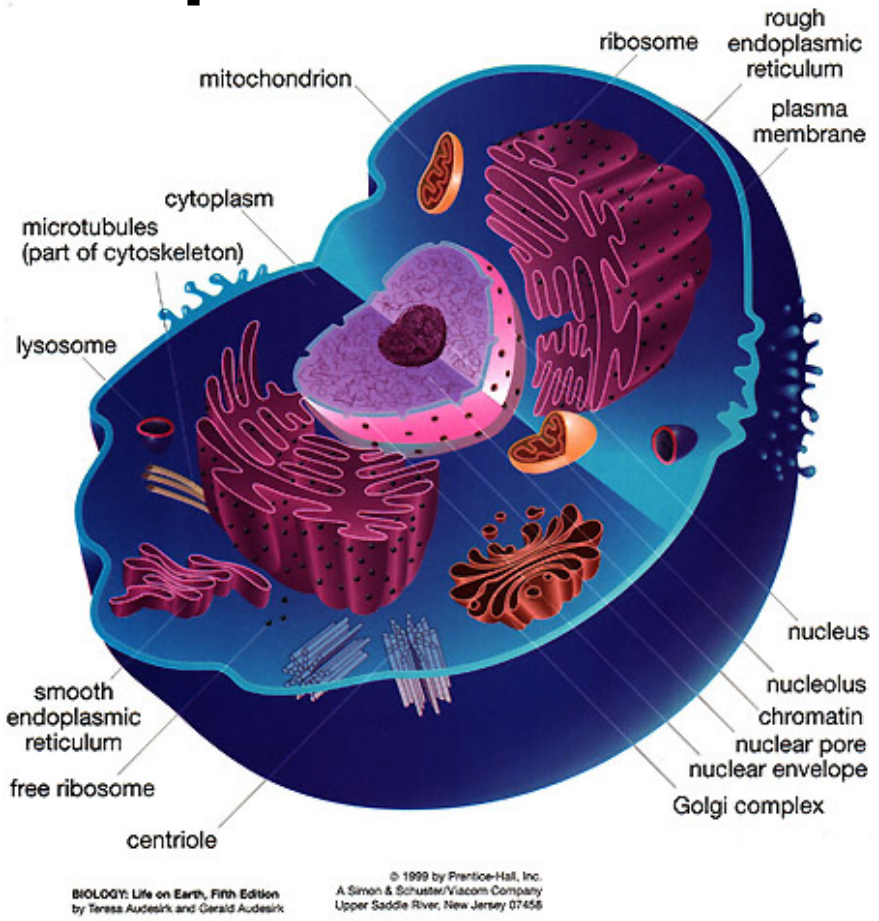
Impedance- detector for cells



Resistance of WBC is much greater than the fluid -> voltage pulse is created in the circuit.
Averaging
Cells with volumes greater than 35.9 fl = RBC

Figure 11.12 Coulter STKS aperture bath.

Cellular composition

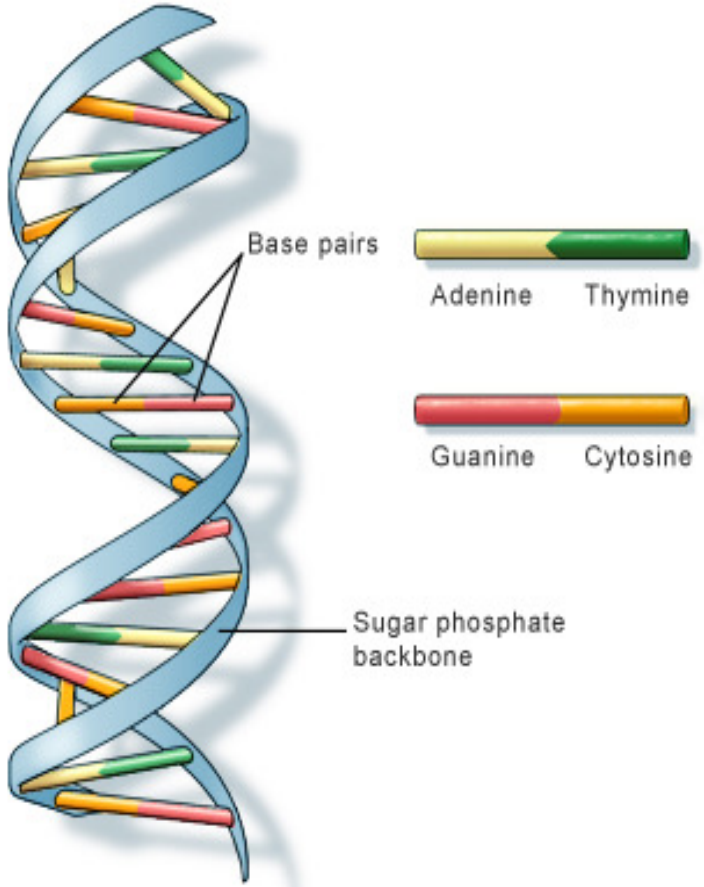


- Source: Todd Rightmire, mt Baker High School

DNA is located in the cell nucleus

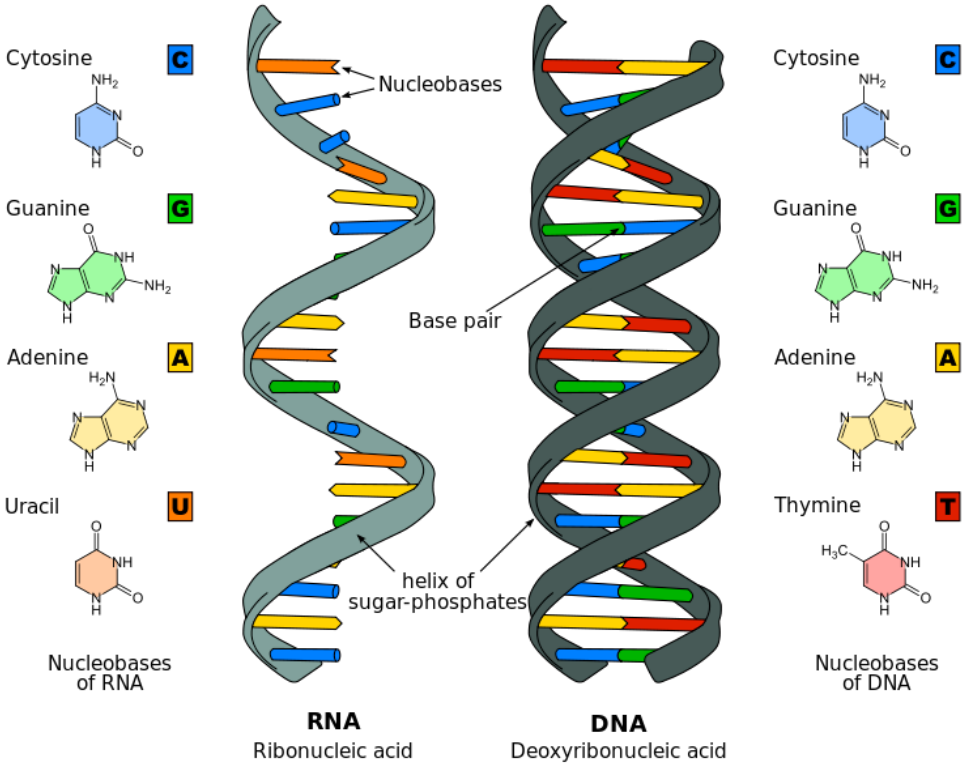
Deoxyribo Nucleic Acid (DNA)

- A double helix built of nucleotides, connected to long chains
- Base pairs of Adenine (A), Thymine (T), Guanine (G) and Cytosine (C). Guanine will always combine with Cytosine, and Thymine will always bind with Adenine.
- Backbone contains sugar-phosphate
- Each triplet of ATGC codes for a certain amino acid that will build a protein
- The genetic code is determined of the order of the nitrogenbases in the DNA-chain, the so called genetic code



Ribo Nucleic Acid (RNA)

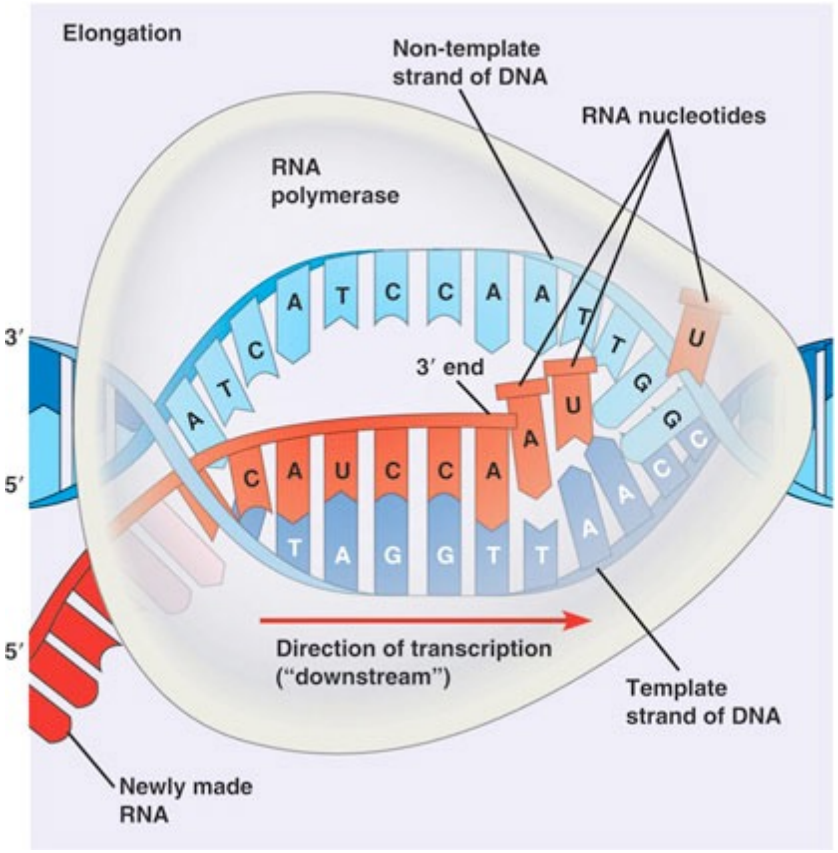
- DNA contains all the necessary information for protein synthesis, but the job is done in the ribosomes
- DNA molecules are too big to penetrate the nucleus-membrane, transcription gives m-RNA that can move freely into cytosol
- RNA is an information transference of the DNA into the ribosomes where amino acids are connected to form proteins
- ACG are the same as for DNA, but thymin is replaced with Uracil (U)



http://upload.wikimedia.org/wikipedia/commons/thumb/3/37/Difference_DNA_RNA-EN.svg/749px-Difference_DNA_RNA-EN.svg.png

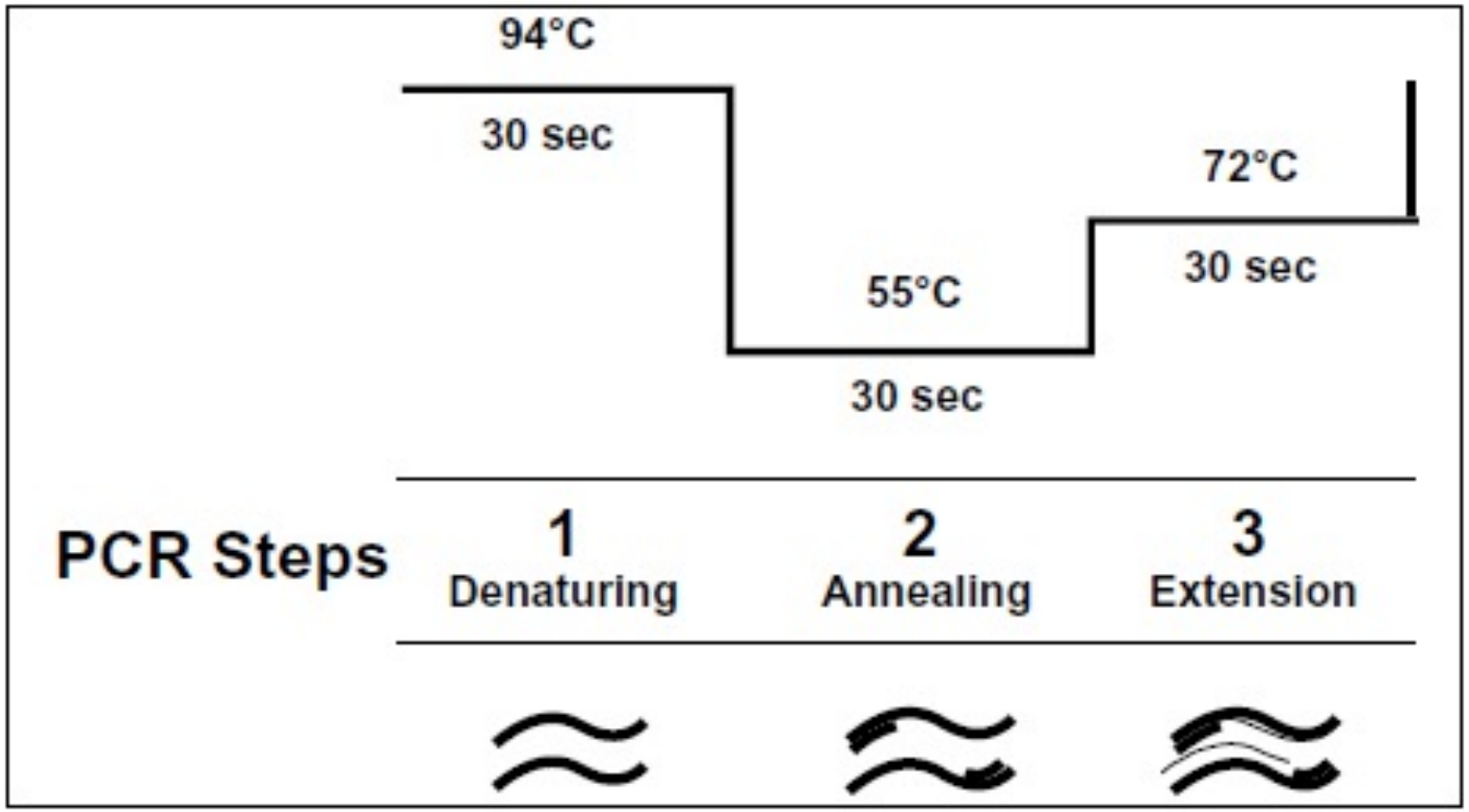
M-RNA syntesis

- The two DNA-chains are separated in order to release the nitrogen bases. RNA polymerase binds free ribonucleotides complementary to the nucleotides in the DNA-chain
- Each triplet in DNA gives a complementary triplett in m-RNA
- At the start of each gene there is a promotor defining the starting point of the polymerase
- t-RNA connects to specific amino-acids and if the m-RNA code is matched, this can be used by the ribosome for decoding the m-RNA and building chains of amino acids



http://meyerbio1b.wikispaces.com/file/view/transcription.jpg/72711585/transcription.jpg

The three cycles of PCR



Palumbi: The simple fool's guide to PCR

Denaturation - Renaturation

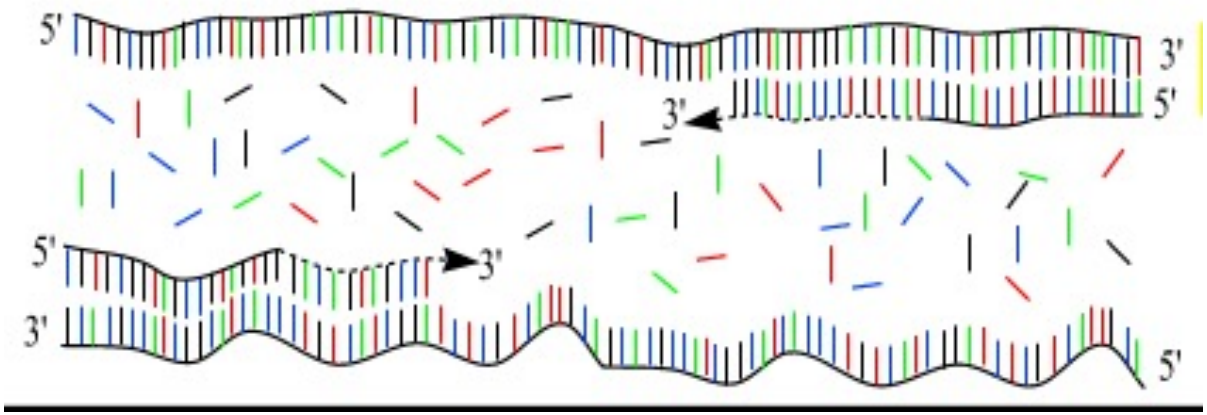
- Separating the double helix DNA by applying heat = Denaturation
- Careful cooling anneals the helix = renaturation
- All DNA becomes single strands

Annealing

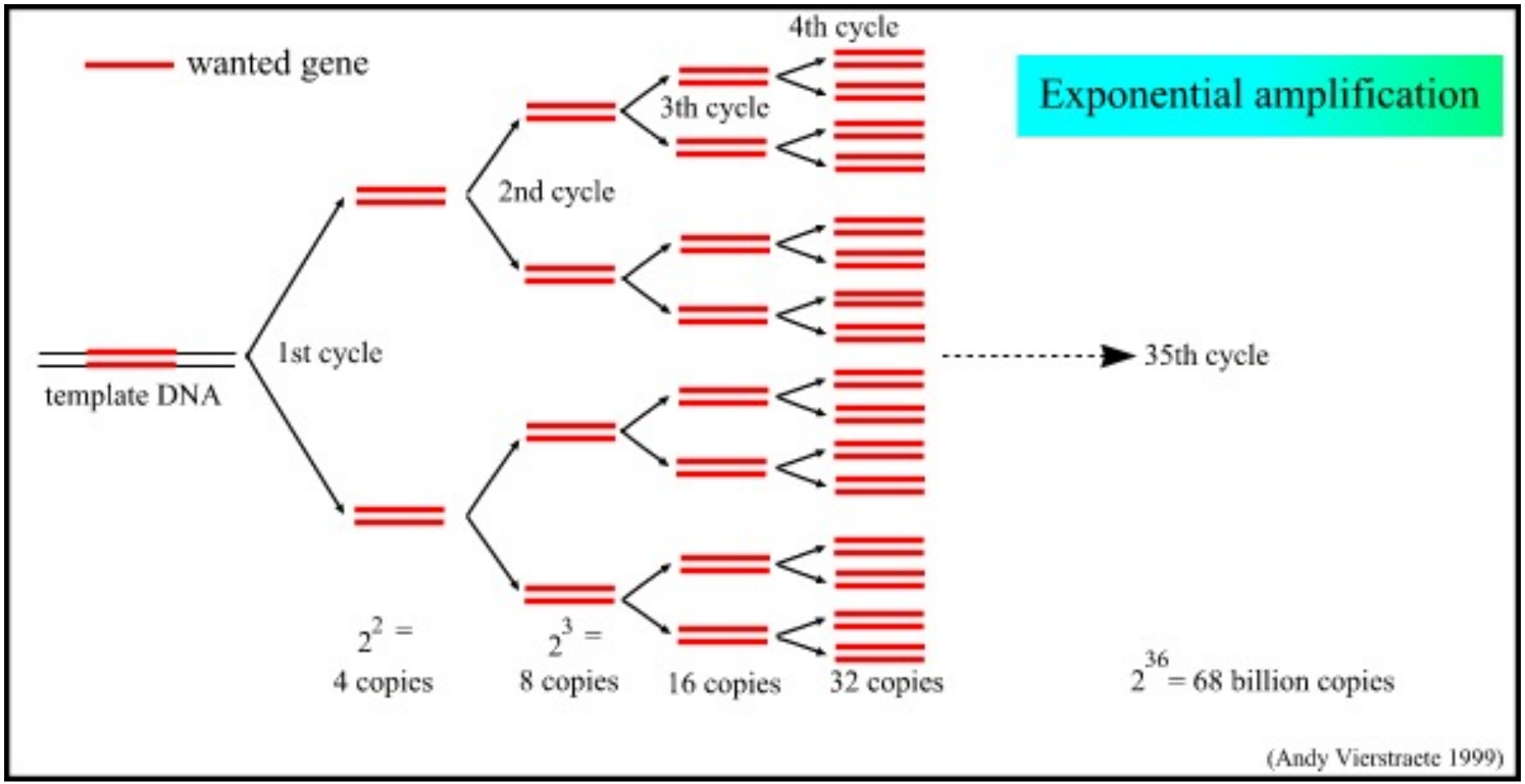
- In order to bind to each of the complementary regions, two primers are supplied in molar excess
- Temperature is lowered to allow primers to anneal. (Too low temperature will allow randomly annealing, too high temperature will avoid any binding at all)
- Typically temperature between 40 – 60 degrees C

Extension

- DNA polymerase duplicates DNA, typically between 72-75˚C for maximal polymerase function.
- Polymerase must add nucleotides to the 3’ end of the primer sequence annealed to the template DNA
- Primers are critical for the initiation of the reaction



PCR amplification

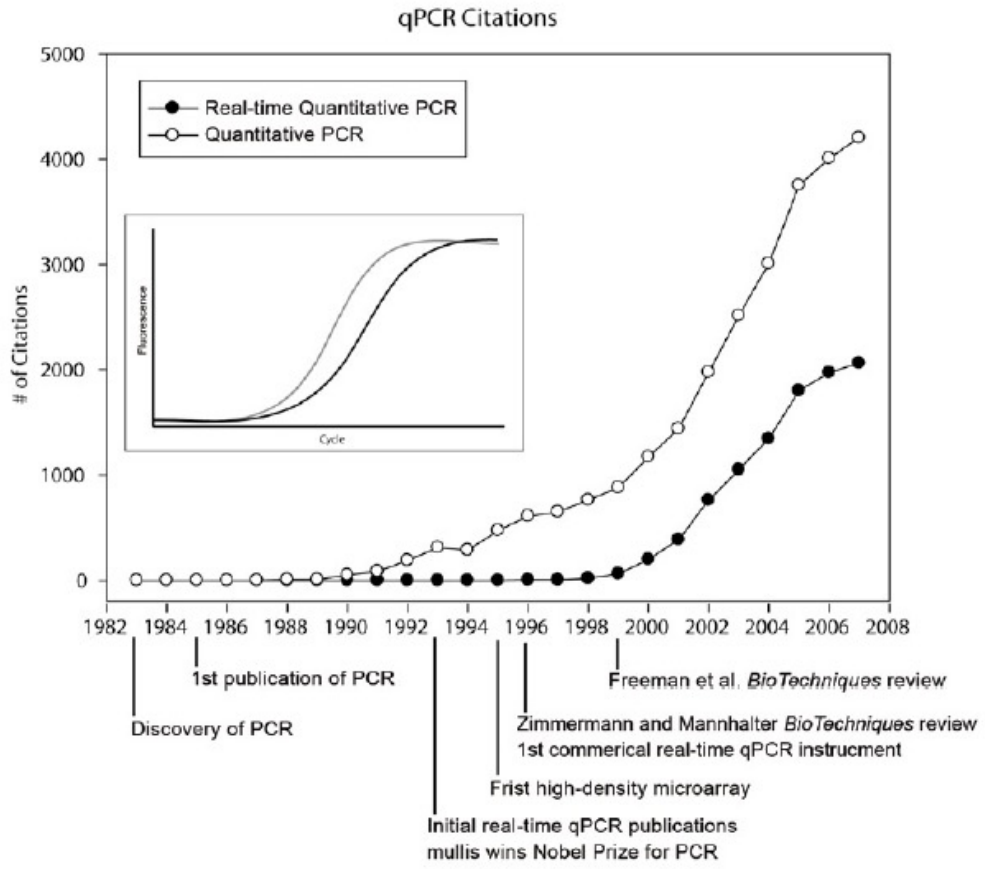


Problem with traditional PCR?

- What is the main problem with traditional PCR?

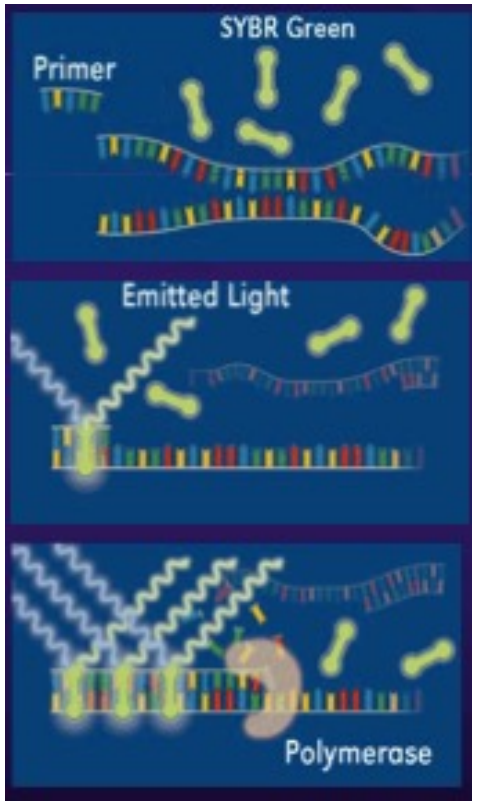
  Answer: There is no quantification of the wanted sequence

qPCR or realtime PCR



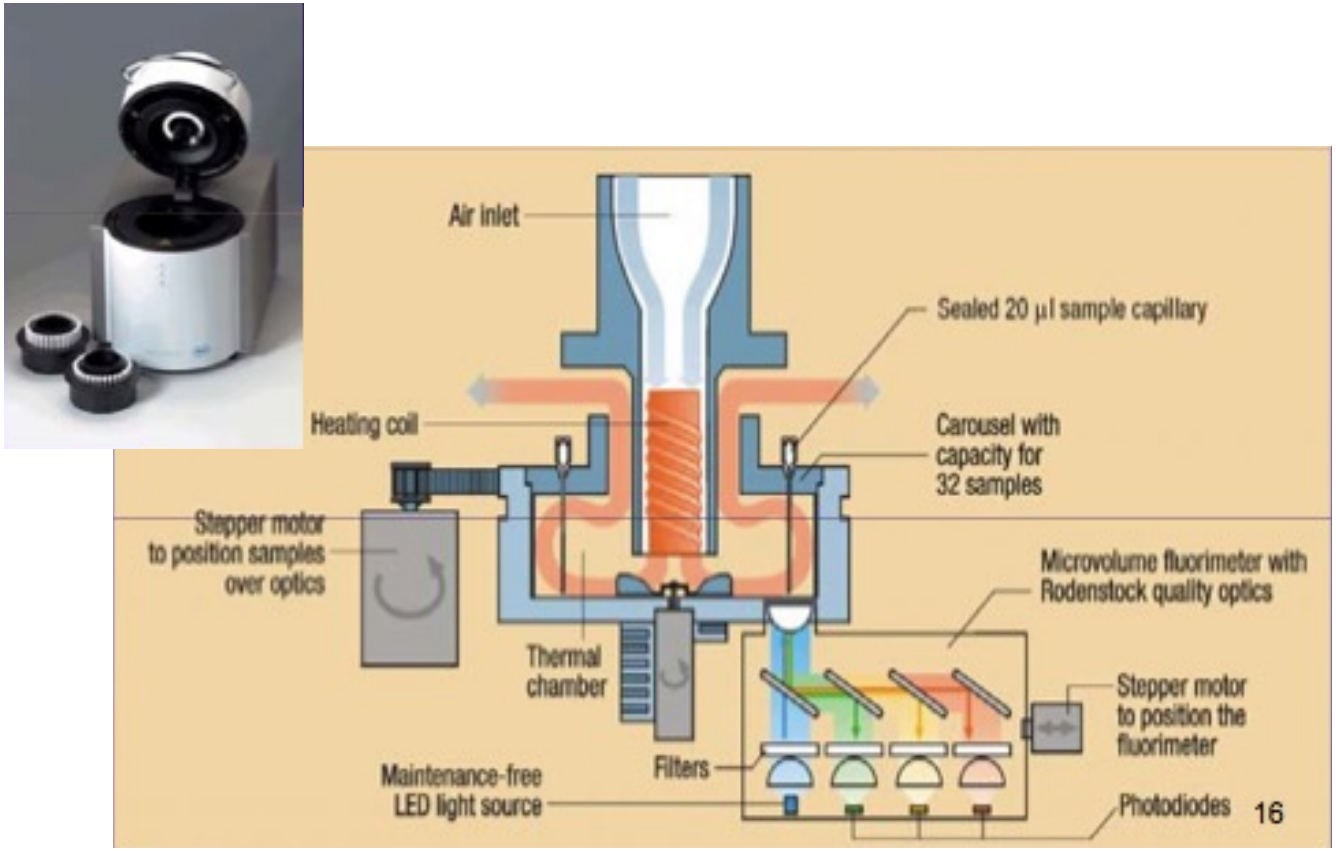
1953 Watson & Crick and Franklin & Gosling DNA papers in *Nature*
1975 Southern paper on DNA blotting
1977 1st description of Northern Blot

Real-time qPCR



Source:Viraphong Lulitanond, Ph.D.

Real-time qPCR



Source:Viraphong Lulitanond, Ph.D.

Advantages and disadvantages with PCR

Adv:

- Extremely sensitive, can amplify the DNA of interest from one single cell (Even for old, degraded DNA)

Disadvantage:

- The sensitivity. If contamined, the contaminated DNA will also be amplified.

Advantages with Real-time PCR (qPCR)

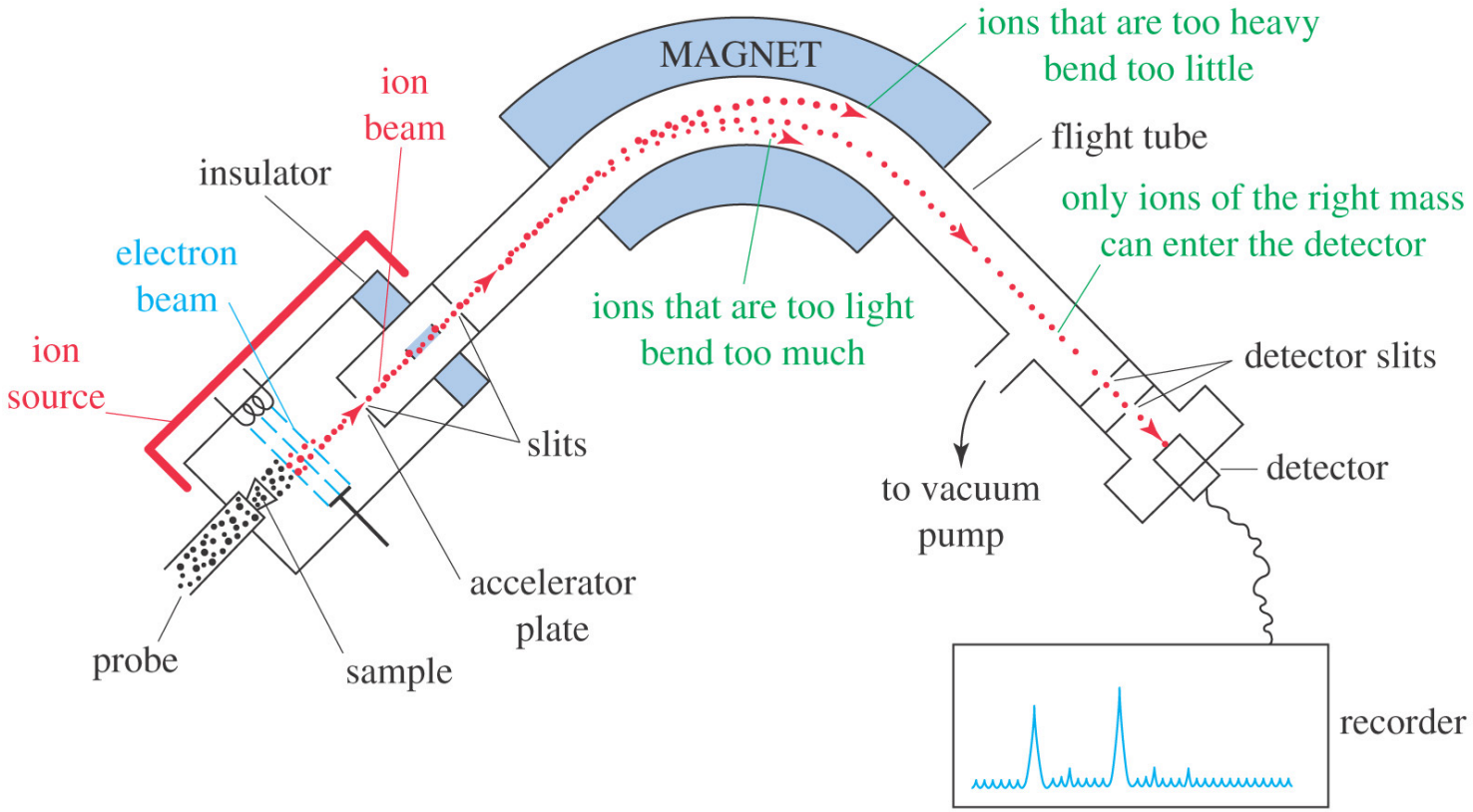
- Identify amplified fragments during the PCR process (exponential phase, traditional PCR measures during the plateau phase) = a good measurement of the starting quantity of the material

- Standard PCR requires post-PCR analysis (typ electrophoresis), possibly agarose gel electrophoresis;. Real-time PCR eliminates these needs. Amplicon recognition is achieved by monitoring the accumulation of specific products during each cycle.

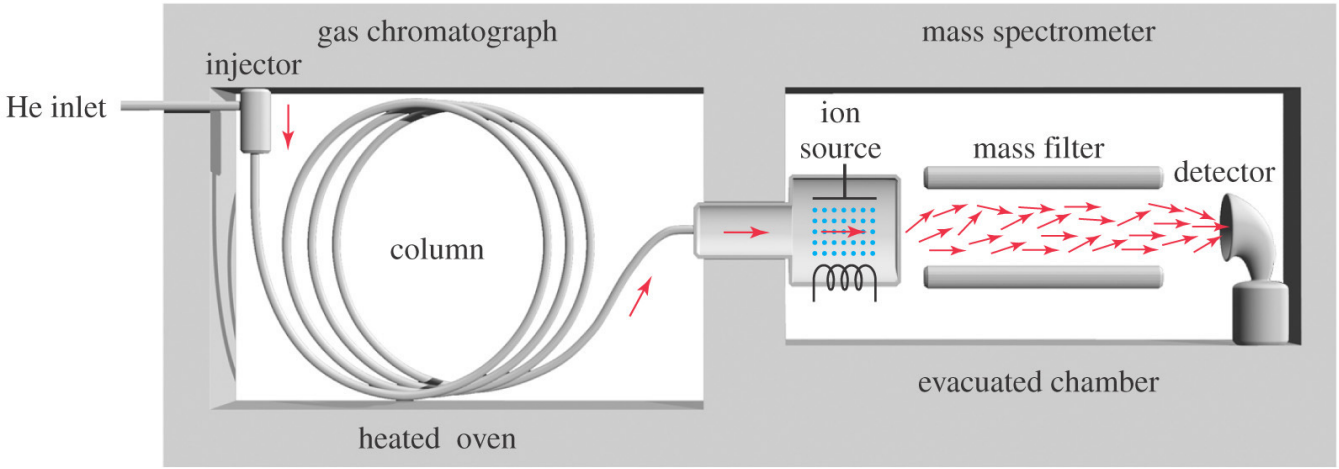
- qPCR is performed in the same tube for the whole prosess. Regular PCR is transferred to other formats = increased risk of contamination

Mass spectrometry

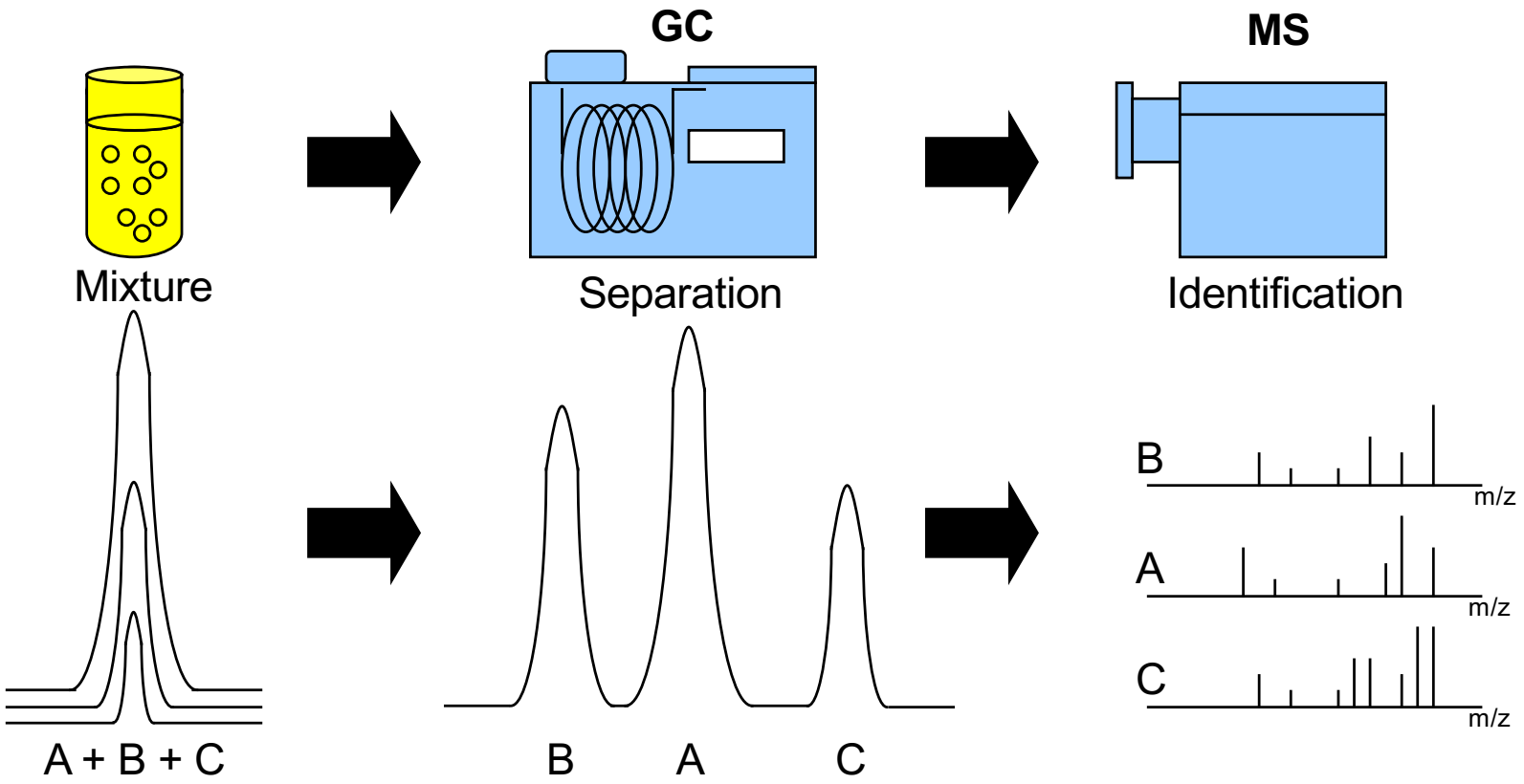
Mass spectrometry



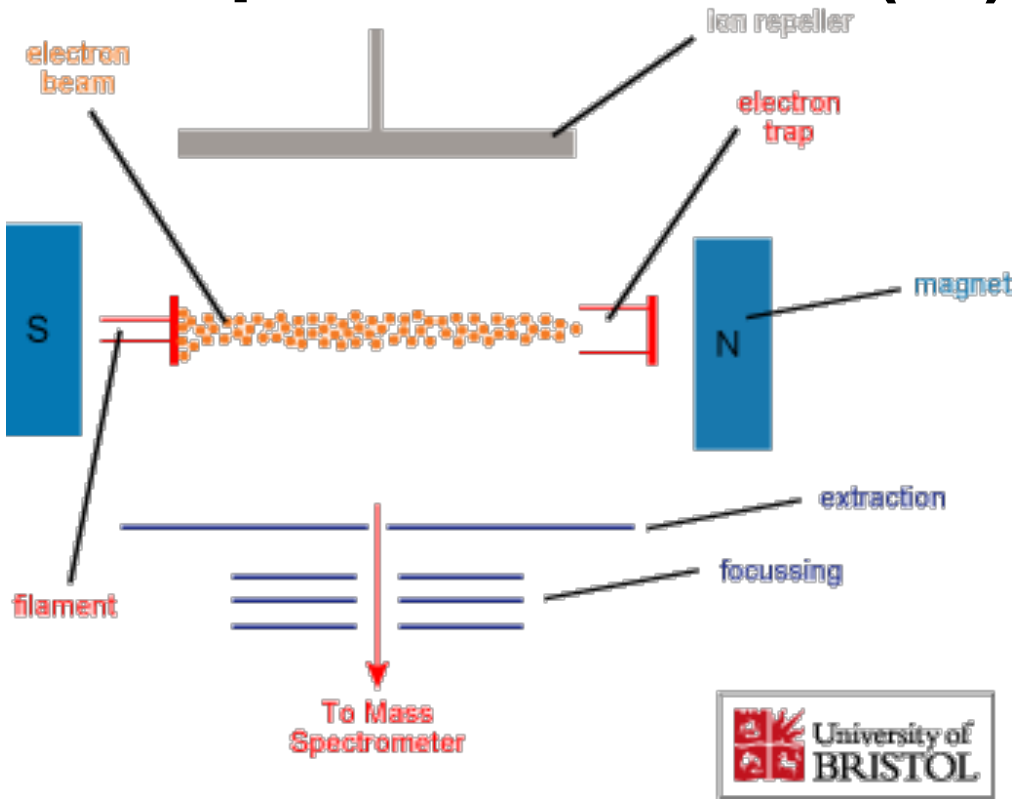
Combination of gas chromatography mass spectrometry



Analysis by GC-MS



Electron impact ionization (EI)

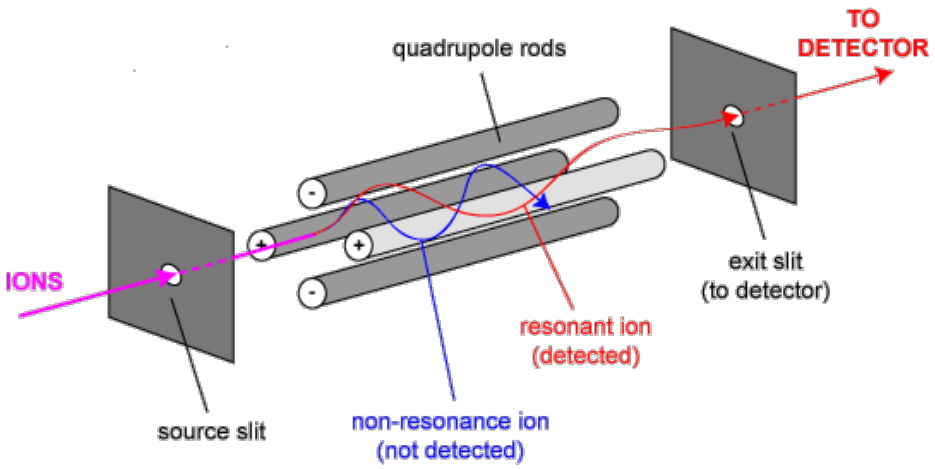


Bombardment with high-energy electrons, typically 70 eV.
Due to collision, an electron is removed from the analytes (M), which results in a molecular ion M+.

$M + e \rightarrow M^+ + 2e^-$

Quadropole mass spectrometers

- 4 cylindrical rods in parallell, ions are sent into the space between the four rods
- A current field is applied to two rods and a radio frequency to the two others. This generates an electric field that the ions will go through
- Only ions with a specific mass and charge are able to pass through the rods for each given DC/RF potential and reach the detector on the other side. All others will collide or change direction and thus miss the detector



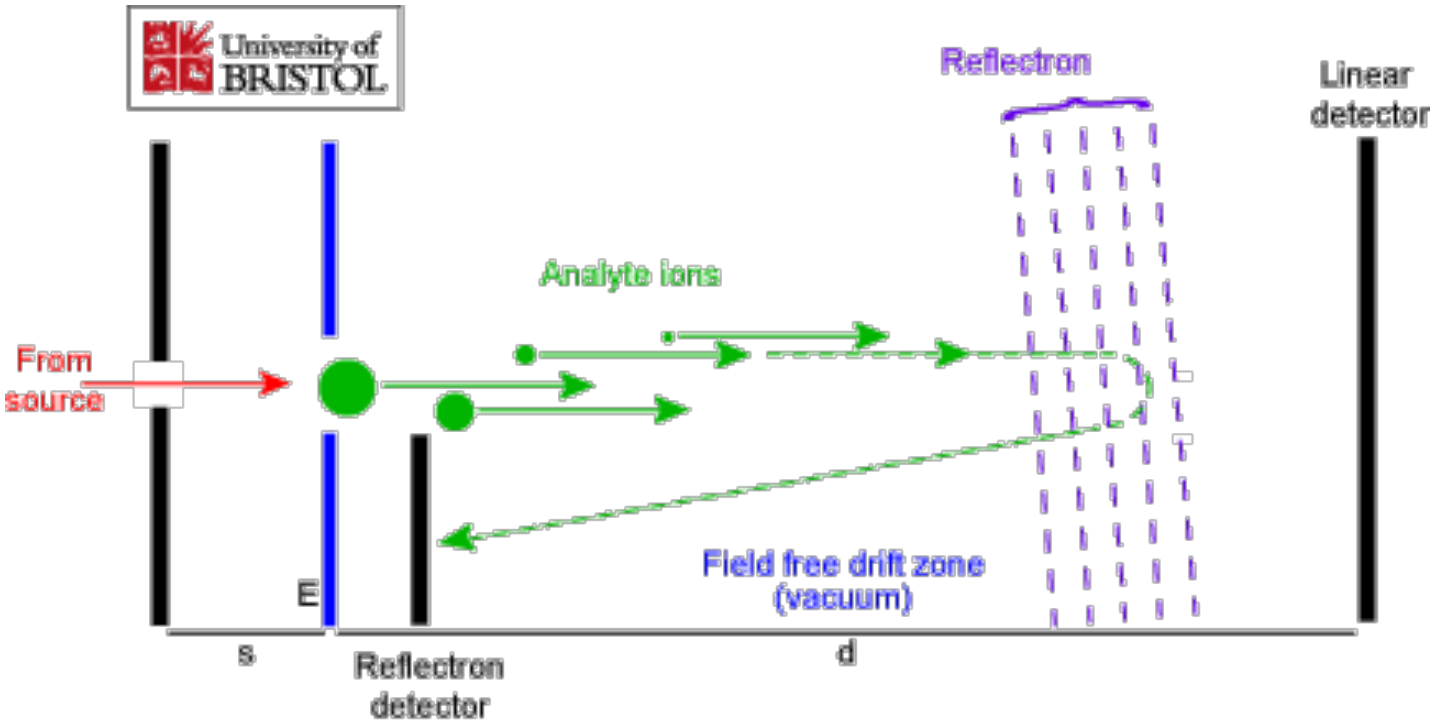
http://www.bris.ac.uk/nerclsmsf/images/quadrupole.gif

http://ael.gsfc.nasa.gov/images/saturn/quadrupole.jpg

Time of flight (TOF)

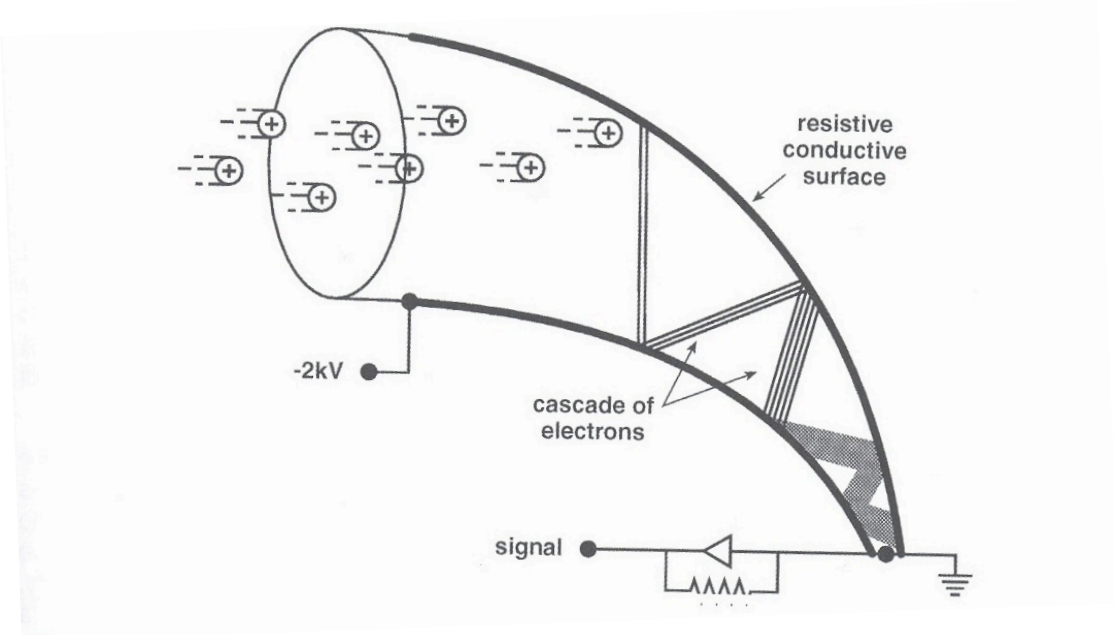
$$\frac{m}{z} = 2eEs\left(\frac{t}{d}\right)^2$$

- High resolution
- Heavier ions require more time to travel a fixed distance, TOF will separate ions with the same kinetic energy but different mass/charge because the heavier the ion, the more time it will need to travel the distance



http://www.chm.bris.ac.uk/ms/images/tof-schematic.gif

Detector – Continuous Dynode EM



- Each ion will release two electrons that is accelerated and will release 4 electrons on the next impact and so on. The resulting current is proportional to the amount of analyte in the sample
- Advantage: Quick response, high sensitivity
- Drawback: Limited lifetime depending on the number of ions hitting the device.

Watson, Introduction to Mass Spectrometry, 4th ed

Scan mode or SIM mode

- There are two options: Look for a single ion (SIM) or perform a wide scan (SM).
- Scan mode means that the mass filter is adjusted to allow a wide range of masses pass through. A spectrum is obtained for all the different masses
- Scan mode is less sensitive due to the loss of ions in the quadropole rods
- Sim mode increases sensitivity and is typically used for quantitative analysis
- In SIM mode, you need to know the desired specimen that should be monitored

Advantages and disadvantages with MS

advantages:

- Relatively fast process
- Small sample size
- Can differentiate between isotopes

Disadvantages:

- No directly structural information (can often be derived though)
- Only for pure compounds
- Non-volatile compunds are difficult, only gas-phase ions are accepted
- destructive technique

Flow Cytometry

Flow cytometry is used for measurement of multiple characteristics of individual particle. FC can offer:

- Rapid analysis of several characteristics of single cells
- Used for immunophenotyping (= study the protein expressed by the cells, useful for example for detection of tumor markers)
- Inexpensive equipment
- Both quantitative and qualitative information
- Used for immunophenotyping of a number of specimens like whole blood, bone marrow, cerebrospinal fluid, urine and solid tissues

https://www.youtube.com/watch?v=EQXPJ7eeesQ

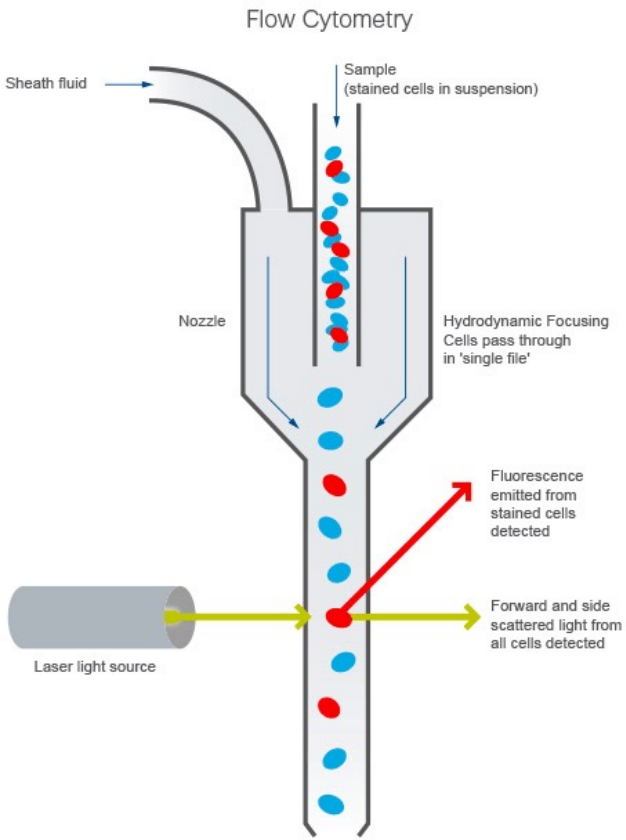
Flow cytometry – general principles

Measures ***optical*** and ***fluorescence*** characteristics of any particle like cells, nuclei, microorganisms ++

Three measurements:

1. Size (forward angle light scatter) and internal complexity (right angle scatter)
2. Fluorescent dyes can bind to specific cellular components as DNA or RNA
3. Antibodies with fluorescent dyes bind to specific proteins both on the cell membranes or inside the cells

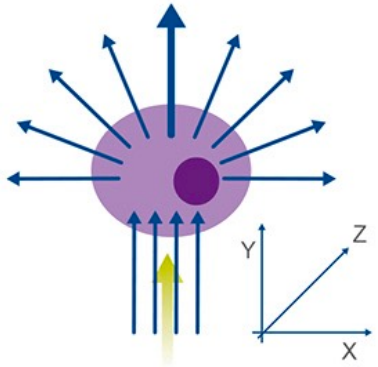
Overview flowcytometer



The fluid will focus the cell suspension so that the cell will pass the laser, one cell at a time

https://www.abcam.com/protocols/introduction-to-flow-cytometry

Overview flowcytometer



When the green laser interrogates the cell, light will scatter. The cell size and granularity will determine the direction of the scattered light.

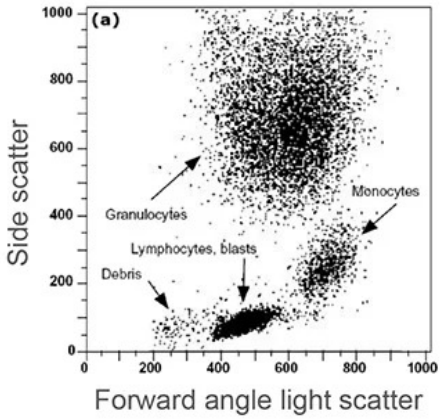
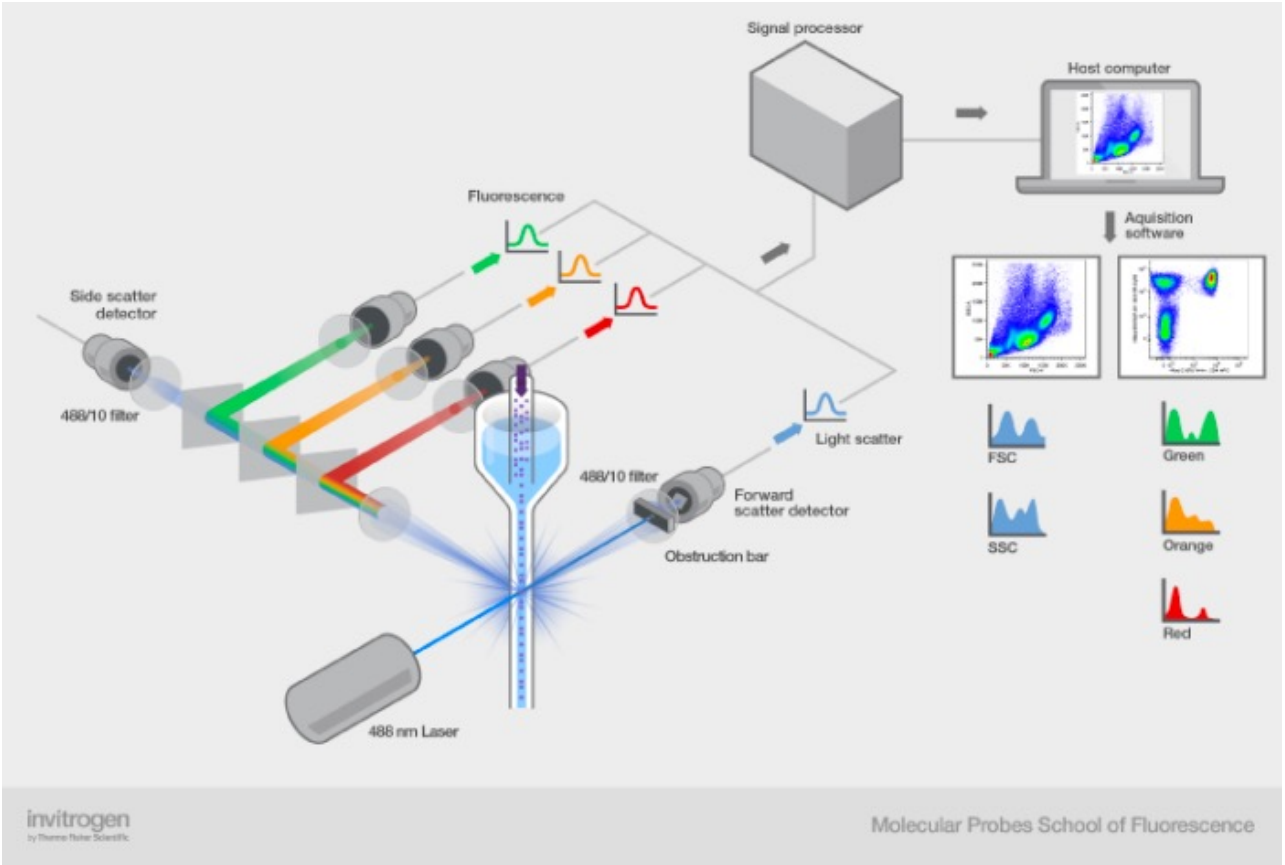


Figure 3. Dot plot of FS versus SS. *Each dot represents a single cell analyzed by the flow cytometer. The characteristic position of different cell populations is determined by differences in cell size and granularity. Image reference: Riley and Idowu. Principles and Applications of Flow Cytometry*[*]

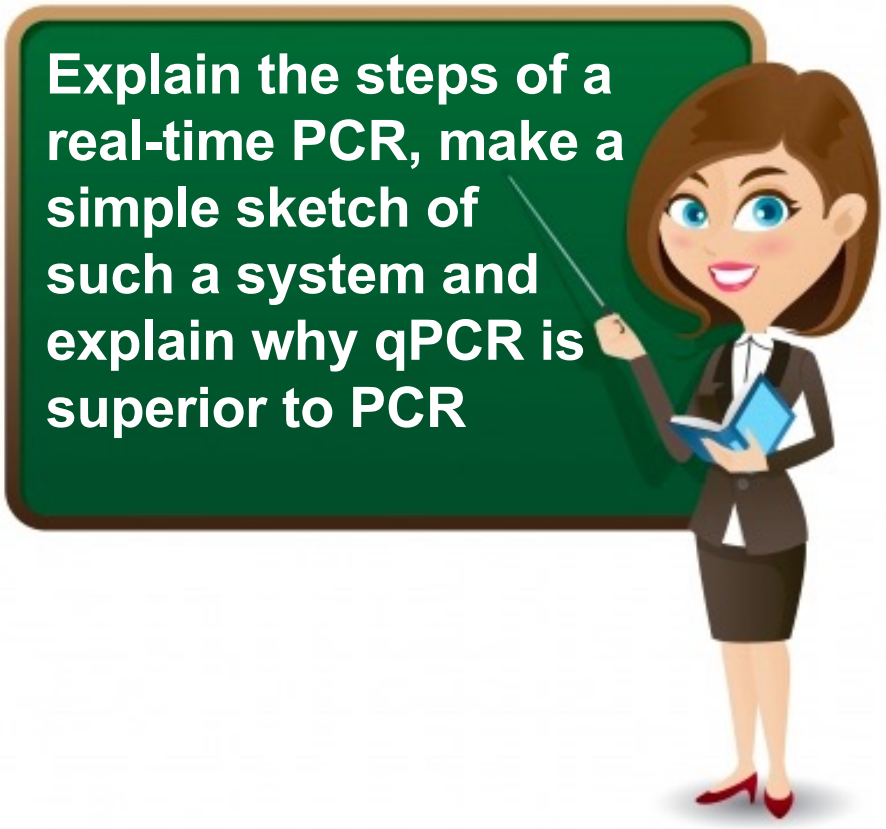
https://www.abcam.com/protocols/introduction-to-flow-cytometry

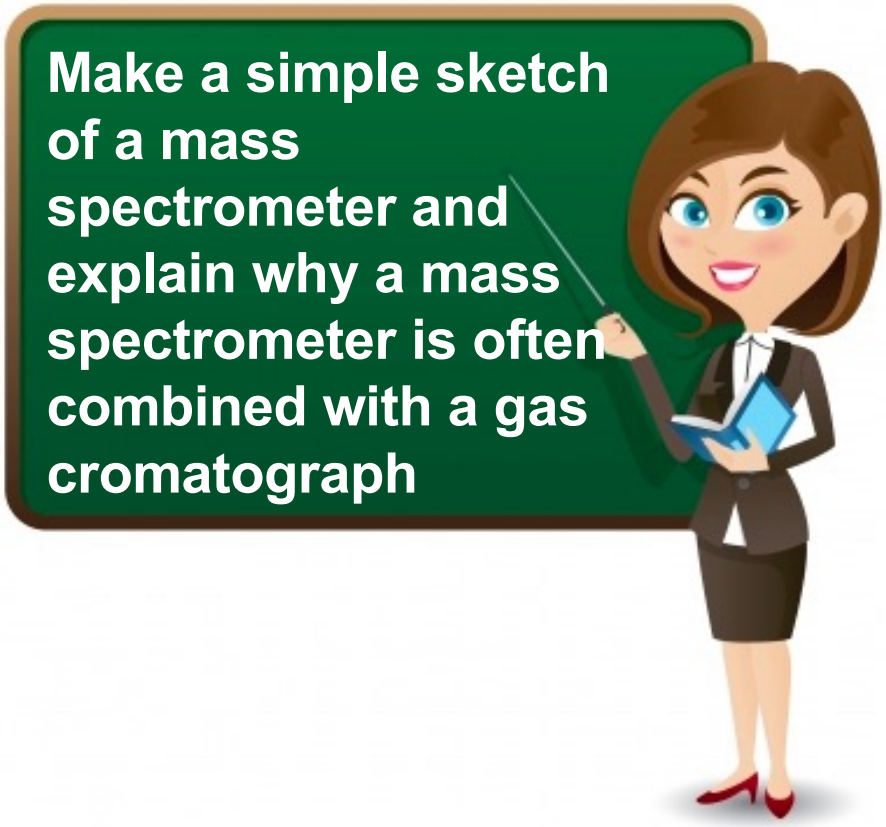
Overview flowcytometer

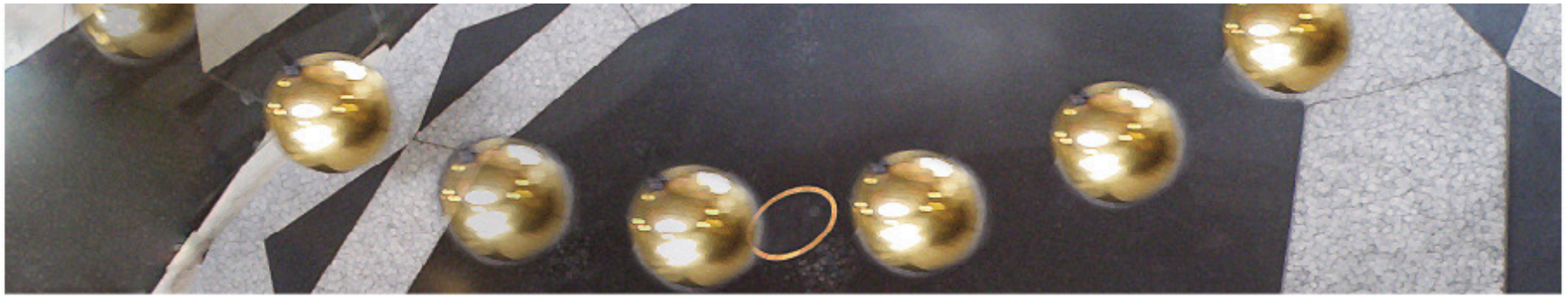


https://www.thermofisher.com/uk/en/home/life-science/cell-analysis/cell-analysis-learning-center/molecular-probes-school-of-fluorescence/flow-cytometry-basics/flow-cytometry-fundamentals/how-flow-cytometer-works.html

Exercise examples







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Lecture 11

An accident rarely comes alone…

Radiation thermometer

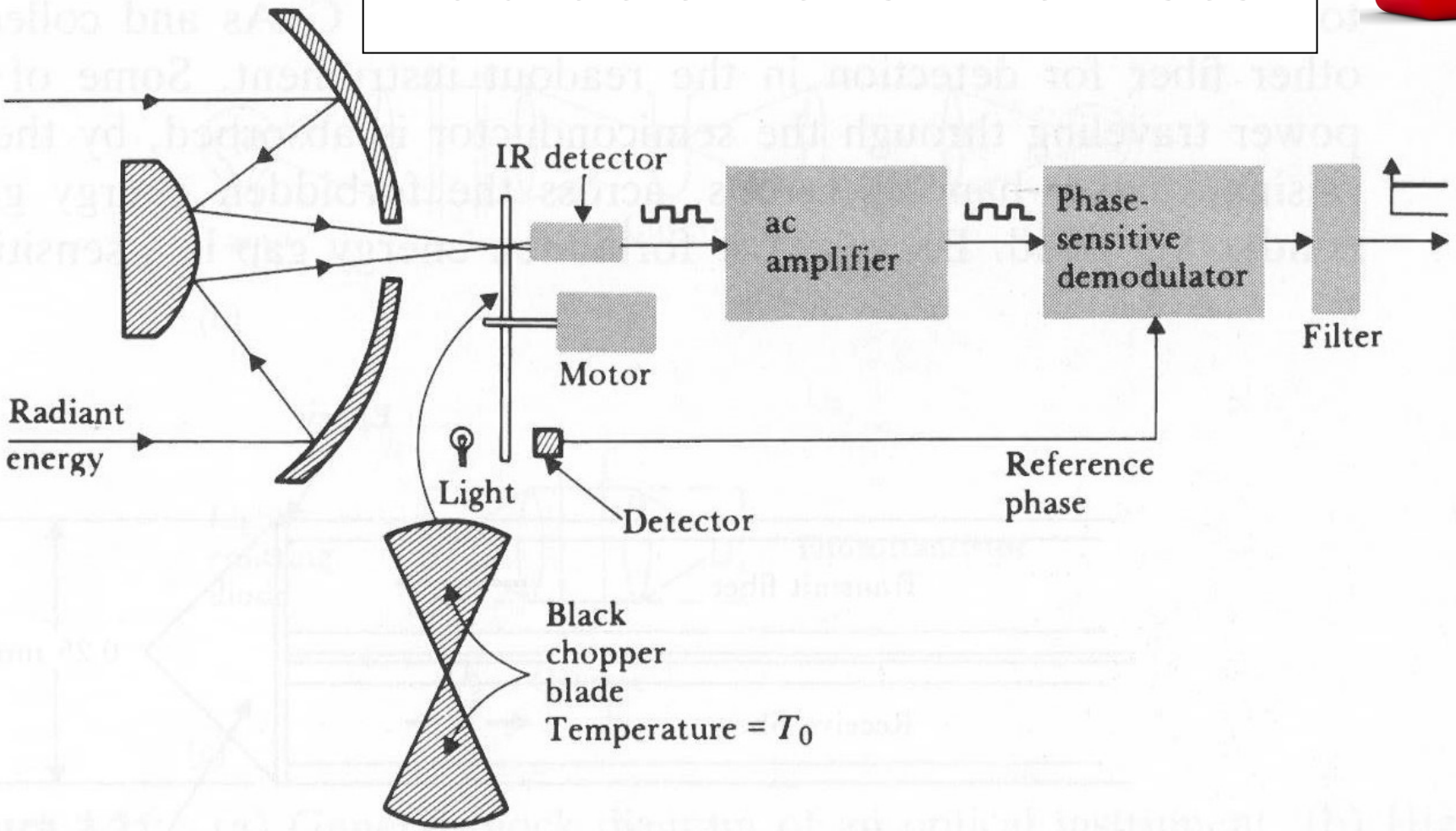


Figure 2.19 Stationary chopped-beam radiation thermometer (From *Transducers for Biomedical Measurements: Principles and Applications*, by R. S. C. Cobbold. Copyright © 1974, John Wiley and Sons, Inc. Reprinted by permission of John Wiley and Sons, Inc.)

Infrared ear thermometer

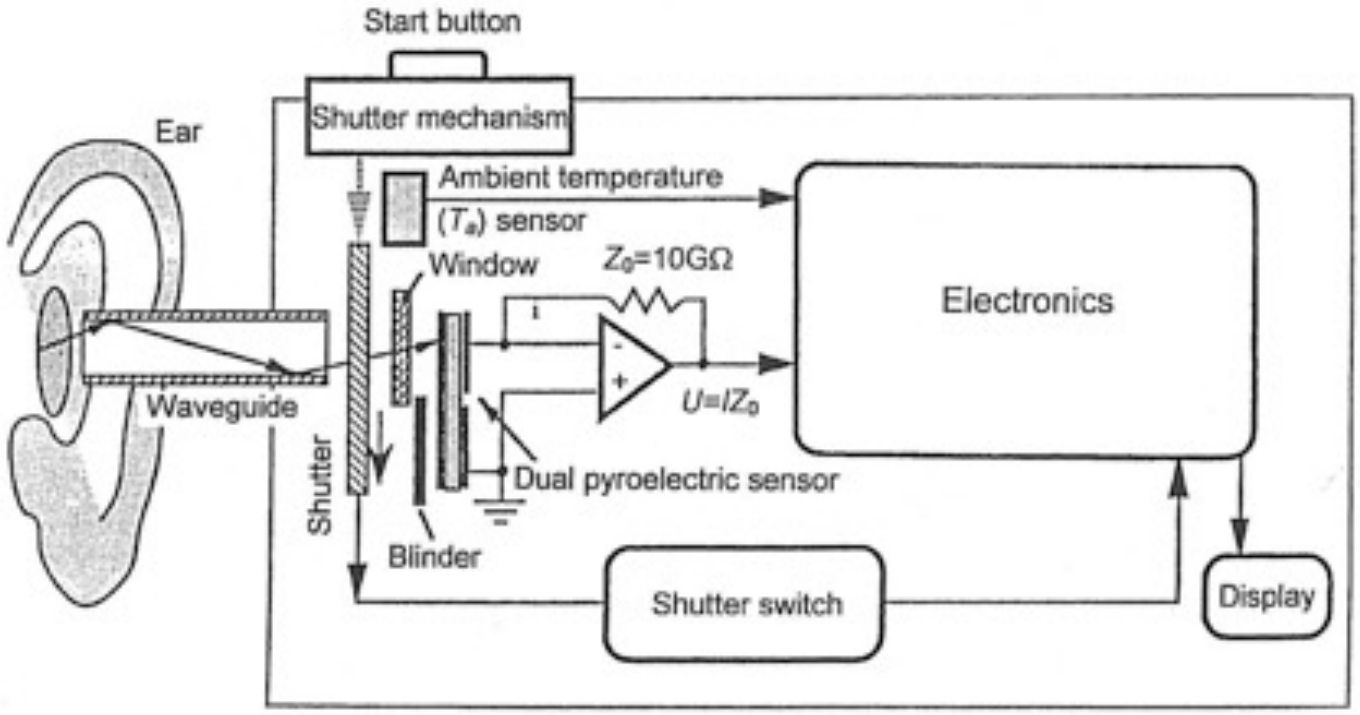


Image: Harsanyi, 2000, p 102

Application of radiation thermometry, determines core body temperature by measuring the magnitude of infrared radiation emitted from tympanic membrane and surrounding ear canal. (Tympanic membrane and hypothalamus are perfused by the same vasculature -> Hypothalamus is the body thermostat

Kidney stone crusher (Lithotripter)

Source: www.dornier.com

Kidney stone crusher

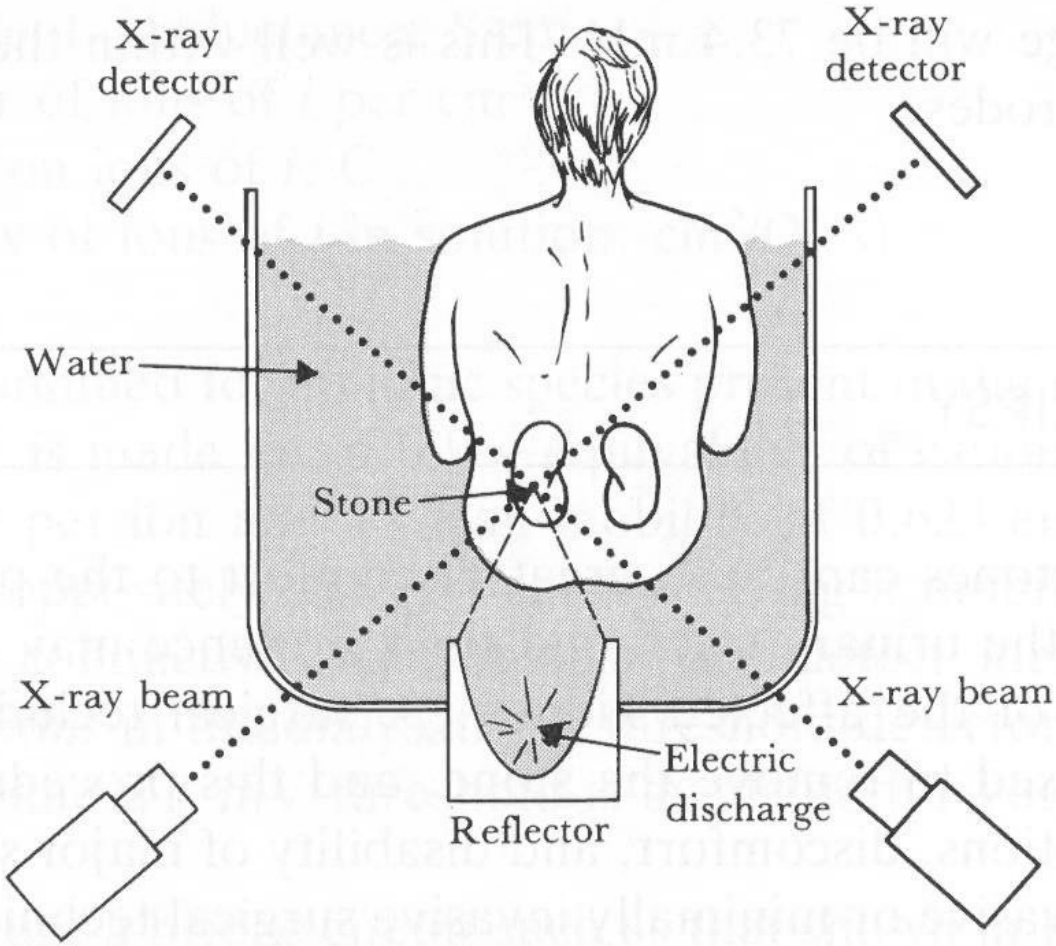


Figure 13.18 In extracorporeal shock-wave lithotripsy, a biplane x-ray apparatus is used to make sure the stone is at the focal point of spark-generated shock waves from the ellipsoidal reflector.

Active implant bladder stimulators

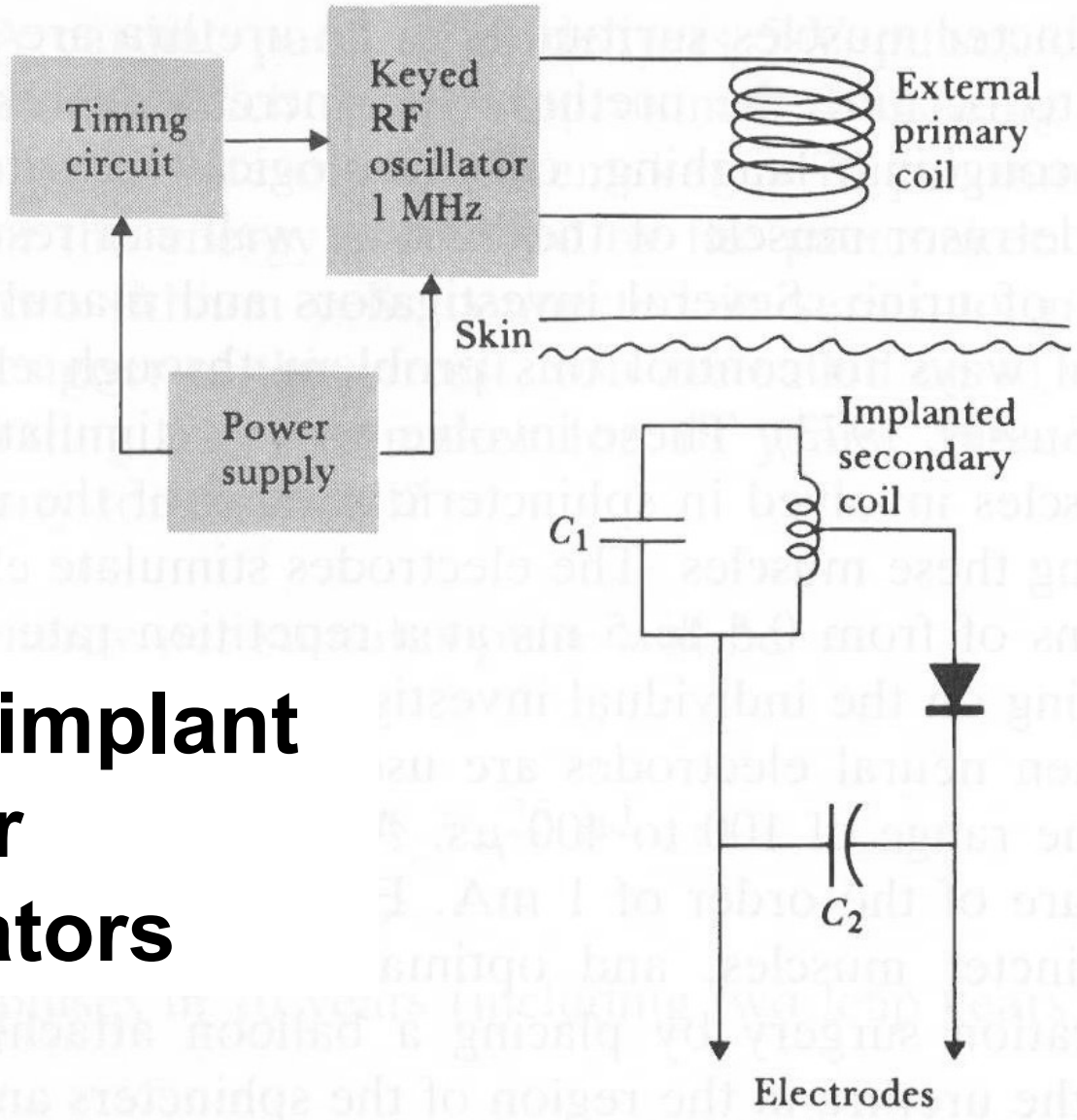


Figure 13.7 A transcutaneous RF-powered electric stimulator Note that the implanted circuit of this stimulator is entirely passive and that the amplitude of the pulse supplied to the electrodes is dependent on the coupling coefficient between the internal and external coils.

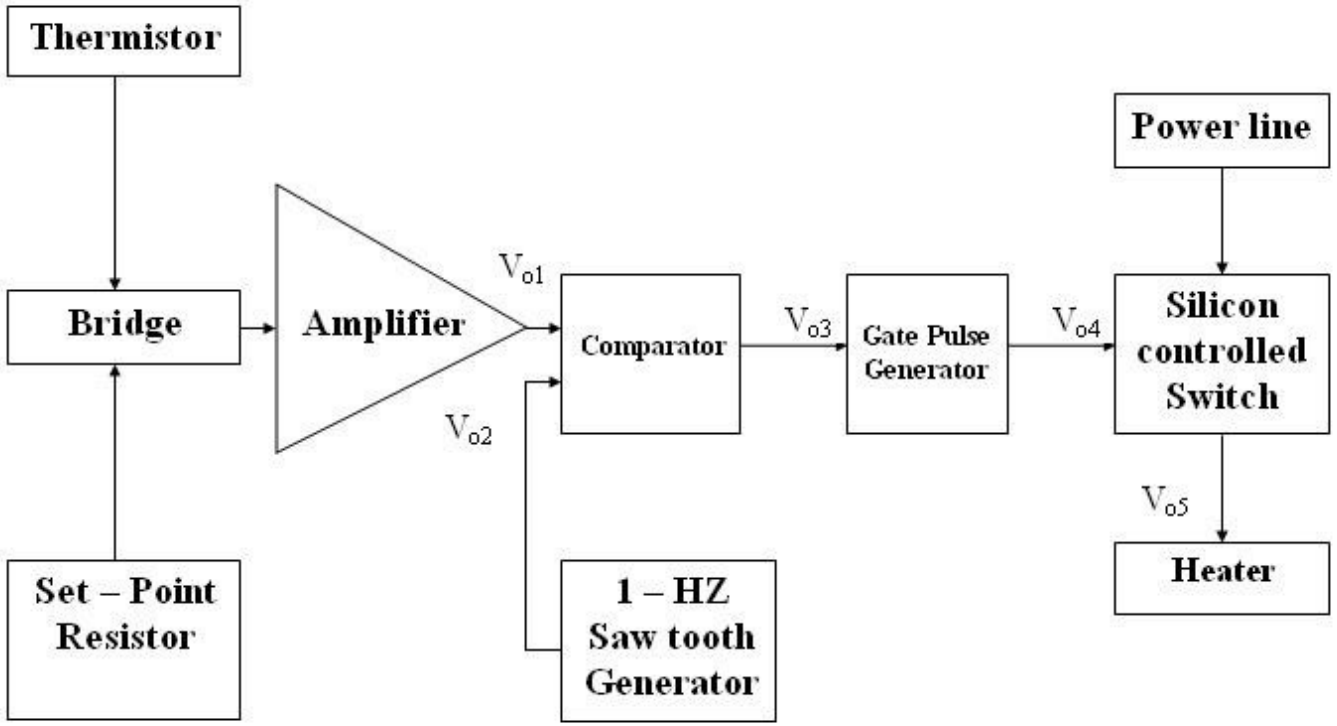
Infant incubator

Medicalexpo.com

Premature infants

Premature infants is a baby born prior to the 37 completed weeks of gestation. A premature infant will typically have problems with the lung function, heat regulation and skin moisture. The incubator tries to counteract this by providing temperature and moisture control and thereby decrease the oxygen requirements. Normally, the temperature is controlled with a proportional control system

Proportional control method



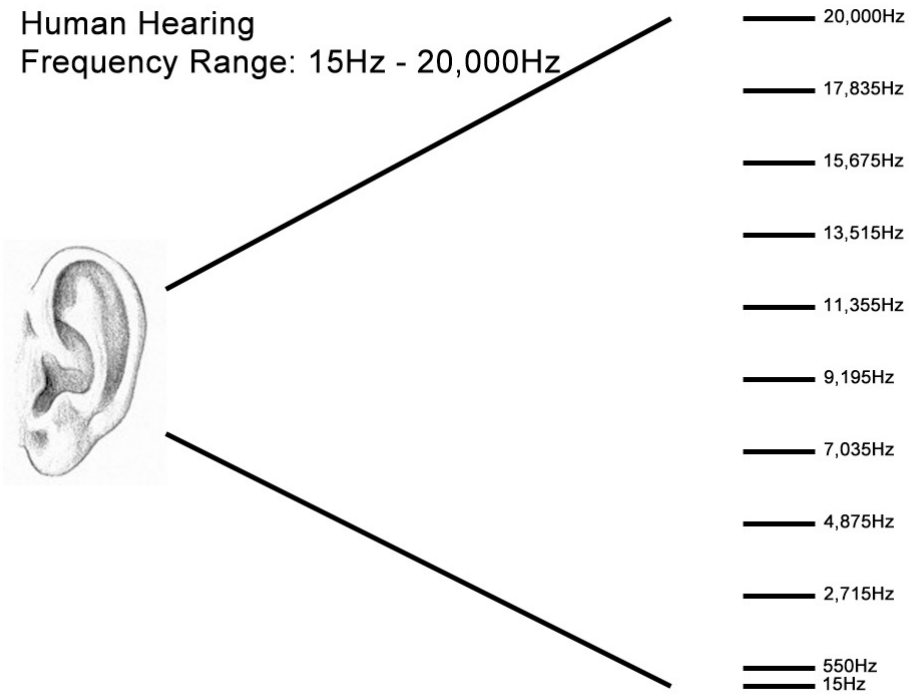
Alarms in Incubators

- High temperature alarms
- Power failure alarms
- Set temperature alarms
- Air flow alarms (fan stop)
- Probe failures

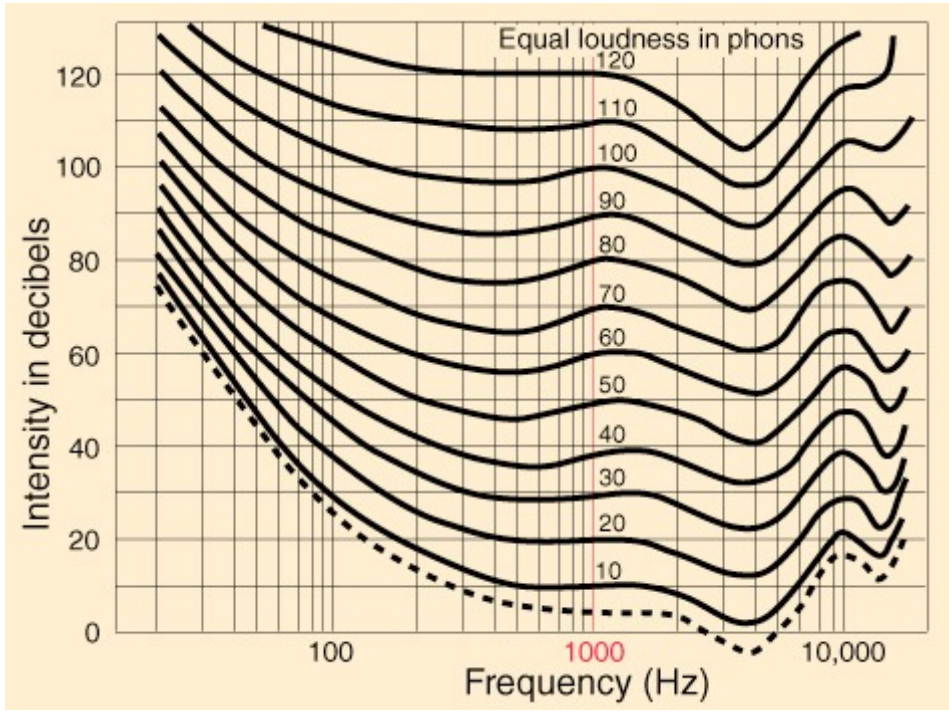
Cochlea implants

Sound intensity I(dB) = 10log (I/I (0)) = sound power per unit area (watts/m*m)
Sound Loudness is a subjective term describing the strength of the ears perception of a sound. Closely related but not identical to sound intensity. The sound intensity must be factored by he ear's sensitivity to the particular frequencies contained in the sound.

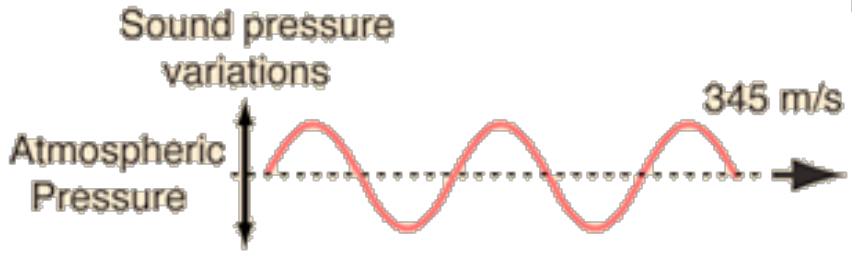
Hearing frequency range

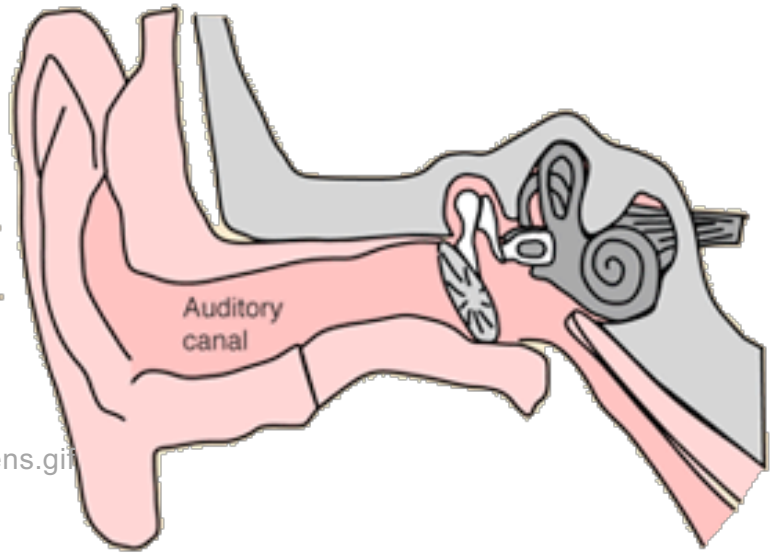


http://www.iigwest.com/investigations/meier/images/Meier_Audio_Hearing.jpg



http://www.nu9n.com/images/fletcher.jpg





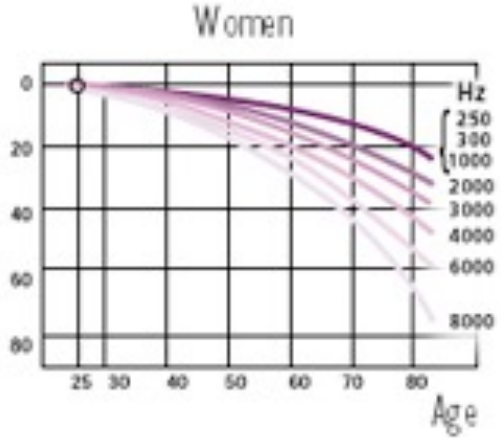
Source:http://hyperphysics.phy-astr.gsu.edu/hbase/sound/imgsou/esens.gif

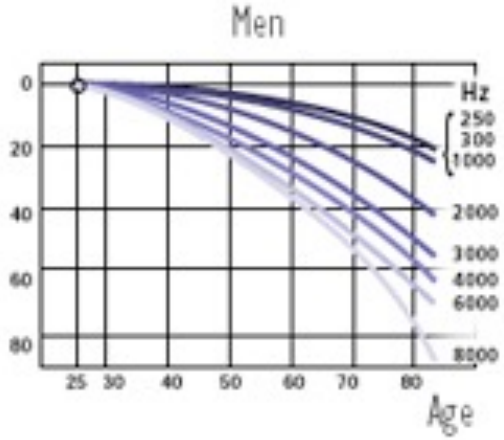
The ear is incredibly sensitive:

- The threshold of hearing is less than one billionth of atmospheric pressure

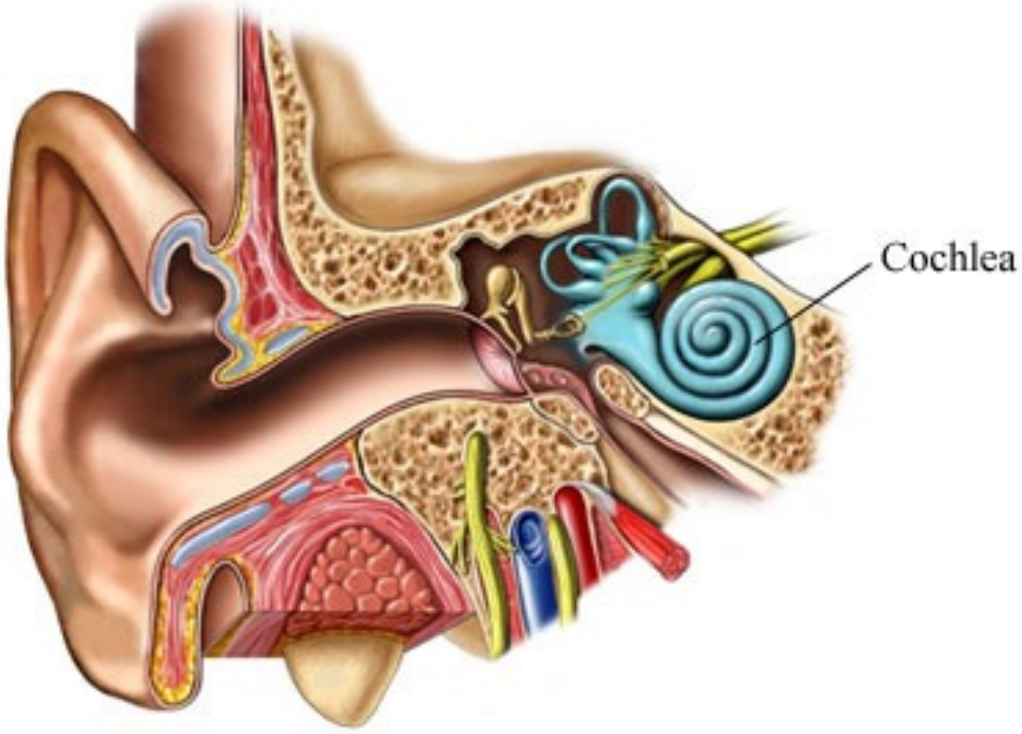
And has an incredible range of operation:

- Threshold of pain is 10^{13} of the threshold of hearing





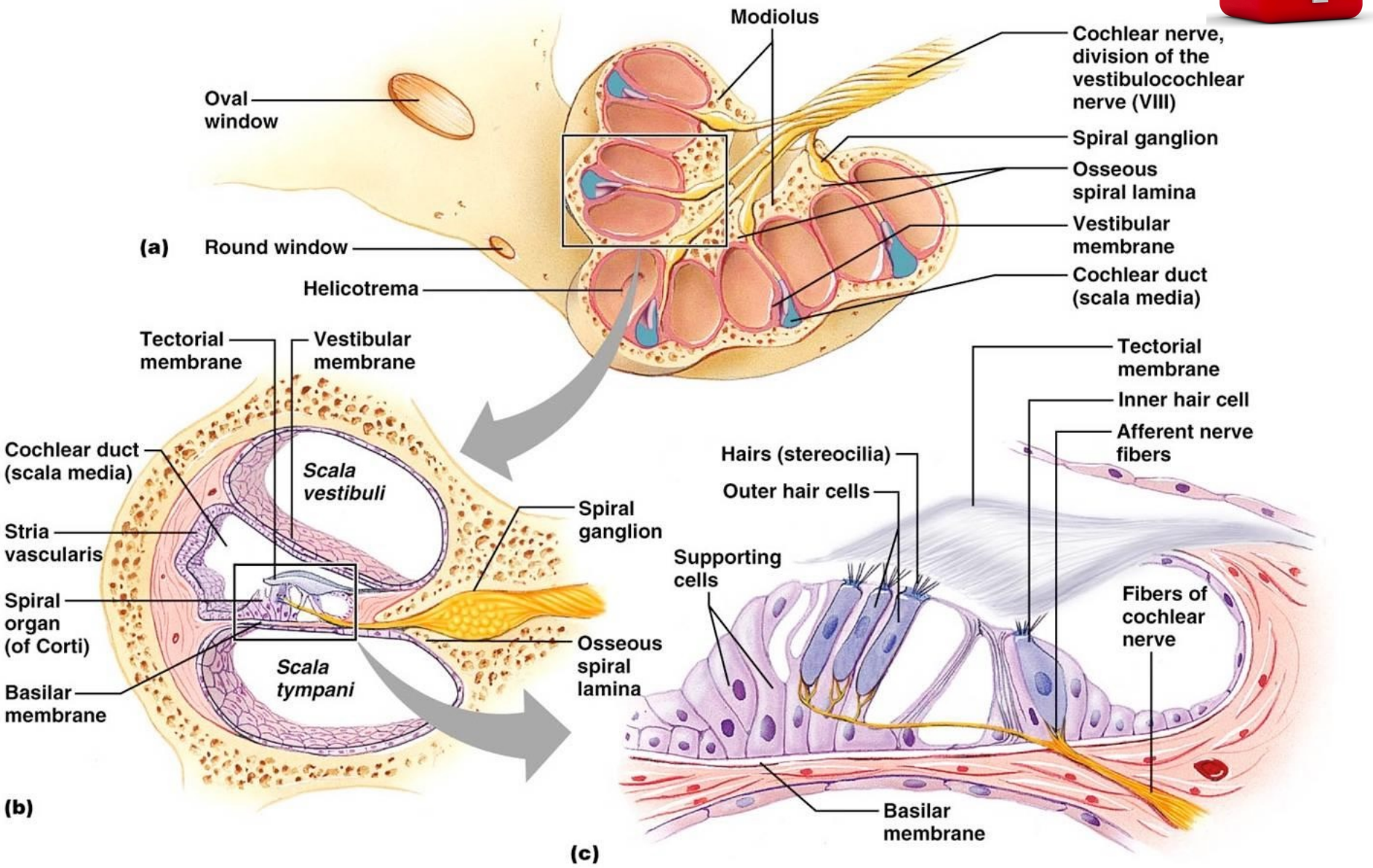
The Cochlea



http://www.odec.ca/projects/2007/park7r2/AQ00008_cochlea.jpg

The cochlea is divided into an upper duct called the scala vestibuli and a lower duct, called the scala tympani, by a thin bony shelf called the osseous **spiral lamina**. It is a narrow shelf of bone arising from the modiolar side of the cochlea.

This division is completed by the membranous cochlear duct or scala media. Its floor is formed by the basilar membrane. The vestibular membrane, or Reissner's membrane, forms the roof of the scala media.



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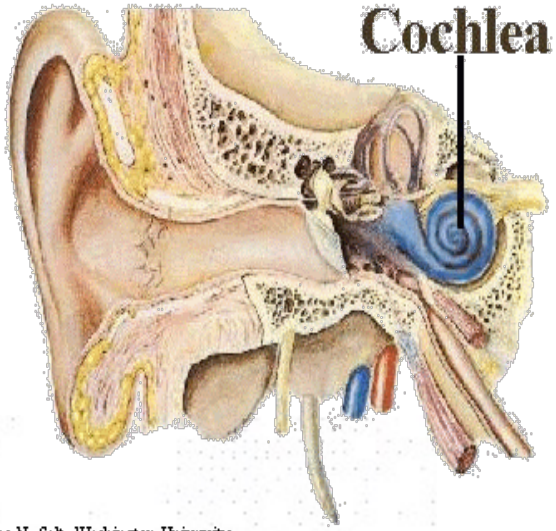
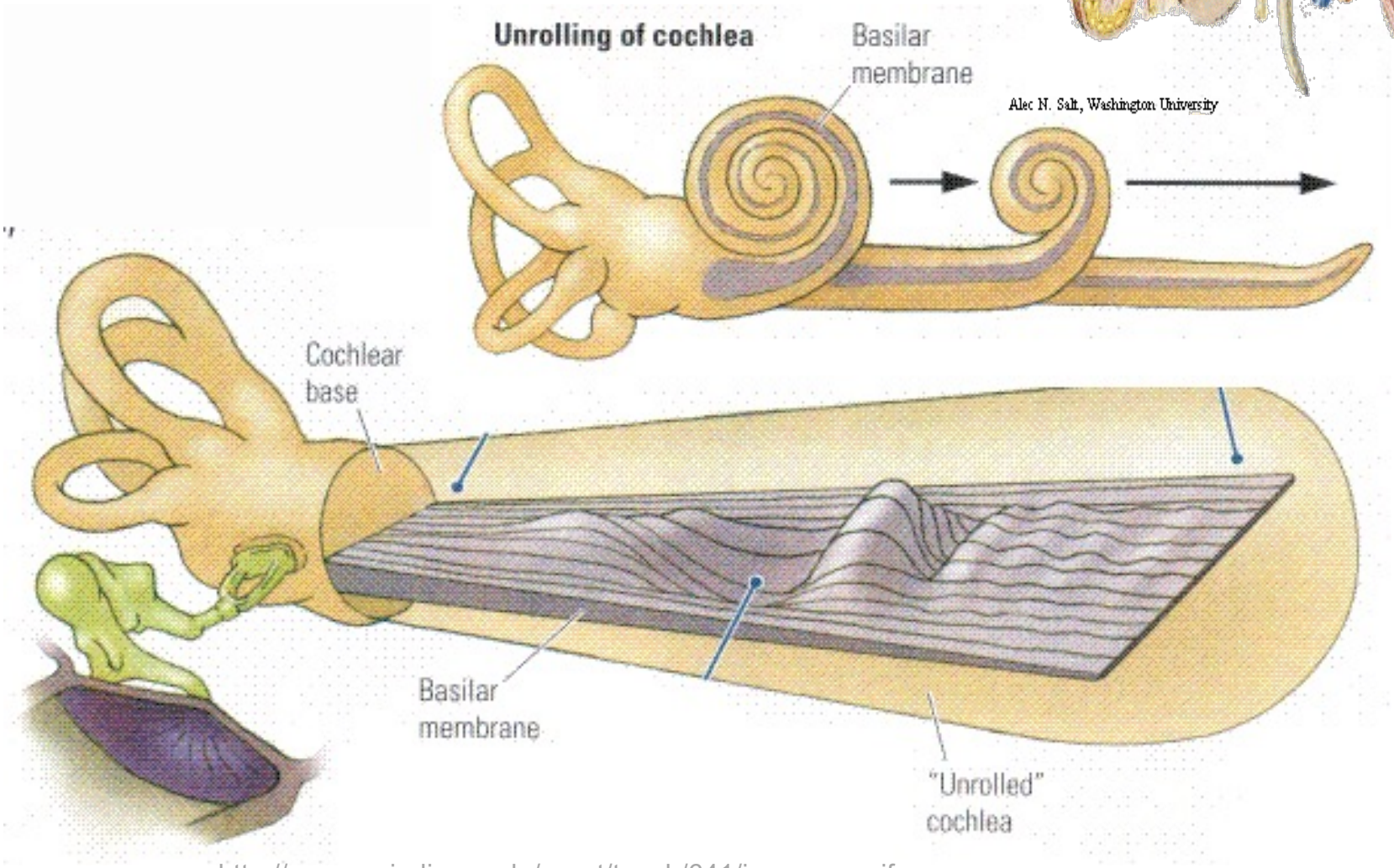
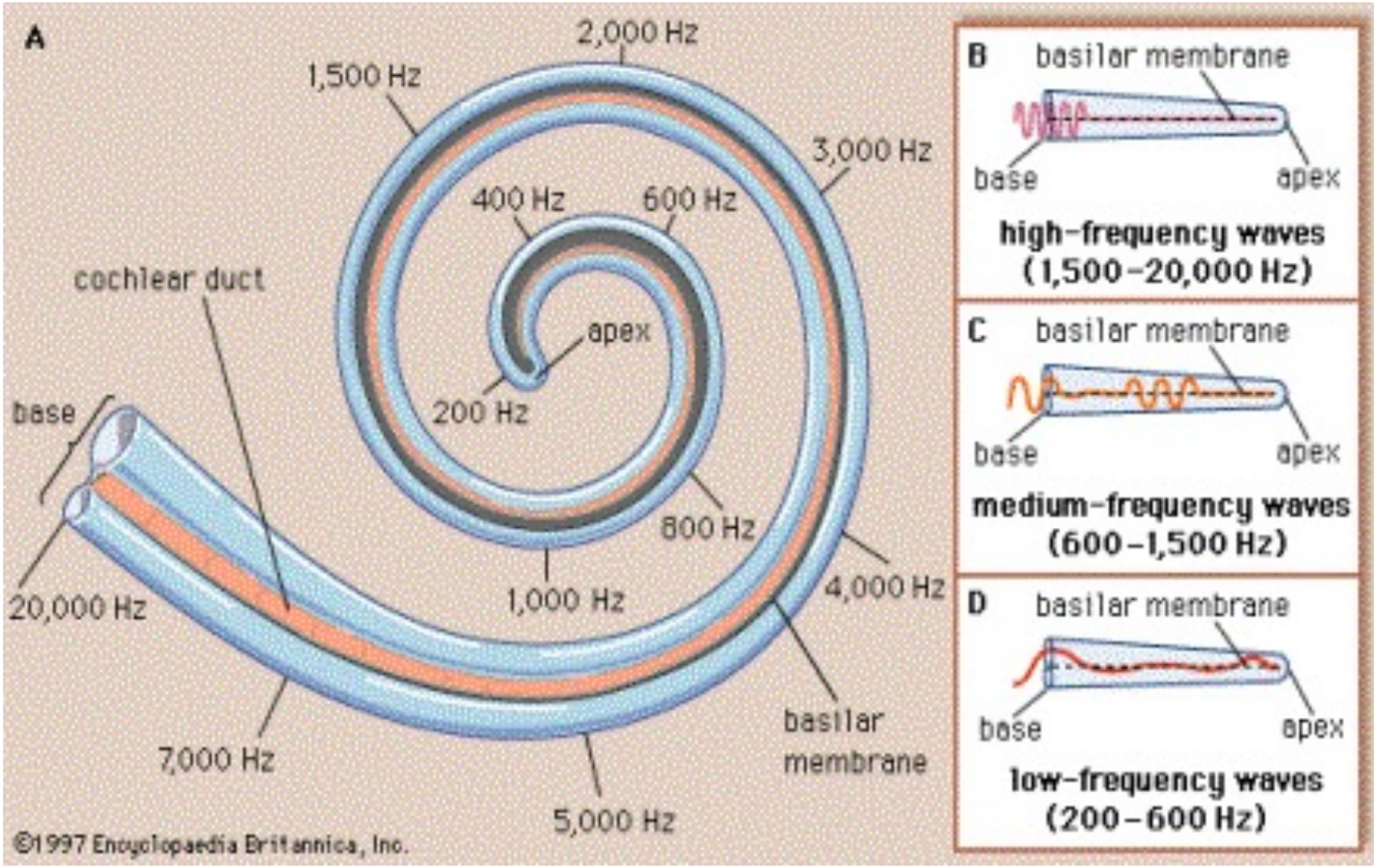
The Cochlea

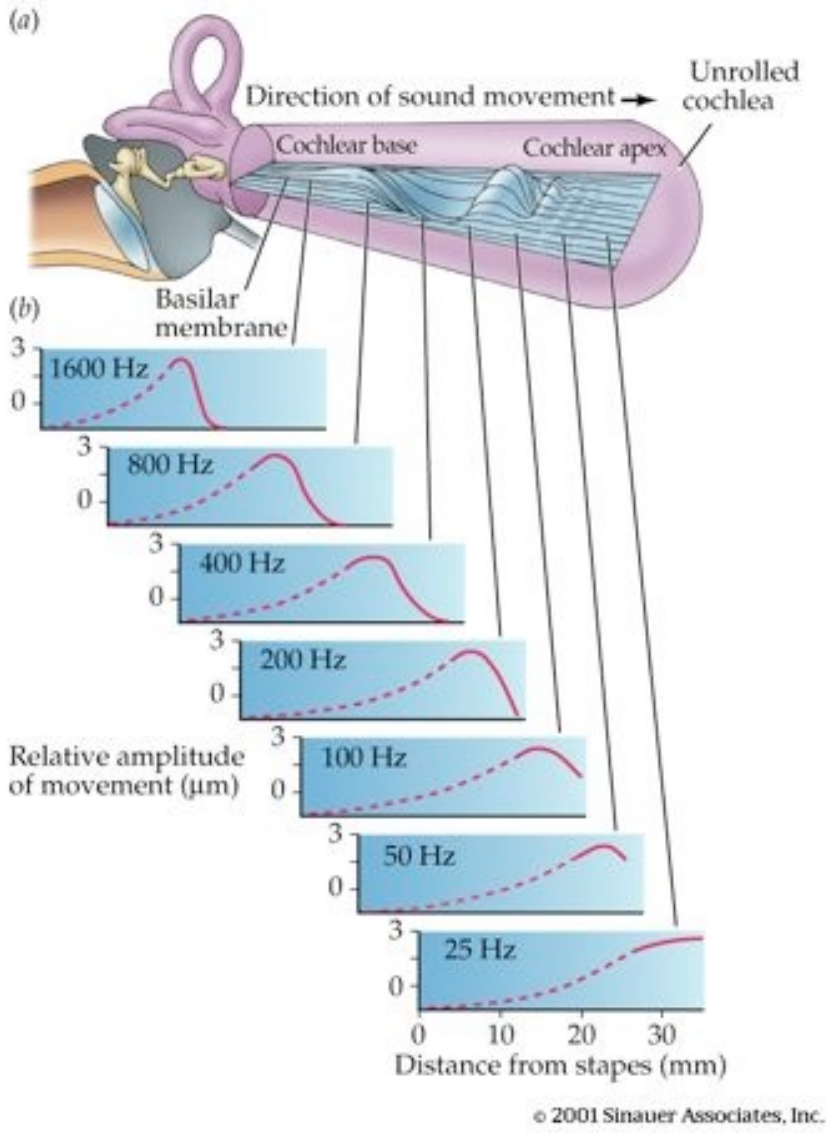




http://www.cs.indiana.edu/~port/teach/641/inner_ear.gif


A
2,000 Hz
1,500 Hz
3,000 Hz
400 Hz
600 Hz
cochlear duct
apex
200 Hz
base
800 Hz
1,000 Hz
4,000 Hz
20,000 Hz
7,000 Hz
basilar membrane
5,000 Hz
©1997 Encyclopaedia Britannica, Inc.
B basilar membrane
base
apex
high-frequency waves (1,500–20,000 Hz)
C basilar membrane
base
apex
medium-frequency waves (600–1,500 Hz)
D basilar membrane
base
apex
low-frequency waves (200–600 Hz)

Frequency tuning



Cochlear implant

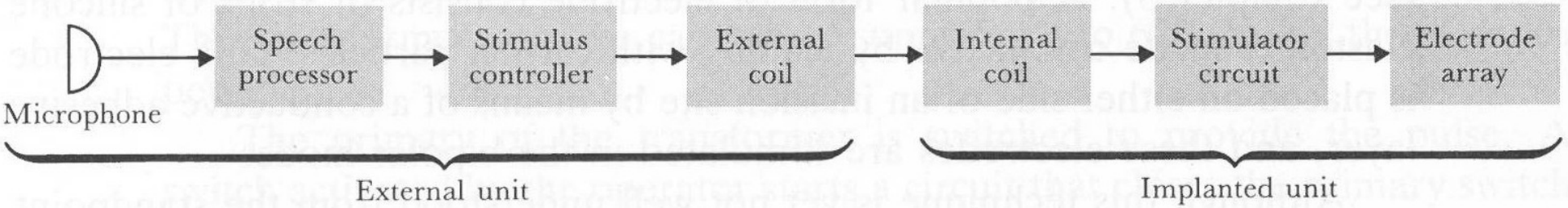
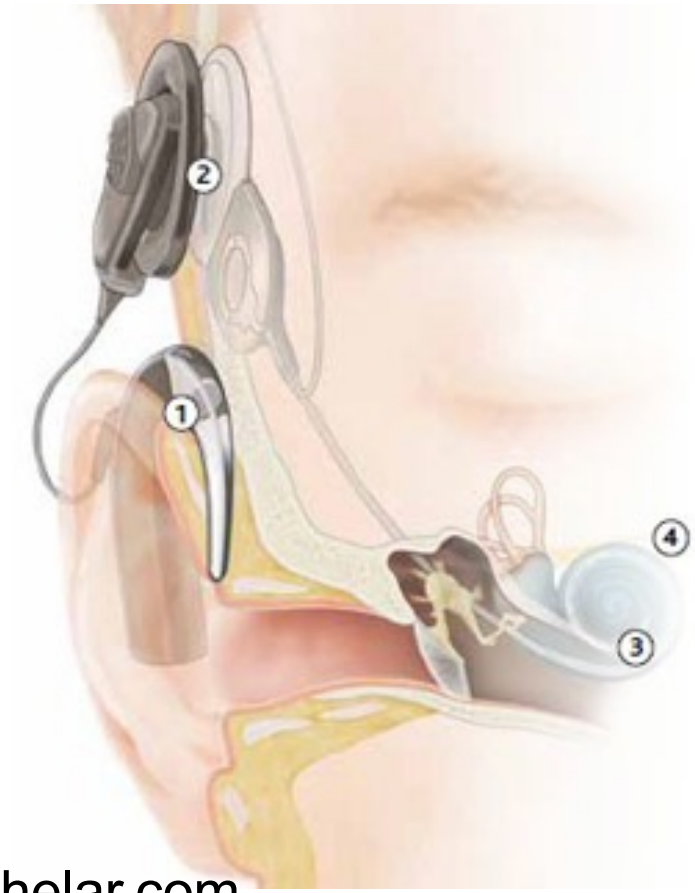


Figure 13.9 Block diagram of a cochlear prosthesis

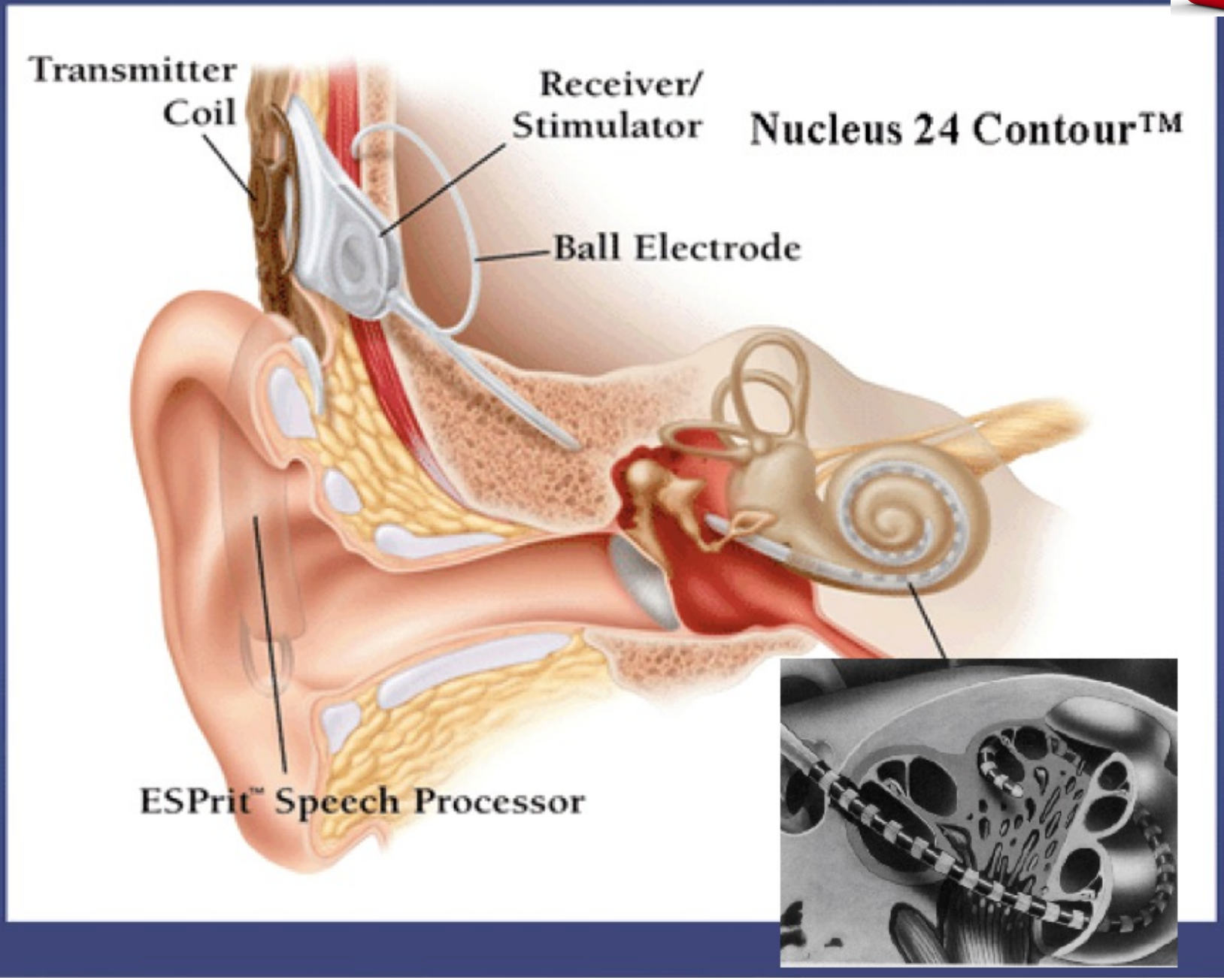
For deaf patients whose hearing impairment results from dysfunction of the sound-transducing elements of the middle and inner ear.
Speech processor = determines what specific characteristics will be used to control stimulating electrodes (Set of bandpass filters)
Stimulus controller = takes information from SP and uses it to determine when a stimulus pulse should be applied to a particular set of electrodes
Electrode array = array placed on a flecible structure that can assume spiral shape of the cochlea in contact with the cochlea-nerves (very small)

The cochlea implant



www.cochelar.com

Source: ESPrit

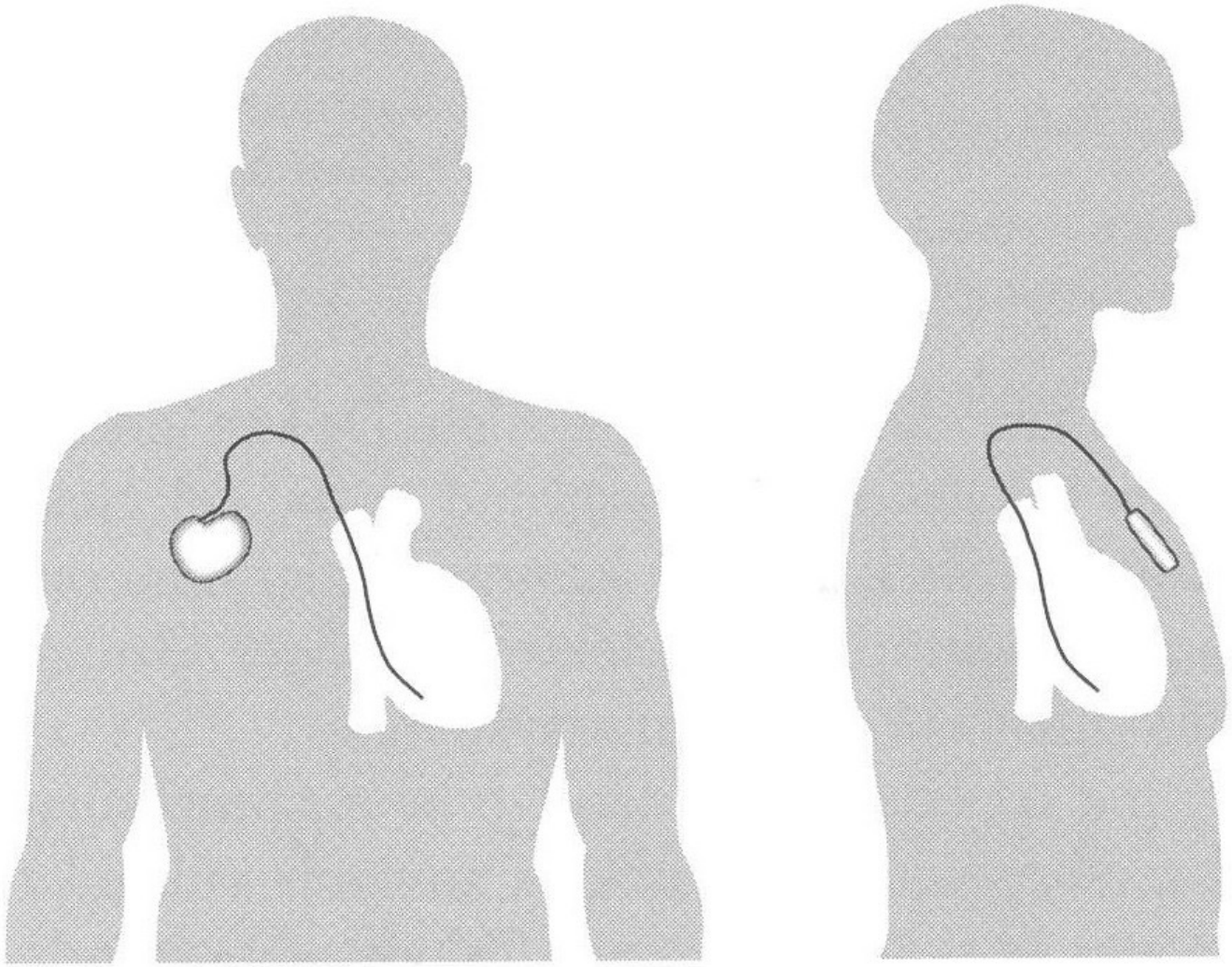


The CI-amplifier

Understanding speech is the ultimate goal, and at the same time a very complex task. Normal speech consists of a number of different frequencies, small shades and sounds that has to be perceived and combined in the brain in order to understand what is said. Deaf patients will typically have a 70-80 dB hearing loss, reaching a dynamic range of approximately 15-25 dB. At the same time very loud sounds have to be attenuated, a general fixed gain will be unpleasant for the patient. Requirements:

- Low power consumption
- Speed,
- A minimum of 60 dB dynamic range
- Variable gain
- The processor needs powerful algorithms to balance the gain and the electrode output

Active implant: pacemaker



Figur 3:51. Subkutant implanterad pacemaker med ledningar.

Pacemaker (Asynchronous)

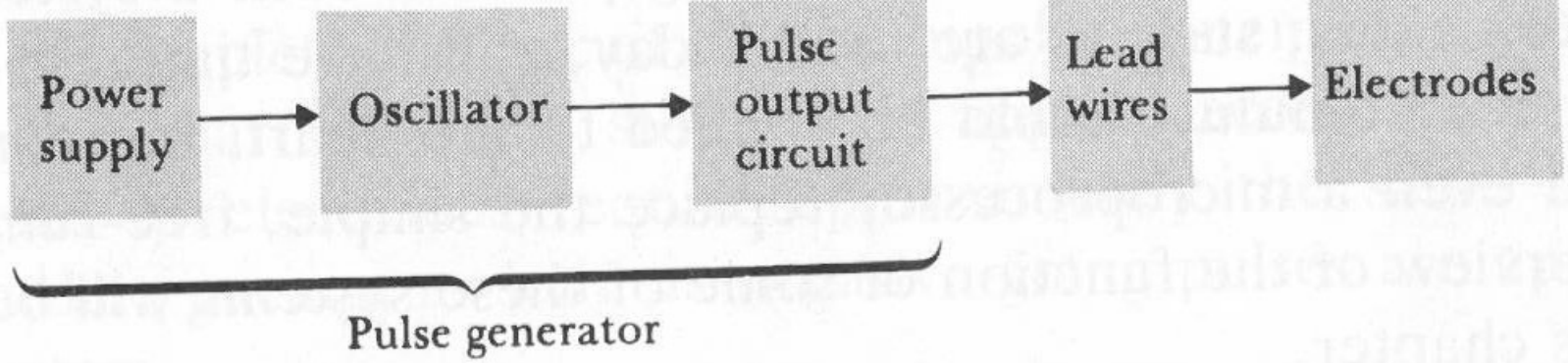


Figure 13.1 Block diagram of an asynchronous cardiac pacemaker

Demand pacemaker (Synchronous)

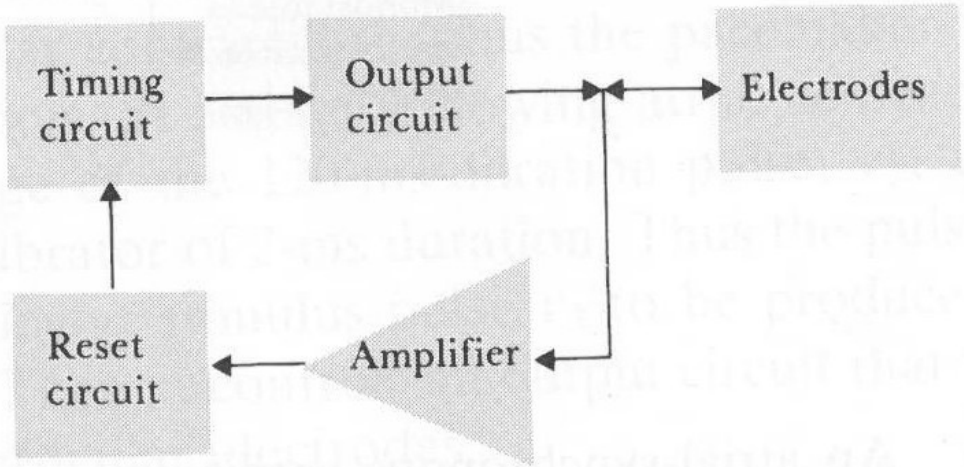


Figure 13.3 A demand-type synchronous pacemaker Electrodes serve as a means of both applying the stimulus pulse and detecting the electric signal from spontaneously occurring ventricular contractions that are used to inhibit the pacemaker's timing circuit.

Patients can establish a normal cardiac rythm between cardiac blocks -> continuous stimulations can result in serious complications. (artificial stimulus falls in repolarization period following a spontaneous ventricular contraction -> ventricular fibrillation).

Must not compete with the hearts' normal pacing action

Two synchronous types:

Atrial-synchronous pacemaker

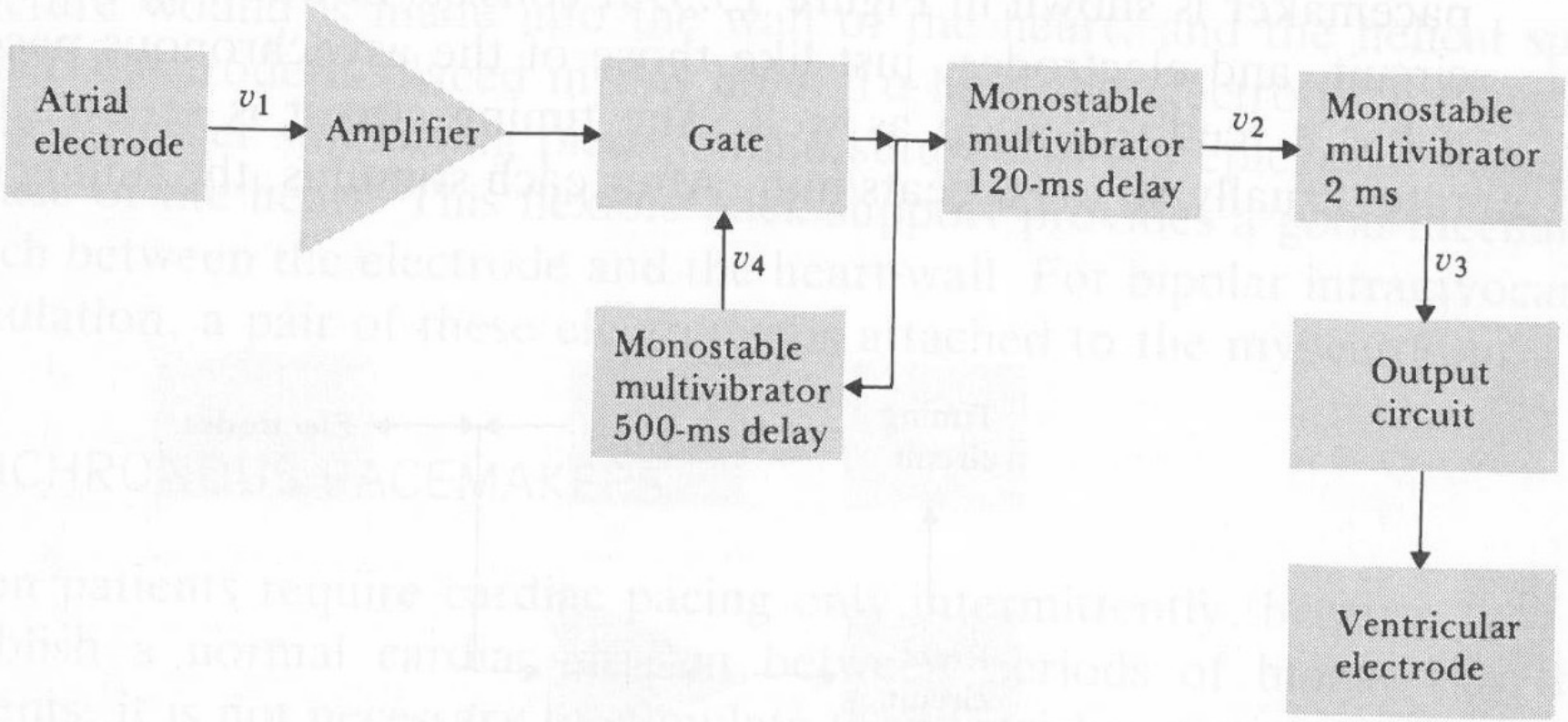


Figure 13.4 An atrial-synchronous cardiac pacemaker, which detects electric signals corresponding to the contraction of the atria and uses appropriate delays to activate a stimulus pulse to the ventricles. Figure 13.5 shows the waveforms corresponding to the voltages noted.

Second type: Atrial-synchronous pacemaker
Replace blocked conduction system of the heart, system is refractory
Fixed rates if atrial stimulus is lost -> combine demand pm with as pm

Physiologically controlled pacemaker

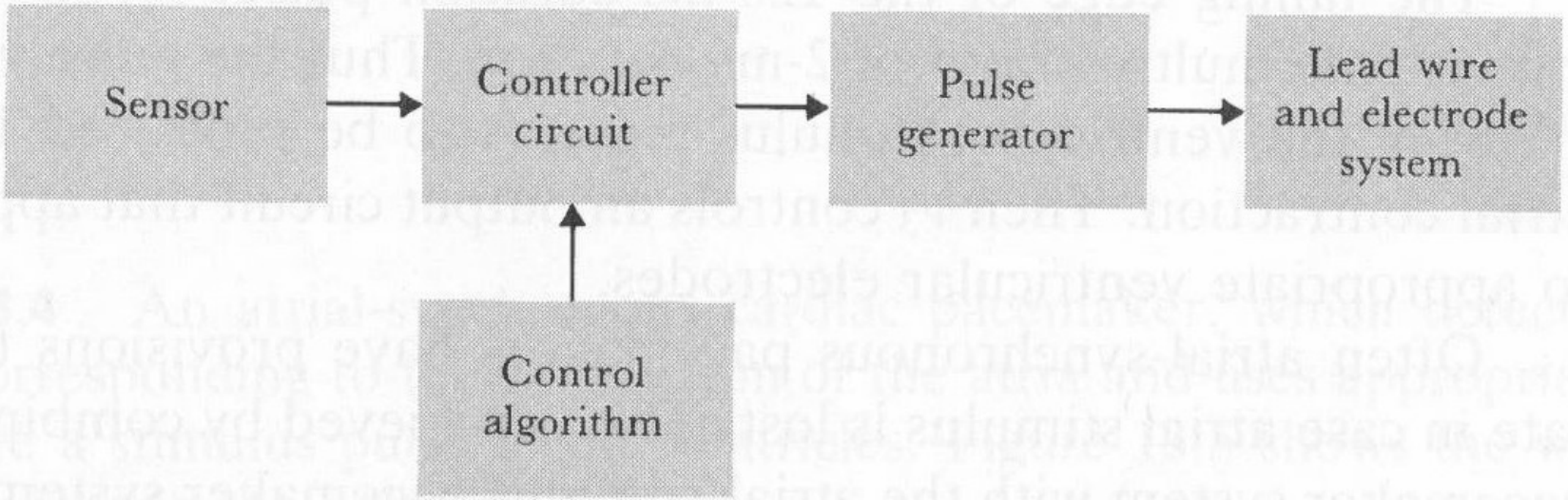
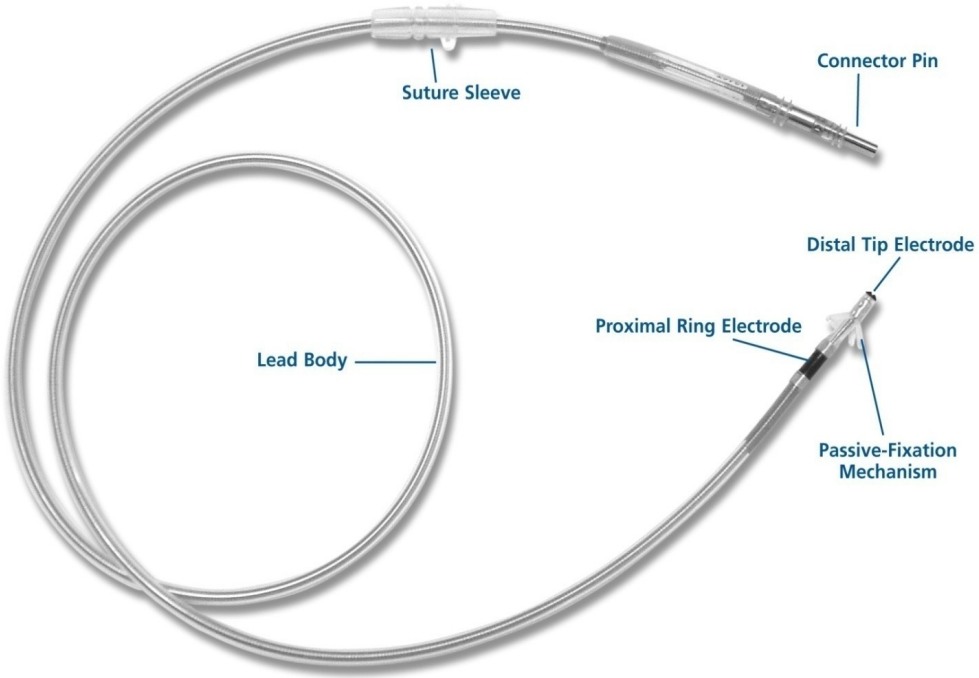
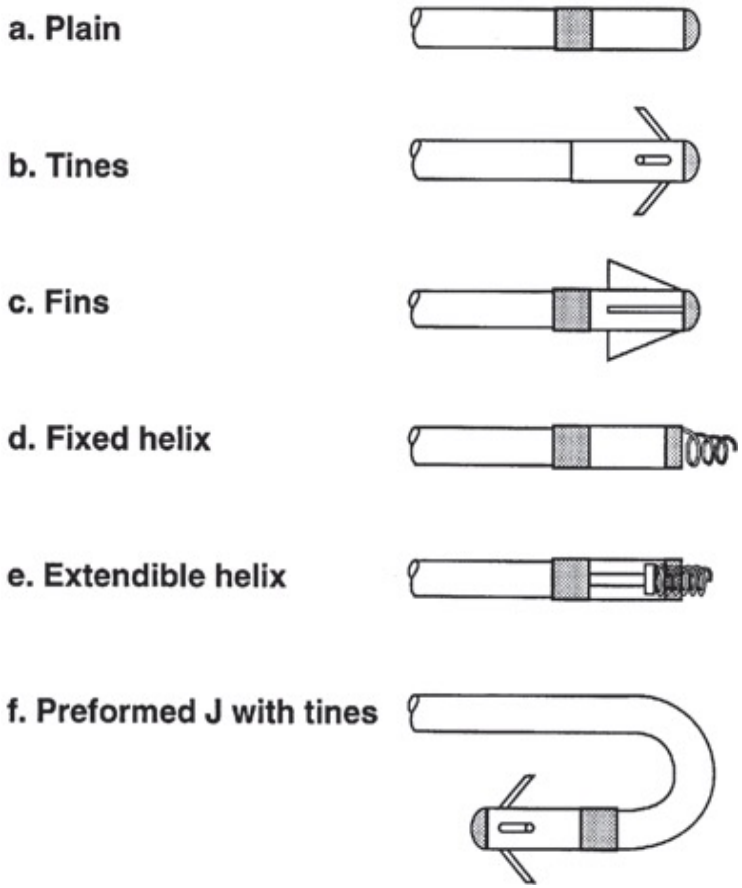


Figure 13.6 Block diagram of a rate-responsive pacemaker

Lead components and fixation mechanisms





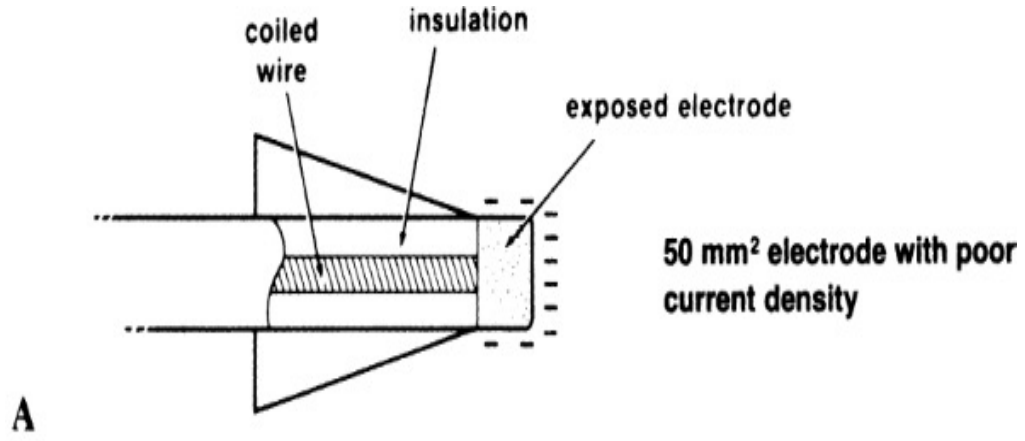
Unipolar vs Bipolar

	Unipolar	Bipolar
Advantages	Smaller diameter Easier to implant Large spike	No pocket stimulation Less susceptible to EMI Programming flexibility
Disadvantages	Pocket stimulation Far-field oversensing No programming flexibility	Larger diameter Stiffer lead body Small spike Higher impedance Voltage threshold is 30% higher

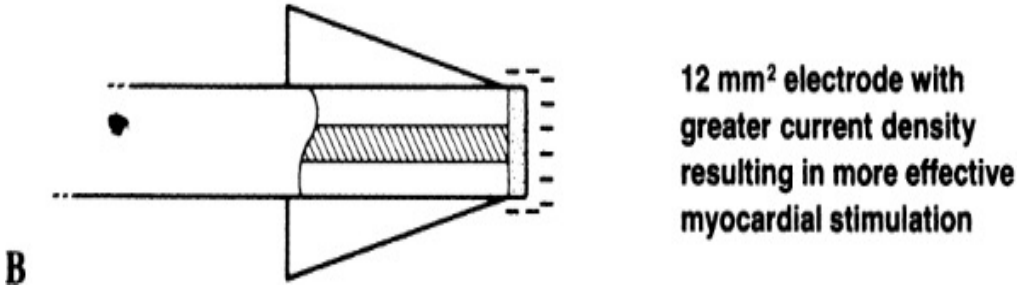
Source: www.Cardiologycmc.in

Impedance and electrodes

- Large electrode tip
  - Threshold ↑
  - Impedance ↓
  - Polarization ↓



- Small electrode tip
  - Threshold ↓
  - Impedance ↑
  - Polarization ↑



Metal / electrolyte = electron / ion transitions

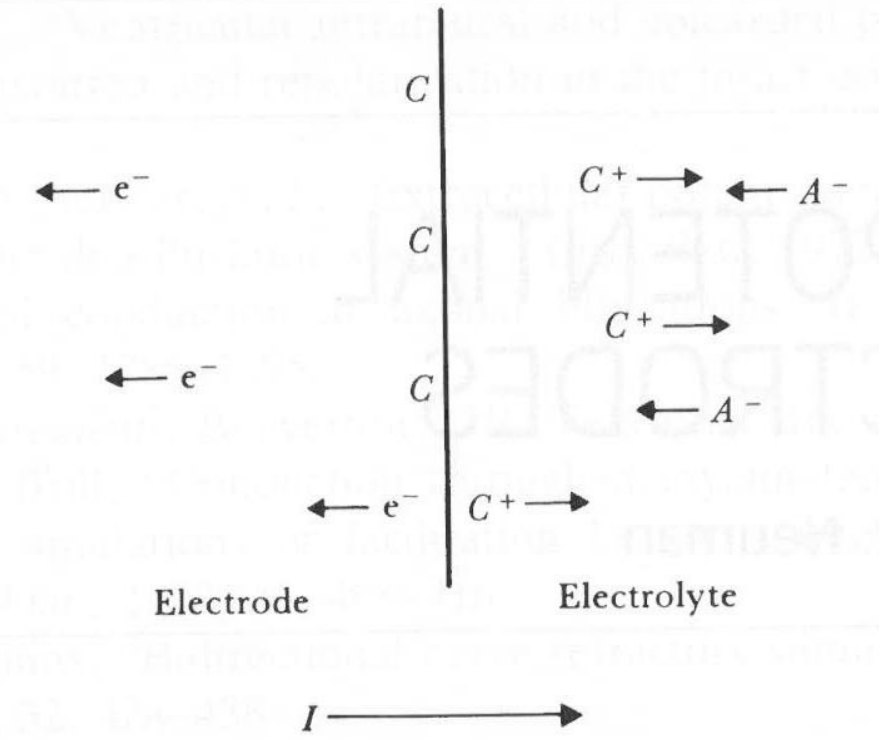


Figure 5.1 Electrode-electrolyte interface The current crosses it from left to right. The electrode consists of metallic atoms C. The electrolyte is an aqueous solution containing cations of the electrode metal C^+ and anions A^-.

A **half-cell** is a structure that contains a conductive electrode and a surrounding conductive electrolyte separated by a naturally occurring Helmholtz double layer. Chemical reactions within this layer momentarily pump electric charges between the electrode and the electrolyte, resulting in a potential difference between the electrode and the electrolyte

Half-cell potential is described for non-current situations
Current will alter the half-cell potential -> due to the polarization of the electrode

Overpotential = Diff betw observed half cell potential and the equilibrium zero-current half-cell potential
Three basic components:

1. Ohmic overpotential: Resistance of the electrolyte, voltage drop along current path in the electrolyte
2. Concentration overpotential: Due to changes in distribution of ions in the electrolyte in the vicinity of the electrode-electrolyte interface. The difference between current induced half-cell potential and equilibrium half-cell potentia = concentration overpotential
3. Activation overpotential: Charge-transfer process in oxidation-reduction reaction are not entirely reversible. (Energy barrier in order to start reaction). Current direction decides if oxidation or reduction predominates and thus the energy barrier = difference in voltage between electrode and electrolyte

All three mechanisms are additive

Theoretically two types of electrodes: Perfectly polarizable and perfectly non-polarizable
PP: no actual charge cross electrode electrolyte interface when current applied. (Behaves as a capacitor) (Platium, noble metals)
PNP: Current passing freely across electrode-electrolyte interface (Ag/Agcl, slightly soluble in water = stable)

Ag / AgCl
Non-polarizable electrode

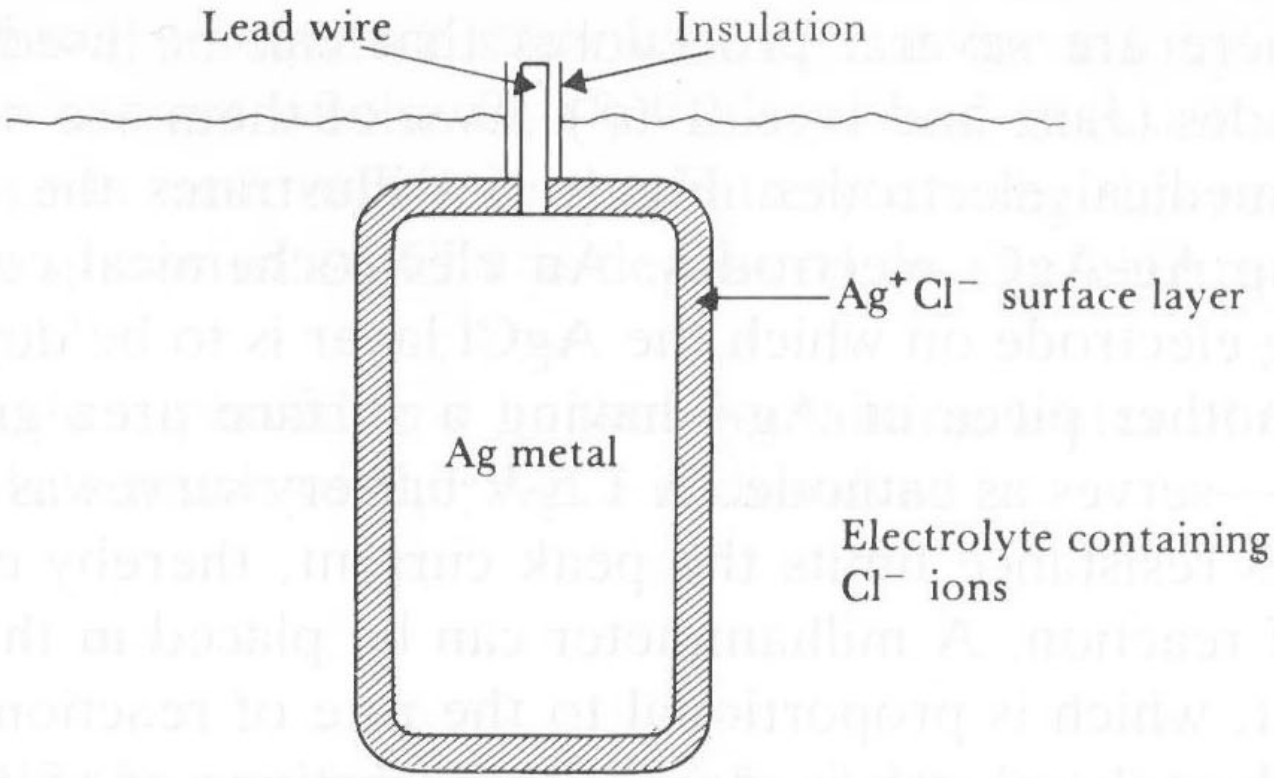
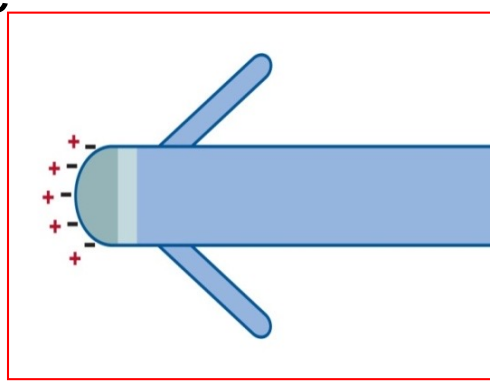


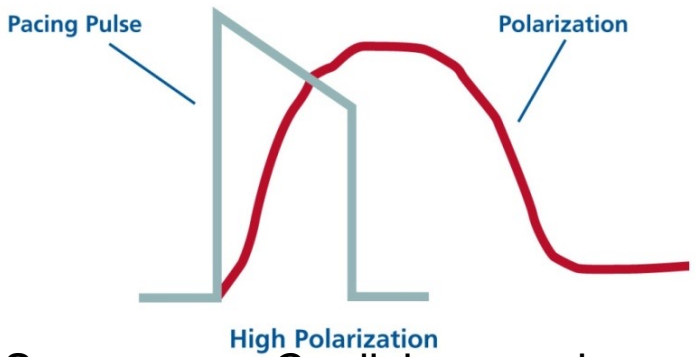
Figure 5.3 A silver–silver chloride electrode, shown in cross section.

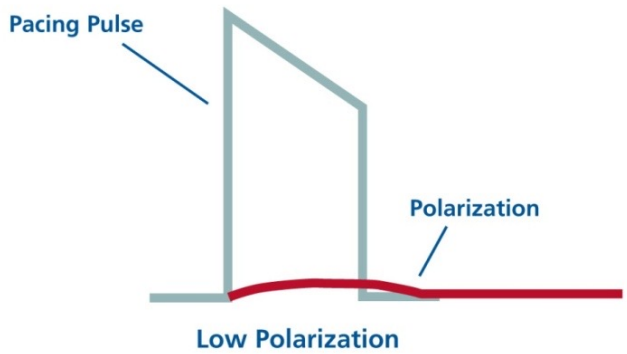
Polarization

- After an output pulse, positively charged particles gather near the electrode.
- The amount of positive charge is
  - Directly proportional to pulse duration
  - Inversely proportional to the functional electrode size (i.e. smaller electrodes offer higher polarization)



Polarization effect may represent 30–40% of the total pacing impedances as high as 70% for smooth surface, small surface area electrodes





Source: www.Cardiologycmc.in

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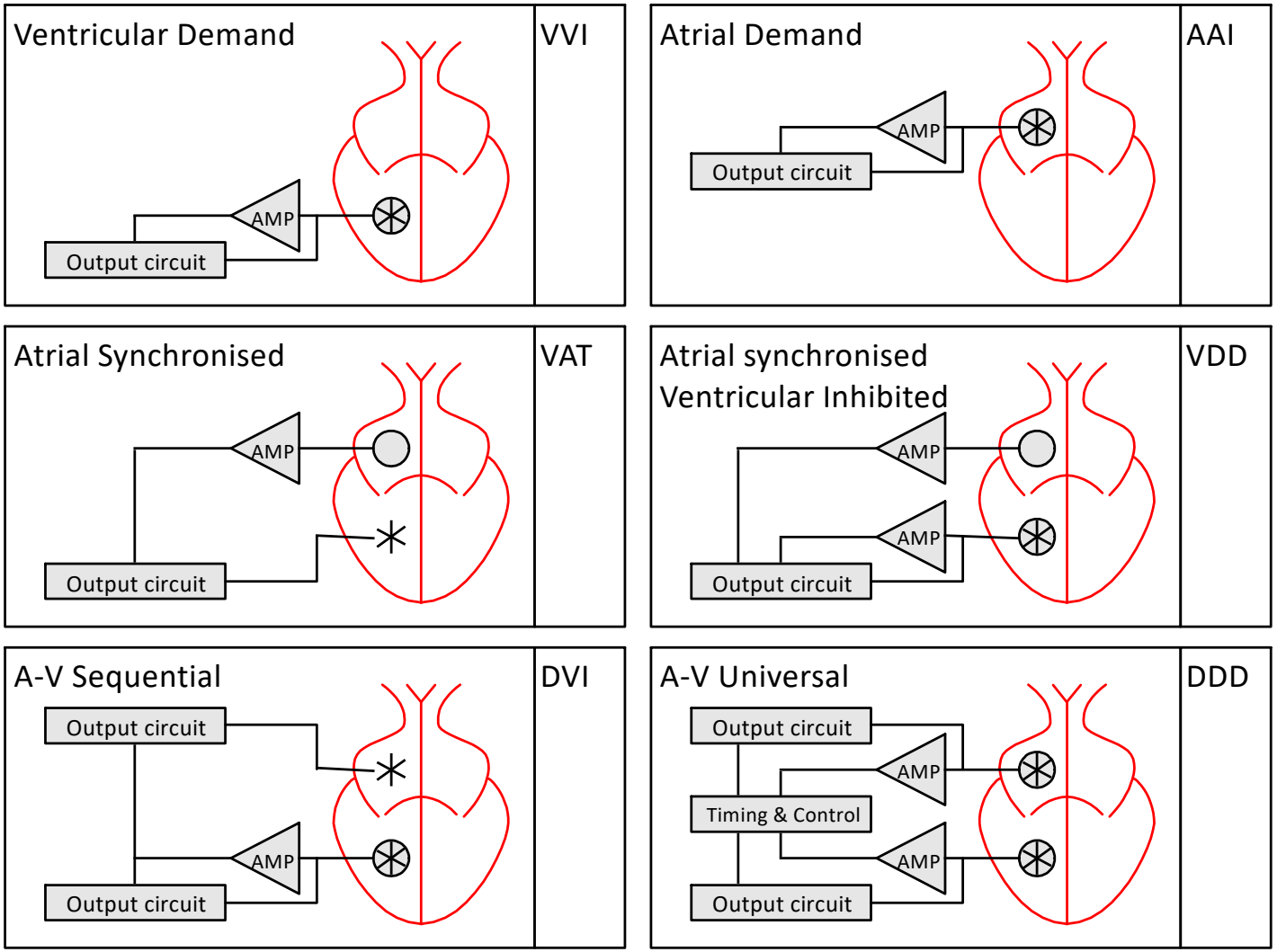
Pacing Modes



Stuart Allen 06

Pacemaker-electrodes

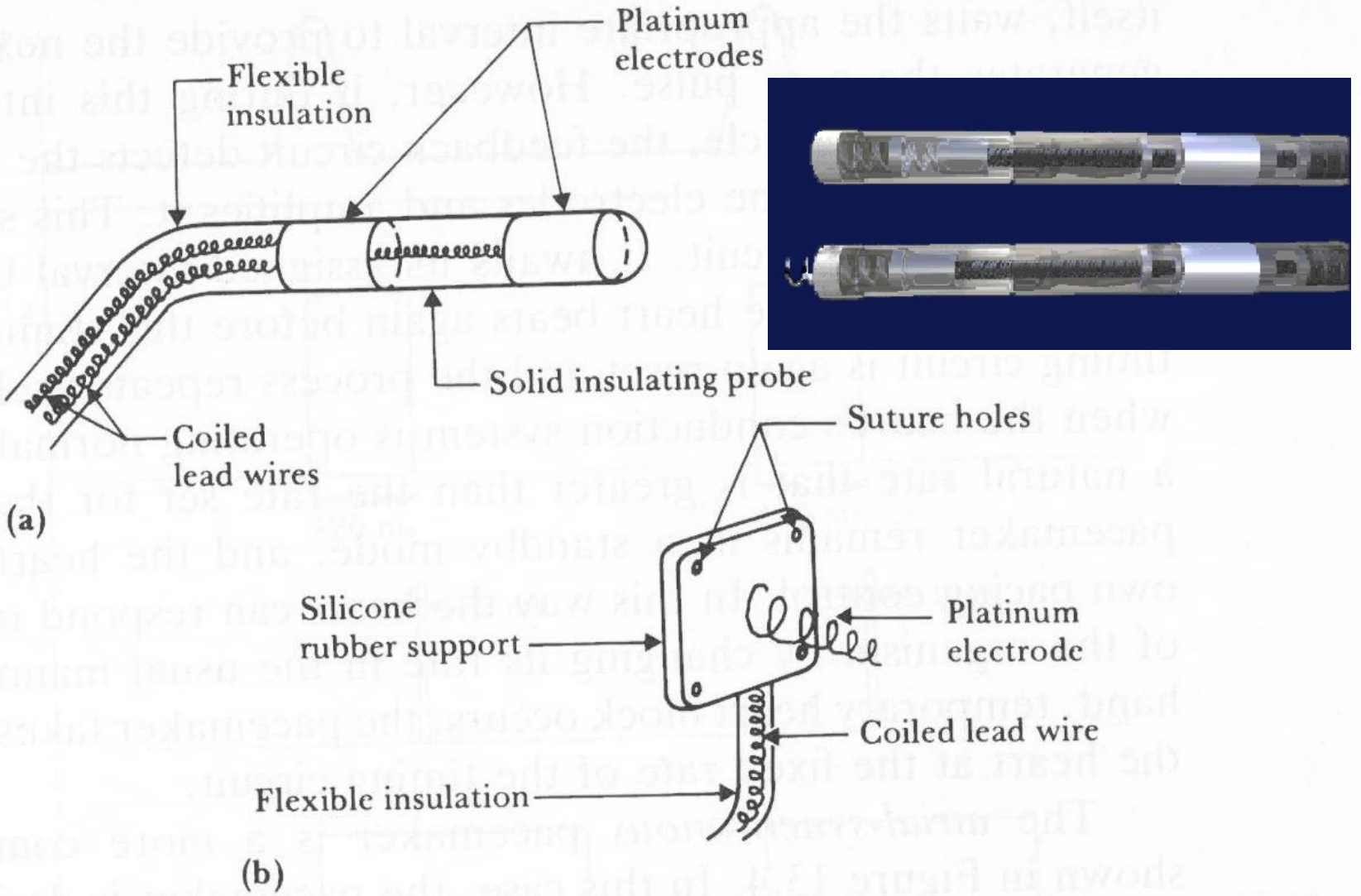
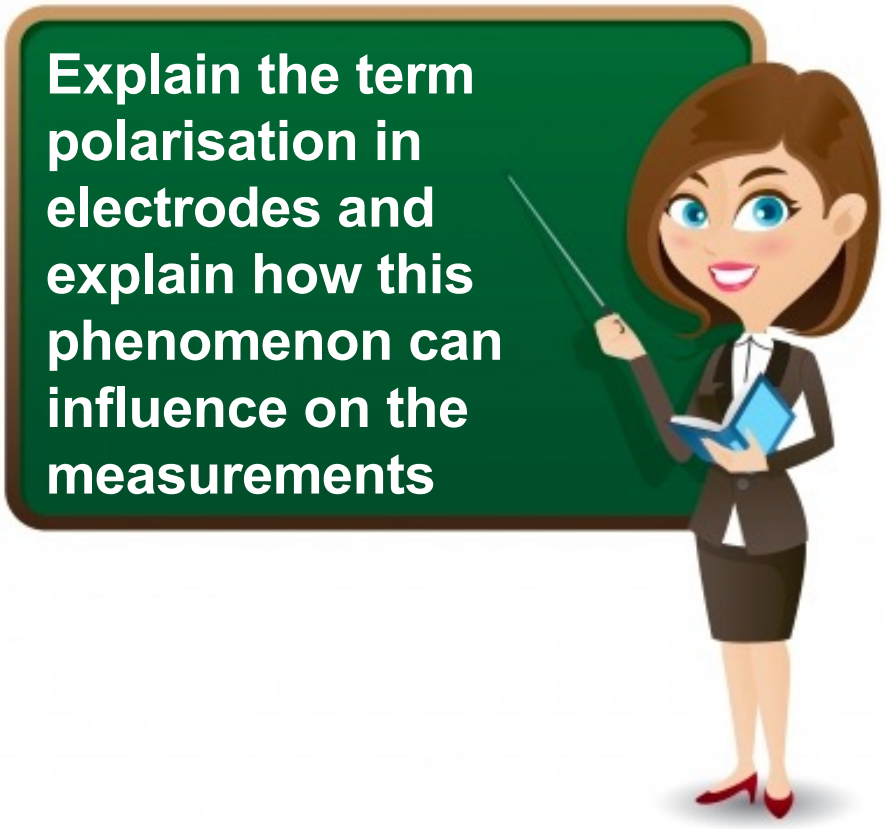
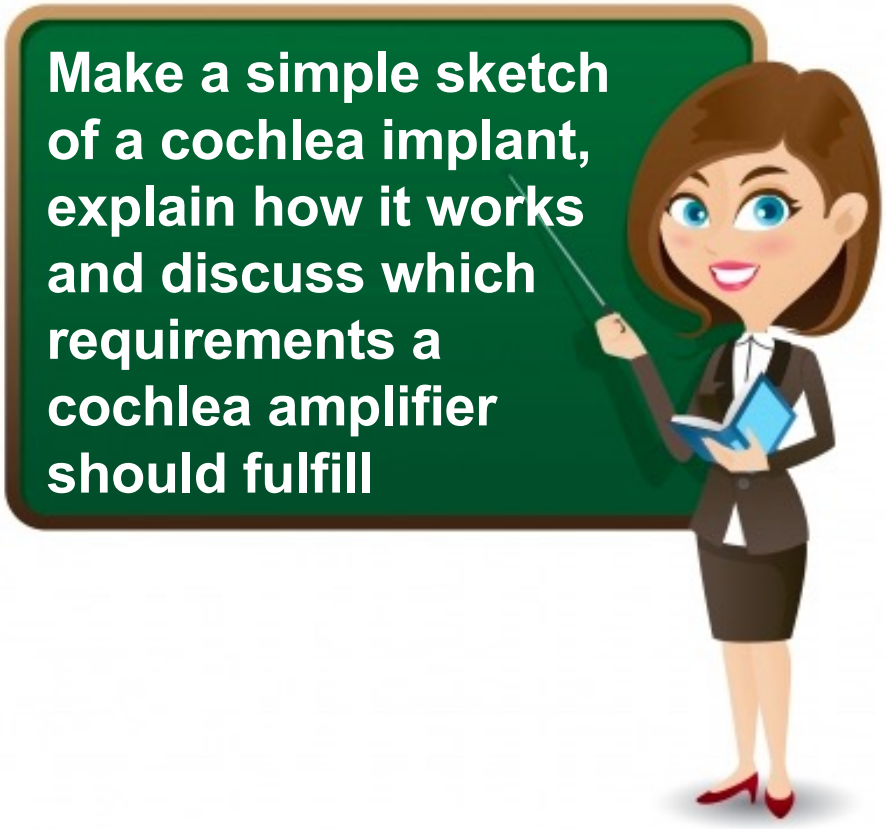
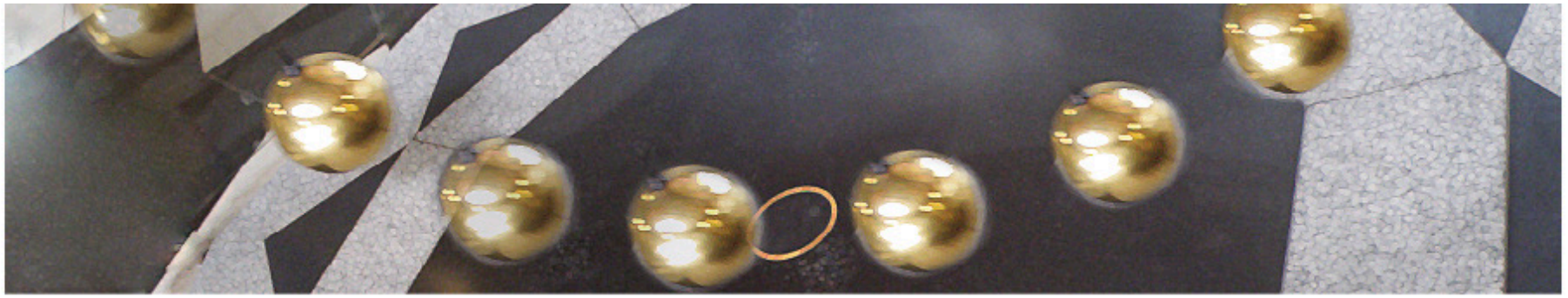


Figure 13.2 Two of the more commonly applied cardiac pacemaker electrodes (a) Bipolar intraluminal electrode. (b) Intramyocardial electrode.

Exercise examples







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Lecture 12

X-ray files: The truth is out there

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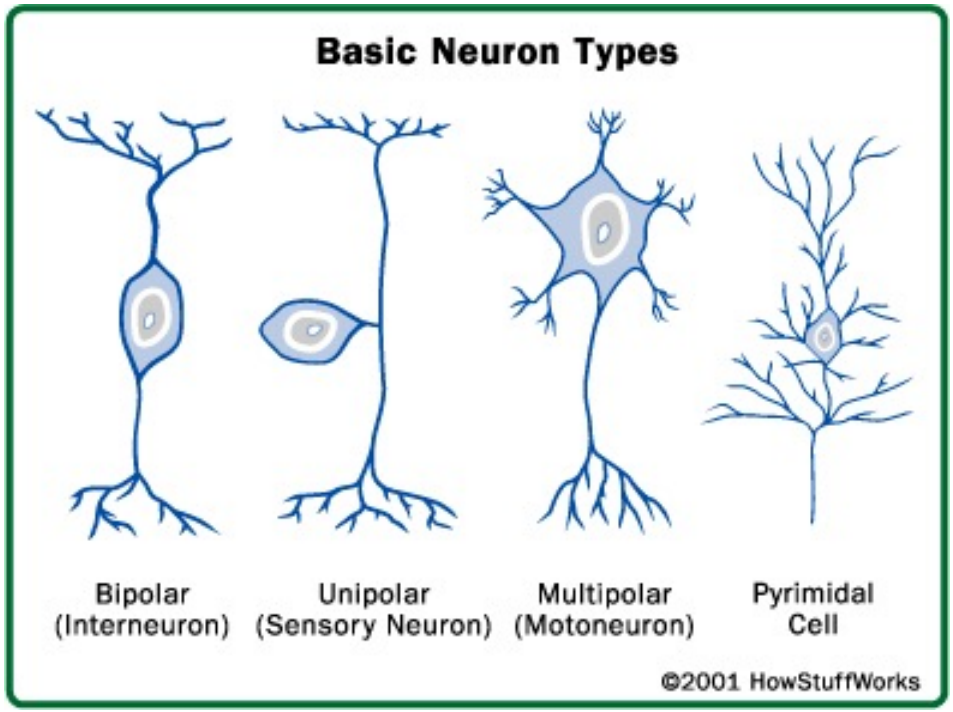
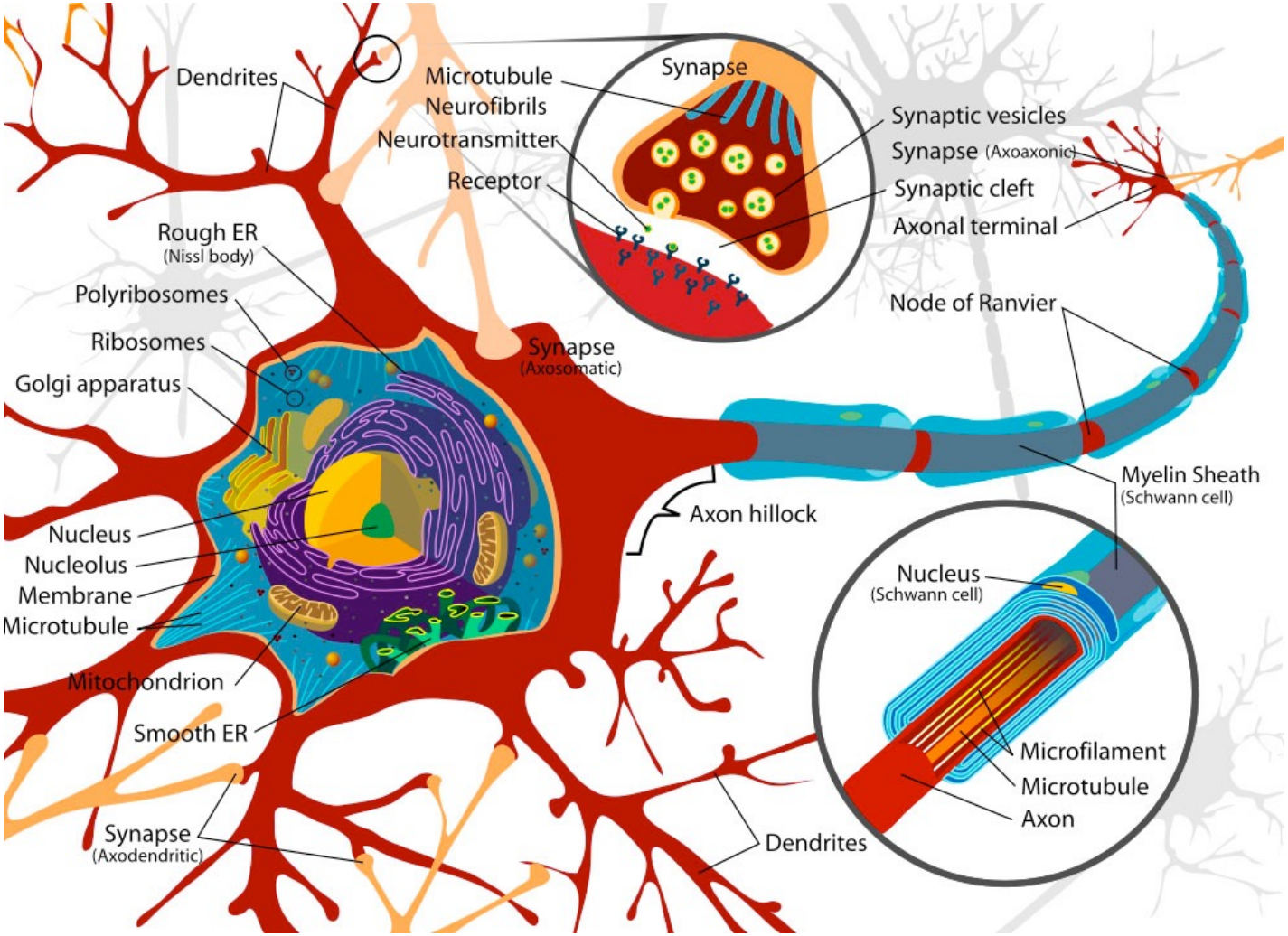
Signalpaths in cortex



Functional part of the cerebrum is the cerebral cortex (bark, outer, covering). (1.5 to 4.0 mm in thickness)
Cell bodies and fiber bundles in a complex architecture, 2 types of neurons, pyramidal and nonpyramidal.
Nonpyramidal is small, dendrites spring in all directions and contribute none to the surface records
Variations in dipole orientation (Dendrite, cell), strength and direction, produce wavelike fluctuations in the recorded potential on the surface

Neuron (Nerve cell)

Dendrite recieve information
Axon send information



http://paleozonenutrition.com/wp-content/uploads/2012/02/nerve-cell.jpg

MEG - Magnetoencefalogram

- EEG measures surfaceactivity
- MEG measures sulcus activity (in the furrow/fure)
- Perpendicular to each other
- MEG is a functional neuroimaging technique, recording magnetic fields produced by current from action potentials
- Extremely sensitive magnetometers (SQUIDS – super conducting quantum interference devices)
- Essential problem of biomagnetism is the weakness of the signal
- 50 000 active neurons is needed to produce a detectable signal
- Must be dipoles with similar orientation = pyramidal cells

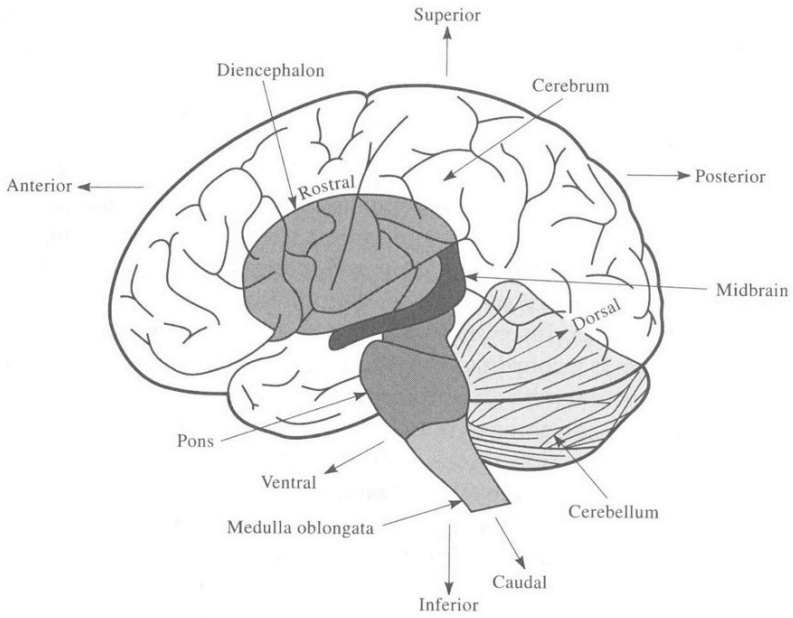


Figure 4.24 (a) Anatomical relationship of brainstem structures (medulla oblongata, pons, midbrain, and diencephalon) to the cerebrum and cerebellum. General anatomic directions of orientation in the nervous system are superimposed on the diagram. Here the terms rostral (toward head), caudal (toward tail), dorsal (back), and ventral (front) are associated with the brainstem; remaining terms are associated with the cerebrum. The terms medial and lateral imply nearness and remoteness, respectively, to or from the central midline axis of the brain. (b) A simplified diagram of the CNS showing a typical general sense pathway from the periphery (neuron 1) to the brain (neuron 3). Note that the axon of the secondary neuron (2) in the pathway

EEG

Thalamus is a major relay station and an integration centre of all sensory systems. Hypothalamus integrates functions of the autonomic nerve system and is a hormone controlling centre, cerebellum is a coordinator in the volyntary muscle system, cerebrum is the main part housing the conscious functions of the nervous system

EEG - electrodes

- An equivalent circuit of the EEG-electrode is shown on the top
- Due to the low amplitude signals, the half-cell potential matters (= E in the figure, see the table below). C is due to the effect of higher freguencies
- The measuerement of a potential between two electrodes is shown in the figure to te right
- G is the cerebral generator, Rg is the internal resistance

TABLE 10.1. *Typical half-cell potential values*

Electrode material	Electrode potential (V)
Lead (Pb)	−0.13
Tin (Sn)	+0.14
Silver chloride (AgCl)	+0.22
Copper (Cu)	+0.52
Silver (Ag)	+0.80
Platinum (Pt)	+0.86
Gold (Au)	+1.50

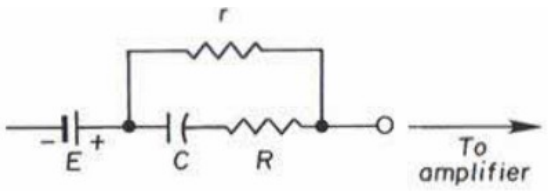


FIG. 10.2. Series equivalent circuit of a single electrode in contact with an electrolyte. Redrawn from Geddes (14).

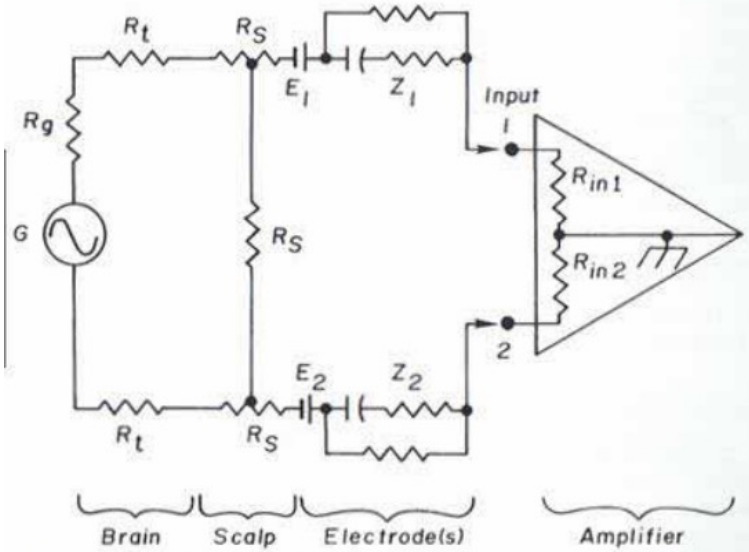


FIG. 10.3. Equivalent circuit of electrode pair with input to an EEG amplifier. G = Cerebral generator; Rg = internal resistance of generator; Rt = tissue resistance; Rs = scalp resistance; $E_{1,2}$ = electrode potential; $Z_{1,2}$ = capacitive and resistive properties of electrodes; $R_{in,1}$ and $R_{in,2}$ = input resistance (impedance) of amplifier. Redrawn from Geddes (14).

Images: Geddes and Baker, 1966

Position dependency

- Measuring a 3-dimentional structure is difficult with surface electrodes
- P2 measures both the negative potential of the near sulcus, but also the positive charge of distal sulcus. Thus a lower signal at P2 than P1 (see figure)

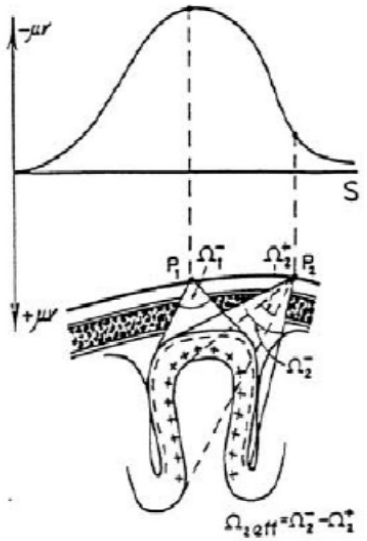


FIG. 7. Potential distribution along line S on the scalp created by the synchronous activation of a curved portion of cortex that occupies the crown of a gyrus and its two sides forming the proximal walls of the two adjacent sulci. At P1, the potential depends only on the solid angle Ω_1^-, since at this point an electrode "sees" only a portion of the negative side of the dipole layer. At P2, an electrode "sees" the negative side of the portion of the dipole layer occupying the crown of the gyrus and the wall of the proximal sulcus under the angle Ω_2^-; however, it also "sees" under the smaller angle Ω_1^+ the positive side of the portion of the dipole layer located in the wall of the distal sulcus. The potential at P2 is therefore smaller than would be expected if only Ω_2^- were the angle determining the size of the potential at P2 and is proportional to the effective solid angle $\Omega_{2\text{eff}}$ which equals the difference between Ω_2^- and Ω_1^+, the polarity being negative, since $\Omega_1^- > \Omega_2^+$. As is the case for a flat area of cortex oriented in parallel to the scalp the potential profile is bell-shaped. (Taken in part from Gloor, 1975.)

Biopotential amplifiers

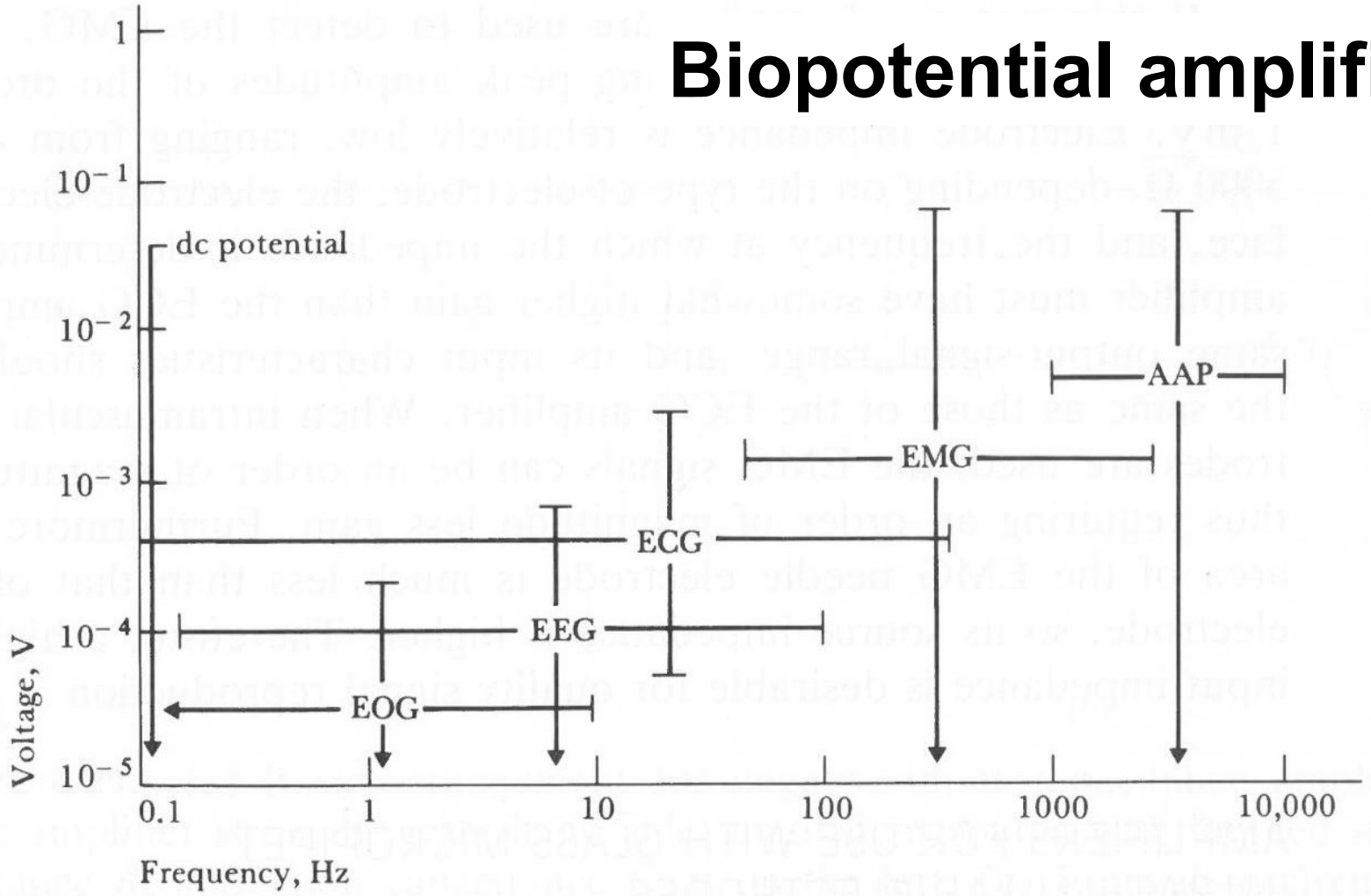
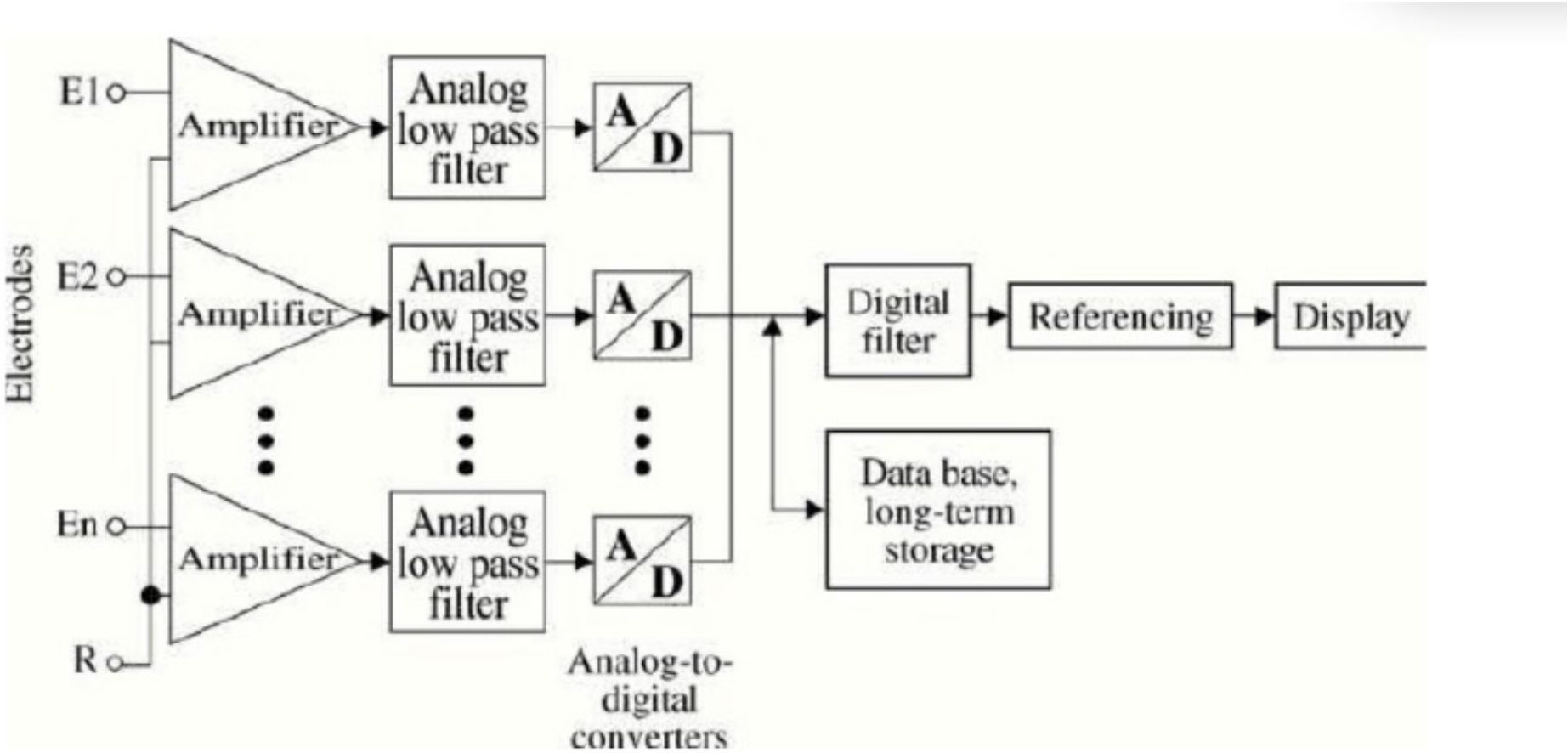


Figure 6.20 Voltage and frequency ranges of some common biopotential signals; dc potentials include intracellular voltages as well as voltages measured from several points on the body. EOG is the electrooculogram, EEG is the electroencephalogram, ECG is the electrocardiogram, EMG is the electromyogram, and AAP is the axon action potential. (From J.M.R. Delgado, "Electrodes for Extracellular Recording and Stimulation," in *Physical Techniques in Biological Research*, edited by W.L. Nastuk, New York: Academic Press, 1964.

A/D-conversion



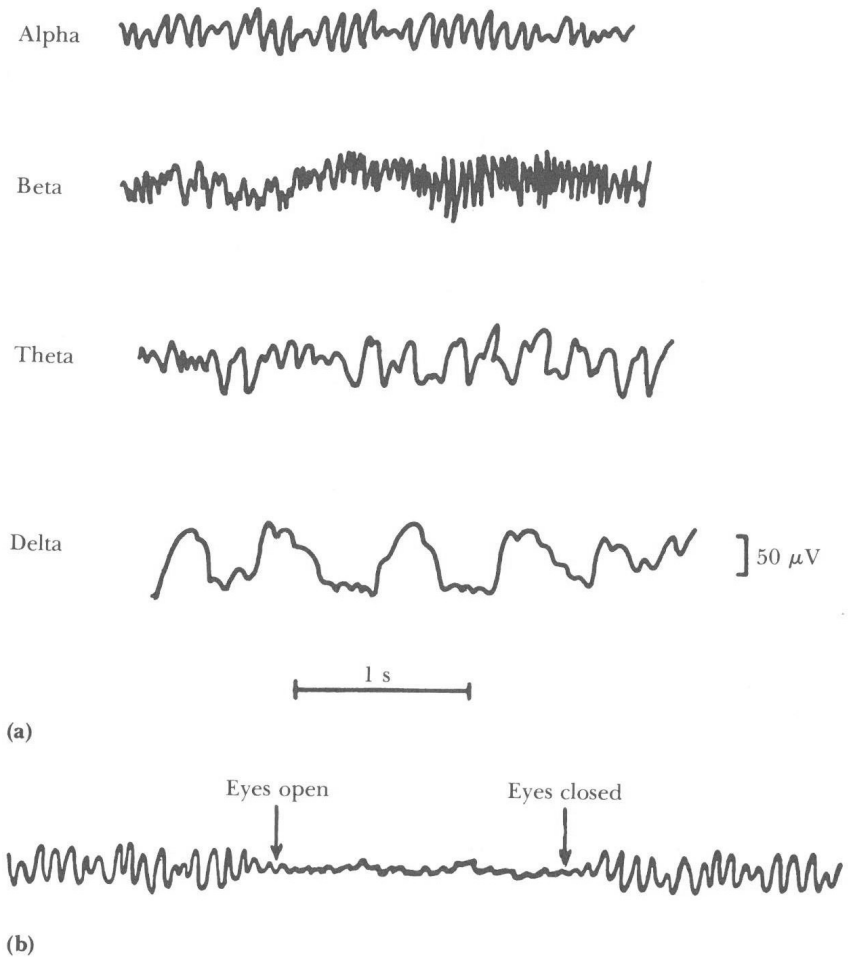
What requirements would you choose for the AD-converters?

Filters

- Necessary for obtaining apropriate signals
- All selective filters are digital, the only analog filter is the analog front end-filter (why?)
- Filters attenuate, not eliminate signal information
- Are often mistakenly used to make smooth curves, not to make correct curves
- Filters will add an error to the curves, depending on the settings
- Risk of aliasing (fold back frequencies)

EEG waves 1

Alpha 8-13 Hz, awake, quiet relaxed 20-200 uV. Disappear during sleep
Beta 14-30 Hz up to 50 Hz if intense mental activity. Beta 1 and beta 2. Affected by mental activity Beta 2 appear during intense activation of the CNS and during tension
Theta 4-7 Hz children, and emotional stress among some adults (disappointment and frustration)
Delta below 3.5 Hz, sometimes only every 2 or 3 second, deep sleep, infancy and serious organic brain diseases



Sleep EEG

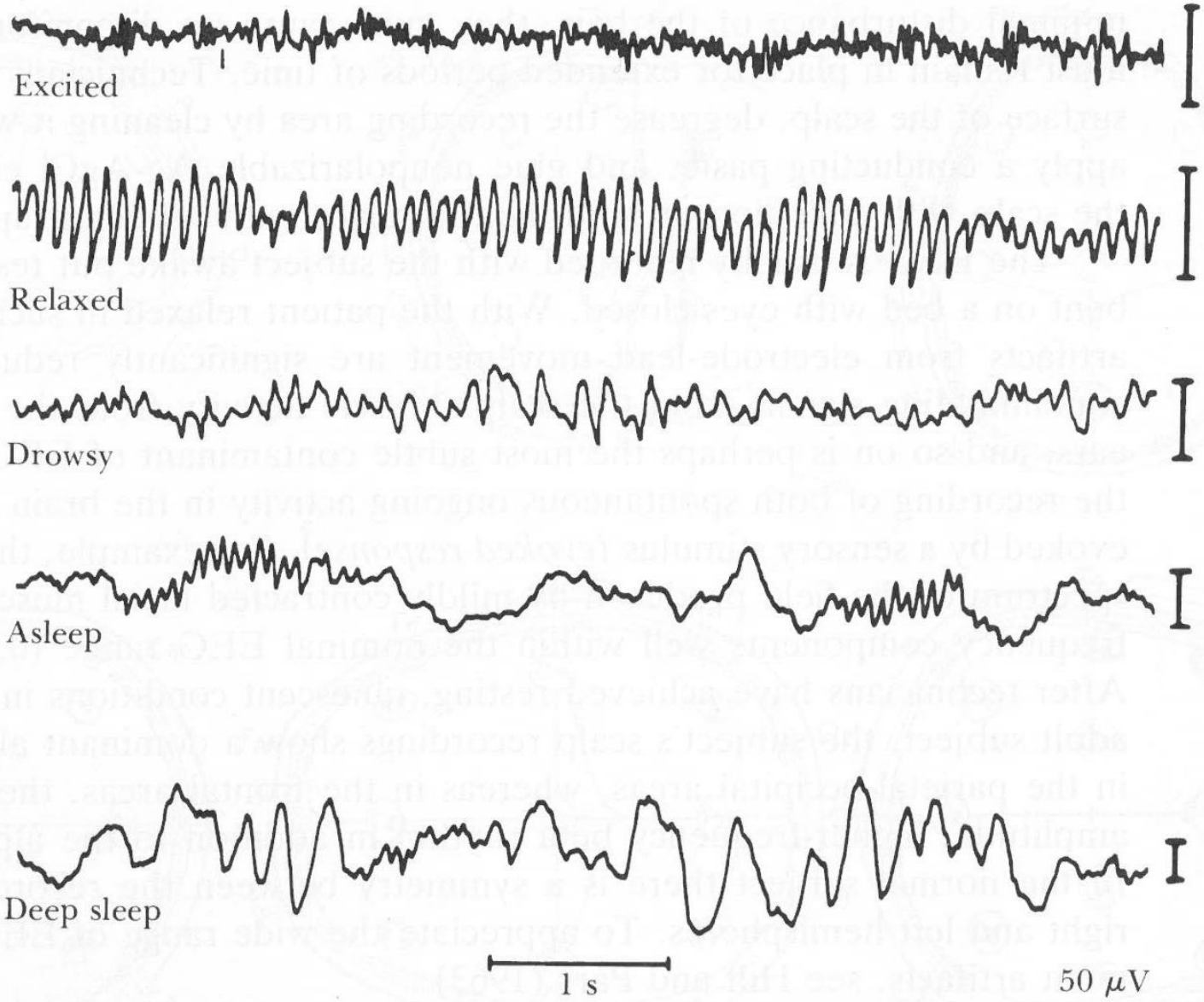


Figure 4.33 The electroencephalographic changes that occur as a human subject goes to sleep The calibration marks on the right represent 50 μV. (From H. H. Jasper, "Electrocephalography," in *Epilepsy and Cerebral Localization,* edited by W. G. Penfield and T. C. Erickson. Springfield, Ill.: Charles C. Thomas, 1941.)

EEG

electrodes

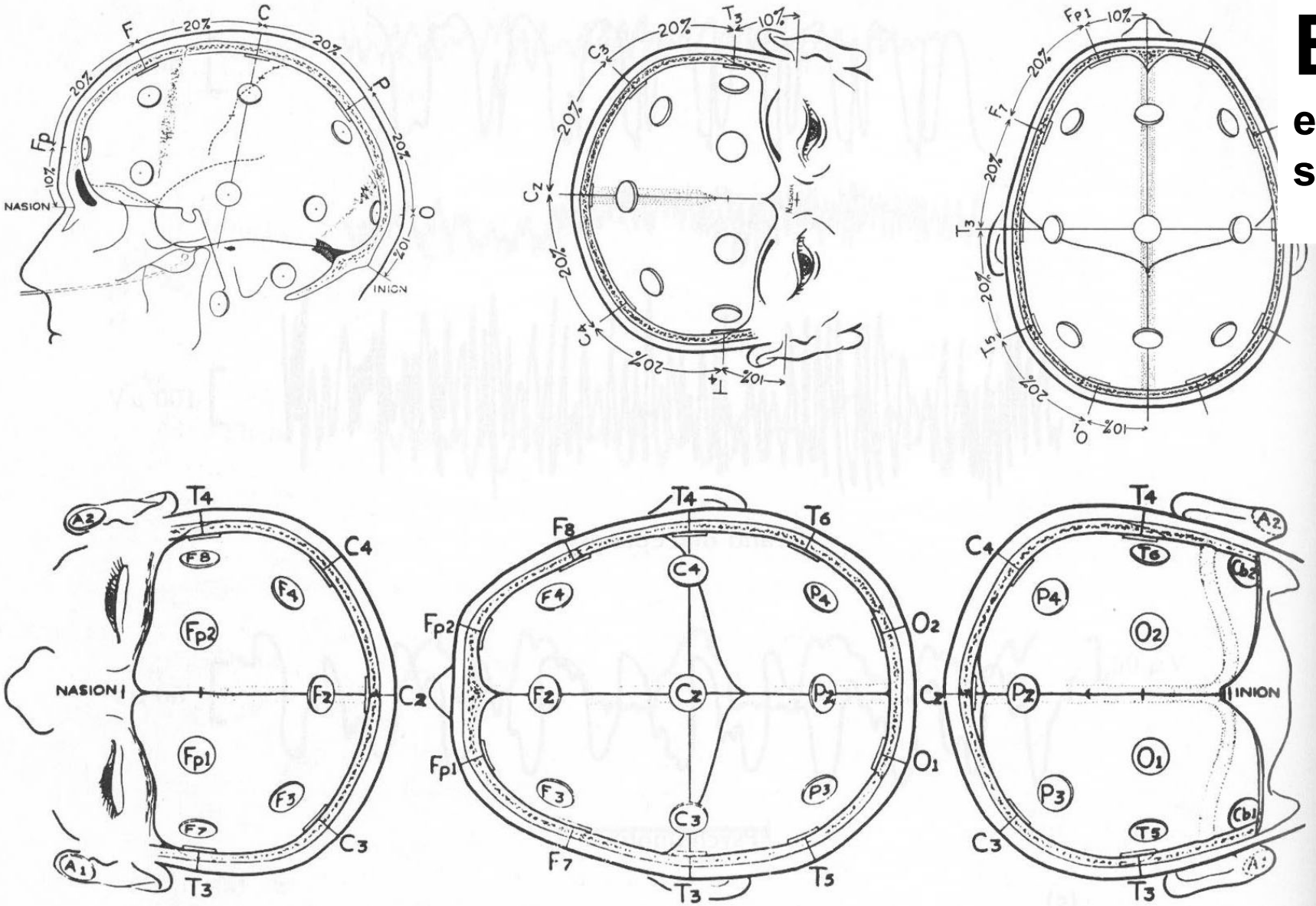


Figure 4.32 The 10-20 electrode system This system is recommended by the International Federation of EEG Societies. (From H. H. Jasper, "The Ten-Twenty Electrode System of the International Federation in Electroencephalography and Clinical Neurophysiology," *EEG Journal*, 1958, **10** (Appendix), 371–375.)

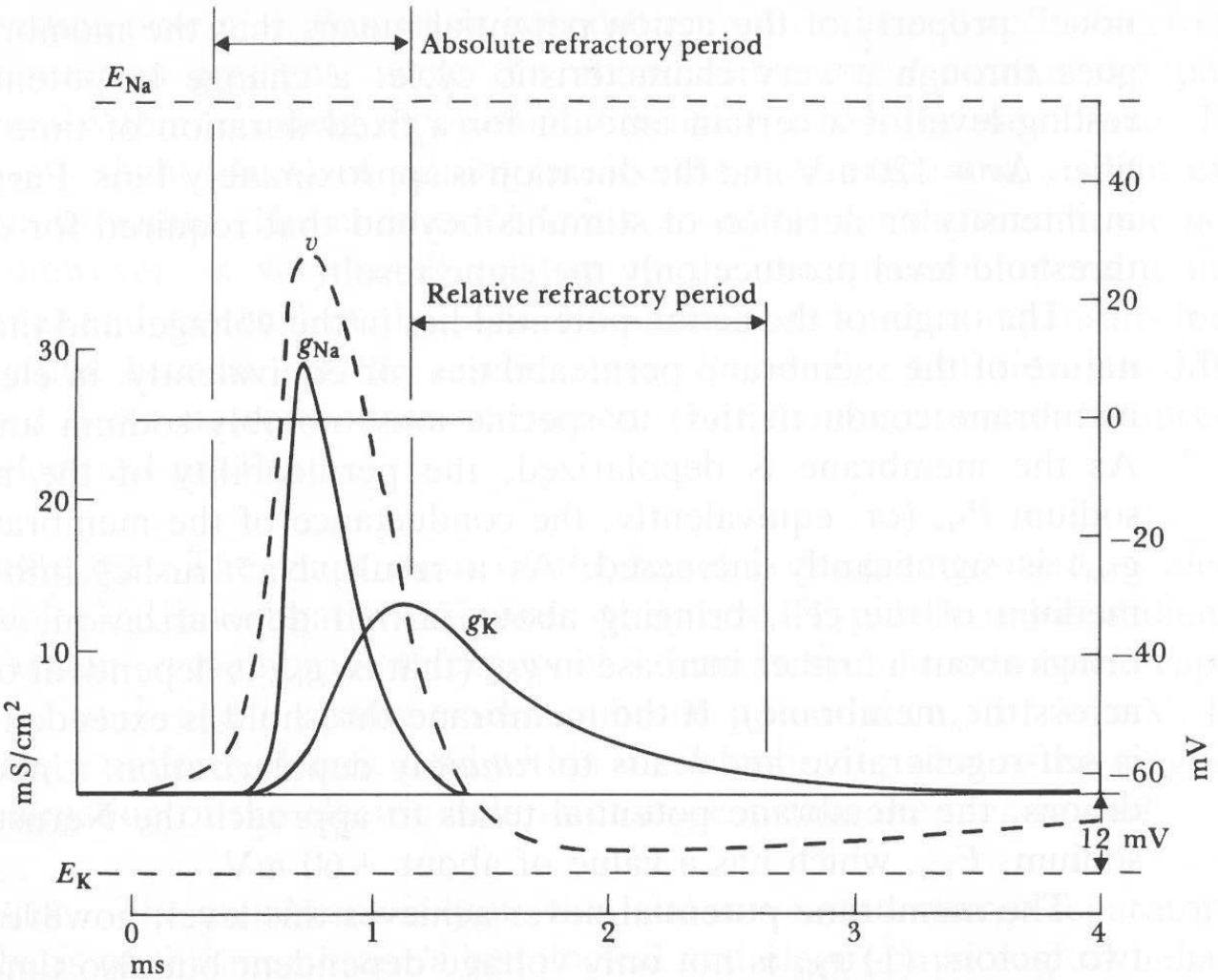
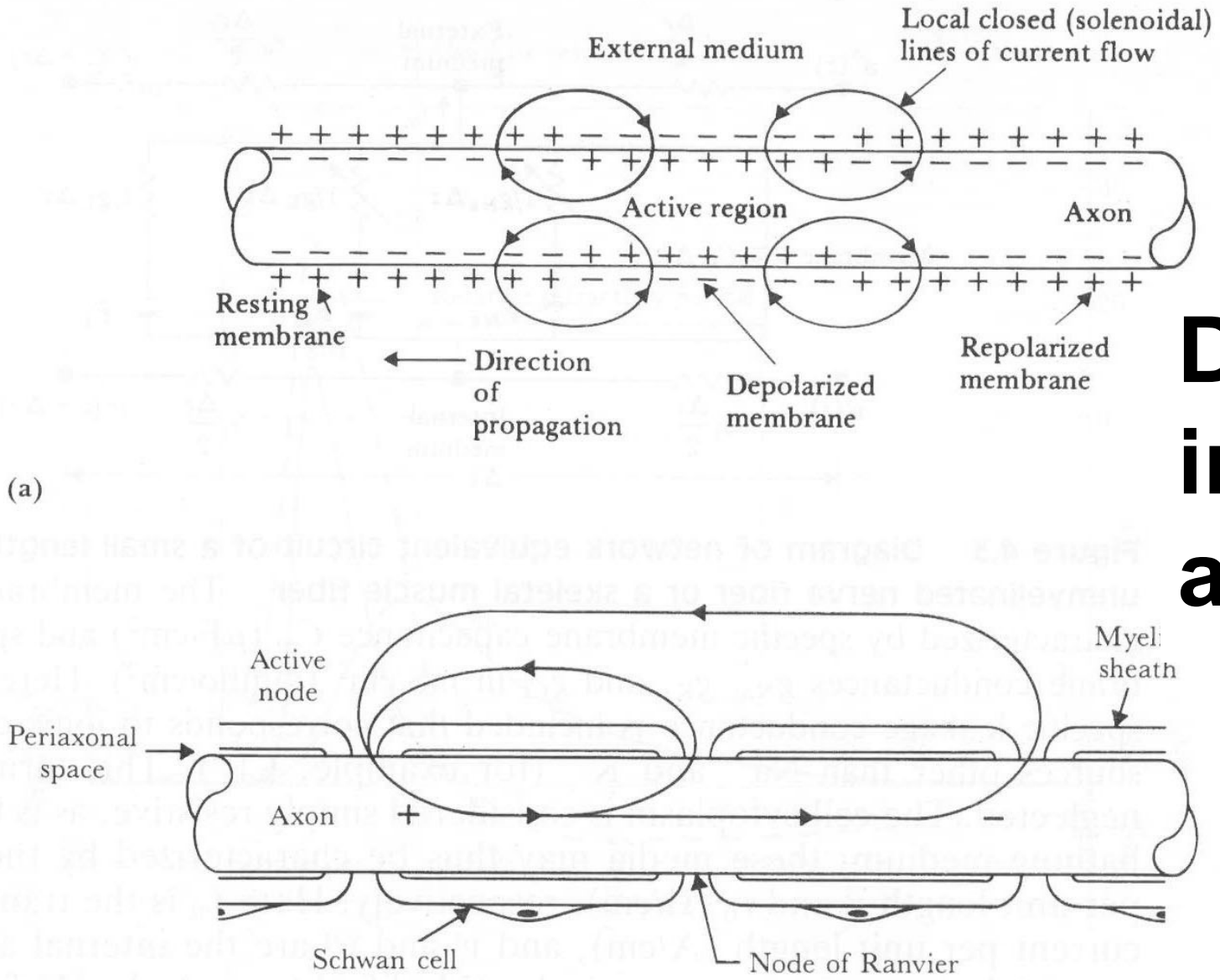


Figure 4.2 Theoretical action potential v and membrane ionic conductance changes for sodium (g_{Na}) and potassium (g_K) are obtained by solving the differential equations developed by Hodgkin and Huxley for the giant axon of the squid at a bathing medium temperature of 18.5°C. E_{Na} and E_K are the Nernst equilibrium potentials for sodium and potassium across the membrane. (Modified from A. L. Hodgkin and A. F. Huxley, "A Quantitative Description of Membrane Current and Its Application to Conduction and Excitation in Nerve," *Journal of Physiology*, 1952, **117**, p. 530.)

Action potential, excitable cell



Dipoles in the axon

Figure 4.4 (a) Charge distribution in the vicinity of the active region of fiber conducting an impulse. (b) Local circuit current flow in the myelinated nerve fiber.

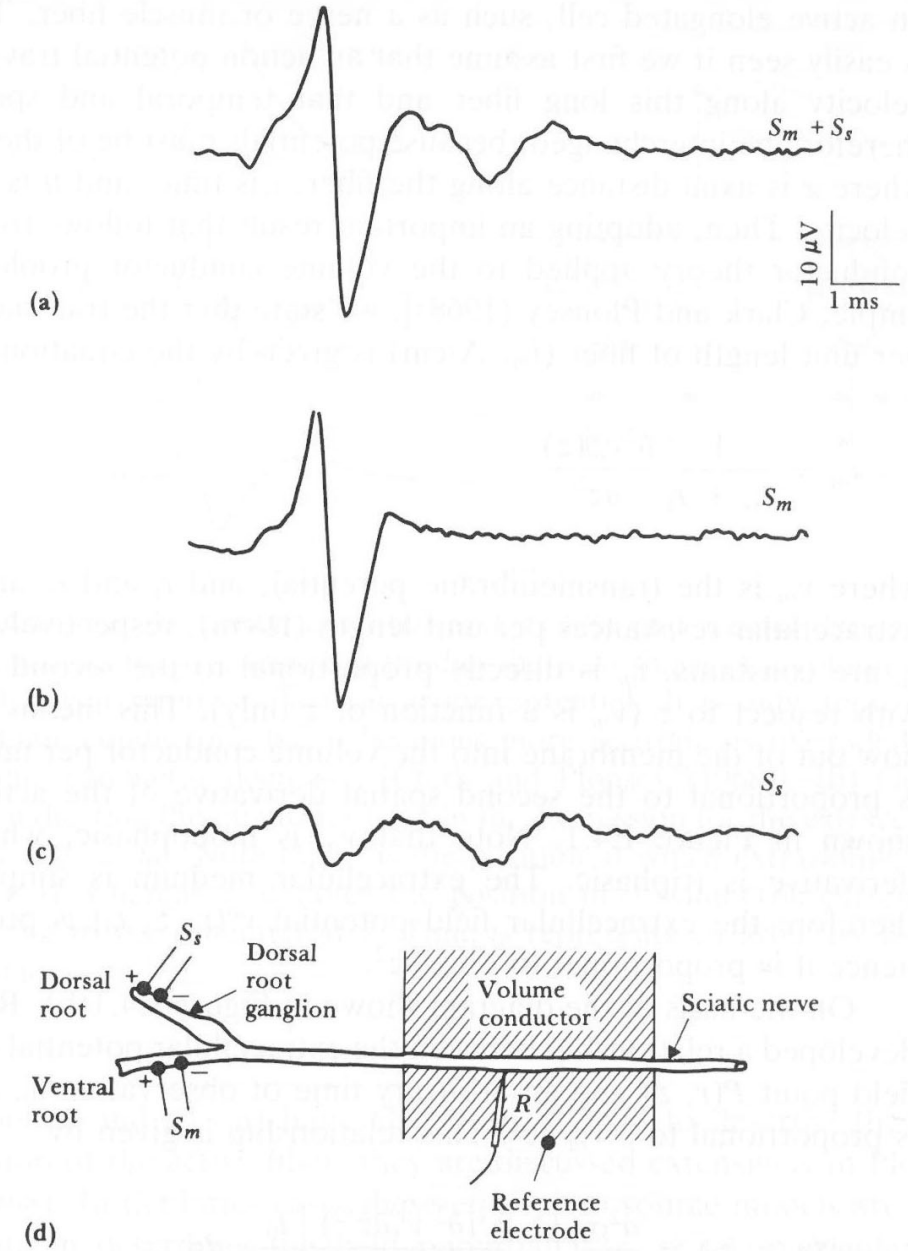
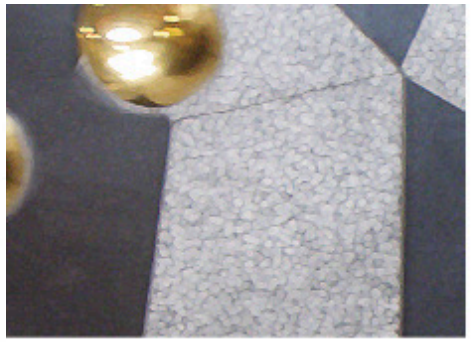


Figure 4.5 Extracellular field potentials (average of 128 responses) were recorded at the surface of an active (1-mm-diameter) frog sciatic nerve in an extensive volume conductor. The potential was recorded with (a) both motor and sensory components excited ($S_m + S_s$), (b) only motor nerve components excited (S_m), and (c) only sensory nerve components excited (S_s).

Summing up in the nerve-cell

Both motorical and sensorical fibers are excited simultaneously by electrical stimulus.
Dorsal root is sensoric
Ventral root is motoric, dorsal root is nervous
Stimulation of the many large diametric motoric fibers will give the largest extracellular response.
Stimulation of sensoric fibers will excite two groups of sensoric fibres.



How to measure action potential
Axon in invertebrate animals

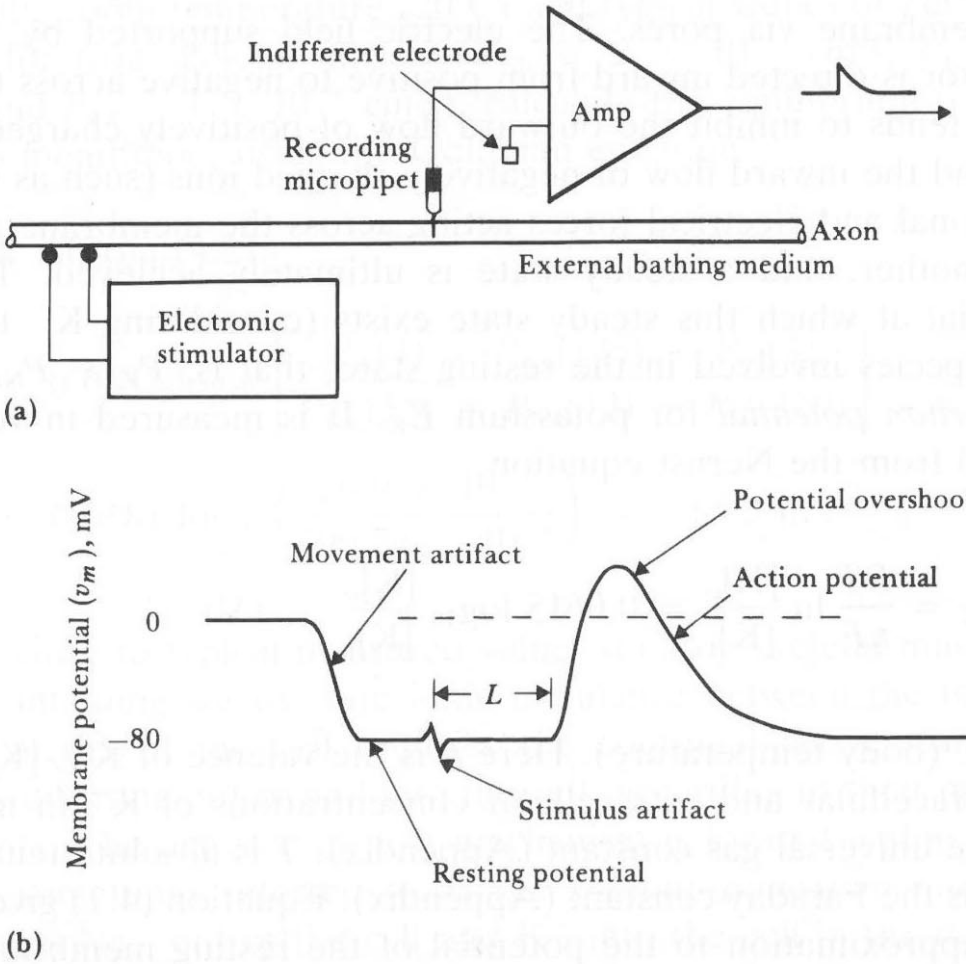
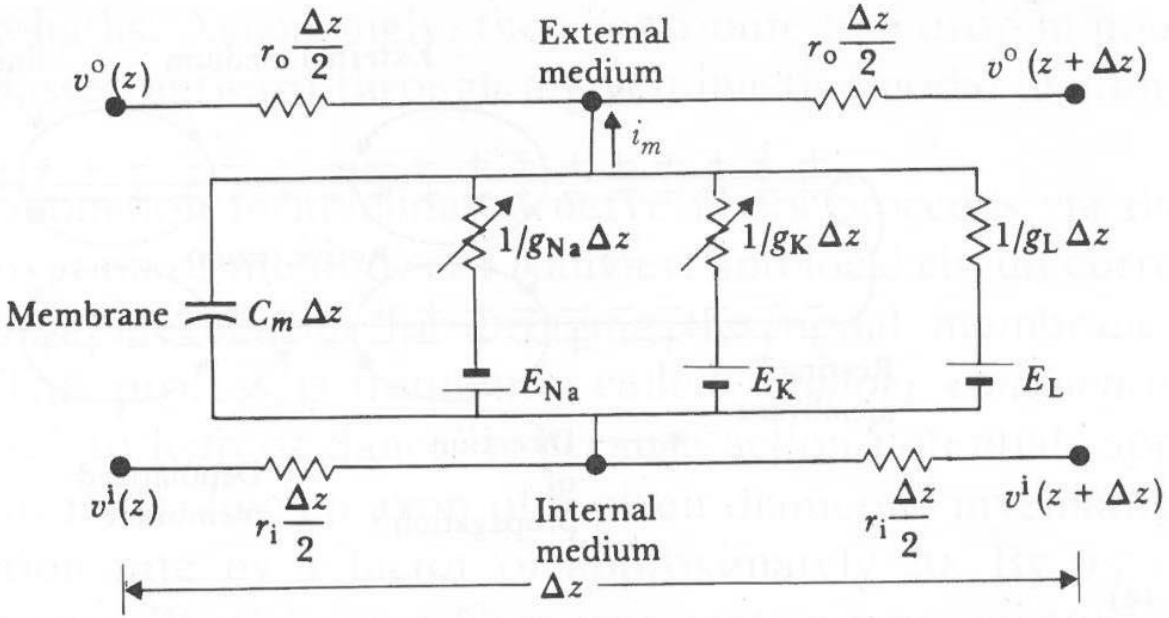


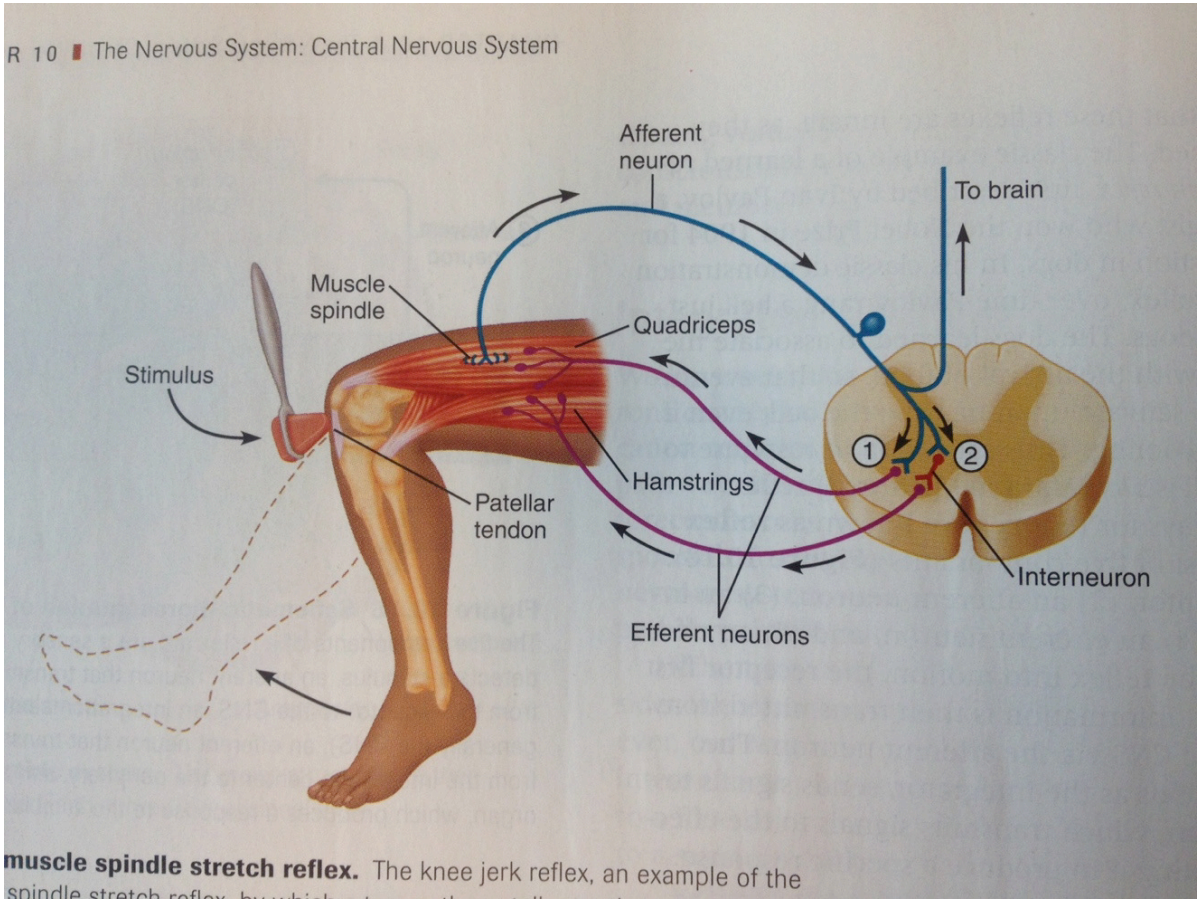
Figure 4.1 Recording of action potential of an invertebrate nerve axon (a) An electronic stimulator supplies a brief pulse of current to the axon, strong enough to excite the axon. A recording of this activity is made at a downstream site via a penetrating micropipet. (b) The movement artifact is recorded as the tip of the micropipet drives through the membrane to record resting potential. A short time later, an electrical stimulus is delivered to the axon; its field effect is recorded instantaneously at downstream measurement site as the stimulus artifact. The action potential proceeds along the axon at a constant propagation velocity. The time period L is the *latent period* or transmission time from stimulus to recording site.



muscle -fibre or axon

Figure 4.3 Diagram of network equivalent circuit of a small length (Δz) of an unmyelinated nerve fiber or a skeletal muscle fiber The membrane proper is characterized by specific membrane capacitance C_m (μF/cm^2) and specific membrane conductances g_{Na}, g_K, and g_{Cl} in mS/cm^2 (mmho/cm^2). Here an average specific leakage conductance is included that corresponds to ionic current from sources other than Na^+ and K^+ (for example, Cl^-). This term is usually neglected. The cell cytoplasm is considered simply resistive, as is the external bathing medium; these media may thus be characterized by the resistance per unit length r_i and r_o (Ω/cm), respectively. Here i_m is the transmembrane current per unit length (A/cm), and v^i and v^o are the internal and external potentials v at point z, respectively. (Modified from A. L. Hodgkin and A. F. Huxley, "A Quantitative Description of Membrane Current and Its Application to Conduction and Excitation in Nerve," *Journal of Physiology*, 1952, **117**, p. 501.)

Reflex


R 10 The Nervous System: Central Nervous System
Afferent neuron
To brain
Muscle spindle
Quadriceps
Stimulus
Hamstrings
Patellar tendon
Interneuron
Efferent neurons
muscle spindle stretch reflex. The knee jerk reflex, an example of the

Muscle control

Reflex arc

- Sense organ
- Sensory nerve, sending information
- CNS, integratorstation. Evaluated -> Motoric decision can be implemented
- Motor nerve, communicating with peripheral muscle
- Effector organ, like skeletal muscle fibers.

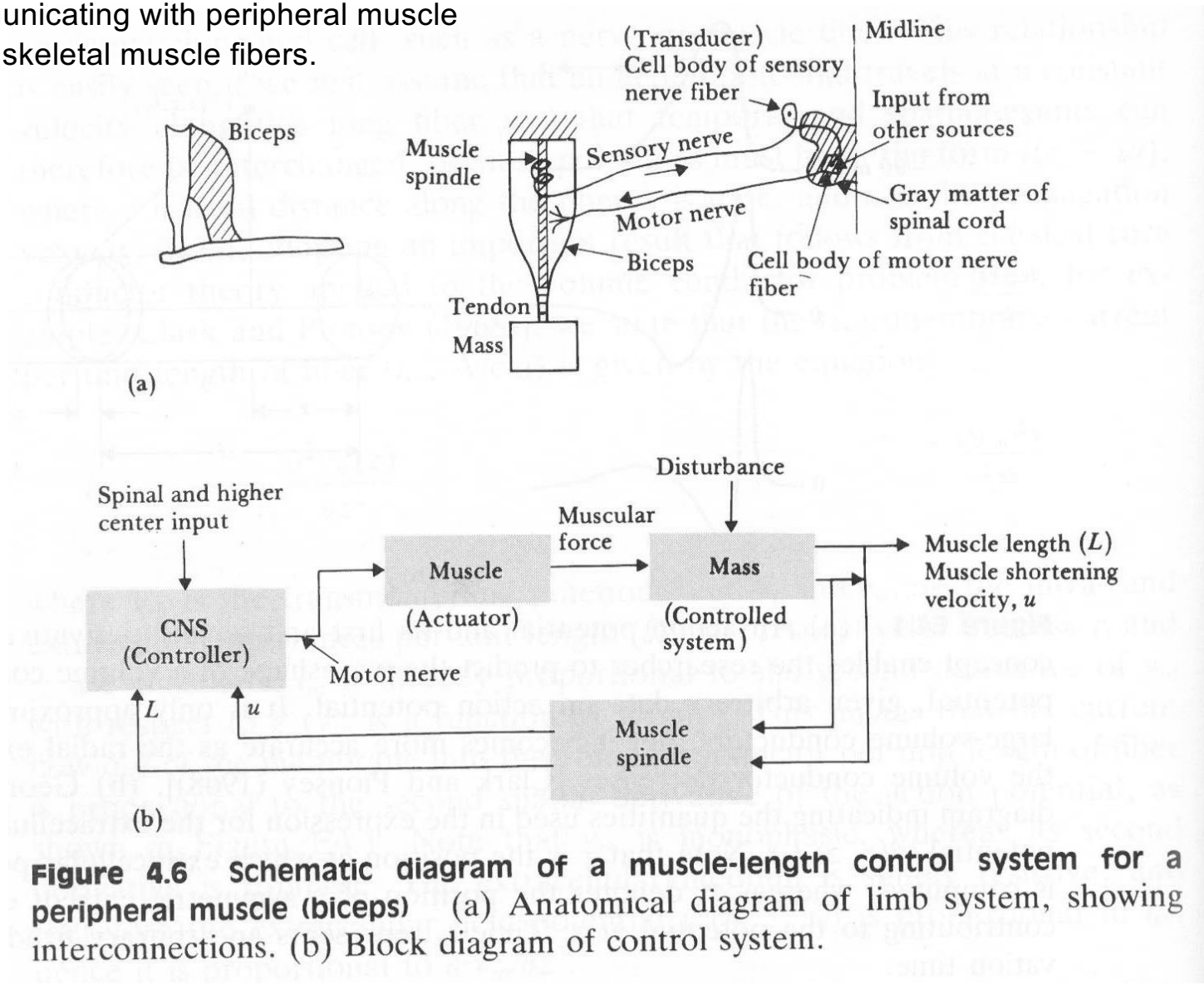


Figure 4.6 Schematic diagram of a muscle-length control system for a peripheral muscle (biceps) (a) Anatomical diagram of limb system, showing interconnections. (b) Block diagram of control system.

Neural velocity

Nerve stimulation at two different sites, subtraction of the shorter latency from the longer latency gives conduction time

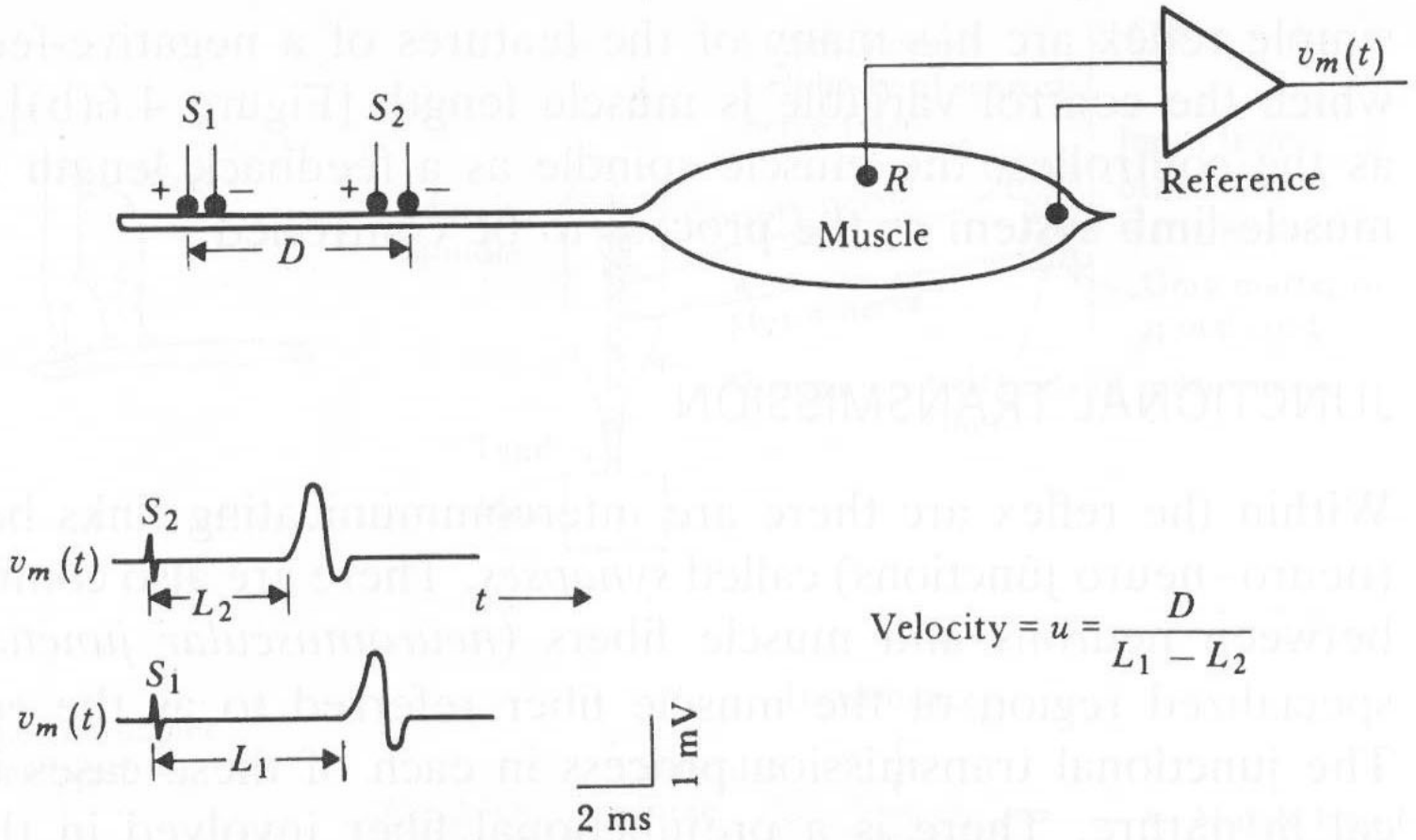


Figure 4.7 Measurement of neural conduction velocity via measurement of latency of evoked electrical response in muscle. The nerve was stimulated at two different sites a known distance D apart.

Neurography

Amp:
High gain
High input imp
Good CMRR
Low amp noise

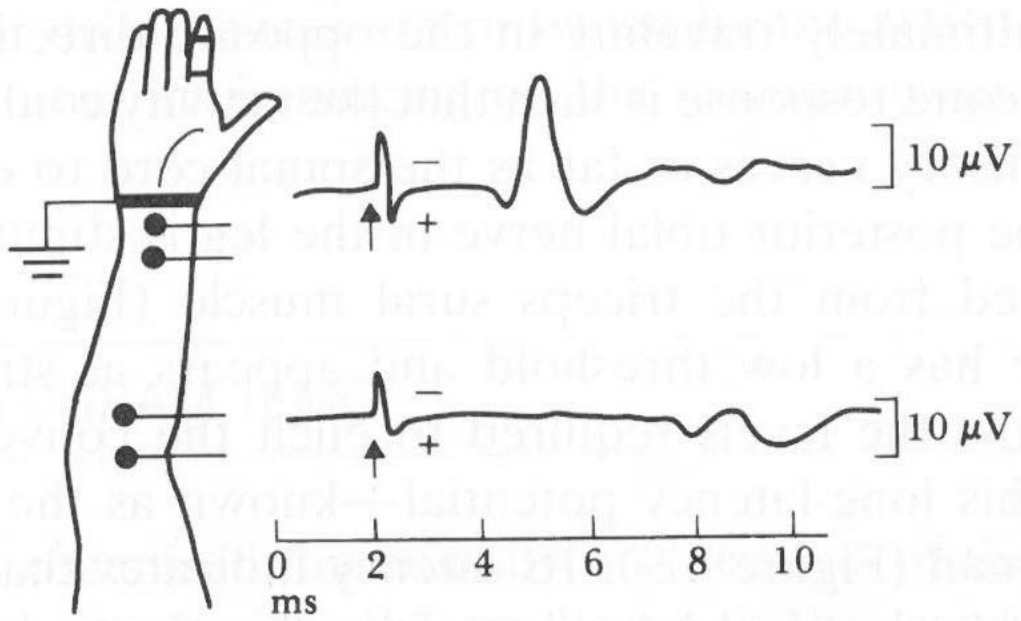


Figure 4.8 Sensory nerve action potentials evoked from median nerve of a healthy subject at elbow and wrist after stimulation of index finger with ring electrodes. The potential at the wrist is triphasic and of much larger magnitude than the delayed potential recorded at the elbow. Considering the median nerve to be of the same size and shape at the elbow as at the wrist, we find that the difference in magnitude and waveshape of the potentials is due to the size of the volume conductor at each location and the radial distance of the measurement point from the neural source. (From J. A. R. Lenman and A. E. Ritchie,

H-reflex

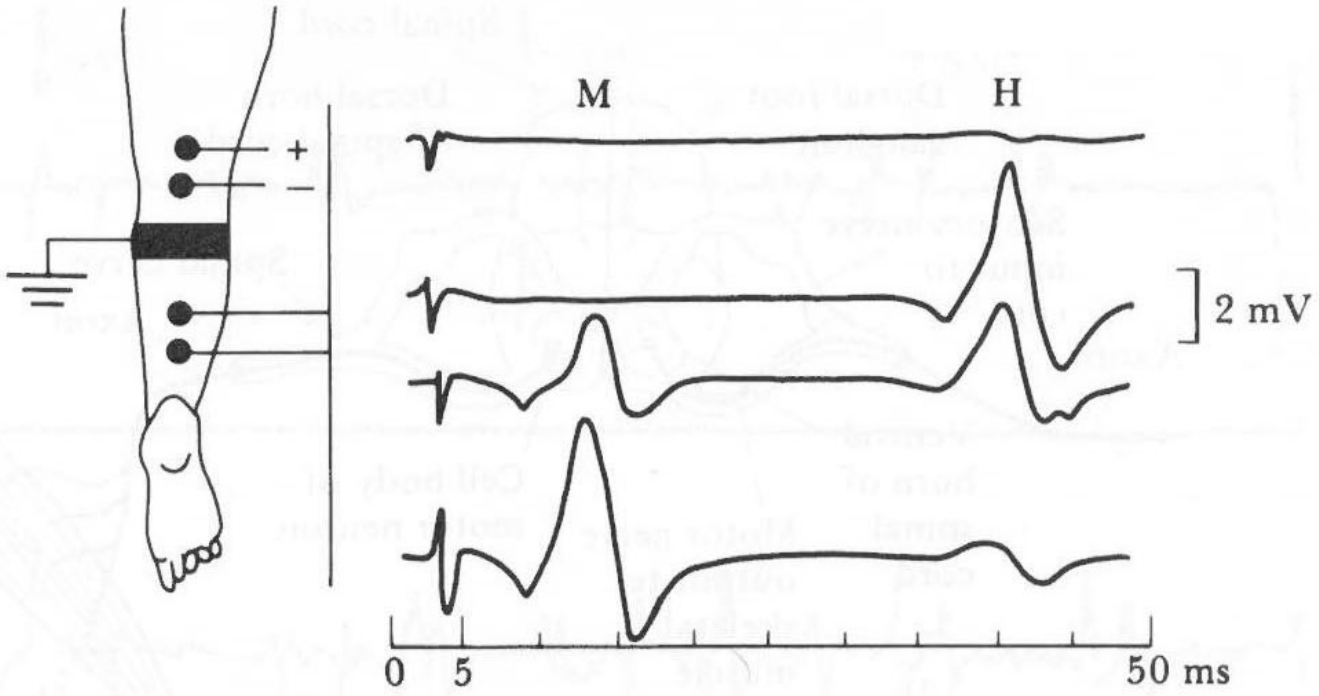


Figure 4.9 The H reflex The four traces show potentials evoked by stimulation of the medial popliteal nerve with pulses of increasing magnitude (the stimulus artifact increases with stimulus magnitude). The later potential or H wave is a low-threshold response, maximally evoked by a stimulus too weak to evoke the muscular response (M wave). As the M wave increases in magnitude, the H wave diminishes. (From J. A. R. Lenman and A. E. Ritchie, *Clinical Electromyography*, 2nd ed., Philadelphia: Lippincott, 1977; reproduced by permission of the authors.)

EMG

Cross sectional view of the spinal cord. A method for distinguishing between myopathic and neurogenic muscle weakness and wasting

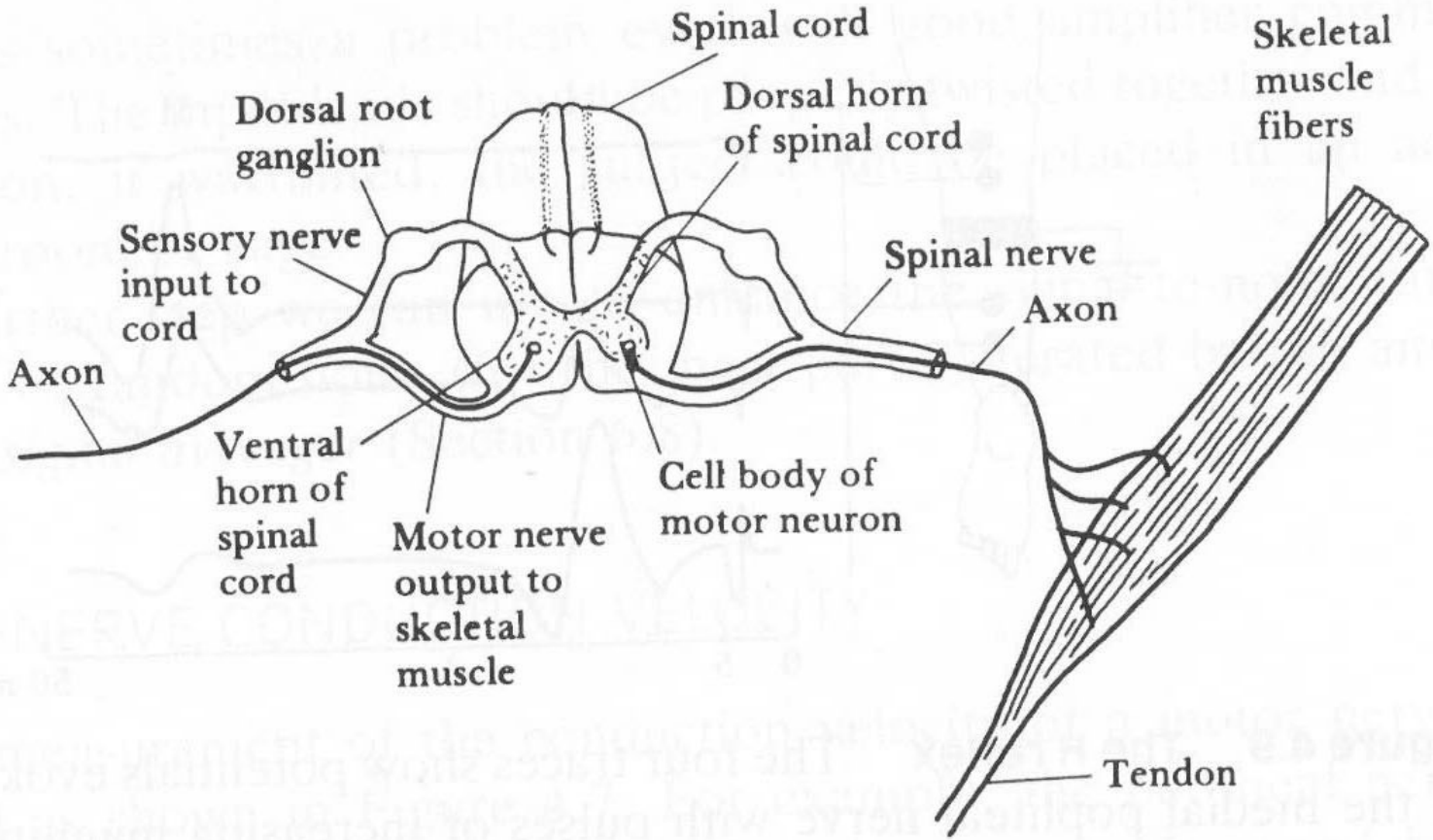


Figure 4.10 Diagram of a single motor unit (SMU), which consists of a single motoneuron and the group of skeletal muscle fibers that it innervates.

EMG

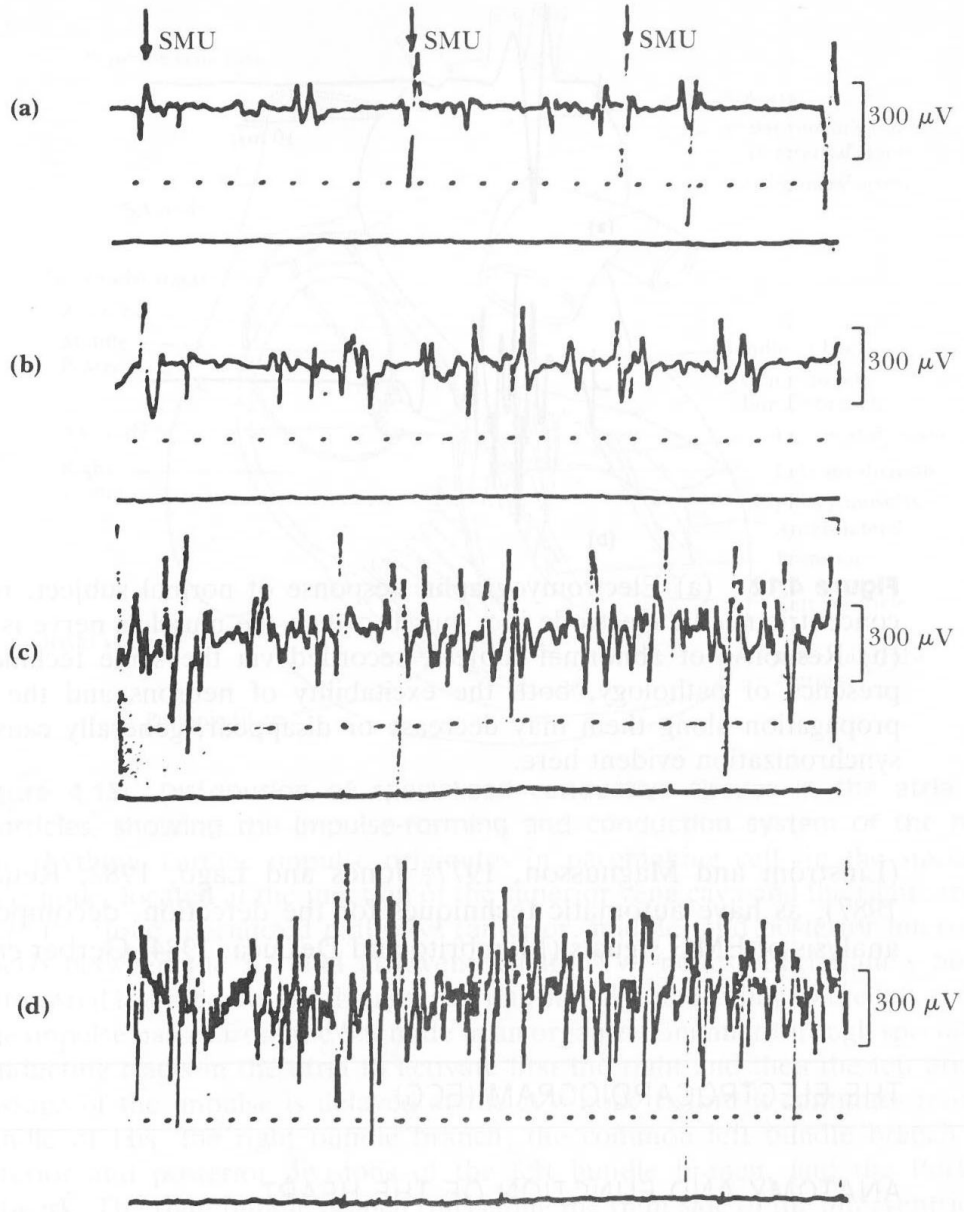


Figure 4.11 Motor unit action potentials from normal dorsal interosseus muscle during progressively more powerful contractions. In the interference pattern (c), individual units can no longer be clearly distinguished. (d) Interference pattern during very strong muscular contraction. Time scale is 10 ms per dot. (From J. A. R. Lenman and A. E. Ritchie, *Clinical Electromyography*, 2nd ed., Philadelphia: Lippincott, 1977; reproduced by permission of the authors.)

ERG

Electroretinogram

Eye 24 mm in diameter. Light transmitting parts -> cornea, anterior chamber, lens and vitreous chamber

A transparent fluid is found in the anterior chamber, vitreous chamber is filled with a transparent gel

Normal pressure 20 – 25 mmHg, necessary for a clear visual image

Glaucoma = high pressure condition, injure the retina. Caused by obstruction of flow between blood and fluid

5 types of nerve cells:

Photoreceptors, bipolar, horizontal, amacrine and ganglion cells (axons)

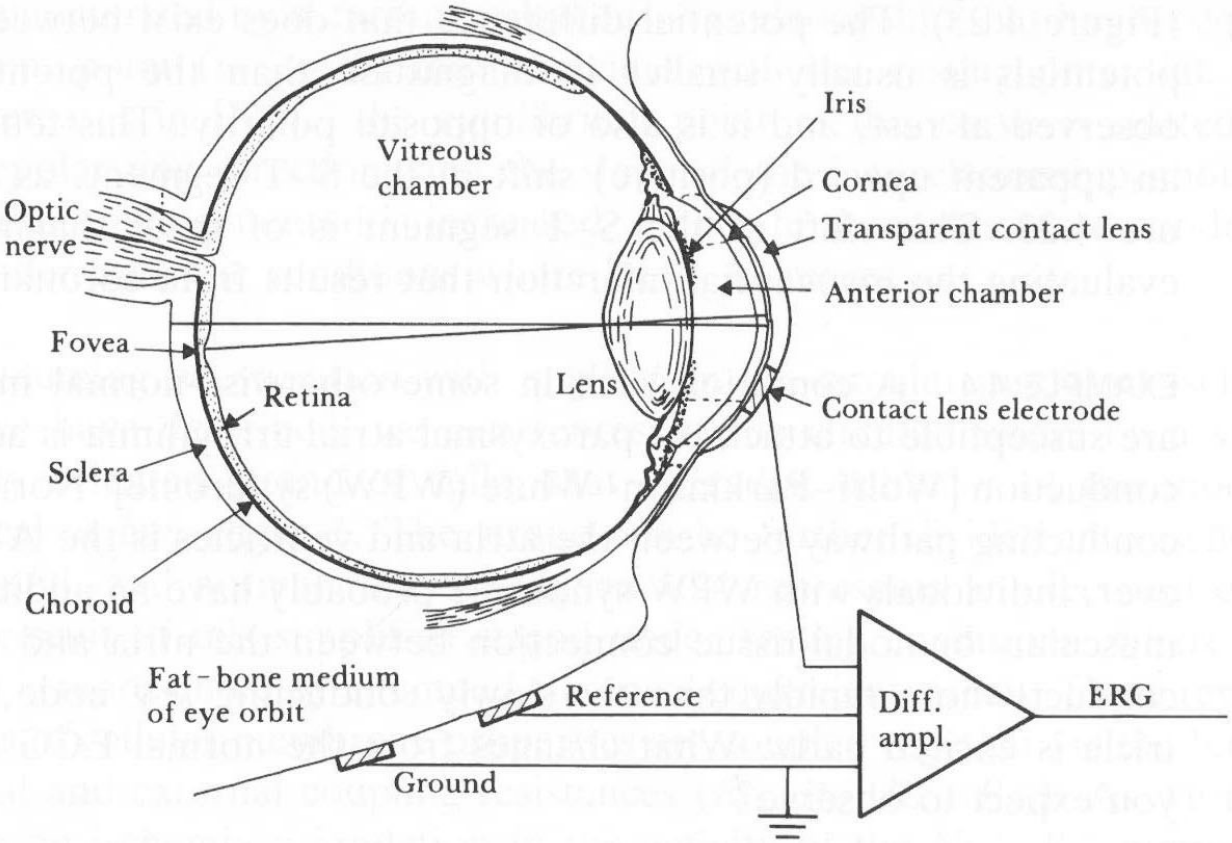


Figure 4.25 The transparent contact lens contains one electrode, shown here on horizontal section of the right eye. Reference electrode is placed on the right temple.

ERG

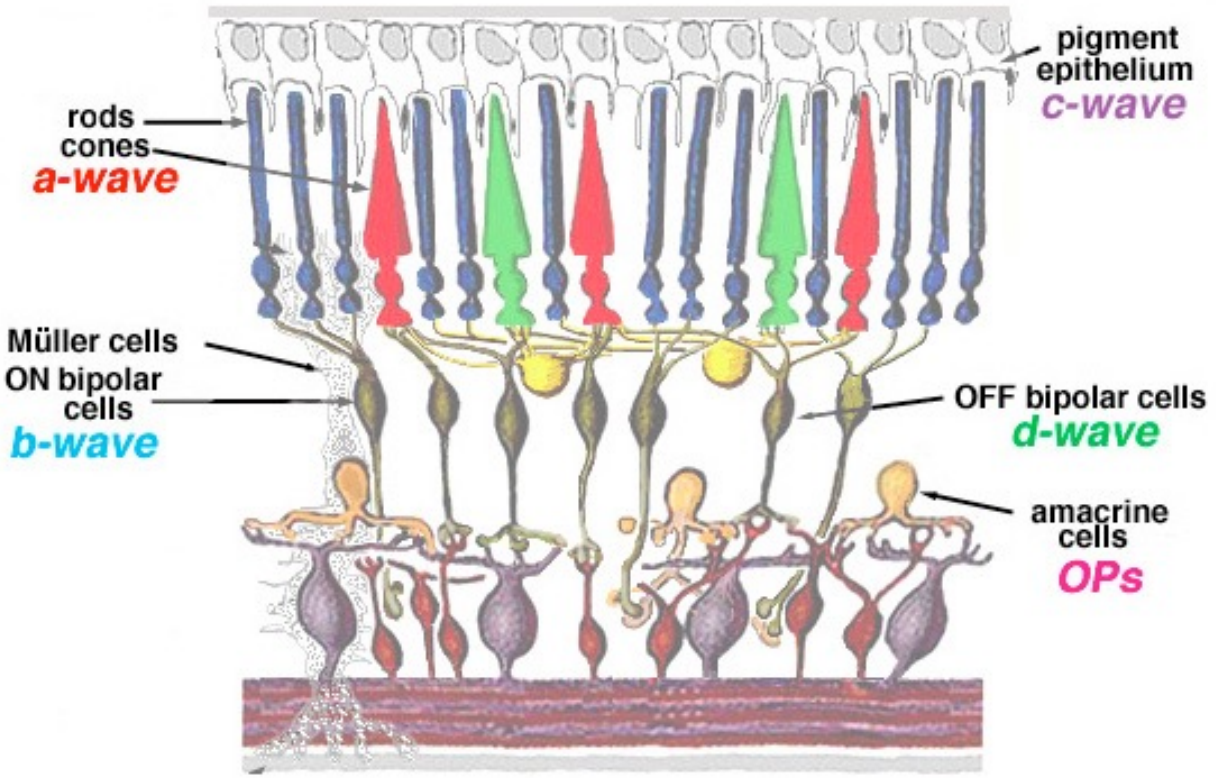


Fig.3 Cartoon of the retina to show where the major components of the ERG originate.

http://webvision.med.utah.edu/gifswv/DONFig3.gif

ERG

A - Early receptor potensial ERP + late receptor potensial LRP
B- Bipolare og ganglion celler i innerste lag av retina
C – pigment epitel-celler
D- av-respond til retina
Early receptor potential (ERP) light-induced changes in photopigment molecules (first part)
Late receptor potential (LRP) output of the photoreceptors (second part)

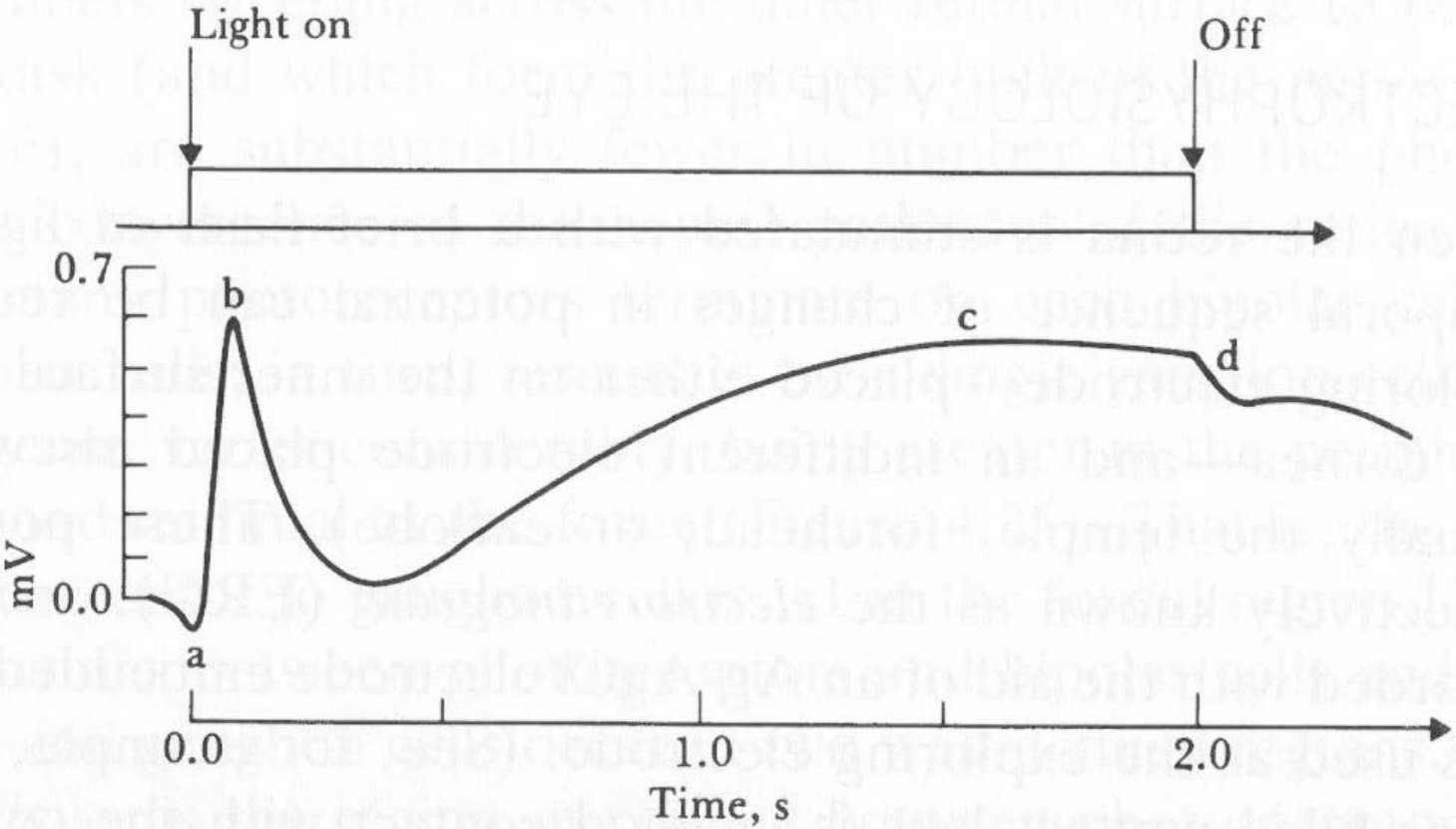
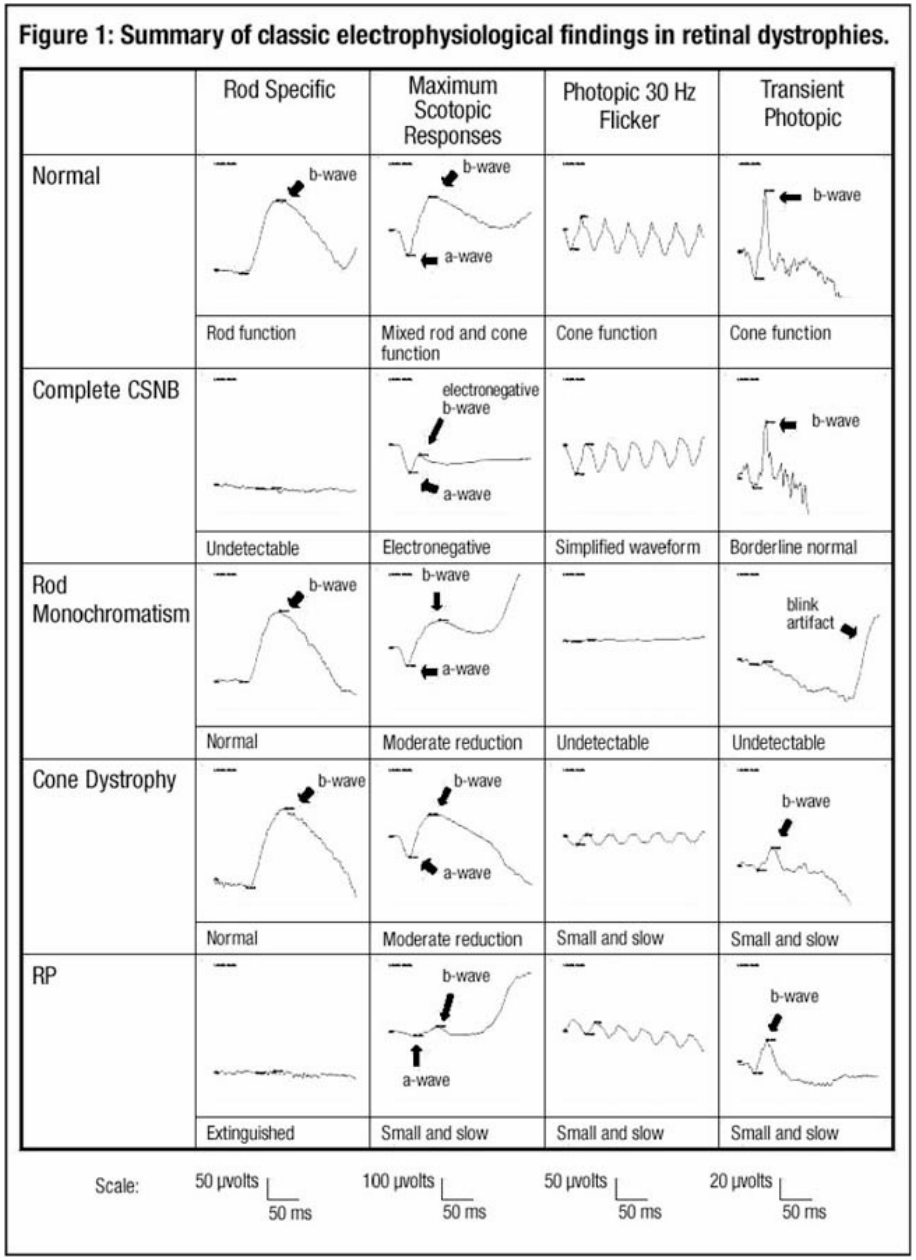


Figure 4.26 Vertebrate electroretinogram

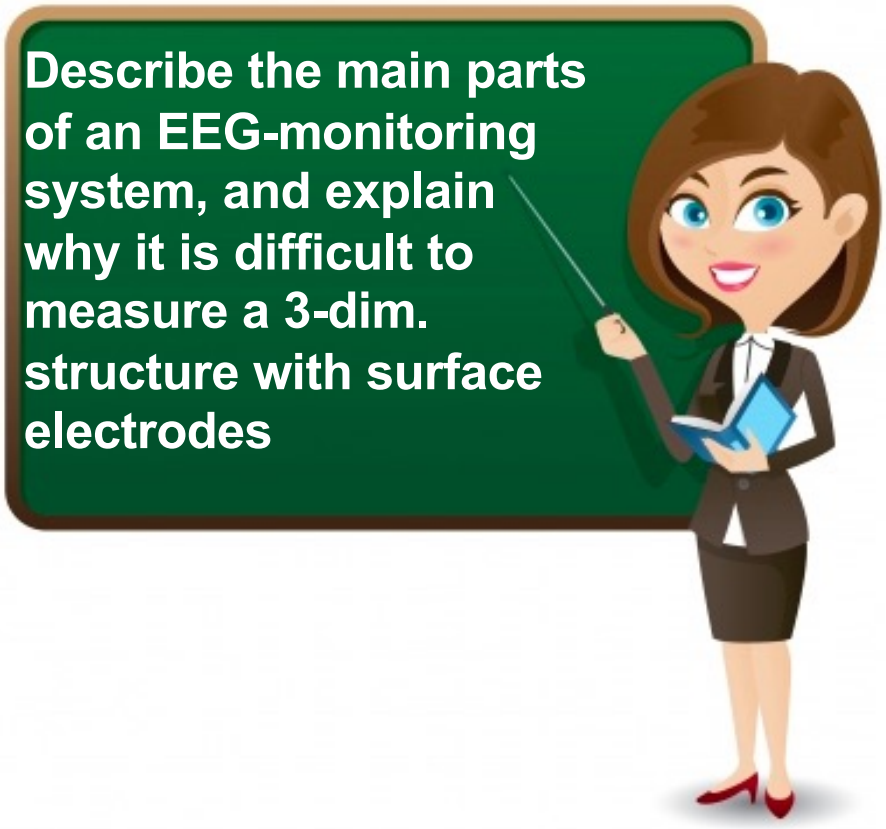
ERG

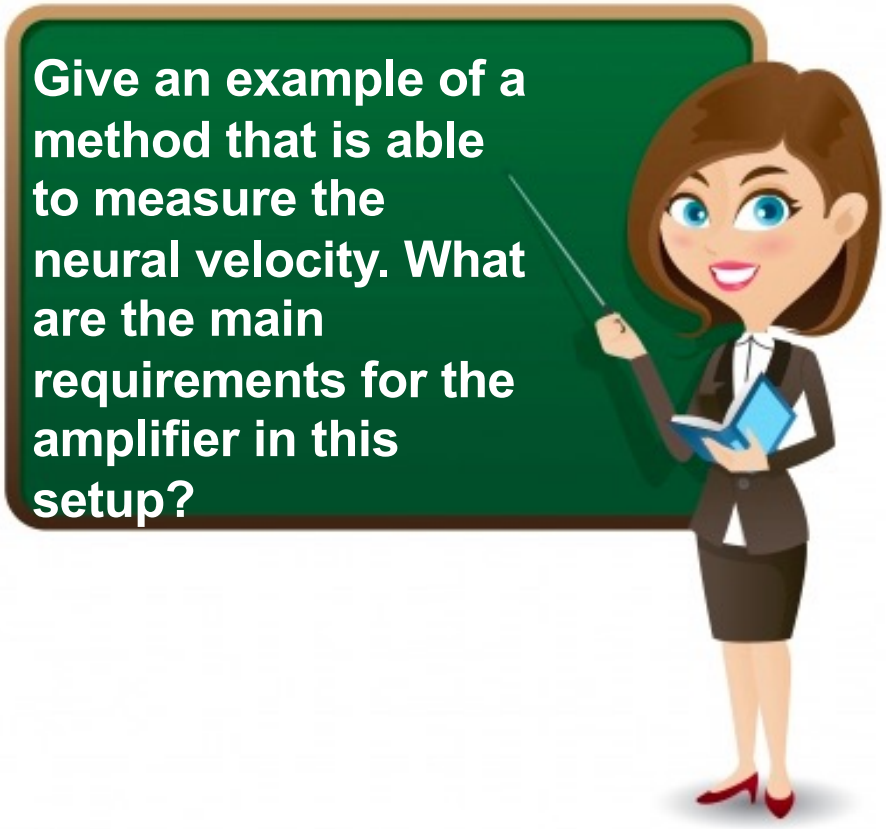
Figure 1: Summary of classic electrophysiological findings in retinal dystrophies.

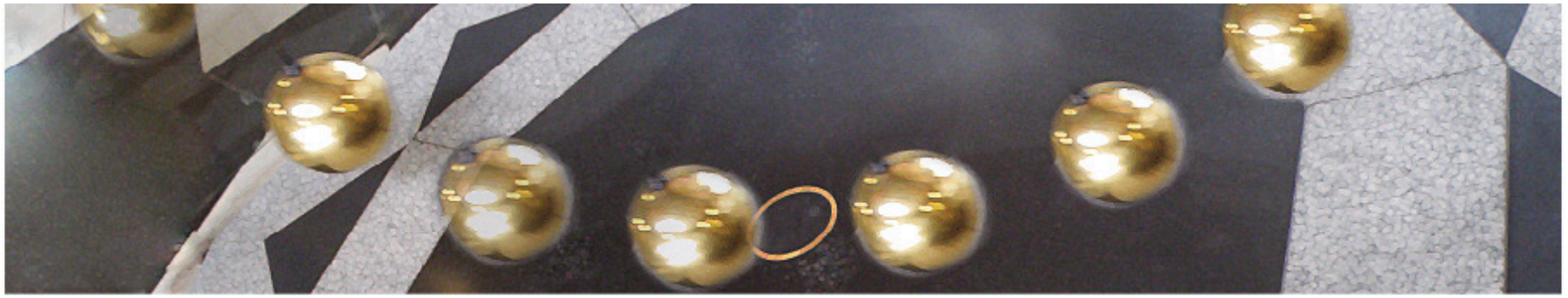


http://www.retinalphysician.com/content/archive/2007/April/jpg%5C9FF1.jpg

Exercise examples







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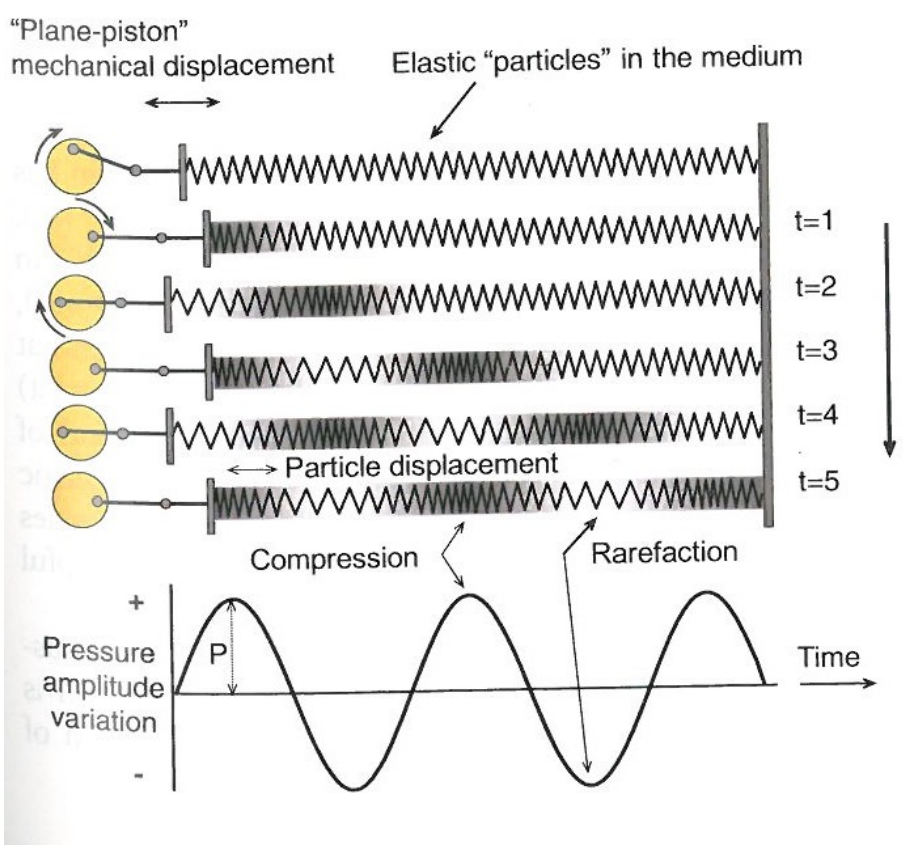
Lecture 13

Ultrasound energy



■ FIGURE 14-2 Ultrasound energy is generated by a mechanical displacement in compressible medium, which is modeled as an elastic spring. Energy propagation is shown as a function of time, resulting in areas of compression and rarefaction with corresponding variations in positive and negative pressure amplitude, *P* (lower diagram). Particles in the medium have only minor displacement as the wave front passes.

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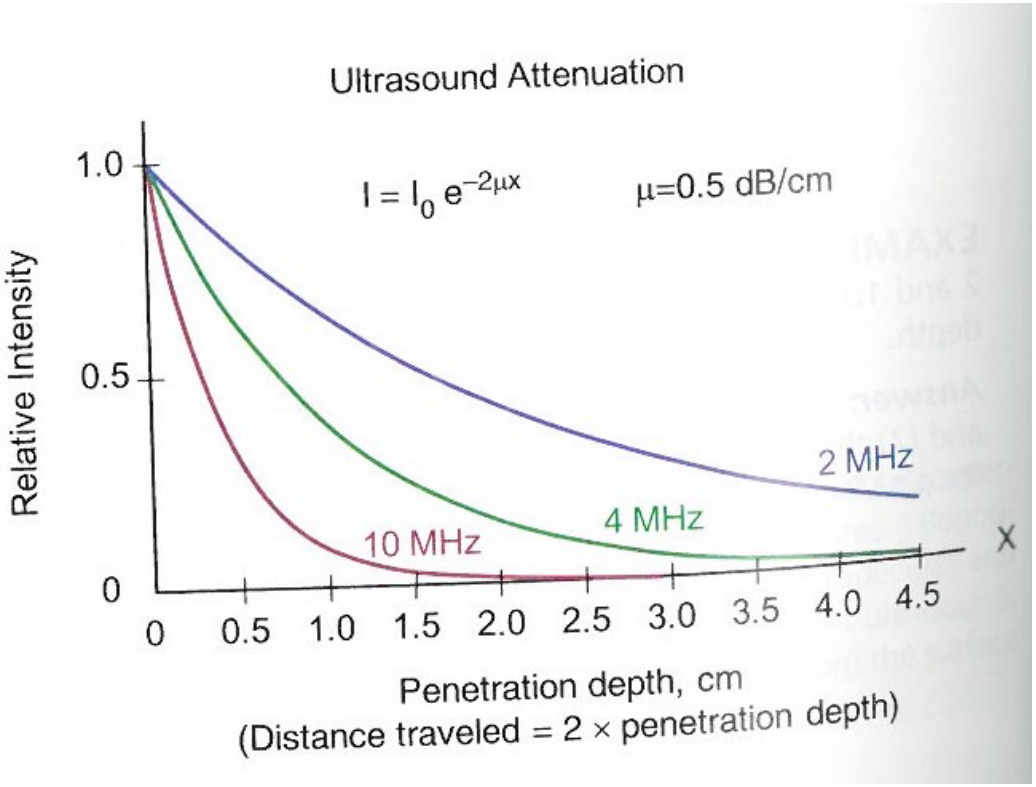
Ultrasound attenuation

■ FIGURE 14-7 Ultrasound attenuation occurs exponentially with penetration depth and increases with increased frequency. The plots are estimates of a single frequency ultrasound wave with an attenuation coefficient of (0.5 dB/cm)/MHz of ultrasound intensity versus penetration depth. Note that the total distance traveled by the ultrasound pulse and echo is twice the penetration depth.

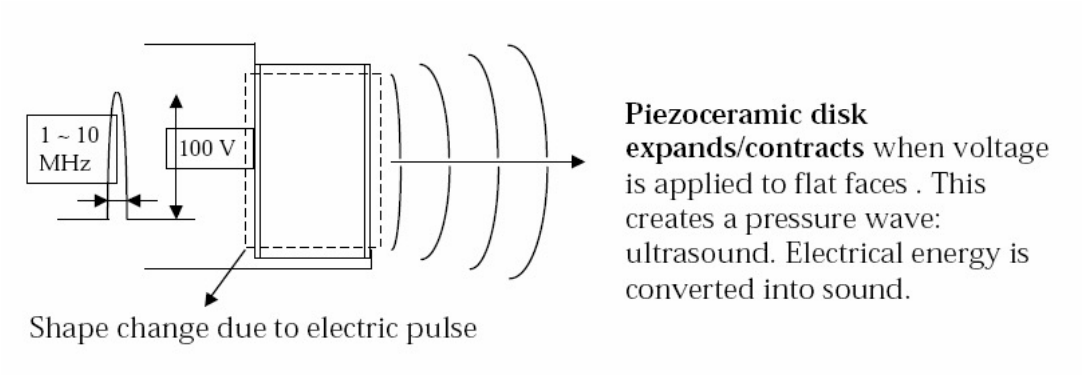


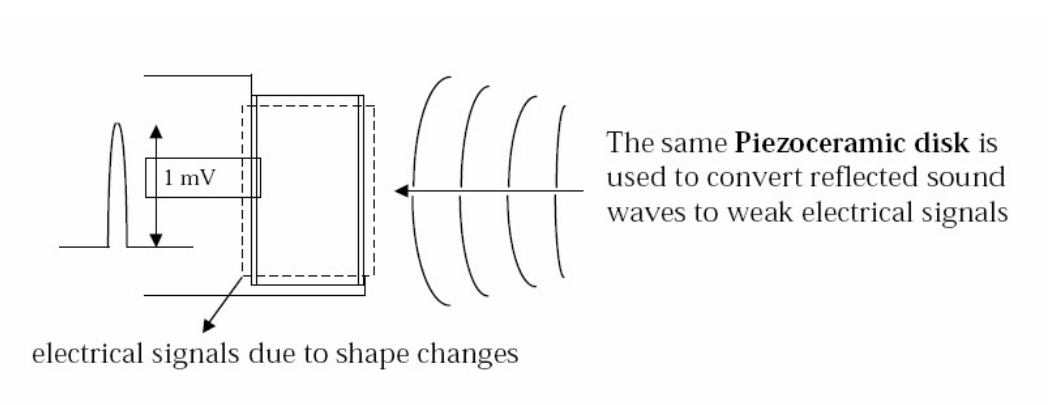
Some of the energy is scattered and lost when hitting small objects with size <= Landa. Absorbed energy is converted to heat. The transducer thickness defines the frequency, the thickness of the transducer equal to ½ Landa

The spatial resolution depends on wavelength, and the attenuation on the frequency

Total reflection, all of the beam is travelling along the boundary

Ultrasound piezo crystal





When stressed, a voltage is produced. When a voltage pulse is applied, the ceramic deforms

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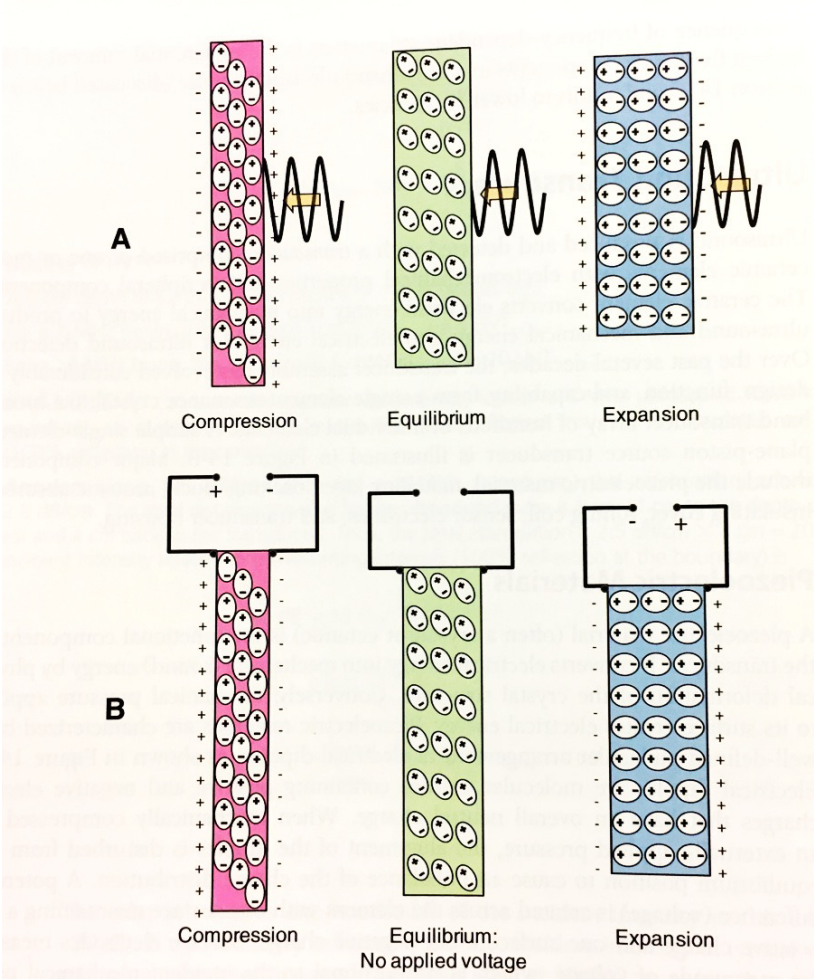
The piezoelectric element



A – under influence of mechanical pressure. Surface electrodes measure the charge variation as a function of time
B – External voltage source applied to surface causes compression or expansion from equilibririum -> realignment of the dipole

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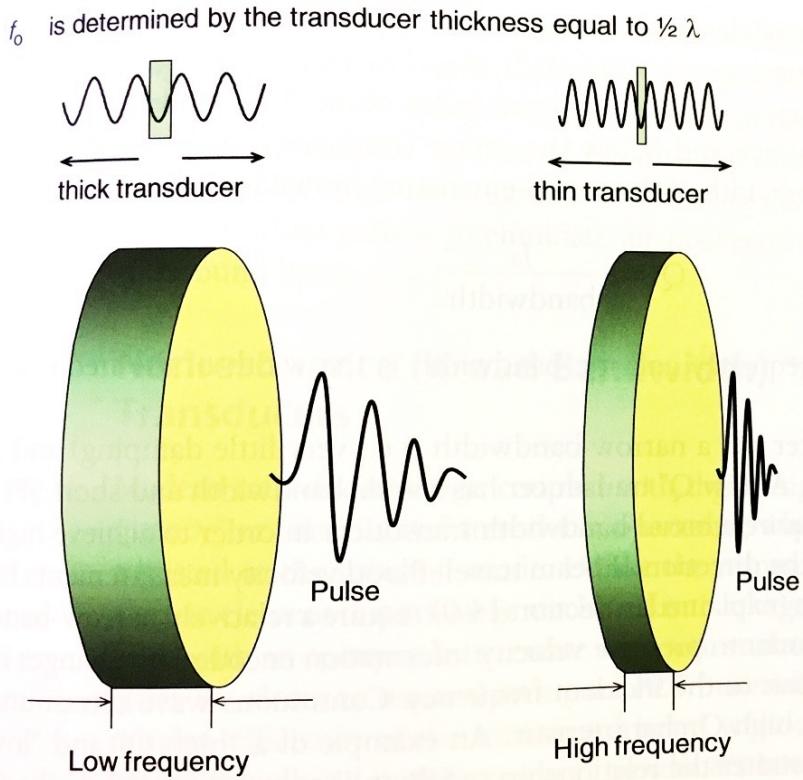
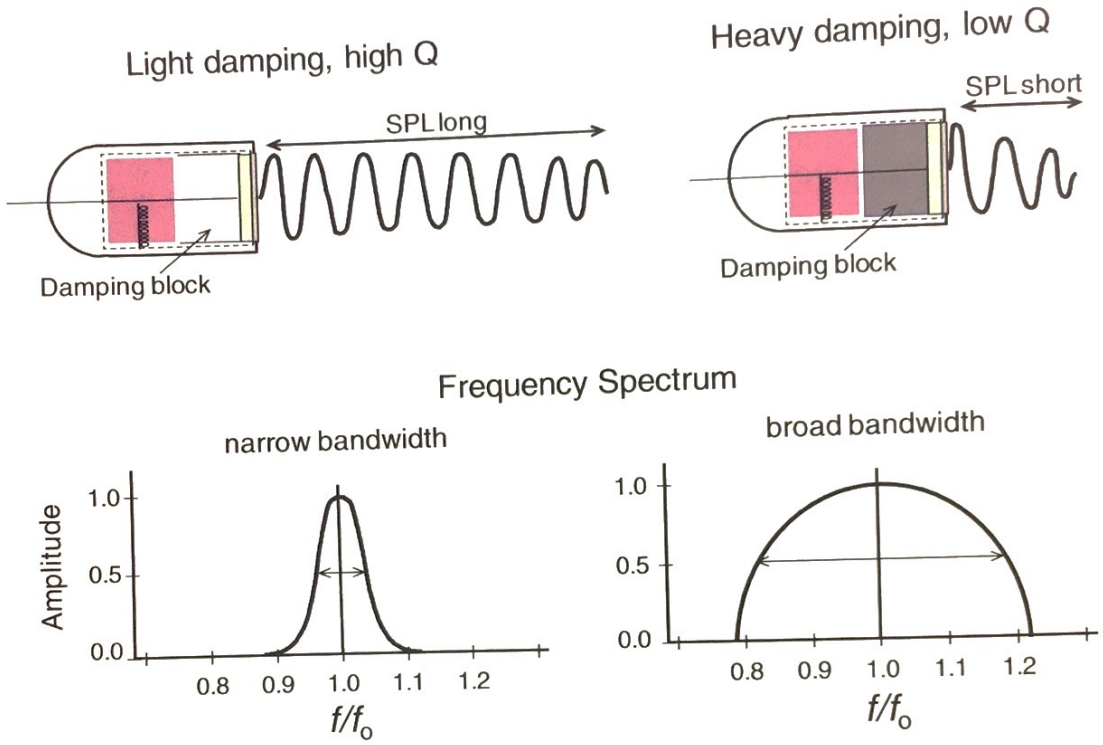
The piezoelectric element



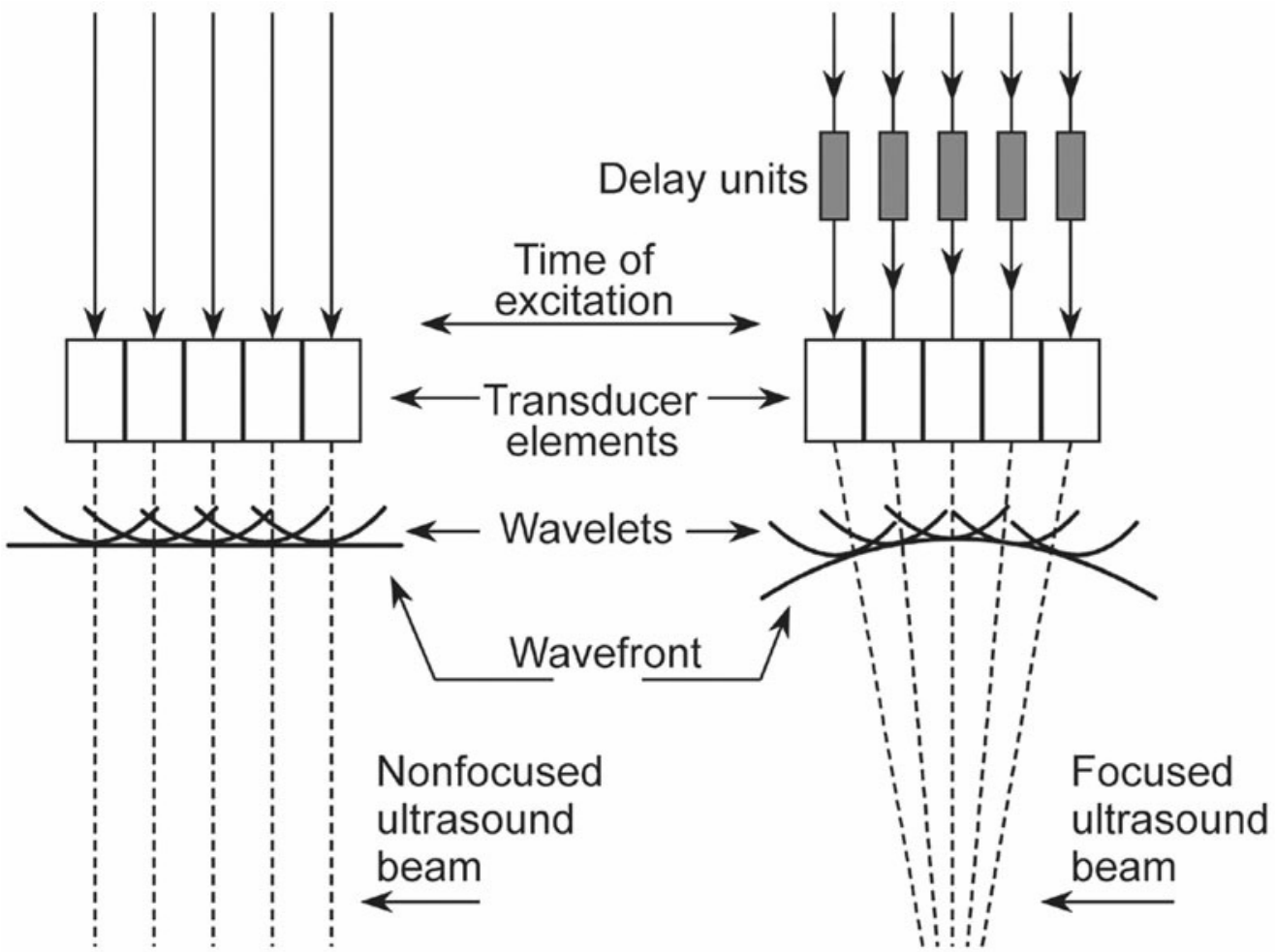
■ **FIGURE 14-10** A short-duration voltage spike causes the resonance piezoelectric element to vibrate at its natural frequency, f_0, which is determined by the thickness of the transducer equal to ½ λ. Low-frequency oscillation is produced with a thicker piezoelectric element. The spatial pulse length (SPL) is a function of the operating frequency and the adjacent damping block.

The damping block



■ **FIGURE 14-11** Effect of damping block on the frequency spectrum. The damping block is adjacent to the backside of the transducer and limits the vibration of the element to a small number of cycles. Light damping allows many cycles to occur (**top left**), which results in an extended SPL (number of cycles times the wavelength) and a narrow frequency bandwidth (range of frequencies contained in the pulse (**bottom left**). Heavy damping reduces the SPL and broadens the frequency bandwidth (**top and bottom right**). The Q factor describes the center frequency divided by the bandwidth.

Piezoelectric crystal, beam shape



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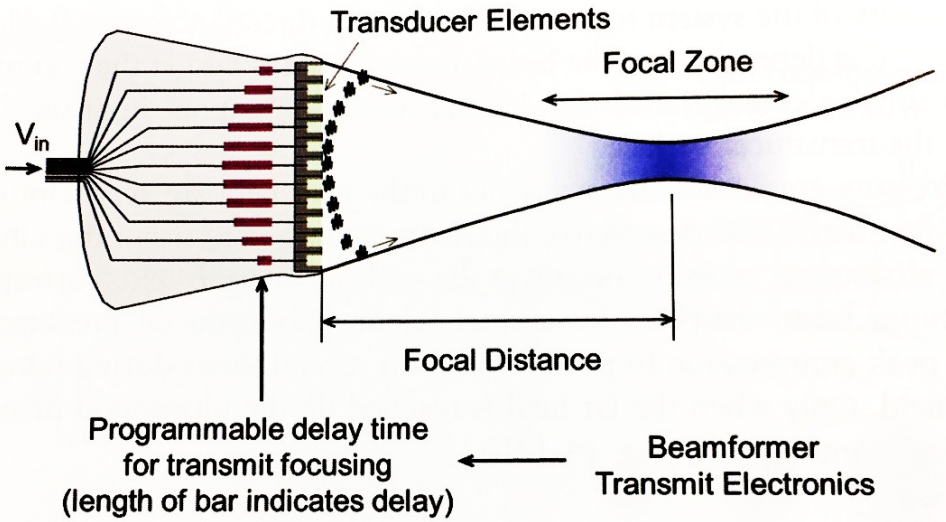
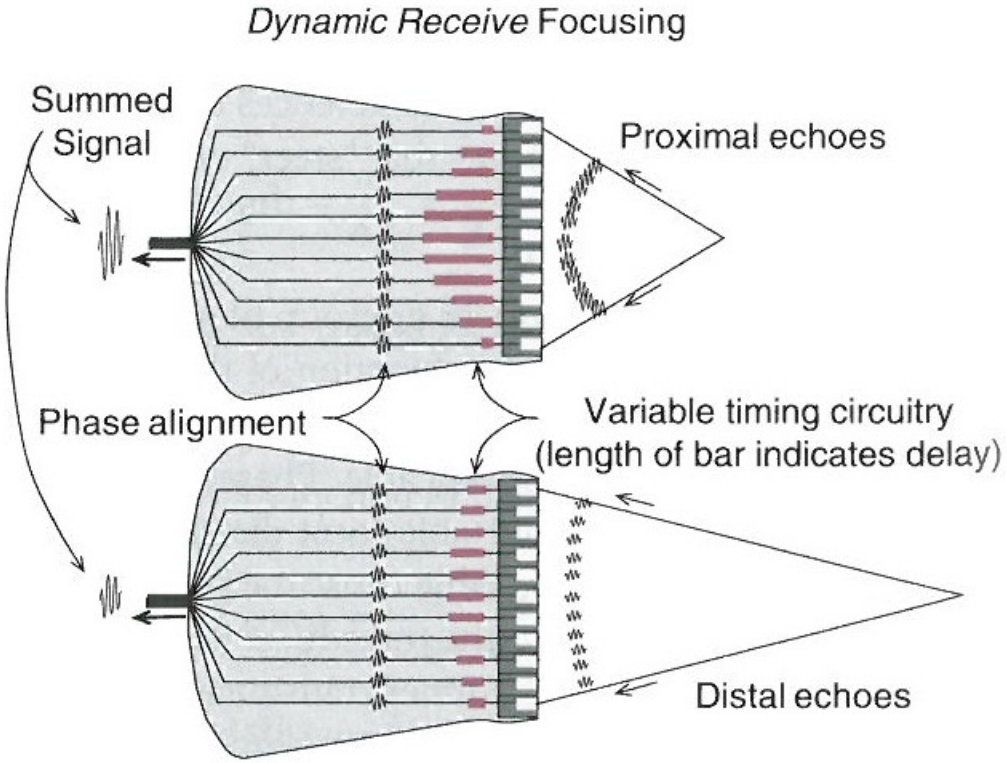
The phased array transducer



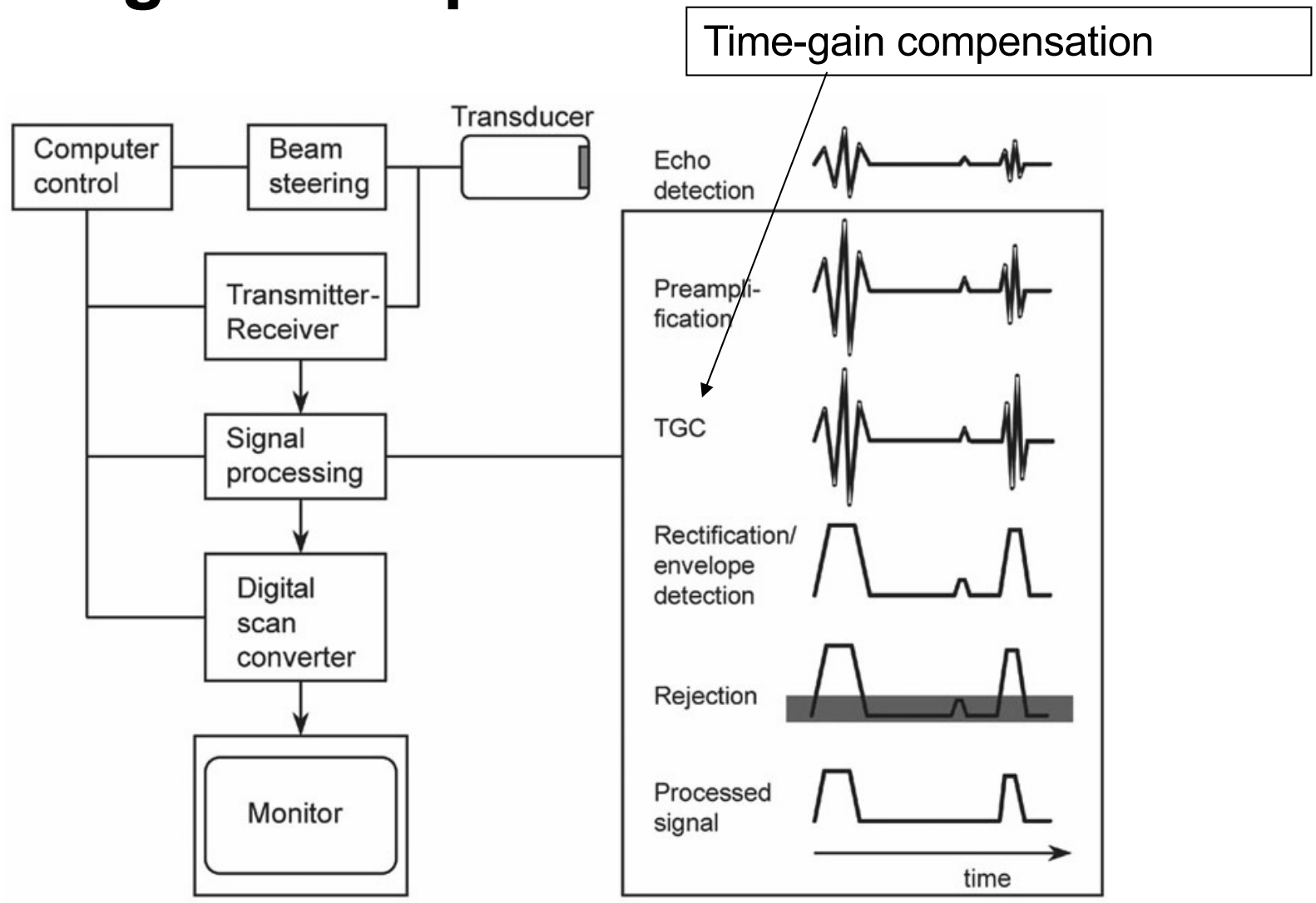
■ FIGURE 14-15 A phased-array transducer assembly uses all elements to produce the ultrasound beam. Focusing is achieved by implementing a programmable delay time (beam former electronics) for the excitation of the individual transducer elements (focusing requires the outer elements in the array be energized first). Phase differences of the individual ultrasound pulses result in a minimum beam diameter (the focal distance) at a predictable depth in tissue.

Dynamic receive focusing

■ FIGURE 14-16 Dynamic receive focusing. All transducer elements in the phased array are active during the receive mode, and to maintain focus, the receive focus timing must be continuously adjusted in order to compensate for differences in arrival time across the array as a function of time (depth of the echo). Depicted are an early time (top illustration) of proximal echo arrival and a later time of distal echo arrival. To achieve phase alignment of the echo responses by all elements, variable timing is implemented as a function of element position after the transmit pulse in the beam former. The output of all phase-aligned echoes is summed.



Time-gain compensation



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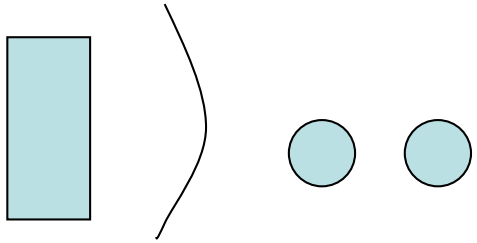
Time-gain compensation: Reducing artifacts in the B-mode intensity images by increasing intensity with depth

Two types of resolution

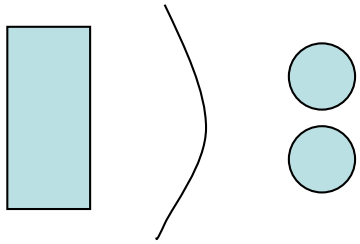
Axial resolution: Ability to discriminate two objects in parallell to the beam.

Best at high frequencies

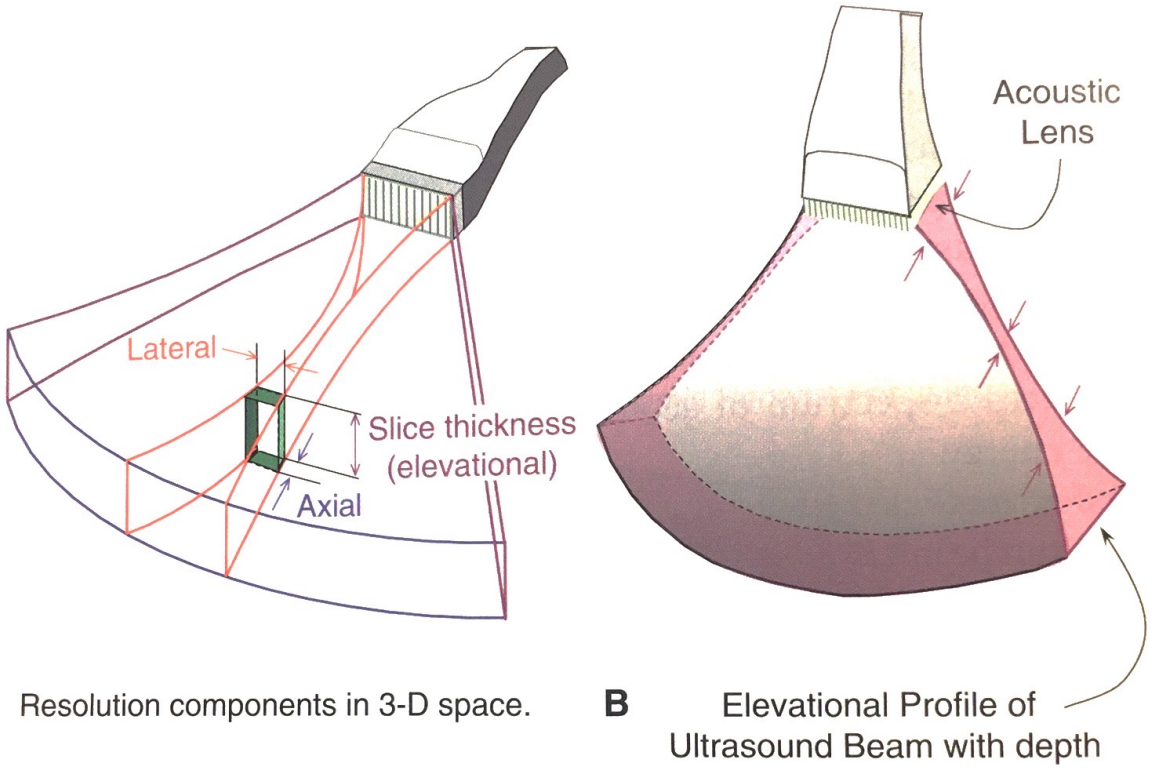


Lateral resolution: Ability to discriminate two objects perpendicular to the beam

Best at the focal zone



Resolution



■ FIGURE 14-19 **A.** The axial, lateral, and elevational (slice-thickness) contributions in three dimensions are shown for a phased-array transducer ultrasound beam. Axial resolution, along the direction of the beam, is independent of depth; lateral resolution and elevational resolution are strongly depth dependent. Lateral resolution is determined by transmit and receive focus electronics; elevational resolution is determined by the height of the transducer elements. At the focal distance, axial is better than lateral and lateral is better than elevational resolution. **B.** Elevational resolution profile with an acoustic lens across the transducer array produces a focal zone in the slice-thickness direction.

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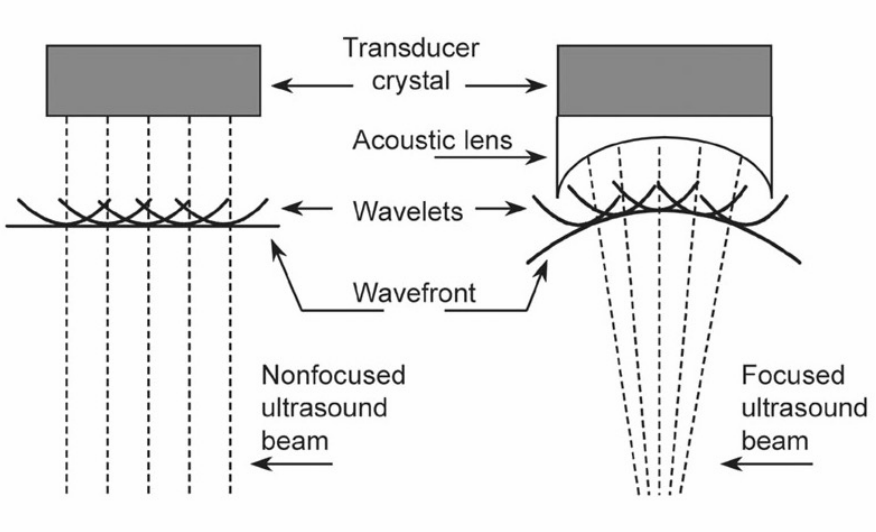
Ultrasound transducer frequency vs resolution

- A 15 MHz scan has very good resolution but penetrates a short distance only
- A 3 MHz scan can penetrate far into the body, but the resolution is poor
  - High frequency = High resolution
  - High frequency = Poor range



Kilde: Alejandro Frangi

Ultrasound (US), A-mode (amplitude)

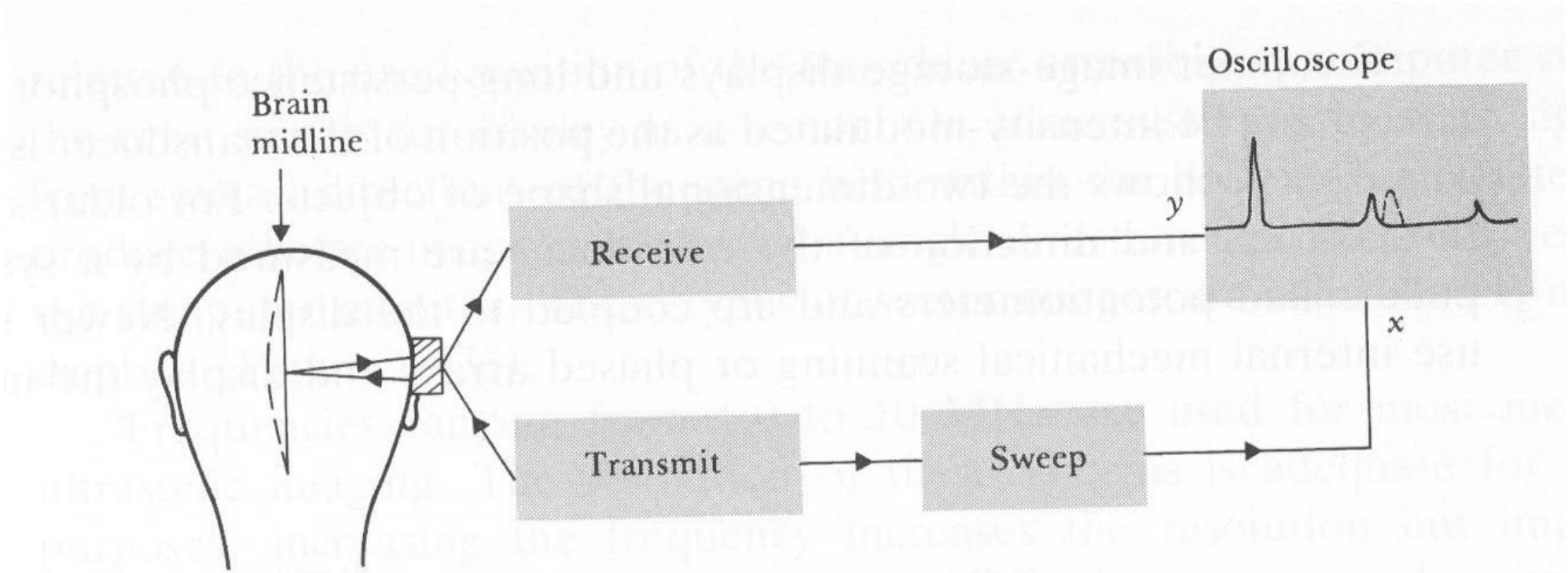
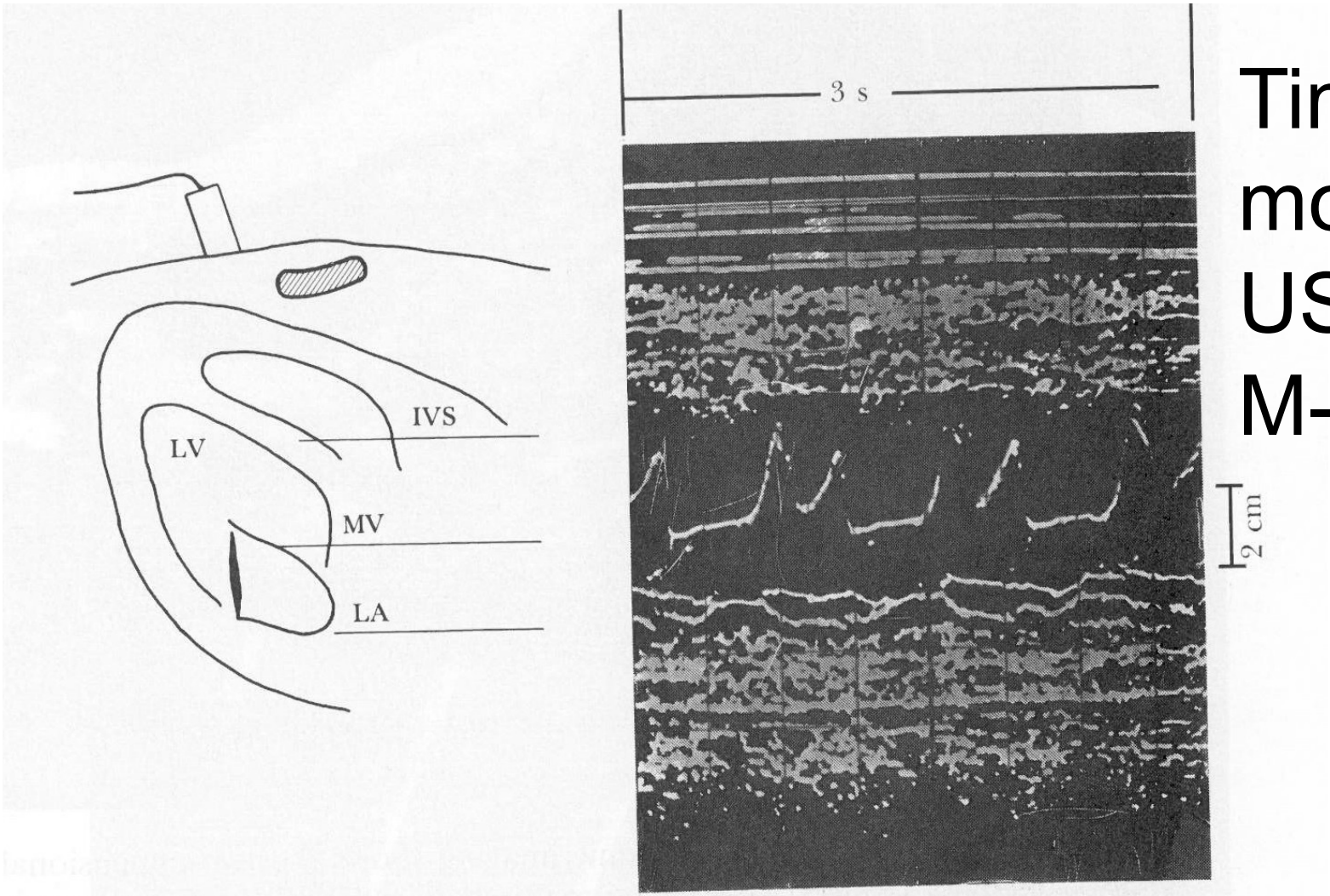


Figure 12.31 A-mode scan of the brain midline

Time delay between transmitted pulse and its echo is a maesure of the depth of the tissue interface
Each change of tissue type, a reflection results
Displacement of the brain midline. Scanning from both sides, should be symmetric, a tumor or blood clot could move the cerebral hemispheres to shift the midline
Obsolete now



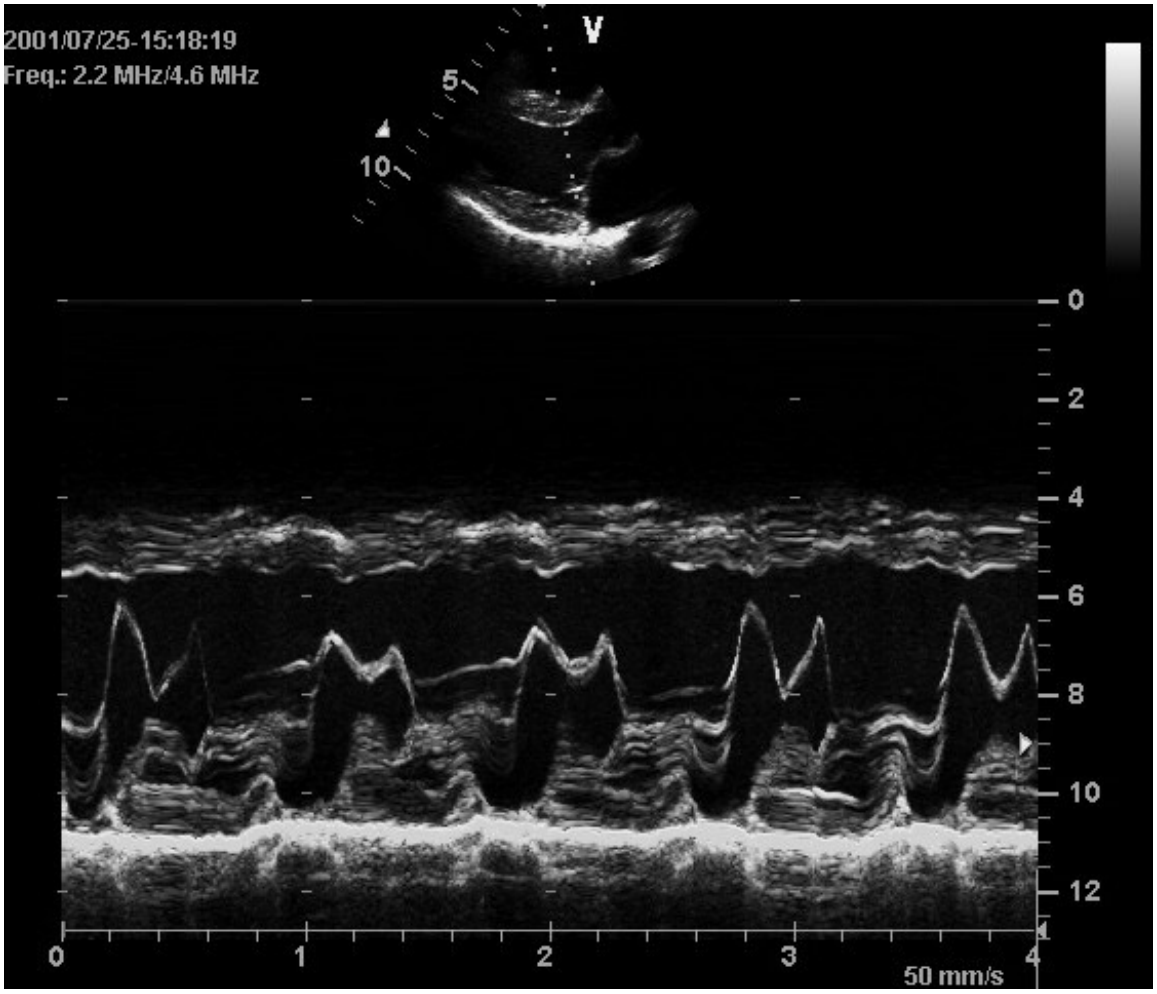
Time motion US, M-mode

Figure 12.32 **Time-motion ultrasound scan of the mitral valve of the heart** The central trace follows the motions of the mitral valve (MV) over a 3-s period, encompassing three cardiac cycles. The other traces correspond to other relatively static structures, such as the interventricular septum (IVS) and the walls of the left atrium (LA).

Strength of the echo is used to modulate intensity of the display against echo-return time with zero time at the top of the display, image can be shown as moving to the right.

Position of tissues as a function of time = Time motion scan

M-mode Ultrasound (motion)



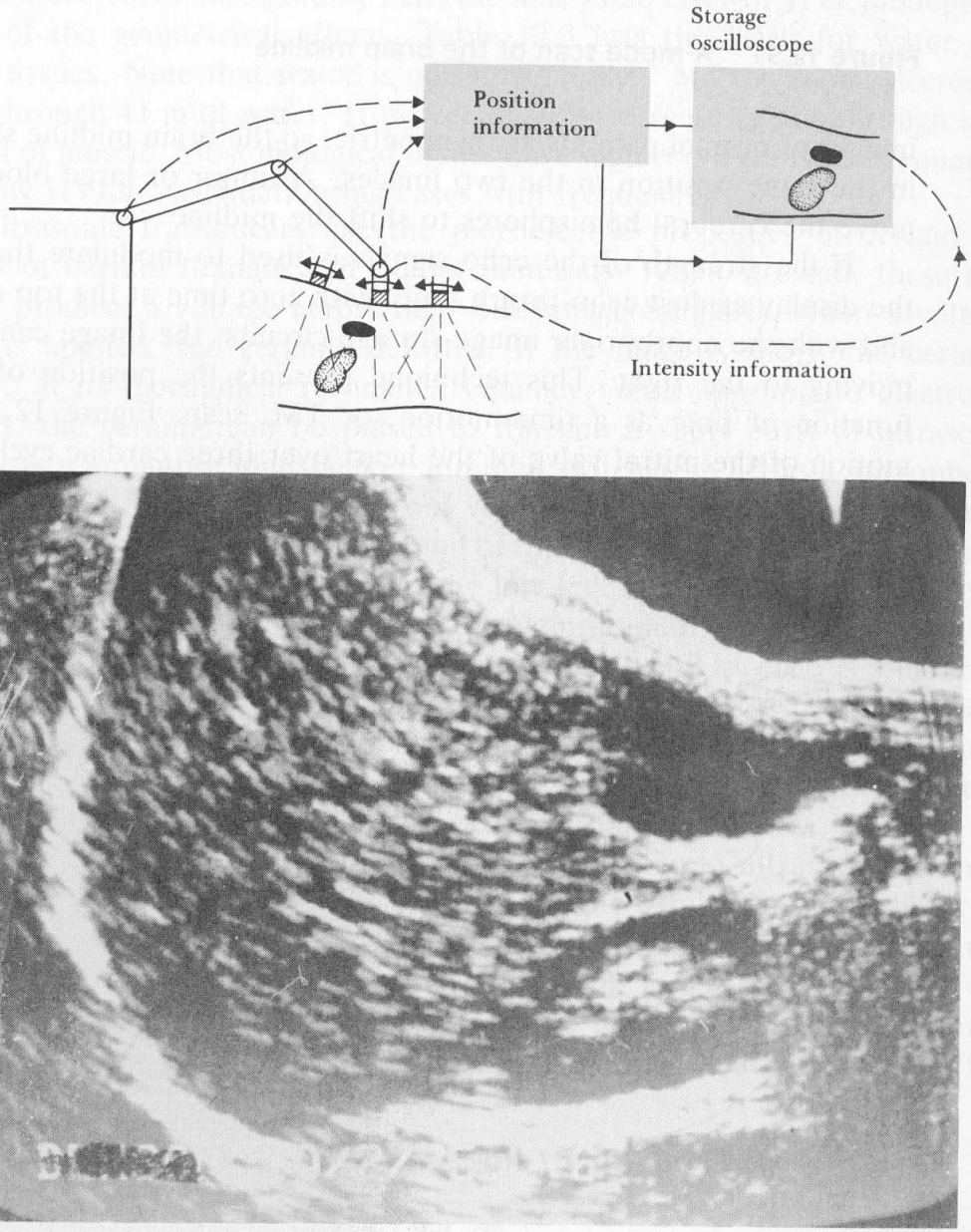


Figure 12.33 (a) B-mode ultrasonic imaging shows the two-dimensional shape and reflectivity of objects by using multiple-scan paths. (b) This B-mode ultrasonic image, which corresponds to (a), shows the skin of the belly at the top right, the liver at the left center, the gall bladder at the right above center, and the kidney at the right below center. The bright areas within the kidney are the collecting ducts.

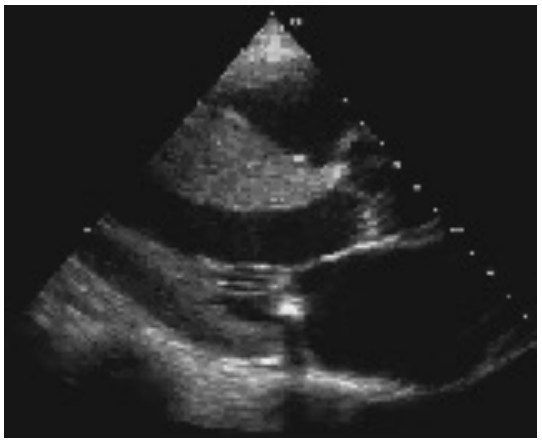
B-mode

B-mode (Brightness)

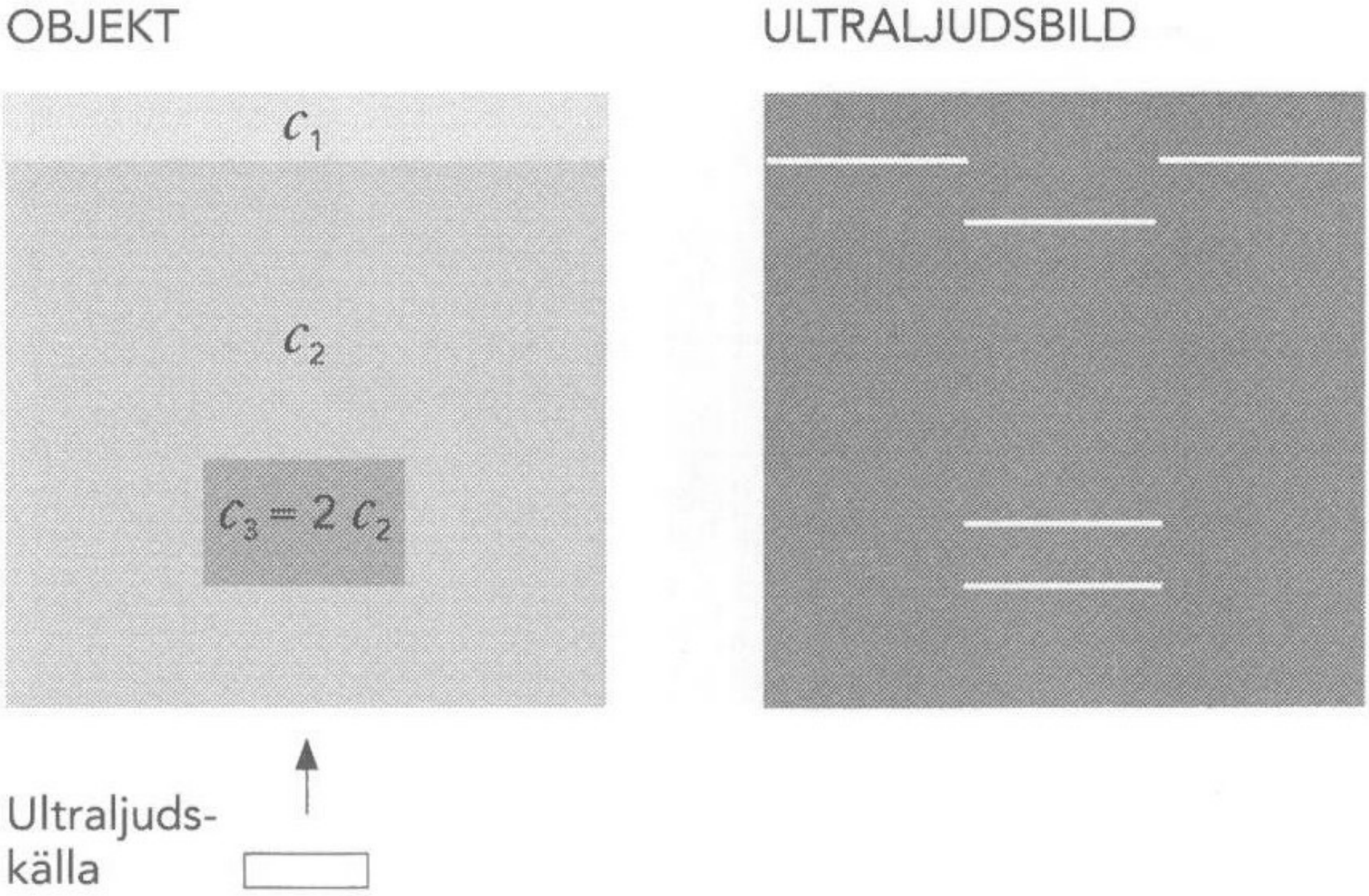
Same as A-mode, but twodimensional graphical display where brightness indicates the amplitude to reflected sound

Most modern US-systems is realtime 2D or 3D. Multiple crystals or mobile crystals

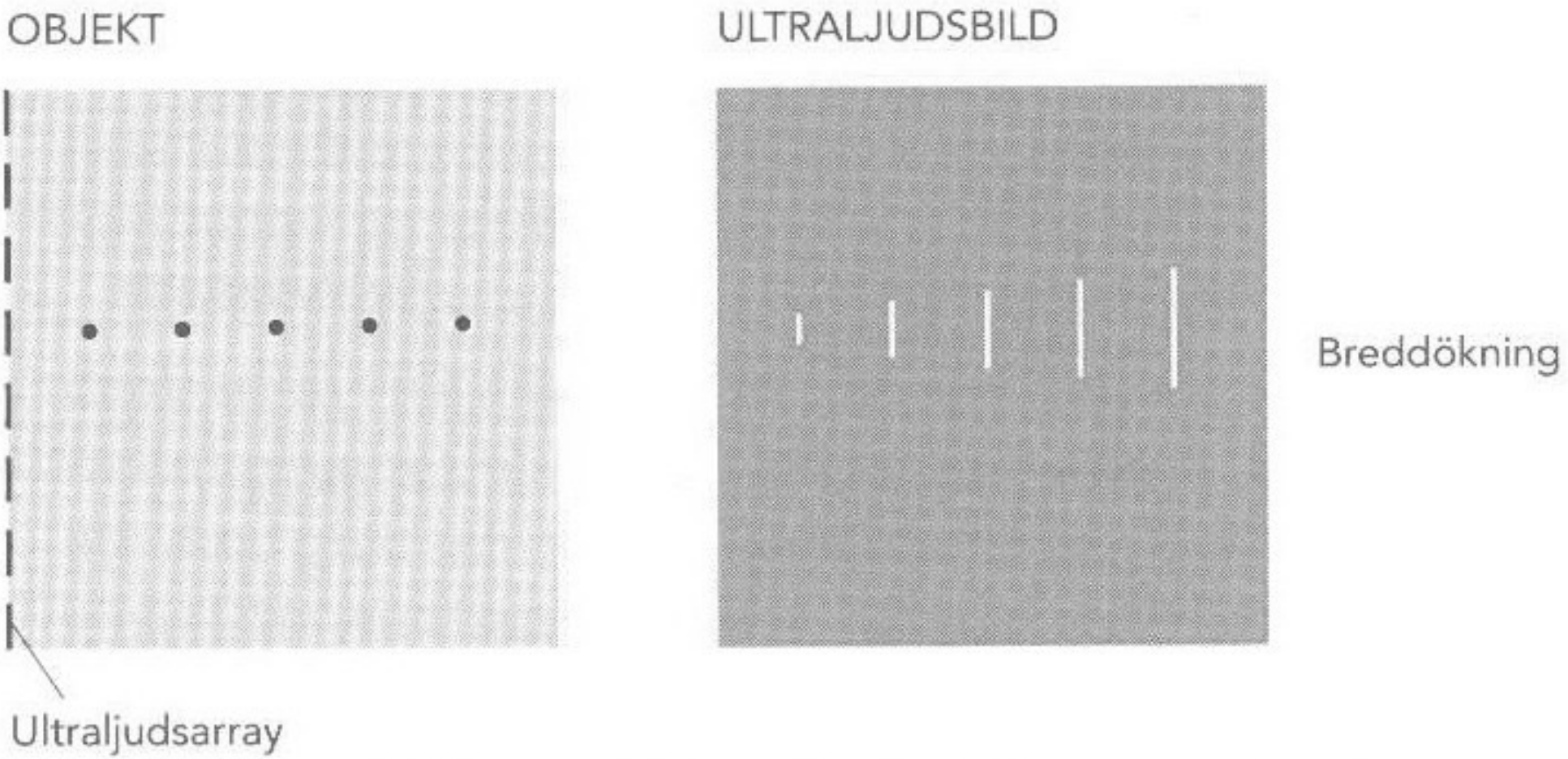
Up to 100 images per second



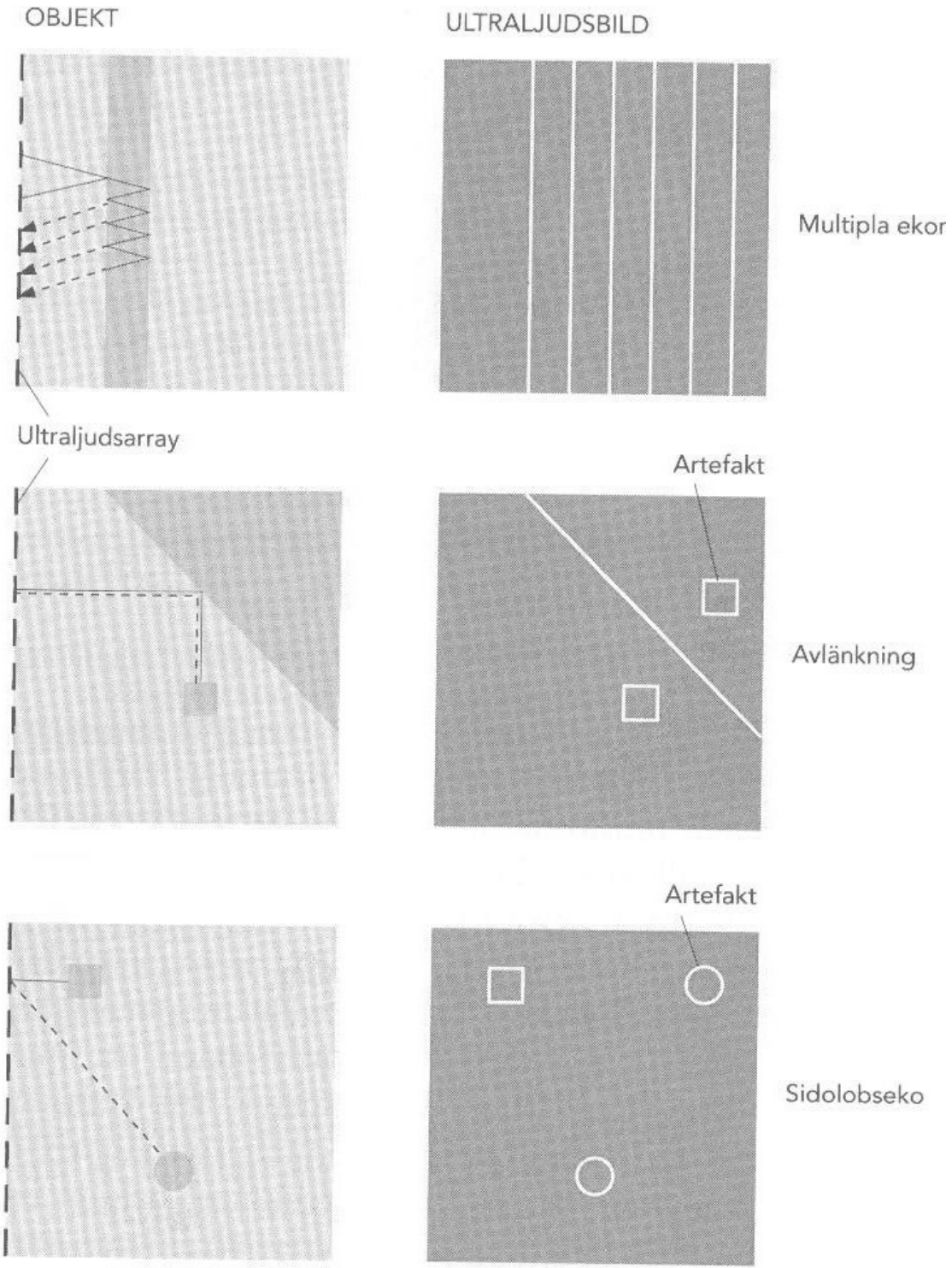
Sources of error (1)



Sources of error (2)



UiO :

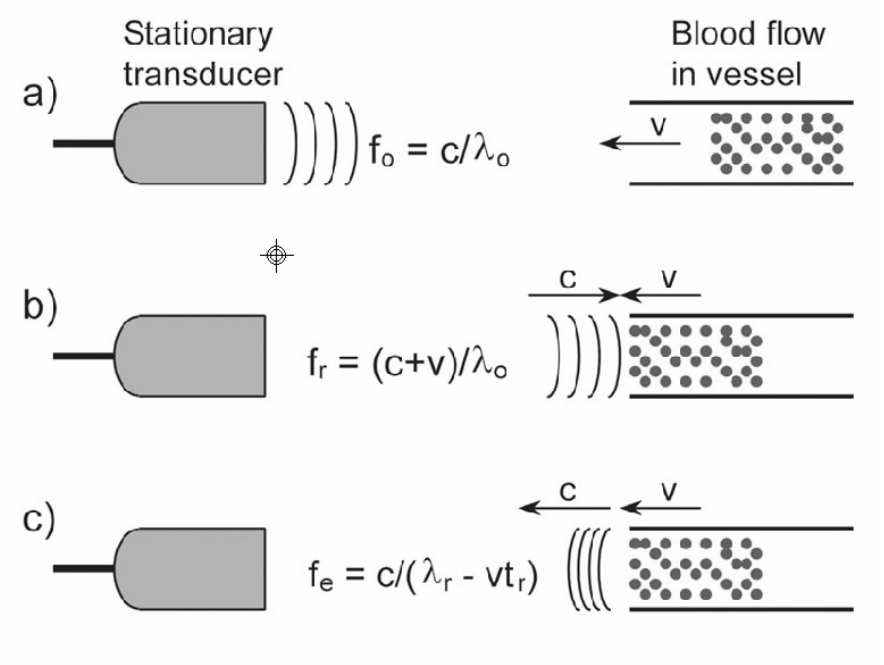


Sources of error (3,4,5)

Doppler ultrasound

Higher frequency = blood towards the transducer

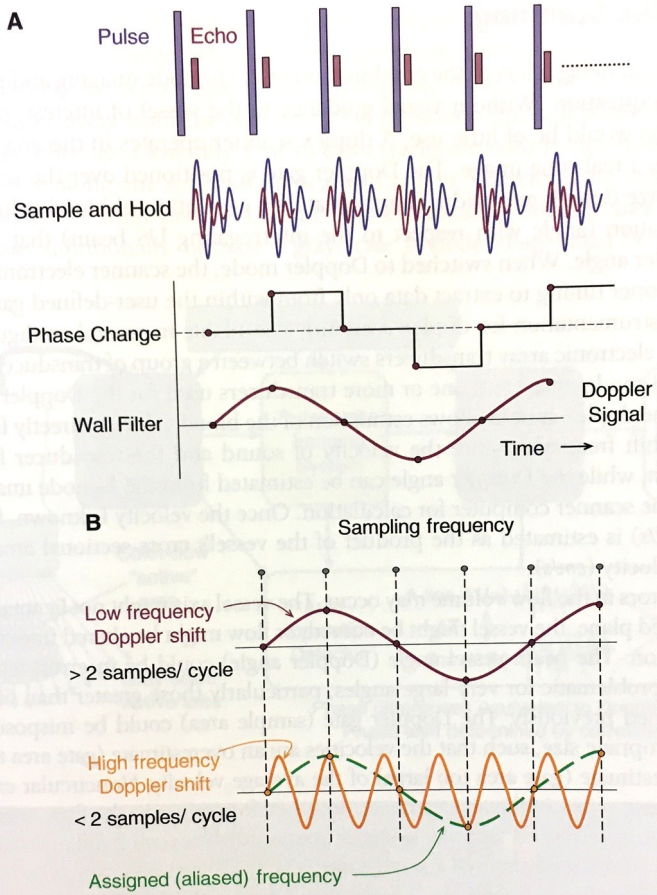
Lower frequency = blood away from the transducer



$$f_D = f_e - f_0 = 2 f_0 \frac{v \cdot \cos\alpha}{c}$$

Kilde: Alejandro Frangi

Doppler Ultrasound Aliasing



■ **FIGURE 14-40** **A.** The returning ultrasound pulses from the Doppler gate are sampled over several pulse-echo cycles (in this example, six times), in order to estimate Doppler shifts (if any) caused by moving blood cells. A sample and hold circuit measures a variation of signal with time (note that the echo [***purple line***] and the pulse [***blue line***] vary in phase, which are recorded and analyzed by Fourier transform methods to determine the Doppler shift frequencies). The wall filter removes the low-frequency degradations caused by transducer and patient motion. **B.** Aliasing occurs when the frequencies in the sampled signal are greater than ½ the PRF (sampling frequency). In this example, a signal of twice the frequency is analyzed as if it were the lower frequency and thus mimics (aliases) the lower frequency.

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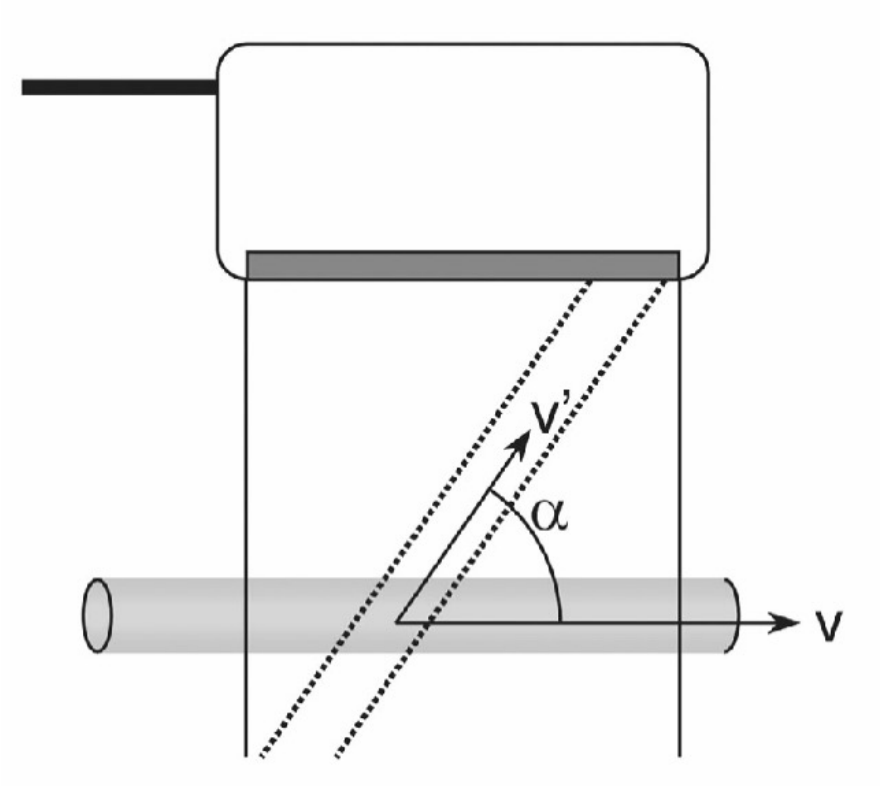
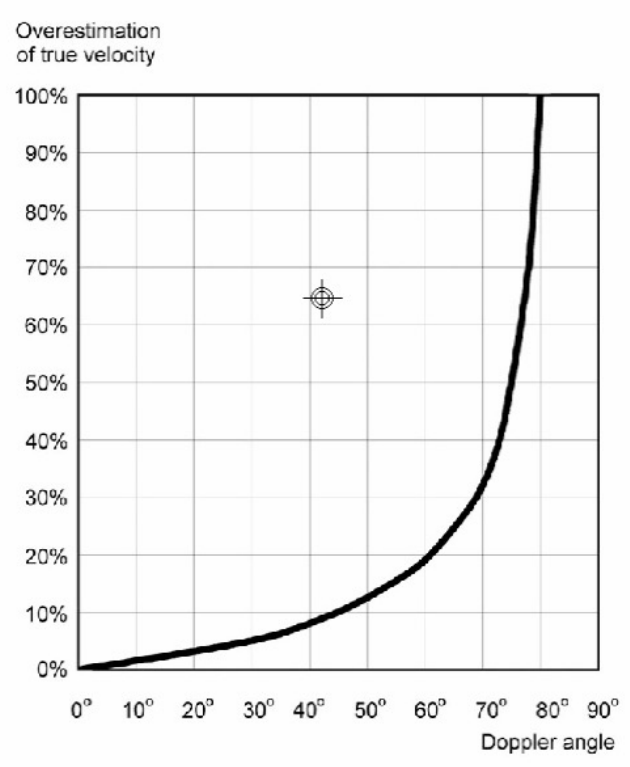
Doppler ultrasound

$$f_D = f_e - f_0 = 2 f_0 \frac{v \cdot \cos\alpha}{c}$$





Doppler image/velocity

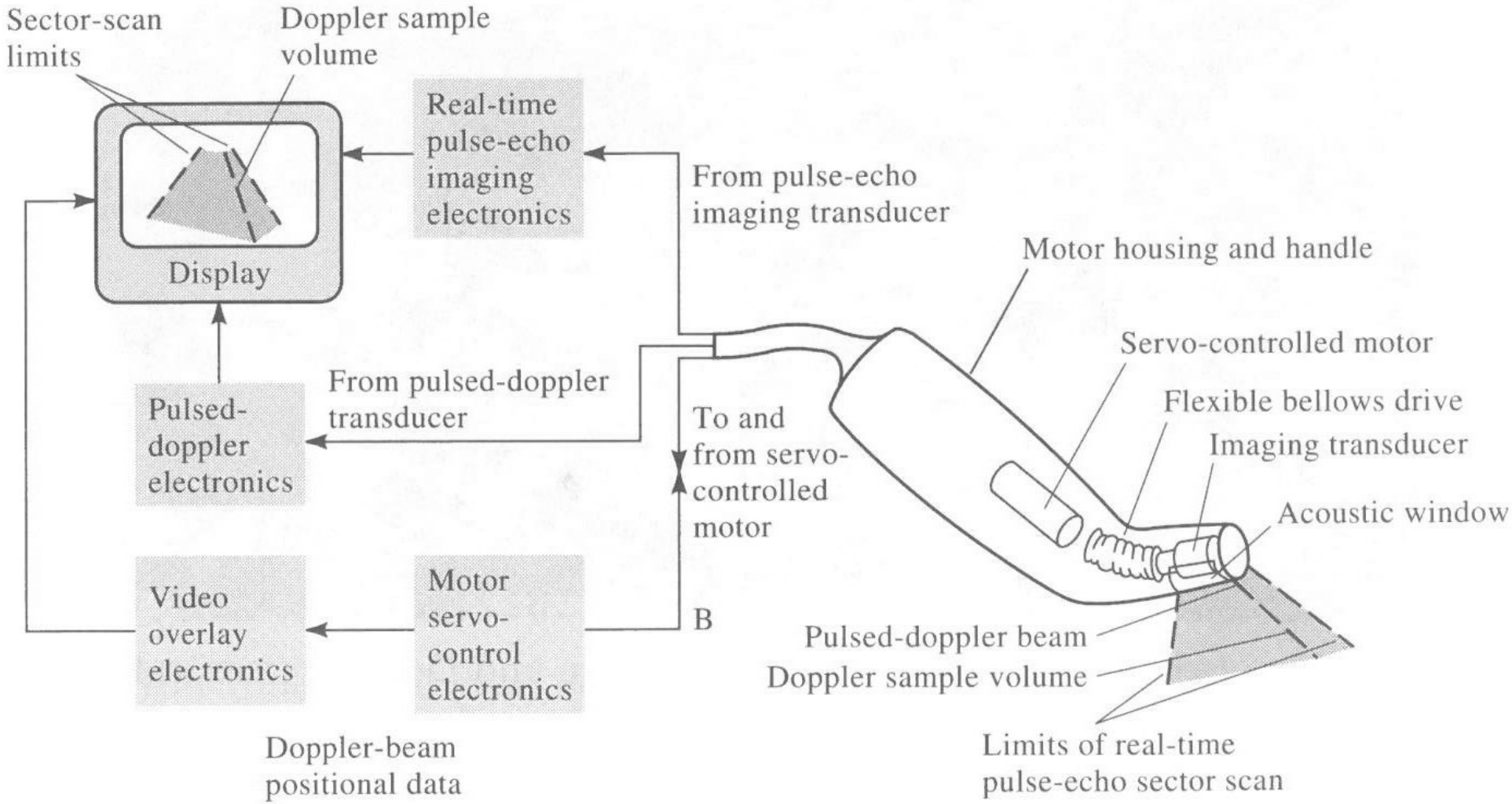


Figure 12.32 The duplex scanner contains a mechanical real-time sector scanner that generates a fan-shaped two-dimensional pulse-echo image. Signals from a selected range along a selected path are processed by pulsed Doppler electronics to yield blood velocity (from Wells, 1984).

Color doppler

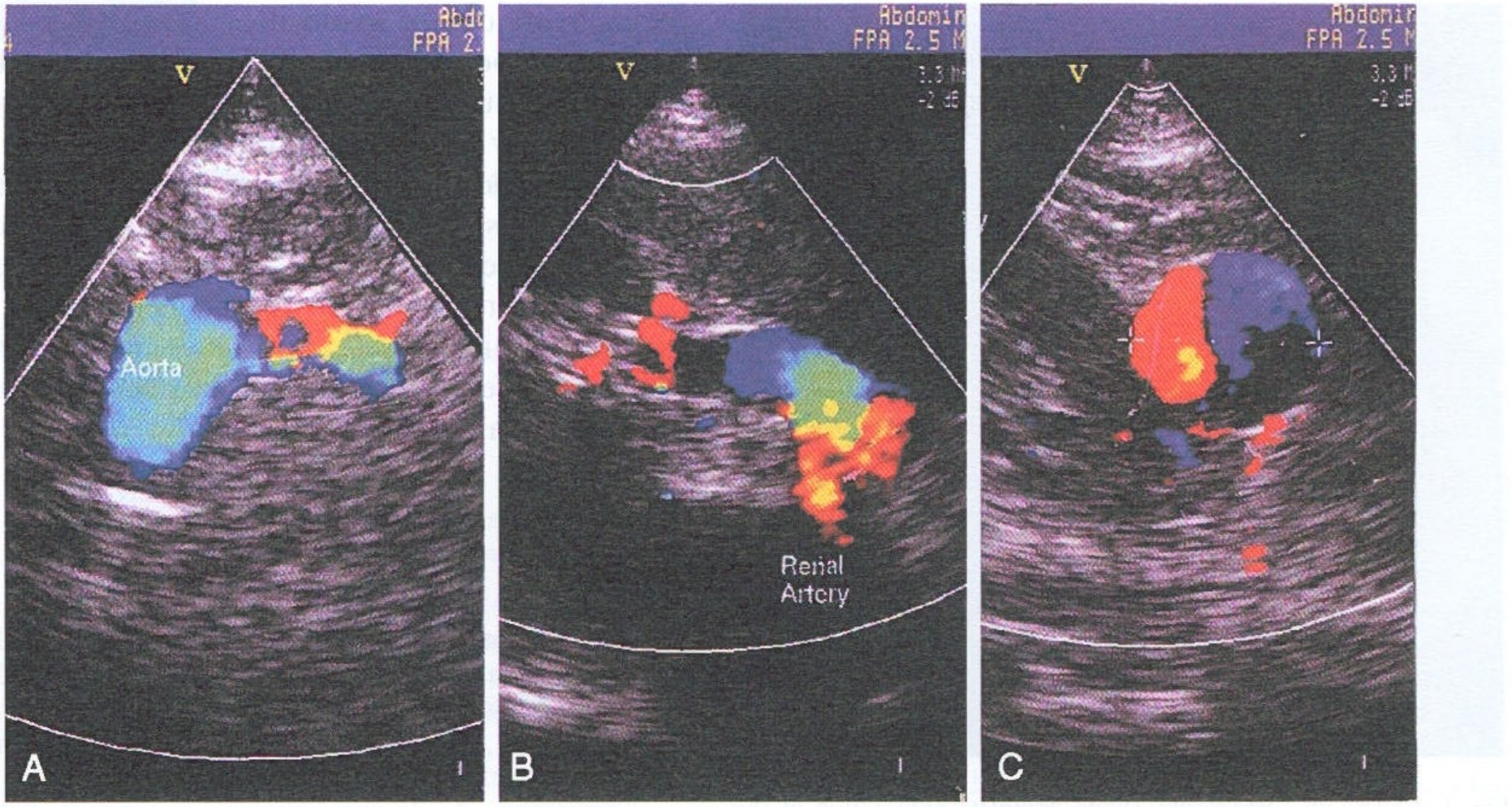


Fig. 1. A–C. Colour ultrasonography examination shows the dilated, tortuous left renal artery. A large aneurysm, partially exophytic, can be seen at the lower pole of the kidney. There is coexistence of both arterial and venous blood flow.

Ultrasound advantages

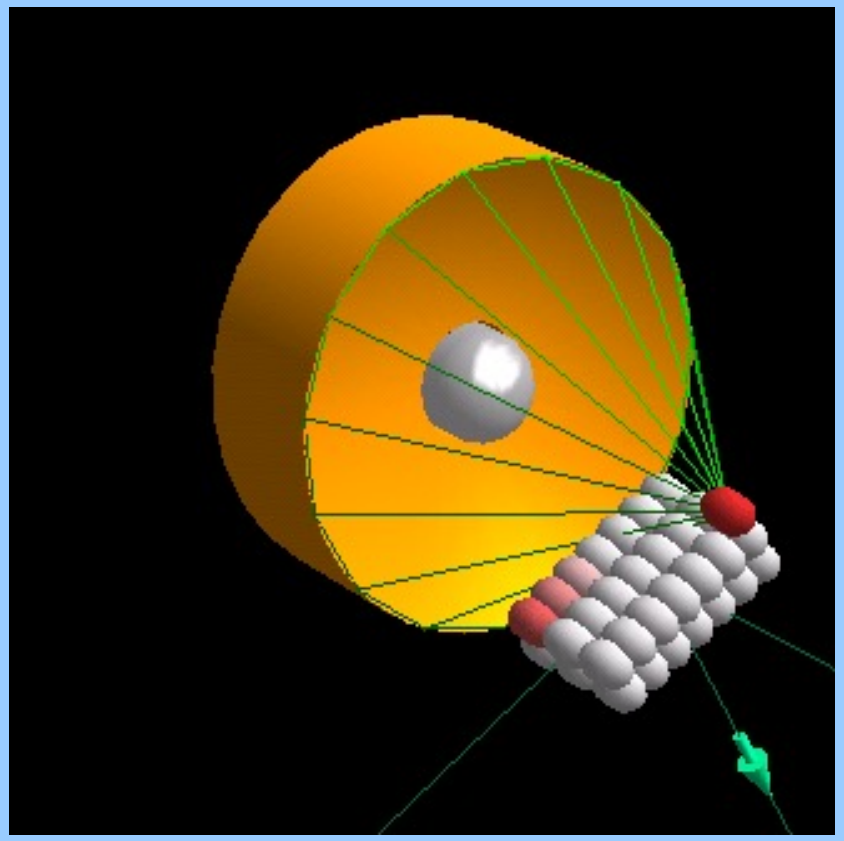
- Muscles and soft tissue are suitable for US-imaging, especially transitions between solid substances and liquid filled areas.
- Real time images = fast diagnosis. Can also be used to biopsy-guiding
- Shows the organ structure
- No well-known side effects, not unpleasant for the patient
- Small scanners compared to other image modalities
- Inexpensive compared to other image modalities
- Spatial resolution is better at high-frequency US than most of the other modalities

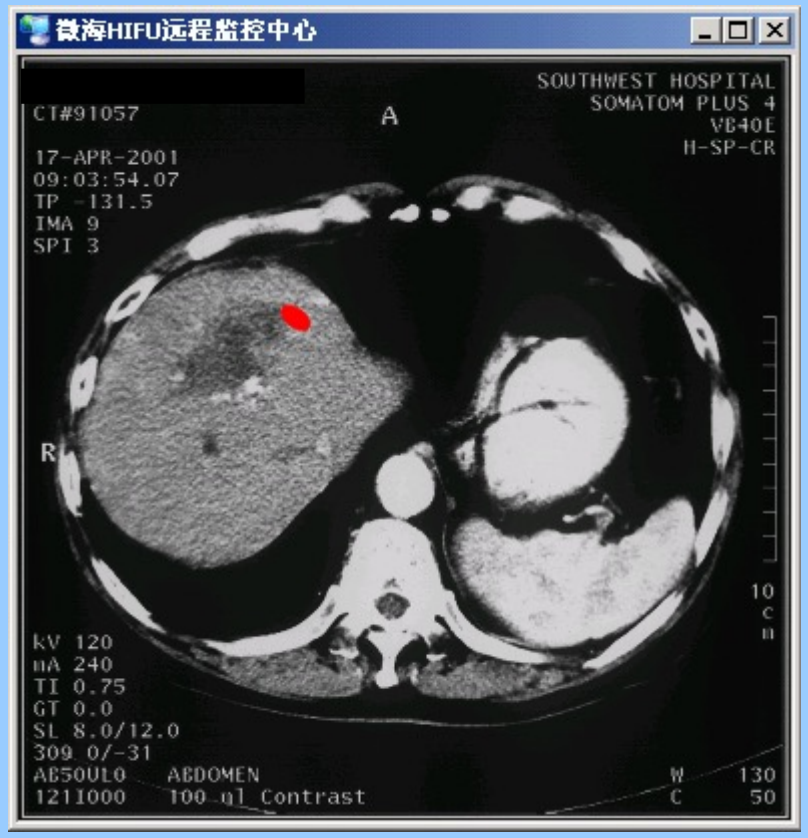
Ultrasound disadvantages

- Unable to penetrate bone tissue
- Poor performance where gas is present
- Limited operating range, dependent on the frequency
- High requrements for the operator, can be difficult to interpret
- Difficult to track back a scanned volume, as soon as the pictures are aquired no exact anchor-pile is available to navigate in the volume

Focused ultrasound

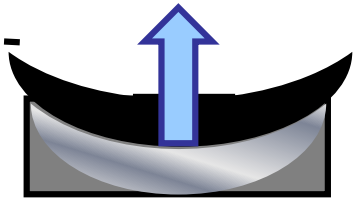
- Volume ablation animation and MR image courtesy of Feng Wu

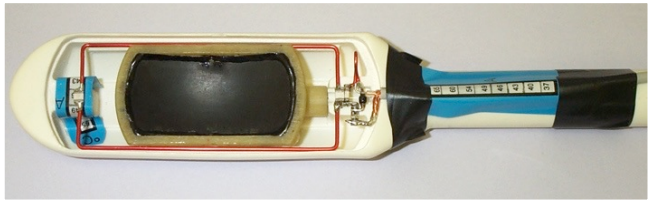




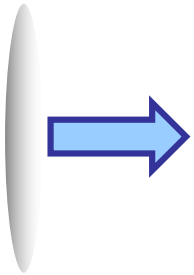
Kennedy JE (2005) Nature Reviews Cancer 18 March 321-327

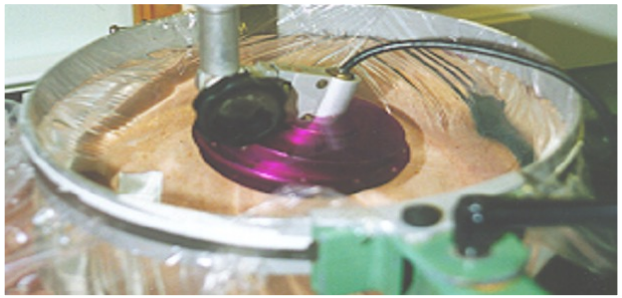
Focused ultrasound



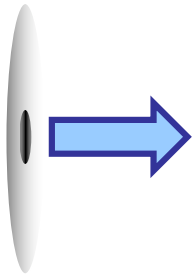


Integrated therapy & MR imaging device for treatment of prostate tumours





Single-element 1.7 MHz extra-corporeal transducer



Single-element HIFU transducer with central aperture for imaging transducer

Frequenses from 0.5 to 4 MHz, intensity up to 20 kWcm^2

Focal length from 3 to 15 cm, Fasearray allows multiple simultaneous foci

Kilde: http://www.maths.bath.ac.uk/~masigg/Godden.ppt#10

Advantages focused ultrasound

- High accuracy (diameter of a few cells)
- Destroyed tissue will be re-absorbed of the body
- Rapid heating of the tissue will destroy the tumor
- Non-invasive or minimal invasive
- No blood loss
- Repeatable
- Rapid convalescence

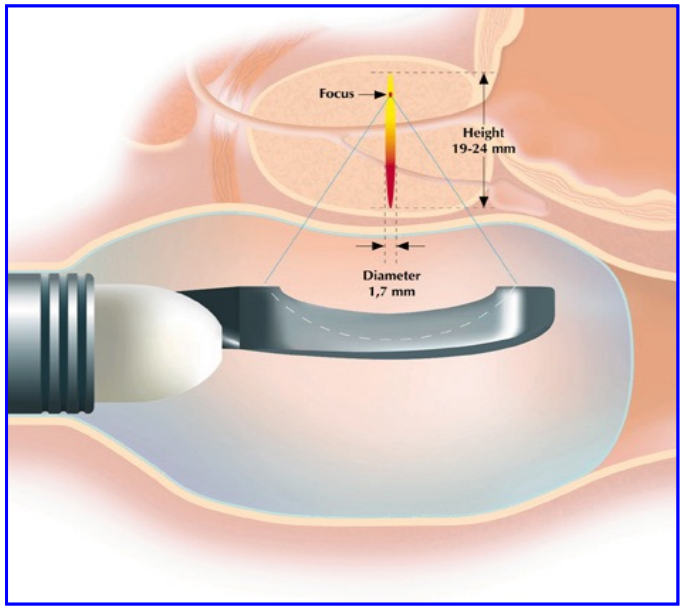
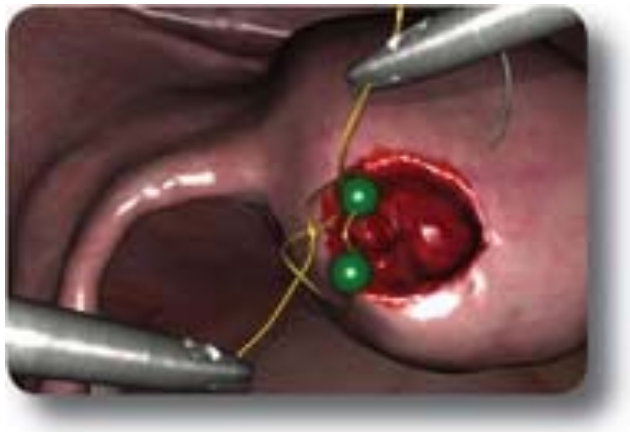


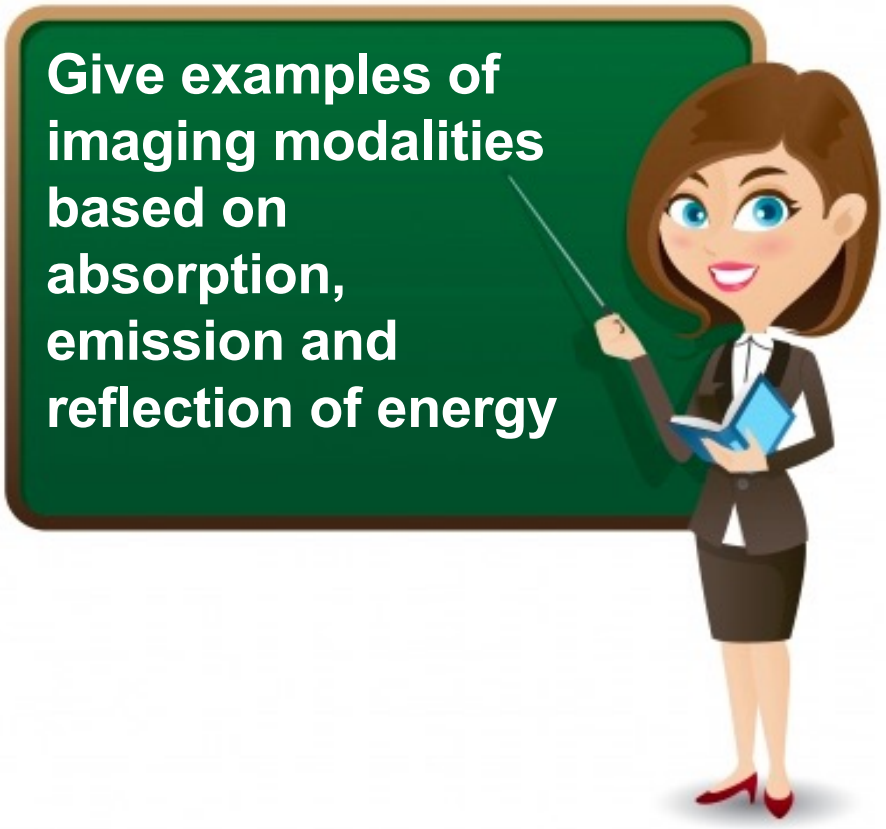
Image: Trans-rectal probe (EDAP)

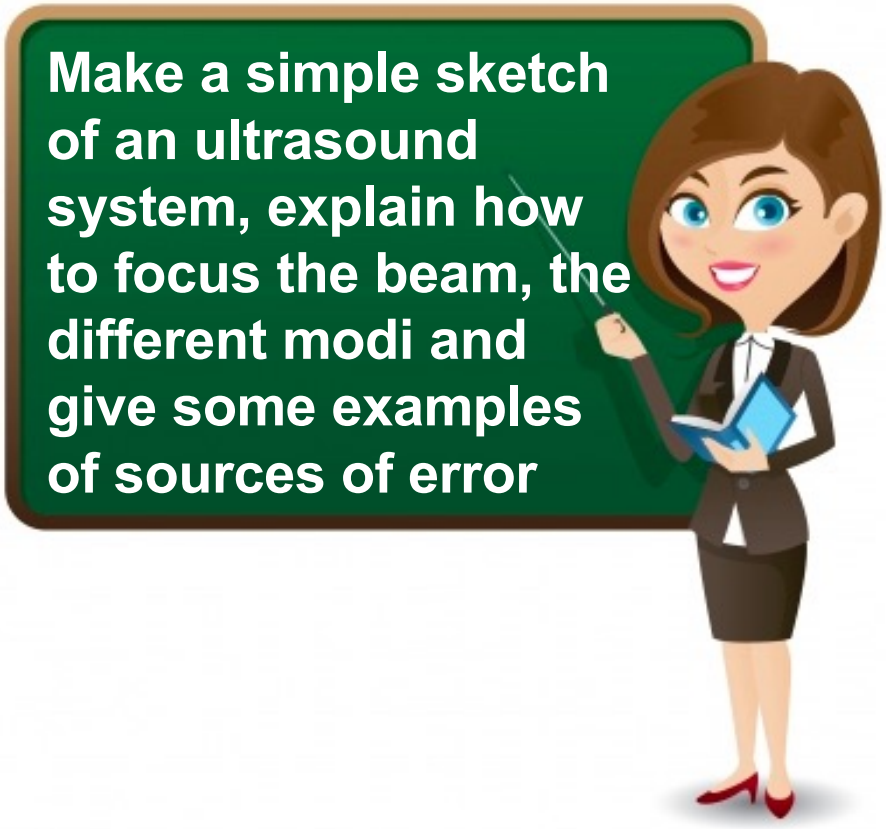
Disadvantages focused ultrasound

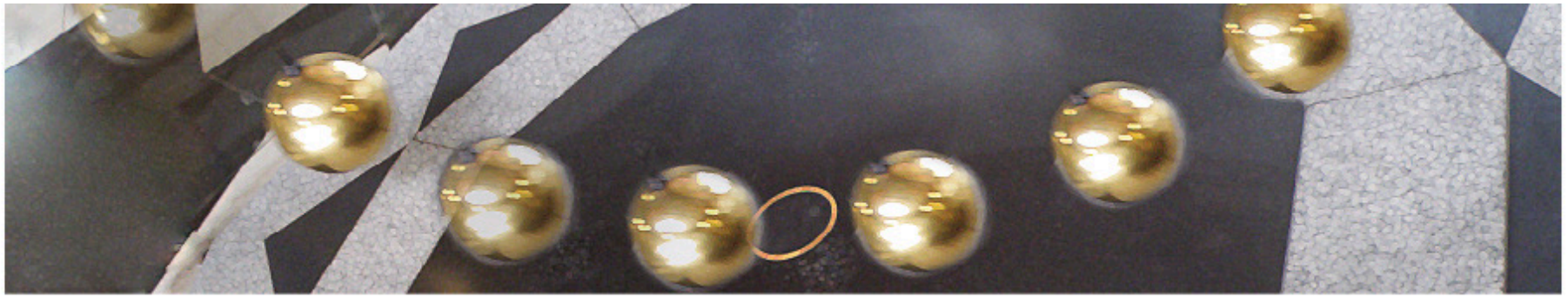
- Capacity problems with large tumors
- New and not established procedure
- Needs direct acoustic access to tumor
- The tumor must be well defined
- The surgeon will not have direct vision of the tissue with the tumor
- Possible side effects of high energetic ultrasound is not clarified (10^4 of the energy of imaging ultrasound)
- Require normally MR-monitoring to verify necrosis



Exercise examples







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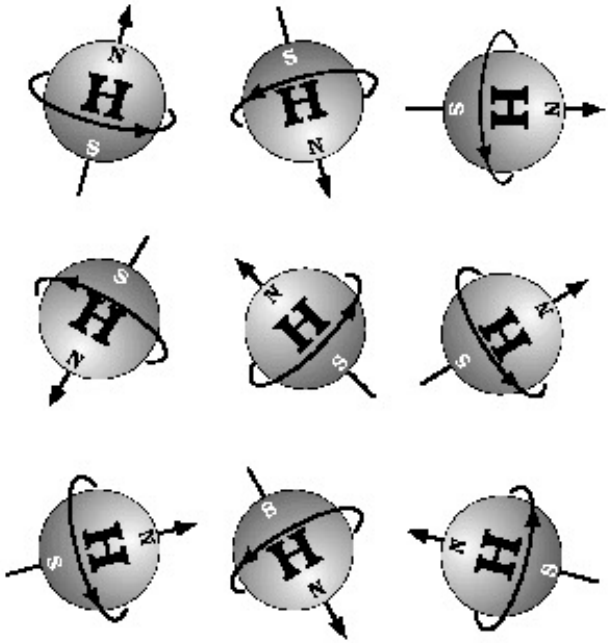
University of Oslo

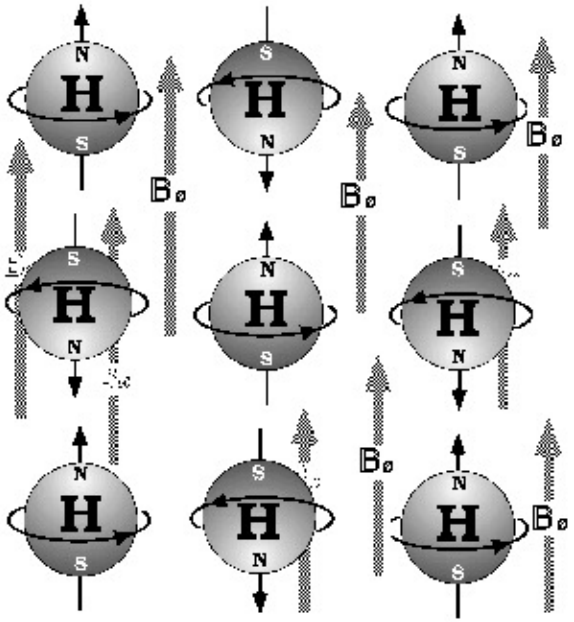
FYS 4250

Lecture 14

Spinning Protons Act Like Little Magnets

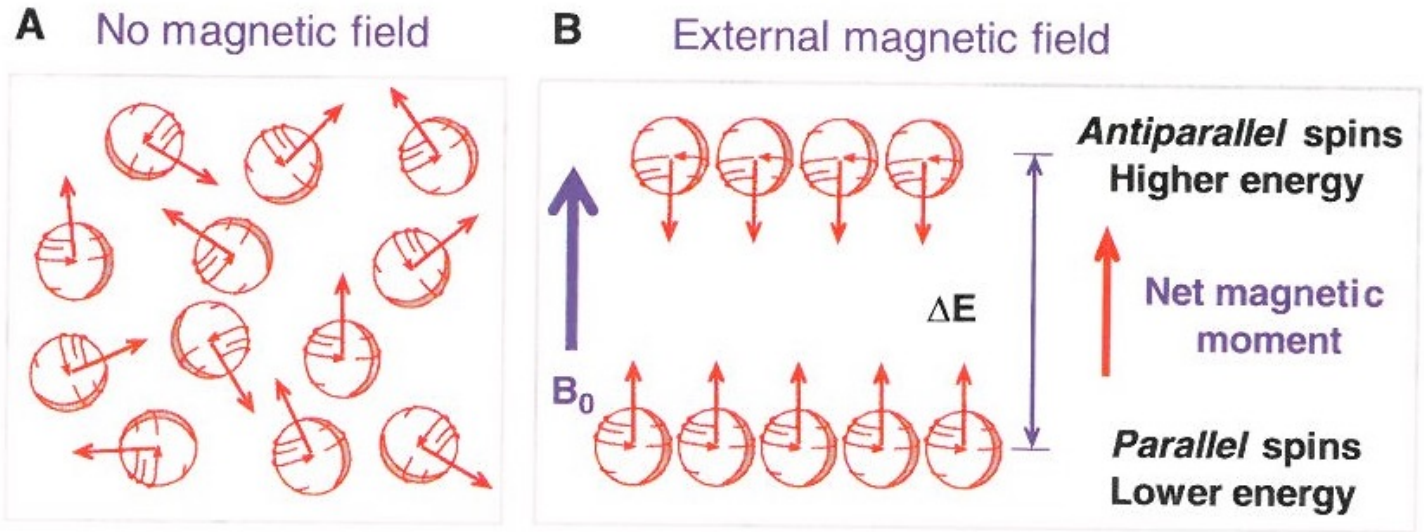


They Align With An External Magnetic Field (Bø)



- Ref:www.simplyphysics.com

Energy levels of free protons



■ **FIGURE 12-7** Simplified distributions of "free" protons without and with an external magnetic field are shown. **A.** Without an external magnetic field, a group of protons assumes a random orientation of magnetic moments, producing an overall magnetic moment of zero. **B.** Under the influence of an applied external magnetic field, B_0, the protons assume a nonrandom alignment in two possible orientations: parallel and antiparallel to the applied magnetic field. A slightly greater number of protons exist in the parallel direction, resulting in a measurable *net magnetic moment* in the direction of B_0.

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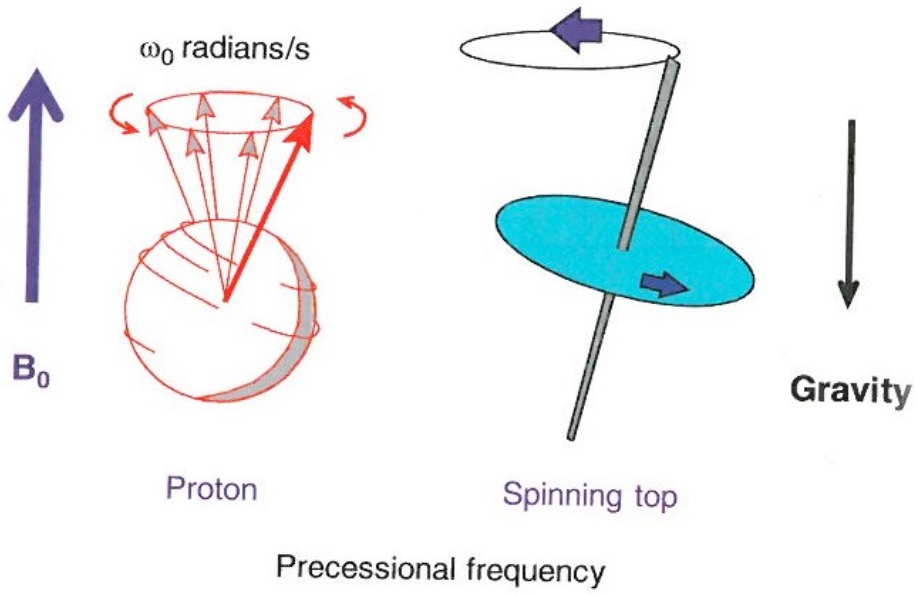
Magnetic characteristics of nucleus

$W_0 = \gamma B_0$

■ FIGURE 12-8 A single proton *precesses* about its axis with an angular frequency, ω, proportional to the externally applied magnetic field strength, according to the *Larmor* equation. A well-known example of precession is the motion a spinning top makes as it interacts with the force of gravity as it slows.



In addition to spin, there is a torque in a perpendicular direction from the applied magnetic field that causes precession. The Larmor equation describes the dependence between the magnetic field B0 and the angular precessional frequency w0.

$$f_0 = \frac{\gamma}{2\pi} B_0$$

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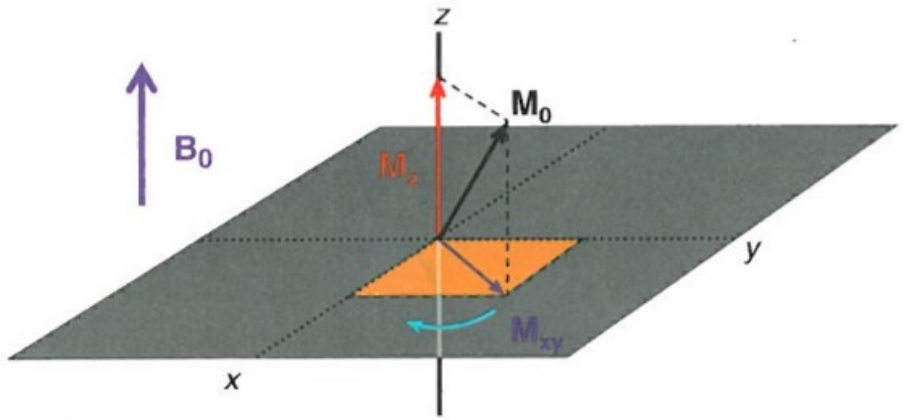
Magnetization in three planes



M_z: Longitudinal Magnetization: in z-axis direction

M_{xy}: Transverse Magnetization: in x-y plane

M_0: Equilibrium Magnetization: maximum magnetization

■ FIGURE 12-11 *Longitudinal magnetization,* M_z, is the vector component of the magnetic moment in the z direction. *Transverse magnetization,* M_{xy}, is the vector component of the magnetic moment in the *x-y* plane. *Equilibrium magnetization,* M_0, is the maximal longitudinal magnetization of the sample, and is shown displaced from the z-axis in this illustration.

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Resonance and exitation

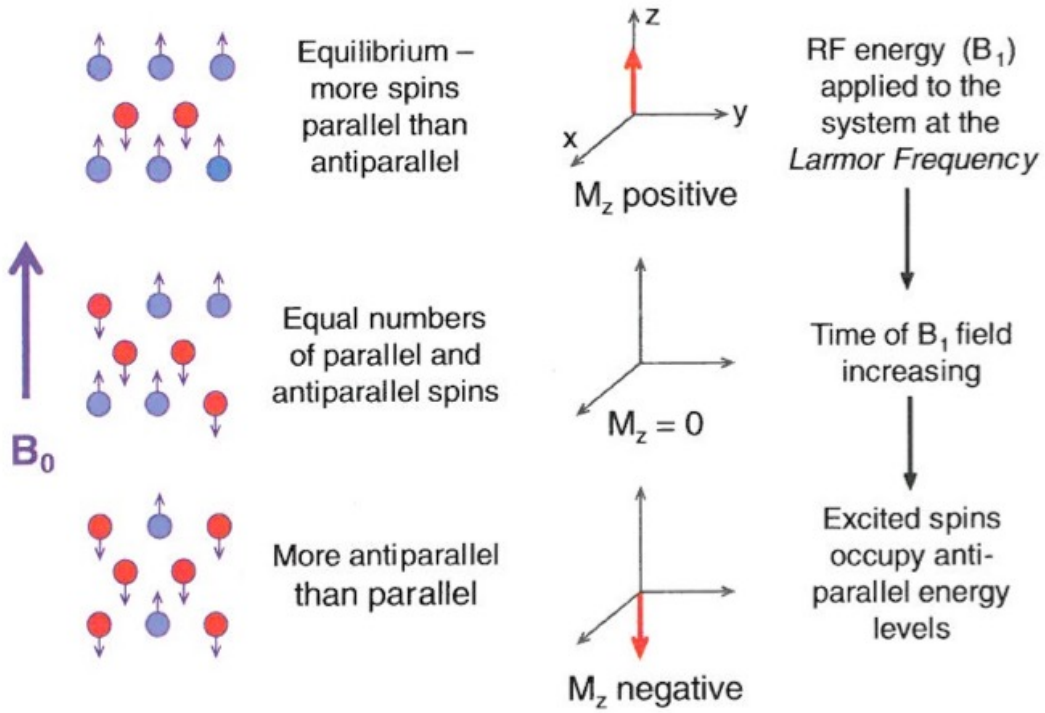


FIGURE 12-12 A simple quantum mechanics process depicts the discrete energy absorption and the time change of the longitudinal magnetization vector as RF energy equal to the energy difference of the parallel and antiparallel spins is applied to the sample (at the Larmor frequency). Discrete quanta absorption changes the proton energy from parallel to antiparallel. With continued application of the RF energy at the Larmor frequency, M_z is displaced from equilibrium, through zero, to the opposite direction (high energy state).

Larmor frequency

The energy difference between the two alignment states depends on the nucleus

$$\Delta E = 2\ \mu_z B_o$$
$$\Delta E = h\ \nu$$

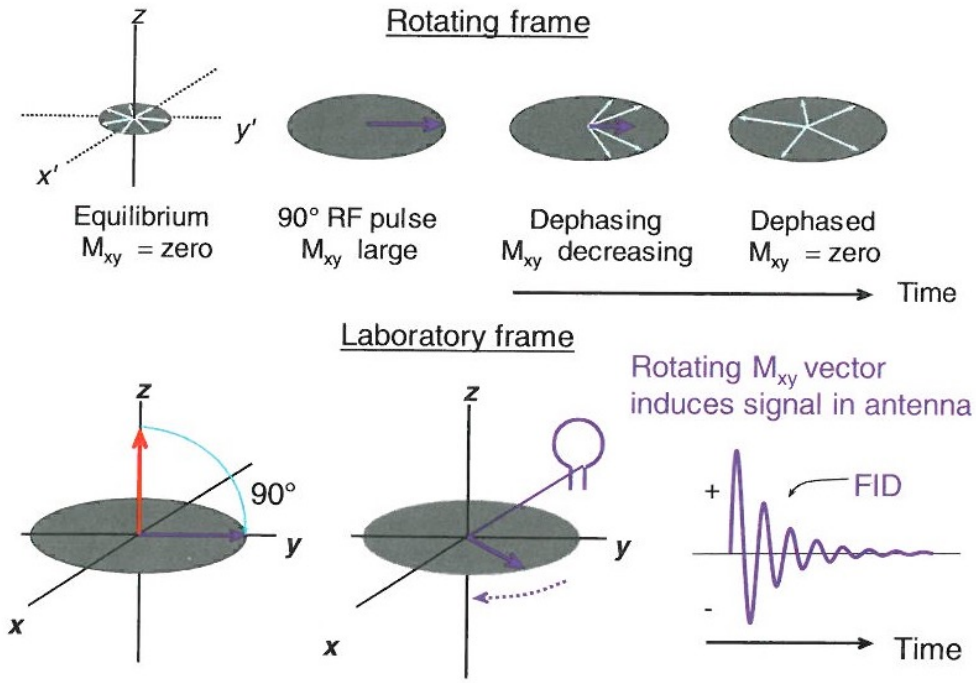
$$\nu = (\gamma/2\pi)\ B_o$$

known as Larmor frequency

$\gamma/2\pi$ **= 42.57 MHz / Tesla for proton**

Free induction decay = a damped sinusoidal electronic signal

Dephasing of magnetic vector



■ FIGURE 12-15 **Top.** Conversion of longitudinal magnetization, M_z, into transverse magnetization, M_{xy}, results in an initial phase coherence of the individual spins of the sample. The magnetic moment vector precesses at the Larmor frequency (stationary in the rotating frame), and dephases with time. **Bottom.** In the laboratory frame, M_{xy} precesses and induces a signal in an antenna receiver sensitive to transverse magnetization. A FID signal is produced with positive and negative variations oscillating at the Larmor frequency, and decaying with time due to the loss of phase coherence.

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Return to equilibrium, T1 relaxation

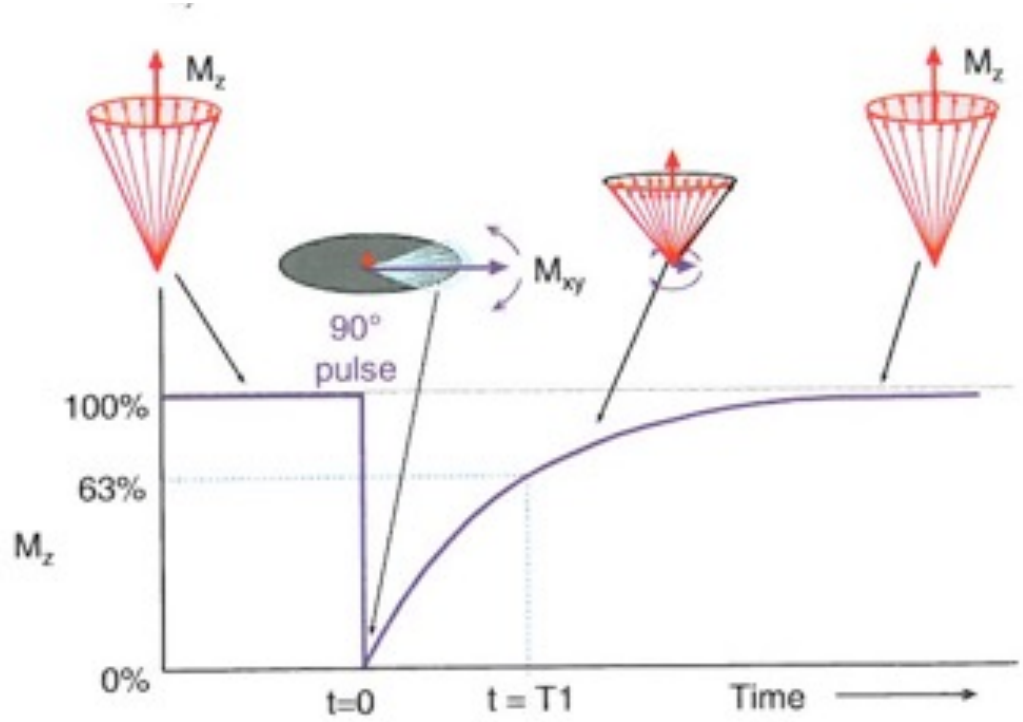

FIGURE 12-17 After a 90-degree pulse, M_z is converted from a maximum value at equilibrium to $M_z = 0$. Return of M_z to equilibrium occurs exponentially and is characterized by the spin-lattice T1 relaxation constant. After an elapsed time equal to T1, 63% of the longitudinal magnetization is recovered. Spin-lattice recovery takes longer than spin-spin decay (T2).

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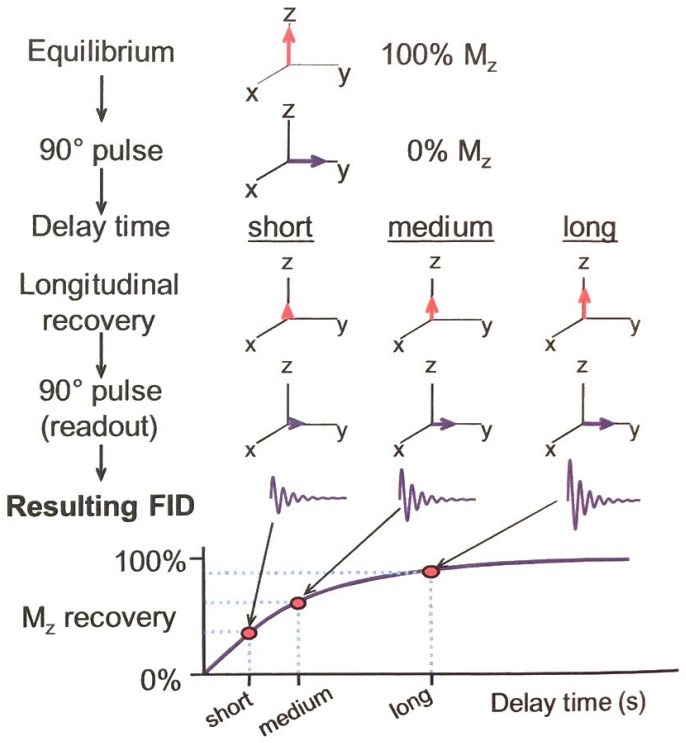
Return to equilibrium, T1 relaxation

■ **FIGURE 12-18** Spin-lattice relaxation for a sample can be measured by using various delay times between two 90-degree RF pulses. After an initial 90-degree pulse, $M_z = 0$, another 90-degree pulse separated by a known delay is applied, and the longitudinal magnetization that has recovered during the delay is converted to transverse magnetization. The maximum amplitude of the resultant FID is recorded as a function of delay times between initial pulse and readout (three different delay time experiments are shown in this example), and the points are fit to an exponential recovery function to determine T1.



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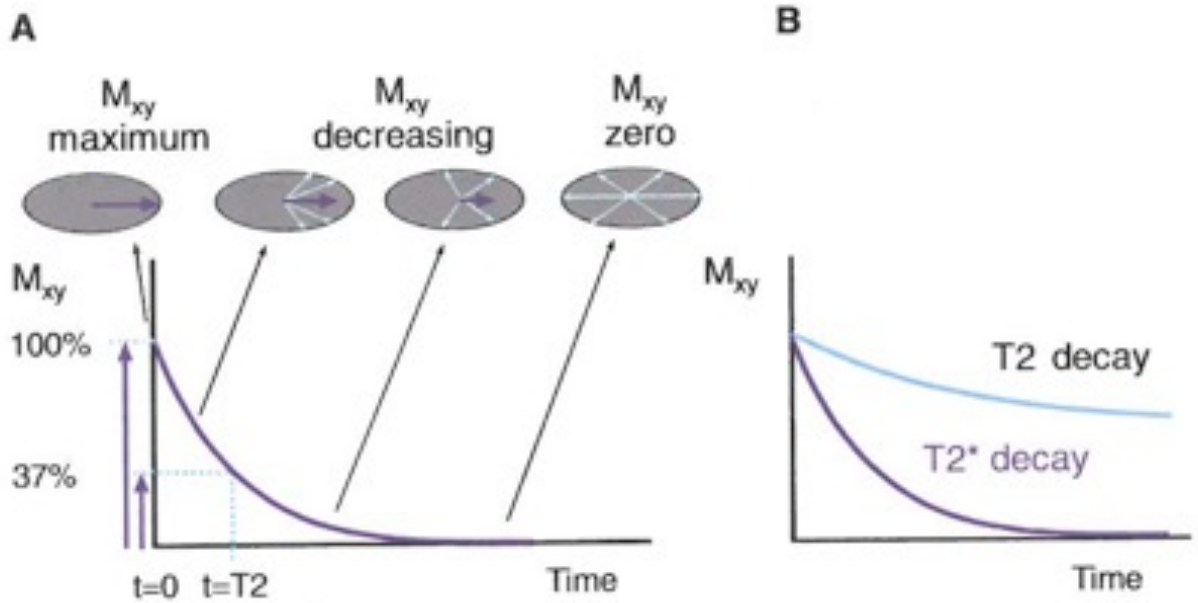
Free induction decay: T2 Relaxation



■ FIGURE 12-16 **A.** The loss of M_{xy} phase coherence occurs exponentially caused by intrinsic spin-spin interactions in the tissues and extrinsic magnetic field inhomogeneities. The exponential decay constant, T2, is the time over which the signal decays to 37% of the initial transverse magnetization (e.g., after a 90-degree pulse). **B.** T2 is the decay time resulting from *intrinsic* magnetic properties of the sample. T2* is the decay time resulting from *both intrinsic and extrinsic magnetic field variations*. T2 is always longer than T2*.

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Comparison of T1 and T2

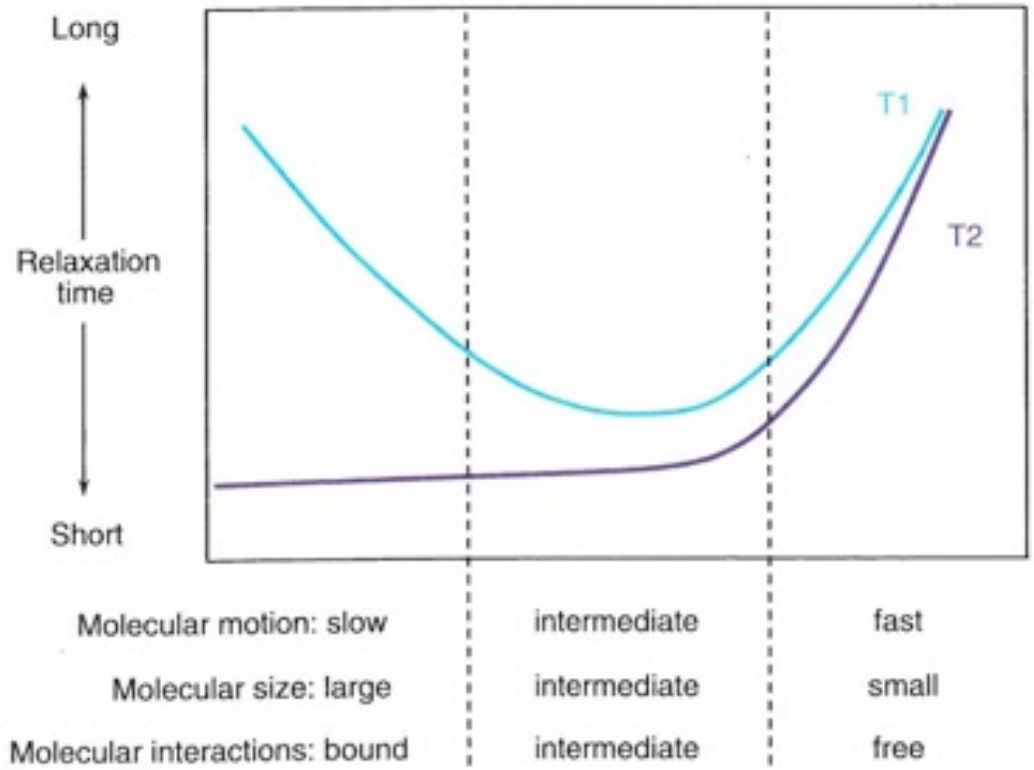

FIGURE 12-20 Factors affecting T1 and T2 relaxation times of different tissues are generally based on molecular motion, size, and interactions that have an impact on the local magnetic field variations (T2 decay) and structure with intrinsic tumbling frequencies coupling to the Larmor frequency (T1 recovery). The relaxation times (vertical axis) are different for T1 and T2.

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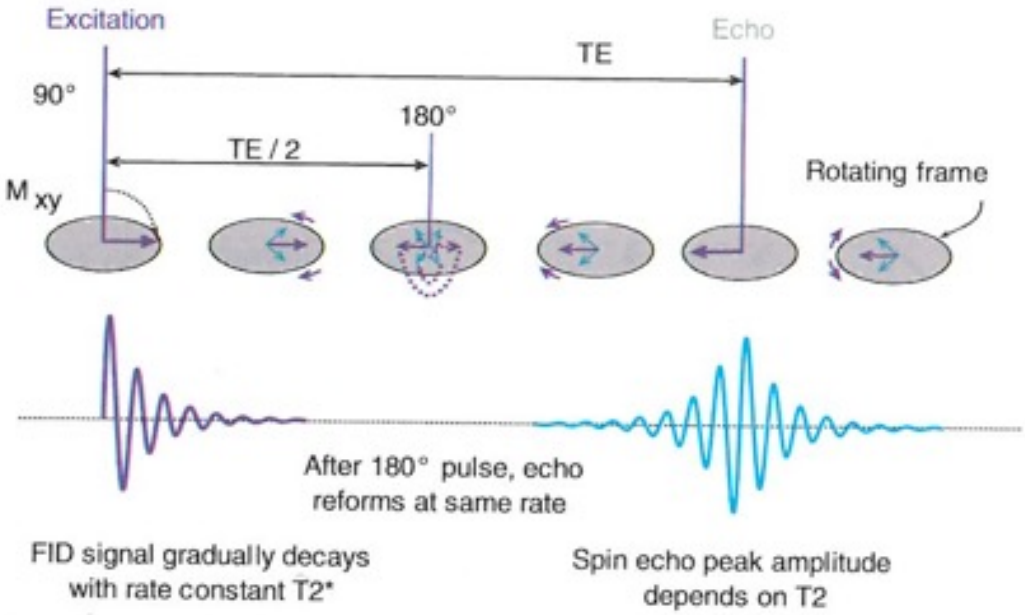
Spin echo contrast weighting

$$S \propto r_H \left[1 - e^{TR/T1}\right] e^{-TE/T2}$$



■ FIGURE 12-22 The SE pulse sequence starts with a 90-degree pulse and produces an FID that decays according to T2* relaxation. After a delay time TE/2, a 180-degree RF pulse inverts the spins that re-establishes phase coherence and produces an echo at a time TE. Inhomogeneities of external magnetic fields are canceled, and the peak amplitude of the echo is determined by T2 decay. The rotating frame shows the evolution of the echo vector in the opposite direction of the FID. The sequence is repeated for each repetition period, TR.

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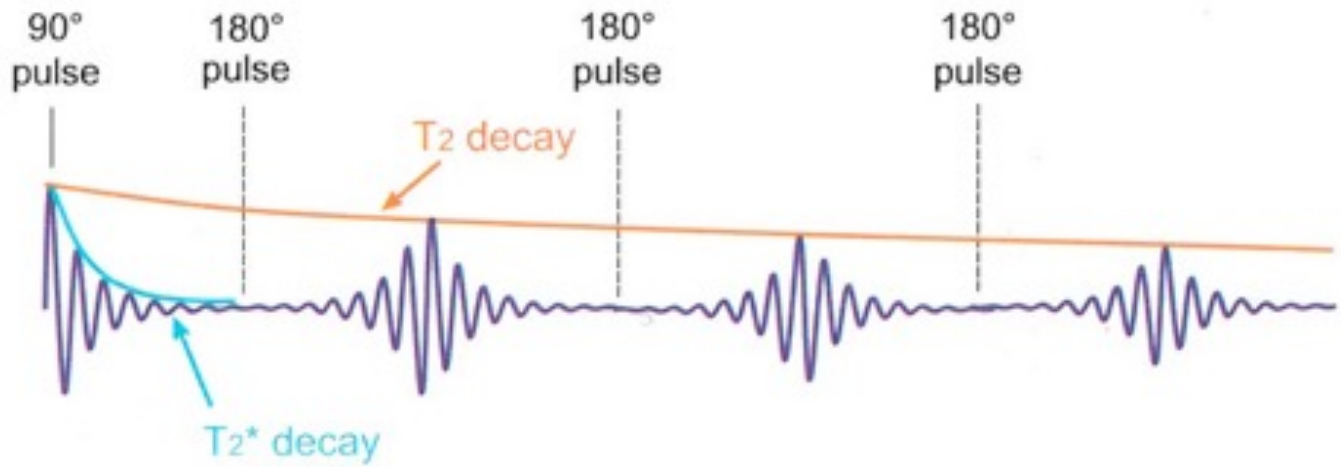
T2-spin echo decay



■ FIGURE 12-23 "True" T2 decay is determined from multiple 180-degree refocusing pulses acquired during the repetition period. While the FID envelope decays with the T2* decay constant, the peak amplitudes of subsequent echoes decay exponentially according to the T2 decay constant, as extrinsic magnetic field inhomogeneities are cancelled.

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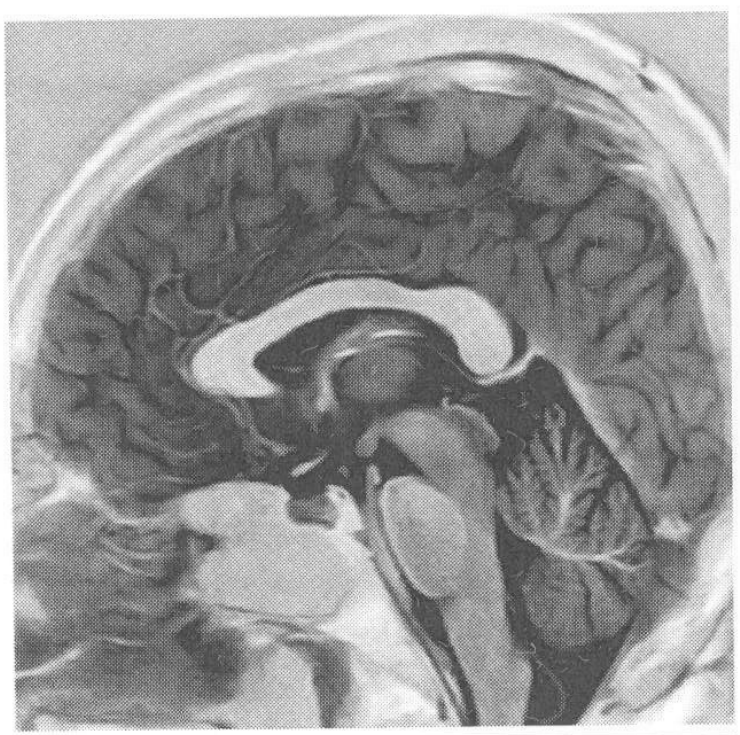
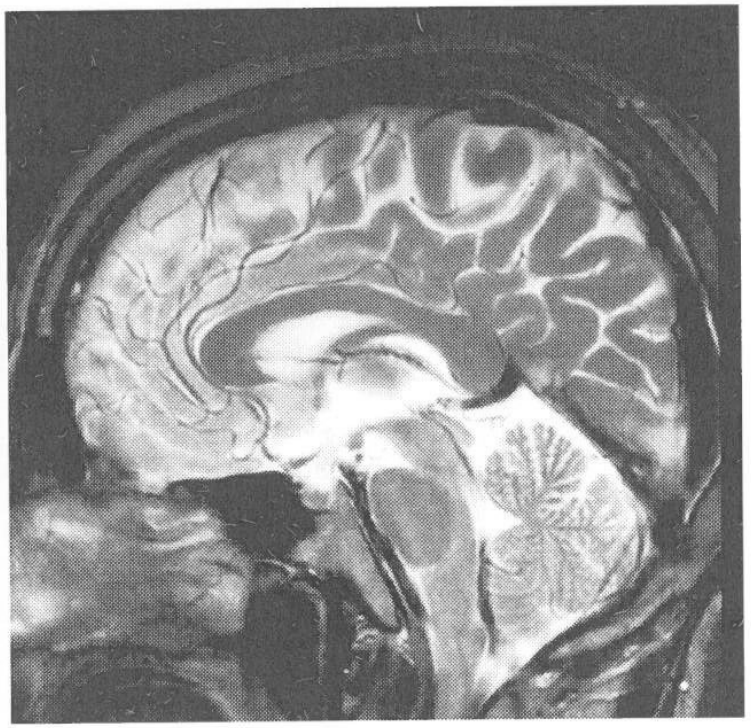
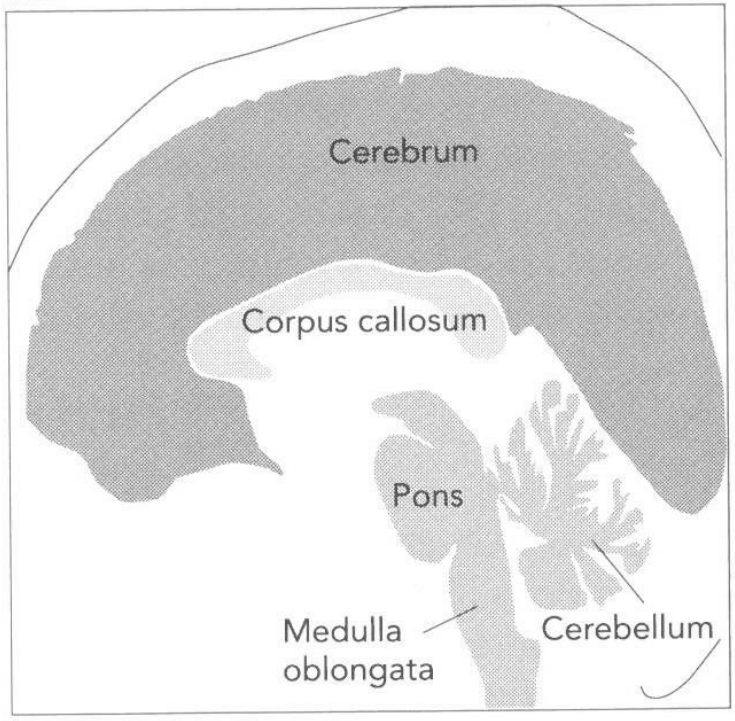


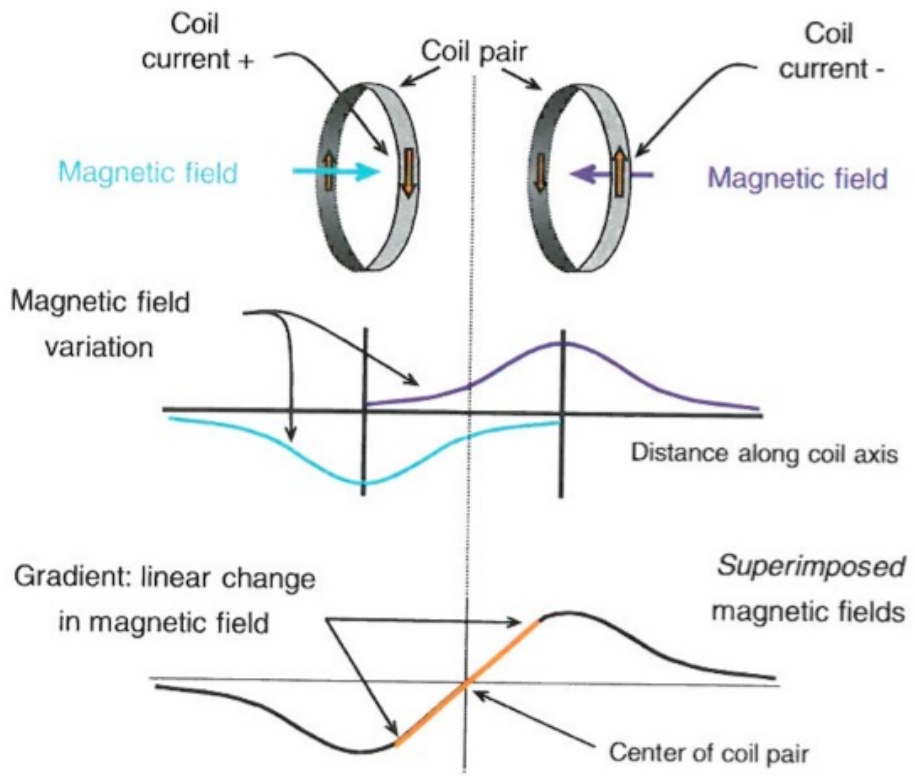




Figur 8:75. Hjärnor avbildade genom utnyttjande av uppmätta relaxationstider. Till vänster T_1-viktad bild och till höger T_2-viktad. (MR-bilder från Philips Medical Systems.)

MR images T1 and T2 contrast

Gradients



■ FIGURE 12-4 Gradients are produced inside the main magnet with coil pairs. Individual conducting wire coils are separately energized with currents of opposite direction to produce magnetic fields of opposite polarity. Magnetic field strength decreases with distance from the center of each coil. When combined, the magnetic field variations form a linear change between the coils, producing a linear magnetic field gradient, as shown in the lower graph.

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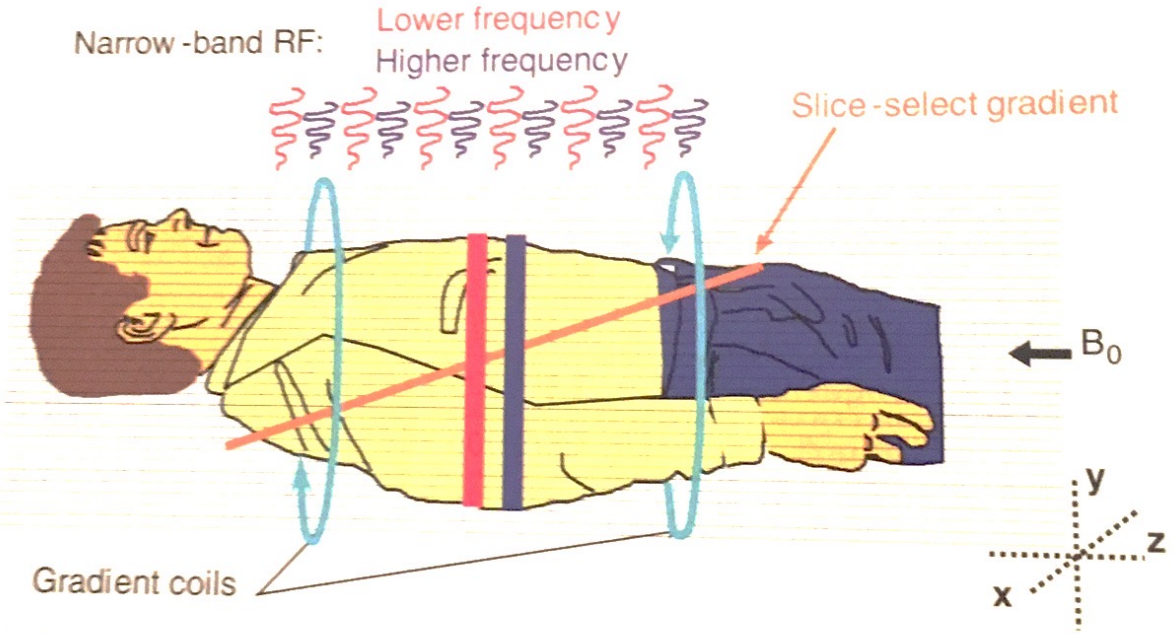
Image construction

Slice select gradient (SSG)

Proton precessional frequencies is increased or decreased dependent on their distance from null

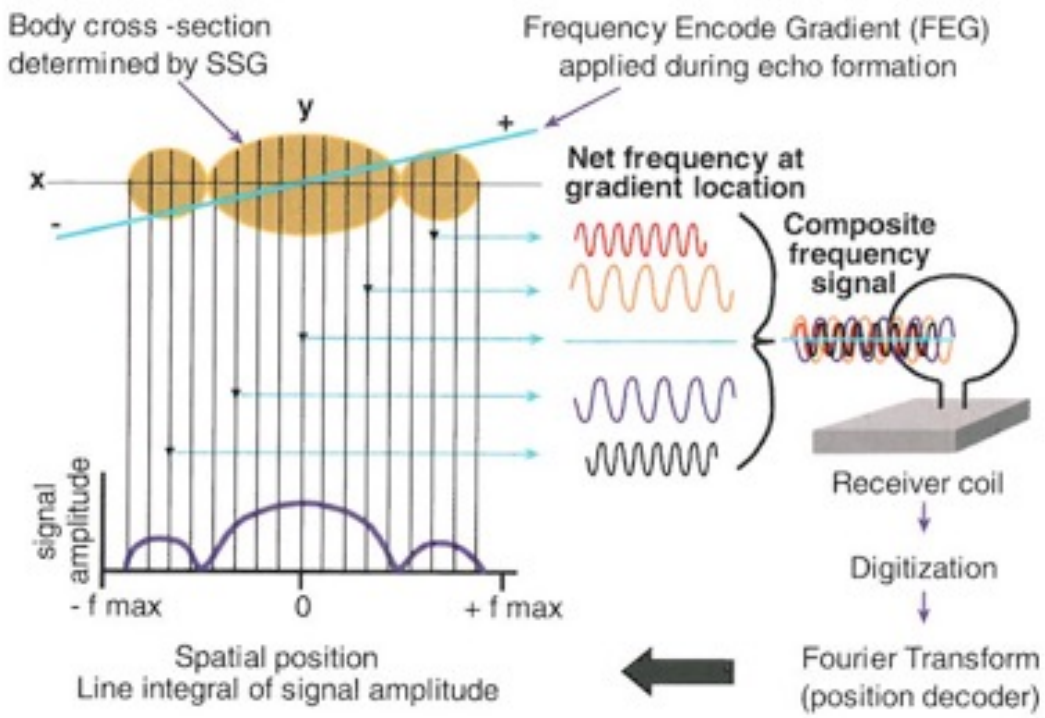
Only protons with precessional frequencies matching RF frequencies will absorb energy = thin slice



■ FIGURE 12-49 The SSG disperses the precessional frequencies of the protons in a known way along the gradient. A narrow band RF pulse excites only a selected volume (slice) of tissues, determined by frequency, BW, and SSG strength. In the example above, two narrow-band RF pulses with different center frequencies irradiate the whole body during the application of the gradient, and only those protons at the same frequencies as the RF pulses will absorb energy. Note that the higher frequency slice is shifted towards the positive pole of the applied gradient.

Frequency encode gradient

Frequency encode gradient = readout gradient, perpendicular to SSG



■ FIGURE 12-52 The *FEG* is applied in an orthogonal direction to the SSG, and confers *a spatially dependent variation* in the precessional frequencies of the protons. Acting only on those protons in a slice determined by the SSG excitation, the composite signal is acquired, digitized, demodulated (Larmor frequency removed), and Fourier transformed into frequency and amplitude information. A one-dimensional array represents a *projection* of the slice of tissue (amplitude and position) at a specific angle. (Demodulation into net frequencies occurs *after* detection by the receiver coil; this is shown in the figure for clarity only.)

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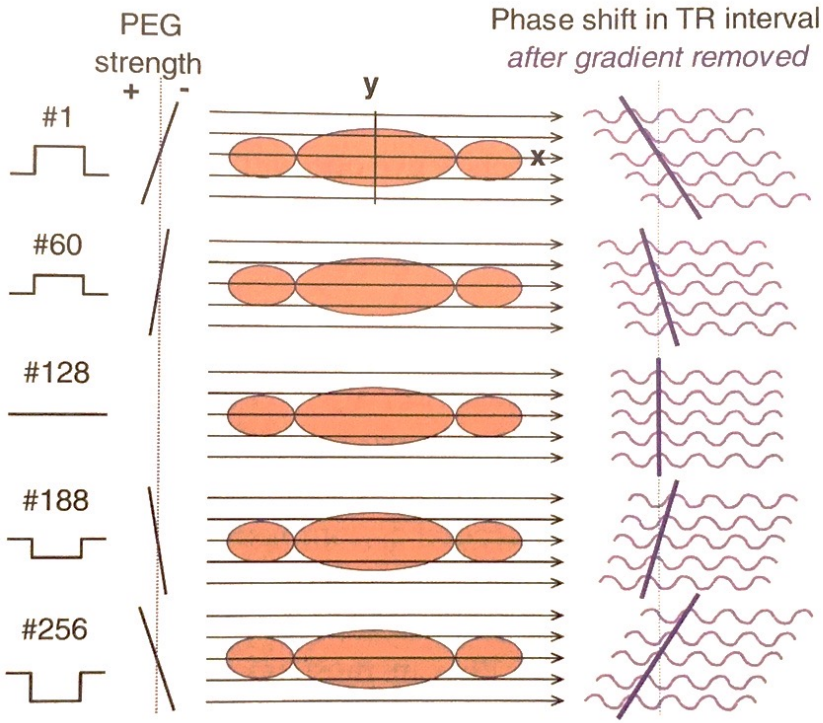
Phase encode gradient (PEG)

Proton position in the third orthogonal dimension is determined with PEG. Introduce a phase change with a short duration PEG



■ **FIGURE 12-55** The PEG is applied *before* the FEG and *after* the SSG. The PEG produces a spatially dependent variation in angular frequency of the excited spins for a brief duration, and generates a spatially dependent variation in phase when the spins return to the Larmor frequency. Incremental changes in the PEG strength for each TR interval spatially encodes the phase variations: protons at the null of the PEG do not experience any phase change, while protons in the periphery experience a large phase change dependent on their distance from the null. The incremental variation of the PEG strength can be thought of as providing specific "views" of the volume because the SSG and FEG remain fixed throughout the acquisition.

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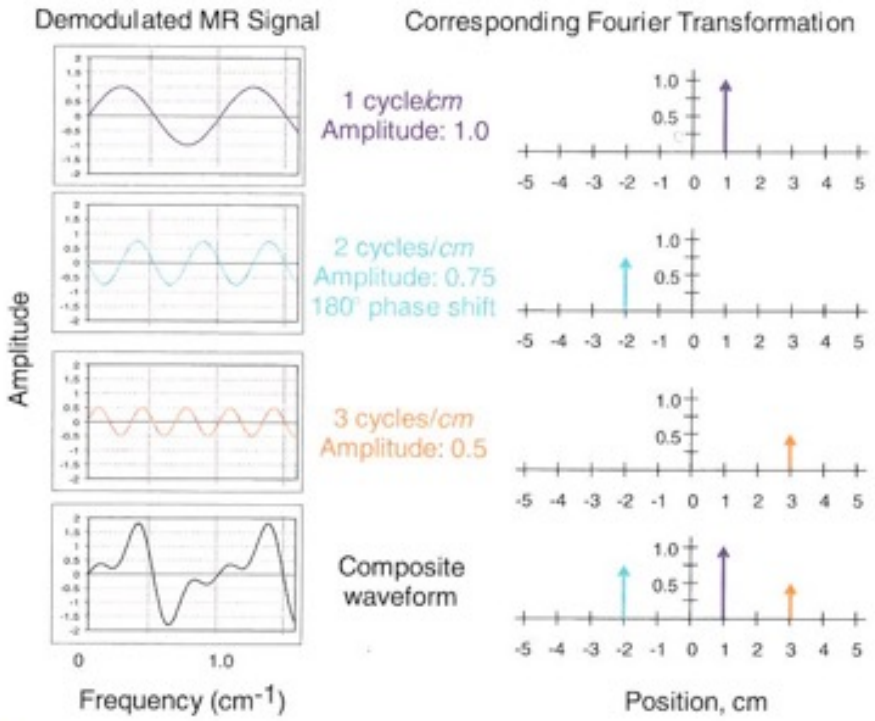
A rotating FEG in the x-y plane will give the acquisition of individual projections as a function of angle.

Fourier transform of spatial freq. signals



■ FIGURE 12-53 Spatial frequency signals (cycles/cm) and their Fourier transforms (spatial position) are shown for three simple sinusoidal waveforms with a specific amplitude and phase. The Fourier transform decodes the frequency, phase and amplitude variations in the spatial frequency domain into a corresponding position and amplitude in the spatial domain. A 180-degree phase shift (second from the top) is shifted in the negative direction from the origin. The composite waveform (a summation of all waveforms, lower left) is decoded by Fourier transformation into the corresponding positions and amplitudes (lower right).

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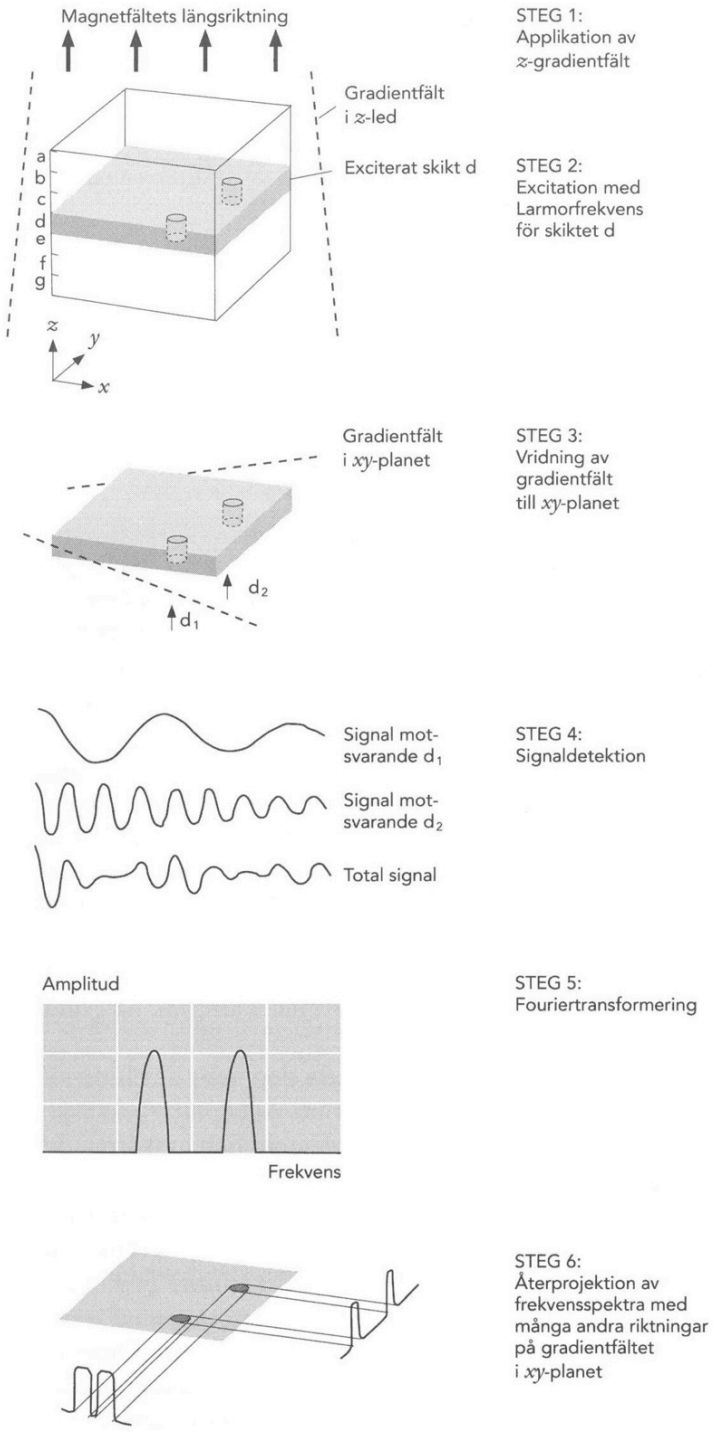


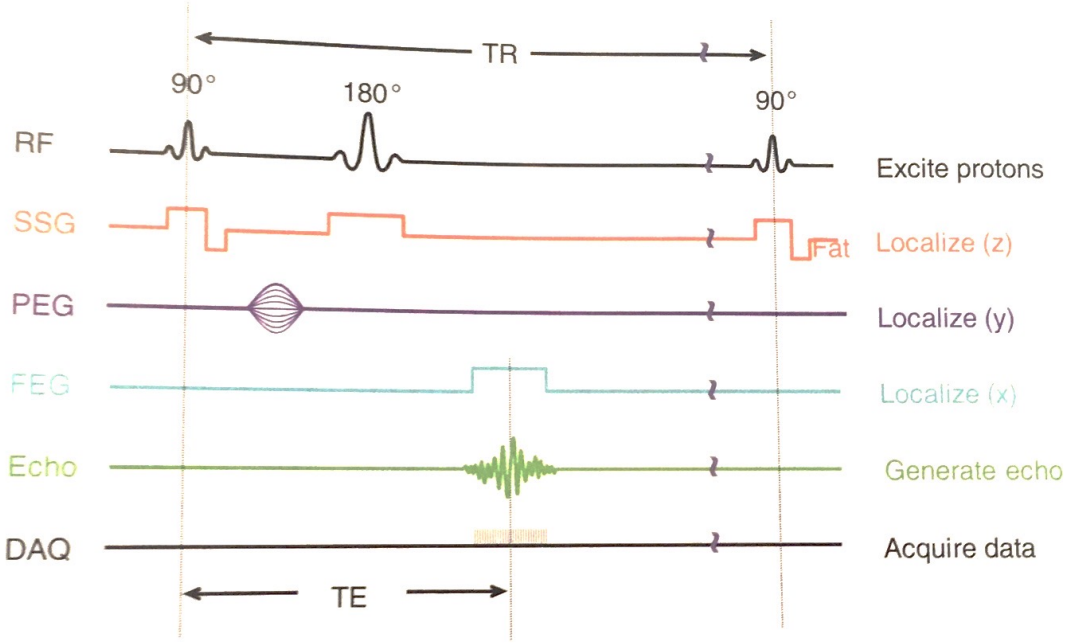
Figur 8:85. En möjlig metod för rekonstruktion av MR-bilder.

3D picture construction (old way)

$$\omega = \gamma B$$

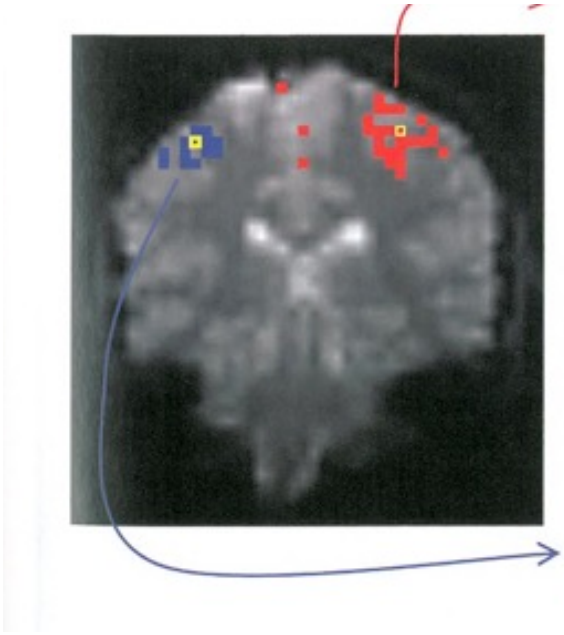
All gradients (SSG + PEG + FEG)

Proton position in the third orthogonal dimension is determined with PEG. Introduce a phase change with a short duration PEG



■ **FIGURE 12-56** A typical spin-echo pulse sequence diagram indicates the timing of the SSG, PEG, and FEG during the repetition time (TR) interval, synchronized with the RF pulses and the DAQ when the echo appears. Each TR interval is repeated with a different PEG strength (this appears as multiple lines in the illustration, but only one PEG strength is applied per TR as indicated by the bold line in this figure).

Functional MRI



Hb differs in how it responds to the magnetic field, the deoxygenated Hb molecule is slightly more attracted to magnetic field.

In consequence, the magnetic field is distorted by causing the nuclei to loose magnetization faster in the *T2 decay = MR pulse sequences sensitive to *T2 will have more signals when the blood is oxygenated than for the deoxygenated blood.

(The effect increases with the square of the magnetic field strength) = Minimum 1.5T

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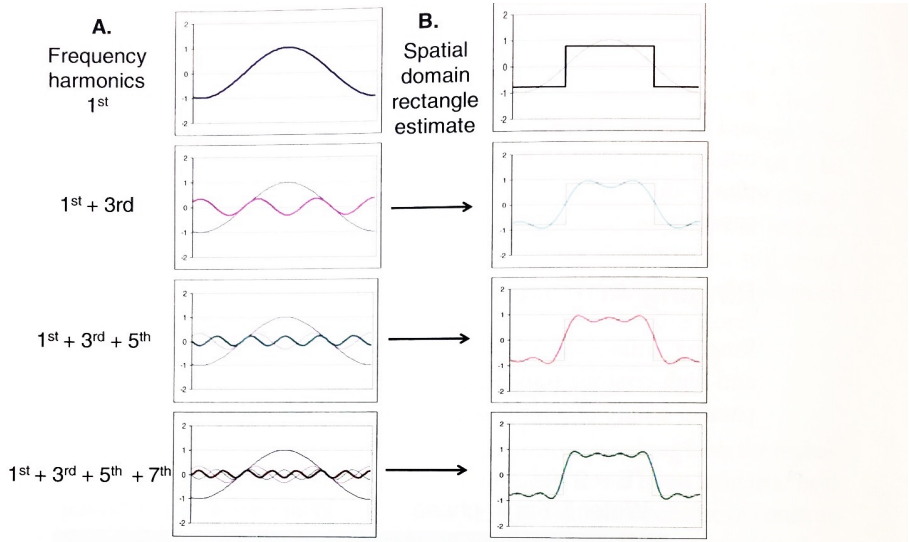
MRI-artefacts

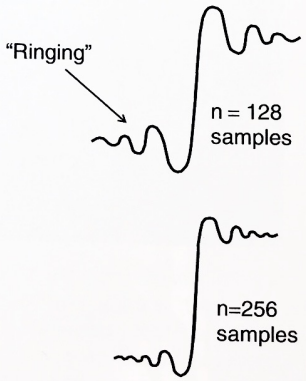
Caused by insufficient sampling, could be reduced with a larger numb

Ringing artefacts



■ FIGURE 13-36 The synthesis of a spatial object occurs by the summation of frequency harmonics in the MR image. **A. Left column**: frequency harmonics that estimate a rectangle function with progressively higher frequencies and lower amplitudes are shown. **B. Middle column**: As higher frequency harmonics are included, the summed result more faithfully represents the object shape, in this example a rectangle with two vertical edges. The number of frequencies encoded in the MR image is dependent on the matrix size. **C. Right column**: A sharp transition boundary in an MR image is represented with 256 samples better than with128 samples (frequency harmonics in k-space). The amount of ringing caused by insufficient sampling is reduced with a larger number of samples.

C. Sharp transition in MR image:



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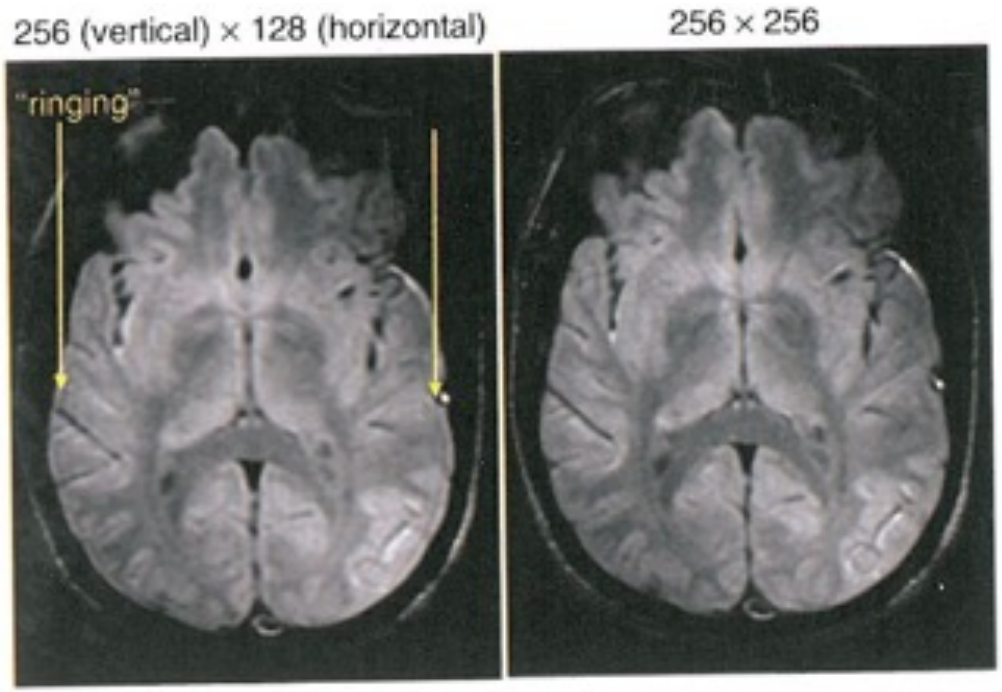
Ringing artefacts



■ FIGURE 13-37 Example of ringing artifacts caused by a sharp signal transition at the skull in a brain image for a 256 × 128 matrix (left) along the short (horizontal) axis, and the elimination of the artifact in a 256 × 256 matrix (right). The short axis defines the PEG direction.

Caused by insufficient sampling, could be reduced with a larger number of samples.

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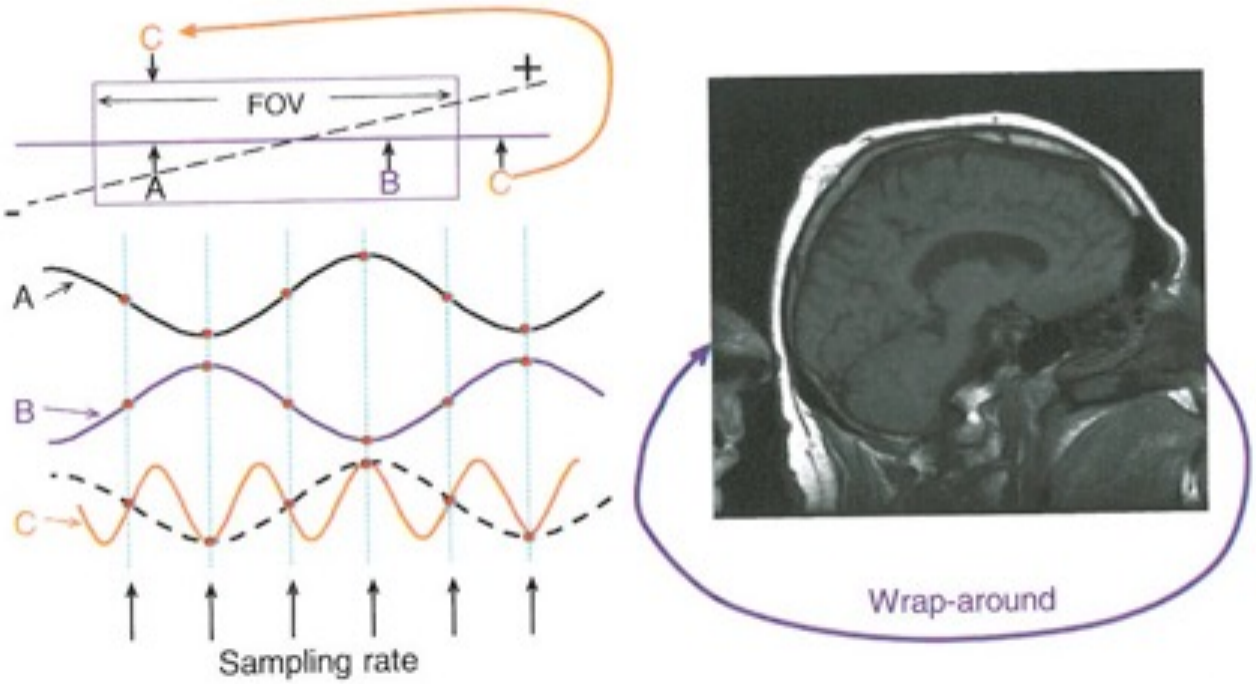
Wraparound artefacts



■ FIGURE 13-38 **Left.** Wraparound artifacts are caused by aliasing. Shown is a fixed sampling rate and net precessional frequencies occurring at position *A* and position *B* within the FOV that have identical frequencies but different phase. If signal from position *C* is at *twice* the frequency of *B* and insufficiently sampled, the same frequency and phase will be assigned to *C* as that assigned to *A*, and therefore will appear at that location. **Right.** A wrap-around artifact example displaces anatomy from one side of the image (or outside of the FOV) to the other side.

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Susceptibility artefacts

Any drastic change in the magnetic susceptibility will distort the magnetic field. Changes in susceptiblity like tissue-air interface, or metals (ferrous or not) may have a significant effect on the local tissues adjacent to changes in susceptibility. Can also be helpful, like diagnosing the age of a hemorrhage based on signal characteristics of the blood degeneration products

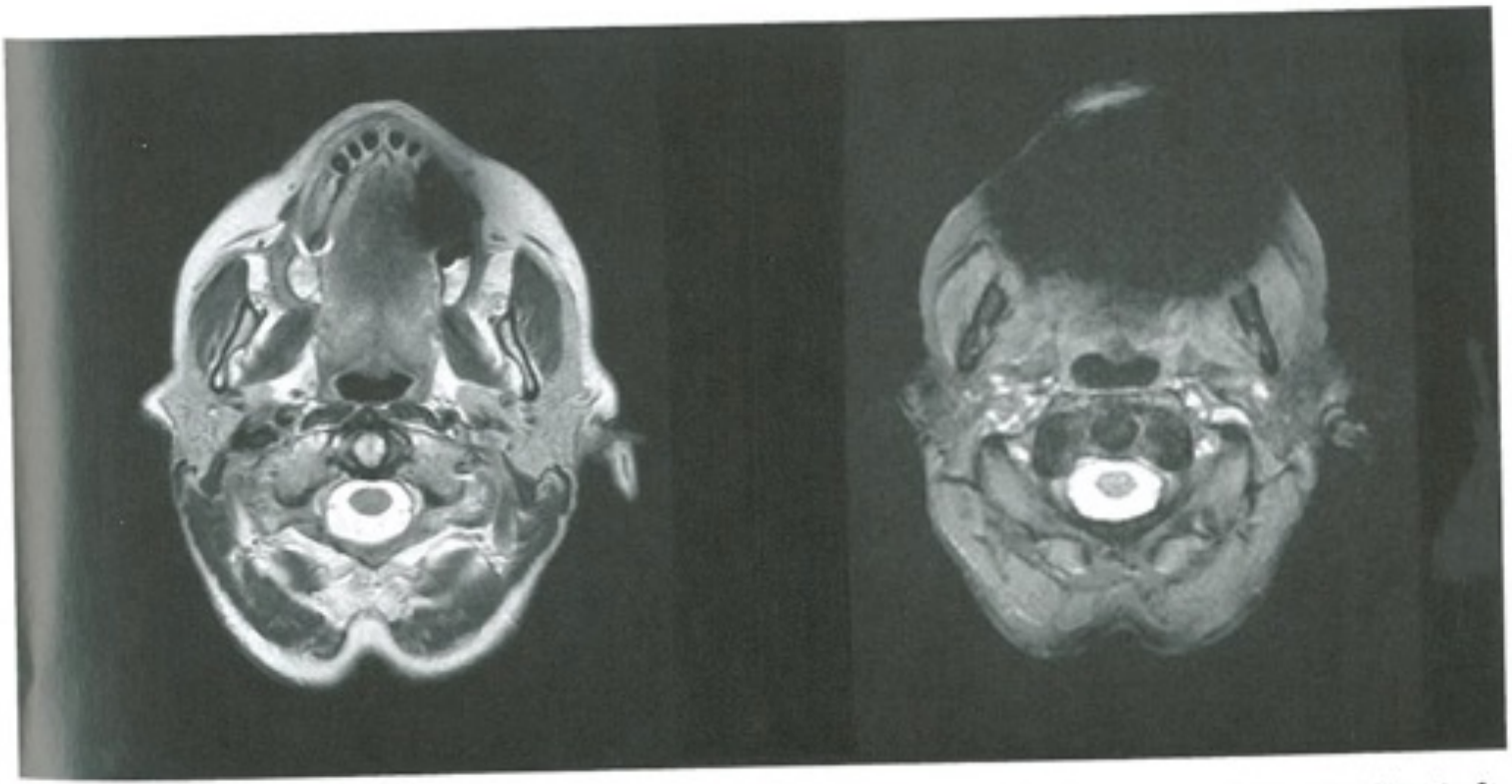

FIGURE 13-24 Susceptibility artifacts due to dental fillings are shown in the same axial image slice. **Left.** Axial T2-weighted fast spin echo image illustrates significant suppression of susceptibility artifacts with 180-degree refocusing pulse. **Right.** Axial T2*-weighted gradient echo image illustrates significant image void exacerbated by the gradient echo, where external inhomogeneities are not canceled in the reformed echo.

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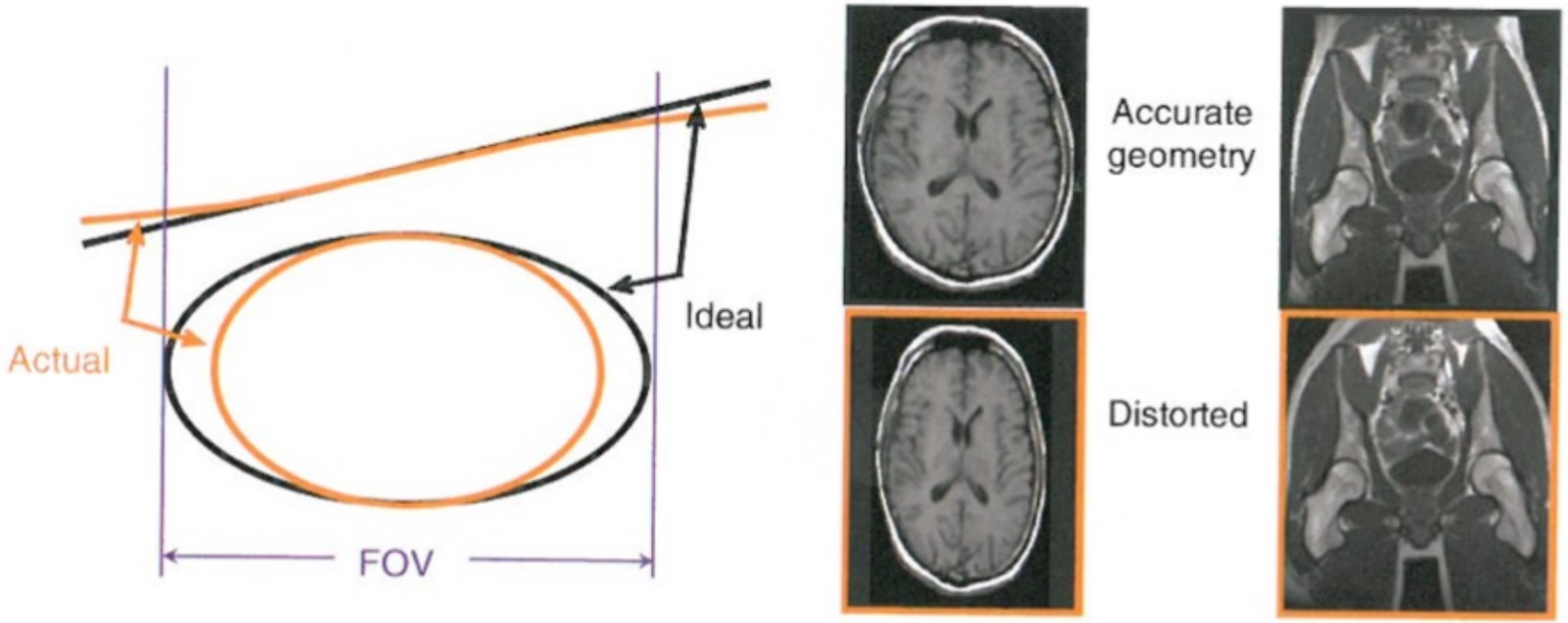
Gradient nonlinearity artefacts



■ **FIGURE 13-25** Gradient nonlinearity causes image distortions by mis-mapping anatomy. In the above examples, the strength of the gradient at the periphery is less than the ideal (*orange line* versus *black line*). This results in a compression of the imaged anatomy, with inaccurate geometry (images with *orange* border). For comparison, images acquired with linear corrections are shown above.

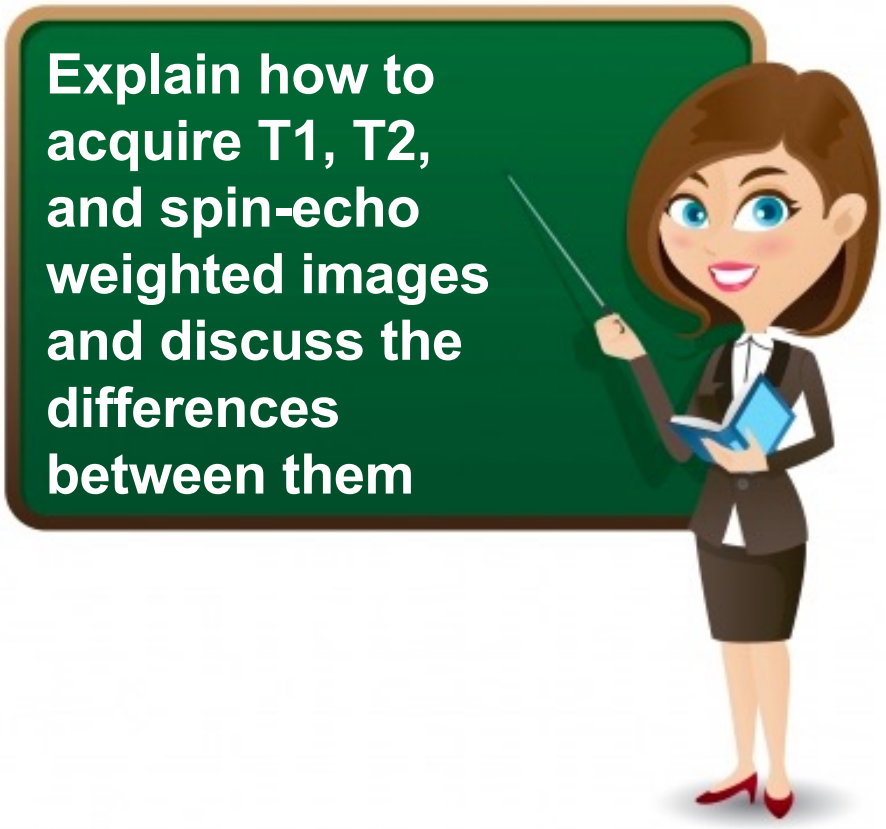
Any deviation or temporal instability in linear gradients will give a distortion. With gradient calibration and limitation of FOV (Lowering gradient field strength) or holding the gradient field strength and number of samples constant while decreasing the frequency bandwidth, minimize spatial distortion

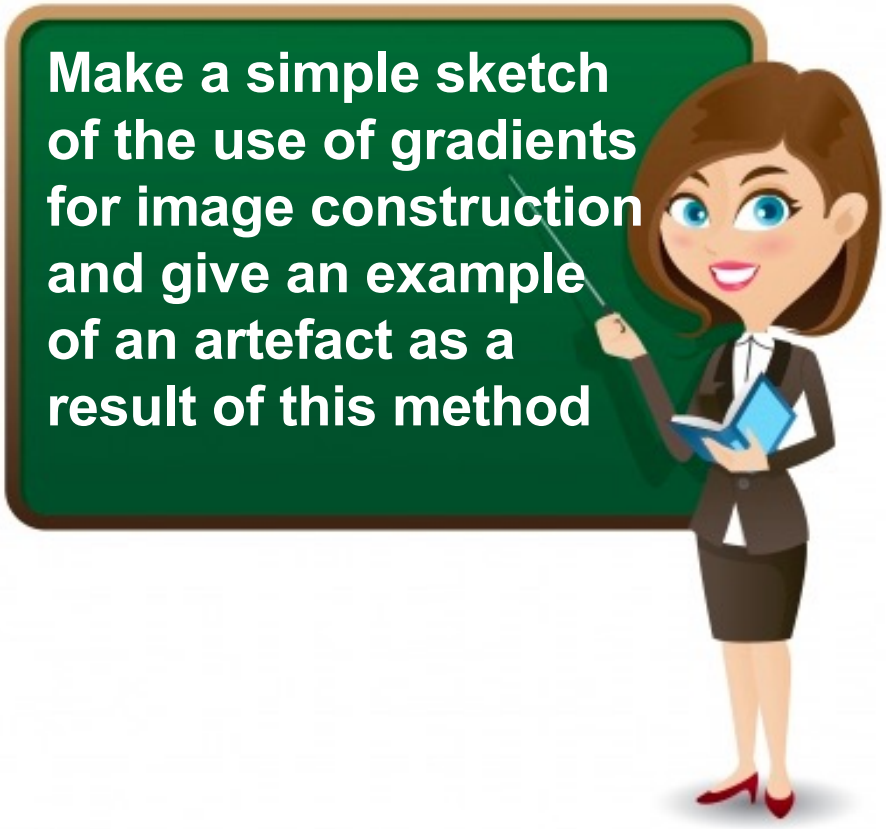
Adv/disadv MRI

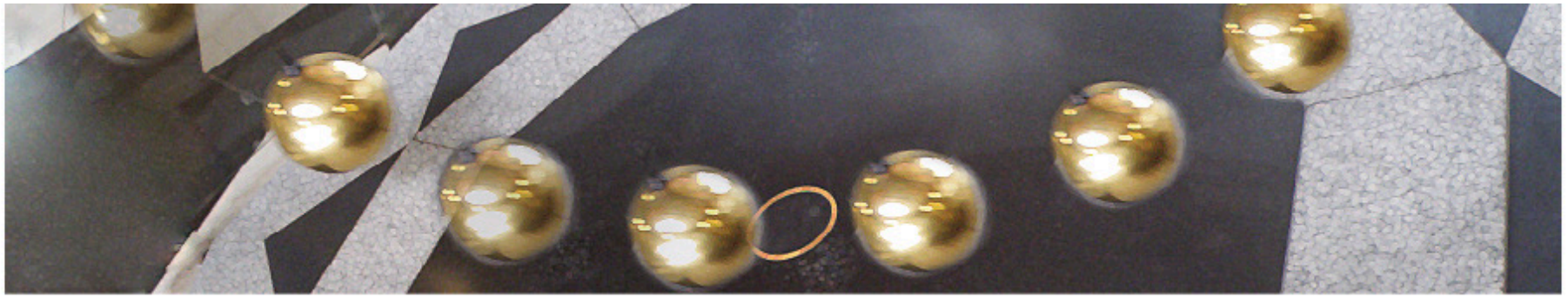
- Advantages
- No harmful radiation
- Soft tissue imaging
- High resolution images of T1 or T2 preferences

- Disadvantages
- Expensive, large installation with superconducting magnets++
- Very strong magnetic field
- Claustrophobic
- Not for frozen tissue
- Time consuming

Exercise examples







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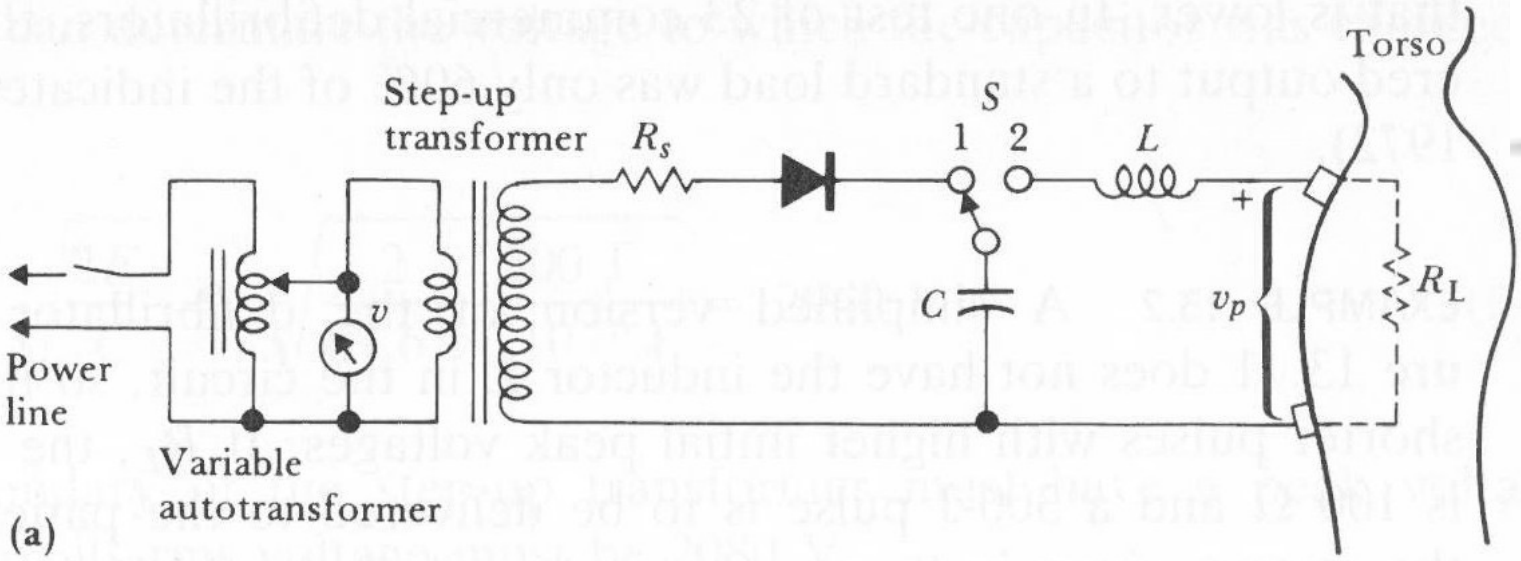
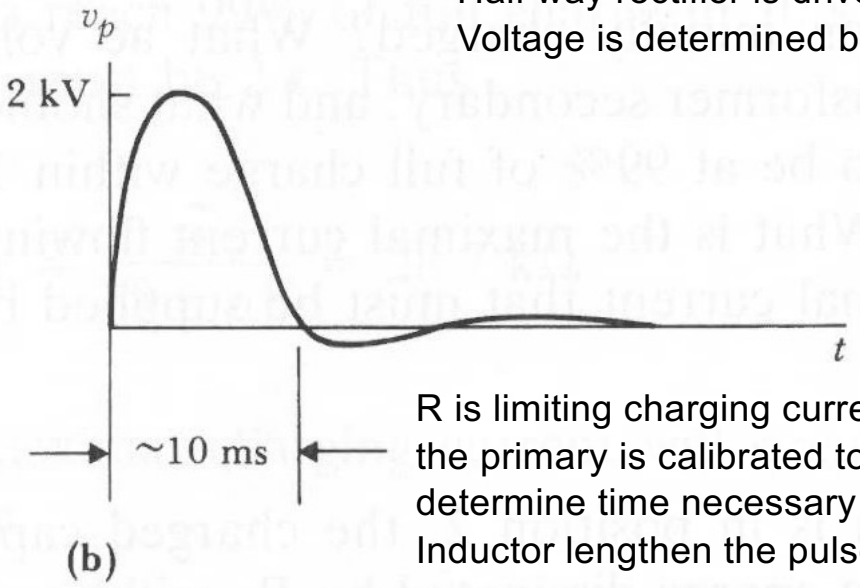
Lecture 15



Half way rectifier is driven by a step-up transformer to charge capacitor C.
Voltage is determined by a variable autotransformator in the primary circuit

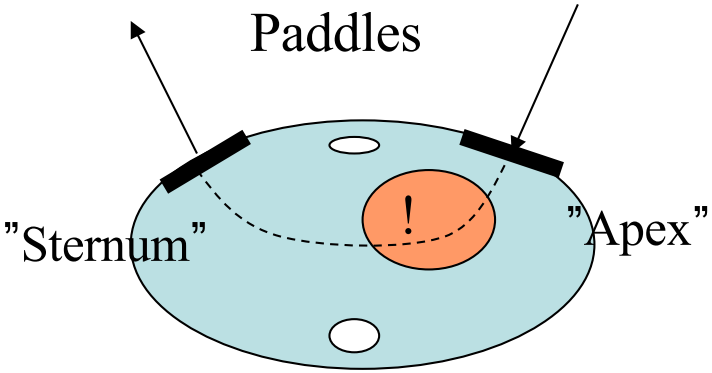
Apparatus

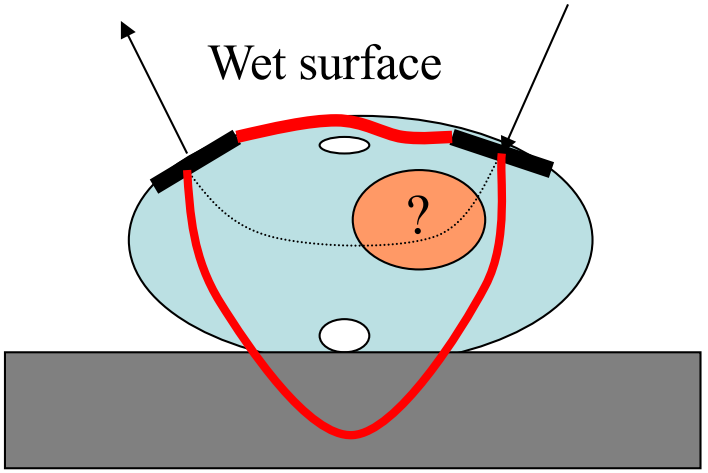


R is limiting charging current to protect circuit components, an AC voltmeter across the primary is calibrated to indicate energy stored in the capacitor. (Also helps to determine time necessary to achieve full charge on capacitor.).
Inductor lengthen the pulse, producing a waveshape.

Figure 13.11 (a) Basic circuit diagram for a capacitive-discharge type of cardiac defibrillator. (b) A typical waveform of the discharge pulse. The actual waveshape is strongly dependent on the values of L, C, and the torso resistance R_L.

Current pattern in the thoracic volume during defibrillation





Defibrillation, typical limits:

Current density 0,6A/cm^2 intracardial or energy 5 J/kg body weight

R_t: 20 - 200 ohm, I_m: 5- 60 A, V_m: 1000 - 6000 V

Ohms law: $V_m = R_t * I_m$

Internal and external electrodes

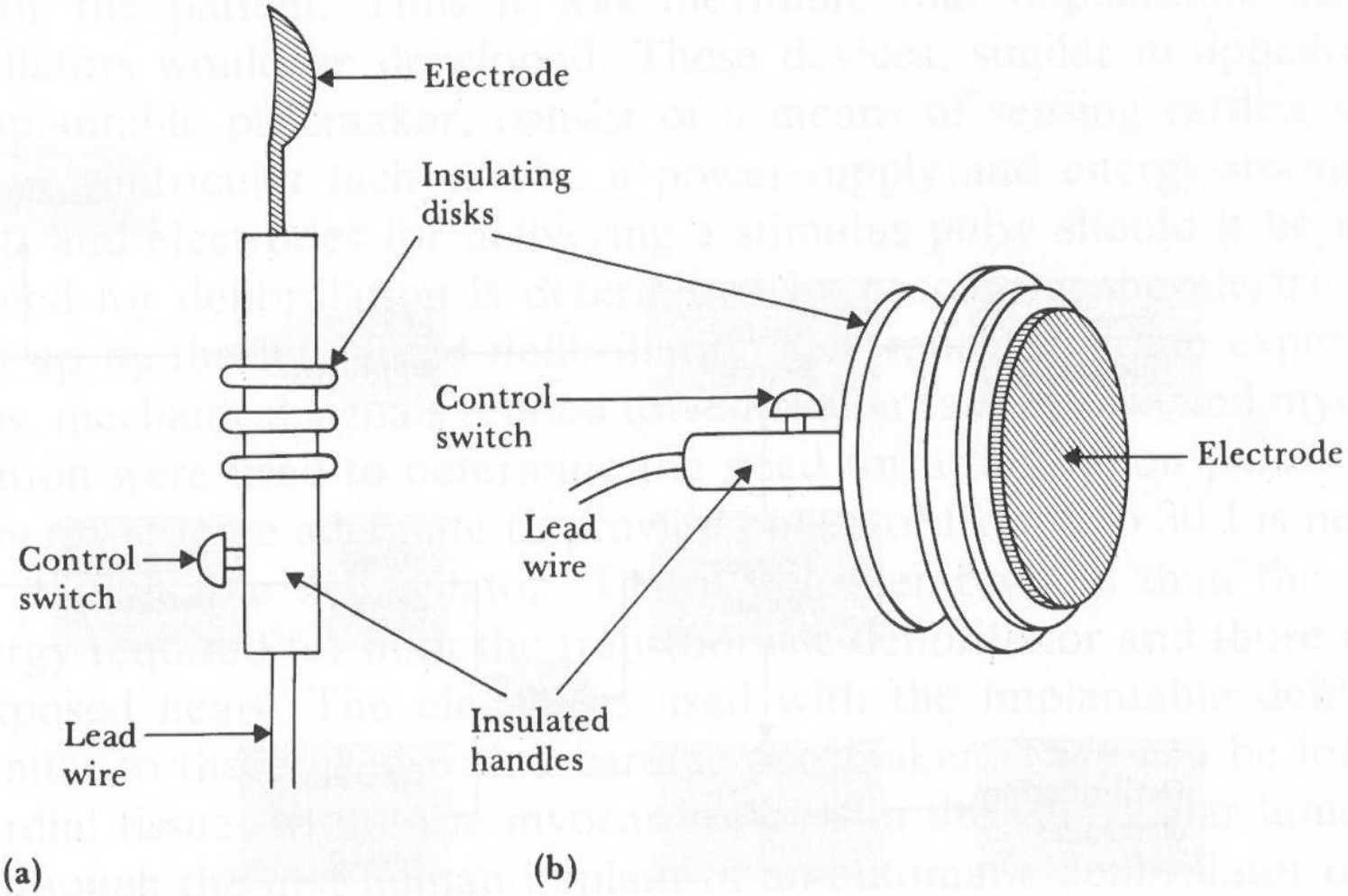
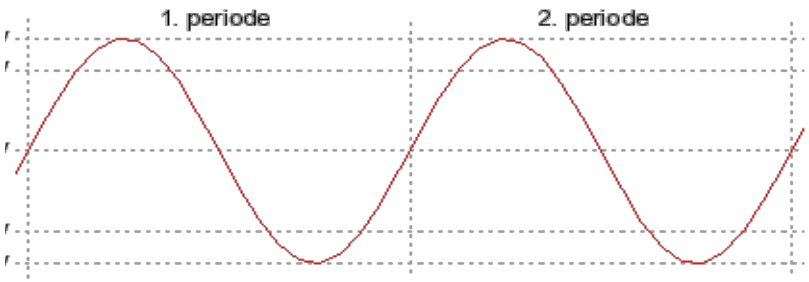


Figure 13.13 Electrodes used in cardiac defibrillation (a) A spoon-shaped internal electrode that is applied directly to the heart. (b) A paddle-type electrode that is applied against the anterior chest wall.

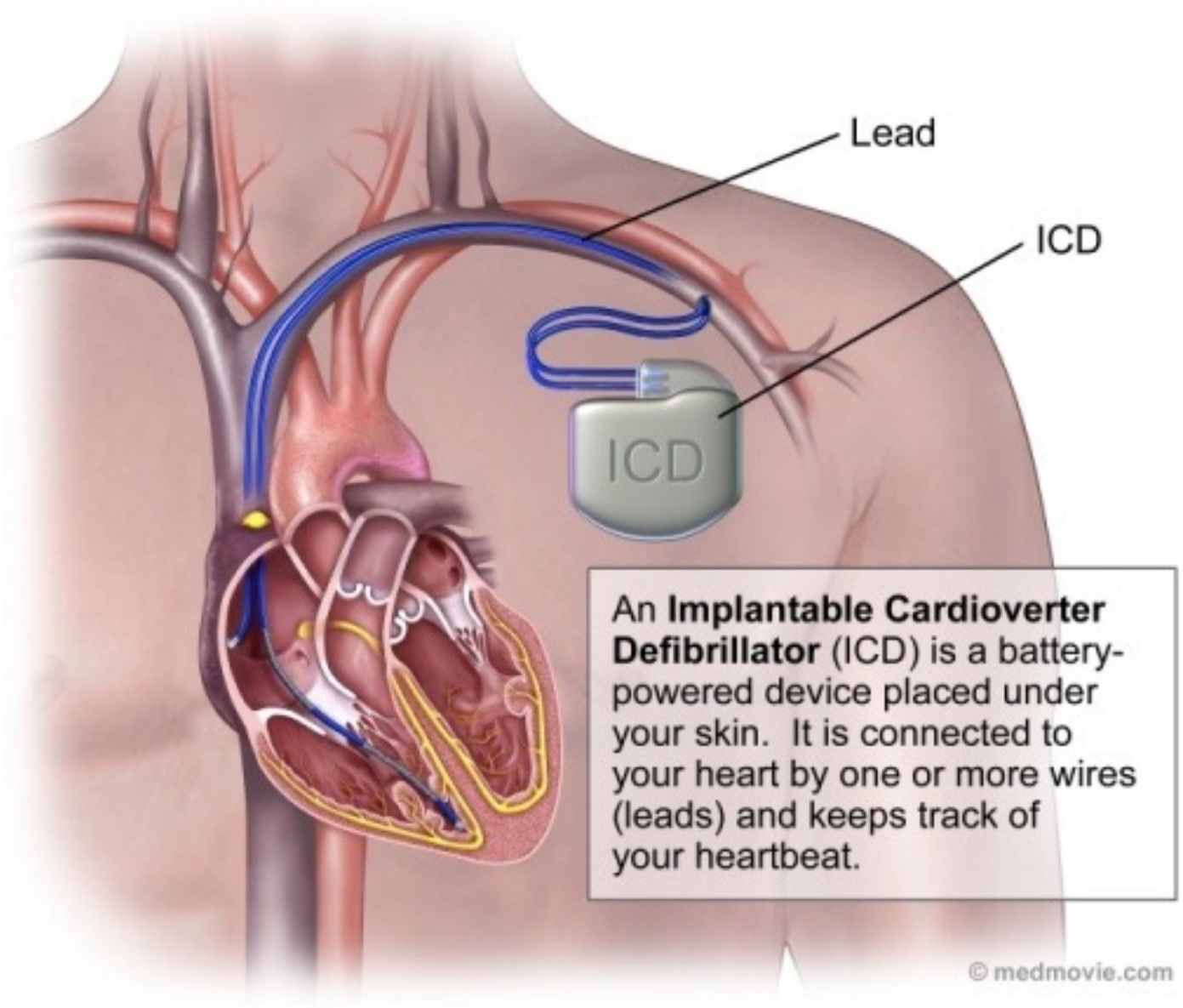
Biphasic defibrillator

- Turns the current path (one syclus = ca 10 ms)
- Less energy consumption -> less risk of fire damages and injuries in myocard
- Higher successrate (90% instead of 60% using monophasic defibrillation[1])



1. Heart Smarter: EMS Implications of the 2005 AHA Guidelines for ECC & CPR pp 15-16

Implantable Cardioverter Defibrillator (ICD)



Electro-conversion (synchronous defibrillation)

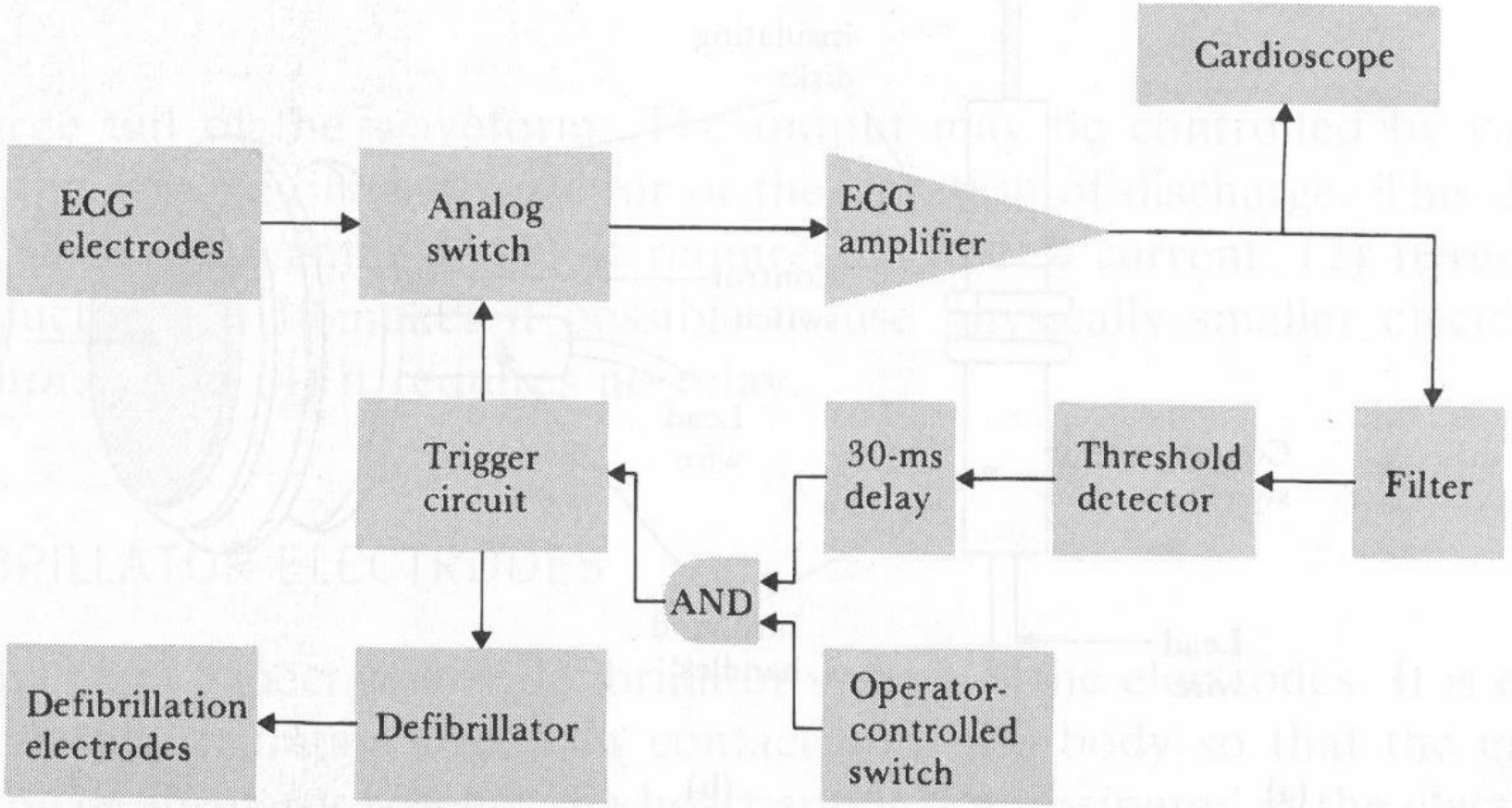


Figure 13.14 A cardioverter The defibrillation pulse in this case must be synchronized with the R wave of the ECG so that it is applied to a patient shortly after the occurrence of the R wave.

Gamma Camera

- A camera for nuclear imaging. The most used so far was invented by H. Anger in the 1960's (The Anger camera)

http://img.medicalexpo.com/images_me/photo-g/70717-3803791.jpg

Principle: The patients drinks a cocktail including a radioactive tracer bound to a sugarlike molecule. Cells with high consumption of energy (e.g. Cancerous cells) will take up more of the tracer than healthy tissue, this can be measured with a gamma camera

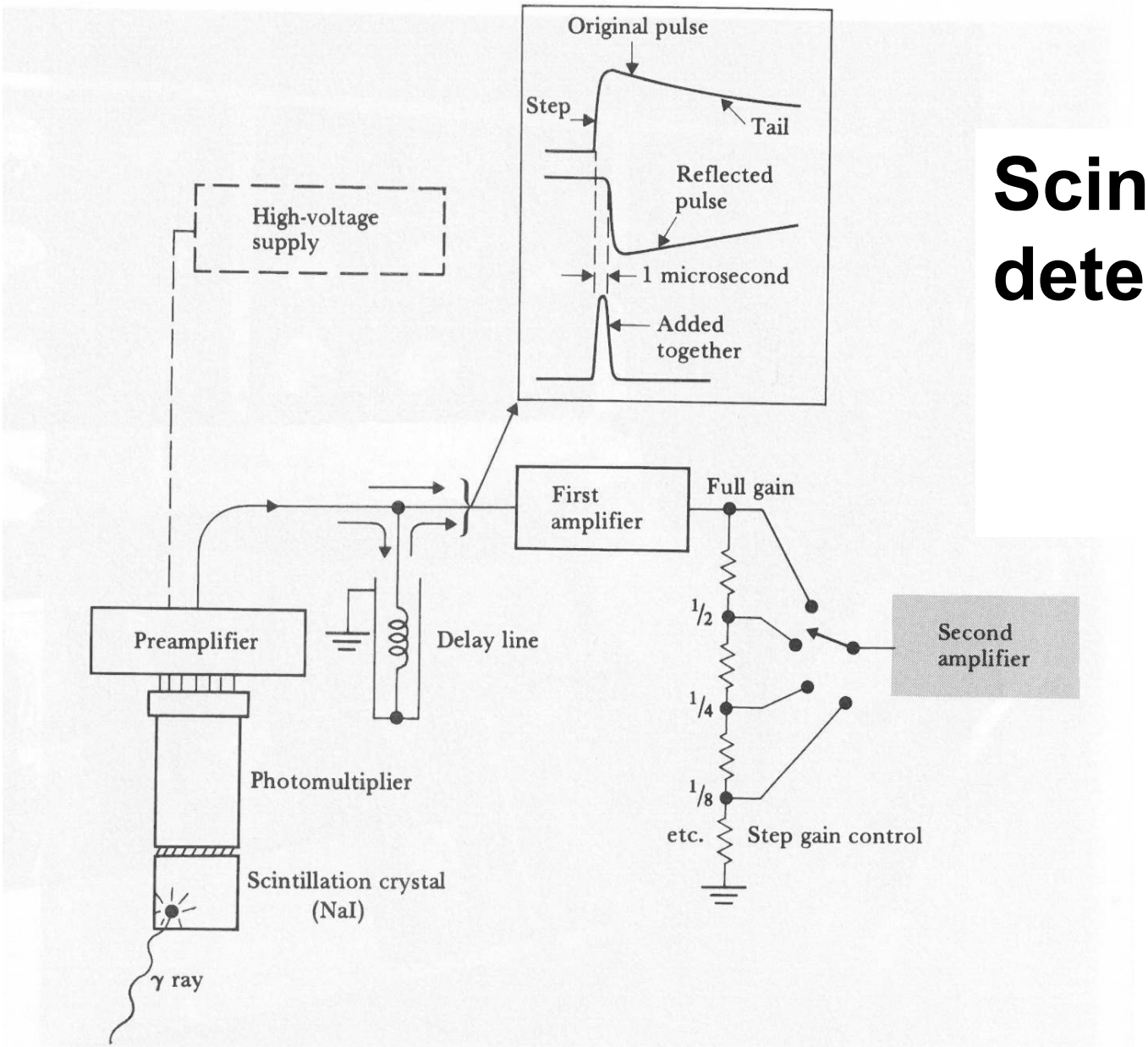
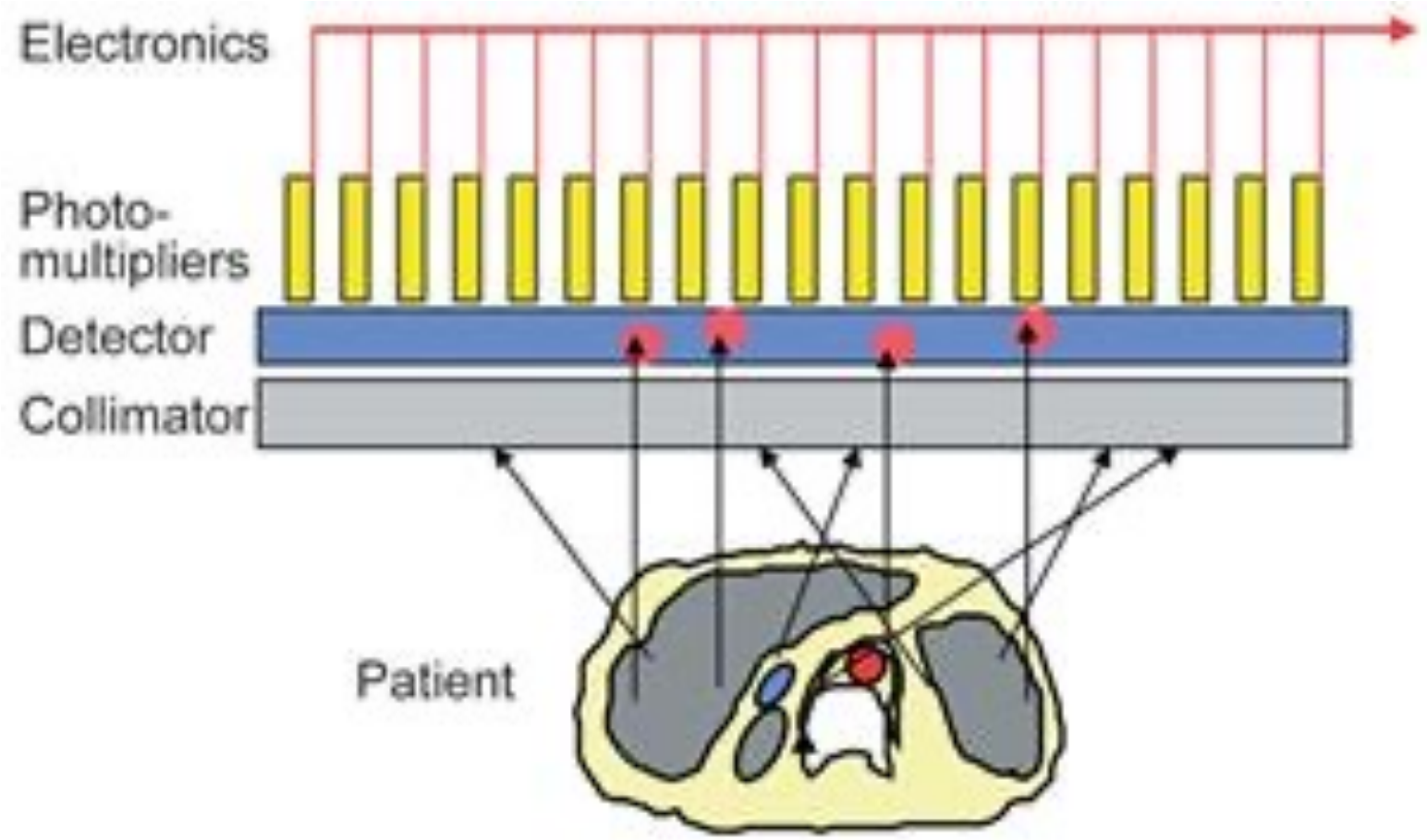


Figure 12.23 Basic implementation of a NaI scintillation detector, showing the scintillator, light-sensitive photomultiplier tube, and support electronics. (From H. N. Wagner, Jr., ed., *Principles of Nuclear Medicine*. Philadelphia: Saunders, 1968. Used with permission of W. B. Saunders Co.)

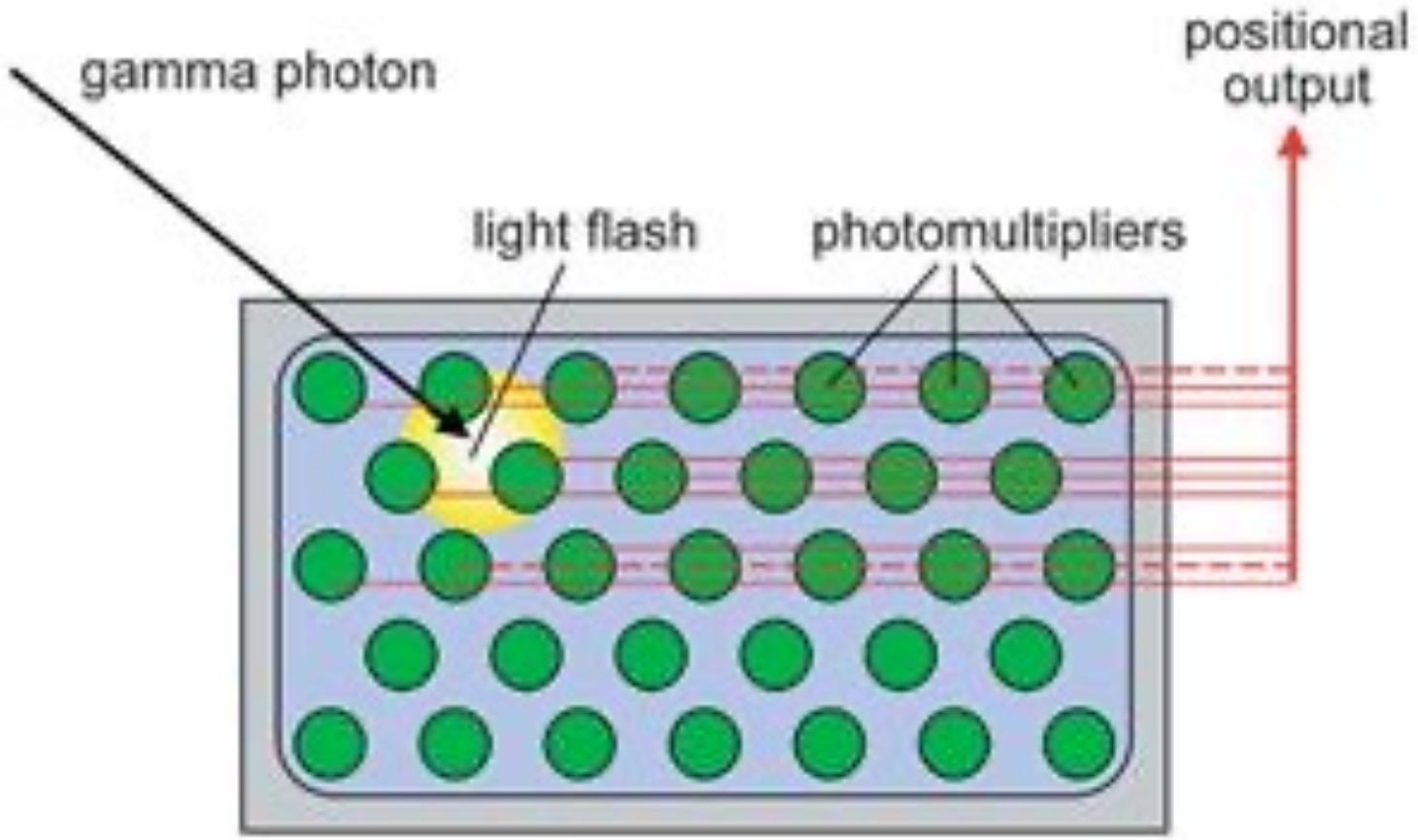
Scintillation-detector

Anger camera



Photons with a proper direction are let through the collimator, into the detector and photomultipliers

Anger Camera (cont.)



SPECT- imaging

Single photon emission computer tomography, systematic use of gamma camera

Image: GE Healtcare

Line spread and MTF

Response of a gamma camera to a line source of radioactivity. Line-spread function of camera was generated by summing over one dimensjon of the digital image aquired in nuclear-medicine computer -> Fourier transformed to generate modulation transfer function

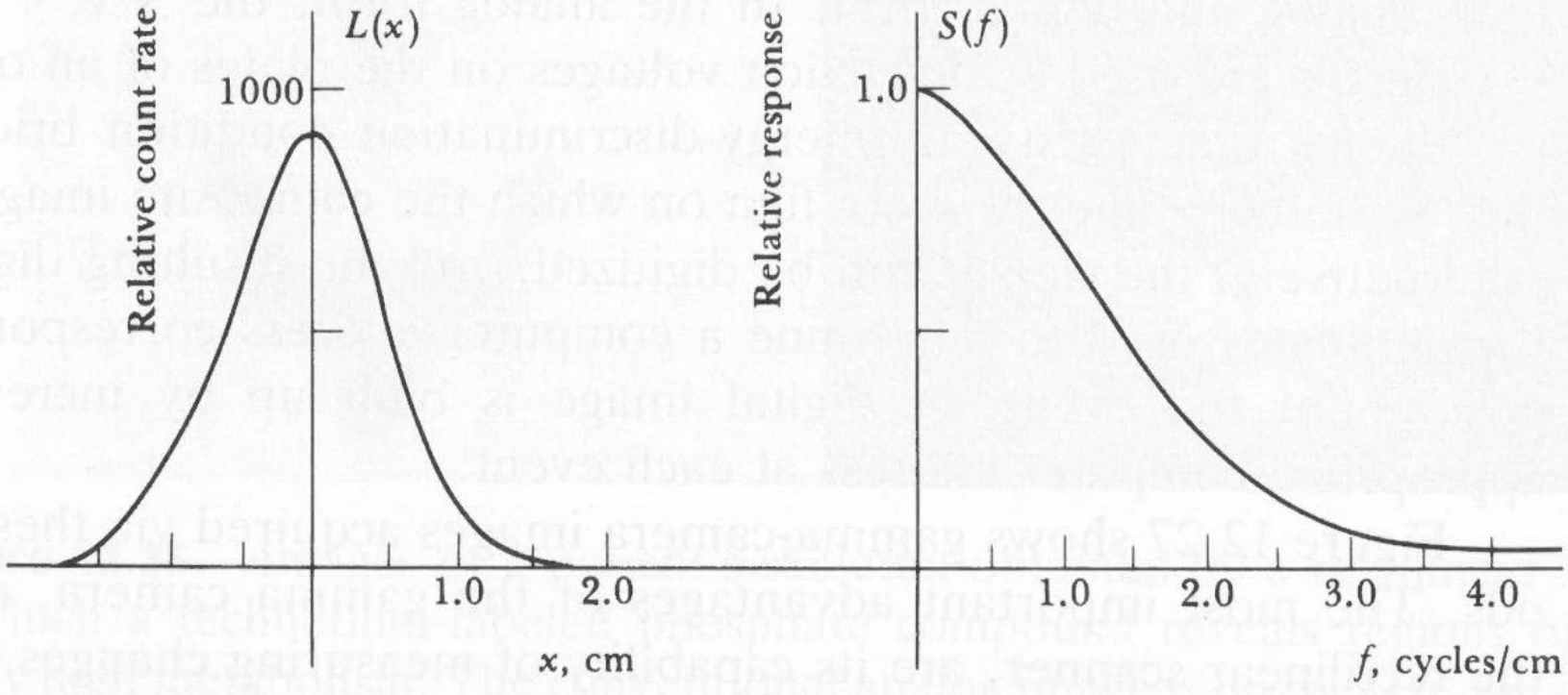


Figure 12.28 Line-spread response function obtained in a gamma camera under computer control, together with the corresponding modulation transfer function.

PET camera

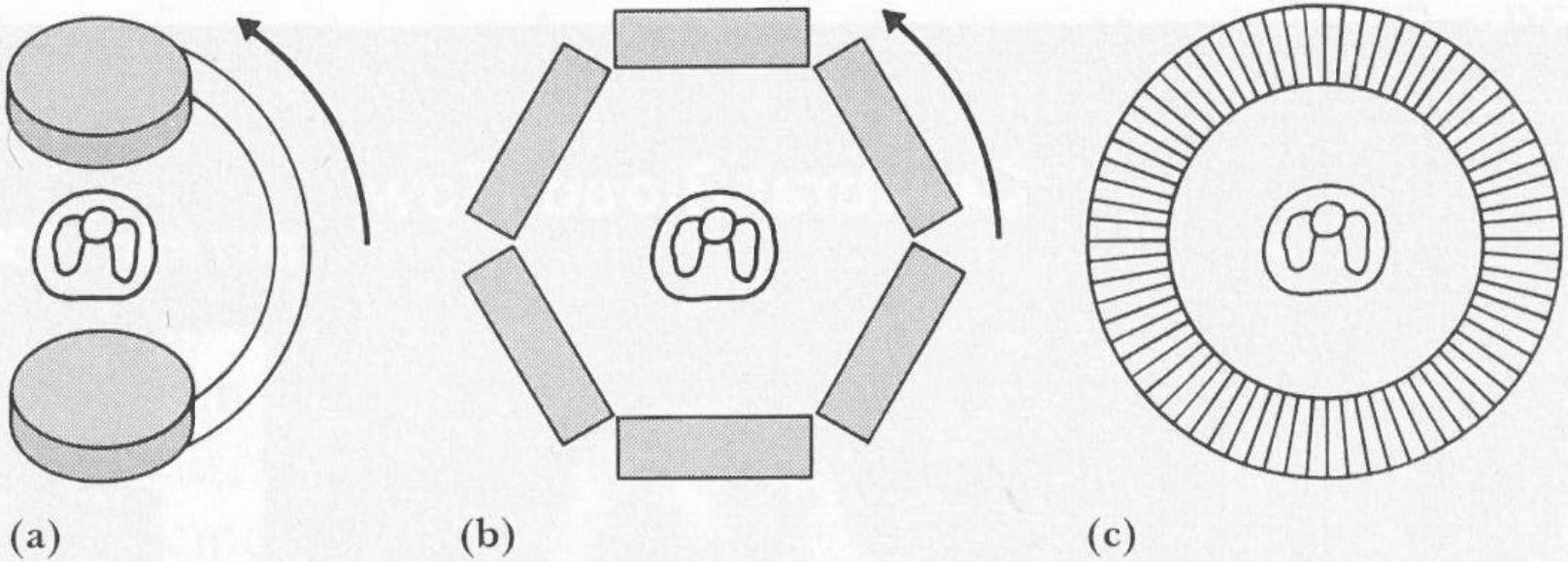
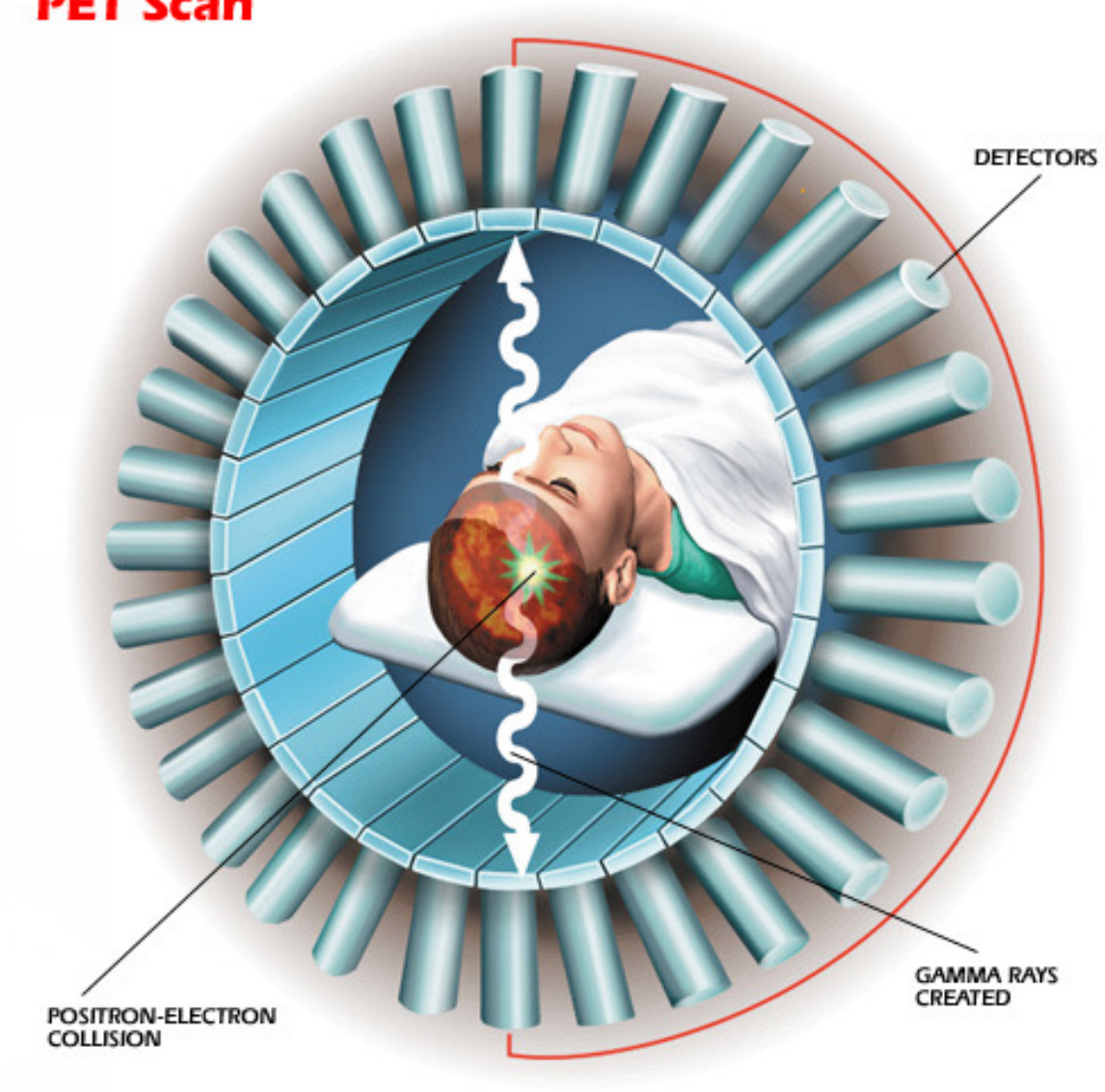


Figure 12.29 Evolution of the circular-ring PET camera (a) The paired (b) the hexagonal ring cameras rotate around the patient. (c) The circular assembly does not rotate but may move slightly—just enough to fill in the between the detectors. The solid-state detectors of the ring camera are integ with the collimator and are similar in construction to detectors used ir machines.

PET/CT scanners

Image: http://2nznub4x5d61ra4q12fyu67t.wpengine.netdna-cdn.com/img/4363ct1.jpg

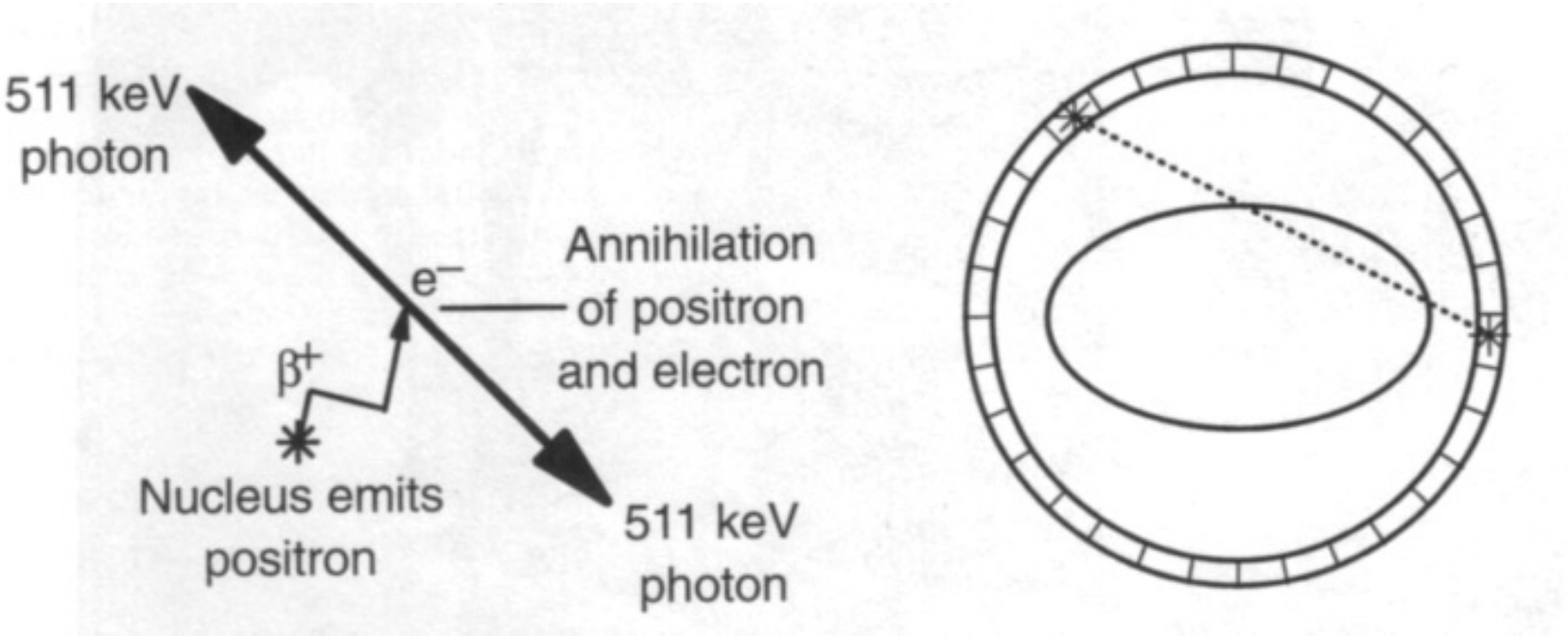
PET Scan



Measured quantity is concentration of positron emitter. To obtain actual concentration -> calibrate and measure the performance of the machine

Annihilation coincidence detection

- Emitted positrons lose their kinetic energy by causing excitation and ionization
- A positron that has lost most of the energy will interact with an electron by an ***annihilation***
- This annihilation will convert the mass of the electron-positron pair into two 511-keV photons, emitted in contrary directions


511 keV
photon
Annihilation
of positron
and electron
e⁻
β⁺
Nucleus emits
positron
511 keV
photon

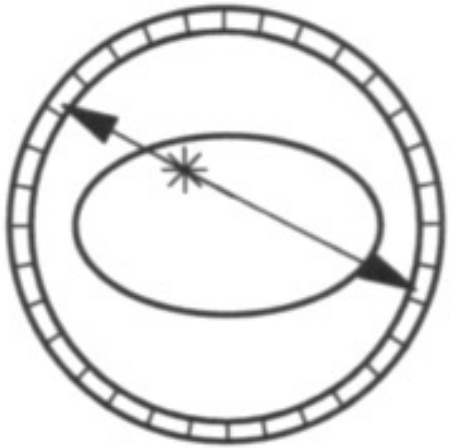
Annihilation coincidence detection

- If a simultaneous photon is registered in two different detectors, the annihilation came into being along a straight line between the two detectors (LOR). The electronics within a scanner detects the simultaneous hits in a process called annihilation coincidence detection
- When two simultaneous hits have been detected, a line between the two detectors is calculated

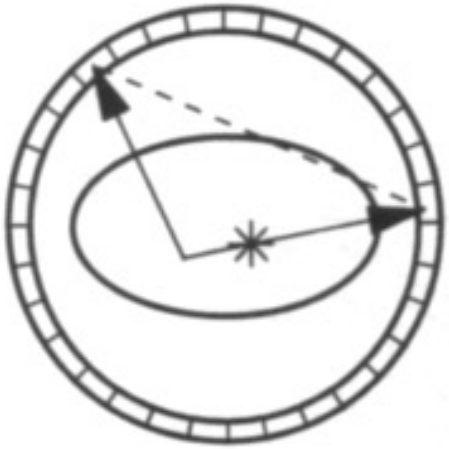
True, random, and scatter coincidences

- A *true coincidence* = detection is the result of a single nuclear annihilation
- A *random coincidence* = photons from different nuclear transformations are detected simultaneously at the detectors. May give erroneous results.
- A *scatter coincidence* = one or both photons from a single annihilation are scattered in different directions but still detected in the detector

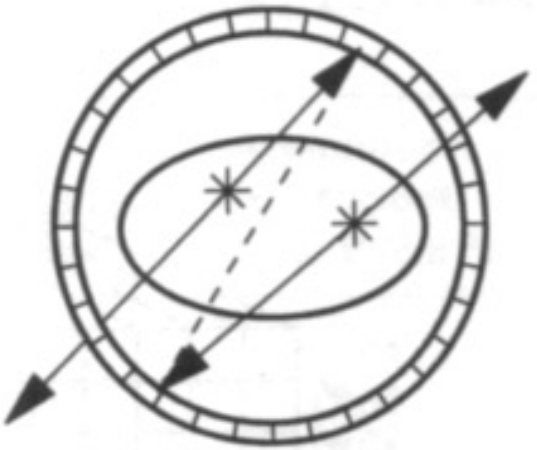
True



Scattered

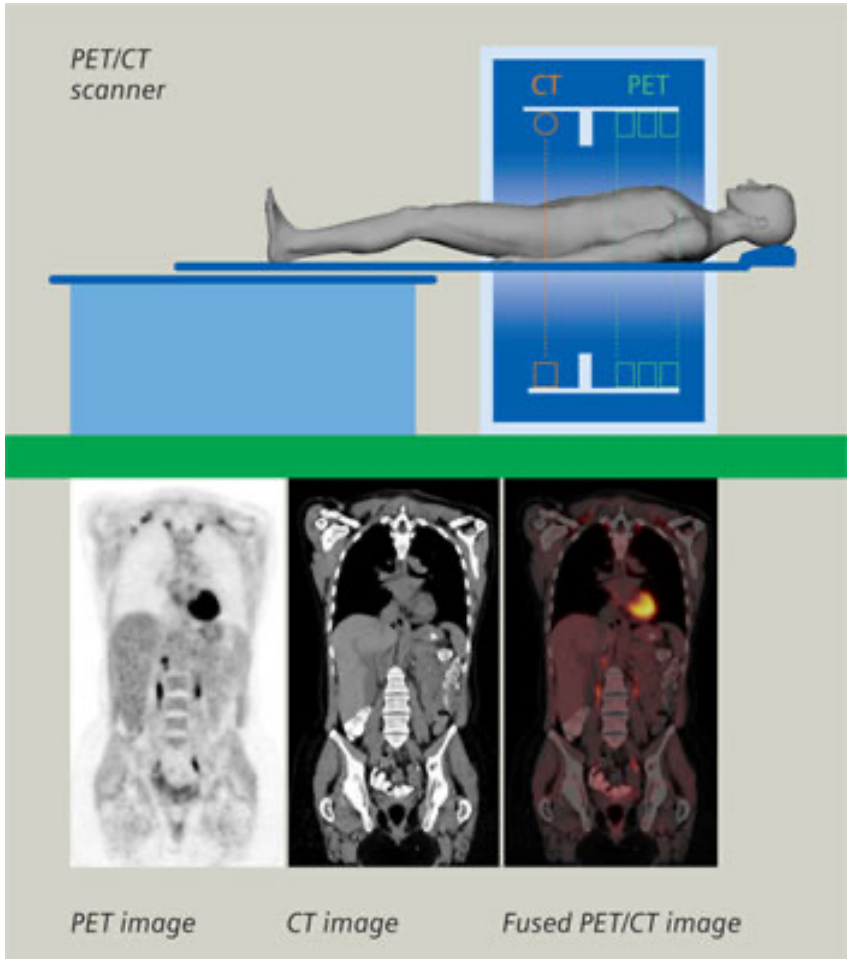


Random

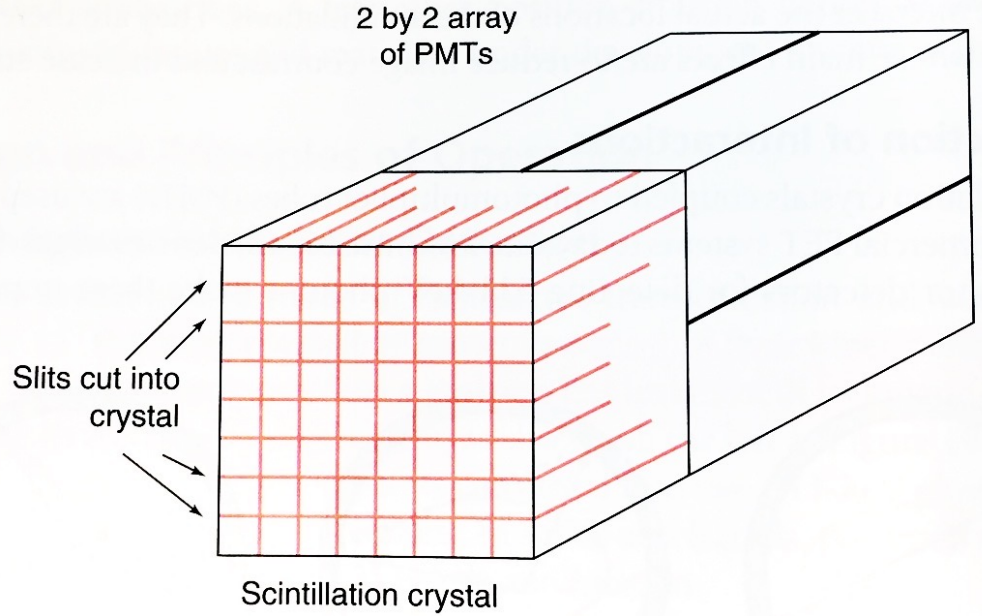


PET-CT

- Usually combined with CT in order to localize activity in the body



Scintillation crystals and photomultiplier tubes

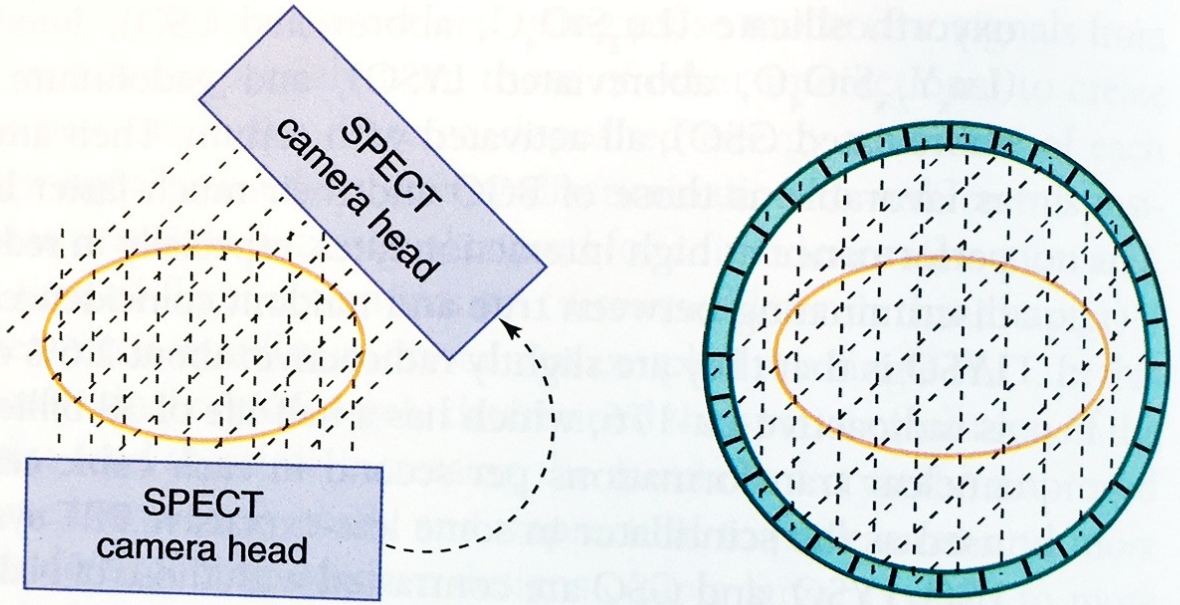


■ **FIGURE 19-17** A technique for coupling scintillation crystals to photomultiplier tubes (PMTs). The relative heights of the pulses from the four PMTs are used to determine the position of each interaction in the crystal. The thick (2 to 3 cm) crystal is necessary to provide a reasonable detection efficiency for the 511-keV annihilation photons. The slits cut in the scintillation crystal form light pipes, limiting the spread of light from interactions in the front portion of the crystal, which otherwise would reduce the spatial resolution. This design permits four PMTs to serve 64 detector elements.

Source: Bushberg et al. The essential physics of Medical Imaging (2012)

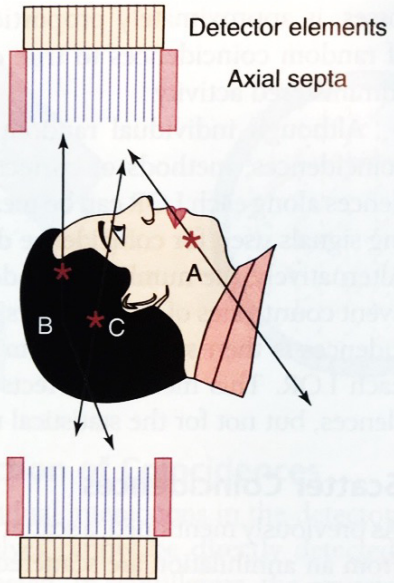
SPECT vs PET scanner systems

■ **FIGURE 19-18** Acquisition of projection data by a SPECT system (**left**) and a PET system (**right**), showing how each system collects data for two projections. However, the PET system collects data for all projections simultaneously, whereas the scintillation camera head of the SPECT system must move to collect data from each projection angle.

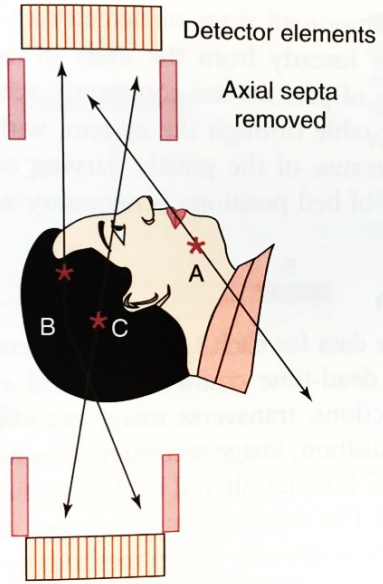


Source: Bushberg et al. The essential physics of Medical Imaging (2012)
Source: Bushberg et al. The essential physics of Medical Imaging (2012)

2D vs 3D PET scanner



■ **FIGURE 19-19** Side view of PET scanner illustrating two-dimensional data acquisition. The axial septa prevent photons from activity outside the field-of-view (**A**) and most scattered photons (**B**) from causing counts in the detectors. However, many valid photon pairs (**C**) are also absorbed.



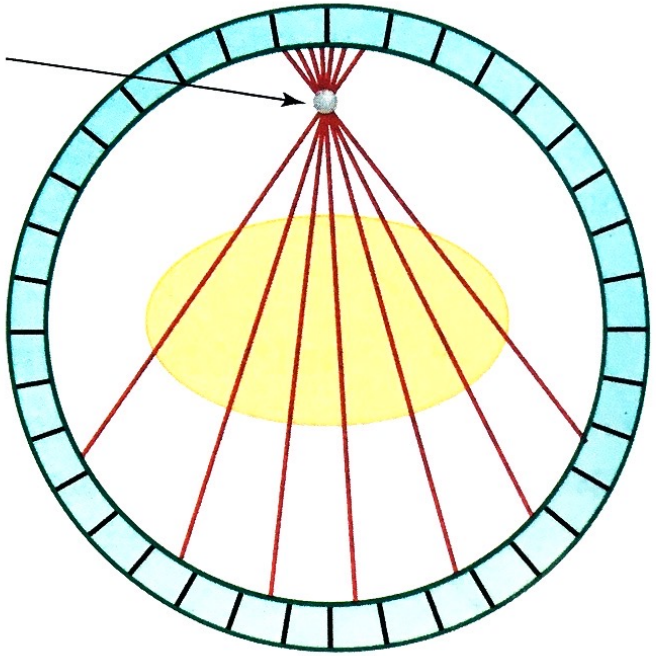
■ **FIGURE 19-21** Side view of PET scanner illustrating three-dimensional data acquisition. Without axial septa, interactions from activity outside the FOV (**A**) and scattered photons (**B**) are greatly increased, increasing the dead time, random coincidence fraction, and scatter coincidence fraction. However, the number of true coincidences (**C**) detected is also greatly increased.

Source: Bushberg et al. The essential physics of Medical Imaging (2012)

Some of the photons are lost on the way to the detectors, this is depending on the tissue they are penetrating. How can we correct for this?

Attenuation correction

■ **FIGURE 19-26** Rod source for attenuation correction in a dedicated PET system.



Attenuation coefficient for 511-keV annihilation photons in soft tissue is lower than photons emitted by most radionuclides, but the average path length for both to escape is much longer = Higher loss in PET

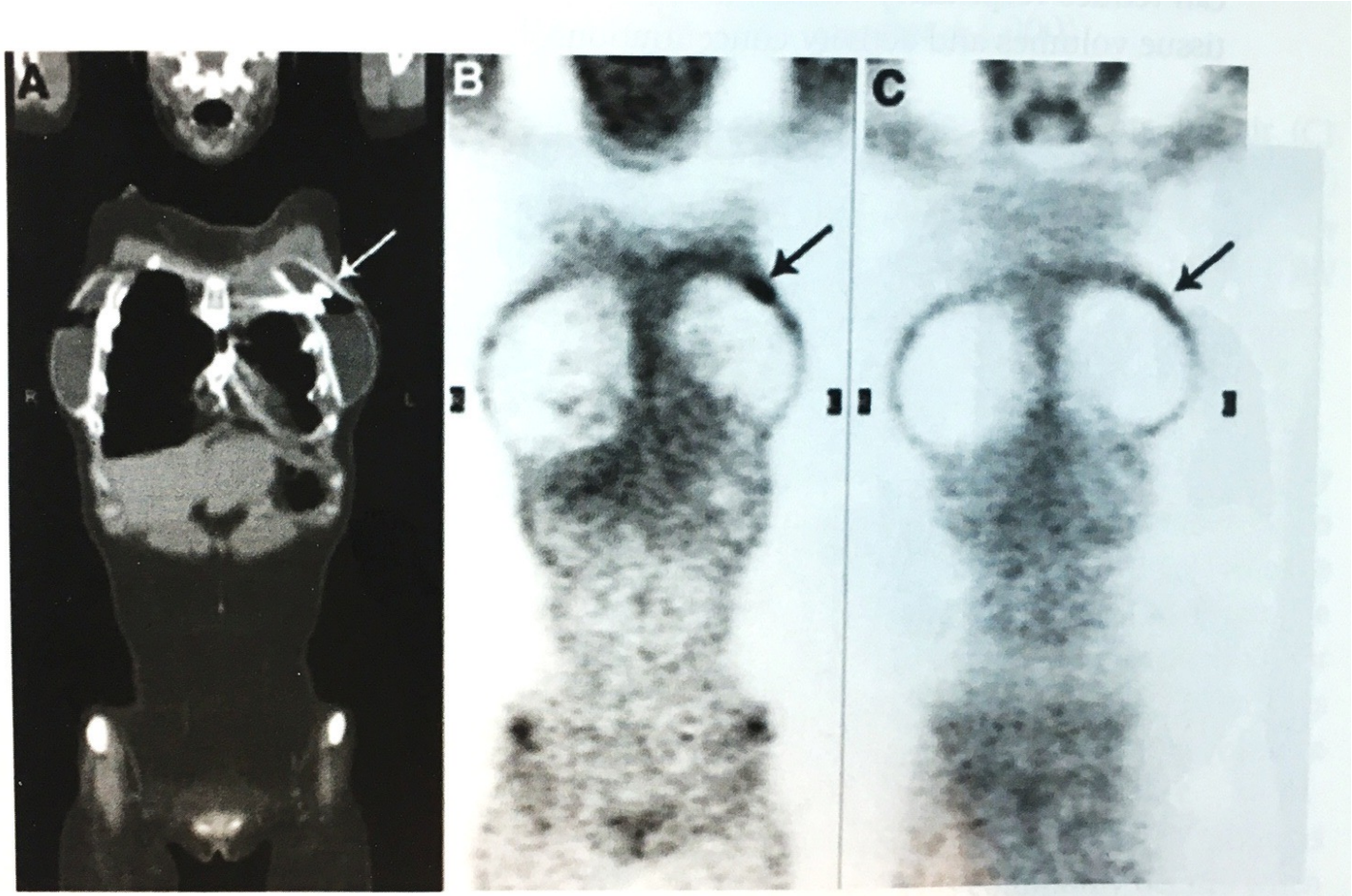
LOR = Line of radiation

Disadvantages – Increased imaging time
-Slightly increased dose
-Increased spatial noise
-Patient movement can give spatial misregistration between attenuation map and emission data when not aquired simultaneously

Today, CT is used for attenuation correction

Source: Bushberg et al. The essential physics of Medical Imaging (2012)

Attenuation correction



■ **FIGURE 19-29** Attenuation correction artifact caused by overestimation of attenuation by a metal object, in this case a body piercing. CT image (**A**) shows a streaking artifact at the location of the metal object on the left breast. Overestimation of attenuation causes the attenuation-corrected PET image (**B**) to display a falsely elevated concentration of F-18 FDG at the location of the metal object. Notice that that concentration of F-18 FDG is not elevated in the PET image (**C**) that is not attenuation corrected. (Images courtesy of Sureshbabu W,

Source: Bushberg et al. The essential physics of Medical Imaging (2012)

Comparison of SPECT and PET

Source: Bushberg et al. The essential physics of Medical Imaging (

TABLE 19-5 COMPARISON OF SPECT AND PET

	SPECT	PET
Principle of projection data collection	Collimation.	Annihilation coincidence detection (ACD).
Transverse image reconstruction	Iterative methods or filtered backprojection.	Iterative methods or filtered backprojection.
Radionuclides	Any emitting x rays, gamma rays, or annihilation photons. Optimal performance for photon energies of 100–200 keV.	Positron emitters only.
Spatial resolution	Depends upon collimator and camera orbit. Within a transaxial image, the resolution in the radial direction is relatively uniform, but the tangential resolution is degraded toward the center. Typically about 10 mm FWHM at center for a 30 cm diameter orbit and ^{99m}Tc. Larger camera orbits produce worse resolution.	Relatively constant across transaxial image, best at center. Typically 4.5–5 mm FWHM at center.
Attenuation	Attenuation less severe. Radioactive attenuation correction sources or x-ray CT can correct for attenuation.	Attenuation more severe. Radioactive attenuation correction sources or x-ray CT can correct for attenuation.

http://www.ucl.ac.uk/nuclear-medicine/referrers/petmr/PETMRschematic.png

PET-MRI

Disadvantages with PET-CT

a. High dose
b. Sequential (no simultaneous acquistion)

Advantages with PET-MR

a. No extra dose
b. Soft tissue imaging
c. Functional imaging

Main problem with PET-MR: Photomultiplier tubes in the PET are sensitive to magnetic fields

Solution:

a. Two scanners in series
b. Integration of PET-hardware into the MRI-gantry

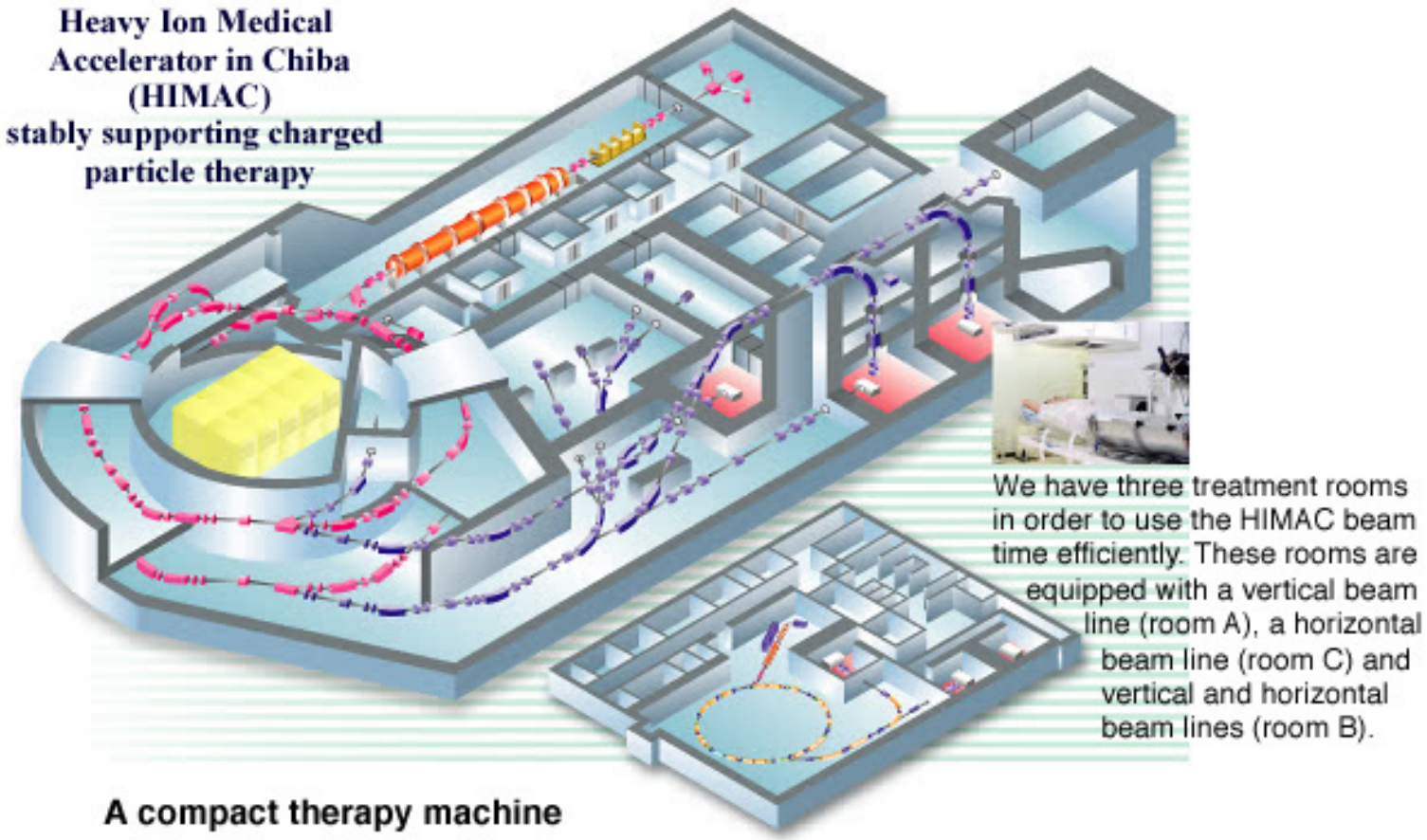
http://www.ucl.ac.uk/nuclear-medicine/referrers/petmr/PETMRschematic.png

PET-MRI

This technology has been available since 2011 (Siemens Biograph mMR), why has it not succeded yet?

a. No attenuation correction, difficult to calculate attenuation coefficients
b. Long time scans compared to PET-CT due to long MR-sequences
c. Expensive
d. Need MRI-compatible detectors instead of photomultipliertubes, more complicated, costly maintenance

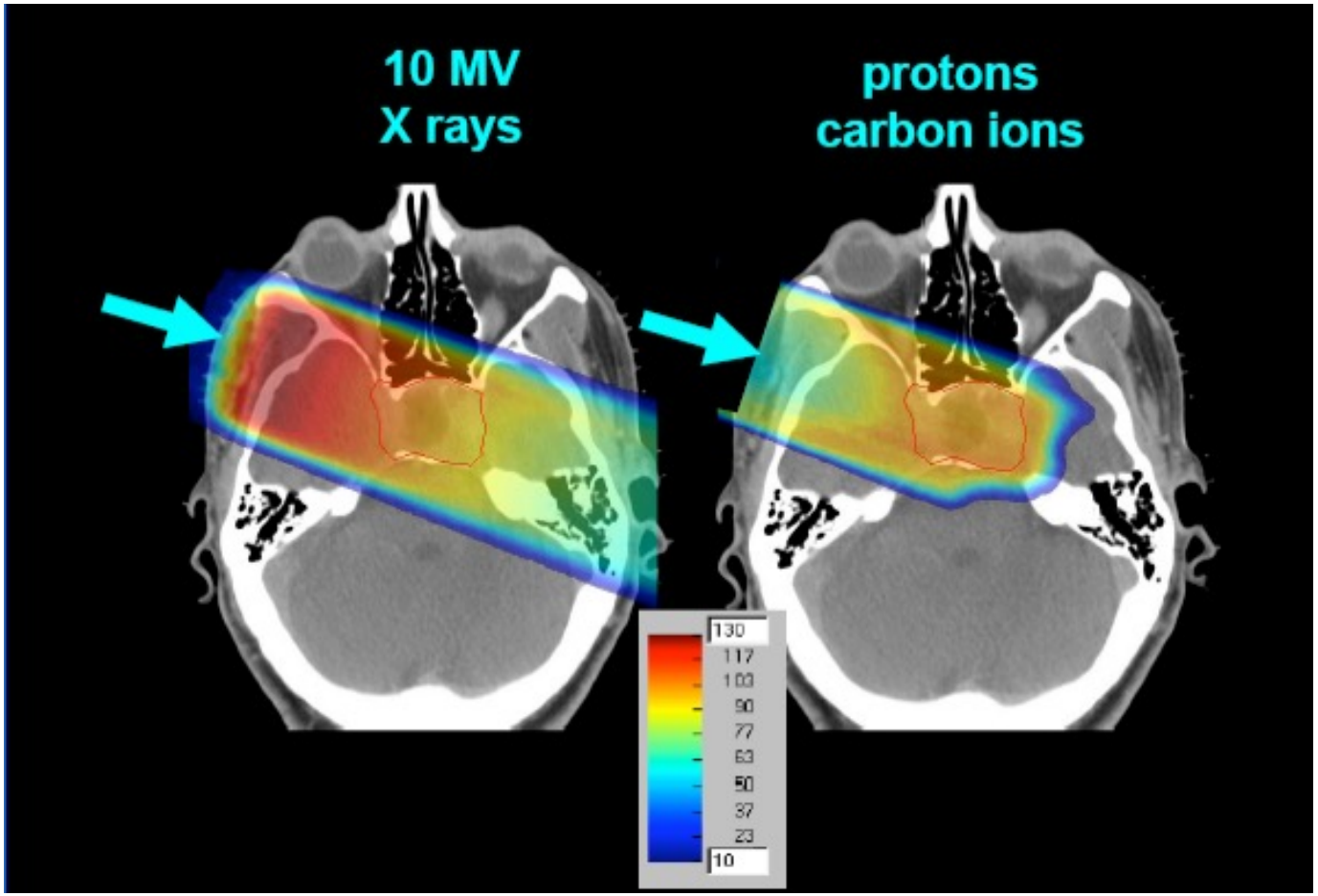
Non-invasive surgery



Kilde: NIRS, Chiba, Japan

Non-invasive surgery

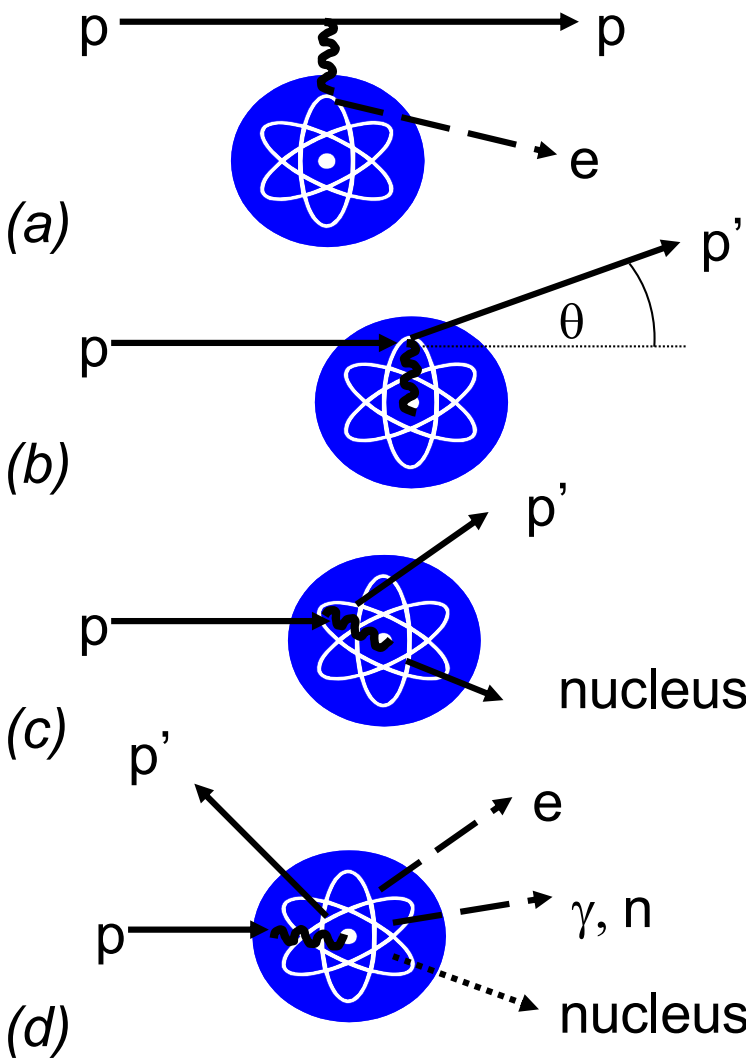
Better dose distribution to the tumor



Source: Magne Guttormsen, Fysisk Institutt, UIO

Proton interactions

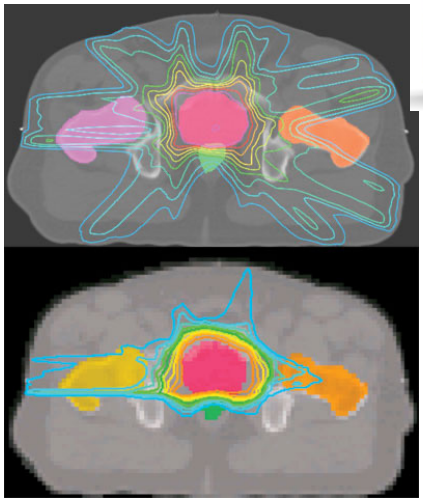
- Electron interactions (*a*)
  - Ionization
  - Excitation
- Nuclear interactions (*b*-*d*)
  - Multiple Coulomb scattering (*b*), small q
  - Elastic nuclear collision (*c*), large q
  - Nonelastic nuclear interaction (*d*)



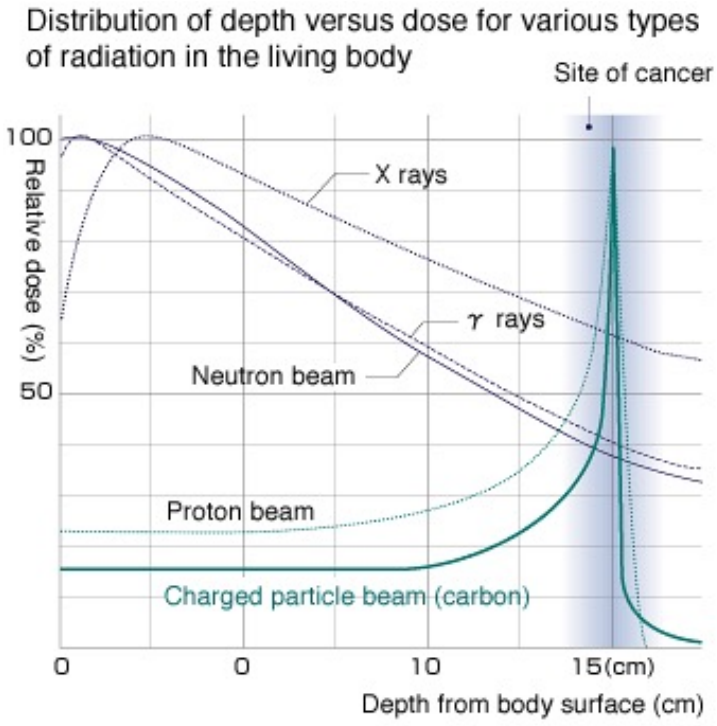
UiO : Department of Physics
University of Oslo

Non-invasive surgery

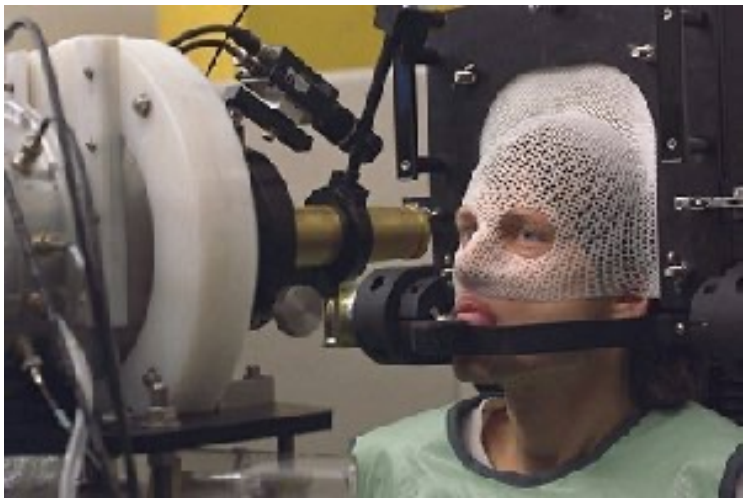
Heavy ion therapy (Proton-terapi)



http://www.nature.com/nature/journal/v449/n7159/box/449133a_BX1.html



Kilde: NIRS, Chiba, Japan



http://www.triumf.info/public/about/virtual_tour.php?section=3&single=18

The ionization density (number of ions per unit of path length) produced by a fast charged particle along its track increases as the particle slows down. It eventually reaches a maximum called the Bragg peak close to the end of its trajectory. After that, the ionization density dwindles quickly to insignificance. In fact, the ionization density follows closely the LET

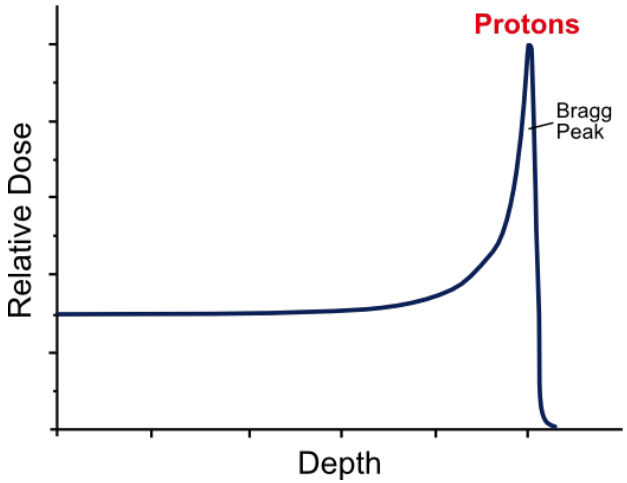
The Bragg Peak

- A moving particle will loose energy according to the Bethe Bloch formula

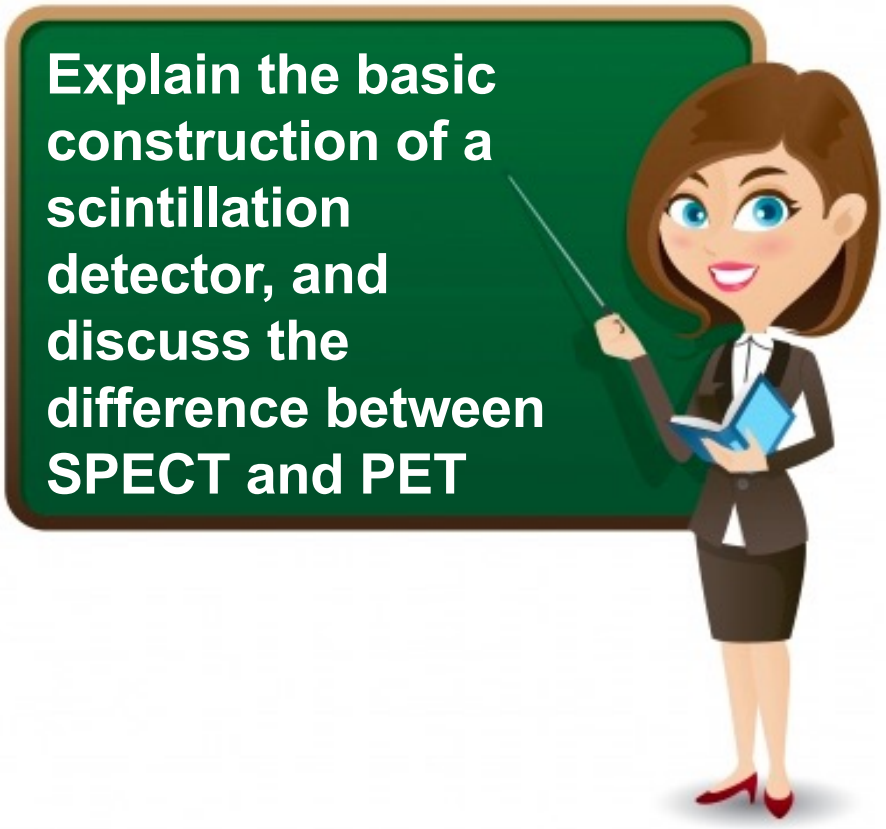
$$-\frac{\mathrm{d}E}{\mathrm{d}x} = \frac{4\pi n z^2}{m_e c^2 \beta^2} \cdot \left(\frac{e^2}{4\pi\epsilon_0}\right)^2 \cdot \left[\ln\left(\frac{2m_e c^2 \beta^2}{I \cdot (1-\beta^2)}\right) - \beta^2\right]$$

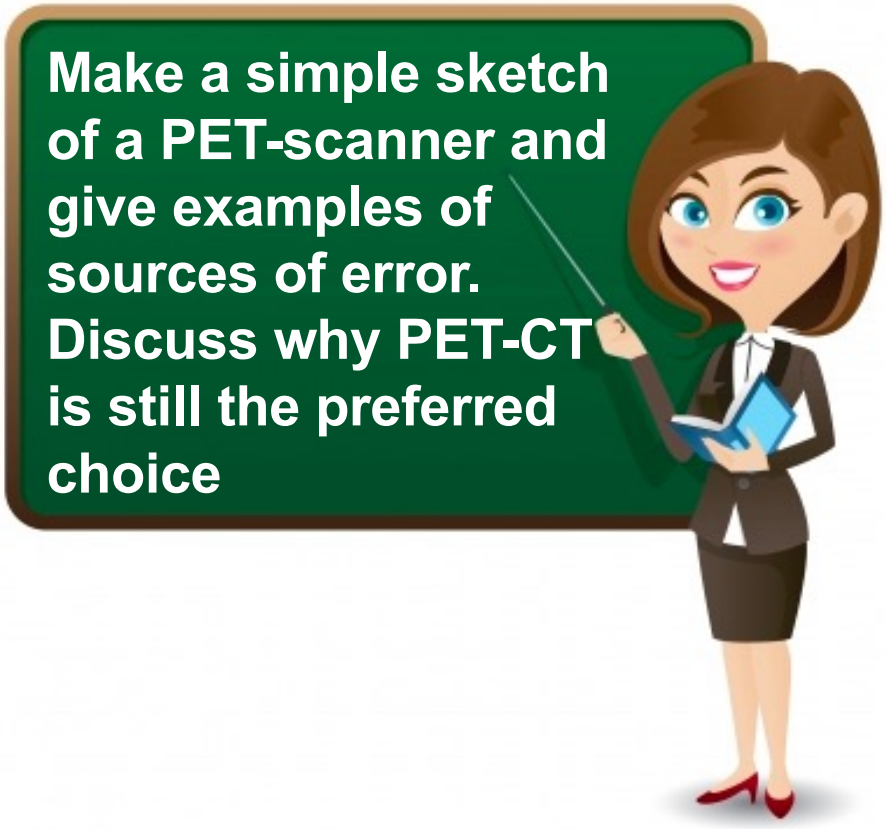
due to collisions with electrons of the absorber material. In addition there is a nuclear fragmentation reaction that gives very complex alterations of the particle field composition

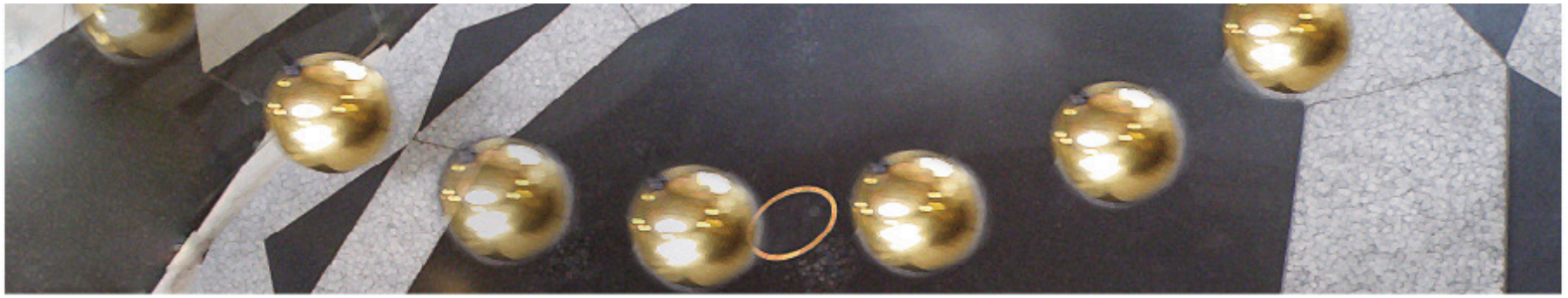
- As energy decreases, the statistical probability of more nuclear interactions increase dramatically, and most of the energy is deposited shortly before the kinetic energy reach zero



Exercise examples







UiO : Department of Physics
University of Oslo

FYS 4250

Lecture 16

Radiotherapy

Kilde: Eva Stabell Bergstrand, Taran Paulsen Hellebust, Avdeling for Medisinsk Fysikk

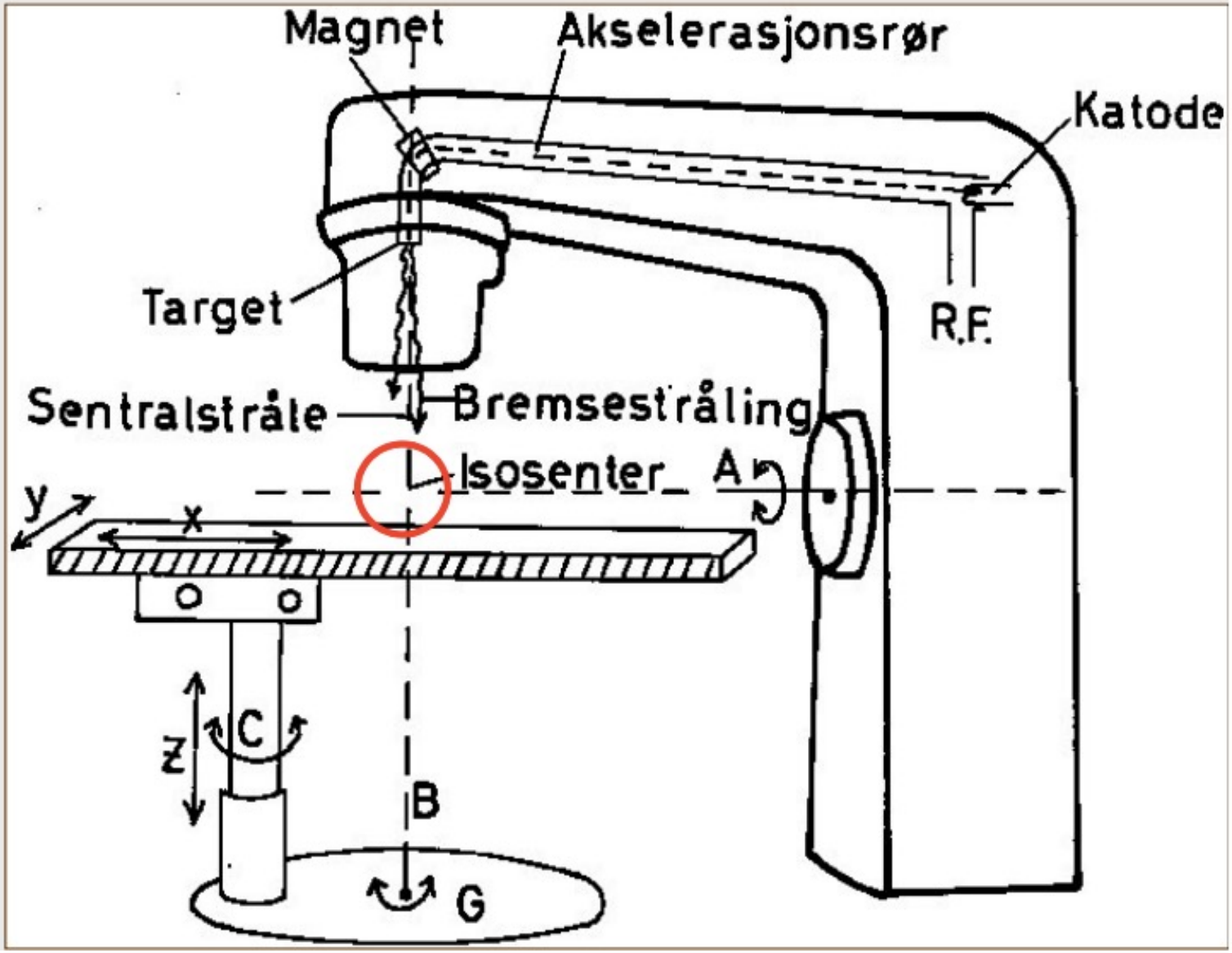
Sketch of a linear accelerator

Comprises the machine

AND

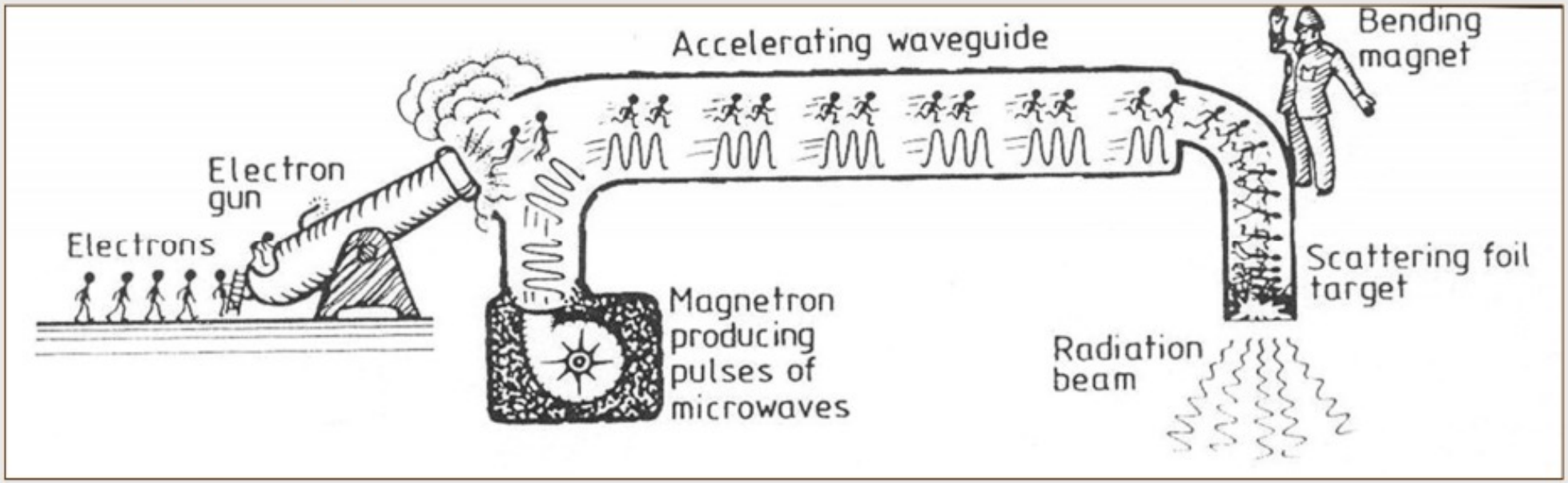
the treatment coach

The machine comprises the accelerator, head and gantry



Kilde: Eva Stabell Bergstrand, Taran Paulsen Hellebust, Avdeling for Medisinsk Fysikk

The principals of a linear accelerator

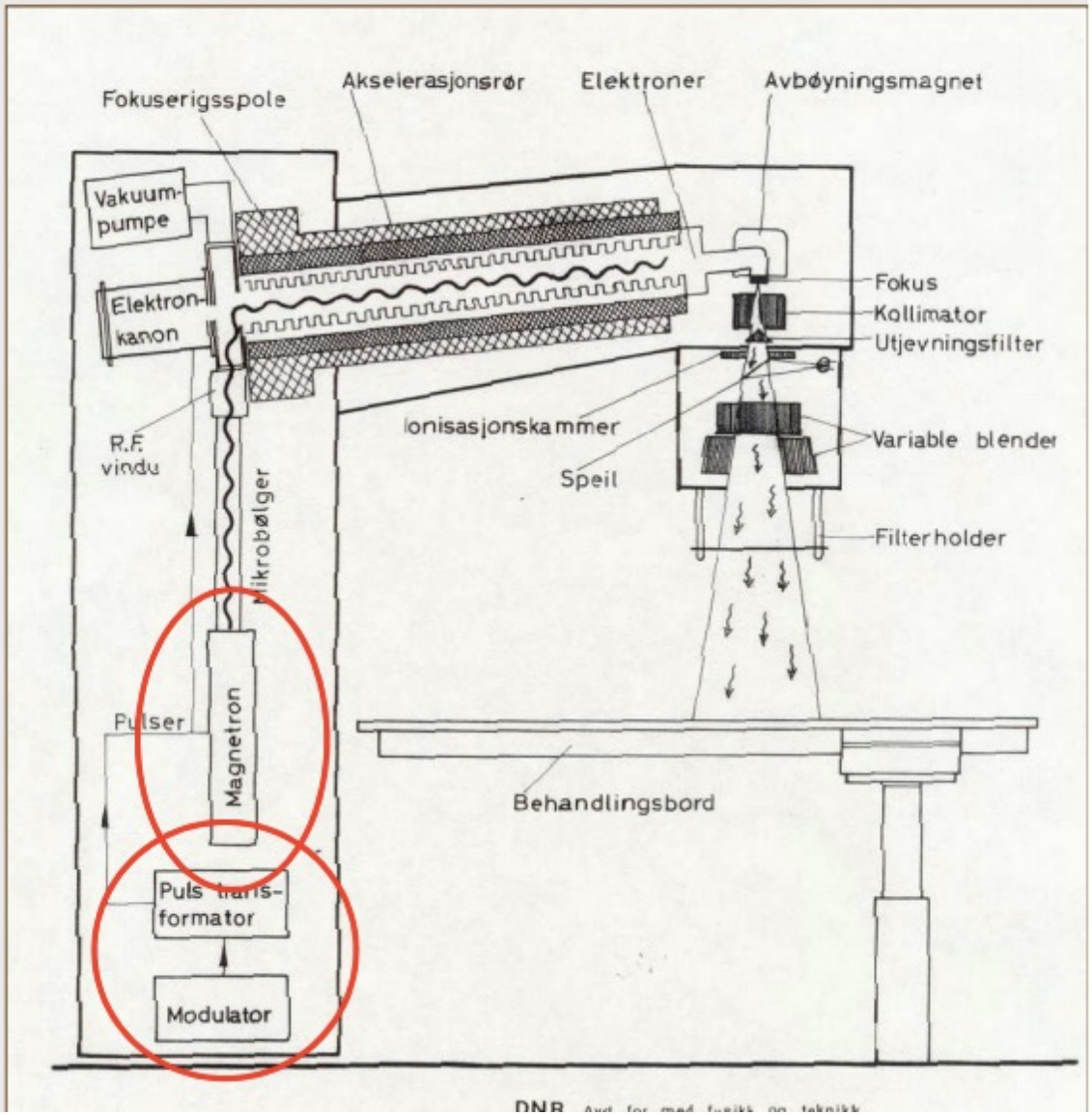


- Pulsed radiation
  - –1-5 µs with 5-500 pulses/s
  - –Dose rate: 3-4 Gy/min at 1 m distance
- The electrons surf on the micro waves and gain energy
- The magnet bends the electrons against the target

Kilde: Eva Stabell Bergstrand, Taran Paulsen Hellebust, Avdeling for Medisinsk Fysikk

The modulator

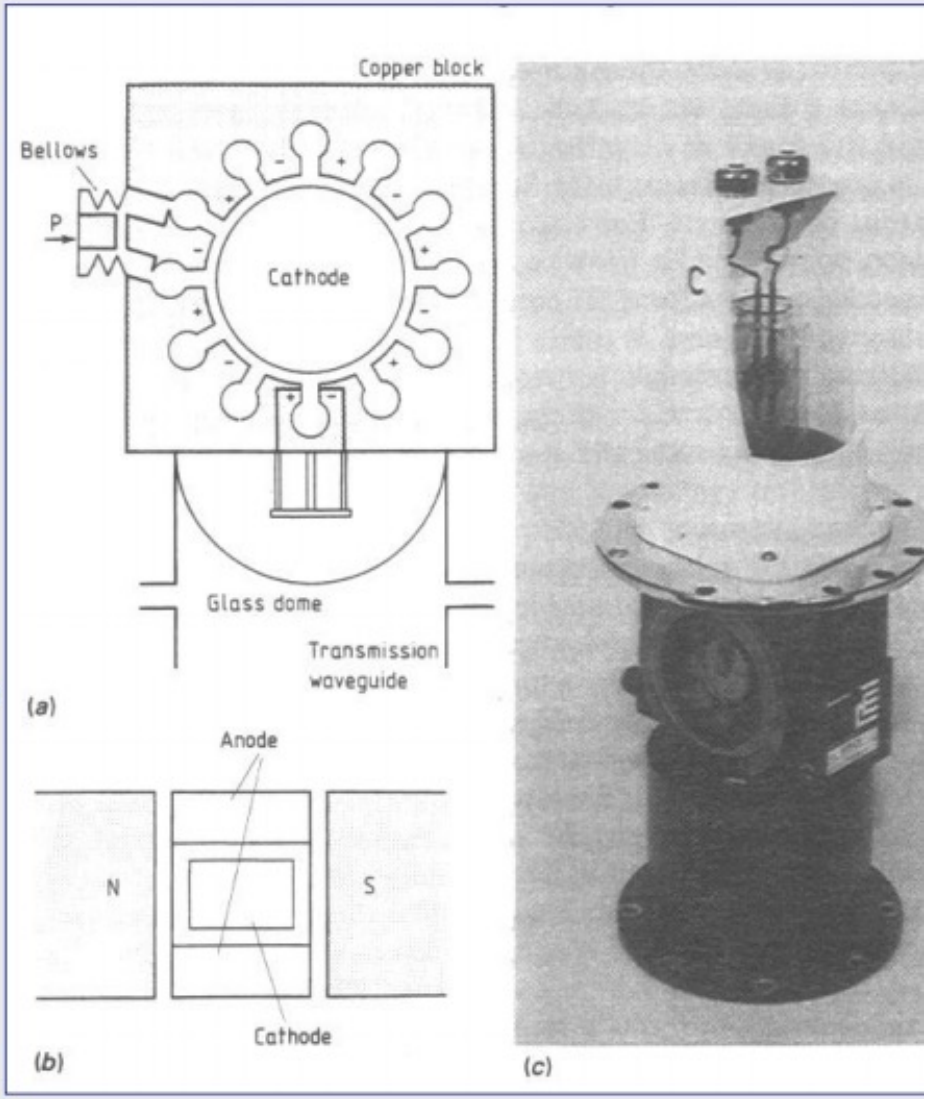
- The modulator generate high-voltage pulses that will be amplified in the transformer and supplied to the magnetron AND the gun
- In the magnetron the micro waves are created; electromagnetic radiation with a frequency of approx. 3 GHz



Kilde: Eva Stabell Bergstrand, Taran Paulsen Hellebust, Avdeling for Medisinsk Fysikk

Micro wave production: The magnetron

- The magnetron use the pulses of high voltage from the modulator to generate micro waves (electromagnetic radiation with wave length of approx. 10 cm)
- The anode and the cathode is placed in a magnetic field
- The high voltage pulses are applied to a heated cylindrical cathode
- Thermionic electrons are then attracted towards an anode of cylindrical cavities
- Magnetic field strength and the voltage is adjusted to have a electronic fields oscillating to create charge clouds and electromagnetic radiation is created in the cavities
- The frequency is determined by the geometry of the cavities (and temperature), can be regulate via the switch P
- The micro waves are transferred by an antenna.



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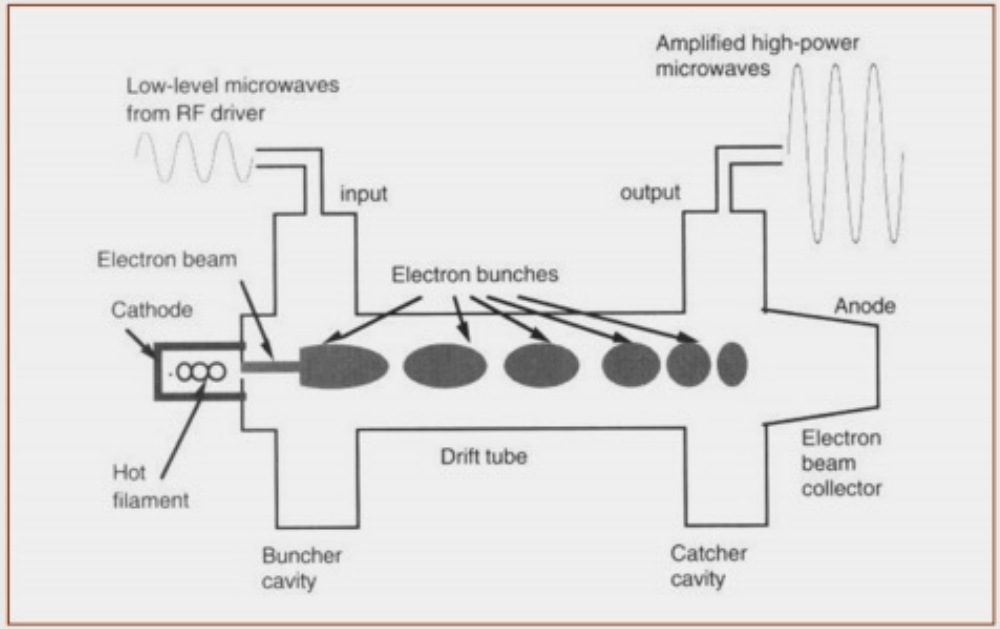
Klystron (microwave amplifier)

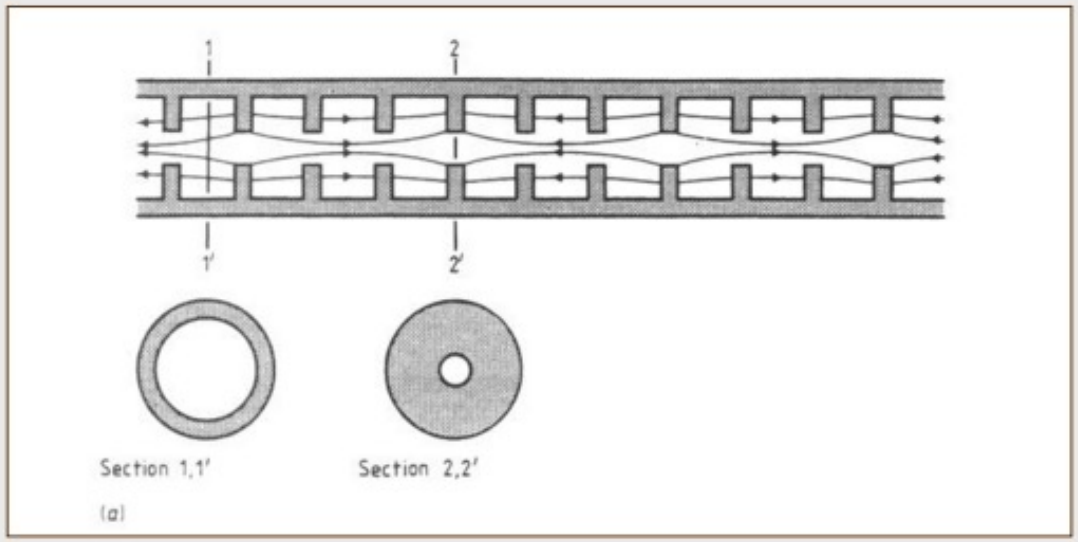
- Machines with high energies often use a klystron instead of a magnetron
- The klystron receive low-level microwaves from a RF-generator
- Electrons from a gun moves from left to right, they interact with the RF waves in the first cavity and will be bunched
- The bunched electrons will loose speed in the next cavity and the energy is transferred to the cavities as strong RF waves



Stanton og Stinson 2009

The waveguide

- If the electron is arranged to move with the same velocity as the field, the electron will receive energy continuously from the field and move from left to right
- The field velocity has to be increased along the waveguide
- Can vary the capacity per unit length by fitting the guide with conducting irises or discs



- The waveguide can be operated in one of two ways:
  - Energy can flow smoothly in and out at opposite ends of the system - **traveling waveguide**
  - Energy is reflected at the ends of the system – **standing waveguide**

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Radiation quality of the photons

10 kV to 20 kV, 0.02 mm to 0.15 mm Al HVL	**Grenz rays**, very little used for therapy
10 kV to 60 kV, 0.02 mm to 3.3 mm Al HVL	**Short distance or contact therapy**, depth up to several millimetres can be treated
50 kV to 150 kV, 1 mm to 8 mm Al HVL	**Superficial therapy**, depth of around 5 mm can be treated
160 kV to 300 kV, 0.5 mm to 4 mm Cu HVL	**Orthovoltage therapy or deep therapy**, depth of 1 to 2 cm can be treated

The choice of energy is determined by the site of the target volume: Skin irradiation, superficial tumors or more deep situated tumors

The quality of the photons is given by an apparent high voltage potential

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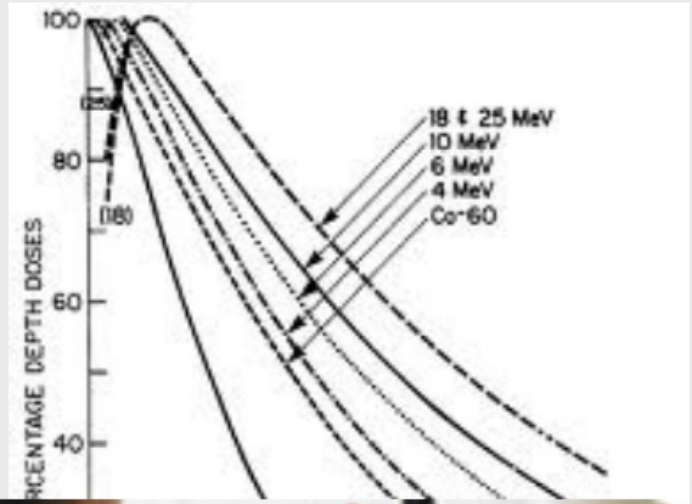
Radiation quality of the photons

X-ray therapy

- Steep dose fall; target volume with maximum extension of a few mm below the skin surface can be treated with such equipment (50-150 kV)
- Sharp edge of the field, short distance from the focus to the treated area



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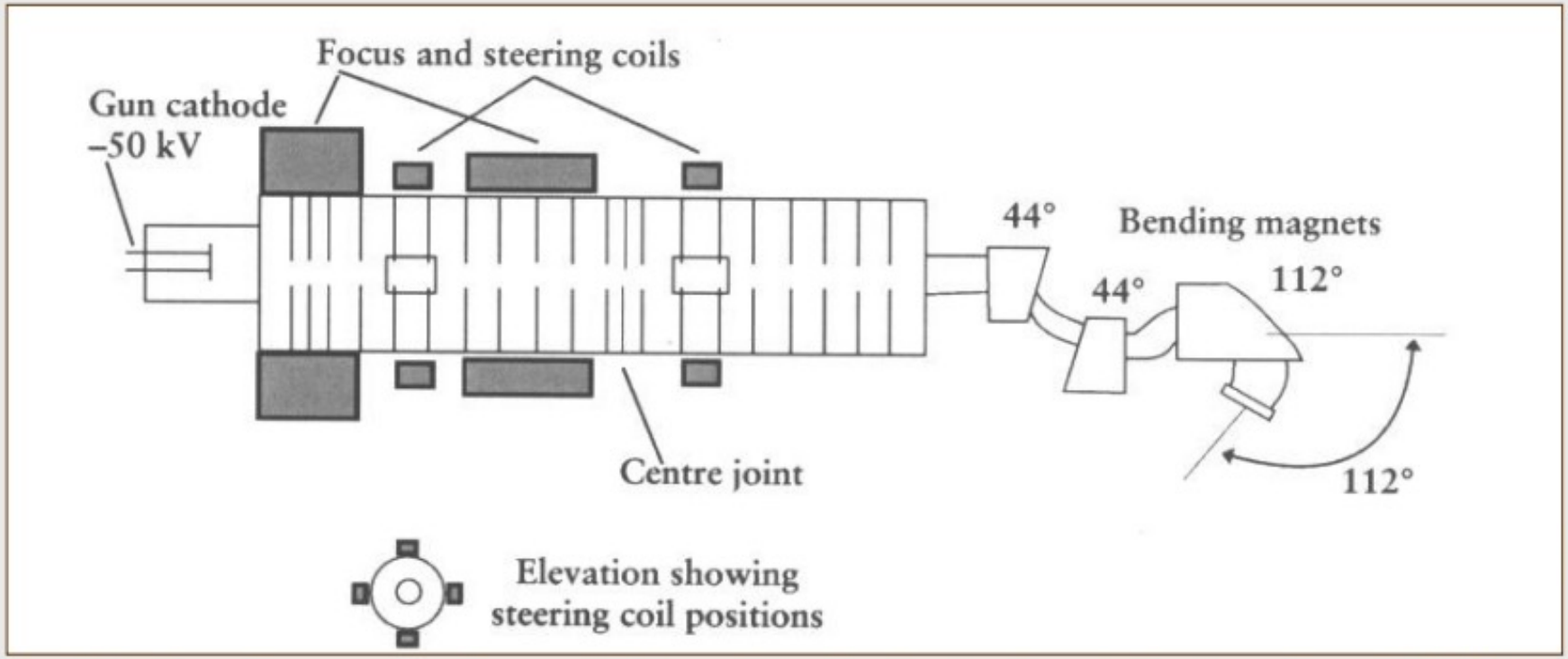
Focusing and steering of the beam



Elekta

The beam have to be focused already in the beginning tube since the E-field has components not only in the direction of the acceleration. Static focusing coils force the electrons to the centre. Steering coils are dynamic and can change the magnetic field if the ionisation chamber shows shallow fields

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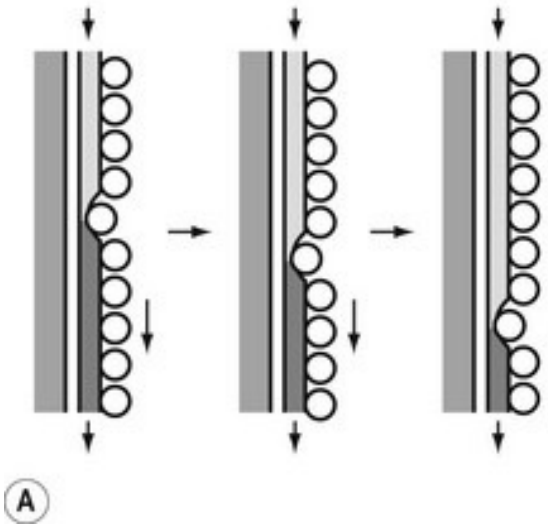
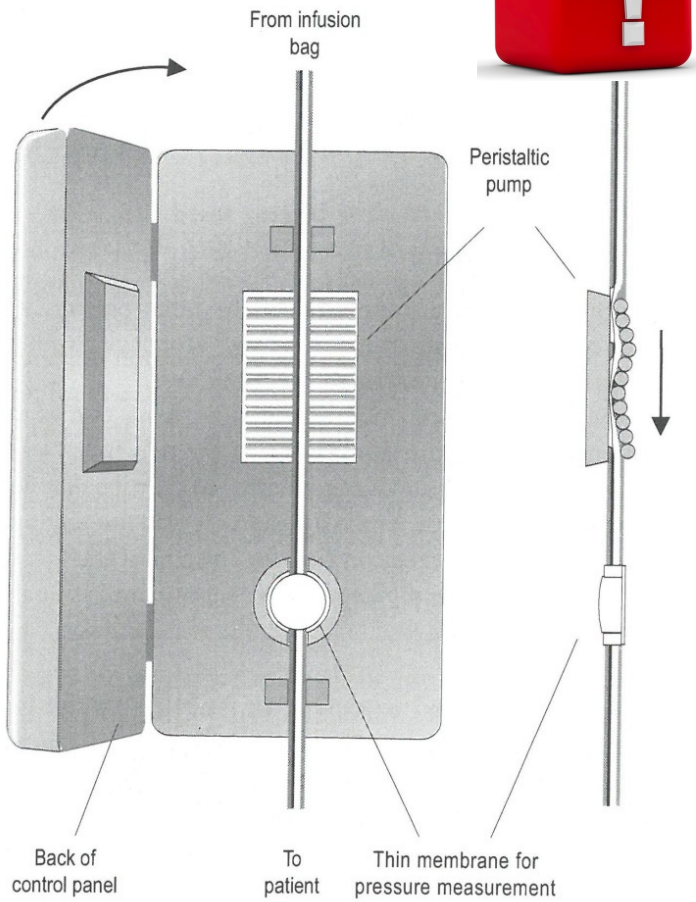
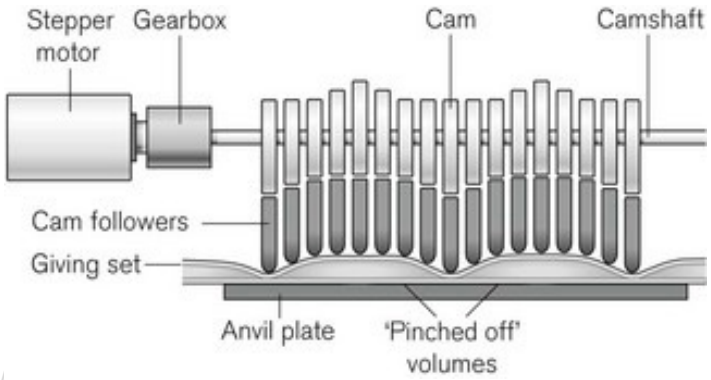
Infusion-pump (peristaltic)

Tubing is compressed by a series of rotating rollers, certain prerequisitions to the tubing:

- Hard wearing
- Known and consistent internal volume
- No ”memory” of compression, easy filling



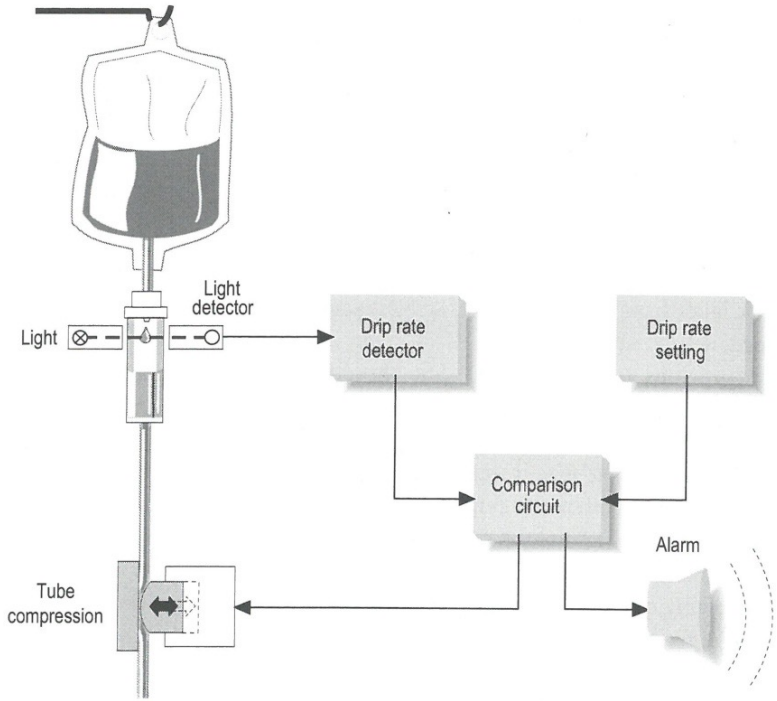




https://aneskey.com/infusion-equipment-and-intravenous-anaesthesia/

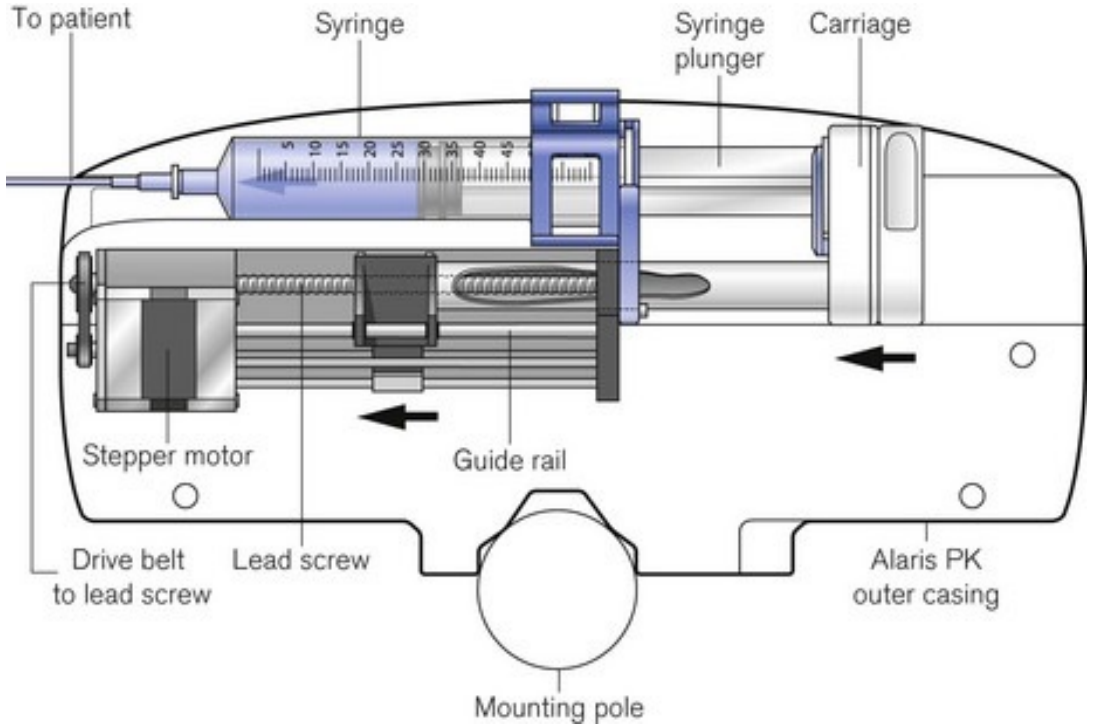
Drop counter

A drop-counter is an essential safety mechanism for controlling the real infusion-rate. Typically optical readings, have to make sure that the medication is detecteable for the drop-counter



https://aneskey.com/infusion-equipment-and-intravenous-anaesthesia/

Syringepump



Microcontrollerbased stepper motor is controlling the movement of at lead screw which is mechanically connected to a syringe through a syringe plunger.

Important pre-requisites:

- Type and size of the syringe
- Type and concentration of medication

https://aneskey.com/infusion-equipment-and-intravenous-anaesthesia/

Multipump challenges

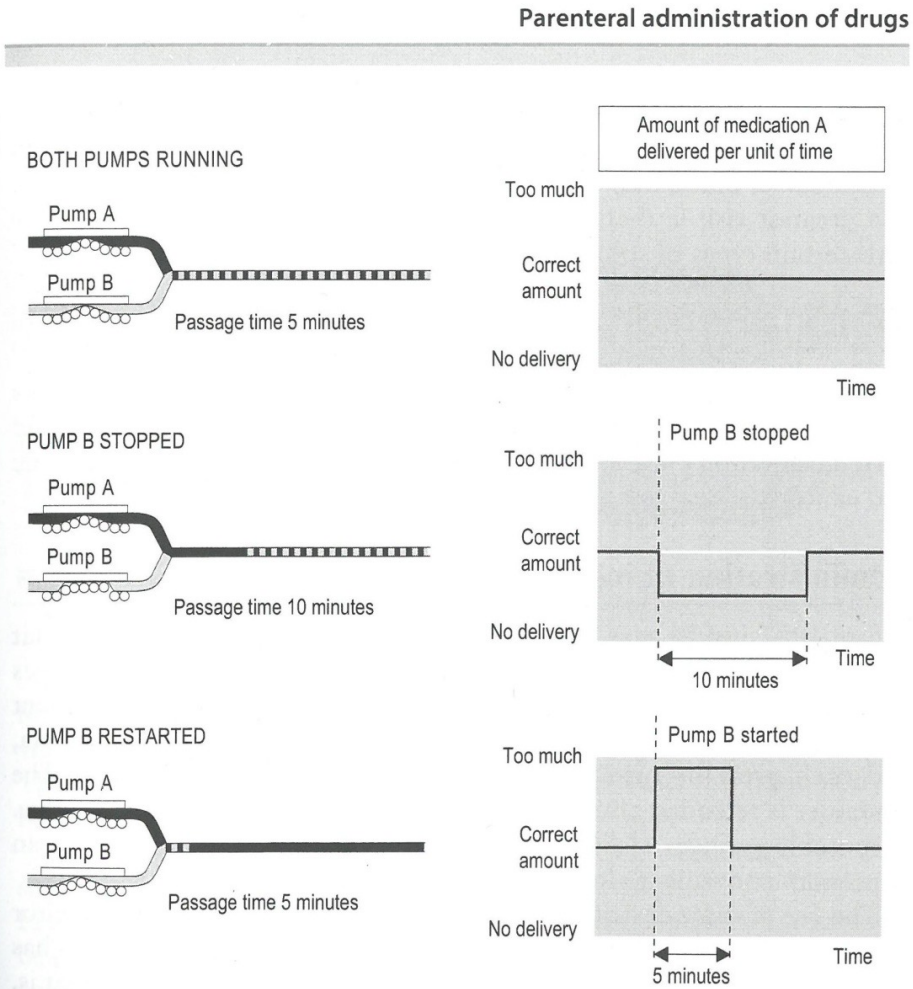


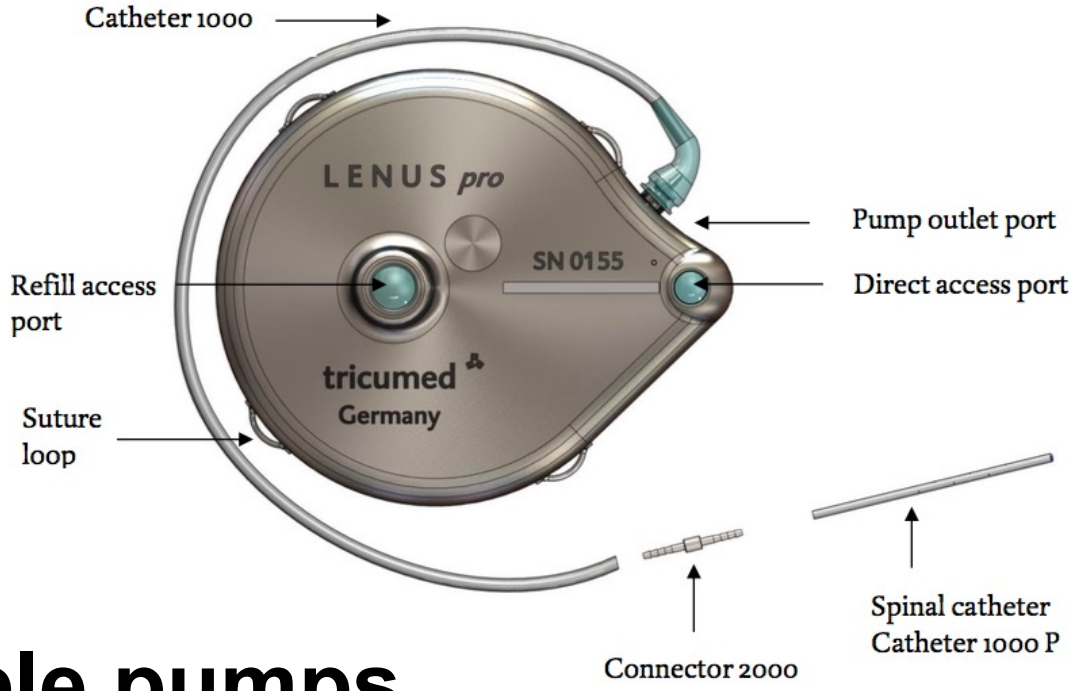
Figure 9:9 When two or more pumps are interconnected and one of them stopped or restarted, the infused volume per unit of time from the running pump is affected. The figure demonstrates what happens to the medication from infusion pump A when pump B is stopped and then restarted

Kilde: Jacobsen og Murray, Medical Devices, use and safety. Elsevier, 2007

Infusion pumps vs syringe pumps

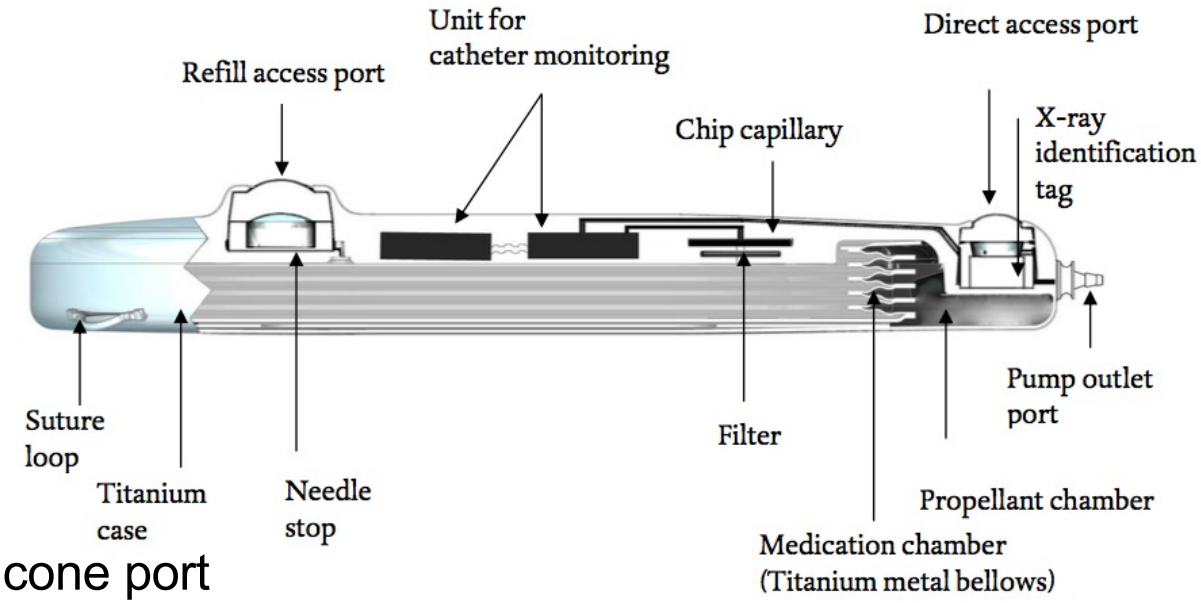
	Advantages	Disadvantages
Infusion pumps	High capacity Need special infusion sets Drop-counter is vulnerable	Less accurate than syringe pump (but still very accurate)
Syringe pumps	High accuracy Syringe recognition Easy transport Low volumes	Limitations in capacity Depending on right medication protocol, syringe type and size

Fully mechanically, only an electronic occlusion alarm



Implantable pumps

Propellant is a compressible gas, able to create a stable pressure in the actual range



Refill access port = silicone port

Percutaneous filling (through the skin)

Emptying before filling, calculating rest-volume. Filling with saline in the beginning and the end. Small volumes, only 1 ml/day

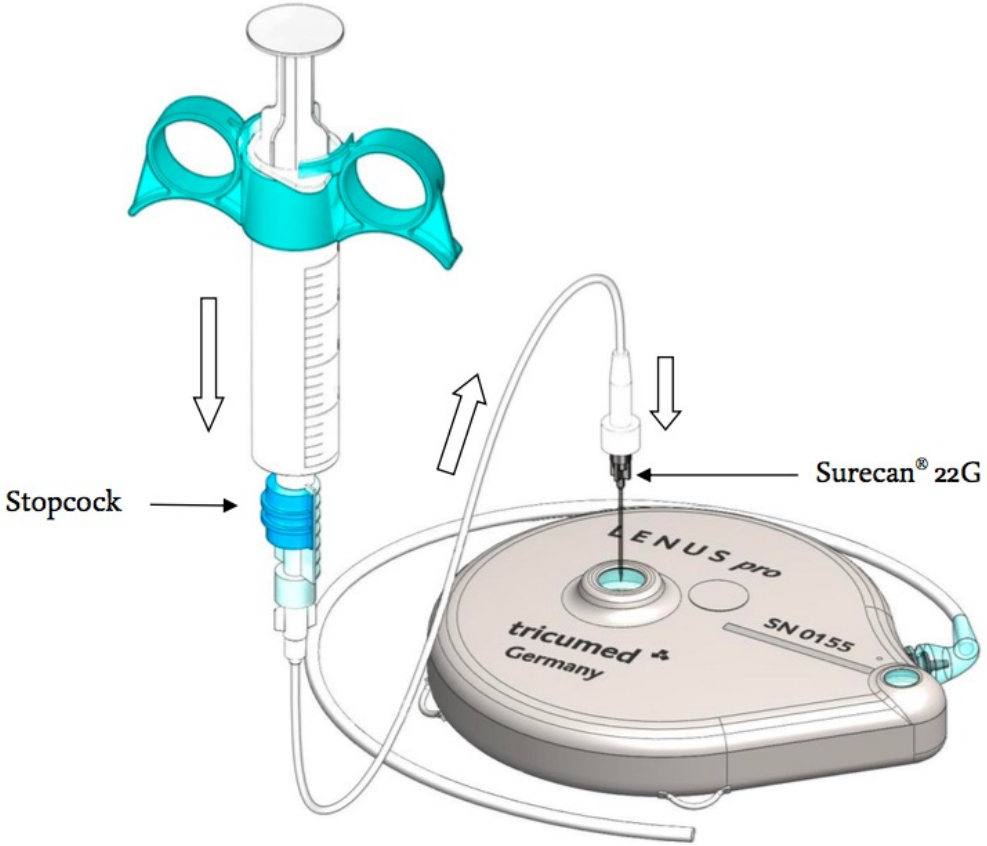
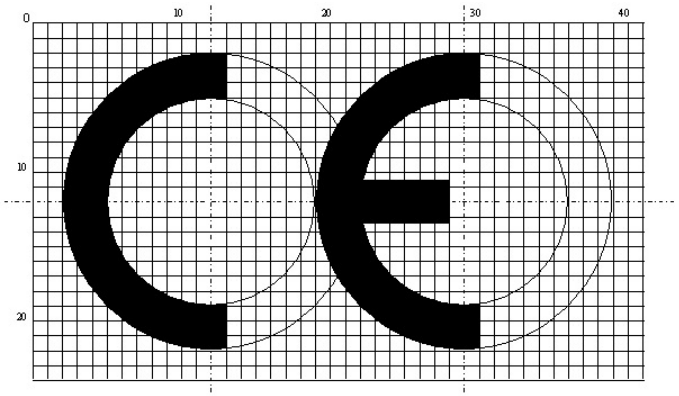


Figure 13: Refilling the infusion pump

Medical Device Directive

- Medical device directive (MDD, 93/42/EEC of June 1993) (På norsk Medisinsk utstyr direktivet 93/42/EØF)
- No manufacturer can market or sell any medical device in the European union unless the product can meet the MDD-requirements. (New version in 2007)
- The manufacturer is responsible to assure that a product is compliant with the requirements
  - Low risk products (class 1): The manufacturer can perform the necessary assessment themselves
  - Medium or high risk (class 2 or 3): Requires an impartial third party (notified body) to
- Safety standards is defined in IEC 60601 series



IEC 60601

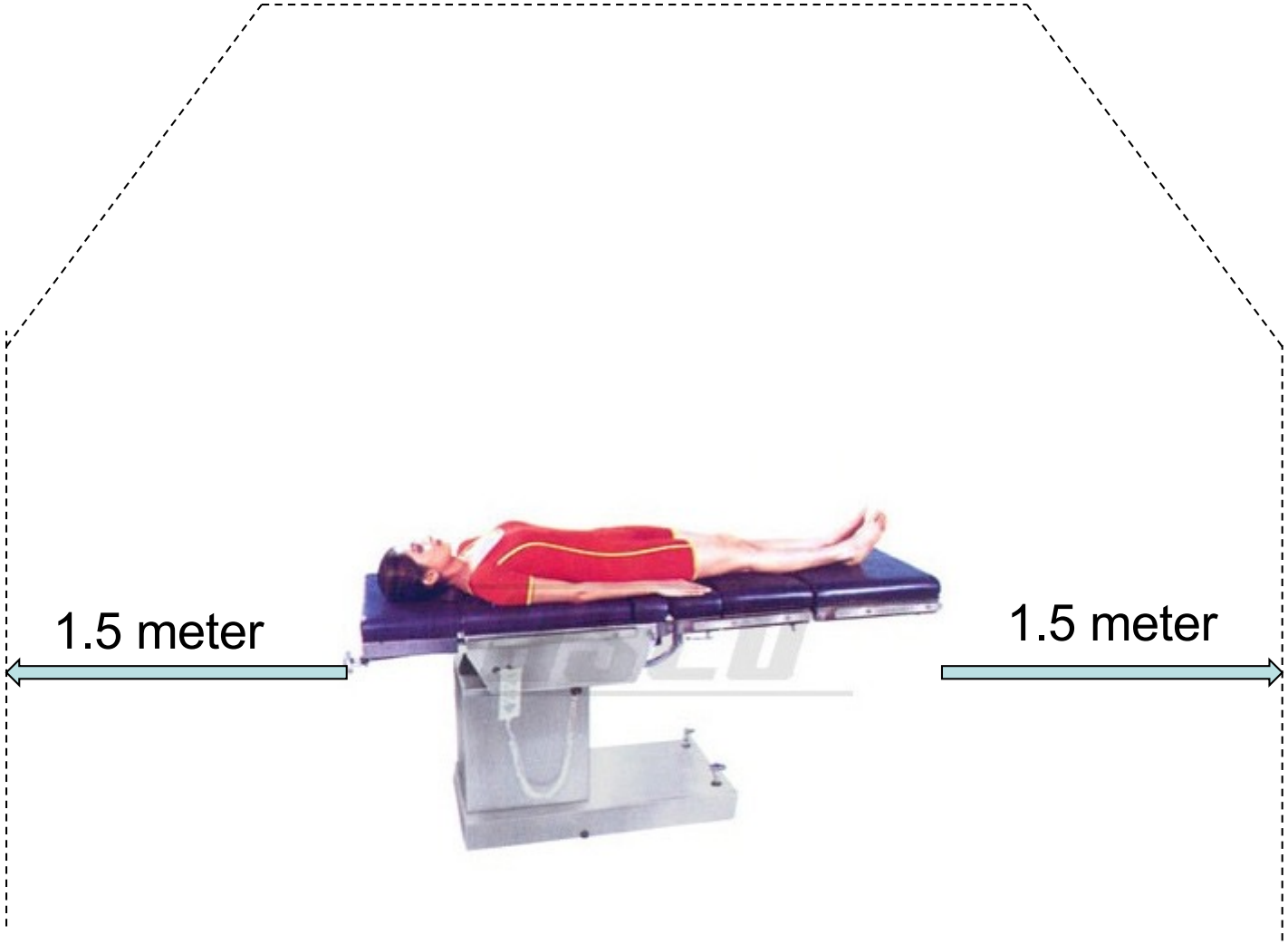
- Technical standards for safety of medical equipment (ME), published in 1977, today's version consists of:
  - 1 general standard (60601-1 Medical electrical equipment – Part 1)
  - 10 collateral standards (60601-1-X) define requirements for particular aspects like electromagnetic compatibility (60601-1-2)
  - 60 particular standards (60601-2-X) define requirments for specific types of medical equipment like MR scanners (IEC 60601-2-33)

The certification process has been criticized for its complexity, cost and risk for the manufacturers.

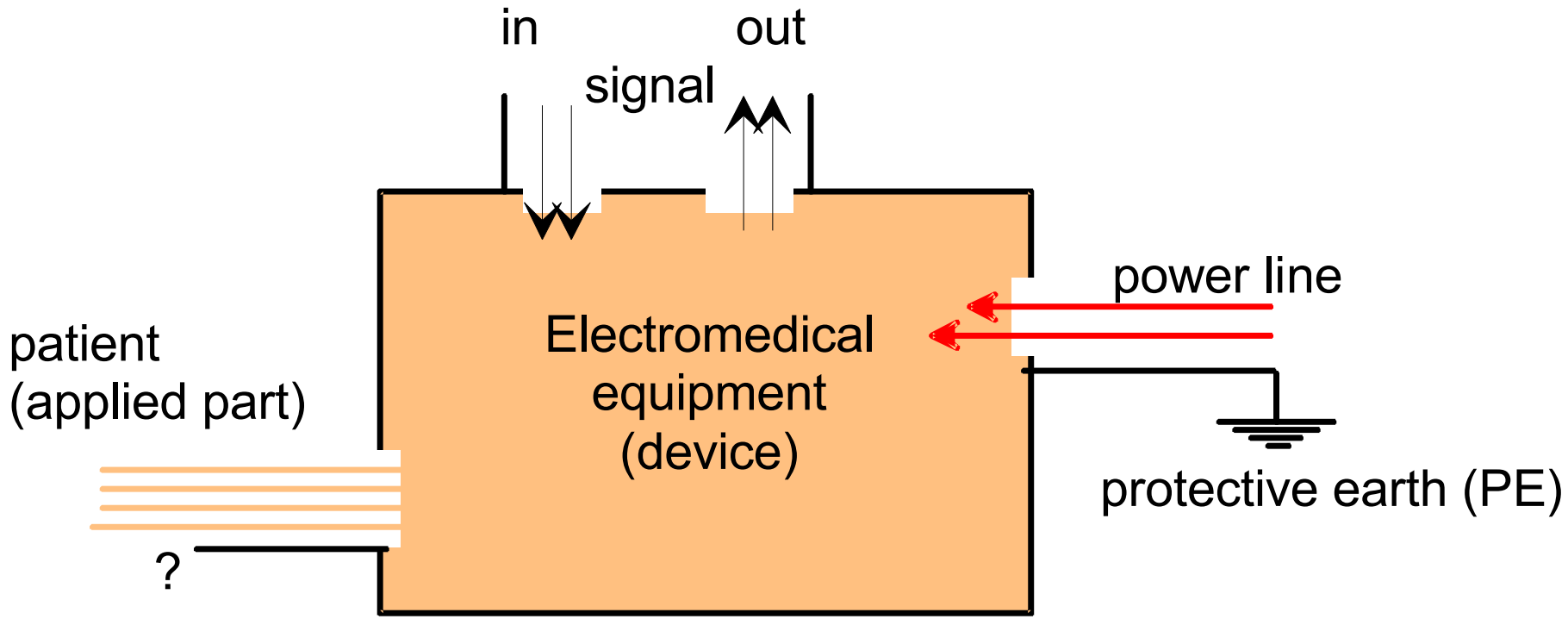
Single fault concept and risk management

- A medical equipment (ME) shall be single fault safe, or the risk shall be acceptable. (This means that a ME in normal condition (NC) is compliant with the standard if a single fault condition does not lead to an unacceptable risk)
- What is acceptable/unacceptable risk?
- Determining the level of acceptable is a responsibility for the manufacturer
- If the ME is compliant to IEC 60601, the residual risks for these requirements can be assumed to be acceptable? Or?

Patient environment

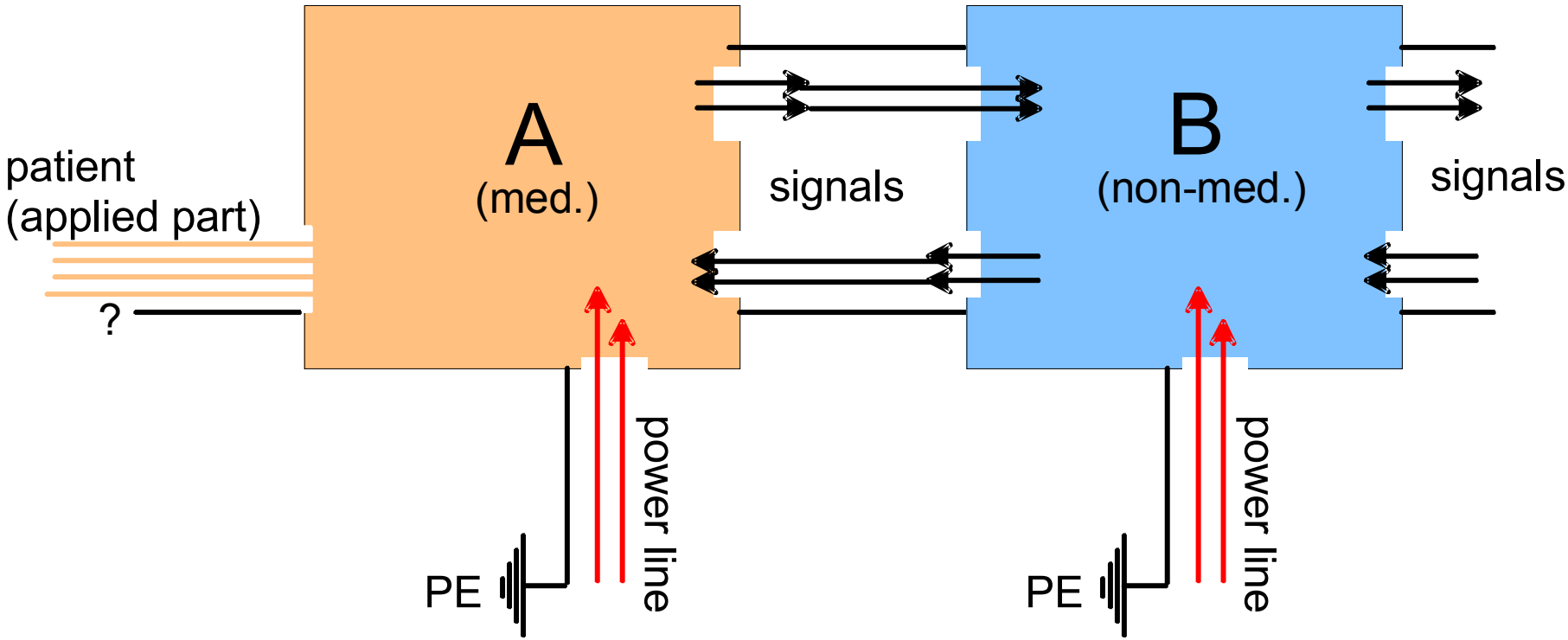


Electromedical devices must be CE-marked (Europe)



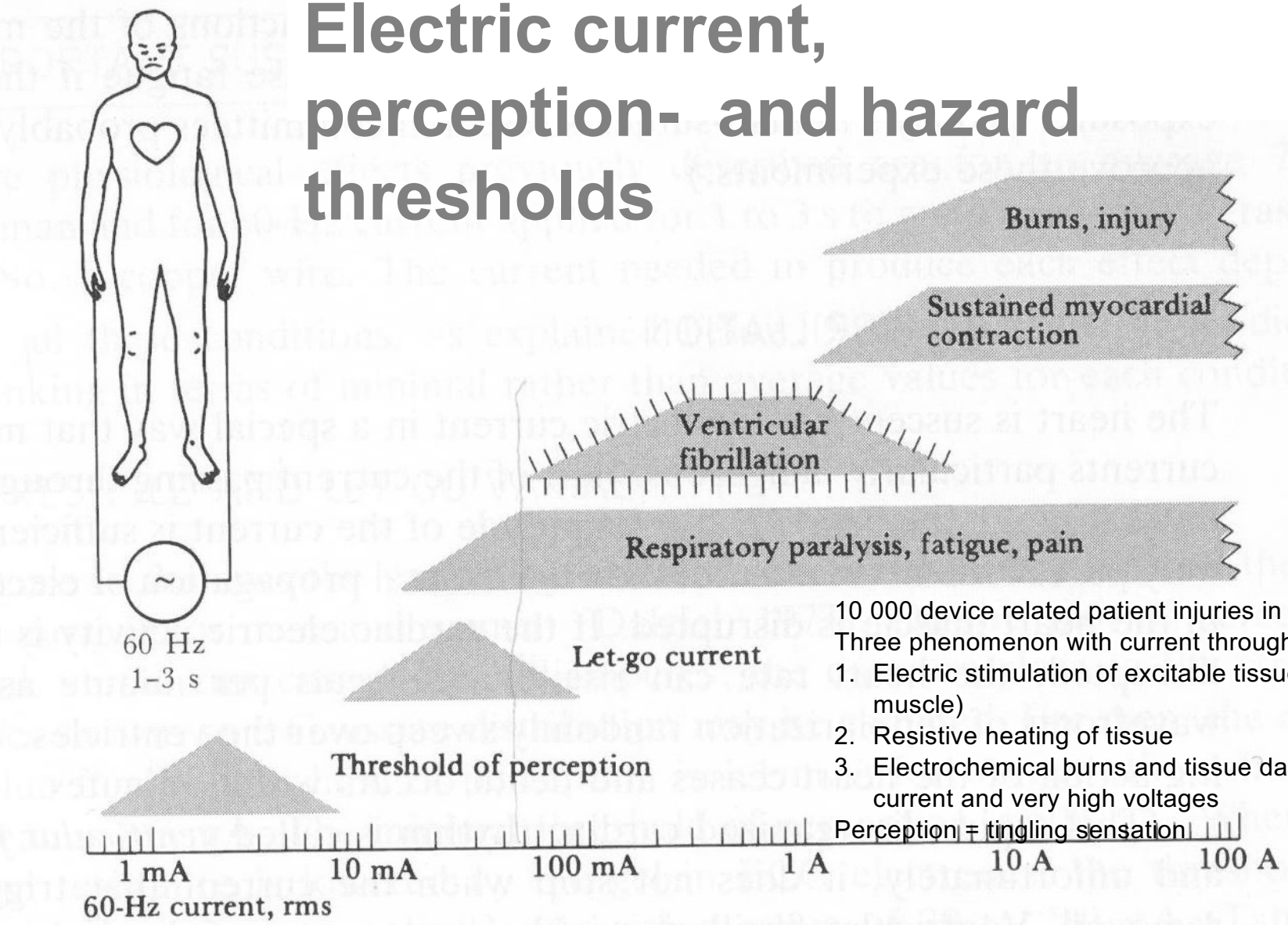
Can be marked by the vendour if class I, all other classes must be approved by a notified body (= NEMKO, TüV and so on)

Patient near PC (B-apparatus)



Special requirements for the B apparatus, typically additional protective earth or a separating transformer

Electric current, perception- and hazard thresholds



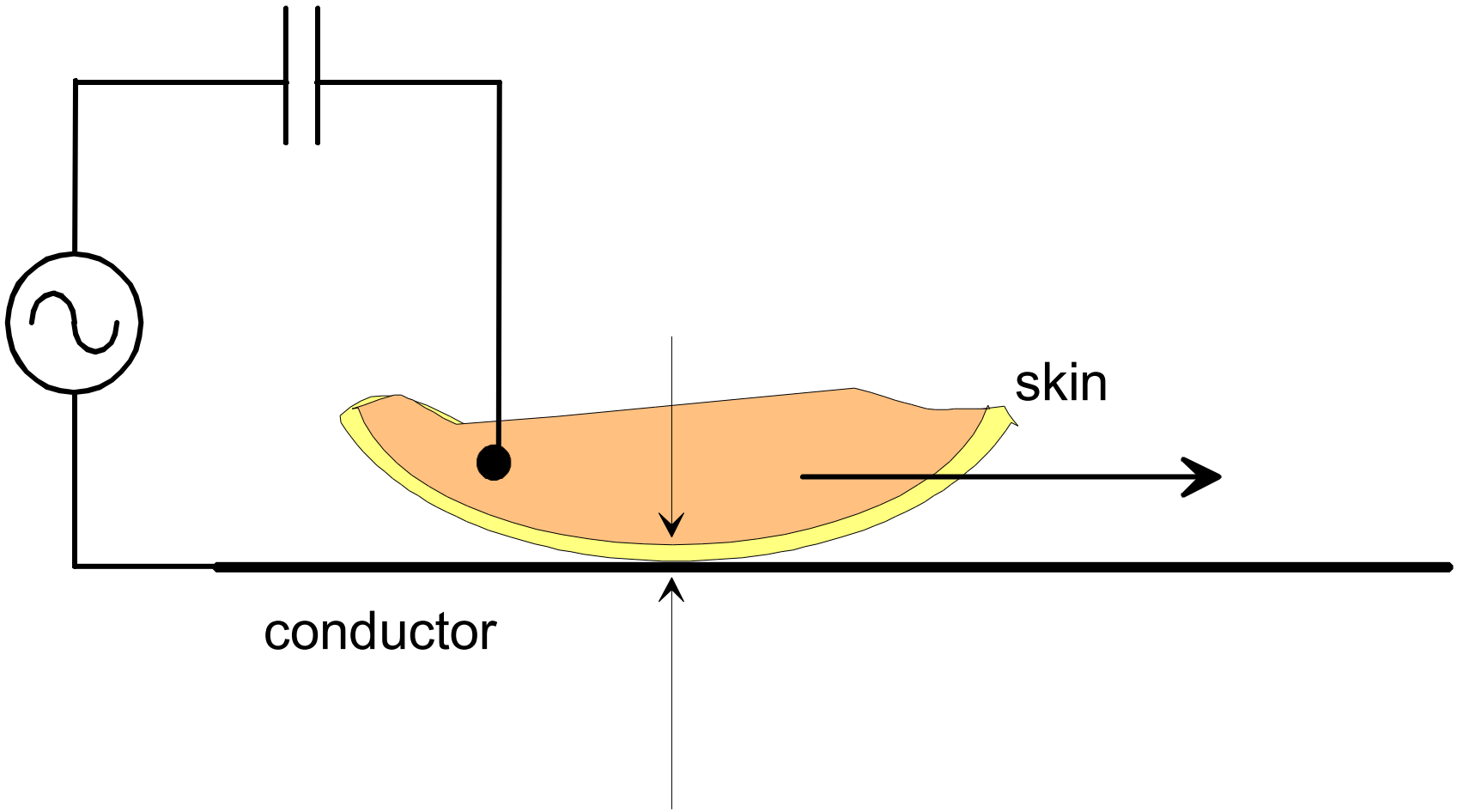
10 000 device related patient injuries in USA each year
Three phenomenon with current through the body:

1. Electric stimulation of excitable tissue (nerve & muscle)
2. Resistive heating of tissue
3. Electrochemical burns and tissue damage for direct current and very high voltages

Perception = tingling sensation

Figure 14.1 Physiological effects of electricity Threshold or estimated mean values are given for each effect in a 70-kg human for a 1- to 3-s exposure to 60-Hz current applied via copper wires grasped by the hands.

Electrovibration (1uA 50Hz)



Statistical scattering of sensitivity for electric current

University of Oslo

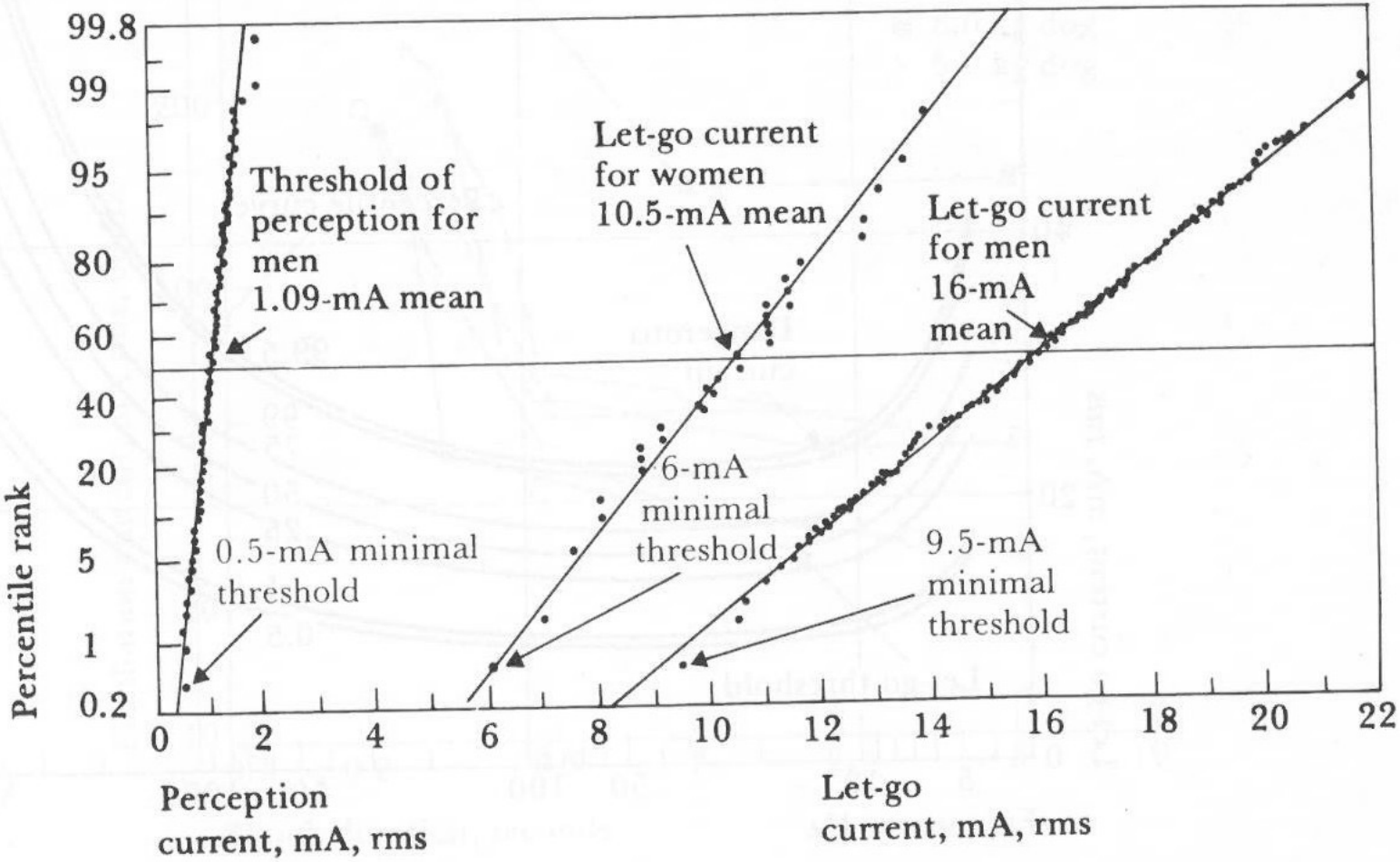


Figure 14.2 Distributions of perception thresholds and let-go currents These data depend on surface area of contact (moistened hand grasping AWG No. 8 copper wire). (Replotted from C. F. Dalziel, "Electric Shock," *Advances in Biomedical Engineering*, edited by J. H. U. Brown and J. F. Dickson III, 1973, 3, 223–248.)

Frequency dependency and spread of the let-go threshold

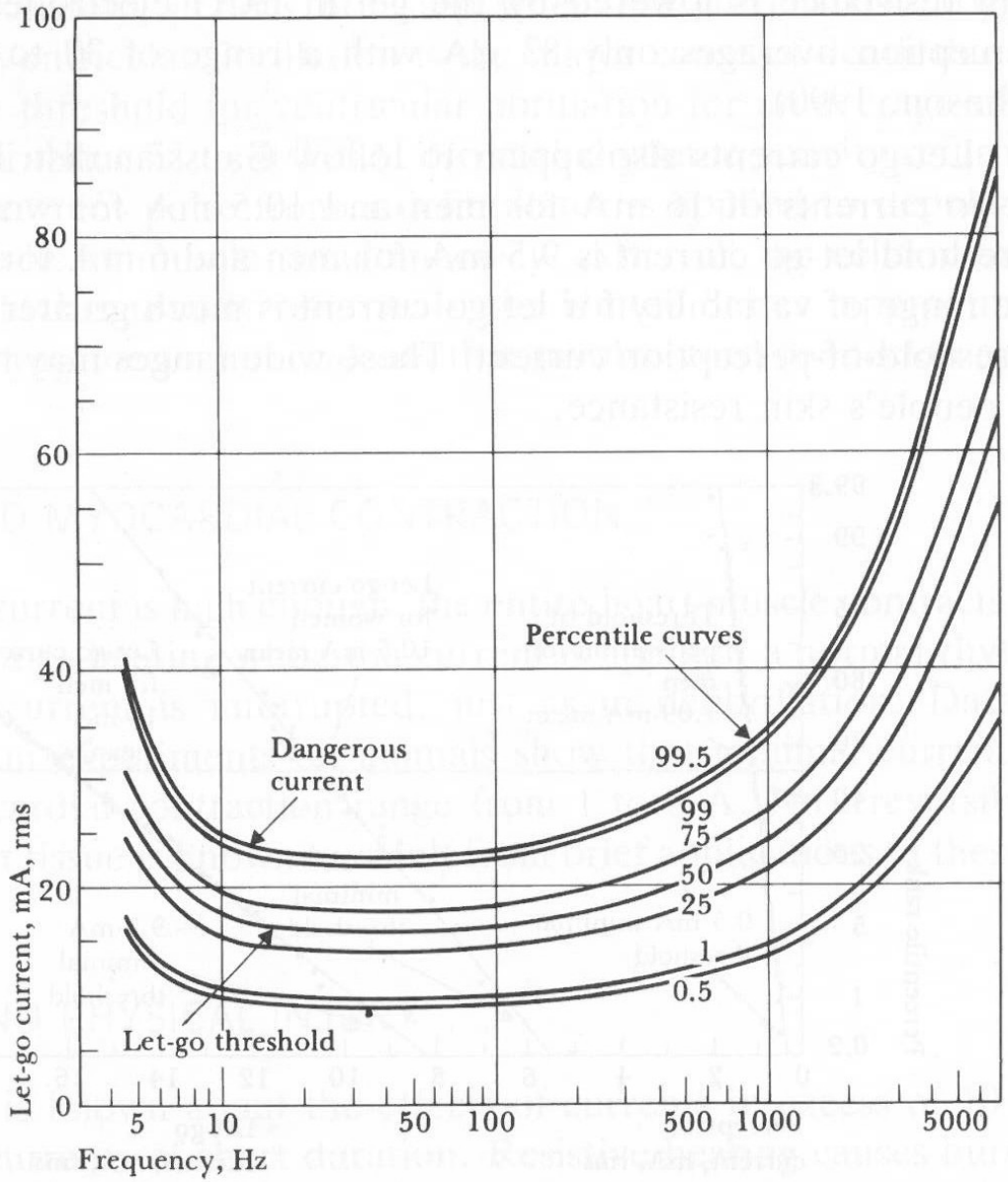


Figure 14.3 Let-go current versus frequency Percentile values indicate variability of let-go current among individuals. Let-go currents for women are about two-thirds the values for men. (Reproduced, with permission, from C. F. Dalziel, "Electric Shock," *Advances in Biomedical Engineering,* edited by J. H. U. Brown and J. F. Dickson III, 1973, 3, 223–248.)

Ventricular fibrillation thresholds in animals

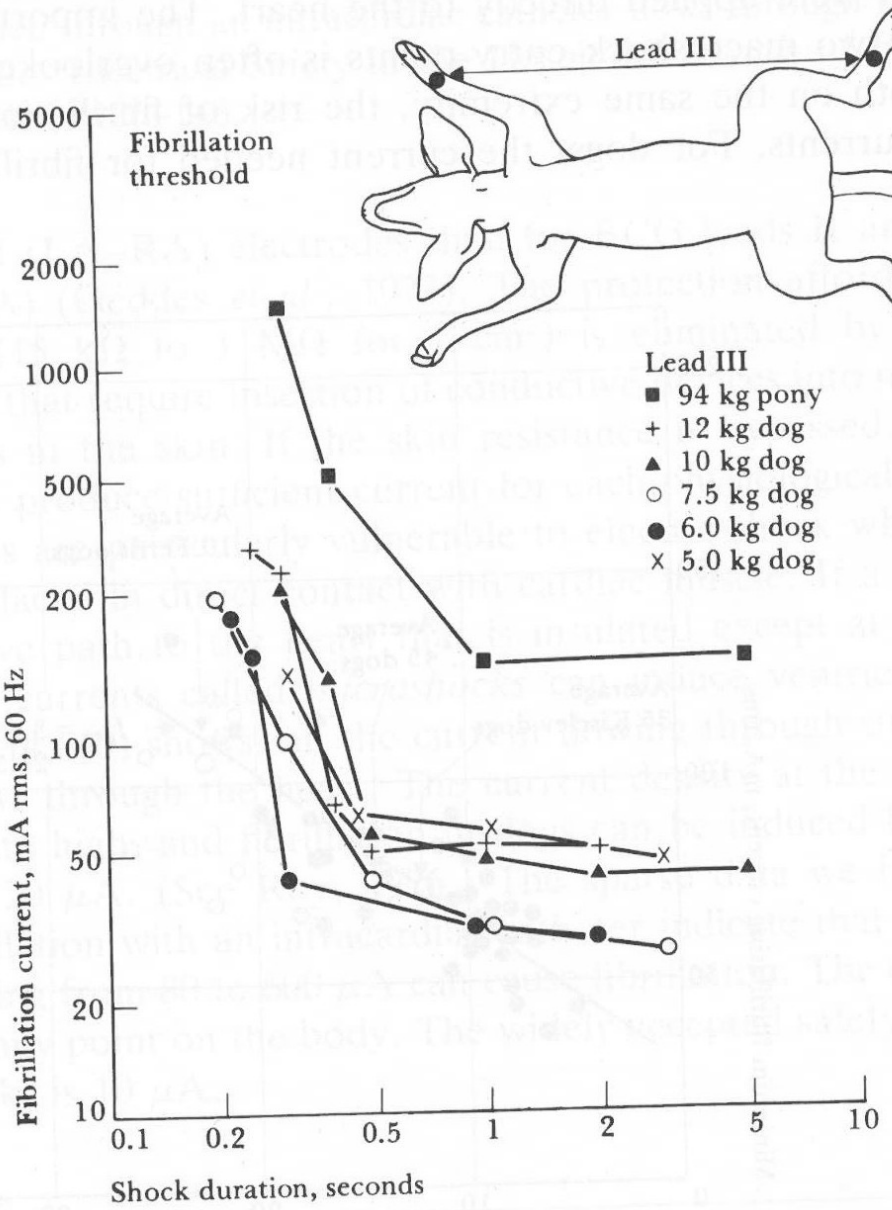


Figure 14.4 Thresholds for ventricular fibrillation in animals for 60-Hz ac current. Duration of current (0.2 to 5 s) and weight of animal body were varied. (From L. A. Geddes, *IEEE Trans. Biomed. Eng.*, 1973, 20, 465–468. Copyright 1973 by the Institute of Electrical and Electronics Engineers. Reproduced with permission.)

Macro- og microshock

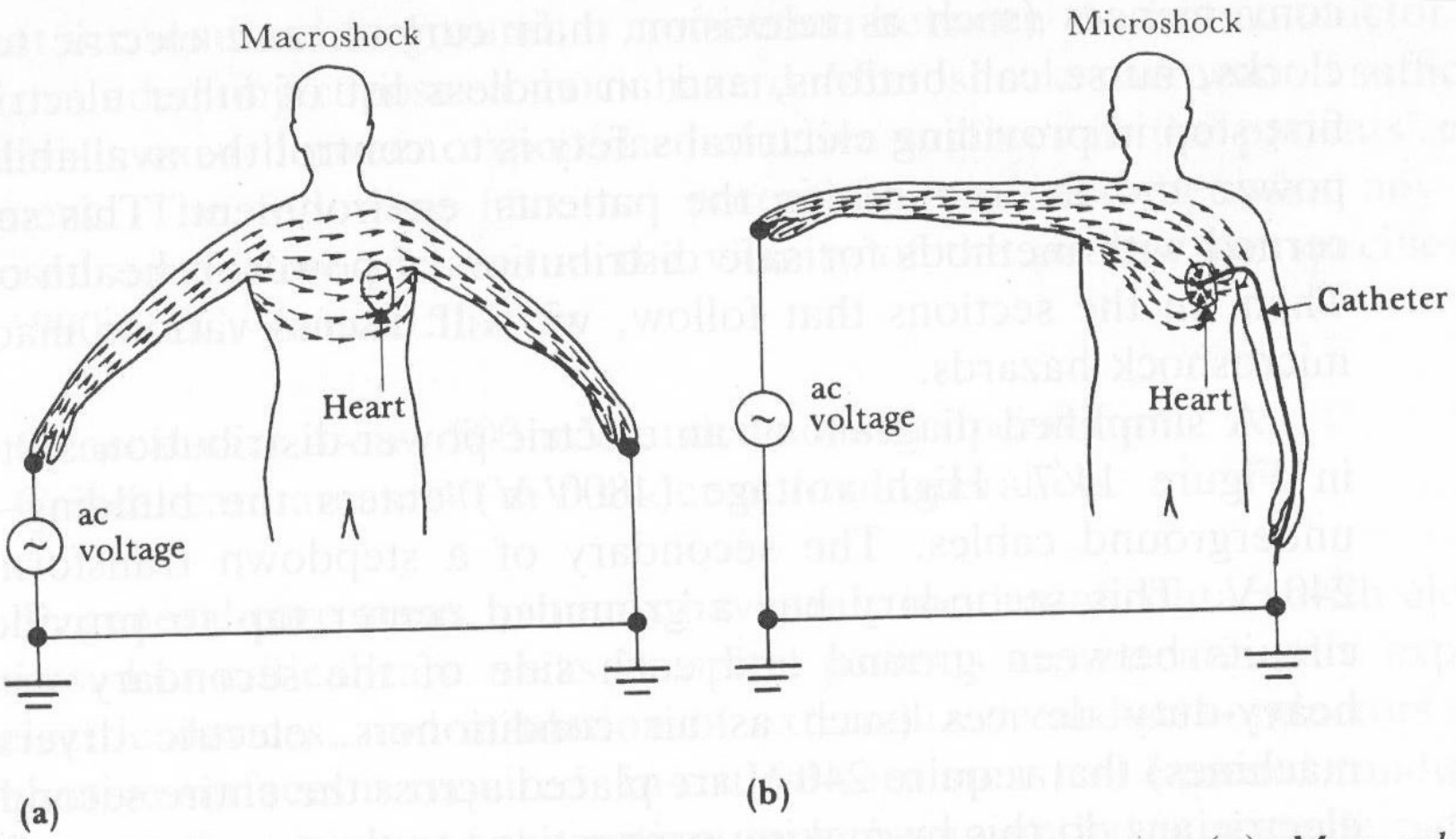
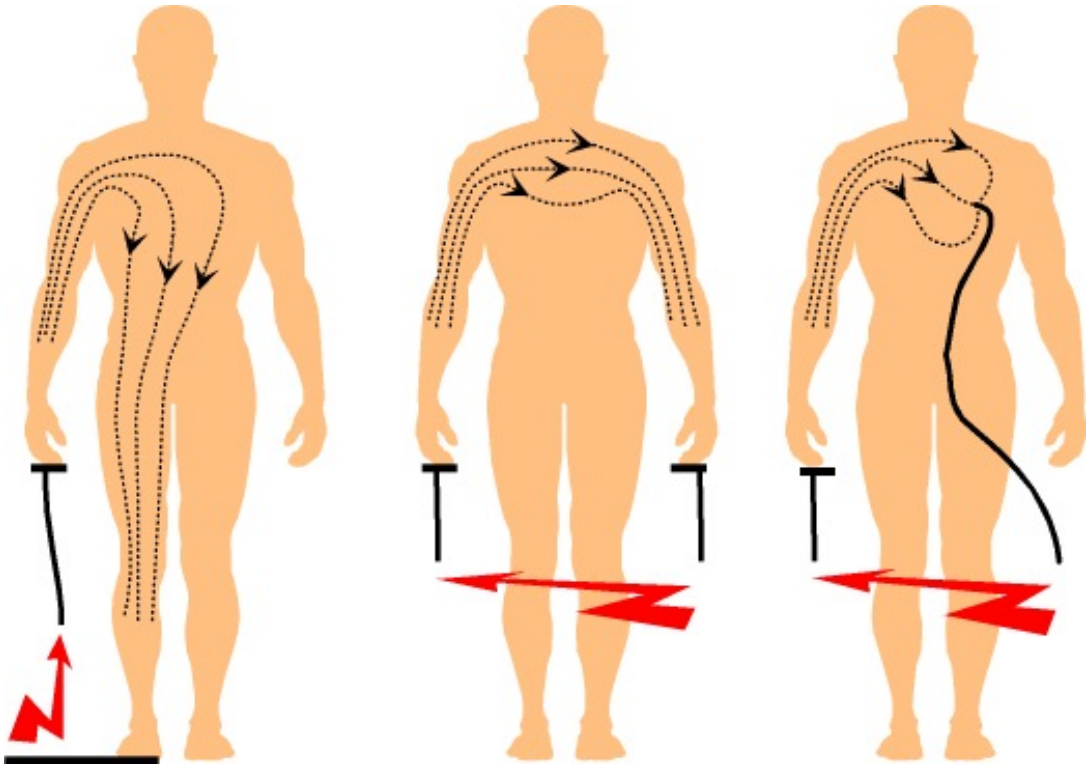


Figure 14.6 Effect of entry points on current distribution (a) *Macroshock*, externally applied current spreads throughout the body. (b) *Microshock*, all the current applied through an intracardiac catheter flows through the heart. (From F. J. Weibell, "Electrical Safety in the Hospital," *Annals of Biomedical Engineering*, 1974, 2, 126–148.)

Macro- og microshock vs current density

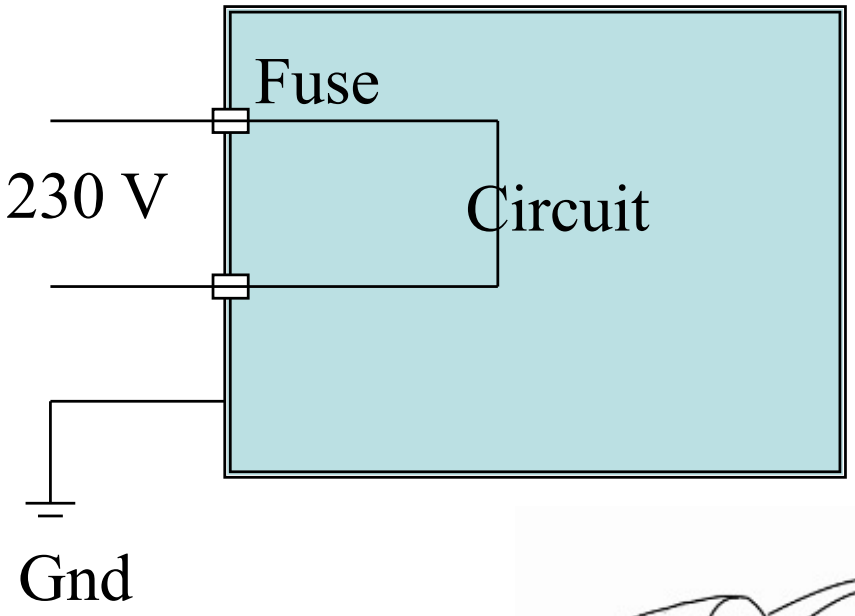


I < 75 milliampére
large volume

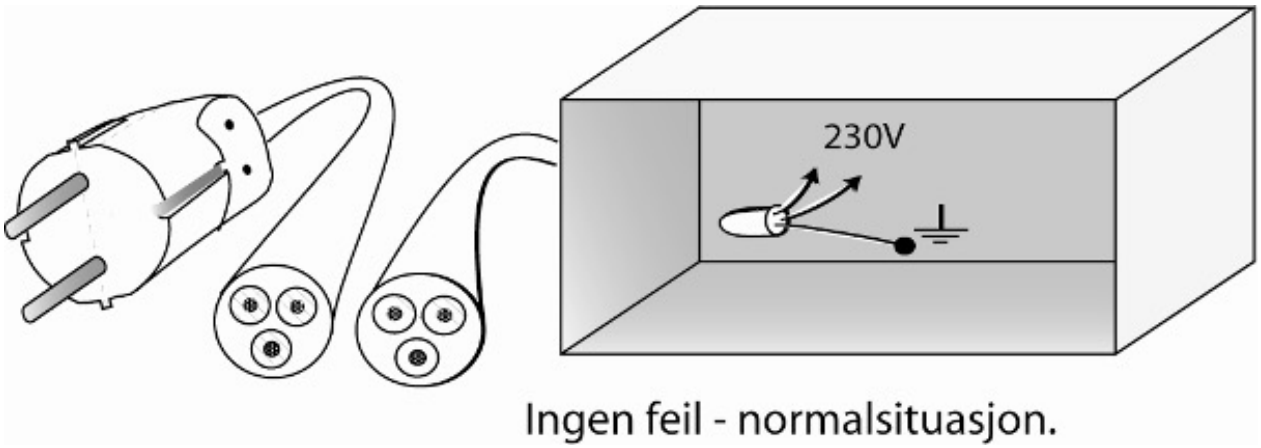
I = 10 mikroampére
small area

Current density = current / area

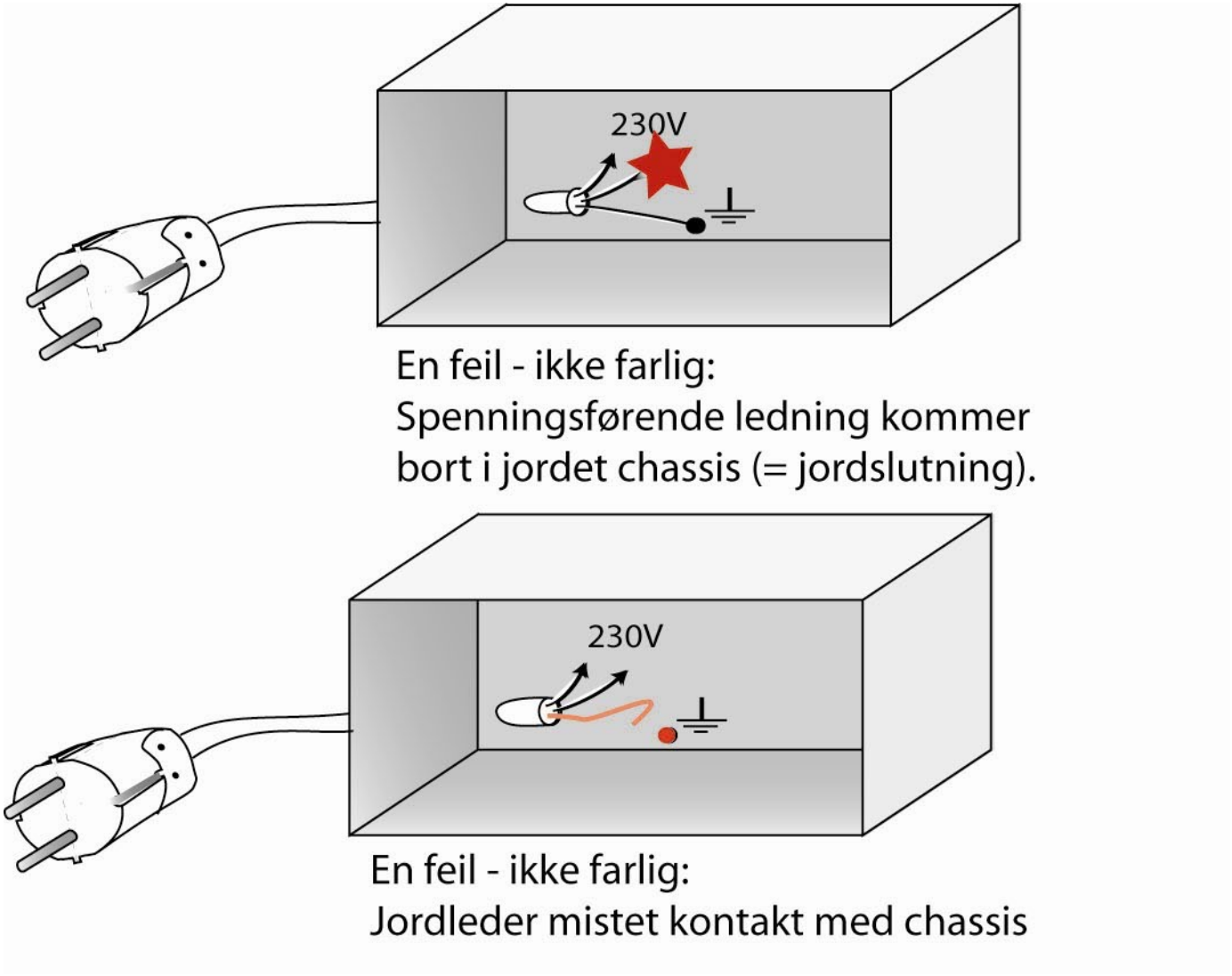
Electrical grounding

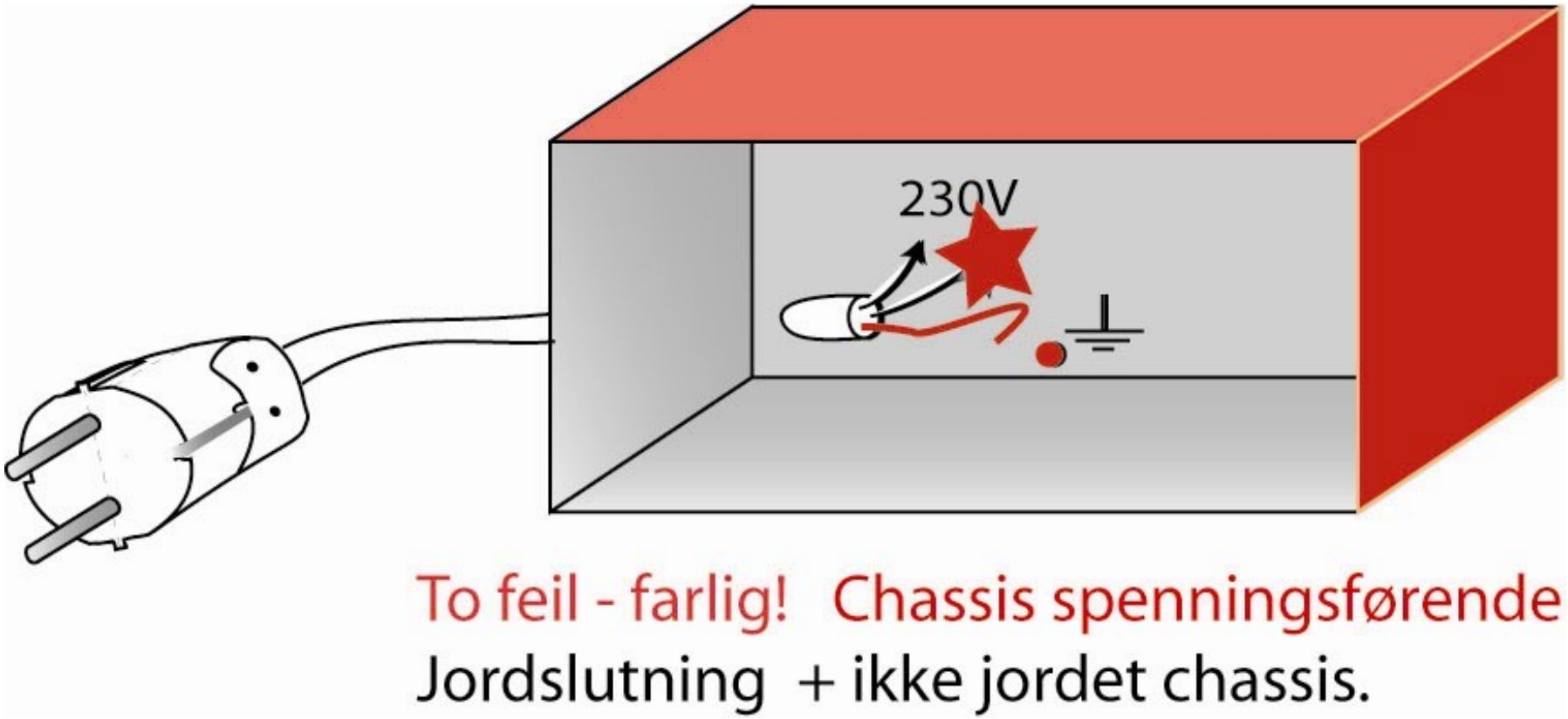


Only devices with a double isolation-tag can be used if not separate ground



One error, not fatal but must be repaired





Two simultaneous errors are dangerous.

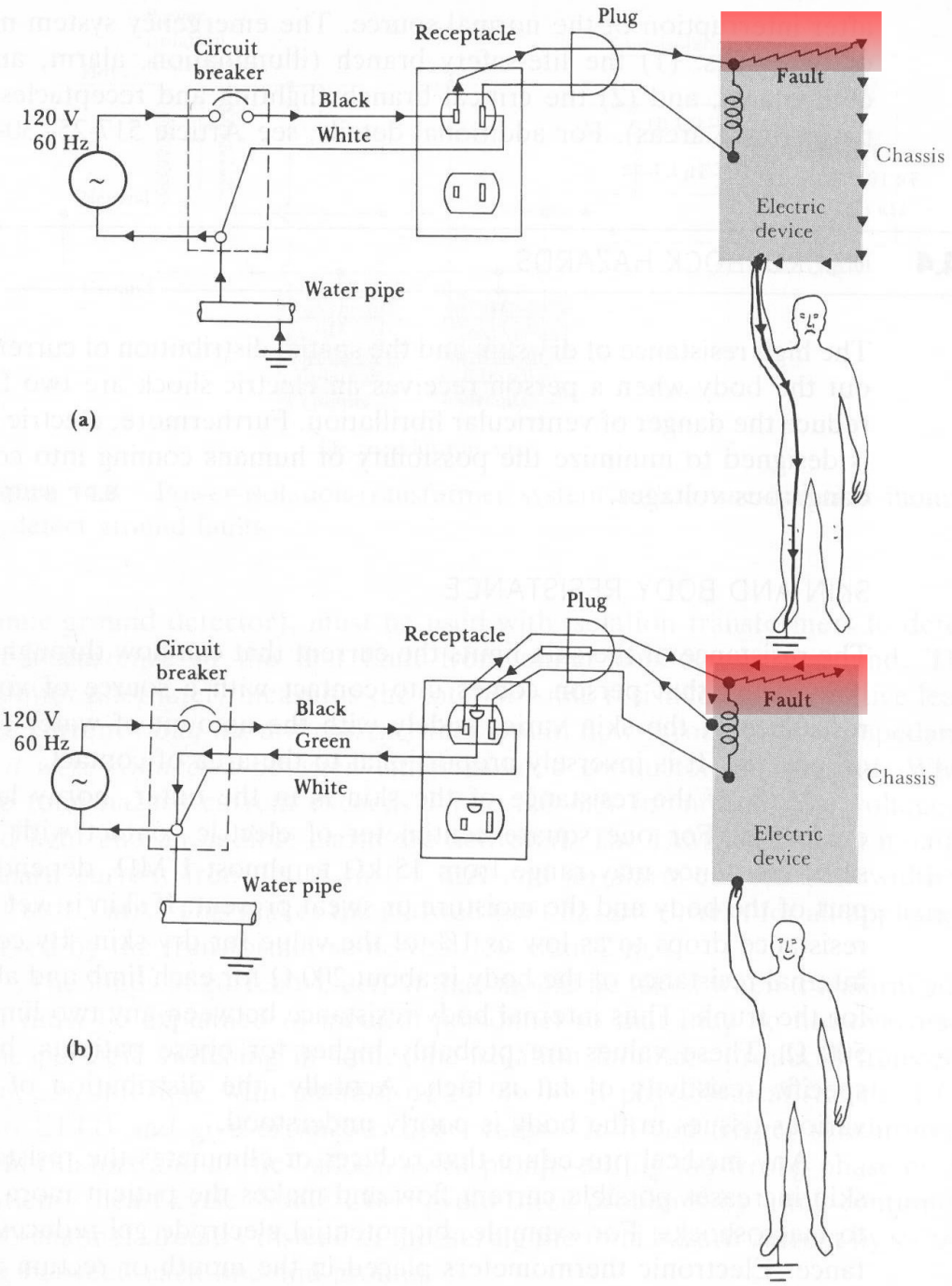


Figure 14.9 Macroshock due to a ground fault from hot line to equipment cases for (a) ungrounded cases and (b) grounded cases.

Macroshock due to ground fault

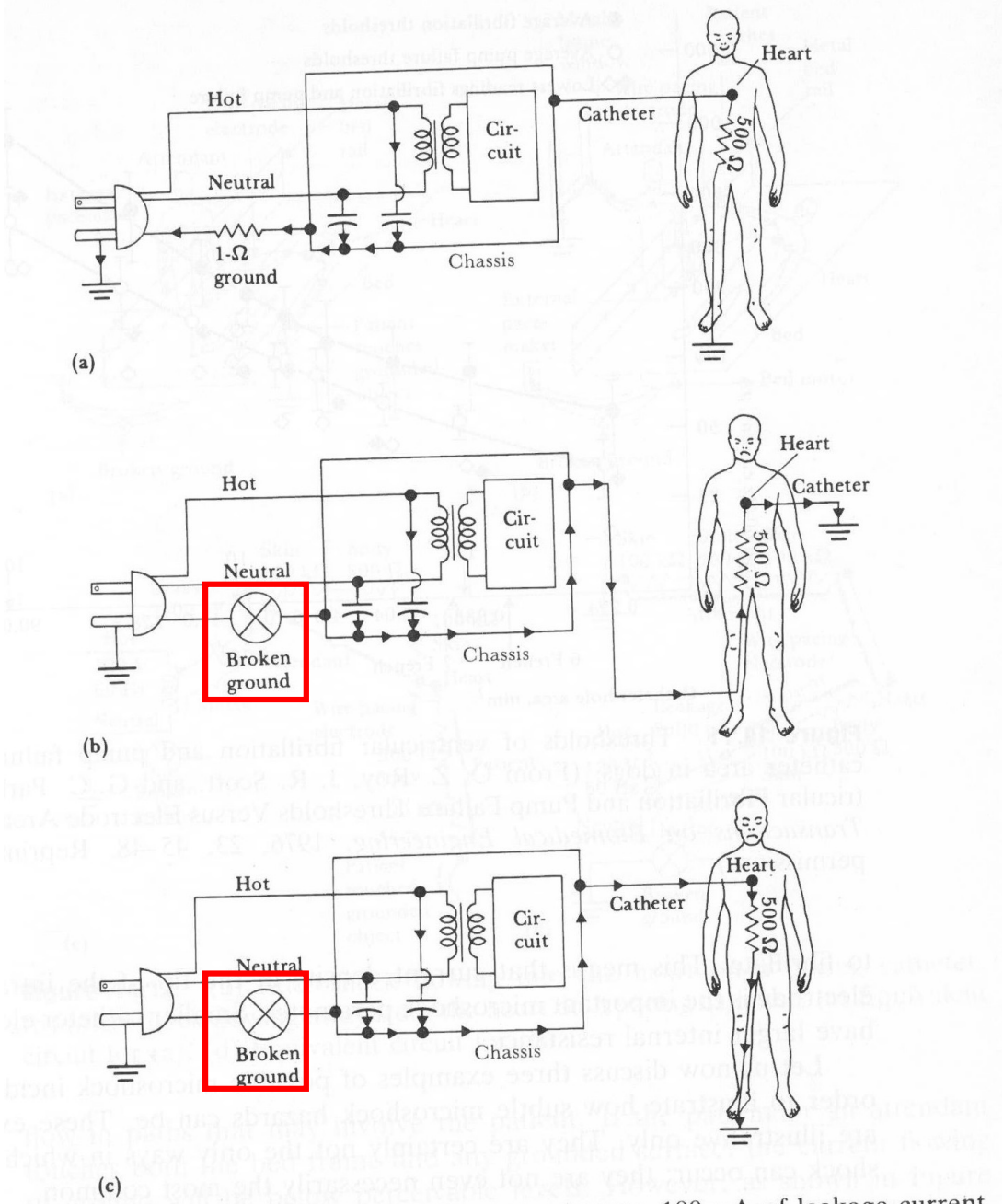


Figure 14.10 **Leakage-current pathways** Assume 100 μA of leakage current from the power line to the instrument chassis. (a) Intact ground, and 99.8 μA flows through the ground. (b) Broken ground, and 100 μA flows through the heart. (c) Broken ground, and 100 μA flows through the heart in the opposite direction.

Microshock, two error situations

Ventricular fibrillation and pump failure vs catheter area

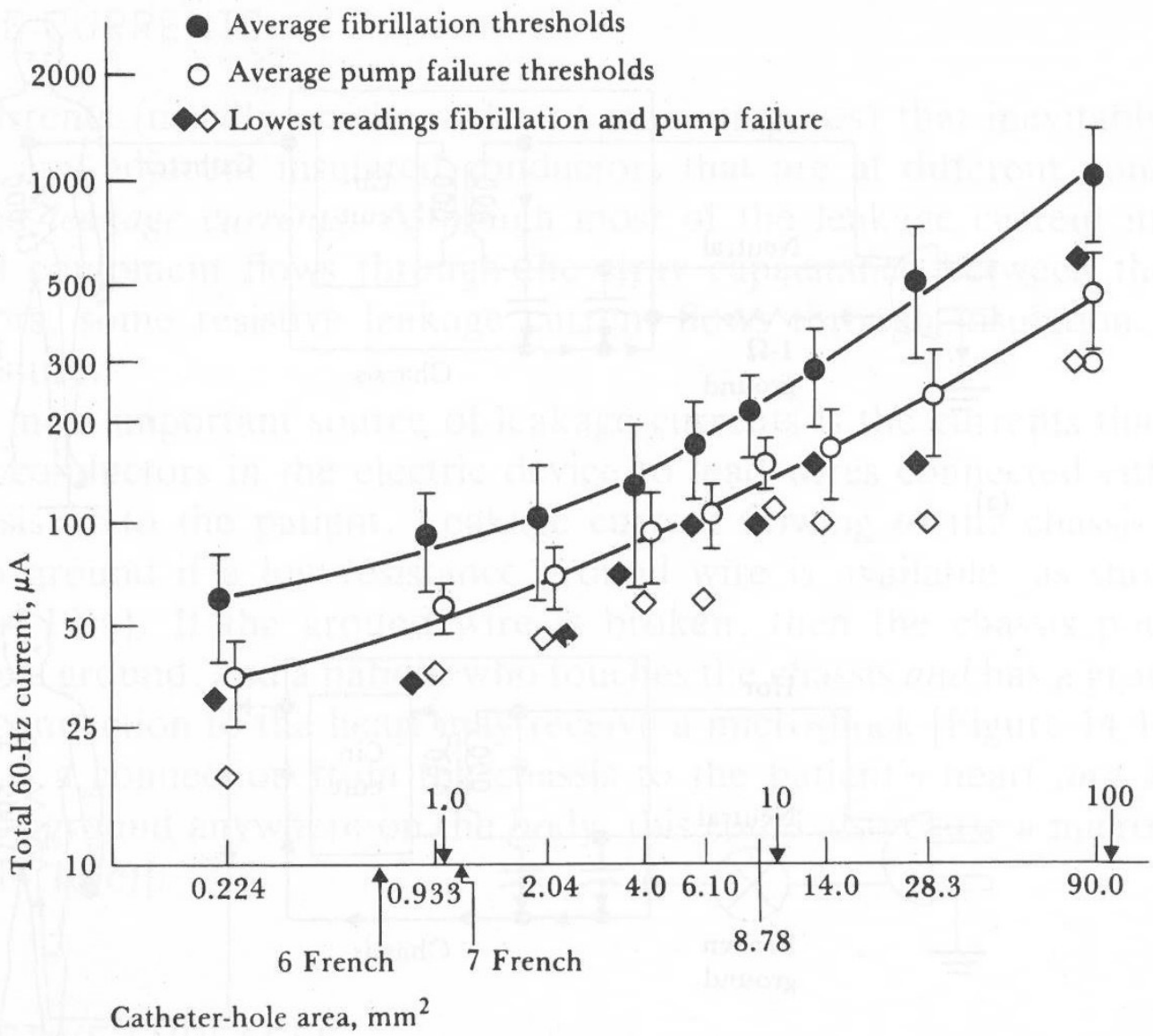


Figure 14.11 Thresholds of ventricular fibrillation and pump failure versus catheter area in dogs. (From O. Z. Roy, J. R. Scott, and G. C. Park, "Ventricular Fibrillation and Pump Failure Thresholds Versus Electrode Area," *IEEE Transactions on Biomedical Engineering*, 1976, 23, 45–48. Reprinted with permission.)

UiC

Micro-shock

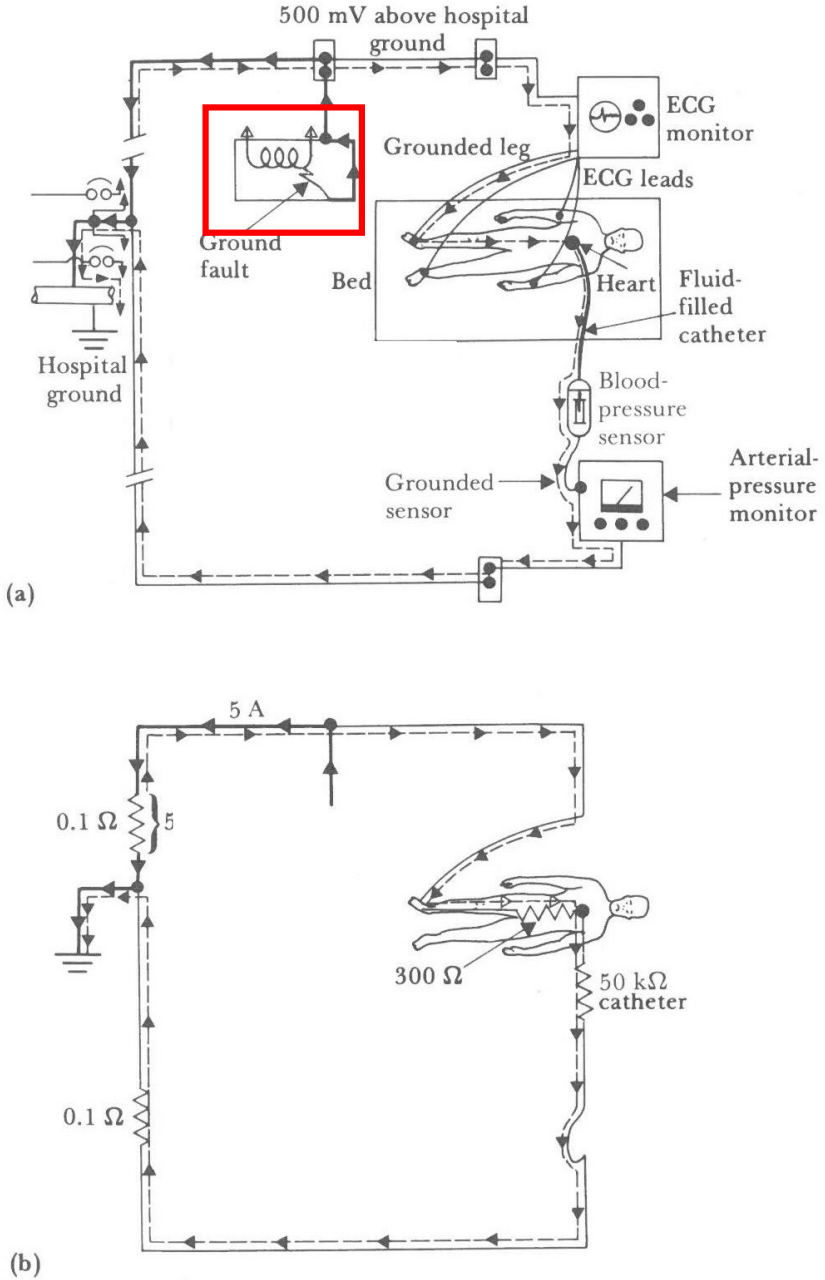


Figure 14.11 (a) Large ground-fault current raises the potential of *one* ground connection to the patient. The microshock current can then flow out through a catheter connected to a different ground. (b) Equivalent circuit. Only power-system grounds are shown.

System for grounding

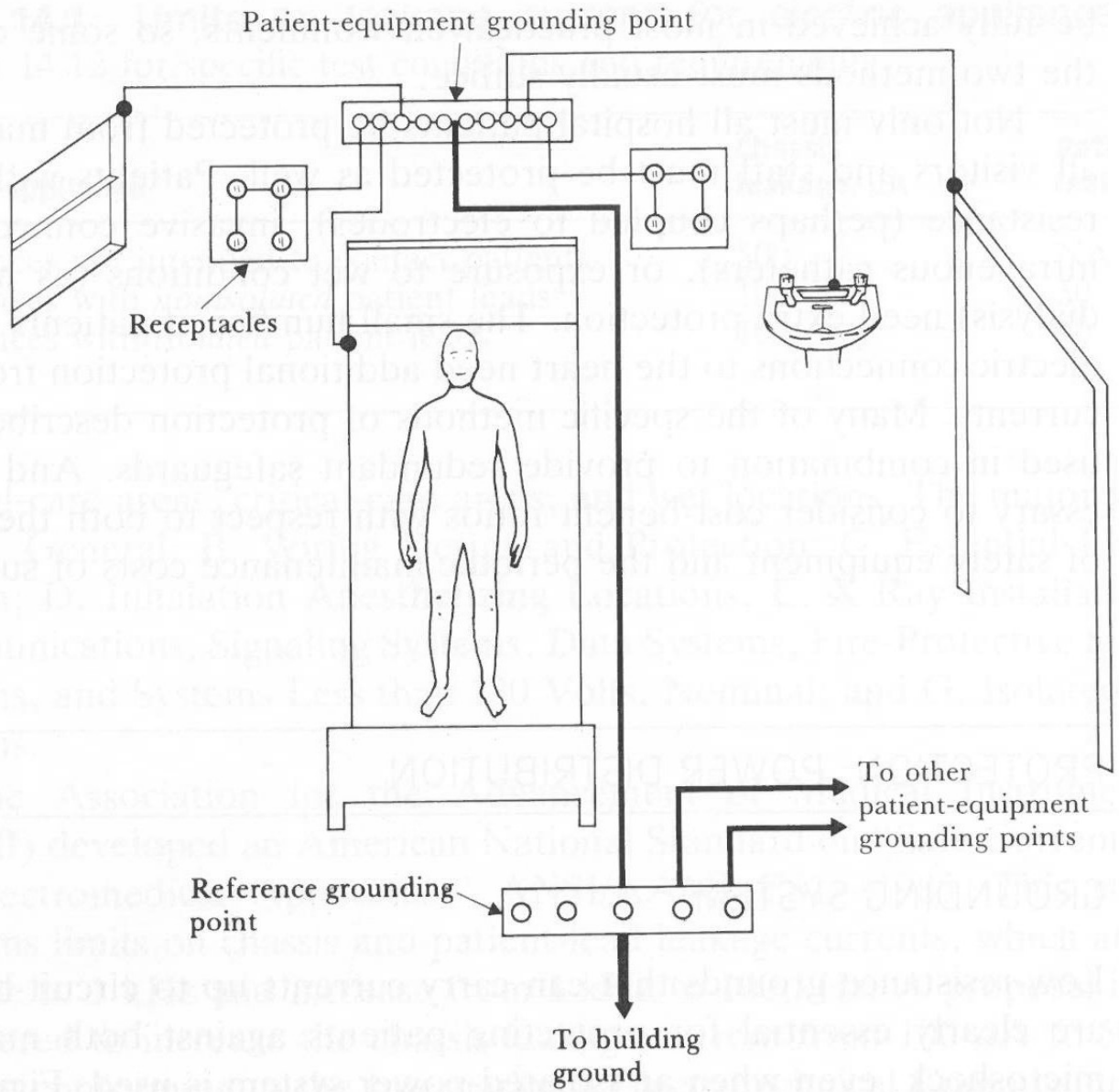
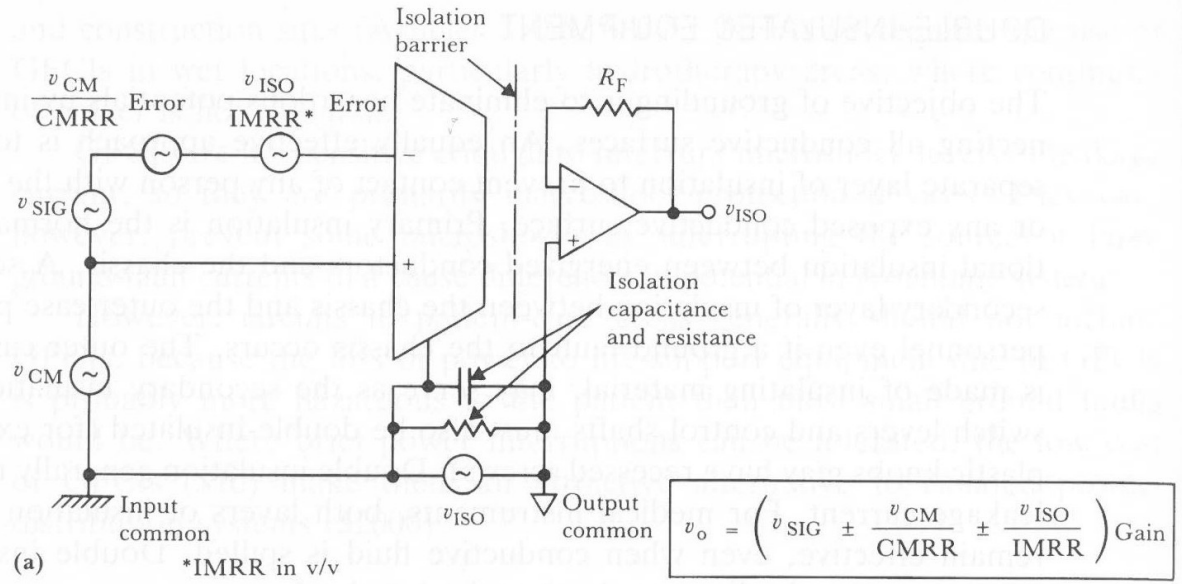


Figure 14.15 Grounding system All the receptacle grounds and conductive surfaces in the vicinity of the patient are connected to the patient-equipment grounding point. Each patient-equipment grounding point is connected to the reference grounding point that makes a single connection to the building ground.

Electrical isolation amplifier



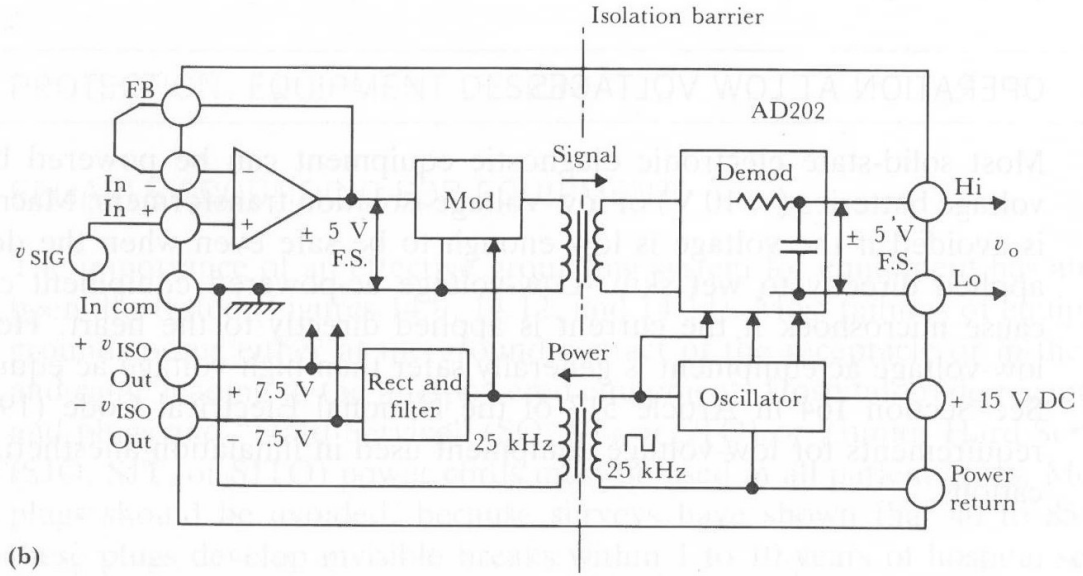


Figure 14.17 **Electrical isolation of patient leads to biopotential amplifiers** (a) General model for an isolation amplifier. (b) Transformer isolation amplifier (Courtesy of Analog Devices, Inc., AD202). (c) Simplified equivalent circuit for an optical isolator (Copyright © 1989 Burr-Brown Corporation. Reprinted in whole or in part, with the permission of Burr-Brown Corporation. Burr Brown ISO100). (d) Capacitively coupled isolation amplifier (Horowitz and Hill, Art of Electronics, Cambridge Univ. Press, Burr Brown ISO106).

Perfect isolation barrier modeled by the isolation capacitance and resistance.
IMRR = isolation mode rejection ratio (potential between the input common and the output common)
The high impedance is modeled by isolation capacitance and resistance

3 main features
- High ohmic isolation input/output (>10MOhm)
- High isolation-mode voltage (> 1000V)
- High common mode-rejection ((> 100 dB)

- Transformer isolation
- Optical isolation
- Capacitive isolation

Ground pin to chassis test

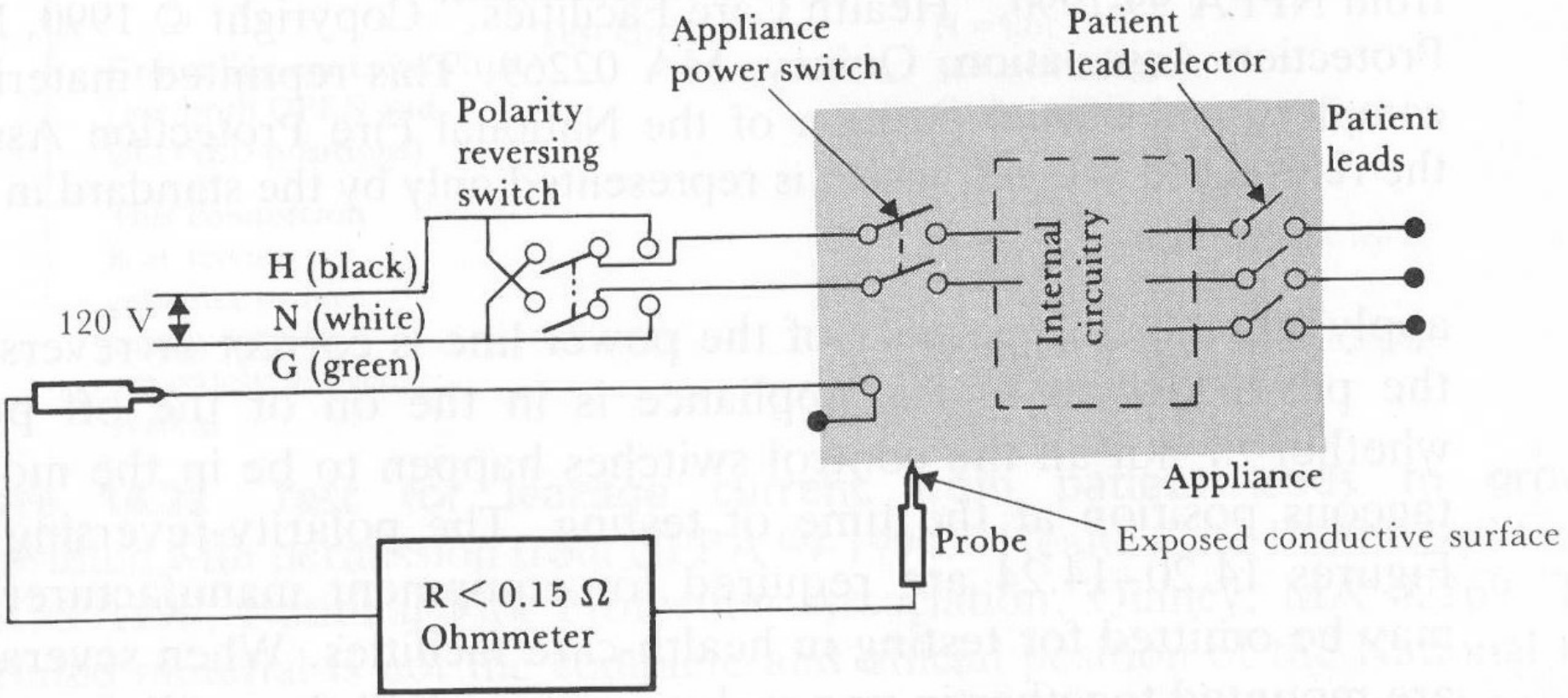


Figure 14.20 Ground-pin-to-chassis resistance test

Chassis leakage current test

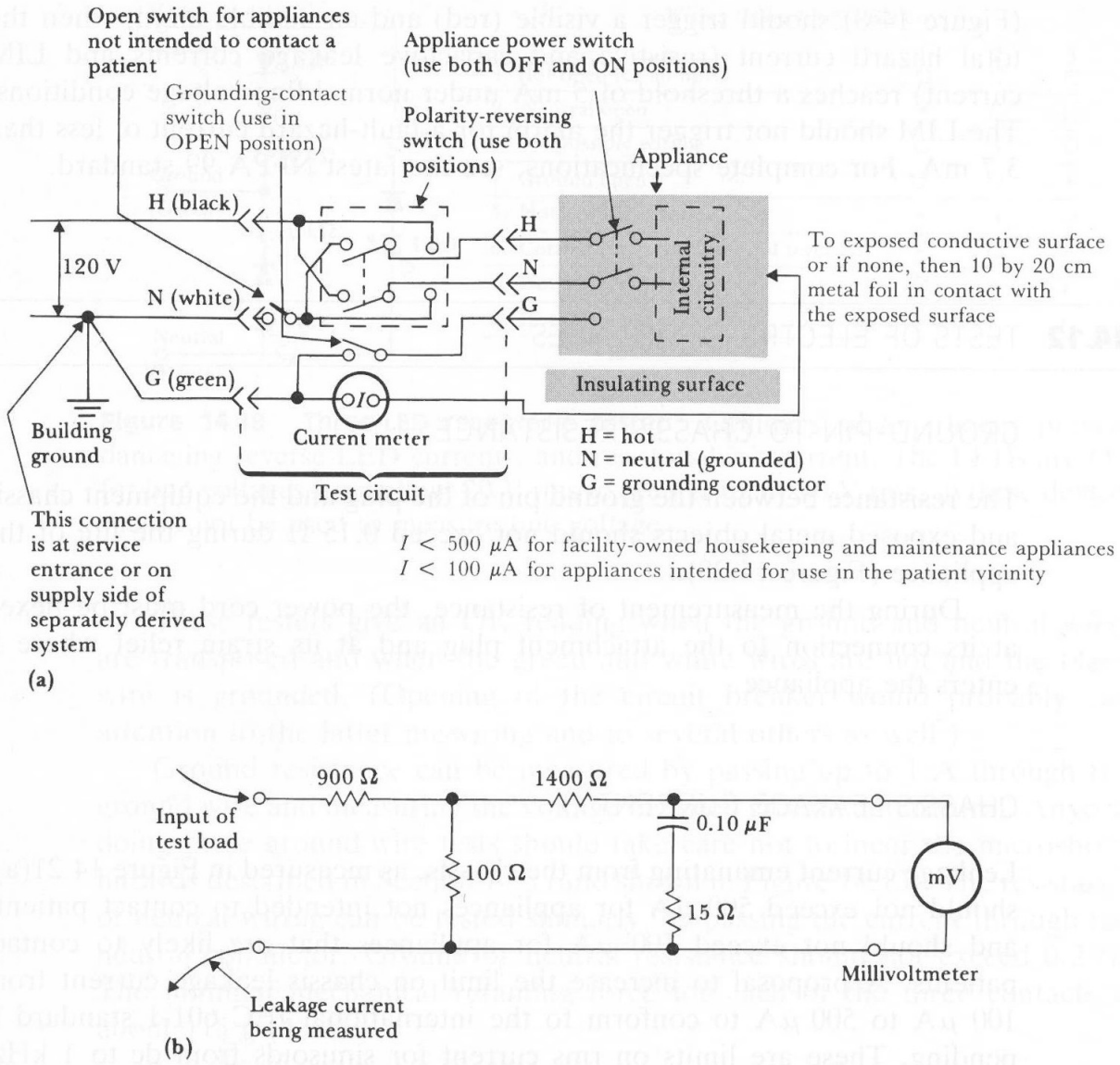


Figure 14.21 (a) Chassis leakage-current test. (b) Current-meter circuit to be used for measuring leakage current. It has an input impedance of 1 kΩ and a frequency characteristic that is flat to 1 kHz, drops at the rate of 20 dB/decade to 100 kHz, and then remains flat to 1 MHz or higher. (Reprinted with permission from NFPA 99-1990, "Health Care Facilities," Copyright © 1990, National Fire Protection Association, Quincy, MA 02269. This reprinted material is not the complete and official position of the National Fire Protection Association, on the referenced subject, which is represented only by the standard in its entirety.)

Patient leakage current test

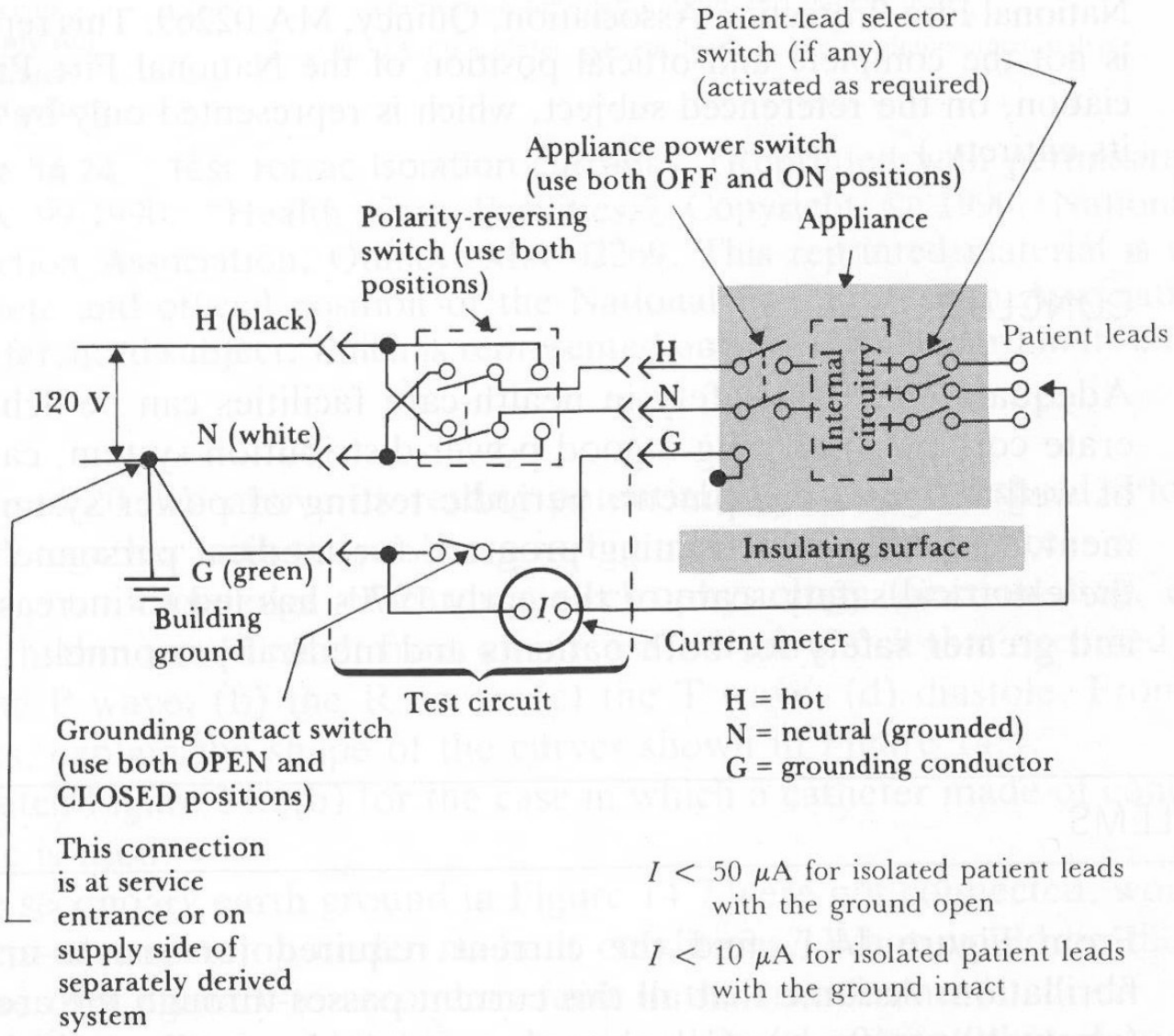
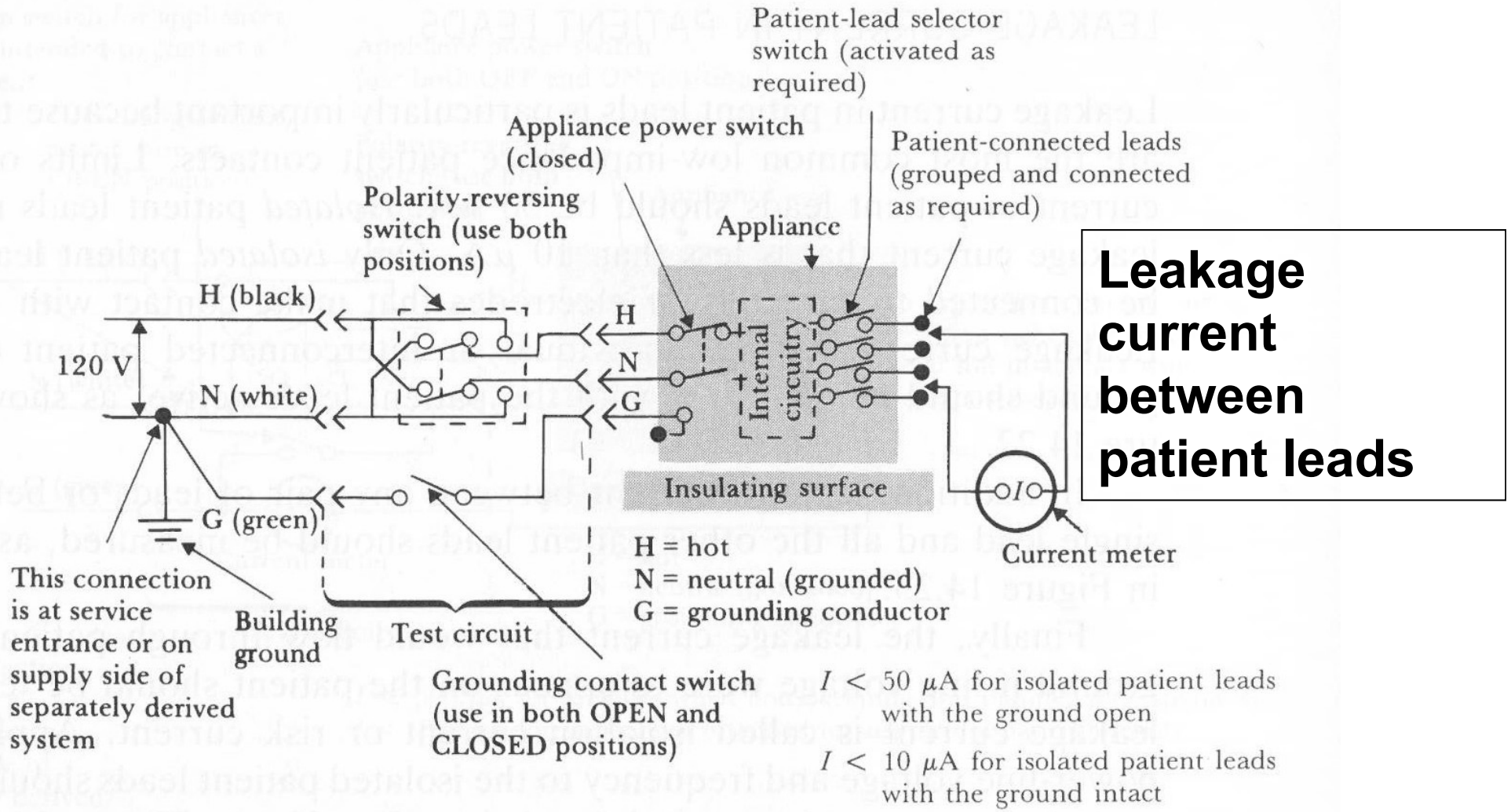


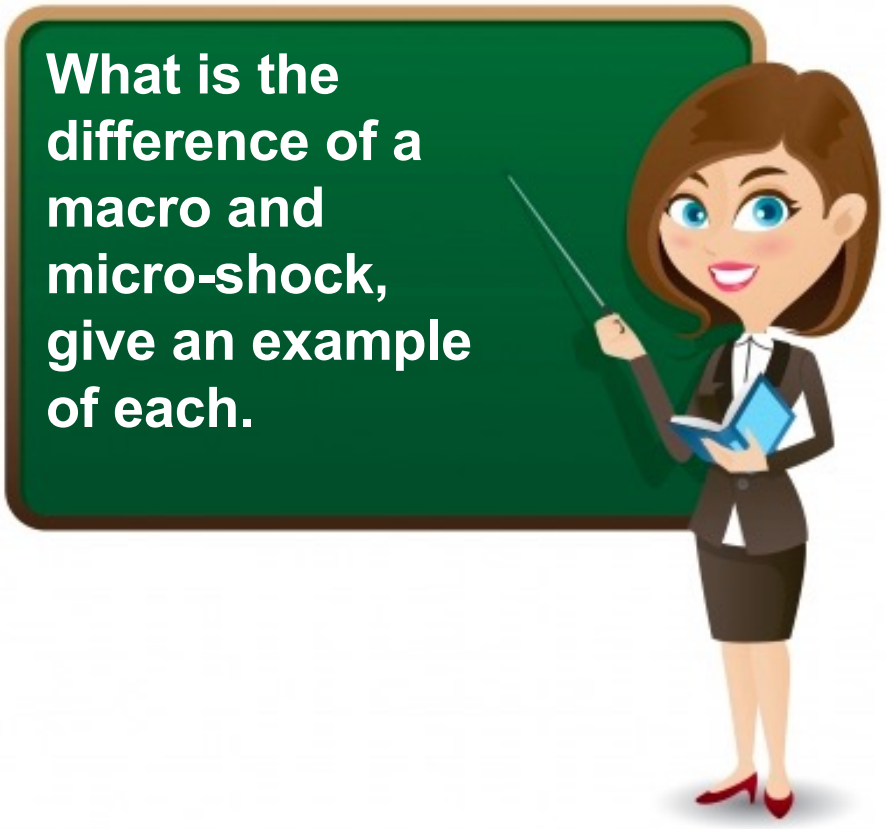
Figure 14.22 Test for leakage current from patient leads to ground (Reprinted with permission from NFPA 99-1990, "Health Care Facilities," Copyright © 1990, National Fire Protection Association, Quincy, MA 02269. This reprinted material is not the complete and official position of the National Fire Protection Association, on the referenced subject, which is represented only by the standard in its entirety.)



Leakage current between patient leads

Figure 14.23 Test for leakage current between patient leads (Reprinted with permission from NFPA 99-1990, "Health Care Facilities," Copyright © 1990, National Fire Protection Association, Quincy, MA 02269. This reprinted material is not the complete and official position of the National Fire Protection Association, on the referenced subject, which is represented only by the standard in its entirety.)

Exercise examples



Finally.....

Slicky tricks

1. When preparing for your exam, don't get lost in details. Start with the main topics and be sure you understand them before you start to drill down in the substance
2. During the exam: Keep talking
3. If you have nothing more to say, try to direct the attention slightly to a related topic of your preferation
4. All amplifiers (more or less), in this course have the same demands: High input impedance, high CMRR, protection to the organism, high gain, easy to calibrate and good frequency characteristics within the physiological spectrum
5. The main goal of this course is to obtain a breadth of outlook in this complicated field, don't forget that. A typical question could be to compare different image modalities across all chapters.
6. If (on a direct question) you don't know the answer, try to talk around the question while closely observing the response from both the examinator and sensor. Very often, it is possible to discuss yourself towards the answer.
7. Don't exaggerate the consequence when you're in, this is no execution. Take your time, breath calmly and think before you speek and we will have a nice, peaceful conversation
8. Even if the curriculum for the exam is all of your textbook (except from chapter 9), the main focus comes from the lectures.

Good luck!