Measurement of Flow and Volume of Blood

The main subject of this lesson is the measurement of blood flow and blood volume

There are various techniques that can be used for these purposes such as:

- Indicator-dilution Method That Uses Continuous Infusion
- Indicator-dilution Method That Uses Rapid Injection
- Electromagnetic Flowmeters
- Ultrasonic Flowmeters
- Thermal-convection Velocity Sensors
- Chamber Plethysmography
- Photoplethysmography
- Electrical-impedance Plethysmography

❑ Indicator-dilution Method That Uses Continuous Infusion

- The indicator-dilution methods do not measure instantaneous pulsatile flow but, rather, flow averaged over a number of heartbeats.

Concentration

- When a given quantity m_0 of an indicator is added to a volume V, the resulting concentration C of the indicator is given by

$$C = m_0/V.$$

- When an additional quantity m of indicator is then added, the incremental increase in concentration is

$$\Delta C = m/V.$$

- When the fluid volume in the measured space is continuously removed and replaced, as in a flowing stream, fixed quantity of indicator per unit time is added

$$\Delta C = (dm/dt)/(dV/dt)$$

- From this equation, we can calculate flow

$$F = \frac{dV}{dt} = \frac{dm/dt}{\Delta C}$$

Fick Technique

- We can measure cardiac output (blood flow from the heart) by using

$$F = \frac{dV}{dt} = \frac{dm/dt}{\Delta C}$$

Fick Technique uses O_2 as an indicator in the equation to calculate the Cardiac output:

$$F = \frac{dm/dt}{C_a - C_v}$$

where

F = blood flow, liters/min

dm/dt = consumption of O_2, liters/min

C_a = arterial concentration of O_2, liters/liter

C_v = venous concentration of O_2, liters/liter

➢ Measurements required to determine O_2 amount

- The blood returning to the heart from the upper half of the body has a different concentration of O_2 from the blood returning from the lower half, because the amount of O_2 extracted by the brain is different from that extracted by the kidneys, muscles, and so forth. Therefore, we cannot accurately measure **Cv** in the right atrium. We must measure it in the **pulmonary artery** after it has been mixed by the pumping action of the right ventricle.

- The clinician can measure the concentration of the oxygenated blood **Ca** in **any artery**, because blood from the lung capillaries is well mixed by the left ventricle and there is no consumption of O_2 in the arteries. An arm or leg artery is generally used.

- The physician may float the catheter into place by temporarily inflating a small balloon surrounding the tip.

- As the blood flows through the lung capillaries, the subject adds the indicator (the O_2) by breathing in pure O_2 from a spirometer

- The exhaled CO_2 is absorbed in a soda-lime canister, so the consumption of O_2 is indicated directly by the **net gas-flow rate**.

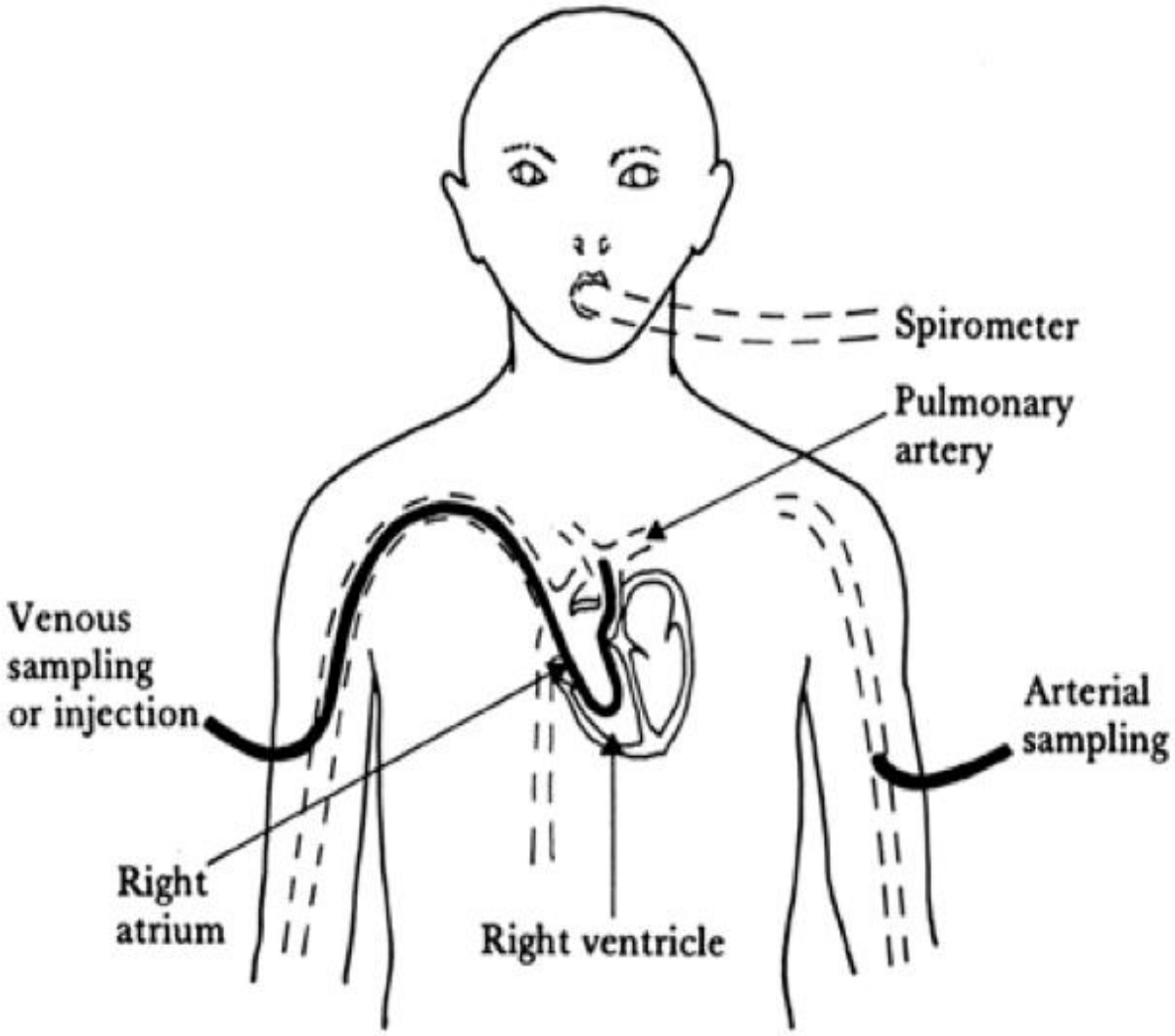


Figure 8.1 Several methods of measuring cardiac output. **In the Fick method**, the indicator is O_2; consumption is measured by a spirometer. The arterialvenous concentration difference is measured by drawing samples through catheters placed in an artery and in the pulmonary artery. **In the dye-dilution method**, dye is injected into the pulmonary artery and samples are taken from an artery. **In the thermodilution method**, cold saline is injected into the right atrium and temperature is measured in the pulmonary artery.

❑ Indicator-dilution Method That Uses Rapid Injection

- A bolus of indicator is rapidly injected into the vessel, and the variation in downstream concentration of the indicator versus time is measured until the bolus has passed.

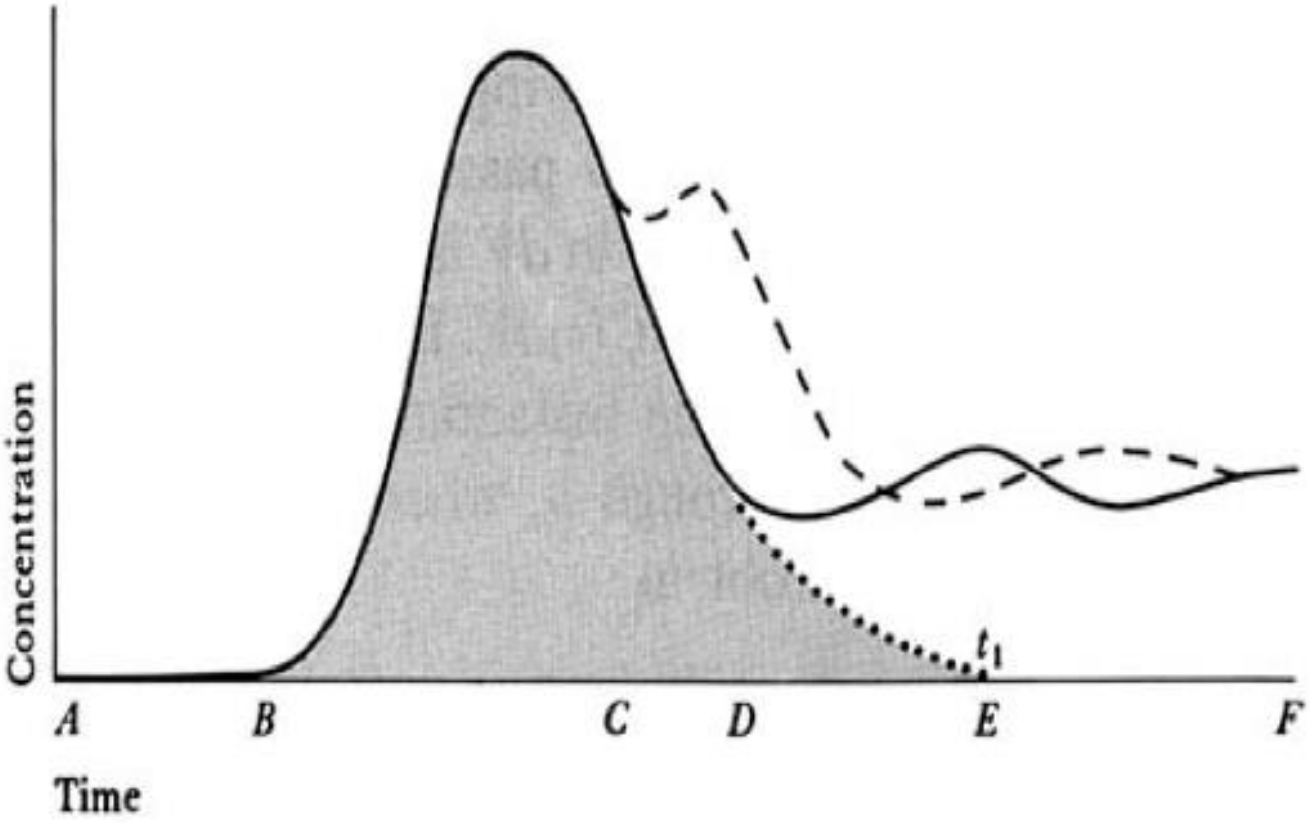
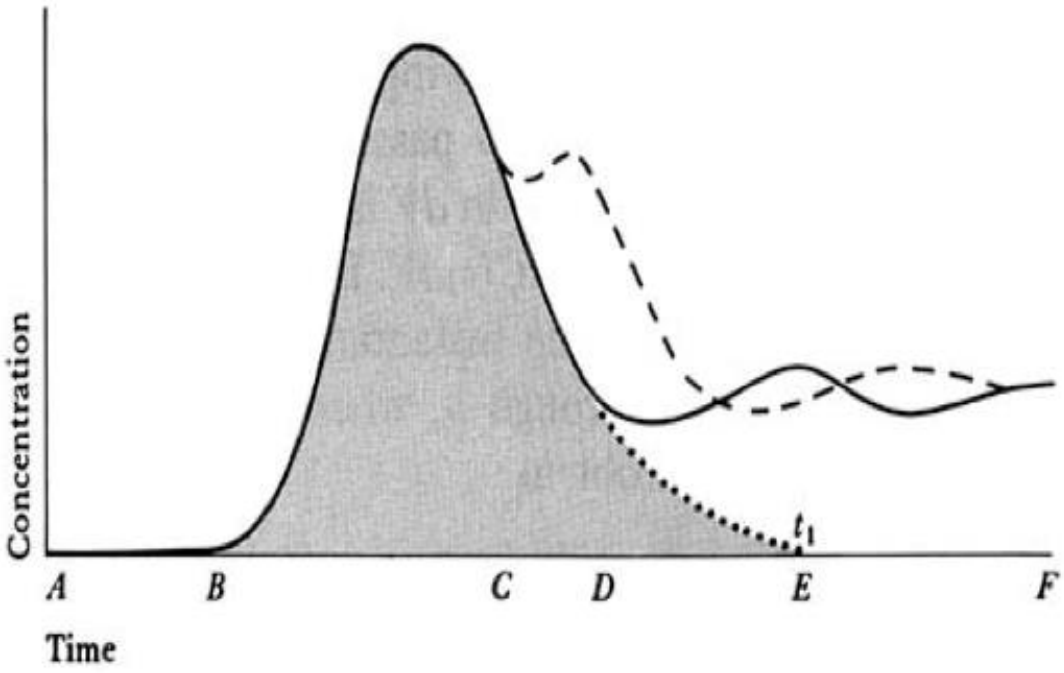


Figure 8.2: Rapid-injection indicator-dilution curve

- After the bolus is injected at time A, there is a transportation delay before the concentration begins rising at time B.
- After the peak is passed, the curve enters an exponential decay region between C and D, which would continue decaying along the dotted curve to t_1 if there were no recirculation.
- However, recirculation causes a second peak at E before the indicator becomes thoroughly mixed in the blood at F.
- The dashed curve indicates the rapid recirculation that occurs when there is a hole between the left and right sides of the heart.
- When a right-left shunt is present, the delay in transport is abnormally short because some indicator reaches the sampling site without passing through the lung vessels.



➢ Rapid-injection indicator-dilution Method That Uses Dye Dilution

- A common method of clinically measuring cardiac output is to use a colored dye, indocyanine green (cardiogreen).

- Colored dye, *indocyanine green* (cardiogreen, a.p 805 nm), meets the requirements for an indicator:
  - inert
  - harmless
  - measurable
  - economical
  - always intravascular

- The dye is available as a liquid that is diluted in isotonic saline and injected directly through a catheter, usually into the pulmonary artery.

- About 50% of the dye is excreted by the kidneys in the first 10 min, so repeat determinations are possible.

- The plot of the curve for concentration versus time is obtained from a constant-flow pump, which draws blood from a catheter placed in the femoral or brachial artery.

- Blood is drawn through a colorimeter cuvette, which continuously measures the concentration of dye, using the principle of absorption photometry.

➢ Rapid-injection indicator-dilution Method That Uses Thermodilution

- The most common method of measuring cardiac output is that of injecting a bolus of cold saline as an indicator.

- A special four-lumen catheter is floated through the brachial vein into place in the pulmonary artery.

- A syringe forces a gas through one lumen; the gas inflates a small, doughnut-shaped balloon at the tip. The force of the flowing blood carries the tip into the pulmonary artery. The cooled saline indicator is injected through the second lumen into the right atrium.

- The indicator is mixed with blood in the right ventricle. The resulting drop in temperature of the blood is detected by a thermistor located near the catheter tip in the pulmonary artery.

- The third lumen carries the thermistor wires.

- The fourth lumen, which is not used for the measurement of thermodilution, can be used for withdrawing blood samples.

- cold saline is injected into the right atrium and temperature is measured in the pulmonary artery.

$$F = \frac{Q}{\rho_b c_b \int_0^{t_1} \Delta T_b(t)\,dt} \left(m^3/s\right)$$

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where

Q= heat content of injectate, J(= $V_i \Delta T_i p_i c_i$)

P_b = density of blood, kg/m^3

c_b = specific heat of blood, J/(kg.K)

- problems of thermodilution method that cause errors.

(1) inadequate mixing between the injection site and the sampling site

(2) exchange of heat between the blood and the walls of the heart chamber.

(3) heat exchange through the catheter walls before, during, and after injection.

❑ Electromagnetic Flowmeters

- The electromagnetic flowmeter measures instantaneous pulsatile flow of blood and thus has a greater capability than indicator-dilution methods, which measure only average flow.

➢ principle

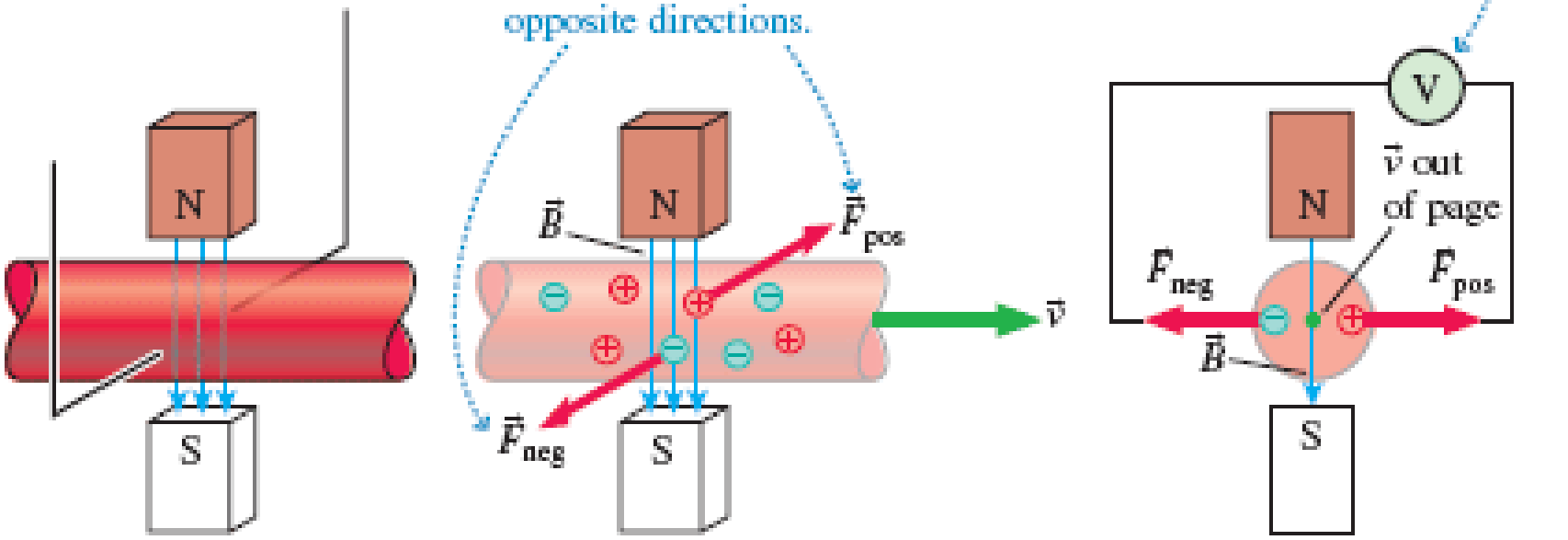
- The electric generator in a car generates electricity by induction. Copper wires move through a magnetic field, cutting the lines of magnetic flux and inducing an emf in the wire. This same principle is exploited in a commonly used blood flowmeter.

- Instead of copper wires, the flowmeter depends on the movement of blood, which has a conductance similar to that of saline.

1. The probe's magnets apply a strong field. The electrodes make contact along an axis perpendicular to this field.

2. The magnetic field exerts forces on ions moving with the blood. Positive and negative ions feel forces in opposite directions.

3. An end view shows that these forces create a separation of charge, producing a potential difference between the electrodes.



- Faraday's law of induction gives the formula for the induced emf.

$$e = \int_0^{L_1} \mathbf{u} \times \mathbf{B} \cdot d\mathbf{L}$$

where

B = magnetic flux density, T
L = length between electrodes, m
u = instaneous velocity of blood, m/s

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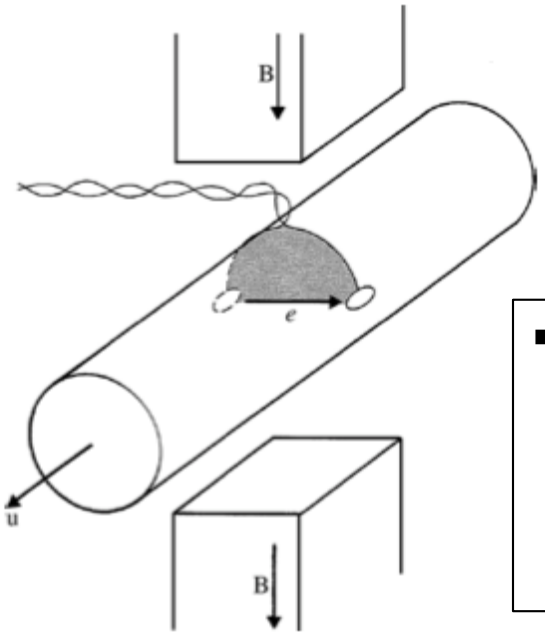


- For a uniform magnetic field B and a uniform velocity profile *u*, the induced emf is

$$e = BLu$$

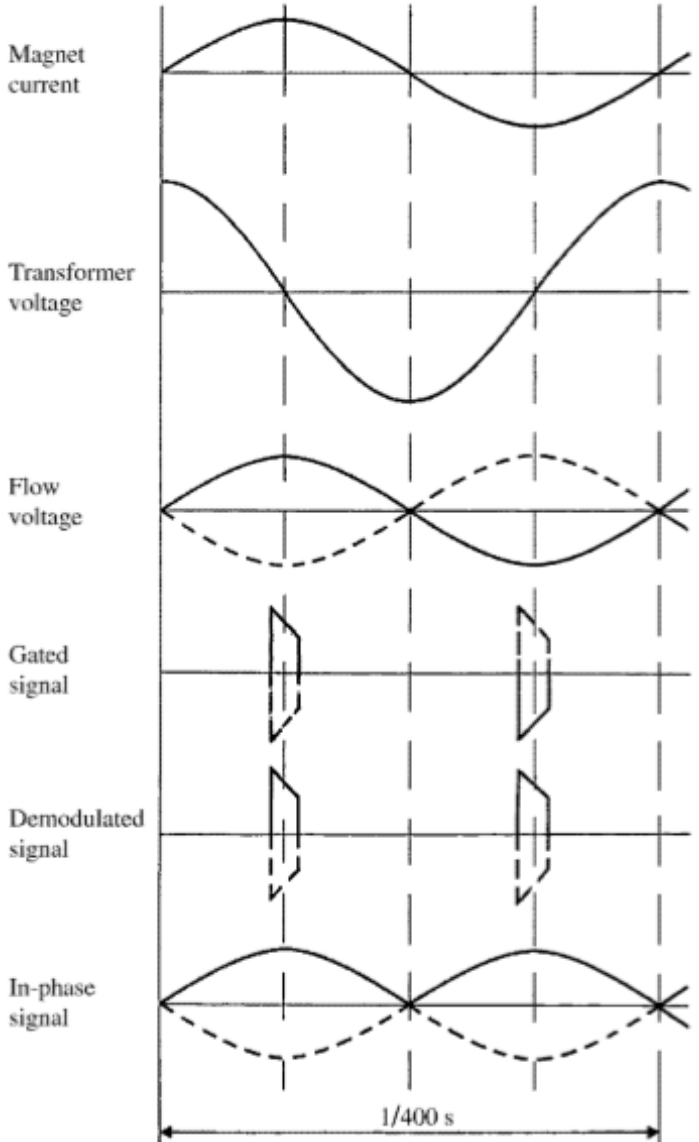
Figure 8.3: Electromagnetic flowmeter: When blood flows in the vessel with velocity u and passes through the magnetic field B, the induced emf e is measured at the electrodes shown. When an ac magnetic field is used, any flux lines cutting the shaded loop induce an undesired transformer voltage.

➢ Direct-current Flowmeter

- The flowmeter shown in Figure 8.3 can use a dc magnetic field, so the output voltage continuously indicates the flow
- However, it is not satisfactory due to
  1. Electrode-electrolyte potential at the same order as the induce voltage due to the flow emf can't be detected
  2. The ECG has similar frequency components and it has larger signal (near the heart), therefore causes interference
  3. In the frequency range of interest, 0 to 30 Hz, 1/f noise in the amplifier is large, which results in a poor SNR

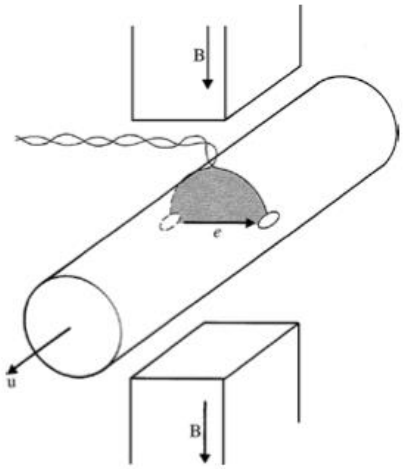
➢ Alternating-current Flowmeter

- The clinician can eliminate the problems of the dc flowmeter by operating the system with an ac magnet current of about 400 Hz.
- The operation of this carrier system results in the ac flow voltage shown in Figure.
- When the flow reverses direction, the voltage changes phase by 180° , so the phase-sensitive demodulator is required to yield directional output.



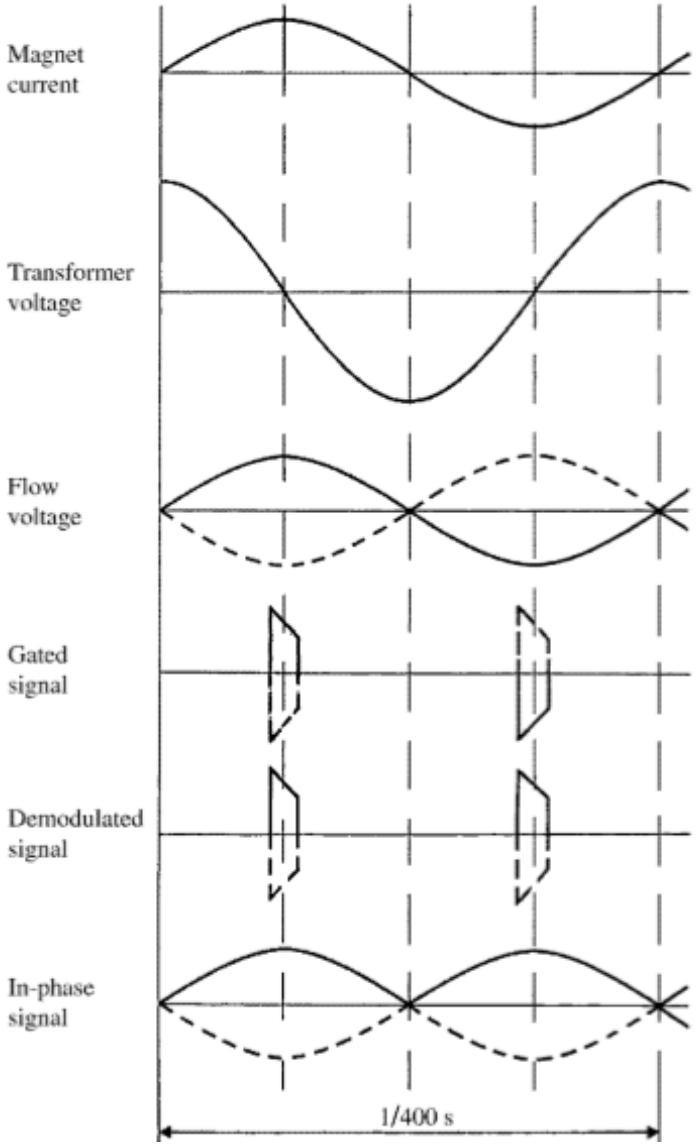
- Although ac operation is superior to dc operation, the new problem of ***transformer voltage*** arises.

- If the shaded loop is not exactly parallel to the B field, some ac magnetic flux intersects the loop and induces a transformer voltage proportional to dB/dt in the output voltage.



- Even when the electrodes and wires are carefully positioned, the transformer voltage is usually many times larger than the flow voltage.

- The amplifier voltage is the sum of the transformer voltage and the flow voltage.



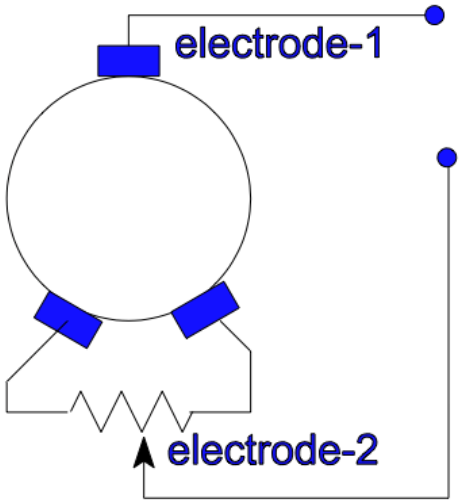
Solutions

– Phantom electrode
– Sampling
– Quadrature suppression
– Square-wave excitation

➢ Phantom electrode

- One of the electrodes is separated into two electrodes in the axial direction. Two wires are led some distance from the electrodes, and a potentiometer is placed between them.

- The shaded loop in Figure 8.3 can thus be tilted forward or backward or placed exactly parallel to the B field.



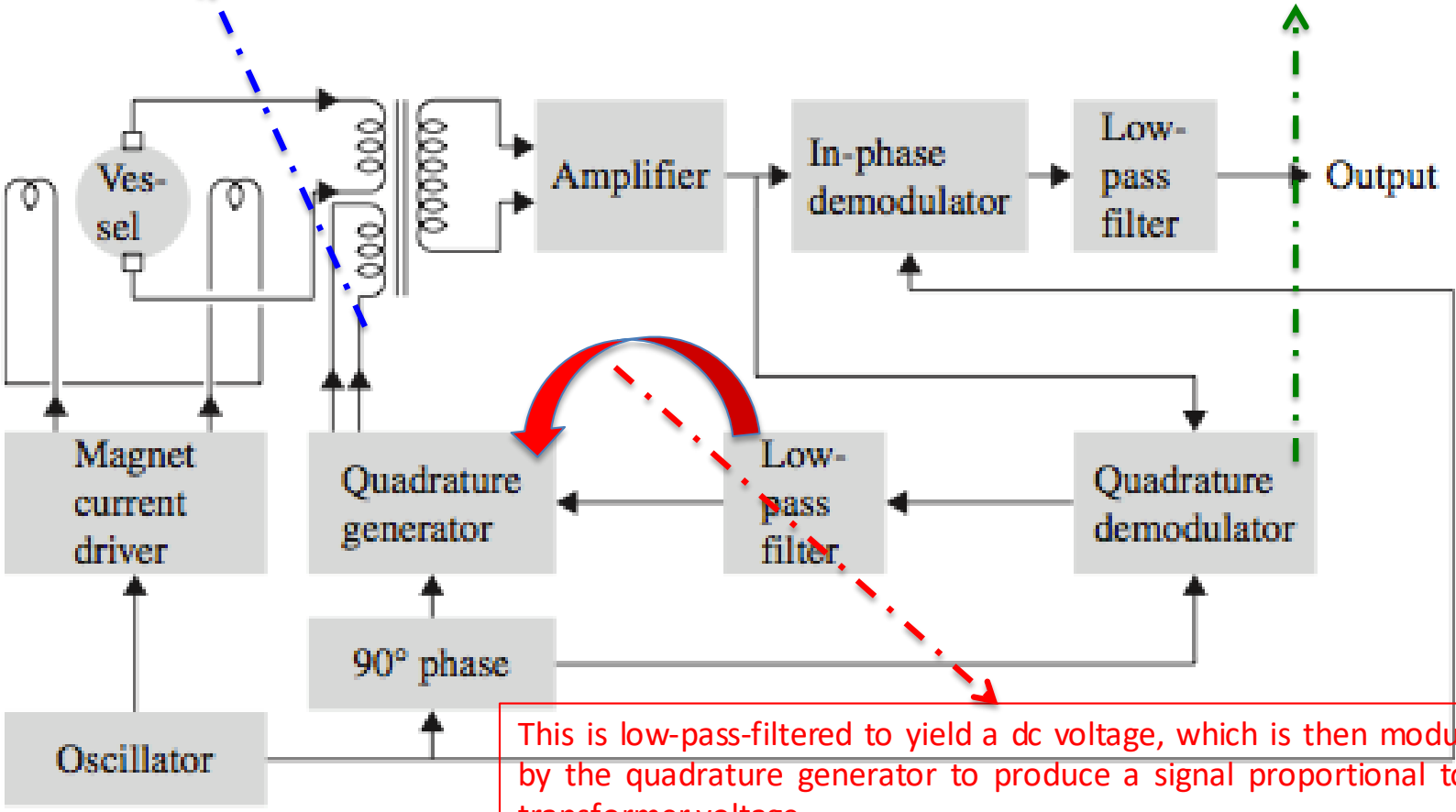
➢ Sampling

- we can sample the composite signal when the transformer voltage is zero. At this time the flow voltage is at its maximum, and the resulting gated signal measures only the flow voltage.

➢ Quadrature suppression

The signal is fed to a balancing coil on the input transformer, thus balancing out the transformer voltage at the input.

The magnitude of the voltage in the transformer at the amplifier output is detected by the quadrature demodulator, which has a full-wave-rectified output

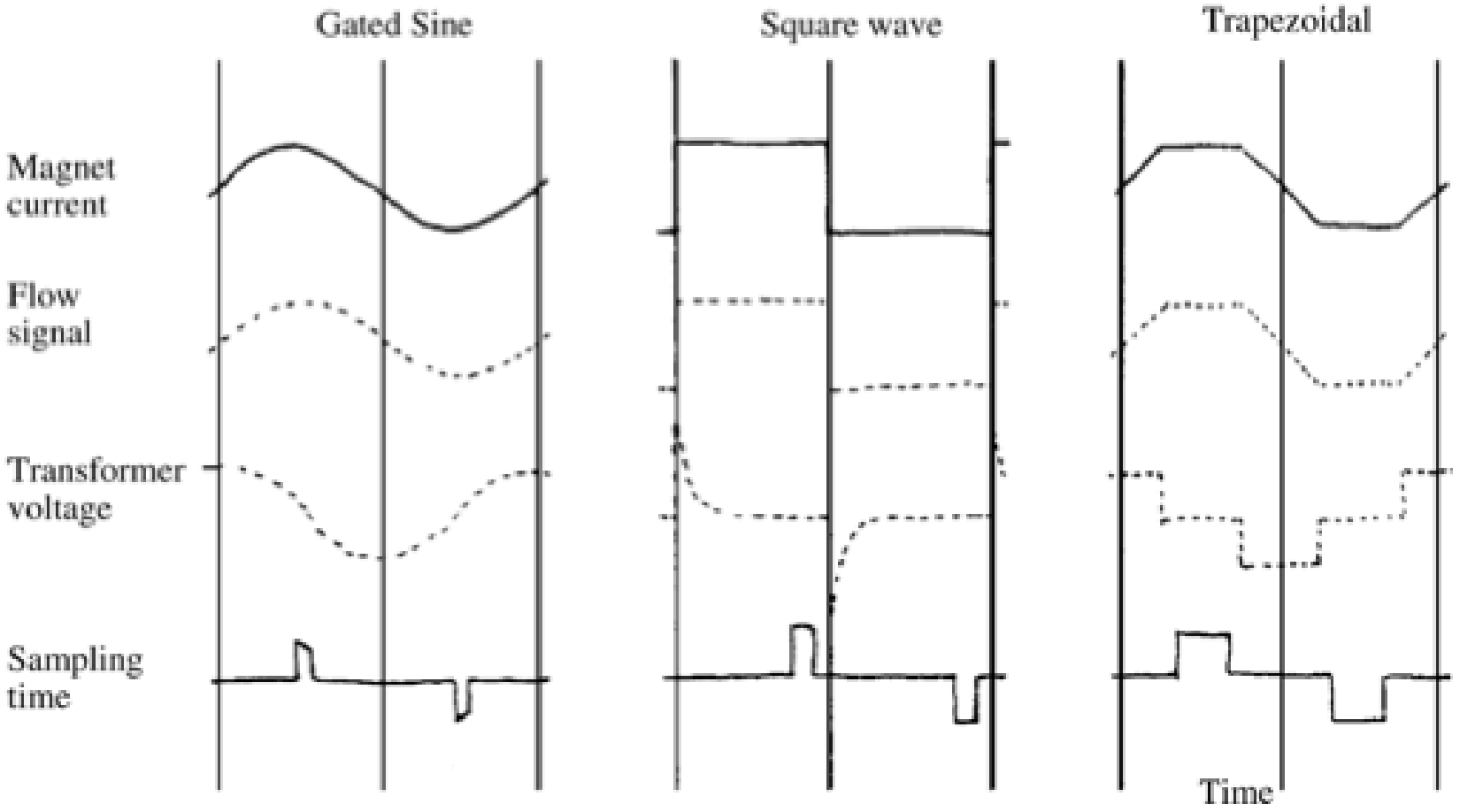


This is low-pass-filtered to yield a dc voltage, which is then modulated by the quadrature generator to produce a signal proportional to the transformer voltage

The quadrature-suppression flowmeter detects the amplifier quadrature voltage. The quadrature generator feeds back a voltage to balance out the probe-generated transformer voltage. With enough gain in this negative-feedback loop, the transformer voltage at the amplifier output is reduced by a factor of 50

➢ Square-wave excitation

- In this case the transformer voltage appears as a very large spike, which overloads the amplifier for a short time. After the amplifier recovers, the circuit samples the square-wave flow voltage and processes it to obtain the flow signal.
- To prevent overload of the amplifier, trapezoidal excitation has also been used.



❑ Ultrasonic Flowmeters

- The ultrasonic flowmeter, like the electromagnetic flowmeter, can measure instantaneous flow of blood.

- The ultrasound can be beamed through the skin, thus making transcutaneous flowmeters practical.

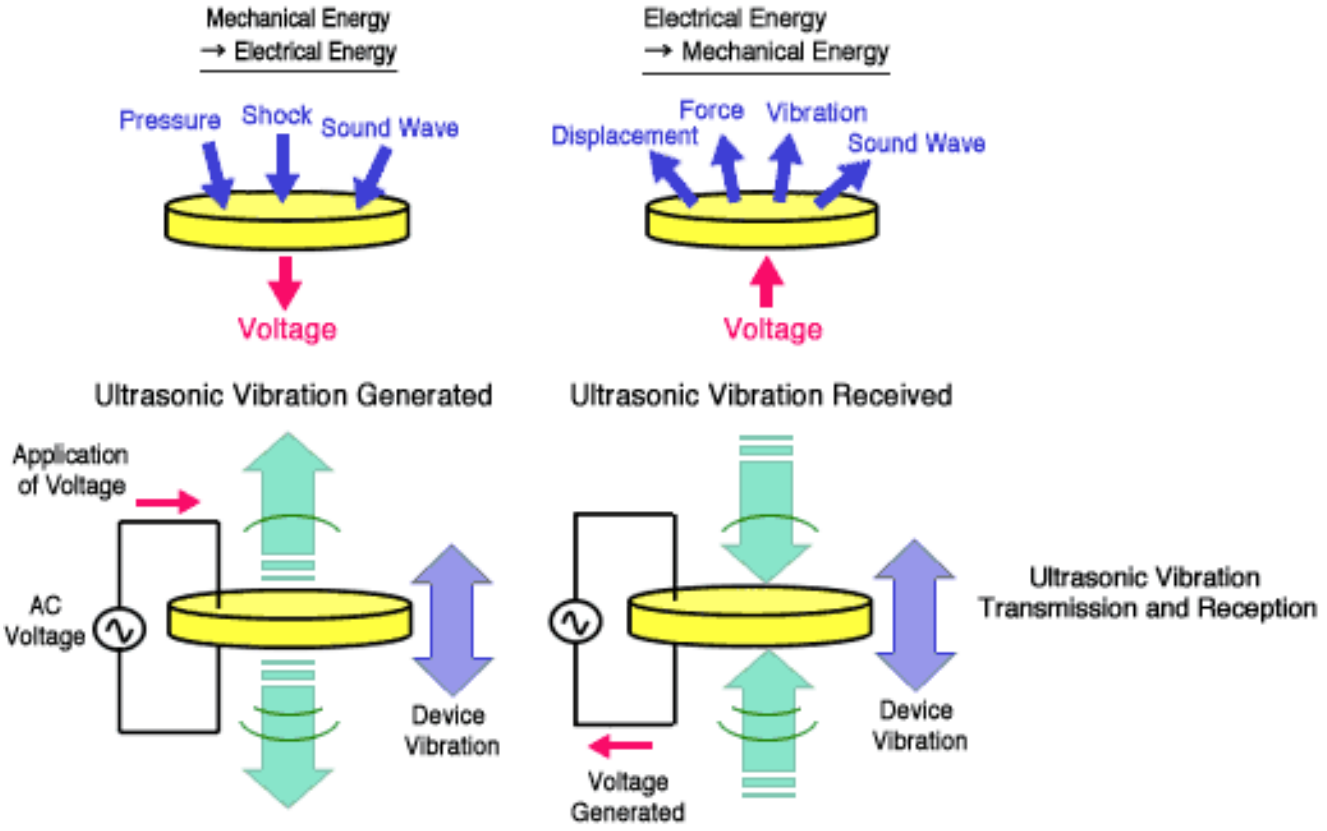
- Two types:

  ① Transit time flow meters
  ② Doppler type

Transducers

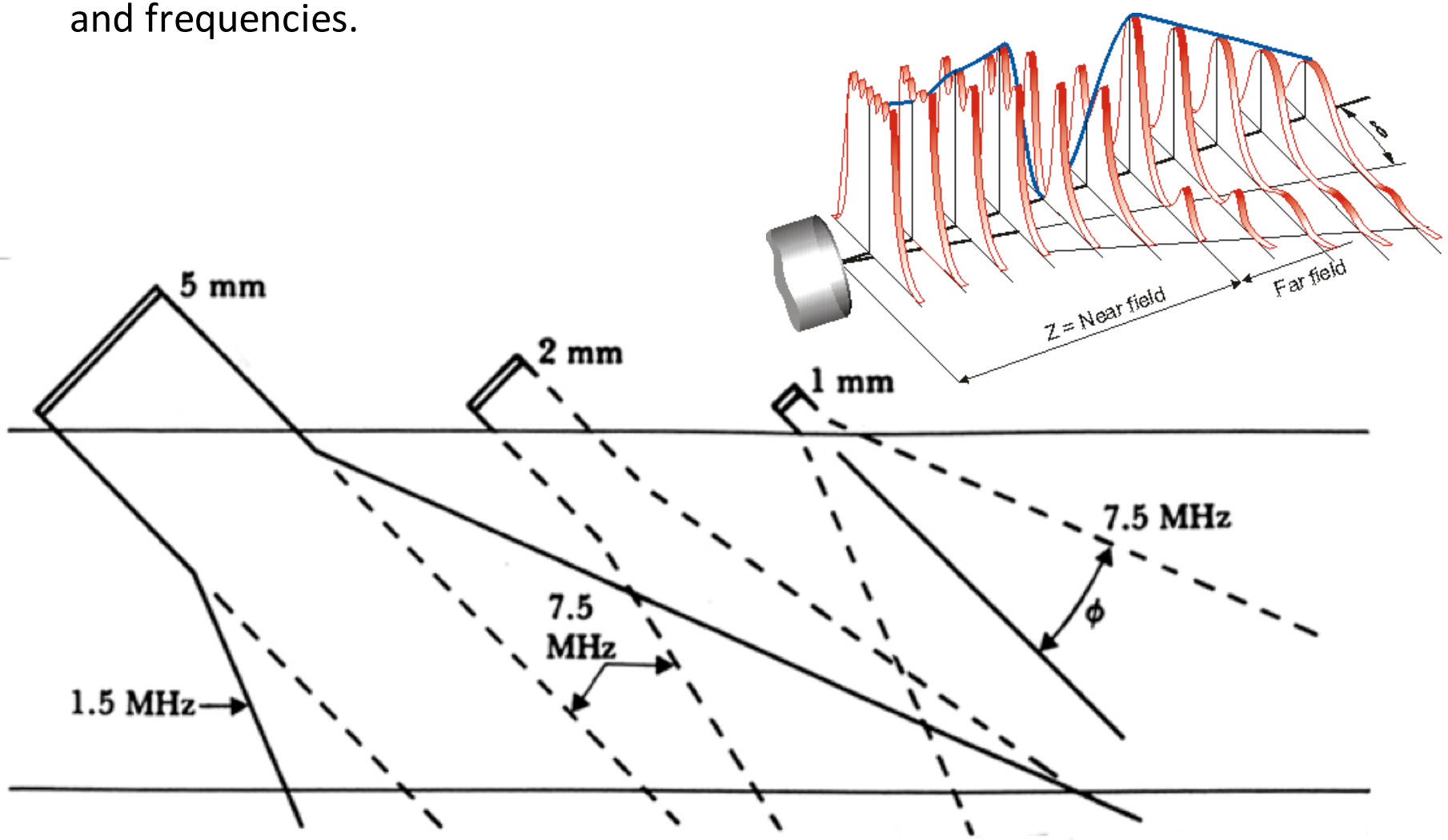
- For the transducer to be used in an ultrasonic flowmeter, we select a piezoelectric material that converts power from electric to acoustic form.

- Lead zirconate titanate is a crystal that has the highest conversion efficiency and the pistonlike movements generate longitudinal plane waves, which propagate into the tissue.



- Because the transducer has a finite diameter, it will produce diffraction patterns.

- Figure shows the outline of the beam patterns for several transducer diameters and frequencies.



Near and far fields for various transducer diameters and frequencies. Beams are drawn to scale, passing through a 10 mm-diameter vessel. Transducer diameters are 5, 2, and 1 mm. Solid lines are for 1.5 MHz, dashed lines for 7.5 MHz.

- In the ***near field*** , the beam is largely contained within a cylindrical outline and there is little spreading.

- The intensity is not uniform, there are multiple maximums and minimums within this region, caused by interference.

- The near field extends a distance d_{nf} given by

$$d_{nf} = \frac{D^2}{4\lambda}$$

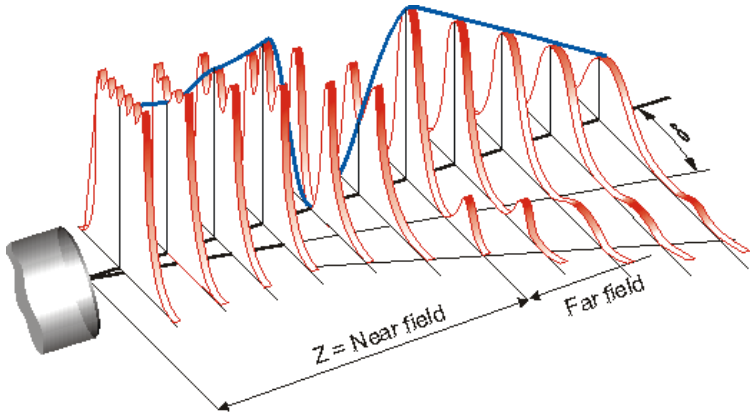
where

D = transducer diameter and
λ = wavelength.

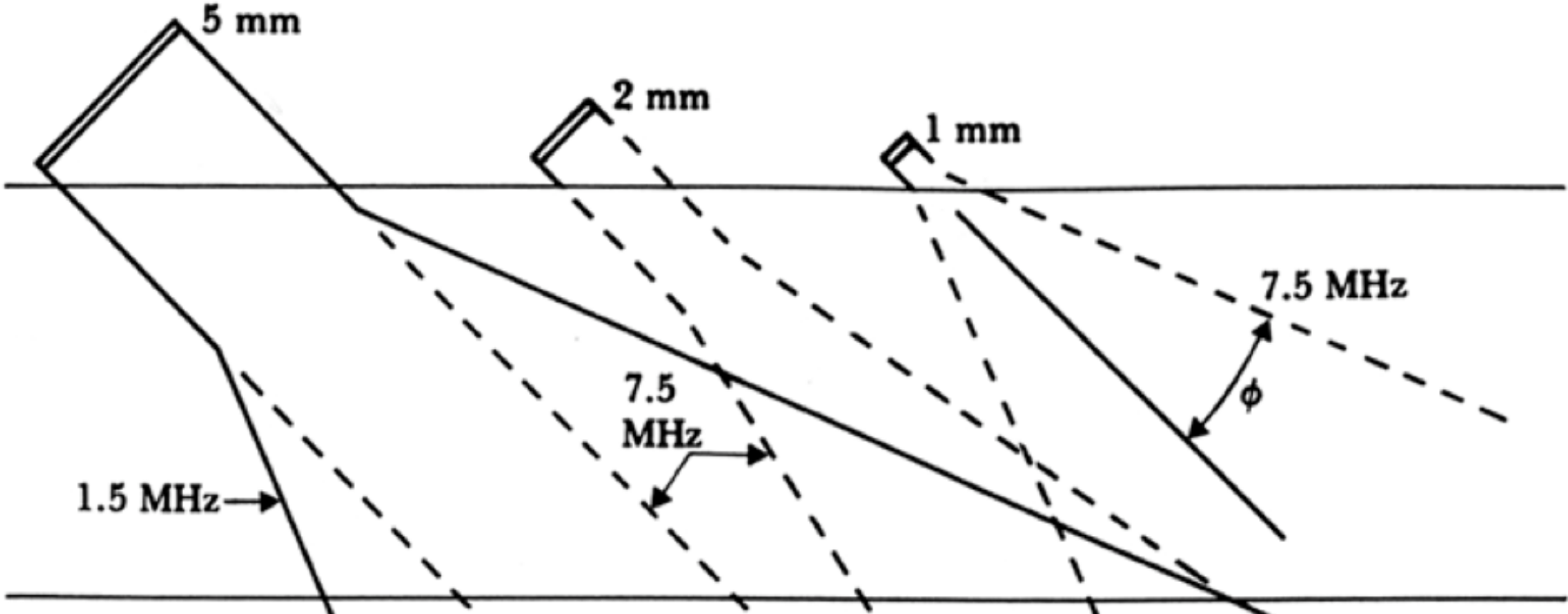
- In the ***far field*** the beam diverges, and the intensity is inversely proportional to the square of the distance from the transducer.

- The angle of beam divergence Φ is given by

$$\sin\theta = \frac{1.2\lambda}{D}$$

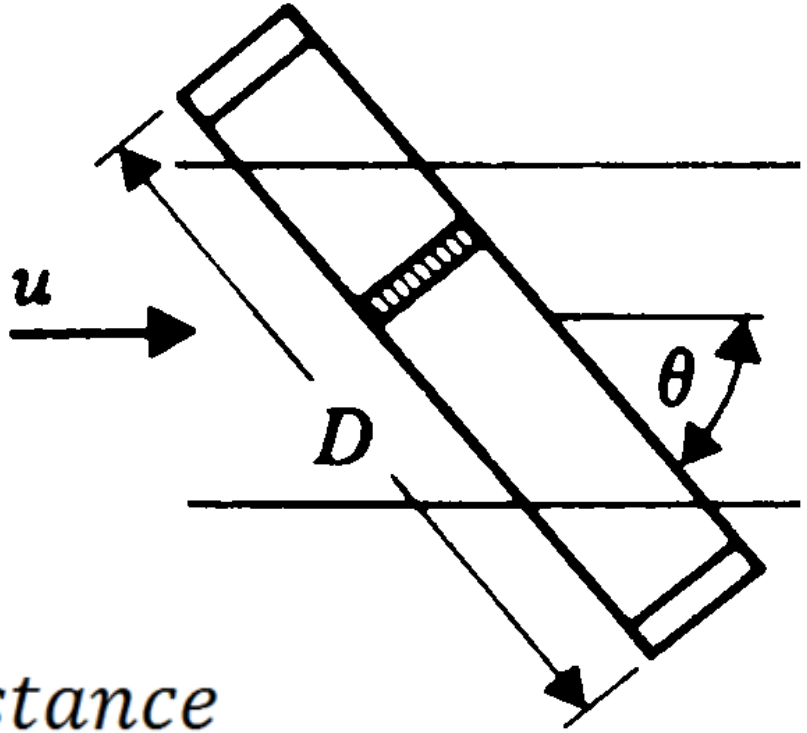


- we should avoid the far field because of its lower spatial resolution. To achieve near-field operation, we must use higher frequencies and larger transducers.



① Transit-Time Flowmeter

- The pulsed beam is directed through a blood vessel at a shallow angle and its transit time is measured.



$$t = \frac{distance}{conduction\ velocity}$$

$$t = \frac{D}{c \pm u\cos\theta}$$

- t - transit time
- D - Distance between the transducers
- c - Sound velocity
- u - blood flow velocity

- The transit time in the downstream (+) and upstream (-) directions is different

- The difference between upstream and downstream transit times is

$$\Delta t = \frac{2D\hat{u}\cos\theta}{(c^2 - \hat{u}^2\cos^2\theta)} \cong \frac{2D\hat{u}\cos\theta}{c^2}$$

Watch video # 16

- Like the electromagnetic flowmeter, the transit-time flowmeter can operate with either saline or blood as a fluid, because they do not require particulate matter for scattering.

- However, they do require <u>invasive</u> surgery to expose the vessel.

②Doppler Type Flowmeters

➢ Continuous-wave Doppler Flowmeter

- When a target recedes from a fixed source that transmits sound, the frequency of the received sound is lowered because of the Doppler effect.

- fractional change in frequency equals the fractional change in velocity

$$\frac{f_d}{f_0} = \frac{u}{c}$$

where

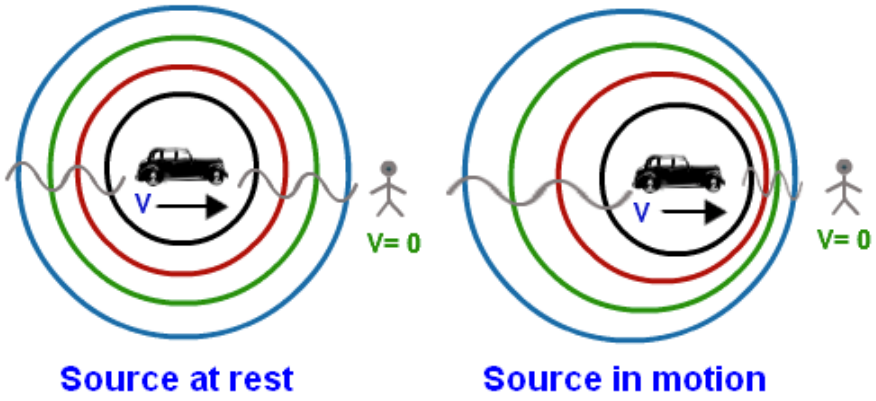
f_d = Doppler frequency shift

f_0 = source frequency

u = target velocity

c = velocity of sound

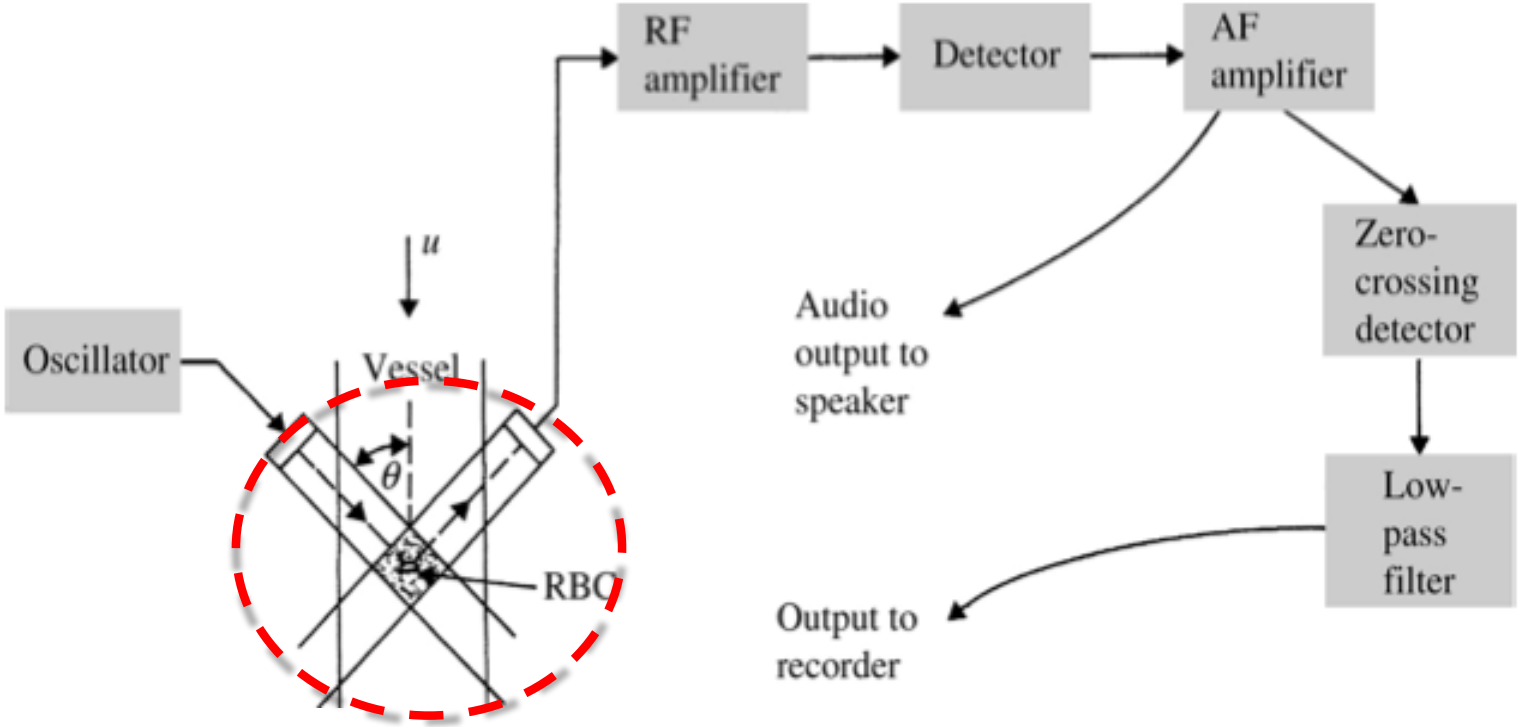
- Doppler Shift was given by Christian Johann Doppler in 1842. The change in the frequency of sound as a result of relative motion between the source and the observer is the Doppler effect.

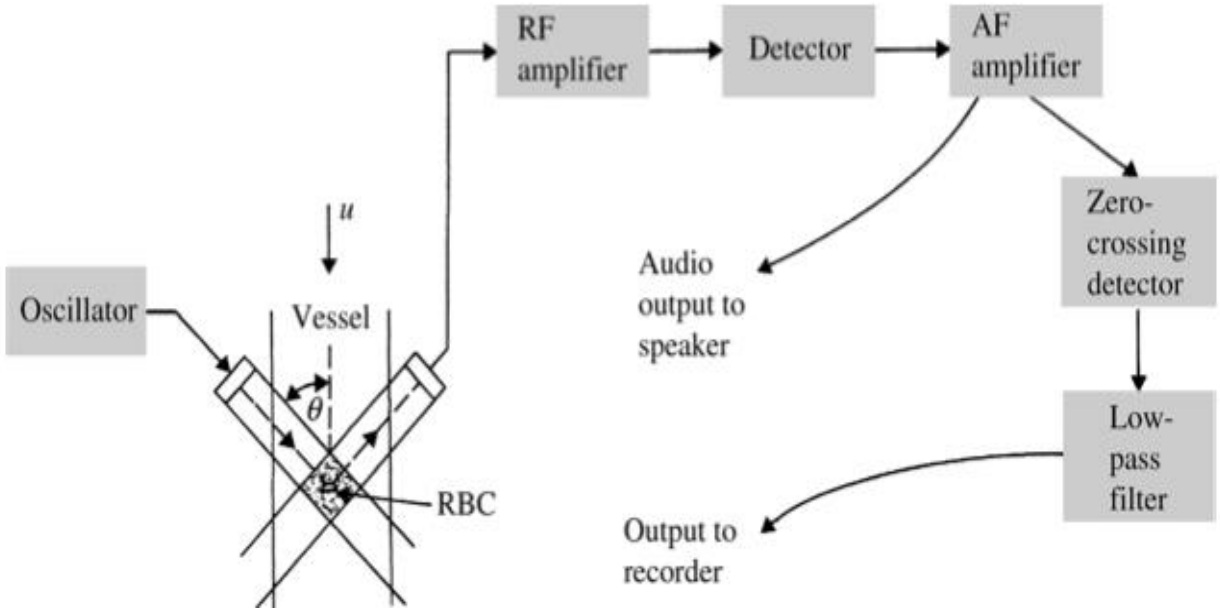


Doppler ultrasonic blood flowmeter:

- ultrasound is beamed through the vessel walls, backscattered by the red blood cells, and received by a piezoelectric crystal.

- <u>blood cells are reflecting targets in the blood</u>





- The frequency is shifted twice.
  - One shift occurs between the transmitting source and the moving cell that receives the signal.
  - One shift occurs between the transmitting cell and the receiving transducer.

$$f_d = \frac{2 f_0 u \cos\theta}{c}$$

➢ **The Doppler-shifted signal is not at a single frequency for several reasons.**

1. Cells move at different velocities, producing different shifts of the Doppler frequency.

2. A given **cell remains** within the beam-intersection volume for **a short time**.

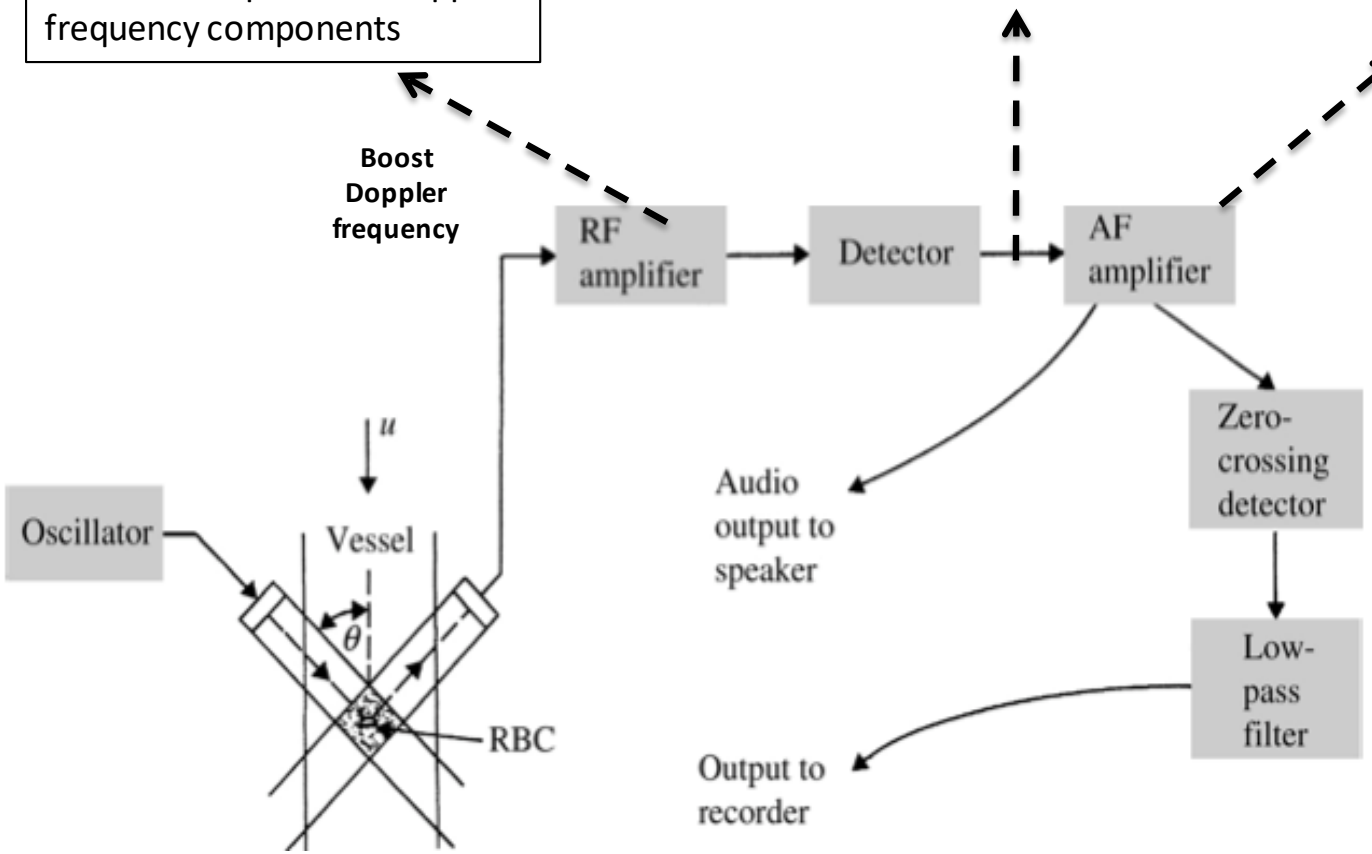
3. Acoustic energy traveling within the main beam, but at **angles** to the beam axis causes different Doppler-frequency shifts due to an effective change in θ .

4. Tumbling of cells and local velocities resulting from **turbulence** cause different Doppler-frequency shifts.

All these factors combine to produce a band of frequencies. The resulting spectrum is similar to band-limited random noise, and from this we must extract flow information.

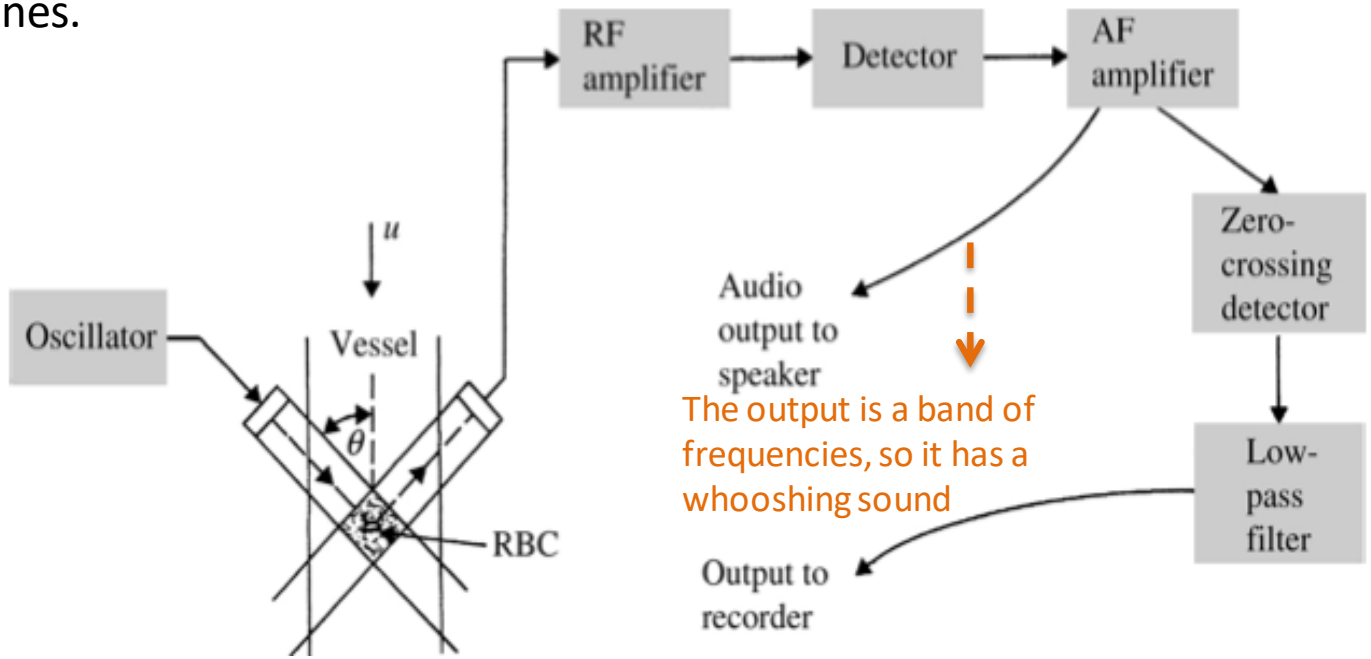
RF amplifier in order to boost the low-amplitude Doppler-frequency components

The output spectrum contains the desired frequencies, which lie in the audio range, plus other undesired frequencies



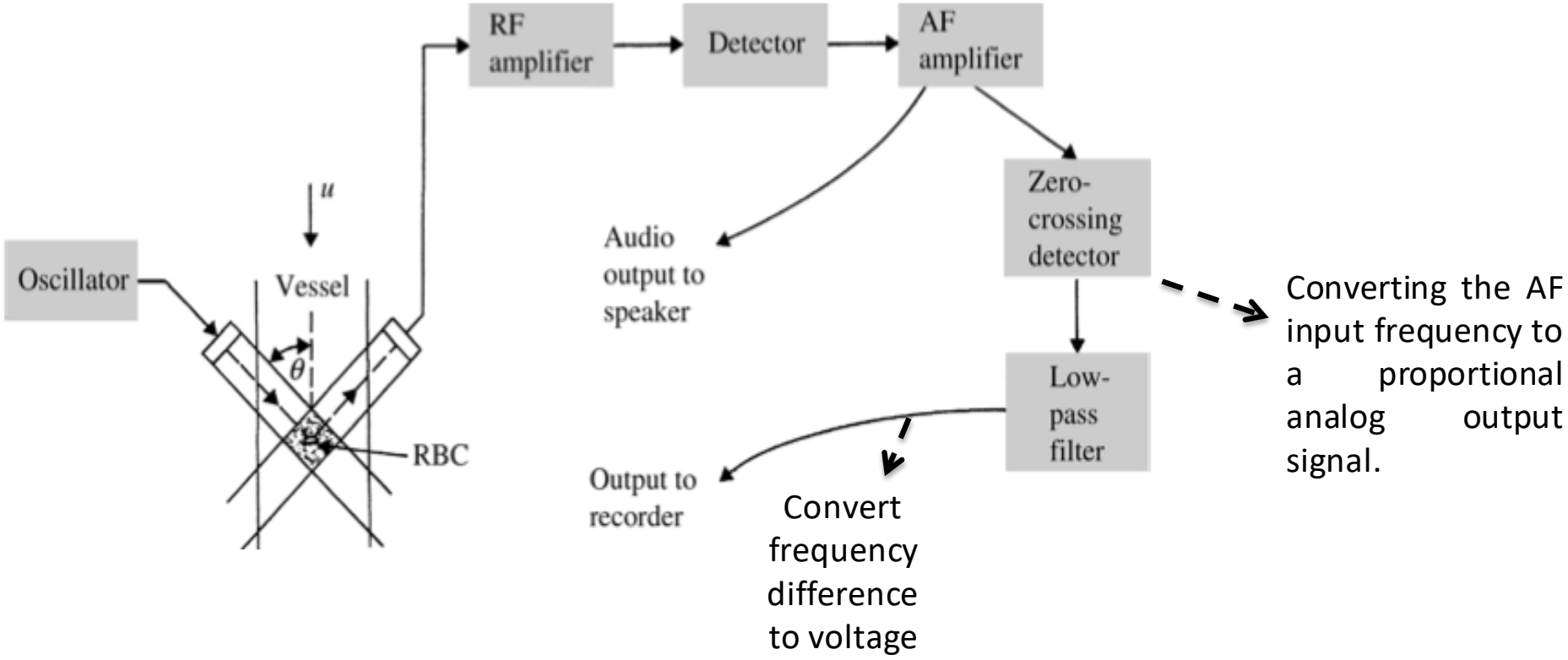
- The dc component must be removed with a high-pass filter in the AF amplifier
  - high-pass filter: corner frequency of about 100 Hz in order to reject large Doppler signals due to motion of vessel walls.
  - A low-pass filter removes high frequencies and also noise. The corner frequency is at about 15 kHz, which includes all frequencies that could result from cell motion, plus an allowance for spectral spreading.

- In the simplest instruments, the AF output drives a power amplifier and speaker or earphones.



- Venous flow sounds like a low-frequency rumble and may be modulated when the subject breathes.

- This simple instrument can be used to trace and qualitatively evaluate blood vessels within 1 cm of the skin in locations in the legs, arms, and neck.



- The spectrum of the AF signal versus time to obtain a more quantitative indication of velocities in the vessel may also be plotted.

- A major defect of the detector used in simple flowmeters is that it cannot detect the direction of flow

- Compared with the electromagnetic flowmeter, this is a real disadvantage, because reverse flow occurs frequently in the body.

- ***quadrature-phase detector*** from radar technology, which is used to determine not only the speed at which an aircraft is flying but also its direction can be used to detect the direction of blood flow.

- Figure 8.11(a) shows the analog portion of the quadrature-phase detector. A phase-shift network splits the carrier into two components that are 90° apart.
- The reference waves and the RF-amplifier output are linearly summed

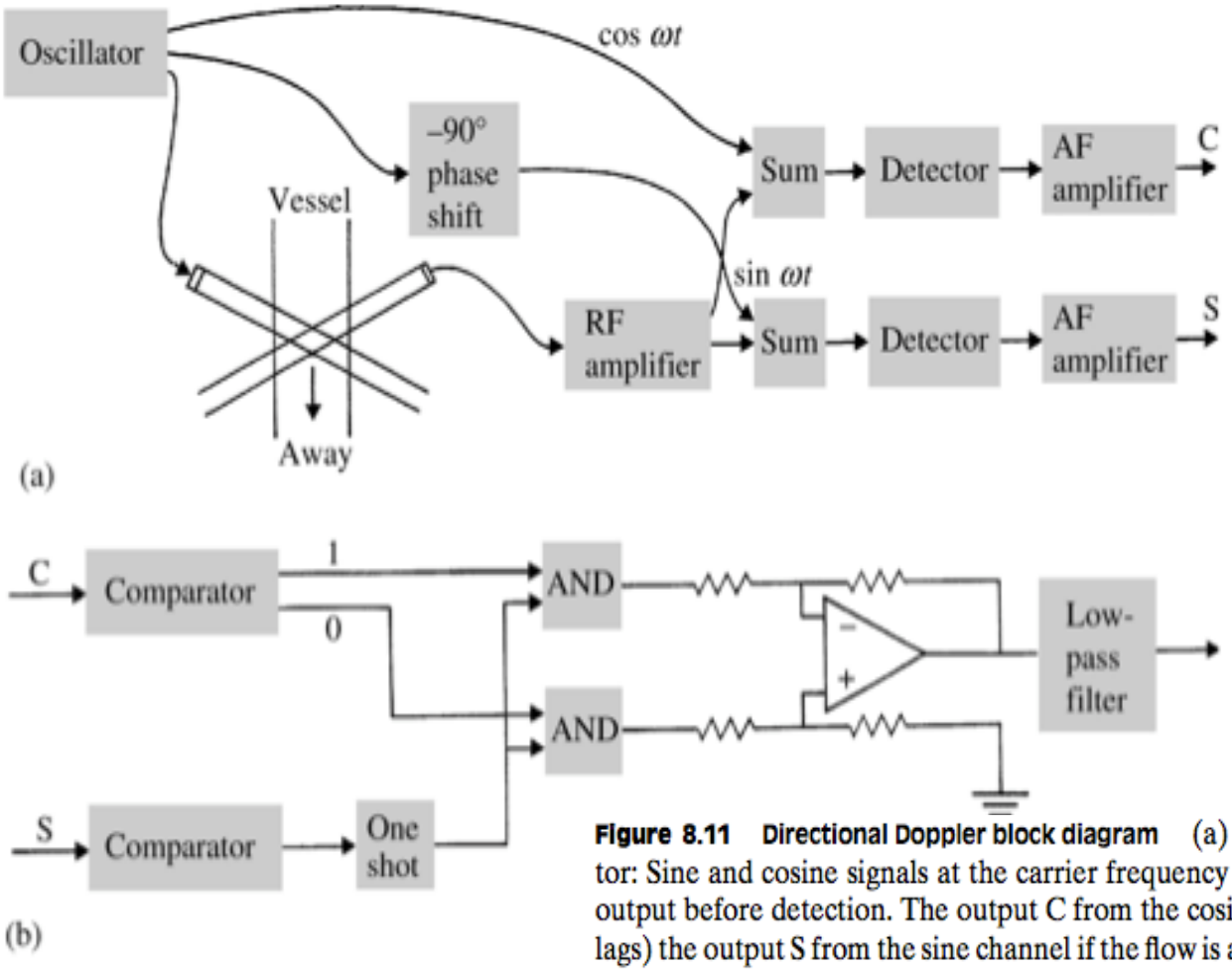


Figure 8.11 Directional Doppler block diagram (a) Quadrature-phase detector: Sine and cosine signals at the carrier frequency are summed with the RF output before detection. The output C from the cosine channel then leads (or lags) the output S from the sine channel if the flow is away from (or toward) the transducer. (b) Logic circuits route one-shot pulses through the top (or bottom) AND gate when the flow is away from (or toward) the transducer. The differential amplifier provides bidirectional output pulses that are then filtered.

- If the flow of blood is in the same direction as the ultrasonic beam, we consider the blood to be flowing **away** from the transducer.
- The phase of the Doppler wave lags behind that of the reference carrier, and the Doppler vector [see Figure 8.12(a)] rotates clockwise.
- Note that the sine channel lags behind the cosine channel

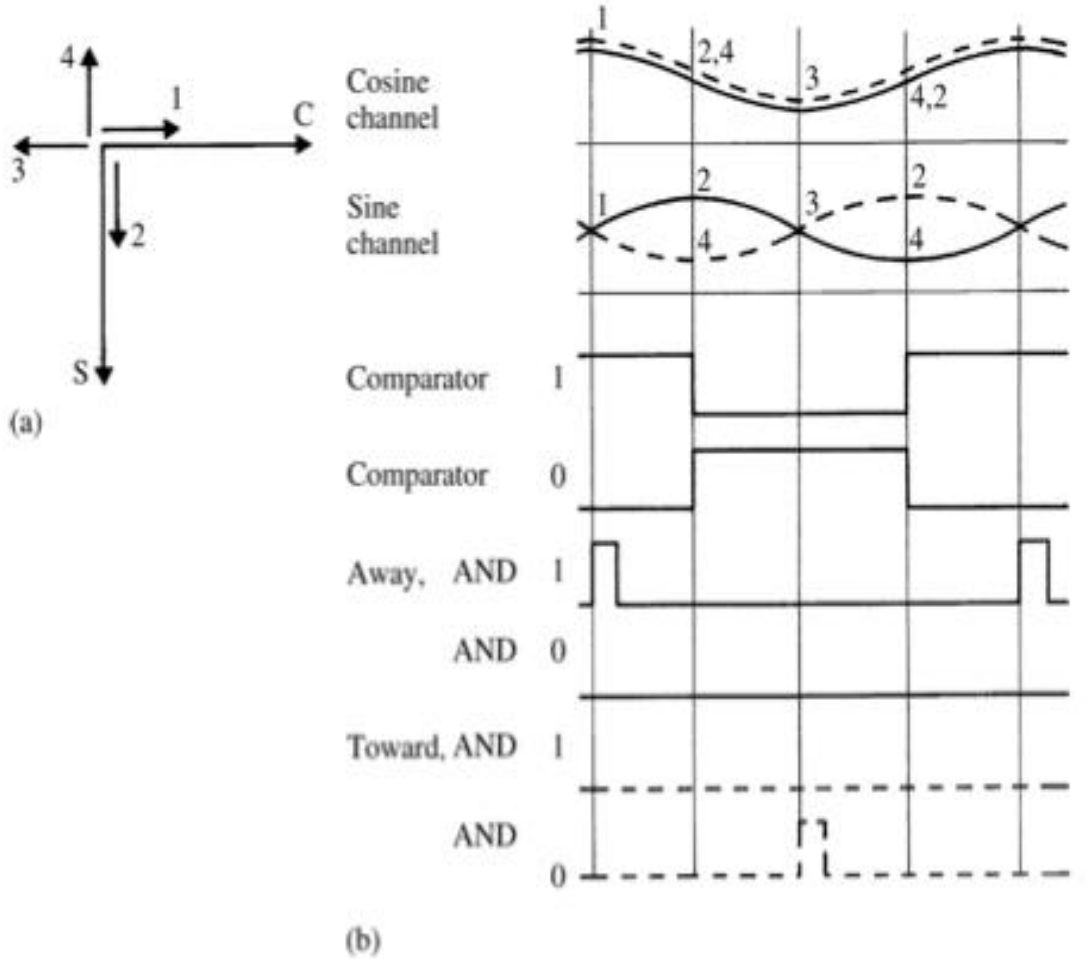
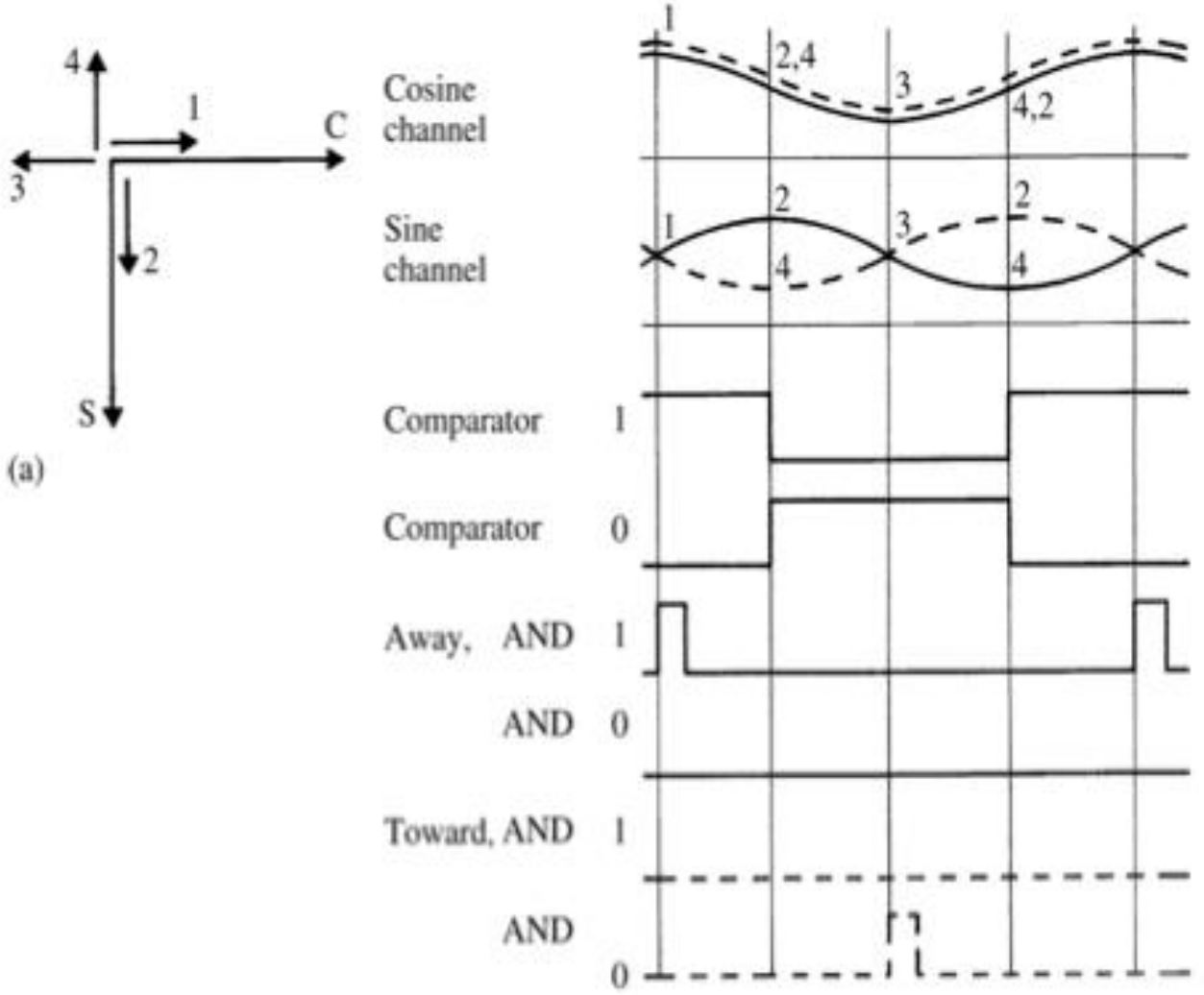
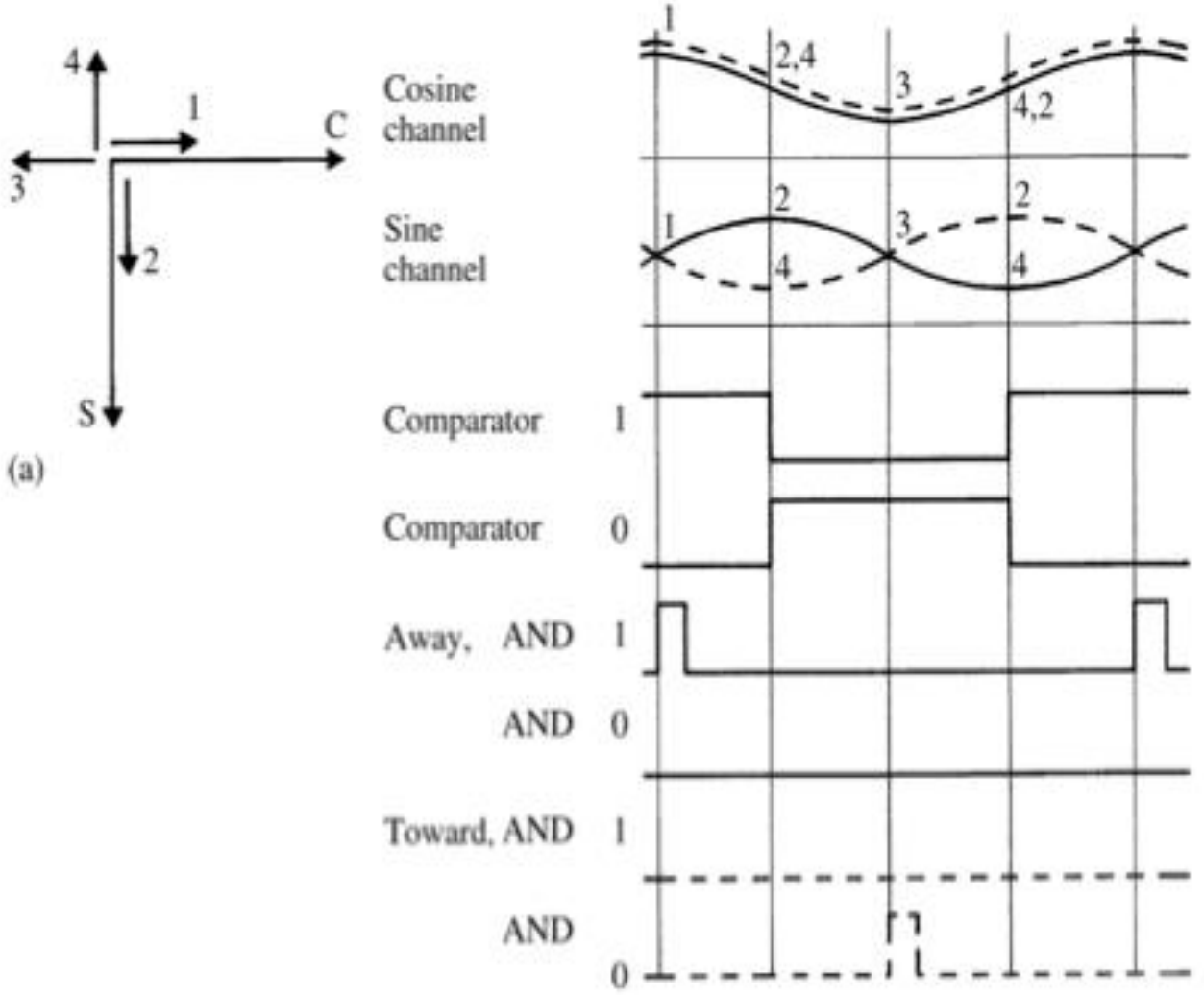


Figure 8.12 Directional Doppler signal waveforms (a) Vector diagram: The sine wave at the carrier frequency lags the cosine wave by 908. If flow is away from the transducer, the Doppler frequency is lower than the carrier. The short vector represents the Doppler signal and rotates clockwise, as shown by the numbers 1, 2, 3, and 4. (b) Timing diagram: The top two waves represent the single-peak envelope of the carrier plus the Doppler before detection. Comparator outputs respond to the cosine channel audio signal after detection. One-shot pulses are derived from the sine channel and are gated through the correct AND gate by comparator outputs. The dashed lines indicate flow toward the transducer.

- **For time 1**, the carrier and the Doppler add, producing a larger sum in the cosine channel. The sine channel is unchanged.
- **For time 2**, the carrier and the Doppler add, producing a larger sum in the sine channel.
- Similar reasoning produces the rest of the wave for **times 3 and 4**.



- If the **flow of blood is toward the transducer**, the Doppler vector rotates counterclockwise.
- This produces the dashed waves, and the phase relation between the cosine and sine channels is reversed.
- By examining the sign of the phase, we measure direction of flow.
- logic detects the sign of the phase.



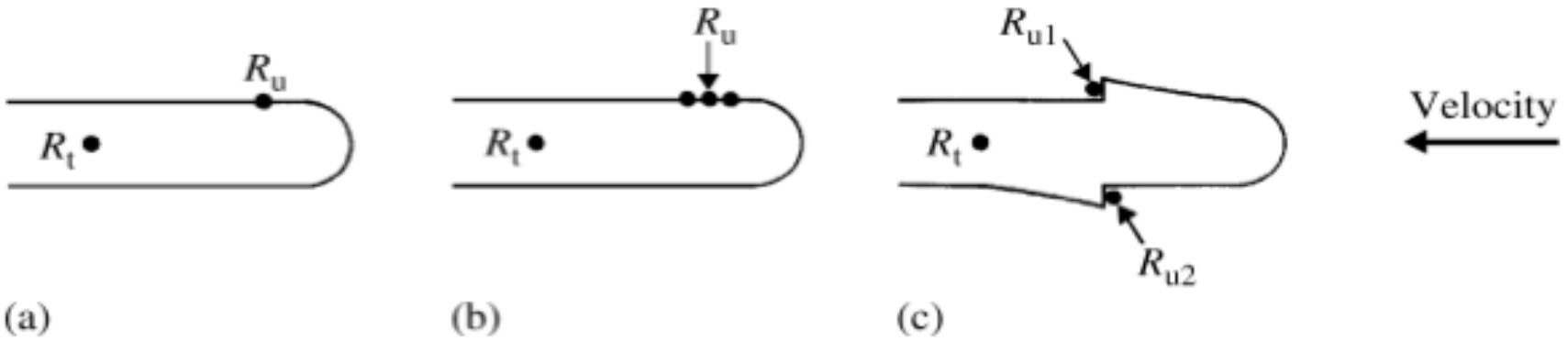
➢ Pulsed doppler

- Instruments have been built that operate in a radar like mode.
- The transmitter is excited with a brief burst of signal. The transmitted wave travels in a single packet.
- The transmitter can also be used as a receiver, reflections are received at a later time.
- The delay between transmission and reception is a direct indication of distance, so we can obtain a complete plot of reflections across the blood vessel.
- By examining the Doppler shift at various delays, we can obtain a velocity profile across the vessel.

❑ Thermal-convection Velocity Sensors

- Thermal velocity sensors depend on convective cooling of a heated sensor and sensitive only to local velocity.

Principle: The flow lowers the temperature of a heated thermistor. The temperature reduction and velocity are non linearly related. Large sensitivity at low velocities and a small sensitivity at high velocities.



Thermal velocity probes (a) Velocity-sensitive thermistor R_u is exposed to the velocity stream. Temperature-compensating thermistor R_t is placed within the probe. (b) Thermistors placed down- and upstream from R_u are heated or not heated by R_u, thus indicating velocity direction. (c) Thermistors exposed to and shielded from flow can also indicate velocity direction.

Heat dissipated by the thermistor

$$\frac{W}{\Delta T} = a + b \log u$$

velocity

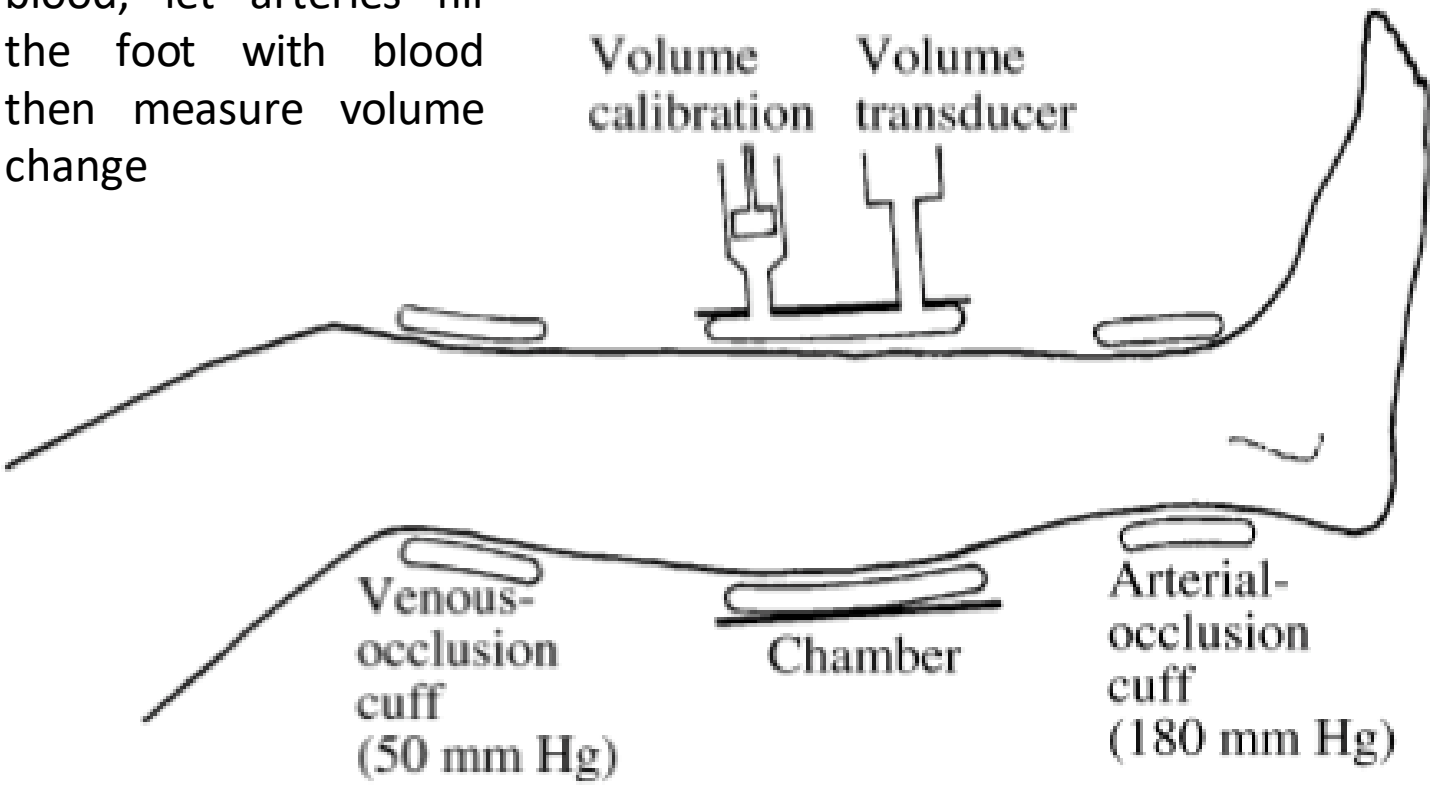
Temperature difference

constants

❑ Chamber Plethysmography

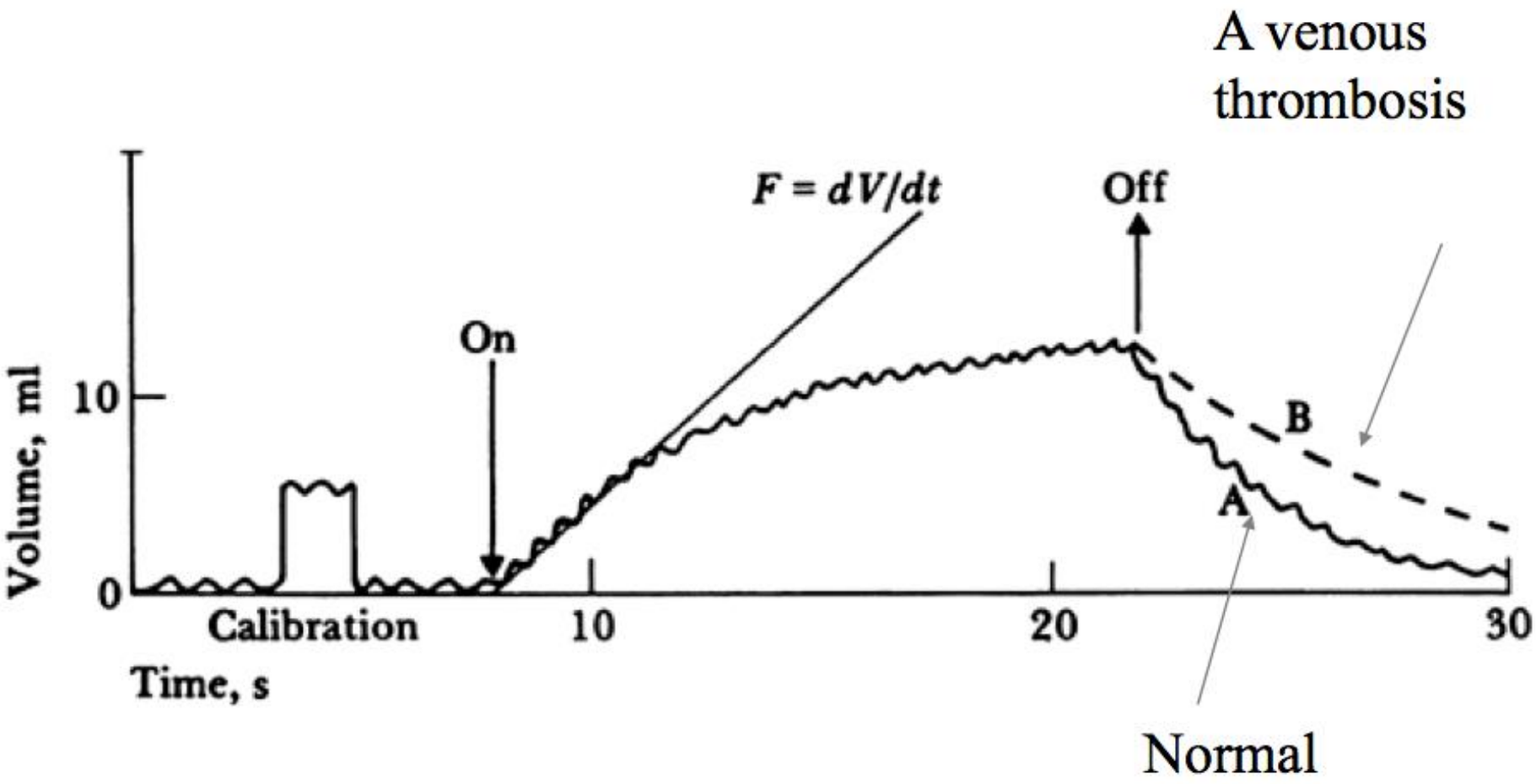
- A non-invasive technique to measure changes in volume; F= d*V*/dt

Principle: Stop venous blood, let arteries fill the foot with blood then measure volume change



- As the volume of the leg increases, the leg squeezes some type of bladder.
- If the bladder is filled with water, the change in volume may be measured by observing the water rising in a calibrated tube.
- For recording purposes, some air may be introduced above the water and the change in air pressure may be measured

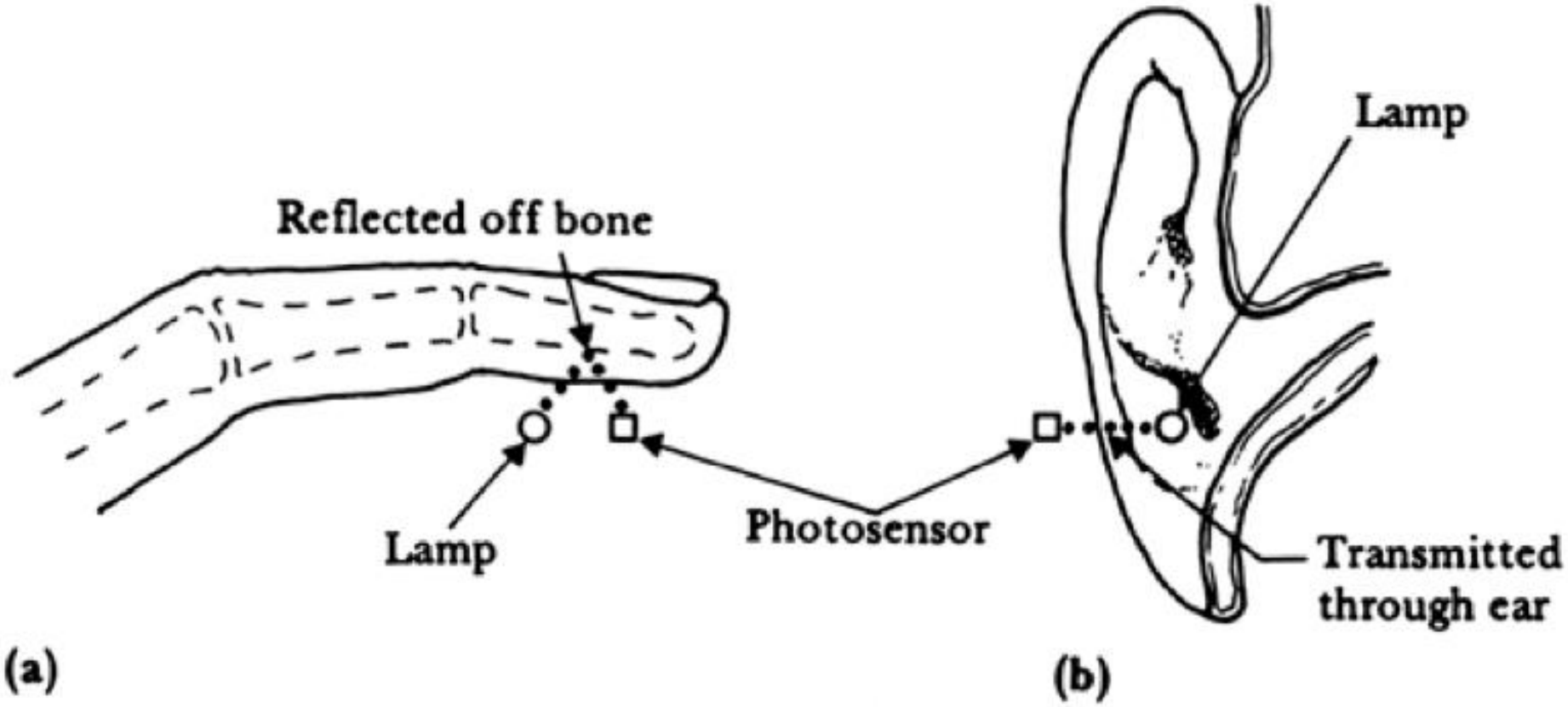
In chamber plethysmography, the venous-occlusion cuff is inflated to 50 mm Hg (6.7 kPa), stopping venous return. Arterial flow causes an increase in volume of the leg segment, which the chamber measures.



After venous-occlusion cuff pressure is turned on, the initial volume-versus-time slope is caused by arterial inflow. After the cuff is released, segment volume rapidly returns to normal (A). If a venous thrombosis blocks the vein, return to normal is slower (B).

❑ Photoplethysmography

- Reflection, absorption and scattering of light depends on how much blood is flowing into the organ.
- Although photoplethysmography is simple and indicates the timing of events such as heart rate, it provides a poor measure of changes in volume.
- Use LED with narrow band light and peak at 940nm as the source



(a) Light transmitted into the finger pad is reflected off bone and detected by a photosensor. (b) Light transmitted through the aural pinna is detected by a photosensor.

❑ Electrical-impedance Plethysmography

- It is simple to attach electrodes to a segment of tissue and measure the resulting impedance of the tissue.
- As the volume of the tissue changes in response to pulsations of blood (as happens in a limb) or the resistivity changes in response to increased air in the tissue (as happens in the lung), the impedance of the tissue changes.

- **Swanson's model** for impedance plethysmography (for a cylindrical limb).

- The derivation requires **three assumptions**:

1. The expansion of the arteries is uniform. This assumption is probably valid in healthy vessels, but it may not be valid in diseased ones.
2. The resistivity of blood, ρ_b , does not change. ($u_b \uparrow \rightarrow \rho_b \downarrow$)
3. Lines of current are parallel to the arteries.

impedance of the blood

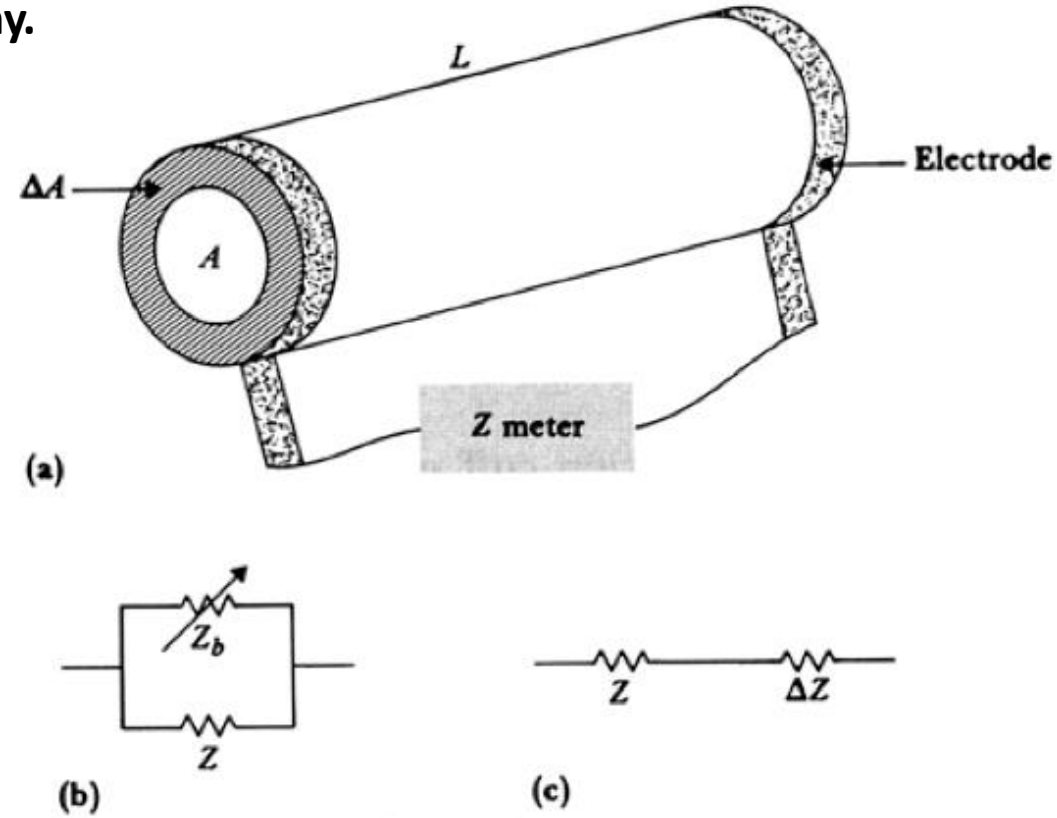
$$Z_b = \frac{\rho_b L}{\Delta A}$$

$$\Delta V = L\,\Delta A = \frac{\rho_b L^2}{Z_b}$$

additional blood volume

➢ A model for impedance pletysmography.

a) a model for impedance plethysmography. A cylindrical limb has length L and cross-sectional area A. With each pressure pulse, A increases by the shaded area ΔA. (b) This causes impedance of the blood, Z_b, to be added in parallel to Z. (c) Usually ΔZ is measured instead of Z_b.



$$\Delta Z = [(Z_b \,||\, Z) - Z] \quad \Delta Z = \frac{ZZ_b}{Z+Z_b} - Z = \frac{-Z^2}{Z+Z_b}$$

because $Z \ll Z_b$,

$$\frac{1}{Z_b} \cong \frac{-\Delta Z}{Z^2} \quad \Rightarrow \quad \Delta V = \frac{-\rho_b L^2 \Delta Z}{Z^2}$$

Although this model is valid at any frequency, there are several considerations such as SNR that suggest the use of a frequency of about 100 kHz.