STANFORD UNIVERSITY

EE122B

Introduction to Biomedical Electronics

Tissue Impedance

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Content

Review of tissue impedance concepts and the use of impedance measurement in the determination of physiological parameters.

- Tissue Impedance Characteristics
- Impedance Measurement Techniques
- Applications
  - Impedance plethysmography (Respiration)
  - Impedance cardiography (ICG)
  - Tissue characterization (Body Composition Analyzers)
  - Electrical Impedance Tomography (EIT)

Science

Tissue Impedance Characteristics

A Few Basics First

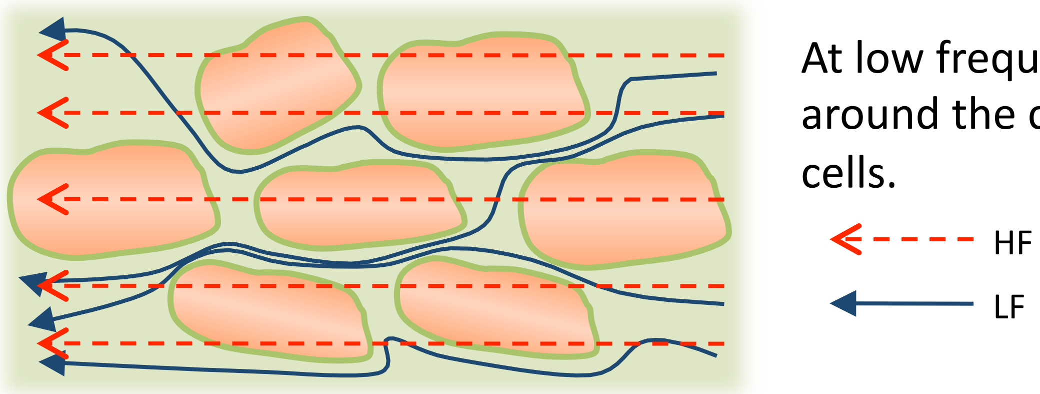
- Tissue bioimpedance includes electrical conduction from both a conduction and dielectric point of view, and focuses on two main parameters:
  - Conductivity (charge transport)
  - Permittivity (charge storage)
- Current transport in a lossy medium is defined by:
  - σ : conductivity
  - ε : permittivity

$$J = J_c + J_d = \sigma E - i\omega\varepsilon E$$

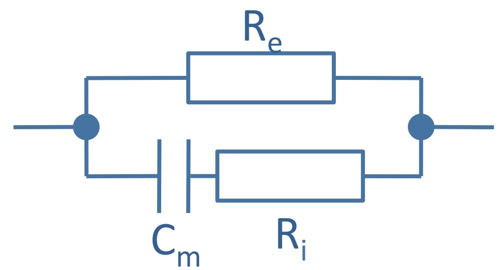
Or: $J = -i\omega\hat{\varepsilon}E, \quad with\ \hat{\varepsilon} = \varepsilon + i\dfrac{\sigma}{\omega}$ (complex permittivity)

- Permittivity is usually frequency-dependent, due to *relaxation* effects (dipoles can follow field change only so fast), leading to so-called *dispersions* (frequency response peaks) in the frequency domain.

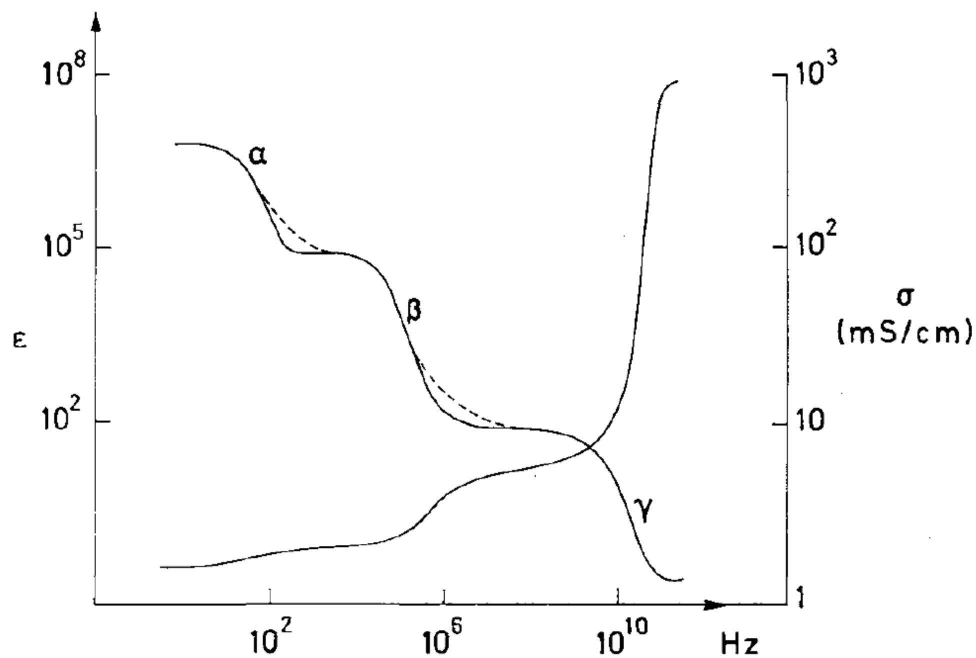
Tissue Impedance Model



At low frequencies (DC-kHz), the current goes around the cells. Higher, it flows through the cells.



Simplified equivalent model for conductivity



Dielectric dispersion regimes:

α **(mHz-kHz)**: counter-ion effect around membrane glycocalix, ionic diffusion, intracellular structures.

β **(kHz-100MHz)**: Maxwell-Wagner effect, membrane capacitance, protein response.

γ **(GHz)**: polarization of water molecules

Source: Schwan, Annals of Biomedical Engineering, 16, 1988

Tissue Conductivity Examples

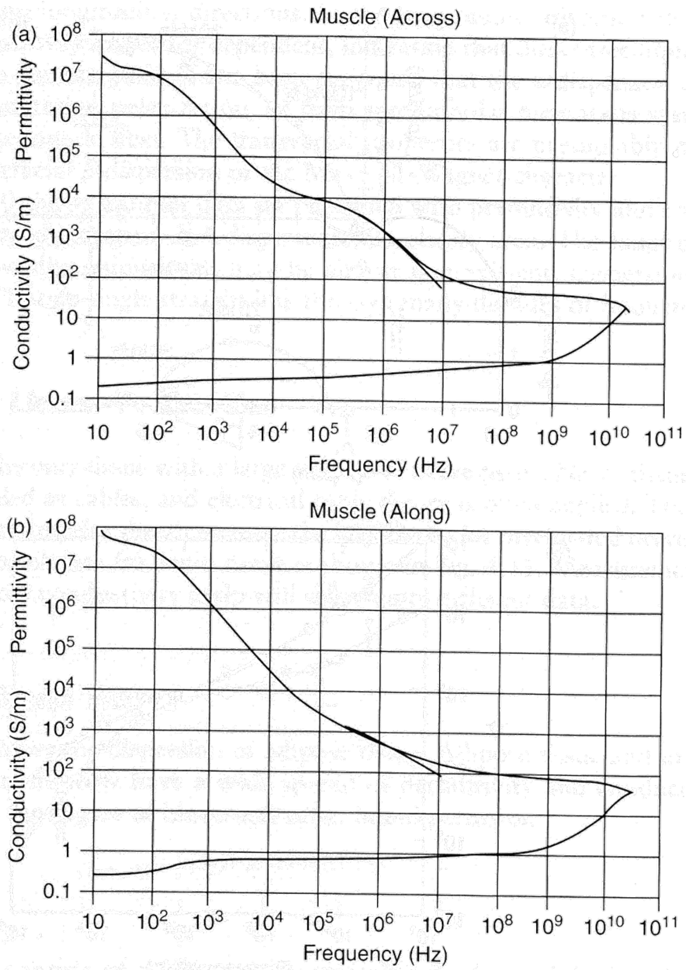


Figure 4.10 Dispersion of muscle tissue. (a) transversal; (b) longitudinal. *Source*: From Gabriel et al. (1996b) by permission.

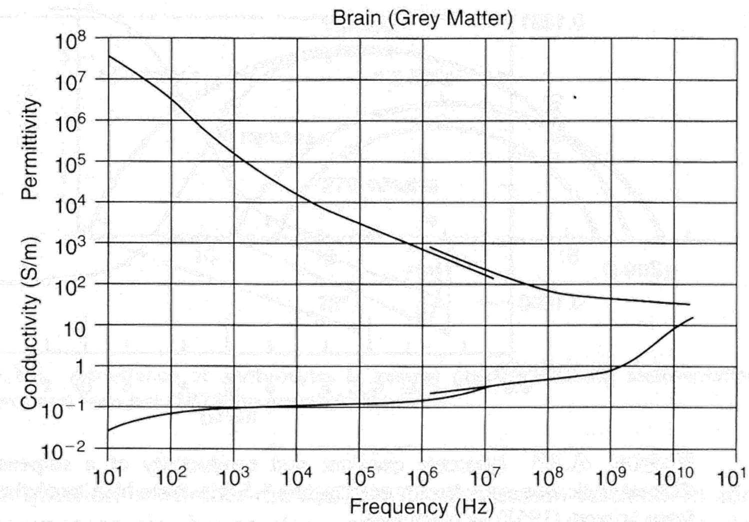


Figure 4.11 Dispersion of brain tissue. *Source*: From Gabriel et al. (1996b) by permission.

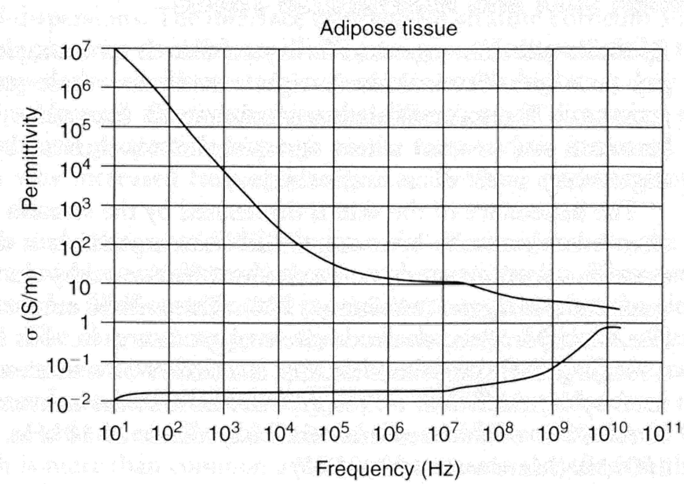


Figure 4.12 Dispersion of adipose tissue. *Source*: From Gabriel et al. (1996b) by permission.

Source: Bioimpedance and Bioelectricity Basics, Grimnes & Martinsen, Elsevier, 2008

Tissue Conductivity Examples

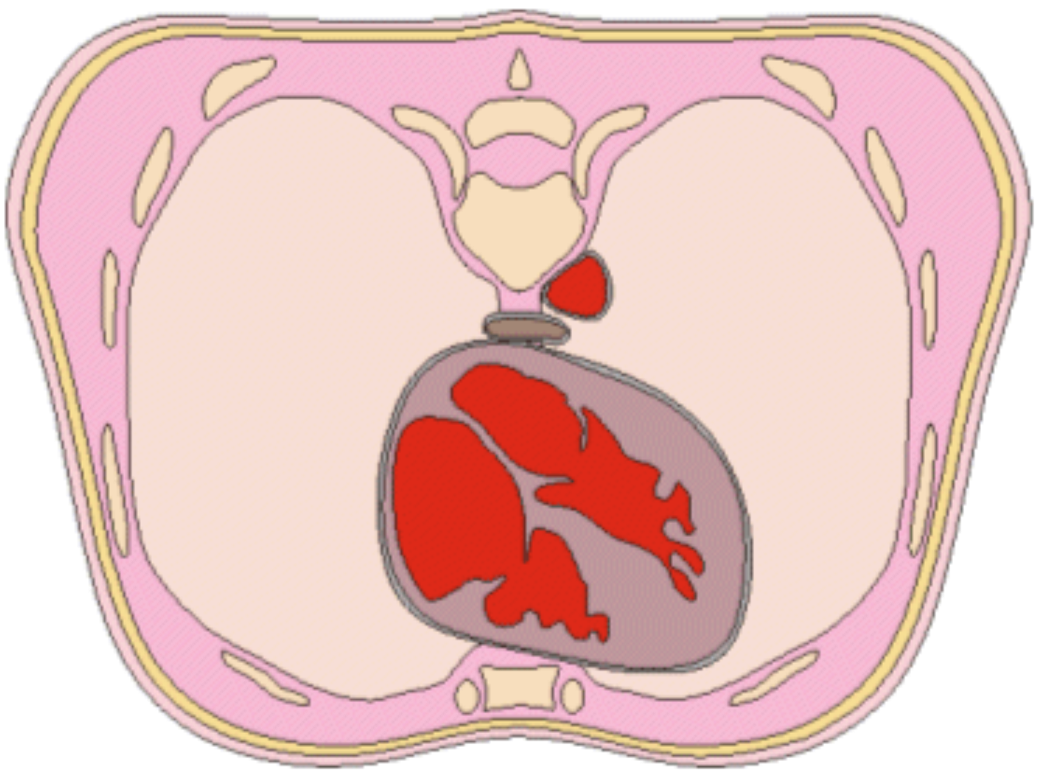
TABLE 4.1 Tissue Conductivity, LF and 1 MHz

Tissue	σ (S/m) 1 Hz–10 kHz	σ (S/m) *ca* 1 MHz	φ_{max} @<10 MHz	anisotropy
Human skin, dry	10^{-7}	10^{-4}	80°	?
Human skin, wet	10^{-5}	10^{-4}	30°	?
Bone	0.005–0.06		20°	Strong
Fat	0.02–0.05	0.02–0.05	3°	Small
Lung	0.05–0.4	0.1–0.6	15°	Local
Brain (grey matter)	0.03–0.4	0.15	15°	Small
Brain (white matter)	0.03–0.3			Strong
Liver	0.2	0.3	5°	?
Muscle	0.05–0.4	0.6	30°	Strong
Whole blood	0.7	0.7	20°	Flow dependent
Urine	0.5–2.6	0.5–2.6	0°	0
CSF	1.6	1.6	0°	0
Saline, 0.9%, 20°C	1.3	1.3	0°	0
Saline, 0.9%, 37°C	2	2	0°	0
Seawater	5	5	0°	0

A key research question is whether or not malignancies can be detected via impedance. (e.g., http://www.ncbi.nlm.nih.gov/pubmed/8058021)

Source: Bioimpedance and Bioelectricity Basics, Grimnes & Martinsen, Elsevier, 2008

Tissue Resistivity in Thorax



Tissue	Resistivity [Ohm·m]
Blood	1.6
Heart muscle	2.5 parallel 5.6 normal
Skeletal muscle	1.9 parallel 13.2 normal
Lungs	20
Fat	25
Bone	177

Source: Bioelectromagnetism, Malmivuo & Plonsey, http://www.bem.fi

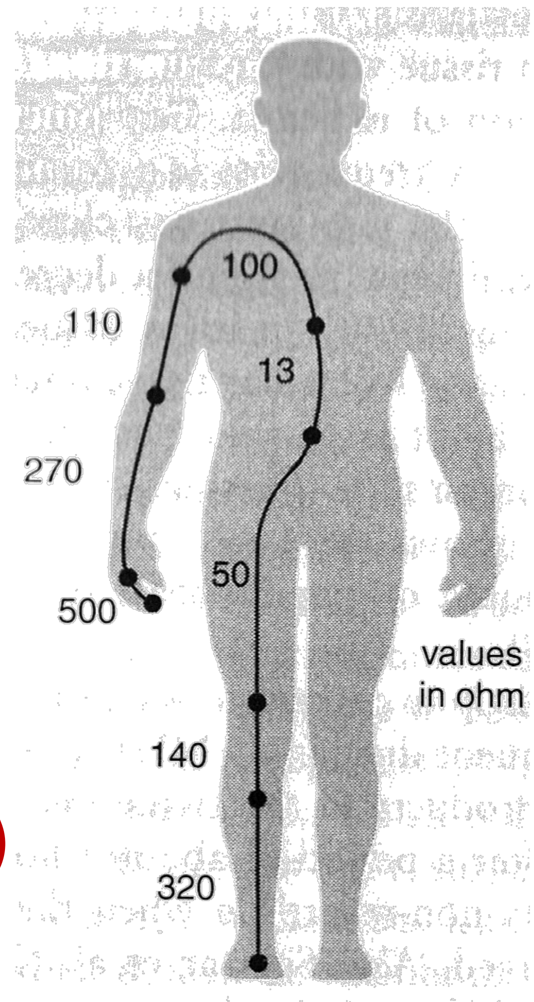
Body Impedance Examples

At low frequencies (100Hz-100kHz):

- Whole-body (hand-foot): 500 Ω
- Limb: 100-200 Ω
- Trunk: 50-100 Ω
  - Variation due to respiration: 1-10 Ω
  - Variation due to blood flow: 100-500 mΩ

Requires mΩ resolution !!

(Kelvin connections, typically)



Source: Bioimpedance and Bioelectricity Basics, Grimnes & Martinsen, Elsevier, 2008

Technology

Impedance Measurements

Impedance Measurement Methods

- Bridges (LCR meter)

  Adjustment of variable element to match unknown impedance.

- *I-V* method

  Direct measurement of current/voltage characteristic.

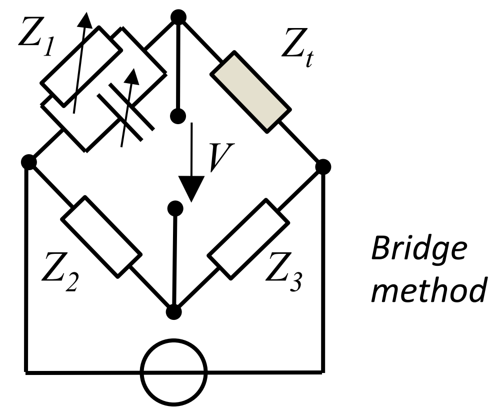
  – Lock-in amplification

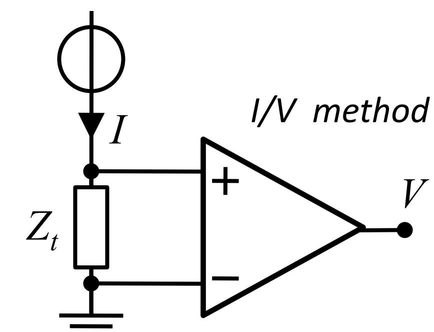
- Time domain spectroscopy

  Broadband excitation recorded in time-domain, analyzed in frequency domain.

- Time domain transmissometry

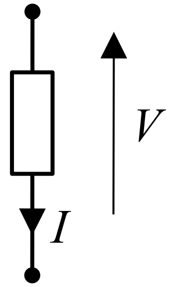
  Model-based current-voltage fitting.





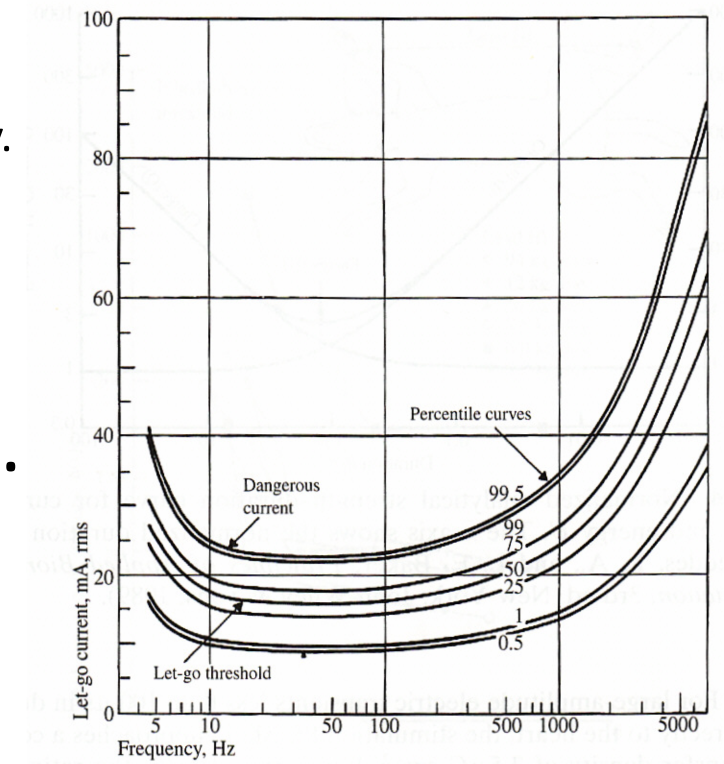
Is It Safe?

$$Z = \frac{V}{I}$$



Of course, isolation is necessary.

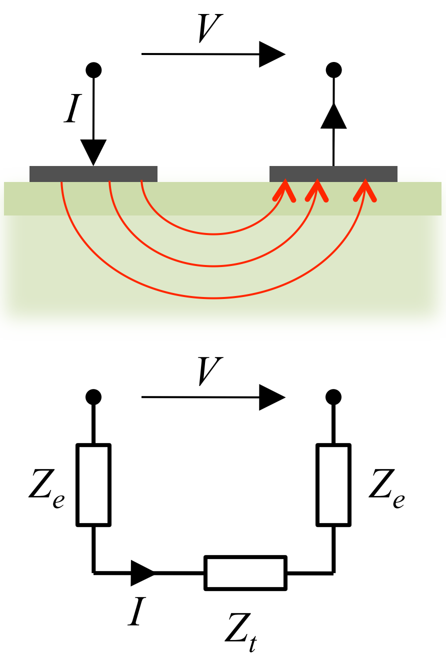
- Impedance measurement implies injection of a current. *Is it safe?*
- Yes… but must be careful.
  - Keep excitation above 1 kHz!
    Perception threshold increases with frequency.
  - Keep current below 4 mA RMS
    Generally accepted safe limit.



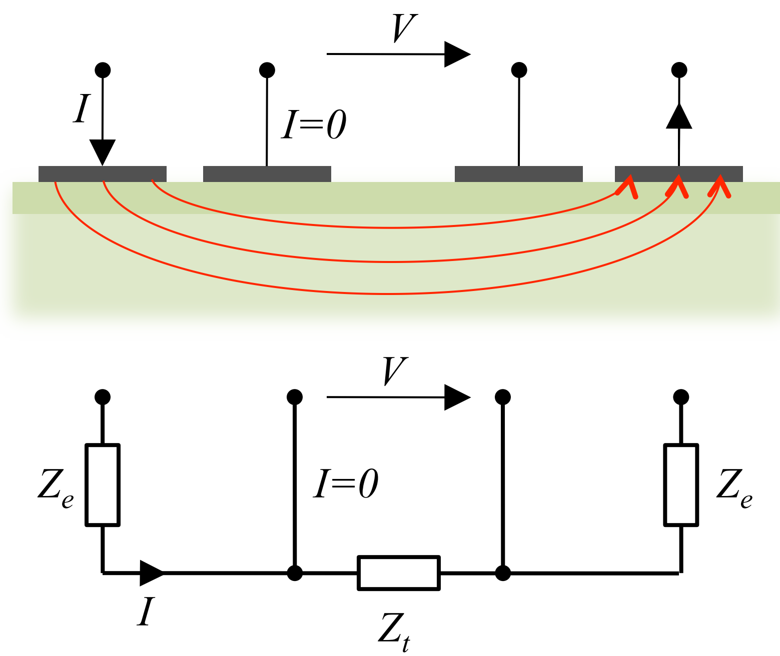
Source: Medical Instrumentation, J. Webster, 2009

Electrode Configurations

Preferably, a four-electrode configuration (Kelvin) is used to measure tissue impedance, in order to reduce contributions of the electrodes (1-10 kΩ) on the measured impedance (usually 10-1000 Ω):



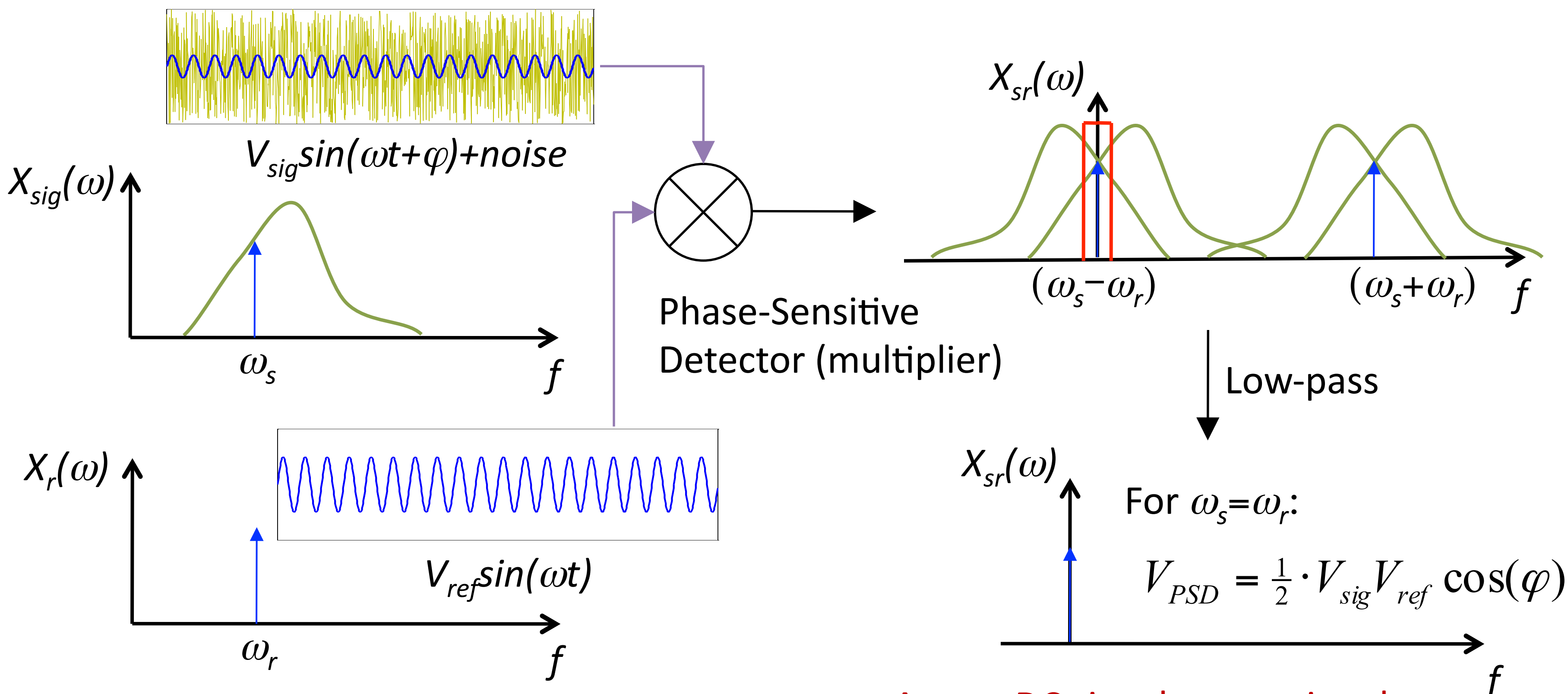
$$Z_t = \frac{V}{I} - \underbrace{2Z_e}_{\text{Unknown}}$$



Direct: $Z_t = \dfrac{V}{I}$

Lock-in Amplification

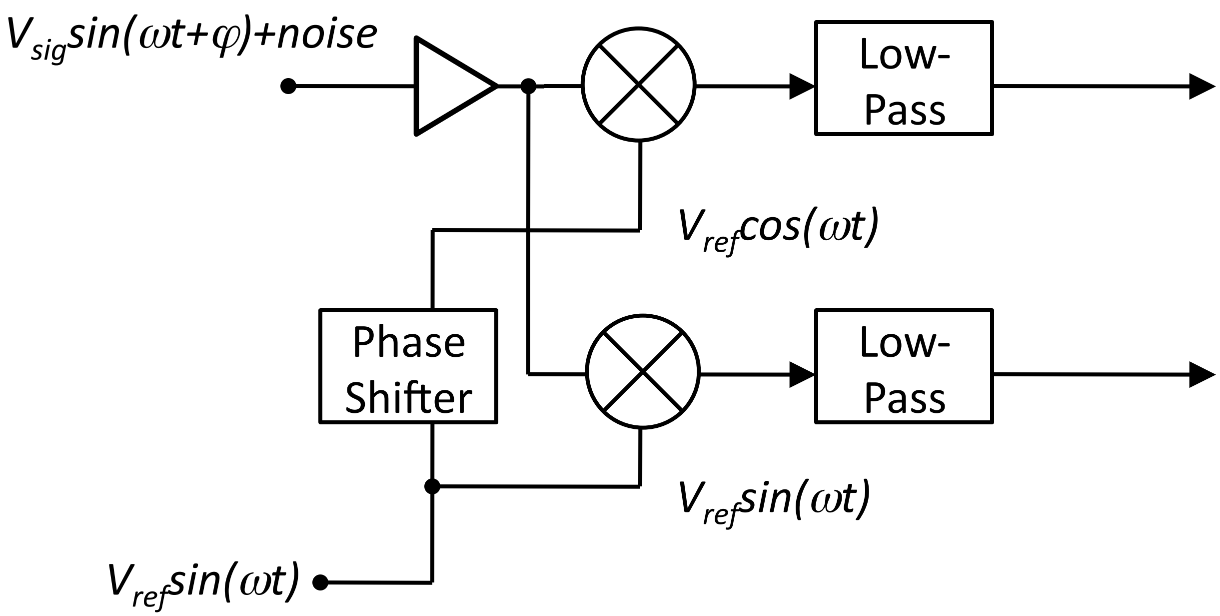
Lock-in amplifiers act as extreme narrow-band filters which selectively amplify a signal of a given frequency.



A near-DC signal proportional to signal amplitude and phase!

Lock-in Amplification

By using two reference signals with a 90° phase-shift (sine/cosine), the lock-in amplifier can separate amplitude and phase:



$$X = \tfrac{1}{2} \cdot V_{sig} V_{ref} \cos(\varphi)$$

$$Y = \tfrac{1}{2} \cdot V_{sig} V_{ref} \sin(\varphi)$$

$$R = \sqrt{X^2 + Y^2} = V_{sig} \qquad \varphi = \arctan\left(\frac{X}{Y}\right)$$

Squarewave Lock-in Amplification

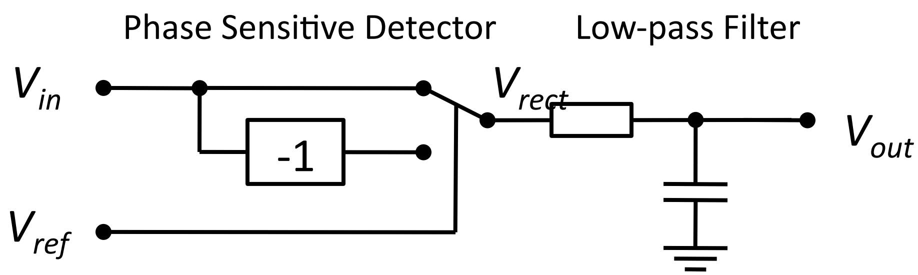
- Can do this also using any waveform (e.g., squarewave), whereby each harmonic is also heterodyned (more correctly, homodyned) to DC.
- The, of course, one is "sampling" a bigger fraction of the impedance of the target system and lumping the results together.
- For basic research, single-frequency lock-in approaches are generally used.
- For low-cost consumer applications, squarewave techniques are often used because the "multiplier" is simply a switch driven digitally to pass or block the signal.

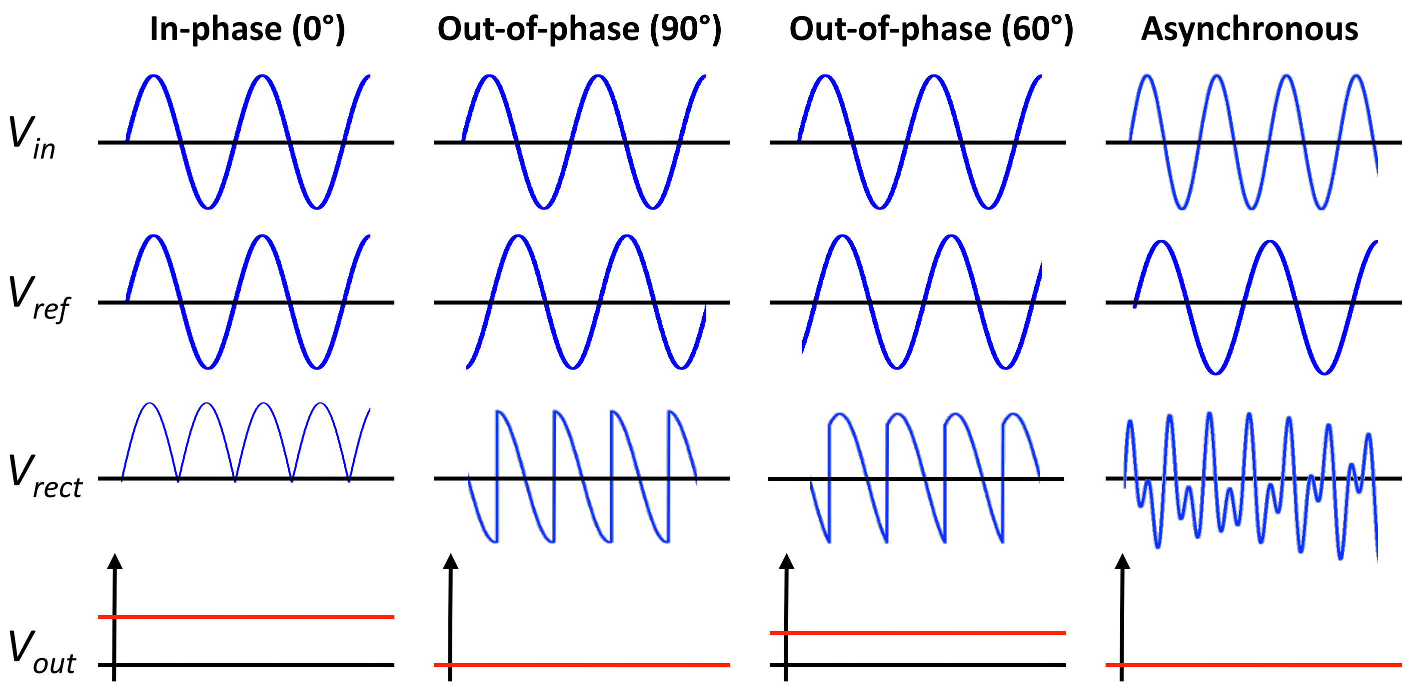
Phase-Sensitive Demodulator

- The heart of the lock-in amplifier is the synchronous rectifier, consisting of a phase-sensitive detector (PSD) and a low pass-filter.
- Phase-sensitive detector:
  - Multiplier (analog or digital)
  - Switched gain stage (+1/-1 gain)
  - Diode bridge (double balanced mixer)

    Typically used for RF applications

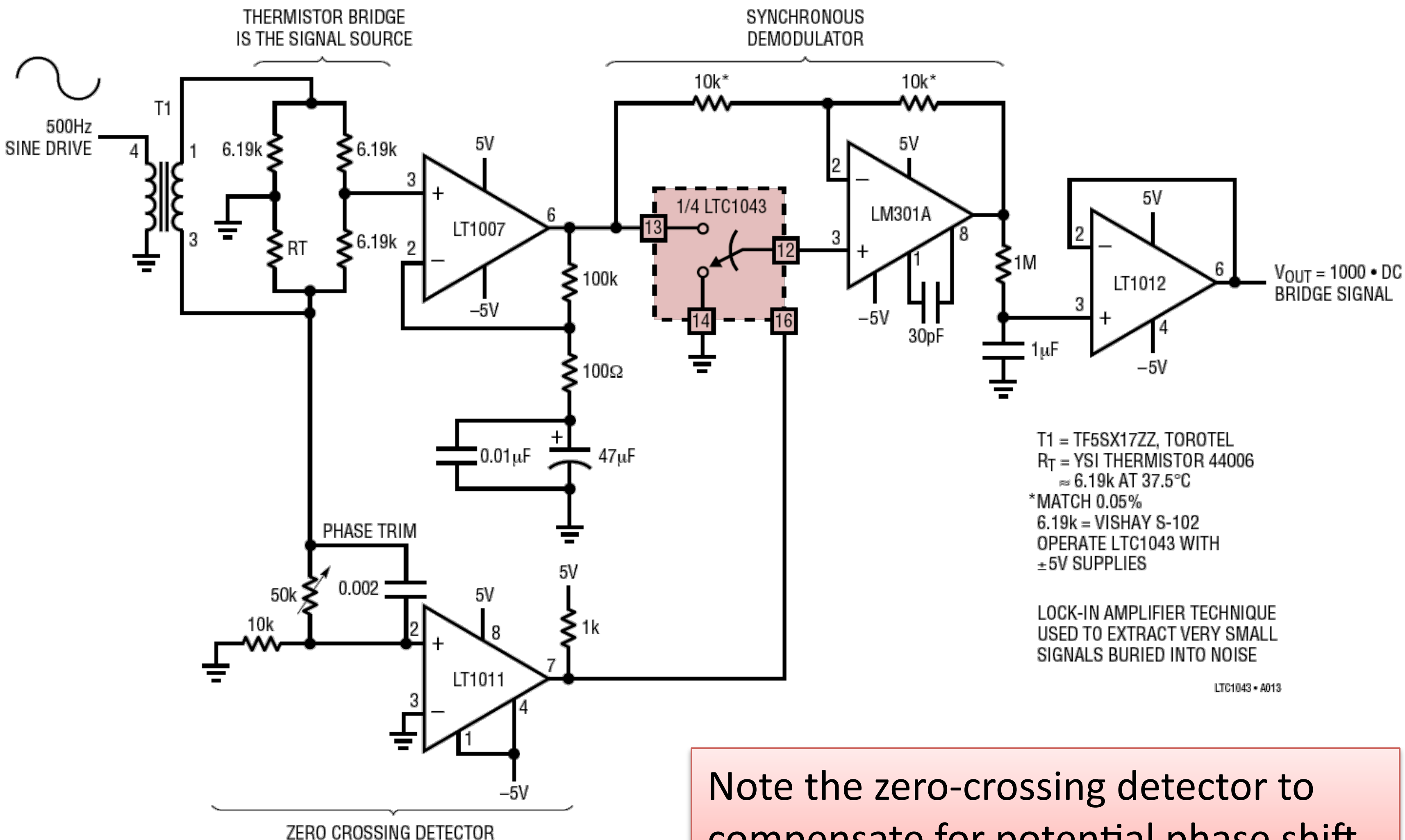
Phase-Sensitive Demodulator





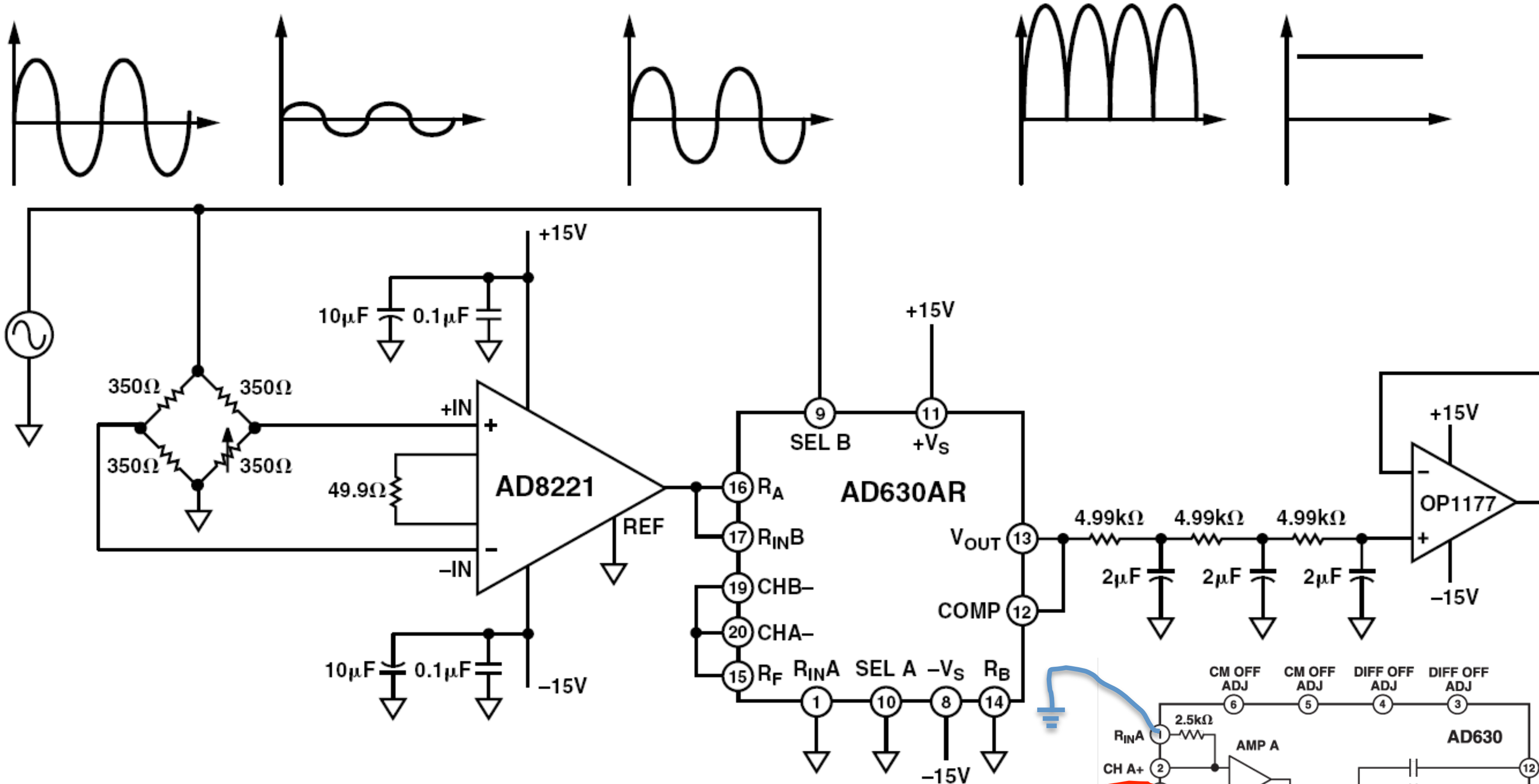
Lock-in Amplifier

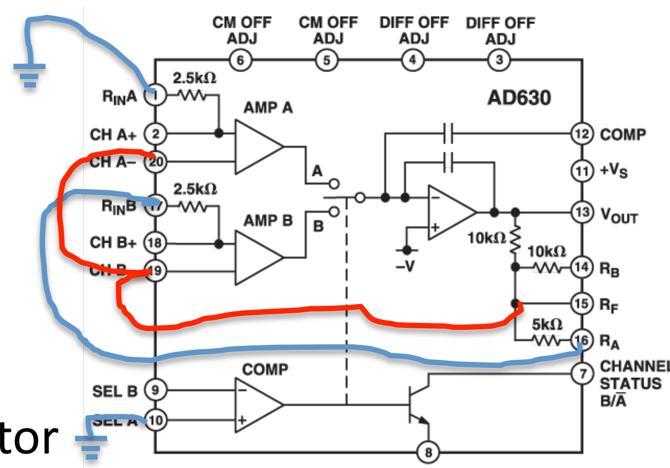
Synchronous demodulator based on switched-cap block (Linear Technologies LT1043)



Note the zero-crossing detector to compensate for potential phase shift

Precision Synchronous Demodulator

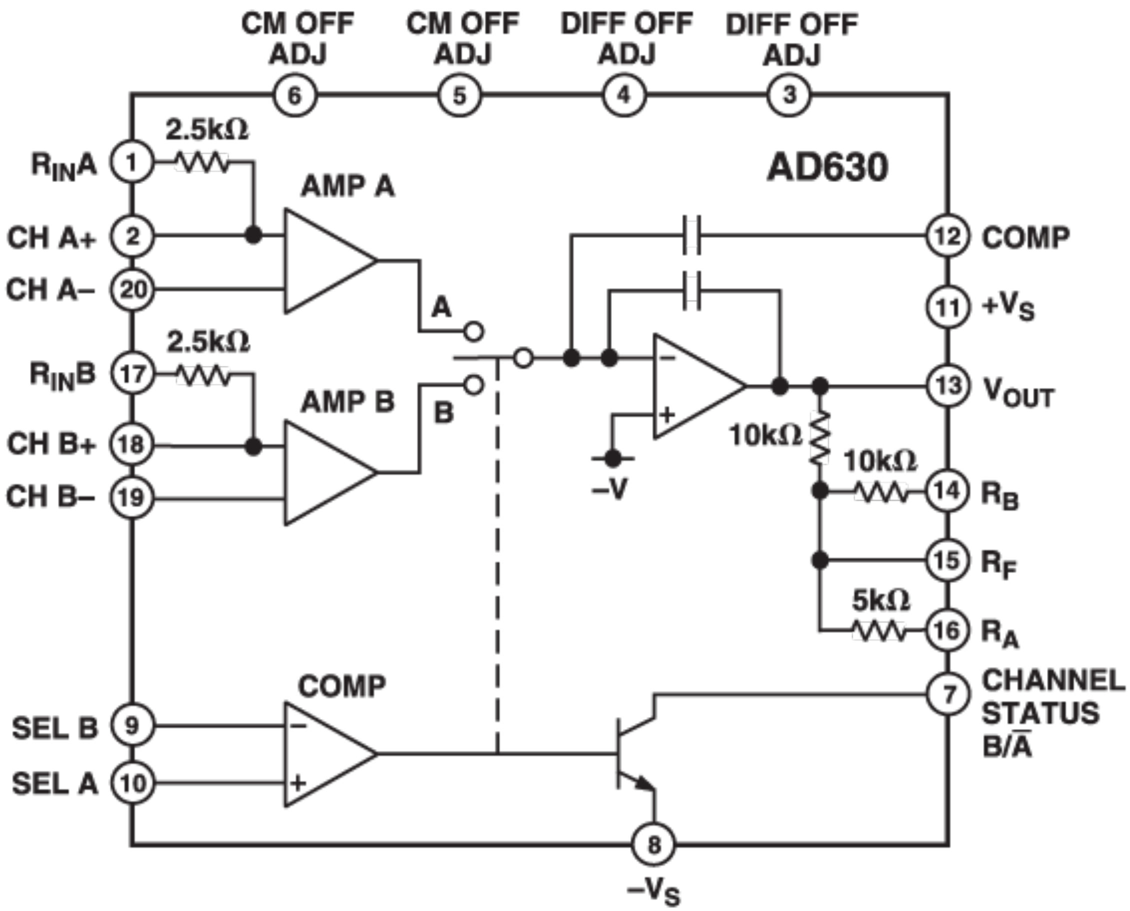




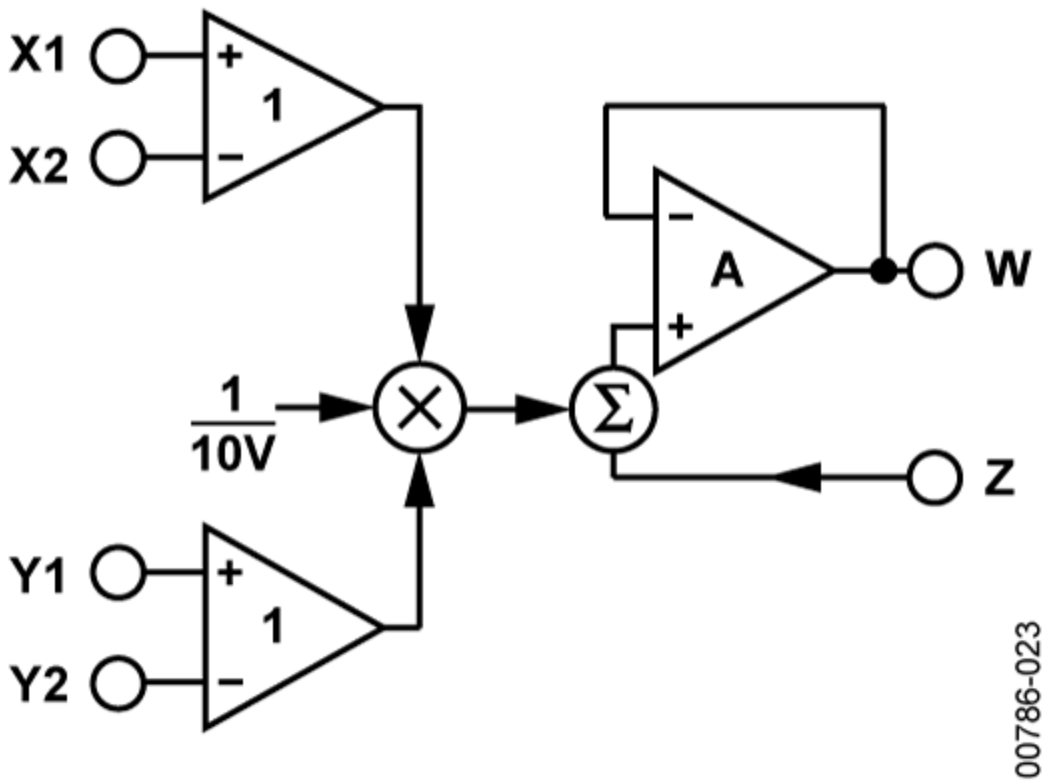
Analog Devices AD630 Balanced Modulator/Demodulator

Source: Analog Devices, Application Note AN-683

AD630 Detail



AD633: True Multiplier



Commercial Lock-In Amplifiers

Stanford Research Systems (SRS) SR-830
http://www.thinksrs.com/index.htm

Digital multiplication!

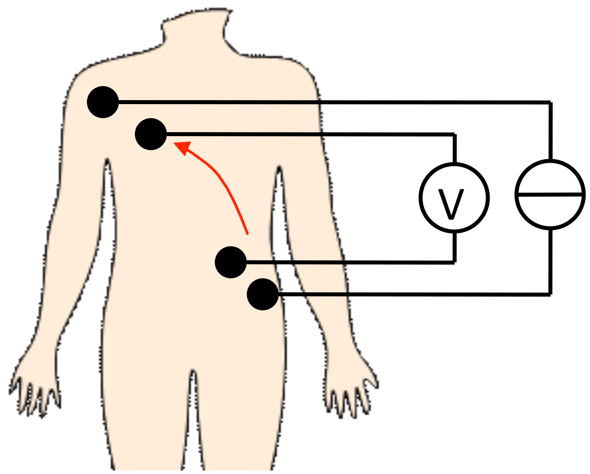
Zurich Instruments HF2LI Lock-in amplifier
http://www.zhinst.com/

Applications

Respiration Measurements

Impedance Plethysmography

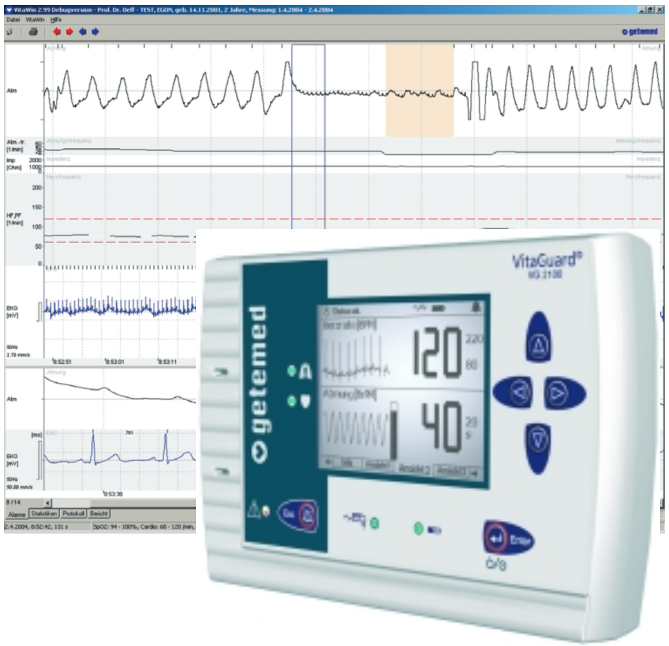
- Impedance plethysmography ("measurement of volume") can be readily applied to respiration monitoring.
- Intake of air in lungs increases thoracic resistance.
- 1-10 Ω modulation, 0.01-0.5 Hz bandwidth.
- Can be calibrated to measure tidal volume.
- Sensitive to motion artifacts.



Ambulatory Systems

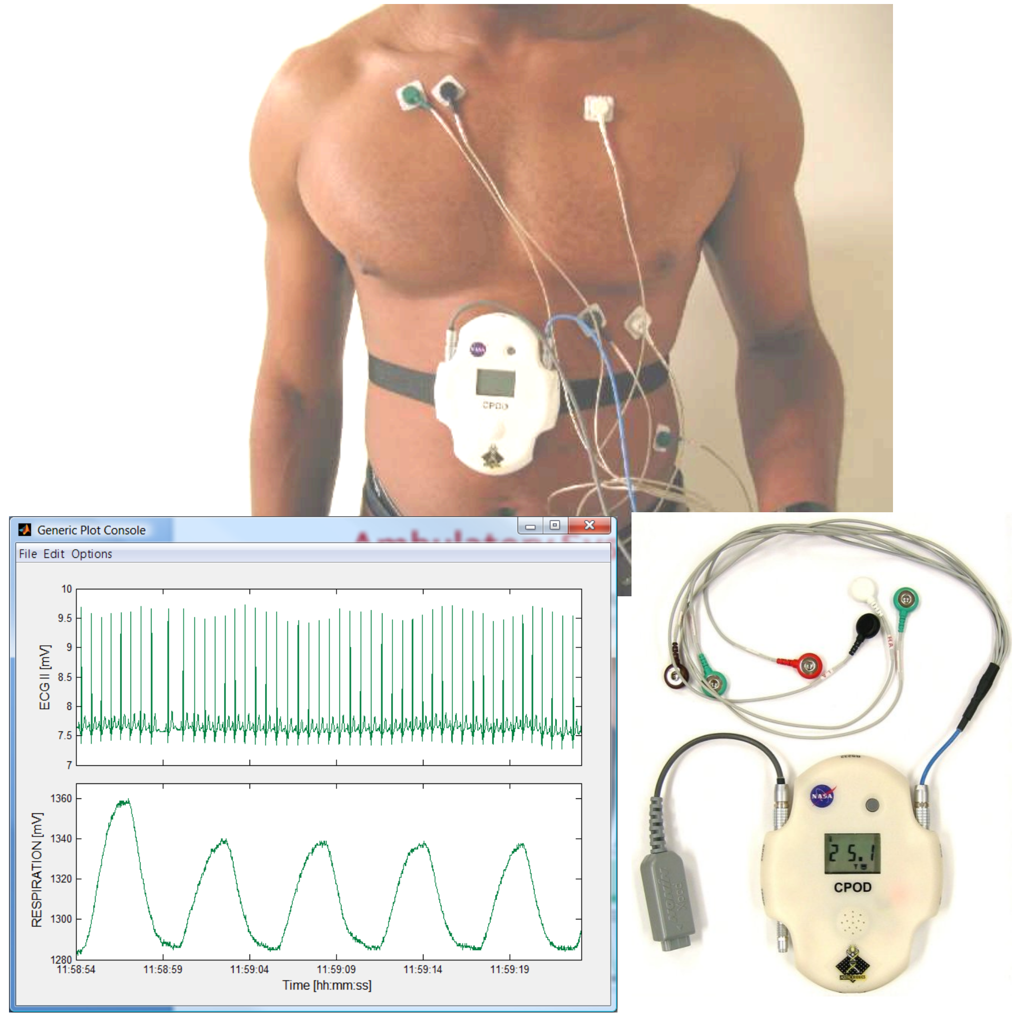
NASA/Stanford LifeGuard CPOD

Multiparameter physiologic monitor



getemed VitaGuard® VG2100

Heart and Apnea monitor



Applications

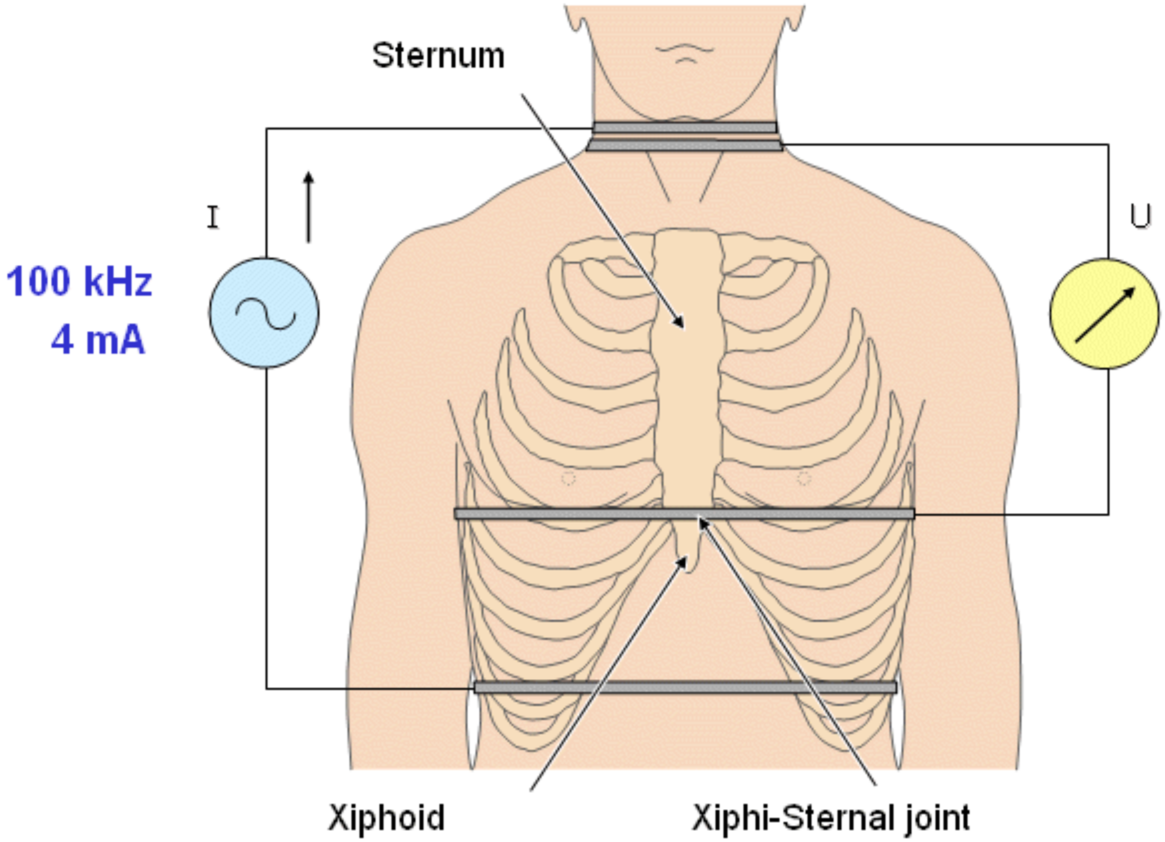
Impedance Cardiography

Impedance Cardiography

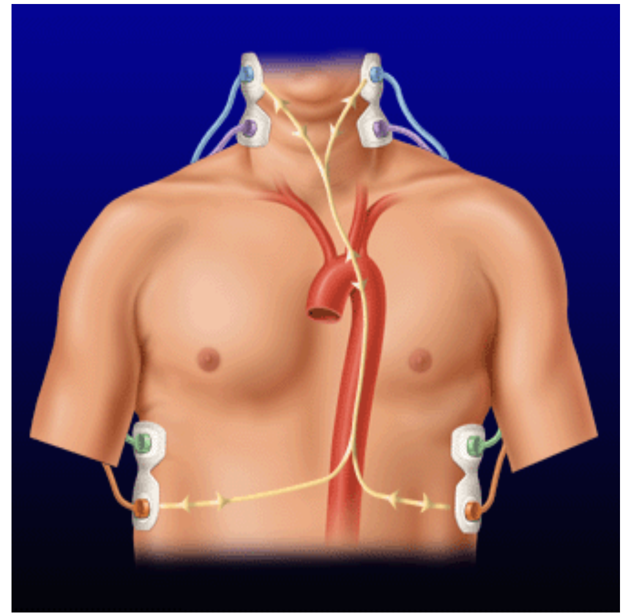
To be tested in lab !!

- Impedance cardiography (ICG) aims at evaluating hemodynamic parameters:
  - Heart rate
  - Stroke volume (amount of blood ejected at each heart beat), cardiac output
  - Timings (Left Ventricular Ejection Time, Pre-ejection Period,…)
  - Fluid status (Z_0).
- 10-200 mΩ modulation, DC-30 Hz bandwidth.
- Typically, 50-100 kHz/1-4 mA RMS current.

ICG Electrode Setup



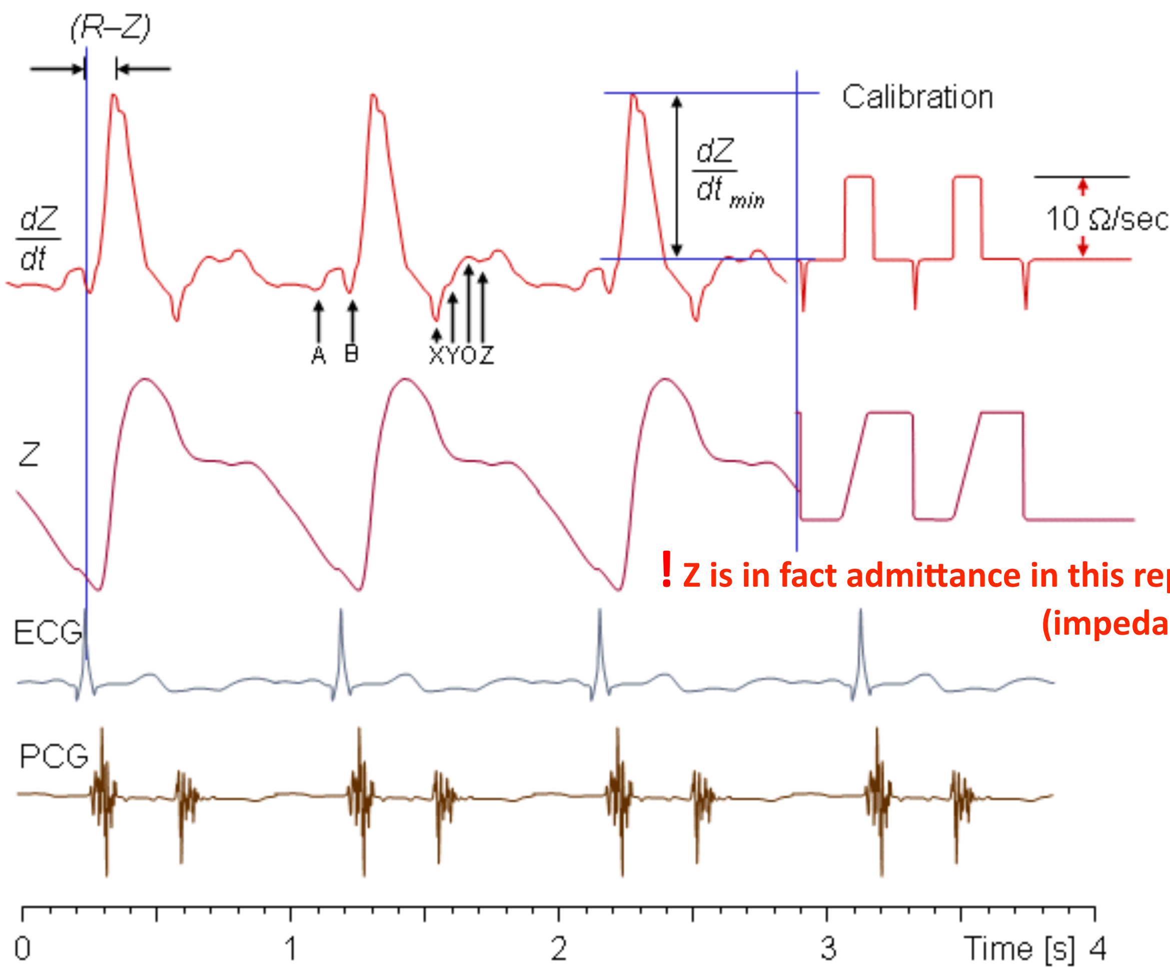
Original band-type electrodes



Current discrete gel-type electrodes (8 total)

Source: Bioelectromagnetism, Malmivuo & Plonsey, http://www.bem.fi & http://www.cardiodynamics.com/

ICG Waveform



! Z is in fact admittance in this representation (impedance decreases during systole)!

Points:

A: Contraction of atrium
B: Opening of aortic valve
C: Maximum flow from left ventricle into aorta
X: Closing of aortic valve
Y: Closing of pulmonary valve
O: Widest open of mitral valve

Signals:

Z: Impedance
dZ/dt: derivative of impedance
ECG: Electrocardiogram
PCG: Phonocardiogram

Source: Bioelectromagnetism, Malmivuo & Plonsey, http://www.bem.fi

Cardiac Output Derivation

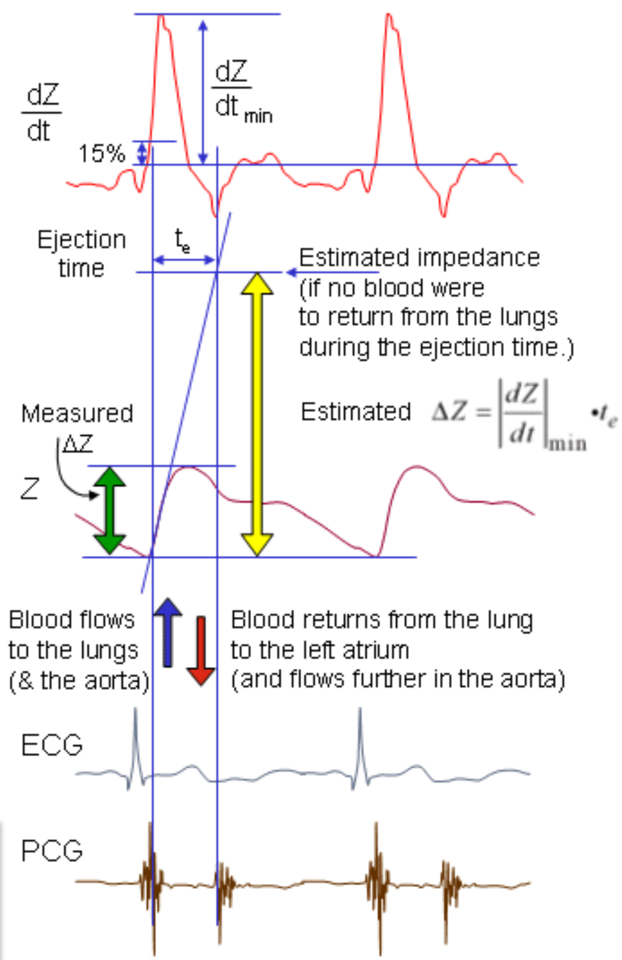
- Challenge: deriving the stroke volume (SV) & cardiac output (CO) from changes in thoracic impedance.

- Nyboer: $\Delta v = \Delta Z \rho \left(\frac{L}{Z_0} \right)^2 \quad [\mathrm{m}^3]$
  (1950)

- Kubicek: $SV = \rho \left(\frac{L}{Z_0} \right)^2 \left| \frac{dZ}{dt} \right|_{\min} \cdot t_e \quad [\mathrm{m}^3]$
  (1966)

$$CO = SV \cdot HR$$

SV	stroke volume [ml]
ρ	blood resistivity [Ω·cm], typically 160 Ω·cm
L	distance between sensing electrodes
Z_0	mean impedance of the thorax [Ω]
$\left\| \frac{dZ}{dt} \right\|_{\min}$	absolute value of the maximum deviation of the first derivative signal during systole [Ω/s]
t_e	ejection time (=LVET) [s]
CO	cardiac output [l/min]
HR	heart rate [bpm]



Many empirical refinements have been made, and are still being made…

Commercial Systems

CardioDynamics/SonoSite

BioZ® Dx

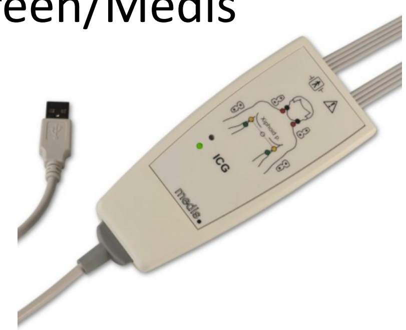
ICG DIAGNOSTICS

FDA-approved

Niccomo™/Medis

(Now CardioDynamics/SonoSite)

CardioScreen/Medis

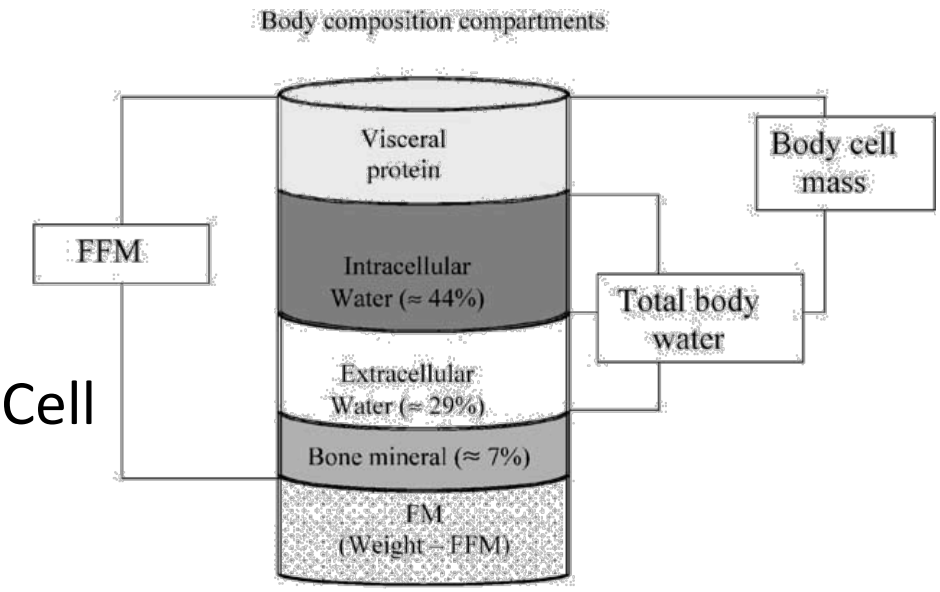


Applications

Body Composition Analysis

Body Composition Analysis

- Estimation of body composition based on whole-body or segmental impedance:
  - Total Body Water (TBW)
  - Extracellular Water (ECW)/ Intracellular Water (ICW) balance
  - Fat-Free Mass (FFM, or Body Cell Mass or Muscle Mass)
  - Fat Mass



- Various Configurations:
  - Single frequency (typ. 50 kHz)
  - Multiple frequencies (5-500 kHz)
  - Whole body
  - Segmental

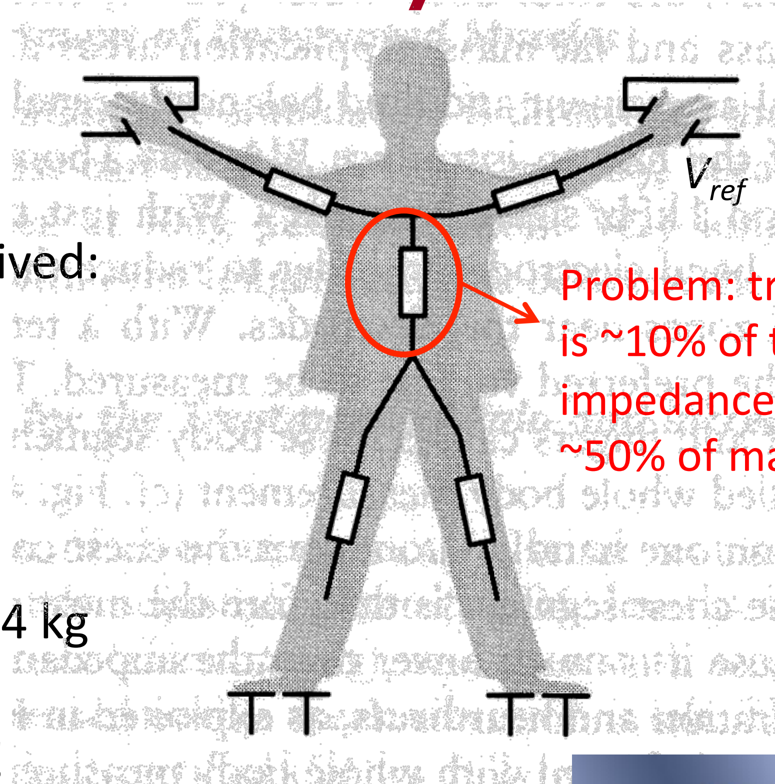
Source: Kyle, Clinical Nutrition, 23, 2004

Body Composition Analysis

- Whole-body, single frequency (SF-BIA – most common)
  - TBW from resistance, FFM & FM derived:

$$TBW = k_1 \frac{H^2}{R} + k_2 W + k_3$$

  - Phase sometimes used as index of nutrition.
  - Typical errors of 3-4 l for TBW and 3-4 kg for FFM).
  - Ok for home, but not for clinical use!
- Refinements (multiple frequencies, segments) help selectively, but the method remains very sensitive to *calibration* and *fluid abnormalities*.



Problem: trunk is ~10% of total impedance, but ~50% of mass!

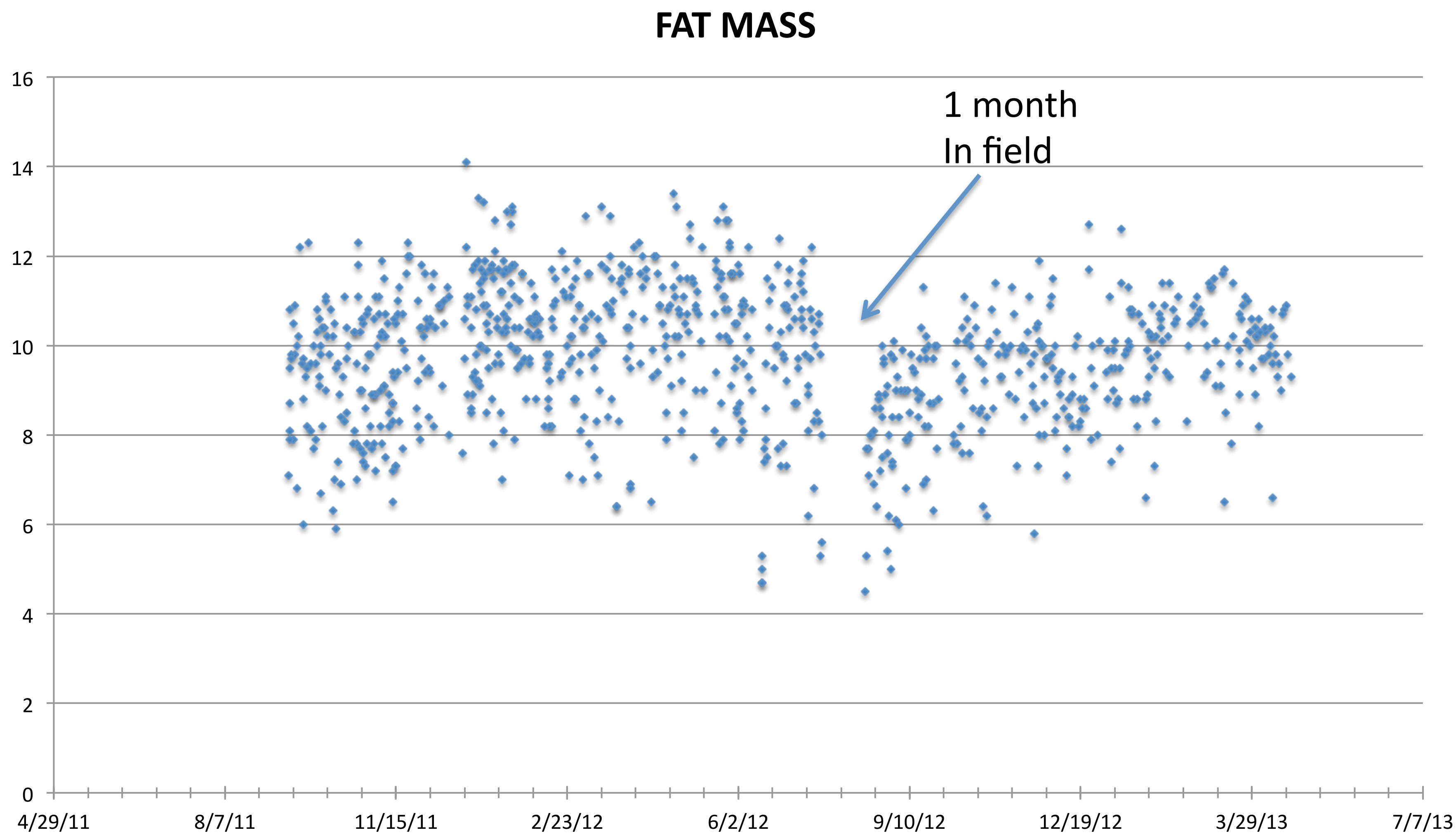
Omron scale

BioScan 916, Maltron
http://www.maltronint.com

Source: Bioimpedance and Bioelectricity Basics, Grimnes & Martinsen, Elsevier, 2008

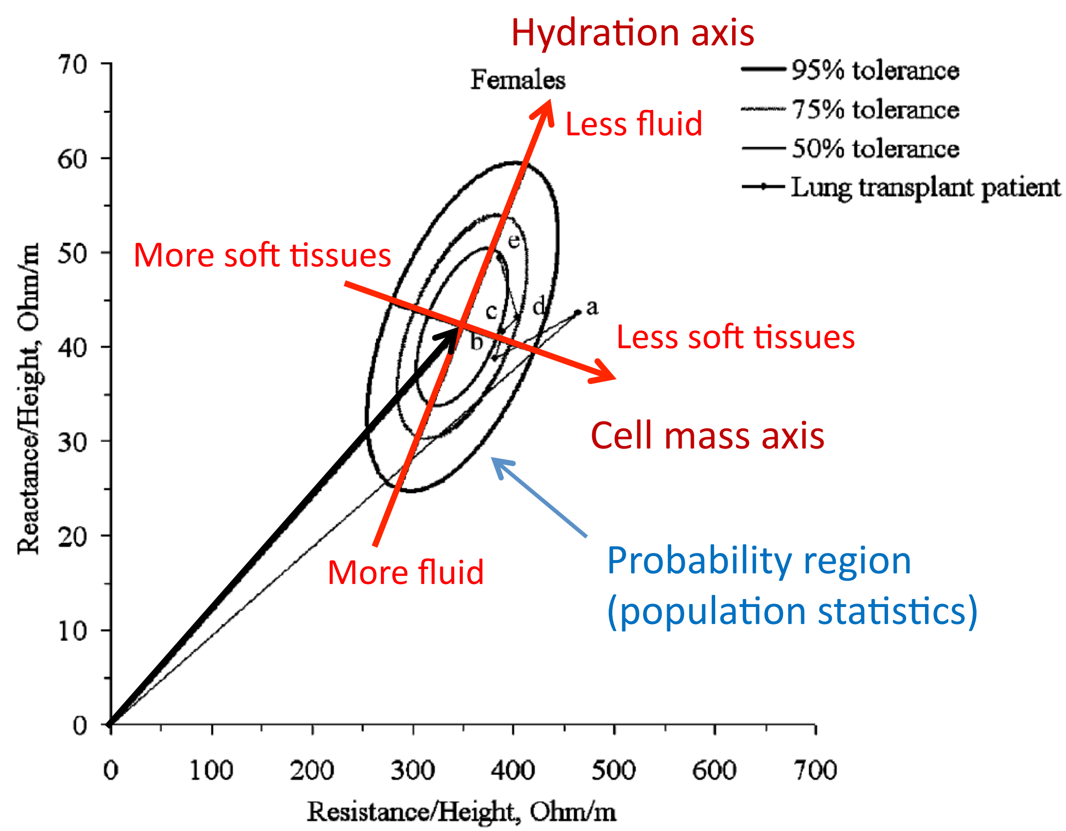
Body Composition Example

- Wiithings Scale data, fat mass vs time, ≈ 150 lb male.



Bioelectrical Impedance Vector Analysis

- ‘Black-box’ approach looking only at patterns in height-normalized resistance/reactance vector.
- No regression, no assumption about models.
- Useful for trending.



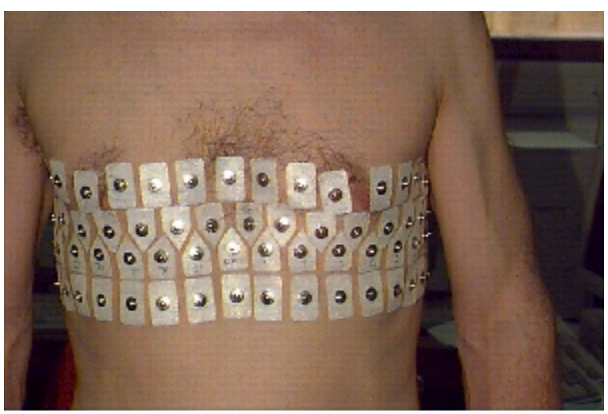
After: Kyle, Clinical Nutrition, 23, 2004

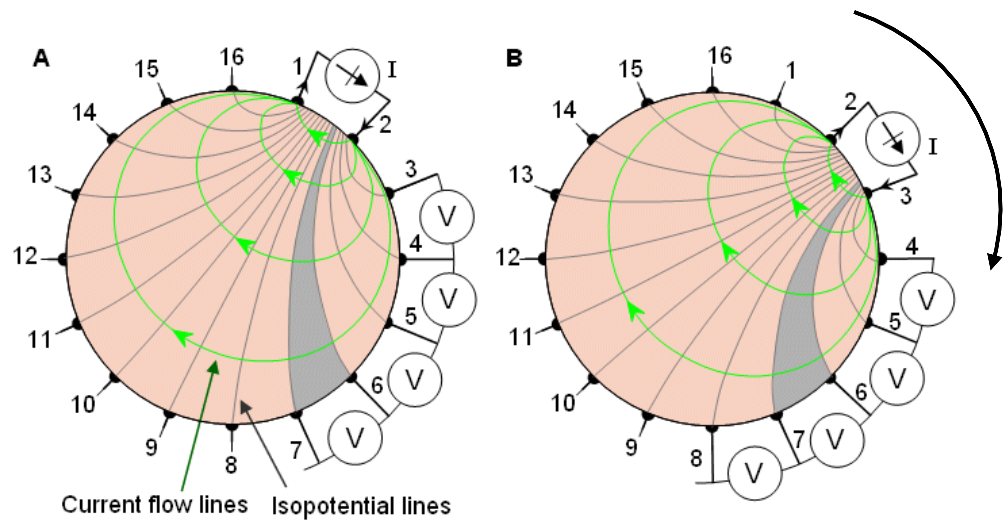
Applications

Electrical Impedance Tomography

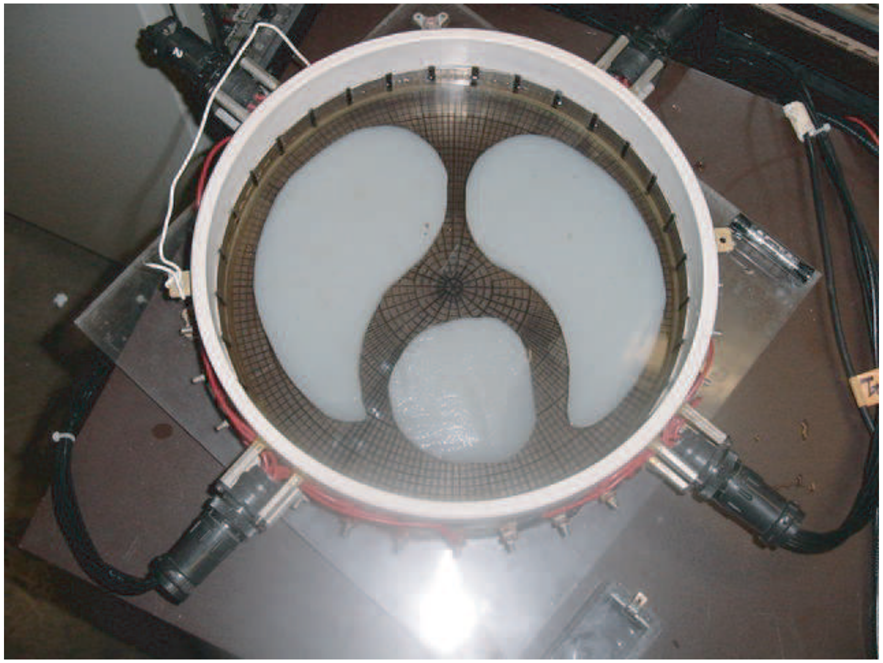
Electrical Impedance Tomography

- By using many electrodes to take independent measurements, tissue impedance can be imaged.
- Typically 8-16 frequencies used, spanning 10kHz-1MHz.
- 16-128 electrodes, currents in the milliampere range.
- Resolution currently limited (≈centimeters).
- High sensitivity to anisotropy of tissue in these frequencies.
- Limited clinical use so far.

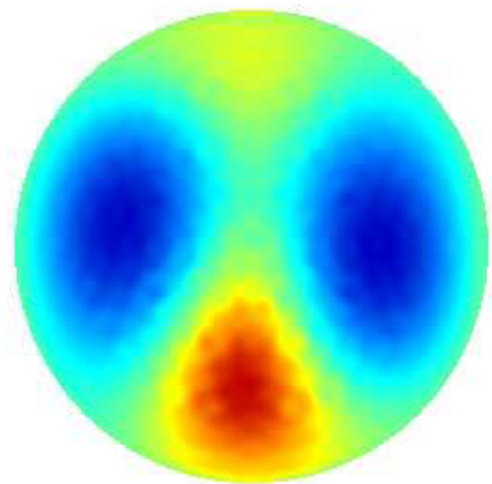




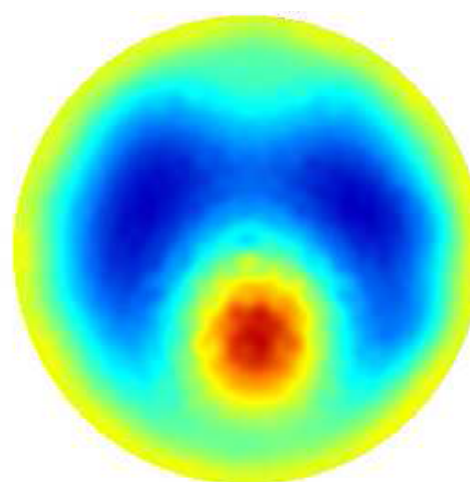
EIT: Reconstruction Challenges



Phantom Chest



'D-bar' algorithm



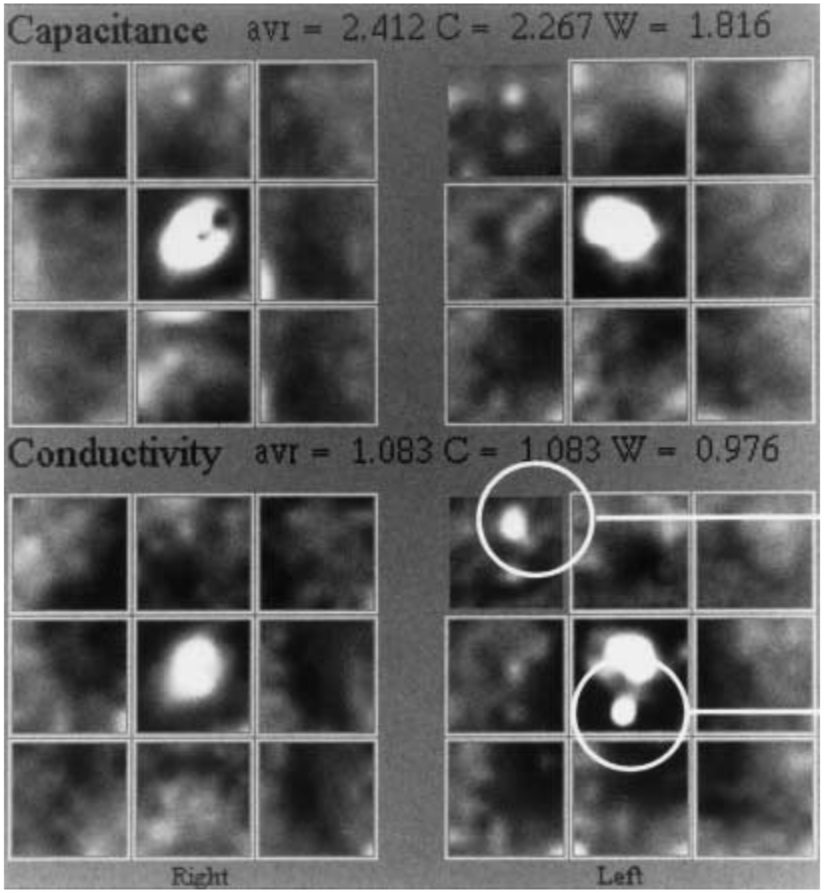
'NOSER' algorithm

Problem is ill-defined: many degree of freedom, few inputs (inverse conductivity problem)

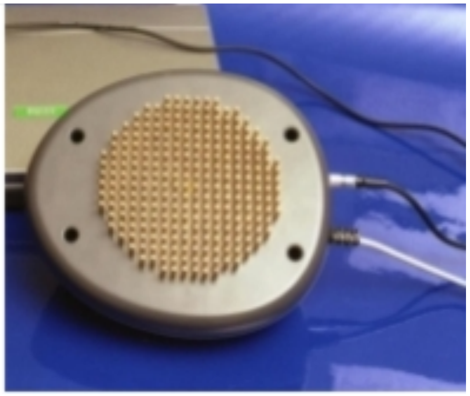
Source: Isaacson et al., Physiological Measurement, 27 (2006)

EIT Examples

Aide to breast cancer detection

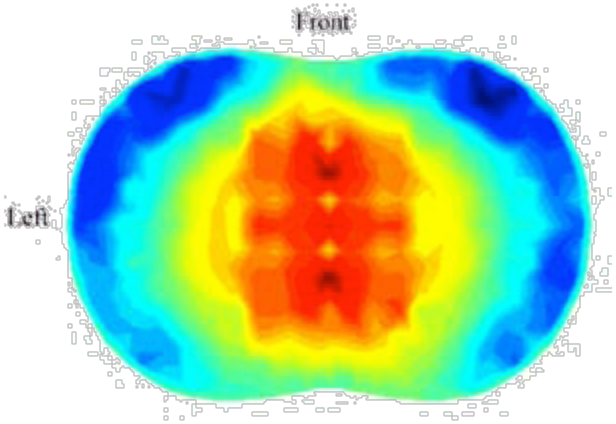


T-Scan 2000 from Siemens (no longer available)
Source: Malich *et al.*, Eur. Radiology, 2000



ITM, LD Technologies (256 electrodes)
http://www.ldteck.com/

Chest imaging



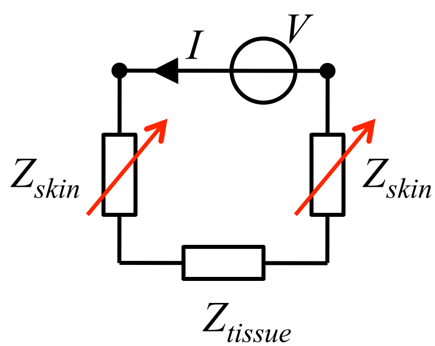
Kerrouche, *et al.*, Physiological Measurement, 21, 2001

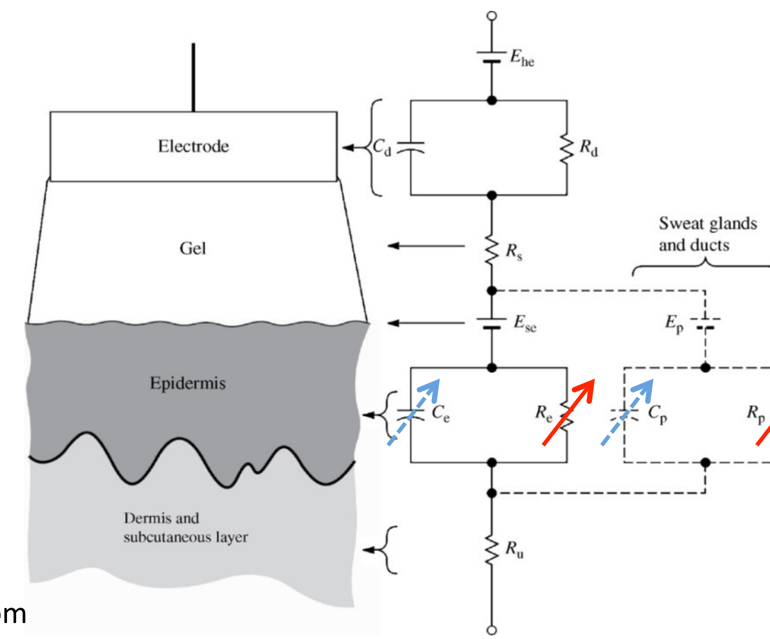
Applications

Other Applications of Impedance Measurements

Galvanic Skin Response (GSR)

- Changes in skin resistance associated with the modulation of sweat (eccrine) glands activity, also known as *Electrodermal Response* (EDR).
- Measured as *Galvanic Skin Resistance* (GSR) or *Conductance* (GSC).
- Most pronounced on plantar/palmar (glabrous) regions.
- Measured at DC (electrode polarization!) or low-frequency AC.
- Indicator of the psychological state (relaxed, nervous, anxious).
- Used in biofeedback, polygraph.

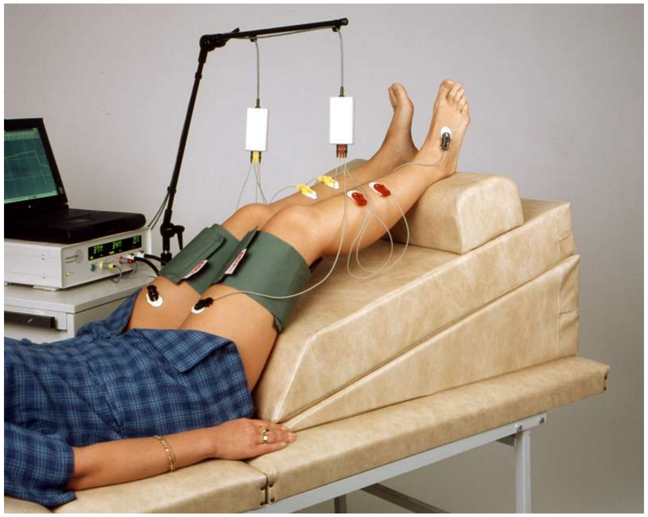


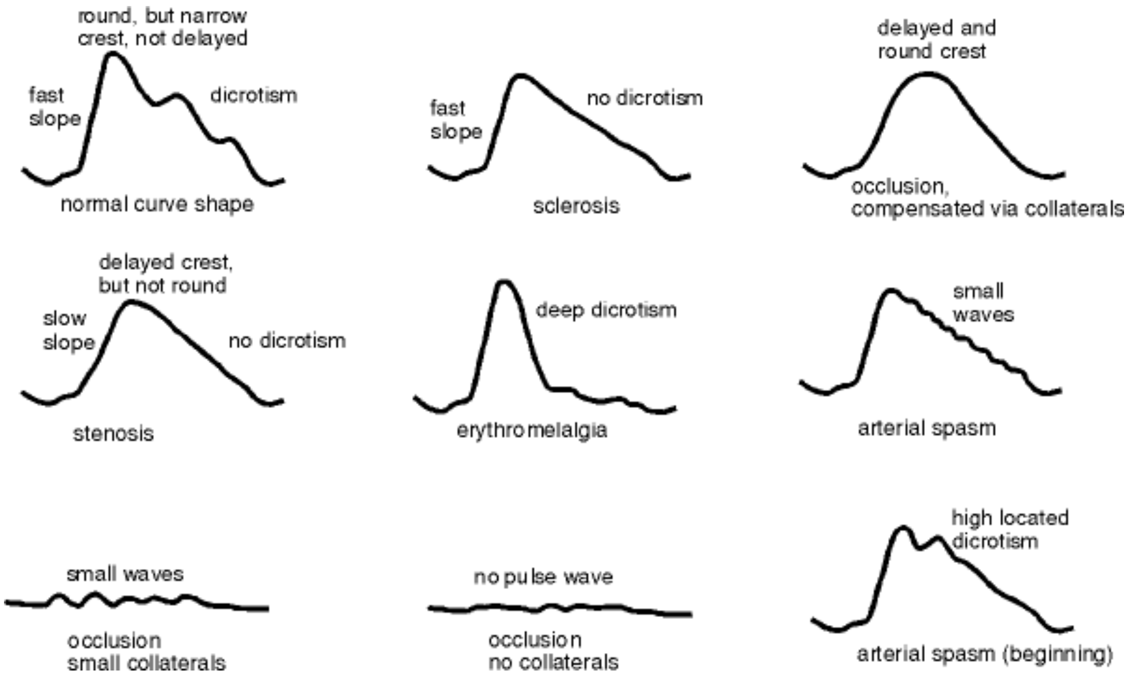


Sources: Webster & http://www.iworx.com

Blood Flow in Limbs

- Venous Occlusion Plethysmography
  - Measure arterial and venous flows
  - e.g., diagnosis of deep vein thrombosis
- Arterial Pulse Wave
  - Arteriosclerosis, stenosis,…





Source: http://www.medis-de.com

Lab this week

Respiration and Impedance Cardiography (ICG)