STANFORD UNIVERSITY

EE122B

Introduction to Biomedical Electronics

Miscellaneous Biomedical Sensors and Interfaces

Gregory Kovacs, Laurent Giovangrandi

Department of Electrical Engineering
Stanford University

Content

Selected biomedical sensor applications, their transduction mechanisms, and associated interface circuitry.

- Temperature sensing
- Displacement and motion sensing
- Electrochemical sensors
  - Potentiometric
  - Amperometric

Technology

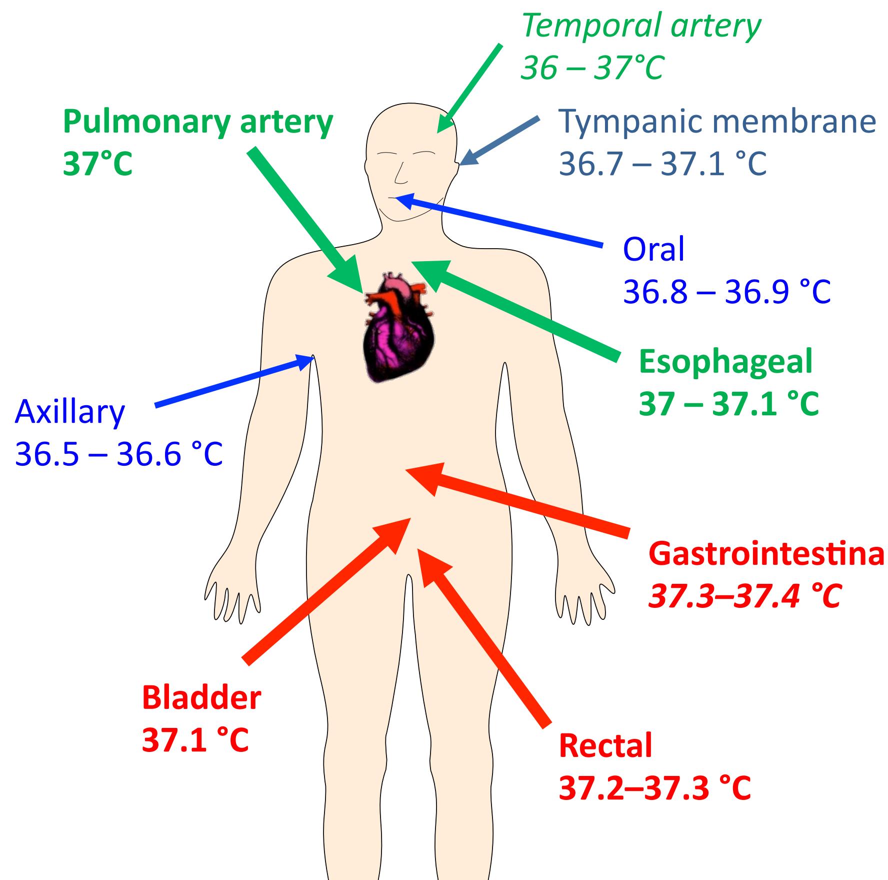
Temperature Sensing

Temperature Physiology

- We (mammals) are a warm-blooded species (*endotherm*).
- Thermoregulation is critical for biological processes to function properly (e.g., protein function).
  Temperature is affected by many processes, some of which are of high diagnostic value (fever, local inflammation,…).
- Thermoregulation is mainly under the control of *hypothalamus.*
  Temperature-sensitive neurons in the hypothalamus, skin and spinal cord relay temperature to the hypothalamus.
- At rest, the body generates ≈ 90 W of heat, and maintain an average temperature of 37°C.
- Heat transfer mechanisms are *radiation*, *conduction* and *convection* and *evaporation of perspiration.*
- *Cooling* is mainly achieved through *perspiration*, aided by vasodilation.
- *Heating* is performed through increased metabolism, muscle activity (shivering), vasoconstriction and shut down of perspiration.

Measurement Locations

- Core temperature
  - Catheter (pulmonary artery)
- Pseudo-core
  - Rectal
  - Gastrointestinal (pill)
  - Esophageal
  - Oral (sublingual)
  - Temporal artery
  - Tympanic membrane
- Surface temperature
  - Skin temperature



Desired measurement range: 30-44°C
Resolution: 0.1°C
Bandwidth: DC - 0.1Hz (up to 1Hz)

Derived from : Mary Frances D. Pate, *Thermal Regulation* in 'Principles and Practice of Pediatrics', 1999; Suleman, Anesthesia & analgesia, 95, 2002; Byrne, Br. J. Sports Med, 41, 2007.

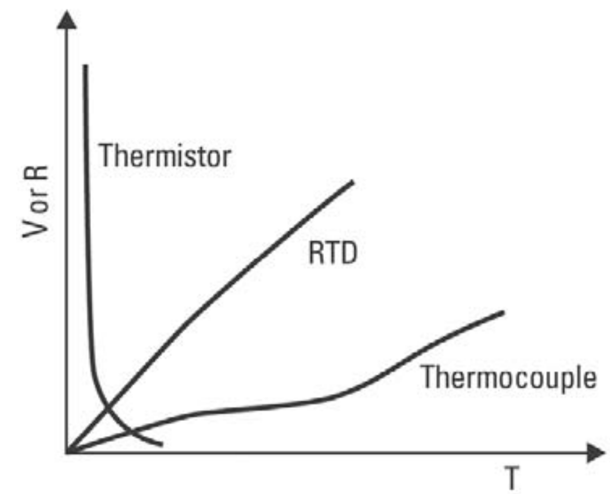
Measurement Technology

- Resistance-based
  - Resistor Temperature Devices (RTD)
  - Thermistors
- Thermocouples
- Radiation-based
- Fiber Optic-based
  Modulation of total internal reflection, fluorescence or absorption in semiconductor.
- Thermochromic
  Temperature-based color change (liquid crystals, thermometer patches).
- Many other technique sensitive to temperature…

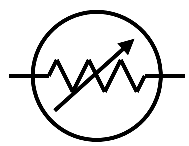
Thermistors & RTDs

- Resistance-based temperature sensors
- Resistor Temperature Device (RTD) 
  - Positive temperature coefficient of resistance (TCR, or TEMPCO).
  - Fairly linear, very accurate.

    Example platinum RTD : TCR = 0.00385 Ω/Ω/°C.
    For 100Ω (typical) at 0°C, 0.38 Ω per °C



Source: Agilent Application Note 290

- Thermistor 
  - Large negative temperature coefficient.
  - Good sensitivity, but not linear.

$$R = R_0 e^{\beta\left(1/T - 1/T_0\right)}$$

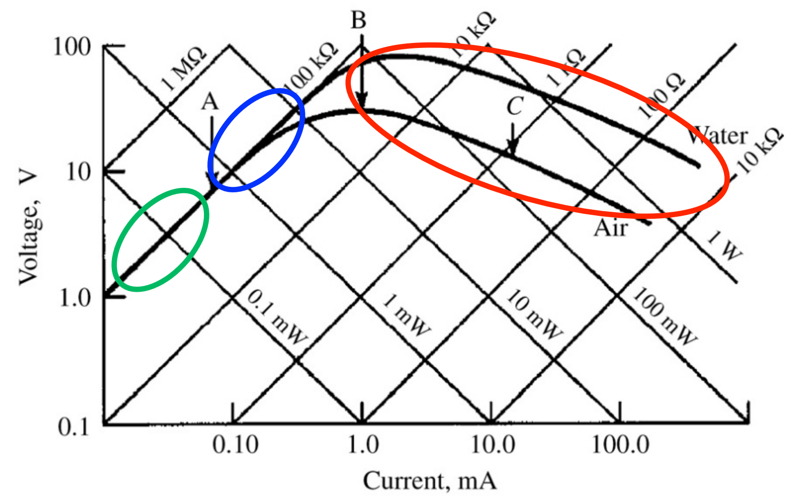
Example YSI 401 (ceramic): R_0 = 2.25 kΩ, β = 3976 Ω (at 25°C) → -100 Ω per °C

  - Typically used for catheters, rectal, esophageal probes (example: series 400 from YSI)

Thermistor Conditioning

- Problem: “Self-heating”

  Current through thermistor should stay low to avoid self-heating.
  Bad: inaccurate temperature measurement
  Worse: destruction of sensor
  (thermal run-off if NTC)

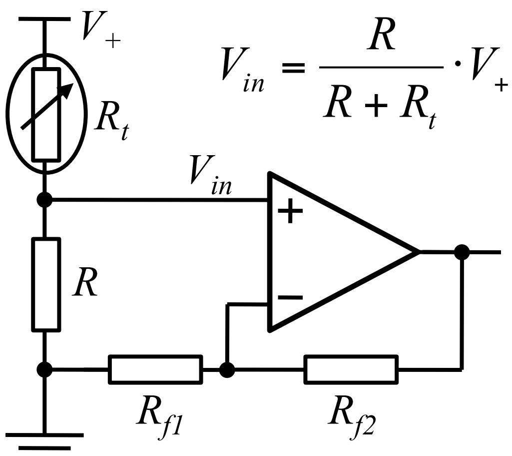


- Linearization
  - Digital, look-up table (third-order polynomial, Steinhart-Hart equation)
  - Analog

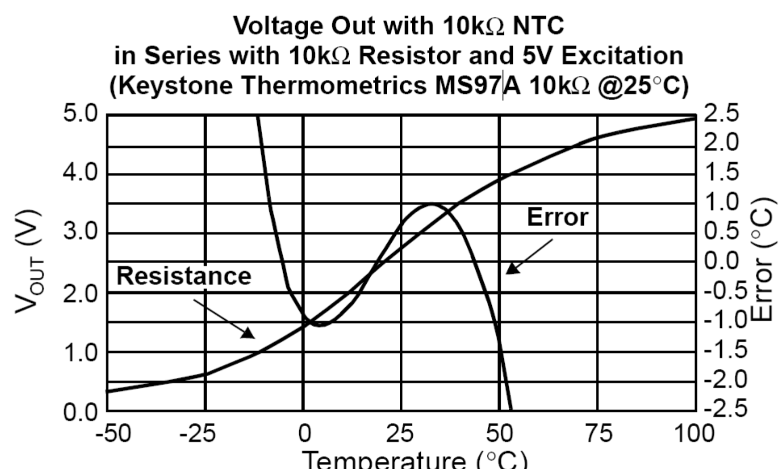
http://en.wikipedia.org/wiki/Steinhart–Hart_equation

Example: series resistance linearizes behavior around R.

$$V_{in} = \frac{R}{R + R_t} \cdot V_+$$



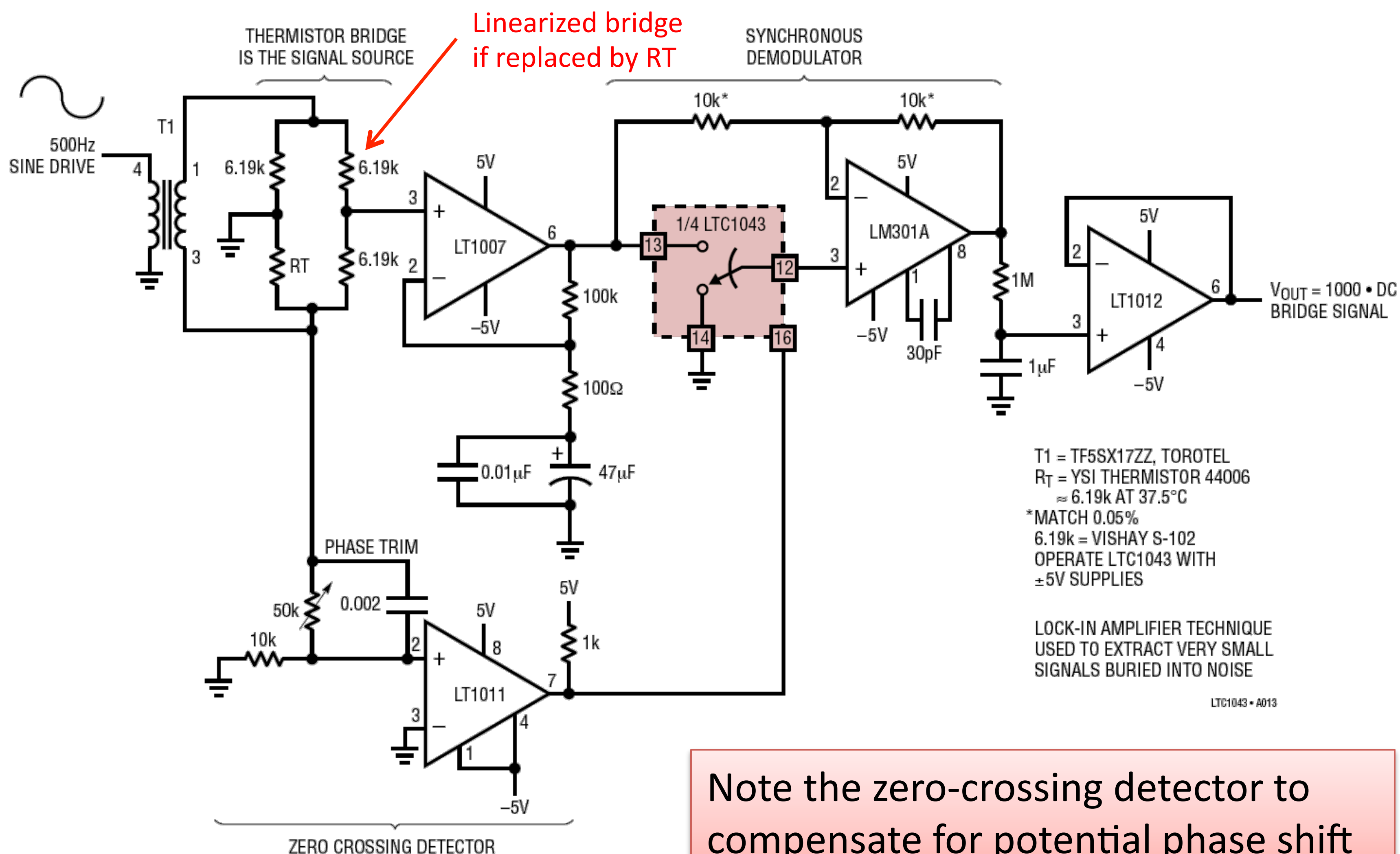
Maximum linearization around T for $R = R_t(T)$



Source: Microchip AN685

Thermistor Conditioning

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



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

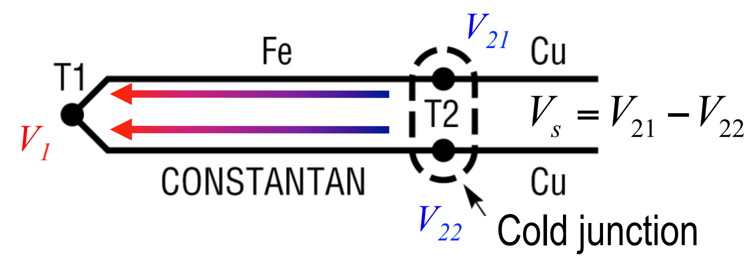
Source: LT1043 datasheet

Thermocouples

- An electromotive force (EMF) appears at the junction of two dissimilar metals. This voltage is a function of the temperature at the metal junction, and at the other end of the metal conductors.

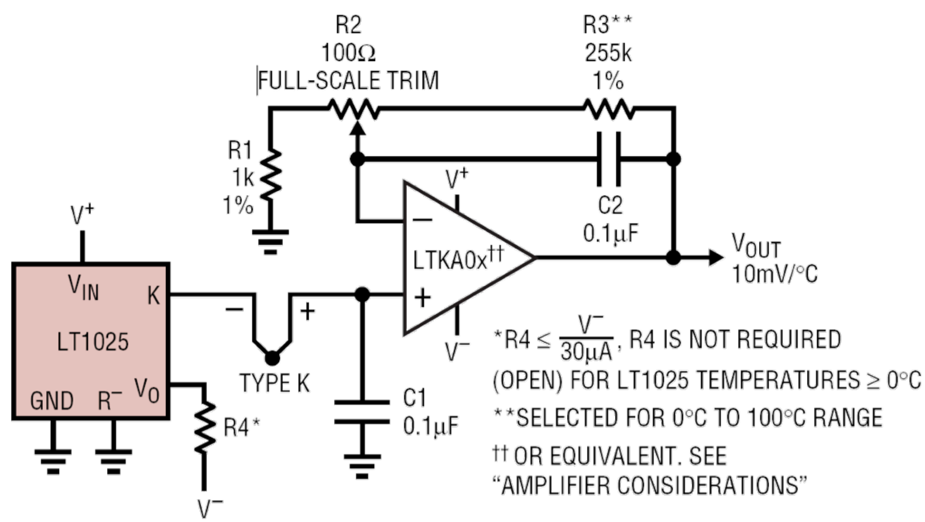
$$V_s = \alpha(T_1 - T_2)$$

α : Seebeck coefficient



Accurate measurements require the “cold junction” to be at a *reference* (ice) or a *known temperature*.

- Typical sensitivities:
  - Type K (chromel-alumel): α = 41 µV/°C
  - Type J (iron-constantan) : α = 50 µV/°C
- Small size, fast response time
  - 10 - 20mm diameter, 1 millisecond
- Special IC provide cold-junction compensation (LT1025, AD597)

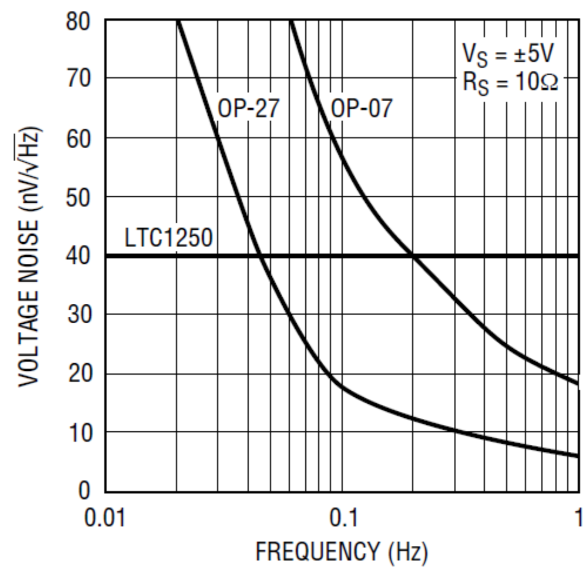


Source: LT1025 datasheet

Zero-Drift Amplifiers

- DC performances of conventional op-amps are usually not stellar (offsets, drift, 1/f noise).
- Precision, chopper amplifiers are optimized for low frequency operation.
- Two main approaches:
  - **Auto-nulling**: periodic sampling of input offset and compensation.
  - **Chopper** amplification: input modulation, AC amplification, demodulation

Example: LT1250
  Offset voltage : 5 μV
  (LT1056 offset voltage : 150 μV)
Noise:



Other circuits: MAX4238, LMV2011, OPA734,…

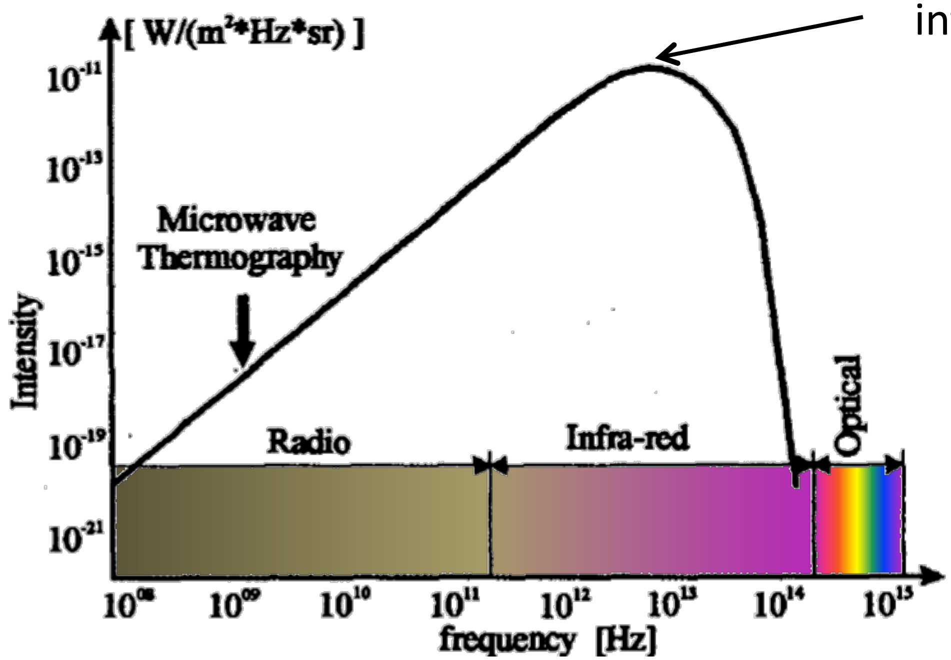
Radiative Measurements

Based on radiation emitted by any body at temperature above absolute zero (AKA black body radiation).

Microwave thermometry (tissue)

Infrared thermometry (surface)

For T = 310K, maximum intensity at ~10 μm



$$I(f,T)=\frac{2\cdot f^2}{c^2}\cdot\frac{h\cdot f}{\exp\left(\frac{hf}{kT}\right)-1}$$

Planck's law

B. Stec, W. Susek, *A 4.4 GHz microwave thermometer with compensation of reflection coefficient*, *13th IEEE International Conference on Microwaves, Radar and Wireless Communications, 2000.*

Infrared Thermometry

- Infrared sensors (quantum or thermal) measure surface temperature.
- Tympanic membranes and temporal regions are usually used.
  They are perfused with blood coming directly from the heart, which also perfuses the hypothalamus.
- Sensitive to surface emissivity ε .
  5% change equals to 1°C at 300K and 3 μm
  Skin emissivity is generally 0.92 - 0.97
- Also used in imaging
  Single and multispectral

Infrared Thermometer

US Patent 4,797,840 (1989, ThermoScan, bought by Braun)

Braun ThermoScan® Pro 4000

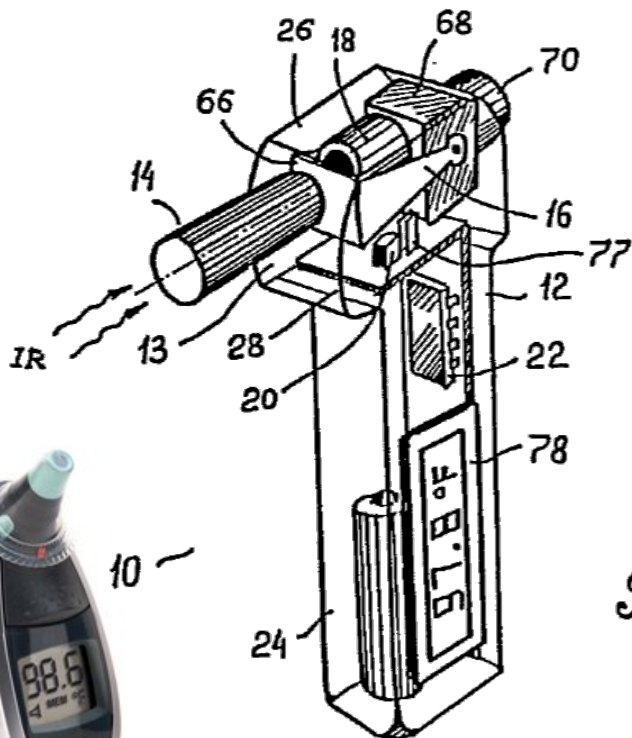


Fig. 1

Sensing circuit (transimpedance amplifier)

PVDF pyroelectric film

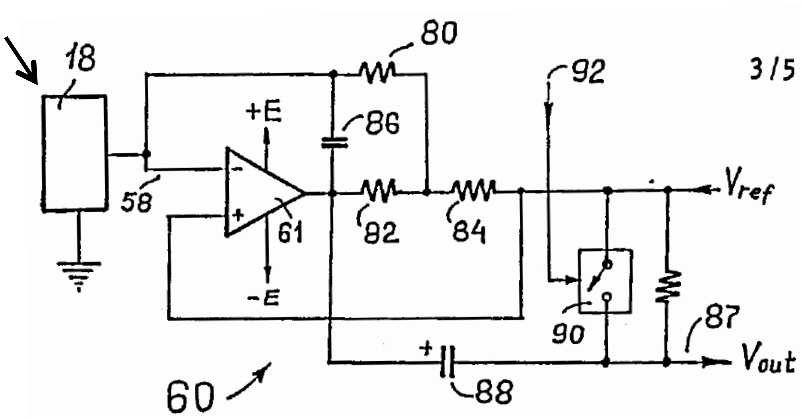


Fig. 7

Typical sensor response

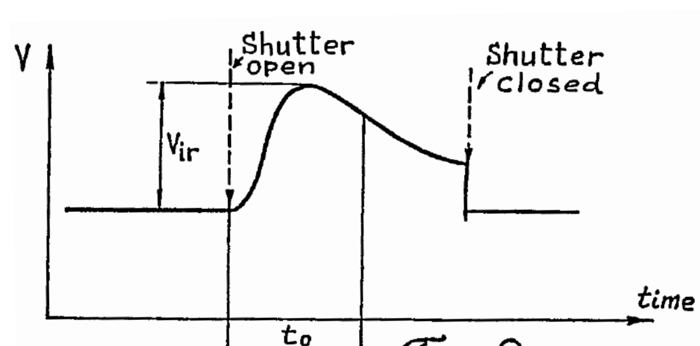


Fig. 8

Mechanical sensing

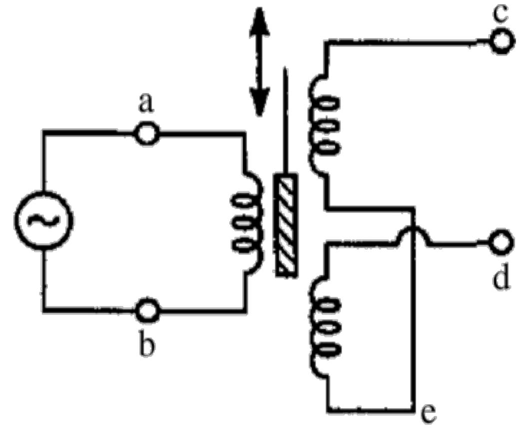
Displacement and Motion Sensing

Displacement and Motion Sensors

- Displacement and motion sensor are at the core of most mechanical sensing application.
  Example: Pressure can displace a membrane
- Displacement, velocity, acceleration and force are all interrelated ($a = \dot{v} = \ddot{x}, F = ma$).
- Wide applicability to biomechanics, rehabilitation and physiologic monitoring,…
- We will review three useful sensors:
  - Linear Variable Differential Transformer (LVDT, displacement)
  - Strain gauges
  - Accelerometers

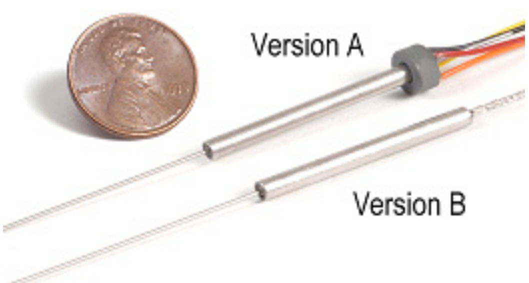
Displacement Sensor - LVDT

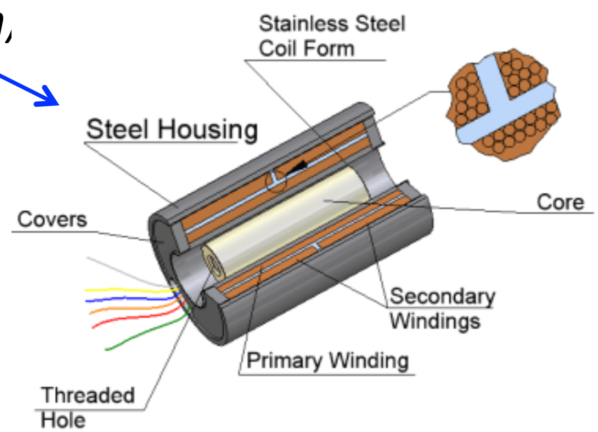
- An electromechanical sensor for displacement is the *Linear Variable Differential Transformer* (LVDT).
- A ferromagnetic core moves between two transformers, splitting the excitation signal proportionally.
- Wide range of spans (millimeter to meter) and resolutions (down to μm).

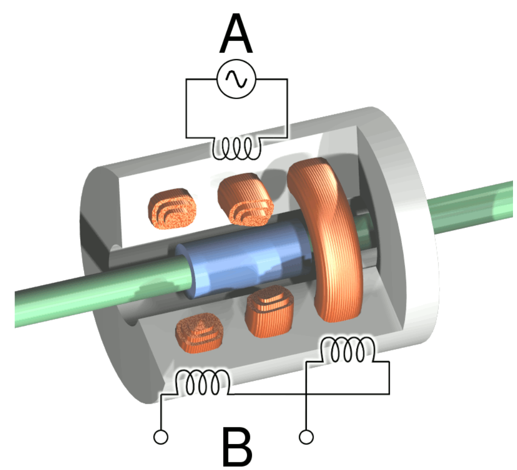


Note: even at full scale, the core still overlaps the three coils (linear range).

Miniature LVDT (∅2.3 mm,
Singer SM Series



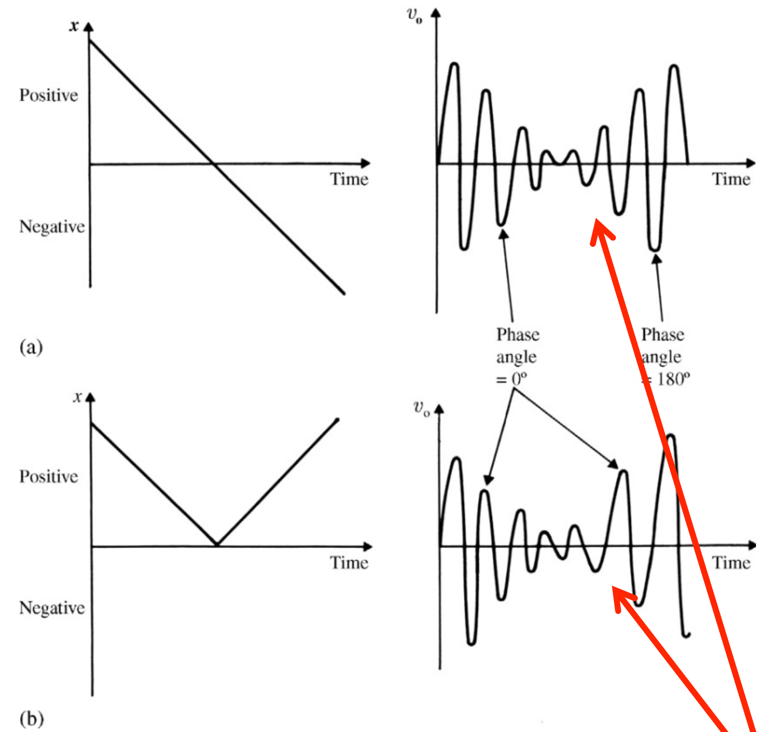




Sources: http://www.transtekinc.com , http://www.singer-instruments.com, Wikipedia

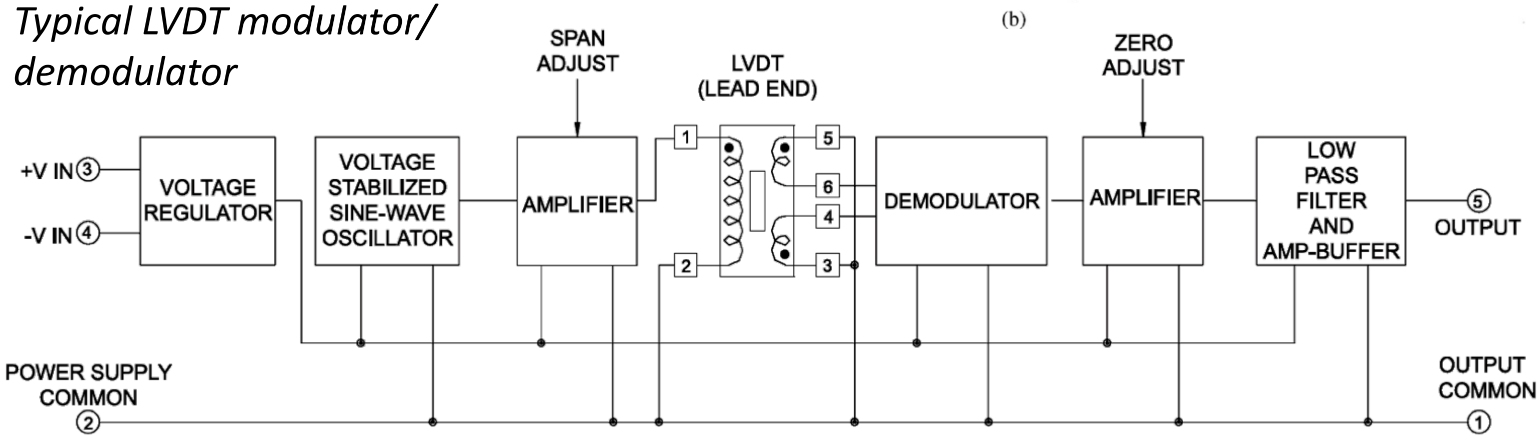
LVDT – Signal Conditioning

- LVDTs require a phase-sensitive demodulation to differentiate sides.
  Simple diode rectifiers blind to phase-inversion at neutral point.
- Typical excitations are in the 50 Hz – 20 kHz range, at levels of 1 - 24V.



A simple rectifier would give the same output

Typical LVDT modulator/ demodulator



Single-chip solution to LVDT modulation/demodulation: **ADI 598/698**

Strain Gauges

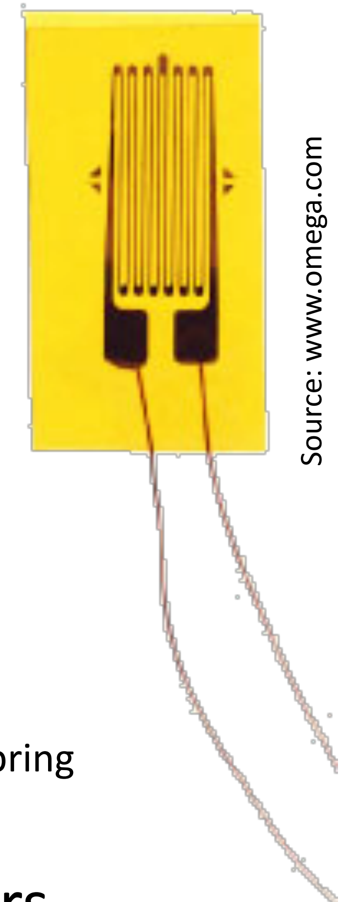
- Strain gauges are resistance sensitive to strain (relative length change).
- Defined by their *Gauge Factor* (GF):

$$GF = \frac{\text{relative resistance change}}{\text{relative length change}} = \underbrace{(1+2\mu)}_{\text{Geometrical effect}} + \underbrace{\frac{d\rho/\rho}{\varepsilon}}_{\text{Piezoresistive effect}}$$

μ : Poisson ratio
ρ : resistivity
ε: strain (dL/L)

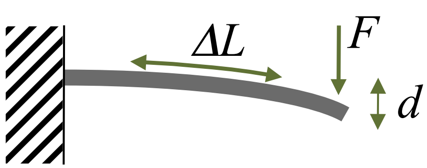
Typical gauge factors:

Metal:	~2
Semiconductor:	80-200



Source: www.omega.com

- Through deformation of a beam, they can measure force:



$$\Delta R \propto \Delta L \propto d \propto kF$$

where k is the spring constant

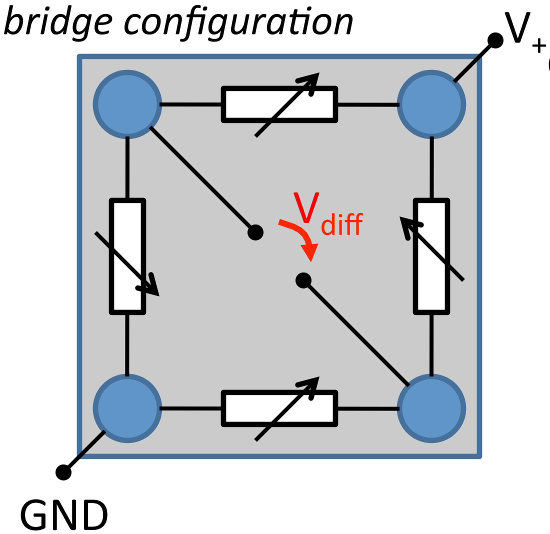
- Typical application: weighing scales, pressure sensors, biomechanical measurements (e.g., heel strike force).

Application: Scales and Force Plates

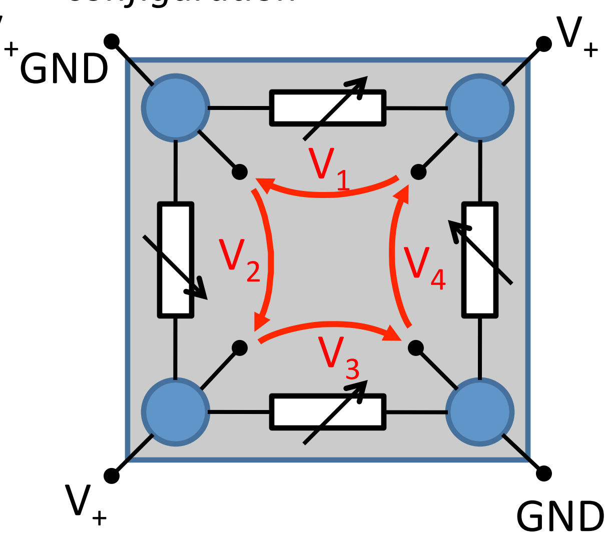
- Scales measure static body weight.
- Force plates add dynamic capabilities and measurement of center of pressure and independent component of force (F_x, F_y, F_z, M_x, M_y, M_z).
- Used in rehabilitation, gait and balance measurements.

Nintendo Wii Fit™

Weight measurement bridge configuration



Center of pressure measurement configuration

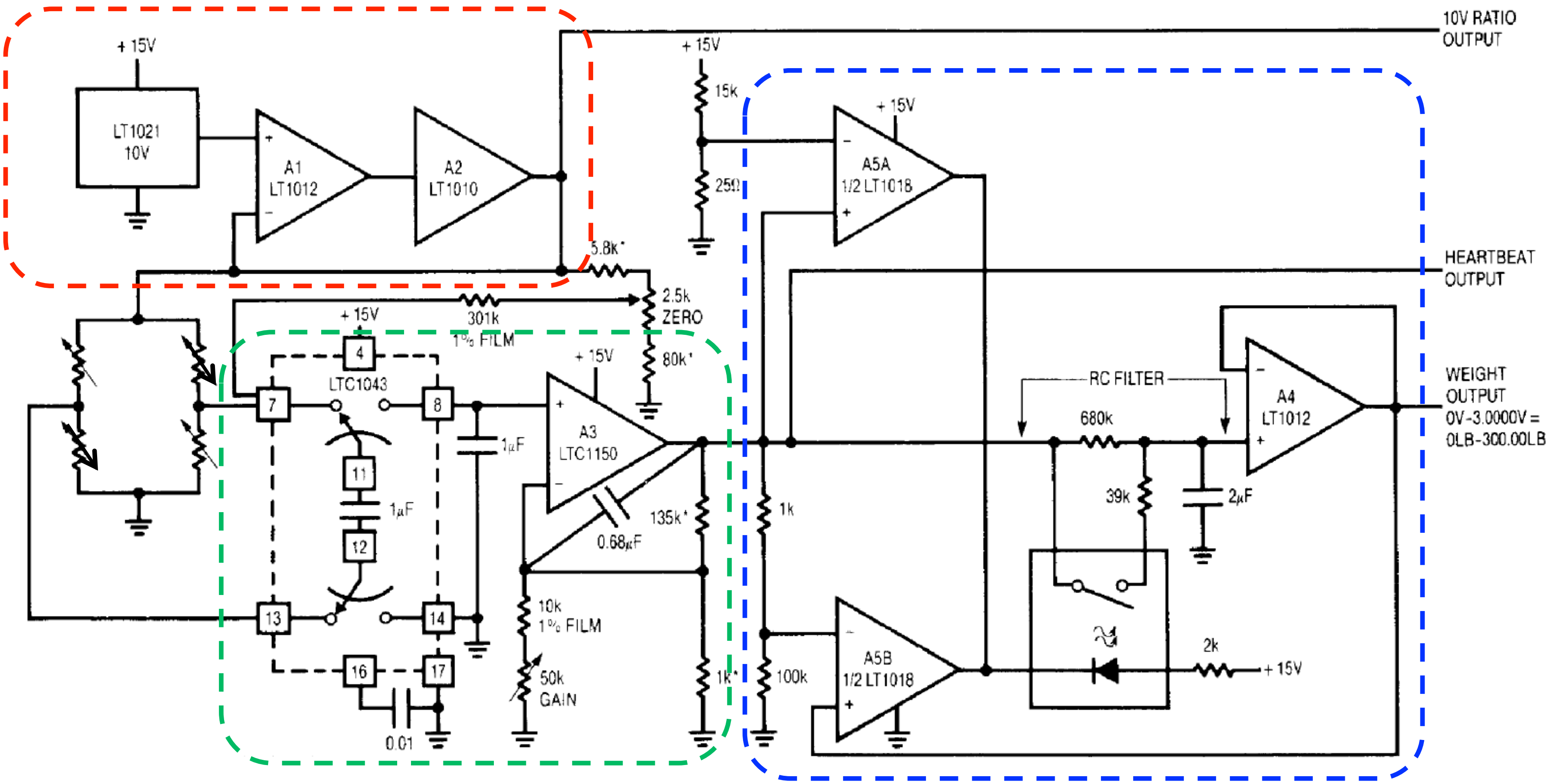


Neurocom Basic Balance Master®

Scale Signal Conditioning

Another bridge conditioning circuit…

Precision bridge excitation



High CMRR amplifier

Dual time-constant filter, automatic switching

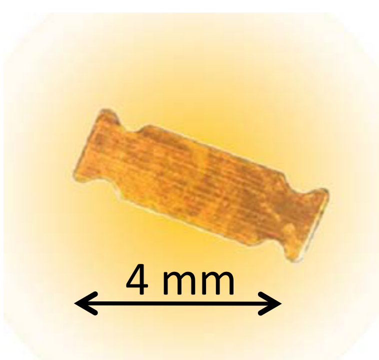
Source: Linear Tech AN-43 - Bridge Circuits

Accelerometers

- Accelerometers are based on Newton's law $F=ma$. They measure the force generated by a proof mass (or seismic mass), usually through the displacement of a mounting spring.
- Applications in activity monitoring, pacemakers, biomechanics (joint acceleration), CPR (depth and rate of compression)…
- Primary technologies for medical applications:
  - Piezoelectric
  - Capacitive
  - (Piezoresistive)
- MEMS technology enables very small devices.
  Volume under one cubic millimeter

Piezoelectric Accelerometers

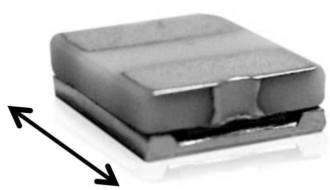
- Piezoelectric material compressed by proof mass generates charges.
- Do not require power.
  Good reason for pacemaker use…
- High output impedance, unless buffered.
  Require adequate conditioning (charge amplifier)
- No DC response (but can be close)



Piezo film used in pacemaker

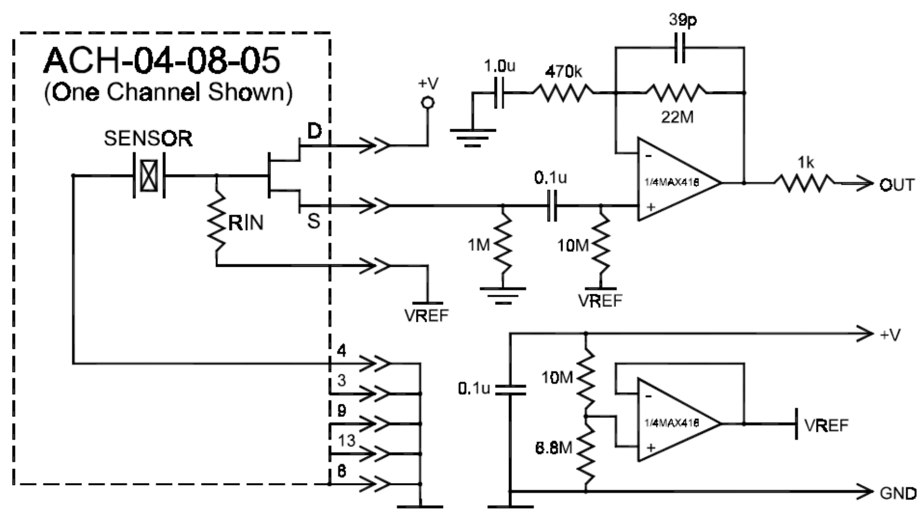
(Measurement Specialties, used without permission)

Endevco 12M1A



5 mm

Buffered Piezoelectric Accelerometer



Source: Measurement Specialties ACH-04-08-05 datasheet

Reminder: Charge Amplifiers

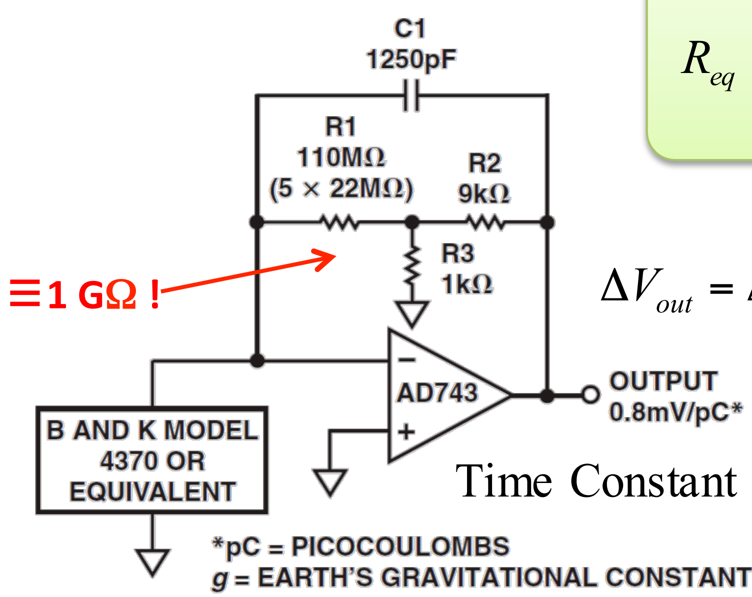
Piezoelectric accelerometers (as other charge generating sensors) require high sensitivity charge amplifiers (integrators).

Circuit requires:

- Low I_b, high Z_{in} op-amps
- Low-leakage capacitor
- Large resistors

T network:

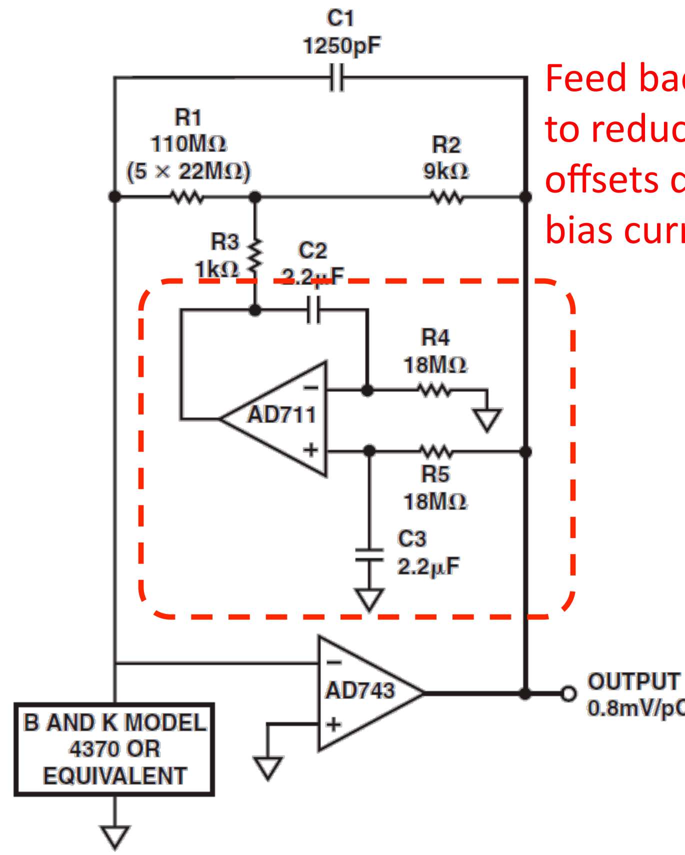
$$R_{eq} = R_1 \cdot \left(1 + \frac{R_2}{R_3}\right)$$



$$\Delta V_{out} = \Delta Q_{out} \cdot \frac{1}{C_1}$$

$$\text{Time Constant} = 2\pi \cdot R_{eq} C_1$$

Figure 14a. Basic Accelerometer Circuit



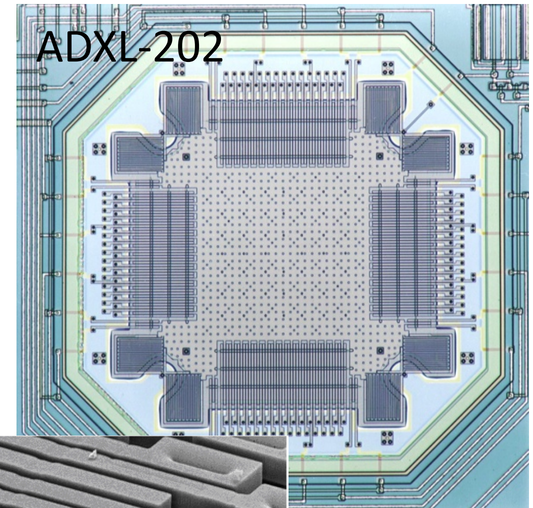
Feed back DC to reduce offsets due to bias currents

Figure 14b. Accelerometer Circuit Using a DC Servo Amplifier

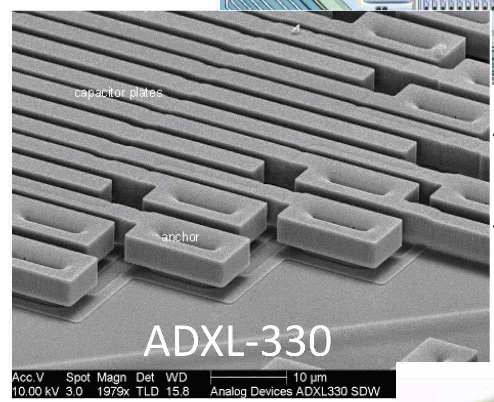
Source: Analog Device AD743 Datasheet

Capacitive Accelerometers

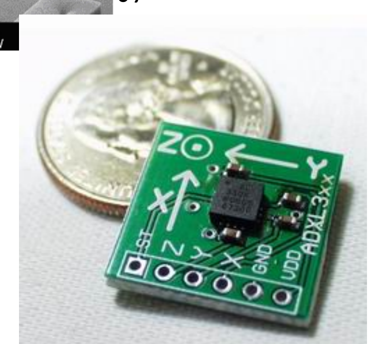
- A proof mass is the movable plate of a variable capacitor. Changes in capacitance is related to movement of the proof mass against a spring OR force to hold proof mass in place [force-feedback].
- Conditioned output
  Buffered, low-impedance, analog or digital
- Require power
  3-axis usually requires 500 μW
- DC response
  Useful for orientation determination
- Miniature 3-axis available
  Analog Devices ADXL330,
  ST Microelectronics, Freescale…



Courtesy Dr. M. Judy, Analog Devices, Inc.



Source: Chipworks,



ADXL-330
- ±3 g, 4x4x1.5 mm
- 300 mV/g
- 380 μg/Hz½ noise
- 1.6 kHz BW (x,y)
- 320 μA @ 3V

Application: CPR Quality Control

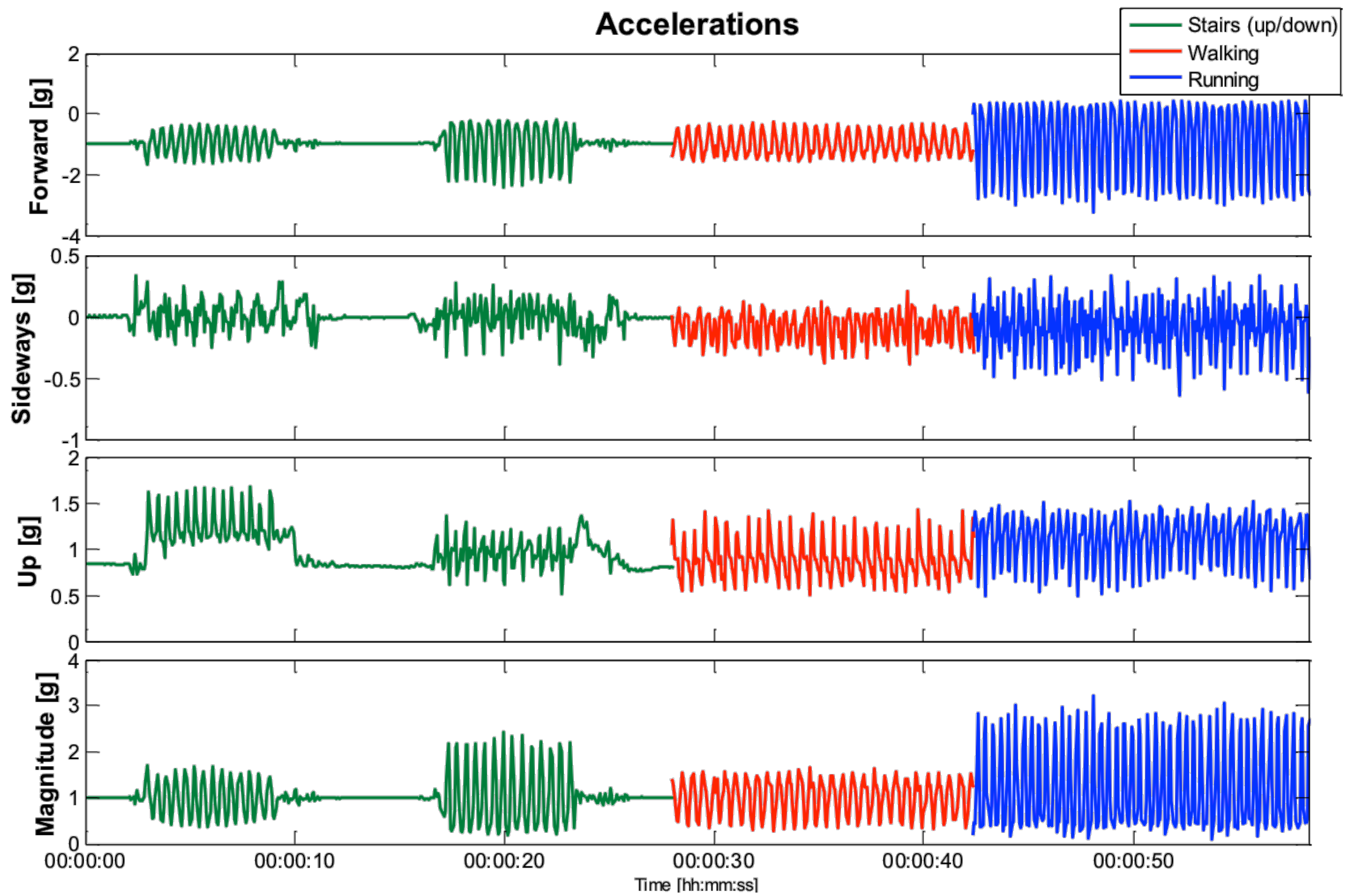
ZOLL® AED Plus Automated External Defibrillator

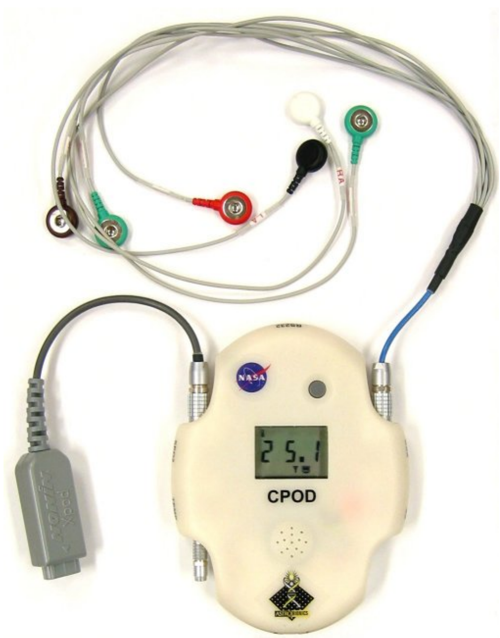
Measures compression depth (double integration of acceleration) and rate to guide CPR

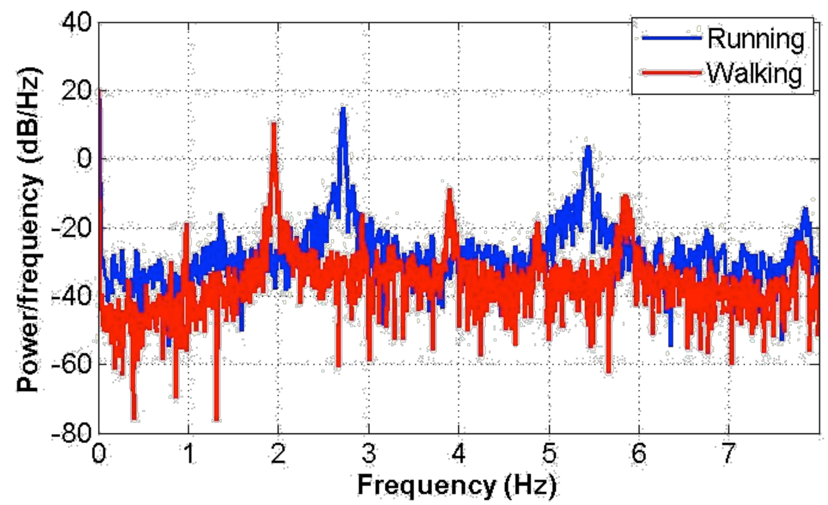
Accelerometer $\iint a\, dt \rightarrow \text{Compression depth}$

Source: www.zoll.com, product brochure & video

Application: Activity Monitoring







Technology

Chemical Sensing

Chemical Sensing

- Measurements of metabolites, blood gases, electrolytes, molecules (hormones,…) and proteins in bodily fluids.
- Historically done in centralized laboratories, but now pushed to point-of-care.
- Large field, impossible to cover all here.
- Focus on a few electrochemical examples for blood chemistry analysis, representative of current point-of-care systems.

Blood Chemistry

Table 10.1 Critical-Care Analytes and Their Normal Ranges in Blood

Blood Gases and Related Parameters		Electrolytes		Metabolites	
P_{O_2}	80–104 mm Hg	Na^+	135–155 mmol/l	Glucose	70–110 mg/100 ml
P_{CO_2}	33–48 mm Hg	K^+	3.6–5.5 mmol/l	Lactate	3–7 mg/100 ml
pH	7.31–7.45	Ca^{2+}	1.14–1.31 mmol/l	Creatinine	0.9–1.4 mg/100 ml
Hematocrit	40–54%	Cl^-	98–109 mmol/l	Urea	8–26 mg/100 ml
Total hemoglobin	13–18 g/100 ml				
O_2-saturation	95–100%				

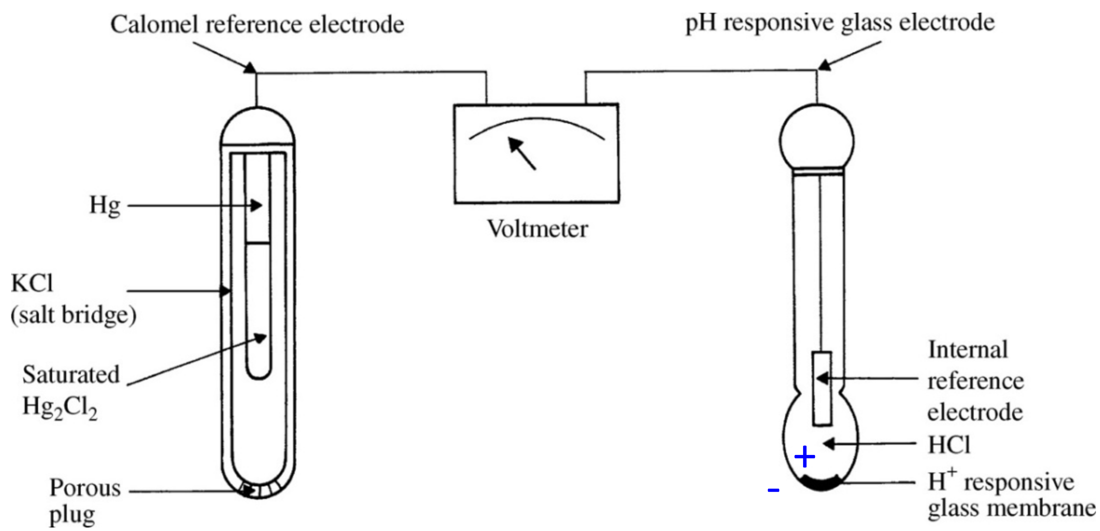
SOURCE: M. E. Collison and M. E. Meyerhoff, "Chemical sensors for bedside monitoring of critically ill patients," *Anal. Chem.*, 1990, 62, 425A–437A.

Electrochemical Sensors

- Electrochemical sensors can be categorized in two groups:
  - *Potentiometric*
    The sensor measures the potential of an electrochemical reaction (e.g., pH).
  - *Amperometric*
    The sensor measures the current generated by an electrochemical reaction at a given potential (e.g., O_2).
- As examples, we will see one of each.
- Beside electrochemical sensors, other classes of chemical sensors include conductimetric sensors, or ISFET/ChemFET sensors.

pH - Potentiometric Sensor

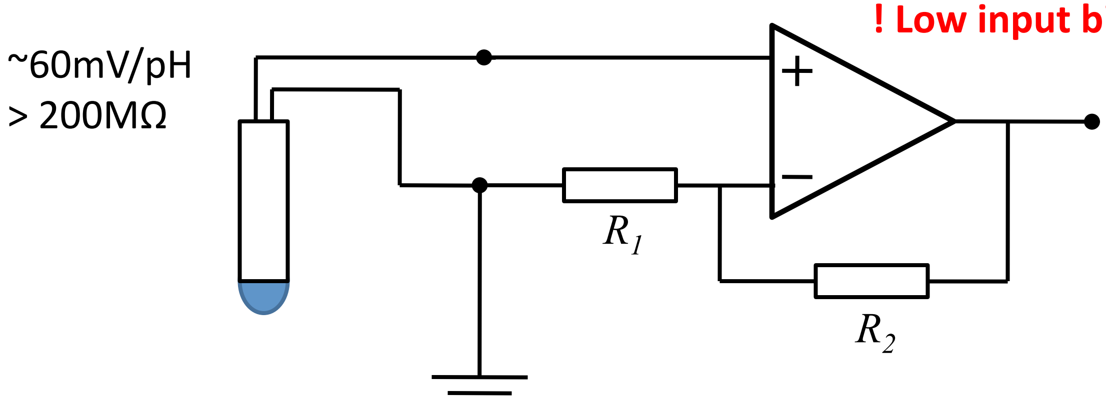
- A ion-selective membrane separates the specimen from a cavity with a fixed concentration of H^+ (pH).
- A *potential* develops across the membrane, defined by the Nernst equation.
  Recall the lecture on cell membrane potential!
- The measurement of this potential, with respect to a reference, yields the pH.



pH - Potentiometric Sensor

- The pH meter is essentially a two-electrode system.
- The reference electrode is often an Ag/AgCl electrode.
- Potentials generated are in the millivolt range.
  ~60mV/pH unit
- Output impedance of the pH electrode is very high (ion-sensitive membrane highly resistive).
- Signal conditioning straightforward.

! High input impedance (>GΩ)
! Low input bias current (pA or less)



O_2 – Amperometric Sensor

Dissolved oxygen concentration can be sensed by plateau current proportional to rate of reduction at a noble metal cathode (*Clark polarographic method*):

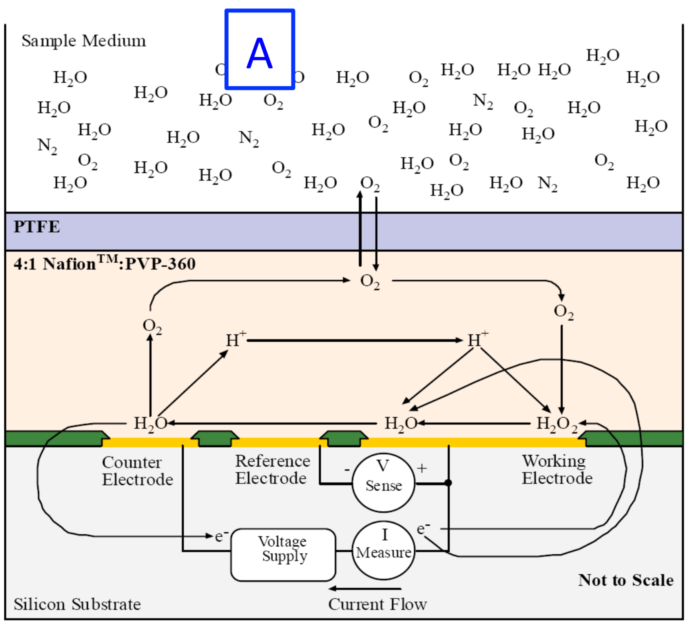
Cathode (reduction of O_2) : $O_2 + 4\ e^- + 2\ H_2O \rightarrow 4\ OH^-$ **A**

Anode (oxidation of Ag): $4\ Ag + 4\ Cl^- \rightarrow 4\ AgCl + 4\ e^-$

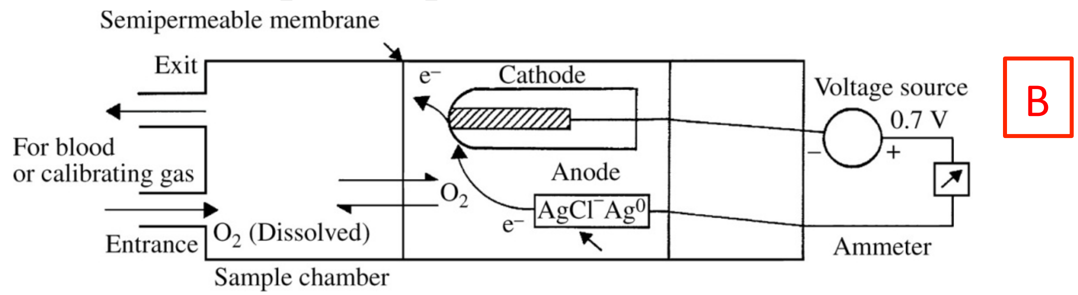
Or

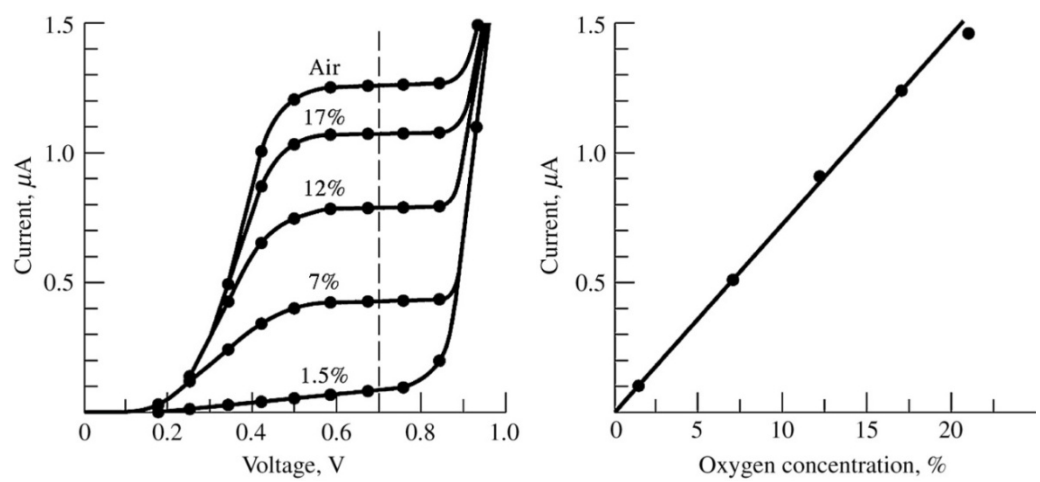
Cathode (reduction of O_2) : $O_2 + 4\ H^+ + 4\ e^- \rightarrow 2\ H_2O$ **B**

Anode (oxidation of H_2O): $2\ H_2O \rightarrow O_2 + 4\ H^+ + 4\ e^-$



Source: G. McLaughlin, PhD thesis, Stanford University.

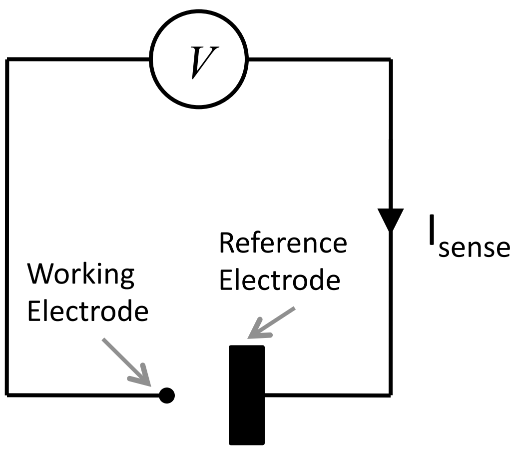




O_2 Sensing - Potentiostat

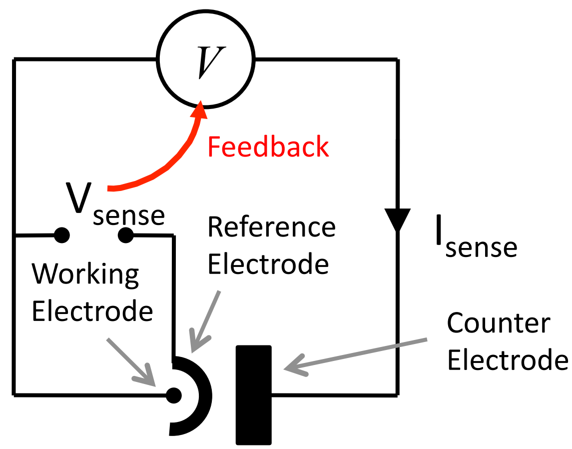
- A potentiostat is typically used to hold the cathode at a fixed voltage with respect to a reference (such as Ag/AgCl electrode), and measure the resulting current.
- Reference electrode must keep a stable potential, which is not trivial if current is passing (redox events).
- Solution: Decouple voltage sensing (reference) from current passing (counter). This is similar to a Kelvin connection.

Two-electrode configuration



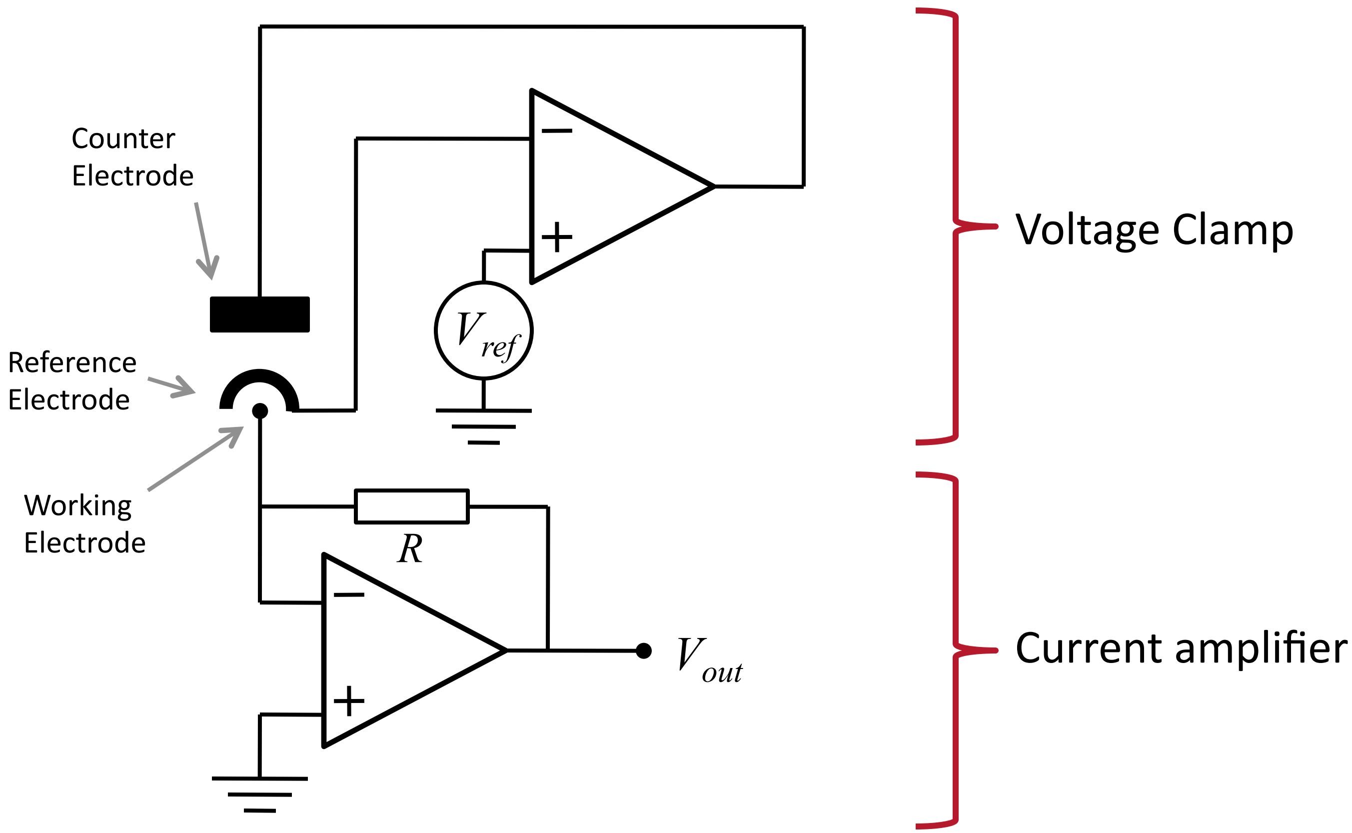
Suitable with stable reference/counter electrode (e.g., Ag/AgCl, Calomel)

Three-electrode configuration



Better with pseudo references (e.g., Au, Pt)

Basic Three-Electrode Potentiostat



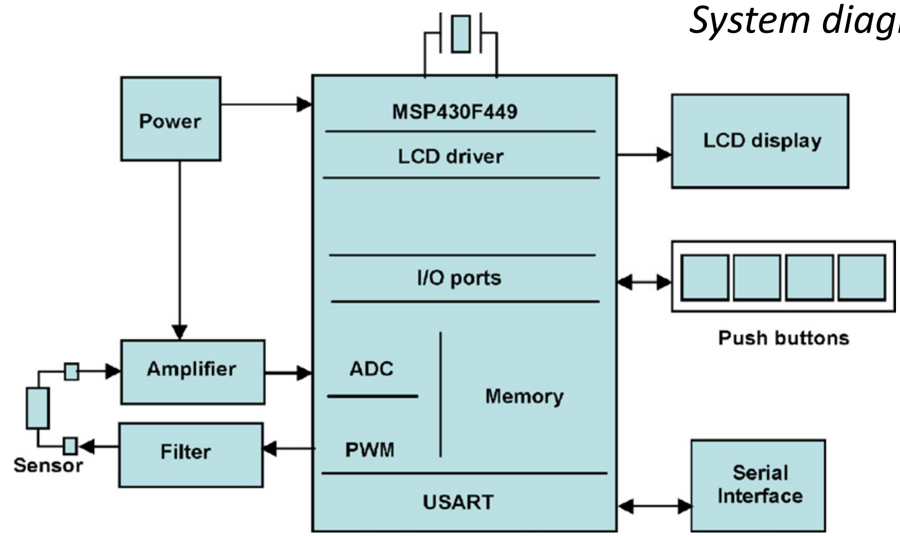
Both operational amplifiers should be electrometer-grade (input impedance > GΩ, bias current < fA)

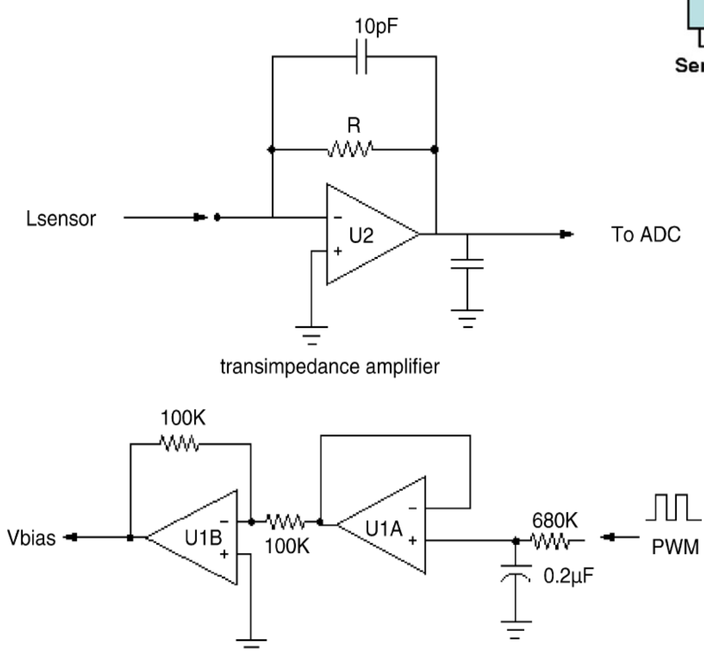
Low-Power Electrochemical Unit

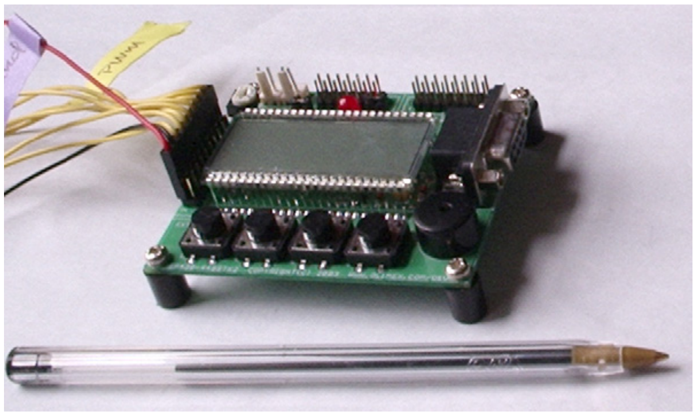
Low power, two-electrode potentiostat:

- Microcontroller-driven
- PWM-controlled reference voltage

System diagram







Source: *An embedded system for portable electrochemical detection*, Kwakye & Baeumner, Sensors Actuators B, 2007

Diabetes and Glucose Sensing

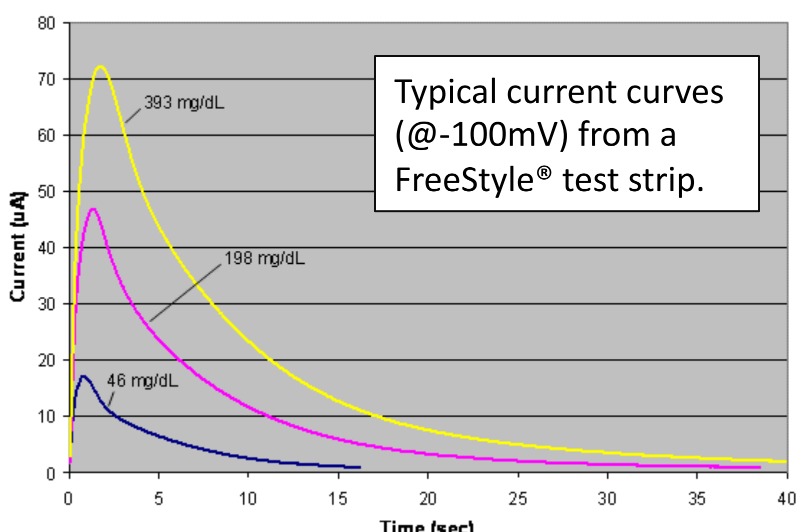
- Diabetes is a condition where the body cannot process glucose into energy, due to lack of insulin production (Type I), or inadequate response to insulin (Type II, most common).
- ~8% of US population (25 million) has diabetes!
- Diabetes management requires frequent (~ four times a day) blood glucose level measurements to direct insulin intake/diet.
- 25 million x 4 x 365 = **36.5 billion tests** per year!
- Cost of diabetes management (per person): $1000-2000/year.
- Glucose sensing performed with handheld blood glucose sensors, using either optical or electrochemical (growing majority) sensing.

Electrochemical Glucose Sensors

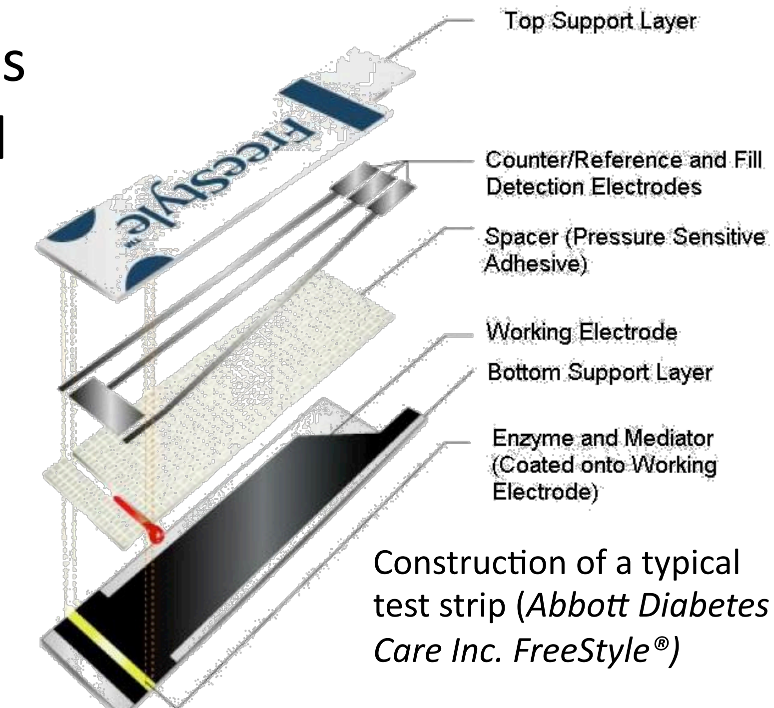
Principle:

- Oxidation of glucose by an ***enzyme*** (e.g., glucose oxidase) generates either directly a measurable *current*, or another species (O_2, H_2O_2) measurable by a conventional sensor.
- Most commonly, the measurement is *amperometric* – current is measured for an applied potential:

Example: OneTouch® blood glucose sensor from LifeScan.



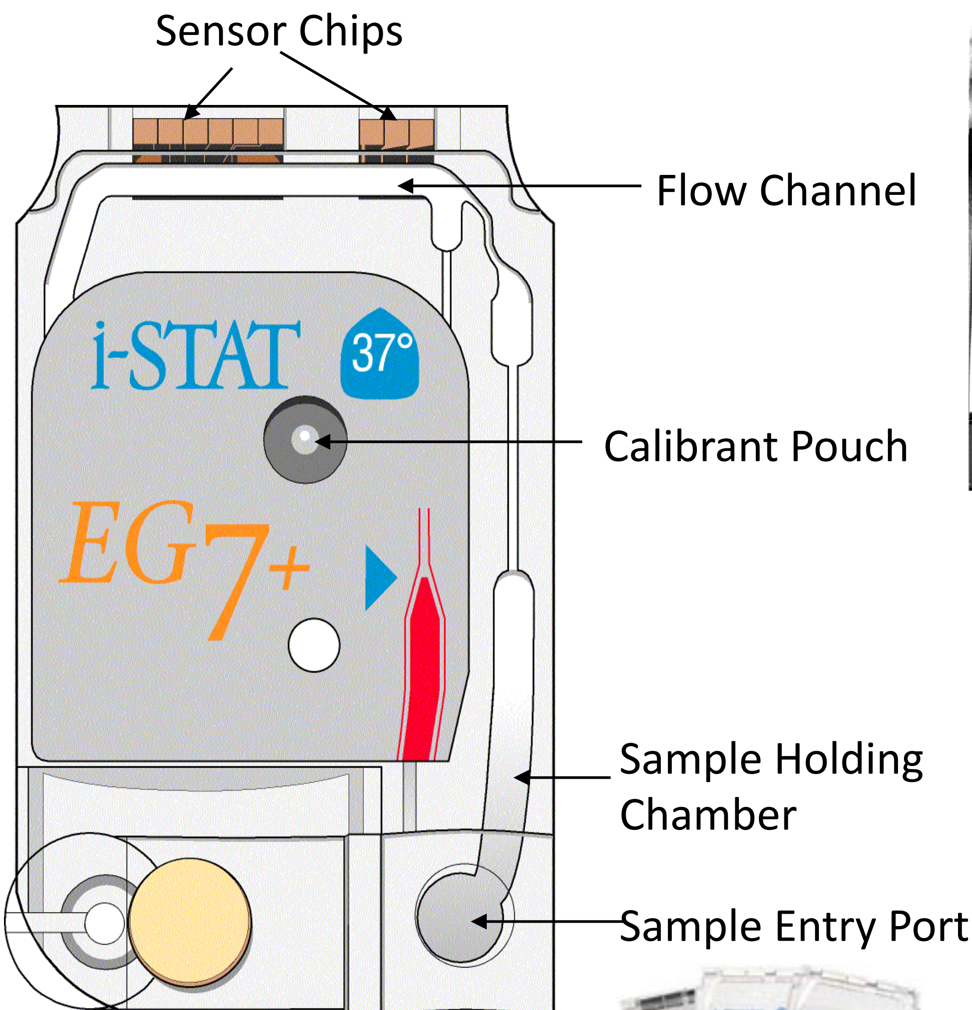
Typical current curves (@-100mV) from a FreeStyle® test strip.

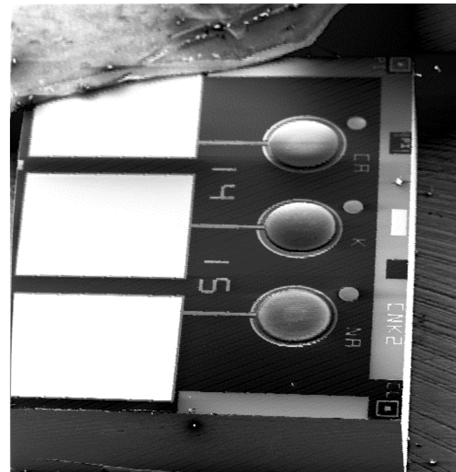


Construction of a typical test strip (*Abbott Diabetes Care Inc. FreeStyle®)*

Source: Feldman, *Electrochemistry Encyclopedia*, 2009 (http://electrochem.cwru.edu/encycl/)

Blood Analyzer Example – *i-STAT®*





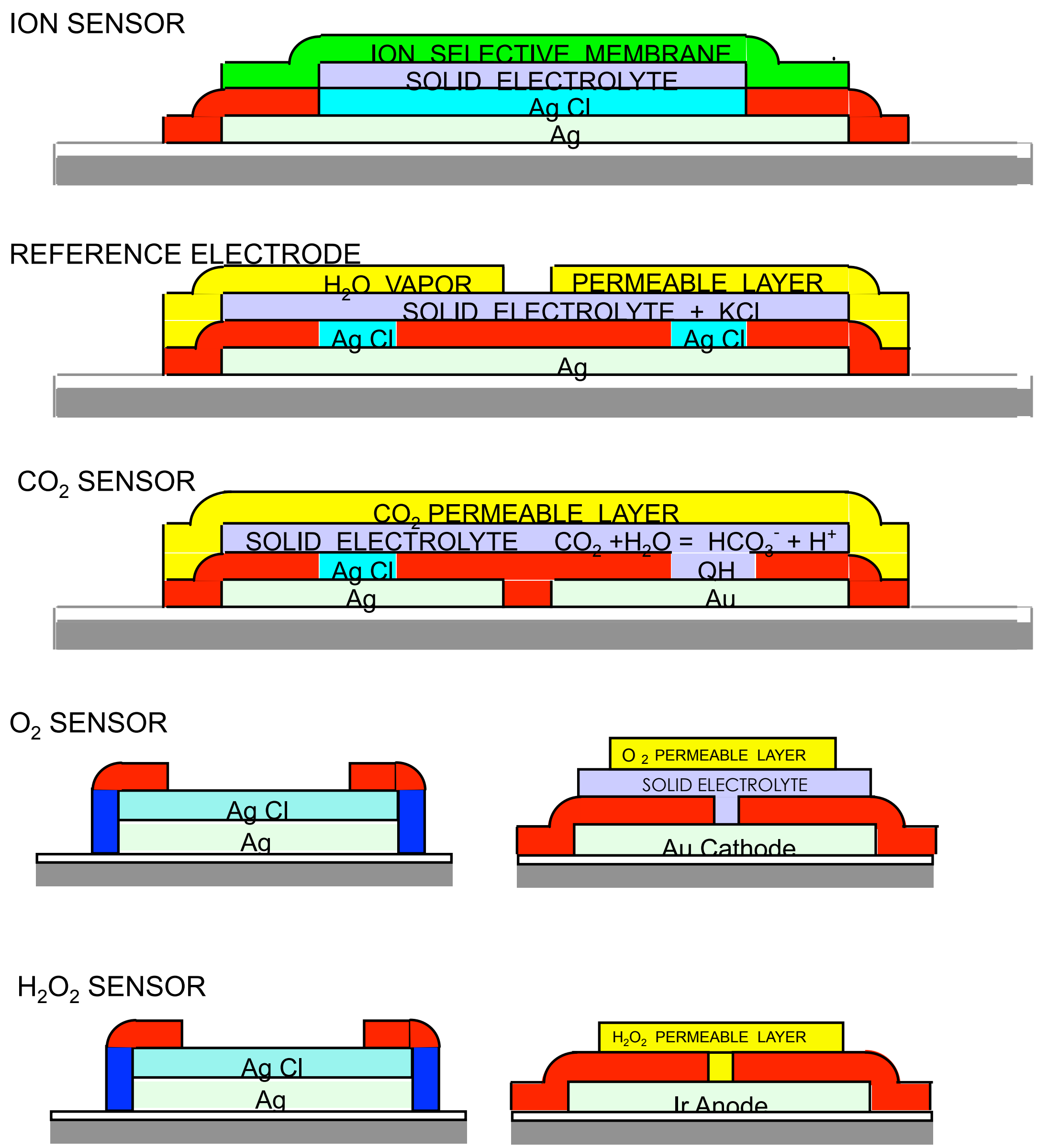
Courtesy Dr. Anca Varlan, I-Stat. Slide from EE312

Blood Analyzer Example – *i-STAT®*

Sensor structure and chemistry for basic blood chemistry.

Based on similar principles, sensing has been extended to many other relevant blood analytes :

- Glucose
- Creatinine
- Cardiac markers (troponin, BNP, CK-MB)
- Urea nitrogen
- …



Courtesy Dr. Anca Varlan, I-Stat. Slide from EE312

Lab this week

Project Time !!!