Medical Instrumentation

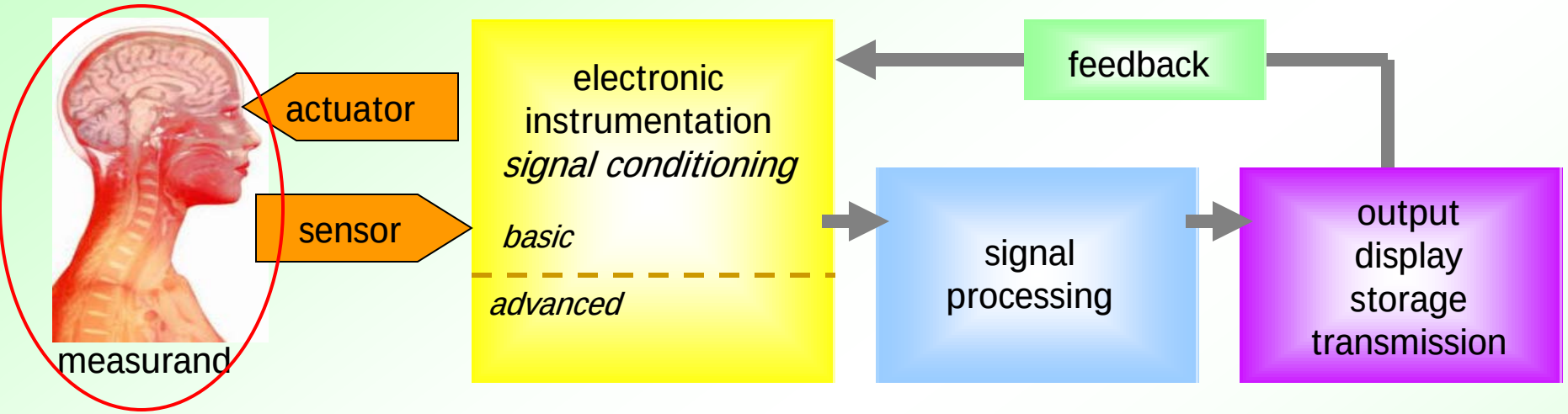
- Design of instrument must match
  - Measurement needs (environmental conditions, safety, reliability, etc)
  - Instrument performance (speed, power, resolution, range, etc)

- A medical device is
  - "any item promoted for a medical purpose that does not rely on chemical action to achieve its intended effect"
    - [Medical Device Amendments (Public law 94-295)]
  - i.e., any electrical or mechanical device for medical applications
    - this class will focus on electrical (including electromechanical and electrochemical)

- Difference from any conventional instrument
  - source of signals is living tissue
  - energy is applied to the living tissue

- Impact on biomedical instrumentation (BI) design requirements?
  - *Reliability* and *Safety*

Generalized Medical Instrumentation System

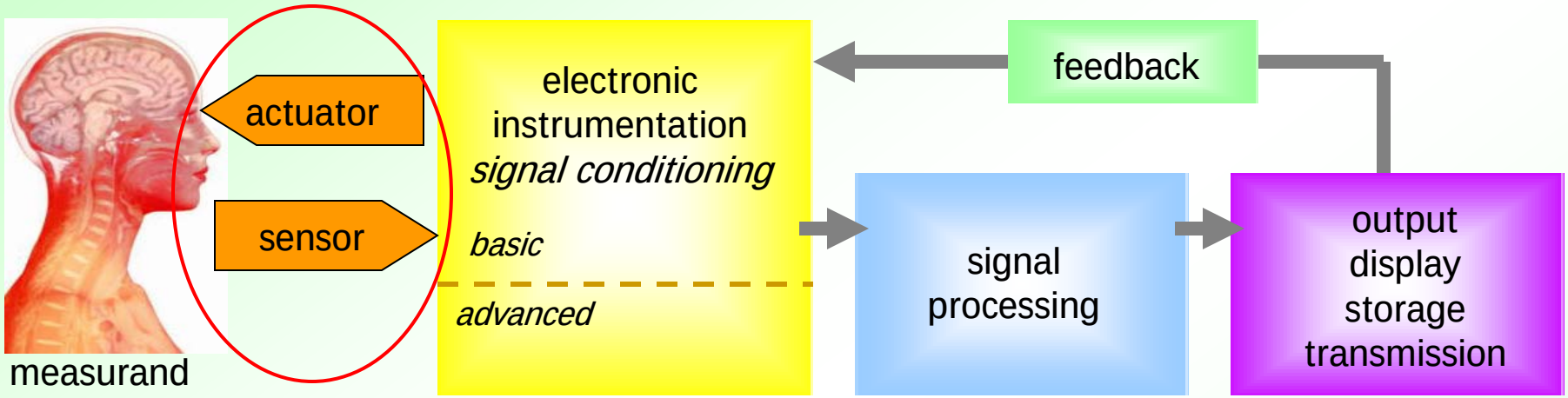


- **Measurand**: Physical quantity, property or condition that the system measures
- Types of biomedical measurands
  - Internal – Blood pressure
  - Body surface – ECG or EEG potentials
  - Peripheral – Infrared radiation
  - Offline – Extract tissue sample, blood analysis, or biopsy
- Typical biomedical measurand quantities
  - Biopotential, pressure, flow, dimensions (imaging), displacement (velocity, acceleration and force), impedance, temperature and chemical concentration

Medical and Physiological Parameters

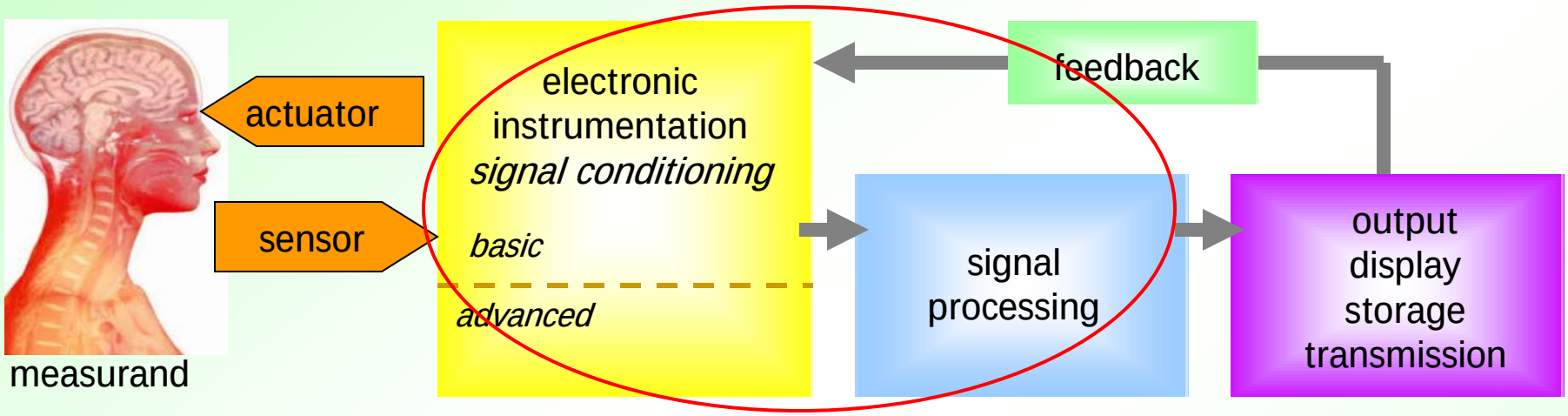
Parameter	Range	Frequency	Sensor
Blood flow	1-300 ml/s	dc – 20 Hz	Flowmeter (ultrasonic)
Arterial blood pressure	25-400mm Hg	dc – 50 Hz	Cuff, strain-gage
ECG	0.5 – 4 mV	0.01 – 250 Hz	Skin electrodes
EEG	5 – 300 microV	dc – 150 Hz	Scalp electrodes
EMG	0.1 – 5 mV	dc – 10,000 Hz	Needle electrodes
Respiratory rate	2 – 50 breaths/min	0.1 – 10 Hz	Strain-gage, nasal thermistor

Sensor



- A **sensor** converts physical measurand to an electrical output
- Sensor requirements
  - Selective – should respond to a specific form of energy in the measurand
  - Minimally invasive (invasive = requiring entry into a part of the body)
    - sensor should not affect the response of the living tissue
- Most common types of sensors in biomedical systems
  - displacement
  - pressure

Signal Conditioning



- **Signal Conditioning**: Amplification and filtering of the signal acquired from the sensor to make it suitable for display
- General categories
  - Analog, digital or mixed-signal signal conditioning
  - Time/frequency/spatial domain processing (e.g., filtering)
  - Calibration (adjustment of output to match parameter measured)
  - Compensation (remove of undesirable secondary sensitivities)

Units of Measurement

- Fundamental SI units
  - SI = Systemes Internationales d'Unites

Quantity	*Standard unit*	*Symbol*
Length	metre	m
Mass	kilogram	kg
Time	second	s
Electric current	ampere	A
Temperature	kelvin	K
Luminous intensity	candela	cd
Matter	mole	mol

- Derived SI units

Quantity	*Standard unit*	*Symbol*	*Derivation formula*
Area	square metre	m^2	
Volume	cubic metre	m^3	
Velocity	metre per second	m/s	
Acceleration	metre per second squared	m/s^2	
Angular velocity	radian per second	rad/s	
Angular acceleration	radian per second squared	rad/s^2	
Density	kilogram per cubic metre	kg/m^3	
Specific volume	cubic metre per kilogram	m^3/kg	
Mass flow rate	kilogram per second	kg/s	
Volume flow rate	cubic metre per second	m^3/s	
Force	newton	N	$kg\ m/s^2$
Pressure	newton per square metre	N/m^2	
Torque	newton metre	N m	
Momentum	kilogram metre per second	kg m/s	
Moment of inertia	kilogram metre squared	$kg\ m^2$	
Kinematic viscosity	square metre per second	m^2/s	
Dynamic viscosity	newton second per square metre	$N\ s/m^2$	
Work, energy, heat	joule	J	Nm
Specific energy	joule per cubic metre	J/m^3	
Power	watt	W	J/s
Thermal conductivity	watt per metre kelvin	W/m K	

Quantity	*Standard unit*	*Symbol*	*Derivation formula*
Electric charge	coulomb	C	A s
Voltage, e.m.f., pot. diff.	volt	V	W/A
Electric field strength	volt per metre	V/m	
Electric resistance	ohm	Ω	V/A
Electric capacitance	farad	F	A s/V
Electric inductance	henry	H	V s/A
Electric conductance	siemen	S	A/V
Resistivity	ohm metre	Ωm	
Permittivity	farad per metre	F/m	
Permeability	henry per metre	H/m	
Current density	ampere per square metre	A/m^2	
Magnetic flux	weber	Wb	V s
Magnetic flux density	tesla	T	Wb/m^2
Magnetic field strength	ampere per metre	A/m	
Frequency	hertz	Hz	s^{-1}
Luminous flux	lumen	lm	cd sr
Luminance	candela per square metre	cd/m^2	
Illumination	lux	lx	lm/m^2
Molar volume	cubic metre per mole	m^3/mol	
Molarity	mole per kilogram	mol/kg	
Molar energy	joule per mole	J/mol	

source: A. Morris, Principles of Instrumentation and Measurement, 3rd Ed., Butterworth-Heinemann, 2001.

Units of Measurement

- Unit Definitions

Physical quantity	*Standard unit*	*Definition*
Length	metre	The length of path travelled by light in an interval of 1/299 792 458 seconds
Mass	kilogram	The mass of a platinum–iridium cylinder kept in the International Bureau of Weights and Measures, Sèvres, Paris
Time	second	$9.192631770 \times 10^{9}$ cycles of radiation from vaporized caesium-133 (an accuracy of 1 in 10^{12} or 1 second in 36 000 years)
Temperature	kelvin	The temperature difference between absolute zero and the triple point of water is defined as 273.16 kelvin
Current	ampere	One ampere is the current flowing through two infinitely long parallel conductors of negligible cross-section placed 1 metre apart in a vacuum and producing a force of 2×10^{-7} newtons per metre length of conductor
Luminous intensity	candela	One candela is the luminous intensity in a given direction from a source emitting monochromatic radiation at a frequency of 540 terahertz ($\text{Hz} \times 10^{12}$) and with a radiant density in that direction of 1.4641 mW/steradian. (1 steradian is the solid angle which, having its vertex at the centre of a sphere, cuts off an area of the sphere surface equal to that of a square with sides of length equal to the sphere radius)
Matter	mole	The number of atoms in a 0.012 kg mass of carbon-12

source: A. Morris, Principles of Instrumentation and Measurement, 3rd Ed., Butterworth-Heinemann, 2001.

BI = biomedical instrumentation

BI Operational Modes

- Direct vs. Indirect
  - Direct mode: measure desired measurand directly
    - if the sensor is invasive, direct contact with the measurand is possible but expensive, risky and least acceptable
  - Indirect mode: measure a quantity that is accessible and related to the desired measurand
    - assumption: the relationship between the measurands is already known
    - often chosen when the measurand requires invasive procedures to measure directly

- Example *indirect mode*
  - Cardiac output (volume of blood pumped per minute by the heart)
    - can be determined from measurement of respiration, blood gas concentration & dye dilution
  - Organ morphology
    - can be determined from x-ray shadows

BI Operational Modes

- Sampling vs. Continuous mode
  - Sampling: for slow varying measurands that are sensed infrequently
    - like body temperature & ion concentrations
  - Continuous: for critical measurements requiring constant monitoring
    - like electro-cardiogram and respiratory gas flow

- Generating vs. Modulating
  - Generating: also known as self-powered mode
    - derive their operational energy from the measurand itself
    - Example: piezoelectric sensors, solar cells
  - Modulating: measurand modulates the electrical signal which is supplied externally
    - modulation affects output of the sensor
    - Example: photoconductive or piezoresistive sensor

BI Operational Modes

- Analog vs. digital modes
  - most sensors are inherently analog
    - (some optical sensors are exceptions)
  - require analog-to-digital converters before any DSP techniques could be applied for filtering

- Real-time vs. Delayed-time mode
  - Real-time
    - Example: ECG signals need to measured in real-time to determine an impending cardiac arrest
  - Delayed-time
    - Example: cell cultures which requires several days before any output is acquired

Measurement Constraints

- The signal to be measured imposes constraints on how it should be acquired and processed

- Signal/frequency ranges
  - Most medical measurands parameters are typically much lower than conventional sensing parameters (microvolts, mm Hg, low frequency)

- Interference and cross-talk
  - Noise from environment, instruments, etc.
  - Other measurands affect measurement (and can't be isolated)
    - e.g., Cannot measure EEG without interference from EMG
  - Require filtering and/or compensation

- *Placement* of sensor(s) in/on/near the body plays a key role in any bio-instrumentation design

Measurement Constraints

- Measurement variability is inherent at molecular, organ and body level
  - Primary cause
    - interaction between different physiological systems
    - existence of numerous feedback loops whose properties are poorly understood
- Therefore evaluation of biomedical devices rely on probabilistic/statistical methods (biostatistics)

- SAFETY
  - Due to interaction of sensor with living tissue, safety is a primary consideration in all phases of the design & testing process
    - the damage caused could be irreversible
  - In many cases, safe levels of energy is difficult to establish
  - Safety of medical personnel also must be considered

- Operator constraints
  - Reliable, easy to operate, rugged and durable

Classification of biomedical instruments

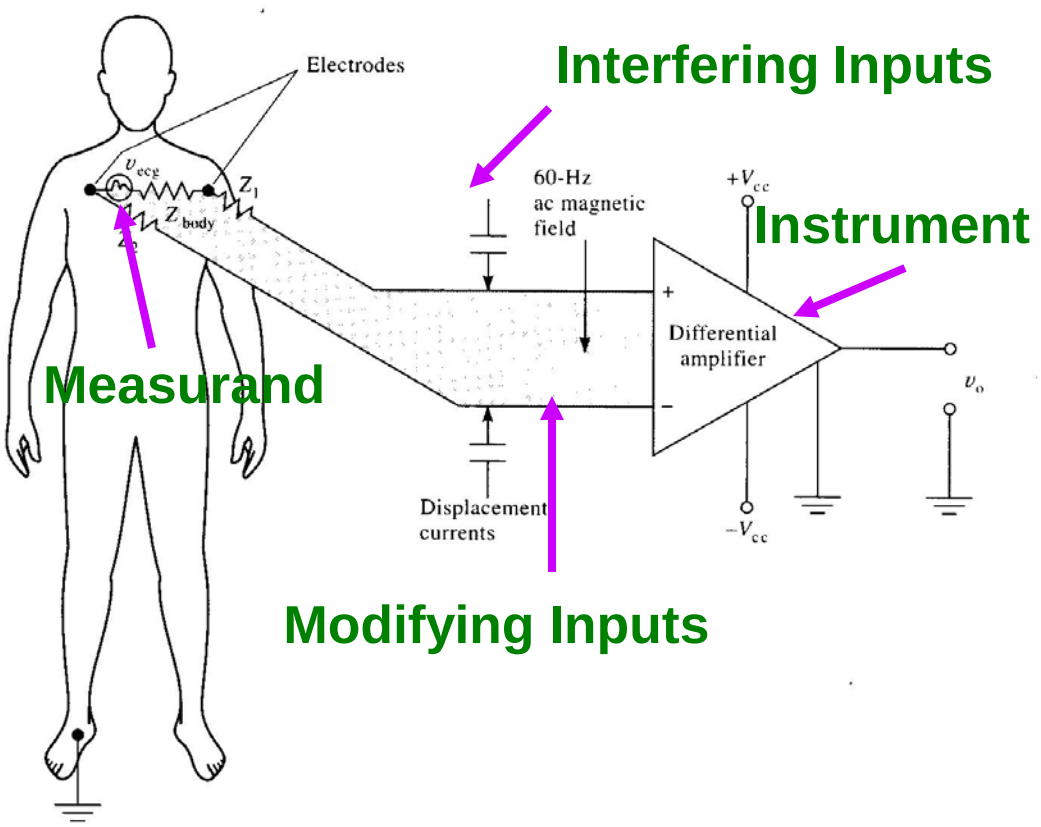
- Quantity being sensed
  - pressure, flow or temperature
  - makes comparison of different technologies easy
- Principle of transduction
  - resistive, inductive, capacitive, ultrasonic or electrochemical
  - makes development of new applications easy
- Organ systems
  - cardiovascular, pulmonary, nervous, endocrine
  - isolates all important measurements for specialists who need to know about a specific area
- Clinical specialties
  - pediatrics, obstetrics, cardiology or radiology
  - easy for medical personnel interested in specialized equipment.

Measurement Input Sources

- Desired inputs
  - measurands that the instrument is designed to isolate
- Interfering inputs
  - quantities that inadvertently affect the instrument as a consequence of the principles used to acquire and process the desired inputs
- Modifying inputs
  - undesired quantities that indirectly affect the output by altering the performance of the instrument itself

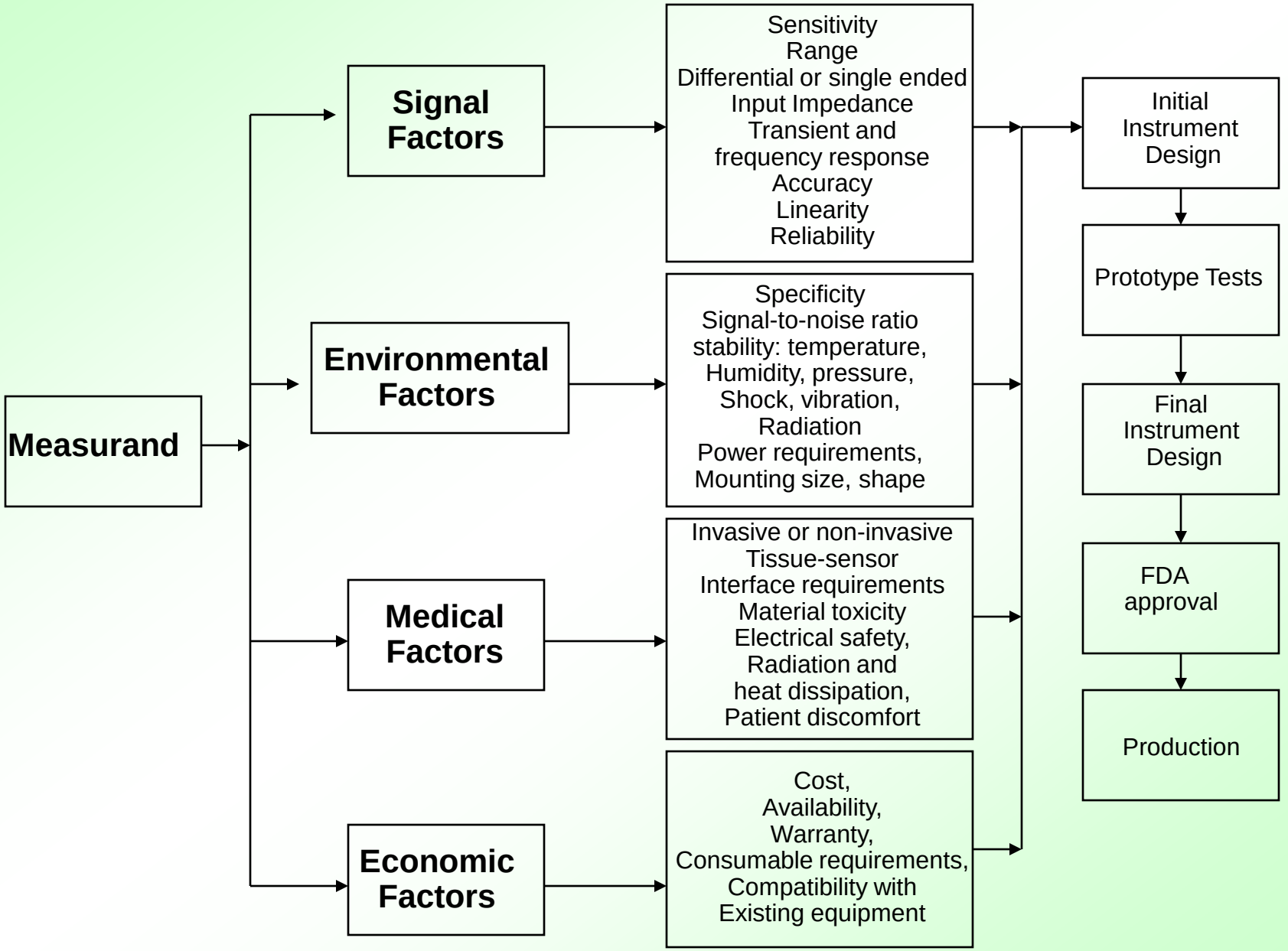
ECG example

- Desired input – ECG voltage
- Interfering input – 60 Hz noise voltage, displacement currents
- Modifying input – orientation of the patient cables
  - when the plane of the cable is perpendicular to the magnetic field the magnetic interference is maximal



- Interfering inputs generally not correlated to measurand
  - often easy to remove/cancel
- Modifying inputs may be correlated to the measurand
  - more difficult to remove

Design Criteria and Process



Regulation of Medical Devices <OPTIONAL>

Regulatory division of medical devices: class I, II and III
- more regulation for devices that pose greater risk

- Class I (General controls)
  - Manufacturers are required to perform registration, premarketing notification, record keeping, labeling, reporting of adverse experiences and good manufacturing practices

- Class II (Performance standards)
  - 800 standards needed to be met

- Class III (Premarketing approval)
  - Manufacturers have to prove the safety of these devices prior to market release

- Implanted devices (pacemakers etc.) are typically designated class III
- Investigational devices are typically exempt

Compensation Techniques

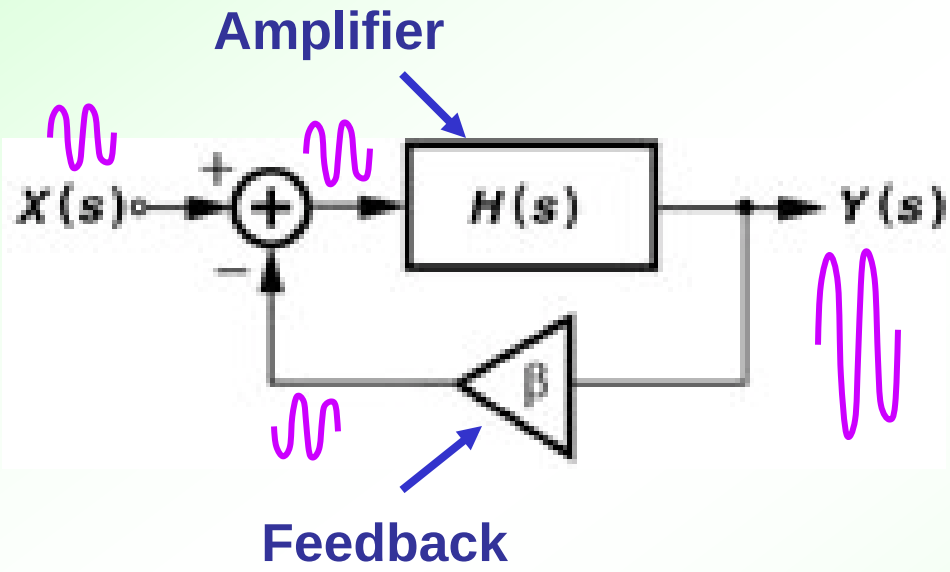
Compensation: elimination or reduction of *interfering* and *modifying* inputs

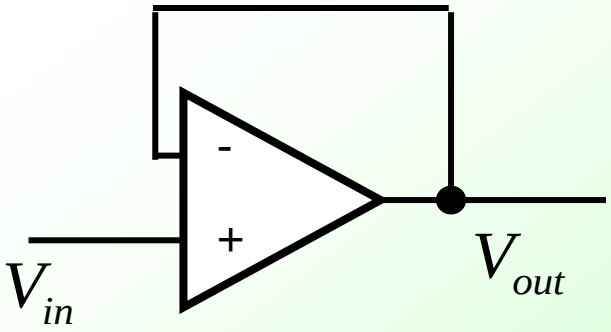
- Techniques
  - Altering the design of essential instrument components
    - simple to implement
  - Adding new components to offset the undesired inputs

- Methods
  - Reduce sensitivity to interfering and modifying inputs
    - Example: use twisted cables and reduce number of electrical loops
  - Signal Filtering
    - temporal, frequency and spatial separation of signal from noise

Compensation: Negative Feedback

- When modifying input cannot be avoided, negative feedback is used to make the output less dependent on the transfer function of the device

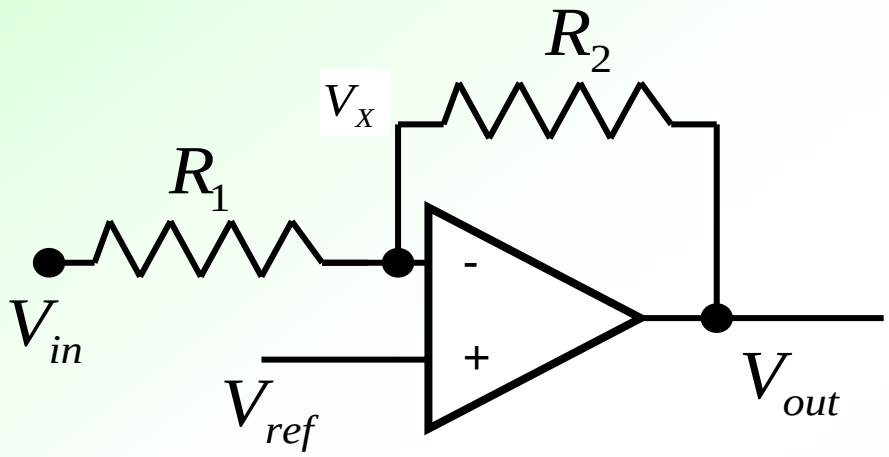




- Feedback devices must be accurate and linear

Feedback

- Open loop amplifiers are seldom used for precise amplification
- Using feedback generates precision amplifiers



$$\frac{V_{in}-V_X}{R_1}=\frac{V_X-V_{out}}{R_2}$$

$$V_{out}=A(V_{ref}-V_X)$$

$$\Delta V_{out}=\frac{-\frac{R_2}{R_1}\Delta V_{in}}{[1+\frac{1}{A}(1+\frac{R_2}{R_1})]}$$

For a large open-loop gain

$$A >> (1+\frac{R_2}{R_1})$$

$$\Delta V_{out}=-\frac{R_2}{R_1}\Delta V_{in}$$

closed-loop gain

Feedback II

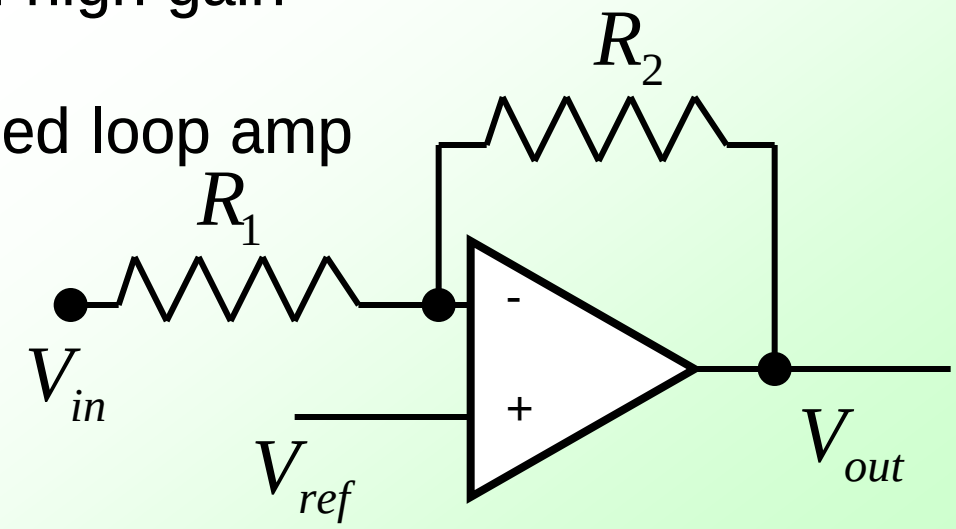
- Large open loop gain criterion
  - easy to satisfy

$$A >> (1 + \frac{R_2}{R_1})$$

- Irrespective of the open loop gain A, closed loop gain can be set to almost any value
  - e.g., 100, 200 or 1000

$$\Delta V_{out} = -\frac{R_2}{R_1} \Delta V_{in}$$

- Easy to design amplifiers with high gain
  - precision not required
- Linearity and precision of closed loop amp
  - determined by ratio of resistors



Other Compensation Techniques

Opposing inputs or noise cancellation

- When *interfering* and *modifying* inputs cannot be filtered
  - additional inputs can be used to cancel undesired output components
  - similar to differential signal representation

Next Lecture Topics

- Biostatistics
  - statistics terms and definitions
  - biomedical studies
- Instrumentation characteristics
  - static
  - dynamic

Biostatistics

- Used to design experiments and clinical studies:
  - To summarize, explore, analyze and present data
  - To draw inferences from data by estimation or by hypothesis testing
  - To evaluate diagnostic procedures
  - To assist clinical decision making

- Medical research studies can be classified as:
  - Observational studies: Characteristics of one or more groups of patients are observed and recorded.
  - Experimental intervention studies: Effect of a medical procedure or treatment is investigated.

Biostatistics Studies

- Observational studies – case-series studies
  - Case-control studies
    - use of individuals selected because they have some outcome or disease
    - then look backward to determine possible causes

- Cross-sectional studies:
  - Analyze characteristics of patients at one particular time to determine the status of a disease or condition.

- Cohort observational studies:
  - A particular characteristics is a precursor for an outcome or disease

- Controlled studies:
  - If procedures compared to the outcome for patients given a placebo or other accepted treatment

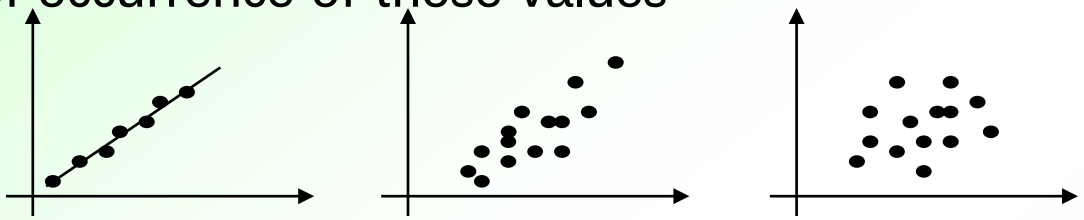
Biostatistics Studies II

- Concurrent control:
  - Patients are selected in the same way and for the same duration

- Double-blind study:
  - Randomized selection of patients to treatment options to minimize investigator or patient bias

Biostatistics: Data Analysis

- Distributions of data reflect the values of a variable/characteristic and frequency of occurrence of those values



- Mean: ($\overline{X}$)average of *N* values (arithmetic or geometric mean)
- Median: middle of ranked values
- Mode: most frequent value

$$\overline{X} = \frac{\sum_i X_i}{N}$$

$$GM = \sqrt[N]{X_1 X_2 \ldots X_N}$$

- Standard deviation: (s) spread of data
  - 75% of values lie between $\overline{X} \pm 2s$

$$s = \sqrt{\frac{\sum_i \left(X_i - \overline{X}\right)^2}{N-1}}$$

- Coefficient of Variation: (CV)
  - permits comparison of different scales

$$CV = \left(\frac{s}{\overline{X}}\right) 100\%$$

- Percentile
  - Percentage of distribution that is less than or equal to the percentile number

More Biostatistics

- Correlation coefficient (r)
  - Measure of the relationship between two numerical variables for paired observations
  - values between +1 and -1 (+1 means strong correlation)

$$r = \frac{\sum \left(X_i - \overline{X}\right)\left(Y_i - \overline{Y}\right)}{\sqrt{\sum \left(X_i - \overline{X}\right)^2} \bullet \sqrt{\sum \left(Y_i - \overline{Y}\right)^2}}$$

- Estimation and Hypothesis Testing
  - Confidence intervals
    - indicates the degree of confidence that data contains the true mean
  - Hypothesis testing
    - reveals whether the sample gives enough evidence for us to reject the *null hypothesis* (statement expressing the opposite of what we think is true)
  - P-value:
    - how often the observed difference would occur by chance alone
- Methods for measuring the accuracy of a diagnostic procedure:
  - *Sensitivity*: probability of the test yielding positive results in patients who actually have the disease
    - opposite: *false-negative rate*
  - *Specificity*: probability of the test yielding negative results in patients who do not have the disease
    - opposite: *false-positive rate*

Instrument Characterization

- Enable comparison of available instruments
- Permit evaluation of new instrument designs

Generalized static characteristics

- Static characteristics:
  - performance of instruments for dc or very low frequency inputs
  - some sensors respond only to time-varying inputs and have no static characteristics
- Dynamic characteristics:
  - require temporal relationships to describe the quality of measurements

Static Characteristics

- **Accuracy**
  - Difference between the true value and the measured value normalized by the magnitude of the true value
  - Several ways to express accuracy
    - most popular is in terms of percentage of full-scale measurement
- **Precision**
  - Expresses number of distinguishable alternatives from which a given result is selected
  - High-precision does not mean high accuracy.
- **Resolution**
  - Smallest incremental quantity that can be measured with certainty
- **Reproducibility**
  - Ability of an instrument to give the same output for equal inputs applied over some period of time

Statistical Control and Static Sensitivity

- Measurement conditions have to take into account *randomness* introduced by environmental conditions
  - If the source of variation can not be removed, then use averaging

- Statistic sensitivity (dc-gain)
  - To perform calibration between output and input
  - For linear calibration

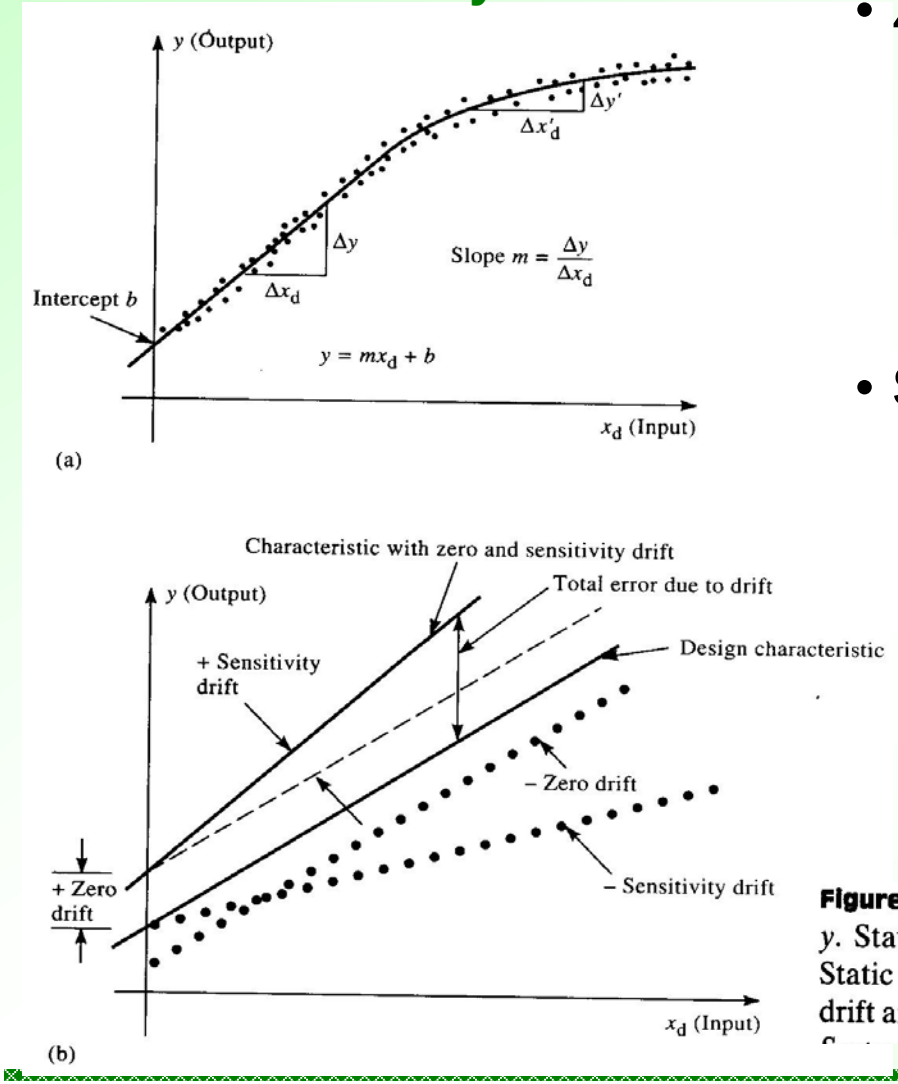
$$m = \frac{n\sum_d x_d y - \left(\sum_d x_d\right)\left(\sum_d y\right)}{n\sum_d x_d^2 - \left(\sum_d x_d\right)^2}$$

$$b = \frac{\left(\sum_d y\right)\left(\sum_d x_d^2\right) - \left(\sum_d x_d y\right)\left(\sum_d x_d\right)}{n\sum_d x_d^2 - \left(\sum_d x_d\right)^2}$$

$$y = mx_d + b$$

Static Characteristics

static sensitivity curves



- Zero drift (offset error)
  - When all measurements increases or decrease by the same absolute amount
  - Causes: manufacturing misalignment, variations in ambient temperature, hysteresis vibration, shock, dc-offset voltage at electrodes
- Sensitivity drift (gain error)
  - When the slope of the calibration curve changes as a result of interfering or modifying input
  - Causes: manufacturing tolerances, variations in power supply, non-linearity
  - Example: ECG amplifier gain changes due to dc power-supply variation

Figure 1.3 (a) Static-sensitivity curve that relates desired input x_d to output y. Static sensitivity may be constant for only a limited range of inputs. (b) Static sensitivity: zero drift and sensitivity drift. Dotted lines indicate that zero drift and sensitivity drift can be negative. [Part (b) modified from *Measurement*

Linearity

- Linearity (formally) : A system that demonstrates superposition principle
  - If system inputs x1, x2 generate outputs y1, y2,
    - i.e., (x1 → y1 AND x2 → y2)
  - Then system is linear if (x1 + x2 → y1 + y2) AND (Kx1 → Ky1)
- Linearity (informally): Output is linearly proportional to measurand quantity
  - data is "fit" to linear curve, generally using "least-squares" technique

outputs, y_i
linear fit, z_i

minimize $\Sigma (z_i - y_i)^2$

- Non-linearity defined as maximum deviation of any output reading from linear fit line
  - Non-linearity is usually expressed as a percentage of full-scale reading

Dynamic Characteristics <OPTIONAL>

- Quantify response of medical equipment with respect to *time-varying* inputs
- Many engineering instruments can be described by ordinary linear differential equations

$$a_n \frac{d^n y}{dt^n} + \ldots + a_1 \frac{dy}{dt} + a_0 y(t) = b_m \frac{d^m x}{dt^m} + \ldots + b_1 \frac{dx}{dt} + b_0 x(t)$$

- Most practical instruments have a first or second order response
- Practical evaluation of a system
  - Apply input as a unit-step function, sinusoidal function or white noise

Dynamic Characteristics

- Operational transfer function:

$$H(s) = \frac{Y(s)}{X(s)} = \frac{b_n s^n + \ldots + b_1 s + b_0}{a_m s^m + \ldots + a_1 s + a_0}$$

- Frequency response of a system

$$s = j\omega$$

- For a sinusoidal input
  - the output is a sinusoid with different magnitude and phase

$$H(s) = K\, H_1(s) \ldots H_m(s)$$

- Magnitude:

$$|H(s)| = K\,|H_1(s)| \ldots |H_m(s)|$$

- Phase:

$$\angle H(s) = \angle H_1(s) + \ldots + \angle H_m(s)$$

Zero-order Instrument

$$a_0 y(t) = b_0 x(t)$$

$$H(s) = \frac{Y(s)}{X(s)} = \frac{b_0}{a_0}$$

- Linear potentiometer is an example of a zero order instrument
- In practice, at high frequencies parasitic capacitance and inductance will cause distortion
- Step response is proportional to the input amplitude; no variation with frequency

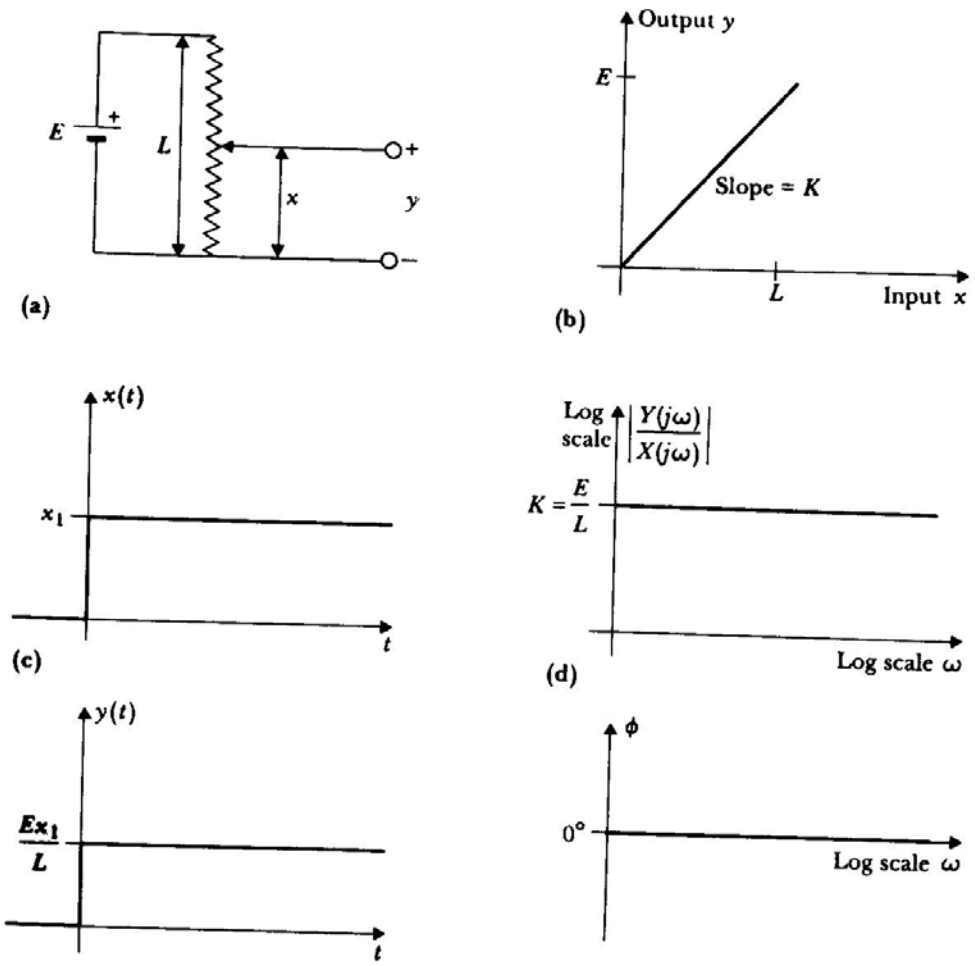


Figure 1.5 (a) A linear potentiometer, an example of a zero-order system. (b) Linear static characteristic for this system. (c) Step response is proportional to input. (d) Sinusoidal frequency response is constant with zero phase shift.

First-order Instrument

- First-order instrument contains a single energy-storage element

$$a_1 \frac{dy}{dt} + a_0 y(t) = b_0 x(t)$$

$$H(s) = \frac{Y(s)}{X(s)} = \frac{K}{(1+\tau s)}$$

- $K = b_0 / a_0$ is the static sensitivity (dc-gain)
- $\tau = a_1 / a_0$ is the time-constant of the system
  - Step response is characterized by a single time constant

- A frequency transfer function is given by

$$|H(j\omega)| = \frac{K}{\sqrt{1+\omega^2\tau^2}}$$

$$\angle H(j\omega) = \arctan(-\omega\tau)$$

Second-order Instrument

- Second-order instrument contains a minimum of two energy-storage element.

$$a_2 \frac{d^2 y}{dt^2} + a_1 \frac{dy}{dt} + a_0 y(t) = b_0 x(t)$$

$$H(s) = \frac{K}{(1 + \frac{2\zeta s}{\omega_0} + \frac{s^2}{\omega_0^2})}$$

- where
  - $K = b_0 / a_0$ is the static sensitivity (dc-gain)
  - $\omega_0 = \sqrt{\frac{a_0}{a_2}}$ is the undamped natural frequency
  - $\zeta = \frac{a_1}{2\sqrt{a_0 a_2}}$ is the damping ratio

- Step response is characterized by *undamped natural frequency* and the *damping ratio*

1st & 2nd order Instruments

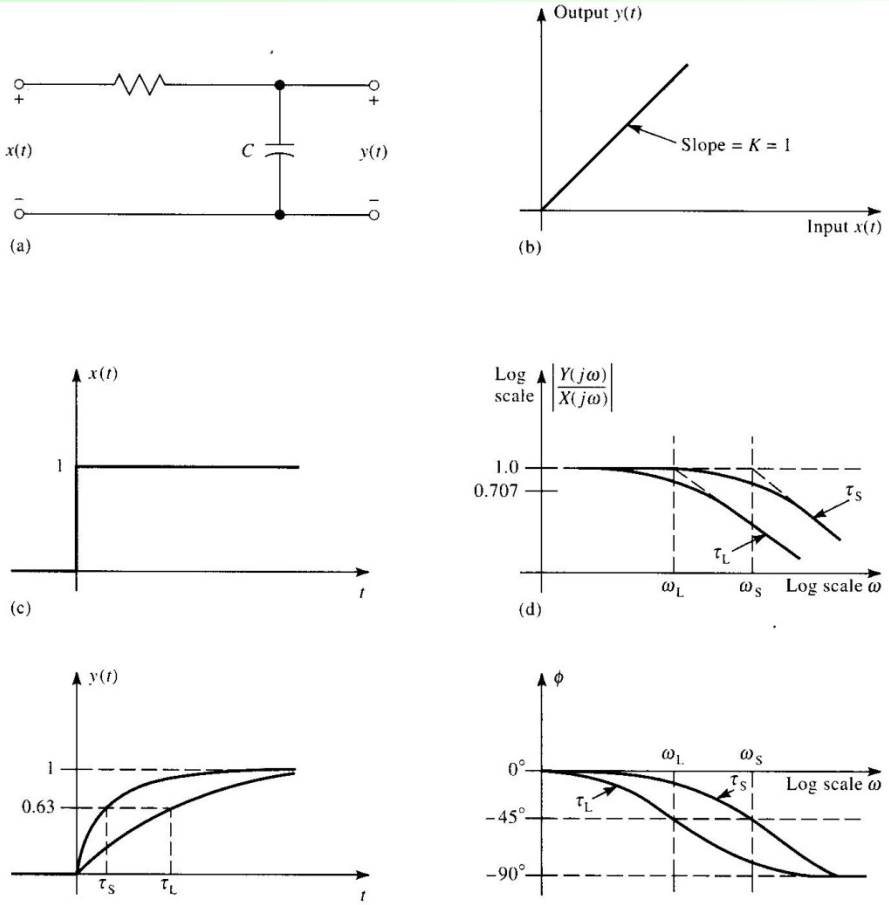


Figure 1.6 (a) A low-pass *RC* filter, an example of a first-order instrument (b) Static sensitivity for constant inputs. (c) Step response for large time constants (τ_L) and small time constants (τ_S). (d) Sinusoidal frequency response for large and small time constants.

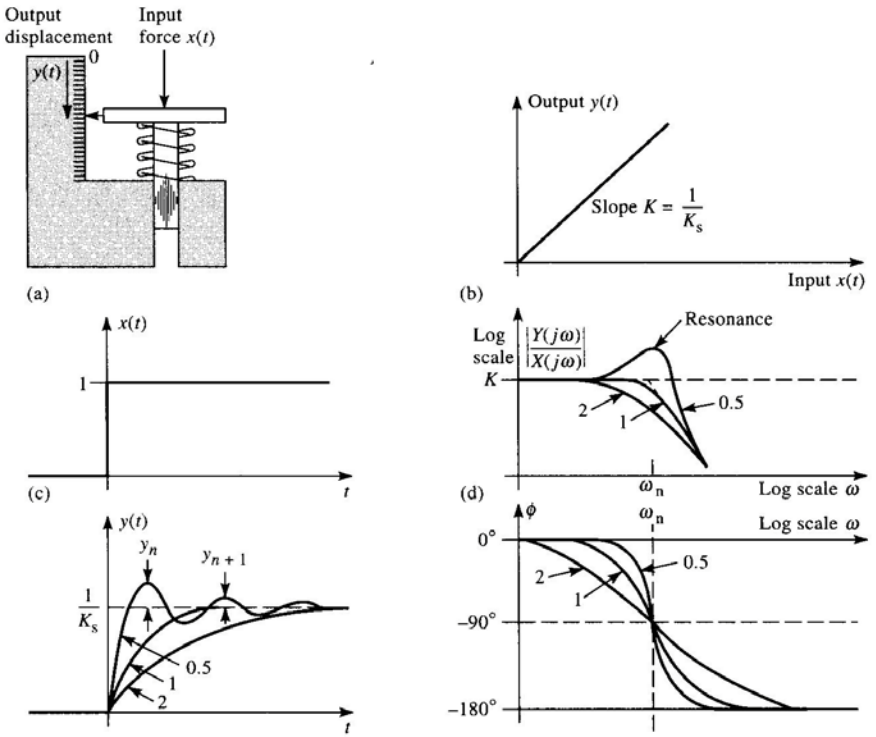


Figure 1.7 (a) Force-measuring spring scale, an example of a second-order instrument. (b) Static sensitivity. (c) Step response for overdamped case $\zeta = 2$, critically damped case $\zeta = 1$, underdamped case $\zeta = 0.5$. (d) Sinusoidal steady-state frequency response, $\zeta = 2$, $\zeta = 1$, $\zeta = 0.5$. [Part (a) modified