Chapter 1. Basic Concepts of Medical Instrumentation

- Invention ⇒ prototype design ⇒ product development ⇒ clinical testing ⇒ regulatory approval ⇒ manufacturing ⇒ sale
  - ❍ Clear vision of the final new product and exactly how it will be used
  - ❍ Commitment and persistence to overcome unexpected technical problems, convince the nay-sayers, and cope with the bureaucratic apparatus

1.1. Terminology of Medicine and Medical Devices

- ❍ Medical Terminology: An Illustrated Guide (Cohen, 1994)
- ❍ Dorland's Illustrated Medical Dictionary, 28th ed. (Dorland, 1994)
- ❍ Dictionary of Medical Eponyms (Firkin and Whitworth, 1987)
- ❍ Health Devices Sourcebook
- ❍ Product Development Directory
- ❍ Encyclopedia of Medical Devices and Instrumentation (Webster, 1988)

1.2 Generalized Medical Instrumentation System

- ❍ Generalized instrumentation system

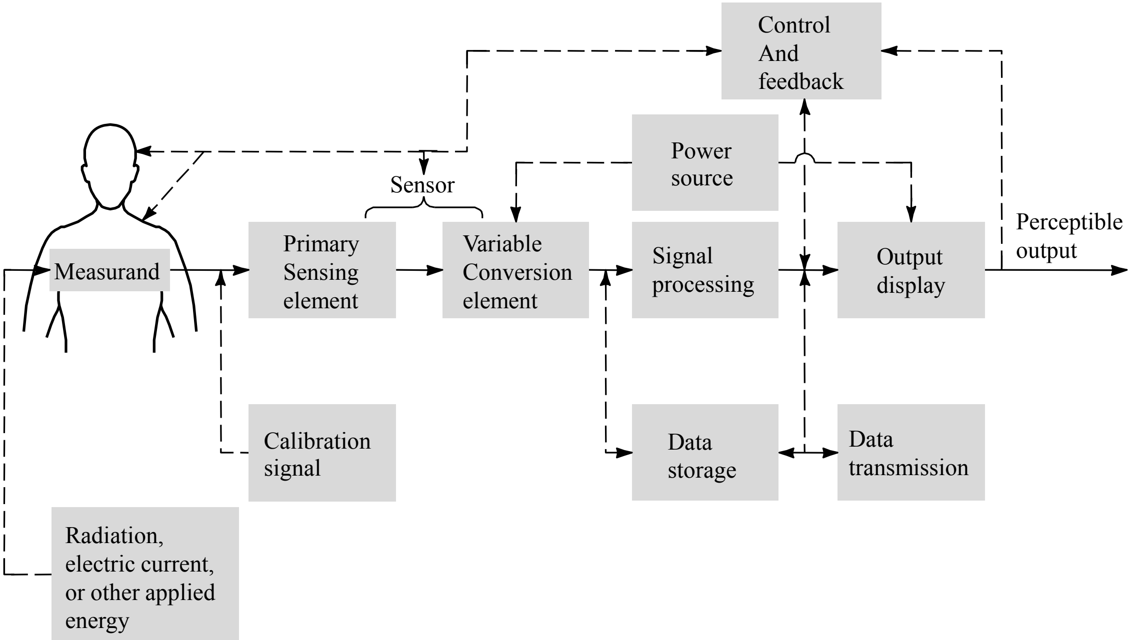

Figure 1.1 Generalized instrumentation system The sensor converts energy or information from the measurand to another form (usually electric). This signal is the processed and displayed so that humans can perceive the information. Elements and connections shown by dashed lines are optional for some applications.

Measurand

- Physical quantity, property, or condition that the system measures
- Accessibility: internal, body surface, emanation from the body, or tissue sample
- Category: biopotential, pressure, flow, dimensions, displacement, impedance, temperature, and chemical concentration
- Localization: organ or anatomical structure

Sensor

- Transducer (sensor) is a device that converts one form of energy to another (electric)
  - Specific
  - Minimization of the extracted energy
  - Minimally invasive
- Primary sensing element and variable conversion element

Signal Conditioning

- Amplification, filtering, impedance matching, A/C conversion, DSP, etc.

Output Display

- Visual sense
    - Numerical or graphical
    - Discrete or continuous
    - Permanent or temporary
- Auditory sense
- Tactile sense
- Human factors engineering guidelines and preferred practices for the design of medical devices (AAMI, 1993)

Auxiliary Elements

- Calibration
- Control and feedback
- Storage
- Transmission

1.3 Alternative Operating Modes

Direct-Indirect Modes

- Accessible (noninvasive or invasive) ⇒ direct mode
- Not accessible ⇒ indirect mode
    - Cardiac output (CO) by Fick method, dye dilution, or thermodilution
    - Morphology of internal organs by X-ray shadows
    - Pulmonary volumes by thoracic impedance plethysmography

Sampling and Continuous Modes

- Frequency content of the measurand: temperature (sampling) or ECG (continuous)
- Objective of the measurement
- Condition of the patient
- Potential liability of the physician

Generating and Modulating Sensors

- Generating sensor: measurand produces output from the energy taken directly from itself, photovoltaic cell
- Modulating sensors: measurand alters the flow of energy from an external source,

photoconductive cell

Analog and Digital Modes

- Analog: continuous in time and continuous in amplitude
- Digital: discrete in time and take only a finite number of different values
  - Greater accuracy
  - Repeatability
  - Reliability
  - Noise immunity
  - No periodic calibration
  - Readability (in display)
- Analog sensor, indirect digital sensor, quasi-digital sensor, and digital sensor
- Data conversions: ADC and DAC

Real-Time and Delayed-Time Modes

- Short processing time ⇒ real-time mode
- Long processing time ⇒ delayed-time mode

1.4 Medical Measurement Constraints

- Typical medical parameter magnitude and frequency ranges: Table 1.1
- Small amplitude and low frequency (AF or below to dc)
- Frequent inaccessibility due to the lack of proper measurand-sensor interface
- Not possible to turn it off or remove a part of it during measurements
- Inherent variability with time and among subjects
- Many feedback loops among physiological systems
- Unknown safety level of the externally applied energy
- Additional constraints of a medical equipment
  - Reliability
  - Easy to use
  - Must withstand physical abuse and exposure to corrosive chemicals
  - Minimized electric-shock hazards

1.5 Classifications of Biomedical Instruments

- Quantity that is sensed: pressure, flow, temperature, etc.
- Principle of transduction: resistive, inductive, capacitive, ultrasonic, electrochemical, etc.
- Organ system: cardiovascular, pulmonary, nervous, endocrine, etc.
- Clinical medicine specialties: pediatrics, obstetrics, cardiology, radiology, etc.

1.6 Interfering and Modifying Inputs

- Desired input: v_{ecg} in Fig. 1.2
- Interfering input: 60-Hz noise in Fig. 1.2
- Modifying input: orientation of the patient cables in Fig. 1.2

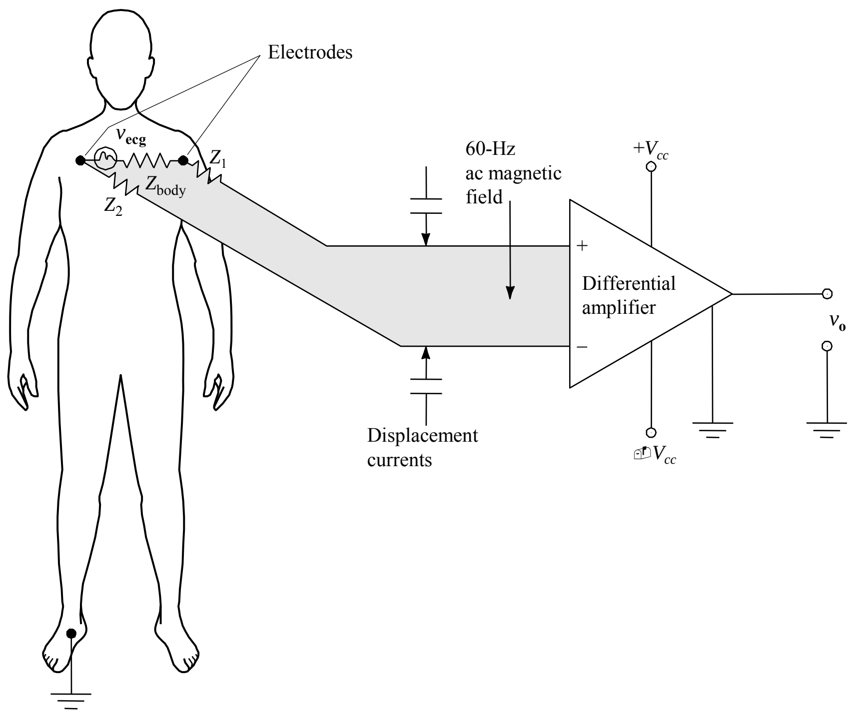

Figure 1.2 Simplified electrocardiographic recording system Two possible interfering inputs are stray magnetic fields and capacitively coupled noise. Orientation of patient cables and changes in electrode-skin impedance are two possible modifying inputs. Z_1 and Z_2 represent the electrode-skin interface impedances.

1.7 Compensation Techniques

❍ Alter design and/or add new components

Inherent Insensitivity

- Make all components inherently sensitive only to desired inputs
  - Twisting the lead wires in Fig. 1.2
  - Use Ag/AgCl electrode to reduce motion artifact

Negative Feedback

- If the transfer function G_d is affected by modifying inputs, negative feedback the output *y* by $(H_f y)$ to the input x_d and make H_f insensitive to modifying inputs
  - $(x_d - H_f y)G_d = y \Rightarrow y = \dfrac{G_d}{1 + H_f G_d} x_d$
  - If $H_f G_d >> 1$, $y \cong \dfrac{1}{H_f} x_d$
- Advantages: less power, more accurate and linear, less loading
- Disadvantages: possible oscillation

Signal Filtering

- A filter is "a device or program that separates data, signals, or material in accordance with specific criteria" (a filter usually separates signals according to their frequencies)
- Electrical, mechanical, pneumatic, thermal, or electromagnetic filters
- Filters at input, intermediate, and output stage

Opposing Inputs

- Use additional interfering inputs to cancel undesired output due to interfering and/or modifying inputs
- Opposing inputs before or after the appearance of undesired signals

1.8 Biostatistics

❍ Application of statistics
- Design experiments or clinical studies

- Summarize, explore, analyze, and present data
- Draw inferences from data by estimation or hypothesis testing
- Evaluate diagnostic procedure
- Assist clinical decision making

❍ Medical research studies

- Observational studies
    - Case-series: no control subjects, describe characteristics of a group, identify questions
    - Case-control: selected subjects, find possible causes or risk factors
    - Cross-sectional: analyze characteristics of patients at one particular time, determine the status of a disease or condition
    - Cohort: ask whether a particular characteristic is a precursor or risk factor for an outcome or disease
- Experimental intervention studies
    - Controlled: comparisons between patients with drug, device, or procedure and patients with a placebo or another accepted treatment
    - Uncontrolled: no such comparison
    - Concurrent control: double-blind, randomized patient selection, for the same time period, minimize investigator or patient bias

❍ Data measurement

- Quantitative data: on a continuous or discrete numerical scale with some precision
- Qualitative data
    - Nominal scale for categorization
    - Ordinal scale for an inherently ordered categories

❍ Descriptive statistics

- Distributions: values and the frequency of occurrence
- Measures of the middle or central tendency
    - Mean
    - Median
    - Mode
    - Geometric mean
- Measures of spread or dispersion
    - Range
    - Standard deviation
    - Coefficient of variation
    - Percentile

    - Interquartile range
    - Standard error of the mean, SEM
  - Relationship between two variables
    - Correlation coefficient
- Inference
  - Estimation
    - Confidence interval
  - Hypothesis testing
    - Null-hypothesis
    - P-value
- Accuracy
  - Sensitivity
  - Specificity
  - Prior probability
- Optimal decision: decision analysis such as decision tree analysis

1.9 Generalized Static Characteristics

- Quantitative criteria for the performance of instruments
  - Static characteristics
  - Dynamic characteristics

Accuracy

- $\text{Accuracy} = \dfrac{\text{true value} - \text{measured value}}{\text{true value}} \times 100(\%)$
  - Measure of the total error
  - True or reference value: NIST (National Institute of Standards and Technology)
- Varies with the normal range and frequency of inputs
- Expressions
  - % of reading
  - % of FS (or simply %)
  - $\pm$ number of digits
  - $\pm\dfrac{1}{2}$ the smallest division of an analog scale
  - Sum of the above

Precision

- Number of distinguishable alternatives from which a given result is selected
- High precision does not necessarily implies high accuracy

Resolution

- Smallest incremental quantity that can be measured with certainty
- Degree to which nearly equal two values of a quantity can be discriminated
- Same as threshold when it starts from zero

Reproducibility or repeatability

- Ability to give the same output for equal inputs applied over some period of time
- Reproducibility does not imply accuracy

Statistical Control

- Random variations in measurements ⇒ statistical analysis ⇒ determine error variation
- Averaging can improve the estimate of the true value

Static Sensitivity

- Static calibration
  - Hold all inputs constant except one
  - Increase the input over the normal operating range and measure the output
- Static sensitivity = $\dfrac{\text{incremental output}}{\text{incremental input}}$
- Static-sensitivity curve in Fig. 1.3 with linear regression of $y = mx_d + b$
- Example: blood pressure sensor with 50 $\mu V \cdot V^{-1} \cdot mmHg^{-1}$

Zero Drift

- All output values increase or decrease by the same absolute amount (Fig. 1.3(b))
- Causes
  - Manufacturing misalignment
  - Variations in ambient temperature
  - Hysteresis
  - Vibration

  - Shock
  - Sensitivity to forces from undesired direction
- Example: slow changes of dc offset voltage of ECG electrodes

Sensitivity Drift

- Changes in the slope of the calibration curve (Fig. 1.3(b))
- Error is proportional to the magnitude of input
- Causes
  - Manufacturing tolerance
  - Variations in power supply
  - Nonlinearities
  - Change in ambient temperature and pressure
- Example: variations of ECG amplifier gain due to the fluctuation of dc power supply voltage or temperature

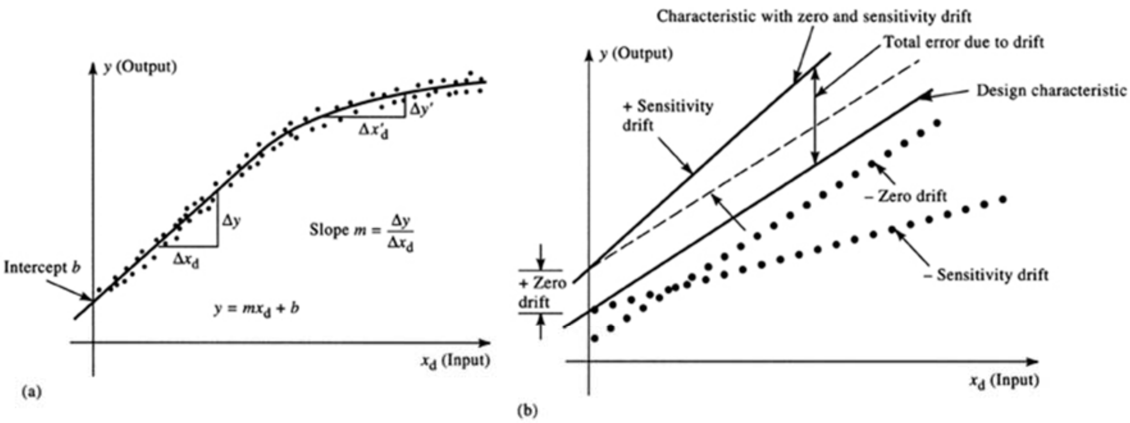

Figure 1.3 (a) Static-sensitivity curve that relates desired input x_d to output y. Static sensitivity may be constant for only a limited range of inputs. (b) Static sensitivity: zero drift and sensitivity drift. Dotted lines indicate that zero drift and sensitivity drift can be negative. [Part (b) modified from *Measurement Systems: Application and Design*, by E. O. Doebelin. Copyright © 1990 by McGraw-Hill, Inc. Used with permission of McGraw-Hill Book Co.]

Linearity

- Requirements: Fig. 1.4(a), $K_1x_1 + K_2x_2 \rightarrow \text{LinearSystem} \rightarrow K_1y_1 + K_2y_2$
- High accuracy does not necessarily implies linearity
- Independent nonlinearity
  - Measure of deviation from linearity
  - ±*A*% of reading or ±*B*% of full scale, whichever is greater (Fig. 1.4(b))

- Equal to the accuracy of a linear instrument if other sources of error are minimal

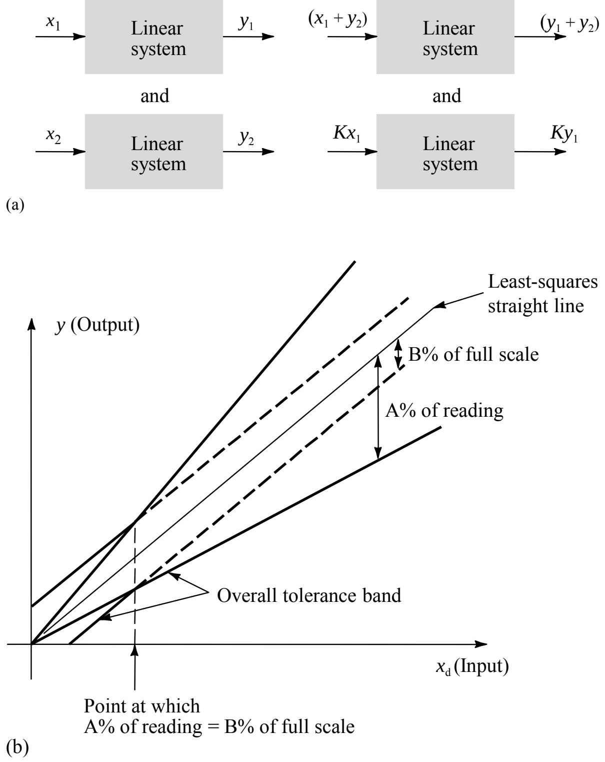

Figure 1.4 (a) Basic definition of linearity for a system or element. The same linear system or element is shown four times for different inputs. (b) A graphical illustration of independent nonlinearity equals ±A% of the reading, or ±B% of full scale, whichever is greater (that is, whichever permits the larger error). [Part (b) modified from *Measurement Systems: Application and Design*, by E. O. Doebelin. Copyright © 1990 by McGraw-Hill, Inc. Used with permission of McGraw-Hill Book Co.]

Input Ranges

- Static linear range may be different from dynamic linear range
- Minimal resolvable inputs ⇒ lower bound
- Normal linear range ⇒ maximal or near-maximal input for linear output
- Maximal operating range ⇒ largest input without damage to the instrument
- Storage conditions

Input Impedance

- Input impedance, $Z_x = \dfrac{X_{d1}}{X_{d2}}$
    - X_{d1} is the phasor equivalent of a steady state sinusoidal effort variable (voltage, force, pressure)
    - X_{d2} is the phasor equivalent of a steady state sinusoidal flow variable (current,

velocity, flow)

- Power, $P = X_{d1} \cdot X_{d2} = \dfrac{X_{d1}^2}{Z_x} = Z_x X_{d2}^2$
  - Instantaneous rate at which energy is transferred across the tissue-sensor interface
  - Measuring X_{d1} $\Rightarrow$ minimize X_{d2} $\Rightarrow$ maximize Z_x $\Rightarrow$ minimize P
  - Measuring X_{d2} $\Rightarrow$ minimize X_{d1} $\Rightarrow$ minimize Z_x $\Rightarrow$ minimize P
- Unknown source impedance $Z_s \Rightarrow$ maximize Z_x to reduce the loading effect in measuring X_{d1}
- Loading effect

1.10 Generalized Dynamic Characteristics

- Dynamic inputs and outputs in continuous system $\Rightarrow$ differential or integral equations (usually linear, ODE with constant coefficients)

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

- With the differential operator, $D^k \equiv \dfrac{d^k()}{dt^k}$,

$$\left(a_n D^n + \cdots + a_1 D + a_0\right) y(t) = \left(b_m D^m + \cdots + b_1 D + b_0\right) x(t)$$

- Test input signals: step, sinusoids, band-limited white noise

Transfer Functions

- Operational transfer function
  - $H(D) = \dfrac{y(D)}{x(D)} = \dfrac{b_m D^m + \cdots + b_1 D + b_0}{a_n D^n + \cdots + a_1 D + a_0}$
  - Useful for transient inputs
- Frequency transfer function
  - $H(j\omega) = \dfrac{Y(j\omega)}{X(j\omega)} = \dfrac{b_m (j\omega)^m + \cdots + b_1 (j\omega) + b_0}{a_n (j\omega)^n + \cdots + a_1 (j\omega) + a_0}$

- For steady state and sinusoidal input
- Input, $x(t) = A_x \sin(\omega t)$ and output, $y(t) = B(\omega)\sin[\omega t + \phi(\omega)]$

Zero-Order Instrument

- $a_0 y(t) = b_0 x(t)$ and $\dfrac{y(D)}{x(D)} = \dfrac{y(j\omega)}{x(j\omega)} = \dfrac{b_0}{a_0} = K =$ static sensitivity
- No amplitude and phase distortion
- Linear potentiometer at low frequency and small load (Fig. 1.5)

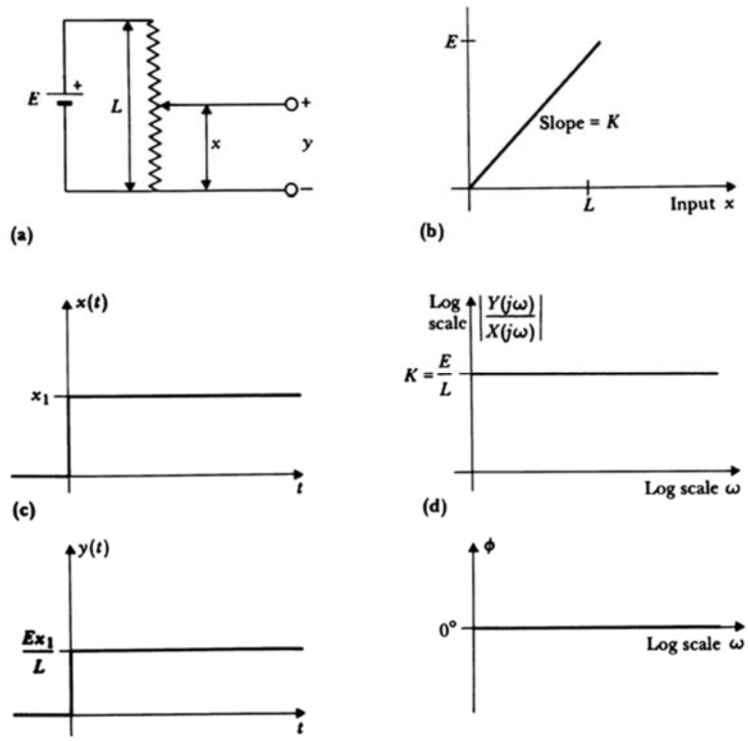

Figure 1.5 (a) A linear potentiometer, an example of a zero-order system. (b) Linear static characteristic for this system. (c) Step response is proportional to input. (d) Sinusoidal frequency response is constant with zero phase shift.

First-Order Instrument

- $a_1 \dfrac{dy(t)}{dt} + a_0 y(t) = b_0 x(t)$ or $(\tau D + 1)y(t) = Kx(t)$
  - $K = \dfrac{b_0}{a_0} =$ static sensitivity
  - $\tau = \dfrac{a_1}{a_0} =$ time constant

- $\dfrac{y(D)}{x(D)} = \dfrac{K}{1+\tau D}$ and $\dfrac{Y(j\omega)}{X(j\omega)} = \dfrac{K}{1+j\omega\tau} = \dfrac{K}{\sqrt{1+j\omega^2\tau^2}} \angle\phi = \arctan\left(\dfrac{-1}{\omega\tau}\right)$
- RC LPF in Fig. 1.6 with $RC\dfrac{dy}{dt} + y(t) = Kx(t)$
  - $y(t) = K\left(1-e^{-t/\tau}\right)$
  - At $\omega = 1/\tau$ (corner, cutoff, or break frequency), the magnitude is $1/\sqrt{2} = 0.707$ times smaller and the phase angle is -45°
  - $\text{dB} = 20\log_{10}\left(\dfrac{Y(j\omega)}{X(j\omega)}\right)$
- RC HPF with R and C in Fig. 1.6 interchanged
  - $y(t) = Ke^{-t/\tau}$
  - $\dfrac{Y(j\omega)}{X(j\omega)} = \dfrac{j\omega\tau}{1+j\omega\tau}$

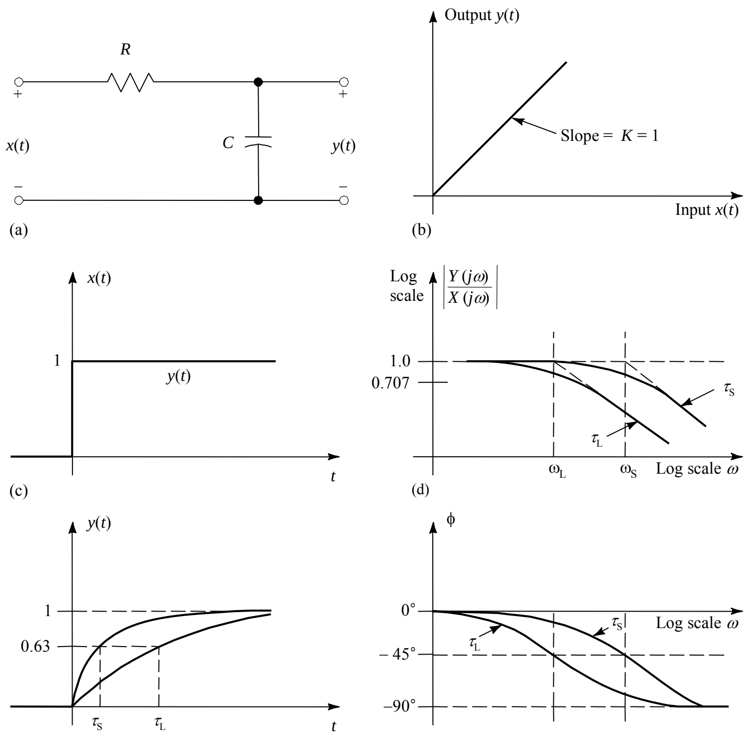

Figure 1.6 (a) A low-pass *RC* filter, an example of a first-order instrument. (b) Static sensitivity for constant inputs. (c) Step response for larger time constants (τ_L) and small time constants (τ_S). (d) Sinusoidal frequency response for large and small time constants.

Second-Order Instrument

- $a_2 \frac{d^2 y(t)}{dt^2} + a_1 \frac{dy(t)}{dt} + a_0 y(t) = b_0 x(t)$ or $\left\{ \frac{D^2}{\omega_n^2} + \frac{2\zeta D}{\omega_n} + 1 \right\} y(t) = Kx(t)$
  - $K = \frac{b_0}{a_0} =$ static sensitivity, output units divided by input units
  - $\omega_n = \sqrt{\frac{a_0}{a_2}} =$ undamped natural frequency, rad/s
  - $\zeta = \frac{a_1}{2\sqrt{a_0 a_2}} =$ damping ratio, dimensionless
- $\frac{y(D)}{x(D)} = \frac{K}{\frac{D^2}{\omega_n^2} + \frac{2\zeta D}{\omega_n} + 1}$ and

$$\frac{Y(j\omega)}{X(j\omega)} = \frac{K}{\left(j\omega/\omega_n\right)^2 + \left(2\zeta\, j\omega/\omega_n\right) + 1}$$

$$= \frac{K}{\sqrt{\left[1 - \left(\omega/\omega_n\right)^2\right]^2 + 4\zeta^2\, \omega^2/\omega_n^2}} \angle\phi = \arctan\left(\frac{2\zeta}{\omega/\omega_n - \omega_n/\omega}\right)$$

- Step response of the mechanical force-measuring instrument in Fig. 1.7
  - Overdamped, $\zeta > 1$:

$$y(t) = -\frac{\zeta + \sqrt{\zeta^2 - 1}}{2\sqrt{\zeta^2 - 1}} K e^{\left(-\zeta + \sqrt{\zeta^2 - 1}\right)\omega_n t} + \frac{\zeta - \sqrt{\zeta^2 - 1}}{2\sqrt{\zeta^2 - 1}} K e^{\left(-\zeta - \sqrt{\zeta^2 - 1}\right)\omega_n t} + K$$

  - Critically damped, $\zeta = 1$: $y(t) = -\left(1 + \omega_n t\right) K e^{-\omega_n t} + K$
  - Underdamped, $\zeta < 1$:

$$y(t) = -\frac{e^{-\zeta\omega_n t}}{\sqrt{1-\zeta^2}} K \sin\left(\sqrt{1-\zeta^2}\,\omega_n t + \phi\right) + K \text{ and } \phi = \arcsin\sqrt{1-\zeta^2} \text{ and}$$

    damped natural frequency, $\omega_d = \omega_n \sqrt{1-\zeta^2}$ (Fig. 1.7(c))
  - Damping ratio of 0.7: practical compromise between rapid rise time and minimal overshoot
  - In Fig. 1.7(c), for $\zeta < 0.3$, $t_n = \frac{3\pi/2 - \phi}{\omega_n\sqrt{1-\zeta^2}}$ and $t_{n+1} = \frac{7\pi/2 - \phi}{\omega_n\sqrt{1-\zeta^2}}$

$$\frac{y_n}{y_{n+1}} = \exp\left(\frac{2\pi\zeta}{\sqrt{1-\zeta^2}}\right), \text{ logarithmic increment } \Lambda = \ln\left(\frac{y_n}{y_{n+1}}\right) = \frac{2\pi\zeta}{\sqrt{1-\zeta^2}} \text{ and}$$

$$\zeta = \frac{\Lambda}{\sqrt{4\pi^2 + \Lambda^2}}$$

- Frequency transfer function: Fig. 1.7(d)
  - -40 dB/dec roll-off (1st order system: -20 dB/dec)
  - Small damping ratio resonance
  - Maximal phase lag of 180° (1st order system: 90°)

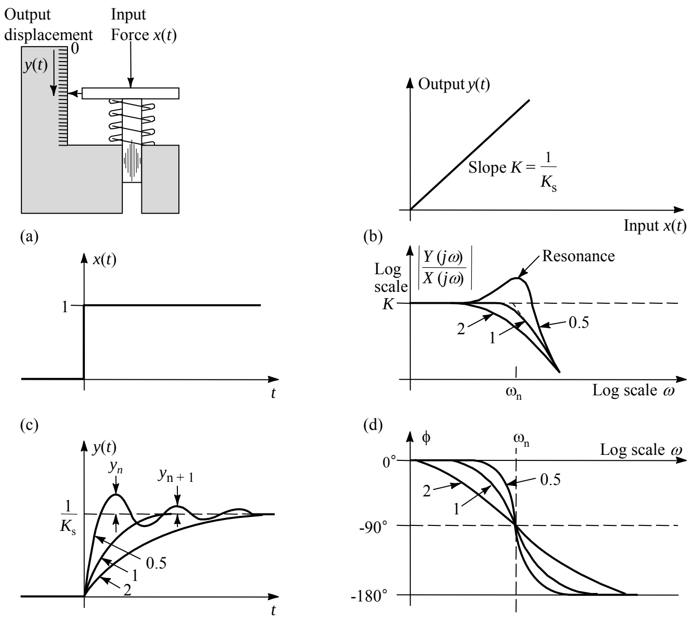

Figure 1.7 (a) Force-measuring spring scale, an example of a second-order instrument. (b) Static sensitivity. (c) Step response for overdamped case $\zeta = 2$, critically damped case $\zeta = 1$, underdamped case $\zeta = 0.5$. (d) Sinusoidal steady-state frequency response, $\zeta = 2$, $\zeta = 1$, $\zeta = 0.5$. [Part (a) modified from *Measurement Systems: Application and Design*, by E. O. Doebelin. Copyright © 1990 by McGraw-Hill, Inc. Used with permission of McGraw-Hill Book Co.]

Time Delay

- $y(t) = Kx(t-\tau_d),\ t > \tau_d$ and $\frac{Y(j\omega)}{X(j\omega)} = Ke^{-j\omega\tau_d}$
- Time-delay element, analog delay line, transport lag, or dead time
- Negative phase angle $\Rightarrow$ time delay
- Varying phase with frequency $\Rightarrow$ varying time delay with frequency
- Undistorted signal reproduction with time delay $\Leftrightarrow$ $\frac{Y(j\omega)}{X(j\omega)} = K\angle -\omega\tau_d$
- Overall instrument transfer function

1.11 Design Criteria

- Design process for medical instruments: Fig. 1.8
- Compromises in specifications

1.12 Commercial Medical Instrumentation Development Process

- Sources of ideas: physicians, nurses, clinical engineers, sales personnel
- Feasibility analysis and product description
  - Medical need for the product
    - Patient indications
    - Number of patients
    - Clinical specialty
    - How, why, and by whom the device will be utilized
  - Technical feasibility
    - Core technology
    - Suitability of existing or readily modifiable components
    - Breakthroughs or inventions required
    - System analysis
    - Preliminary cost analysis
  - Marketing research and analysis for evolutionary products (not for revolutionary products)
  - Fitness with company's current or planned product lines and sales method
- Manufacturing feasibility analysis
- Business plan
  - Financial aspects
  - Personnel requirements
  - Competition patents
  - Standards
  - Manufacturing requirements
  - Sales and service requirements
  - Time schedule for the project
- Development of functional prototype
  - Sensor, signal processing elements, and new or unique components
  - Animal and/or human experiments

- Favorable feasibility review ⇒ <u>product specification</u>
  - Everything about 'what' is required and nothing about 'how'
  - Numerical values for performance
  - Internal testing requirements
  - Size, weight, and color
- Product specification ⇒ design and development engineers
  - Function partitioning into hardware and software
  - Circuit diagrams, software requirements and mechanical designs using CAD
  - Simulations of functional operations
  - Manufacturable prototype: test (animal and/or human), design assurance
  - Design review
- Test equipment design engineers
- Quality assurance engineers
- Manufacturing or production engineers
- ECO (Engineering Change Order)
- Technical support

1.13 Regulation of Medical Devices

- Ensure the safety and efficacy of new medical devices prior to marketing of the device
- Medical device is "any item promoted for a medical purpose that does not rely on chemical action to achieve its intended effect."
- First classification
  - Class I general control
  - Class II performance standards
  - Class III premarket approval
- Second classification (Table 1.2)
  - Preamendment
  - Postamendment
  - Substantially equivalent
  - Implant
  - Custom
  - Investigational
  - Transitional