Introduction to Biomedical Instrumentation

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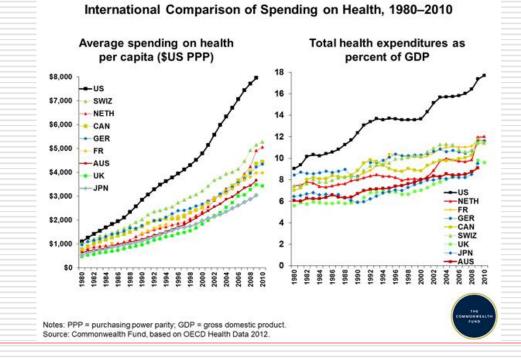


INTRODUCTION

- Biomedical instruments" refer to a very broad class of devices and systems.
- A biomedical instrument is an ECG machine to many people. To others, it's a chemical biosensor, and to some it's a medical imaging system.
- Biomedical instruments are ubiquitous; they are significant to the broader technology and biotechnology sectors; and, finally, they are vital to many medical and scientific fields.
- The global medical device market is expected to reach an estimated \$343 billion by 2021.

Why Should Engineers Care about Medicine?

- □ This figure illustrates that health care costs have been rising steadily in all developed countries.
- □ Total cost of health care in the U.S. currently stands at \$2.7 trillion.



INTRODUCTION

- In this course, the principles, applications, and design of the medical instruments, most commonly used in hospitals are described.
- Relying on electric circuits, electronics, mathematics through differential equations and physics, this course provides required background to be able to design medical instrument.

Content

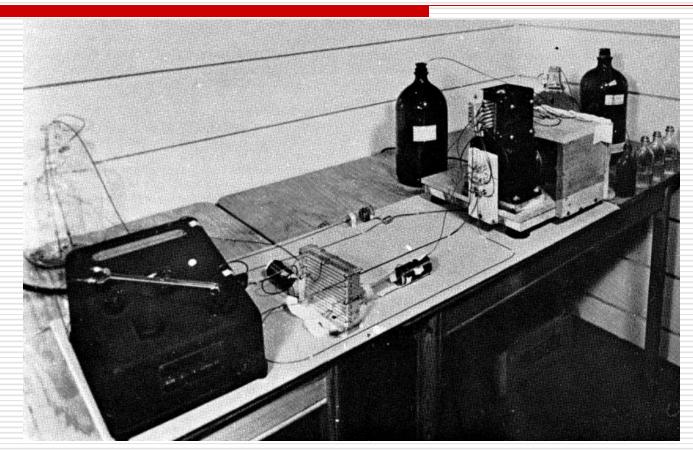
- General concepts that are applicable to all instrumentation systems, including on the commercial development of medical instruments, on biostatistics, and on the regulation of medical devices are covered.
- Basic sensors are described.
- Design of amplifiers for these sensors are introduced.
- Biopotentials, tracing the topic from the origin of biopotentials, through electrodes, to the special amplifier design required are investigated.
- Measurement of cardiovascular dynamics— pressure, sound, flow, and volume of blood are covered.

Content

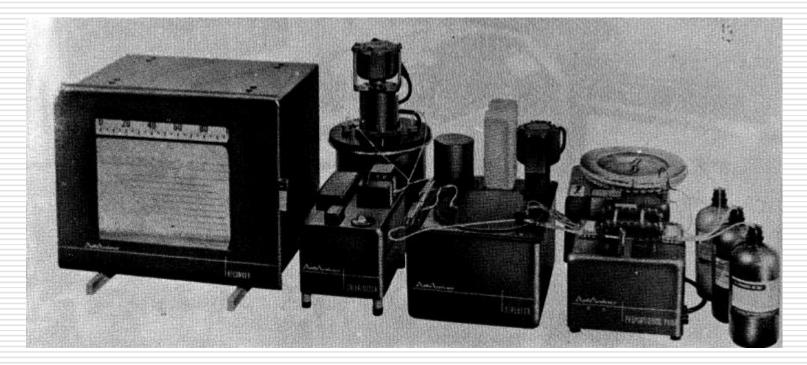
- Measurement of respiratory dynamics—pressure, flow, and concentration of gases are introduced.
- Developing field of biosensors: sensors that measure chemical concentrations within the body via catheters or implants is described.
- The clinical laboratory the area in the hospital where the greatest number of measurements is made, is descirbed.
- General concepts of medical imaging and shows their applications to x-ray techniques, magnetic resonance imaging, positron emission tomography, and Doppler ultrasonic images are introduced.
- A guide both to electric safety in the hospital and to minimization of hazards is presented.

Development of Technicon's Auto Analyzer

- In 1950, Leonard Skeggs developed and instrument and inform Technicon Corporation about it but somehow both sides did not interest in each other.
- Skeggs initially made an agreement with Heinecke Instrument Company and then Harshaw chemical company. However within 3 years period both company could not develop a commercial product out of this design.
- Three years later, salesman of Technicon Corporation heart about the device which can automate chemical analysis.
- Initial demonstration of device worked promisingly and Skeggs and Techicon agreed on a initial payment \$6000 and 3 percent share from the profit.
- Technicon spent three years to refine the initial design into a commercial product. In 1957 contious flow aotu analyzer was introduced.
- Technicon could afford to pursue expensive development of this device since Technicon has the patent on Skegg's original invention.



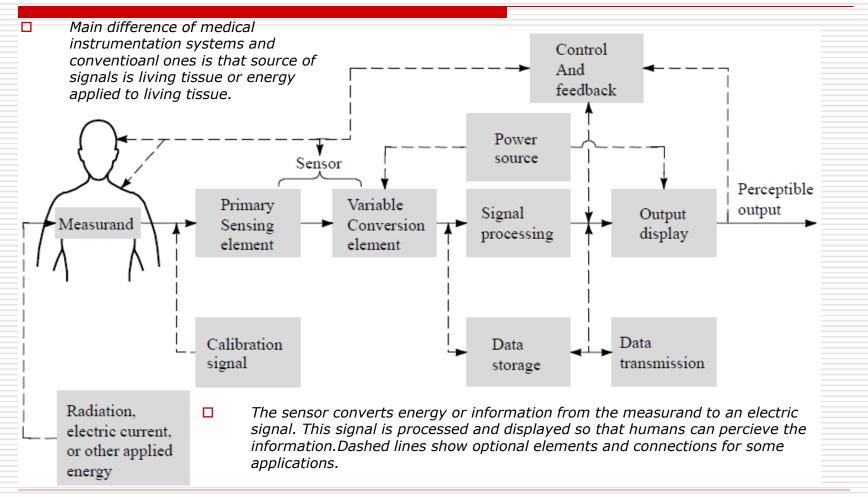
Prototype No. of the AutoAnalyzer (May 1951)



Technicon AutoAnalyzer AAI--commercial instrument (1957).

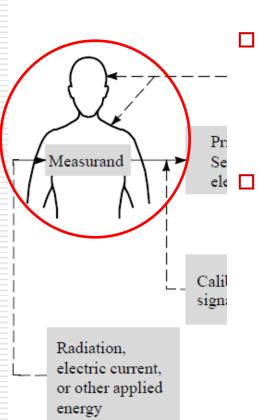
- To introduce technology as radical as the Auto analyzer into conservative clinical laboratories, Technicon performed clinical evaluations and sponsored 25 symposia and attracted around 4500 scientists.
- Incompotent users could damage the market accaptance of the Auto analyzer irreparably.Technicon set up a broadscale training program for purchaser of Auto analyzer and trained 50000 people.
- In 1953, a potential market of 250 units was estimated. By 1988, more than 50000 Auto Analyzer Channels are estimated to be in use around the world.
- Several factors influenced the success.
 - Enormous improvement in the quality of laboratory test results,
 - Enormous reduction in the cost of doing chemical analysis.
 - Physicans began to realize that accurate laboratory data are useful in diagnosis

Generalized Medical Instrumentation System



Generalized Medical Instrumentation System

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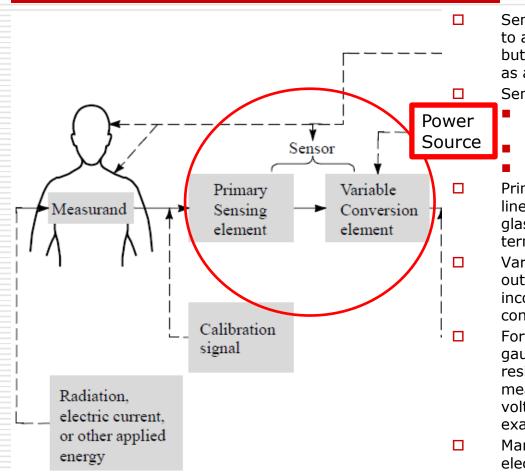


- Measurand is defined as physical quantity, property, or condition that the system measures.
- The accessibility of measurand may be
 - internal (blood pressure),
 - body surface (electrocardiogram potential),
 - emanation from the body, or tissue sample (infrared radiation)
 - derived from a tissue sample (blood or biopsy)

Measurands can be grouped into:

- biopotential,
- pressure,
- flow,
- imaging,
- displacement,
- impedance,
- temperature,
- chemical concentration

Sensor

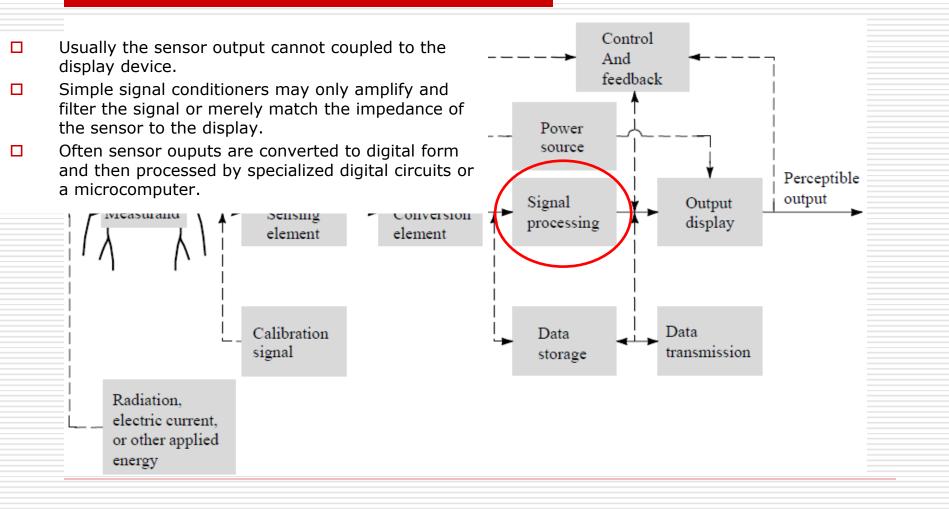


Sensor is a device that converts physical measurand to an electric signal. (Sensor is a type of transducer but transducer is not necessarily a transducer such as an actuator.)

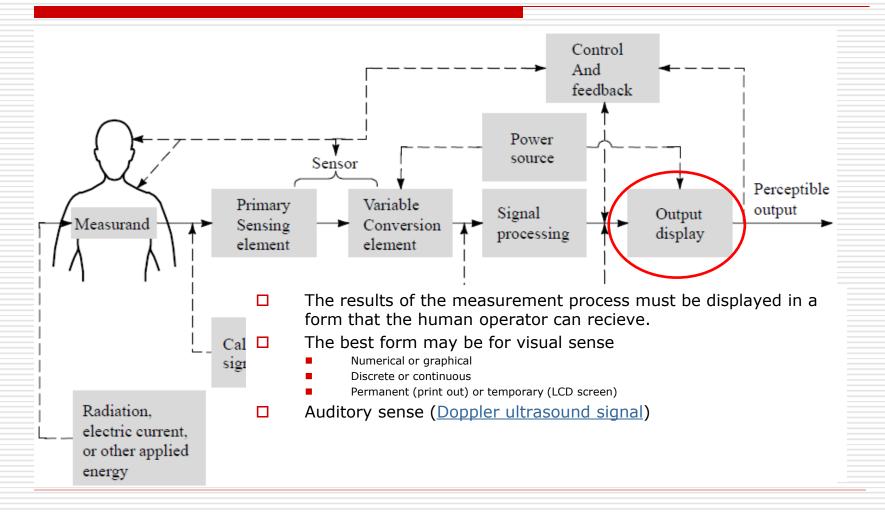
Sensor should

- respond only to the form energy present in the measurand and exclude others.
- Minimize the energy extracted
- Be minimally invasive.
- Primary sensing element gives an output (mostly linear) that is a function of measurand. Mercury-inglass thermometer outputs temperature reading in terms of the level of the mercury.
- Variable conversion elements are needed where the output variable of a primary sensing element is in an inconvenient form and has to be converted to a more convenient form.
- For instance, the displacement-measuring strain gauge has an output in the form of a varying resistance. The resistance change cannot be easily measured and so it is converted to a change in voltage by a bridge circuit, which is a typical example of a variable conversion element.
- Many variable conversion elements need an external electric power to obtain a sensor output.

Signal Contioning

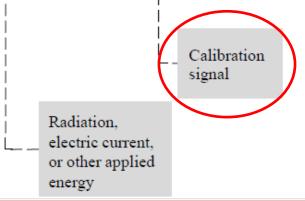


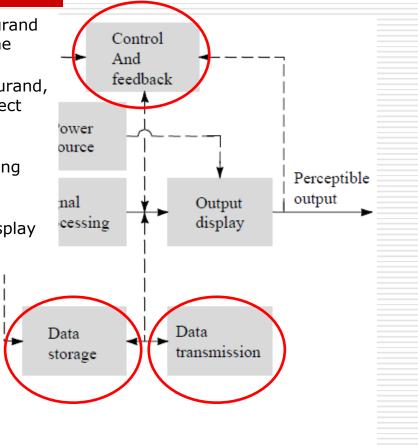
Output Display



Auxiliary Elements

- □ **Calibration** according to the properties of the measurand should be applied to the sensor input or as early in the signal processing chain as possible.
- Control and feedback is required to elicit the measurand, to adjust the sensor and signal conditioner and to direct the flow of output for display, storage and signal conditioner.
- Data Storage may be necessary for signal conditioning and signal processing and to enable the operator to examine data that precede alarm conditions.
- Data Transmission may be required for remote deisplay at nurses's statins, medical centers, or medical dataprocessing facillities.





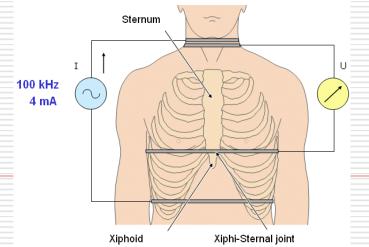
Alternative Operational Modes Direct-Indirect Modes

Direct mode, accessible,

- Invasive, e.g. Blood glucose meter
- Non invasive, e.g. Thermometer
- When the desiren measurand is not accessible, we can use either another measurand that bears a known relation to the desired one or some form of energy or material that interacts with the desired measurand to generate a new measurand that is accessible

Indirect mode, not accessible,

- □ Cardiac output (volume of blood pumped per minute by the heart) determined from
 - Measurements of respiration and blood gas concentration (invasive or non-invasive)
 - Dye dilution (invasive): measured from the speed of indicator substance passing from injection site to measurement site.
- Morphology of internal organs determined from x-ray shadows (non-invasive)
- Pulmonary volumes determined from variations in thoracic impedance plethysmography (non invasive).

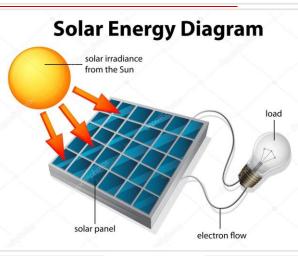


Sampling and Continuous Modes

- Measurands such as body temperature and ion concentrations that change slowly sampled infrequently
- Fastly changing measurands such as ECG, repiratory gas flow is measured continuously
- Measuring mode such as sampling or continuus are determined based on
 - objective of the measurement
 - condition of the patient
 - potential liability of the physician

Generating and Modulating Sensors

- Generating sensor produce their signal output from energy taken directly from the measurand. Example, photovoltaic cell.
- Photovoltaic light sensor is the Solar Cell. Solarcells convert light energy directly into DC electrical energy in the form of a voltage or current to a power a resistive load such as a light, battery or motor.
- Modulating sensors use the measurand to alter the flow of energy from an external source in a way that affects the output of the sensor. Example, photoconductive cell.
- Photoconductive Cell is called the Light Dependent Resistor or LDR. A Photoconductive light sensor does not produce electricity but simply changes its physical properties when subjected to light energy. The most common type of photoconductive device is the Photoresistor which changes its electrical resistance in response to changes in the light intensity.

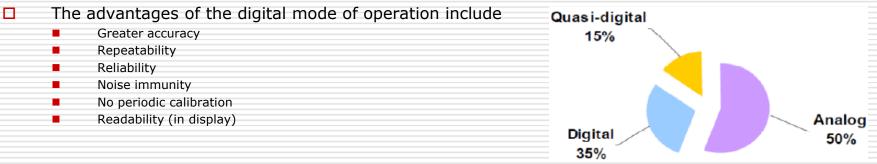




Analog and Digital Modes

Sensor types are

- Analog: continuous in time and continuous in amplitude,
- Digital: discrete in time and take only a finite number of different values
- Quasi digital: variable frequency, pulse rate, or pulse duration that are easily converted to digital signals
- Analog sensors require analog-to-digital converters for digital signal processing
- Digital sensors require digital-to-analog converters to interfaace with analog display devices.
- □ There are indirect digital sensors that use analog primary sensing elements and digital variable-conversion elements, e.g. optical shaft encoders.
- Quasi-digital sensors combine a simplicity and universatility that is inherent to analog devices and accuracy and noise immunity, proper to sensors with digital output.



Many clinicians prefer analog display to check whether a physiological variable is within certain limits or to observe a fastly changing variable such as heart rate since it is annoying to observe it on digital display

Real-Time and Delayed-Time Modes

- Sensors acquire signals in real time as the signals actually occur. The putput of the measurement system may not display the result immediately.
- Some types of signal processing such as averaging and transformations need considerable input before any results can be produced.
- In the case of some measurements such as cell cultures, several days may be required before an output is obtained.

1.4 Medical Measurement Constraints

- □ Typical medical parameter magnitude and frequency ranges: Table 1.1
- Most of the parameter measurement ranges are quite low compared with nonmedical parameters
 - Small amplitude. Most voltages are in microvolt range
 - Low frequency. Signals are in the audio-frequency range (20*20000Hz) or below.
- Frequent inaccessibility due to the lack of proper measurand-sensor interface. Cardiac output.
- To isolate measurand from other systems of body, it is not possible to turn it off or remove a part of it during measurements.
- Inherent variability with time and among subjects.Body temperature changes between 36.5 and 37.5 degrees. Temperature depends on time of the day, person
- Many feedback loops among physiological systems exist and it is seldom feasible to control or neutralize the effects of these systems on the measurand. The most common method of coping with this variablility is to assume empirical statistical and probalistic distribution functions.
- □ It is difficult to establish safety level of the externally applied energy. X-ray, ultrasonic imaging. The heating of tissue is one effect that must be limited.
- Additional constraints of a medical equipment
 - Reliability
 - Easy to use
 - Must withstand physical abuse and exposure to corrosive chemicals
 - Minimized electric-shock hazards

Table 1.1: Examples of medical and physological paramaters

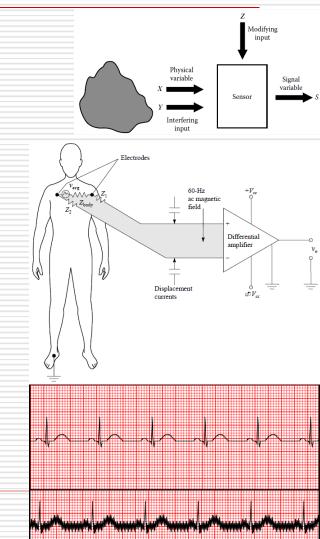
| Parameter or Measuring Technique | Principal Measurement Range of Parameter | Signal Frequency Range, Hz | Standard Sensor or Method |
|---|---|-------------------------------|-----------------------------------|
| Electrocardiography (ECG) | 0.5–4 mV | 0.01–250 | Skin electrodes |
| Electroencephalography (EEG) | 5–300 µV | dc-150 | Scalp electrodes |
| (Electrocorticography and brain depth) | 10–5000 μV | dc-150 | Brain-surface or depth electrodes |
| Electrogastrography (EGG) | 10–1000 µV | dc-1 | Skin-surface electrodes |
| | 0.5–80 mV | dc-1 | Stomach-surface electrodes |
| Electromyography (EMG) | 0.1–5 mV | dc-10,000 | Needle electrodes |
| Eye potentials | | | |
| Electro-oculogram (EOG) | 50–3500 μV | dc-50 | Contact electrodes |
| Electroretinogram (ERG) | 0–900 μV | dc-50 | Contact electrodes |

1.5 Classifications of Biomedical Instruments

- Classification helps comparing different methods of measuring
- Biomedical instruments can be classified into:
- **Quantity** that is sensed: pressure, flow, temperature, etc.
- Principle of transduction: resistive, inductive, capacitive, ultrasonic, electrochemical, etc.
- Organ system: cardiovascular, pulmonary, nervous, endocrine, etc. This class is for specialists who need to know only about a specific area.
- Clinical medicine specialties: pediatrics, obstetrics, cardiology, radiology, etc. This class is for medical personnel who are interested in specialized instruments.

1.6 Interfering and Modifying Inputs

- **Desired input** is the measurand that the instrument is designed to isolate: V_{eca} in Fig. 1.2
- □ **Interfering input** represent the transducer inputs to which the instrument is unintentionally sensitive.
- □ 60-Hz noise, in Fig. 1.2
 - A changing magnetic field B produced by AC can induce in any nearby conductive loop an electromotive force (EMF).
 - A changing electric field E produced by an alternating potential can also produce interference by causing ac currents to flow to ground through the system.
- Modifying input is an undesired quantity that indirectly affect the output by altering the performance of the instrument itself. Modifying inputs can affect processing of either desired or the interferring input: orientation of the patient cables in Fig. 1.2
- If plane of cables are perpendicular to the ac magnetic field, magnetically introduce interference is maximal, otherwise it is zero.
- Interfering inputs generally not correlated to measurand often easy to remove/cancel
- Modifying inputs may be correlated to the measurand more difficult to remove



1.7 Compensation Techniques

- The effects of most interfering and modifying inputs can be reduced or eliminated either by altering the design of essential instrument components or by adding new components.
- □ The first way is preferred since it is simple.

Inherent Insensitivity

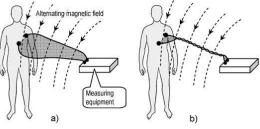
- Make all components inherently insensitive to undesired inputs.
- Twisting the lead wires as done in figure.

Negative Feedback

If the transfer function G_d is affected by modifying inputs, negative feedback the output y by (H_fy) to the input x_d and make H_f insensitive to modifying inputs.

$$(x_d - H_f y)G_d = y \Longrightarrow y = \frac{G_d}{1 + H_f G_d} x_d \qquad \text{If} \ H_f G_d >> 1, \ y \cong \frac{1}{H_f} x_d$$

- This strategy fails if H_f is also affected by modifying inputs.
- Advantages are less power consumption, more accurate and linear response, less loading.
- Disadvantage is dynamic instability leading to oscillations particularly if G_d contains time delays.



1.7 Compensation Techniques

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)
- Instead of input filters composed of electric circuits, many designers prefer electrical, mechanical, pneumatic, thermal, or electromagnetic filters such as shock-proof casings, electromagnetic shielding.
- Electronic filters are often incorporated at some intermediate stage within the instrument. Mixers and modulators are used to shift signals to another frequency range where filtering is more effective. Digital computers are used to filter signals.Filters at input, intermediate, and output stage

Opposing Inputs

- When undesired inputs cannot be filtered, additional interfering inputs can be used to cancel undesired outputs.
- Opposing inputs before or after the appearance of undesired signals
- Output corrections are applied after data collected by having the knowledge of the interfering and/or modifying input.
- To cancel the noise resulting from 60Hz magnetic field, an induced voltage which is produced from present magnetic field by inverting and amplifying, is subtracted from the measured signal.
- Thermistors (temperature dependent resistors) are often used to counteract unavoidable temperature dependent changes in characteristics of active circuit elements such as transistors and integrated circuits.

1.8 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.

1.9 Generalized Static Characteristics

- □ To enable purchasers to compare commercially available instruments and evaluate new instrument designs, quantitative criteria for the performance of instruments are needed.
- □ These criteria must clearly specify how well an instrument measures the desired input and how much the output depends on **interferring and modifying inputs**.
- Characteristics of instrument performance are usually subdivided into two classes on the basis of the frequency of the input signals.
- **Static characteristics**: describe the performance of instruments for dc or very low frequency inputs.
- **Dynamic characteristics**: require the use of differential and/or integral equations to describe the quality of the measurements, neglects the nonlinearities and statistical variability. This simplification is resposible for the difference between ideal and real instrument.

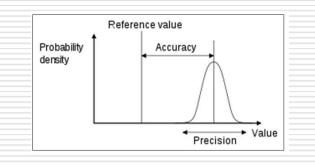


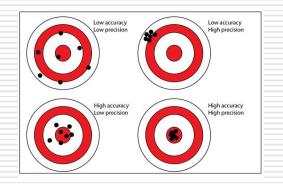
Accuracy

- □ The accuracy (how wrong your measurement is) of a single measured quatitiy is the difference between the true value and the measured value divided by the true value.
- Accuracy usually varies over the normal range of quantity , decreases as the full scale value of the quatitiy decreases on a multirange instrument and also varies with the frequency of inputs.
- Accuracy can be expressed as
 - Percentage of reading
 - Percentage of full scale
 - \pm number of digits for digital readouts, $\pm \frac{1}{2}$ the smallest dvision on an analog scale
- Analog meters usually have their accuracy listed as a percentage of the full-scale reading. When a measured value is close to full scale, or at least above 2/3 of full scale, the published accuracy is meaningful. However, the further away the reading is from full scale, the greater it can deviate from the true value.
- An analog voltmeter with a ±3% accuracy, If the true measured value is, for example, 90.0 V, the meter might read between 87 V and 93 V.
- Digital multimeter (DMM) manufacturers present accuracy specifications in the following format: Complete accuracy specifications: ±(% of reading + number of LSD)
- Accuracy may also include a specified amount of digits (counts) added to the basic accuracy rating. For example, an accuracy of ±(2%+2) means that a reading of 100.0 V on the multimeter can be from 97.8 V to 102.2 V.

Precision

- Precision is too often confused with Accuracy and many consider those two words as synonyms. However, precision has absolutely nothing to do with accuracy.
- Precision is the average value of a set of readings, taken repeatedly with the same measuring device in the same conditions. The deviation of the readings from the mean (average) value determines the precision of the instrument. The figure below illustrates this:





- □ Repeatability and reproducibility are ways of measuring precision.
- For repeatability to be established, the following conditions must be in place: the same location; the same measurement procedure; the same observer; the same measuring instrument, used under the same conditions; and repetition over a short period of time.
- Reproducibility, on the other hand, refers to the degree of agreement between the results of experiments conducted by different individuals, at different locations, with different instruments.

Resolution

- Resolution is the smallest increment a tool can detect and display.
- A digital multi meter having a 20,000 counts meter (4 ½ digit) on its 100 V range will display up to 100.00V. The smallest value it can display on that range would be 0.01V. This is the resolution for this range. The same meter on the 10 V range will display 10.000 V. So its resolution for this range would be 0.001 V (the smallest value it can display on that range).
- The resolution of an analog meter corresponds to the smallest scale subdivision for a particular range.
- The resolution of the instrument above is 0.1 V for the 6VDC range, 0.2 V for the 12VDC range and 0.5V for the 30VDC range.

Counts

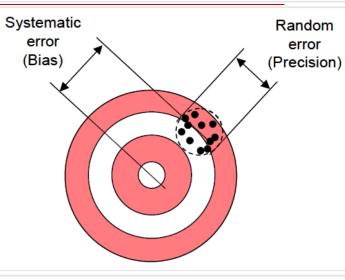
Counts provide the same information as digits but is less ambiguous: The number of counts represents the maximum number the meter can display +1

| 4 ½ Digit Me 20,000 Cour | | 199 199 | 98 |
|---|--------------------|--|----|
| 3 ½ Digit = +- 1999 4 ½ Digit = +- 19999 3 ¾ Digit = +- 3999 4 ^{4/5} Digit = +- 49999 | = 20,00 = 4,000 | Counts 0 Counts 0 Counts 0 Counts | |

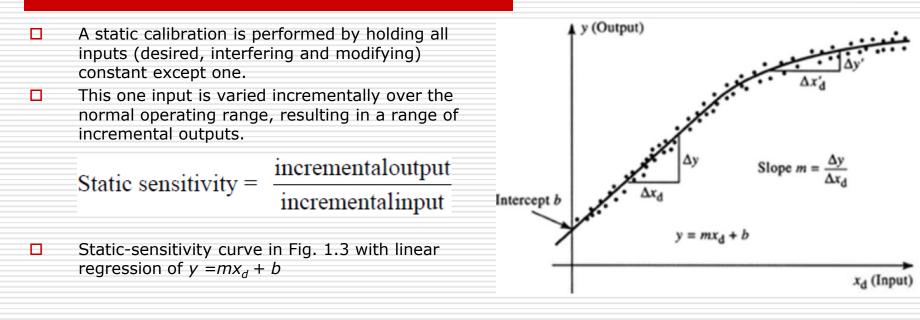


Statistical Control

- Any systematic errors or bias can be removed by calibration and correction factors, but random variations pose a more difficult problem.
- Random errors makes output unreproducible.
- □ If the cause of variability cannot be eliminated, statistical analysis must be done.
- Make multiple measurements and averaging the results can improve the estimate of the true value.
- □ Systematic errors Result from a variety of factors
 - Interfering or modifying variables (i.e., temperature)
 - Drift (i.e., changes in chemical structure or mechanical stresses)
 - The measurement process changes the measurand (i.e., loading errors)
 - The transmission process changes the signal (i.e., attenuation)
 - Human observers (i.e., parallax errors)
- Systematic errors can be corrected with COMPENSATION methods (i.e., feedback, filtering)
- Random errors are also called NOISE: a signal that carries no information such as true random errors (white noise) following a Gaussian distribution. Sources of randomness:
 - Repeatability of the measurand itself (i.e., height of a rough surface)
 - Environmental noise (i.e., background noise picked by a microphone)
 - Transmission noise (i.e., 60Hz hum)

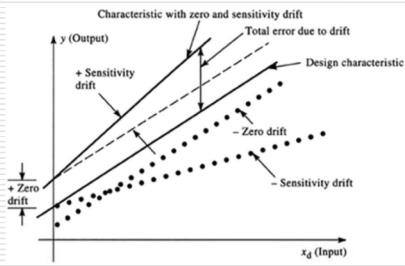


Static Sensitivity



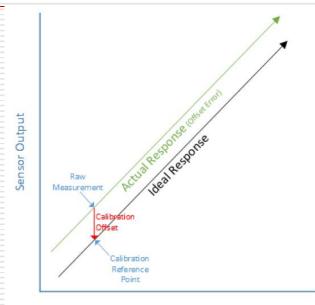
Zero Drift

- Interfering and/or modifying inputs can affect the static calibaration curve.
- Zero drift occurs when all output values increase or decrease by the same absolute amount. The slope of teh sensitivity curve is unchanged.
- Causes
 - Manufacturing misalignment
 - Variations in ambient temperature
 - Hysteresis
 - Vibration
- □ A change in the dc-offset voltage at the electrodes in the electrocardiograph.
- Offsets are easy to correct with a single-point calibration.



One Point Calibration

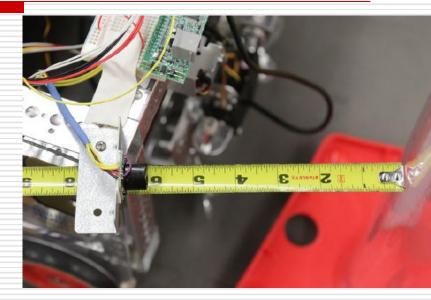
- For example, thermocouples used at very high temperatures exhibit an 'aging' effect. This can be detected by performing periodic one point calibrations, and comparing the resulting offset with the previous calibration.
- To perform a one point calibration:
 - 1. Take a measurement with your sensor.
 - 2. Compare that measurement with your reference standard.
 - 3. Subtract the sensor reading from the reference reading to get the offset.
 - 4. In your code, add the offset to every sensor reading to obtain the calibrated value.





One Point Calibration

- Example: Imagine that you have a competition robot that needs to position itself exactly 6" from a goal in preparation for scoring. You have an ultrasonic rangefinder for your distance sensor. Since you only require maximum accuracy at one distance, a one point calibration is a simple and effictive solution.
 - Using a measuring tape as your reference standard, position the robot exactly 6" from the goal.
 - If you take a reading with your sensor and it says 6.3", then you have a -0.3" offset.
 - Now edit your code to subtract 0.3" from every reading. Since this is known to be a linear sensor it will likely be pretty accurate over most of its
 - range. But you know with great confidence that it will be spot-on at the critical distance of 6".

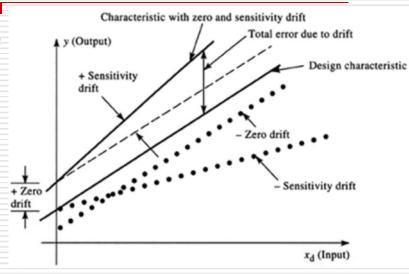


Sensistivity Drift

- Sensistivity drift which is changes in the slope of the calibration curve occurs due to interfering and/or modifying input.
- Sensitivity drift causes error that is proportional to the magnitude of input
- The slope of the calibartion curve can either increase or decrease.

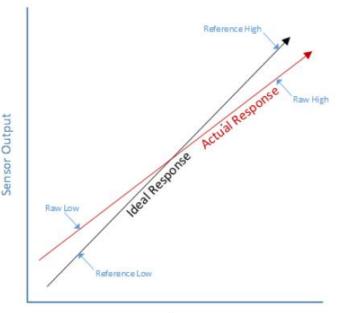
Causes

- 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
- The Two-point calibration process can correct differences in slope.



Two Point Calibration

- A Two Point calibration essentially rescales the output and is capable of correcting both slope and offset errors. Two point calibration can be used in cases where the sensor output is known to be reasonably linear over the measurement range.
- □ To perform a two point calibration:
 - 1. Take two measurement with your sensor: One near the low end of the measurement range and one near the high end of the measurement range. Record these readings as "RawLow" and "RawHigh"
 - 2. Repeat these measurements with your reference instrument. Record these readings as "ReferenceLow" and "ReferenceHigh"
 - 3. Calculate "RawRange" as RawHigh RawLow.
 - 4. Calculate "ReferenceRange" as ReferenceHigh ReferenceLow
 - 5. In your code, calculate the "CorrectedValue" using the formula below:
 - CorrectedValue = (((RawValue RawLow) * ReferenceRange) / RawRange) + ReferenceLow





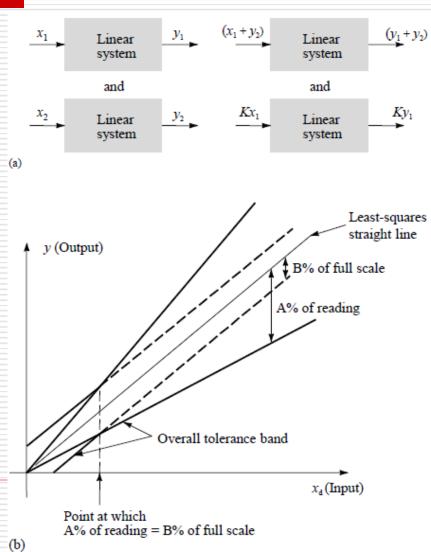
Two Point Calibration

- A common example of a two-point calibration is to calibrate a temperature sensor using an icewater bath and boiling water for the two references. Thermocouples and other temperature sensors are quite linear within this temperature range, so two point calibration should produce good resuts.
- Since these are physical standards, we know that at normal sea-level atmospheric pressure, water boils at 100°C and the <u>"triple point"</u> is 0.01°C. We can use these known values as our reference values:
- **ReferenceLow = 0.01°C**, ReferenceHigh = 100°C, ReferenceRange = 99.99
- RawLow = -0.5°C, RawHigh = 96.0°C, RawRange = 96.5°C
- □ So, if we get a raw reading of **37°C** with this thermometer, we can plug the numbers into the equation to get the corrected reading:
- $\square \quad (((37 + 0.5) * 99.99) / 96.5) + 0.01 = 38.9^{\circ}C$



Linearity

- A system is linear if following requirements are satisfied.
- Linearity eliminates the need to do any complex curve-fitting and simplifies the calibration process.
- High accuracy does not necessarily implies linearity. A sensor can be highly accurate but also have a totally non-linear output function, and sensors with very linear outputs can be highly inaccurate.
- In practice, no instrument has a perfect linear response, so a measure of deviation from linearity is needed.
- Independent nonlinearity expresses the maximal deviation of points from the least squares fitted line.
- Measure of deviation from linearity is A% of reading or B% of full scale, whichever is greater (Fig. b)



Text Book

John G. Webster, Medical Instrumentation Application and Design, 4th Edition