Chapter 1
Bio-optoelectronic Measurements
光電生醫量測技術

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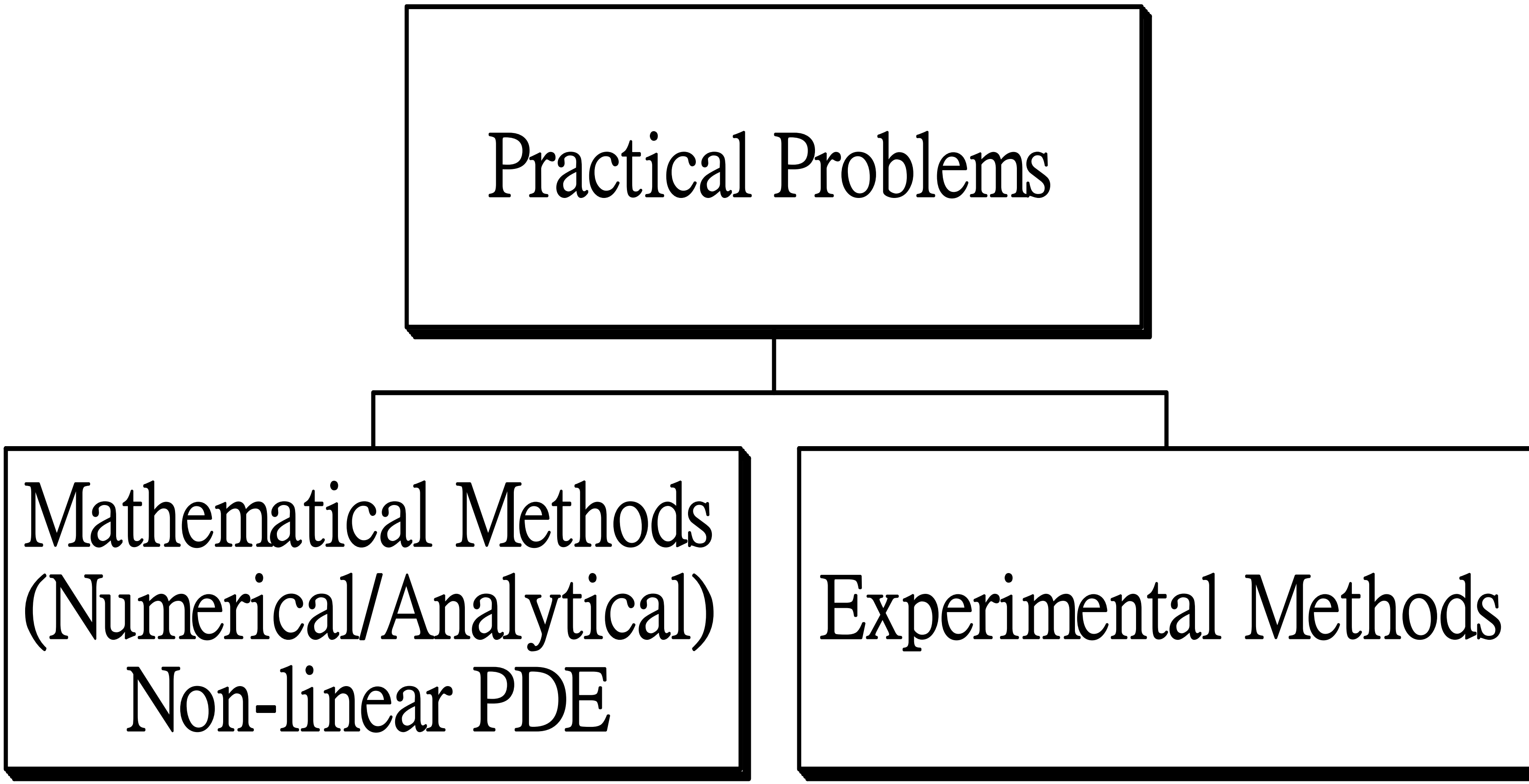
Lecture Contents

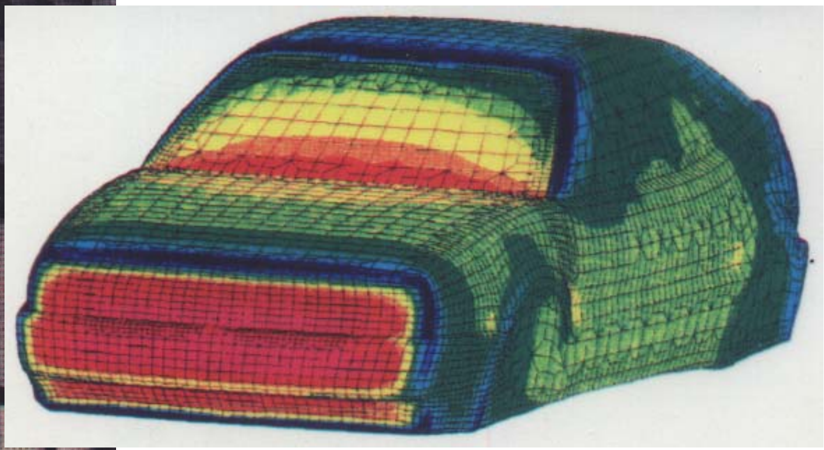
Date	課程名稱	週數	授課教師
2/22	光電生醫量測簡介	1	王安邦
3/1; 3/8; 3/15; 3/22	紅外線溫度量測理論與實習	4	楊丙?
3/29*	紅外線生醫影像應用與診斷	1	楊永健
4/11; 4/18; 4/25* (Mon.)	核磁共振掃描技術、應用及其發展	3	曾文毅
5/3	光電速度與粒徑量測理論	1	王安邦
5/10	光電速度量測之生醫應用	1	余幸司
5/17	內視鏡原理應用與未來發展	1	謝銘鈞
5/24	雷射光電技術於眼科之量測、診斷、應用與未來發展	1	尤之浩
5/31; 6/7; 6/14	奈米光電生醫量測原理、應用與未來發展: (1) 原子力顯微術、掃描穿隧顯微術、近場光學顯微術：生物奈米量測與奈米診斷。 (2) 光學生物晶片與生物感測器：生物分子間相互作用動力學與量論。 (3) 雙極性干涉術：蛋白構形形變奈米量測。	3	林世明
6/21	期末報告	1	王安邦/林世明

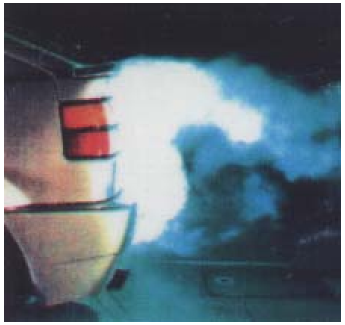
*** 18:30 ~ 21:15**

Tools for Solving Problems in Engineering



Experiments & Simulations in Engineering

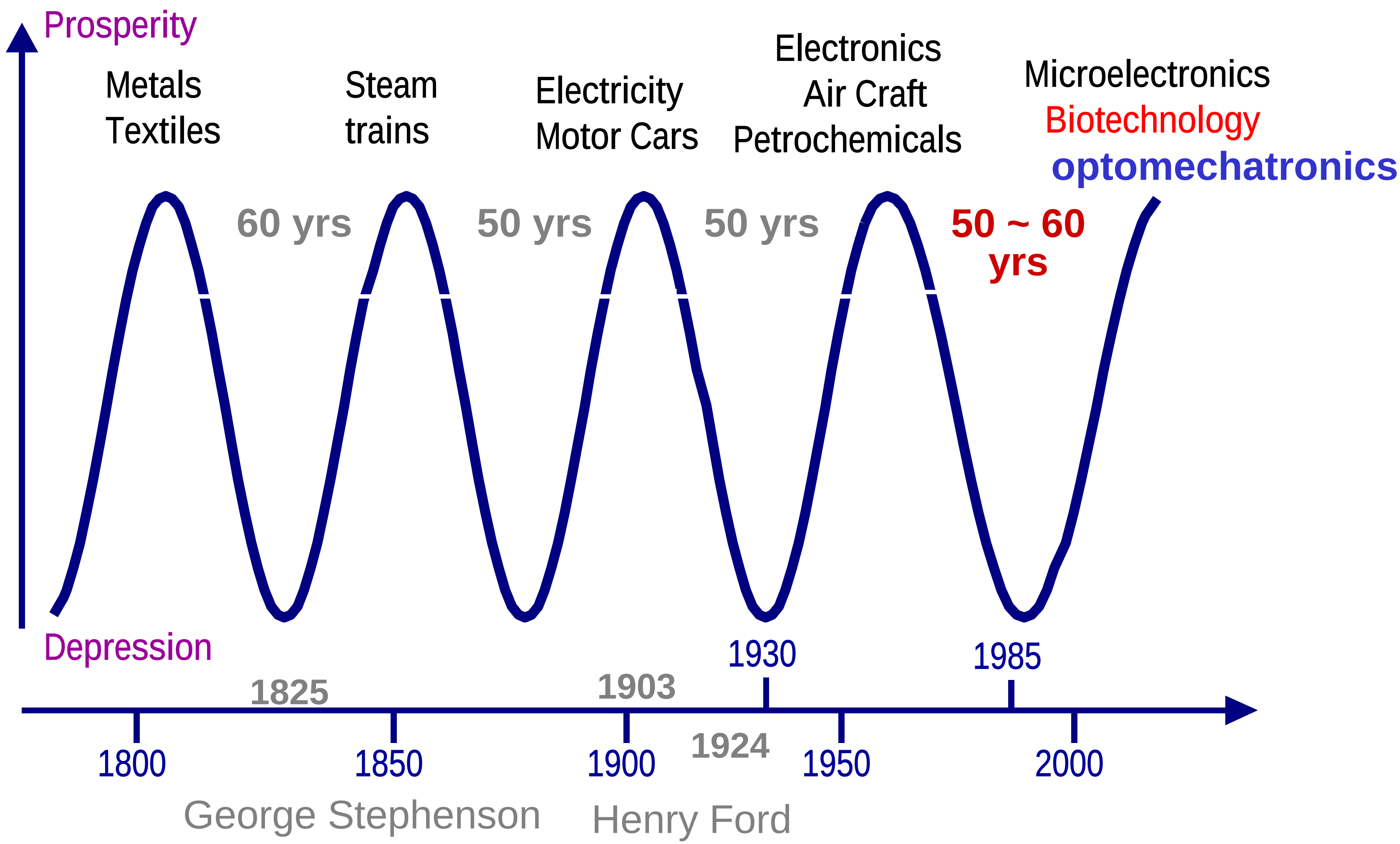




From Pure Engineering to Bio-optoelectronic measurements

- Life is invaluable
- Life is environmental-condition-dependent
- Life is time-dependent
- The bio-medical measurements are much more complicated …
- More interactions between engineering and medical colleges are needed

Trend of the world



What is Temperature?

❑ Qualitative Definitions:

1. The degree of hotness or coldness of a body.
2. All bodies have the same temperature if they are in thermal equilibrium.
3. The level of thermal energy. (cf. Electrical energy; Mechanical potential energy.)

❑ Units of temperature (one of System International units, SI) :

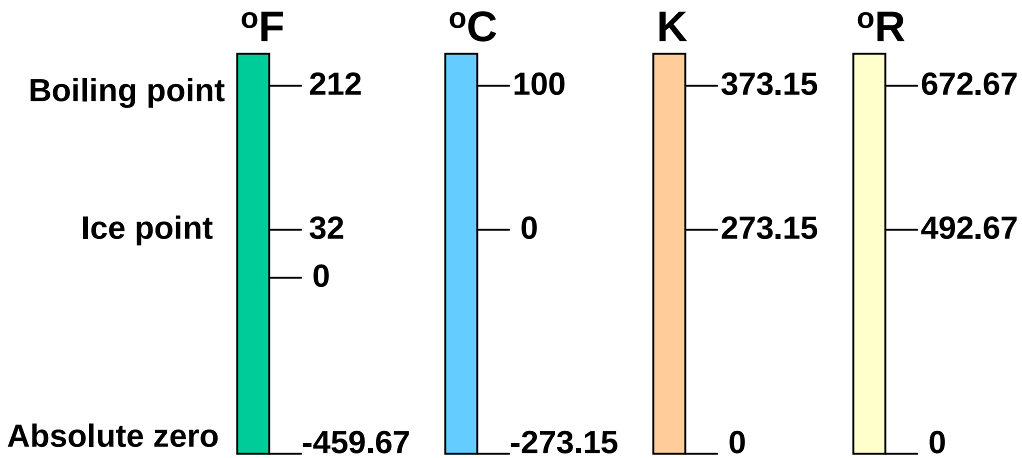
Unit		Symbol	Quantity measured
Dimensional	1. Meter	m	Length
	2. Kilogram	kg	Mass
	3. Second	s	Time
	4. Ampere	A	Electric current
	5. Kelvin	K	Temperature
	6. Mole	mol	Amount of substance
	7. Candela	cd	Luminous intensity
Dimensionless	8. Radian	rad	Plane angle
	9. Steradian	sr	Solid angle

(from Lee (2001))

How to Quantify the temperature?

- **Four common temperature scales:**

  Fahrenheit(1708), Celsius(1740), Kelvin(1848), Rankine(1730)



$$^{o}F = \frac{9}{5}(^{o}C) + 32$$

$$^{o}C = \frac{5}{9}(^{o}F - 32)$$

$$K = 273.15 + {}^{o}C$$

$$^{o}R = 459.67 + {}^{o}F$$

- **Fundamental temperature scales:**

  The relationship of measured variable to temperature depends only on fundamental physical constants, not on arbitrary calibrating constants.

  Examples:

  1.Thermodynamic, PV=PV(T, $\underline{N_A}$, $\underline{k}$)

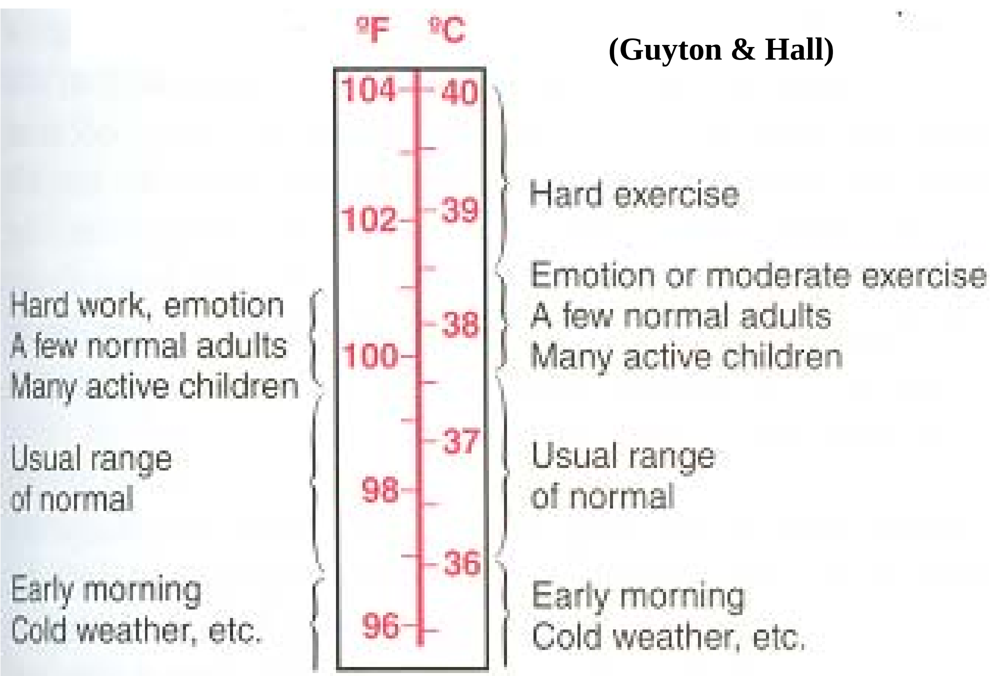
  2.Thermal radiance, W=W(T, $\underline{k}$, $\underline{c}$, $\underline{h}$)

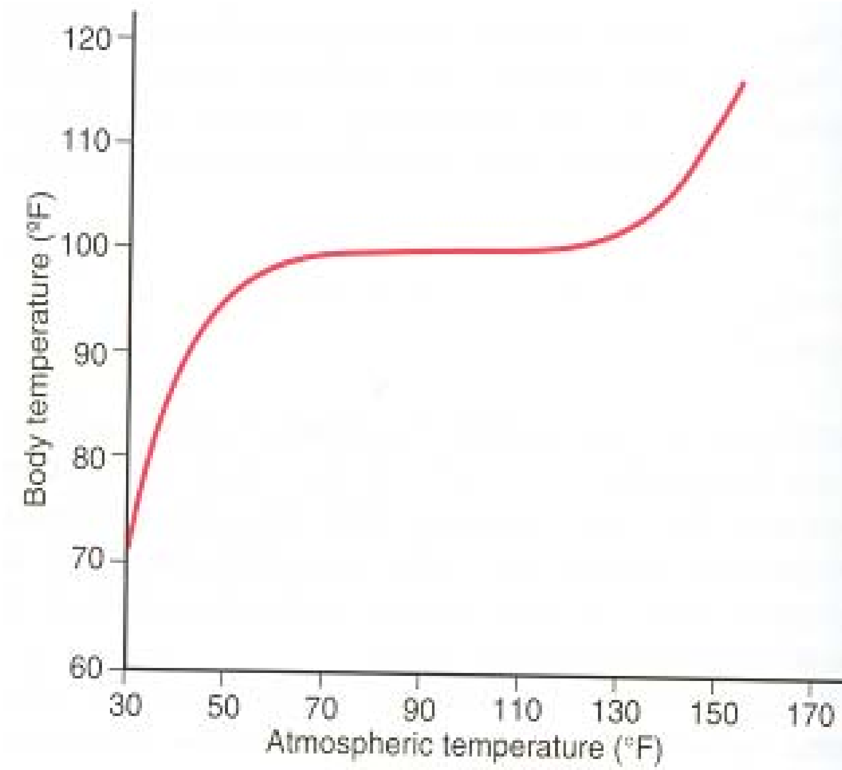
(from Lee (2001))

Body temperature & it's control

- Core temperature and skin temperature
- Core temperature remains almost constant 98~98.6±1ºF, (36.7~37±0.6ºC) except illness.

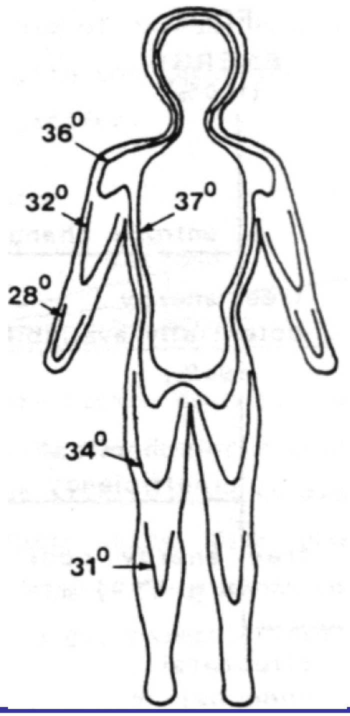
(Guyton & Hall)





Body temperature & it's control

- Temperature measurement depends on position (rectal ~ oral + 0.6^{o}C), exercise and surrounding conditions.
- Body temp. is controlled by balancing heat production against heat loss
- Most heat of body is produced from liver, brain, heart (and skeletal muscles during exercise) and lost through skin to the air.



Heat production & lose

- **Heat production is main by-product of metabolism**
- **Metabolic rate of body is influenced by**

  - **basal metabolism of all cells of body**

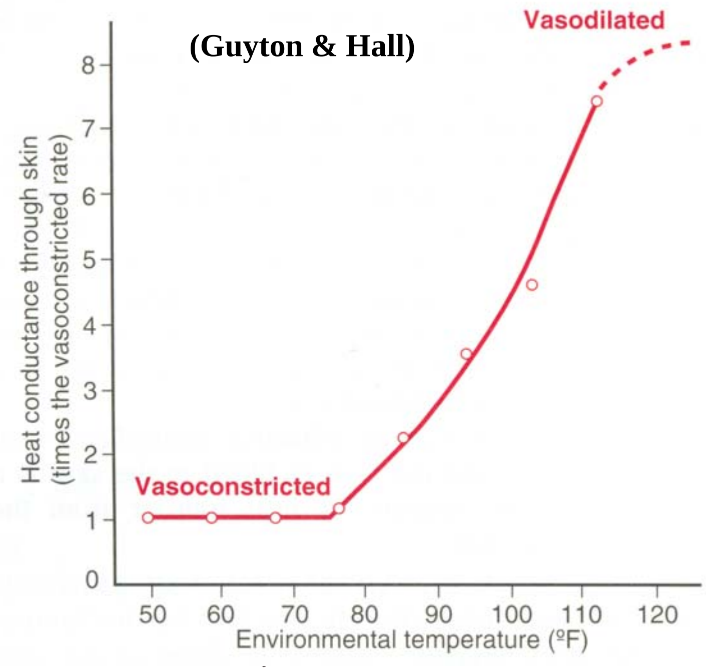
  - **extra metabolism of muscle activity**

  - **extra metabolism by thyroxine (甲狀腺素), epinephrine(腎上腺素), norepinephrine (正腎上腺素), sympathetic stimulation on the cells.**

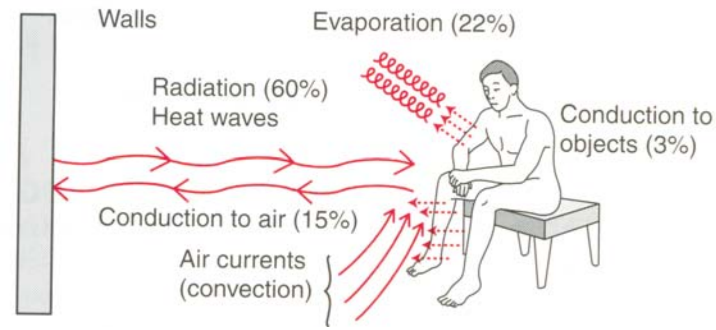
  - **extra metabolism by increased chemical activity in cells**

Thermal Insulation of body

- **The fat of subcutaneous tissues, conduct heat only 1/3 as other tissues, act as the main heat insulator of body.**
- **Heat loss decreases ~50% for usual suit of clothes. About 50% heat transmitted from skin to the clothing by radiation. Insulating property could increase by Au-coating inside of clothing**
- **Blood flow from the body core to the skin, the effective *heat radiator*, provides heat transfer of the body**
- **Heat transfer to skin by blood is controlled by sympathetic nervous system**



How does heat loss from skin ?

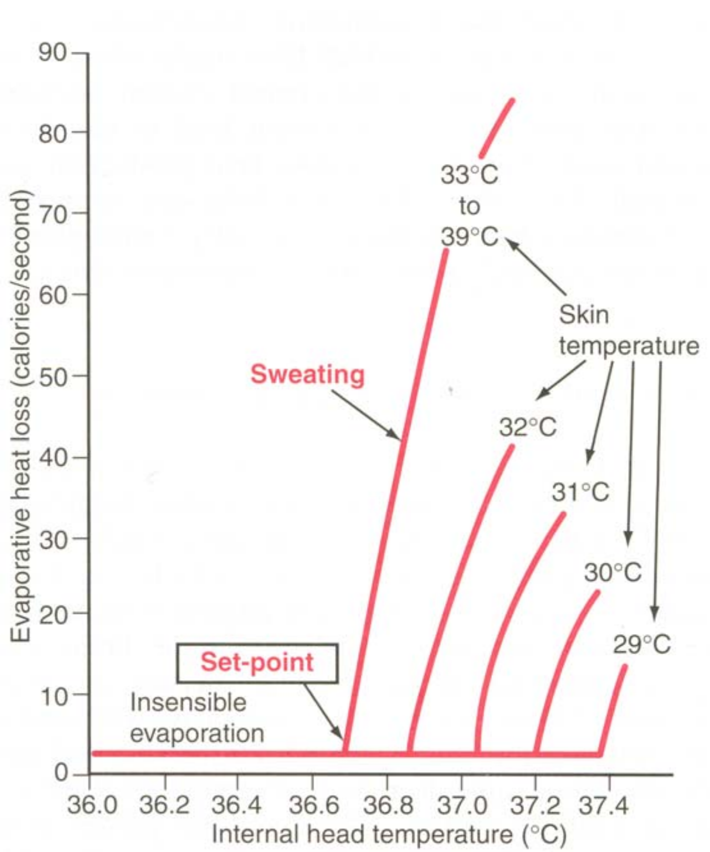


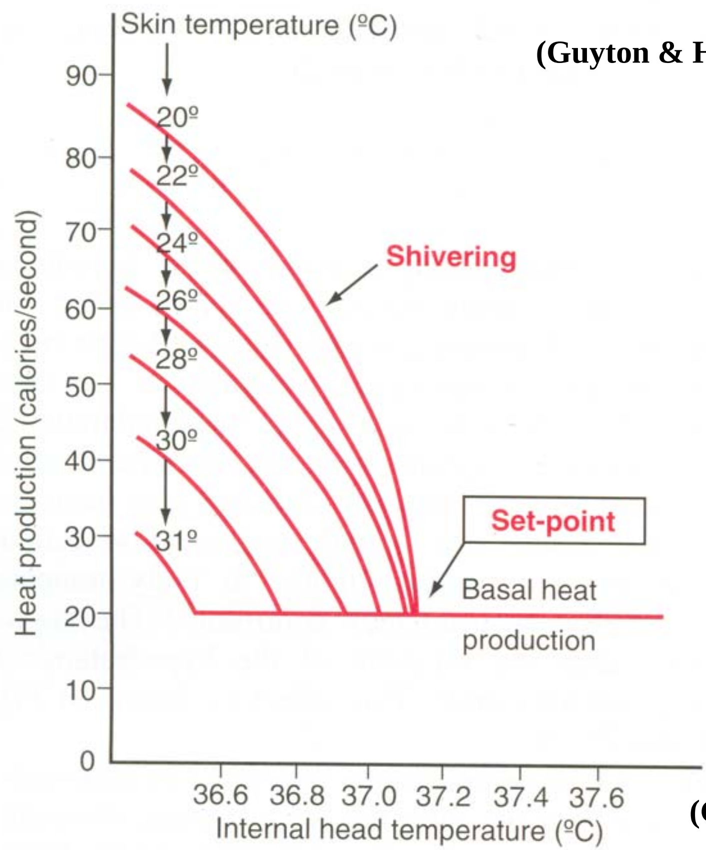
(Guyton & Hall)

- **Body heat is lost by radiation, conduction and evaporation**
- **Radiation of a nude person in room at T_{room} is ~60% total heat loss. Wave length of radiation: 5 ~ 20 μm.**
- **About 15% of total heat loss is conducted to the air. The cooling effect of wind (at low wind velocity) is proportional to (wind velocity)$^{0.5}$**
- **Evaporation heat of water: 0.58 kcal/g.**
  Water is insensibly evaporated from skin and lungs (without sweating) at a rate of 450~600 ml/day (12 ~ 16 Kcal/hr). Evaporation is necessary cooling mechanism at very high air temperature.

Skin temperature v.s. Core temperature

Thermostatic detection of temperature in the Hypothalamus (下視丘)



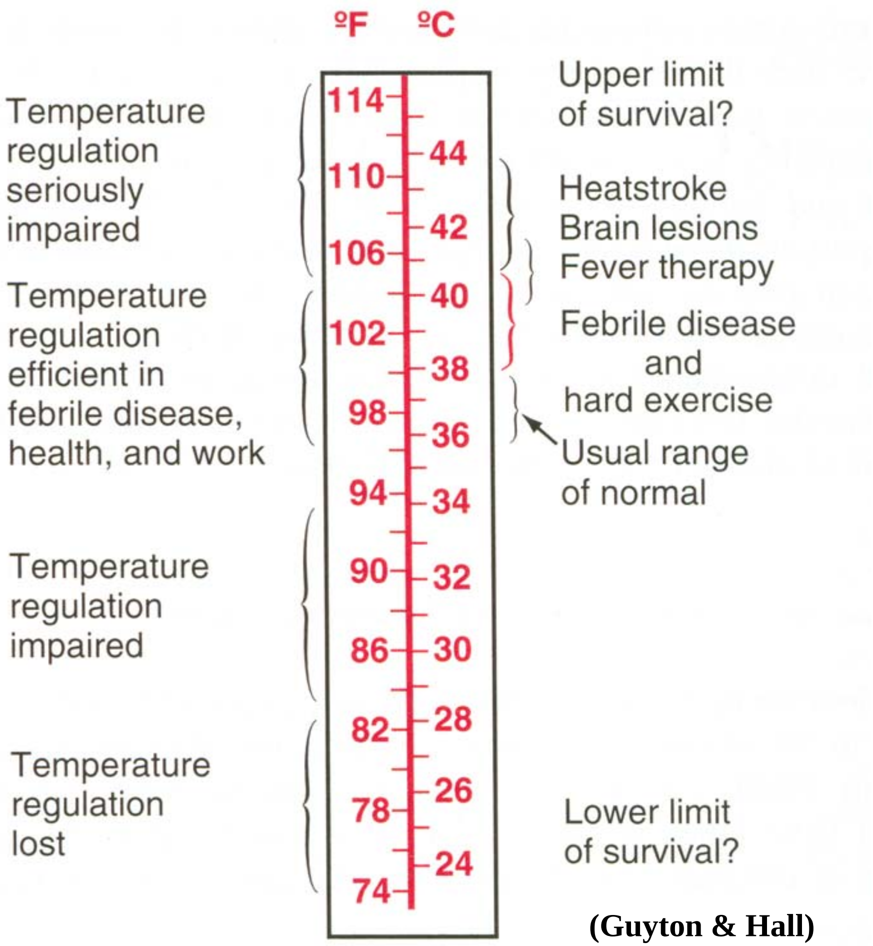


(Guyton & Hall)

(Guyton & Hall)

Abnormality of temperature regulation

Fever means body temperature above the normal range that can be caused by abnormalities in the brain itself or by toxic substances that affect the temperature regulation system. They include bacterial diseases, brain tumors, … etc.



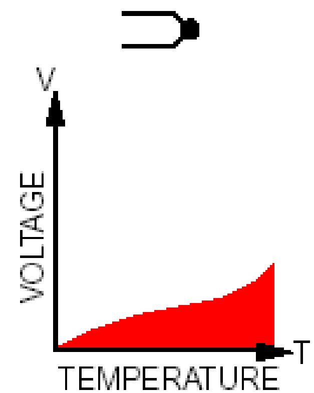
(Guyton & Hall)

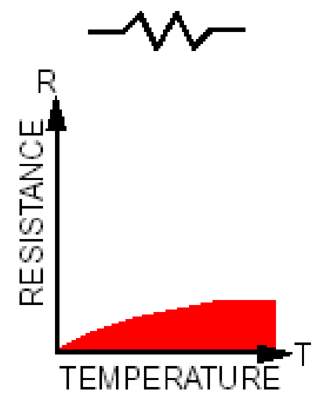
Classification of Temperature Sensors

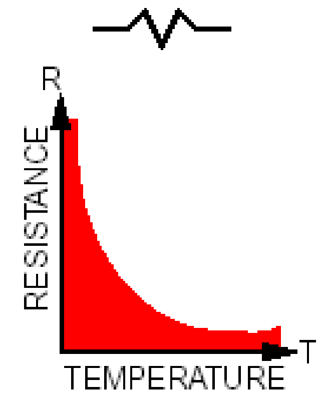
	Principle							
Sensor	**Thermo-electric**	**Electrical Resistance**	**Carrier Mobility**	**Thermal Radiation**	**Electrical Capacitance**	**Thermal Expansion**	**Resonant Frequency**	**Others**
Thermocouple	■							
Thermopile	■							
RTD(PTC, NTC)		■						
Thermistor		■	■					
P-N junction			■					
Optical pyrometer				■				
Pyro-electric				■	■			
Quantum			■	■				
Spectroradiometer			■	■				
Cooling IR imager			■	■				
Uncooled IR imager	■	■	■	■	■	■		
Gas						■		
Liquid						■		
Bi-metal						■		
Quartz							■	
Liquid Crystal								1
Others								2,3,4,5
[Remark]: 1.Reflectance, 2.Index of Refraction, 3.Ultrasonic, 4.Microwave, 5.Acoustic								

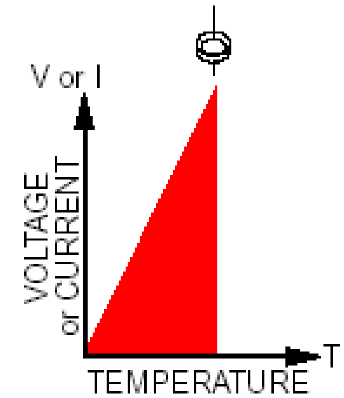
(from Lee (2001))

Analysis of common temperature sensors









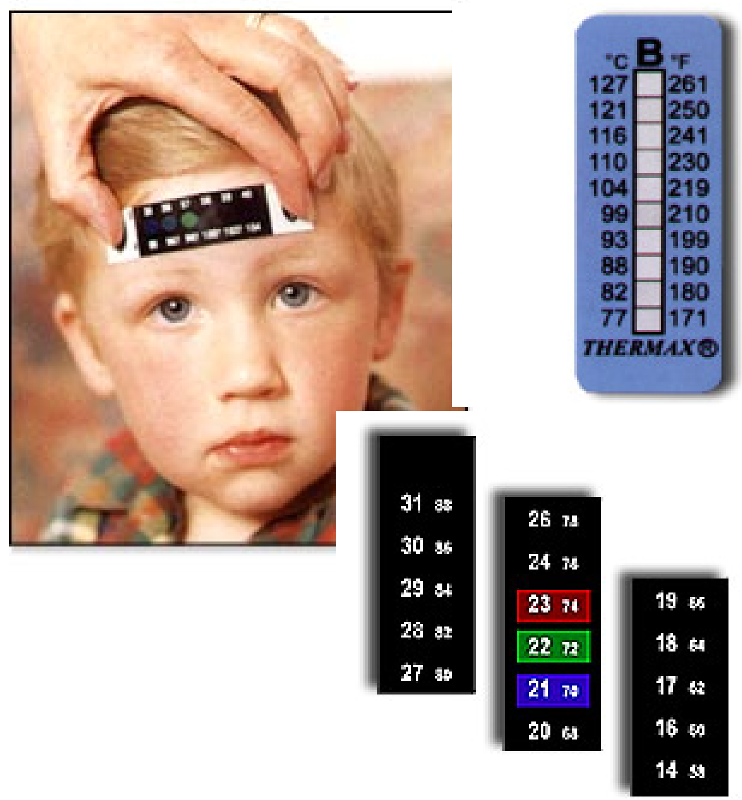
	Thermocouple	RTD	Thermistor	I. C. Sensor
Advantages	☐ Self-powered ☐ Simple ☐ Rugged ☐ Inexpensive ☐ Wide variety ☐ Wide temperature range	☐ Most stable ☐ Most accurate ☐ More linear than thermocouple	☐ High output ☐ Fast ☐ Two-wire ohms measurement	☐ Most linear ☐ Highest output ☐ Inexpensive
Disadvantages	☐ Non-linear ☐ Low voltage ☐ Reference required ☐ Least stable ☐ Least sensitive	☐ Expensive ☐ Current source required ☐ Small Δ R ☐ Low absolute resistance ☐ Self-heating	☐ Non-linear ☐ Limited temperature range ☐ Fragile ☐ Current source required ☐ Self-heating	☐ T<200°C ☐ Power supply required ☐ Slow ☐ Self-heating ☐ Limited configurations

(Omega)

Liquid crystal Thermometer

Forehead Thermometer
Fish box thermometer

- **Safe**
- **convenient**
- **accurate**
- **Time constant: some seconds**
- **Mirror or observer is needed.**



From: Taiwah Charts Corp.

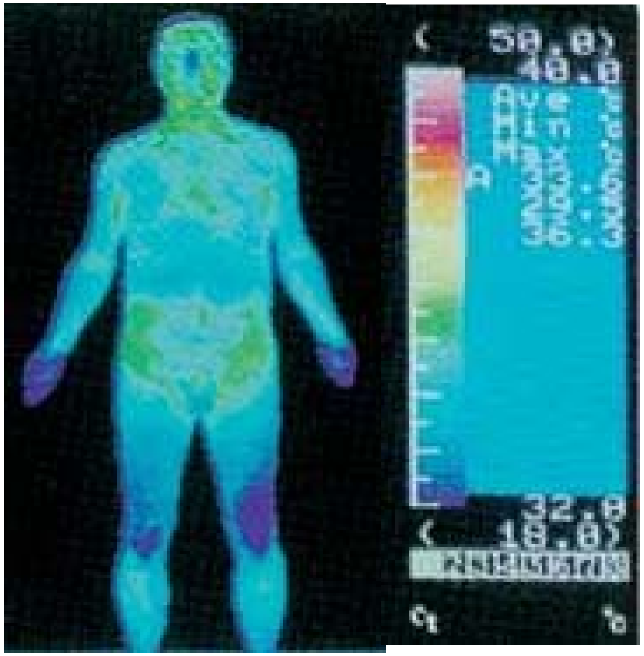
IR measurement

www.vega.org.uk/. ../index.php

- All bodies radiate Infrared wave
- Infrared measurement technology is counted among the key applications in the medical field.
- Thermal examinations of the human body have no harmful effects.
- One of the main applications is the early diagnosis of tumors and skin cancer. A classical use of thermal imaging systems is the detection of disturbances in the venous blood circulation and the early diagnosis of thrombosis and strictures of vessels.

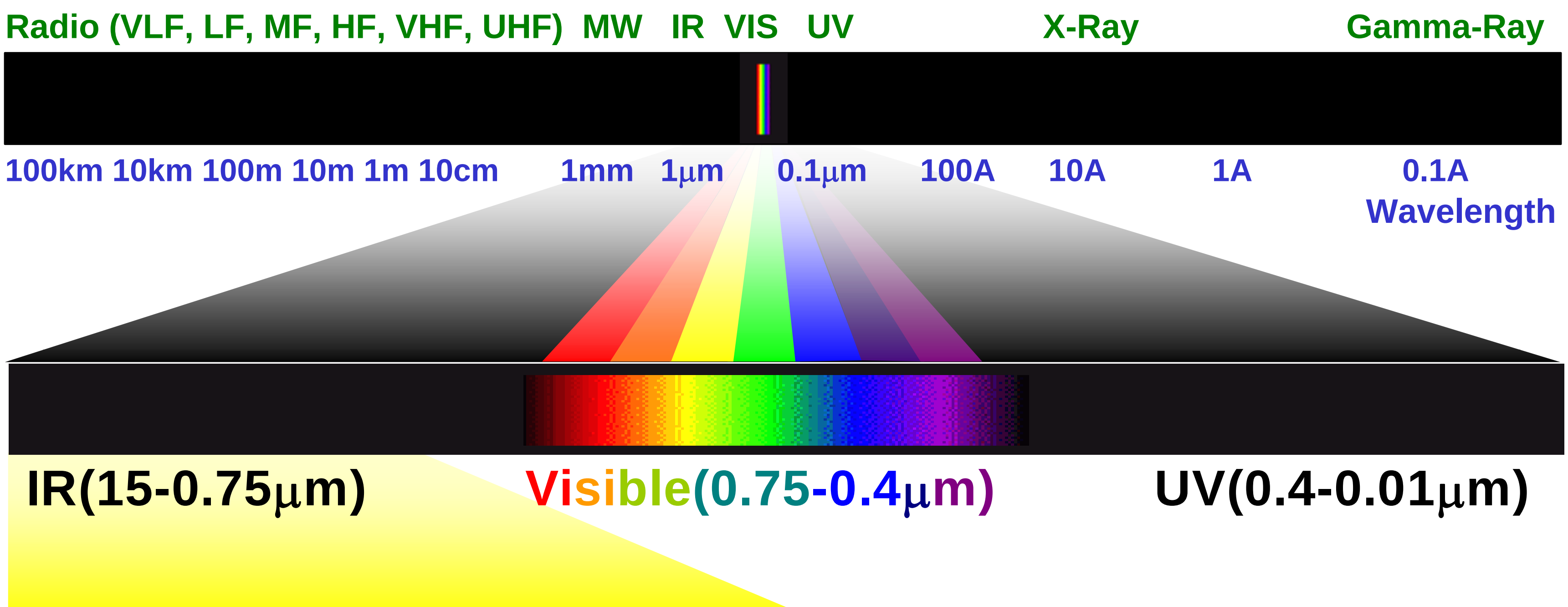
Thermography

Thermography also holds a firm place with transplantations of organs especially of the heart. While implanting the organ the acceptance and the blood circulation can be monitored online and exactly determined. New experiences open up in the surveillance of laser based ablations (i. e. with ophthalmology).



(www.livengood-lifestyles.com)

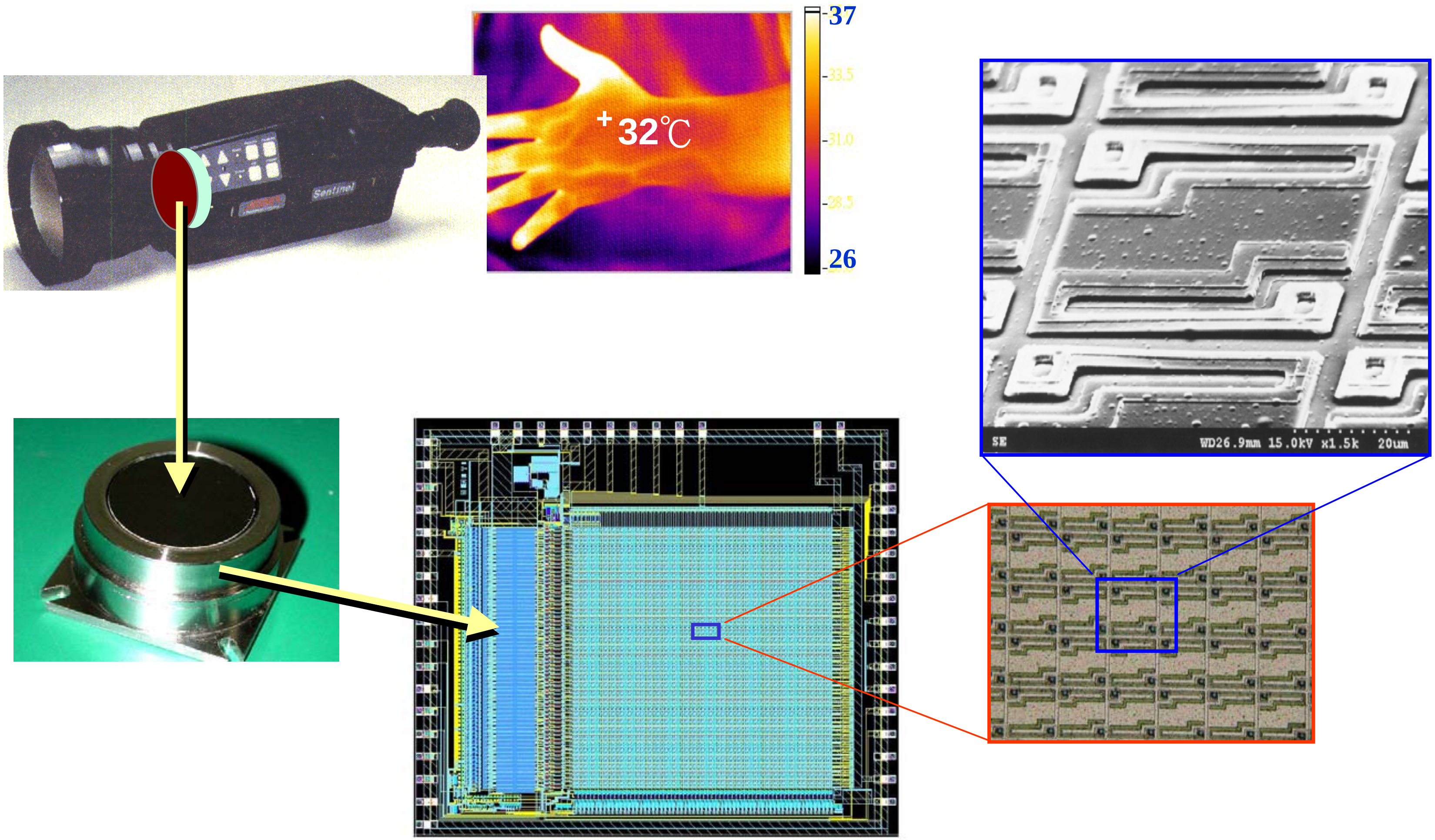
The Electromagnetic Spectrum



Near IR	(NIR)	:	0.75 - 3μm
Middle IR	(MIR)	:	3 - 6μm
Far IR	(FIR)	:	6 - 15μm
Extreme IR	(XIR)	:	15 - 1000μm

(from Lee (2001))

Infrared Imager

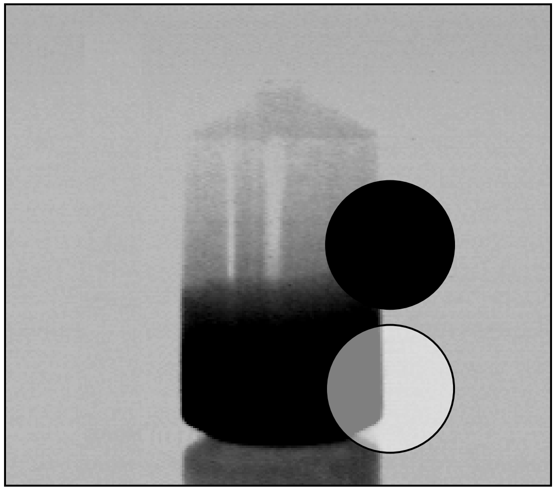


(from Lee (2001))

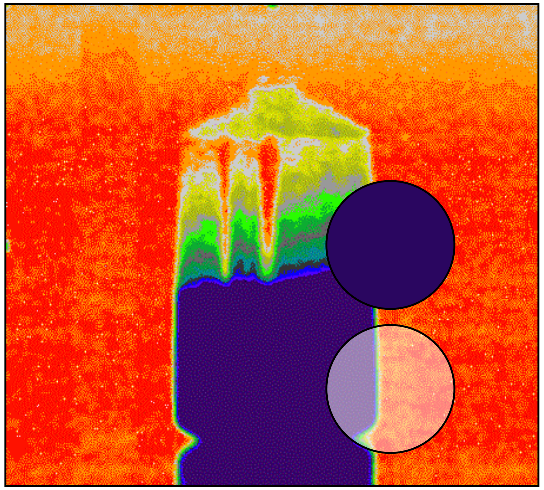
Visible cf. Thermal Radiation (1)

❑ Target signature (Spatial Distribution)

Visible(0.4-0.75μm)



FIR(8-12μm)



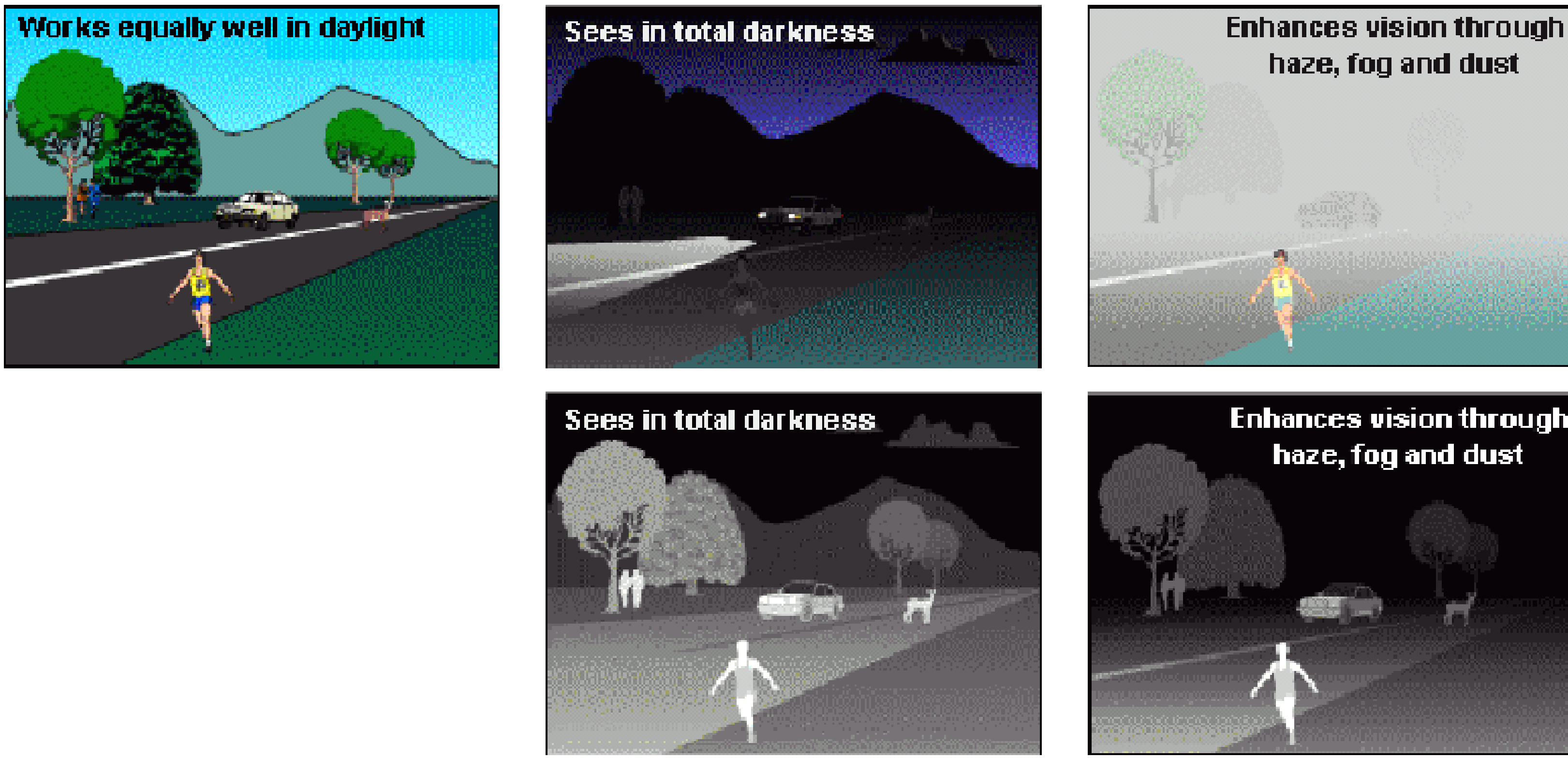
FIR(8-12μm)

- Active sensing：Visible, NIR
- Passive Sensing：Visible, NIR, MIR, FIR

(from Lee (2001))

Visible cf. Thermal Radiation(2)

- ❑ **Background signature (Spatial Distribution)**

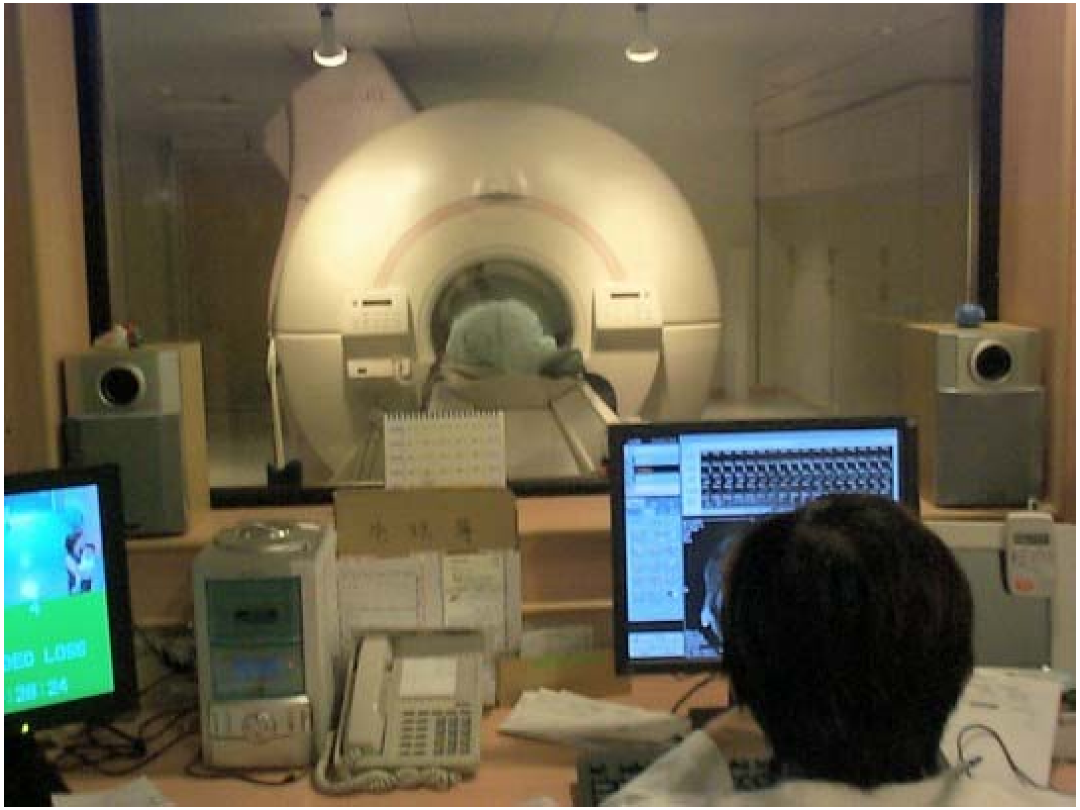


Ref. “Thermal imaging solutions”, TI NIGHTSIGHT interactive explorer.

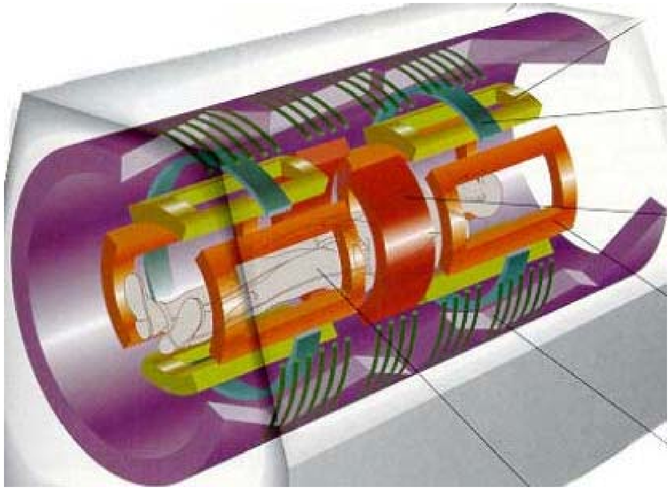
(from Lee (2001))

核磁共振掃瞄

核磁共振掃瞄儀 (Magnetic Resonance Imaging,MRI)



MRI = NMR + Imaging



(From莊凱翔)

膠囊內視鏡

(From: minho.show.org.tw)

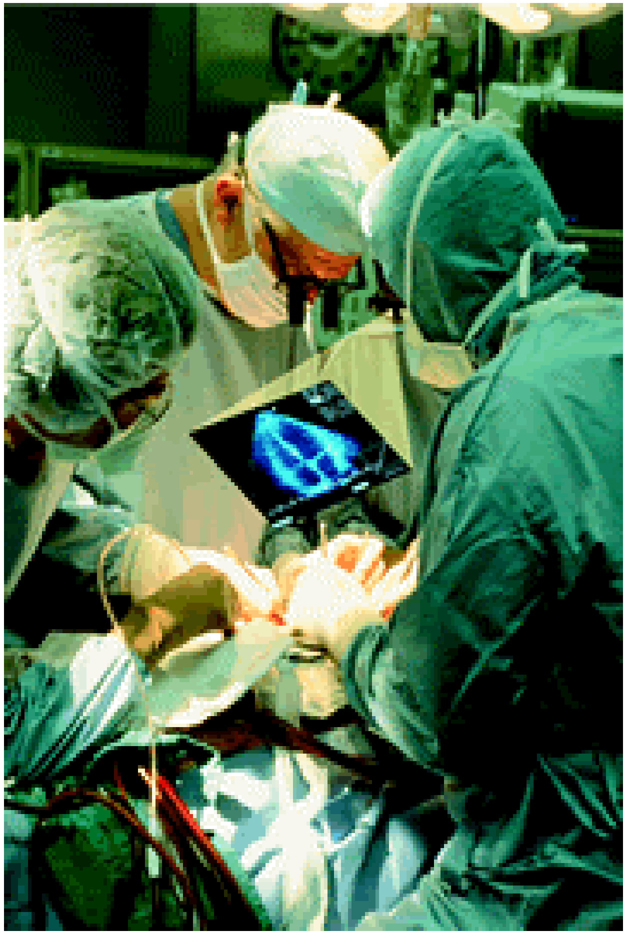
膠囊內視鏡，約11x26釐米大小，內含前端攝影機、影像感應傳送器和精密電池(八小時的電池待命期)。現有的小腸鏡僅能檢查小腸的前三分之一段，檢出率僅三成，而血管攝影與核醫檢查則必須在病灶出血時才能檢出，相較之下，膠囊內視鏡更容易檢出小腸病灶，檢出率約六至七成。限制性，它無法向胃鏡般重覆觀看同一部位，且無法切片，所以有時較難判斷。

眼科光電技術

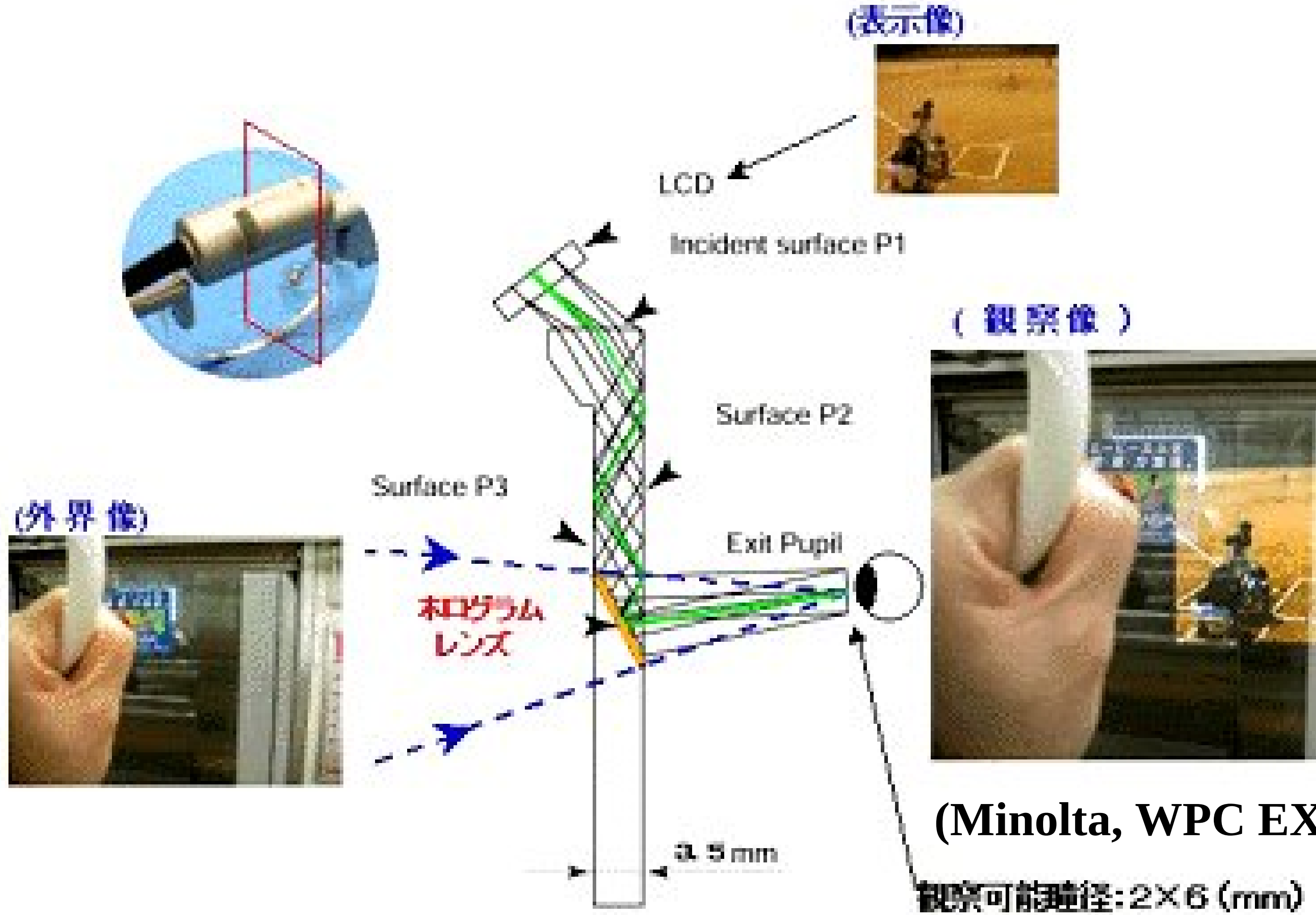
Imaging and Display technology

Picture Archiving and Communication System, (PACS)

醫療影像擷取儲存傳輸系統

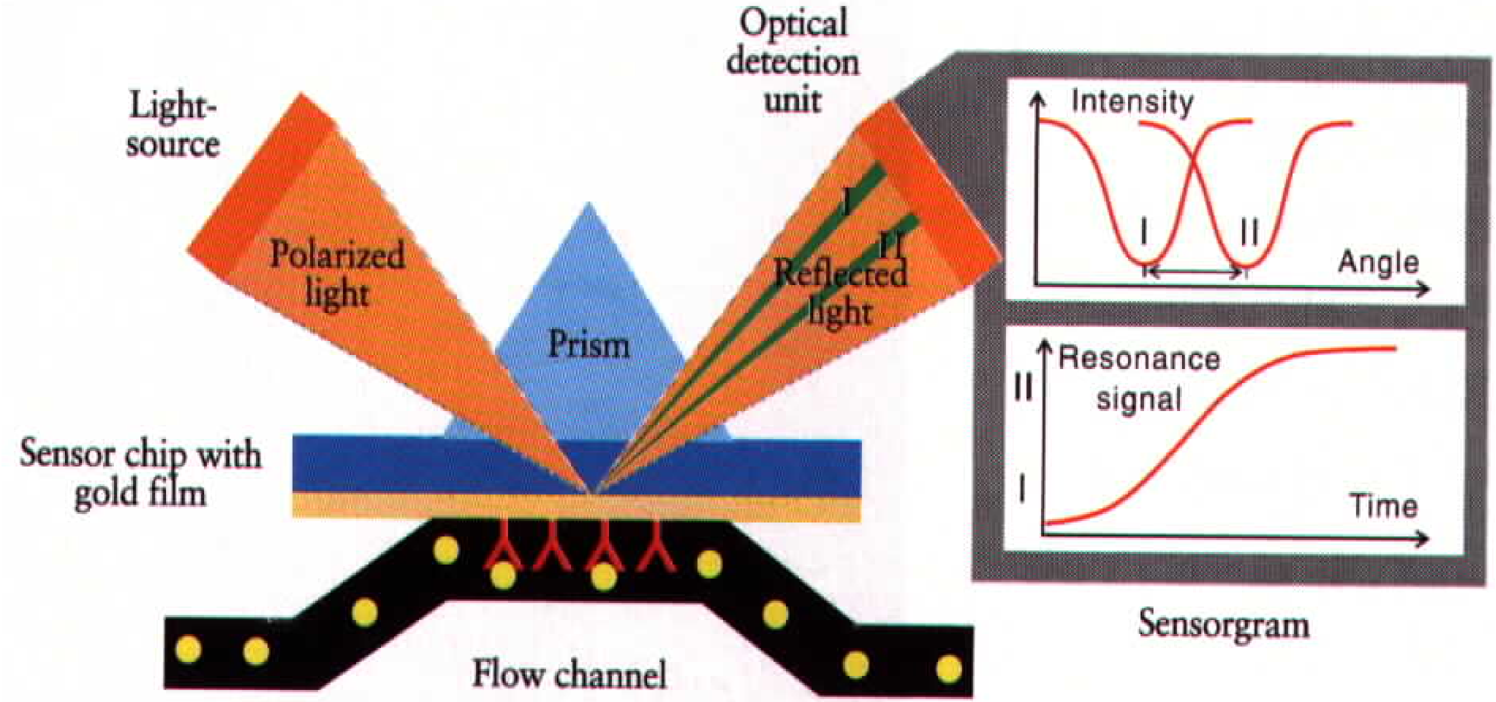


Holographic See-through Browser



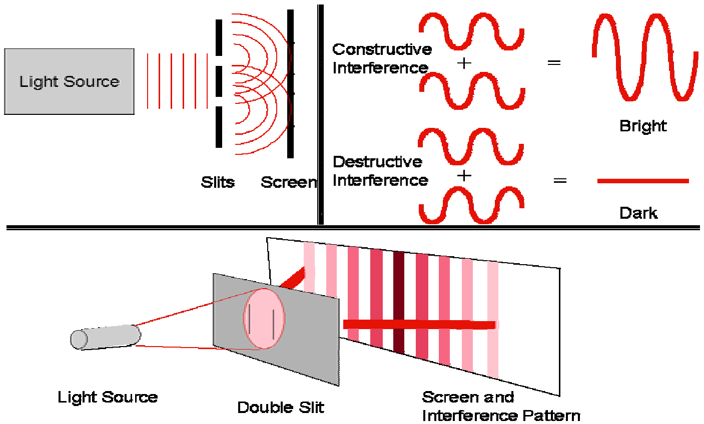
(Minolta, WPC EXPO 2003/9)

Surface Plasmon Resonance (SPR)

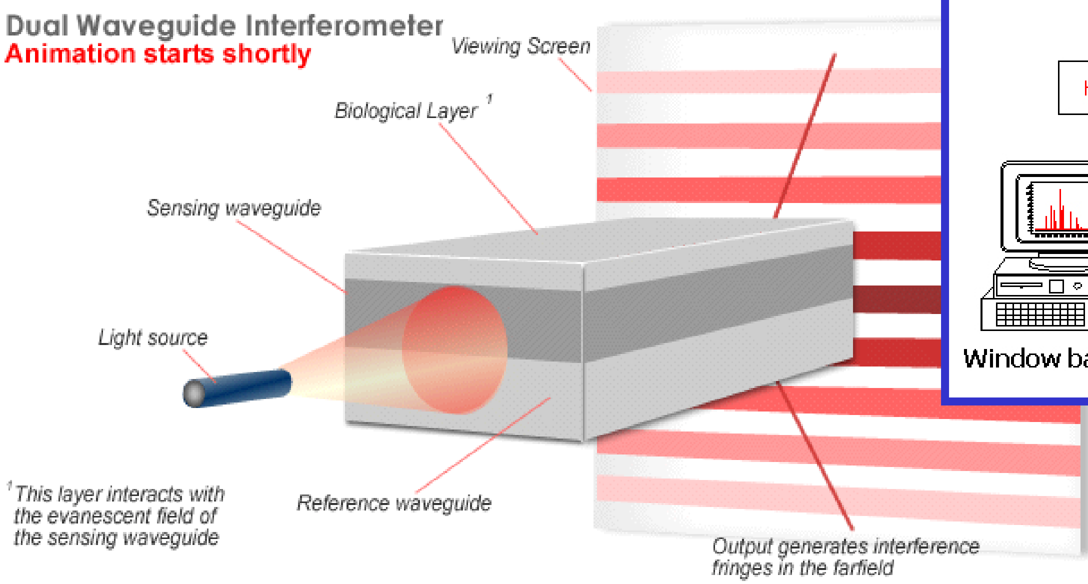


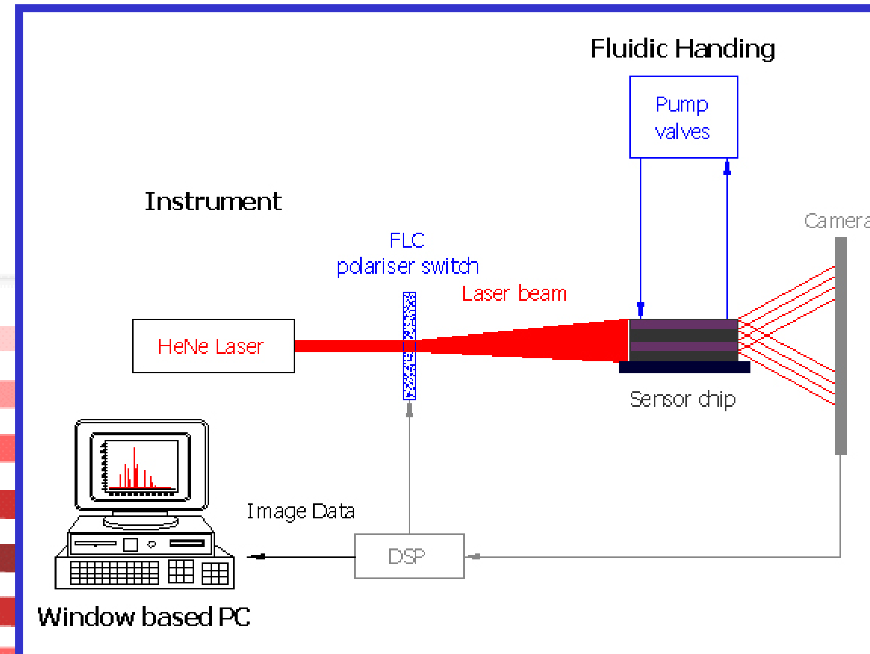
in)

Dual Polarization Interferometry (I)



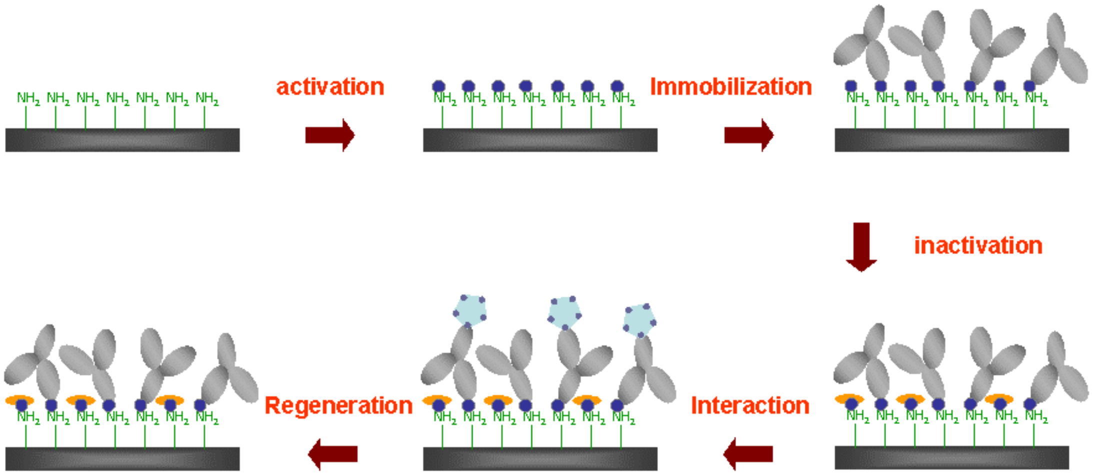
Young's interference experiment





$$\Delta\phi = k_0 L \Delta n_s$$

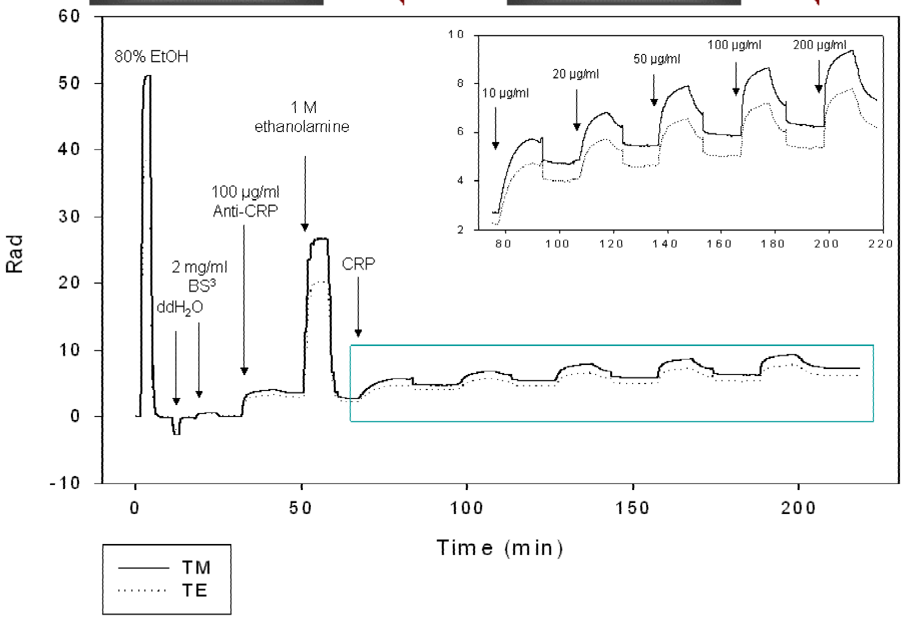
Dual Polarization Interferometry (II)

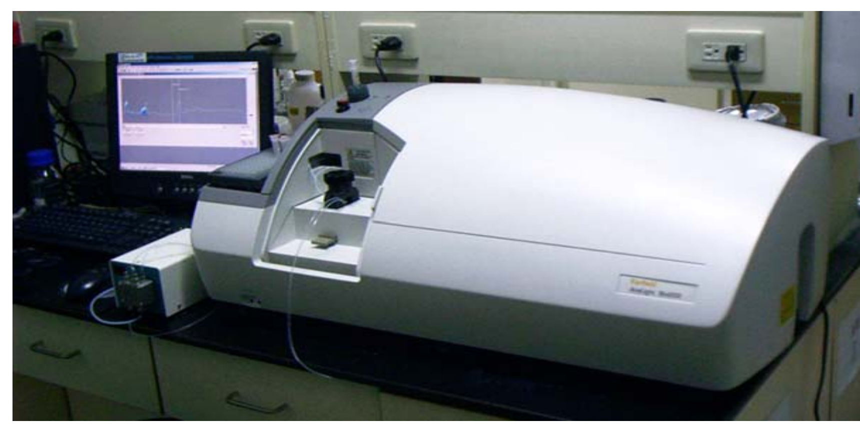


$$\Delta\phi = k_0 L \Delta n_s$$

$\Delta T < 1mK$

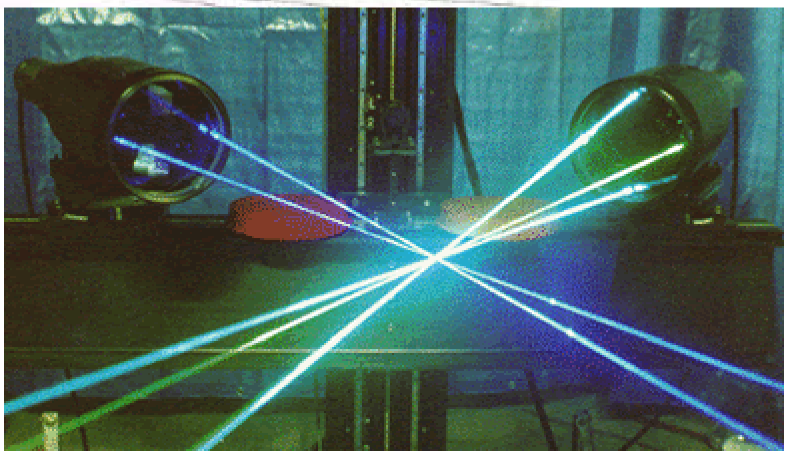
Dead volume < 2μl





(Farfield Sensors Ltd)

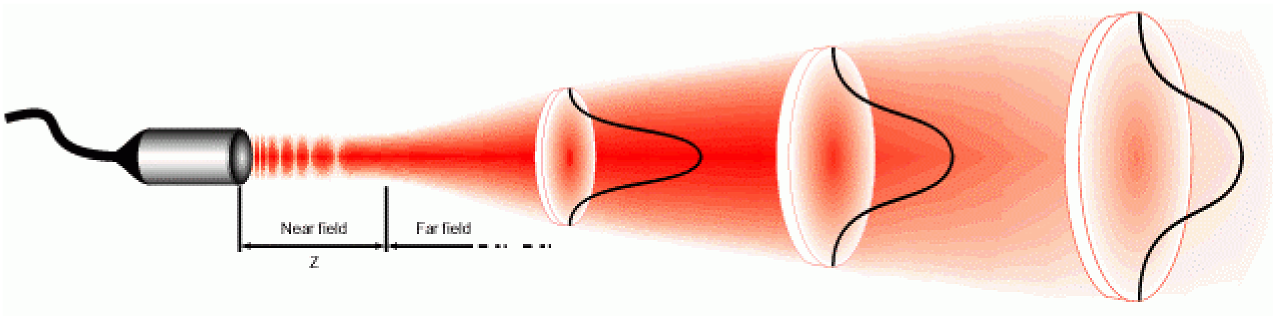
Optical Velocity measurement

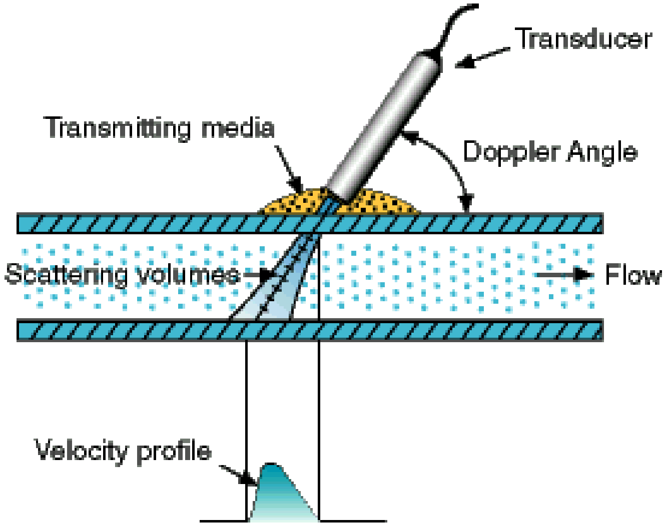


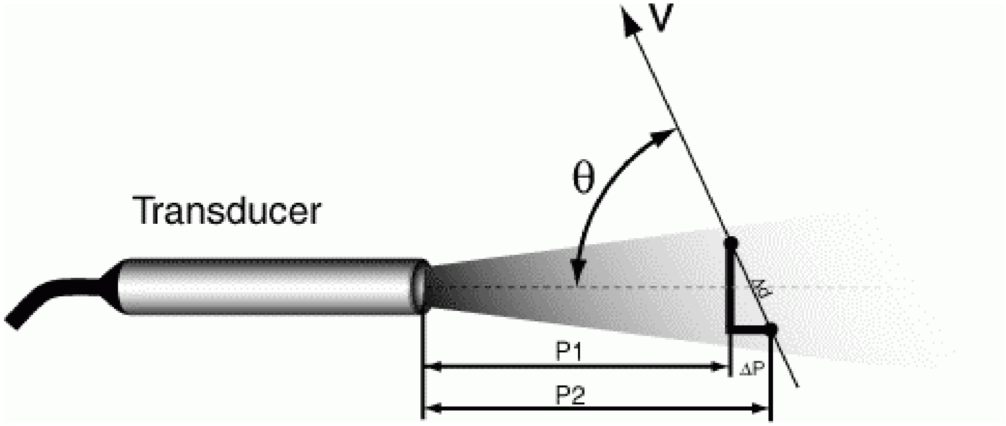
(From Y.H. Shau)

Pulsed Doppler Ultrasonic technique

- *Pulsed Doppler Ultrasonic technique*







History of Physiological Fluid Dynamics I

- Fluid: a substance which moves continuously under the action of shearing forces, no matter how small that shearing force may be. (i.e. Liquid or Gas).
- Leonardo da Vinci (1452-1519)
  – scientific approach to human anatomy
  – illustration of the cardiovascular system
  – remark on the thickening and hardening of arterial walls with age (Atherosclerosis)
- William Harvey (1578-1658)
  – Circulation of Blood flow
- Stephen Hales (1677-1761)
  – Measurement of blood pressure, arterial dimension, Blood Flow velocity

(From Y.H. Shau)

History of Physiological Fluid Dynamics II

- Stephen Hales (1677-1761)
  - Measurement of blood pressure, arterial dimension, Blood Flow velocity
- Leonhard Euler (1775)
  - One-dimensional inviscid incompressible flow in an elastic tube.
- Thomas Young (1808)
  - propagation of sound through an elastic solid or compressible fluid
- Poiseuille (1840)
  - Viscous pressure drop in blood vessels
- Otto Frank (1898)
  - Theory of wave propagation in the circulatory system

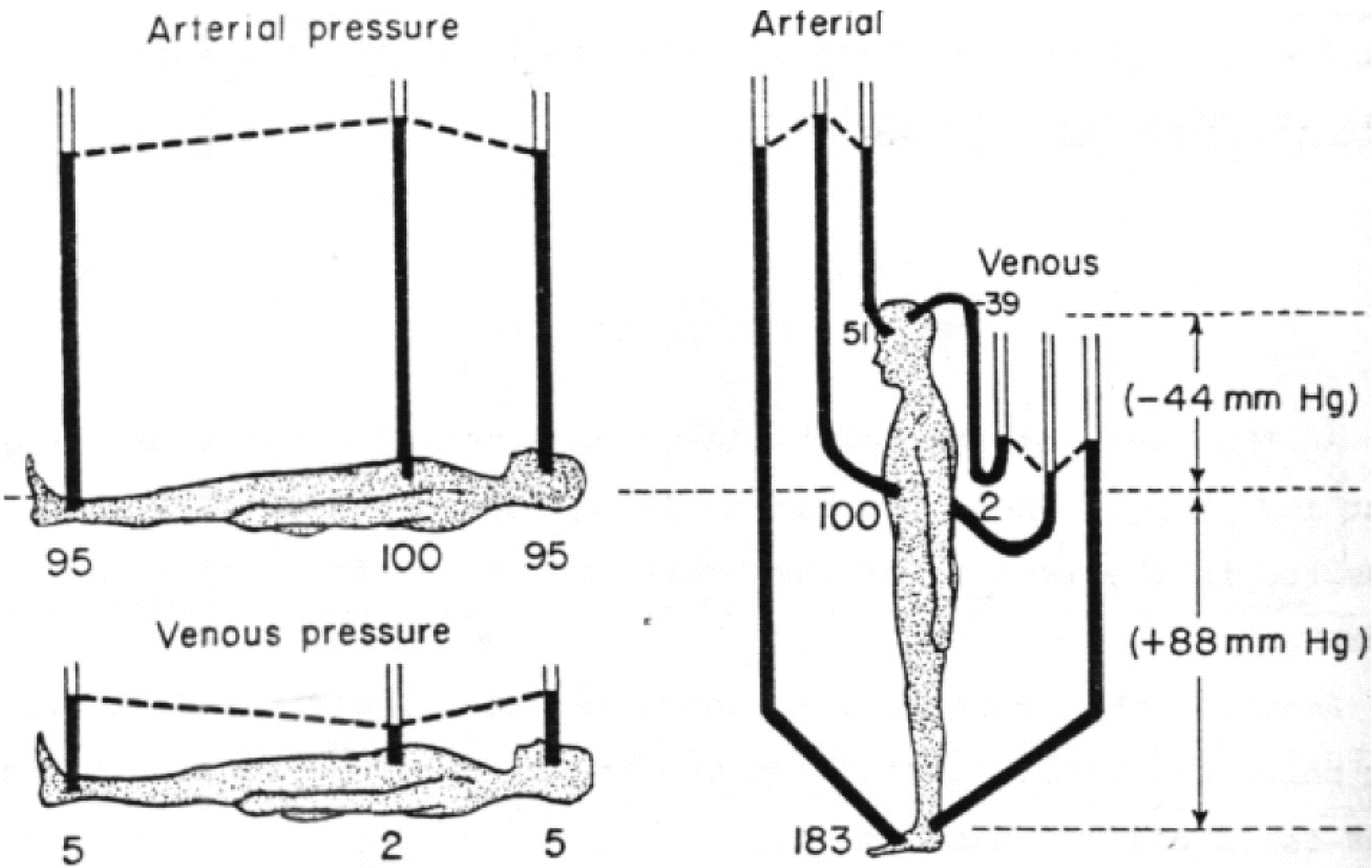
(From Y.H. Shau)

History of Physiological Fluid Dynamics III

- Fahraeus and Lindqvist (1931)
  - apparent viscosity of blood decreases as the tube diameter decreases
- McDonald and Womersley (1950)
  - Modern linear theory of wave propagation in the circulatory system
- Lambert (1958)
  - Nonlinear theory of wave propagation and Fluid flow in non-rigid tube
- Pedley (1980)
  - Fluid mechanics of large blood vessels

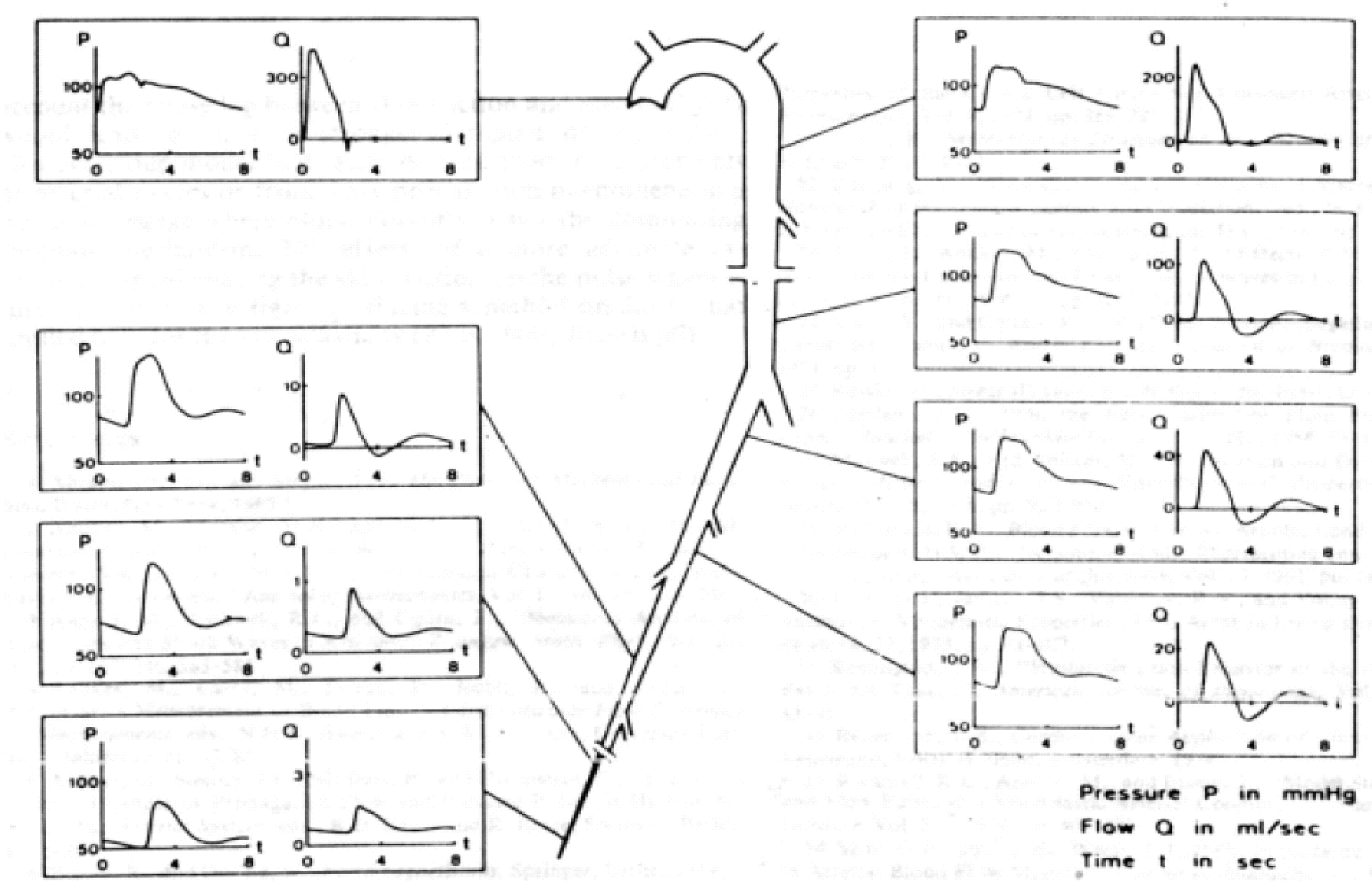
(From Y.H. Shau)

Hydrostatics of circulation



(From Y.H. Shau)

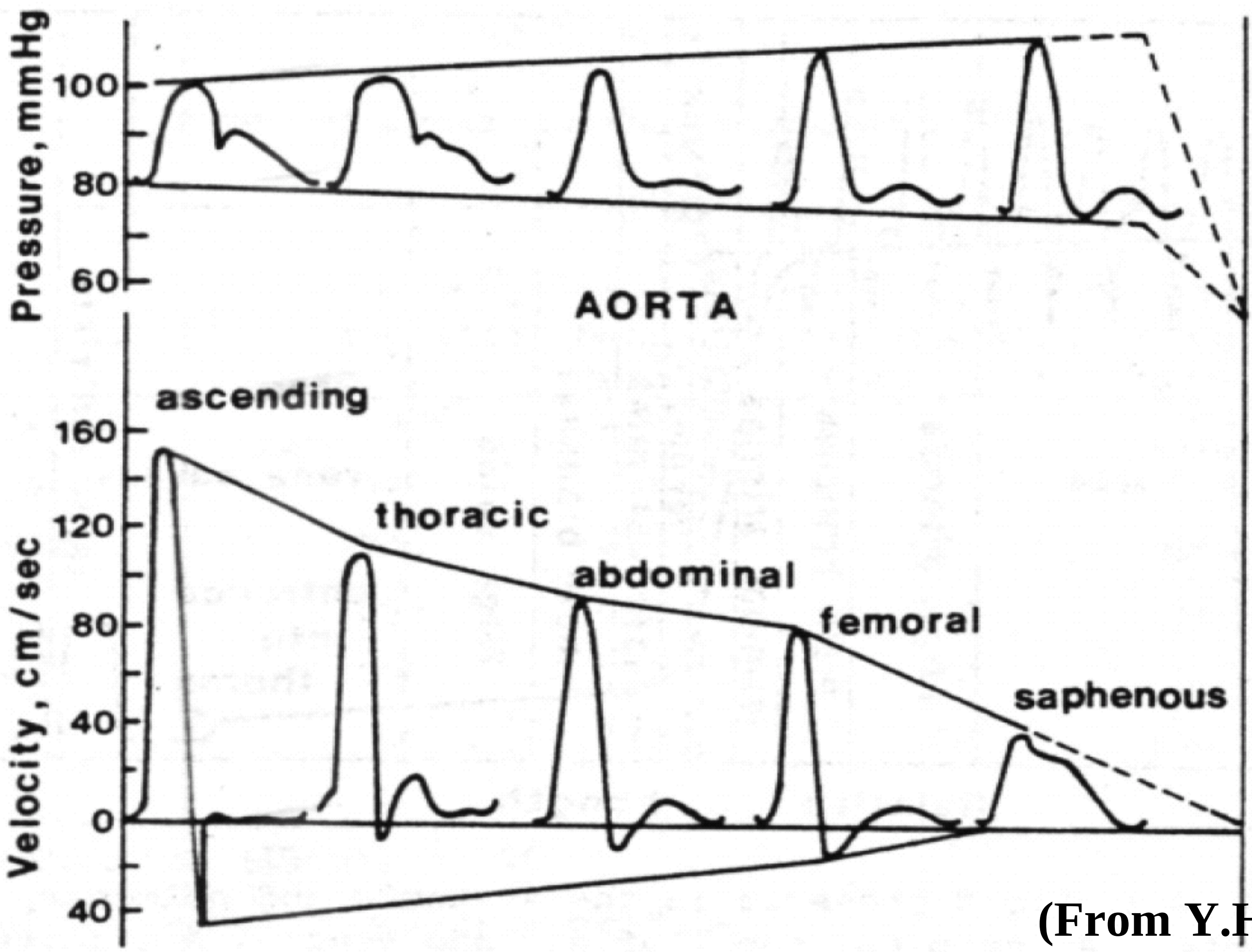
Pressure and Flow Pulse



Pressure and flow pulses predicted by the new viscoelastic model for different locations in the arterial conduit

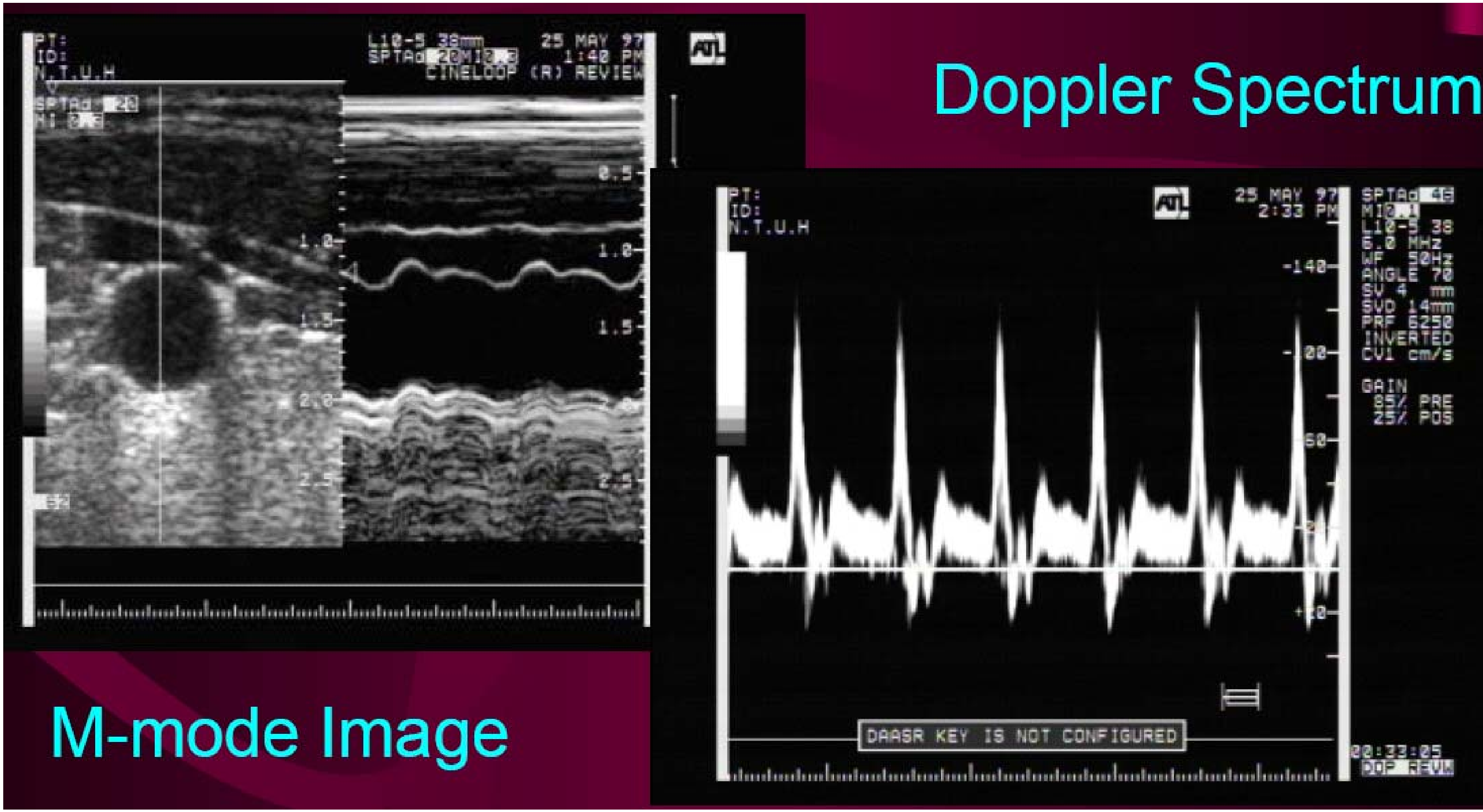
(From Y.H. Shau)

Velocity and pressure of blood flow



(From Y.H. Shau)

Ultrasound Flow measurement



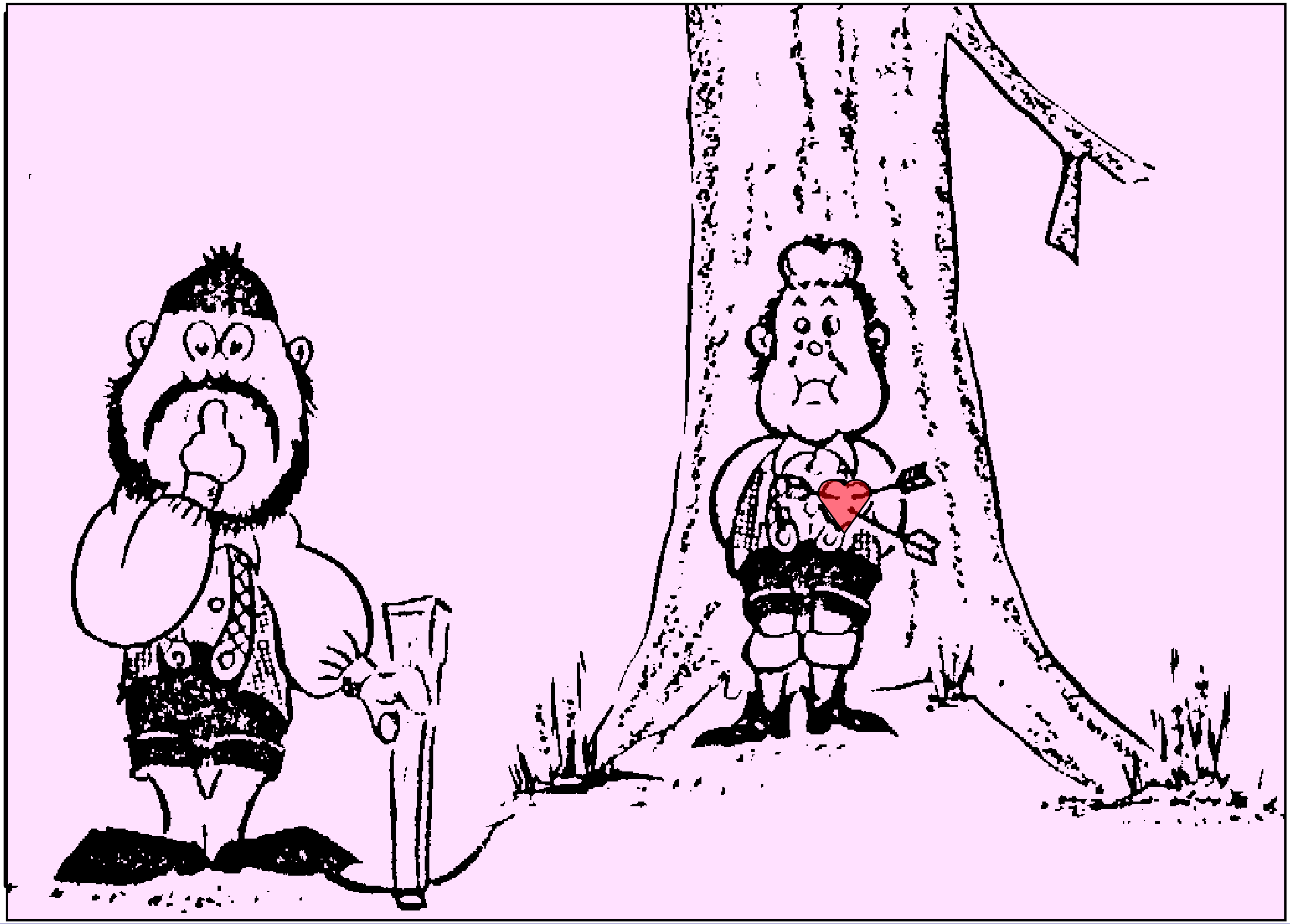
(From Y.H. Shau)

Terminology for Error Analysis

Terminology

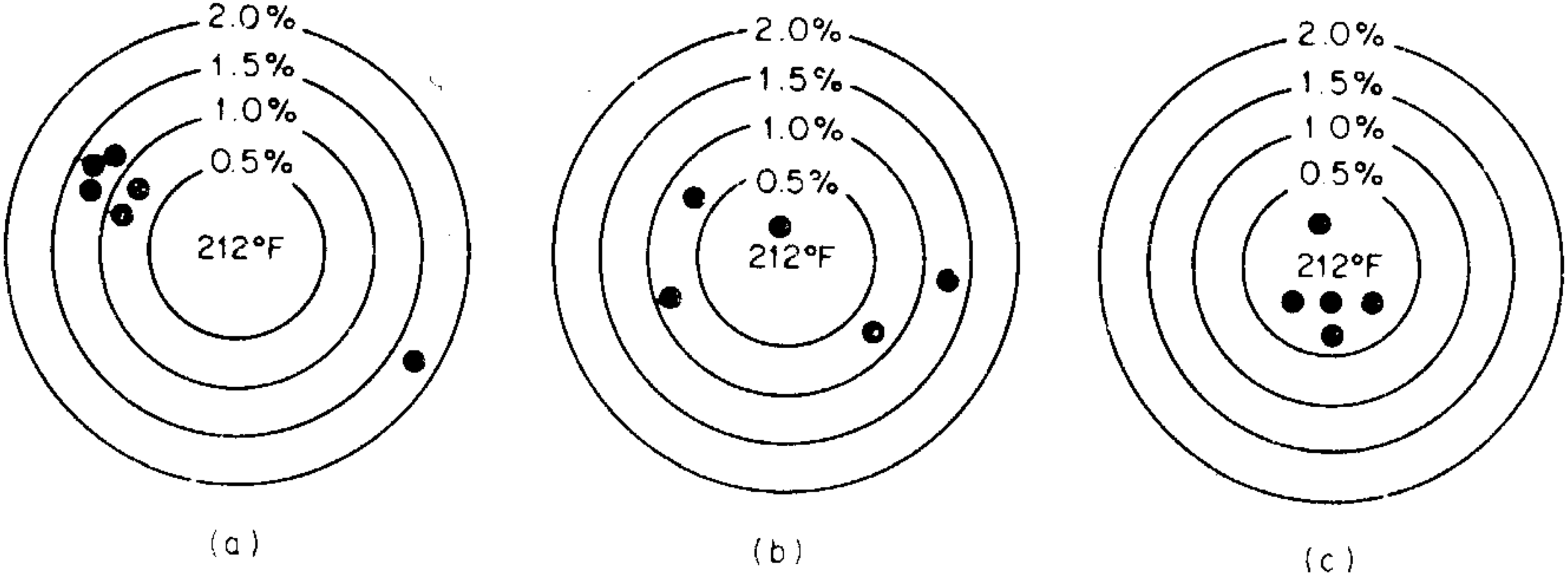
- ***Error***: deviation of the reading from a known input
- ***Accuracy***: Error, usually expressed as a percentage of full-scale reading.for industrial or laboratory instruments.
- ***Uncertainty***: range within the error is likely to fall with specified confidence limits (or fiducial limit).
- ***Precision*** (Repeatability):
  - ***reproducibility*** of the reading for a given input.
  - an instrument can be precise, but ***not*** calibrated or misused
  - accuracy of an instrument cannot be better than its precision.
- ***Traceability***: The ability to trace the accuracy of a standard back to its ultimate source in the fundamental standards (e.g., NIST)
- ***Sensitivity*** : ratio of instrument output to input.

Precision(repeatability) & Accuracy



Precision, Bias error & Accuracy (I)

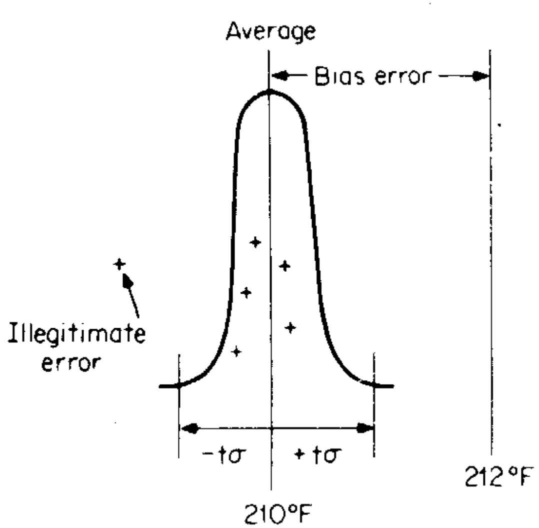
Calibration Data for Three Temperature-Measuring Devices



†Possible illegitimate error or an outlier.

(From Miller, 1983)

Precision, Bias error & Accuracy (II)



(From Miller, 1983)

With the outlier omitted, the average of the reading

$$\bar{I}=\frac{\sum I_i}{n}$$ **=(210.1+210.0+209.8+210.2+209.9)/5=210.0**

the standard deviation is:

$$\sigma=\left[\frac{\sum (I_i-\bar{I})/\bar{I})\times 100\%}{n-1}\right]^{0.5}$$

=[(0.0023+0+0.0090+0.0090+0.0023)/(5-1)]$^{0.5}$ =0.0753%

∴ the *precision* at the 95% confidence level is then:

σ_p=t_{st} σ, where t_{st} is two-tailed student's t-value, could be found from table (t_{st} = 2.776 for n=5).

∴ the precision is then σ_p=2.776×0.0753%=0.21%

The *direction bias error* is

$$B=\frac{\bar{I}-I_t}{I_t}\times 100\%$$ **=[(210-212)/(212)] × 100%=-0.94%**

∴ the *accuracy* is $A_{cc}=B\pm\sqrt{(1+\frac{1}{n})}\sigma_p$ **=-0.7%~-1.2%**

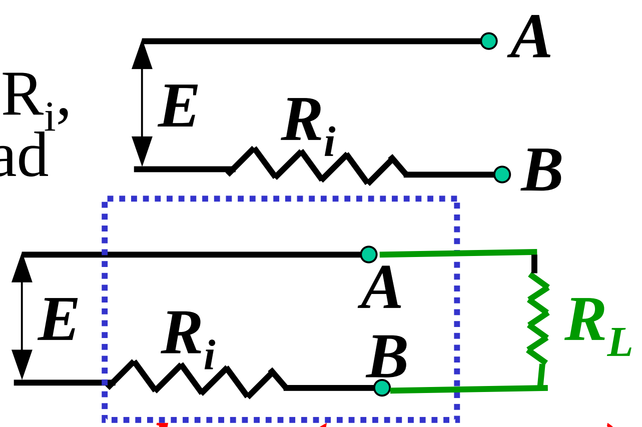
Error Analysis

- Almost all bio-measurements are indirect.
- In experimental work, errors of two different types can occur :
  - Systematic Errors
    - poorly adjusted instruments
    - improper calibration
    - false instrument specification
    - incorrect or biased statistical estimators
  - Statistical or random errors
    - improper reading from a scale
    - statistical variance of the measured quantity.
- Some errors can be corrected or controlled, others (uncertainty) cannot. All must be estimated !

Some notes for electronics

- Impedance Matching

It is continually necessary to connect various electronic instruments in different combinations



Every instrument has an internal resistance R_i, in series with an externally connected load resistance R_L ,

The voltage

$$E_{AB} = E \frac{R_L}{R_L + R_i}$$

- If E_{AB} is to be measured, R_L should be chosen ***large (e.g. scopes)***.
- If power is to be transmitted

$P = E_{AB}^2 / R_L$ or $P = E^2 R_L / (R_L + R_i)^2$

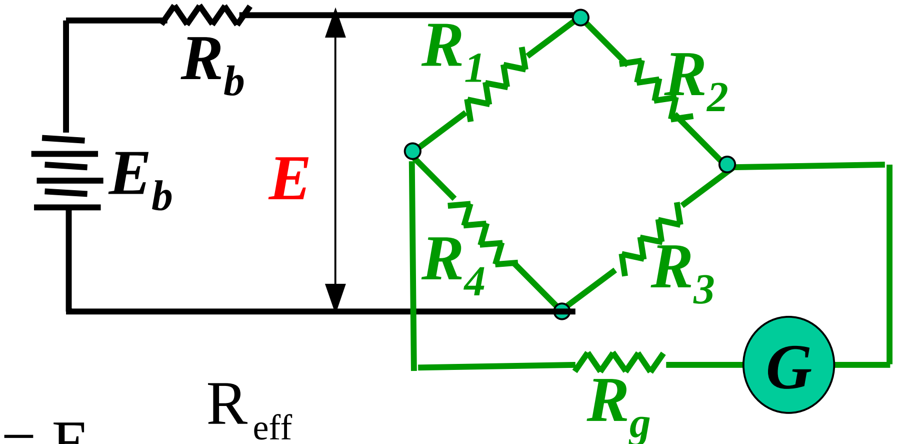
For a maximum transmission : $dP/dR_L = 0$ then $R_L = R_i$

i.e. resistive part of impedance should be match.The inductive and capacitive terms must also be considered when dynamic response is important.

Wheatstone bridge

The Wheatstone bridge is a basic building block of many measuring instruments. It allows precise measurement of minute change in resistance, capacitance or inductance. It has many applications in

- hot-wire anemometry
- strain gauges
- Inductive pressure transducers or condenser microphones



- effective bridge resistance:

$$R_{eff} = \frac{(R_1+R_4)(R_2+R_3)}{R_1+R_2+R_3+R_4}, \quad E = E_b \frac{R_{eff}}{R_{eff}+R_b}$$

- Voltage measured at galvanometer:

$$E_g = E\left(\frac{R_1}{R_1+R_4} - \frac{R_2}{R_2+R_3}\right)$$

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