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# Clinical laboratory instrumentation

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BIOEN 302

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# Medical instrumentation

- ❑ Diagnostic instrumentation
- ❑ Therapeutic instrumentation
- ❑ Clinical laboratory instrumentation



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# Clinical laboratory

- Analyzes patient specimens (e.g. **blood, bone marrow, urine, or tissue samples**) in order to provide information to aid in the diagnosis of disease and evaluate the effectiveness of therapy.



Clinical laboratory

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# Clinical laboratory

- Major divisions:
  - Hematology
  - Biochemistry
  - Molecular diagnostics
  - Microbiology
  - Histology

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# Hematology laboratory instrument

- Determine the numbers and characteristics of elements in the blood (RBC, WBC, platelets, etc) and test the blood clotting.



Coulter counter

ITEM	DATA	UNITS
WBC	12.38	$10^9/L$
RBC	4.13	$10^{12}/L$
HGB	127	g/L
HCT	0.386	L/L
MCV	93.5	fL
MCH	30.8	pg
MCHC	329	g/L
PLT	222	$10^9/L$
RDW-SD		fL
RDW-CV	13.2	%
PDW		fL
MPV	10.3	fL

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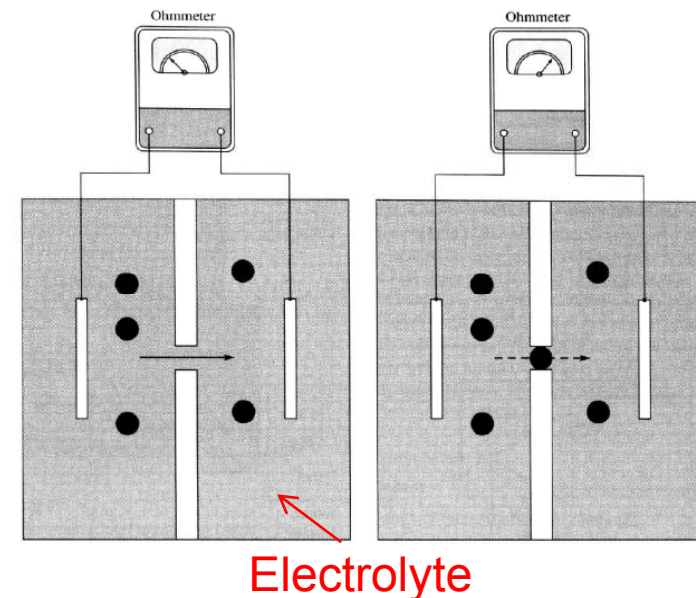
# Coulter counter

- A device for **counting** and **sizing** cells.
- Coulter Principle:
  - Devised by Wallace H. Coulter in 1947.



# Coulter counter

- Coulter Principle:
  - A hole with a small diameter (e.g. 50  $\mu\text{m}$ ) is between two chambers.
  - As particles pass across the hole, the resistance between the two probes changes.
  - Ohmmeter measure the change on the resistance.



$$R = k \times \frac{\text{Particle volume}}{\text{Aperture size}}$$



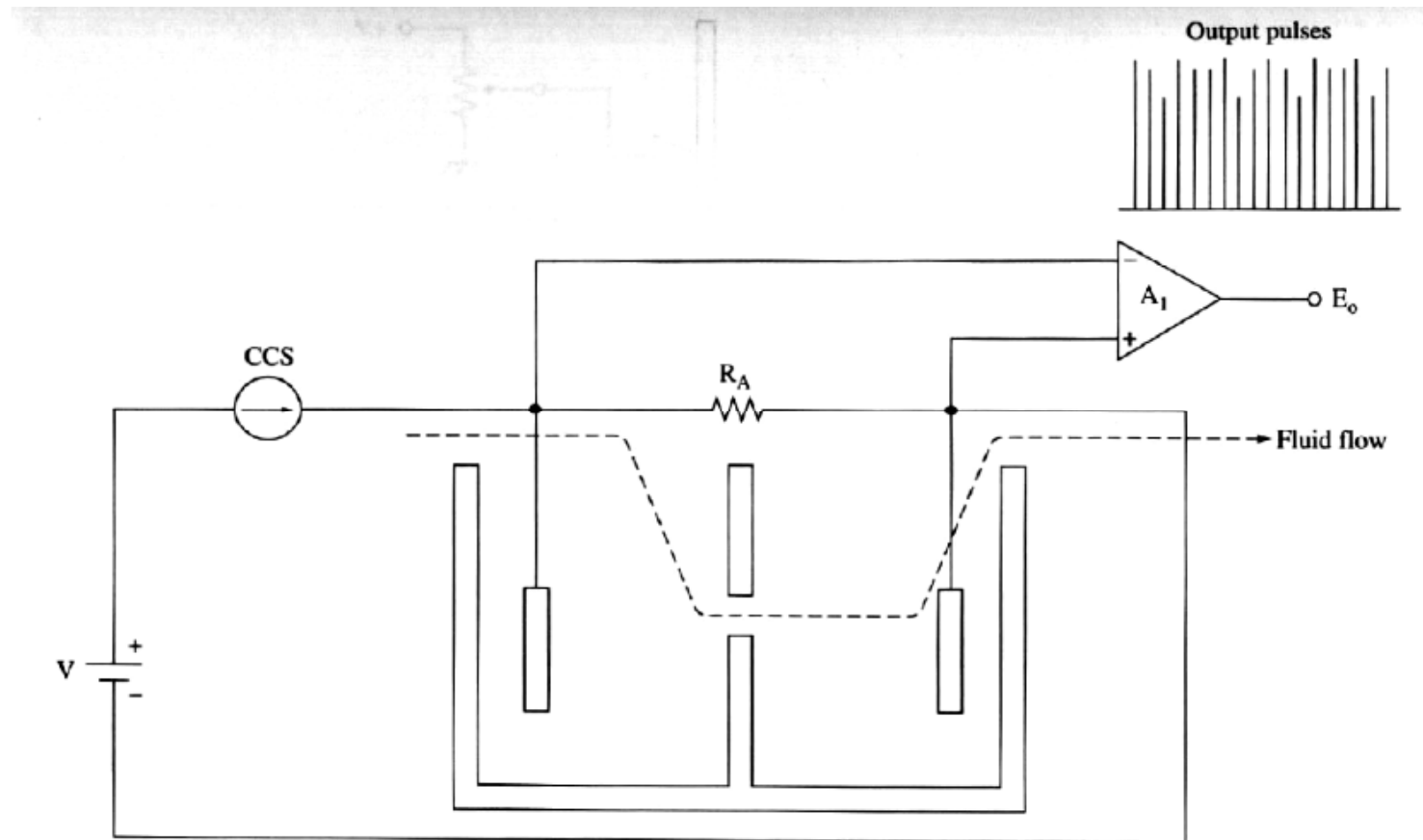
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# Coulter counter

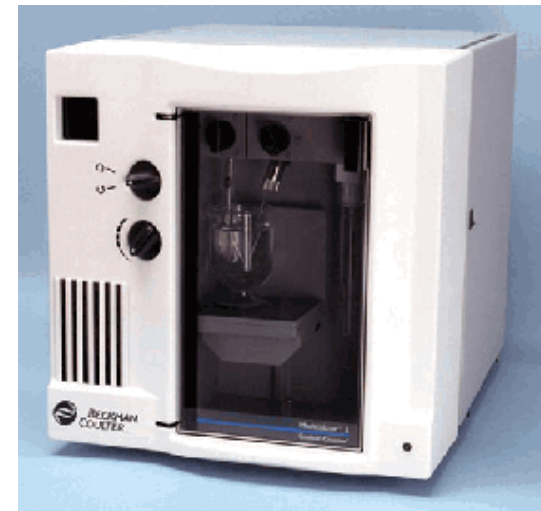
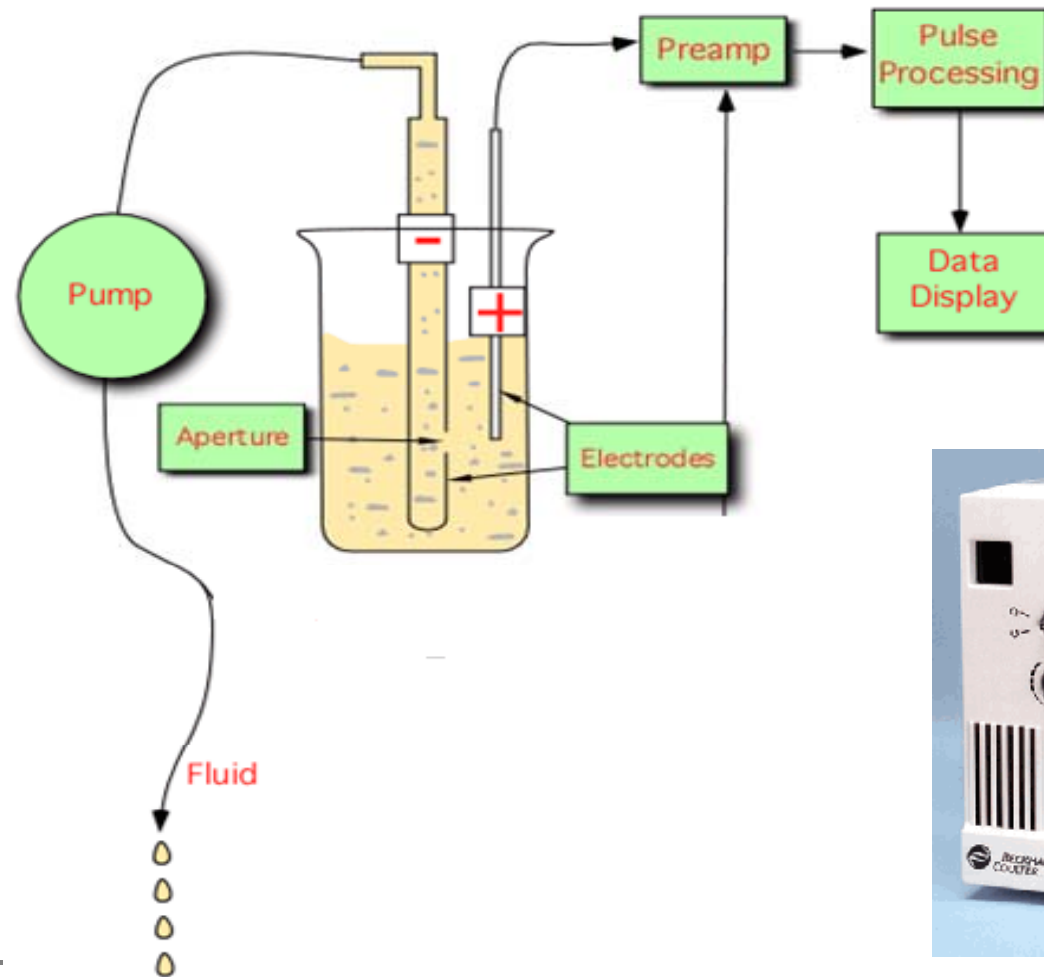
- Constant current source (CCS) and voltage amplifier replace the ohmmeter.
- $R_A$  is the resistance of the aperture and will be either high or low, depending on whether or not the particle is inside the aperture.

# Coulter counter

- Schematic:



# Coulter counter



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# Biochemistry laboratory instrument

- Analyze blood, urine, and other fluids to determine how much clinically important substances is present.



Spectrophotometer

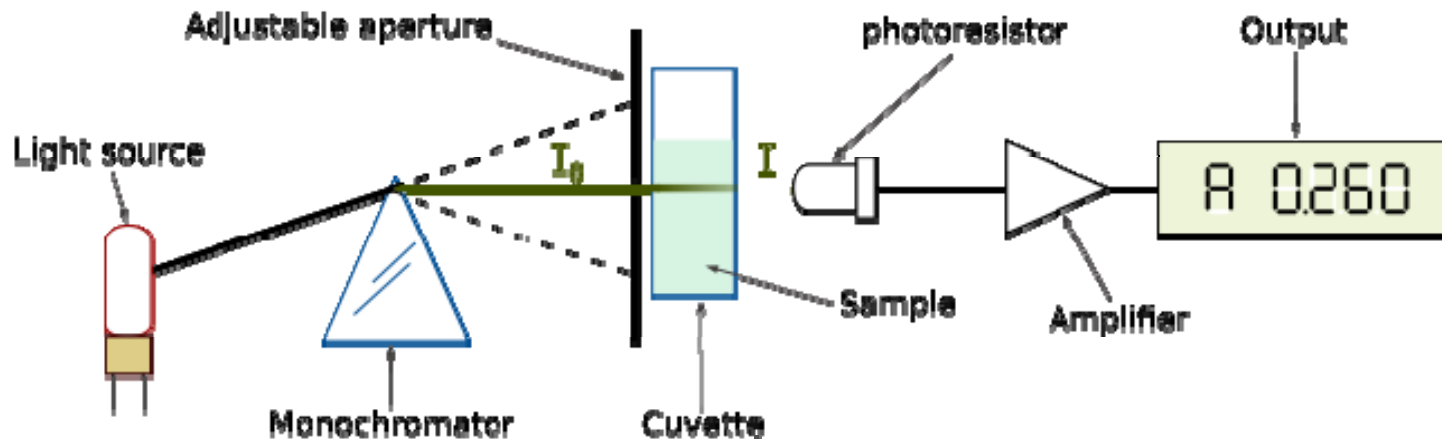
Glucose level (nmol/L)	Indication
3.5—5.5	Normal
5.6—6.9	Pre-diabetes
>7	Diabetes

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# Spectrophotometer

- A photometer that can measure intensity as a function of the light source wavelength.
- The wavelength used is typically in the ultraviolet (200-400 nm), visible (400-700nm) or infrared (700 to 800 nm) range.
- It can be used to determine the entity of an **unknown substance**, or the concentration of a number of **known substances**.

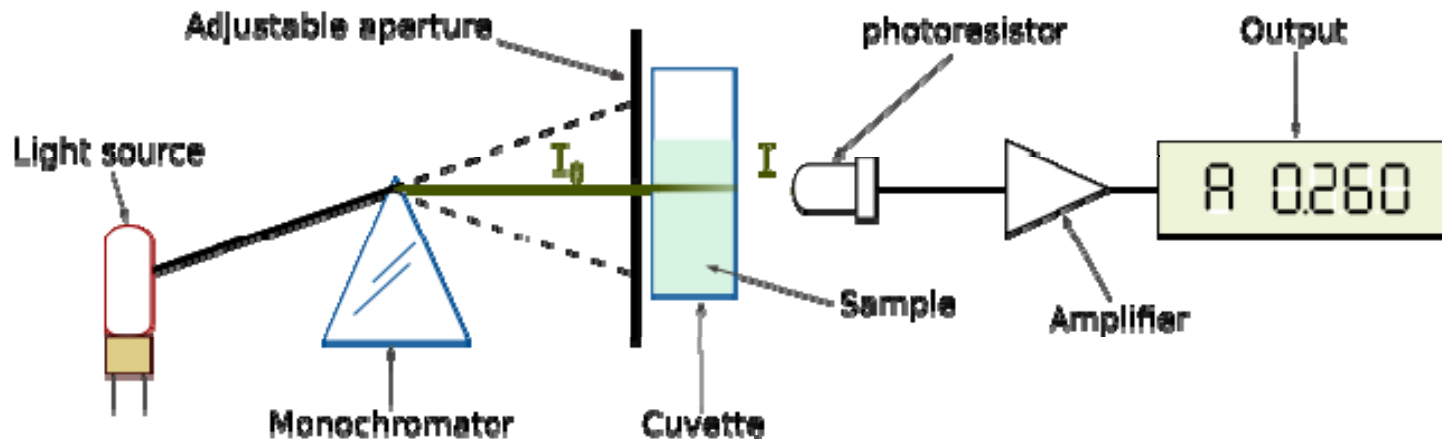
# Spectrophotometer



## Light source:

- Hydrogen lamp for 200 to 360 nm range.
- Tungsten filament lamp for 360 to 800 nm range.

# Spectrophotometer

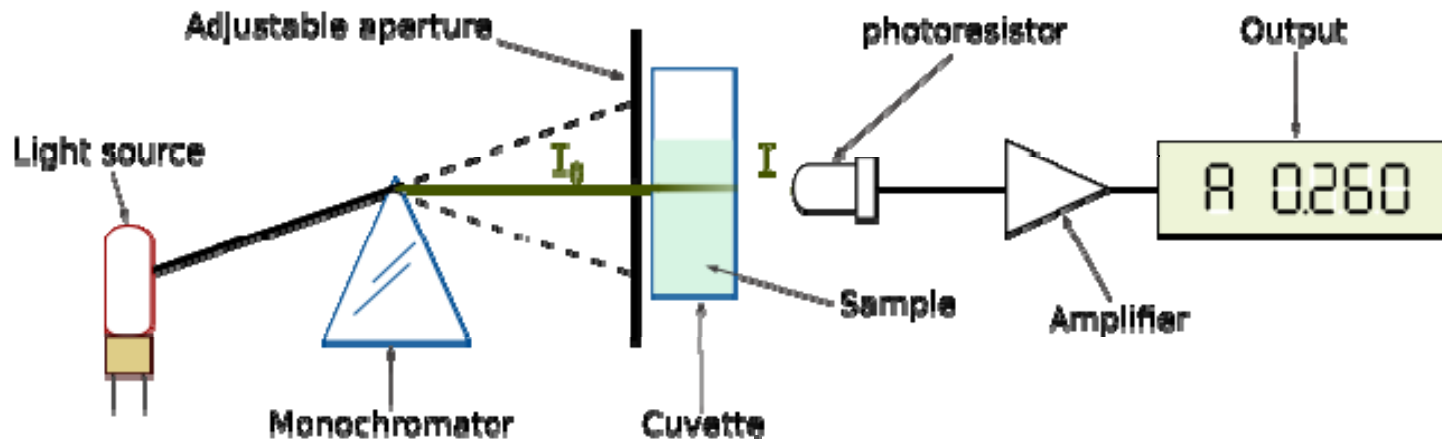


## Wavelength selector:

- Glass filter: wavelengths in the band of interest to pass
- Monochromator: use a prism or diffraction grating to disperse the input beam spatially as a function of wavelength and a mechanical device is used to select the wavelength.



# Spectrophotometer



## Photometric system:

- Light sensor: e.g. photoresistor and phototransistor
- Amplifier
- Output display device

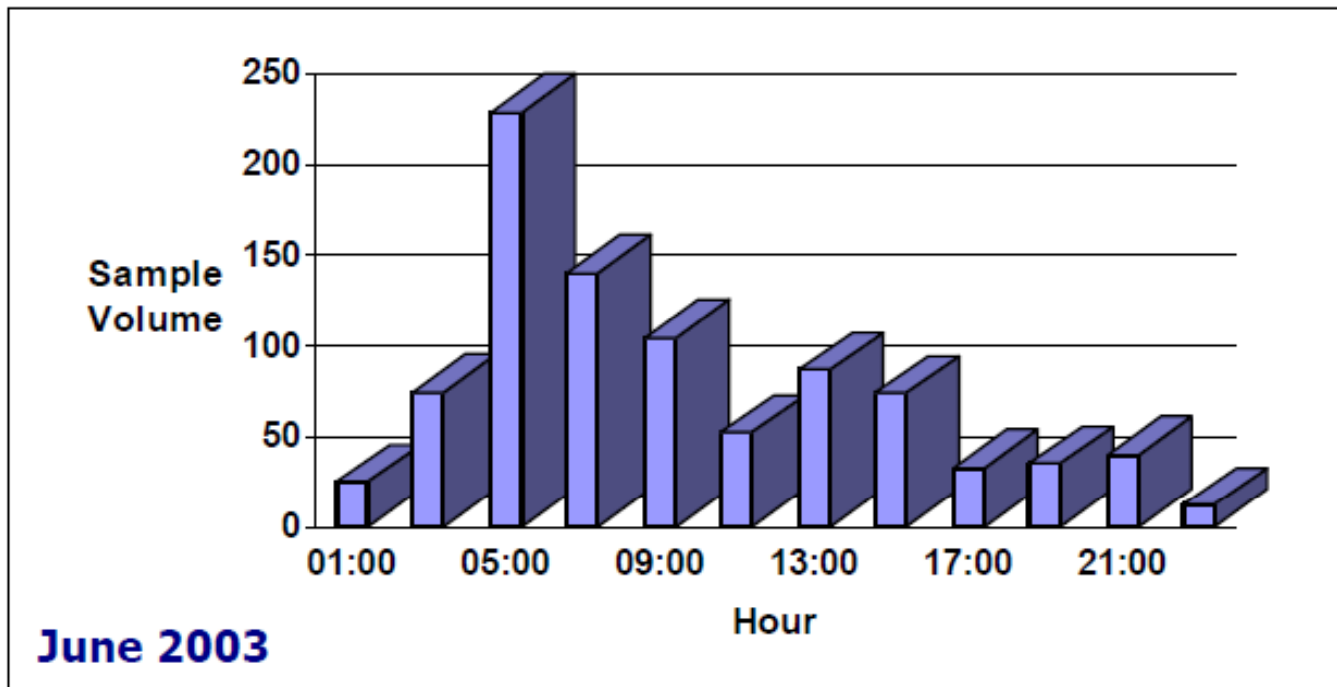


# Labor



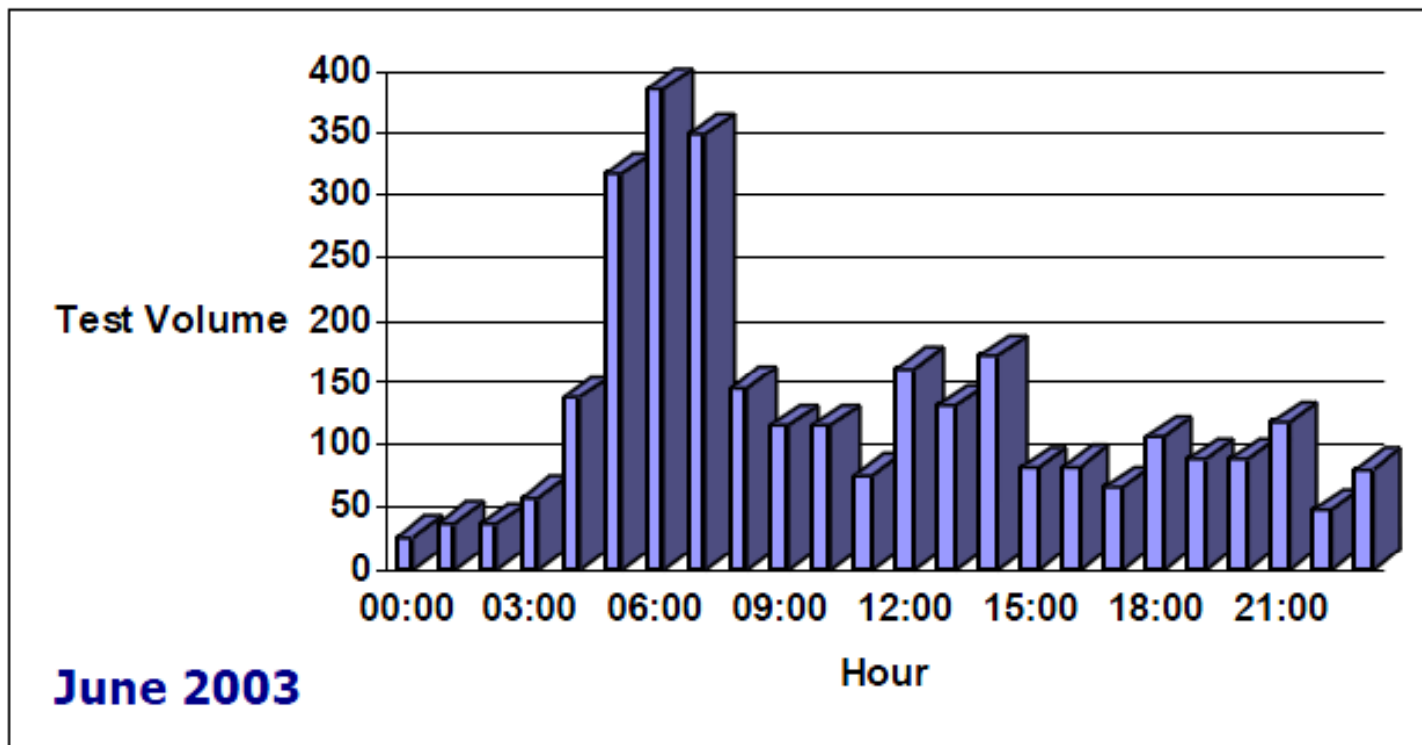
# Total sample volume per hour

Includes hematology and chemistry testing  
Approximately 900 samples received per day



# Chemistry test volume per hour

Approximately 3,000 chemistry results reported per day

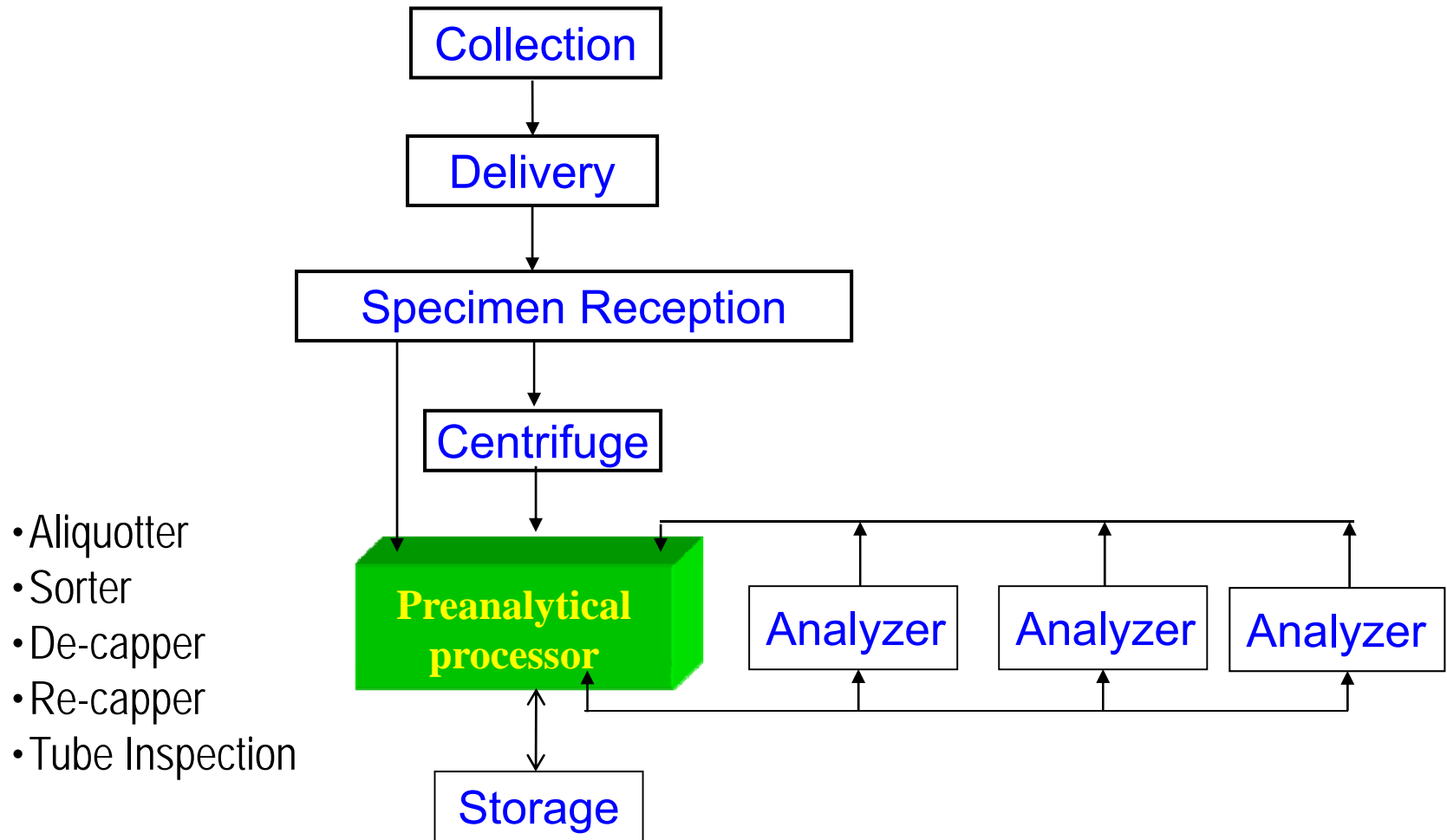


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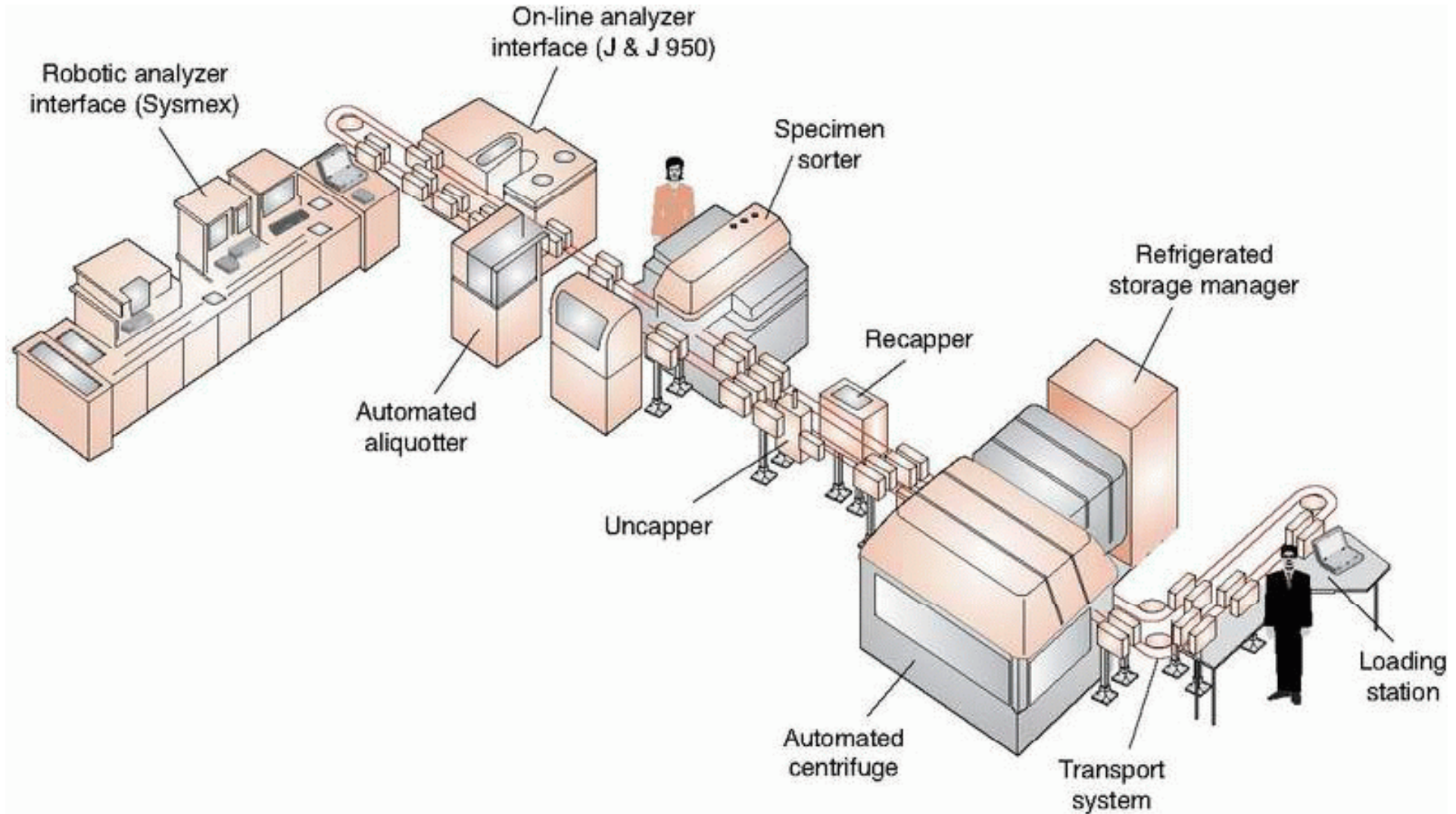
# Chemistry test automation benefits

- Labor reduction
- Gain productivity and efficiencies
- Improve quality by reducing sample handling and processing errors
- Increase safety due to lower exposure

# Automated workflow



# Total laboratory automation



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# Total laboratory automation



A video to show automated clinical chemistry laboratory

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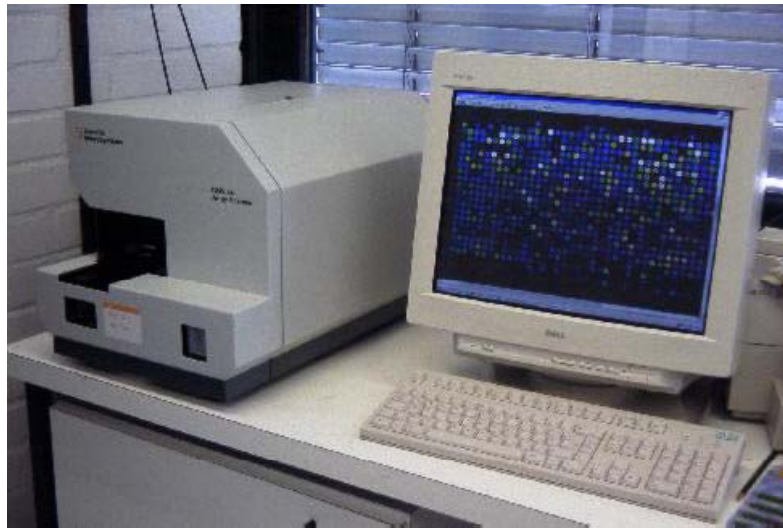
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# Molecular diagnostic instrument

- Detect the formation, structure, and function of DNA, RNA, and proteins.



DNA microarray

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# DNA microarray

- What is a DNA microarray?
  - Also known as DNA Chip
  - A high throughput technology that allows detection of thousands of genes simultaneously
  - Principle: base-pairing (DNA: A-T and G-C)

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# DNA microarray

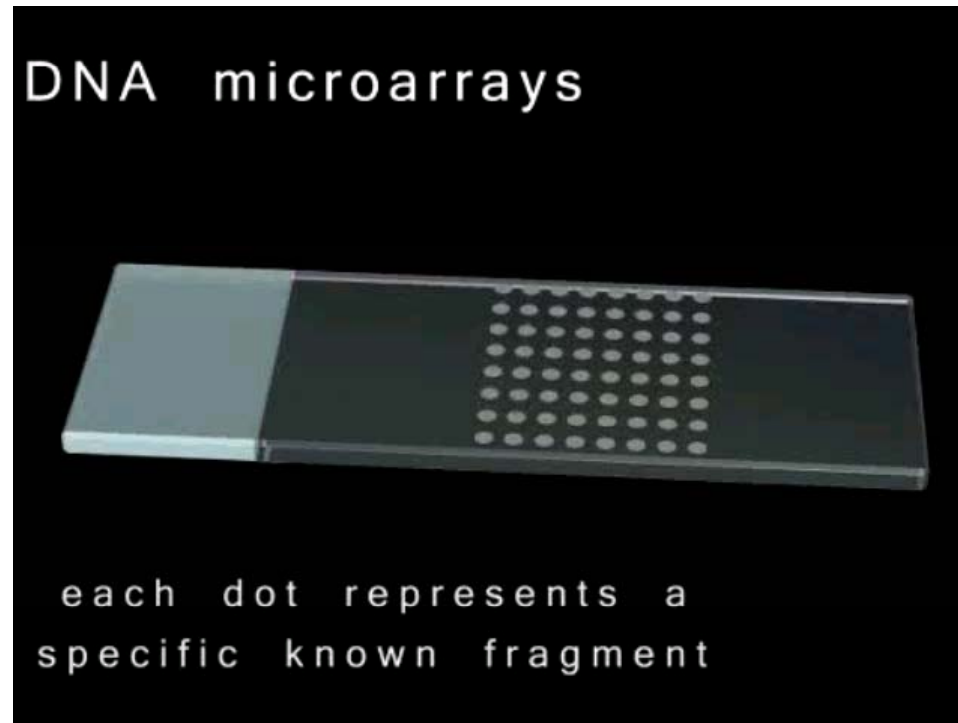
## ■ How does it work?

- Extract mRNA from a cell
- Convert mRNA into colored cDNA (fluorescently labeled)
- Mix labeled cDNA together and wash over the microarray
- Each cDNA sequence hybridizes specifically with the corresponding gene sequence in the array
- Wash unhybridized cDNA off
- Read array with fluorescent microscope
- Analyze images generating a profile of gene expression in the cell

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# Microarray

- How does it work?



A video to show how DNA microarrays work

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# DNA Microarray

- Applications:
  - Identification of complex genetic diseases
  - Cancer diagnosis
  - Drug discovery

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# Microbiology laboratory instrument

- Test various fluids and tissue culture for presence of pathological microorganisms (E. coli, fungi, parasites, etc).



Incubator



A video to show how urine sample is processed



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# Histology laboratory instrument

- Study the microscopic anatomy of tissue to analyze disease states at a cellular level by light or electron microscopy.



Tissue processor



Microtome



Autostainer

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# Tissue

- Biopsy: removal of tissues for diagnostic purposes.
  - Surgical resection
  - Needle
  - Trephine



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# Standard histological technique

- Fixation
- Processing
  - Dehydration
  - Clearing
  - Infiltration
  - Embedding
- Sectioning
- Staining (H&E: haematoxylin & eosin)

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# Standard histological technique

- Fixation

- Chemical: formaldehyde

- Aims:

- Close to a living form

- Prevent alteration from subsequent treatment

# Standard histological technique

- Processing
  - Dehydration: remove water using graded alcohol series
  - Clearing: use a hydrophobic clearing agent to remove the alcohol (not miscible with wax)
  - Infiltration: replace clearing agent with paraffin wax
  - Embedding: in paraffin wax

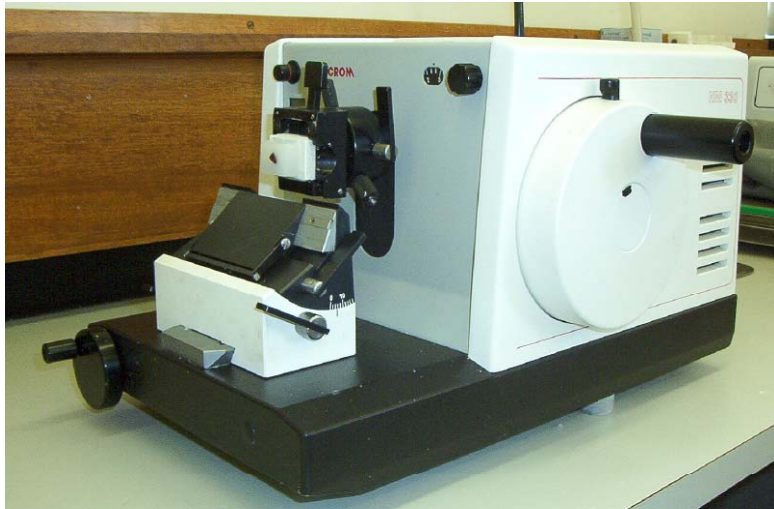


Tissue processor

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# Standard histological technique

- Sectioning: cut 3-5  $\mu\text{m}$  tissue section from the block
- Staining



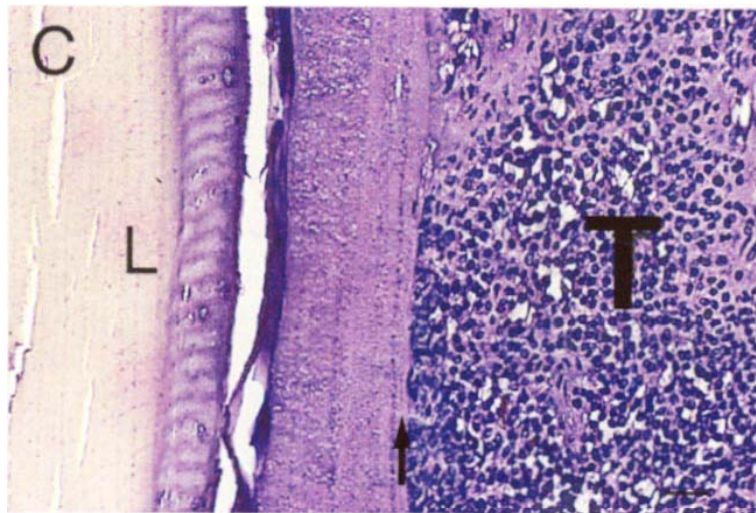
Microtome



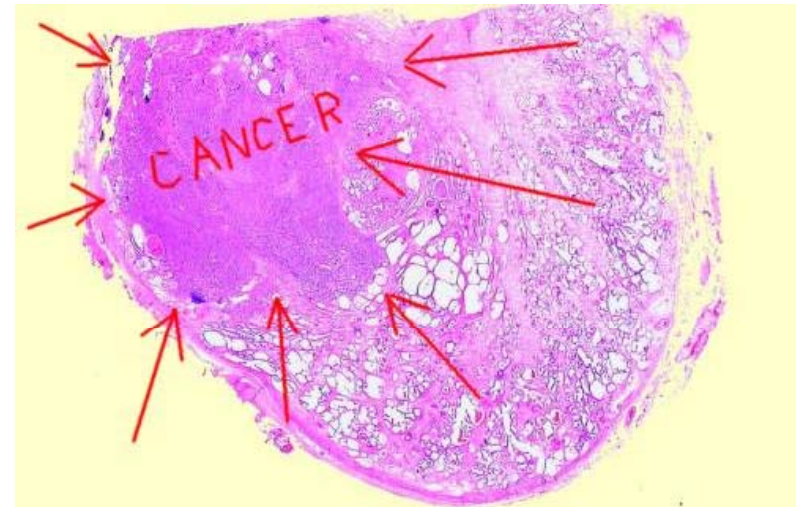
Autostainer

# Histology laboratory instrument

- Examples:



Tumor of the retina



Prostate tumor



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Questions?