



# Pharmaceutical Instrumental Analysis

الأستاذ الدكتور جمعة الزهوري ( دكتوراه صيدلة-ألمانيا 1991 )

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# Simeticone for Oral Use

## Action and use

Antifoaming agent

## DEFINITION

Simeticone for Oral Use contains not less than 4.5% and not more than 8.0% w/w of silica,  $\text{SiO}_2$ , and not less than 91.0% and not more than 97.0% w/w of Dimeticone 1000. It is prepared by the addition of finely powdered silica to Dimeticone 1000.

IR معيارية

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# ASSAY

## ***For silica***

To 1 g add 50 ml of *toluene*, mix well and filter through an ignited silica crucible. Wash the residue thoroughly with toluene, dry at  $105^{\circ}$  and ignite to constant weight at  $500^{\circ}$ .

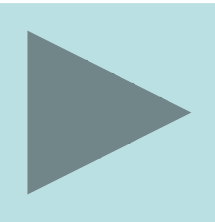
## ***For dimeticone***

Place 40 mg in a stoppered centrifuge tube, add 20 ml of toluene and shake for 20 minutes. Filter and **record the infrared absorption spectrum**, Appendix II A, of a 0.5-mm layer of the filtrate over the range  $1330$  to  $1180\text{ cm}^{-1}$  ( $7.52$  to  $8.47\text{ }\mu\text{m}$ ). Measure the absorbance of the  $\text{CH}_3\text{Si}$  stretching band at the maximum at  $1261\text{ cm}^{-1}$  ( $7.93\text{ }\mu\text{m}$ ). Repeat the operation using dimeticone EPCRS in place of the preparation being examined..



# An Introduction to Infrared Spectrometry

Prof. Dr. J. Al-Zehouri





**T**he infrared region of the spectrum encompasses radiation with wavenumbers ranging from about 12,800 to  $10\text{ cm}^{-1}$  or wavelengths from 0.78 to  $1000\text{ }\mu\text{m}$ .<sup>1</sup> From the standpoint of both application and instrumentation, the infrared spectrum is conveniently divided into near-, mid-, and far-infrared radiation;

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## Infrared Spectral Regions

Region	Wavelength ( $\lambda$ ) Range, $\mu\text{m}$	Wavenumber ( $\bar{\nu}$ ) Range, $\text{cm}^{-1}$	Frequency ( $\nu$ ) Range, Hz
Near	0.78 to 2.5	12,800 to 4000	$3.8 \times 10^{14}$ to $1.2 \times 10^{14}$
Middle	2.5 to 50	4000 to 200	$1.2 \times 10^{14}$ to $6.0 \times 10^{12}$
Far	50 to 1000	200 to 10	$6.0 \times 10^{12}$ to $3.0 \times 10^{11}$
Most used	2.5 to 15	4000 to 670	$1.2 \times 10^{14}$ to $2.0 \times 10^{13}$

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## IR absorption

**IR radiation is of too low an energy to excite electronic transitions.**

**Absorption is limited to vibrational and rotational levels.**

**For liquids and solids, molecular rotation is often limited so the major type of interaction is vibrational.**



# Theory of Infrared Absorption spectroscopy

Infrared absorption spectra for molecular species can be rationalized by assuming that all arise from various changes in energy brought about by transition of molecules from one vibration or rotational energy state to another. In this section we use molecular absorption to illustrate the nature of these transitions.

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For a harmonic oscillator consisting of two balls of mass  $m_1$  and  $m_2$  connected by a spring, the equation for the potential energy is a function of the force constant,  $k$ , and the total displacement of the two balls from the equilibrium position ( $d_1 + d_2$ ). The frequency of vibration for the system is a function of the force constant and the mass of each ball.



$$E_p = \frac{1}{2} k (d_1 + d_2)^2$$

$$\nu = \frac{1}{2\pi} \sqrt{\frac{k}{m_1 + m_2}}$$

← Hooke's law



What is the *frequency* of vibration for the following spring system?

$$k = 5 \times 10^{-5} \text{ N/cm}$$



$$m = 1.0 \text{ g}$$

$$m = 1.0 \text{ g}$$

14.14

$$\nu = \frac{1}{2\pi} \sqrt{\frac{5.0 \times 10^{-5} \text{ N/cm}}{\frac{(1.0)(1.0)\text{g}^2}{(1.0 + 1.0)\text{g}}}}$$

$$= \frac{1}{2\pi} \sqrt{5.0 \times 10^{-5} \text{ N/cm} / 0.5\text{g}}$$

$$= \frac{1}{2\pi} \sqrt{10} \text{ s}^{-1}$$

$$\pi = 3.14$$

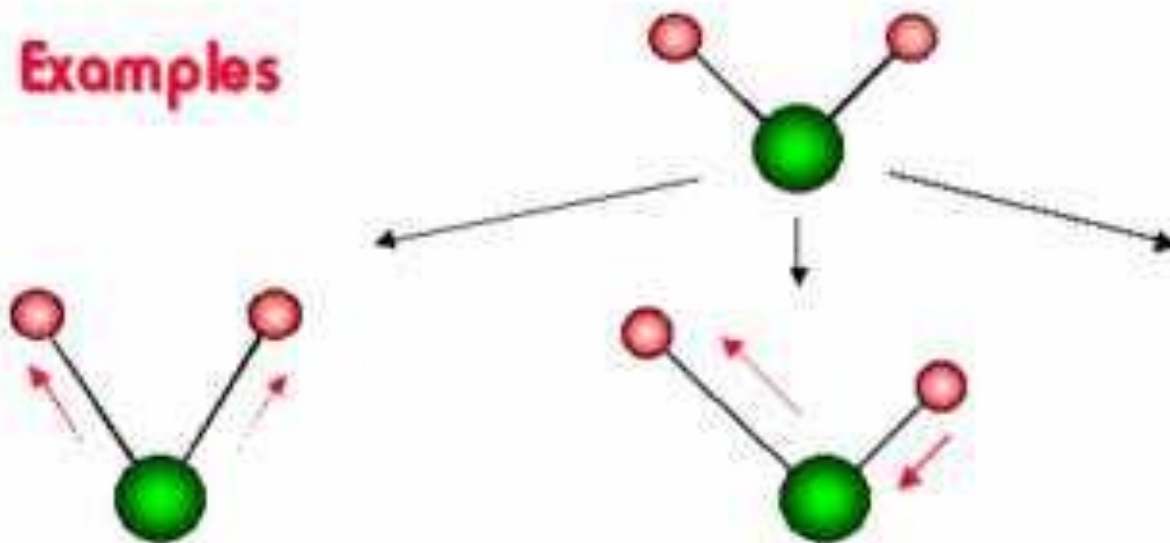
$$\nu = 0.5 \text{ cycle/s}$$

Pr

# IR absorption

Each molecule can have a large number of vibrations that it can undergo.

## Examples



symmetrical stretching

asymmetrical stretching

scissoring



# IR absorption

The types of vibrations available to a molecule is determined by the:

Number atoms

Types of atoms

Type of bonding between the atoms

As a result, IR absorption spectroscopy is a powerful tool in characterizing pure organic and inorganic compounds.

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الجزىء ىمك ثلاث أنواع من الحركات : انتقالية  
(إلكرونيةة) ودورانية واهتزازية هذا يعنى أن طاقة  
الجزىء الكلية = مجموع الطاقات الثلاث أى الطاقة  
الانتقالية (الإكرونيةة) والطاقة الدورانية والطاقة  
الاهتزازية

$$E_{\text{total}} = E_t + E_r + E_v \text{ (or s)}$$



# Vibrational Modes

- It is ordinarily possible to deduce the number and kinds of vibrations in simple diatomic and triatomic molecules and whether these vibration will lead to absorption .

استنتج  
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The number of possible vibrations in a polyatomic molecule can be calculated as follows

- a molecule containing  $N$  atoms have  $3N$  degree of freedom ( due to translational motion  $F_t$  )
- The rotational motion (  $F_r$  ) have 2 degree of freedom for linear molecule and 3 degree of freedom for non –linear molecule.
- vibrational motion (  $F_s$  )



3 N degree of  
freedom=translational+rotational+vibrational

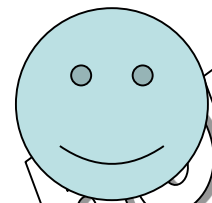
$$F = 3N$$

$$F = F_r + F_t + F_s$$

$$F_s = F - F_t - F_r$$

$$F_s = 3N - 3 - 2 \quad (\text{linear})$$

$$F_s = 3N - 3 - 3 \quad (\text{nonlinear})$$



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$$F_s = 3N - 3 - 2$$

$$9 - 5 = 4$$

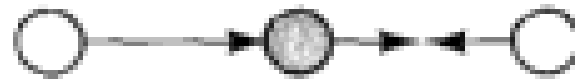
Example : Carbon dioxide

- a linear molecule and thus has  $3N - 5 = 4$  normal modes
- Practical have only 2 absorption peak why ?

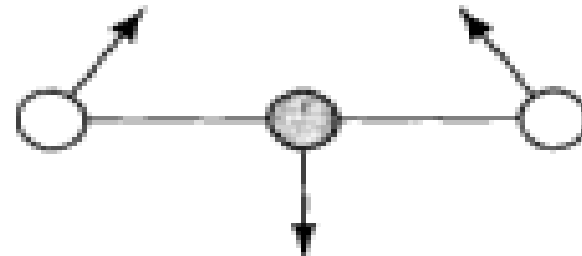
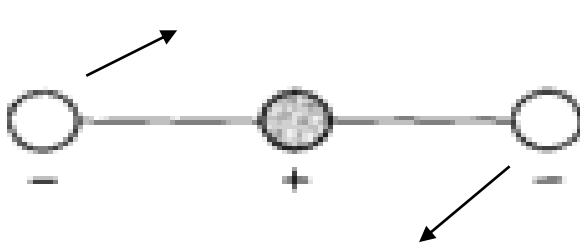
Because one of the coupled vibration is symmetric and the other is asymmetric. The symmetric vibration causes no change in dipole, since the two oxygen atoms simultaneously move away from or toward the central carbon atom. Thus, the symmetric vibration is infrared inactive. But the asymmetric vibration is infrared active.



Symmetric

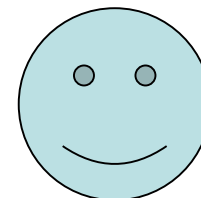


Asymmetric





Q. Give the number of translational, rotational, and vibrational degrees of freedom for  $\text{CO}_2$ .



A. Total degrees of freedom =  $3n = 9$

Translational = 3

Rotational = 2

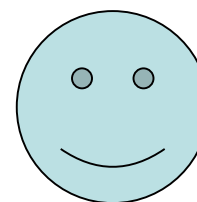
Vibrational =  $3n - 5 = 4$

Pro



Q

Give the number of translational, rotational, and vibrational degrees of freedom for acetylene.



A

Total degrees of freedom =  $3n = 12$

Translational = 3

Rotational = 2

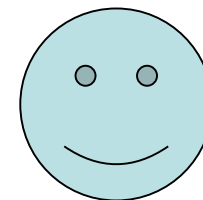
Vibrational =  $3n - 5 = 7$

PIU



Q Give the number of translational, rotational, and vibrational degrees of freedom for the non-linear molecule, water.

A Total degrees of freedom =  $3n = 9$   
Translational = 3  
Rotational = 3  
Vibrational =  $3n - 6 = 3$



PROF.



Q

Give the number of translational, rotational, and vibrational degrees of freedom for the non-linear molecule,  $\text{CH}_4$ .

A

Total degrees of freedom =  $3n = 15$

Translational = 3

Rotational = 3

Vibrational =  $3n - 6 = 9$

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**R**

A molecule with  $n$  atoms has  $3n$  degrees of freedom.

$3n$  degrees of freedom = translational + rotational + vibrational.

For linear molecules:

Vibrational degrees of freedom =  $3n-5$ .

For non-linear molecules:

Vibrational degrees of freedom =  $3n-6$ .

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An infrared absorption band will be observed for each vibrational degree of freedom provided:

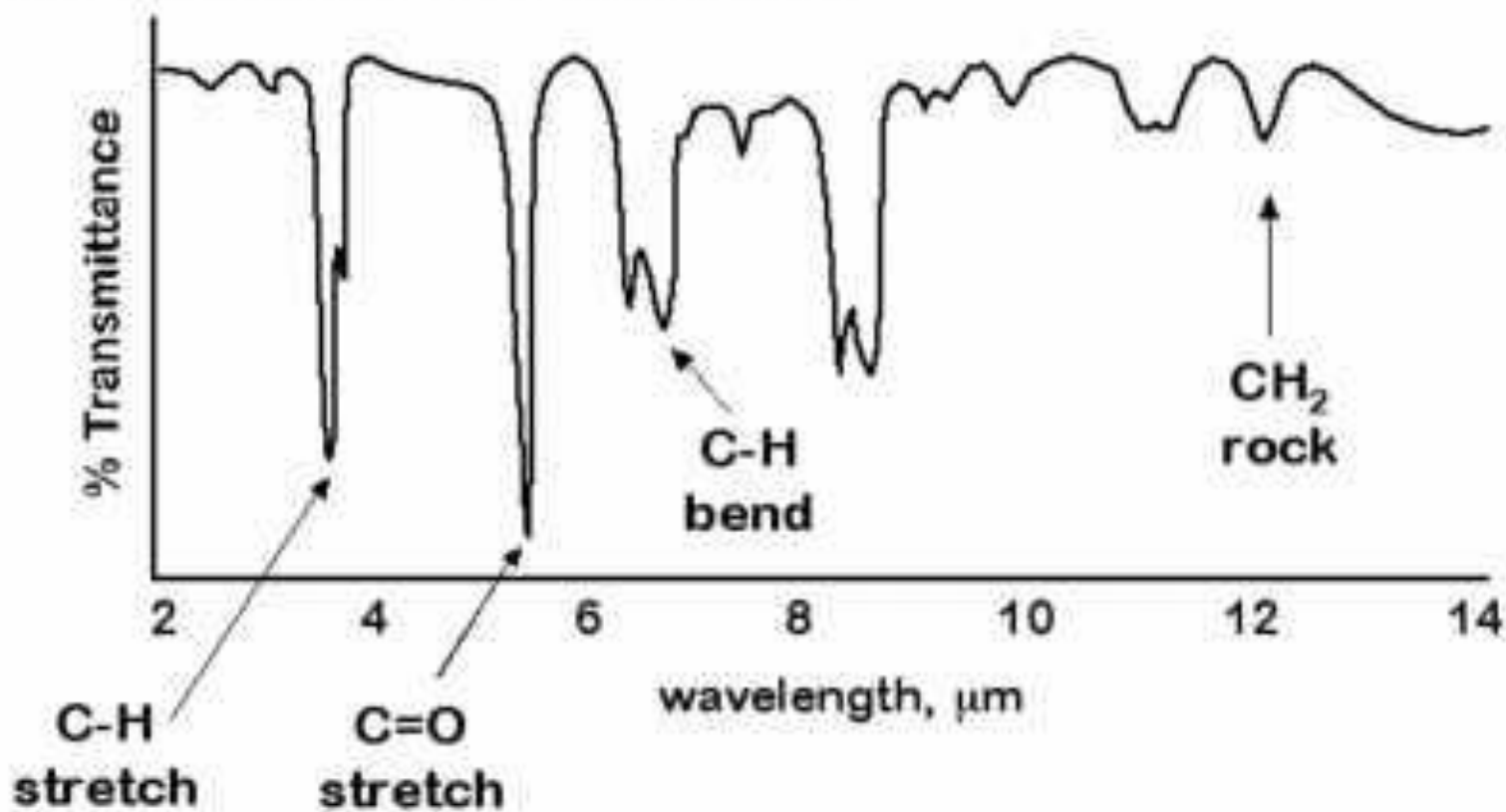
1. A change in the dipole moment of the molecule occurs during the vibration.
2. The band does not coincide in frequency with some other fundamental vibration (the energy levels are degenerate).  
تزامن
3. The absorption falls within the infrared region.
4. The intensity of the absorption is strong enough to be detected.

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# IR absorption

Due to the large number of vibrational states, IR spectra can be very complex.







## IR sources

All are essentially heater elements. IR radiation is produced by passing a current through the element.

**Nernst glower** -  $ZrO_2$ /yttrium oxides

400 - 20,000 nm

**NiChrome wire** - 750 - 20,000 nm

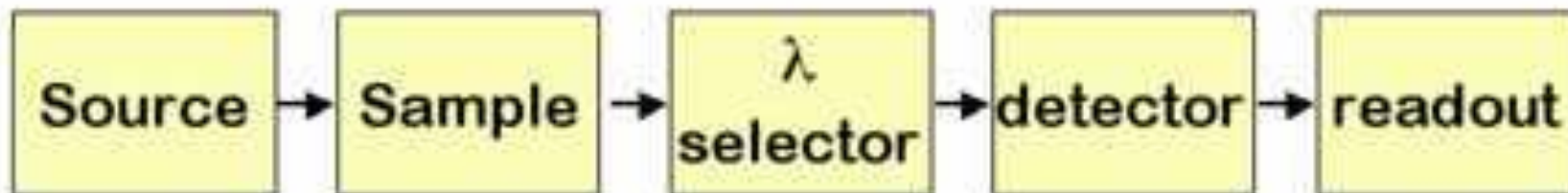
**Globalar** - SiC rod - 1200 - 40,000 nm



# Absorbance



**Common arrangement for UV/Vis**



**Common arrangement for IR**



# IR spectrophotometers

IR equipment is available in two types of configurations.

## Dispersive

Relies on a monochromator system and scanning to produce a spectrum.

## FT

Uses a combination of constructive and destructive interference along with Fourier transformation to produce a spectrum.



# IR spectrophotometers

## Dispersive instruments.

Double beam instruments are the rule.

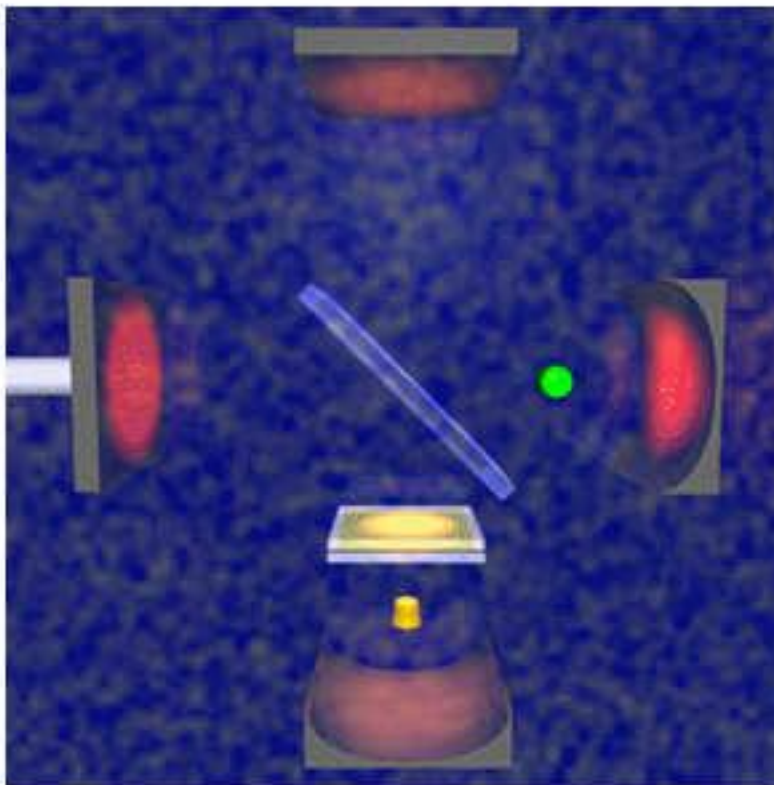
Only significant difference is that the monochromator is after the sample - not before like in UV/Vis equipment.





## FTIR system

A complex signal is produced by passing light through an interference filter and varying the path length.

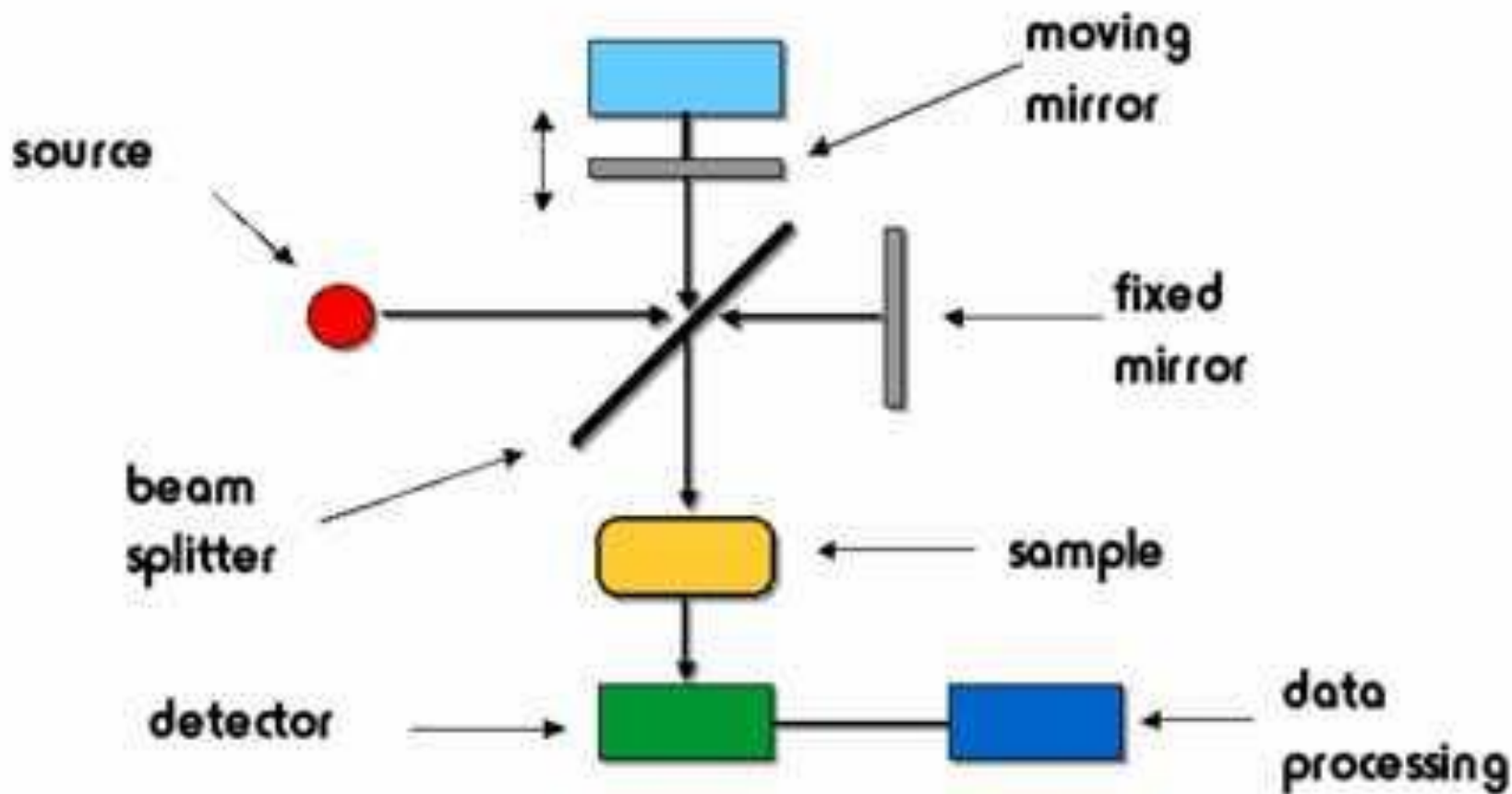


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# IR spectrophotometers

## FT-IR instrument





# IR spectrophotometers

## FT-IR

Since each cycle of the mirror results in several measurements at each  $\lambda$ :

Very fast spectra can be obtained (<1 sec).

Signal to noise can be increased by obtaining many spectra.

You must determine which of the two is most important when developing the method.



# IR spectrophotometers

## FT-IR

The resulting data set is very complex since each data point actually represents the transmittance for several  $\lambda$ .

Each point will contain information for different  $\lambda$  and the data overlaps.

The mathematical process of Fourier transformation is required to convert the data to a usable data.





# IR spectrophotometers

**FT-IR** ( Fourier Transform Infrared Spectrometer)

**At any given time, many  $\lambda$  are passed through the sample cell and recorded.**

**As the movable mirror goes through its cycle, the type of constructive and destructive interference changes, altering the  $\lambda$  that are allowed to pass.**

**With each cycle, any given  $\lambda$  will pass through the cell many times.**



## Lens materials

The material used for construction of lenses must allow light to pass.

This is a function of the  $\lambda$  range that the instrument is designed to work with.

**Visible** - ordinary glass or silica

**UV** - fused silica or quartz

**IR** - KCl, NaCl



# Sample cells

## Cell materials

<b>UV</b>	<b>quartz, fused silica</b>
<b>Visible</b>	<b>glass, plastic (UV cells can be used)</b>
<b>IR</b>	<b>KBr, NaCl crystals are most common</b>

<b>material</b>	<b>nm range</b>
<b>silica</b>	<b>150 - 3000</b>
<b>glass</b>	<b>375 - 2000</b>
<b>plastic</b>	<b>380 - 800</b>



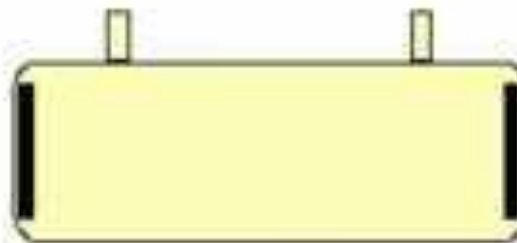
# Sample cells



standard liquid  
cuvette



liquid  
sandwiched  
between  
two NaCl  
plates  
for IR



sample cell  
for gases



# Detectors

IR (heat) detectors.

**Thermocouple** مزدوجة حرارية

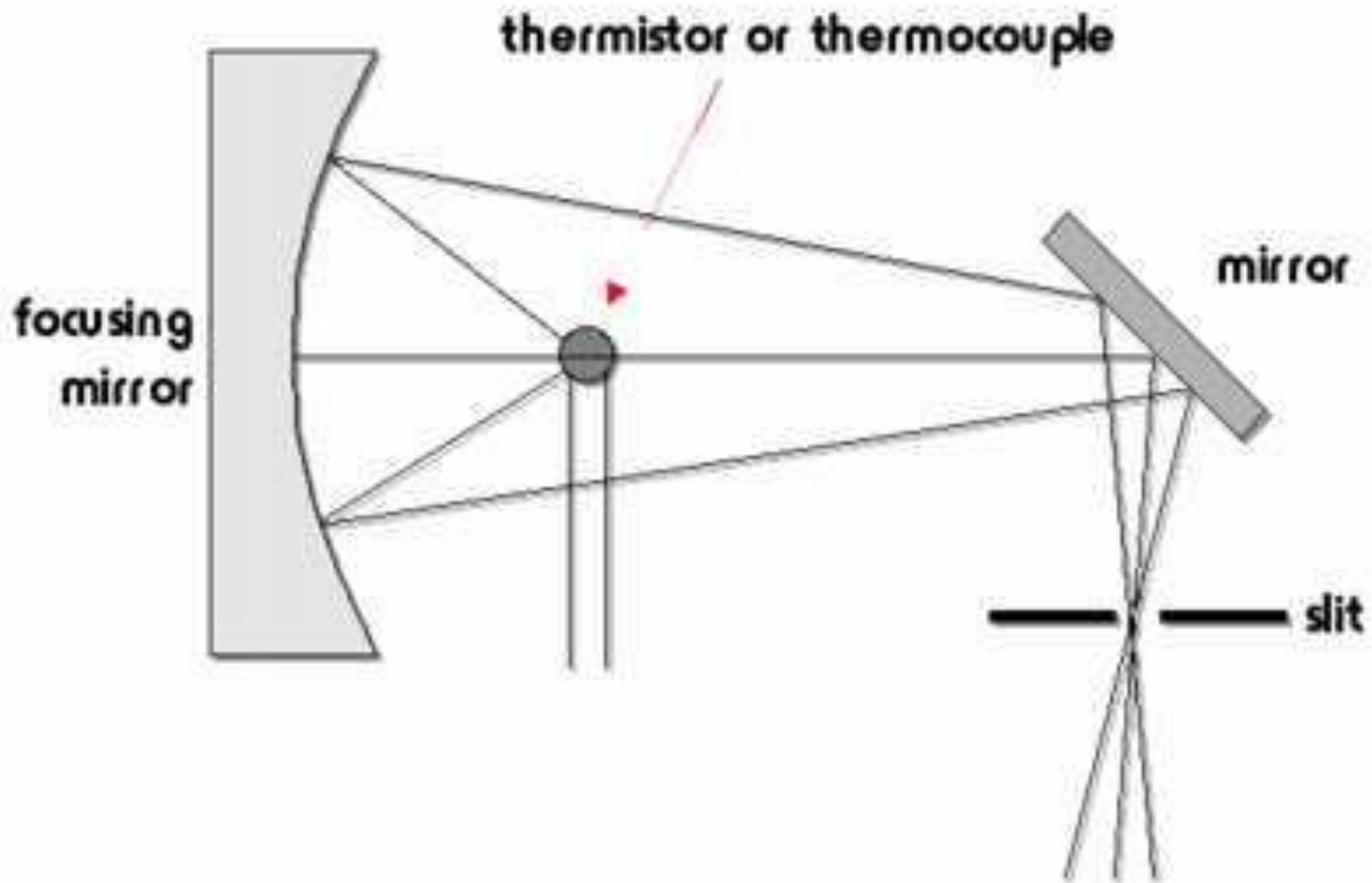
Two dissimilar metals are welded together.  
You get a potential difference  $E_{\text{cell}}$  that is  
temperature dependent.

**Thermister** حساس حرار

Resistance changes as a function of  
temperature.



# Detectors





# IR absorption

The real strength of IR is its ability to identify functional groups.

Functional Group	wavenumber ( $\text{cm}^{-1}$ )	wavelength ( $\mu\text{m}$ )
C-H, aliphatic	3000-2850	3.3-3.5
C-H, aromatic	3150-3000	3.2-3.3
O-H	3600-3000	2.8-3.3
C=O, aldehyde/ketone	1740-1660	5.7-6.0
-CH <sub>2</sub> Cl	1300-1200	7.6-8.2
	850-890	13.2-14



# Applications of Infrared Spectrometry

1- Qualitative analysis

2- Structure analysis

3- Quantitative analysis

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# Sample Handling

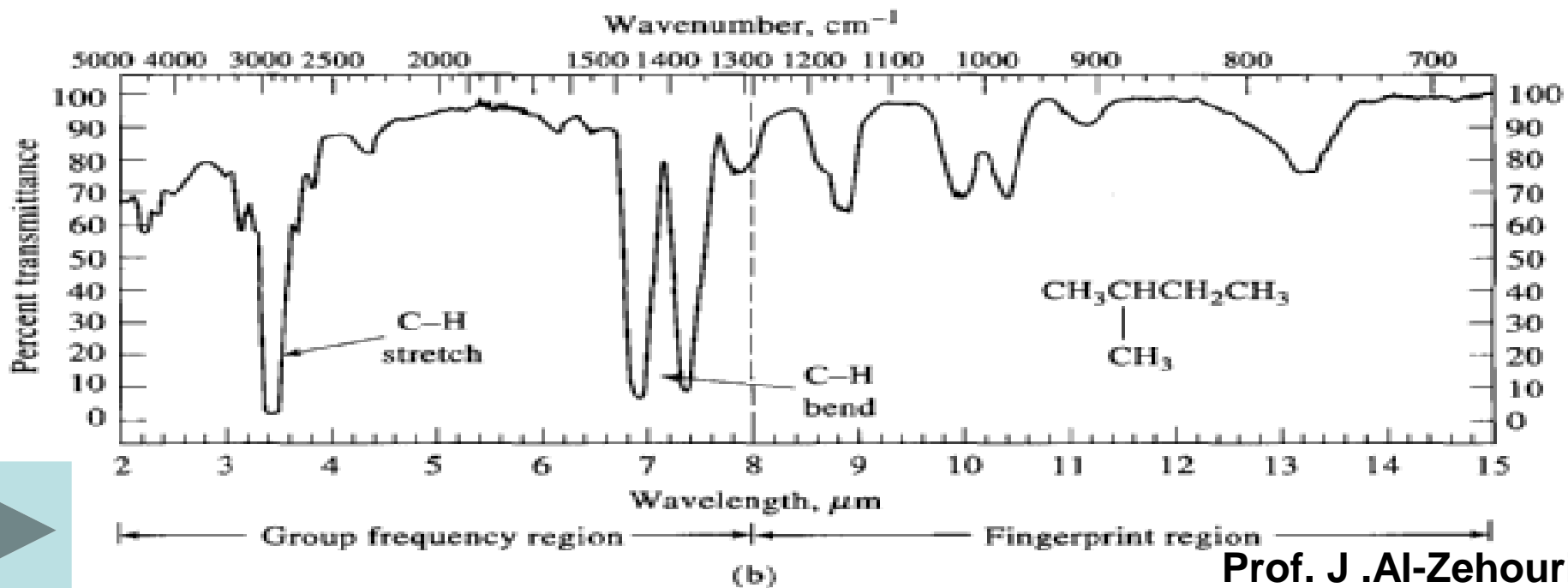
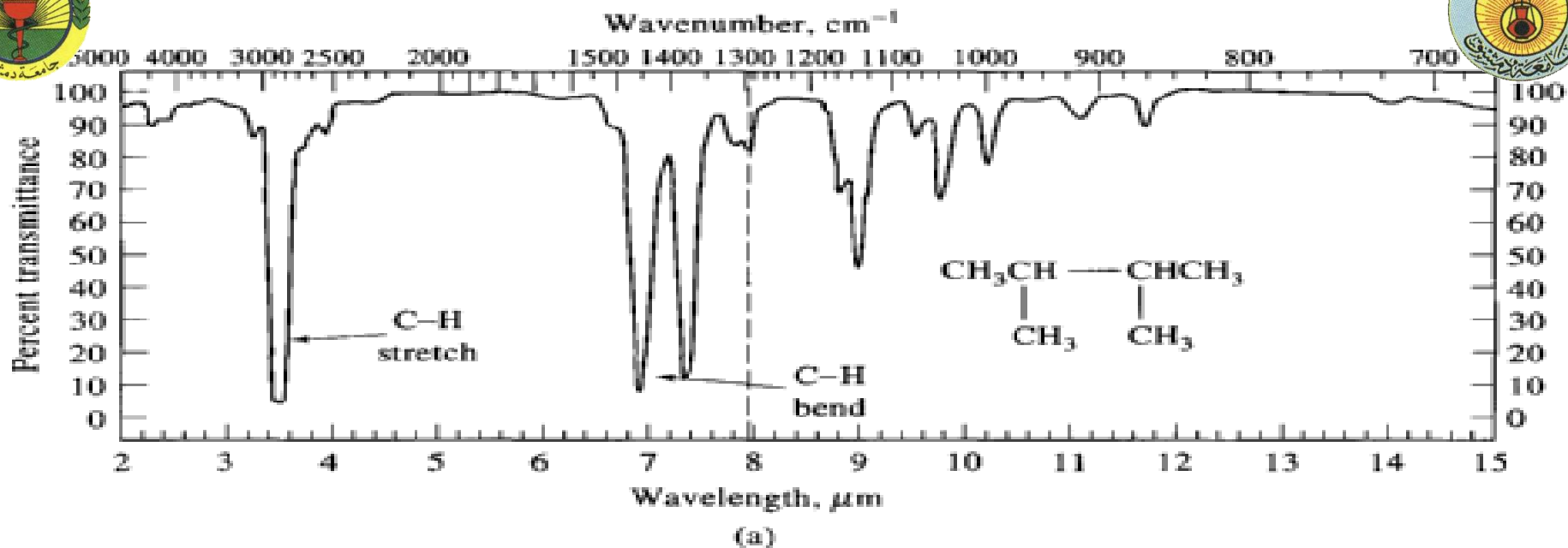
- Solids : one of the most popular techniques for handling solid samples has been KBr pelleting .
- Gases : The spectrum of gas can be obtained by permitting the sample to expand into an evacuated cylindrical cell equipped with suitable windows.
- Liquid ; using sodium chloride cells.



# Qualitative Analysis

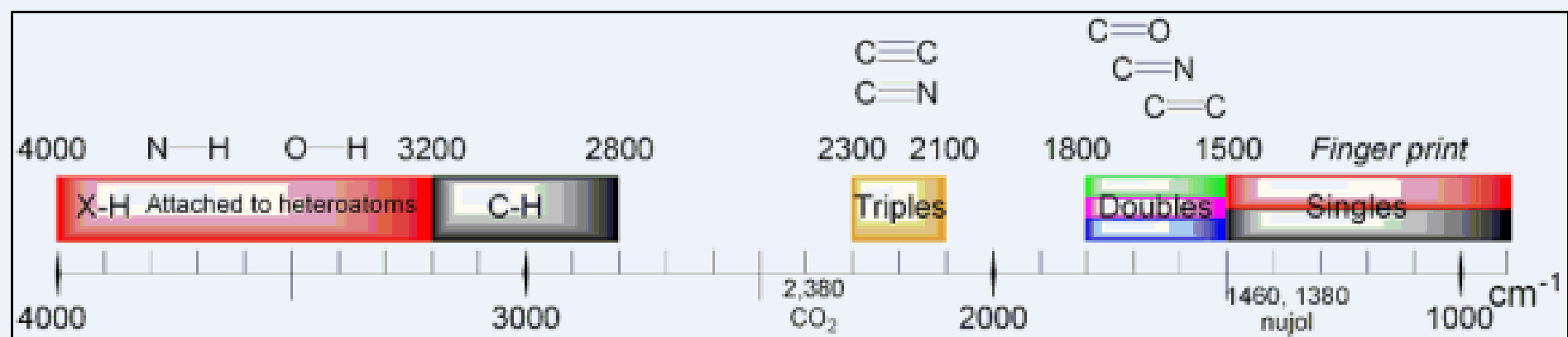
- IR- Spectroscopy : Primarily used for qualitative analysis.
- The general use in pharmacy for identification of drugs.
- We compare the spectrum with the standard.
- Fingerprint region :  $1200 - 700 \text{ cm}^{-1}$  (8-14 $\mu\text{m}$ )

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Zehouli



Prof. Dr. Jowh



# Structure analysis

(functional analysis)

- Identification of characteristic absorption band caused by different functional groups is the basic for the interpretation of infrared spectra. thus O-H stretching frequencies give rise to strong absorption bands in the  $3350 \text{ cm}^{-1}$  .....

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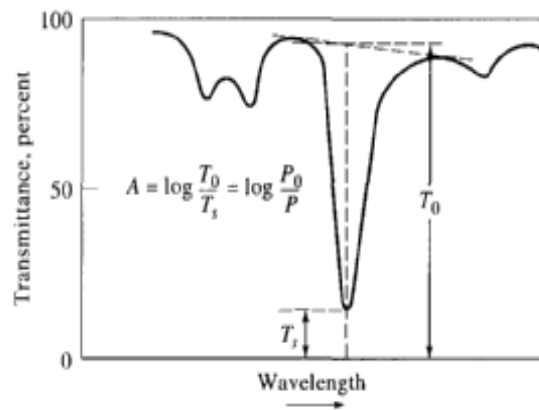
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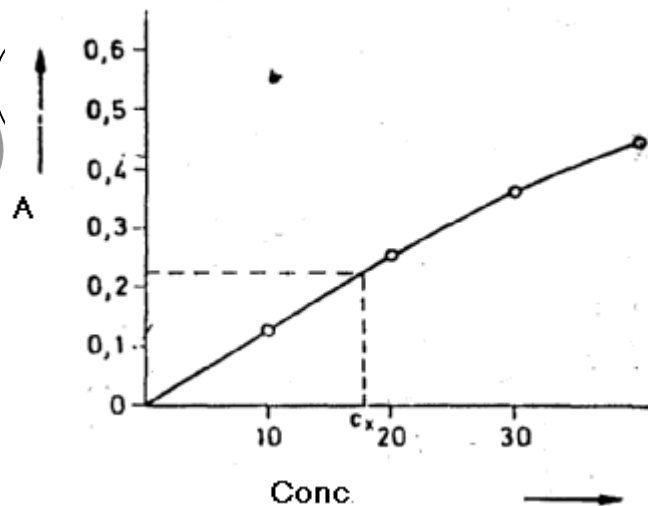
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-CH <sub>2</sub> Cl	1300-1200	7.6-8.2
	850-890	13.2-14



# Quantitative analysis



Baseline method for determination of absorbance.



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# Molecular absorption methods

## IR quantitative analysis

The bands observed in the IR region tend to be very narrow compared to UV/Vis.

As a result, IR absorption typically shows significant deviations from the Beer-Lambert relationship.

Overall, IR is not an overly useful quantitative tool.





***Thank you***

# Q&A

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