Spectral methods

basic aspects in theory, instrumental scheme, and utilization + new trends

Analytical Chemistry: Instrumental Analysis

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Definition of group of spectral methods

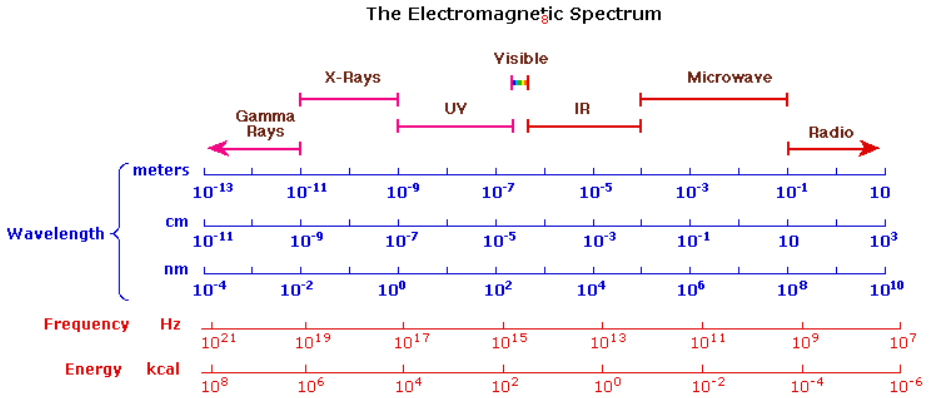
- techniques in analytical chemistry which study an analyte (quality and quantity) by measuring a spectral dependence such as:
  - Absorbance vs. wavelength (UV-VIS absorption spectrometry)
  - Fluorescence vs. wavelength (fluorescence spectrometry)
  - Transmittance vs. wavenumber (infrared spectrometry)
  - Intensity vs. chemical shift (NMR spectrometry)
  - Rel. Abundance vs. m/z (mass spectrometry)
  - and other

  in a suitable part (cuvette, mass analyzer) of spectral analyzer containing the analyte

Principle of spectroscopy

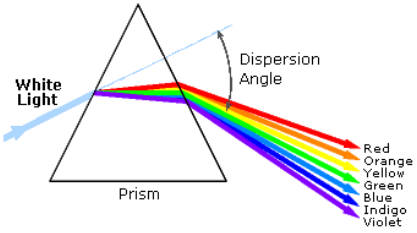
The term "**spectroscopy**" defines a large number of techniques that use radiation to obtain information on the structure and properties of matter. The basic **principle** shared by all **spectroscopic** techniques is to shine a beam of electromagnetic radiation onto a sample, and observe how it responds to such a stimulus.

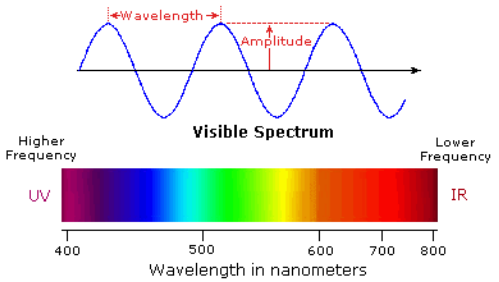
Spectroscopy refers to the study of how radiated energy and matter interact. The energy is absorbed by the matter, creating an excited state. **Spectrometry** deals with the measurement of a specific spectrum so that there are quantifiable results that can then be assessed.



https://www2.chemistry.msu.edu/faculty/reusch/VirtTxtJml/Spectrpy/UV-Vis/spectrum.htm

optical





- **Violet:** 400 - 420 nm
- **Indigo:** 420 - 440 nm
- **Blue:** 440 - 490 nm
- **Green:** 490 - 570 nm
- **Yellow:** 570 - 585 nm
- **Orange:** 585 - 620 nm
- **Red:** 620 - 780 nm

Main categories of spectral methods

- Spectral methods can be broken down into several categories depending on measuring principles and used radiation interacting with the sample:

- **Spectral methods**
  - Optical spectral methods (optical methods are physical-chemical methods of analysis that are based on the optical range of the scale of electromagnetic waves).
  - Atomic spectral analytical methods: Atomic absorption spectral analysis, atomic emission analysis, flame photometry, X-ray fluorescence spectrometry
  - Molecular spectral methods: Molecular absorption spectrometry, fluorescence spectrometry, UV-VIS, infrared spectrometry, Raman spectrometry, nuclear magnetic resonance, mass spectrometry

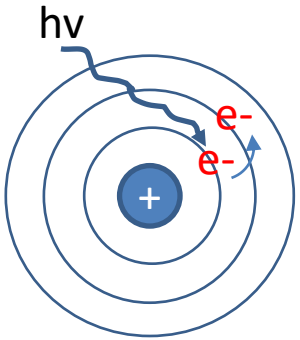
- **Optical methods non-spectral**
  - Refractometry, polarimetry, light scattering photometry
  - Crystallography, X-ray diffraction

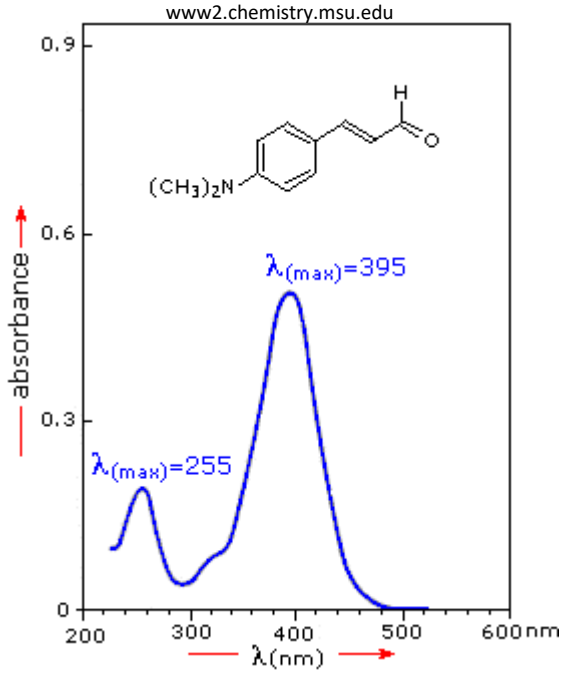
UV-VIS absorption spectroscopy

Principle

- The **Principle of UV-Visible Spectroscopy** is based on the absorption of **ultraviolet** light or **visible** light by chemical compounds, which results in the production of distinct **spectra**.

What chemical compounds are suitable for UV-VIS absorption analysis?
– those with chromophores (conjugated aliphatic and aromatic systems) can absorb UV-VIS radiation



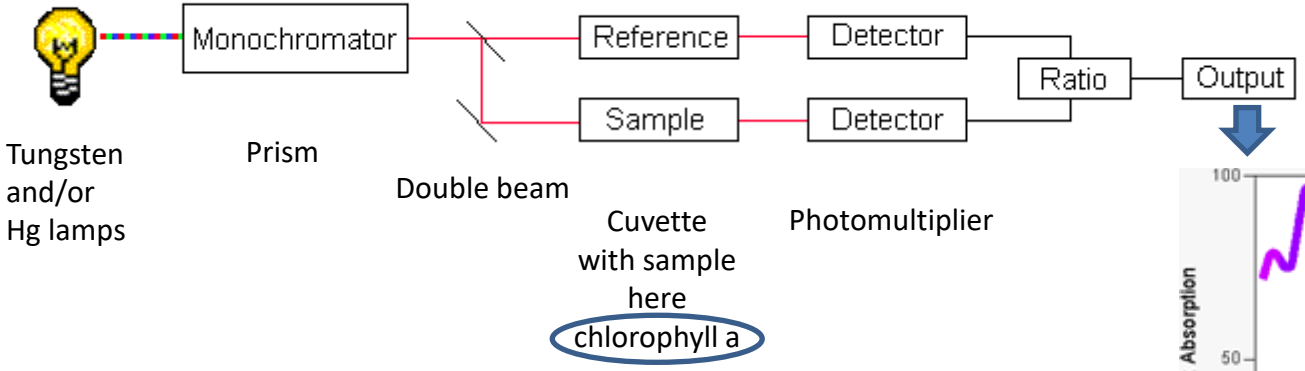


UV-VIS absorption spectroscopy

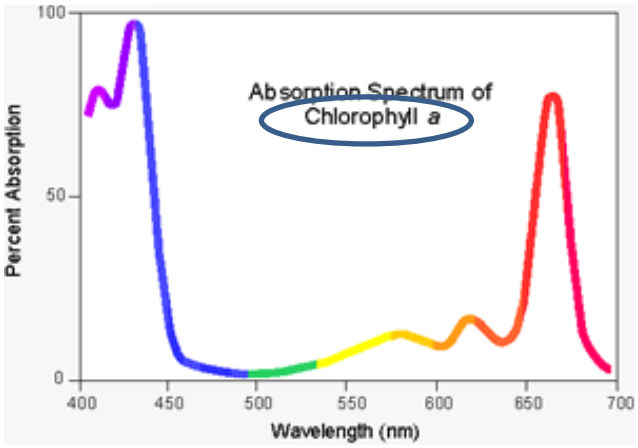
Experimental arrangement

Instruments for measuring the absorption of UV or visible radiation are made up of the following components:

- Sources of radiation (UV and visible lamps)
- Wavelength selector (monochromator)
- Sample containers (cuvettes)
- Detector (photomultiplier)
- Signal processor and readout



Absorption spectrum



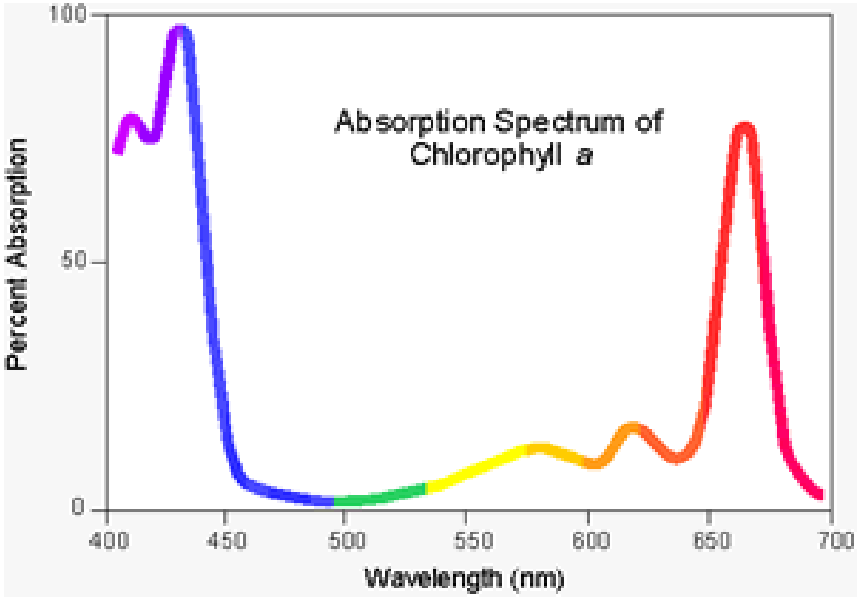
dynamicscience.com.au

UV-VIS absorption spectroscopy

Qualitative analysis

Qualitative analysis is based on the evaluation (comparison) of profiles of absorption spectra of UV-VIS absorbing compounds. Different UV-VIS absorption profiles are results of different chemical structures of various compounds.

Absorption spectrum



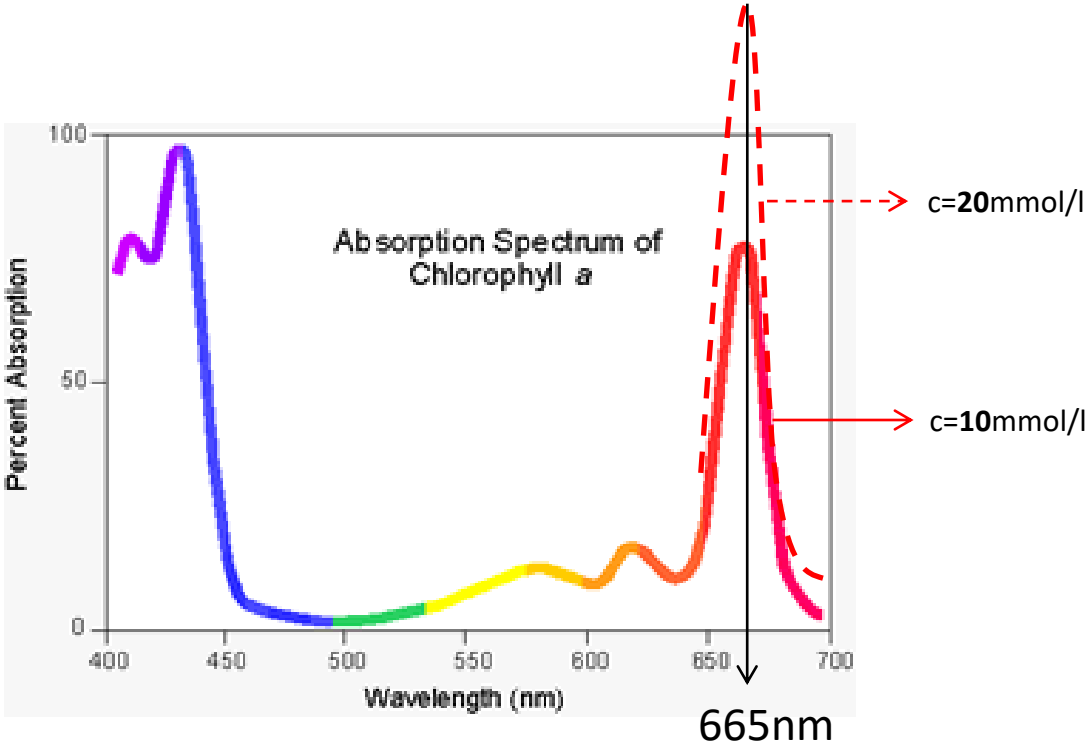
dynamicscience.com.au

Notice:
Absorption spectra do not give precise information in detail chemical structure of an analyzed compound (as it can do e.g. NMR or MS). UV-VIS absorption spectra serve rather to a preliminary confirmation of a given structure in the sample via comparison with a spectrum of corresponding reference compound.

UV-VIS absorption spectroscopy

Quantitative analysis

Quantitative analysis is based on the evaluation of intensity of absorption spectrum (or, in practice, one selected wavelenght of the spectrum) of UV-VIS absorbing compound. Intensity of absorbance is proportional to the concentration of absorbing compound according to the **Lambert-Beer law**: A = c . d . e, where A is absorbance, c is concentration of absorbing compound, d is width of the cuvette (the radiation pass length) and e is absorption coefficient (characteristic for given chemical structure/chromophore)



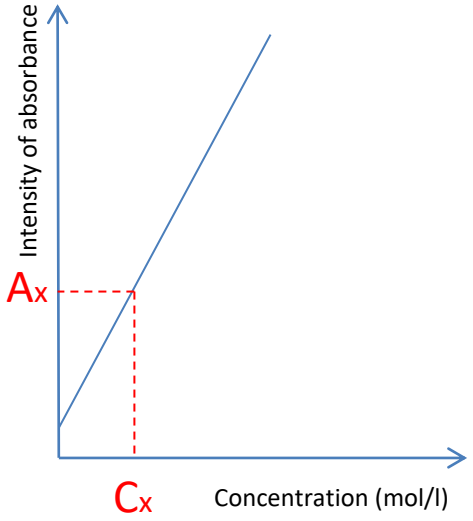
Calibration curve

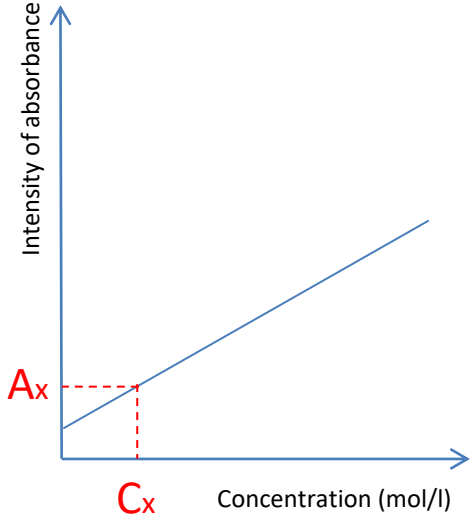
Based on A_{665} = f(c)

UV-VIS absorption spectroscopy

what is sensitivity?
what is calibration curve?

Sensitivity of the UV-VIS analyzer is a measure of its ability to discriminate between small differences in analyte concentration (i.e. when response increases more/less for a given concentration of the analyte, the analyzer is more/less sensitive). So, it is actually the slope of the calibration curve (i.e. the higher the slope of a calibration curve the higher the sensitivity of the analyzer for that particular component). Highly sensitive analyzers are prefered.





Calibration curve is a dependence of intensity of absorbance on concentration of given analyte. This dependence is prepared from measuring a series of standard solutions of given analyte with known concentrations. Mathematical expression of calibration line is following: y=ax+b, where *y* is intensity of absorbance, *x* is concentration of given compound, *a* is slope of calibration line, *b* is intercept of calibration line. Given calibration line is described by *a* and *b*, so that measuring intensity of absorbance of given compound we can easily recalculate its unknown concentration.

Calibration curves obtained with a more sensitive analyzer (left dependence) or a less sensitive analyzer (right dependence). For a given concentration c_x of the analyte X was obtained higher (left dependence) or lower (right dependence) analytical signal (absorbance).

Notice 1: Sensitivity of an analyzer is not the minimum amount that can be detected, this is the Limit of detection, LOD (see later). This value (LOD) is influenced by the experimental conditions , namely a noise of the baseline.
Notice 2: These facts are applicable for spectral, electrochemical and separation methods as well.

UV-VIS absorption spectroscopy

Benefits, limitations and application possibilities

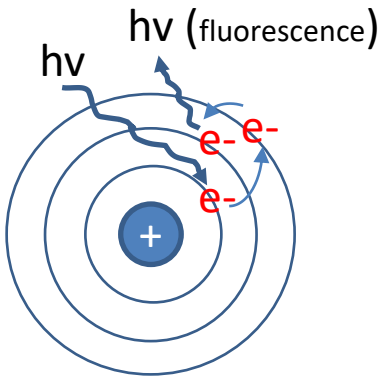
- Simple equipment and analyses
- Cheap equipment and measurements
- Almost universal (large number of UV-VIS absorbing compounds)
- Fast measurements
- Less sensitive
- Less selective
- Unsuitable for exact structural analysis
- Unable to analyze samples with complex matrices
- Preliminary identity confirmation
- Preliminary purity testing
- Fast quantification
- Most frequently used detection step in separation techniques

New trends: libraries of spectra are enhanced, sensitivity is enhanced, precision is enhanced, scaning rate is higher

Fluorescence spectroscopy

Principle

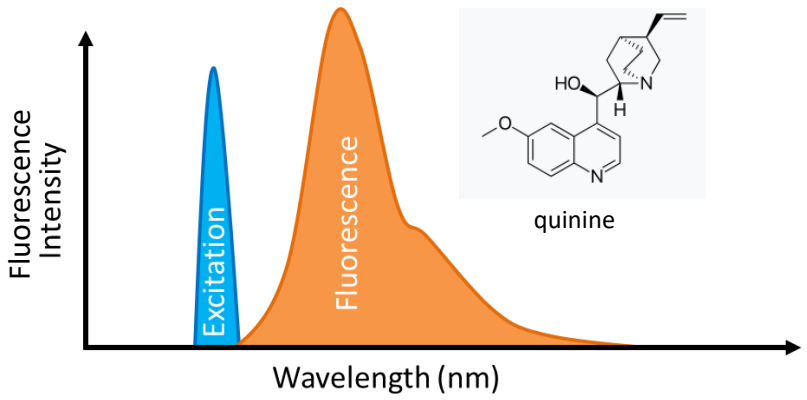
Molecular fluorescence is measured by exciting the sample at the absorption wavelength, also called ***excitation wavelength***, and measuring the emission at a longer wavelength called the emission or ***fluorescence wavelength***. Usually, fluorescence emission is measured at right angles to the incident beam so as to avoid measuring the incident radiation. The short-lived emission that occurs is called ***fluorescence***, whereas luminescence that is much longer lasting is called ***phosphorescence***.



What chemical compounds are suitable for fluorescence analysis?

– those with fluorophores (more complex conjugated aliphatic and aromatic systems often with various heteroatoms and charge) can absorb UV radiation and emit fluorescence radiation

Fluorescence spectrum

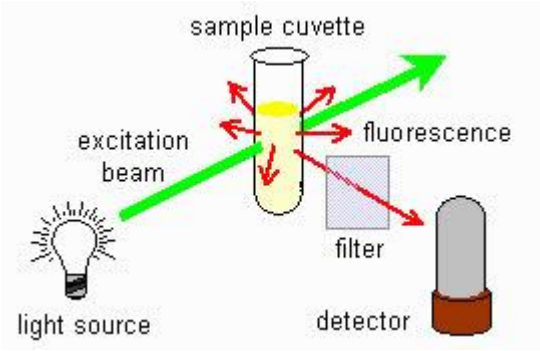


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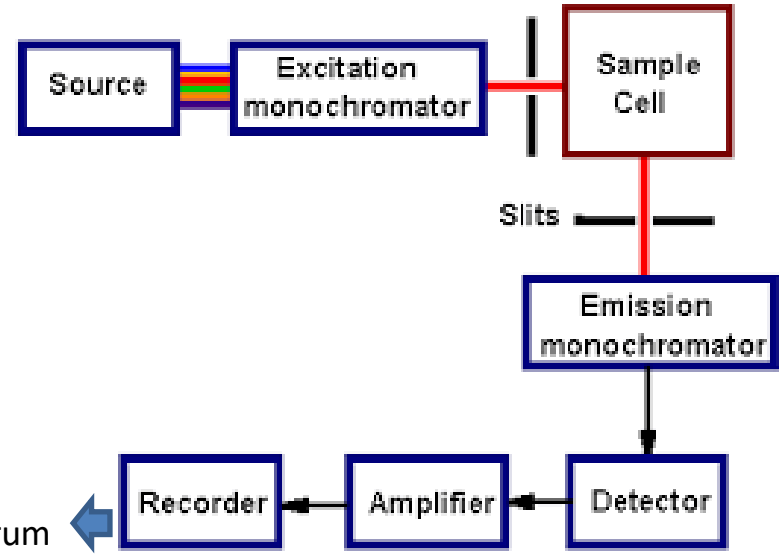
Fluorescence spectroscopy

Experimental arrangement

Instruments for measuring the fluorescence radiation are made up of the following components:

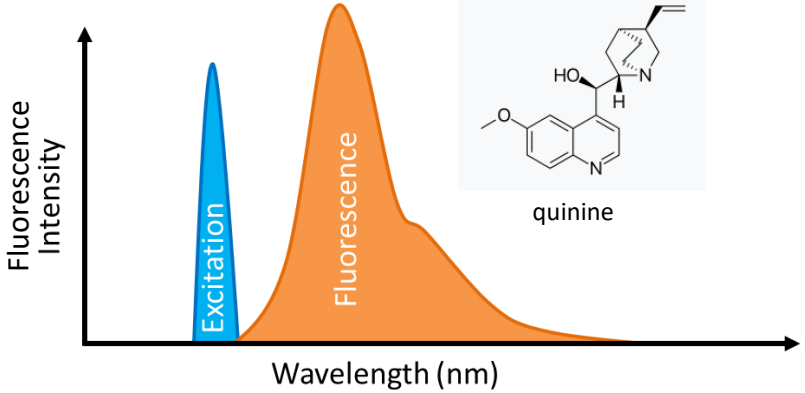


chromedia.org



pci.tu-bs.de

Fluorescence spectrum



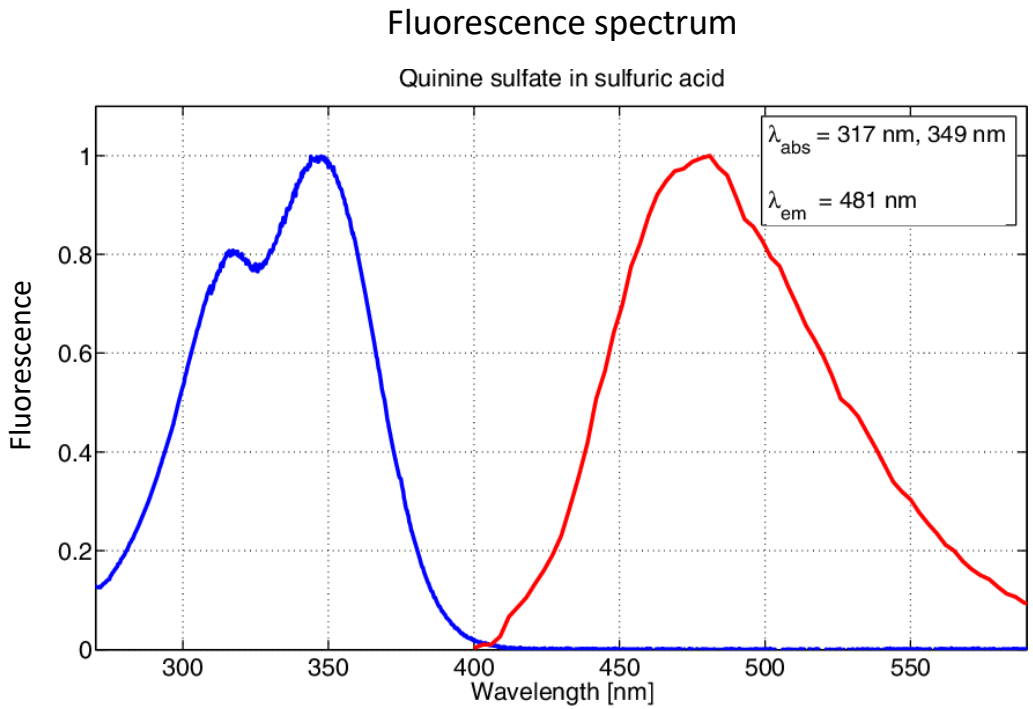
ibsen.com

quinine

Fluorescence spectroscopy

Qualitative analysis

Qualitative analysis is based on the evaluation (comparison) of profiles of fluorescence spectra of (UV absorbing and subsequently) fluorescing compounds. Different fluorescence profiles are results of different chemical structures of various compounds.



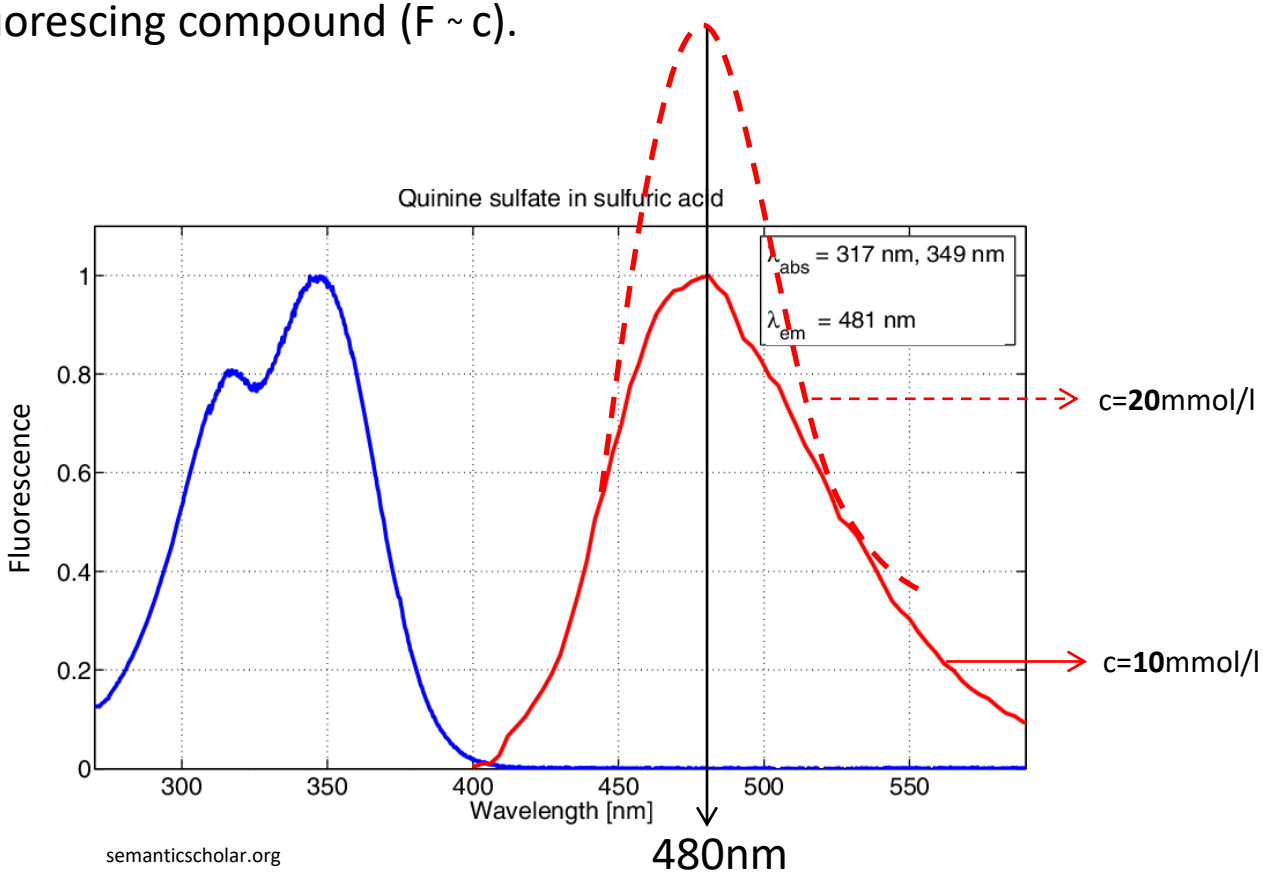
semanticscholar.org

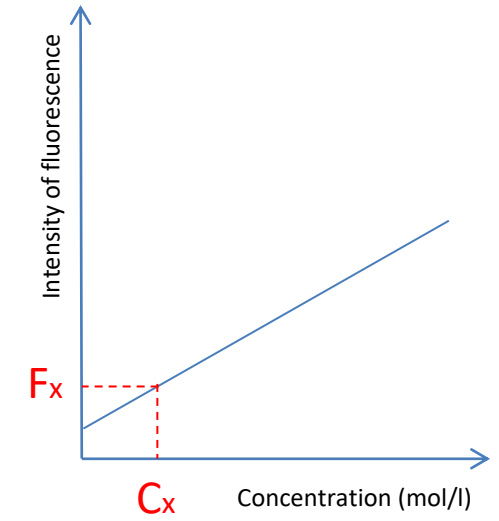
Notice:
Fluorescence spectra do not give precise information in detail chemical structure of an analyzed compound (as it can do e.g. NMR or MS). Fluorescence spectra serve rather to a preliminary confirmation of a given structure in the sample via comparison with a spectrum of corresponding reference compound.

Fluorescence spectroscopy

Quantitative analysis

Quantitative analysis is based on the evaluation of intensity of fluorescence spectrum (or, in practice, one selected wavelenght of the spectrum) of (UV absorbing and subsequently) fluorescing compound. Intensity of fluorescence is proportional to the concentration of fluorescing compound (F ~ c).



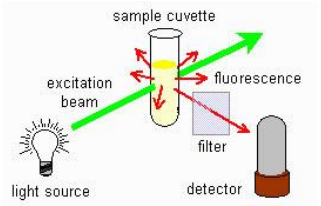


Calibration curve

Based on F_{480} = f(c)

Fluorescence spectroscopy

Benefits, limitations and application possibilities



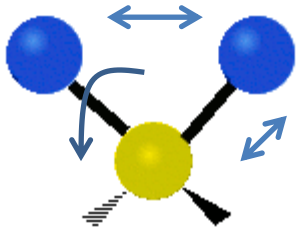
- Highly sensitive (especially LIF, laser induced fluorescence)
- Highly selective
- Relatively simple equipment and analyses
- Fast measurements
- More expensive equipment than UV-VIS (especially LIF)
- Less universal (non-fluorescing compounds must be derivatized)
- Unsuitable for exact structural analysis
- Unable to analyze samples with complex matrices
- Preliminary identity confirmation
- Preliminary purity testing
- Fast quantification
- Most sensitive detection step in separation techniques

Laser as a source of light in LIF

Higest sensitivity
Highest selectivity
Fmol-amol amounts of the analytes can be determined

New trends: libraries of spectra are enhanced, sensitivity is enhanced, precision is enhanced, scaning rate is higher

IR spectroscopy

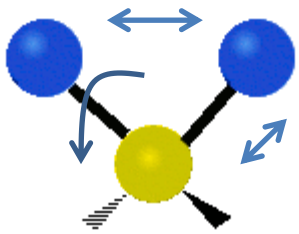


Principle

Infrared spectroscopy exploits the fact that molecules absorb frequencies that are characteristic of their structure. These absorptions occur at resonant frequencies, i.e. the frequency of the absorbed radiation matches the vibrational frequency. The energies are affected by the shape of the molecular potential energy surfaces, the masses of the atoms, and the associated vibronic coupling.

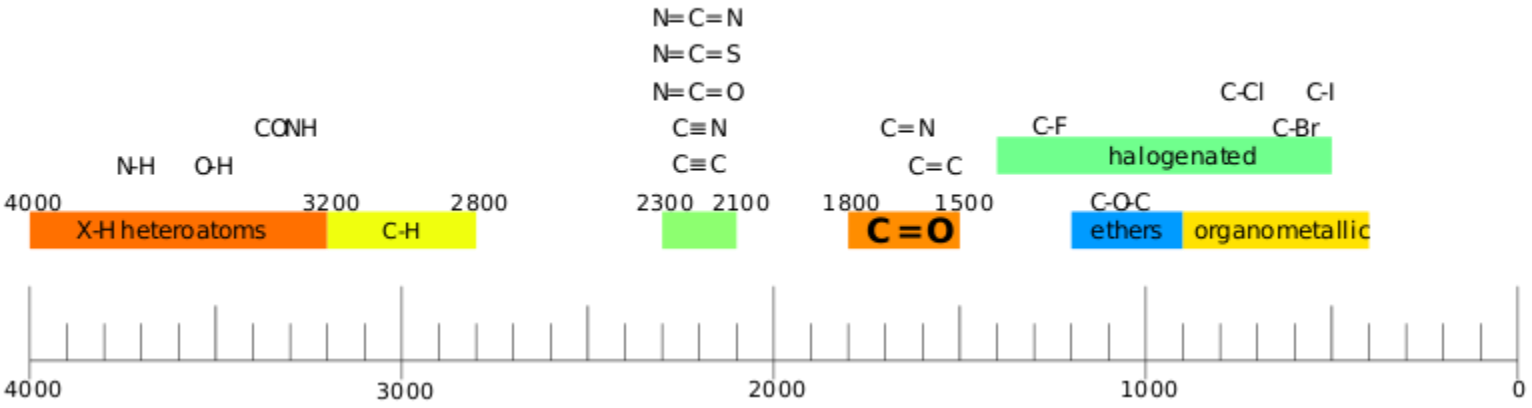
Infrared spectroscopy (**IR spectroscopy** or **vibrational spectroscopy**) is the measurement of the interaction of infrared radiation with matter by absorption, emission, or reflection. It is used to study and identify chemical substances or functional groups in solid, liquid, or gaseous forms.

IR spectroscopy



Principle

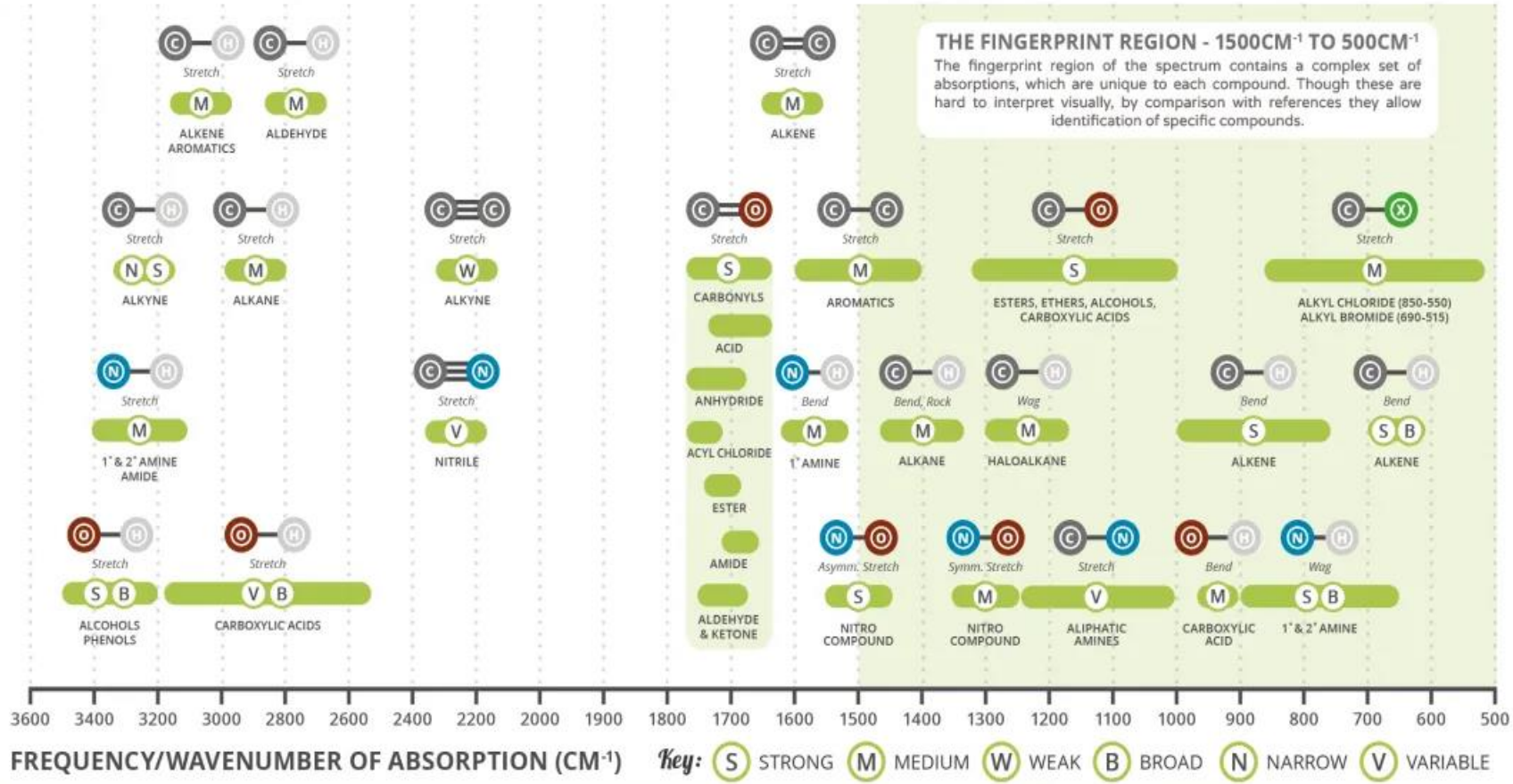
The infrared portion of the electromagnetic spectrum is usually divided into three regions: the near-, mid- and far- infrared, named for their relation to the visible spectrum. The higher-energy near-IR, approximately 14000–4000 cm^{-1} (0.7–2.5 µm wavelength) can excite combination modes of molecular vibrations. The mid-infrared, approximately 4000–400 cm^{-1} (2.5–25 µm) is generally used to study the fundamental vibrations and associated rotational–vibrational structure. The far-infrared, approximately 400–10 cm^{-1} (25–1000 µm) has low energy and may be used for rotational spectroscopy and low frequency vibrations. The region from 2–130 cm^{-1}, bordering the microwave region, is considered the terahertz region and may probe intermolecular vibrations.



Smith JG (2011). "Chapter 13 Mass Spectrometry and Infrared Spectroscopy" (Book). Organic chemistry (3rd ed.). New York, NY: McGraw-Hill. pp. 463–488.

ANALYTICAL CHEMISTRY - INFRARED SPECTROSCOPY

Commonly referred to as IR spectroscopy, this technique allows chemists to identify characteristic groups of atoms (functional groups) present in molecules.



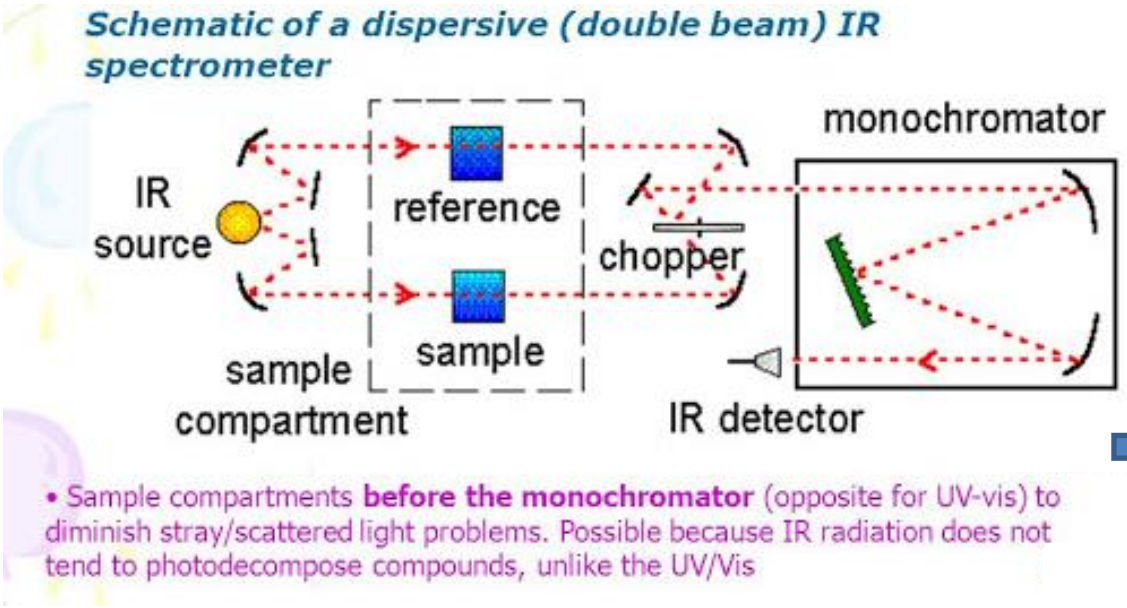
Infrared frequencies make up a portion of the electromagnetic spectrum. If a range of infrared frequencies are shone through an organic compound, some of the frequencies are absorbed by the chemical bonds within the compound. Different chemical bonds absorb different frequencies of infrared radiation. There are a number of characteristic absorptions which allow functional groups (the parts of a compound which give it its particular reactivity) to be identified. This graphic shows a number of these absorptions.

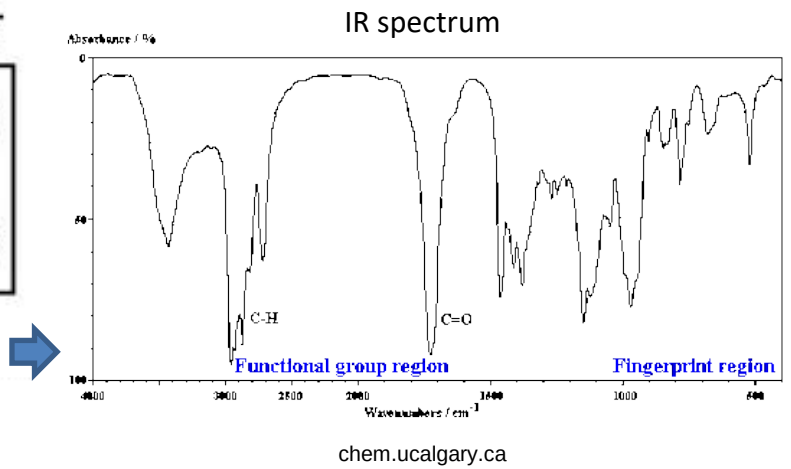
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IR spectroscopy

Experimental arrangement

The method or technique of infrared spectroscopy is conducted with an instrument called an **infrared spectrometer** which produces an **infrared spectrum**. An IR spectrum can be visualized in a graph of infrared light absorbance (or transmittance) on the vertical axis vs. frequency or wavelength on the horizontal axis. Typical units of frequency used in IR spectra are reciprocal centimeters (sometimes called wave numbers), with the symbol cm^{-1}. A common laboratory instrument that uses this technique is a Fourier transform infrared (FTIR) spectrometer.



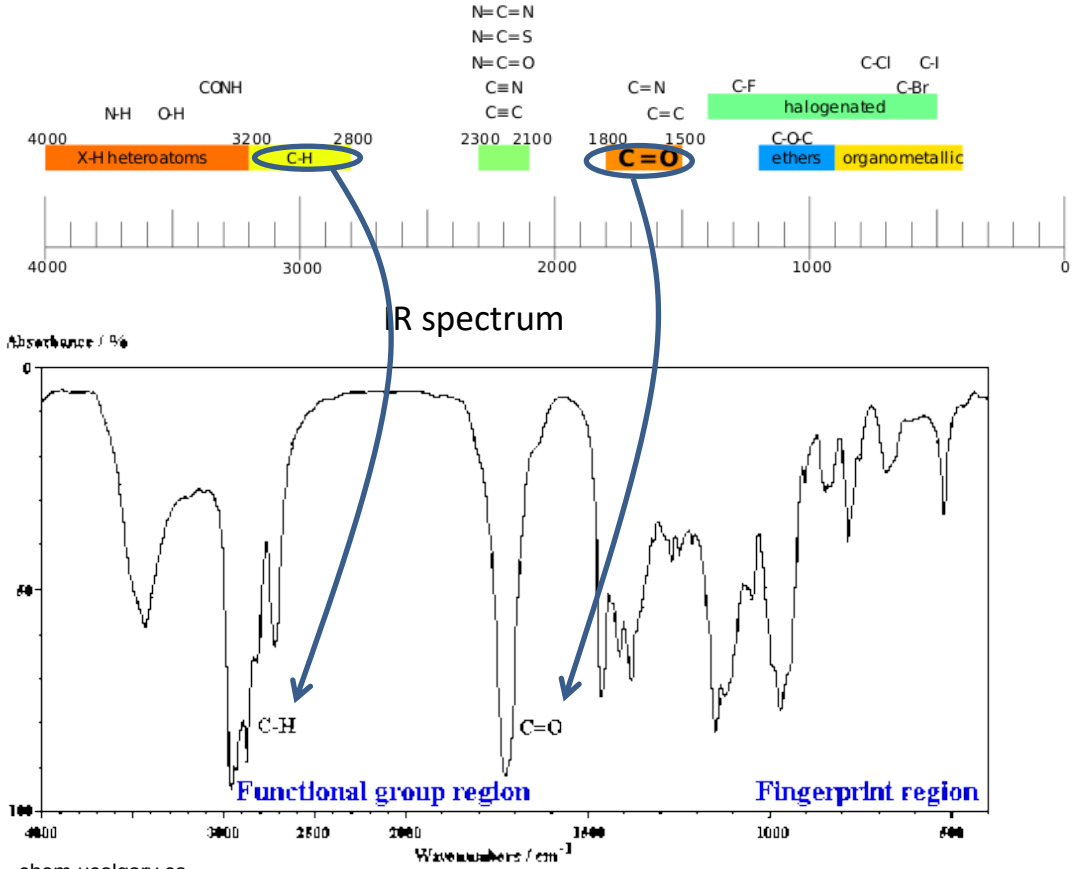


http://delloyd.50megs.com/MOBILE/infrared_spectroscopy.html

IR spectroscopy

Qualitative analysis

IR spectroscopy can identify structures because functional groups give rise to characteristic bands both in terms of intensity and position (frequency).



Notice:
IR spectra give precise information in detail chemical structure of analyzed compounds (their functional groups). Identity of known compounds can be verified via comparison with an IR spectrum of corresponding reference compound.

IR spectra along with NMR and MS represent powerful tandem for a detail structural analysis of known and unknown molecules.

IR spectroscopy

Benefits, limitations and application possibilities

- Relatively simple equipment and analyses
- Fast measurements
- Measurement of liquid and solid samples
- Suitable for exact structural analysis – functional groups
- Universal
- More expensive equipment than UV-VIS
- Identification of chemical structure – functional groups

New trends: libraries of spectra are enhanced, sensitivity is enhanced, precision is enhanced, scaning rate is higher

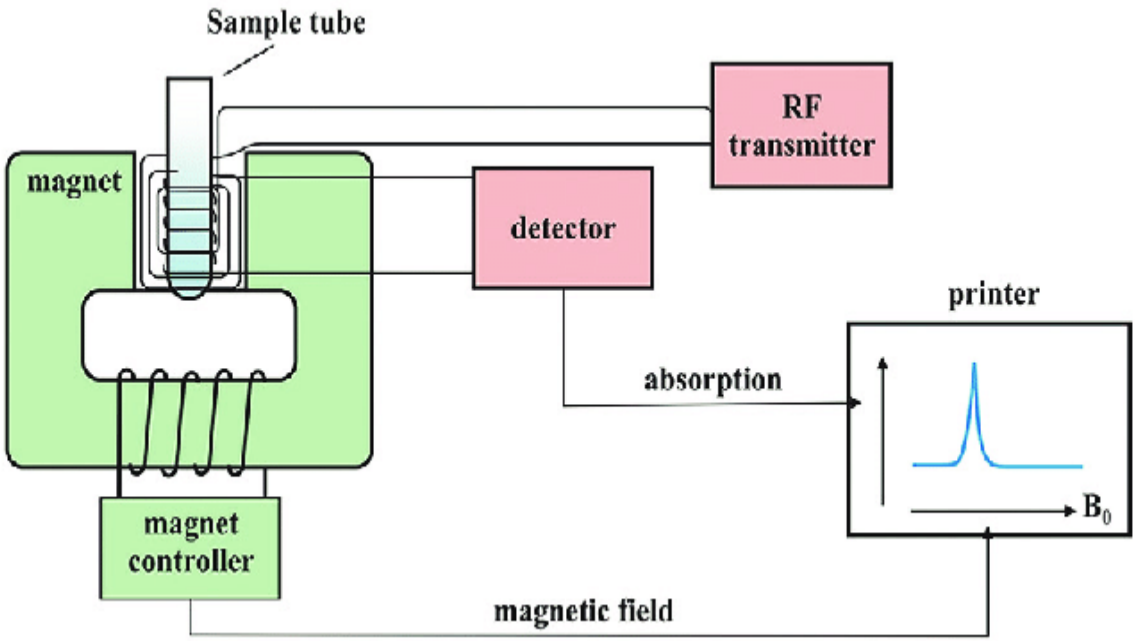
NMR spectroscopy

Principle

Nuclear magnetic resonance (NMR) spectroscopy, is a spectroscopic technique to observe local magnetic fields around atomic nuclei. The sample is placed in a magnetic field and the NMR signal is produced by excitation of the nuclei sample with radio waves resulting in nuclear magnetic resonance, which is detected with sensitive radio receivers. The intramolecular magnetic field around an atom in a molecule changes the resonance frequency, thus giving access to details of the electronic structure of a molecule and its individual functional groups. As the fields are unique or highly characteristic to individual compounds, in modern organic chemistry practice, NMR spectroscopy is the definitive method to identify monomolecular organic compounds. Similarly, biochemists use NMR to identify proteins and other complex molecules. Besides identification, NMR spectroscopy provides detailed information about the structure, dynamics, reaction state, and chemical environment of molecules. The most common types of NMR are proton and carbon-13 NMR spectroscopy, but it is applicable to any kind of sample that contains nuclei possessing spin.

NMR spectroscopy

Experimental arrangement



https://www.google.com/search?q=nmr+instrumental+scheme&client=firefox-b-d&source=lnms&tbm=isch&sa=X&ved=2ahUKEwiVhsq108_rAhWP26QKHZ_ABOQQ_AUoAXoECAwQAw&biw=1920&bih=938#imgrc=VKEwrJxmldhssM&imgdii=WmqLqZDAAQZBBM



A 900 MHz NMR instrument with a 21.1 T magnet



Cutaway of an NMR magnet that shows its structure: radiation shield, vacuum chamber, liquid nitrogen vessel, liquid helium vessel, and cryogenic shims.

https://en.wikipedia.org/wiki/Nuclear_magnetic_resonance_spectroscopy

Modern NMR spectrometers have a very strong, large and expensive liquid helium-cooled superconducting magnet, because resolution directly depends on magnetic field strength. Less expensive machines using permanent magnets and lower resolution are also available, which still give sufficient performance for certain applications such as reaction monitoring and quick checking of samples. There are even benchtop nuclear magnetic resonance spectrometers. NMR can be observed in magnetic fields less than a millitesla. Low-resolution NMR produces broader peaks which can easily overlap one another causing issues in resolving complex structures. The use of higher strength magnetic fields result in clear resolution of the peaks and is the standard in industry.

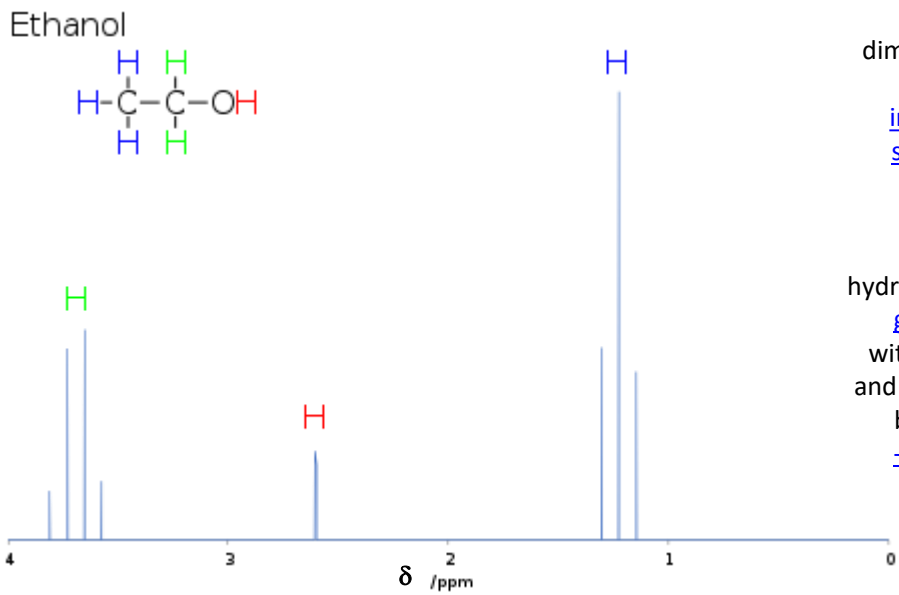
Paudler, William (1974). Nuclear Magnetic Resonance. Boston: Allyn and Bacon Chemistry Series. pp. 9–11.

NMR spectroscopy

Qualitative analysis

NMR spectra are unique, well-resolved, analytically tractable and often highly predictable for small molecules. Different functional groups are obviously distinguishable, and identical functional groups with differing neighboring substituents still give distinguishable signals. NMR has largely replaced traditional wet chemistry tests such as color reagents or typical chromatography for identification. A disadvantage is that a relatively large amount, 2–50 mg, of a purified substance is required, although it may be recovered through a workup. Preferably, the sample should be dissolved in a solvent, because NMR analysis of solids requires a dedicated magic angle spinning machine and may not give equally well-resolved spectra. The timescale of NMR is relatively long, and thus it is not suitable for observing fast phenomena, producing only an averaged spectrum. Although large amounts of impurities do show on an NMR spectrum, better methods exist for detecting impurities, as NMR is inherently not very sensitive - though at higher frequencies, sensitivity is higher.

NMR spectrum



Example ^{1}H NMR spectrum (1-dimensional) of ethanol plotted as signal intensity vs. chemical shift. There are three different types of H atoms in ethanol regarding NMR. The hydrogen (H) on the –OH group is not coupling with the other H atoms and appears as a singlet, but the CH_3– and the –CH_2– hydrogens are coupling with each other, resulting in a triplet and quartet respectively.

Notice:

NMR spectra give precise information in detail chemical structure of analyzed compounds (complex structural info). Identity of known compounds can be verified via comparison with an NMR spectrum of corresponding reference compound.

NMR spectra along with IR and MS represent powerful tandem for a detail structural analysis of known and unknown molecules.

https://en.wikipedia.org/wiki/Nuclear_magnetic_resonance_spectroscopy

NMR spectroscopy

Benefits, limitations and application possibilities

- Suitable for exact structural analysis – complex view, detail structural arrangement, isomerism, intra- and inter-molecular interactions
- Universal (for diamagnetic compounds, current approaches even for paramagnetic ones)
- Very expensive equipment and measurements
- Very complex equipment
- Superconducting magnet requires liquid helium-cooling
- Realtively long timescale (high analysis time)
- Low sensitivity (e.g. in comparison with MS)
- The most complex characterization of chemical structure and intra- and inter- molecular interactions

New trends: libraries of spectra are enhanced, sensitivity is enhanced, precision is enhanced, scaning rate is higher, improvements in magnets

Mass spectrometry

Principle

Mass spectrometry (**MS**) is an analytical technique that measures the mass-to-charge ratio (m/z) of ions in vacuum. The results are typically presented as a mass spectrum, a plot of intensity as a function of the mass-to-charge ratio. Mass spectrometry is used in many different fields and is applied to pure samples as well as complex mixtures. Mass spectra are used to determine the elemental or isotopic signature of a sample, the masses of particles and of molecules, and to elucidate the chemical identity or structure of molecules and other chemical compounds.

In a typical MS procedure, a sample, which may be solid, liquid, or gaseous, is ionized, for example by bombarding it with electrons. This may cause some of the sample's molecules to break into charged fragments or simply become charged without fragmenting. These ions are then separated according to their mass-to-charge ratio, for example by accelerating them and subjecting them to an electric or magnetic field: ions of the same mass-to-charge ratio will undergo the same amount of deflection. The ions are detected by a mechanism capable of detecting charged particles, such as an electron multiplier.

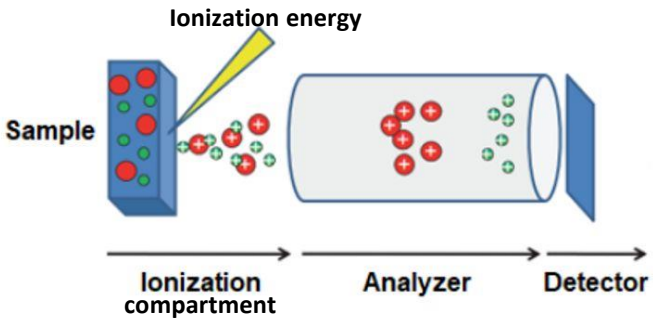
Sparkman, O. David (2000). Mass spectrometry desk reference. Pittsburgh: Global View Pub. ISBN 978-0-9660813-2-9.

Mass spectrometry

Experimental arrangement

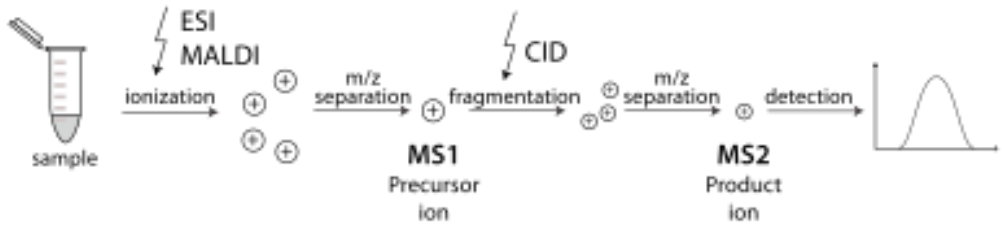
A mass spectrometer consists of three components: an ion source, a mass analyzer, and a detector. The **ionizer** converts a portion of the sample into ions. There is a wide variety of ionization techniques, depending on the phase (solid, liquid, gas) of the sample and the efficiency of various ionization mechanisms for the unknown species. An extraction system removes ions from the sample, which are then targeted through the **mass analyzer** and separated in it according to m/z, and subsequently into the **detector** to detect individual separated ions.

Mass spectrometer (MS)
(basic scheme)



https://www.google.sk/search?q=mass+spectrometry&source=lnms&tbm=isch&sa=X&ved=2ahUKEwiZxeaK5s_rAhXHTsAKHd1wA1IQ_AUoAXoECBEQAw&biw=1920&bih=938#imgrc=S7hWKocl3RhGrM&imgdii=QYxXDHio44iMoM

Tandem mass spectrometry (MS/MS)
(basic procedure)



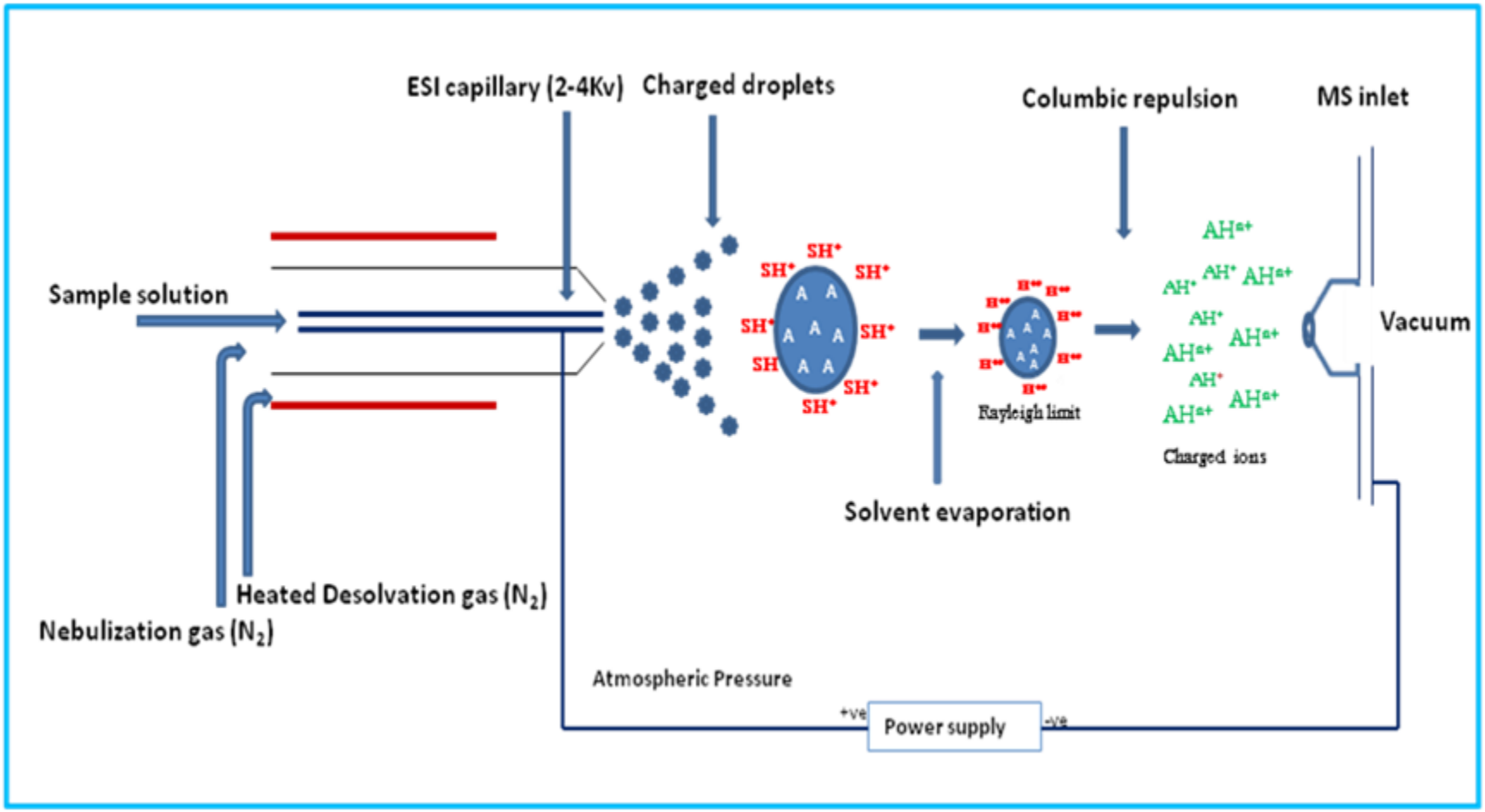
https://en.wikipedia.org/wiki/Mass_spectrometry

Mass spectrometry

Ionic source

Most frequently used

Electrospray ionization (ESI)



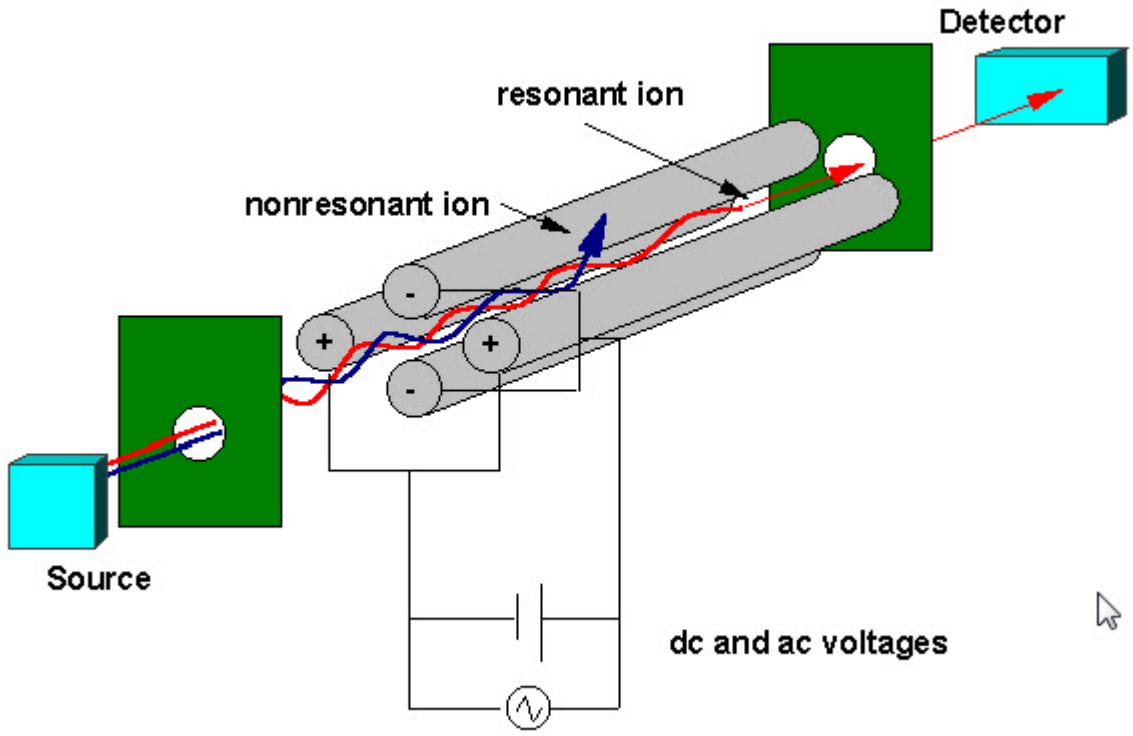
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Mass spectrometry

Mass analyzer

Simple
Fast

Quadrupole (Q)



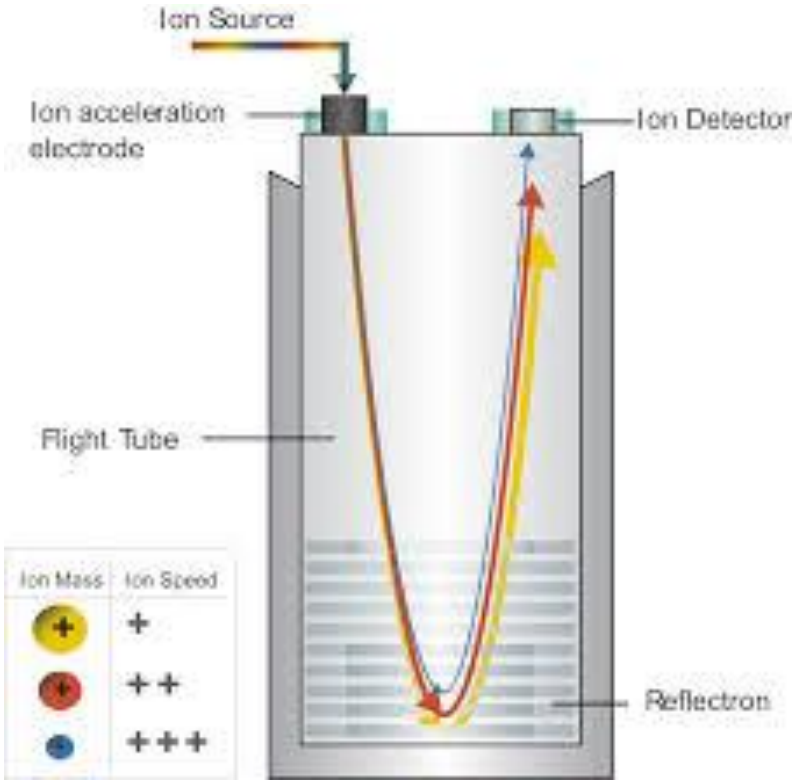
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Mass spectrometry

Mass analyzer

Simple
Fast

Time of flight (TOF)



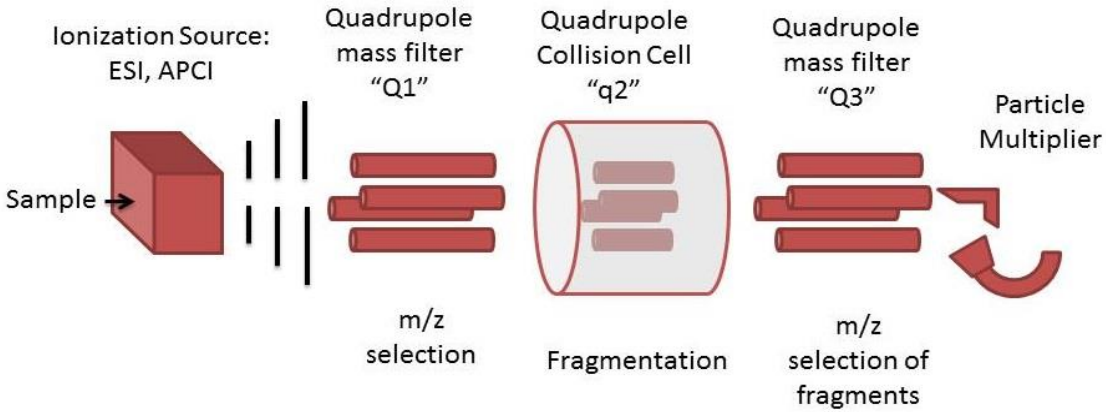
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Mass spectrometry

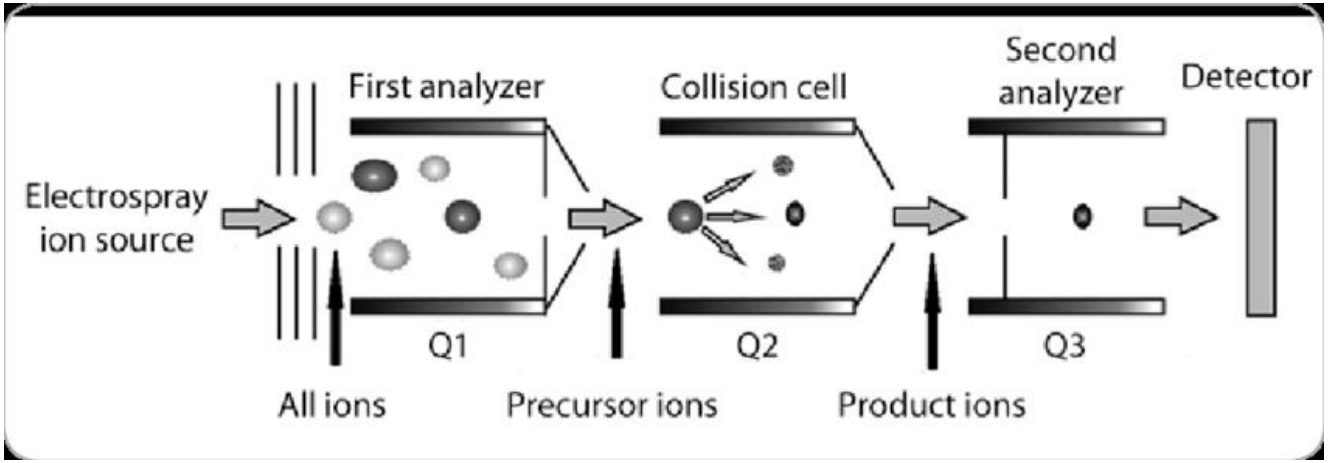
Mass analyzer

Triple quadrupole (QqQ)

Frequently used
Very sensitive
For target analysis



https://www.google.sk/search?q=mass+spectrometry+mass+analyzer+qqq&source=lnms&tbm=isch&sa=X&ved=2ahUKEwjKkJWMgNDrAhXC_KQKHWzAB4oQ_AUoAXoECA0QAw&biw=1920&bih=938#imgrc=BX8cYkjku2zrlM&imgdii=oMnoERtwR3EV2M



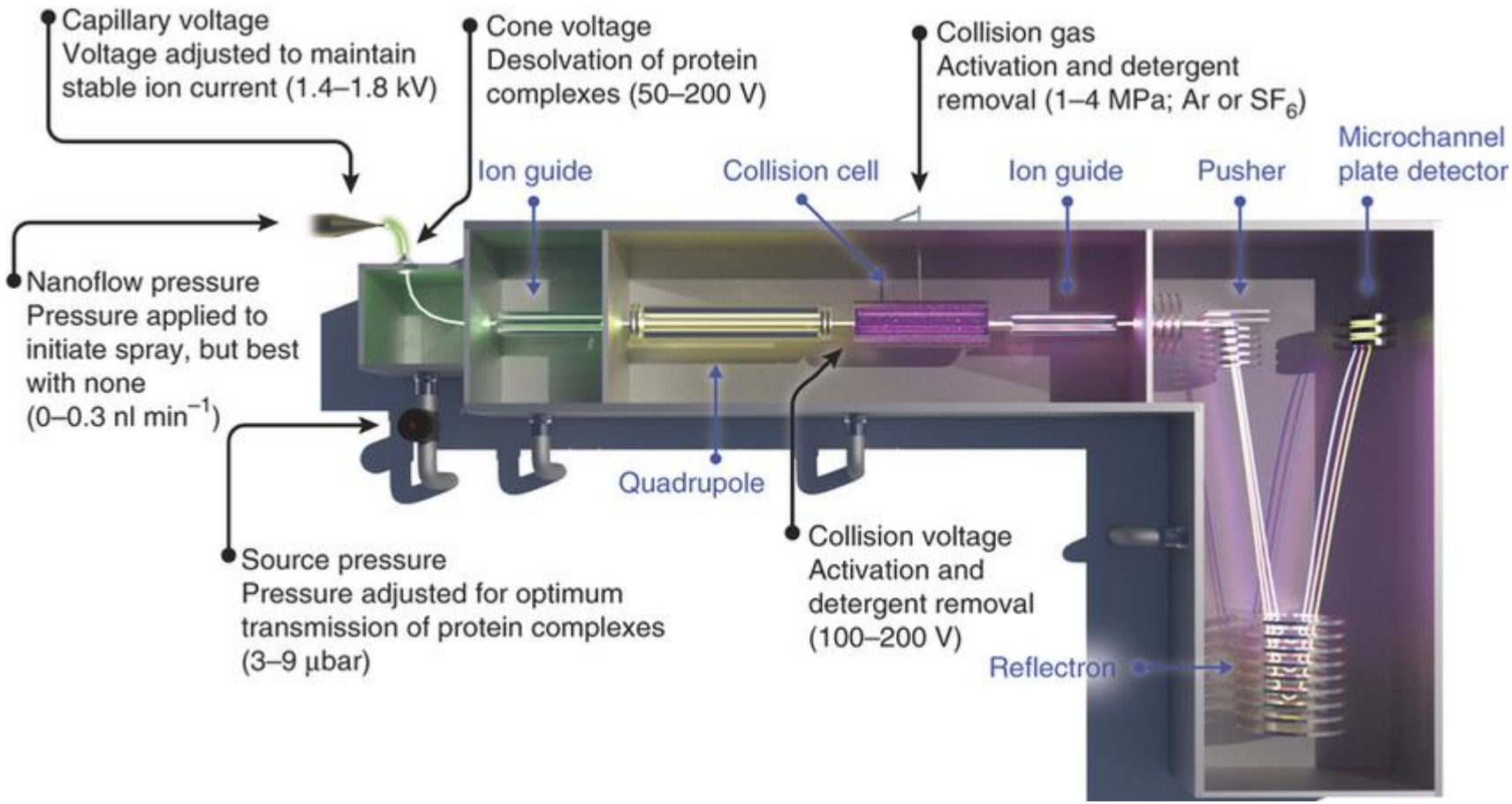
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Mass spectrometry

Mass analyzer

Quadrupole – time of flight (Q-TOF)

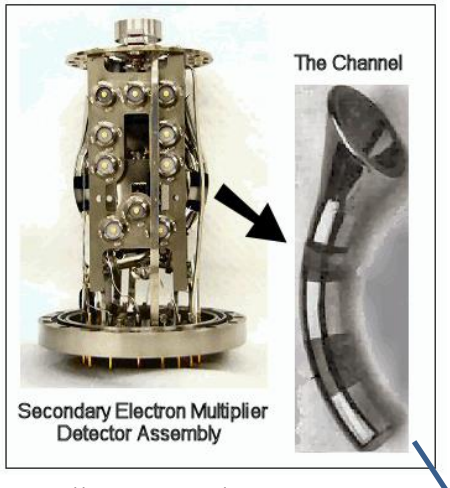
Frequently used
Sensitive
For untarget analysis



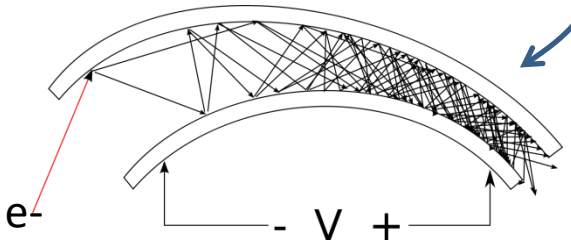
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Mass spectrometry

Detector

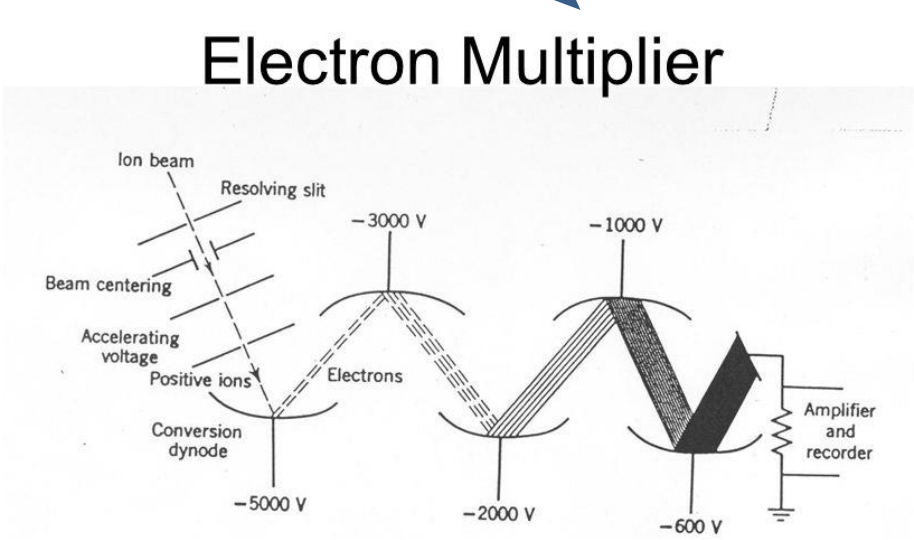


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Frequently used



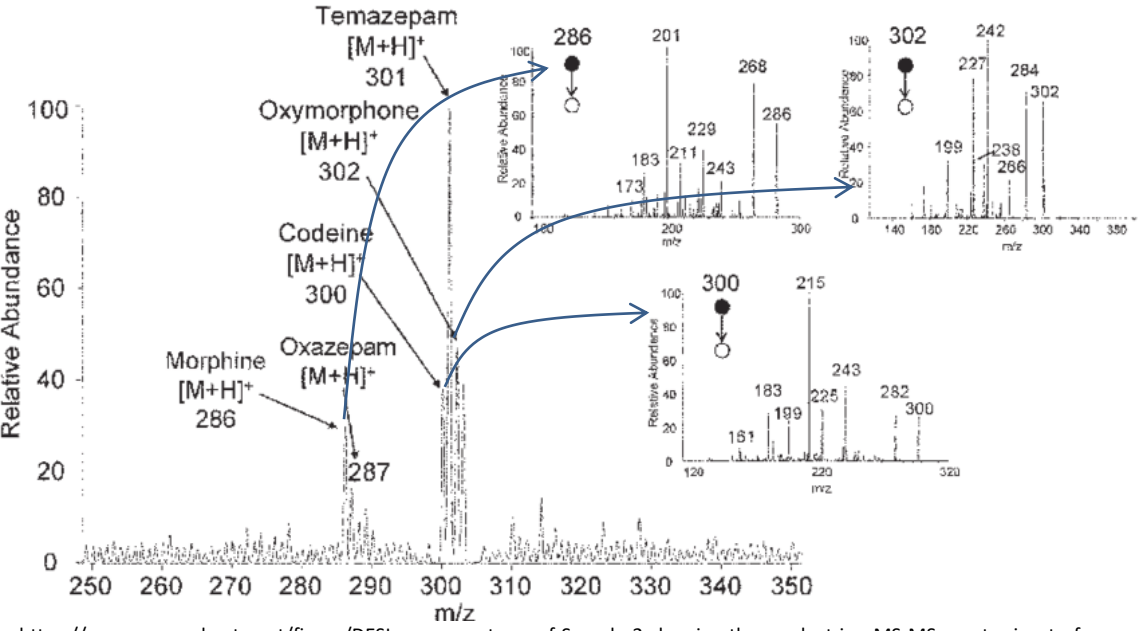
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Mass spectrometry

Qualitative analysis

Results are displayed as mass spectra of the signal intensity of detected ions as a function of the mass-to-charge ratio. The differences in masses of the ions and/or their fragments allow the mass analyzer to sort the ions by their mass-to-charge ratio (for identification). The atoms or molecules in the sample can be identified by correlating known masses (e.g. an entire molecule) to the identified masses or through a characteristic fragmentation pattern. Notice: fragment ion – higher selectivity; molecular ion – lower selectivity. Hence, tandem MS/MS is more selective than MS.

Mass spectra



https://www.researchgate.net/figure/DESI-mass-spectrum-of-Sample-2-showing-the-product-ion-MS-MS-spectra-inset-of-m-z-286_fig7_6130203

Total mass spectrum of drugs mixture and the product ion MS/MS spectra of three selected drugs (insets).
Enhanced (unequivocal) MS/MS identification according to the characteristic mass (fragmentation) spectra of the separated compounds (two identifiers: Mr and m/z spectrum). Mass spectra of compounds with different structures are differing from each other.

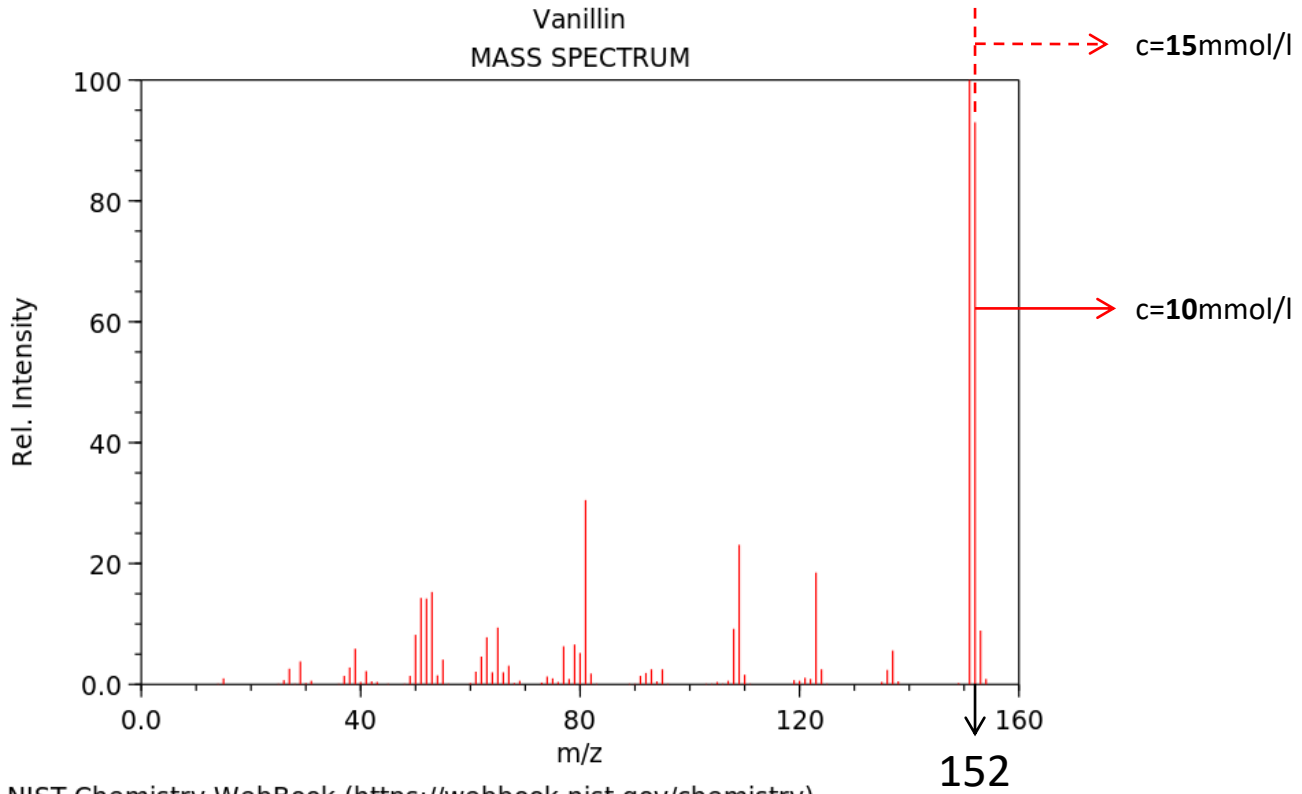
Notice:
Mass spectra give precise information in detail chemical structure of analyzed compounds (Mr, fragments typical for given stucture). Identity of known compounds can be verified via comparison with an mass spectrum of corresponding reference compound.

Mass spectra along with IR and NMR represent powerful tandem for a detail structural analysis of known and unknown molecules.

Mass spectrometry

Quantitative analysis

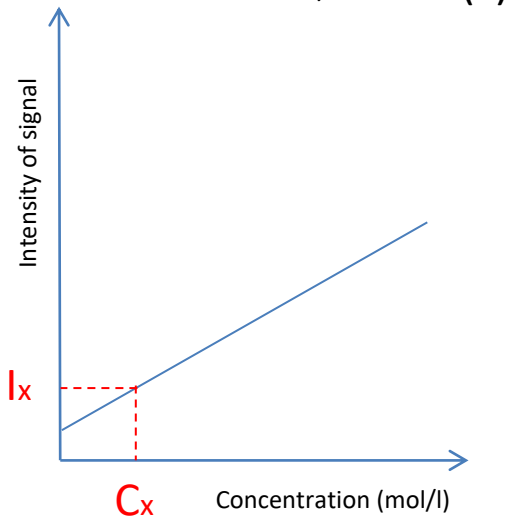
The detector measures the value of an indicator quantity and thus provides data for calculating the abundances of each ion present (for quantification). Quantitative analysis is based on the evaluation of intensity of MS signal of given analyzed compound (via its molecular ion or fragment ion). Intensity of MS signal is proportional to the concentration of analyzed compound (I ~ c). Notice: fragment ion – higher S/N – higher sensitivity; molecular ion – lower S/N – lower sensitivity. Hence, tandem MS/MS is more sensitive



NIST Chemistry WebBook (https://webbook.nist.gov/chemistry)

Calibration curve

Based on $I_{m/z=152} = f(c)$



Mass spectrometry

Benefits, limitations and application possibilities

- Suitable for exact structural analysis – molecular mass, structural arrangement (predicted from fragments of the analyzed compounds)
- Universal (for ionic compounds, non-ionic compounds are turn to ionic ones in an ionic source)
- Able to analyze samples with complex matrices
- Highly sensitive
- Fast analysis
- Expensive equipment and measurements
- Complex equipment
- Interface (ionic source) is necessary
- Complex characterization of chemical structure plus Mr
- Analysis of trace compounds in multicomponent matrices
- Most powerful detection step in separation techniques

New trends: libraries of spectra are enhanced, sensitivity is enhanced, precision is enhanced, scaning rate is higher, enhanced mass resolution and accuracy, ambient MS techniques

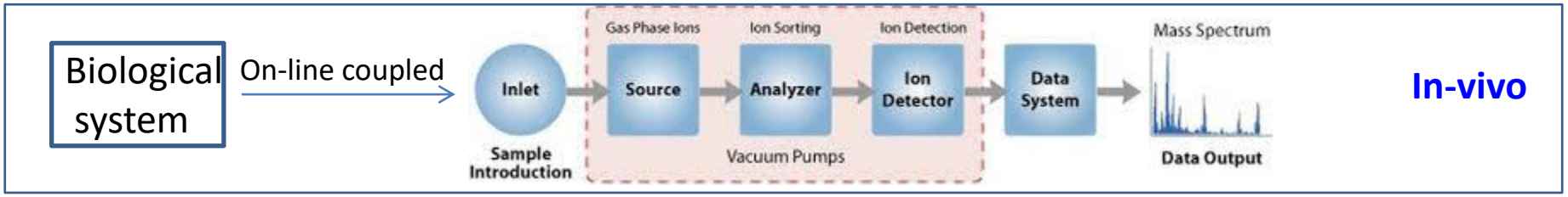
Mass spectrometry

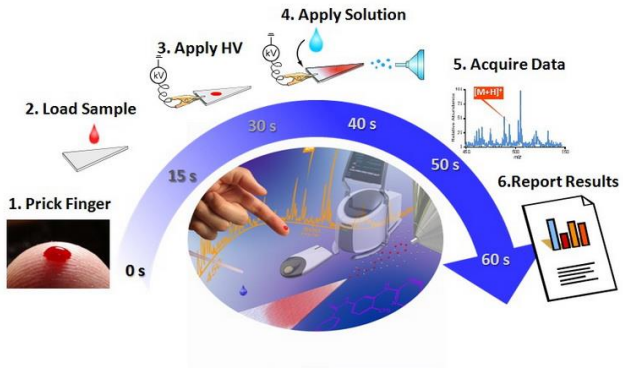
New trends – additional benefits/limitations/utilization

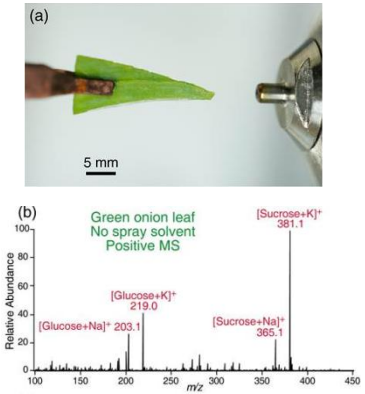
- Enhanced performance parameters of ionization process and measuring of masses and mass spectra, cheap measurements (for ambient techniques)

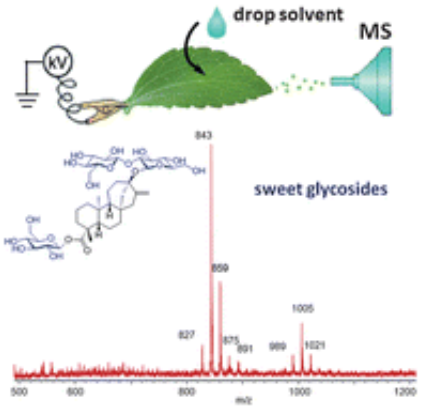
Analyzer	Resolution ability ($x10^3$)	Resolution (Δm/z)	Accuracy of mass determination (ppm)	Mass range – upper limit ($x10^3$)	Linear dynamic range	Scan rate (Hz)	Cost
Q	3 – 5	0,1 – 0,7	< 100	2 – 3	$10^5 – 10^6$	2 – 10	€
QIT	4 – 20	0,1 – 0,7	50 – 200	4 – 6	$10^4 – 10^5$	2 – 10	€
TOF	10 – 60	0,006 – 0,1	1 – 5	10 – 20	$10^4 – 10^5$	10 – 50	€€
Orbitrap	100 – 240	0,002	1 – 3	4	$5x10^3$	1 – 5	€€€
ICR	750 – 2500	0,0002	0,3 – 1	4 – 10	10^4	0,5 – 2	€€€€

- Yet more expensive equipment and measurements (for some techniques, e.g. ICR)
- Miniaturized and automated analysis, in-vivo analysis, direct analysis of materials under ambient conditions









direct analysis of materials

https://engineering.purdue.edu/BioMS/ionization.htm; https://pubs.rsc.org/en/content/articlelanding/2012/AN/c2an16263f#!divAbstract