IONIZATION AND ION SOURCES, DETECTOR, VACUUM SYSTEMS
Mass spectrometer

- Ion source - devices which produce positive or negative electrically charged molecules in gas phase
- Mass analysers - separate the ions according to their mass-to-charge ratio (m/z)
- Detectors - record the charge induced or the current produced, when an ion passes by or hits a surface
ION SOURCE

Produce positive or negative electrically charged molecules in gas phase

- Choice depends on compound
  - Universal ionization technique does not exist

- Differentiation
  - By energy
    - Hard (EI)
      - Cation radical with high energy - fragmentation in ion source – many fragments in the spectra
    - Soft (CI, ESI, APCI, MALDI,...)
      - Molecular adduct with low energy – no or a few fragments in the spectra
  - By pressure
    - Vacuum (EI, CI, MALDI,...)
    - Atmospheric pressure (ESI, APCI, APPI, AP MALDI,...)
      - Ambient ionization technique

- Ions
  - $M + e^- \rightarrow M^{++} + 2e^-$  \hspace{1cm} Cation radicals
  - $M + HA \rightarrow [M+H]^+ + A^-$  \hspace{1cm} Molecular adducts
  - $M + B^- \rightarrow [M-H]^+ + HB$  \hspace{1cm} Deprotonatet molecules
DIFFERENT IONIZATION TECHNIQUE

- Molecular Analysis
  - Electron Ionization (EI)
  - Chemical Ionization (CI)
  - Electrospray (ESI)
    - Nanoelektrospray (nanoESI)
  - Atmospheric Pressure Chemical Ionization (APCI)
  - Atmospheric Pressure Photoionization (APPI)
  - Matrix-Assisted Laser Desorption/Ionization (MALDI)
  - Laser Desorption Ionization (LDI)
  - Secondary Ion Mass Spectrometry (SIMS)
  - Fast Atom Bombardment (FAB)
  - Termospray (TSI)
    - Ambient ionization technique
      - Desorption Electrospray Ionization (DESI)
      - Desorption Atmospheric Pressure Photoionization (DAPPI)
      - Direct Analysis in Real Time (DART)

- .....
**Electron Ionization (EI)**

- An ionization method in which energetic electrons interact with gas phase molecules to produce ions.
  - Electron emission by heating a tungsten wire filament
  - Good reproducibility – spectral library – easy interpretation
    - (energy of the electrons 70eV)

- \[ M + e^- \rightarrow M^{++} + 2 \ e^- \]
  - M is the analyte molecule being ionized
  - \(e^-\) is the electron and
  - \(M^{++}\) is the resulting ion

- Widely used for volatile organic molecules
- Often coupled with GC = GC/EI-MS
CHEMICAL IONIZATION (CI)

- Analyzed ions are produced through the collision of the analyte with ions of a reagent gas, that are present in the ion source
  - **Methane**, ammonia, isobutane, acetonitrile,.....
- Soft ionization technique
  - \([M+H]^+\), \([M+\text{reagent gas}]^+\), fragments (depend on condition)
- Example
  - CH$_4$ as a reagent gas

Primary ion formation
\[ CH_4 + e^- \rightarrow CH_4^+ + 2e^- \]

Product ion formation
\[ M + CH_5^+ \rightarrow CH_4 + [M + H]^+ \]

Secondary reagent ions
\[ CH_4 + CH_4^+ \rightarrow CH_5^+ + CH_3 \]
\[ CH_4 + CH_3^+ \rightarrow C_2H_5^+ + H_2 \]

- Coupled with GC = GC/CI-MS
- Used for volatile organic molecules
**Electrospray (ESI)**

- The liquid containing the analyte(s) is dispersed by electrospray into an aerosol
  - Charged droplets
  - Solvent evaporation
  - Coulombic explosion
- Soft ionization technique
  - \([\text{M+H}]^+\), \([\text{M+ Na}]^+\), \([\text{M+ K}]^+\), .......... molecular adducts
  - Multiply charged ions, dimers

http://www.chm.bris.ac.uk/ms/theory/esi-ionisation.html
Nanoelectrospray (nanoESI)

- Flow of mobile phase usually hundreds nl/min
  - Higher sensitivity
  - Easier interpretation of the spectra

Important parameters
- Mobile Phase Flow
- Tip Inner Diameters (IDs)
- Mobile Phase Composition
- Applied Voltage
ELECTROSPRAY TECHNIQUE

- Polar analytes in broad mass range
- Obtaining multiply charged
  - Analysis of molecules with Mr behind the range of analyzer
- Coupled with HPLC or UHPLC
  - Polar solvent (mobile phase) as a donor of H⁺

Electrospray Wings for Molecular Elephants (Nobel Lecture)

John B. Fenn
Nobel prize in Chemistry
2002
ATMOSPHERIC PRESSURE CHEMICAL IONIZATION (APCI)

- The mobile phase containing eluting analyte is heated to high temperature (above 400°C), sprayed with high flow rates of nitrogen.
- Molecules of solvent and gas are ionized by corona discharge.
- Analyte are ionized by ionized gas molecules and solvent.
**Atmospheric Pressure Chemical Ionization (APCI)**

- APCI can be performed in a modified ESI source
  - Device similar to ESI source
  - However, mechanism of ionization similar to CI
- The ionization occurs in the gas phase

- APCI is a less "soft" ionization technique than ESI
  - Generates more fragment ions

- Coupled with HPLC or UHPLC
  - Advantage of APCI - it is possible to use a nonpolar solvent (mobile phase)
**Matrix-Assisted Laser Desorption/Ionization (MALDI)**

- Laser-based soft ionization method
  - Matrix and analyte are mixed on the target plate
  - The laser (UV, IR) shoots the mixture
  - The energy is transferred to the matrix, which is vaporized, carrying analyte into the vapour phase and charging it

- The mechanism of MALDI is still debated

http://www.fasmatech.net/content-61-2.html
Matrix-Assisted Laser Desorption/Ionization (MALDI)

- Analysis of
  - Biomolecules (DNA, proteins, peptides and sugars)
  - Large organic molecules (polymers, dendrimers, ...)
    - Which tend to fragment, when are ionized by more conventional ionization methods.
  - Singly charged molecular adduct
    - Molecular adducts ([M+H]^+, [2M+H]^+, [M+2H]^{2+}) or loss of proton [M-H]^-
    - Other molecular adducts [M+metal]^+ with salts in sample (Na, K, ......, )

Franz Hillenkamp  
Koichi Tanaka

Nobel prize in Chemistry 2002
MALDI MATRICES: PROPERTIES AND REQUIREMENTS

- Small molecules, usually small organic acids
  - 2,5-dihydroxybenzoic acid, sinapic acid, α-cyano-4-hydroxycinnamic acid,......

- The MALDI matrix of requirements
  - Be able to embed analytes (by co-crystallization)
  - Be soluble in solvents compatible with analyte
  - Be vacuum stable
  - Absorb the laser wavelength
  - Cause co-desorption of the analyte upon laser irradiation
  - Promote analyte ionization
MALDI IMAGING

„Airbrush“

Sublimation

D. melanogaster

TIC

cis-vacenyl acetate

Cholesterol
PC
SM
d=a+b+c.

Metformin - [M+H]+; m/z 130,16

LASER DESORPTION/IONIZATION (LDI)

- **LDI** (laser desorption/ionization)
  - Energy of laser is directly absorbed by analyte
  - Without matrix
  - For small molecules only
    - Spectra without matrix ions
    - Better reproducibility than MALDI
    - Harder ionization technique than MALDI — fragments in spectra
    - Sensitivity depends on analyte

- Useful for imaging

- Instrumentation is same as for MALDI
Almost all compounds can be ionized by more than one technique.

- Depends on **molecular mass, polarity, ionization energy, solubility, ...**
Detectors - record the charge induced or the current produced, when an ion passes by or hits a surface.
DETECTORS

- Records the current produced, when an ion hits a surface of detector

- In commercial instrument detectors with conversion dynode
  - Ions strike a conversion dynode to produce electrons – electron multiplied by
    - Electron multiplier
    - Ion-to-photon detector

- Record the charge induced, when an ion passes by
  - FT-ICR-MS and Orbitrap
    - The detector is part of analyser
    - Ions only pass near the electrodes
**DETECTORS**

- **Elektromultiplier with discrete dynodes**
  - Amplification $10^6$

- **Chaneltron**
  - PbO - sensitive surface
  - Amplification $10^6$

- **Microchannel Plate Detectors (MCP)**
  - PbO - sensitive service
  - Amplification $10^3$
    - Two detectors – $10^6$
  - For TOF analyser

- **Ion-to-photon detector**
  - Electron strike a phosphor and the resulting photons are detected by a photomultiplier
VACUUM SYSTEM
**Vacuum Systems**

- Usually two steps
  - **Rough vacuum** (roughing pump - membrane pump, scroll pump, oil-sealed roughing pump)
    - 100 – 0.1 Pa
    - all type of instruments
  - **High vacuum** *(turbomolecular pump, diffusion pump)*
    - 0.1-10^{-6} Pa,
    - TOF, Q, IT
  - **Ultra-high vacuum** *(turbomolecular pump)*
    - (10^{-10}-10^{-12} Pa)
    - Orbitrap, ICR