École Pratique des Hautes Études

PSL RESEARCH UNIVERSITY PARIS

M1 D2HP – 2024 Environment

Analytical Methods in Environmental Chemistry
Focus on pharmaceutical analysis

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Analytical chemistry, definition

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Applied to environmental matrices

Analytical chemistry, applied to environmental matrices

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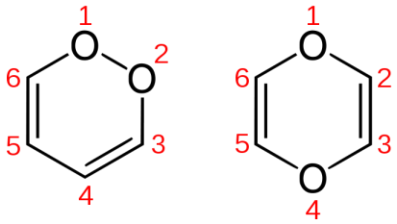
Applied to environmental matrices

Enables the measurement/quantification of in/organic substances (known or unknown at the outset) present in the environments

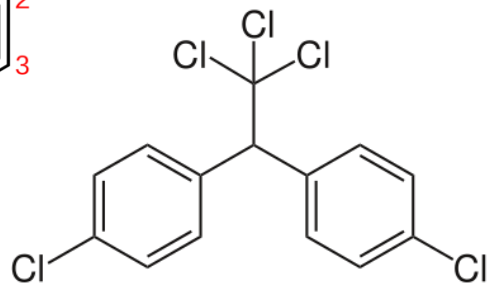
What kind of organic contaminants to consider

Persistent Organic Pollutants (POPs)

- Dioxins

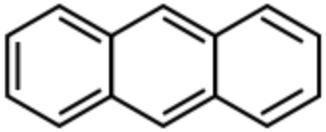


- Pesticides



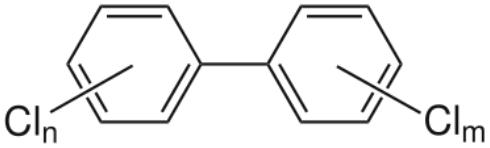
DDT

- PAHs



Anthracene

- PCBs



What kind of organic contaminants to consider

Persistent Organic Pollutants (POPs)

- Dioxins, Pesticides, PAHs, PCBs

Physico-chemical characteristics

- **Semi-volatile** (Pv < 1000 Pa)

Water/Atmosphere distribution, long distance transport

- **Resistant** to degradation

Chemical degradation, photolysis, or biological activity ineffective
Persistent in environments over long time scales

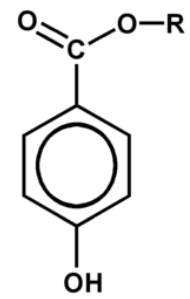
- High **bioaccumulation**

Concentration up trophic chains
Proven impacts on biota

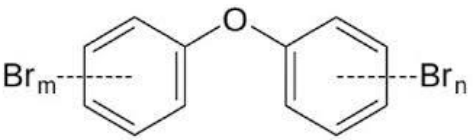
What kind of organic contaminants to consider

Chemical of **emerging** concerns

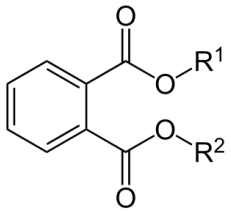
- Flame retardants
- Surfactants
- Phthalates
- Disinfectants
- PFAS
- **Pharmaceutical products**
- Illicit drugs
- Personal care products
- *etc.*



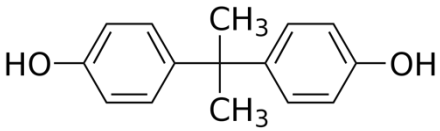
Phenols



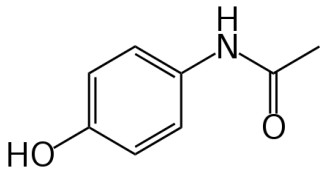
PBDE



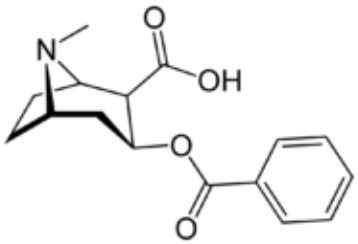
Phthalate



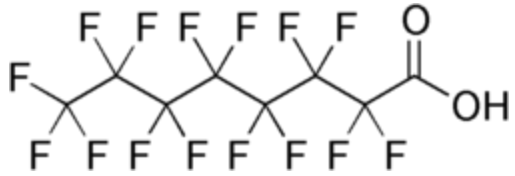
Bisphenol A



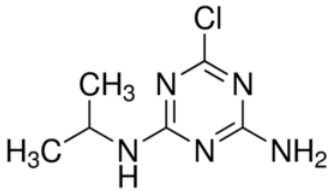
Acetaminophen



Benzoylecgonine



PFOA



Atrazine

What kind of organic contaminants to consider

Chemical of emerging concerns

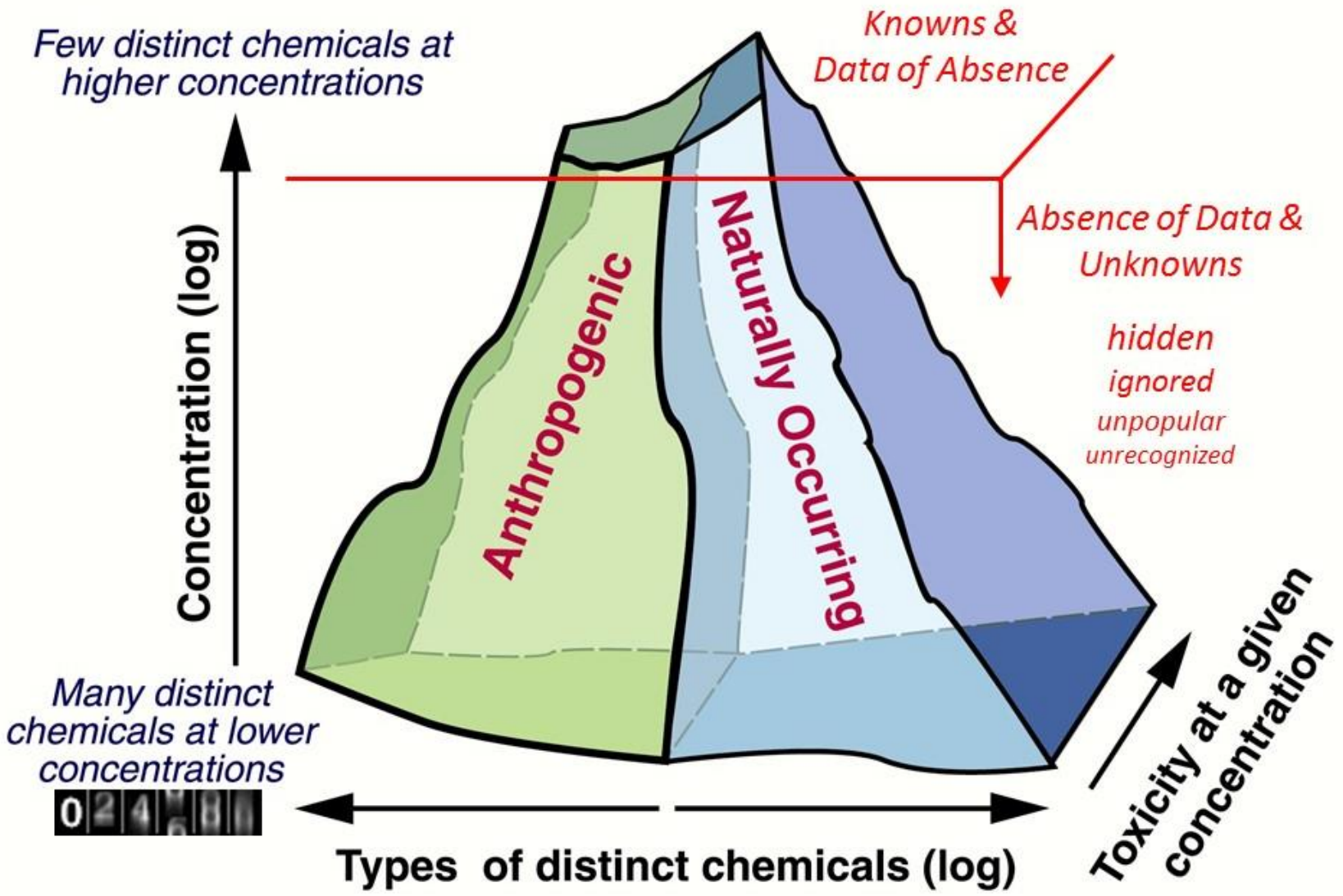
Definition : « Organic substances newly detected in the environment, which are not regulated and whose fate and toxicity are in question »

emerging ≠ « new »

Physico-chemical characteristics

- High solubility
- Very low volatility
- **Pseudo-persistence**
- Generally **hydrophilic** and **polar**

Challenges posed by these contaminants, the iceberg effect



Daughton, 2013, USEPA

An analytical challenge

Concentration level

- ng/L range
- targeted analysis or screening approach

- in a barrel?
- in an olympic swimming pool?
- in a tanker?

Matrix

- complex and loaded matrix

  Drinking water --- raw wastewater !

- temporal variability

  Daily, weekly monthly, seasonnally?

5 steps to assess the environmental contamination

Step 1 : Sampling of environmental matrices

The sampling must:

- Be adequately representative of the objective
- Allow good conservation of the analytes
- Limit secondary pollution

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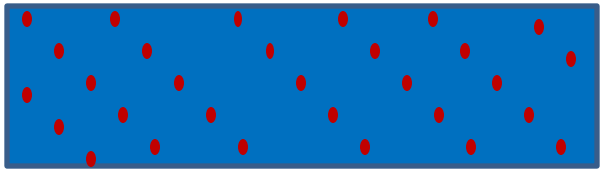
- Be adequately representative of the objective
- Allow good conservation of the analytes
- Limit secondary pollution

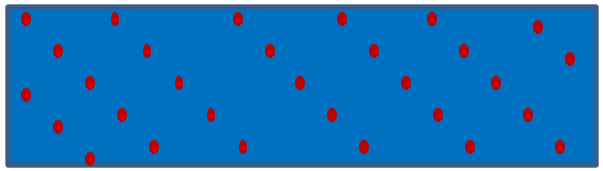
But above all!

The sampling method must be designed according to the levels, their temporal variations, and the physico-chemical characteristics of the targeted contaminants

Sampling methods

Two main types of sampling methods





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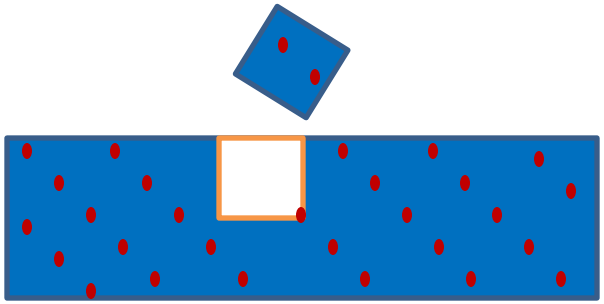
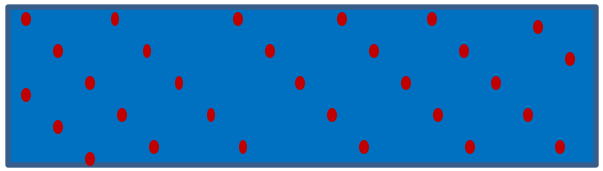


Grab sampling



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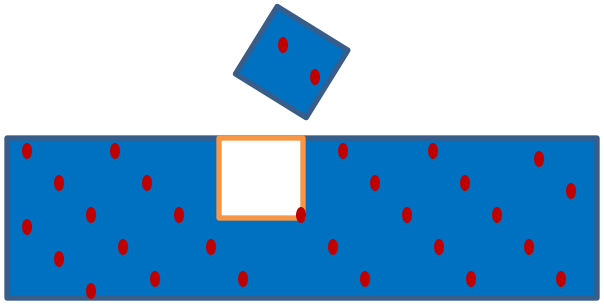

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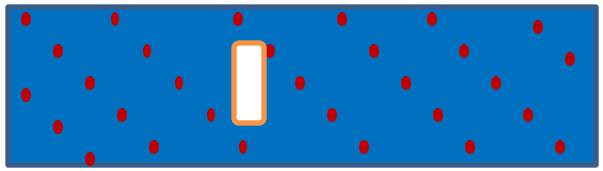
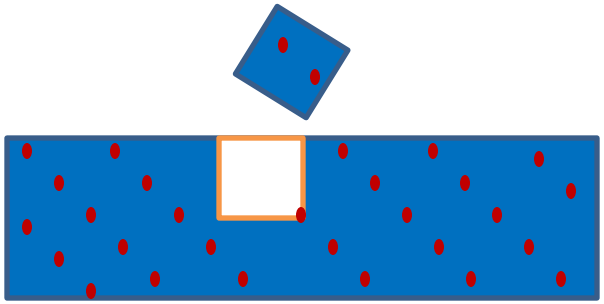


Passive sampling

Sampling methods

Two main types of sampling methods



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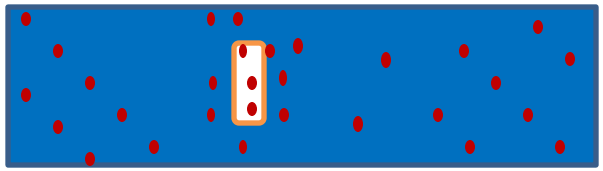

Passive sampling

Grab sampling

Sample a volume of water

Two types of sampling, single or composite

Advantage -> Contaminant concentration in the sample directly reflects the concentration in the sampled matrix

Disadvantage -> The representativeness of these samples can be questioned

Grab sampling

Unique sampling

- Sampling of a given volume at a given time
- Widely used (low human cost, low material risk)
- Ideal case of application

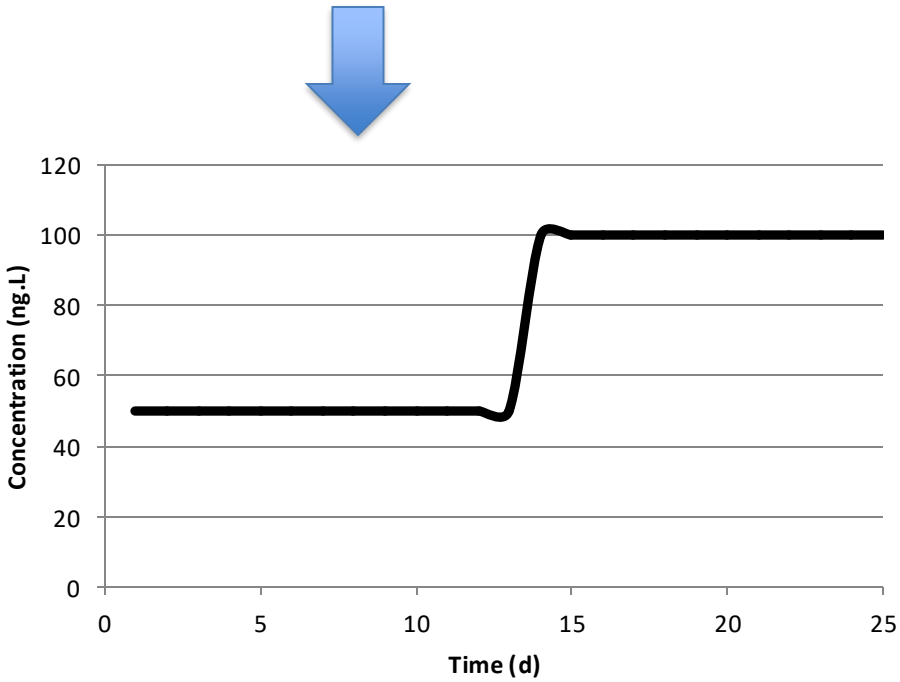

Photo credit: aurea.eu

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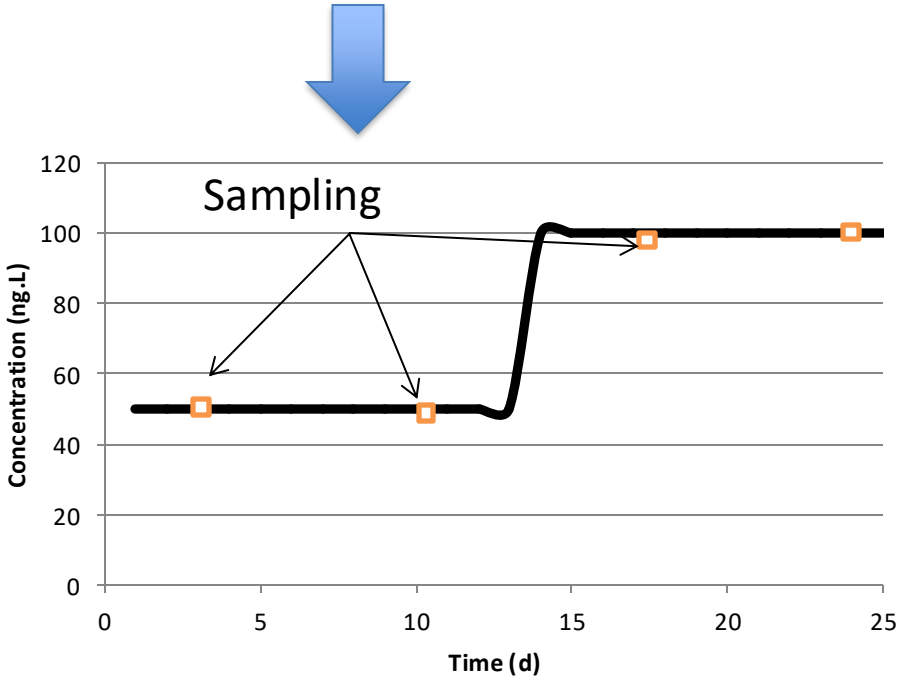

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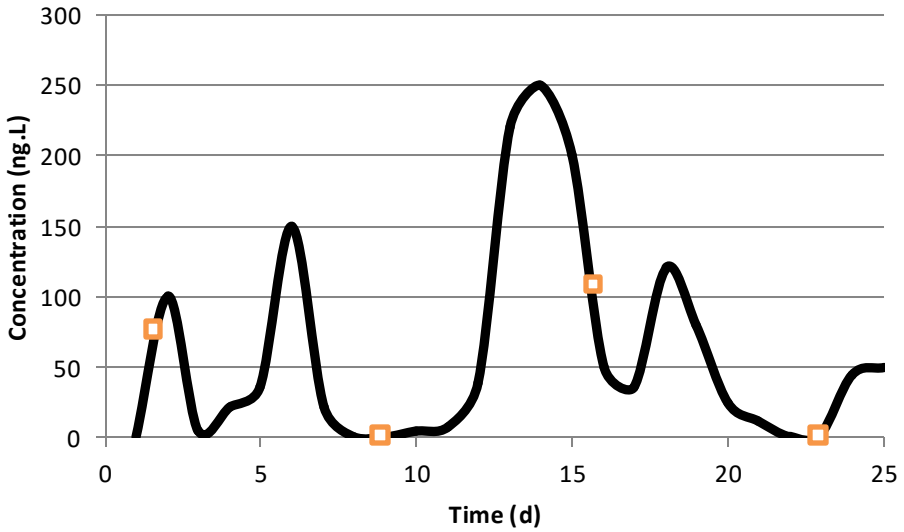

Photo credit : aurea.eu

Grab sampling

Non-composite grab sampling:

- *Saves human time/Limits material risk*
- *Easy access to urban/remote areas*
- *Can be useful for initial screening of contaminants present*
- *Not recommended for temporal/quantitative monitoring of contamination*

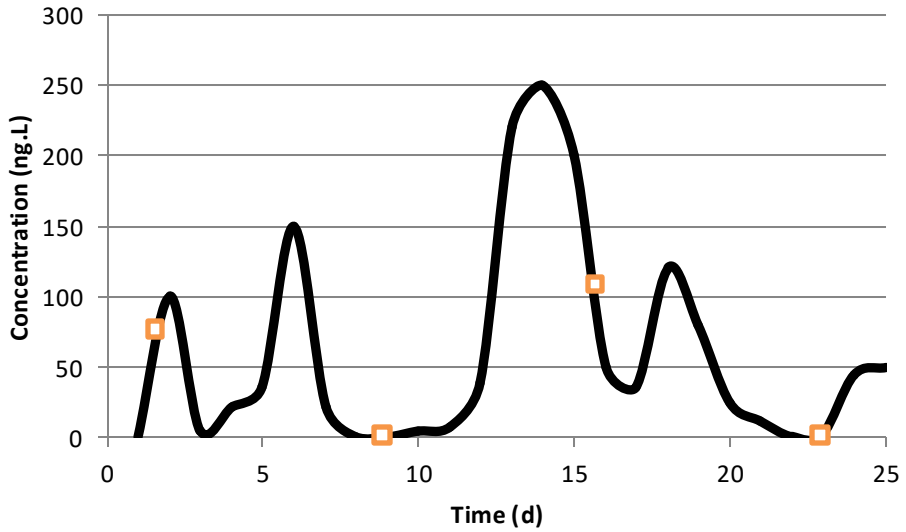

Photo credit : aurea.eu

Grab sampling

Time enslaved composite sampling

- Sampling of a volume V at a predefined time step
- Each sample has the same representativeness as a single sample
- The final sample is a composite of each of the samples

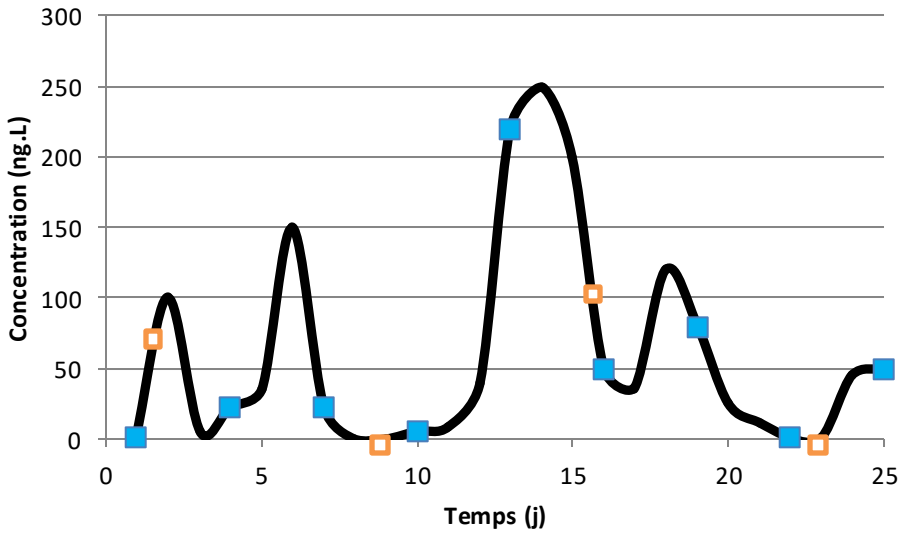

Photo credit : philippe-crochet.com

Grab sampling

Time enslaved composite sampling

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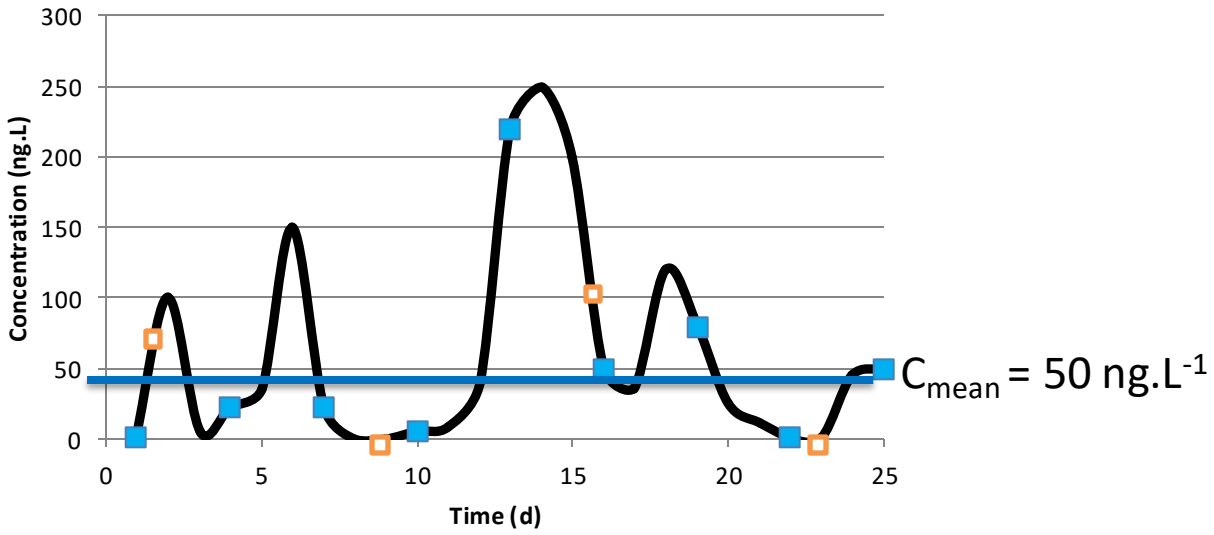
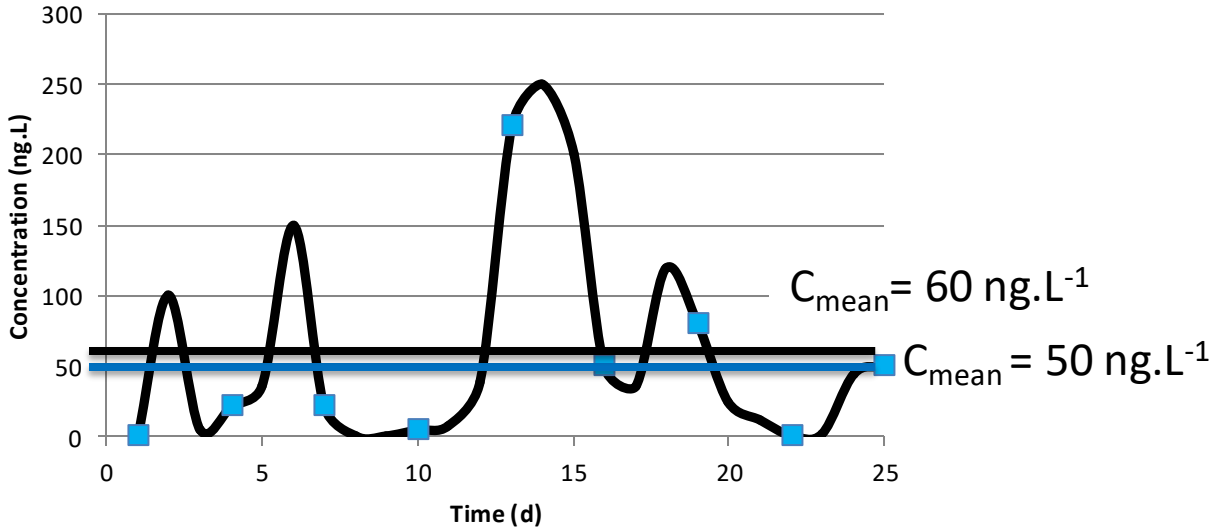
- **Allow the estimation of a mean concentration**



Prélèvements ponctuels

Time-enslaved composite sampling :

- *Allows calculation of an average concentration over a given period*
- *Useful in environments with low variability in flow rates*
- *Concentration is an important parameter for toxicity/fate*
- *Be careful with the time step between each sample*



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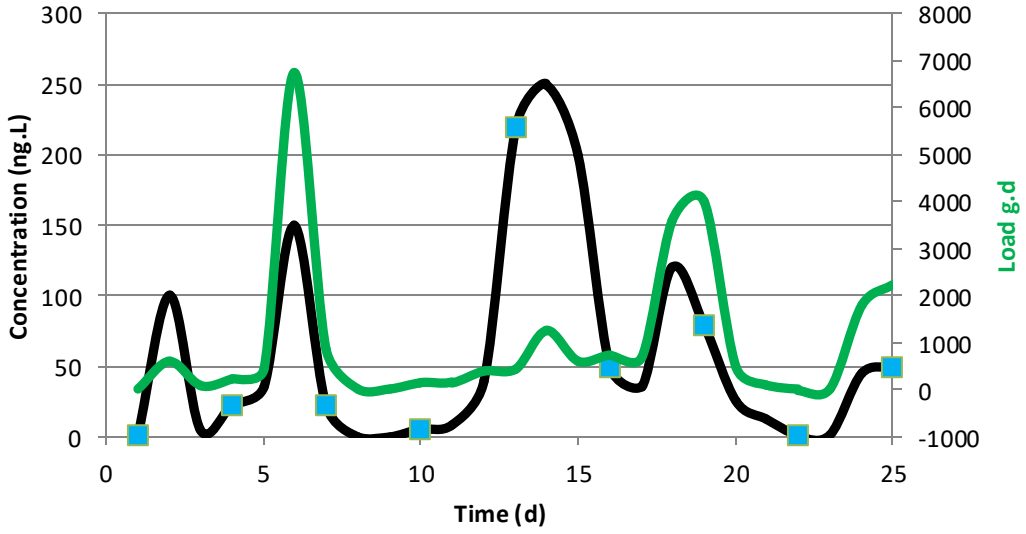
Main limitation -> Does not take into account flow variations!

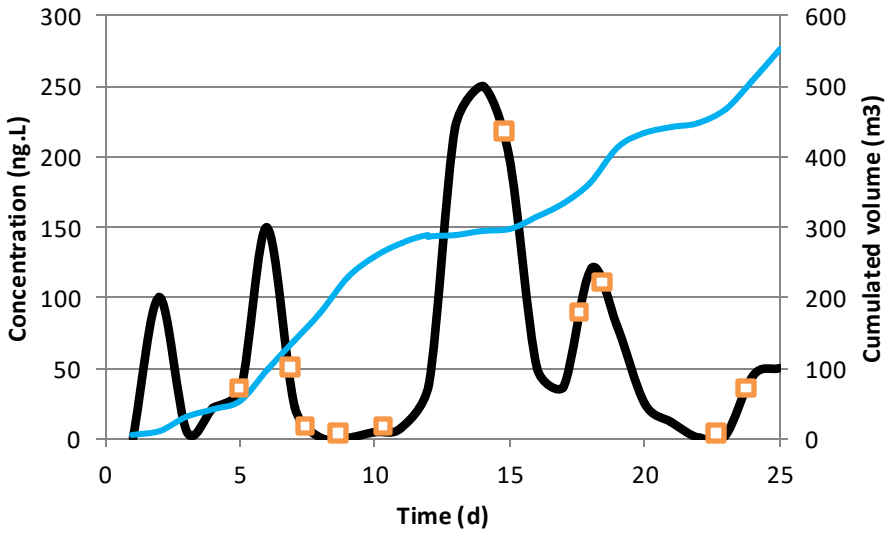


Load = Flow x Concentration

Grab sampling

Flow-enslaved composite sampling

- Sampling of one volume V all volumes V' (recalculated from flow rate)
- The final sample is a mixture of all samples taken



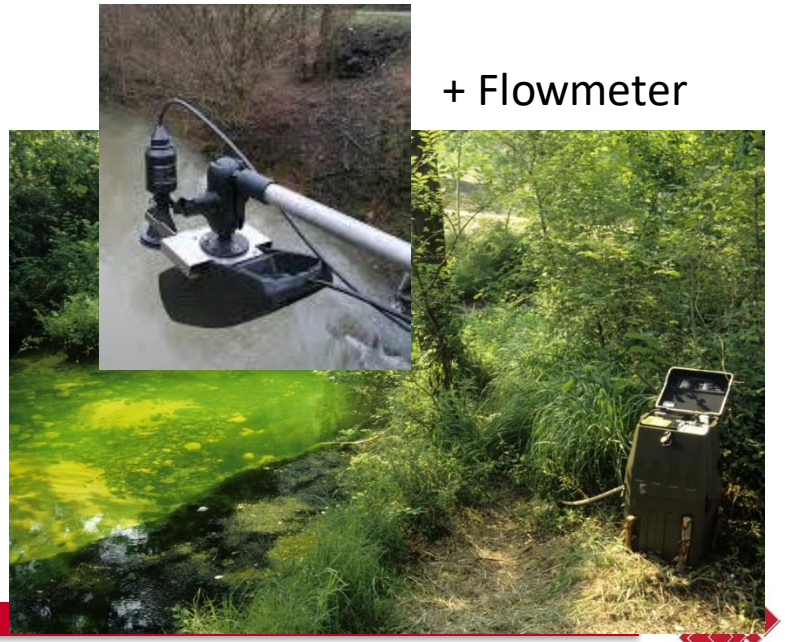
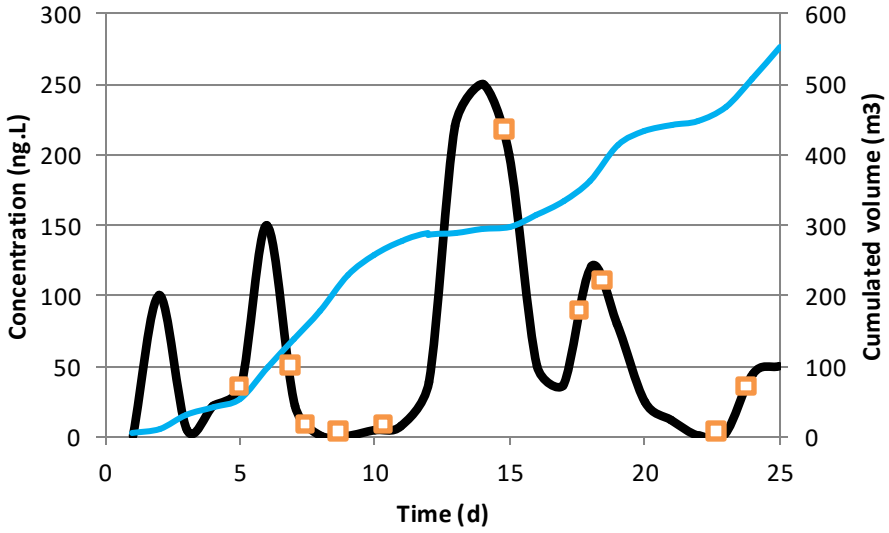


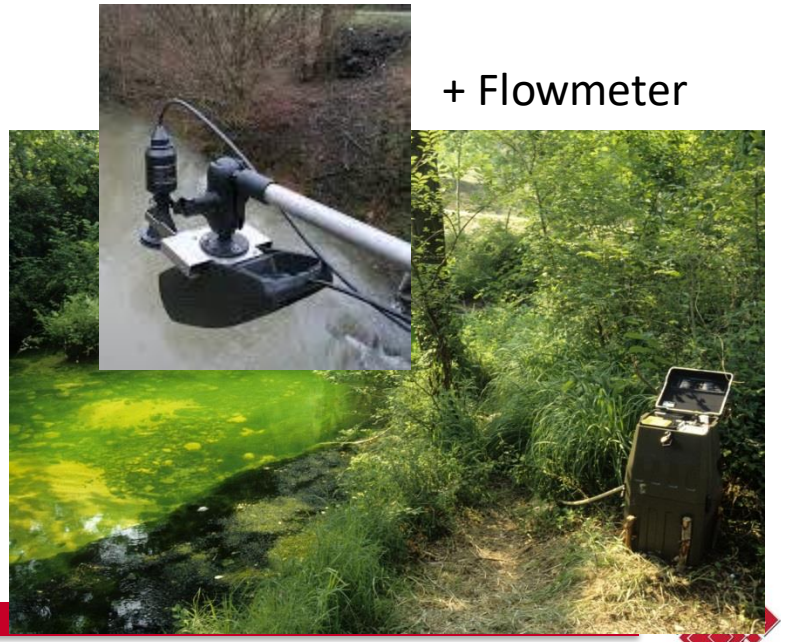
Photo credit : philippe-crochet.com

Grab sampling

Flow-sensitive composite sampling:

- *Allows calculation of an average flow over a given period*
- *Useful in environments with highly variable flows*
- *Flows are useful data for calculating contaminant load*
- *Beware of the volume selected between each sample*
- *Parallel flow measurement, sometimes tricky in natural environments*





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About grab sampling…

Adapting the sampling method to my scientific question

3 examples:

- How much ibuprofen is discharged from the wastewater treatment plant?

- What are the contaminants in this river?

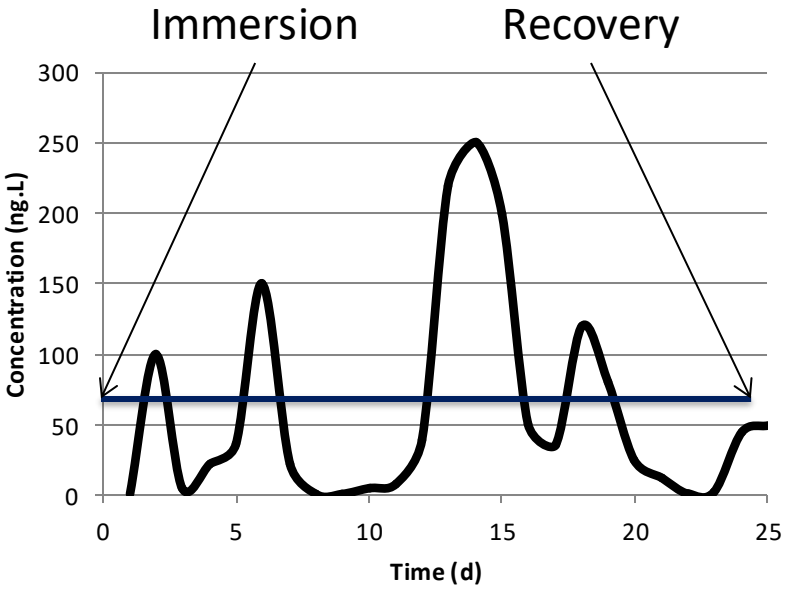
- Is this contaminated river toxic to biota?

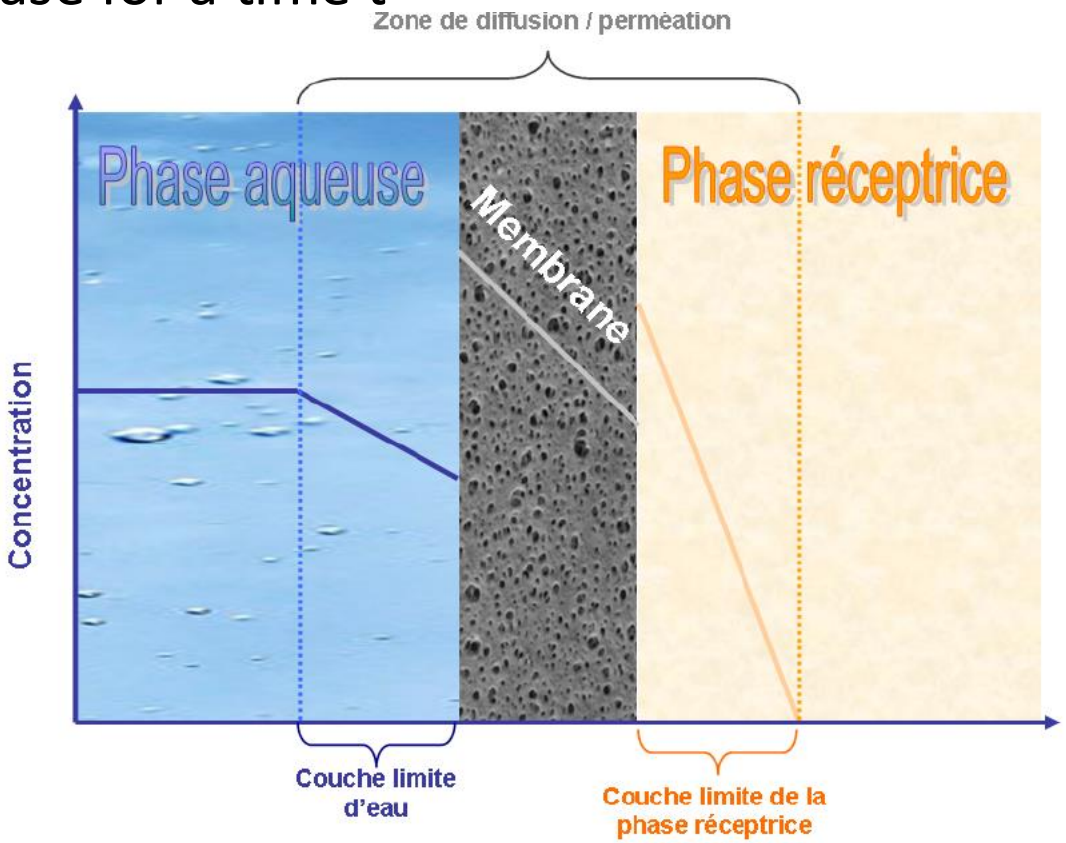
Passive sampling

General :

"Passive"; As opposed to active/grab sampling

Immersion of a receiving phase for a time t





Mazella et al. 2014

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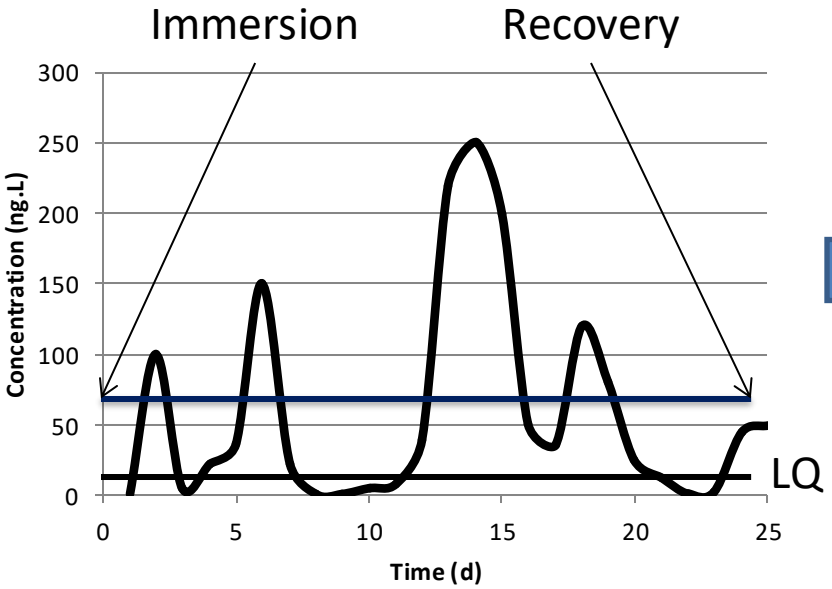


Advantages

- Integrated (good representativeness)
- Low cost
- Pre-concentration of contaminants

Difficulties

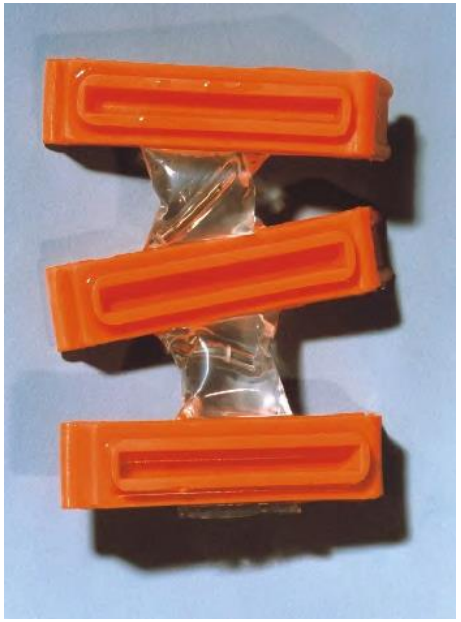
- Influence of external parameters
- Approximate calibration of devices

Mazella et al. 2014

Passive samplers

Diffusion Gradient in Thin films

Passive Diffusive Bags



Semi Permeable Membrane Device

Chemcatcher®

Polar Organic Chemical Integrative Sampler

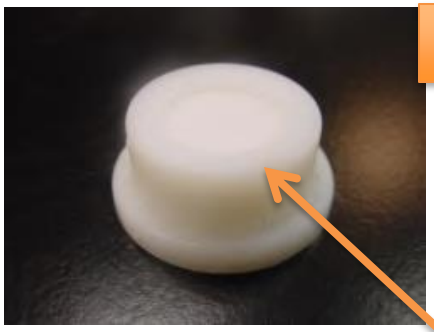
Stir Bar Sorptive Extraction

Passive samplers

Partition/Absorption

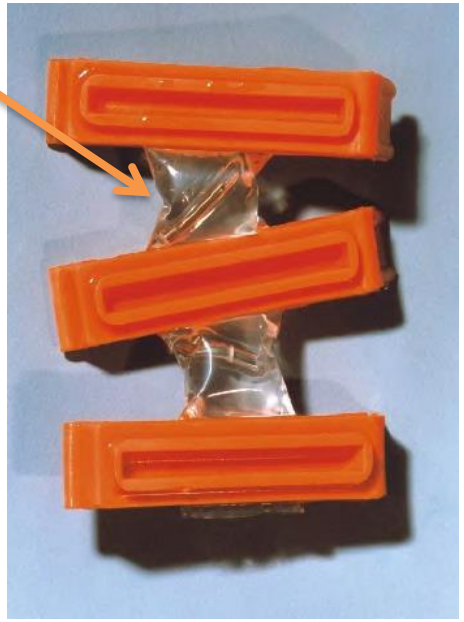
Adsorption

Chelation

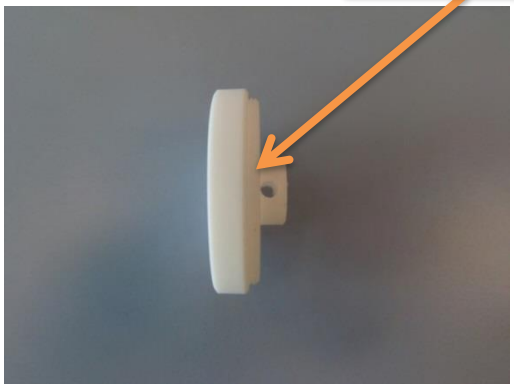


DGTs

PDB



SPMD



Chemcatcher

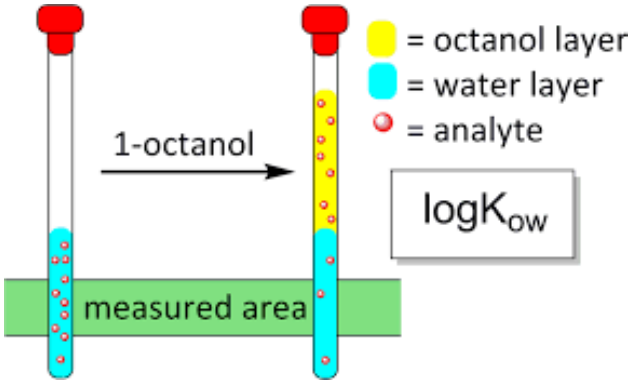
POCIS

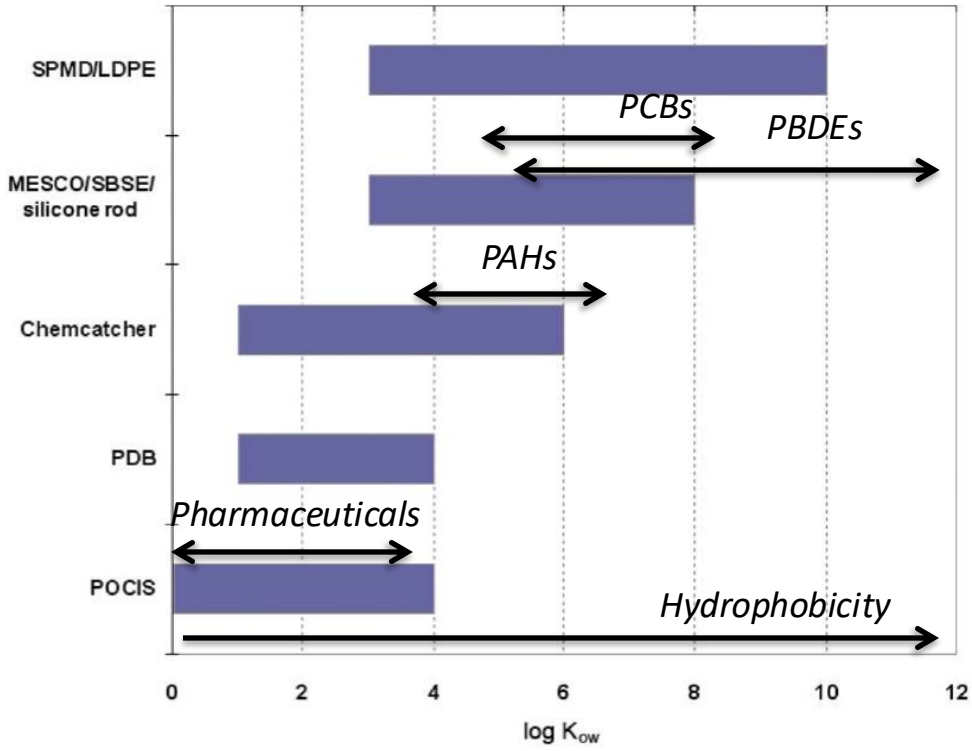
SBSE

Passive samplers

Areas of application

- What type of passive sampler for each type of molecule?
- Adapting the receiving phase to the hydrophobicity of the target compounds





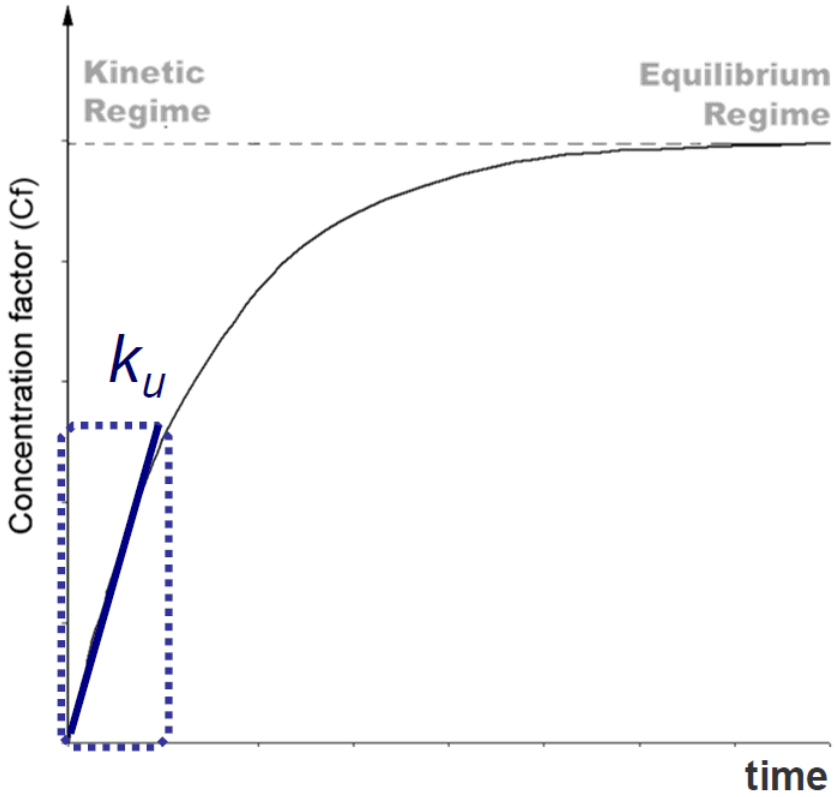
Passive samplers

Simplified functioning

1 -> Contaminant concentration
2 -> Equilibrium

$$C_{water} = \frac{C_{Adsorbent}}{k_u \, x \, t}$$

$$C_{water} = \frac{C_{Adsorbent}}{K_d}$$



With t the time, and k_u the accumulation constant, and K_d the solid/water partition

Bairds, 2010

Passive samplers

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1 -> Contaminant concentration
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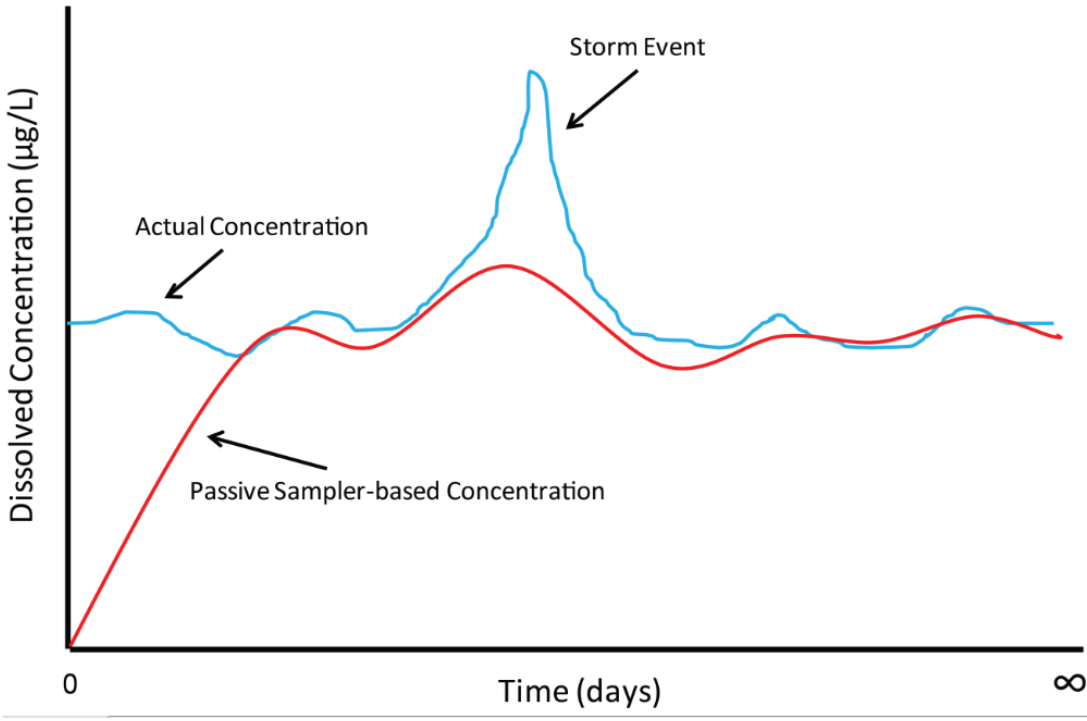
What phase is integrative ?

With t the time, and k_u the accumulation constant, and K_d the solid/water partition



Bairds, 2010

Passive Samplers

$$C_{water} = \frac{C_{Adsorbent}}{k_u \, x \, t}$$

With t the time, and k_u the accumulation constant

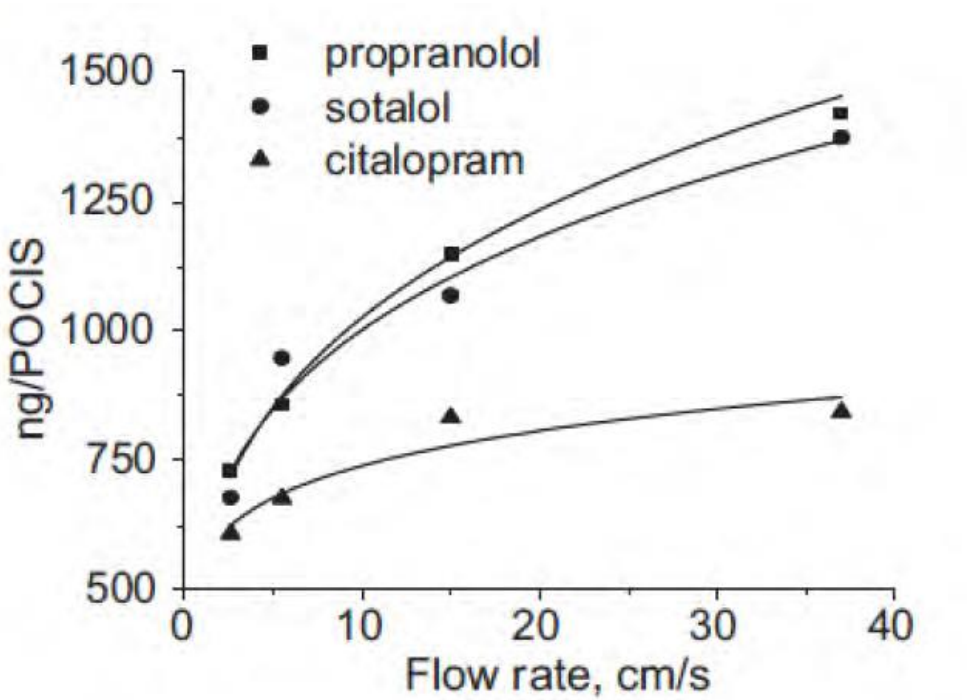
- Measurement of ku
- Specific value for each compound on a given phase
- Requires calibration

Passive Samplers

$$C_{water} = \frac{C_{Adsorbent}}{k_u \, x \, t}$$

With t the time, and k_u the accumulation constant

- Measurement of k_u (or Rs)
- Specific value for each compound on a given phase
- Depends on hydrological conditions (flow, pH, temperature, etc.)



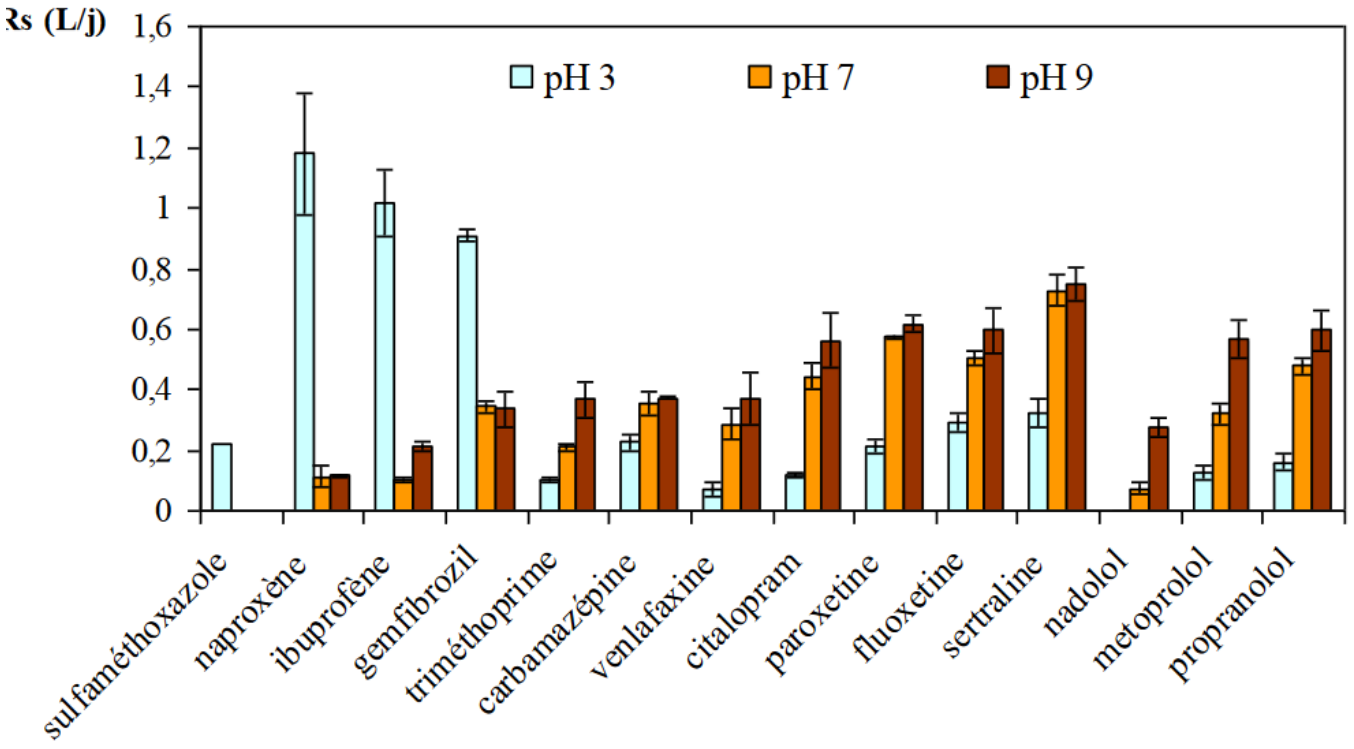
Li et al., 2010, *Env. Tox. & Chem.* **29**, 2461-2469

Passive Samplers

$$C_{water} = \frac{C_{Adsorbent}}{k_u \, x \, t}$$

With t the time, and k_u the accumulation constant

- Measurement of ku (or Rs) -> **always relative value !**
- Specific value for each compound on a given phase
- Depends on hydrological conditions (flow, pH, temperature, etc.)



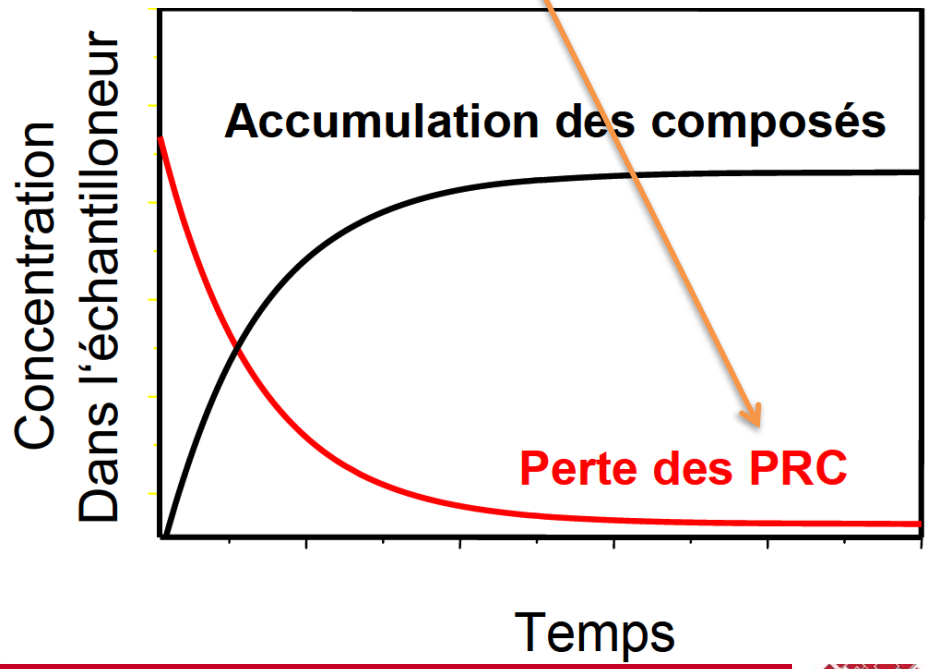
Li et al., 2011, *Chemosphere* **83**, 271-280

Passive Samplers

1 -> Contaminant concentration
2 -> Equilibrium

Two equilibrium:
i. Initial equilibrium
ii. Buffered equilibrium with concentration variations

Performance Reference Compound
Isotopically labelled compounds
Spiked POCIS with PRC



US EPA, 2012

Passive Samplers

Areas of application

What type of passive sampler for each type of molecule?

- Adapting the receptor phase to the hydrophobicity of the target compounds
- Adapting the receptor phase to the contamination levels
- AdvantagesLow cost of implementation, monitoring
- Integrative sampling

Disadvantages

- Need to calibrate for each target compound according to the target matrix
- Little knowledge of concentration variability

Step 1, Sampling

- The sample must:
  - Be adequately representative of the objective
  - Allow good conservation of the analytes
  - Limit secondary pollution
- But above all!
  - The sampling method must be designed according to the levels, their temporal variations and the physico-chemical characteristics of the targeted contaminants

Key step often neglected!

Step 2, Extraction

Sampling | **Extraction** | Separation | Analysis | Validation

- Objective
  - **Concentrate** the compounds of interest
  - **Purify**/adapt the matrix

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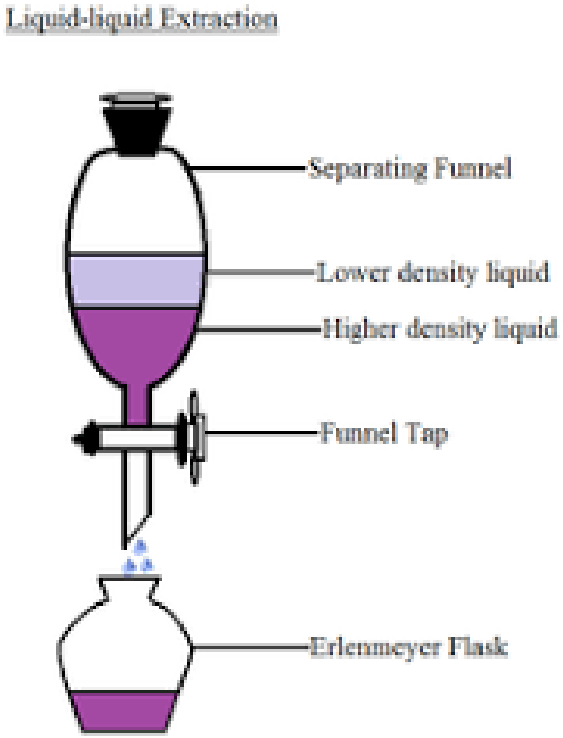
Extraction/concentration technique

Liquid/liquid extraction

Principle

- Use the affinity of molecules for organic solvents
- Involves liquid-liquid phase transfer
- Theory based on a partition coefficient between the two solvents (reminder -> Log Kow)
- Potentially very selective
- Technique not widely used for organic contaminants

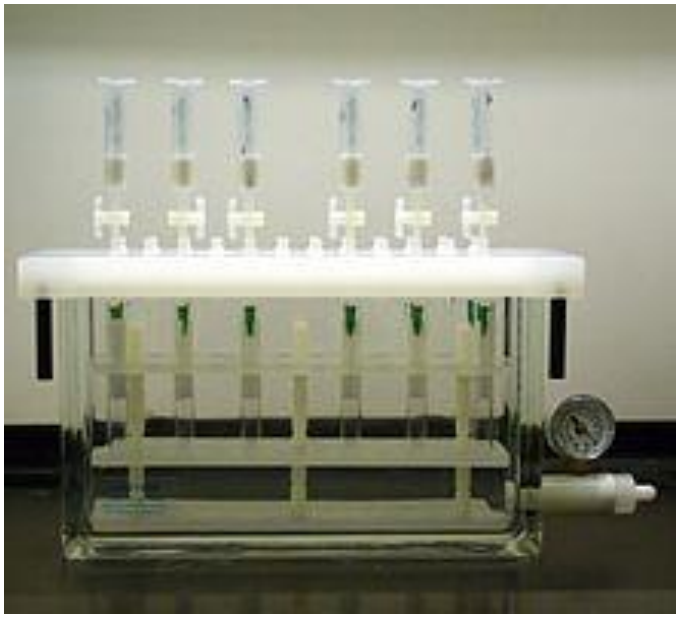
- Necessitate non-miscible solvents
- Large volume of solvents used
- Questionable reproducibility



Extraction/concentration technique

Solid-Phase extraction (SPE)

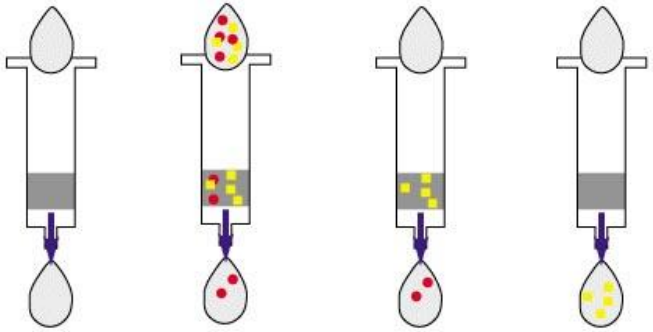
- Aim: To isolate the analyte of interest from a liquid matrix
- Principle: Method based on the theory of adsorption on a solid phase



Extraction/concentration technique

Two types of molecules

- Analyte
- Interferent



1. Conditioning *3. Wash*

2. Load *4. Elution*

Two types of process

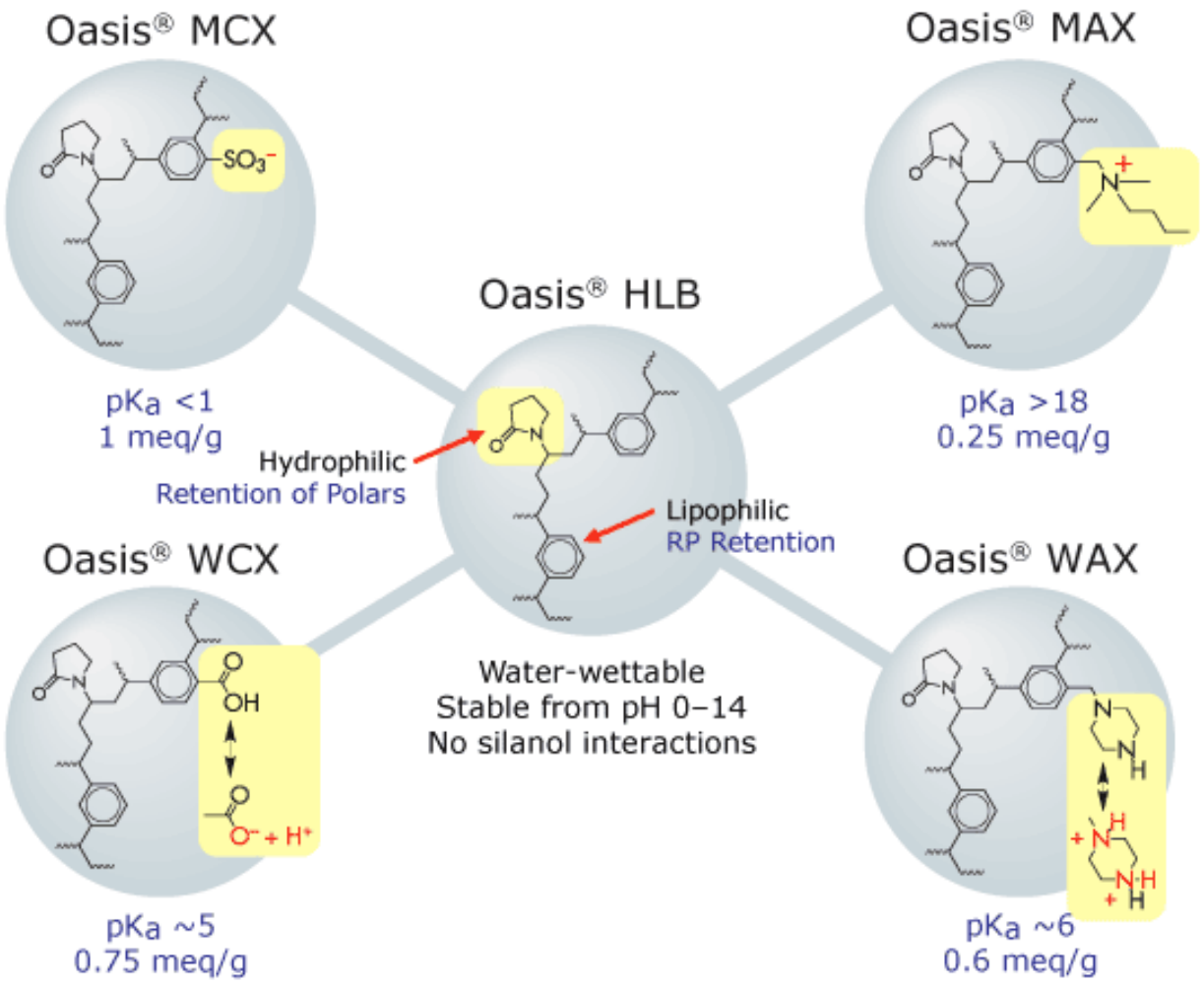
- Rinsing of interferents
- Elution of analytes

This technique allows pre-concentration if the $v_{eluent} < v_{sample}$

the eluent is an organic solvent (or a mixture of) which can also be dried under nitrogen flow

Extraction/concentration technique

Choice of the adsorbent phase



Extraction/concentration technique

SPE extraction is based on the concepts of charges and polarity!

Polarity

Target analytes

hydrocarbures
aldéhydes et cétones
alcools
phénols
acides
hydroxyacides
amines tertiaires
amines secondaires
amines primaires

Phases

polarités de quelques types de phases stationnaires

C18 - C8
phényl (- C6H5)
nitrile (CN)
silice (SiO2...)
amine (NH2)
diol

Solvents

Hexane < Toluene < DCM < Acetonitrile < Methanol < Water

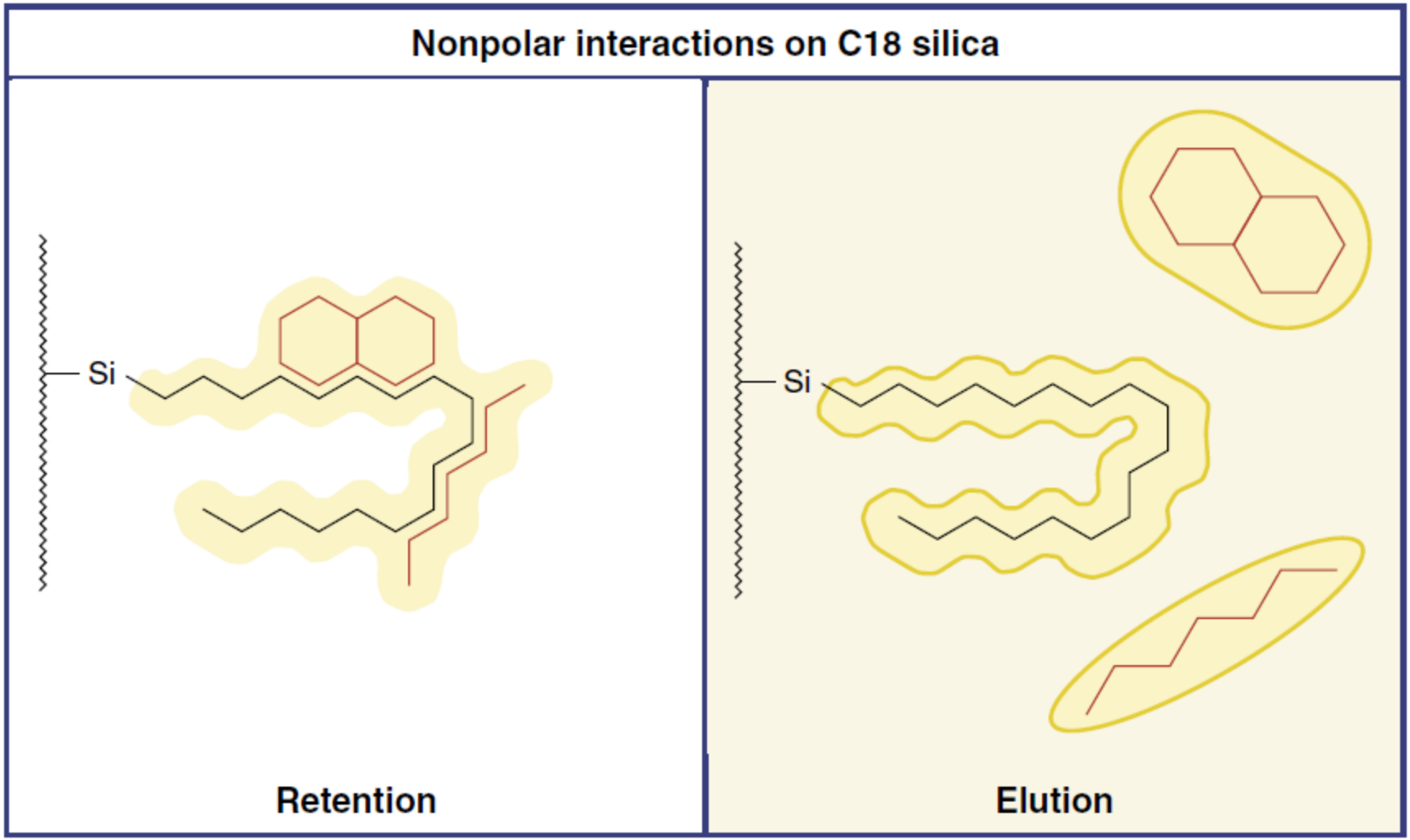
Extraction/concentration technique

Reminder -> Polar substances/Surfaces attract and vice versa!

Reverse phase: Allow the extraction of apolar/weakly polar analytes

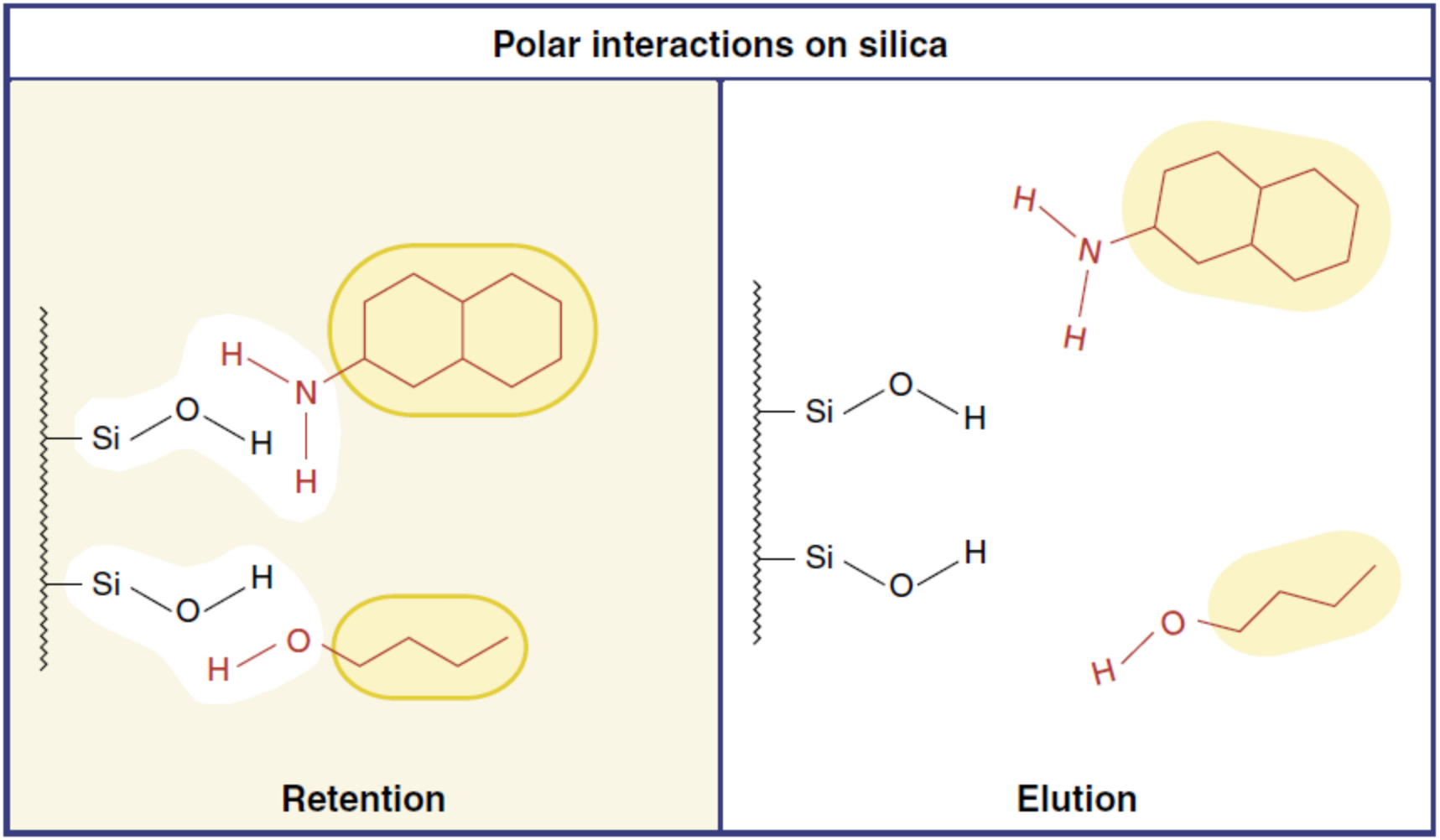
- The liquid sample is polar (e.g. water)
- The solid phase is rather apolar
- Eluent is less polar than water

Techniques d'extraction/concentration



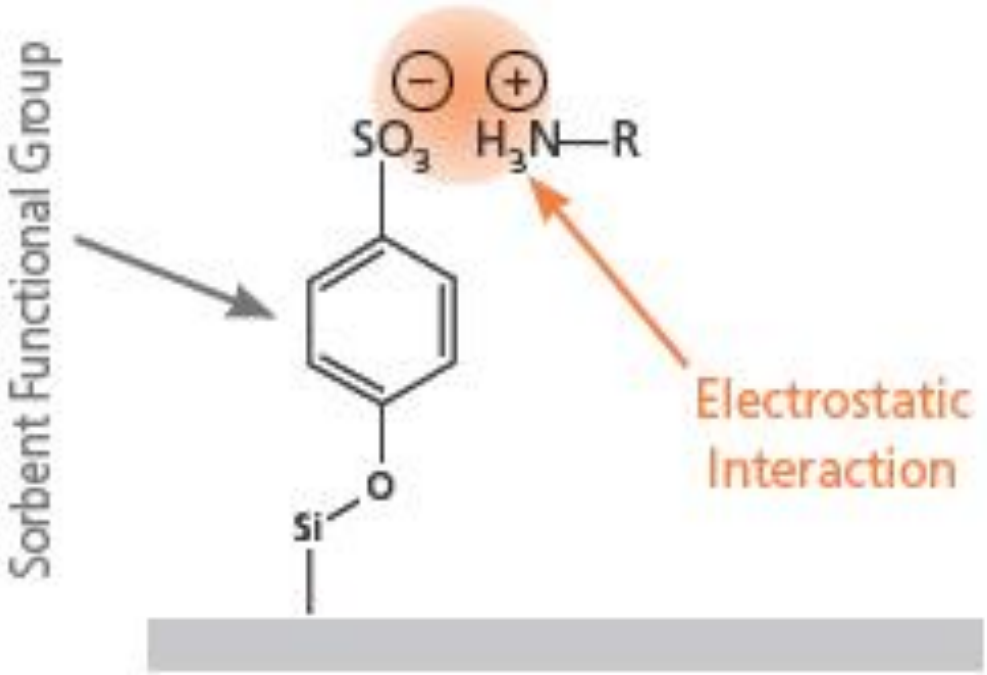
Reversed Phase

Techniques d'extraction/concentration



Normal Phase

Techniques d'extraction/concentration



How to elute ?

Extraction/concentration technique

Reminder -> Polar substances/Surfaces attract and vice versa!

Reverse phase: Allow the extraction of apolar/weakly polar analytes

- The liquid sample is polar (e.g. water)
- The solid phase is rather apolar
- Eluent is less polar than water
- **HLB is a mix between Reversed/normal phase**

Ion exchange:

- Extraction of ionised compounds
- The sample is liquid
- The solid phase is charged (positively or negatively)
- The eluent is usually water at various pHs and/or with high ionic strength

What about selectivity of these two methods ? For which targets ?

SPE

Why is HLB most often used for the simultaneous analysis of several pharmaceuticals ?

HLB used in SPE is exactly the same in POCIS!

Need to estimate the extraction yield in order to be able to recalculate the concentrations for "natural" samples

Step 2, Extraction

Sampling | **Extraction** | Separation | Analysis | Validation

- Conclusion
  - Adapting extraction methods to polarity/charge
  - Adapt selectivity of the method -> purification
  - Need to concentrate samples

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Step 4, Separation

- Objective ?

Chromatography!

Chromatography

- Definition: "a process for separating the constituents of a mixture by means of a mobile phase which carries them through a stationary phase".
- Basic elements: Mobile phase, Stationary phase
- Basic principle: The migration rate (or retention time) of the analytes depends on its solubility in the mobile phase, and its affinity for the stationary phase
- Objective: Separation of analytes before analysis

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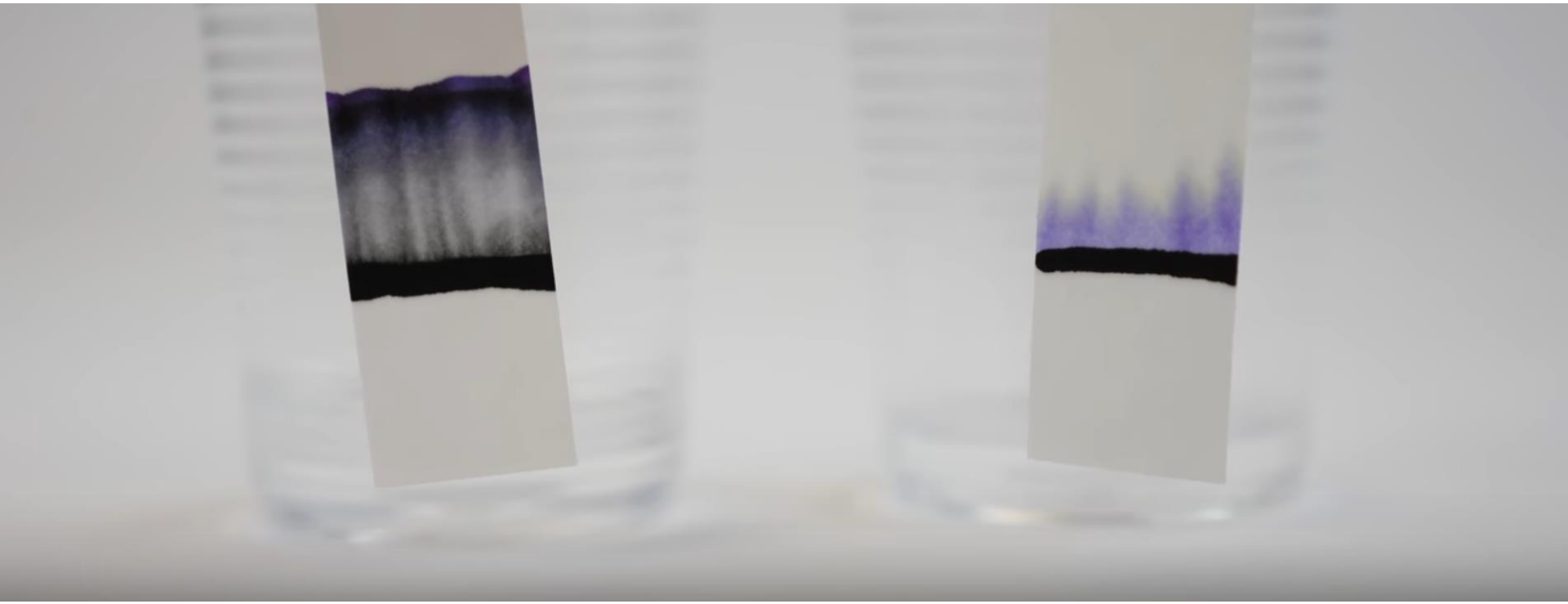
Chromatography, common features

- Mobile phase and stationary phase are immiscible, resulting in a partition equilibrium of the substances between the two phases
- This equilibrium is impacted by the continuous renewal of the mobile phase = migration along the stationary phase
- Migration rate is substance specific = good separation
  - If strong affinity with the stationary phase -> slow migration
  - If strong affinity with the mobile phase -> fast migration

Example



Permanent marker, where is ethanol, where is water ?

Chromatography, common features

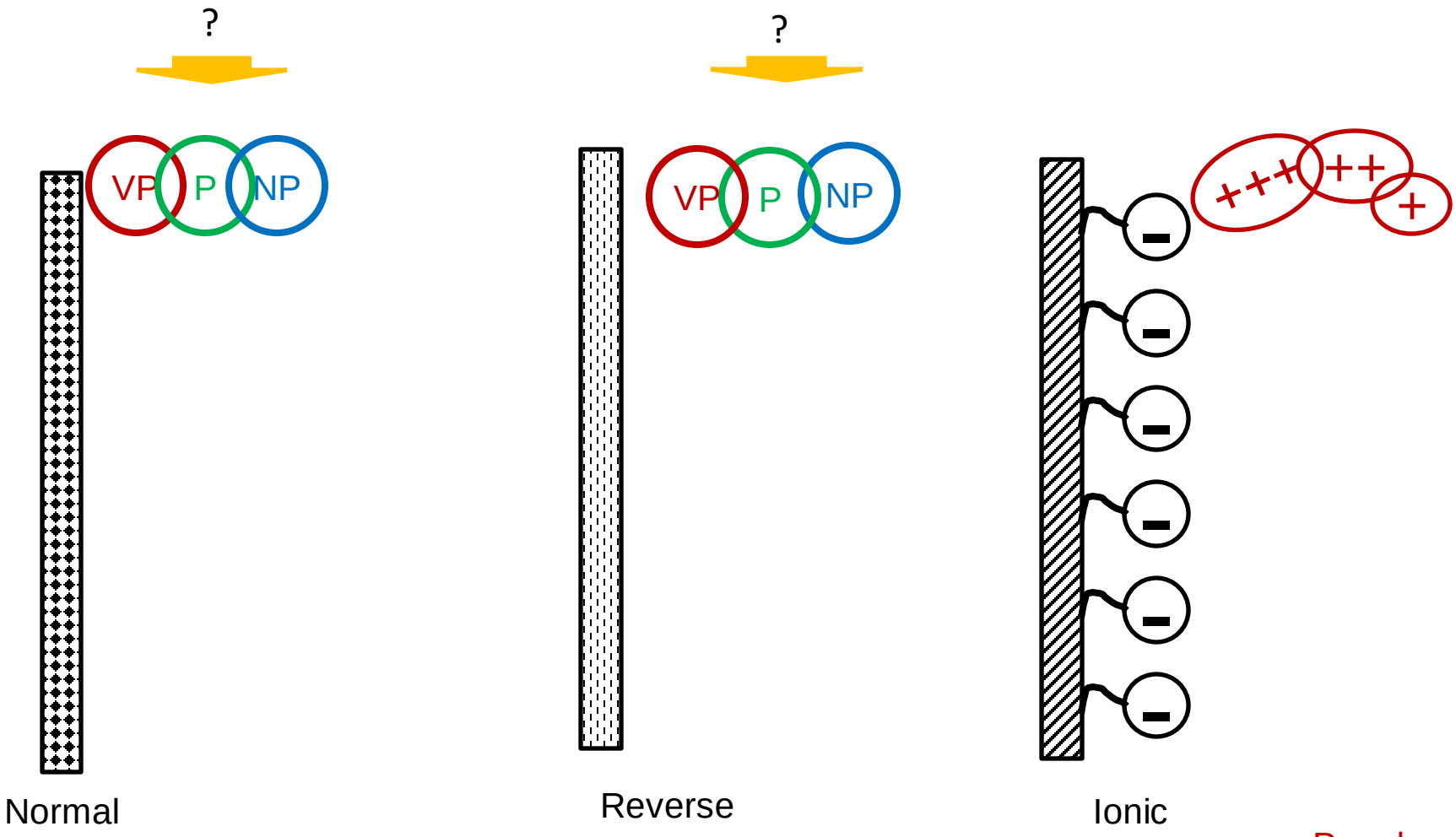
- Mobile phase: fluid by definition, i.e. gas (G), liquid (L) or supercritical fluid (not discussed further here)
- Stationary phase: solid (S) or liquid (L) fixed on a solid
- Relevant techniques for the analysis of organic contaminants :Gas chromatography on column (GSC = GC) Liquid chromatography on column (LSC = LC)

Separation techniques

Different physico-chemical principles

- Electrical charge: ion exchange
- *Size/shape: gel exclusion or permeation*
- **Polarity/hydrophilicity:**
  - **Normal phase: Solvent more polar than stationary phase**
  - **Reverse phase: Solvent less polar than stationary phase**

Separation techniques



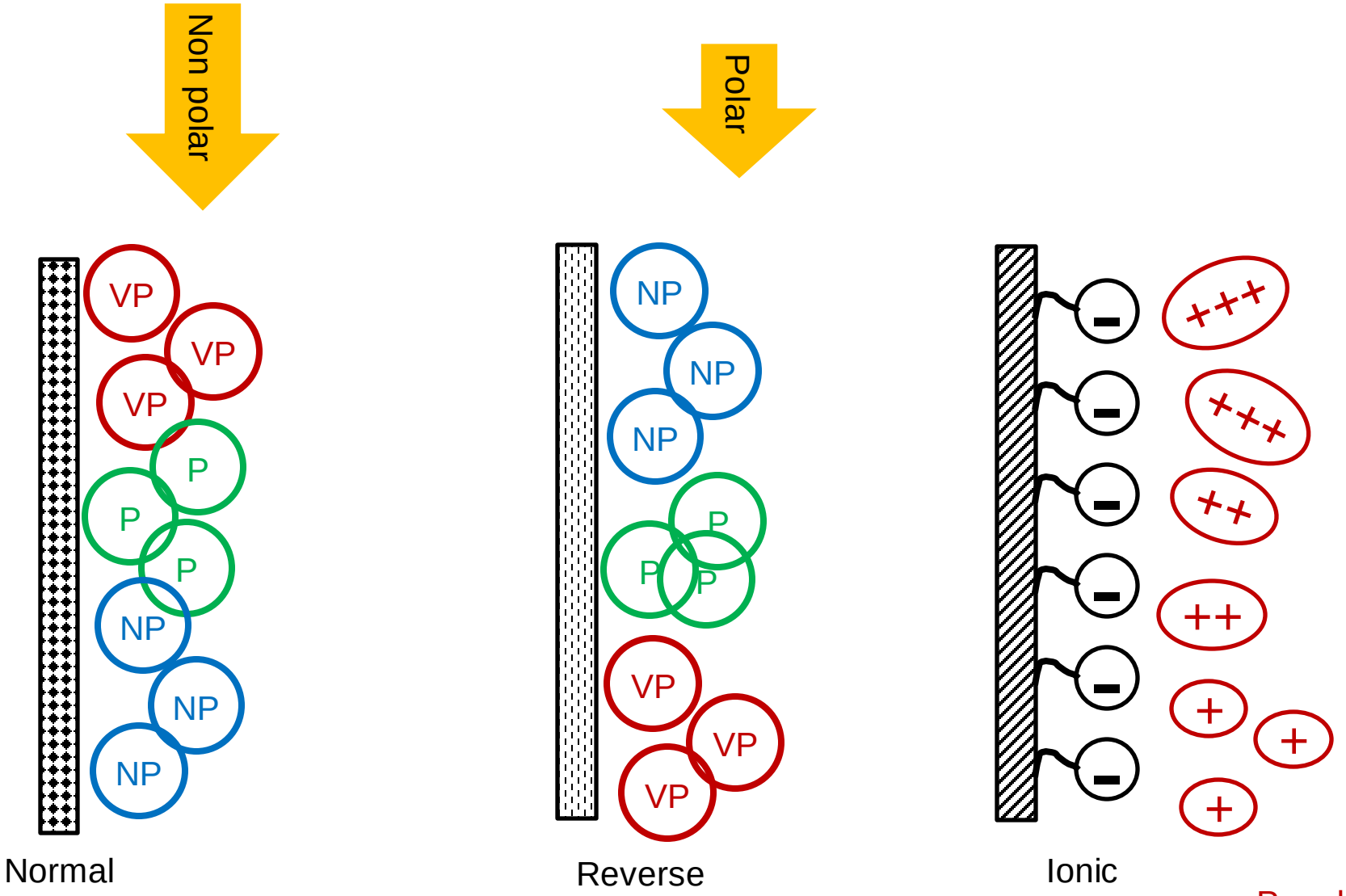
Normal

Reverse

Ionic

P: polar

Separation techniques

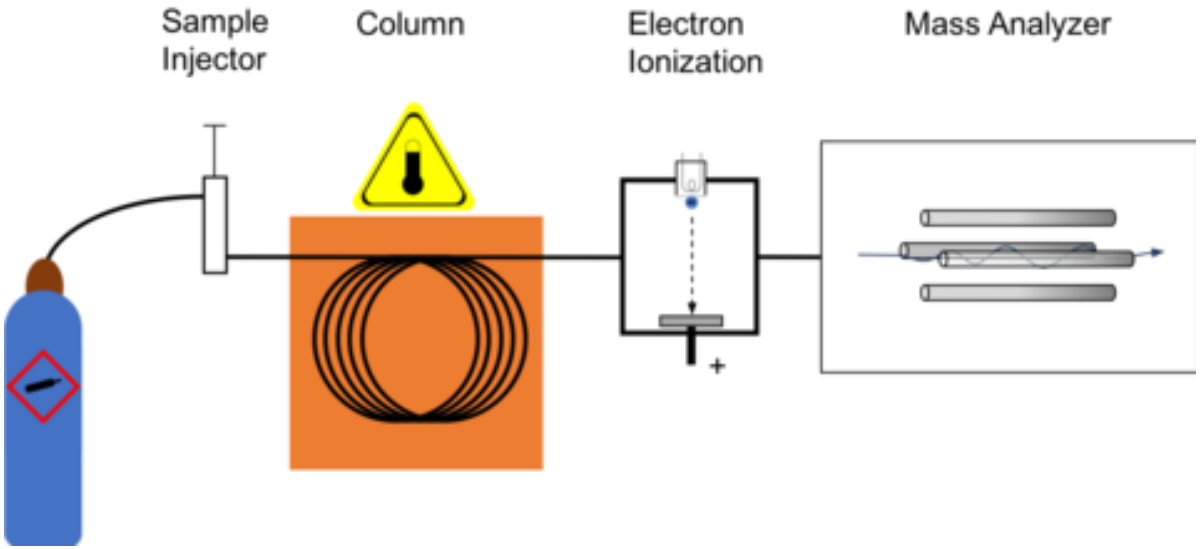


P: polar

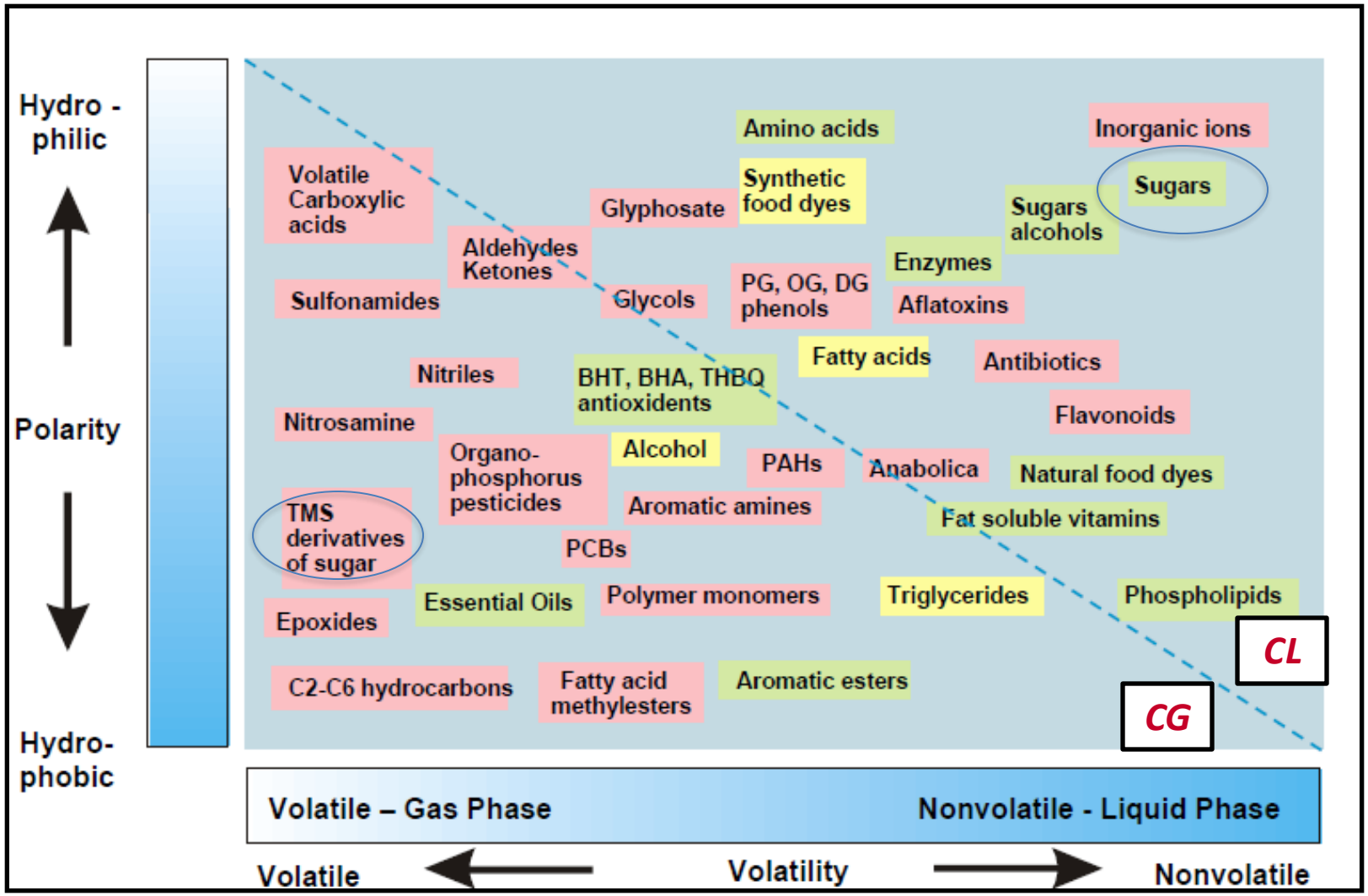
GC, gaseous chromatography

General principle: Separation based on volatility and polarity of molecules

- Separation of compounds in the gaseous state, involves bringing the compounds into the gaseous state by heating
- Suitable for volatile and hydrophobic compounds
- Possibility of **derivatizing** hydrophilic/low volatile compounds



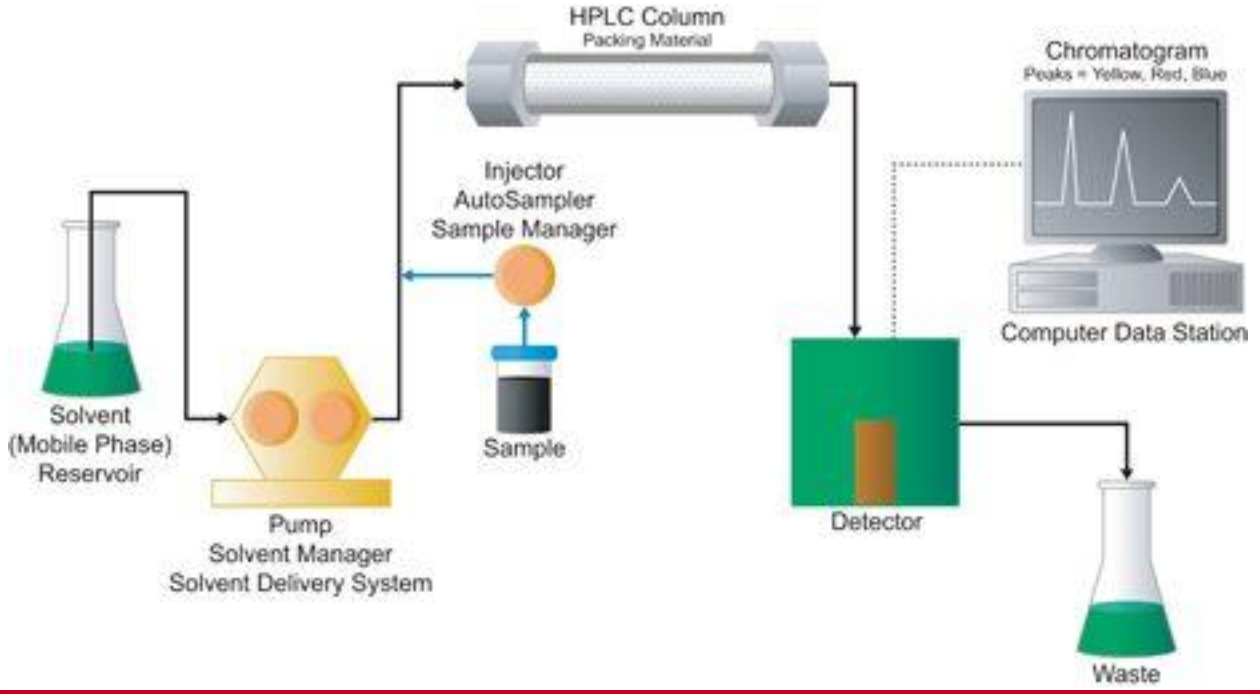
Application Range, GC/LC



LC, Liquid chromatography

General principle: (High) pressure chromatography with separation based on the polarity of the molecules

- Suitable for the analysis of polar and low volatile compounds
- Separation in liquid mode



Step 4, Separation

- Objective ?

Chromatography!

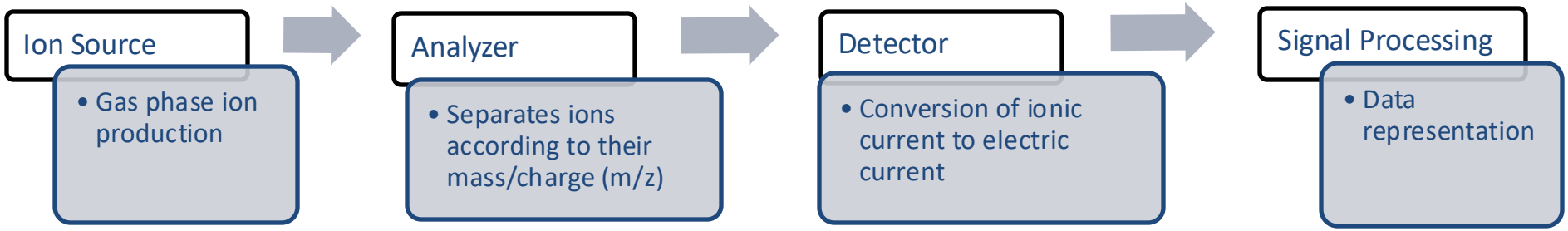
Adapting the mobile phase/stationary phase pair to the polarity/charge of the target compounds
Adapt the mobile phase (gas/liquid) to the physicochemical properties of the target compounds

Step 5, Analysis

- Objective ?

Different types of detectors (FID, UV or MS)

- Only **mass spectrometry** will be discussed here
- To identify/quantify organic molecules
- Principle -> Volatilize / Ionize / Quantify



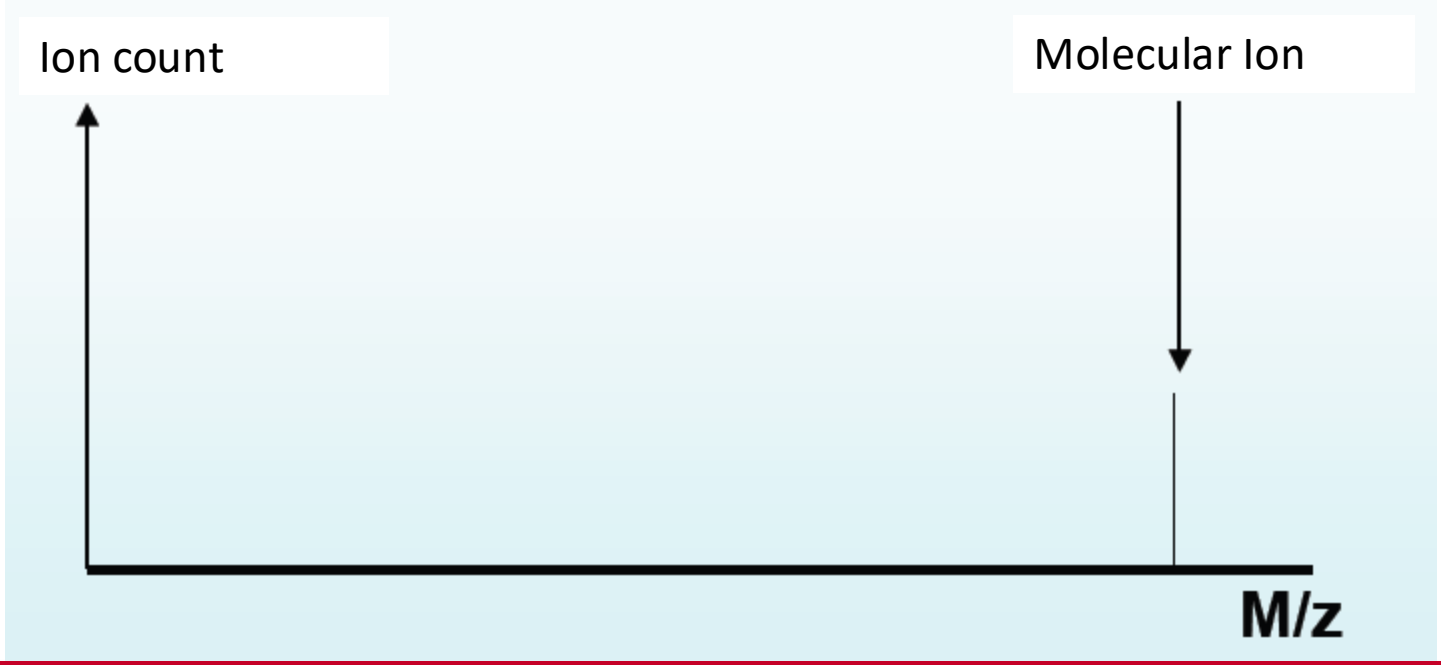
Volatilization/nebulization

- Step that occurs in the source if liquid-gas coupling
- In the case of LC-MS, the mobile phase is liquid, need to nebulise for MS analysis
- In the case of GC-MS, mobile phase = gas, no need to nebulise

- Mobile phase >> analytes

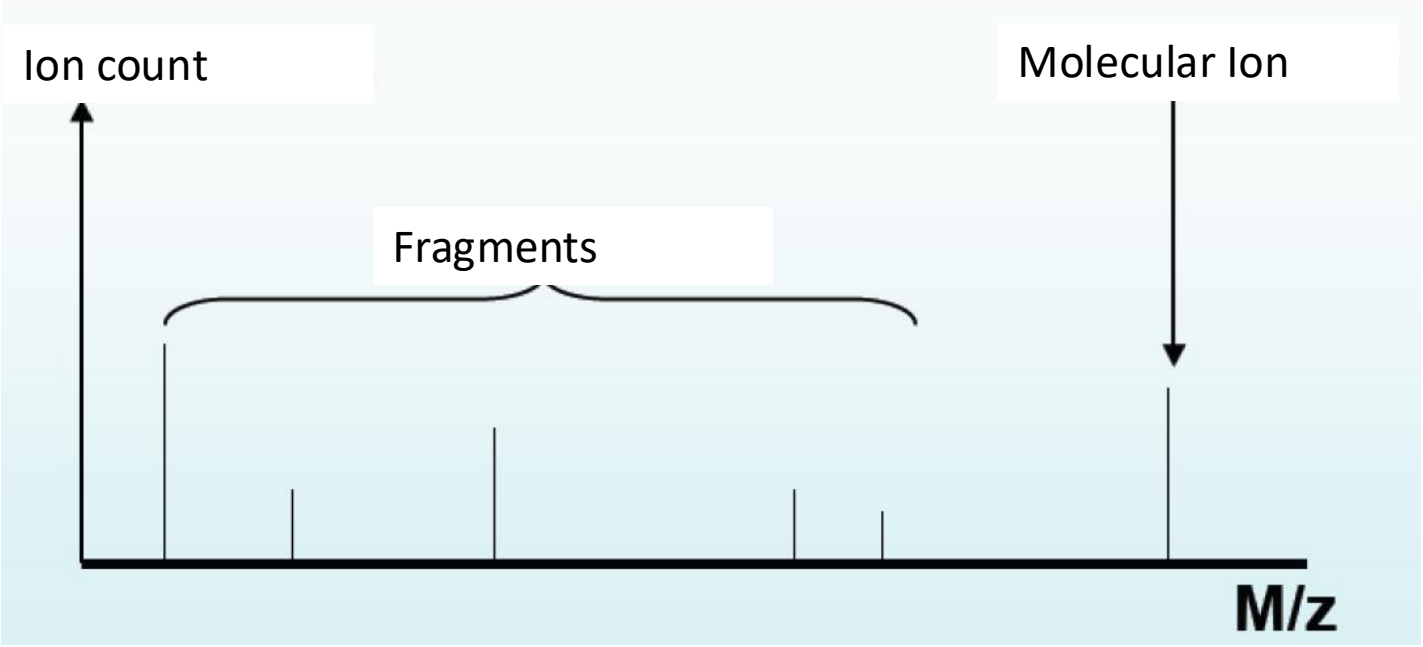
Ionization

- Ionization can be positive or negative!
- There are two main types of ionization:
  - "Soft" ionization



Ionization

- Ionization can be positive or negative!
- There are two main types of ionisation:
  - “Soft” ionization -> mostly ion extraction
  - “Strong” ionization -> fragments production

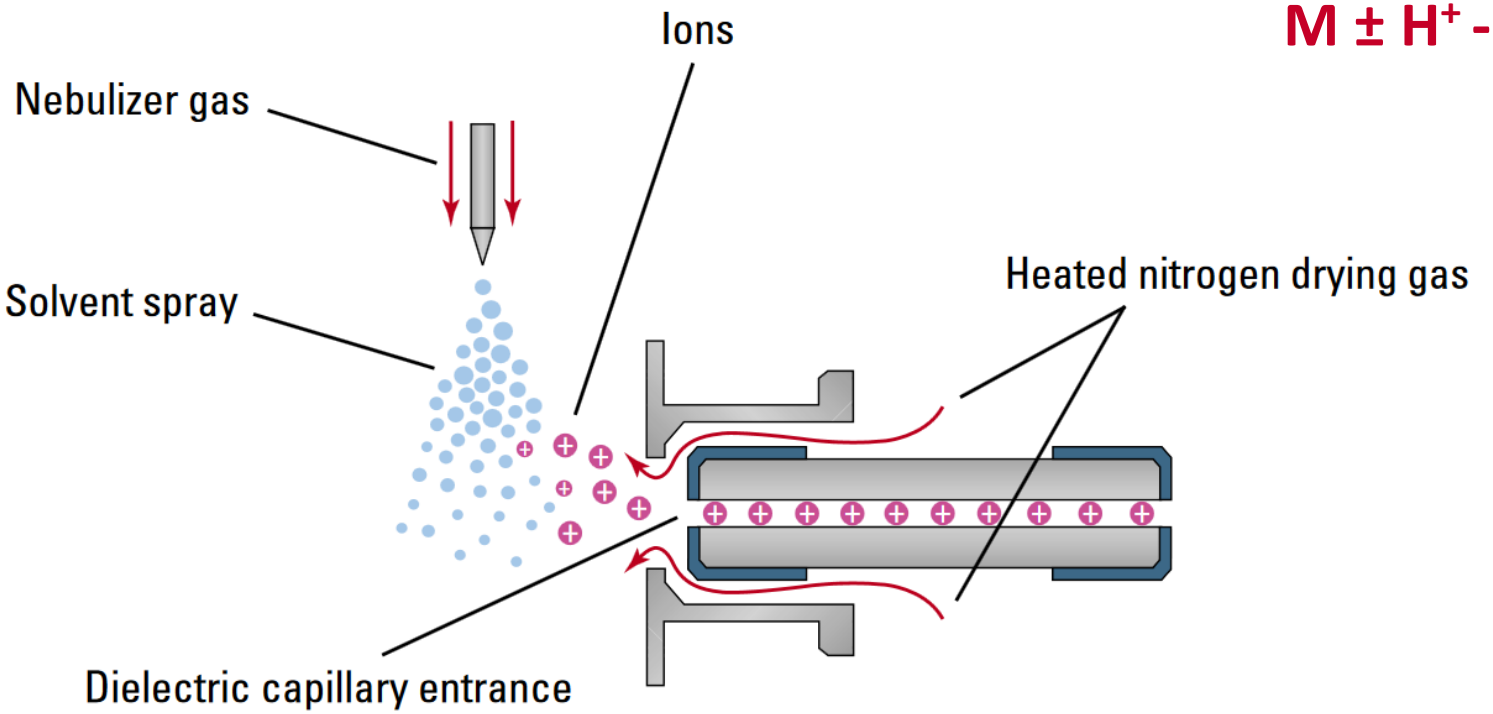


Ionization sources, types

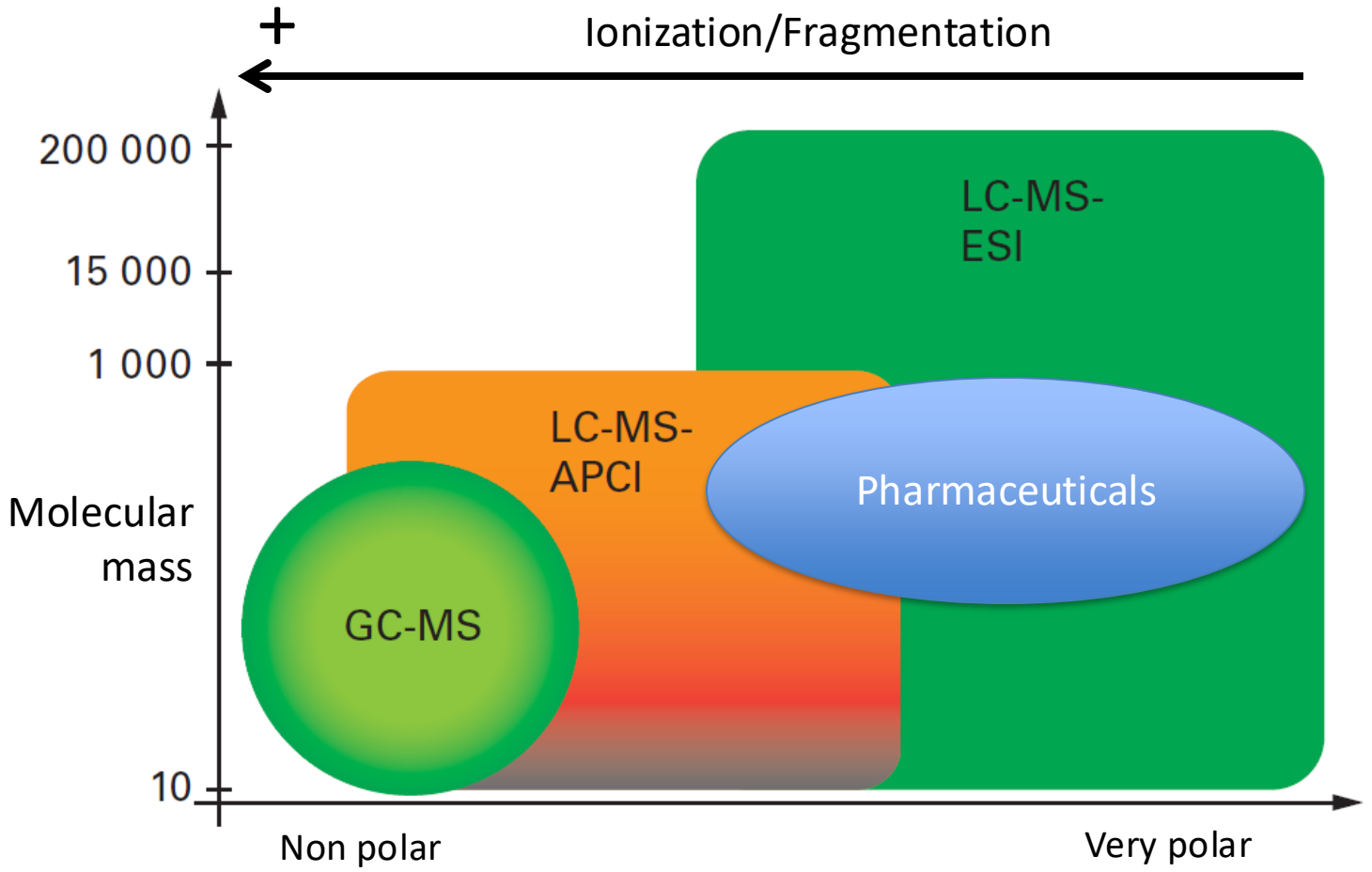
After LC, coupling less easy, phase change necessary (liquid-gas)

- Example of the ESI (electrospray ionisation) source
- Soft ionization
- Suitable for already charged compounds
- Does not produce ionised species as such but acts rather as an ion extractor

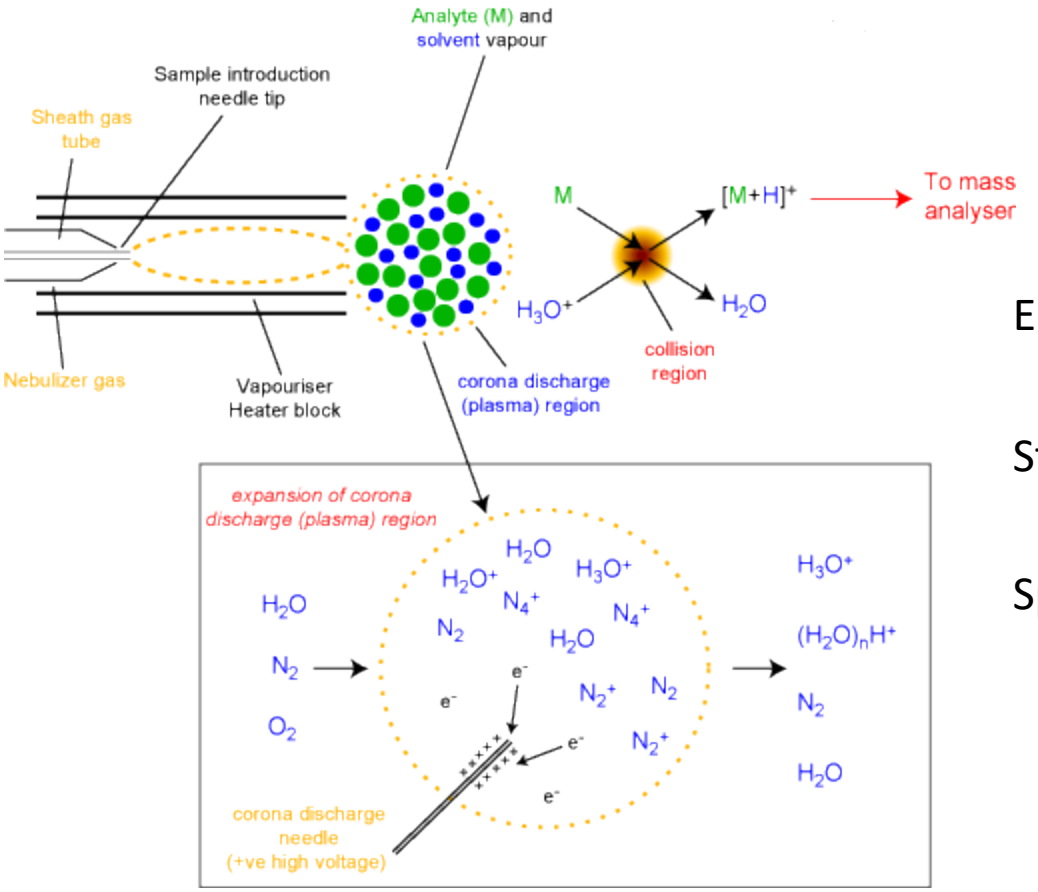
$M \pm H^+ \rightarrow M \pm H^+$



Adapt the ionization source to the analyte!



APCI Source



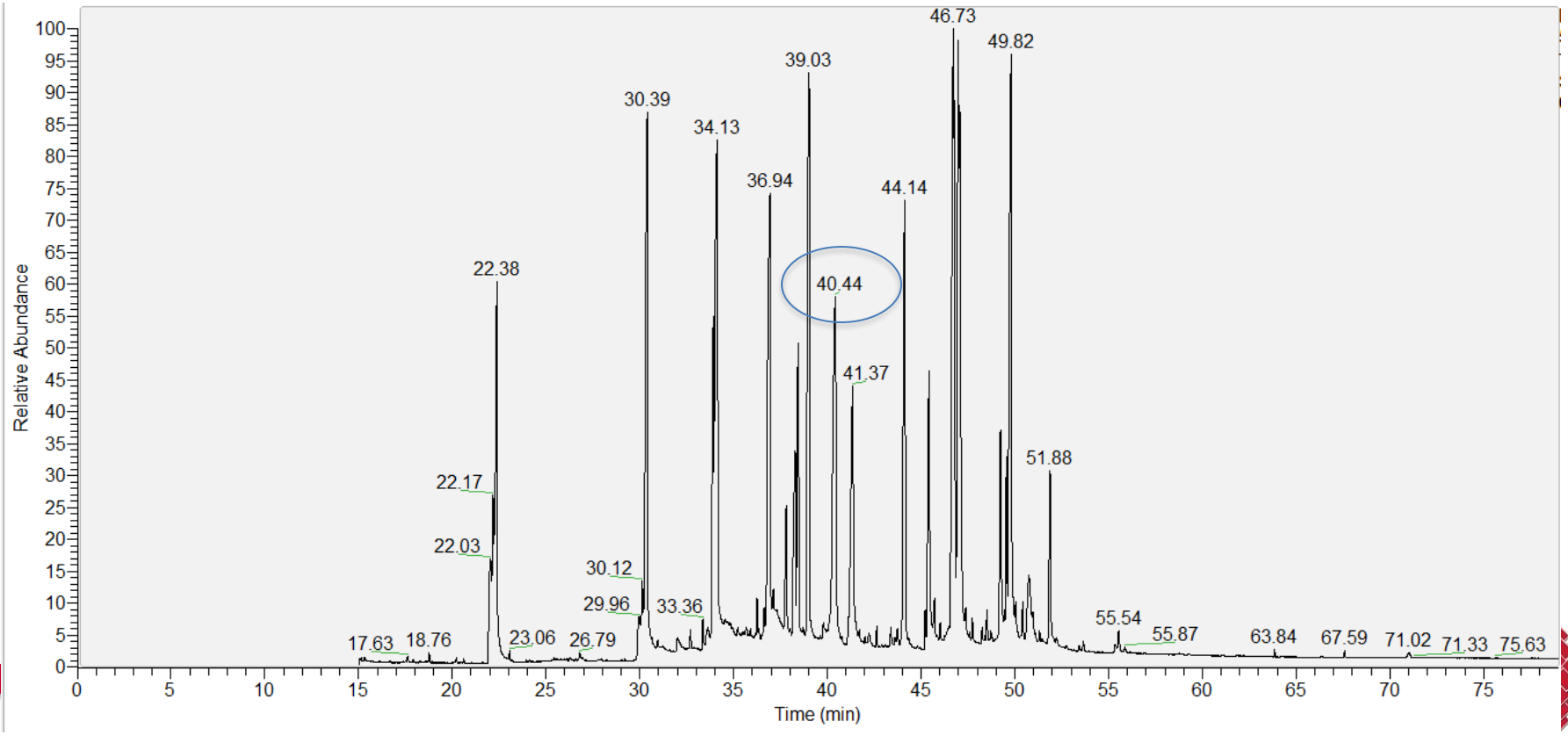
Electron supply through corona needle

Stronger than ESI

Sparsely used for Pharmaceuticals

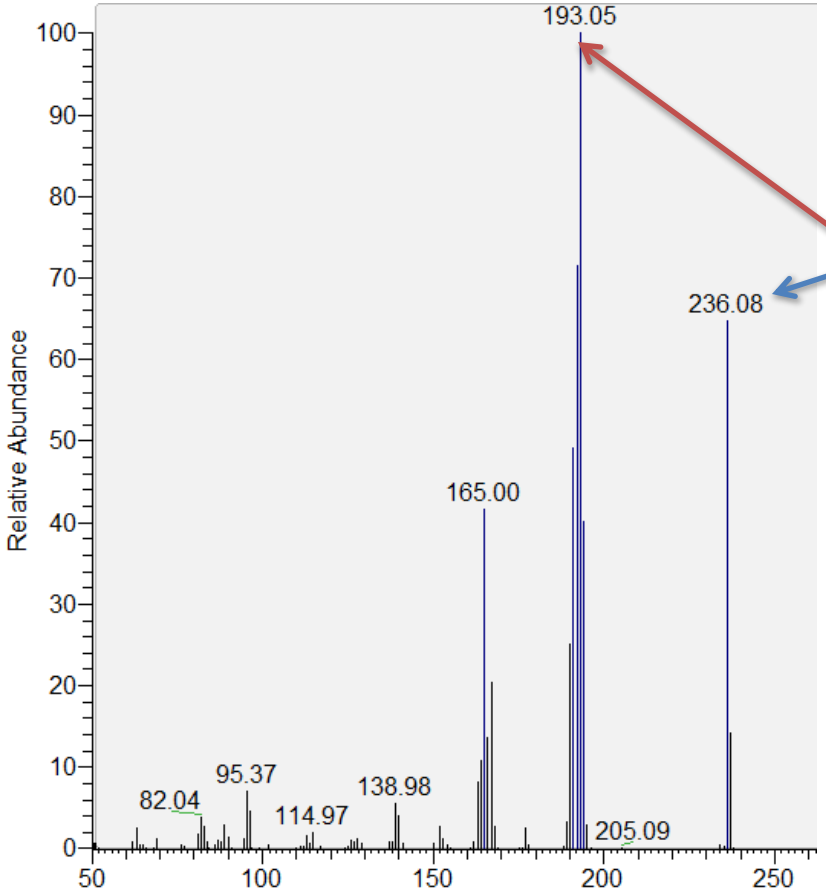
Chromatography/Mass Spectrometry Coupling

- A chromatogram is obtained
- Here the total ionic current (TIC) is represented
- Each peak corresponds to a counted ions accumulation (i.e. one molecule?), its retention time is a first characteristic
- Mass spectrometer counts the ions and assess their m/z



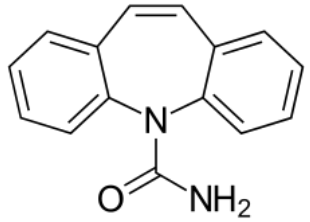
Mass spectrum

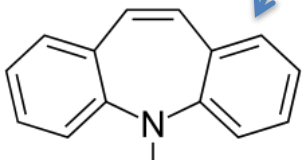
- Retention time alone does not accurately identify a compound!
- Need to observe the mass spectrum



Molecular Ion

Fragment





M = 193 g.mol^{-1}

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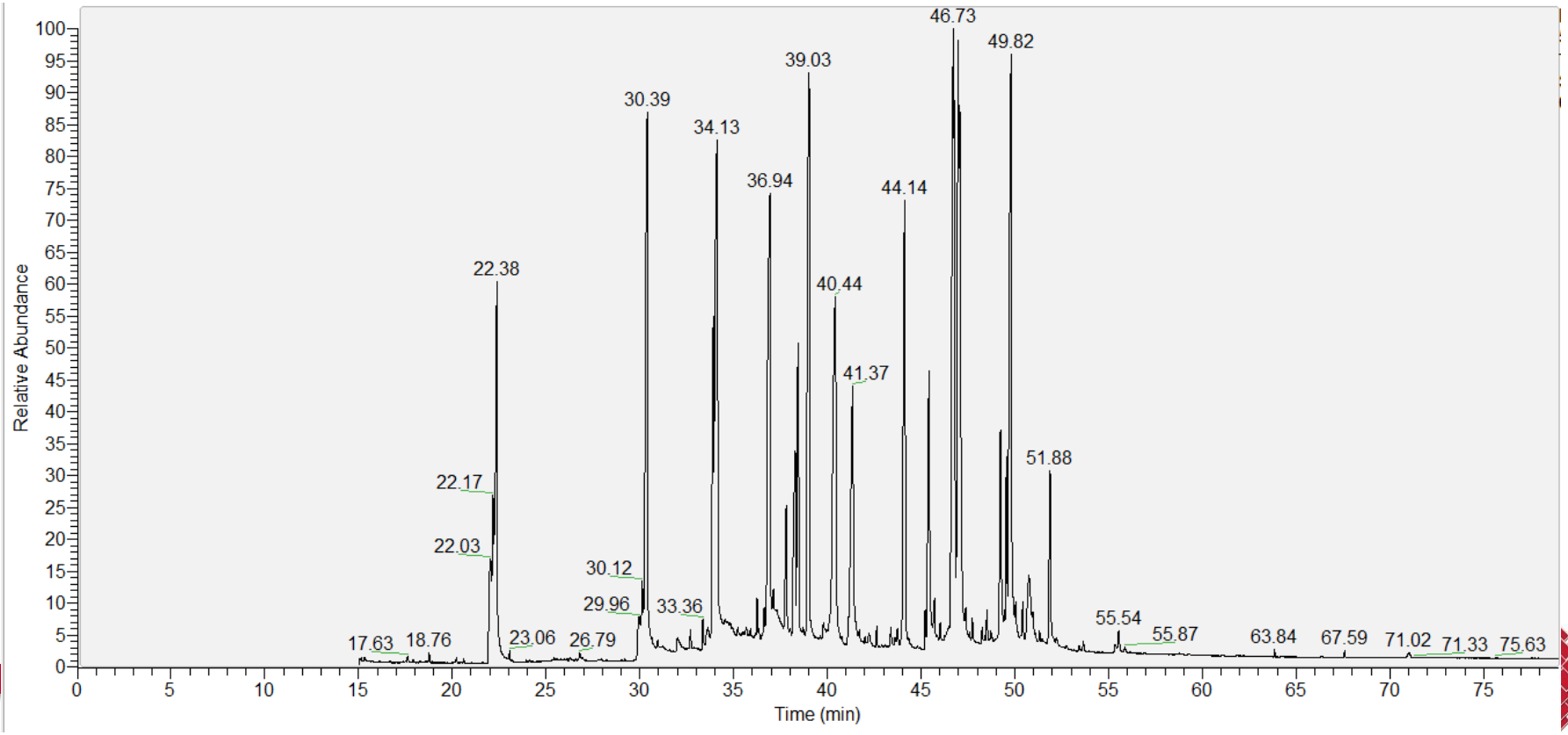
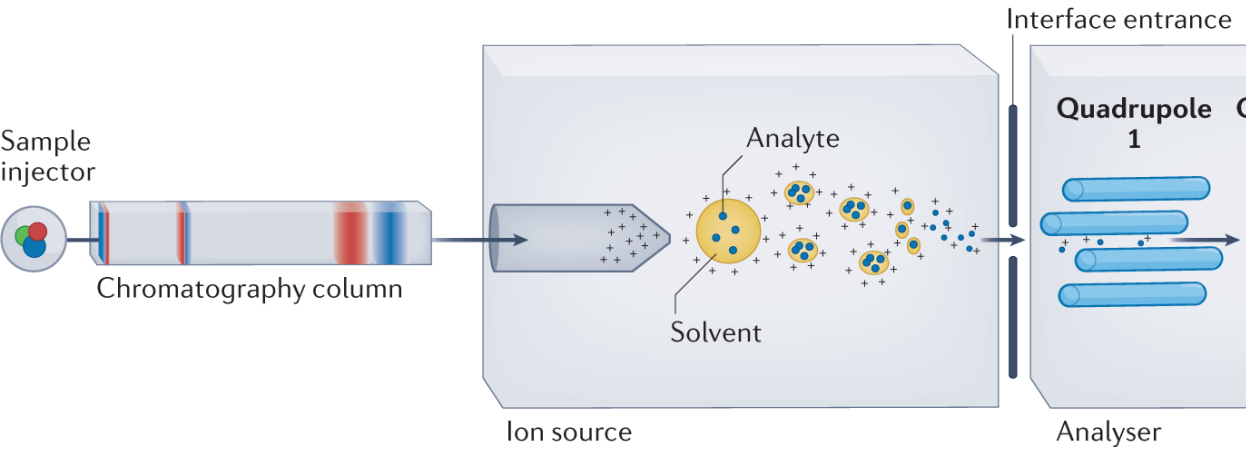
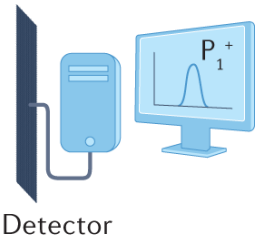
What are the risks to quantitate on TIC?



From MS to tandem MS

- Need to access sometimes very low concentration compounds (very small peaks)
- Classic MS operation





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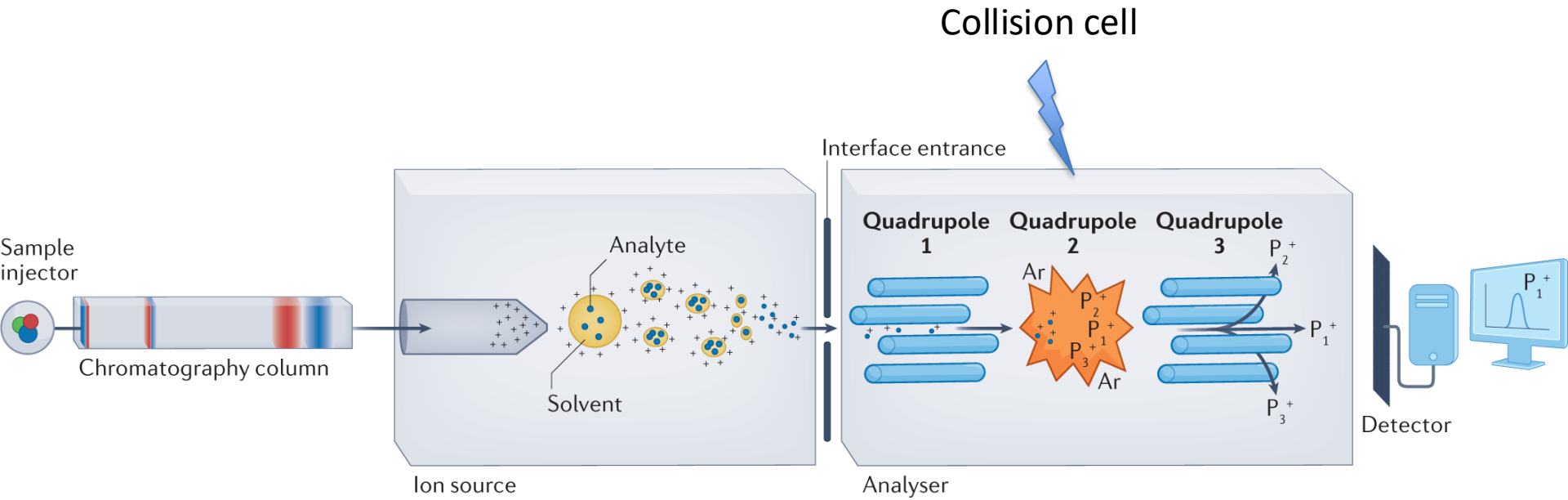
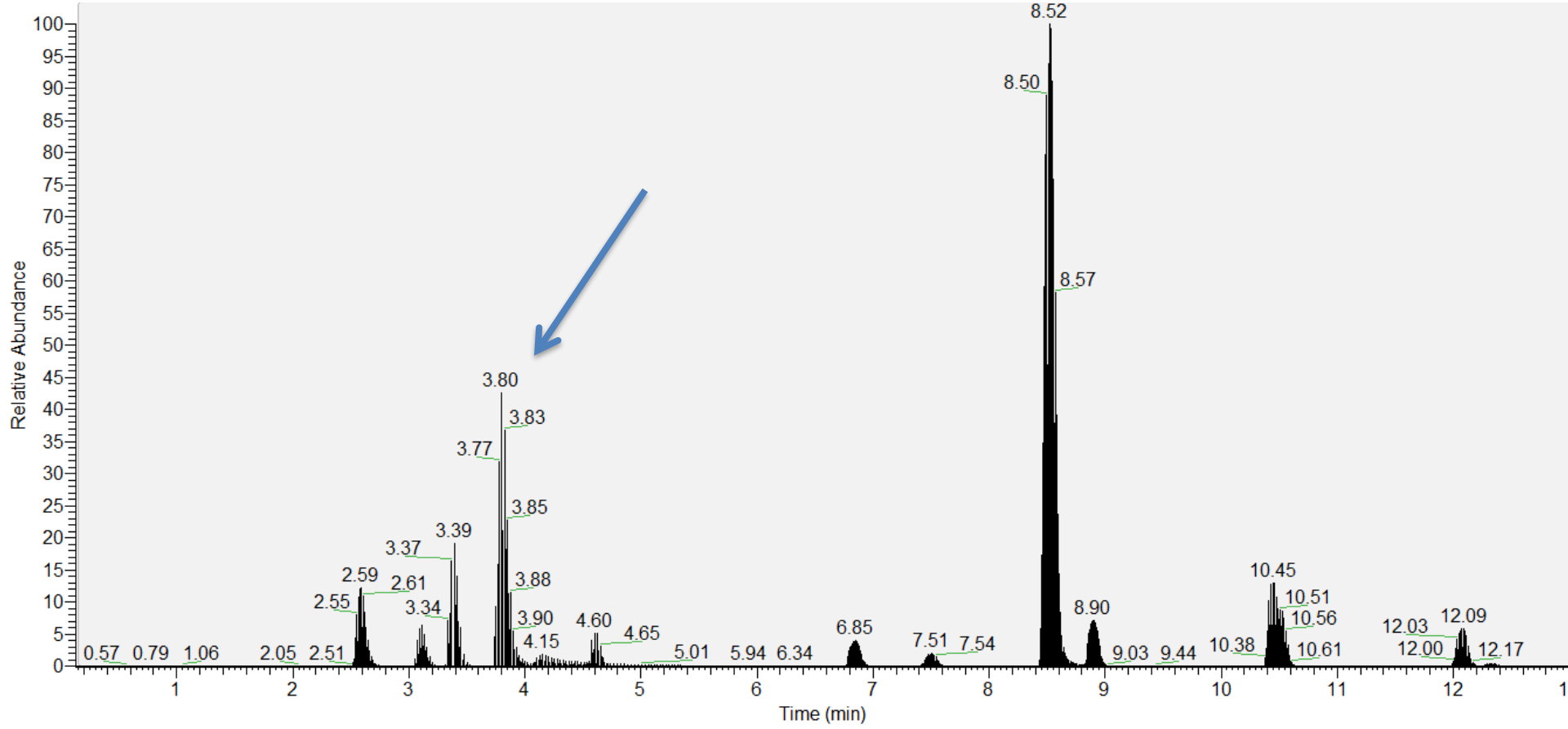


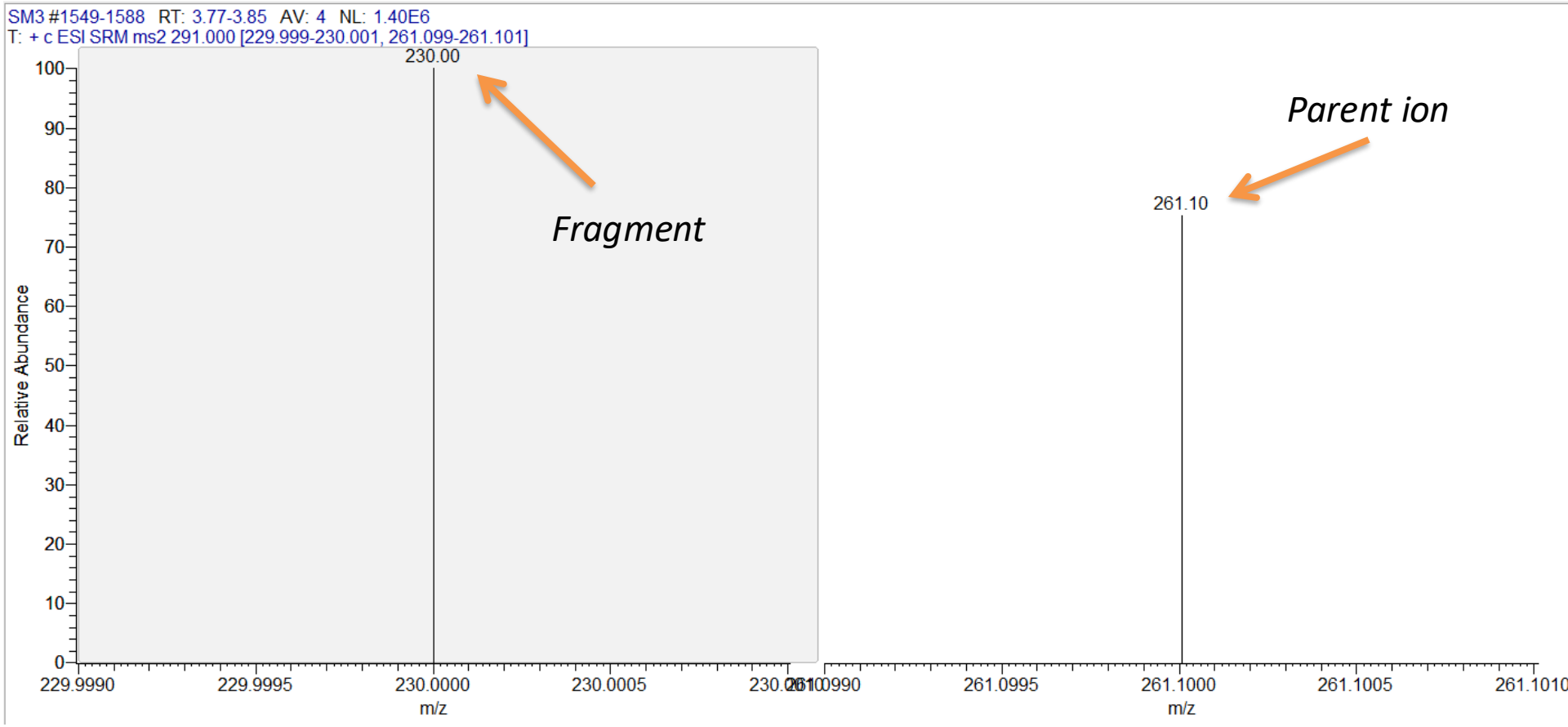
- Objective: Suppression of background noise, limit the false positive
- Technique: A parent/fragment ion pair is determined and specified in a RT range
- Limit the analysis in Q1 to the parent ion and in Q3 to the daughter ion (f(collision energy))

Tandem mass spectrometry



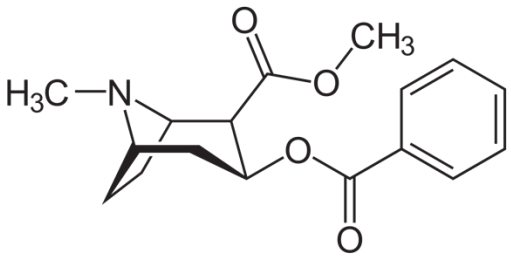
- Objective: Suppression of background noise, limit the false positive
- Technique: A parent/child ion pair is determined and specified in a RT range
- Limit the analysis in Q1 to the parent ion and in Q3 to the fragment (f(collision energy))

Tandem mass spectrometry -> MRM



- Objective: Suppression of background noise, limit the false positive
- Technique: A parent/child ion pair is determined and specified in a RT range
- Limit the analysis in Q1 to the parent ion and in Q3 to the daughter ion (f(collision energy))
- Loss of mass spectrum information / Better resolution

Validation of the specificity of the signal



MW: 303.3

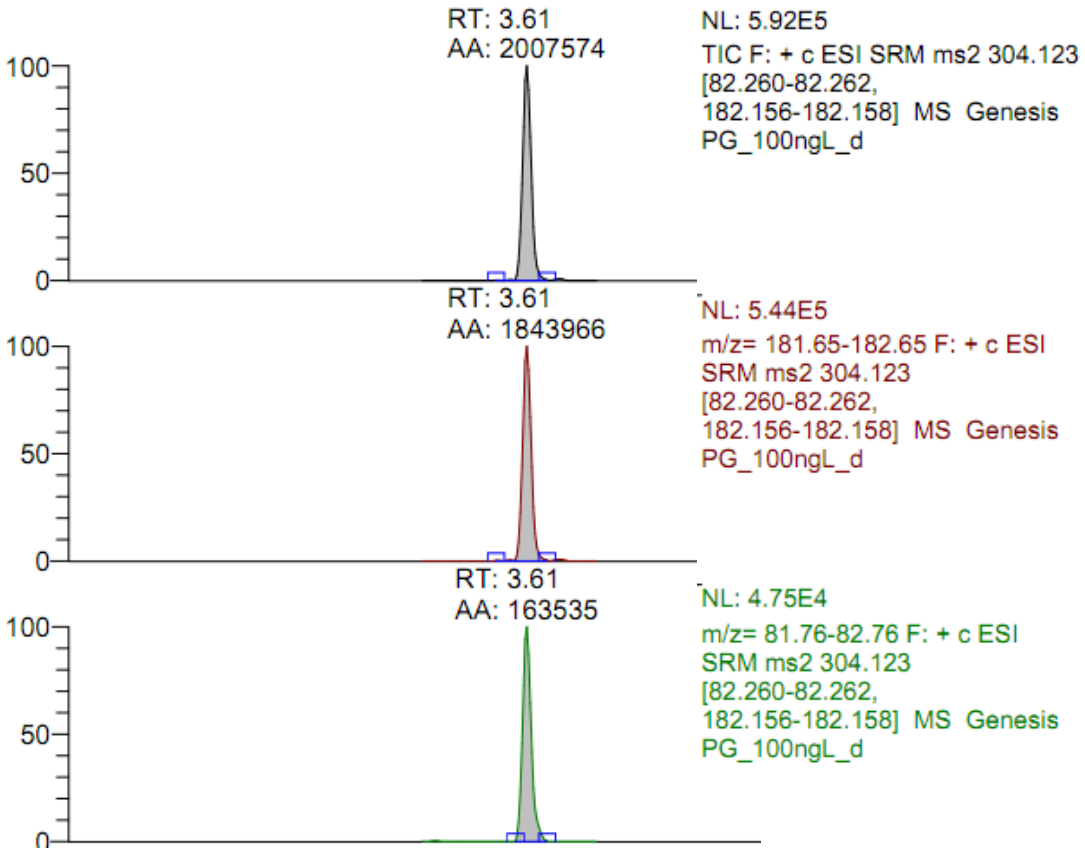
Cocaine

RT = 3,6 min

Quantification:
304,123 → 182,56

Qualification:
304,123 → 82,26

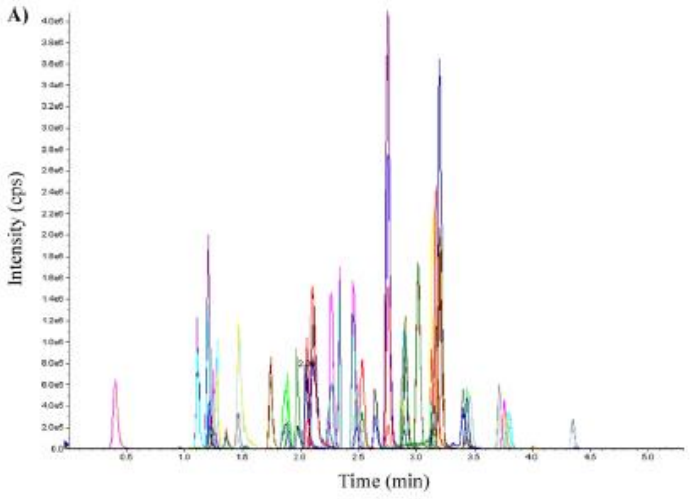
Ratio : 11



Example of application

Gros et al. J. Chromatogr. A, 1248, p 104-121 (2012)

- 81 pharmaceuticals + metabolites
- 2 WWTP influent & effluent, 3 SW, 1 DW
- MS/MS, isotopically-labeled compounds
- SPE (25 ml WW - 500 ml DW)
- LOQ: 1 to 50 ng/L
- Repeat: RSD < 6% - Int. Rep: RSD < 20%.



ESI+ chromatogram of a 10 µg/L solution

Analyte	RT	ESI	MS/MS Quantl / Qual / R	Influent (n=2)	Effluent (n=2)	SW (n=3)	DW (n=1)
SMX	1.98	+	254 / 92-56 / 1.1	768 / nd	222 / nd	16 - 79	0,5
Acetaminophen	0.56	-	150 / 107 & EPI/IDA	16720 / 18681	338 / nd	nd - 243	nd
CBZ	3.19	+	237 / 194-193 / 1.3	95 / 46	158 / 13	8 - 41	2
2-OH-CBZ	2.88	+	258 / 210-208 / 6.8	928 / nd	676 / nd	nd - 52	nd
Codeine	1.36	+	300 / 152-115 / 1.2	800 / 45	142 / nd	4 - 19	nd

WWTP1: urban, hospital - > 1 billion inhbts
WWTP2: urban, industrial – 20 000 inhbts

Concentration in ng/L

Step 6, Validation

- Objective ?

Assessing the following parameters

- Specificity
- Sensitivity
- Sensibility

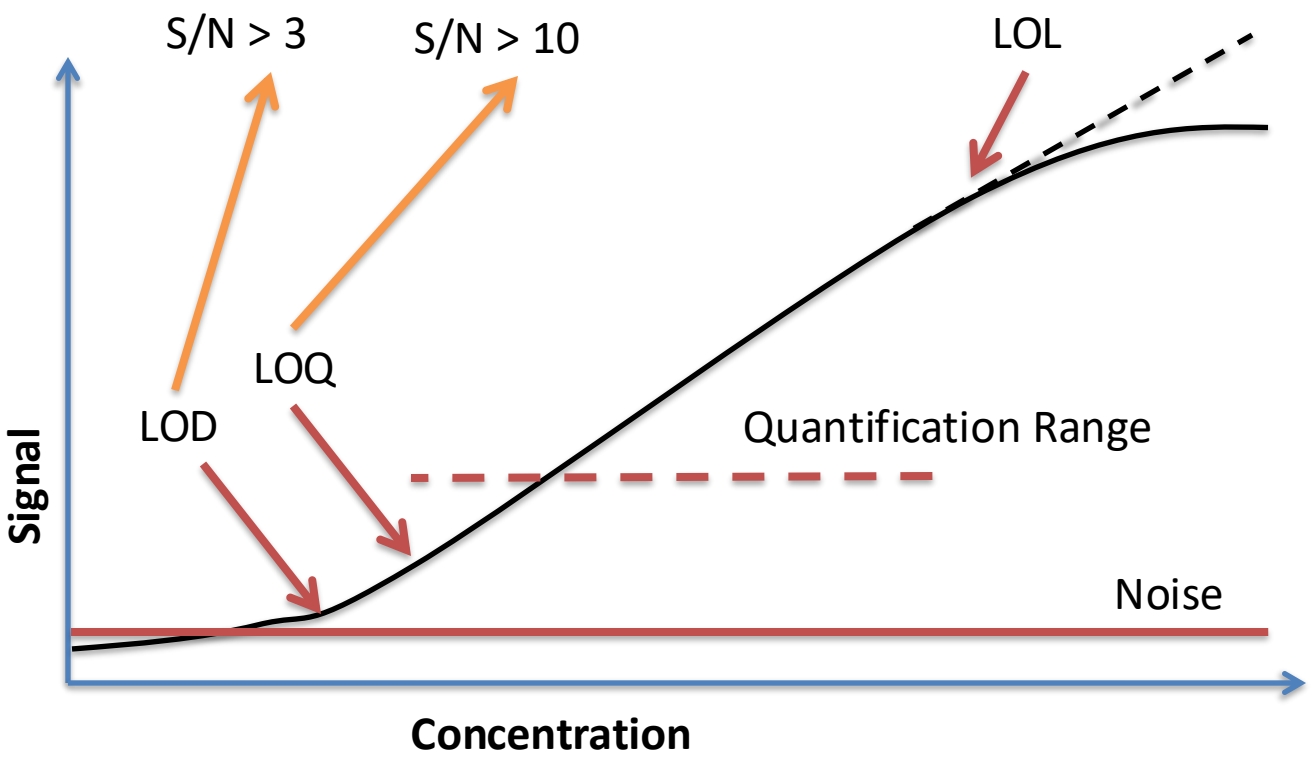
Selectivity/Specificity

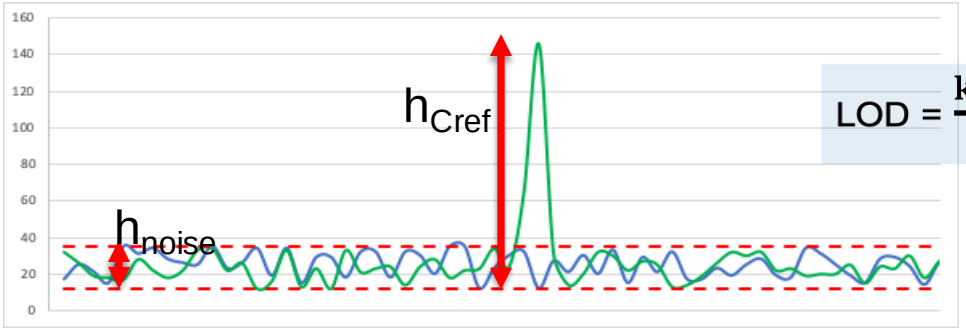
Selectivity ability of a method to measure and differentiate the analyte(s) of interest in the presence of components which may be expected to be present in the sample.
Specificity ability to measure the analyte unequivocally in the presence of other compounds, either exogenous or endogenous, in the matrix.

- Analyse of blank sample and spiked blank sample
- Retention time & peak resolution
- Peak purity profile (DAD detection)
- Specificity of MS response: 4 checkpoints

→ Extent to which a method can determine particular analyte(s) in a complex mixture without interference from the other components in the mixture.
→ The term specific in analysis is considered as the ultimate of selectivity.

Sensibility





$$LOD = \frac{k \times h_{noise} \times C_{ref}}{h_{ref}}$$

0 doesn't exist

LOD wastewater > LOD treated water > LOD drinking water

Matrix effect and Recovery

Matrix effect: The direct or indirect alteration or interference in response of an instrument due to the presence of unintended analytes (for analysis) or other interfering substances in the sample (EMEA).

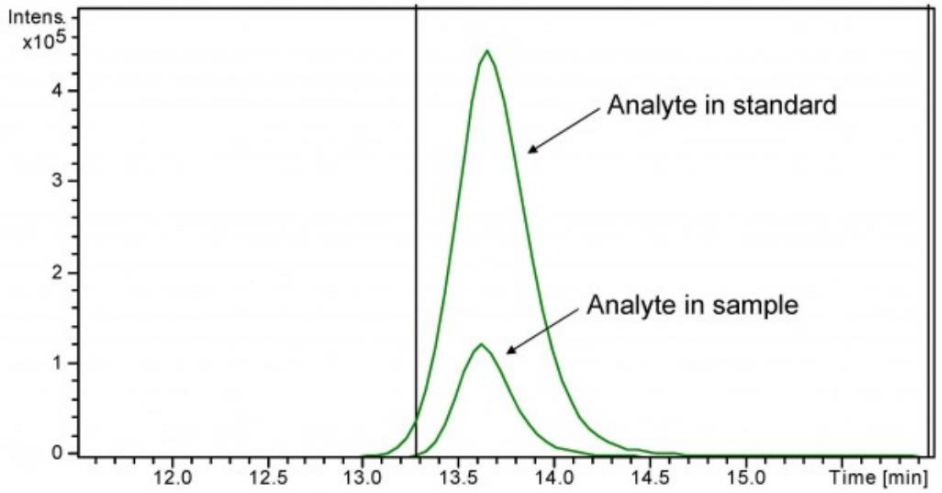
- Signal variation (most often decrease) in LC-MS/MS
- Insufficient separation with interference below the analyte peak also detected

Recovery: Proportion of the amount of analyte, present in or added to the analytical portion of the test material, which is extracted and presented for measurement (IUPAC).

Extraction: efficiency, stability, reproducibility

Matrix effect

Accuracy estimation

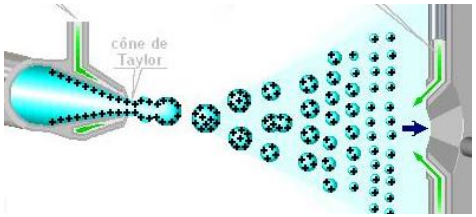


Matrix effect and Recovery

LC-MS/MS use labelled surrogate :

→ Extraction yield

→ Matrix effect compensation

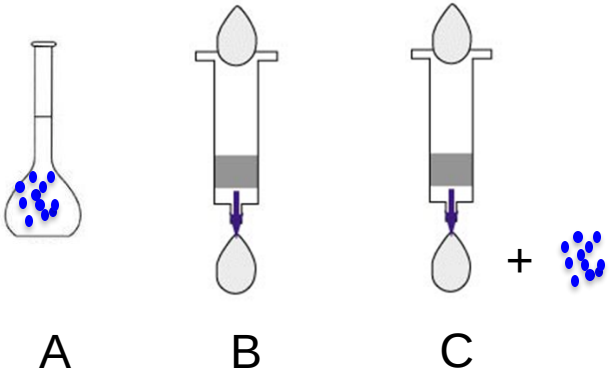


Validation (with labelled surrogate)

A: reference solution in mobile phase

B: spiked sample before SPE

C: matrix sample spiked after SPE



Extraction yield: B/C

Matrix effect: C/A

Efficiency: B/A

	Extraction yield	Matrix effect	Efficiency/recovery
Surface water	92%	- 6%	86%
wastewater	76%	- 51%	37%

Matrix effect and Recovery

Matrix effect: The direct or indirect alteration or interference in response of an instrument due to the presence of unintended analytes (for analysis) or other interfering substances in the sample (EMEA).

- Signal variation (most often decrease) in LC-MS/MS
- Insufficient separation with interference below the analyte peak also detected

Recovery: Proportion of the amount of analyte, present in or added to the analytical portion of the test material, which is extracted and presented for measurement (IUPAC).

- Extraction: efficiency, stability, reproducibility
- Matrix effect
- Accuracy estimation

Internal standard: Test compound added to calibration standards, QC samples and study samples at a known and constant concentration to correct for experimental variability during sample preparation and analysis (EMEA)

- structurally similar analogue → separated from the analyte of interest by chromatography
- stable isotope labelled compound → not separable by chromatography

Quantification with ILIS

- Measurement of area ratio $A_{analyte}/A_{labelled\ surrogate}$

  No chromatographic separation

  Specific MS/MS detection

  Same extraction yield and matrix effect for both molecules

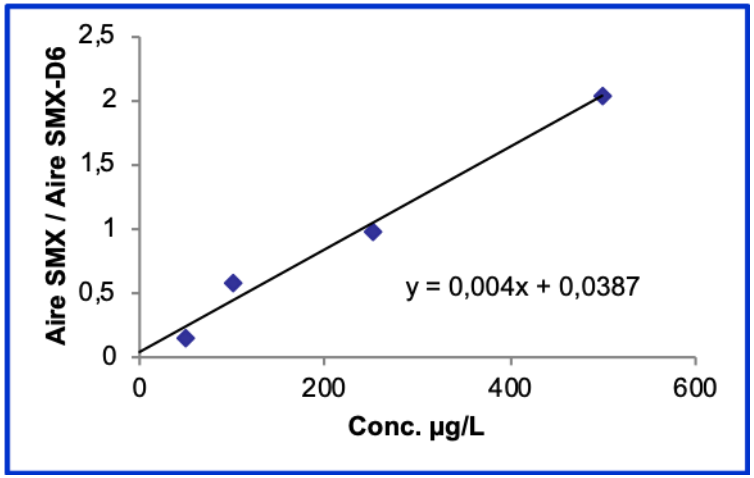
- SPE-LC-MS/MS:

  Addition of labelled surrogate in calibration standards

  Addition of labelled surrogate in samples before SPE extraction

SMX: Q transition 254-92: A = 612941
q transition 254-108: A = 464349
R = 612941/464349 = 1,32

SMX-D6: Q transition 260-98: A = 576196
q transition 260-114: A = 489725
R = 576196 / 489725 = 1,18



Precision

- **Precision**: closeness of agreement between indications or measured quantity values obtained by replicate measurements on the same or similar objects under specified conditions
  - repeatability condition (intra-serie): same measurement procedure, same operators, same measuring system, same operating conditions and same location, and replicate measurements on the same or similar objects over a short period of time.
  - intermediate precision condition (inter-serie): same measurement procedure, same location, and replicate measurements on the same or similar objects over an extended period of time, but may include other conditions involving changes.
  - reproducibility condition: includes different locations, operators, measuring systems, and replicate measurements on the same or similar objects.
- **Precision determination:**
  - repeatability: n measurements of same sample :

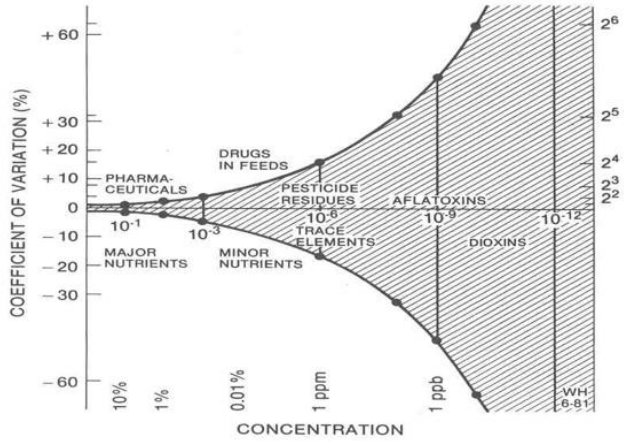
$$\text{RSD (\%)} = \frac{standard\ deviation}{mean} \times 100$$

  - Intermediate precision: n mesurements, k series:
    - X, mean of k means and sem: standard deviation of k means: $\text{RSD (\%)} = \frac{100\ x\ sem}{X}$
    - $\text{RSD (\%)} = \frac{\sqrt{s^2_{intra} + s^2_f}}{X}$ $\qquad s^2_f = sem^2 - s^2_{intra}/n$

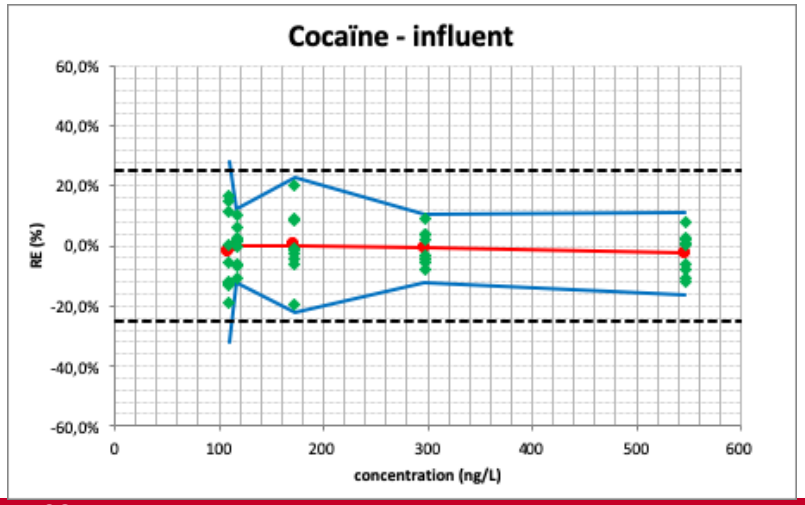
Full validation

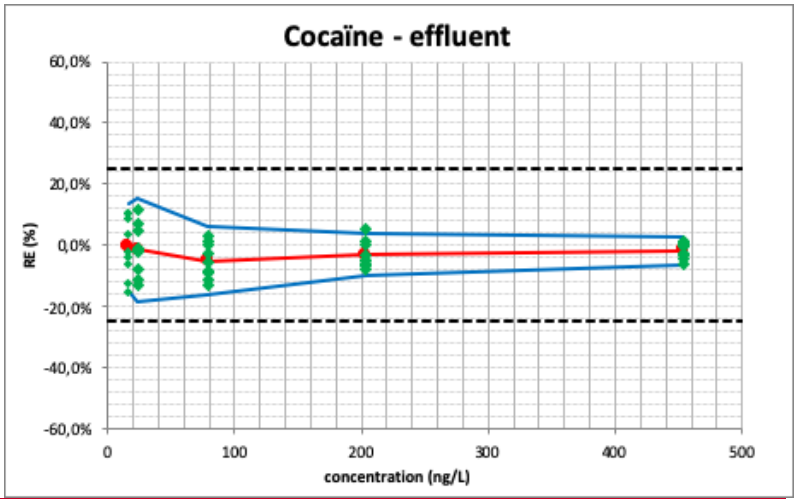
- validation for each analyte and each matrix
- matrix with non-constant composition
  - revised criterion for each measurement series

  → LOD & LOQ
- no specification



- accuracy profile





High Resolution Mass Spectrometry (HRMS)

Conventional MS (i.e. Tandem MS) -> quantification of contaminants traces BUT limited number of analytes

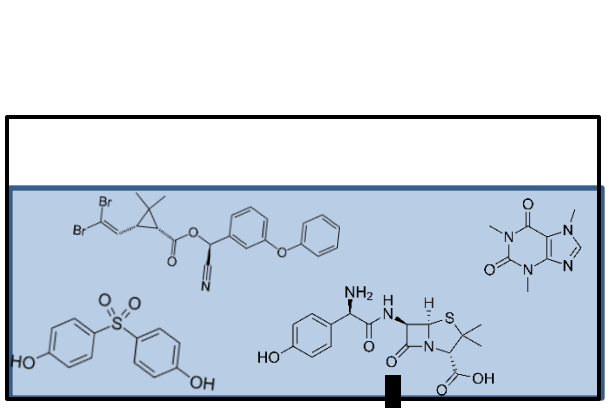
Problem : >100 000 chemical entities exist

→ Conventional MS is not always adapted

(many unknwon molecules in samples)

High Resolution Mass Spectrometry (HRMS)

HRMS : search for unknown molecules in samples

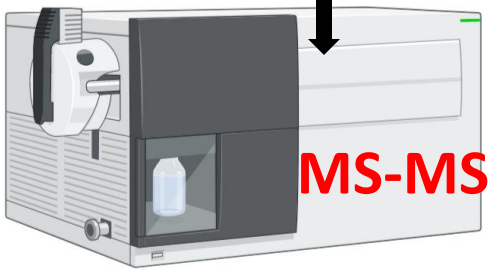


Analysis of all chemical entities

HRMS

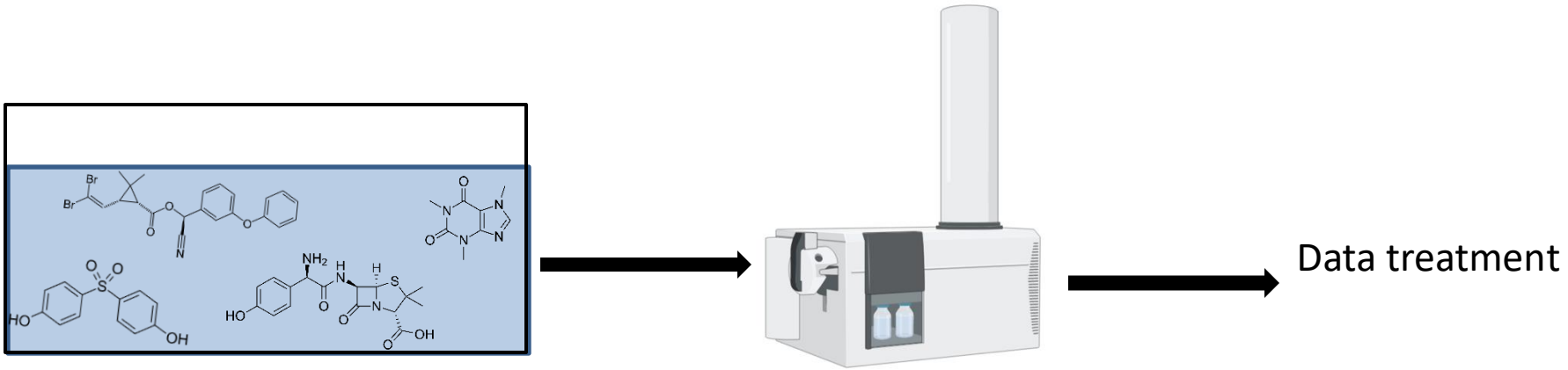
Data treatment

Caffeine quantification



MS-MS

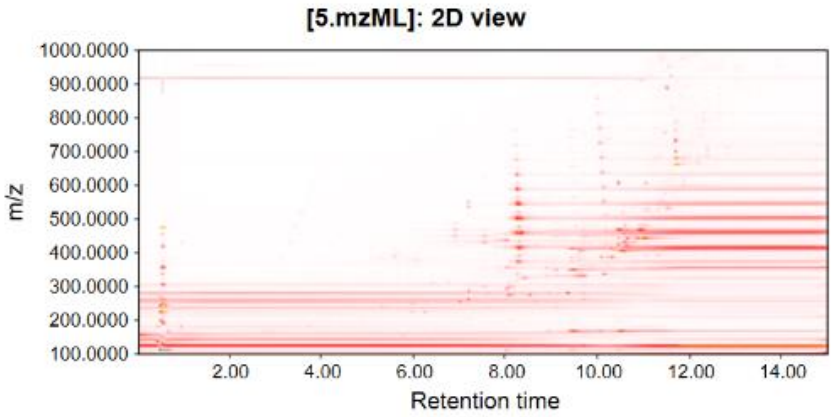
High Resolution Mass Spectrometry (HRMS)



Analysis of the « exact mass » of al chemical entities in the sample

- ✓ High resolution = mass is measured with an accuracy of 4 decimal places
- ✓ Caféine : m/z = 195.0877

High Resolution Mass Spectrometry (HRMS)



Hundreds of masses measured: How do you associate a structure with a mass?

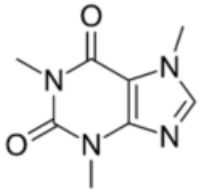
-> Several “tools” are used

High Resolution Mass Spectrometry (HRMS)

Hundreds of masses measured: How do you associate a structure with a mass?

1) Exact mass :

m/z = 195.0877 =

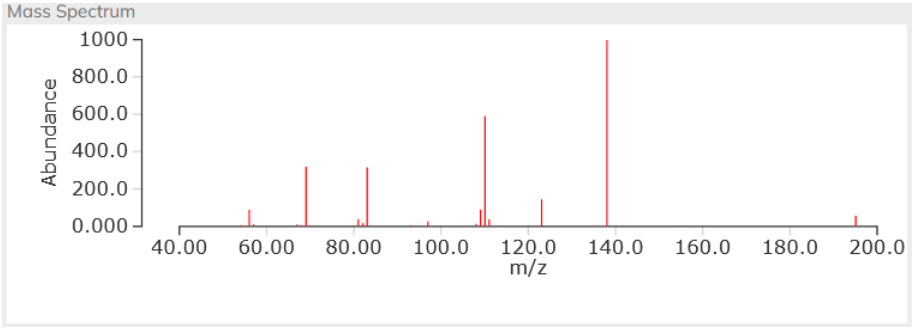


ou $C_5H_{14}ClN_5O$ ou $C_8H_{19}OS_2$ ou $C_3H_{11}ClN_8$

High Resolution Mass Spectrometry (HRMS)

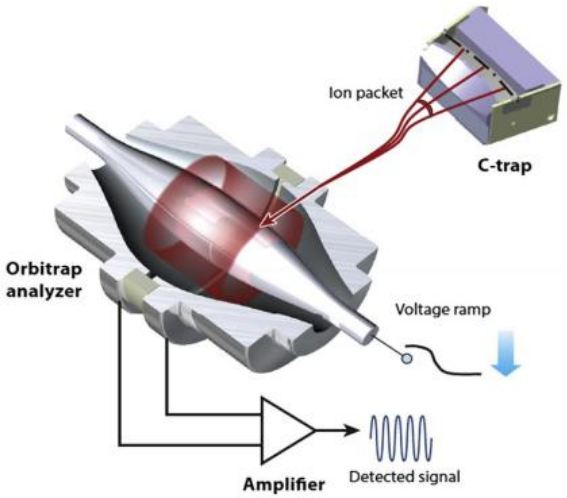
Hundreds of masses measured: How do you associate a structure with a mass?

3) Fragmentation spectra :

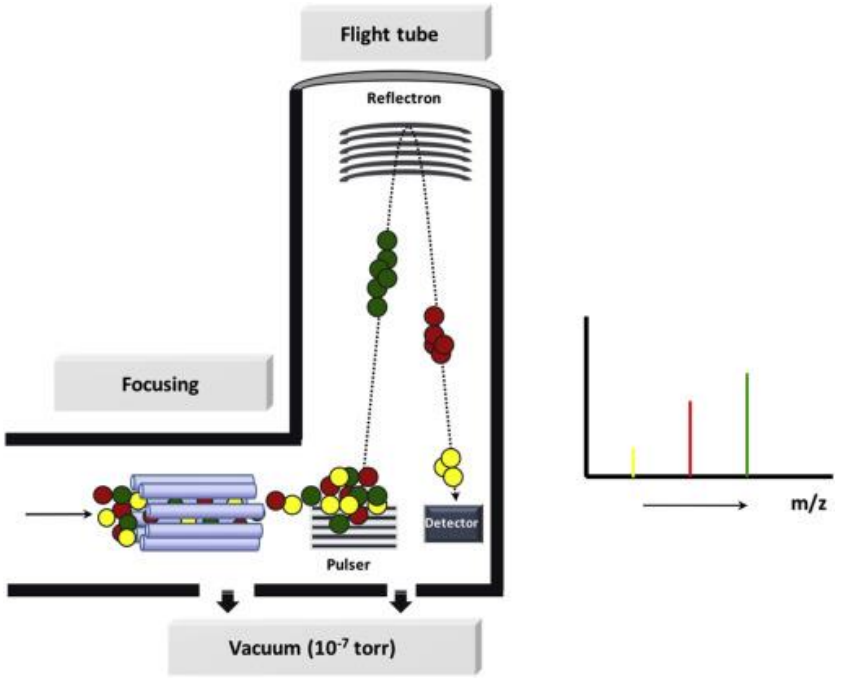


Fragmentation spectra of caffeine

High Resolution Mass Spectrometry (HRMS)



Orbitrap



Time of flight

High Resolution Mass Spectrometry (HRMS)

Table 1. Summary of Prioritization Approaches Used for NTS, with Selected Examples

data-driven	experiment-driven
•frequency, signal intensity of masses[14,33]	•persistence,[34] elimination/formation[29] over process
•component with characteristic isotope pattern (C, Cl, Br, N, O, S)[13,19,35]	•reaction-based search of transformation products to link masses before and after treatment[30]
•part of homologue series (mass difference, Kendrick mass defect)[13,36,37]	•biological,[28] electrochemical,[38] oxidative[32] transformation product formation
•suspect screening (looking for "known" or predicted chemicals without standard)[39,40]	•reaction with isotopically labeled reagents[31]
•specific functional groups (MS/MS, derivatization, neutral loss)[41,42]	•effect-directed selection of masses in toxic fractions[43,44]
•temporal or spatial profile over several samples[24,33]	

Halogenated contaminants

Oxides

Suspect screening

Degradation and WWTP epuration

Effect Directed Analysis

Hollender, Schymanski, Singer, Ferguson, Nontarget Screening with High Resolution Mass Spectrometry in the Environment: Ready to Go? *Environ. Sci. Technol.* 2017.