

Etude du métabolisme : intérêts et limitations de la métabolomique et de la lipidomique.

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IR Inserm, Directrice plateforme MetaToul

24 juin 2026



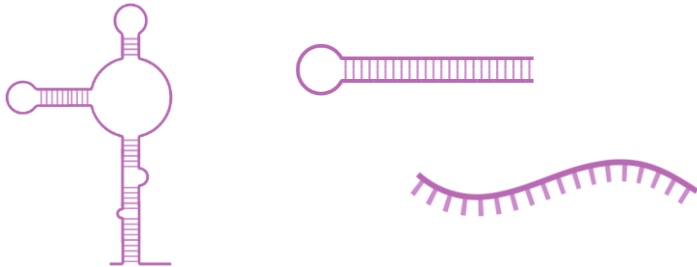
**ACADÉMIE
D'AGRICULTURE
DE FRANCE**

OMIC cascade

❖ Biomolecules



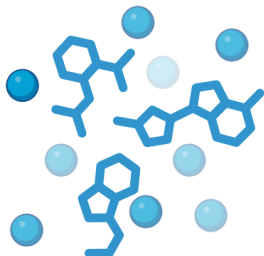
DNA



RNA



Proteins



Metabolites

*Molecules
< 1 500Da*

❖ Analysis

Genome → GENOMICS



Transcriptome → TRANSCRIPTOMICS



Proteome → PROTEOMICS



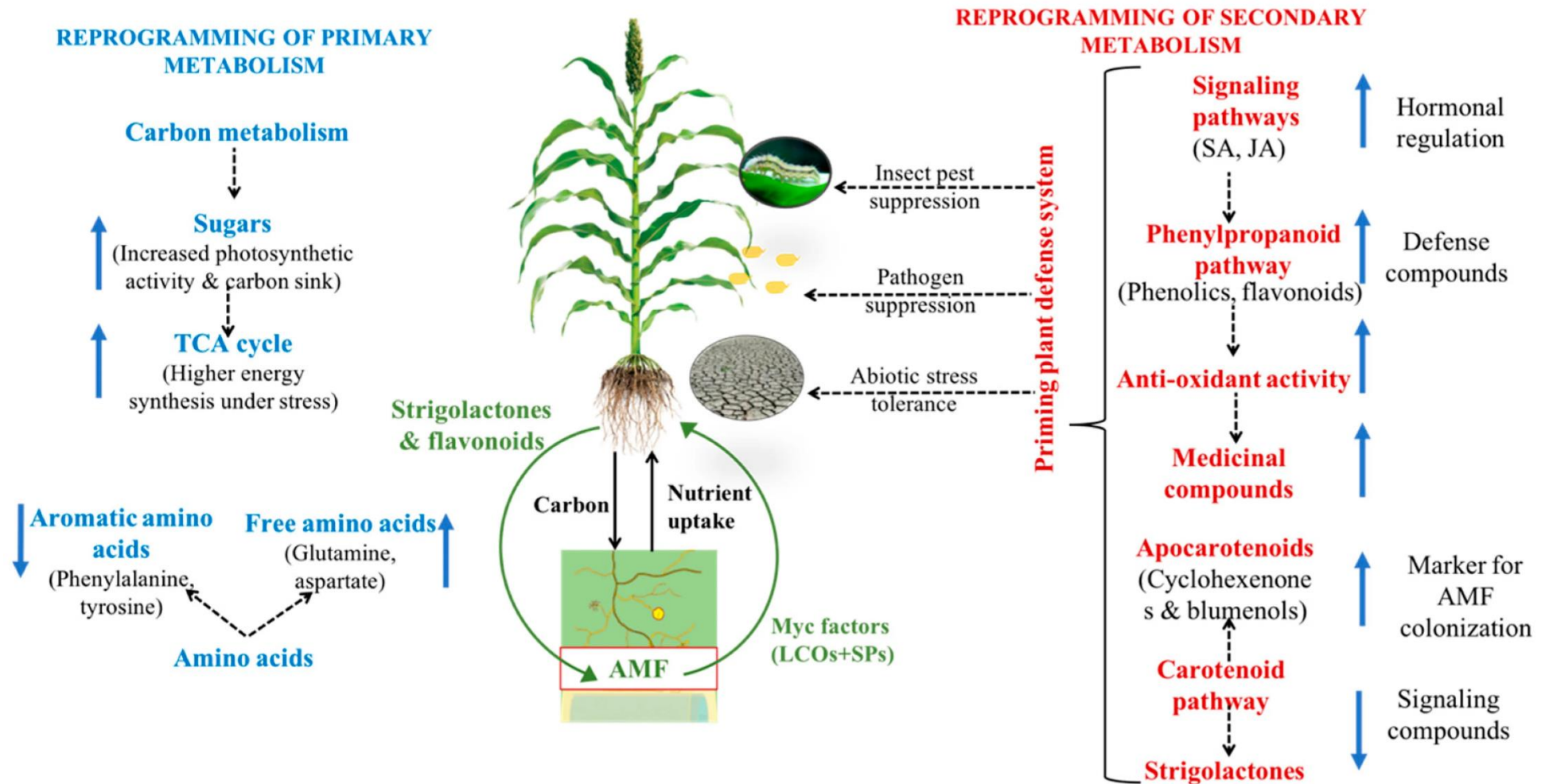
Metabolome → METABOLOMICS



PHENOTYPE

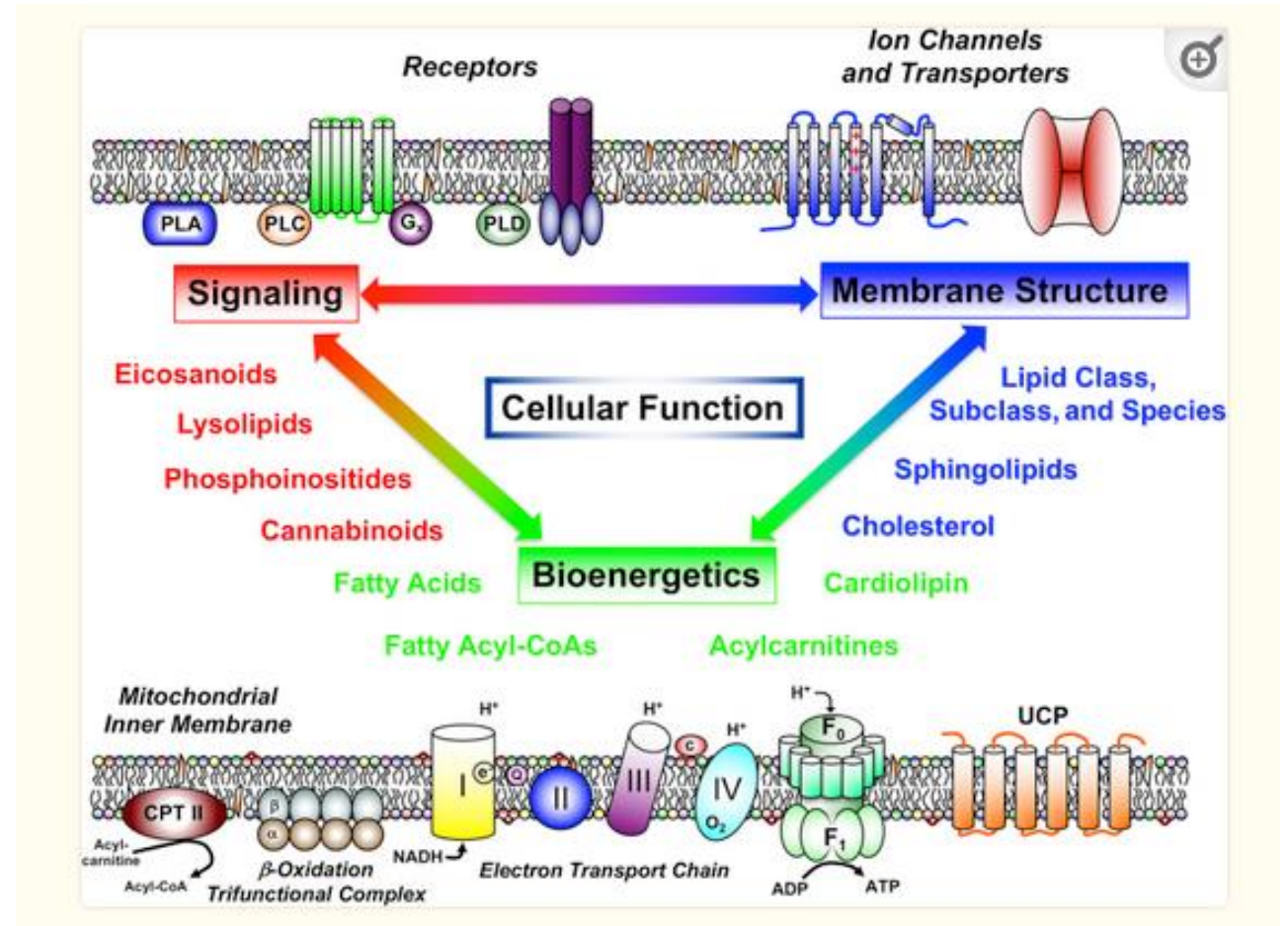
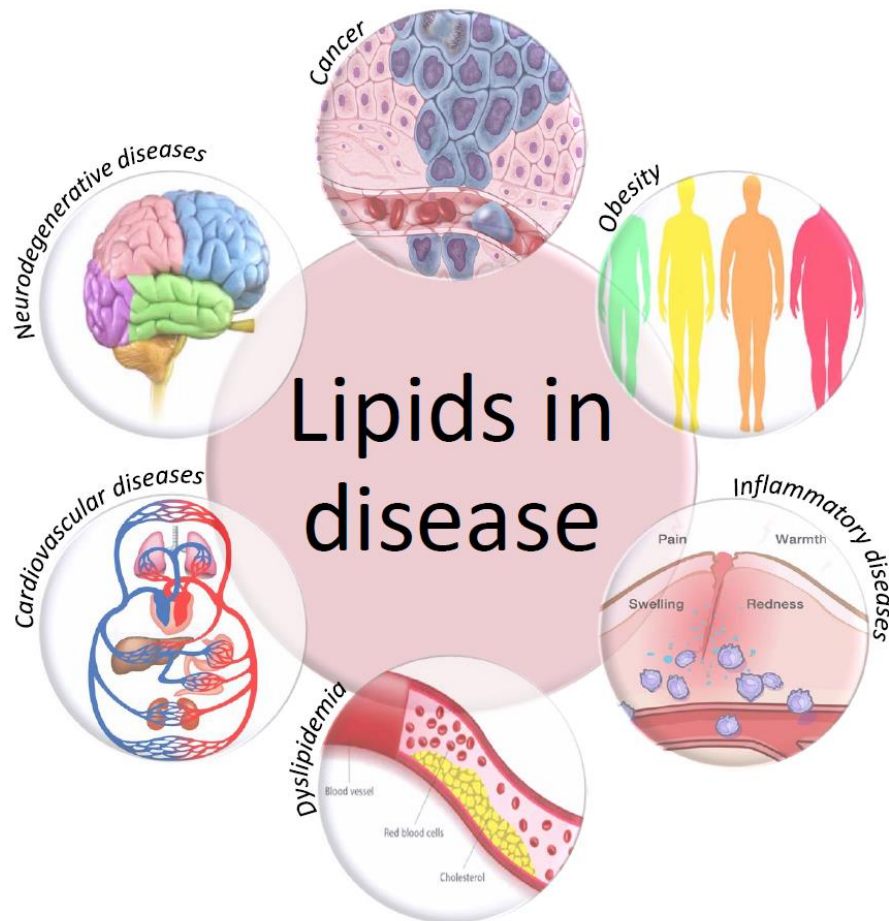
Metabolome & Physiology

❖ In plants



Metabolome & Physiology

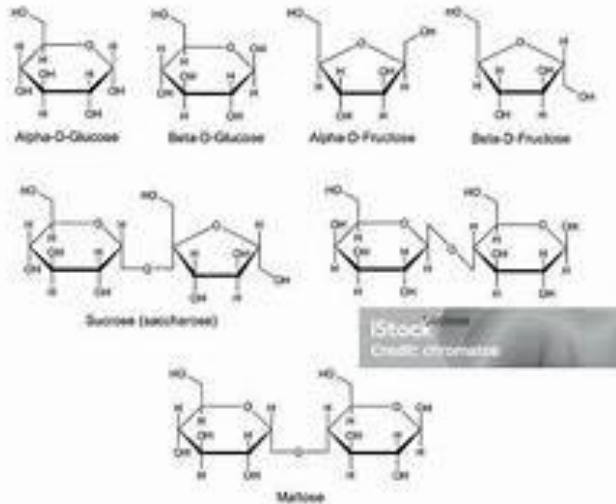
❖ In health



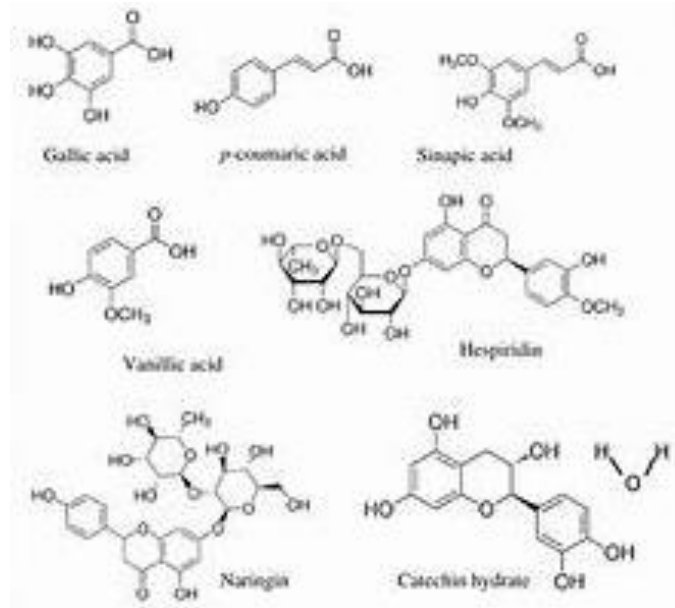
Nature of metabolites?

❖ Polar metabolites = soluble in water

Chemical structures of main sugars

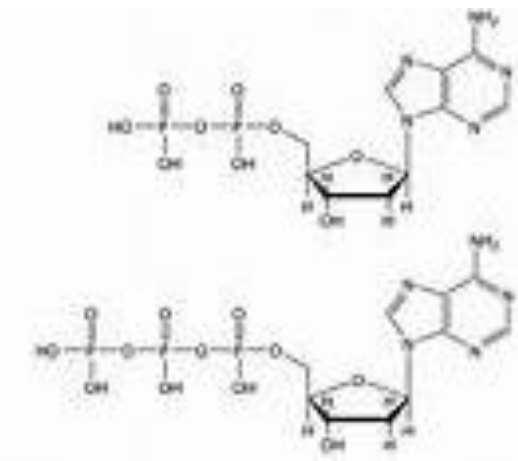
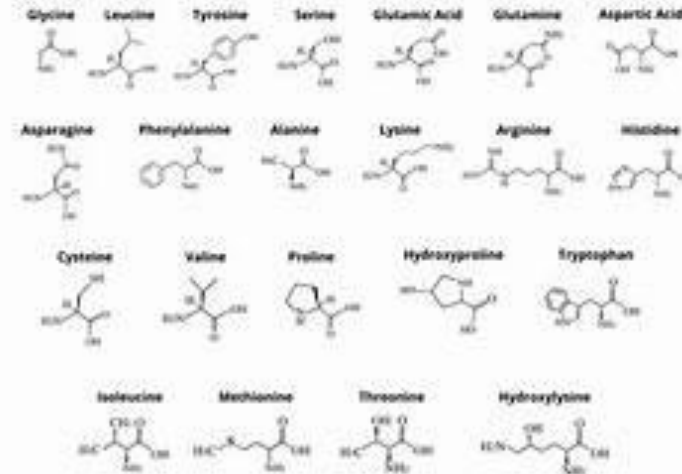


Sugar



Organic acid

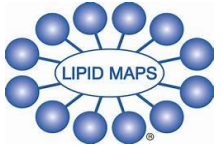
Amino Acids



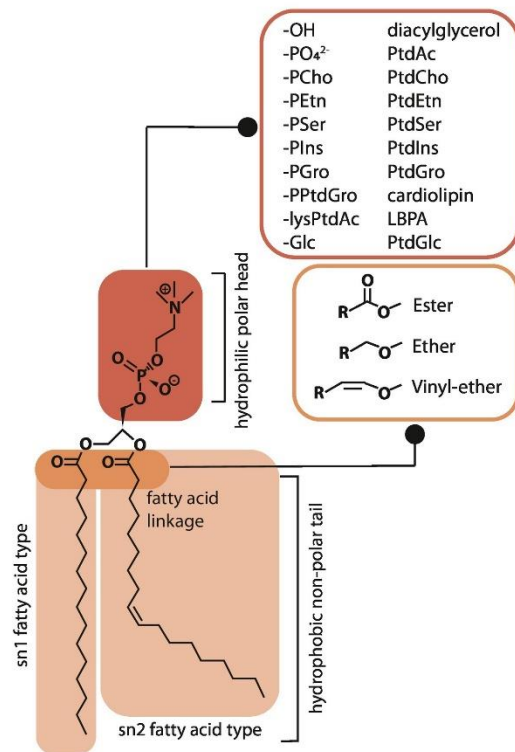
Phosphorilated nucleoside

Nature of metabolites?

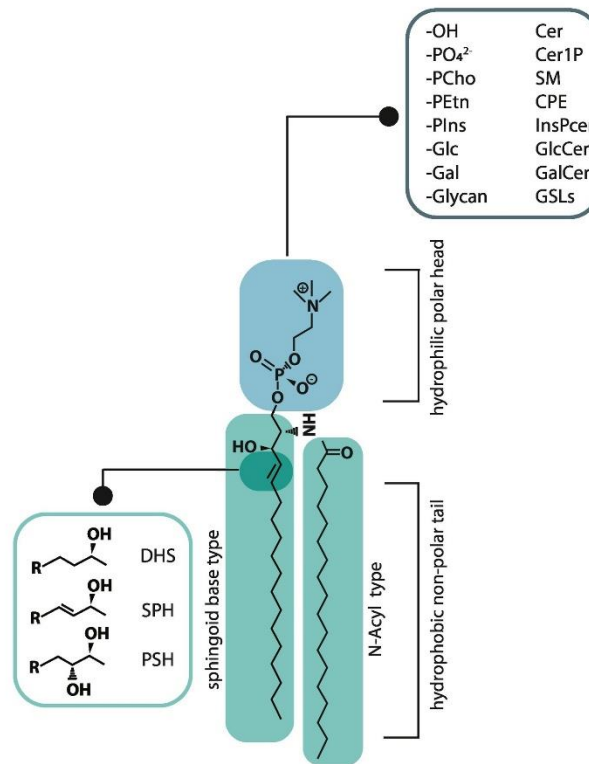
❖ Apolar metabolites = lipids = soluble in organic solvent



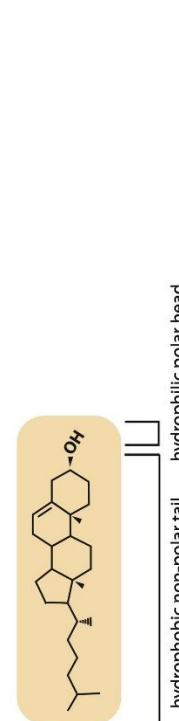
(A) Glycerolipids



(B) Sphingolipids



(C) Sterols



Trends in Cell Biology

Lipid Category	Curated	Computationally-generated	All
Fatty Acyls [FA]	9736	1897	11633
Glycerolipids [GL]	411	7378	7789
Glycerophospholipids [GP]	2308	8297	10605
Sphingolipids [SP]	1844	3168	5012
Sterol Lipids [ST]	4055	0	4055
Prenol Lipids [PR]	2627	0	2627
Saccharolipids [SL]	57	1294	1351
Polyketides [PK]	7205	0	7205
TOTAL	28243	22034	50277

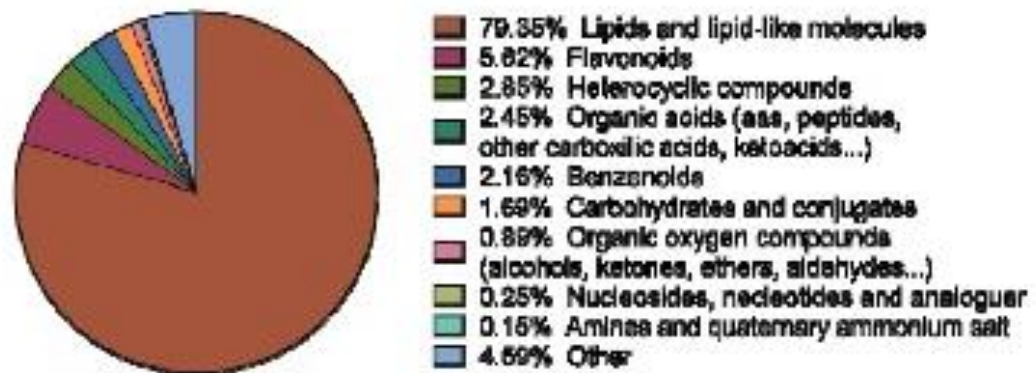
Number of structures per lipid category



Diversity of metabolites

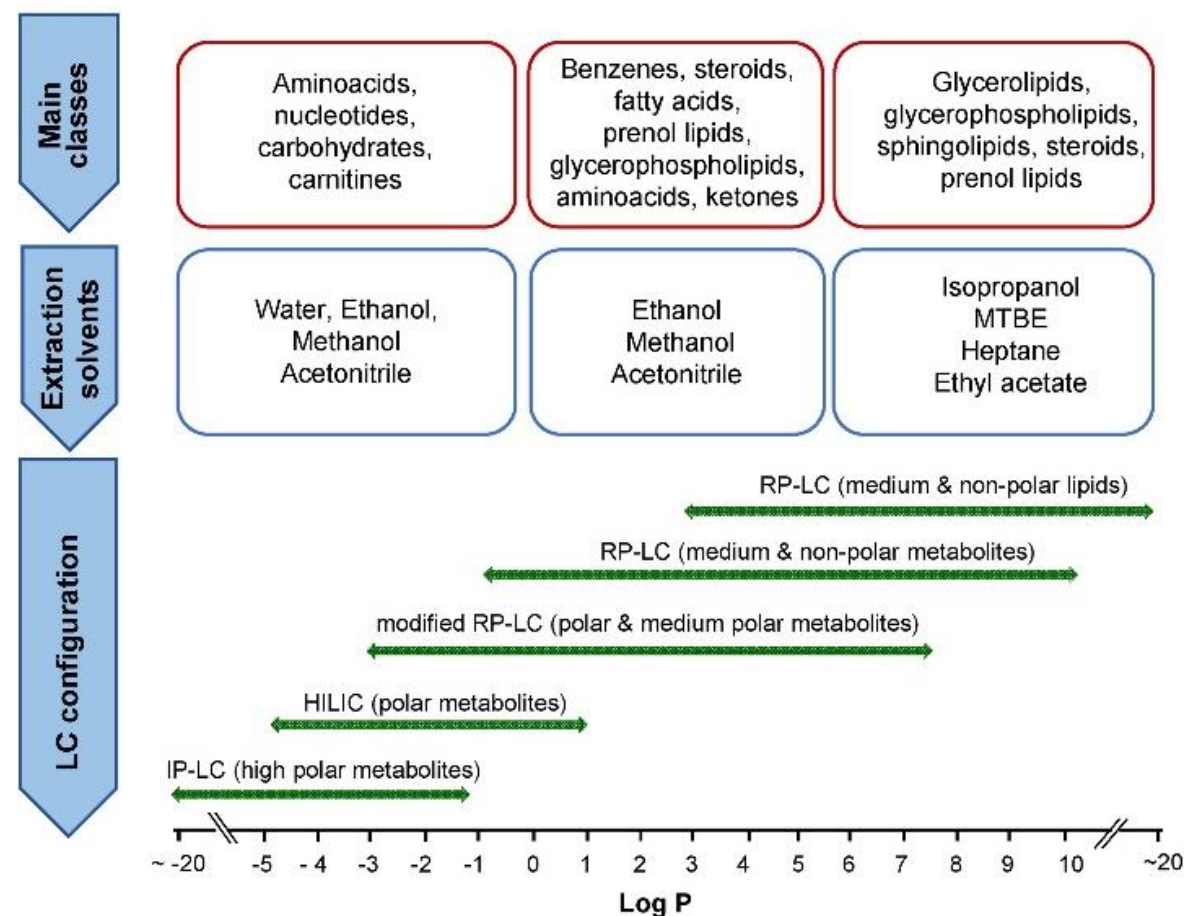
❖ High diversity of structures

Expected human metabolome
~ 118000 COMPOUNDS



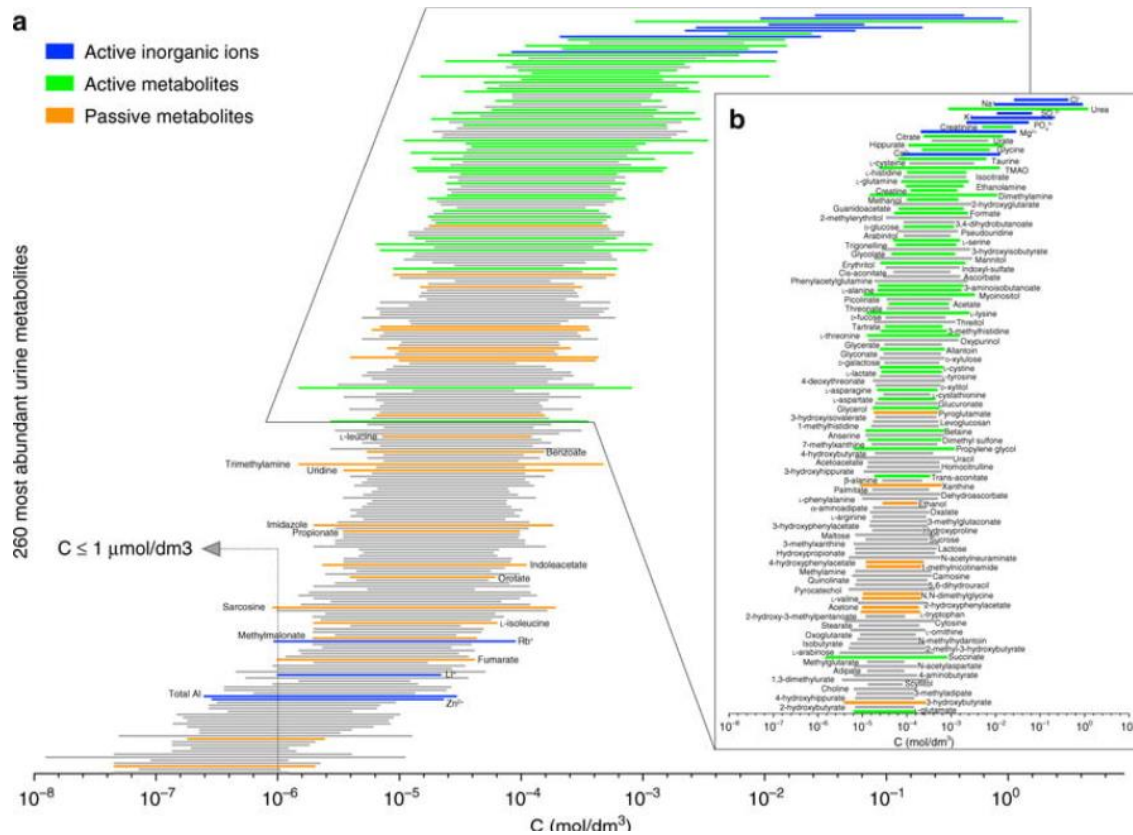
✓ Taxonomic classification (HMDB and KEGG)

❖ Large physical properties



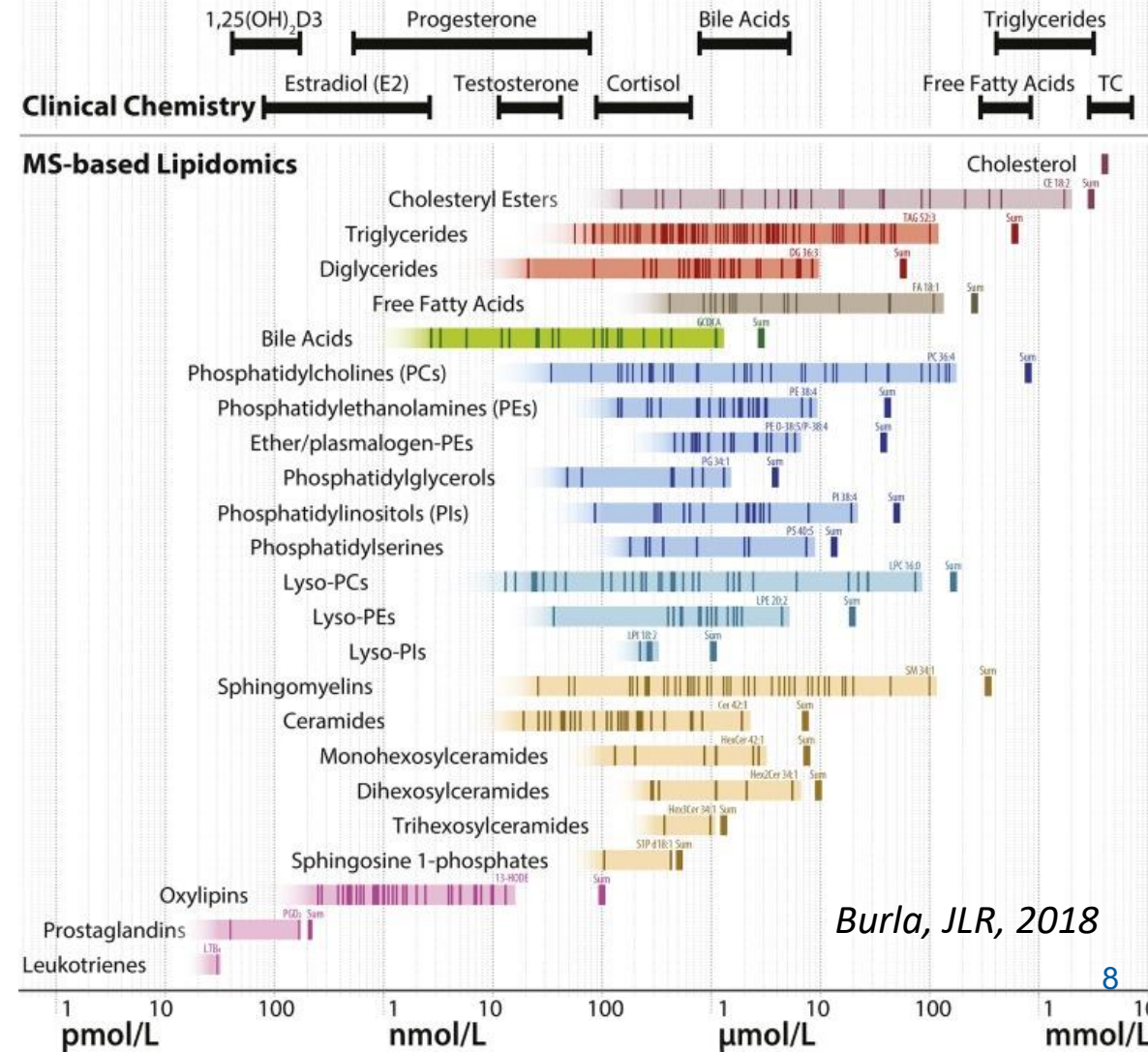
Large gamme of concentration

❖ Metabolites in human urine



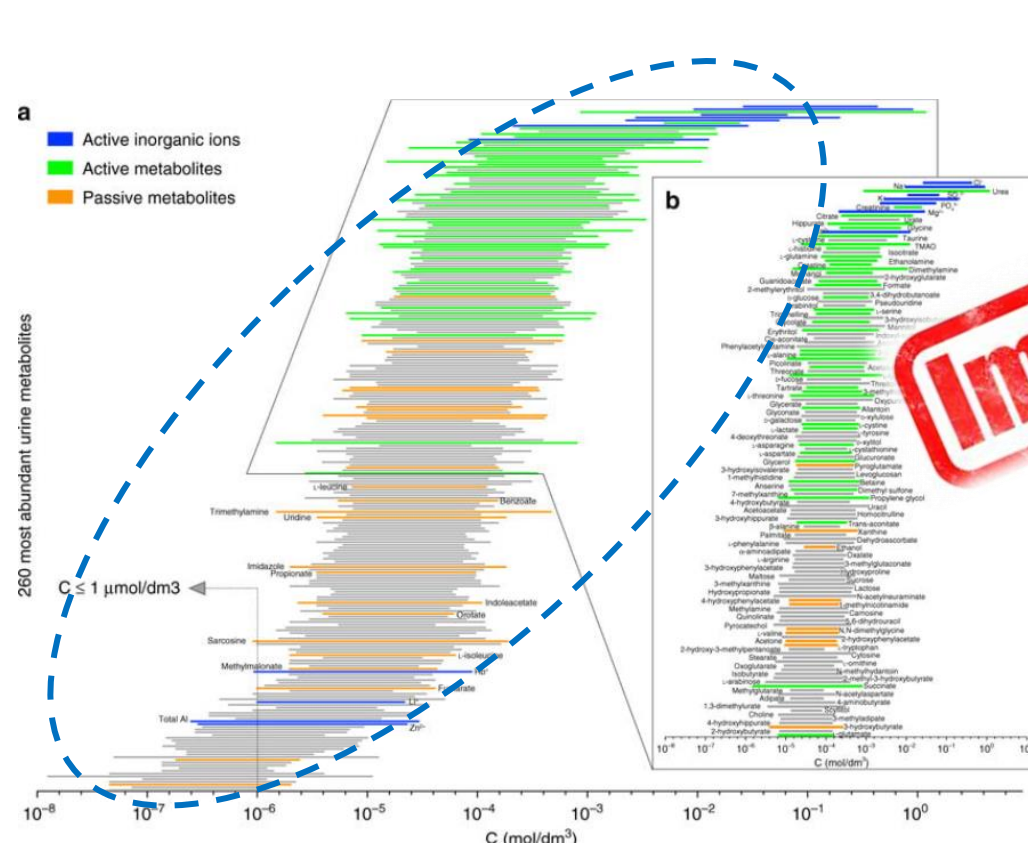
Takis, Nature, 2027

❖ Lipids in human plasma

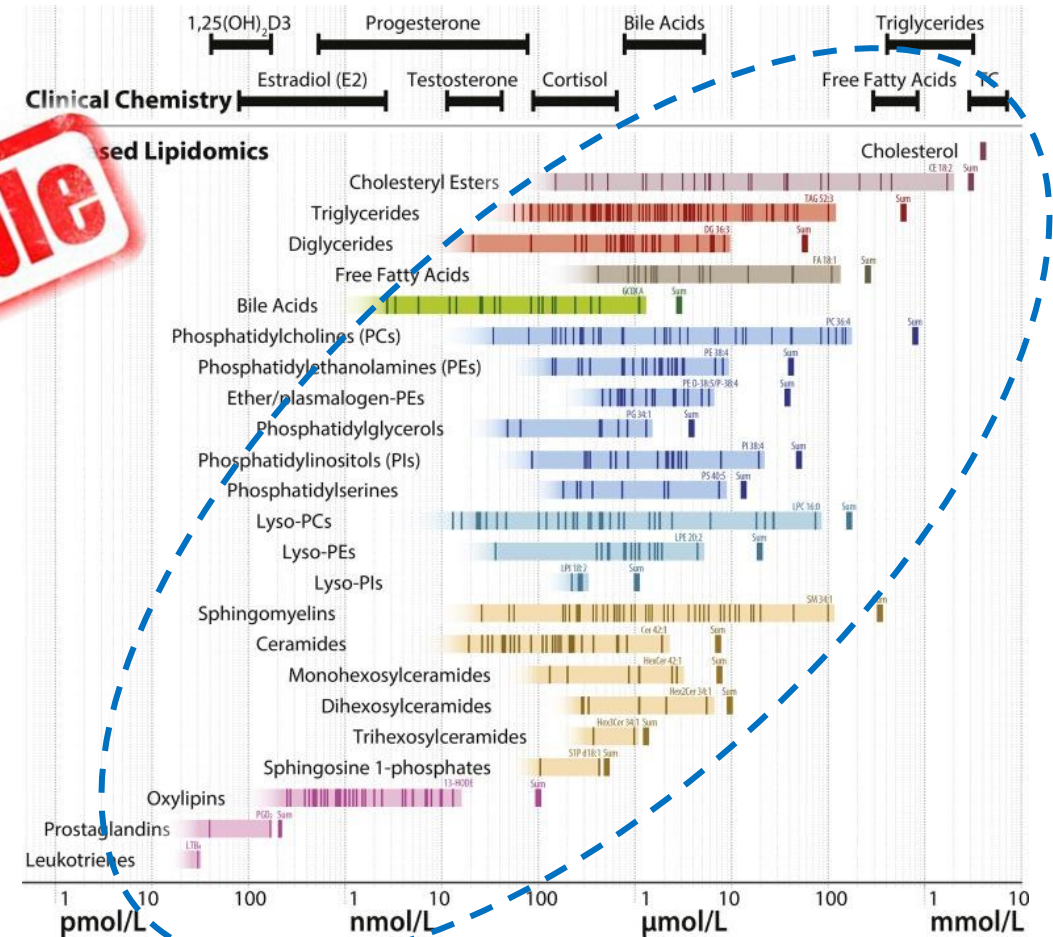


Which approaches in metabolomic?

❖ Analyse a complete metabolome/lipidome ?



Takis, Nature, 2027

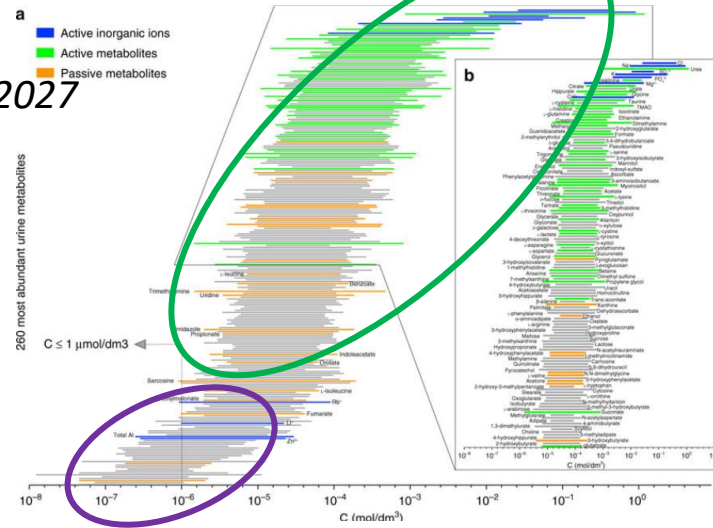


Burla, JLR, 2018

Untargeted & targeted metabolomic

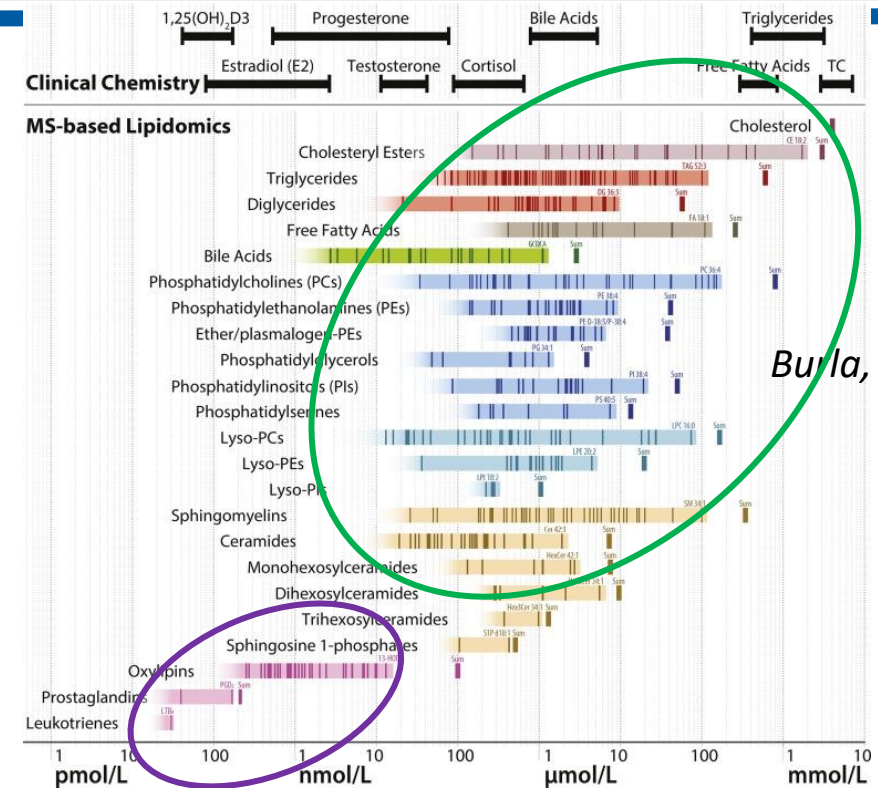
❖ Analyse a complet metabolom/lipidome ?

Takis, Nature, 2027



✓ Untargeted method

- No apriori
- Statistic → discriminant metabolite → annotation
- Most abundant metabolites
- Relative quantification



Buila, JLR, 2018

✓ Targeted method

- Target a metabolite/sub-family
- Lowest abundant metabolites
- Absolute quantification

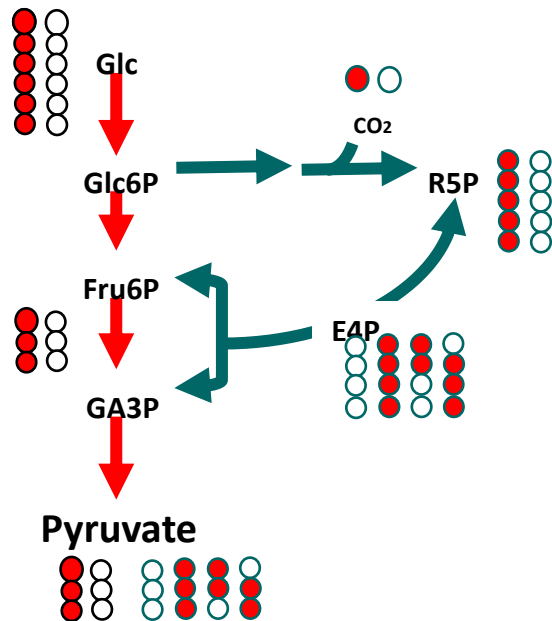


Static situation!

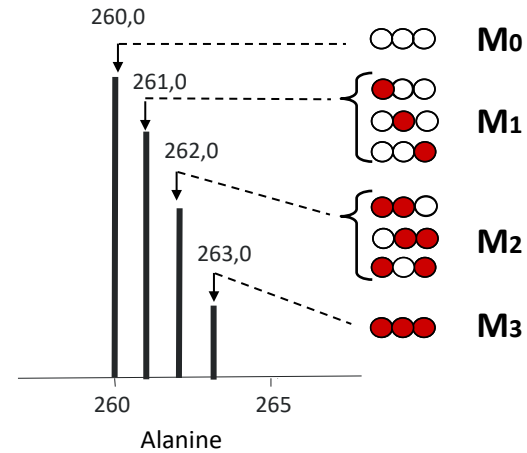


Explore dynamic of metabolism

❖ Tracing and fluxomic



MS: mass isotopomers (isotopic cluster)

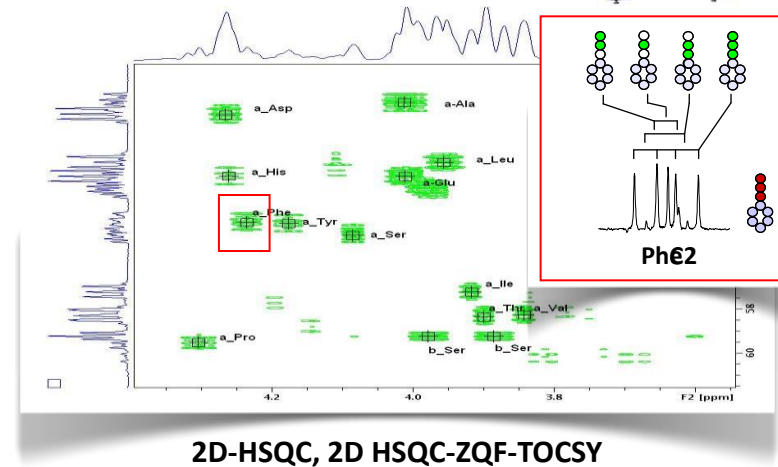
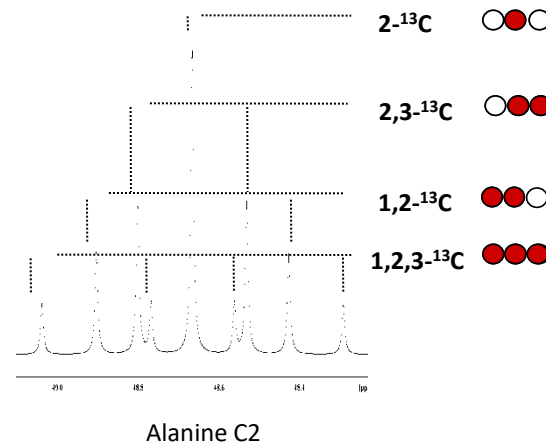


GC-MS
Proteinogenic AA



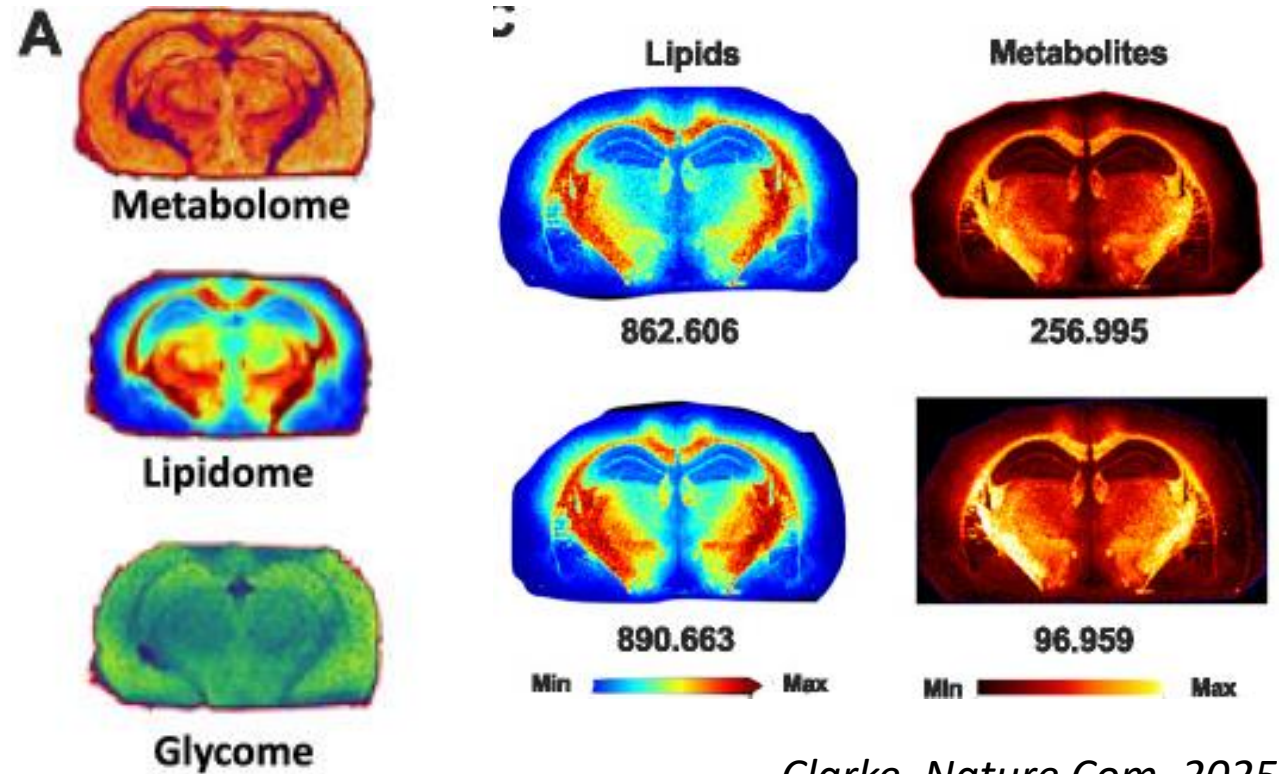
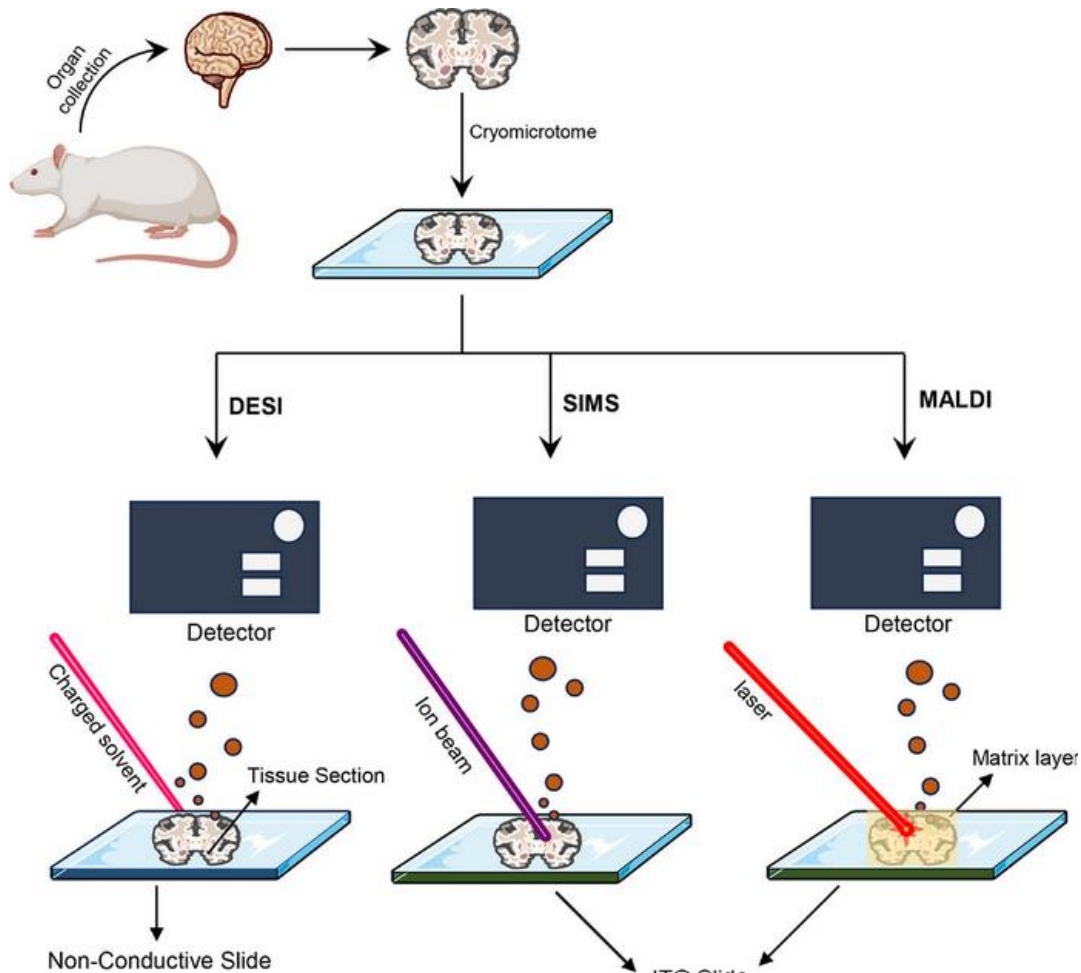
LC-MS
Intracellular metabolites
Extracellular metabolites

NMR: Positional isotopomers (J_{CC} couplings)



Spatial metabolomics

❖ Mass spectrometry Imaging



Clarke, Nature Com, 2025

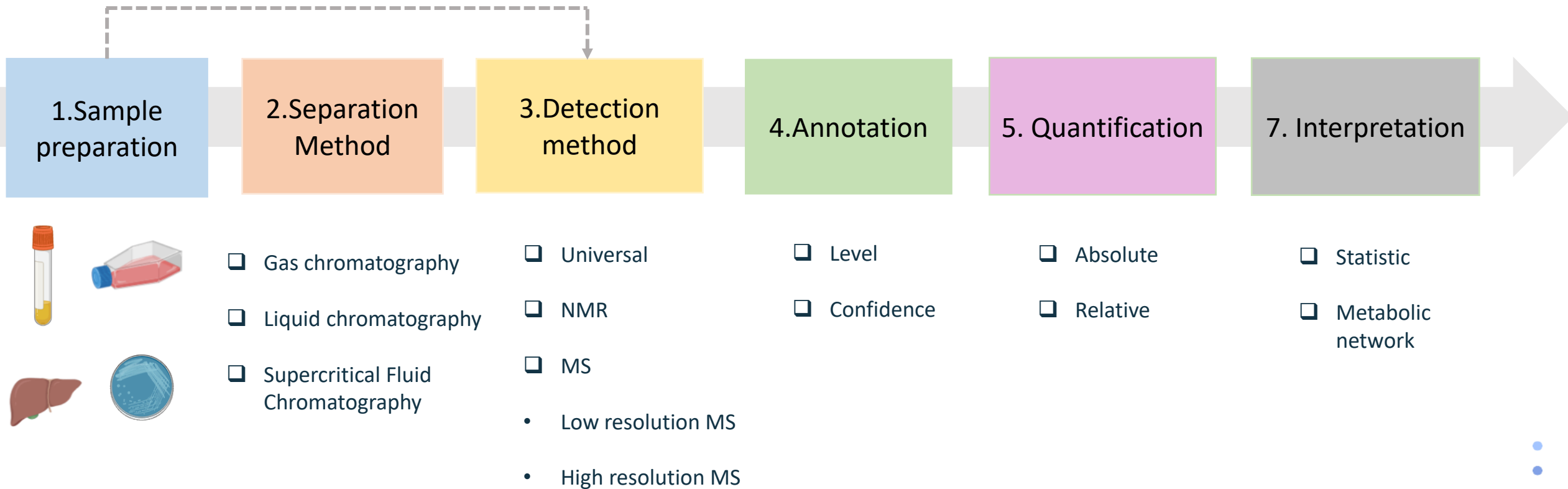
- Localize a metabolite in a tissue
- Spatial resolution 5-20 μ m

Aarika, J Science S, 2025



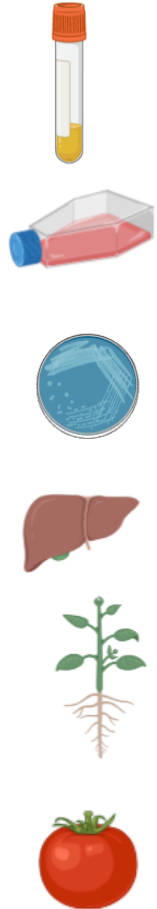
The lipidomic workflow

❖ Metabolomic work flow



Sample preparation

Echantillons



Quenching

- Filtration rapide
- Ajout de solvants Froids
- ...

Normalisation

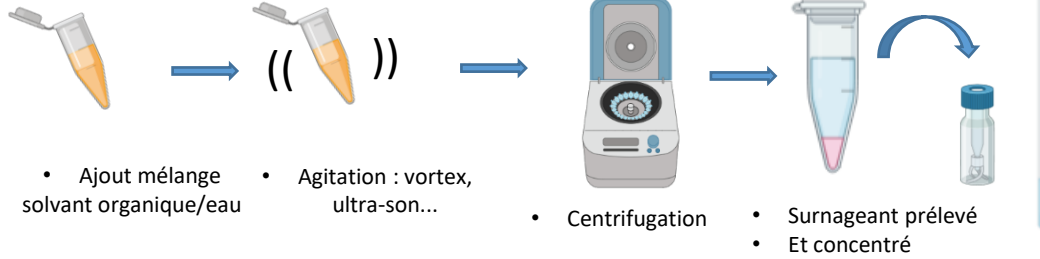
- Volume
- Mg de tissus
- Mg de protéine
- Quantité d'ADN
- Nombre de cellules
- DO...

Broyage

- Broyage en solution
- Broyage à froid
- ...

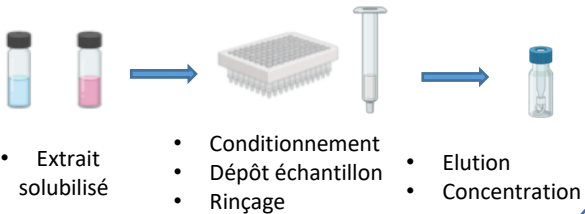


Précipitation des protéines

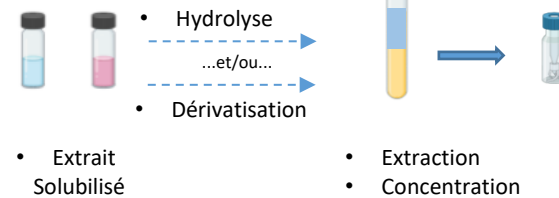


Métabolites
polaires
& lipides

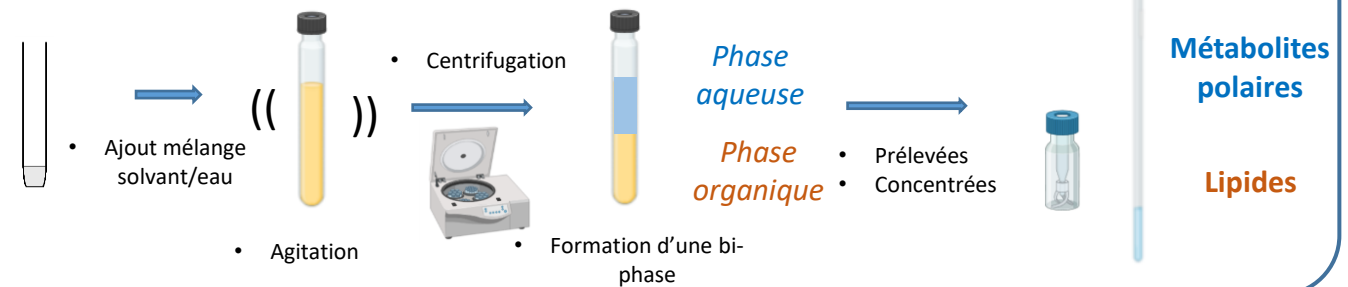
Extraction sur phase solide



Modification chimique

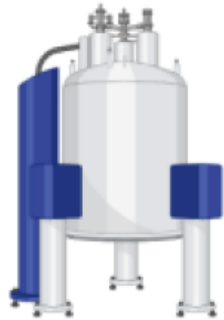


Extraction liquide-liquide



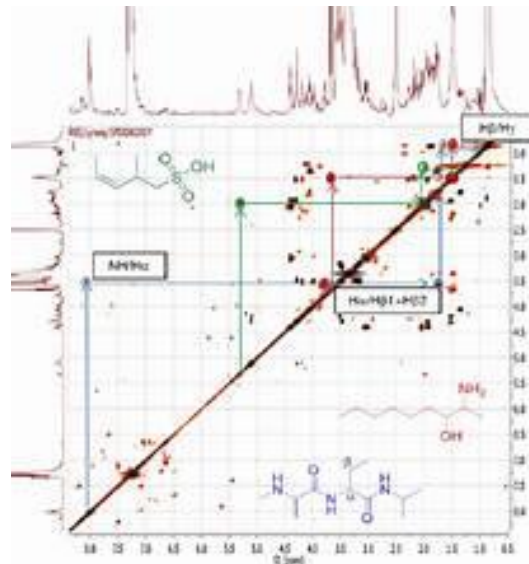
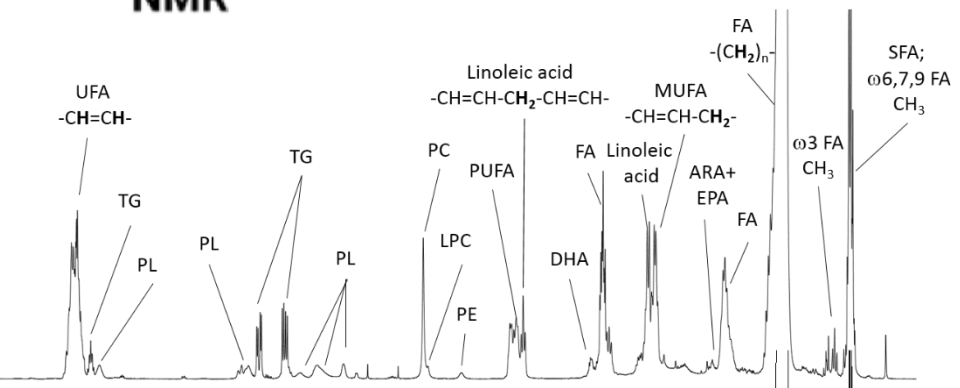
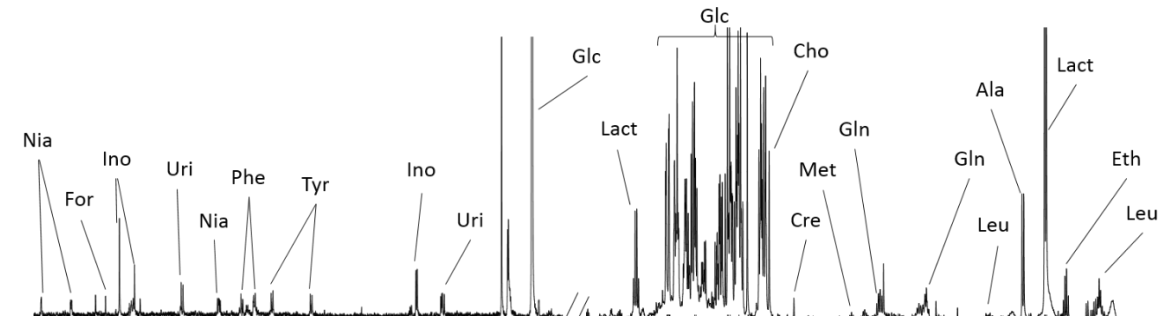
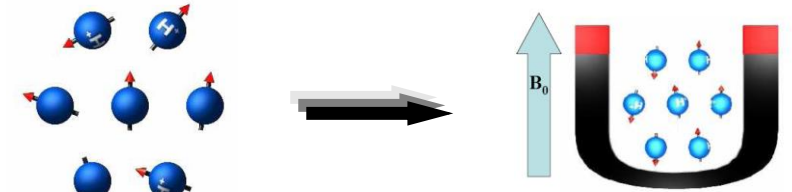
Techniques & instrument in metabolomic

❖ Nuclear Magnetic Resonance



NMR

- Atom with non-zero nuclear spin: ^1H , ^{13}C , ^{31}P , ^{14}N , ^{17}O ...
- Orientation in a magnetic field depending on the molecular environment



- Quantitative
- High throughput
- Non destructive
- Good reproducibility
- Signal overlap
- Lack of sensitivity

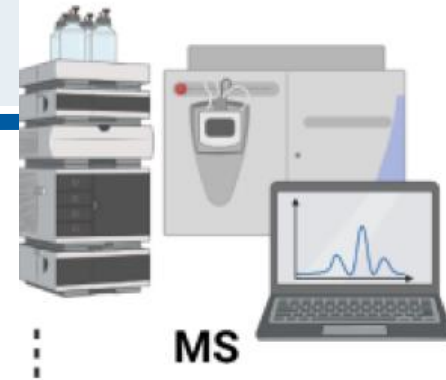
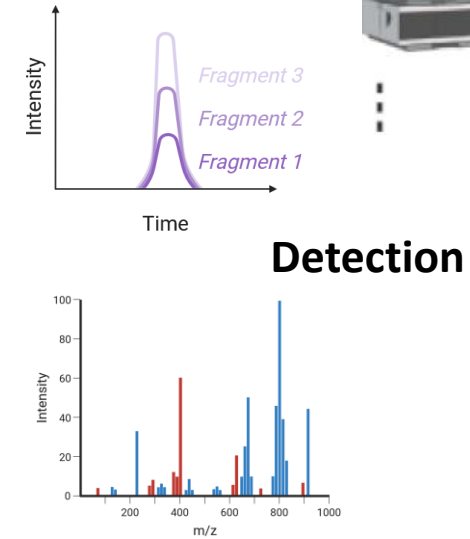
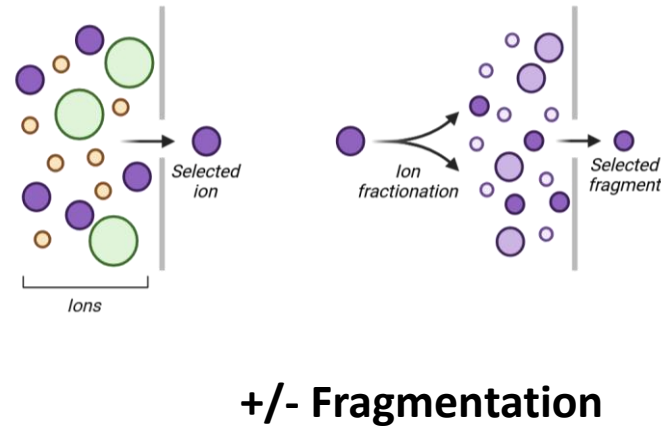
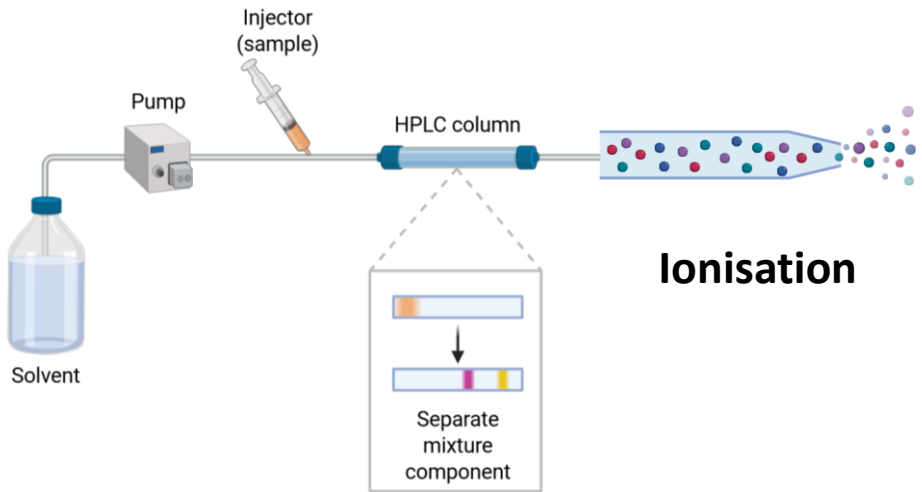
Amiel, Metabolites, 2019

Macyntir, 2014



Techniques & instrument in metabolomic

❖ Mass spectrometry



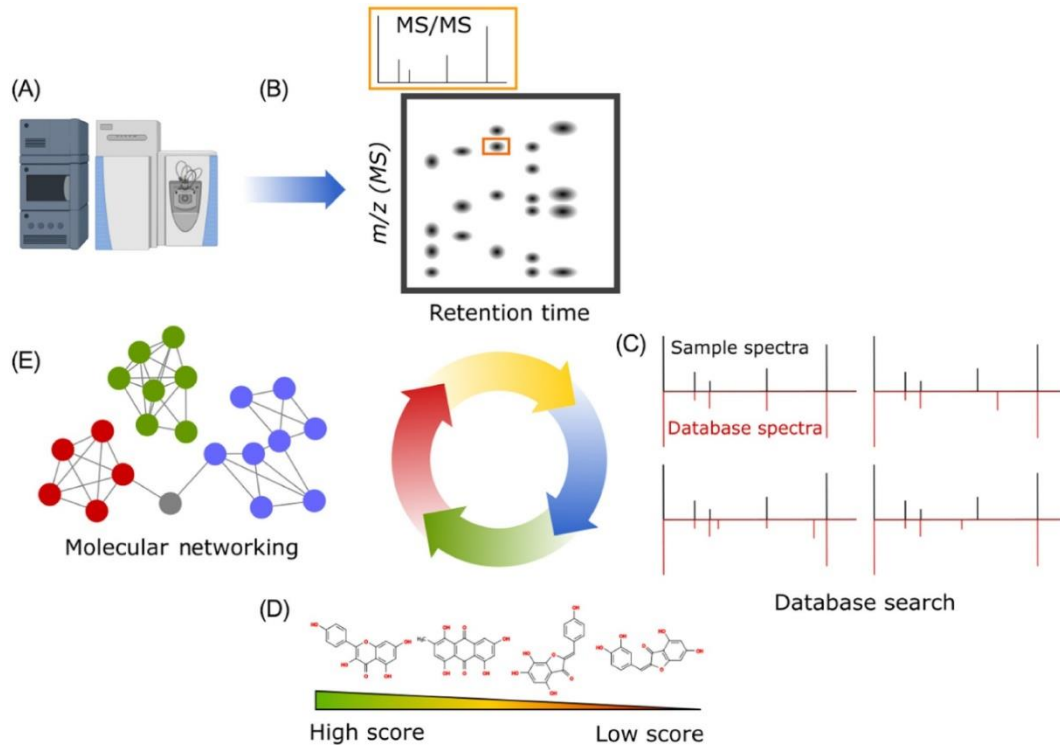
Chromatographic separation
(Liquid, Gaz, Supercritical fluid)

- **Very sensitive**
- **Can analyse complexe mixture**
- **Various instrument/technical options**
- **Very common**
- **Heavy data processing**
- **No robust**



Annotation & identification

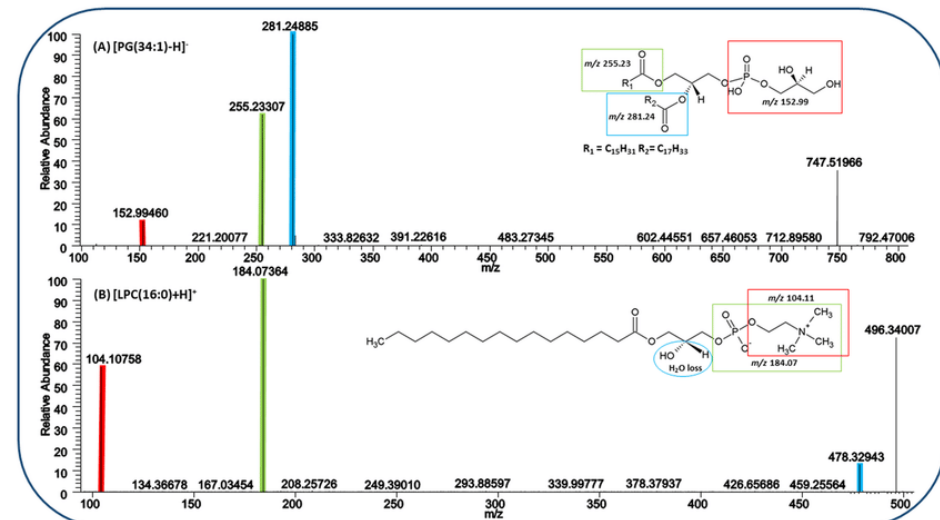
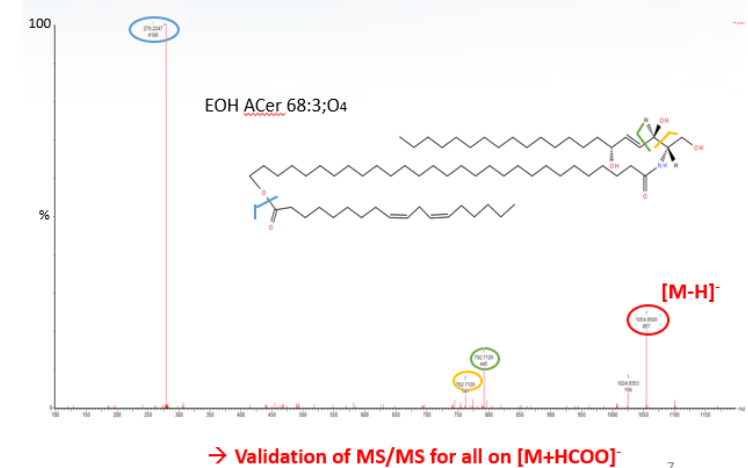
❖ Computational annotation



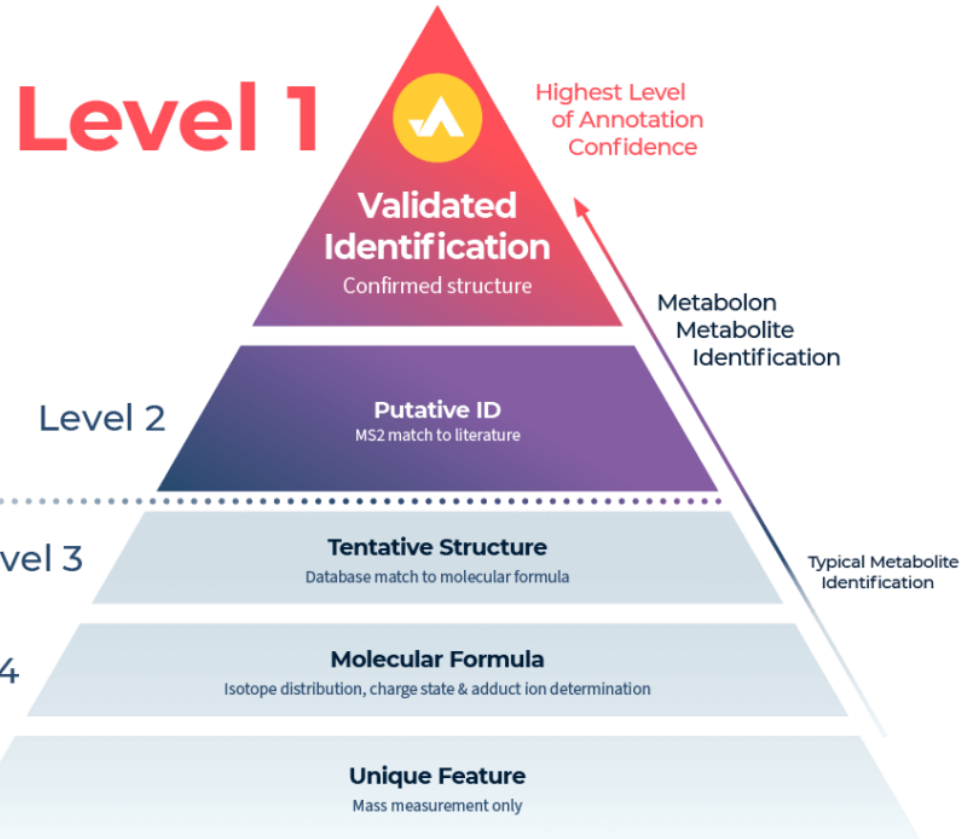
- A lot of software
- Fast...but need to be carefully check

❖ Manual annotation

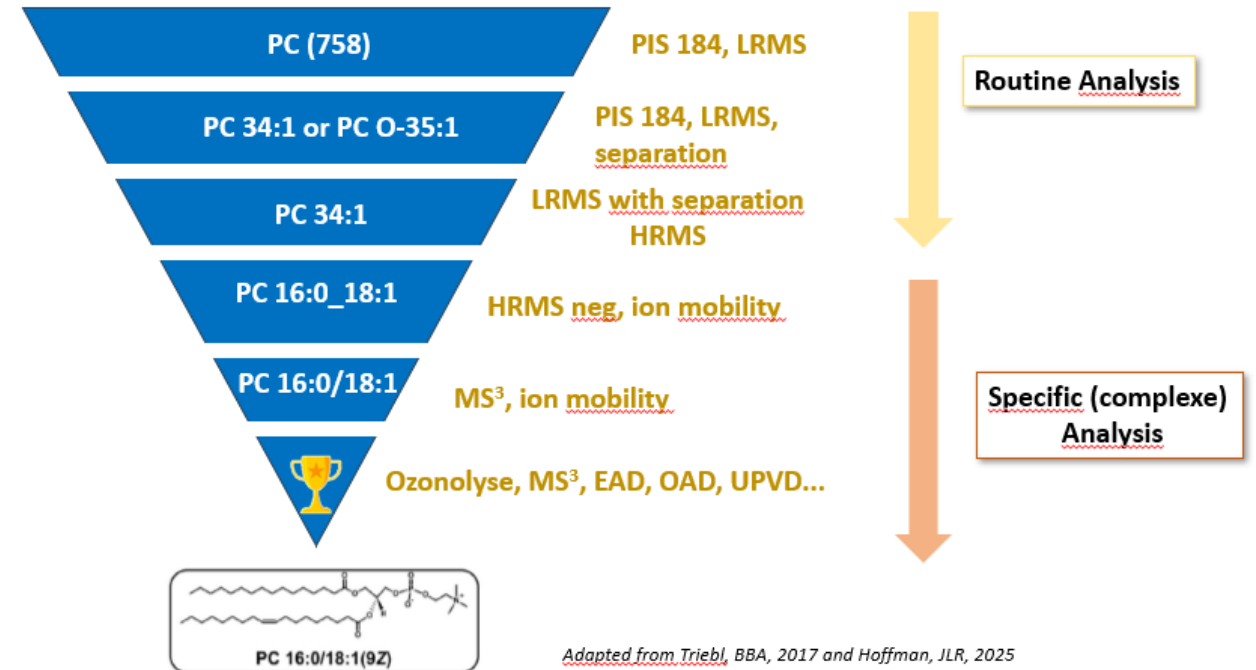
- Time consuming
- Comparison with pure standard
- More confident



Annotation & identification



❖ Level of annotation



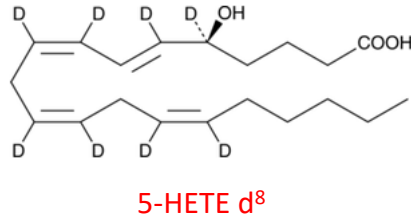
Check them in publications !!



Quantification in MS

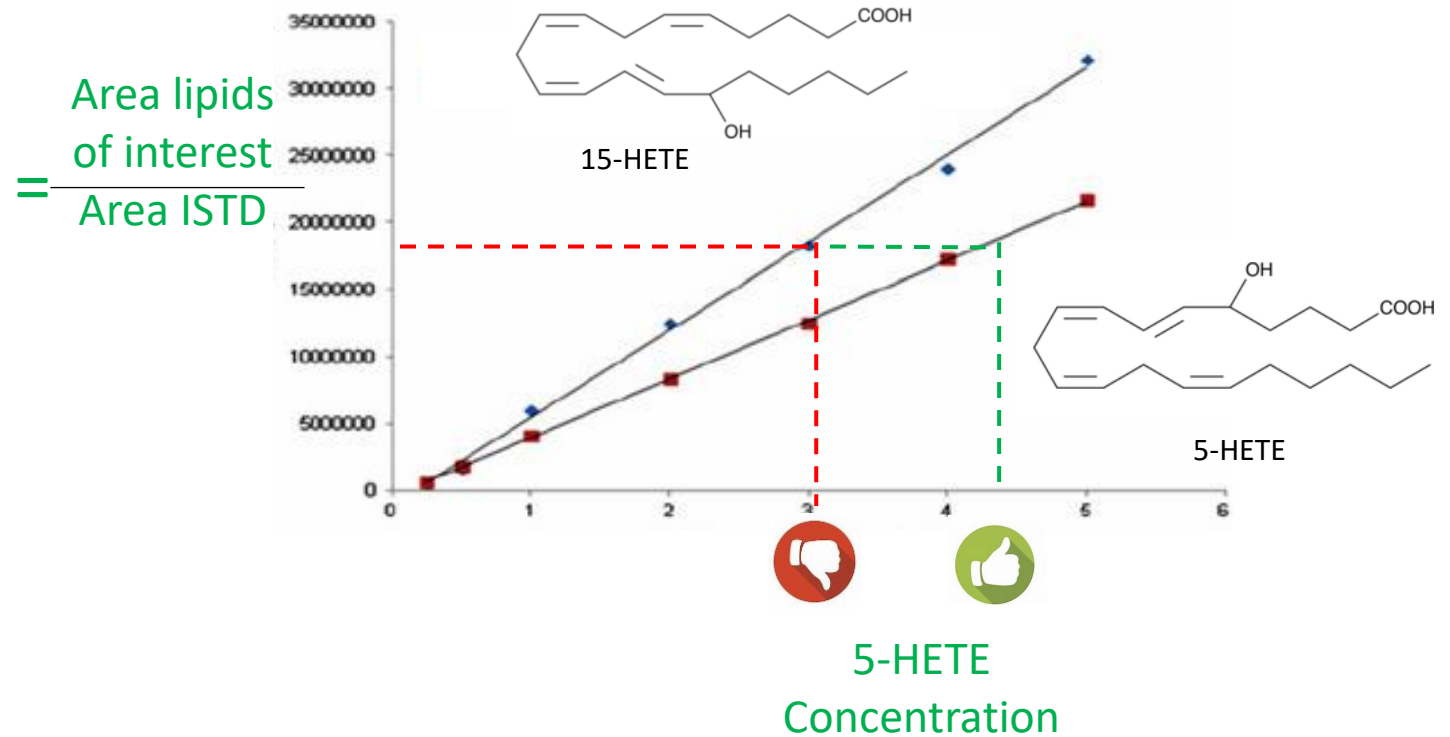
■ Absolute quantification

- The pure metabolite of interest
- A close internal standard
- **Easy with « simple metabolites »**



■ And for complex metabolites/lipids ?

- 1 or more ISTD
- Unavailability of all molecular species
- Prefer « relative or approached » quantities

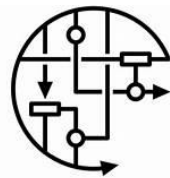


$$= \frac{\text{Area of metabolite}}{\text{Area of internal standard}} \times \text{ISTD extracted quantity}$$

Biological interpretation

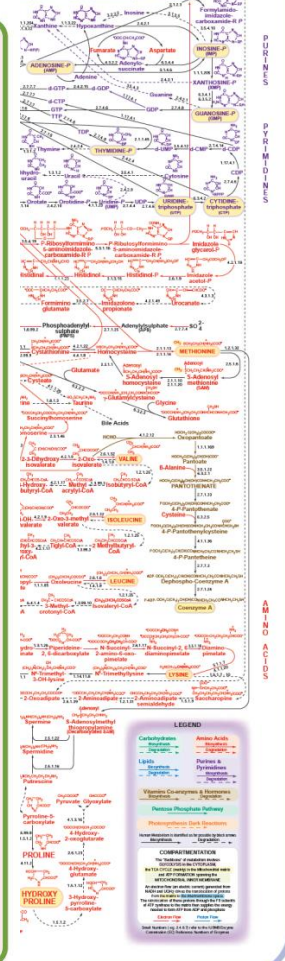
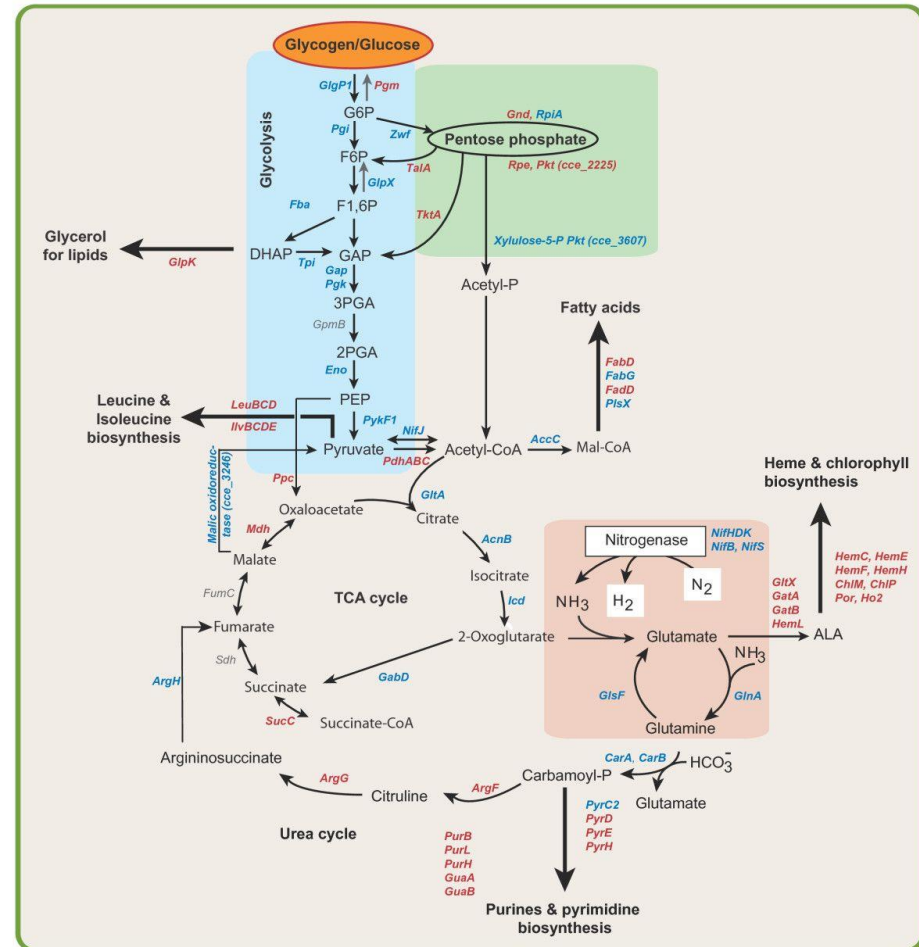
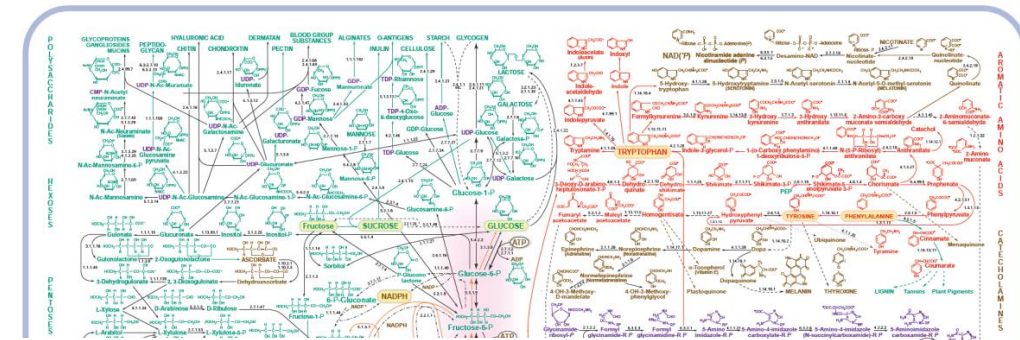
❖ Explore the metabolic network

- Map metabolomic/lipidomic data on a network
- Explore different pathway
- Propose modellisation
- Quality & lack of network

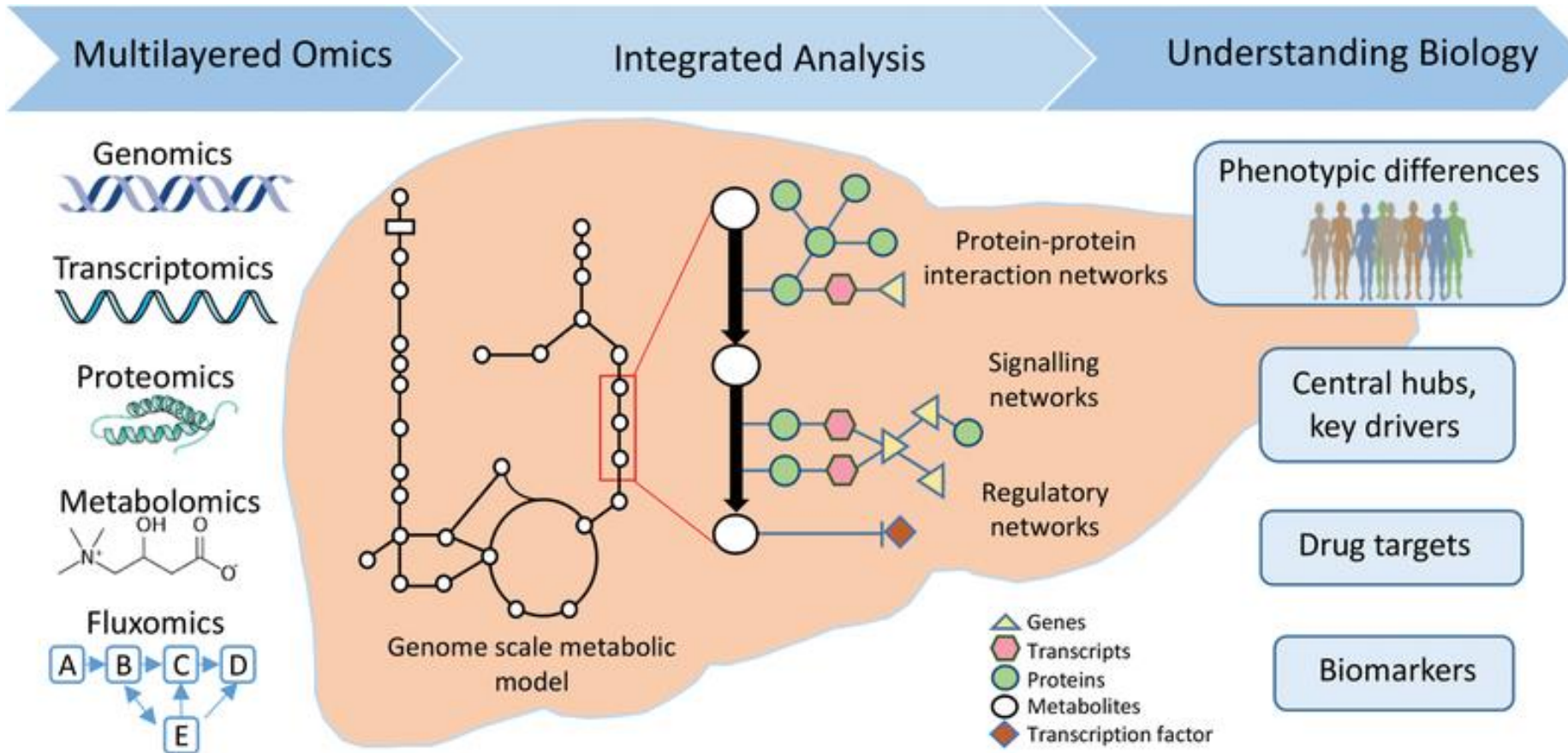


WIKIPATHWAYS
Pathways for the People

Metabolic Pathways



Integrate all OMICS ?



- Different of scale
- How to modelized complexe object
- Specific tools for bio-statistics

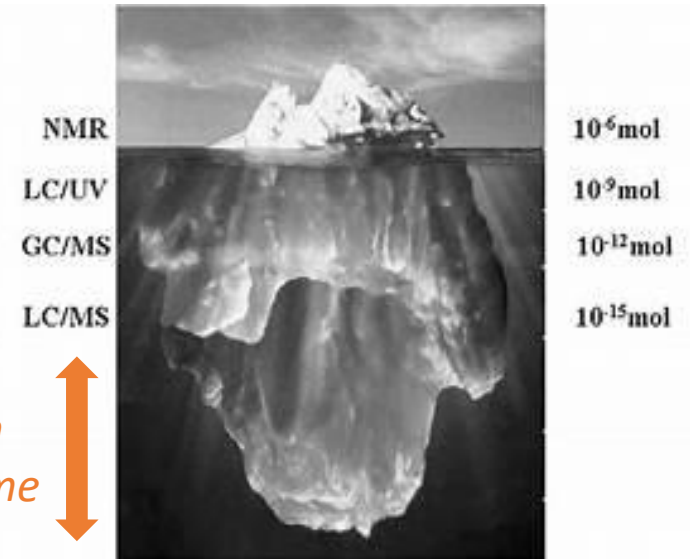
Metabolomic & Lipidomics : interests & limitations



- Powerfull technics
- Large metabolome coverage
- All tissues/fluid, cell... Can be studied
- Great improvement of sensitivity of technics
- « Static », « dynamic » and « spacial» studies
- More and more rapid
- Can be quantitative



*Unknown
metabolome*



- CONS /POS of each technic
- Identification and quantification of metabolite
- Robustness
- Reproducibility : batch effect, instrument/lab reproducibility
- Still a lot of unknown metabolites



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Anaëlle Durbec
Océane Delos
Julia Soullier
Cyrielle Clément
Faustine Vallé
Thibaud Lacroix

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