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The challenge to produce robust data in UHPLC-HRMS/MS based metabolomics for molecular epidemiology studies

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Context : Agricultural activity and cancer



Examples of agricultural tasks associated with exposure to pesticides

Link between occupational exposures and cancers demonstrated in farmers



Pesticides exposure effects?
Other determinants?

- Study cancer biological plausibility, early stages effects, lookout for predictive markers of cancer risks
- Holistic approach of cancers occurrence in farmers population

Utilisation of biobanks samples associated with exposure description and tasks listing for a metabolomic analysis

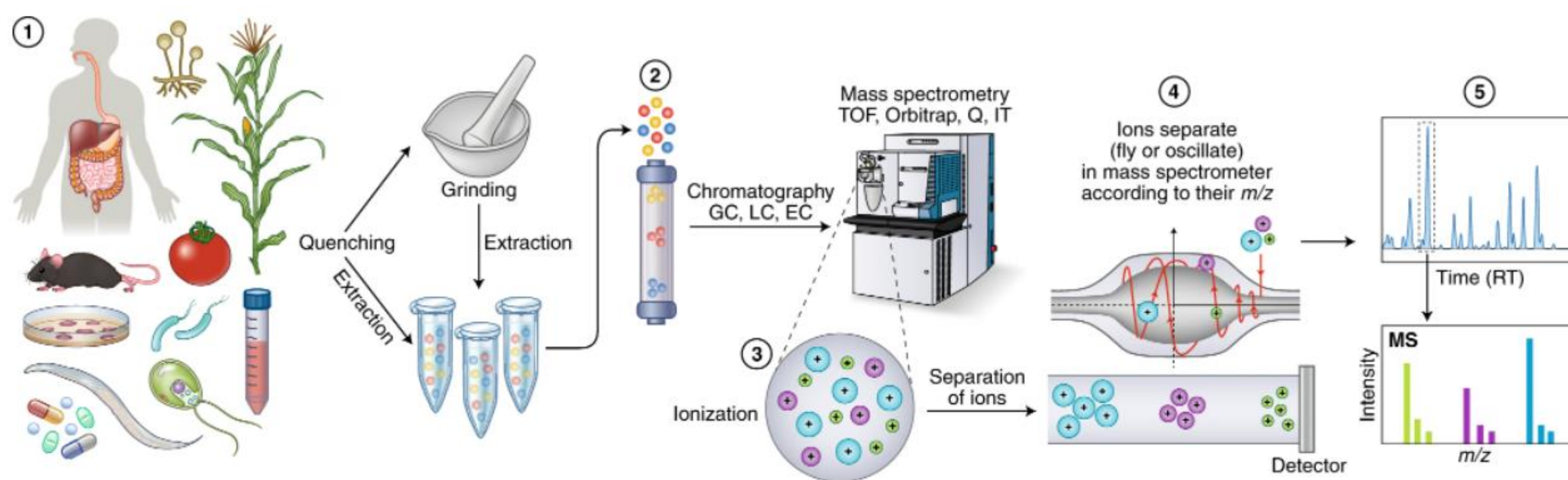


Potential available matrix

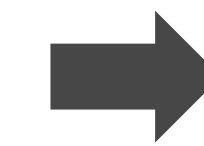
- Blood
- Urine
- Saliva
- Hair

Metabolomic

General Workflow



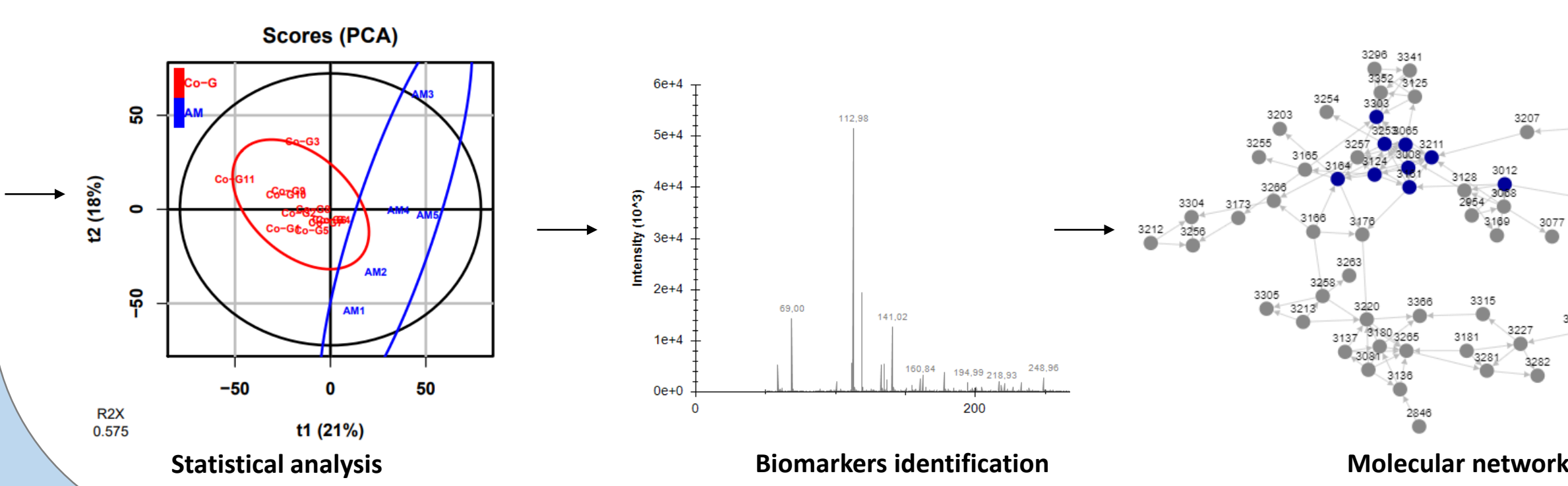
- ❖ Experimental design
- ❖ Sample preparation
- ❖ Metabolites separation
- ❖ Ionisation
- ❖ Detection
- ❖ Data treatment
- ❖ Statistical analysis
- ❖ Metabolites identification
- ❖ Biological interpretation



Many steps to be optimized

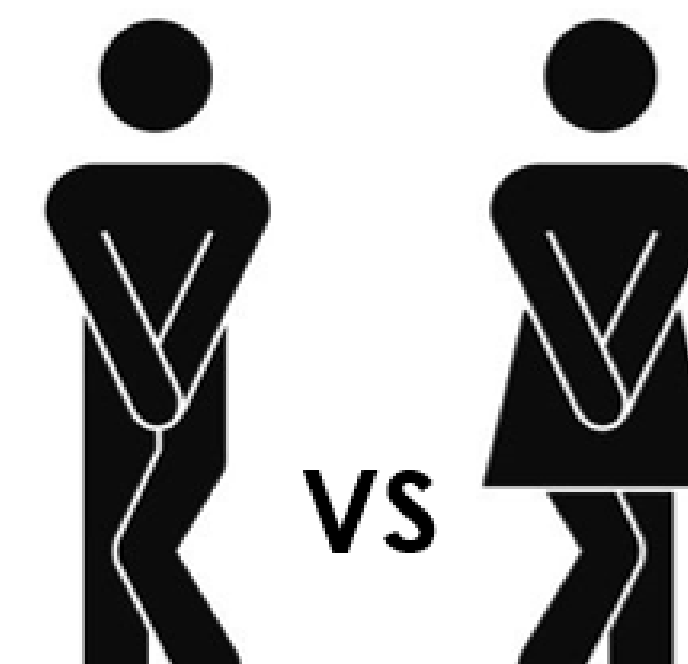
No general method for metabolomic analysis of human urine samples in the literature

Alesek S et al. Mass spectrometry-based metabolomics: a guide for annotation, quantification and best reporting practices. Nat Methods. 2021



Setting up of a test study on healthy volunteers

Men urine samples



Women urine samples



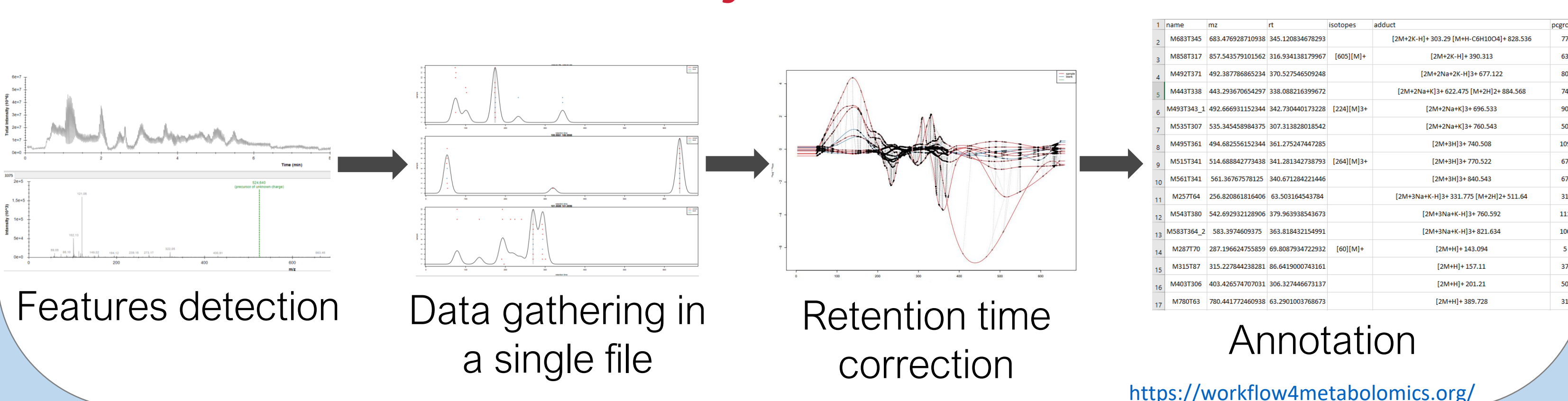
Methodology

Chromatographic parameters and HRMS detection

	ESI Positif	ESI Negatif
Separation of low polarity molecules C18 Waters Acquity® BEH C18 (1x100mm; 1,7 µm)	✓	✓
Separation of high polarity molecules HILIC Waters Acquity® BEH amide (1x100mm; 1,7 µm)	✓	✓

Masse detection : QTOF Agilent 6540, 1 scan/sec, 50-1000 m/z

Data treatment : Galaxy W4M & mixOmics

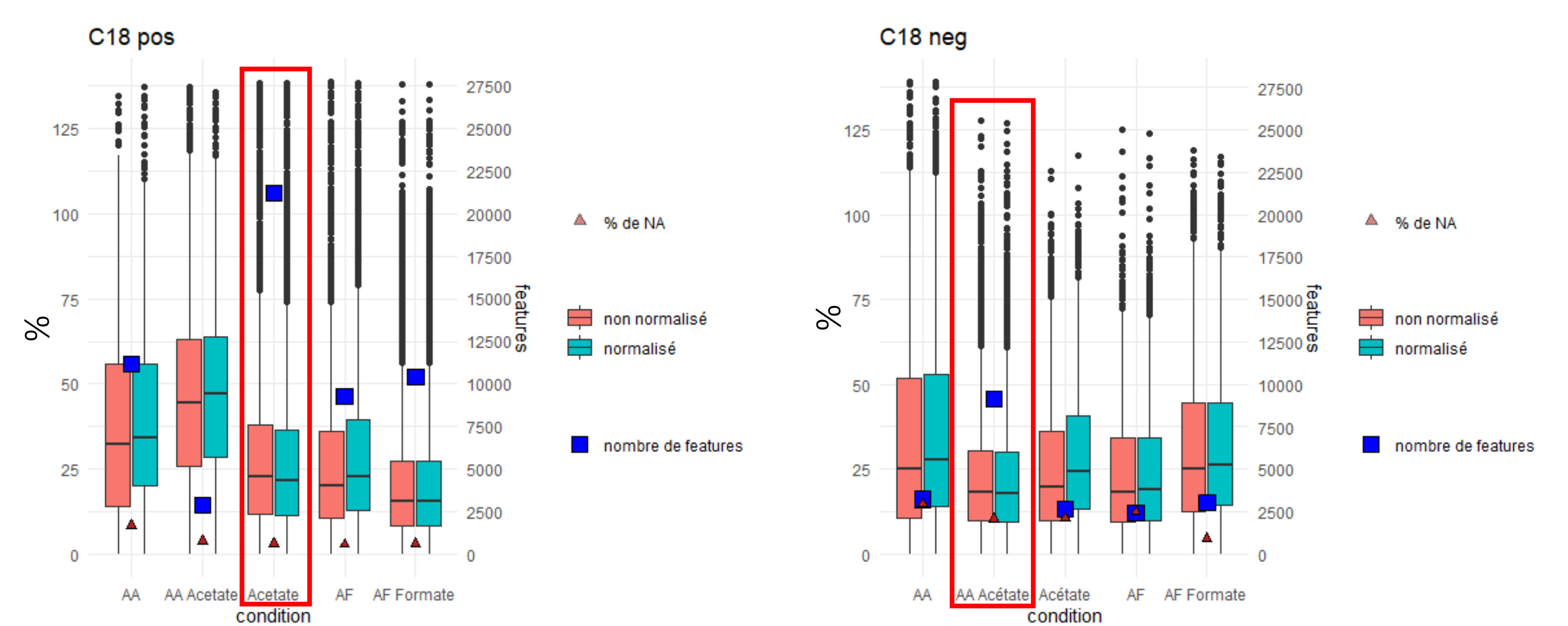


Perspectives

- Ion annotation tool optimisation
- Biobank samples analysis
- Study on blood, hair or saliva
- Use of new statistical tools

Results

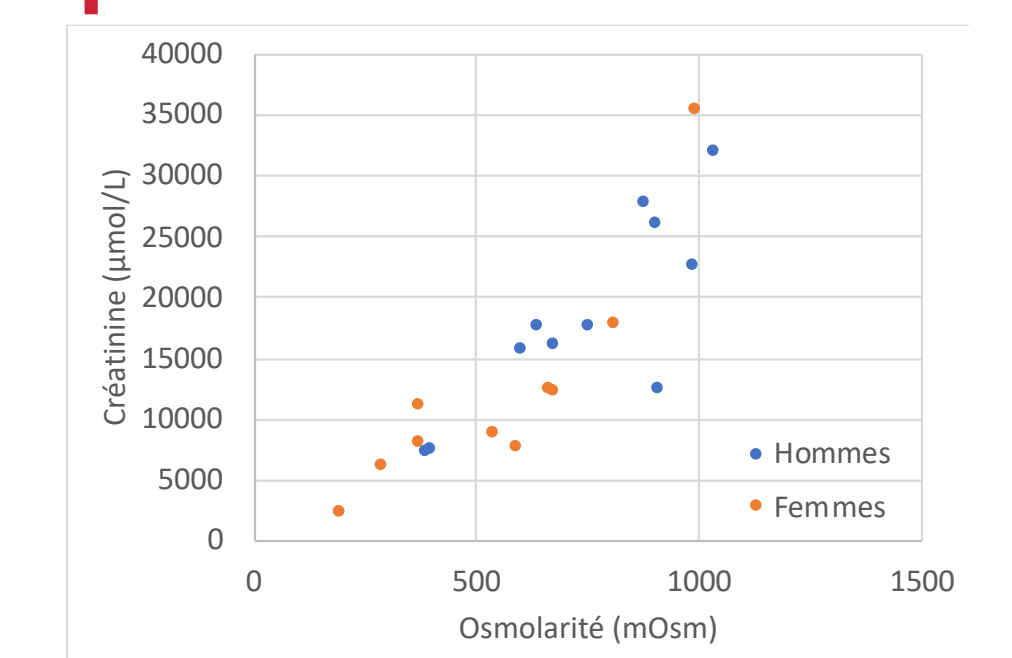
5 mobile phases comparison



Signal normalisation comparison

- Osmolarity
- Creatinine
- Total MS signal

Gagnebin et al., *Analytica chimica Acta*, 2017
Warack et al., *Journal of chromatography B*, 2009



Groups separation and markers highlighted

