Towards the smart lab: A comprehensive approach to mass spectrometry quality control

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Overview

Mass spectrometry (MS) = a powerful analytical technique
↔ because of its high sensitivity even the smallest changes in condition of operation can result in considerable variability
→ quality control (QC) is required to inspire confidence in the experimental results

We present a **comprehensive approach to quality control**:
- Incorporating optimized QC samples within the experimental workflow
- Capturing information at various stages in a mass spectrometry experiment using descriptive QC metrics
- Measuring secondary QC metrics external to the MS instrumentation
- Establishing the qcML standard file format to unambiguously represent, store, and communicate QC information
- Using advanced analytics for automated decision-making

Integration of these elements = the **smart lab**
→ unique "**technological passport**" of an MS instrument
→ objectively assess the instrument's functioning, evaluate the reliability of an experiment

Experimental design

Types of QC samples [1]:
- Simple peptide mixture or protein mixture: BSA, cythochrome c, ...
- Whole-cell lysate: yeast lysate, HeLa cell lysate, ...
- Synthetic peptide mixture: iRT peptides, digestion performance, ...

Incorporating QC samples into the **experimental workflow** [1]:

- At the start and end of a batch

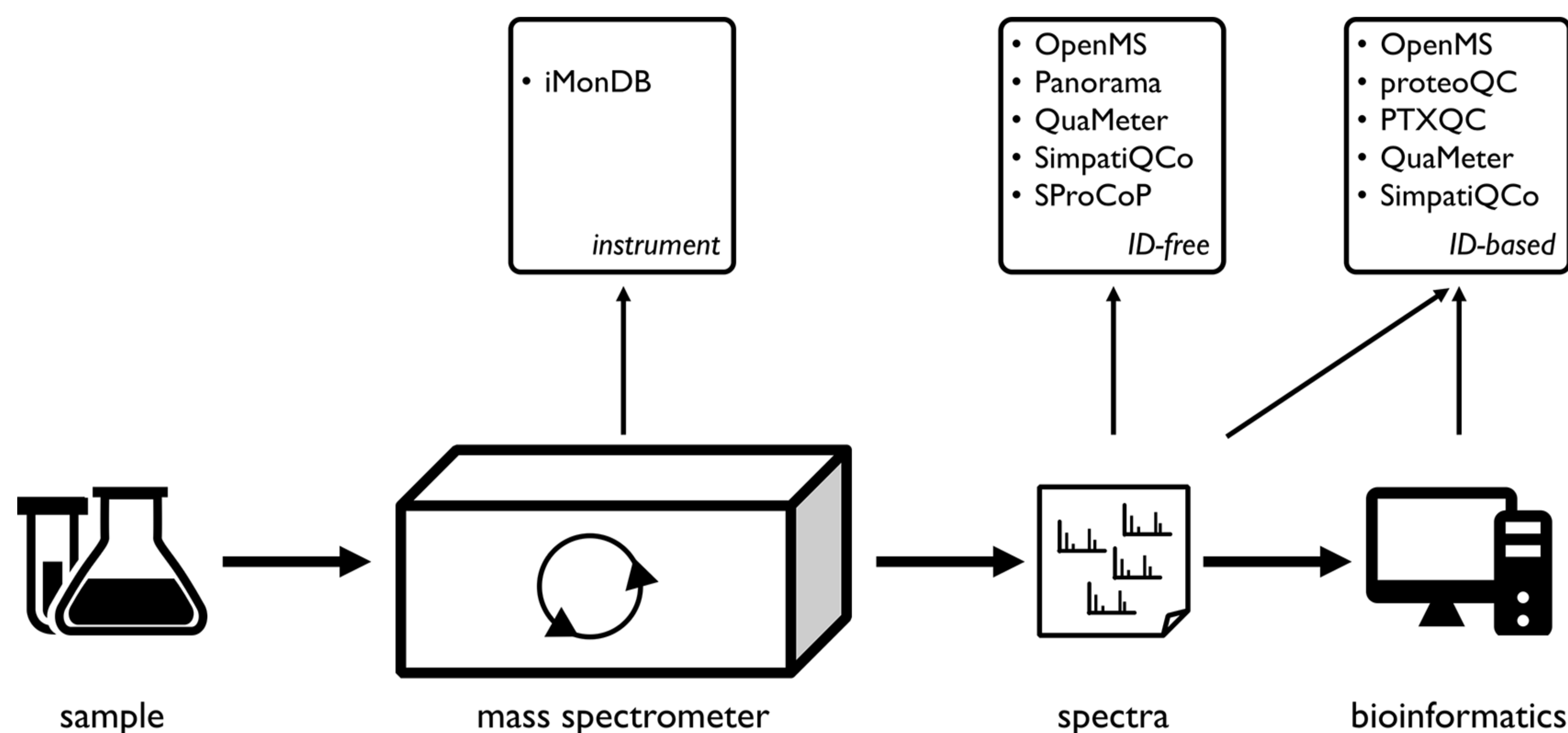- Interleaved with the biological samples

- Reference set

Supplementary data

http://www.bittremieux.be/asms17_smart_lab/

Quality control metrics

QC metrics: assess the reliability of a mass spectrometry experiment

QC metrics can **capture information at various stages** in a mass spectrometry experiment [2]:


sample   mass spectrometer   spectra   bioinformatics

Which metrics to use? All types of metrics can be used to accurately discriminate low-quality from high-quality experiments [2].
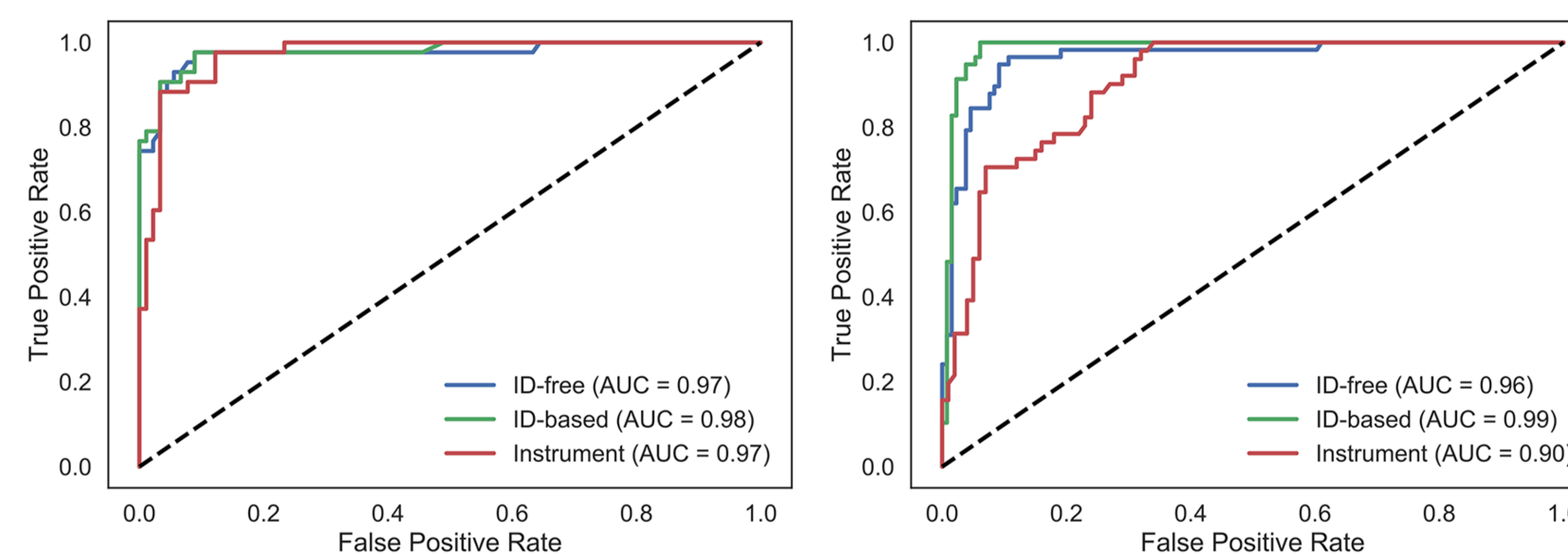
Environment monitoring

External processes: influence the experimental results
↔ effects **not captured** using traditional QC metrics

The **ambient temperature** exhibits weekly and daily patterns, while even the slightest fluctuations in temperature can influence the operation of the mass spectrometer [3]:
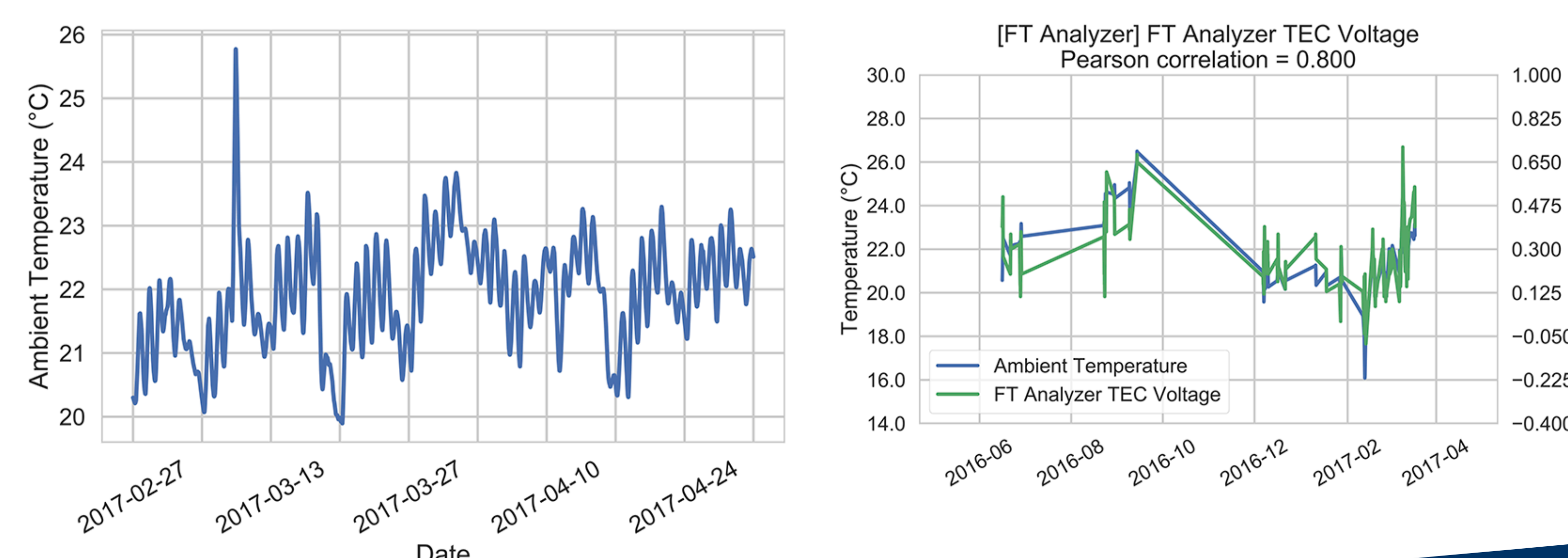
qcML standard format

The **HUPO-PSI Quality Control working group** is developing the qcML format as a community-driven standard file format for mass spectrometry quality control data [4].

The **qcML format** is intended as the focal point for all QC applications:

experimental data → automatic QC generation → qcML file
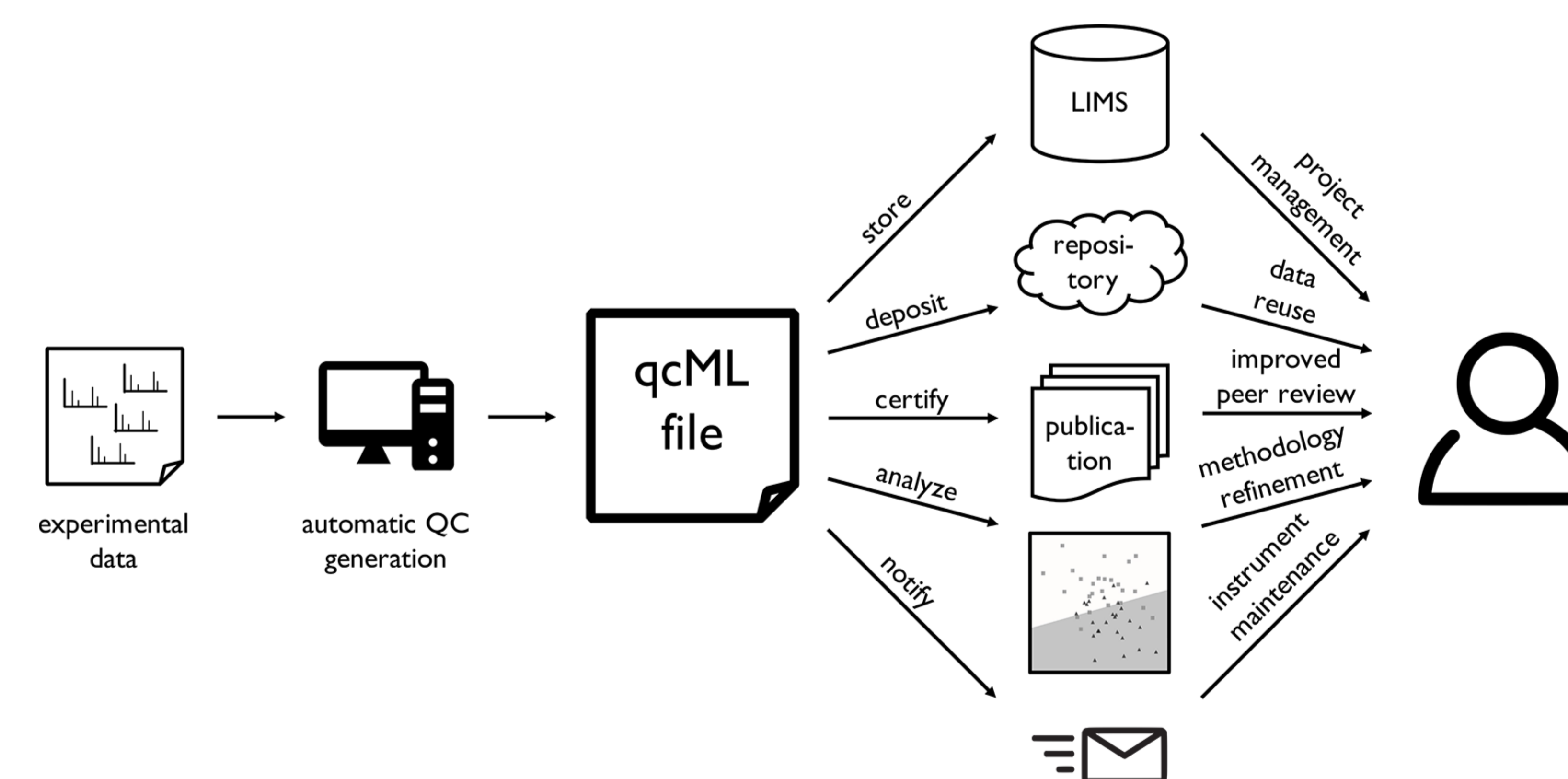
Decision-making

Descriptive QC metrics can be used for **decision-making**. We have developed an algorithmic method to **automatically detect low-quality** mass spectrometry experiments [5]:
- Unsupervised technique: no time-consuming and potentially error-prone manual input required
- Explicitly takes into account the high-dimensional data space
- Emphasis on interpretable results to provide feedback on the quality degradation

QC metrics   unsupervised outlier detection   outlier interpretation
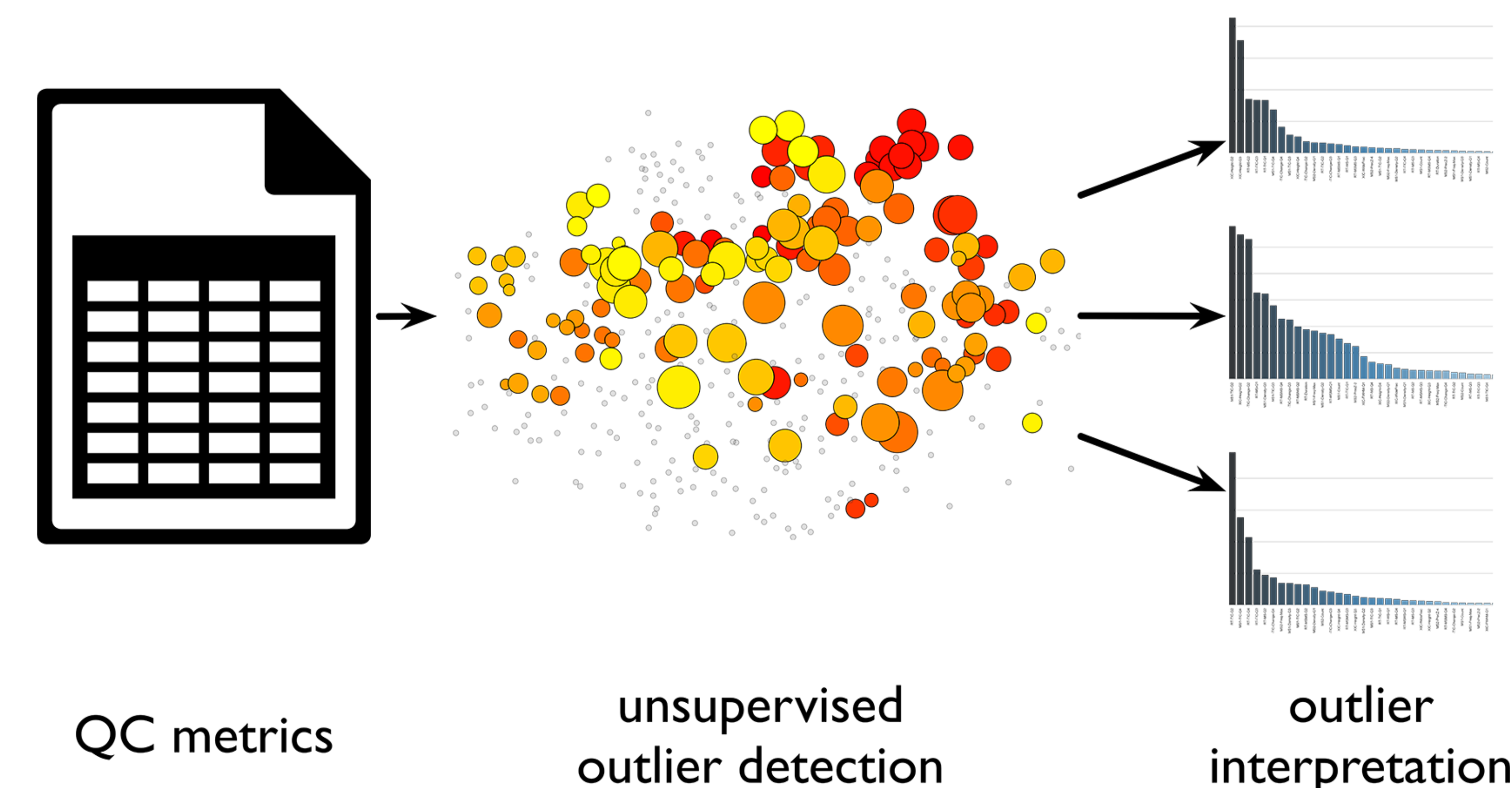
1. Bittremieux *et al*. *Mass Spectrom. Rev.* in revision.
2. Bittremieux *et al*. PROTEOMICS **17,** 1600159 (2017).
3. Bittremieux *et al*. *J. Proteome Res.* **14,** 2360–2366 (2015).
4. Bittremieux *et al*. *Anal. Chem.* **89,** 4474–4479 (2017).
5. Bittremieux *et al*. *J. Proteome Res.* **15,** 1300–1307 (2016).