MetabolomeExplorer: Inferring Metabolic Networks From High Resolution Mass Spectrometry Data

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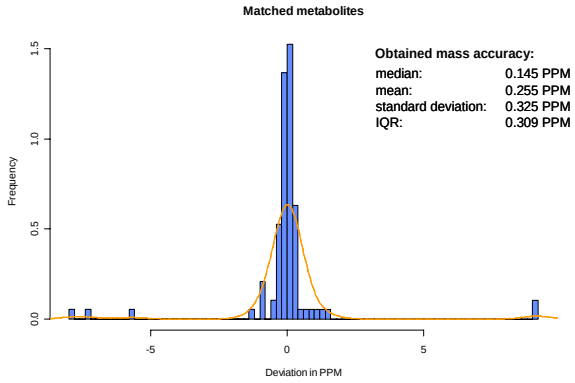
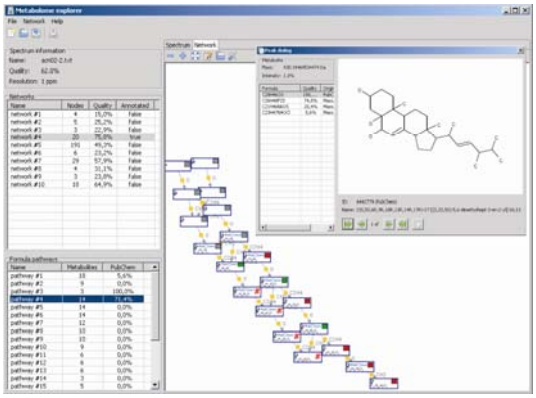
With a new generation of mass spectrometers, capable of mass separation of complex mixtures at very high resolution and mass accuracy, the field of metabolomics gained a powerful tool. However, in order to harness the extra power and overwhelming information abundance generated by the new equipment, novel bioinformatics solutions are needed. As a showcase and test-bed we have developed the MetabolomeExplorer, which implements a number of new concepts for normalizing and analyzing ultra-high resolution mass spectrometry data.





The first step in the analysis of ultra-high resolution mass spectrometry data is to remove bias from the data, peak-selection and combination of multiple samples. For the MetabolomeExplorer a method was developed for calibrating LCMS-measurements, which makes use of ubiquitous pollutants in the laboratory air and setup. These pollutants, present in the majority of scans, are identified for each sample and used to align the different measurements and to correct for the bias in the measurement. Using this approach we are able to achieve a mass accuracy of well below 0.4 PPM. As this is a post-processing operation, the separating power of the machine will not increase, but it does provide much needed accuracy for our network reconstruction approach.

After normalization of the data, a typical analysis with the MetabolomeExplorer consists of the following steps:

1. ***Ab initio* network reconstruction**
2. **Chemical formula prediction**
3. **Molecular structure prediction**
4. **Formula/structure selection**
5. **Network filtering**

Ultra-high resolution metabolomics is a rapidly emerging field. The MetabolomeExplorer will provide a convenient platform for the future development of the bioinformatics tools that are necessary to make full use of the up-coming avalanche of metabolomics data.

Breitling, R., et al. (2006a) Precision mapping of the metabolome, *Trends Biotechnol*, **24**, 543-548.
Breitling, R., et al. (2006b) Ab initio prediction of metabolic networks using Fourier Transform Mass Spectrometry data, *Metabolomics*, **2**, 155-164.