
GAS CHROMATOGRAPHY MASS SPECTROMETRY: KEY TECHNOLOGY IN METABOLOMICS.

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Metabolomics evolved from the conventional profiling techniques combined with the idea to study organisms or biological systems as an integrated system of interacting metabolites, proteins and/or genes in pathways and cellular processes, the so-called systems biology approach. In analogy with other functional genomics technologies, such as transcriptomics (global analysis of gene expression) and proteomics (measure the complete proteome), metabolomics involves the unbiased quantitative and qualitative analysis of the complete set of metabolites present in cells, body fluids and tissues (the metabolome). Ultimately, a successful systems biology approach will open new and exciting ways to improve the quality of human life based on individual phenotypes, for example through personalized health strategies, including medicine, diet and life style. Gas chromatography (GC) coupled to mass spectrometry (MS) is a very suitable technology for metabolomics, as it combines high separation efficiencies and repeatable retention times with generic, sensitive and selective mass detection. In addition, the elaborate fragmentation obtained with electron ionization facilitates the assignment of already identified metabolites and ultimately the de-novo identification of so far unidentified metabolites. However, many metabolites contain polar functional groups and are thermally labile at the temperatures required for their separation or are not volatile at all. Therefore, derivatization of the compounds prior to GC analysis is necessary. We present here the GC(\times GC)-MS based methods used in our laboratory, relying on derivatization via oximation and subsequent silylation. Throughout the development and optimization of the methods emphasis was put on obtaining reliable and quantitative analytical data. The methods facilitate the reliable quantification of hundreds of different metabolites and have been successfully applied in many different studies in the fields of microbial and mammalian metabolomics. In addition, a method is presented capable of measuring metabolite profiles in one single cell.