The identification of all metabolites of a biological system is a tremendous analytical challenge. Not a single instrumental setup can claim to currently isolate, identify, and further quantify all metabolites. Because of its valuable use in identifying potential phenotype changes due to environmental stresses or diseases, metabolomics is nevertheless a growing field of analytical research. Even if ‘true’ metabolomics cannot yet be achieved with the available instrumentation, both metabolic profiling and metabolic fingerprinting can be performed and offer specific sets of information.

Various hyphenated analytical techniques have been used for profiling and fingerprinting in the past years. Among them, gas chromatography (GC) coupled to mass spectrometry (MS) in electron impact (EI) mode is one of the most frequently used. GC-MS can be used in both area, with a preference for target analysis when using scanning MS instruments like quadrupoles and magnetic sectors. Both polar and lipophilic metabolites are GC-MS amenable when a suited derivatization procedure is used after a comprehensive sample preparation. Classical GC-MS however often suffers of peak capacity issues due to the large number of analytes to be chromatographically separated.

Comprehensive two-dimensional GC (GCxGC) has been developed 20 years ago\(^1\). Among various advantages over classical GC, it helps to palliate chromatographic resolution issues. When coupled to Time-of-Flight MS (TOFMS) operated with efficient deconvolution algorithms, the enhanced chromatographic resolution of (GCxGC) is further backed up by analytical resolution in the MS domain. This makes GCxGC-TOFMS a powerful tool for complex sample analyses\(^2\). This setup is capable of target analyses based on internal standards but can also be used for unknown screening and pattern recognition for complex sample mapping. Additionally, zone compression due to the modulation process further enhances the detection power of the technique.

This report will present the main characteristics of GCxGC and TOFMS in terms of analytical and sample dimensionality. Some examples of GCxGC-TOFMS applications in metabolic profiling will also be highlighted.