§ Improvement of methods for the structural characterisation of drug metabolites based on collisional cross sections

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Ion Mobility Mass Spectrometry (IM/MS) is a technique that allows separation of isomeric species based on differences in their collision cross sections (CCSs) in the gas-phase, thus providing specific information on the potential structure of a compound [1]. In combination with Molecular Modelling, it is considered as a potential tool for small molecule identification by measuring their gas-phase CCSs and comparing them to theoretically derived CCS databases. A protocol for theoretical determination of CCS has been introduced in [2] and its improvement is at the core of this project.

In the initial stage of the project we have developed a script – an extensive automation of the protocol, which allows all the routine and necessary steps of the algorithm to be performed automatically. It minimises human intervention and saves valuable time. Further research is aimed at investigating deeper possible sources responsible for the differences between the theoretical and experimental CCS values.

In the present work, new atomic parameters employed in the CCS determination software (MOBCAL [3]) have been introduced: the protocol has been modified to be able to distinguish between different atom types and to assign appropriate parameters. Other modifications include an additional step in the protocol that calculates root-mean-square deviation (RMSD) of the found conformations and performs filtering based on the level of similarity among structures. Extensive tests of the protocol with the introduced changes are to be made in order to assess the performance of the new script. Additionally, the calculation of the partial charges used by MOBCAL to calculate the ion-induced part of the potential is to be included in the protocol. Further research includes the study of the possible effect of the dipole moment on the CCS of a metabolite and the assessment of the possible use of QSAR in the protocol.

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