

# Short History of QMSA

By

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Soon after the discovery of NMR, it was understood that *energetics* of nuclear spins of a molecule located in magnetic field and moving isotropically in solution, can be treated quantitatively using quantum mechanical theory (QM), using only the two types of NMR-parameters: the chemical shifts and coupling constants [1,2]. The computer program LAOCOON3 was published 1964[2] and became a standard for years. However, handling of spin-systems of more than 8 coupled protons was computationally slow and clumsy. The next landmark in the history of QMSA (Quantum Mechanical Spectral Analysis) was formed by the program NUMARIT [3,4], which allowed an efficient use of symmetry and *X-approximation*. The softwares so far were frequency-based, until the *Total-Line-Shape* programs like DAVINS [5] and DAISY [6], for which the spectrum were given in digital form. The first approach toward ‘Automatic analysis’, meaning start of analyses from rough trial parameters, the use of integral transforms was introduced already in 1975.

The present tools like ChemAdder software [7,8,9] allow treatment of large spin-networks, like steroids, peptides, and mixtures of tens or even hundreds of components, with ordinary personal computers. When also optimized linewidths, baseline and line-shape are added to the analyses, the method allows simulation of an experimental spectrum into very details, using the field strength independent NMR-parameters. The parameters can be then arranged into field (instrument) independent *Adaptive Spectral Libraries*, to be used as discussed below.

The NMR method is *metric*, which means that the NMR signal area is proportional to the number of nuclei, independently of the compounds, on the condition that the spectra are measured properly. This also means that the spectrum of a mixture is sum of the spectra of the components, forming the basis of quantitative QMSA (qQMSA). However, the spectra and the parameters depend significantly on conditions like solvent, concentrations, and pH, which complicates the analysis of complex mixtures and is the reason to that the analysis is done iteratively and is still computationally challenging.

The basics of QMSA are reviewed in ref. [7] and in

<https://www.chemadder.com/letters.html>

[https://www.chemadder.com/presentations/ChemAdder\\_QMSA%20BASICS.pdf](https://www.chemadder.com/presentations/ChemAdder_QMSA%20BASICS.pdf).

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