

In many fields, and more particularly in pharmaceuticals, the use of reference materials is required. In a process of manufacturing new active molecules, getting commercially available and adequate reference materials is not straightforward. Consequently, industries need to create and certify their new products, for example by determining their purity. Regulatory or metrology agencies must be able to verify the quality of reference materials.

The determination of the purity of molecules can be performed by several technologies. Nuclear Magnetic Resonance (NMR) has the advantage to be a primary method by definition. Consequently, this technology can be used to qualify other ones, such as chromatography for instance. Two main advantages of NMR are the possibility to obtain quantitative results with a very high precision (standard deviation lower than 1%) and to establish an exhaustive uncertainty calculation on experimental results.

Which expertise is proposed by SPECTROMAITRISE?

- The determination of a molecule purity by NMR with the desired accuracy, in order to certify it and to give it the status of reference
- The delivery of a certificate of purity recognized internationally, including uncertainty calculation

What are the innovative and differentiating methodologies used or proposed by SPECTROMAITRISE?

- Quantitative ^1H NMR with very high accuracy and trueness ($<0.1\%$)
- Scientific expertise in the optimization of NMR acquisition parameters in getting quantitative results: the measurement of longitudinal relaxation times, the recording of NMR spectra with a very high signal to noise ratio, the use or not of ^{13}C decoupling to avoid the apparition of corresponding satellites, etc.
- Scientific expertise in the optimization of NMR processing parameters in getting quantitative results: spectra manual phasing, baseline correction, spectra deconvolution, result correction if ^{13}C satellites are present, etc.
- Outsourced service of method validation and parameter verification to customers

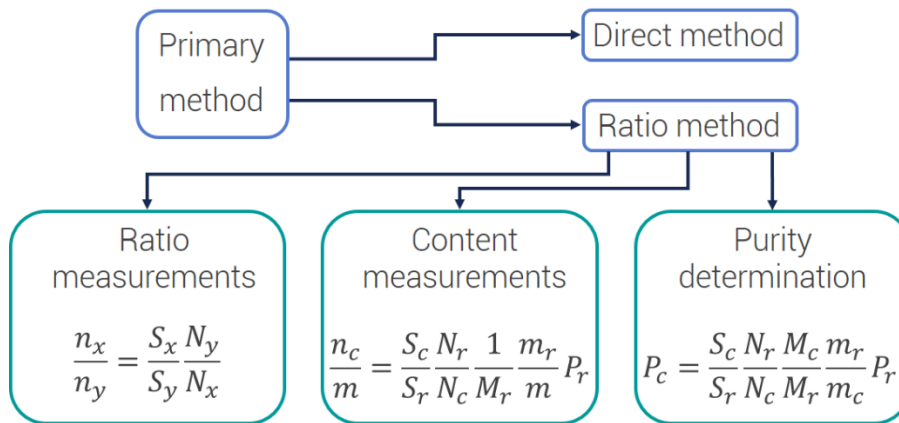
To which matrices can the SPECTROMAITRISE expertise be applied?

- Pure molecules in order to give the status of standard meeting regulatory specifications
- Synthesized or manufactured molecules which are not available as commercial reference

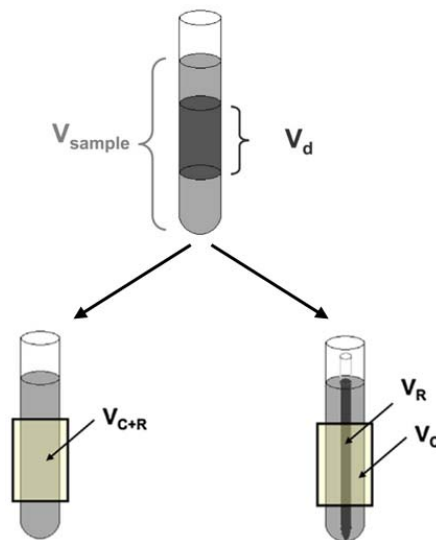
Reference and normalization methods: Essential tools for the intercomparison of NMR spectra,

P. Giraudeau *et al.*, *Journal of Pharmaceutical and Biomedical Analysis*, 2014, 93, 3-16

This publication presents a non-exhaustive list of different reference methods found in the NMR literature. This article helps to choose the most suitable reference method to a given issue. The main acquisition parameters to optimize for each method are listed in order to obtain quantitative NMR measurements.



Schematic illustration of qNMR as a primary analytical technique used to determine purity



Schematic representation of the internal and external referencing methods in qNMR