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SPINEVOLUTION: A powerful tool for the simulation of solid and liquid state NMR experiments

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Abstract

Exact numerical simulations of NMR experiments are often required for the development of new techniques and for the extraction of structural and dynamic information from the spectra. Simulations of solid-state magic angle spinning (MAS) experiments can be particularly demanding both computationally and in terms of the programming required to carry them out, even if special simulation software is used. We recently developed a number of approaches that dramatically improve the efficiency and allow a high degree of automation of these computations. In the present paper, we describe SPINEVOLUTION, a highly optimized computer program that implements the new methodology. The algorithms used in the program will be described separately. Although particularly efficient for the simulation of experiments with complex pulse sequences and multi-spin systems in solids, SPINEVOLUTION is a versatile and easy to use tool for the simulation and optimization of virtually any NMR experiment. The performance of SPINEVOLUTION was compared with that of another recently developed NMR simulation package, SIMPSON. Benchmarked on a series of examples, SPINEVOLUTION was consistently found to be orders of magnitude faster. At the time of publication, the program is available *gratis* for non-commercial use.

Keywords: NMR simulations; Virtual NMR spectrometer; Software; Parameter optimization; Data fitting

1. Introduction

With the continued increase in the complexity of NMR techniques and applications, numerical simulations have become an indispensable part of modern day research. They are now commonly required for the extraction of structural parameters from the data, design of new experiments, and theoretical research. This is especially true for solid-state NMR, where most applications employ magic angle spinning (MAS) and ^{1}H-decoupling to obtain high resolution spectra, while various recoupling methods are used to restore the averaged dipolar and chemical shift anisotropy (CSA) interactions [1,2]. These techniques normally create a homogeneous time-dependent Hamiltonian [3], requiring the use of numerical methods whenever the experiments have to be simulated exactly. Typically, such experiments are designed and interpreted in terms of the first few orders of the average Hamiltonian theory (AHT) [4], which can often be used to obtain approximate solutions. However, while being a powerful analytical tool, AHT is not always applicable or sufficiently accurate. Furthermore, even in the experiments where this formalism provides a reasonably accurate analytic description of the two-spin systems, it remains necessary to invoke numerical methods for most cases involving multiple spins. In solution-state NMR, analytic descriptions of experiments are much more common. However, numerical simulations are still important, for example, when studying non-ideal pulses (including shaped pulses

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[5]), various effects due to strong coupling and relaxation, and even single-scan 2D experiments [6,7].

Driven by demands of the experimental NMR, numerous computer programs were developed over the past four decades for the simulation of NMR experiments [8–41]. Most of this software is easily assigned to one of the following categories: *analytic NMR tools* (typically implemented in Mathematica), *specialized application programs* (e.g., a NOESY spectra simulator), *application programming interfaces* (*API*'s) (providing building blocks for the development of application programs), *general solution-state NMR simulation programs*, and *general NMR simulation programs*. The two later types are called general in the sense that they can be used for the simulation of experiments with a wide variety of pulse sequences and spin systems, and thus have the functionality of a virtual NMR spectrometer (in addition to any other functionalities they may have). Additionally, as opposed to an API, a simulation program must have an abstract, high-level interface, which should not require any programming, in general.

In spite of all these developments, only a few instances of the currently available software are suitable for the simulation of general NMR experiments. As a consequence, until a few years ago, the design of new techniques, particularly in the solid-state NMR, had to be often combined with the development of new problem-specific software [23,25,42–45]. For the solid-state NMR, this had been more than an inconvenience: it seems that the development of the whole field had been held back due to the lack of an appropriate general simulation tool. This rather bold statement is evidenced by the recent popularity enjoyed by SIMPSON [39], and by the vast interest expressed in such a tool in the community.

To the best of our knowledge, the first reasonably general NMR simulation software was ANTIOPE [27]. The program is still maintained and distributed by its author (J.S. Waugh) and has recently acquired a particularly user-friendly interface and undergone other significant changes since its initial publication. An API-type package GAMMA [31], which appeared soon after ANTIOPE, is designed as a library of C++ classes and methods intended as building blocks for the construction of various problem-specific simulation programs. Although the development of these programs is much facilitated by GAMMA, a significant amount of programming is often required to perform a simulation. The package has been extensively used over the years for the simulation of both NMR and EPR experiments. A similar C++ API (BlochLib [40]) has been developed recently that relies on efficient numerical libraries for its core calculations and is superior to GAMMA in terms of efficiency. Currently the most popular in the solid-state NMR community simulation package is SIMPSON [39]. It is designed as a high-level API, where the simulation is driven by an input file written in the scripting language Tcl. SIMPSON requires no compilation and much less programming to perform a simulation. The major application of the program is the simulation of MAS experiments. Overall, it provides a reasonable compromise between efficiency, convenience, and versatility.

The aforementioned three qualities are probably the most important characteristics desired from a general NMR simulation program. Developing software that is not deficient in any of these areas has been a great challenge so far. Indeed, versatility can be achieved in the most straightforward manner by taking the API approach of GAMMA, BlochLib, and, to a lesser degree, SIMPSON. However, an interface that requires writing C++ code for a sophisticated API platform is unlikely to be convenient in most cases. Furthermore, to efficiently propagate a density matrix through a complex MAS experiment with multiple pulse sequences, one has to compute and recycle an elaborate collection of propagators. There is very little support provided to this end in GAMMA, BlochLib, or SIMPSON. As a result, using the most efficient algorithm for such a simulation would be either impossible due to restrictions of the API, or highly challenging due to the substantial amount of expertise and programming required. In addition, the efficiency of any simulation depends also on the efficiency of the computational techniques and algorithms that the simulation package relies upon internally, and which are beyond the user's control. If these techniques comprise only a rather basic set, creation of a simple interface to such a package is relatively straightforward, as exemplified by some older solution-state programs. However, if these techniques comprise an extensive library of highly efficient and often problem-specific algorithms, then their integration into a unified general NMR simulation program with a user-friendly interface presents a significant challenge, which is in addition to the challenge of developing these methods and creating such a library.

In an attempt to solve this problem, we developed SPINEVOLUTION, a general NMR simulation program that implements a number of novel computational techniques and methodological approaches to this end. Although specifically tailored for the simulation of solid-state MAS experiments, SPINEVOLUTION can also be used in the context of solution state NMR, particularly to solve various optimization problems. The program features a friendly, text file based interface, where the pulse sequences are specified in terms of the "canonical representation." The representation is a natural, non-algorithmic description of NMR experiments that captures their periodic structure in a form easily explored for the construction of efficient propagation schemes.