

# Modelling NMR spectra for spins $I = \frac{1}{2}$ using SIMPSON

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This tutorial consists of simple simulations of 1D spectra for systems of  $^1\text{H}$  and  $^{13}\text{C}$  spins, in the solution state and in the solid state.

## 1. Introduction

SIMPSON is a command-line program that relies on a single input file, where the spin system, the NMR interactions and the simulation parameters are described, together with the pulse sequence and a set of instructions to start the simulation and process the resulting data. A typical input file is organized as follows:

spinsys {	<i>Definition of the spin system</i>
channels 13C 1H	NMR isotope(s)
nuclei 13C 1H 1H	List of nuclei
shift 1 0 20p 0 0 0 0	NMR interactions; can be shift, jcoupling, dipole.
dipole 1 2 -25000 0 0 0 0	shift: $i d_{iso} d_{aniso} \eta \delta \alpha \beta \gamma$
dipole 1 3 -25000 0 0 109.4 0	jcoupling: $i j J_{iso} J_{aniso} \eta \delta \alpha \beta \gamma$
dipole 2 3 -22000 0 0 144.7 0	dipole: $i j \omega/(2\pi) \eta \delta \alpha \beta \gamma$
}	
par {	<i>Definition of the parameters</i>
proton_frequency 500e6	<i>"Experimental" acquisition and processing parameters</i>
sw 10000	$^1\text{H}$ Larmor frequency, used to convert ppm to Hz
variable tsw 1e6/sw	spectral width
np 512	new variables can be defined, to be used later in the file
spin_rate 1000	number of points in the simulated data
variable lb 50	spinning frequency, in Hz (0 for liquid and static solids)
variable zfill 4096	
crystal_file rep2000	<i>Simulation parameters</i>
gamma_angles 10	Orientation set for powder averaging (solids only)
method direct	Number of angles for powder averaging (mas only)
start_operator I1x	Algorithm for the simulation
detect_operator I1p	Initial density operator
verbose 1101	Observable operator
}	verbosity
proc pulseseq {} {	<b>Definition of the pulse sequence</b>
global par	
acq_block {	The syntax acq_block defines the pulse sequence during acquisition.
delay \$par(tsw)	Note that the custom variable tsw is used here.
}	
}	
proc main {} {	<b>Main procedure</b>
global par	
set f [fsimpson]	Run the simulation
faddlb \$f \$par(lb) 0	Apodise the FID

fsave \$f \$par(name).fid	Save the fid
fzerofill \$f \$par(zfill)	Zero-fill the fid
fft \$f	Fourier transform of the FID
fsave \$f \$par(name).spe	Save the spectrum
}	

The simulation is started from the command line, by typing  
 simpson <filename>.in

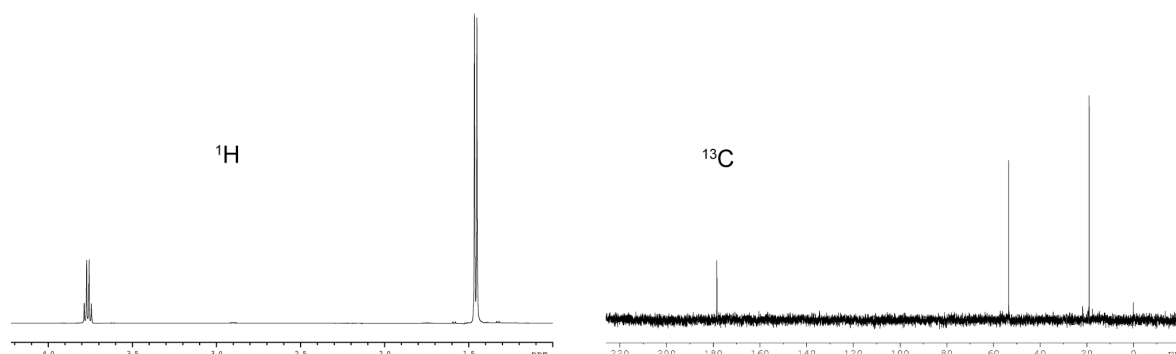
The program generates two files : simpson.fid (FID) and simpson.spe (Spectrum). Those files consist of a header:

SIMP	
NP=65536	Number of complex data points
SW=160000	Spectral width, in Hz
TYPE=SPE	Either SPE (frequency domain) or FID (time domain)
DATA	

followed by the data, either in ASCII or binary format. They can be visualised with Simpson tools: **simplot** or through a drag-and-drop on an empty page of jsnmr (<http://www.jsnmr.net/empty.html> ).

## 2. Liquid-state NMR

In this section, the  $^1\text{H}$  and  $^{13}\text{C}$  spectra of the amino-acid L-alanine are simulated. Experimental spectra, taken from the HMDB ([www.hmdb.ca](http://www.hmdb.ca)) are shown in Fig. 1.



**Fig. 1.** Experimental 1D  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra of L-alanine, recorded at magnetic fields corresponding to  $^1\text{H}$  Larmor frequencies of 500 MHz and 400 MHz, respectively.

### 2.1. $^1\text{H}$

File: liquid\_1H.in

System: 4  $^1\text{H}$  spins, corresponding to the amino-acid L-alanine

Interactions: chemical shift, j coupling

In this first example, the  $^1\text{H}$  1D NMR spectrum of alanine in solution is simulated. Only isotropic interactions are considered.

spinsys {	
channels 1H	
nuclei 1H 1H 1H 1H	
shift 1 1.46p 0 0 0 0	
shift 2 1.46p 0 0 0 0	
shift 3 1.46p 0 0 0 0	
shift 4 3.76p 0 0 0 0	
jcoupling 1 4 7.1 0 0 0 0	
jcoupling 2 4 7.1 0 0 0 0	

Chemical shifts are given in ppm using p

```
jcoupling 3 4 7.1 0 0 0 0
}
```

The simulation is very fast. It can be used as a virtual spectrometer to analyse the effect of acquisition parameters:

- Compare simulations for several values of the spectral width and of the number of points
- Change the lb parameter. What does the result look like for lb = 0? Why?
- Consider the effect of the static magnetic field. Compare simulations with  $^1\text{H}$  Larmor frequencies of 500 MHz and 43 MHz.

Note that in order to compare spectra, the variable index can be changed to save files under a different name. For example, change the variable to

```
variable index 2
```

## 2.2. $^{13}\text{C}$

Files: liquid\_13C.in, liquid\_13C\_freq.in

System: 3  $^{13}\text{C}$  spins and 4  $^1\text{H}$  spins, corresponding to the amino-acid L-alanine

Interactions: chemical shift, j coupling

The second example now considers the  $^{13}\text{C}$  spectrum of alanine in solution. Note the different operators:

```
start_operator I5x+I6x+I7x
detect_operator I5p+I6p+I7p
```

Together with the parameters considered in 2.1, the use of RF decoupling can be simulated here, using a slightly modified acq\_block:

```
proc pulseq {} {
  global par
  offset $par(o1) $par(o2)           Changes the offset on the two channels
  acq_block {
    pulse $par(tsw) 0 0 $par(rf) 0    Continuous-wave decoupling at <rf> Hz on channel 2
  }
}
```

- Start with the file liquid\_13C.in. Compare simulations with and without  $^1\text{H}$  decoupling

The simulation for this 7 spins system takes a little longer. By default, the simulation method is direct time, where direct is the only option for liquids and time means that the density matrix is propagated during the fid.

- How does the simulation time vary with the number of points in the spectrum?

Alternatively, the simulation can be carried out in the frequency domain.

- Try the option method direct frequency; what is the output of the simulation? How does the simulation time vary with the number of points?

Note the different syntax for processing in the file liquid\_13C\_freq.in

set f [fsimpson]	The simulation is a histogram of the calculated frequency,
fsave \$f \$par(name)_\$par(index)_stick.spe	with bins given by sw and np.
	A more realistic spectrum is obtained by
fft \$f -inv	inverse Fourier transform:
faddlb \$f \$par(lb) 0	line broadening
fsave \$f \$par(name)_\$par(index).fid	
fzerofill \$f \$par(zfill)	zero filling
fft \$f	and Fourier transform back to the frequency domain
fsave \$f \$par(name)_\$par(index).spe	

### 3. Static solid-state NMR

#### 3.1. $^{13}\text{C}$ CSA

File: static\_13C\_CSA.in

System: 1  $^{13}\text{C}$  spin

Interactions: CSA

This example consists of a single  $^{13}\text{C}$  spins, in a static solid, with an anisotropic chemical shift tensor.

```
spinsys {  
  channels 13C  
  nuclei 13C  
  shift 1 0 20p 0 0 0  
}
```

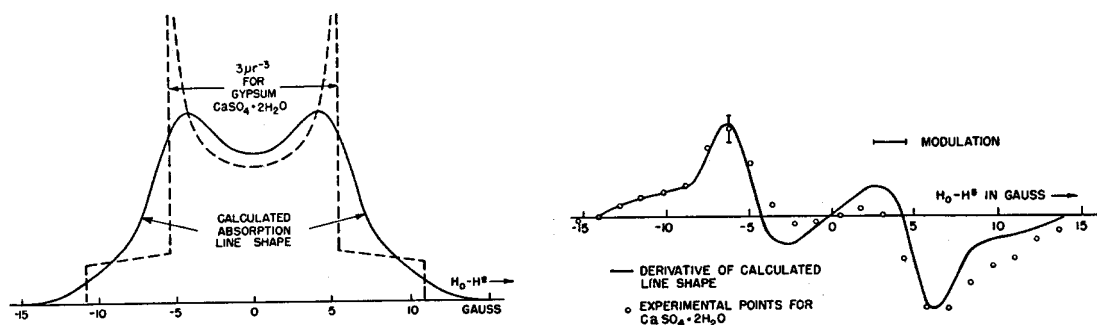
The initial file consists of a single orientation, described in the parameters:

```
crystal_file  alpha0beta0  
gamma_angles  1
```

- Change the orientation of the CSA tensor in its PAS and observe the effect on the simulated spectrum.

To obtain a powder-averaged spectrum, the crystal file alpha0beta0 is replaced by a set of orientations, such as zcw143.

- Increase the number of orientations and observe the slow convergence of the lineshape. The external file zcw28656.cry may be used since single crystal simulations require a large number of orientations. Some line broadening is still necessary to remove discontinuities.
- Change the value of the asymmetry parameter  $\eta$  and observe the effect on the simulated lineshape.



**Fig. 2.** The broken line in the left curve shows the calculated distribution of component line centers for the proton resonance in powdered  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ . The continuous line on the same plot is the calculated line shape obtained by superposing gaussians of width 1.54 gauss according to this distribution function. The right plot contains experimental points for powdered  $\text{CaSO}_4 \cdot 2\text{H}_2\text{O}$ , and a curve which is the derivative of the calculated line shape. Reproduced from G.E. Pake, J. Chem. Phys., 16, 327 (1948).

#### 3.2. $^1\text{H}$ dipolar interaction

File: static\_1H\_DD.in

System: 2  $^1\text{H}$  spins

Interactions: CSA

The following system consists of two protons with a dipolar spin-spin coupling. The converged simulation corresponds to the classic "Pake doublet", first measured on the water signal of gypsum (Fig. 2).

- Run the simulation. How does one measure the dipolar coupling from the spectrum?

## 4. Magic-angle-spinning solid-state NMR

### 4.1. $^{13}\text{C}$ CSA

File: mas\_13C\_CSA.in

System: 1  $^{13}\text{C}$  spin

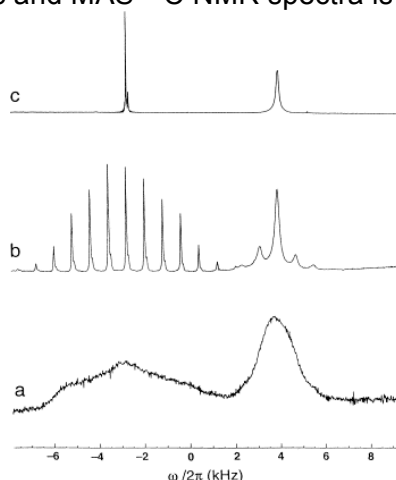
Interaction: CSA

The spin system is the same as in 3.1, but the simulation now considers a sample under magic-angle spinning.

proton_frequency	500e6	
sw	20000	
variable tsw	1e6/sw	
np	512	
spin_rate	200	The spinning frequency is defined here
variable lb	50	
variable zfill	4096	
method	direct	
crystal_file	rep2000	
gamma_angles	16	With MAS, the number of gamma angles is defined

- Compare the simulated spectrum with that obtained in the static case, using the same CSA parameters.
- How does the spinning frequency influence the number, position and intensities of spinning sidebands in the spectrum? What is the influence of the magnetic field?
- This simulation considers a powder average. How does the simulated spectrum converge with the number of orientations?

The relationship between static and MAS  $^{13}\text{C}$  NMR spectra is shown in Fig. 3, for glycine.



**Fig. 3.**  $^1\text{H}$ -decoupled 50.3 MHz  $^{13}\text{C}$  CP spectra of glycine powder: (a) static spectrum; (b) CP/MAS at a rotor frequency 800 Hz; (c) CP/MAS at a rotor frequency 8000 Hz. Reproduced from O.N. Antzutkin, Prog. Nucl. Magn. Reson. Spec. 35, 203 (1999).

### 4.2. $^{13}\text{C}$

File: mas\_13C.in

System: 1  $^{13}\text{C}$  spin and 3  $^1\text{H}$  spins

Interaction: DD, CSA

The previous simulation did not consider any protons and thus assumed perfect decoupling of the  $^1\text{H}$ - $^{13}\text{C}$  dipolar interactions. Now 3 protons are introduced in the spin system, with the geometry of a methyl group and the corresponding interactions:

```
spinsys {
channels 13C 1H
nuclei 13C 1H 1H 1H
shift 2 0 2p 0 0.00 70.50 60.00
shift 3 0 2p 0 0.00 70.50 300.00
shift 4 0 2p 0 0.00 70.50 180.00
dipole 1 2 -22690 0.00 70.50 60.00
dipole 1 3 -22690 0.00 70.50 300.00
dipole 1 4 -22690 0.00 70.50 180.00
dipole 2 3 -20734 0.00 90.00 270.00
dipole 2 4 -20734 0.00 90.00 210.00
dipole 3 4 -20734 0.00 90.00 150.00
}
```

In the simulation, several options are considered for heteronuclear decoupling. Three pulse sequences are available:

```
proc pulseseq_free {} {
  global par
  acq_block {
    delay $par(tsw)
  }
}
Free evolution

proc pulseseq_cw {} {
  global par
  acq_block {
    pulse $par(tsw) 0 0 $par(rf) 0
  }
}
Continuous-wave decoupling

proc pulseseq_tppm {} {
  global par
  acq_block {
    pulse $par(t180) 0 0 $par(rf) $par(tppm_angle)
    pulse $par(t180) 0 0 $par(rf) [expr -$par(tppm_angle)]
  }
}
Two-pulse phase modulation
```

The main procedure is written such that three consecutive simulations are carried out, one for each type of acquisition.

- Compare the simulated spectrum with and without decoupling, using a large spectral width for acquisition. What does the undecoupled spectrum look like?

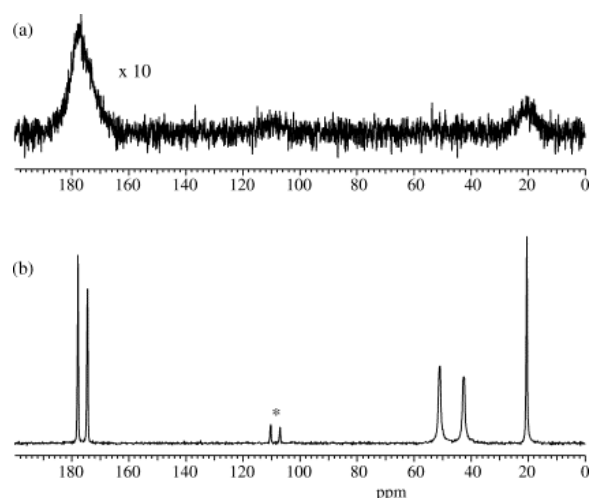
An experimental comparison of decoupled and undecoupled spectra is shown in Fig. 4.

The two decoupling schemes do not have the same performance. This is best observed with a reduced spectral width for acquisition (e.g., equal to the spinning frequency).

- Compare the CW and TPPM spectra, with and without CSA for the  $^1\text{H}$  spins. Try also to remove the dipolar interaction between protons. The angle for the TPPM decoupling scheme can also be optimised.

In the solid state at non-cryogenic temperatures, methyl groups are usually hopping fast.

- How would this hopping motion affect the effective dipolar interactions? How can this be accounted for in the simulation?



**Fig. 4.** Fig. 1.  $^{13}\text{C}$  CP/MAS spectra (spin rate,  $\nu_r=5.1$  kHz,  $^{13}\text{C}$  Larmor frequency, 75.40 MHz) of a glycine/alanine mixture obtained (a) without  $^1\text{H}$  decoupling, and (b) using continuous wave  $^1\text{H}$  decoupling ( $^1\text{H}$  nutation rate,  $\nu_{\text{rf}}$ , 60 kHz). The asterisk marks spinning sidebands from the carbonyl resonances. Reproduced from P. Hodgkinson, Prog. Nucl. Magn. Reson. Spectrosc. 46, 197, (2005).

#### 4.3. $^1\text{H}$

File: mas\_1H.in, mas\_gcompute\_freq.in

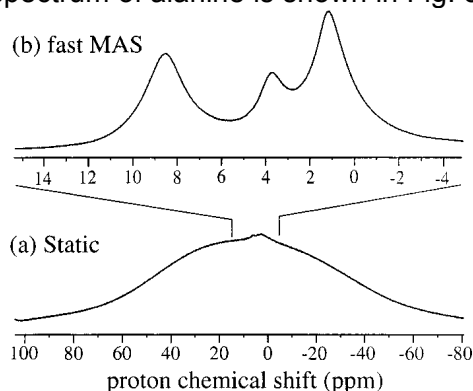
System: up to 7  $^1\text{H}$  spins, corresponding to a molecule of alanine in the solid state

Interactions: DD

The system now consists of a selection of protons from a crystal structure of L-alanine. The spin systems are defined in separate files, which can be called with:

source /Users/jdumez/Downloads/lalnH3\_CS.spinsys

An example of experimental spectrum of alanine is shown in Fig. 5.



**Fig. 5.** One-dimensional proton spectra of powdered L-alanine. (a) Static spectrum. (b) MAS spectrum at 30 kHz rotor spinning frequency. The spectra were acquired at 500 MHz using a one-pulse sequence. Reproduced from A. Lesage *et al.*, J. Am. Chem. Soc. 123, 5747 (2003).

It is difficult to obtain a realistic simulation for  $^1\text{H}$  spins, because crystals typically contain a dense network of strongly coupled spins.

- Start with the file mas\_1H.in, and the 4-spin system. How does the simulated spectrum compare to an experimental one?
- Increase the number of spins to 5. How does the simulation time increase? How does the simulation time scale with the number of points in the fid?

Because of these unfavourable properties, a more efficient simulation algorithm will be used. In the file mas\_gcompute\_freq.in, a frequency domain calculation is used (see 2.2), together with the gcompute algorithm. This requires the spectral width to be the product of the spinning frequency and the number of gamma angles:

```

proton_frequency 1000e6
sw               160000
variable tsw     1e6/sw
np              1024*64
spin_rate       10000

variable lb      10
variable zfill   4096

crystal_file     rep256
gamma_angles     16
method           gcompute freq

```

Note that a very large number of points are required for a correct binning of the frequencies. But the simulation time is virtually independent of the number of points.

- Increase the number of protons in the simulation. How does the lineshape evolve?
- Consider the effect of the spinning frequency. Compare with 4.1. Which spinning frequency is required to observe well resolved peaks for the three sites?

There are several algorithms implemented in SIMPSON to calculate propagators. Their performance depends on the computer and the available libraries. For example:

```
method           gcompute freq cheby1
```

uses a Chebyshev expansion of the exponential.

- Compare the simulation time for several options, which include: cheby1, pade, and taylor.

$^1\text{H}$  CSA parameters are rarely measured.

- Introduce a CSA tensor in the simulation. How does it influence the spectrum?

#### 4.4. Cross polarisation

File: mas\_13C\_CP.in

System: 1  $^{13}\text{C}$  spin and 1  $^1\text{H}$  spin

Interactions: DD

In this final example, the simulation does not yield a spectrum but instead the trajectory of the  $^{13}\text{C}$  transverse magnetization, for an initial state that consists of  $^1\text{H}$  transverse magnetization,

```

start_operator I2x
detect_operator I1p

```

under continuous irradiation on both channels:

```

proc pulseseq {} {
  global par

  acq_block {
    pulse $par(tsw) $par(rfC) x $par(rfH) x
  }
}

```

- Consider the effect of the relative intensity of the  $^{13}\text{C}$  and  $^1\text{H}$  irradiation.
- Run a powder-averaged simulation. How does the transfer curve change?

#### 4.5. To go further

With all the ingredients introduced in this tutorial, a CP MAS experiment on a  $\text{C}_n\text{H}_m$  system may be programmed very efficiently. One can also plot the transverse dephasing time of the  $^{13}\text{C}$  magnetisation for a  $\text{CH}_m$  system, using various decoupling schemes.