Numeric-Symbolic Solutions of the Liouville-von Neumann Equation, Constrained Optimization, and NMR

Christopher Anand[1], Alex Bain[2], Zhenghua Nie[3]

[1]Department of Computing and Software
[2]Department of Chemistry & Chemical Biology
[3]School of Computational Engineering and Science
McMaster University

May 13, 2011
Southern Ontario Numerical Analysis Day

Outline

Motivation

Simulating NMR

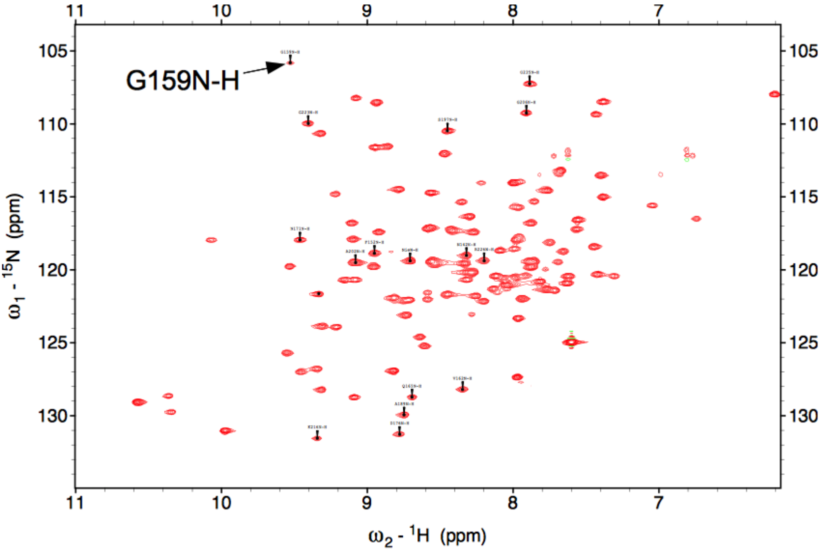
Solution of Single Spin System

Fitting Relaxation Time

Designing Optimal Broadband Universal Rotation Pulses

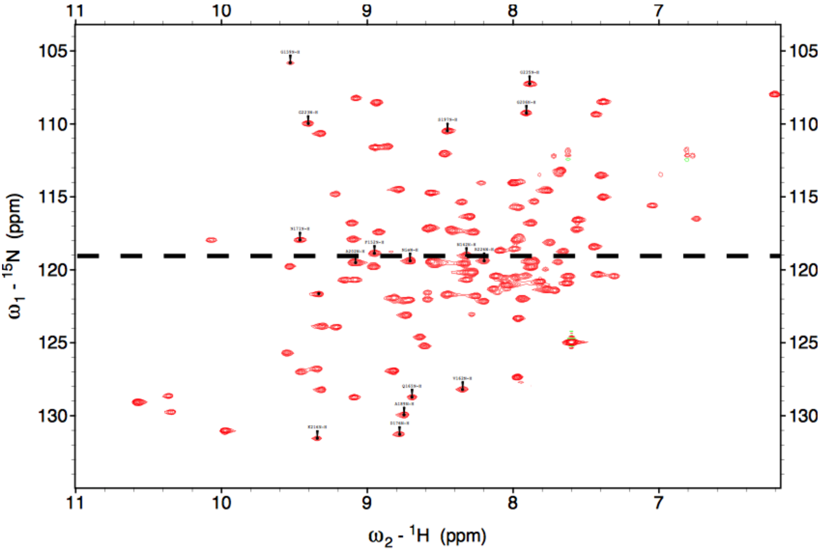
Conclusion & Future Works

Measuring Relaxation Time



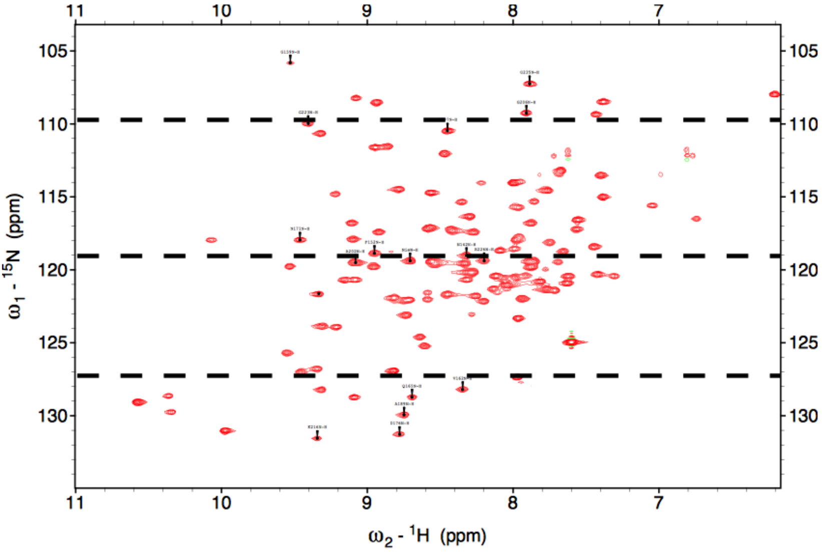
2D spectroscopy of the Iα of Protein Kinase A (PKA). (Provided by Dr. Melacini's Lab)

Measuring Relaxation Time



2D spectroscopy of the Iα of Protein Kinase A (PKA). (Provided by Dr. Melacini's Lab)

Measuring Relaxation Time



2D spectroscopy of the Iα of Protein Kinase A (PKA). (Provided by Dr. Melacini's Lab)

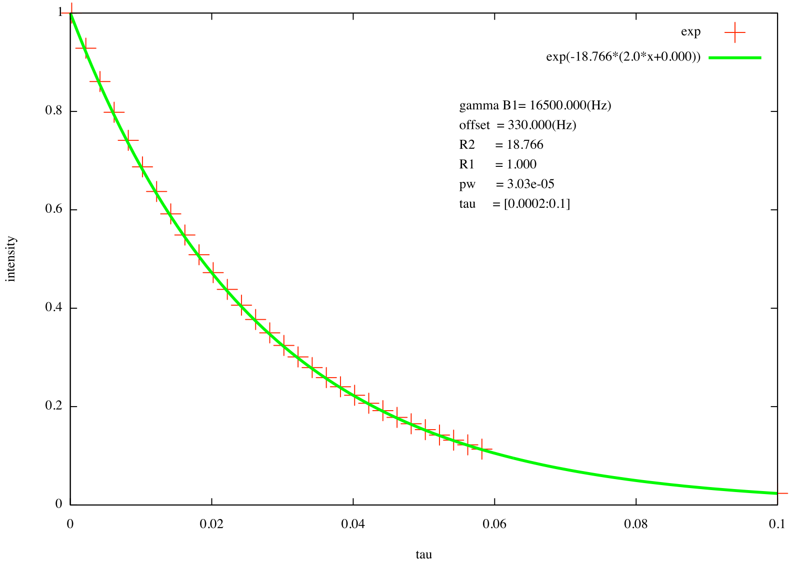
Effect of Offset

The power cannot be infinity.

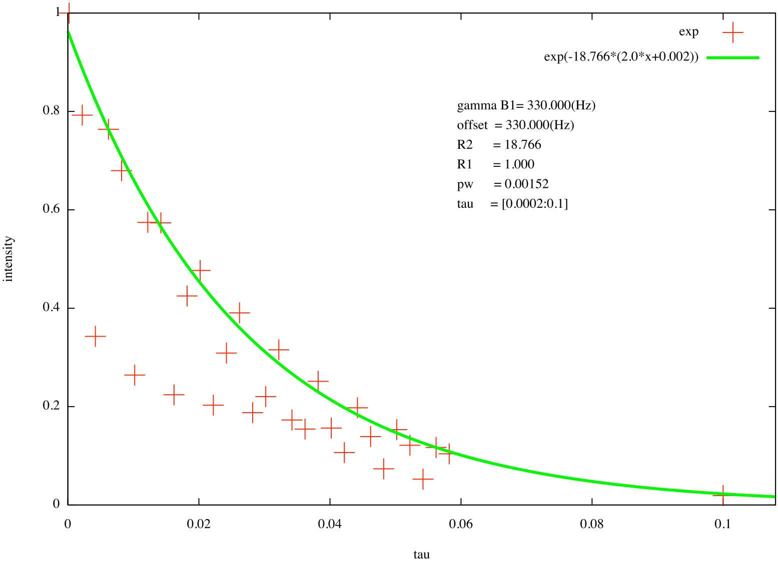
- Some probes require low power;
- Maximum power output by the amplifier is limited;
- Sample may boil if the power is too high;

If sample is a large molecule, the range of offset frequencies may be wide. For example, $\Delta\omega = \gamma B_1$. Offset will significantly affect the measurements.

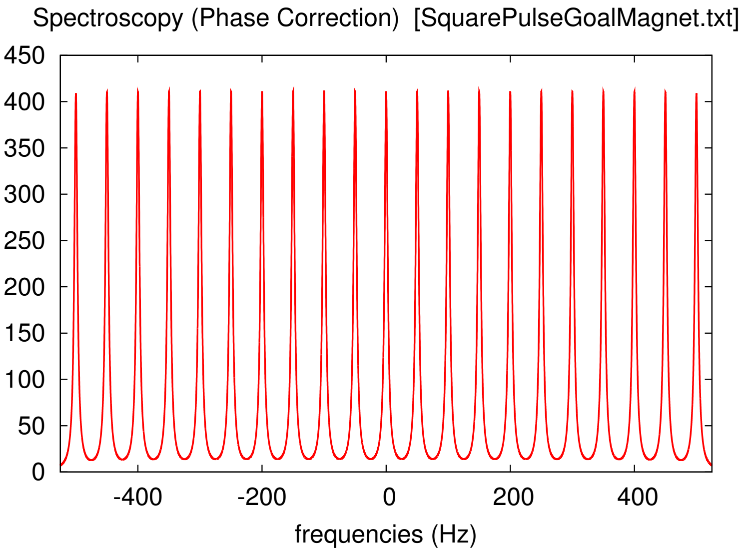
Ideal Experiments



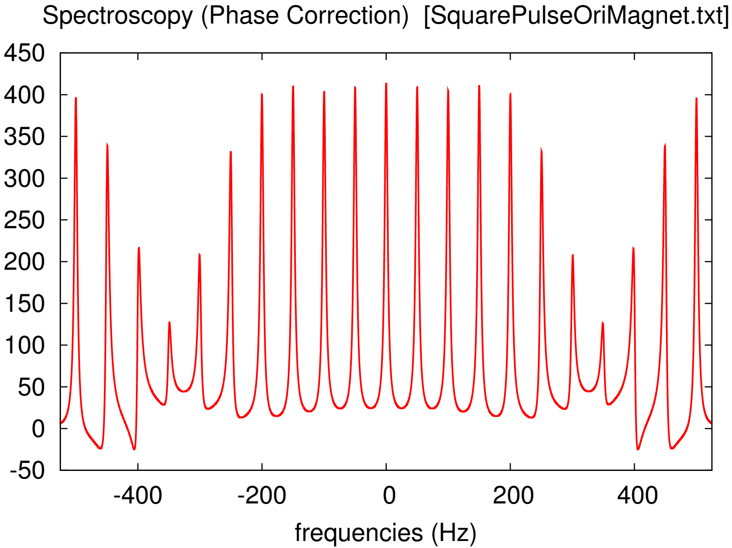
Real Experiments



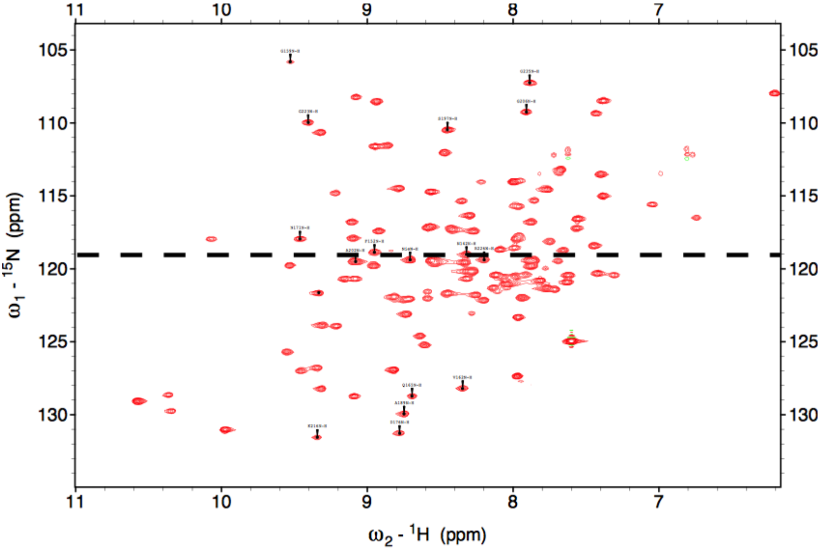
Ideal Experiments



Real Experiments

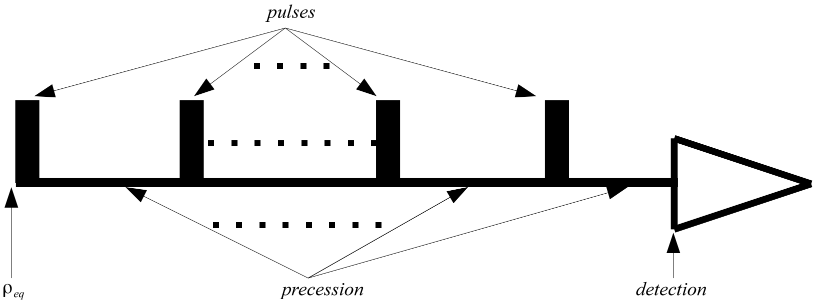


Measuring Relaxation Time



Objective: Can we measure the relaxation time of all nuclei in one time?

Calculation of NMR Using Liouville-von Neumann Equation



- Vector of observables (ρ) in Liouville space method
- Evolution of the spin system in Liouville space method

$$\frac{d\,\rho}{d\,t} = -i(\mathcal{L}+\mathcal{B})\rho - \mathcal{R}(\rho - \rho_{eq}) \quad \textit{(Inhomogeneous)}$$

$$\frac{d\,\rho}{d\,t} = (-i(\mathcal{L}+\mathcal{B}) - \mathcal{R})\rho \quad \textit{(Homogeneous)}$$

Solution of the Liouville Space Method

Precession:

$$\frac{d\rho}{dt} = (-i(\mathcal{L} + \mathcal{B}) - \mathcal{R})\rho$$

Solution of a rectangular pulse:

$$\rho(t) = e^{(-i(\mathcal{L}+\mathcal{B})-\mathcal{R})t}\rho(0)$$

Solution of a shaped pulse or pulse sequence:

$$\rho(t_p) = \hat{L}_N \cdots \hat{L}_1 \rho(0)$$

with

$$\hat{L}_j = e^{(-i(\mathcal{L}+\mathcal{B}_j)-\mathcal{R})\Delta t_j}$$

Solution of the Liouville Space Method (cont.)

- $MatrixExponential((-i(\mathcal{L}+\mathcal{B})-\mathcal{R})t)$
- $A = PDP^{-1} \Rightarrow e^{A} = Pe^{D}P^{-1}$ (spin echo experiments)
  $A = PDP^{-1} \Rightarrow A^{n} = PD^{n}P^{-1}$ (CPMG experiments)
- $e^{(A+B)t} \approx e^{At}e^{Bt}$ when t is small enough. (design of optimal pulses)
- $\frac{d\,\rho}{d\,t} \approx \frac{\rho_a - \rho_b}{\Delta t}$ (steady state)

Computing $Exp(\mathbf{A}t)$ via Lagrange Interpolation

Theorem

If A is an $n \times n$ matrix with n distinct eigenvalues $\lambda_1, \lambda_2, \cdots, \lambda_n$, then we have

$$e^{tA} = \sum_{k=1}^{n} e^{t\lambda_k} L_k(A),$$

where the $L_k(A)$ are Lagrange interpolation coefficients given by

$$L_k(A) = \prod_{j=1, j\neq k}^{n} \frac{A - \lambda_j I}{\lambda_k - \lambda_j}$$

for $k = 1, 2, \cdots, n$.

– *T. M. Apostol, Some Explicit Formulas for the Exponential Matrix e^{tA}, The American Mathematical Monthly 76 (1969) 289 - 292.*

Bloch Equations and Its Solution

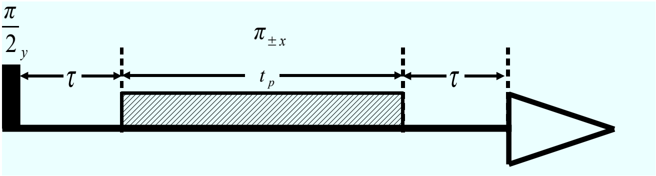
$$\frac{d}{dt}\begin{pmatrix} M_x \\ M_y \\ M_z \\ M_e \end{pmatrix} = \begin{pmatrix} -R_2 & -\omega & \gamma B_1 \sin\phi & 0 \\ \omega & -R_2 & -\gamma B_1 \cos\phi & 0 \\ -\gamma B_1 \sin\phi & \gamma B_1 \cos\phi & -R_1 & R_1 \\ 0 & 0 & 0 & 0 \end{pmatrix} \begin{pmatrix} M_x \\ M_y \\ M_z \\ M_e \end{pmatrix} \tag{1}$$

A is used to represent the coefficient matrix. When **A** is constant, the solution is

$$\mathbf{M}(t) = e^{\mathbf{A}t}\mathbf{M}(0).$$

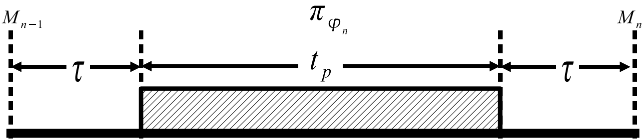
The size of the file to store $e^{\mathbf{A}t}$ solved by `MatrixExponential` of Maple is 11M.

Hahn Echo and Its Solution



$$\mathbf{M}(2\tau + t_p) = e^{\mathbf{A}(\gamma \mathbf{B_1}=\mathbf{0})\tau}.e^{\mathbf{A}(\gamma \mathbf{B_1}=\mathbf{b1})t_p}.e^{\mathbf{A}(\gamma \mathbf{B_1}=\mathbf{0})\tau}.\mathbf{M}(0) \qquad (2)$$

CPMG and Its Solution



$$\mathbf{M}_n = \mathbf{E}_n \mathbf{M}_{n-1}$$

$$\mathbf{E}_n = \mathbf{E}_{fid} \mathbf{E}_{\pi}(\varphi_n) \mathbf{E}_{fid}$$

$$\mathbf{M}_n = \mathbf{E}^n \mathbf{M}_0 \tag{3}$$

Fitting Problem

$$\min \sum_{i=1}^{n} \left|\left| M_{\text{meas}}(i) - I_0 \sqrt{M_{x,i}^2 + M_{y,i}^2} \right|\right|^2$$

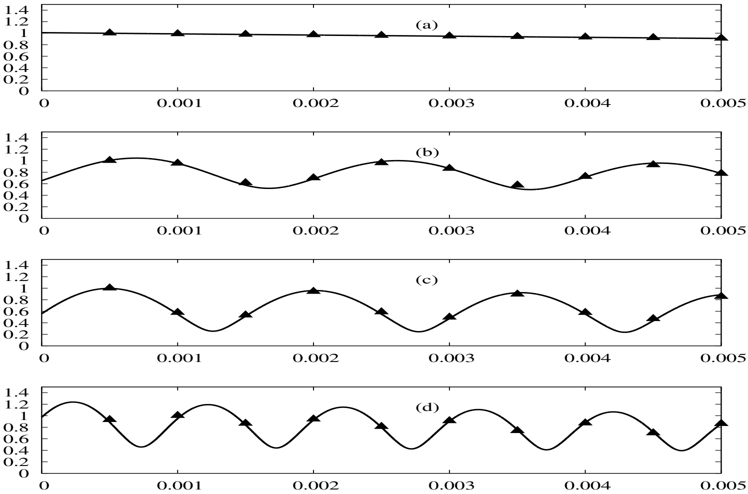
Subject to Eq. (1) which is an first-order Ordinary Differential Equation (ODE).

Reformed Fitting Problem

$$\min \sum_{i=1}^{n} \left\| M_{\text{meas}}(i) - I_0 \sqrt{M_{x,i}^2 + M_{y,i}^2} \right\|^2$$

Subject to Eq. (2) or Eq. (3).

Fitting Results



Design Optimal Broadband Universal Rotation Pulses

$$\frac{d\rho}{dt} = (-i(\mathcal{L} + \mathcal{B}(t)) - \mathcal{R})\rho$$

$$\rho(t_p) = \hat{L}_N \cdots \hat{L}_1 \rho(0)$$

Two Models:

$$\min \quad \sum\sum ||\rho(t_p) - \rho_{\text{target}}||^2 \qquad \text{(Vector Model)}$$

and

$$\min \quad \sum\sum ||\hat{\mathbf{L}}_{\text{effective}} - \hat{\mathbf{L}}_{\text{target}}||^2 \qquad \text{(Matrix Model)}$$

Subject to:

$$\sum_{i=1}^{N} \sqrt{br_i^2 + bi_i^2} \leq MTOTAL$$

$$\sqrt{br_i^2 + bi_i^2} \leq \gamma B_1^{max} \qquad (i \text{ from } 1 \text{ to } N)$$

Derivatives of the Effect of a Shaped Pulse

$$
\begin{aligned}
\frac{\partial \hat{L}_{\text{effective}}}{\partial br_i} &= \hat{L}_N \cdot \hat{L}_{N-1} \cdots \frac{\partial \hat{L}_i}{\partial br_i} \cdots \hat{L}_2 \cdot \hat{L}_1 \\
\frac{\partial^2 \hat{L}_{\text{effective}}}{\partial br_i^2} &= \hat{L}_N \cdot \hat{L}_{N-1} \cdots \frac{\partial^2 \hat{L}_i}{\partial br_i^2} \cdots \hat{L}_2 \cdot \hat{L}_1 \\
\frac{\partial^2 \hat{L}_{\text{effective}}}{\partial br_i \partial bi_i} &= \hat{L}_N \cdot \hat{L}_{N-1} \cdots \frac{\partial \hat{L}_i^2}{\partial br_i \partial bi_i} \cdots \hat{L}_2 \cdot \hat{L}_1 \\
\frac{\partial^2 \hat{L}_{\text{effective}}}{\partial br_i \partial br_j} &= \hat{L}_N \cdots \frac{\partial \hat{L}_i}{\partial br_i} \cdot \hat{L}_{i-1} \cdots \hat{L}_{j+1} \cdot \frac{\partial \hat{L}_j}{\partial br_j} \cdots \hat{L}_1 \\
\frac{\partial^2 \hat{L}_{\text{effective}}}{\partial br_i \partial bi_j} &= \hat{L}_N \cdots \frac{\partial \hat{L}_i}{\partial br_i} \cdot \hat{L}_{i-1} \cdots \hat{L}_{j+1} \cdot \frac{\partial \hat{L}_j}{\partial bi_j} \cdots \hat{L}_1 \\
\cdots\cdots &
\end{aligned}
$$

$$(i \in [1..N], j \in [1..(i-1)])$$

cost: $O(N^3)$ matrix multiplications of $\hat{L}_i$ of $4^n \times 4^n$.

Efficiently Computing Derivatives

Step 1 (*Cost:* $O(N)$)

$$\mathbf{U}_i = \hat{L}_N \cdot \hat{L}_{N-1} \cdots \hat{L}_{i+1}$$

$$\mathbf{V}_i = \mathbf{U}_i^{-1} = \hat{L}_i^{-1} \cdot \hat{L}_{i+1}^{-1} \cdots \hat{L}_{N-1}^{-1} \cdot \hat{L}_N^{-1}$$

(i from N to 1)

Step 2 (*Cost:* $O(N^2)$)

$$\hat{L}_{\text{effective}} = \mathbf{U}_1 \cdot \hat{L}_1$$

$$\mathbf{W1}_i = \mathbf{U}_i \cdot \frac{\partial \hat{L}_i}{\partial br_i} \cdot \mathbf{V}_i$$

$$\mathbf{W3}_i = \mathbf{V}_i \cdot \hat{L}_{\text{effective}}$$

$$\frac{\partial \hat{L}_{\text{effective}}}{\partial br_i} = \mathbf{W1}_i \cdot \hat{L}_{\text{effective}}$$

$$\frac{\partial^2 \hat{L}_{\text{effective}}}{\partial br_i^2} = \mathbf{U}_i \cdot \frac{\partial^2 \hat{L}_i}{\partial br_i^2} \cdot \mathbf{W3}_i$$

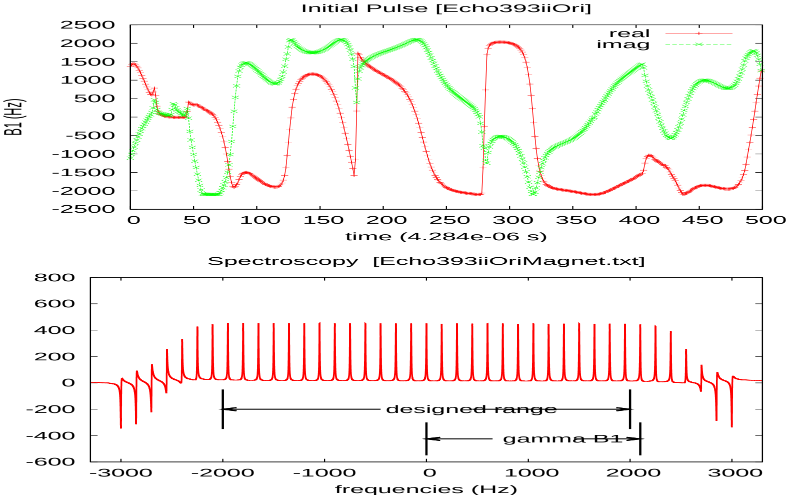
$$\frac{\partial^2 \hat{L}_{\text{effective}}}{\partial br_i \partial br_j} = \mathbf{W1}_i \cdot \frac{\partial \hat{L}_{\text{effective}}}{\partial br_j}$$

$$\frac{\partial^2 \hat{L}_{\text{effective}}}{\partial br_i \partial bi_j} = \mathbf{W1}_i \cdot \frac{\partial \hat{L}_{\text{effective}}}{\partial bi_j}$$

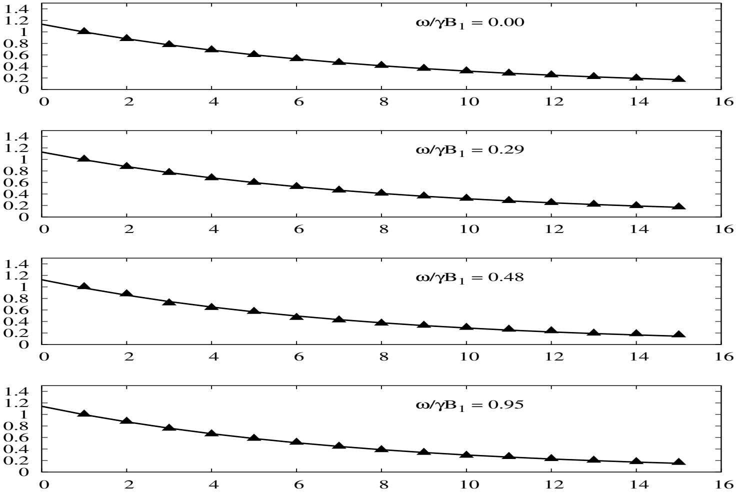
$$\cdots\cdots$$

(i from 1 to N, j from 1 to (i-1))

Spectroscopy Using Optimal Broadband Universal Rotation Pulses



CPMG Using Optimal Broadband Universal Rotation Pulses



Conclution & Future Works

- The exact symbolic solution of the Bloch equations is given in the Lagrange form.
- We are able to apply this exact solution to manipulate arbitrary pulse sequences.
- Combined with complicated data processing, simple experiments such as rectangular pulses can still provide reliable estimates of transverse relaxation in a wide range.
- We are able to design optimal universal shaped pulses with the full solution of the Bloch equations via a second-order optimizer.
- These optimal shaped pulses work similar as rotation pulses and offer more uniform spectra within the designed range than other published pulses.
- In the future, we will explore the limits of designing optimal pulses and extend these methods to solve the Liouville-von Neumann equation of large spin systems.

Reference

1. *Alex D. Bain, Christopher Anand, Zhenghua Nie, Exact Solution to the Bloch Equations and Application to the Hahn Echo, Journal of Magnetic Resonance, 206 (2010) 227-240. (doi:10.1016/j.jmr.2010.07.012)*
2. *Alex D. Bain, Christopher Kumar Anand, Zhenghua Nie, Exact Solution of the CPMG Pulse Sequence with Phase Variation Down the Echo Train: Application to* R_2 *Measurements, Journal of Magnetic Resonance, 209 (2011) 183-194. (doi:10.1016/j.jmr.2011.01.009)*

Thanks!

Abstract

In NMR, a spin system is governed by the Liouville-von Neumann equation which is a set of first-order ordinary differential equations. The spin system will experience different Hamiltonians during a NMR experiment. At the end of a NMR experiment (after a pulse sequence), we obtain signals which can be seen as the integral of the Liouville-von Neumann equation from the equilibrium state. If we set up optimization problems to fit experiment data or design new experiments, the objective functions will depend on the integral of the Liouville-von Neumann equation. Our method to solve these problems is to symbolically solve the ODE system before we solve the optimization, so as to eliminate the process to numerically solve the ODEs during solving the problems. The symbolic solution of a spin system will be huge, even for the simplest (e.g., spin-1/2) system. Since it is impractical to directly substitute the symbolic solution into the unconstrained objective function, we instead add them as equality constraints resulting in a much smaller problem. With the symbolic solutions of the ODEs, we are able to calculate exact derivatives which significantly improve the performance of the optimization and design universal rotation pulses (also called gate pulses in the quantum computing) which are independent of spin states. We will present examples of the single spin-1/2 system, the method is able to extend to large spin systems.