Optimal Control in Solid-State NMR

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Control

Quantum System
Outline:

- Brief introduction to the solid-state NMR spectroscopy
- Optimal control in solid-state NMR
- New solid-state NMR experiments, low-field NMR, DNP, and MRI
NMR spectroscopy: Uses magnetic fields and rf irradiation to manipulate nuclear spins

Polarization by B0
Rf irradiation

RF Pulse

Response

Niels Chr. Nielsen
Chemical Shift – the resonance frequency depends on the electronic surrounding

\[ B_0 \]

Very crowded for big molecules
Scalar couplings and dipolar cross-relaxation allows for communication between spins: 2D NMR

Through-bond (J) coupling

Through-space (dipole-dipole) coupling
Controls in liquid-state NMR spectroscopy

** STATIC FIELD **

\[ H = \omega_0 I_z \]

\[ H_\sigma = \omega_\sigma I_z \]

** CHEMICAL SHIFT **

** RF FIELD **

\[ H = 2\omega_{rf}\cos(\omega_c t) I_x \]

** Rotating frame: **

\[ H = \omega_{rf} I_x \]

** J COUPLING **

Generates two-spin operators, which may be used to drive coherence/polarization transfer between coupled spins

Rotations in 3D \((I_x, I_y, I_z)\) or \((I_x, 2I_y S_z, 2I_z S_z)\) operator spaces

Niels Chr. Nielsen
Structure of proteins in immobile environments

Membrane protein structures

GREEN SULFUR BACTERIA
Chlorobidum tepidum

Pedersen, Dittmer, Miller, and Nielsen, FEBS Lett., 2008

Amyloid fibril structures

Nielsen et al, Angew. Chem. 2009
For solids, anisotropic interactions destroy the resolution and the sensitivity is low.

dipolar coupling between protons:

- $120 \text{ kHz} @ 1.0 \text{ Å}$
- $40 \text{ kHz} @ 1.5 \text{ Å}$

solid-state NMR
no magic angle spinning
no $^1\text{H}-^1\text{H}$ decoupling
Origin to broadening: Chemical shielding anisotropy

The electrons shield the magnetic field – an orientation dependent manner.
Origin to broadening: Dipole-dipole couplings

\[ \beta = 0 \] in isotropic liquids

\[ \beta \neq 0 \] in solids or oriented media
Regain of resolution: Magic-angle spinning

Isotropic chemical shift
To mimic molecular motion we have to spin fast

4.0 mm → 15 kHz (1,400,000 x g)
3.2 mm → 25 kHz (2,700,000 x g)
2.5 mm → 35 kHz (3,500,000 x g)

a 3.2 mm rotor spinning at 24 kHz…

… has a speed of 240 m/s when it would roll on the floor …

… and needs only 46 hours to roll around the earth…

From van Rossum

inSPIN
Center for Insoluble Protein Structures

Niels Chr. Nielsen
Strong rf irradiation: to remove dipolar coupling

From van Rossum

720,844 mm$^3$
(1 mW / mm$^3$)

67 mm$^3$
(15 W / mm$^3$)

15 mm$^3$
(70 W / mm$^3$)
Effect of MAS and strong rf irradiation

A solid protein: Nanocrystals

A good high-resolution solid-state NMR spectrum brings us at the level where liquid-state NMR started

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Detailed structure information
- do we regain control with too much power

Chemical shielding tensor

Dipole-dipole coupling
Tayloring of the Hamiltonian: Recoupling of dipolar coupling interactions

Sample rotation destroys exploitation of dipolar couplings

\[ x \]

\[ + \]

\[ \times \]

\[ \text{for } p=-m \]
Accurate distance in MAS solid-state NMR: Recoupling without dipolar truncation – NMR robotics

Triple-Oscillating-Field-technique

\(^{13}\)C-\(^{13}\)C distances up to 5 Å with 0.1-0.2 Å accuracy

Khaneja and Nielsen, J. Chem. Phys., 2009
Optimal control design of NMR experiments

- improved sensitivity
- band selective operation
- less rf power consumption

\[ \rho_f = U \rho_i U^+ \]

Optimal control => Design of \( \bar{U} \)

\[ J_i = \phi_i - \lambda \int_0^T \sum_k u_k^2(t) dt \]

Final cost Running cost

Final cost \[ \phi_1 = \text{Tr} \left\{ C^\dagger \rho(T) \right\} \]

Kehlet et al, JACS, 2004

Free open source software at www.bionmr.chem.au.dk
A specific case – many exists
Traditional recoupling vs. optimal control

\[
\text{Gain: } \sim 100\% \\
\text{DCP, 10\% L} \\
\text{DCP, 5\% L} \\
\text{RAMP DCP}
\]

\[\text{Excitation time (ms)} \]

\[
\begin{align*}
\text{Efficiency} & = \omega_r \\
\text{adiabatic} & = 4\omega_r \\
\text{SS} & = 3\omega_r
\end{align*}
\]

\text{OPT CONTROL}

\[\text{Gain: } \sim 100\%\]
3D NCOCX: U-^{13}C,^{15}N-ubiquitin

Optimal Control

50-100% Higher sensitivity
Less sample heating (in the order of 1/10 – 1/4 power)

$^{15}\text{N} \rightarrow ^{13}\text{C}$ in NCO and NCA at highfield–sequence&robustness

Traditional recoupling vs. optimal control

Optimal control (OPT CONTROL) shows a gain of ~100% compared to traditional recoupling. Efficiency is plotted against excitation time (ms). The figure illustrates the comparison between different recoupling schemes: 4\omega_r, 3\omega_r, and others. The green line represents an adiabatic process with 5% L. The graph highlights the benefit of using optimal control in terms of efficiency improvement.
Composite Dipolar Recoupling
A marriage between Analytics and Optimal Control Numerics

Rf pulse:

\[
\frac{\pi}{2}y
\]

Improved rf inhom compensation

Dipolar recoupling:

\[
\frac{\pi}{2}y(\pi)x(\pi/2)y
\]

Improved \(\beta\)-angle compensation

ZQ-frame:
\[
\pi
\]

\(l_x \rightarrow S_x\)
Inspiration from optimal control: Composite Dipolar Recoupling

Better compensation towards orientation ($\beta$) variation of dipolar coupling
Optimal Control version with Reduced Dimensionality

Transfer Efficiency

Rf pulses

Recoupling sequence

Excitation time (ms)

DCP

OC\textsubscript{COMB}\textsubscript{9}

COMB\textsubscript{3}

Optimization of Effective Hamiltonians
Sensitivity-enhanced 2D solid-state NMR

\[ 2I_x S_x - 2I_y S_y \]

Only transfer of x- or y-component

\[ 2I_x S_x + 2I_y S_y + 2I_z S_z \]

Transfer of both components after \( t_1 \) evolution \( \Rightarrow \sqrt{2} \) sensitivity enhancement

Symmetry-based optimal control experiments for assignment

OC7 band-selective mixing for 2D CACB, CACX & 3D NCACB

Reducing the RF FIELD’s by a factor of 3-4 => only 10-15’th sample heating

Gain:
X 3-4

Low-field NMR using Optimal Control for Resolution Enhancement
Optimal control and DNP

S(Electron)-I(Nucleus) two-spin system

\[ H_0 = \Omega_n l_z + A S_z l_z + B S_z l_x \]

\[ \Omega_n/2\pi = -14 \text{ MHz} \quad ^1\text{H Zeeman} \]
\[ A/2\pi = 6 \text{ MHz} \]
\[ B/2\pi = 3 \text{ MHz} \]

\[ S_x \rightarrow l_z \]

A: secular part of hyperfine interaction
B: Pseudo secular part of hyperfine interaction

MW @ 9 GHz (X-band) – ca. 0.3 T (14 MHz) NMR

Jeschke, Schweiger, Mol Phys 1996
Maximov, Tosner, Nielsen, JCP (2008)
Optimal control in MRI: Excitation of a HALF BRAIN

Setup

Experiment at 16.4T

Initial optimization

Refined optimization
Talking about half brains – OC can do amazing things

What do you think this pulse will excite?

and NMR/MRI/DNP is an excellent field to the the capabilities in …

we provided open source Software – you do the rest

www.bionmr.chem.au.dk

Niels Chr. Nielsen
Thanks to ....

... and YOU for your attention