WHAT CAN WE LEARN ABOUT DIFFUSION BY NMR ?

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Content

1) Diffusion in NMR
2) Convection
3) The pulse sequences
4) Setup and analysis
5) Mutual diffusion and diffusion of pure compounds

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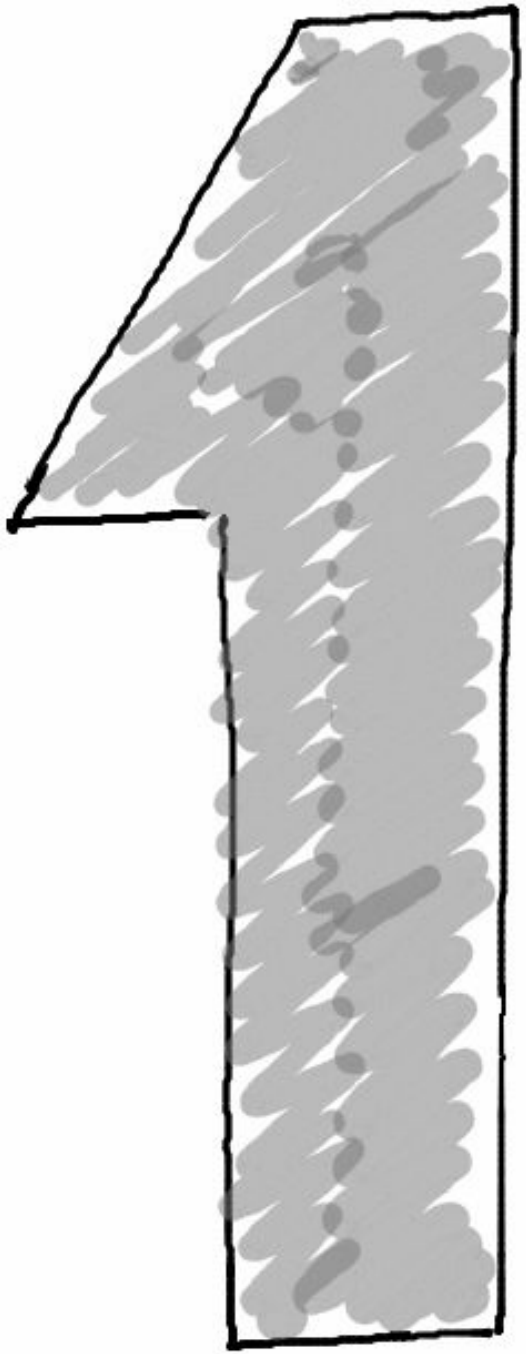

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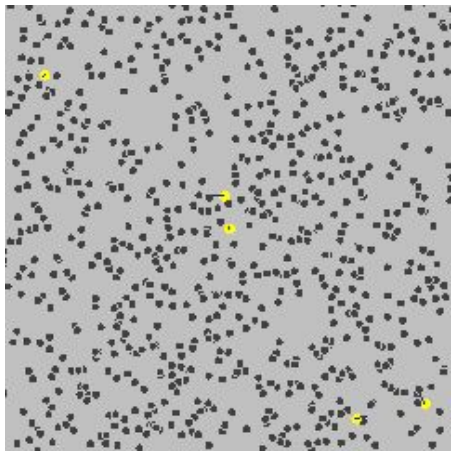
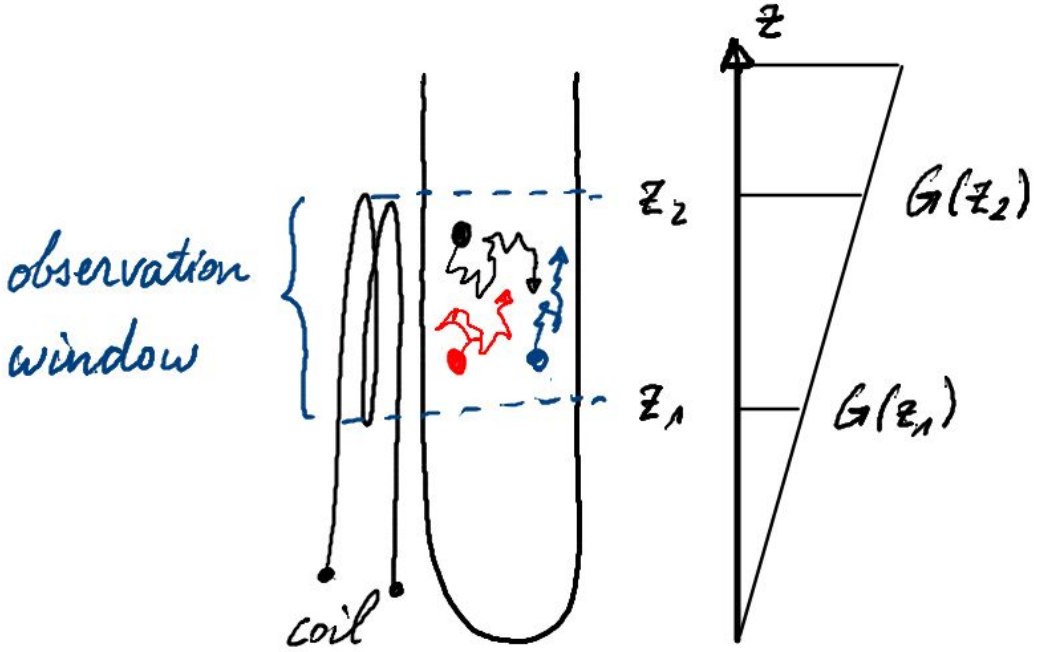
What is diffusion?

Ecuación Stokes-Einstein

$$D = \frac{k_b T}{6\pi\eta r_s}$$



Self-diffusion



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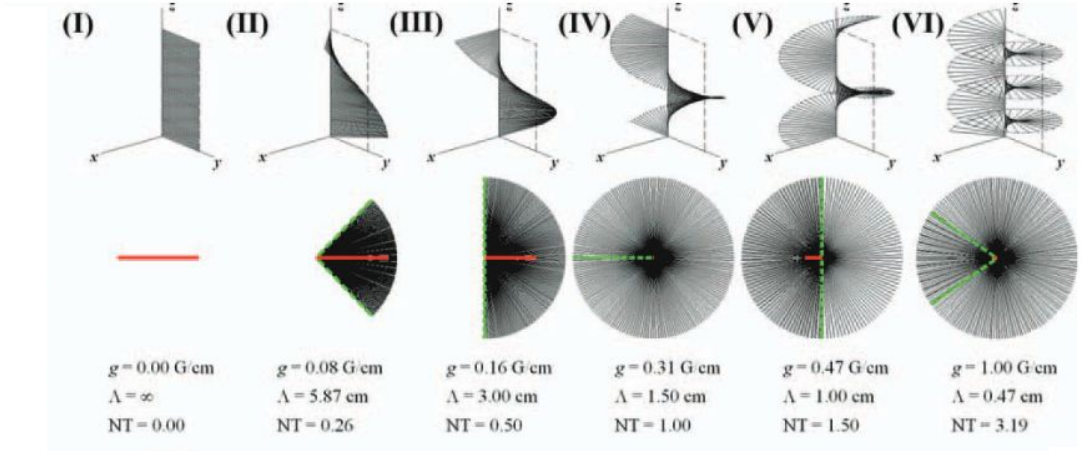
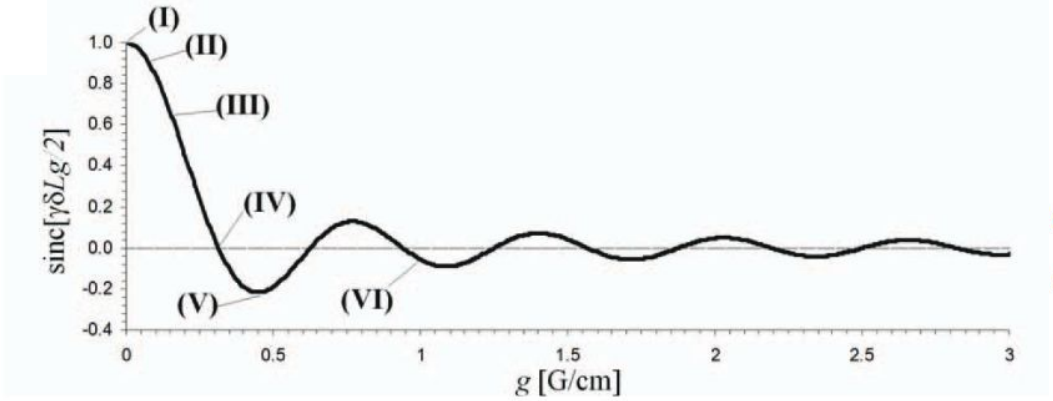
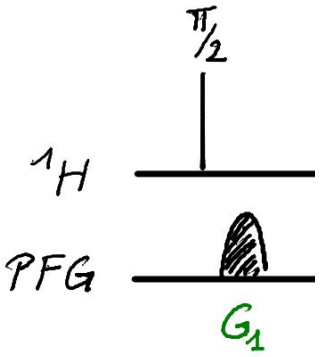
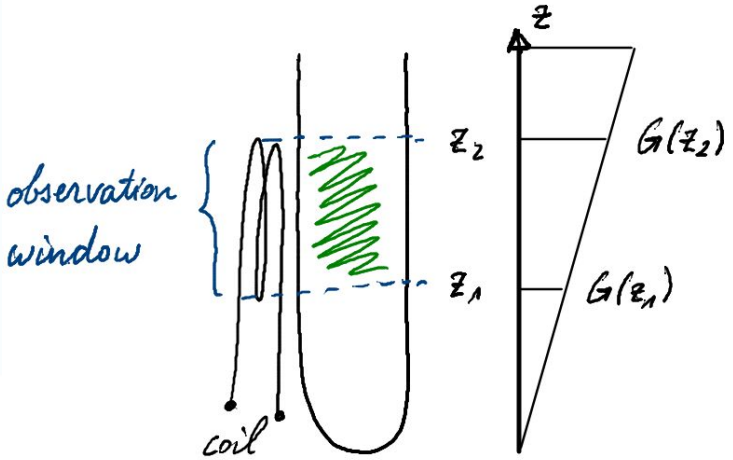
Pulse field gradients

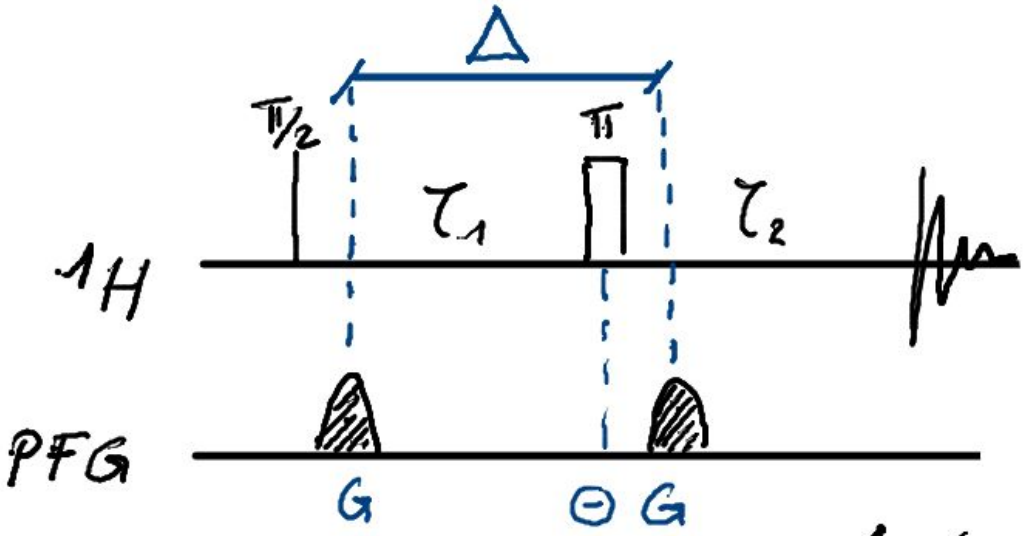




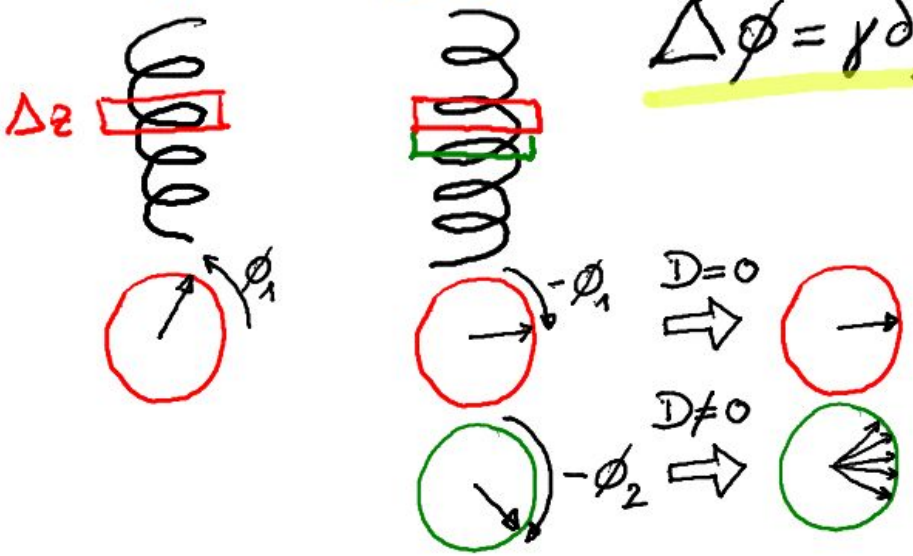


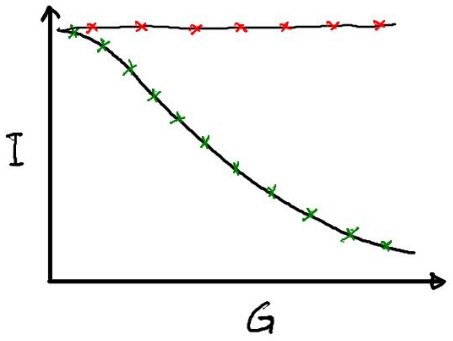


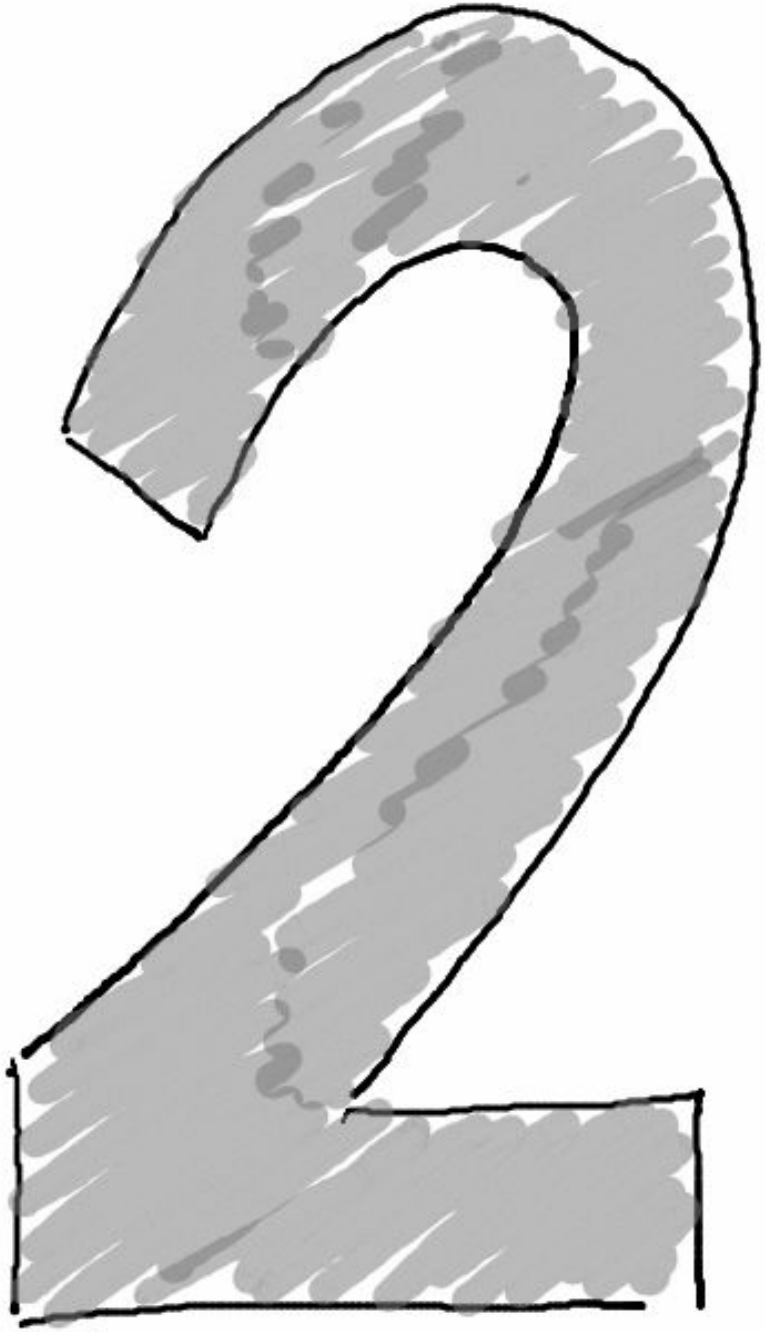
Diffusion measurement: gradient echo



$$\Delta\phi = \gamma \delta g \Delta z$$







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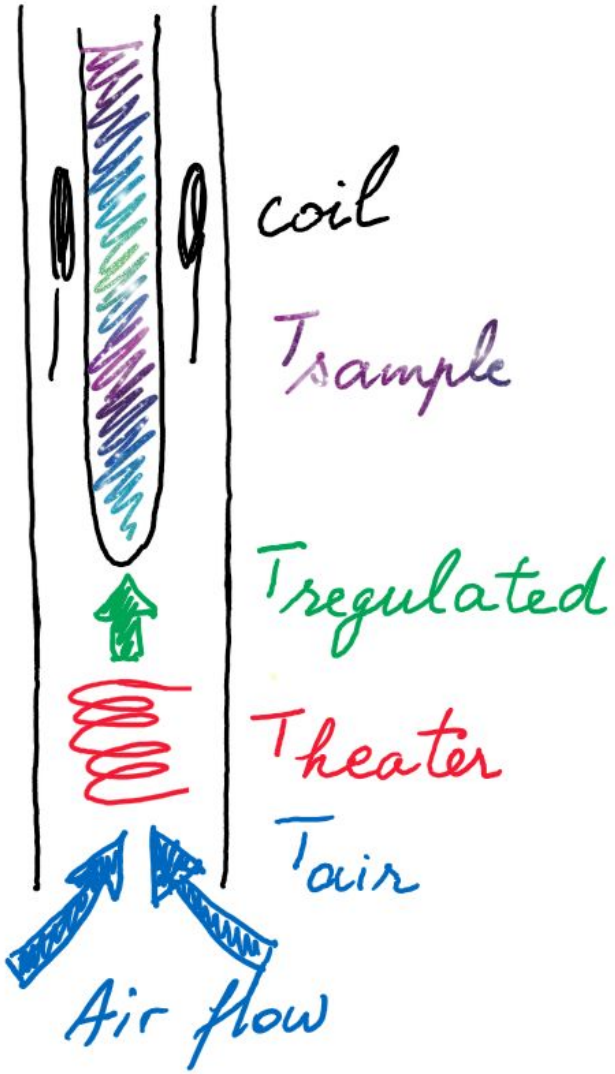
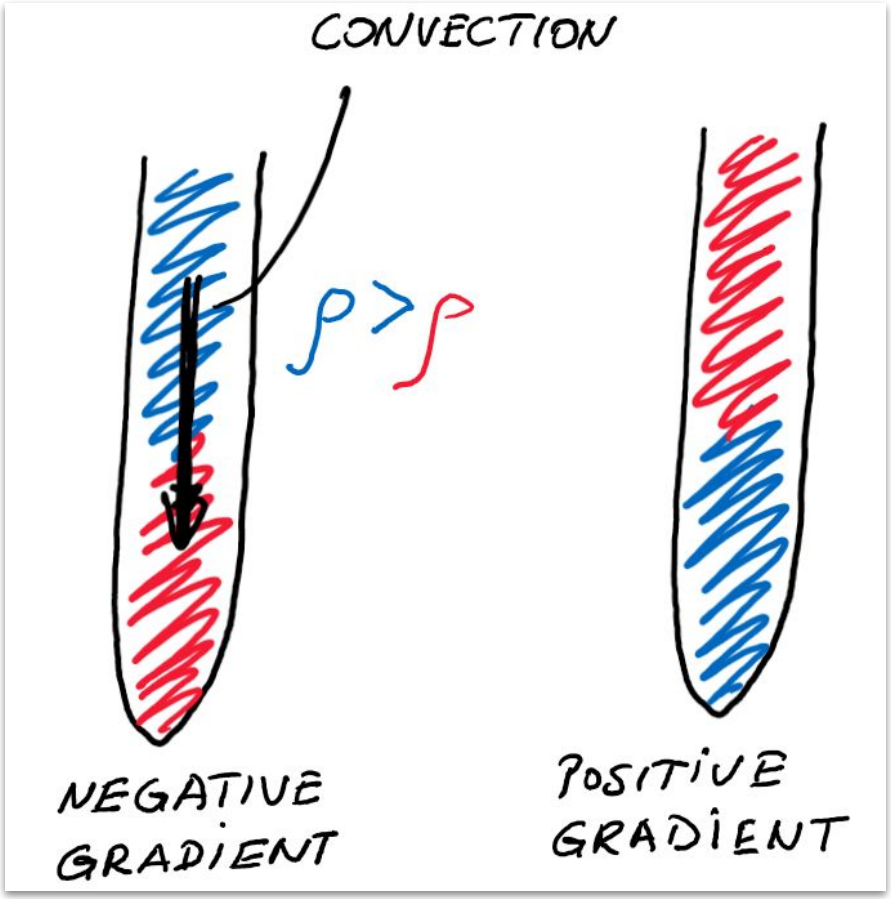
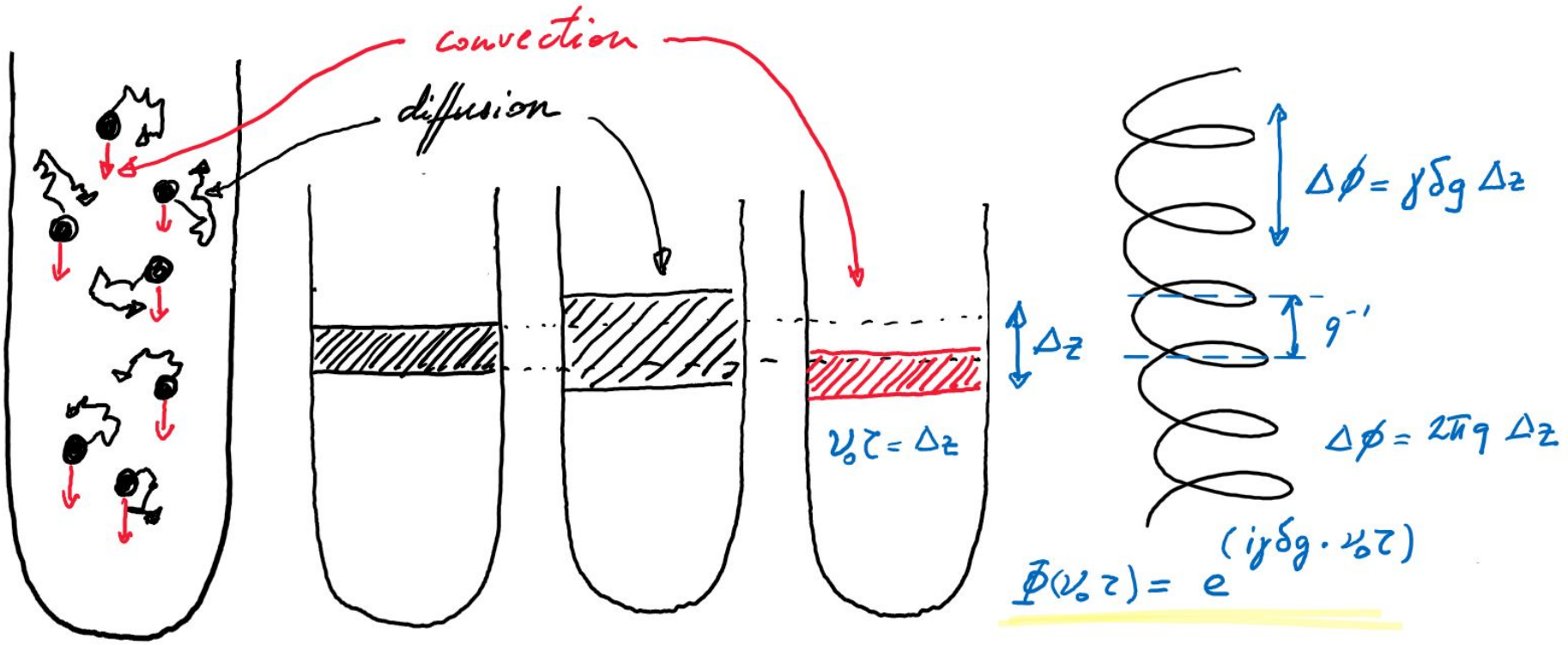
Convection


coil
T sample
T regulated
T heater
T air
Air flow


CONVECTION
ρ > ρ
NEGATIVE GRADIENT
POSITIVE GRADIENT

Diffusion vs convection



- Convection can be compensated
- Diffusion cannot

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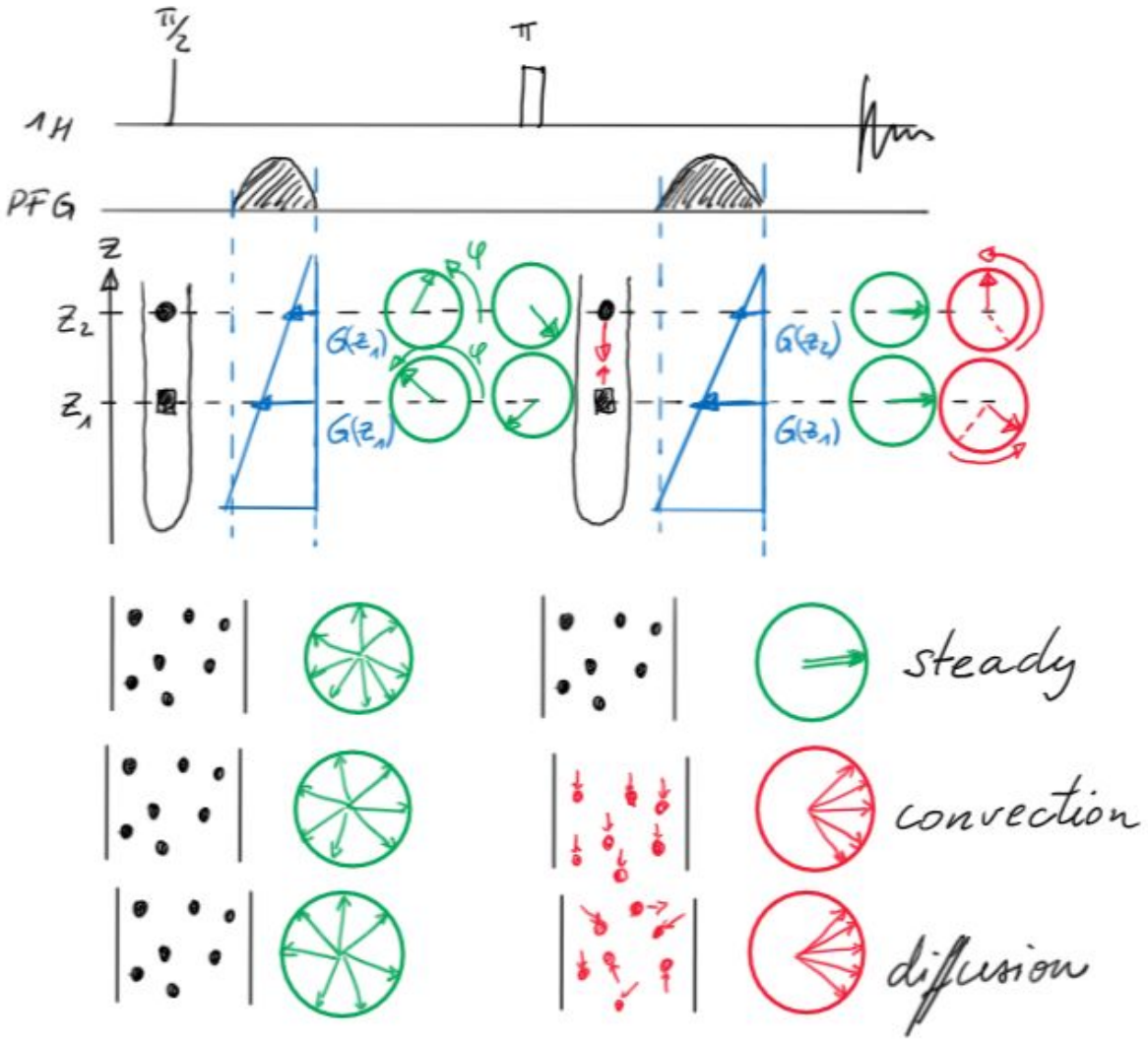
Diffusion vs convection



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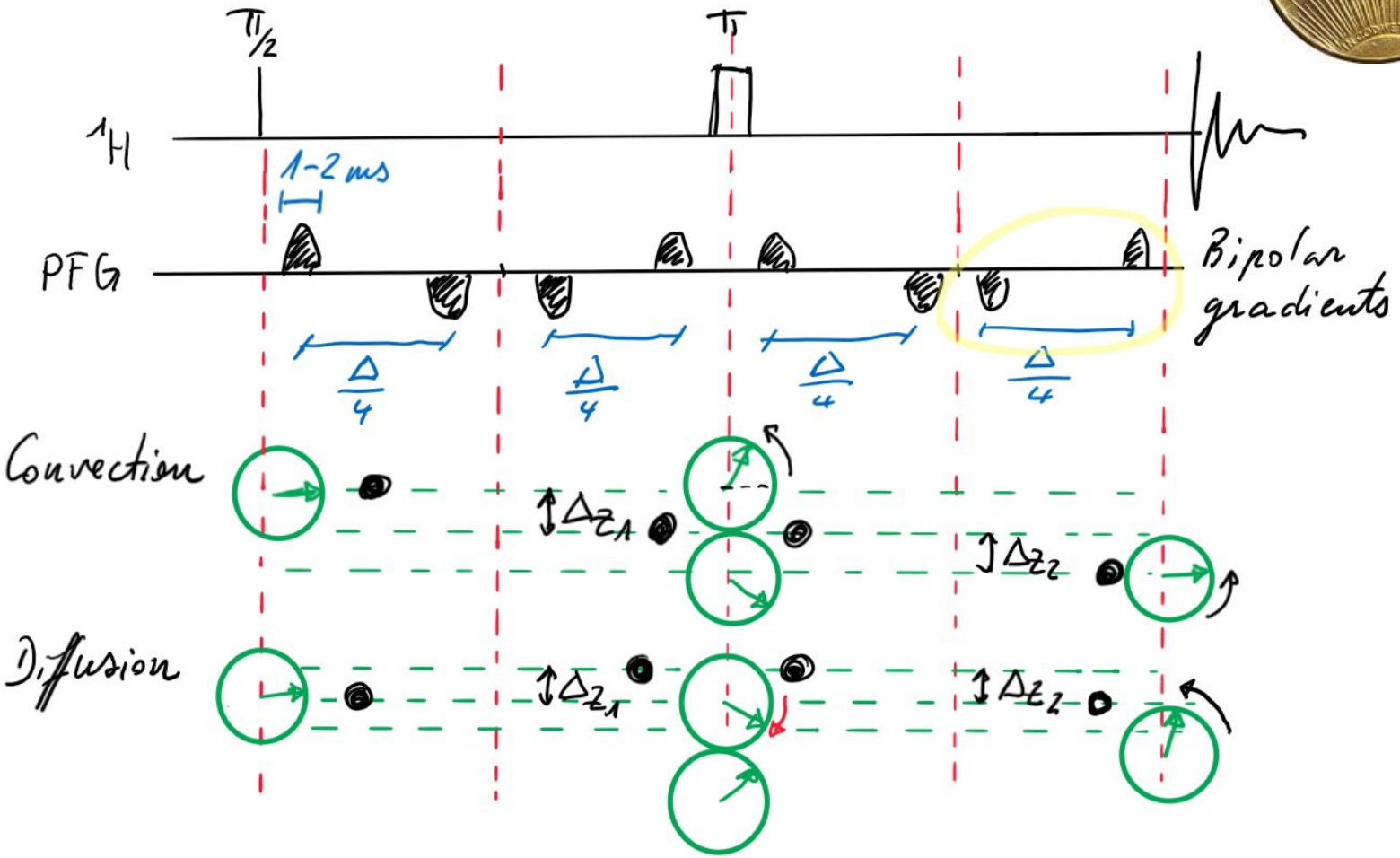
Convection compensated spin echo



- Convection is refocused
- Diffusion isn't

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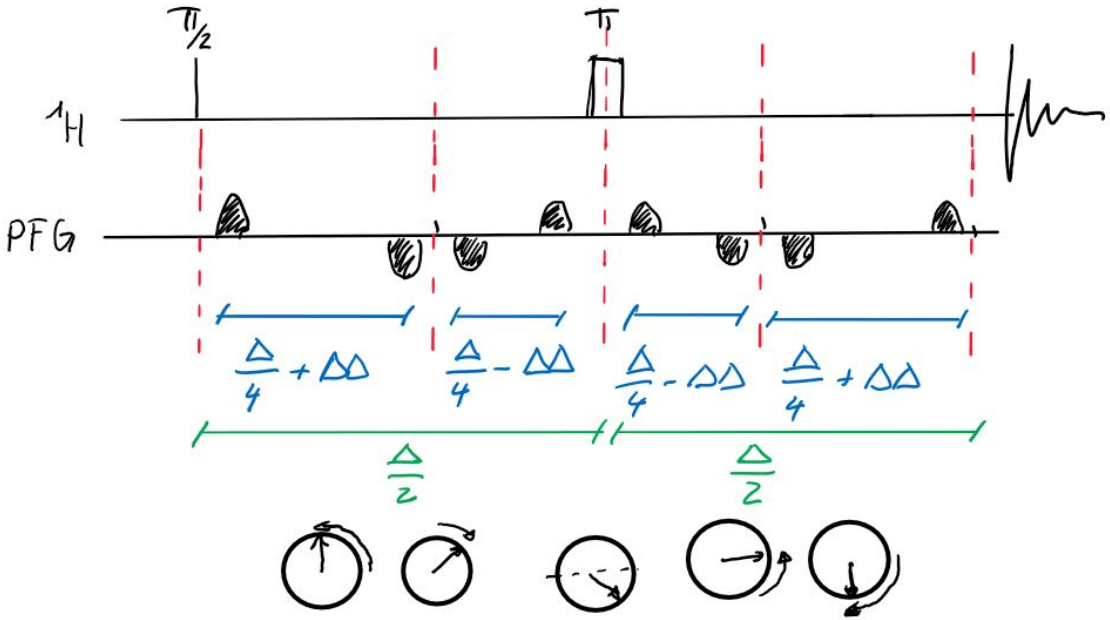
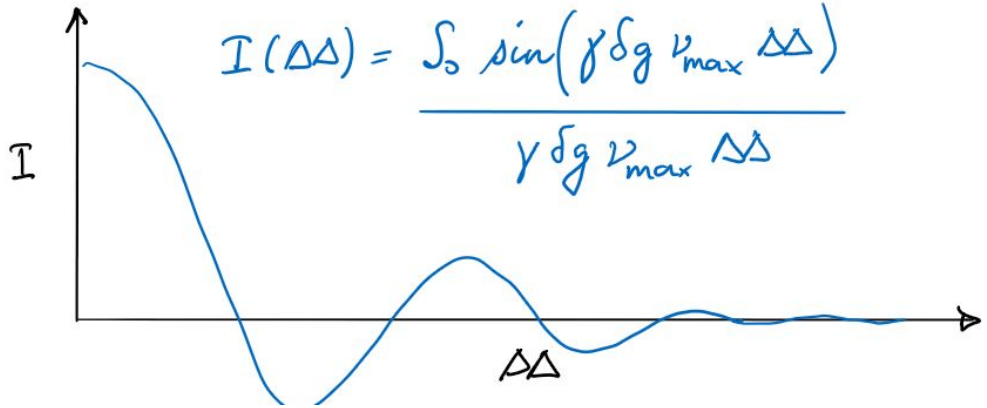
Measurement of convection





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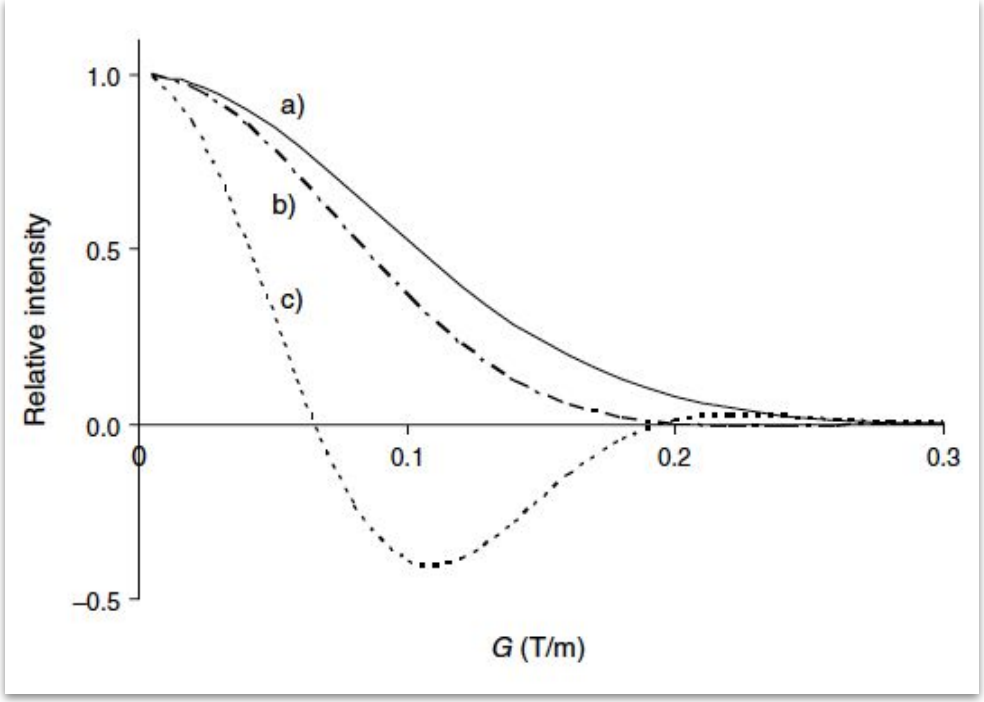
Diffusion + convection



$$I_G \approx I_{G=0} \cos(\gamma \delta G \Delta v) \exp\left(-(\gamma \delta G)^2 D\left(\Delta - \frac{\delta}{3}\right)\right)$$

convection diffusion

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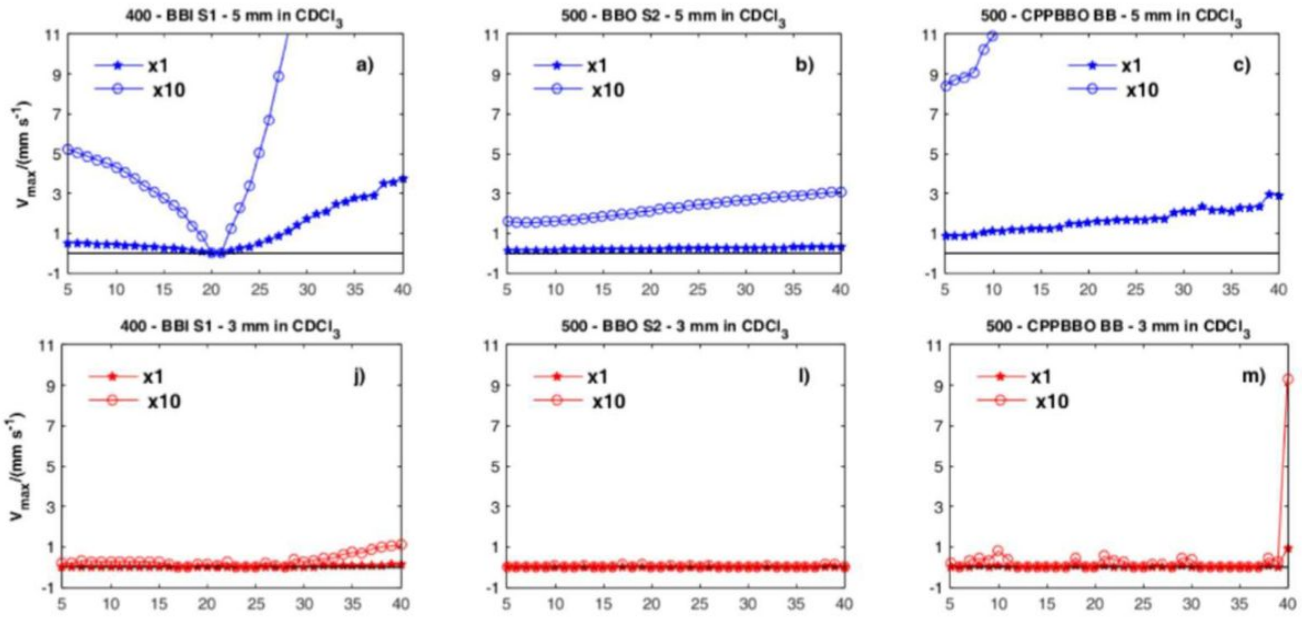
Convection is almost always present

Convection in liquid-state NMR: expect the unexpected

T. M. Barbosa,[a,b] R. Rittner,[a] C. F. Tormena,[a] G. A. Morris,[b] and M. Nilsson[b]



5mm

3mm

- Convection is almost often present
- it depends on T, solvent, probe, geometry of the tube

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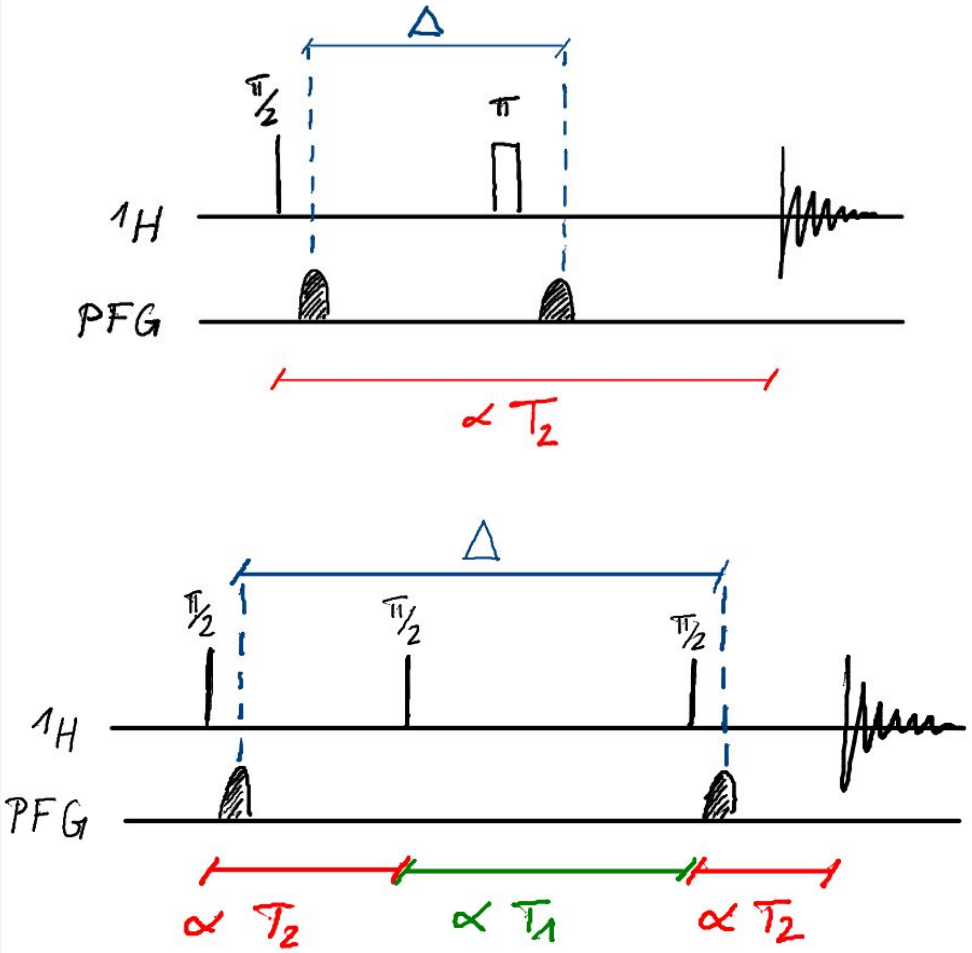
PFG and Stimulated Echo



- Diffusion may be slow compared to T_2
- Stimulated Echo protects the magnetization in z
- STE drop half of magnetization but is still more intense

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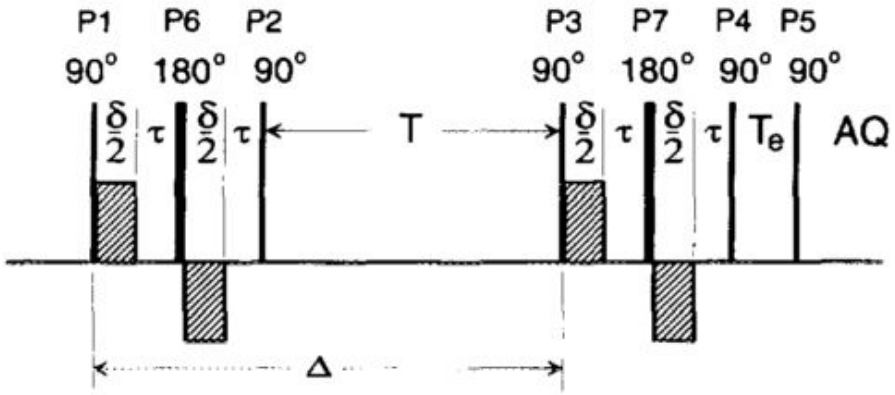
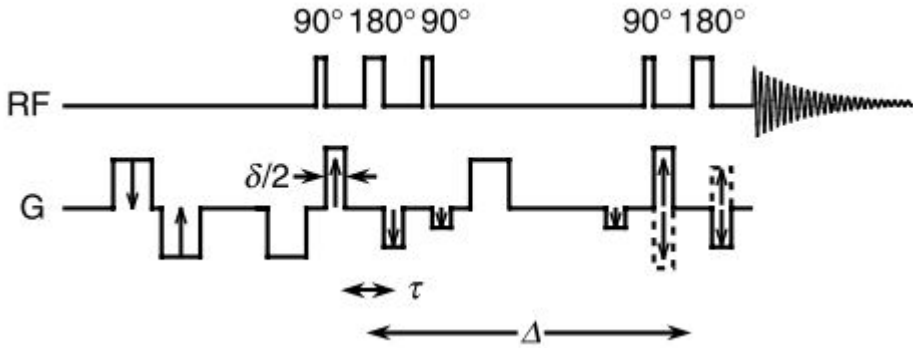
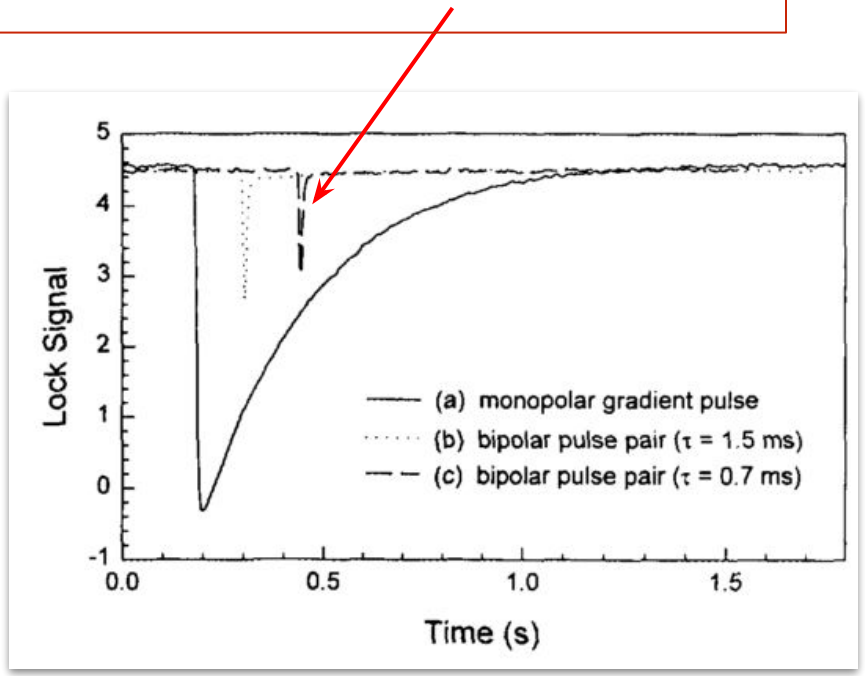
BPPLED and Oneshot







- Bipolar Pulse Pair Longitudinal Eddy Current Delay
  - **reduce eddy current BPP**
  - long phase cycling
- Oneshot
  - **short phase cycling** (one scan)
  - small tilt angle
  - lock refocused by small gradients

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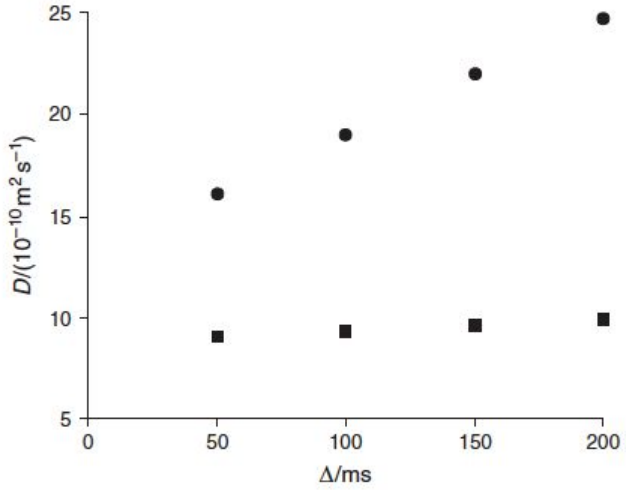
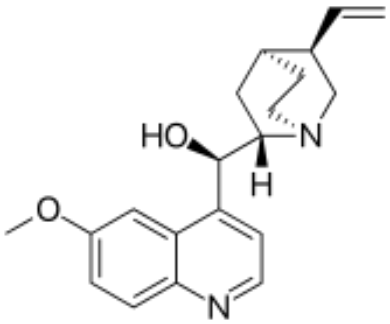
First detect convection

Una forma rápida de rastrear la presencia de convección es usar diferentes valores del diffusion delay para una misma temperatura de trabajo.



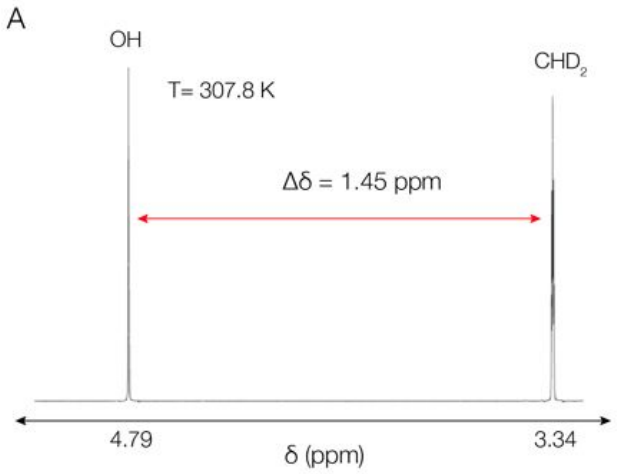


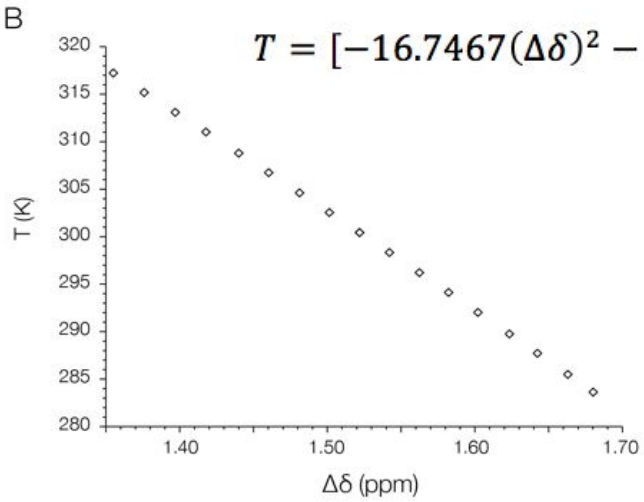
Relación entre el Dapp y el Big delta

$$D_{app} = D + \frac{\Delta\nu^2}{2}$$

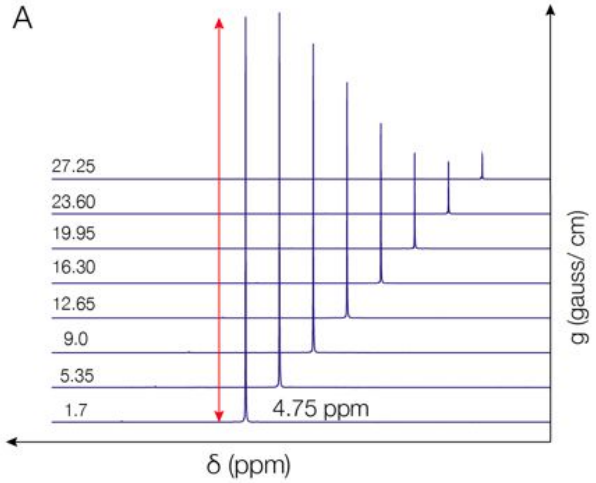
- Convection must be detected first since calibration is performed using known solvents

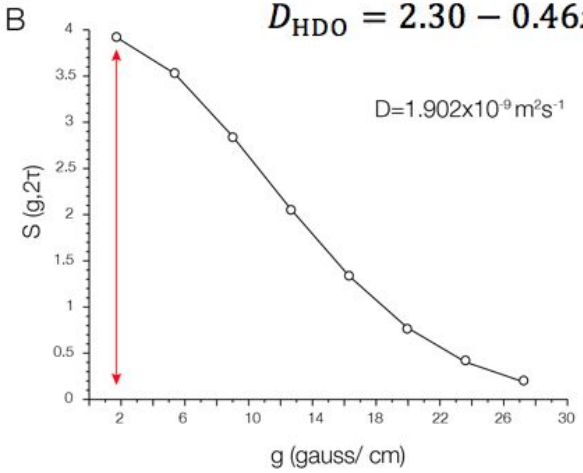
The calibrate your gradients





$$T = [-16.7467(\Delta\delta)^2 - 52.5130(\Delta\delta) + 419.1381]\ \mathrm{K}$$





$$D_{\mathrm{HDO}} = 2.30 - 0.46x_{\mathrm{D_2O}} + 0.0672x_{\mathrm{D_2O}}^2\ 10^{-9}\mathrm{m}^2/\mathrm{s}.$$

$D = 1.902 \times 10^{-9}\ \mathrm{m^2 s^{-1}}$

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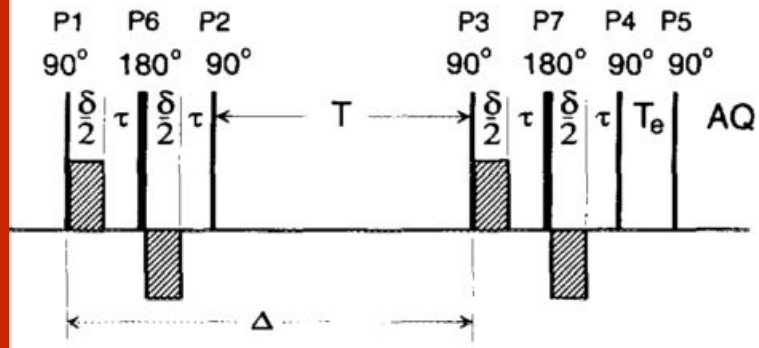
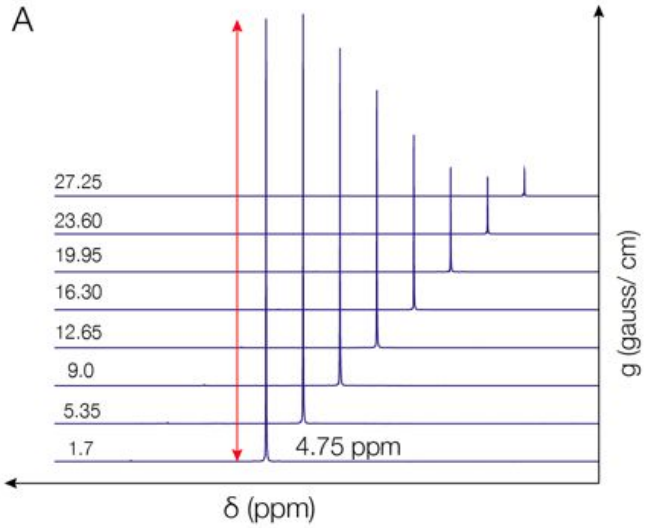
Recalculate the gradients



$$S(q) = S(0)exp\left[-D\gamma^2 g^2 \delta^2(\Delta - \delta/3 - \tau/2)\right]$$

$$g = \sqrt{-\frac{1}{D\gamma^2\delta^2(\Delta - \delta/3 - \tau/2)}\mathrm{Ln}\left[\frac{s(q)}{s(0)}\right]}$$



$$g = \sqrt{\frac{1}{D\gamma^2\delta^2(\Delta - \delta/3 - \tau/2)}\mathrm{Ln}\left[\frac{s(0)}{s(q)}\right]}$$

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Minimize convection

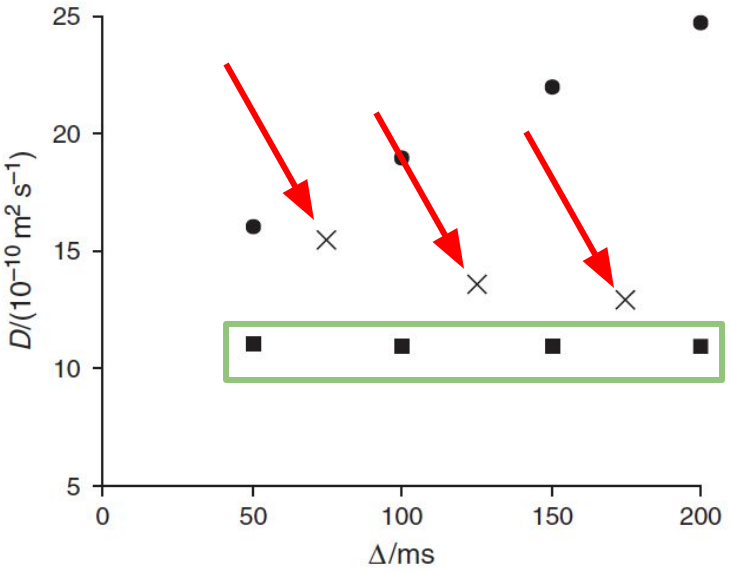
Rayleigh Number

1) Tube diameters : $$R = \frac{g\alpha}{\kappa\nu} r^4 T^*$$

2) Solvent viscosity:

Solvent	Viscosity (mPa.s)
Acetone	0.31
Acetonitrile	0.35
Benzene	0.60
Chloroform	0.54
Dichloromethane	0.41
Dimethylsulfoxide	1.99
Methanol	0.54
Tetrahydrofuran	0.46
Toluene	0.56
Water	0.89

3) Sample spinning :



- Sample spinning rate should be synchronized with Δ

Summary

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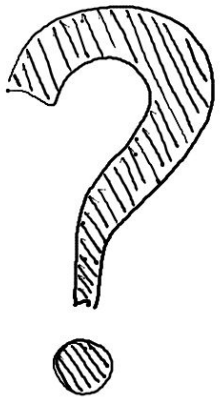
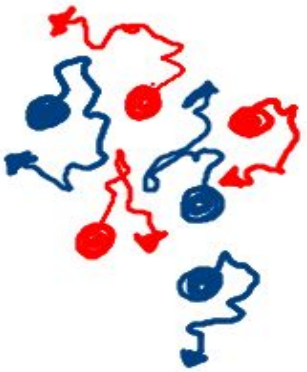
What NMR can tell us about diffusion?

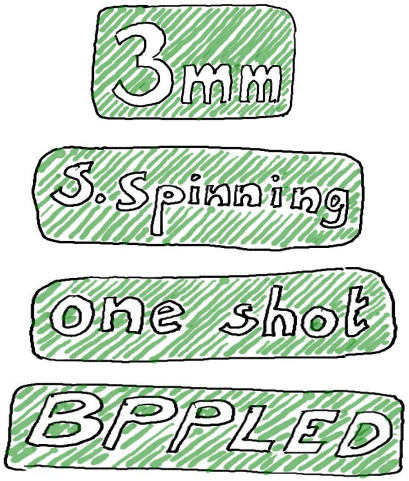
No force applied

self-diffusion





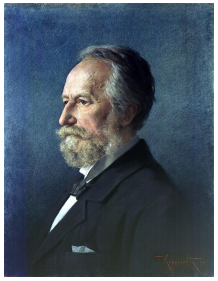
Intra-diffusion



Force is applied

Mutual diffusion

Fick vs Maxwell - Stefan

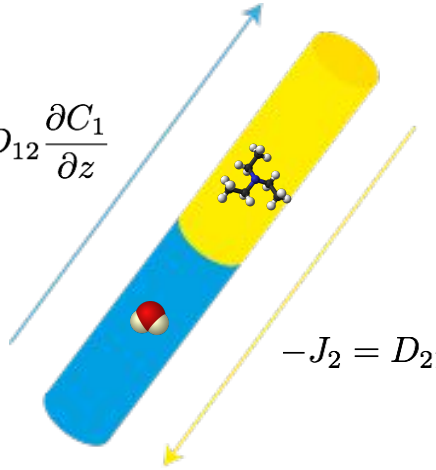


Adolf Eugen Fick

Josef Stefan

James Maxwell

$$-J_1 = D_{12}\frac{\partial C_1}{\partial z}$$

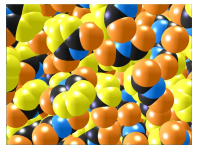


$$-J_2 = D_{21}\frac{\partial C_2}{\partial z}$$

$$Đ = \frac{D}{\Gamma}$$

Thermodynamic correction factor

Maxwell-Stefan



thermodynamic interaction
vs.
molecular friction

D can be measured, while $Đ$ can be calculated

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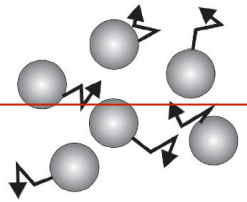
The route to Fick diffusivities



Darken model

$$Đ_{12} = x_2 \hat{D}_1 + x_1 \hat{D}_2$$

Vignes model

$$Đ_{12} = \left(Đ_{12}^{x_1 \to 1}\right)^{x_1} \left(Đ_{12}^{x_2 \to 1}\right)^{x_2}$$

requires experimental data difficult to acquire

TCF must be known difficult to measure **not trivial for multi-comp. mixtures**

Fick diffusion coefficients

Direct prediction

Prediction via Maxwell -Stefan

Darken -type

Vignes -type

require intra-diffusion coefficients

require diffusivities at infinite diffusion (large error in predicted ones)

Krishna & van Baten (2006)

Kooijman & Taylor (1991)

Rehfeldt & Stichlmair (2007)

Wesselingh & Krishna (1990)

Krishna (1981, 1985)

generalized

generalized

combined

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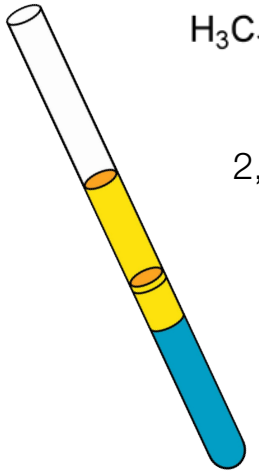
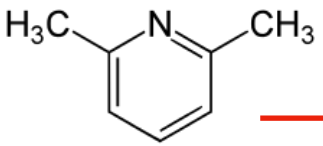
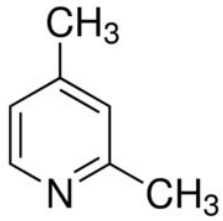
Bardow, A. ***et al.*** Fluid Phase Equilibria. 278, 27-35 (2009)

MD simulation requires self-diffusion



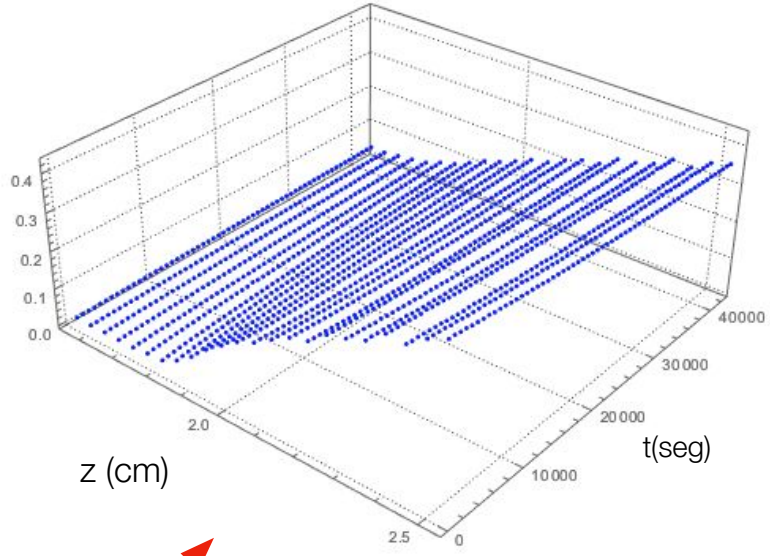


2,6-Lutidine

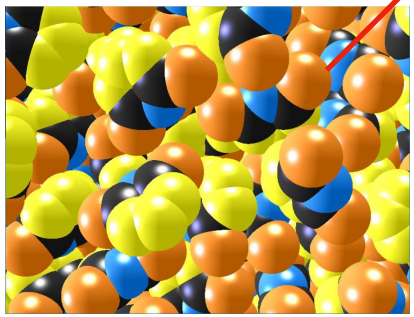


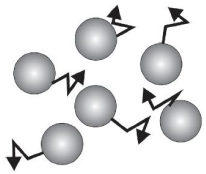
2,4-Lutidine

X 2,6-Lutidine



Molecular Dynamics





Self diffusion coefficient

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Die Universität der Informationsgesellschaft

Awful results!

- Convection
- Eddy current
- Radiation damping
- Relaxation times
- lock?

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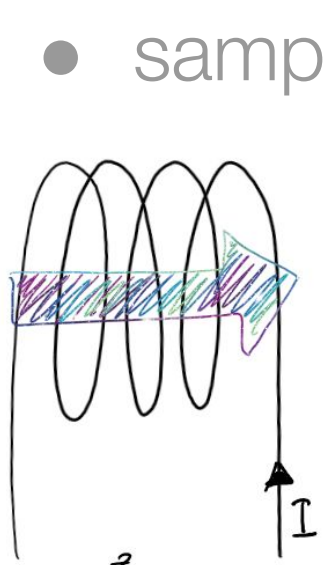
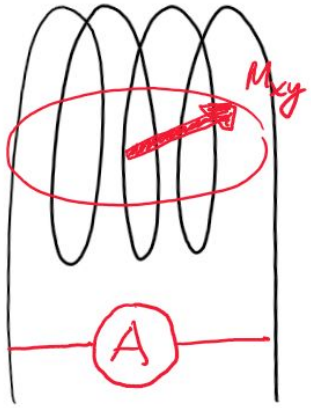
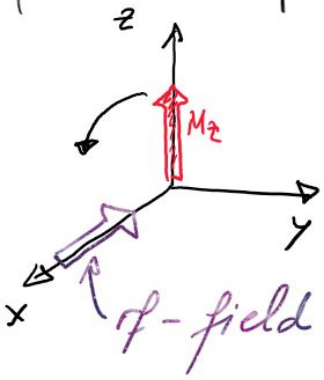
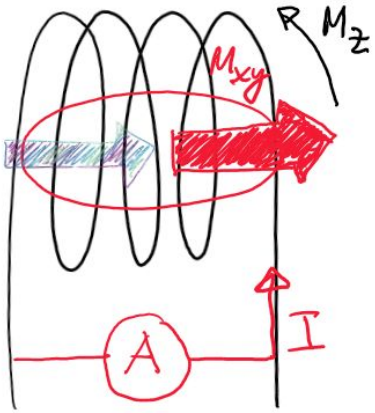
Radiation Damping (RD) / high concentrated samples

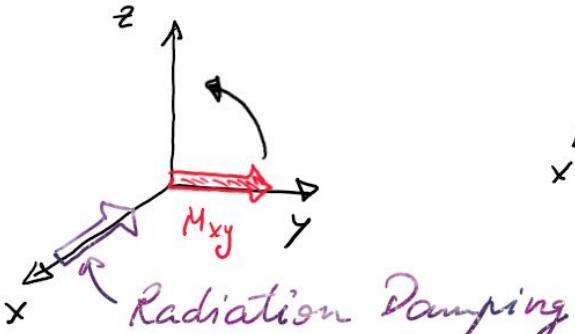
- dilution
- sample volume

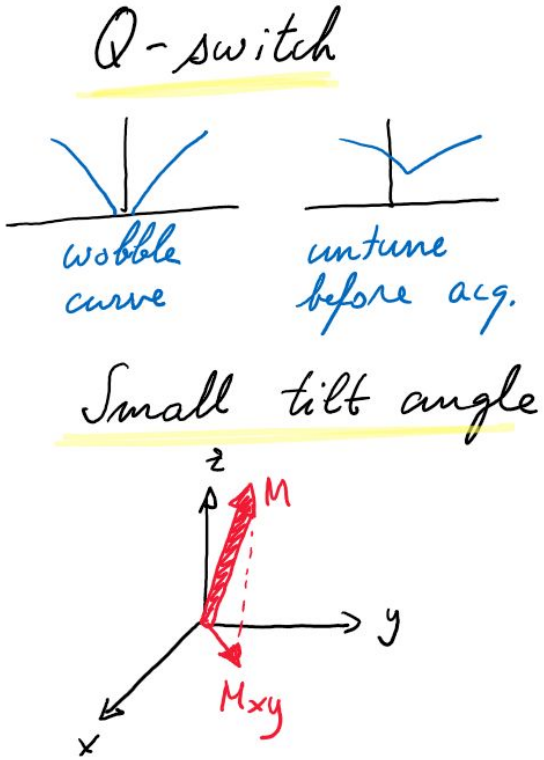












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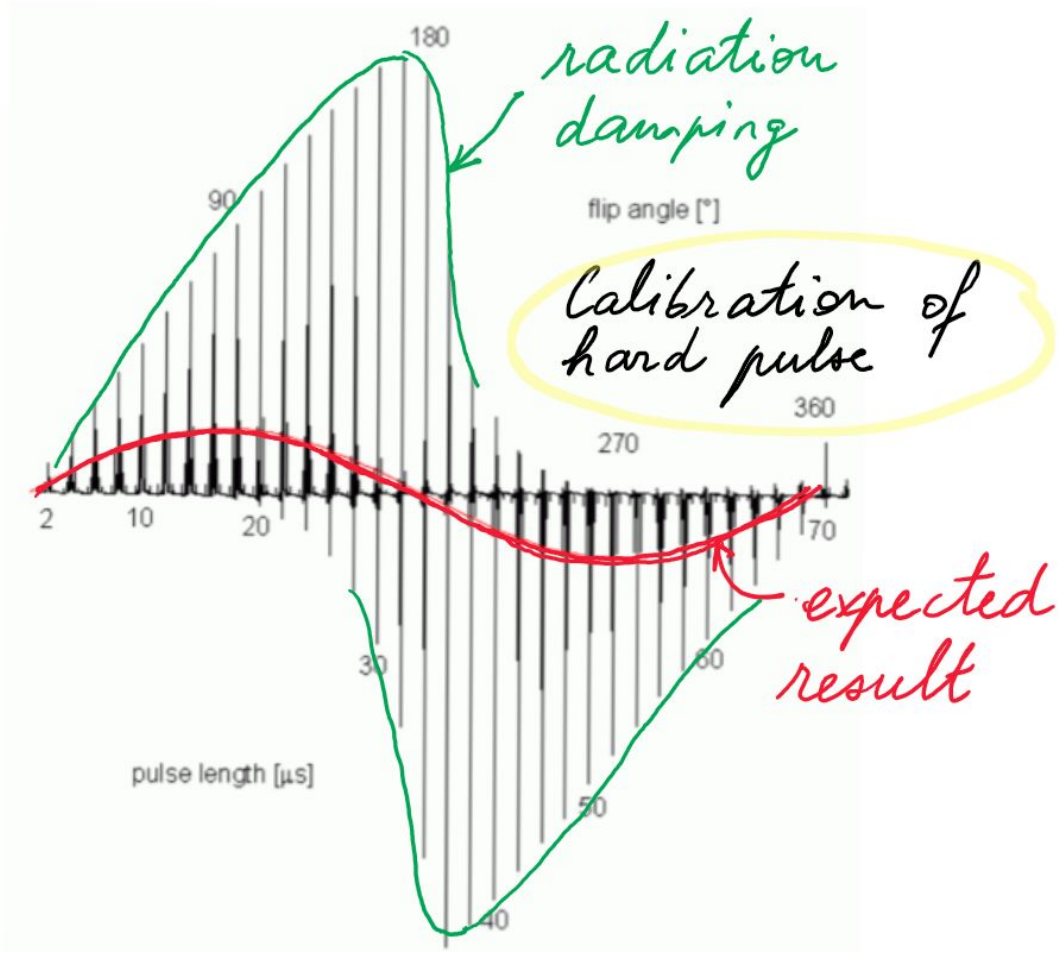
Effects of RD



http://anorganik.uni-tuebingen.de/klaus/nmr/index.php?p=damping/damping

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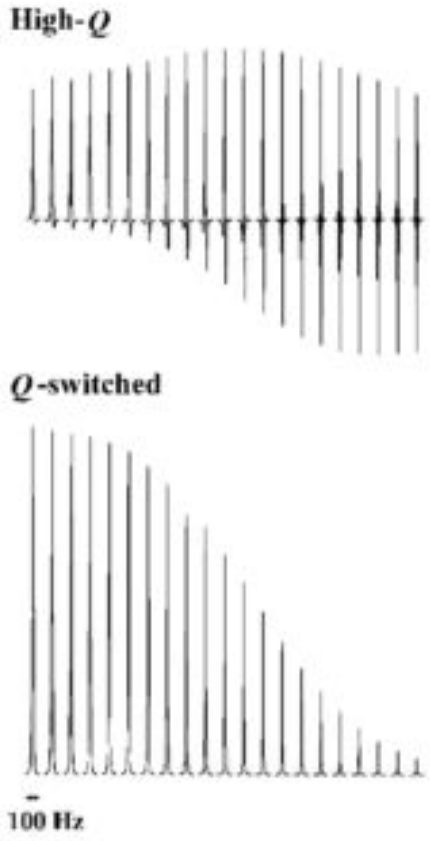
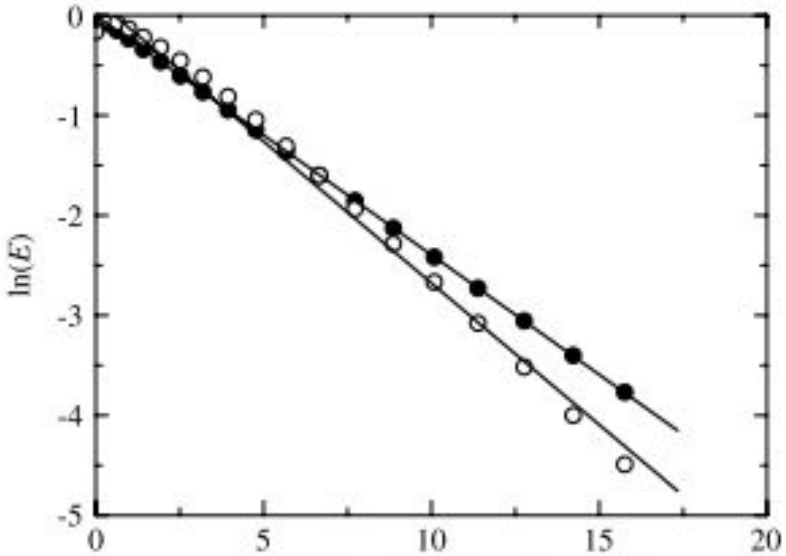
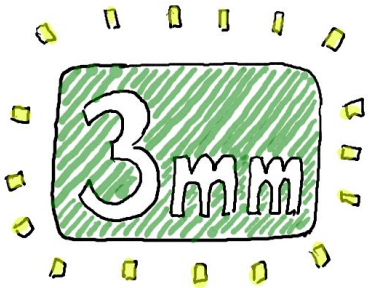
Effects of RD on D



(A)



(B)



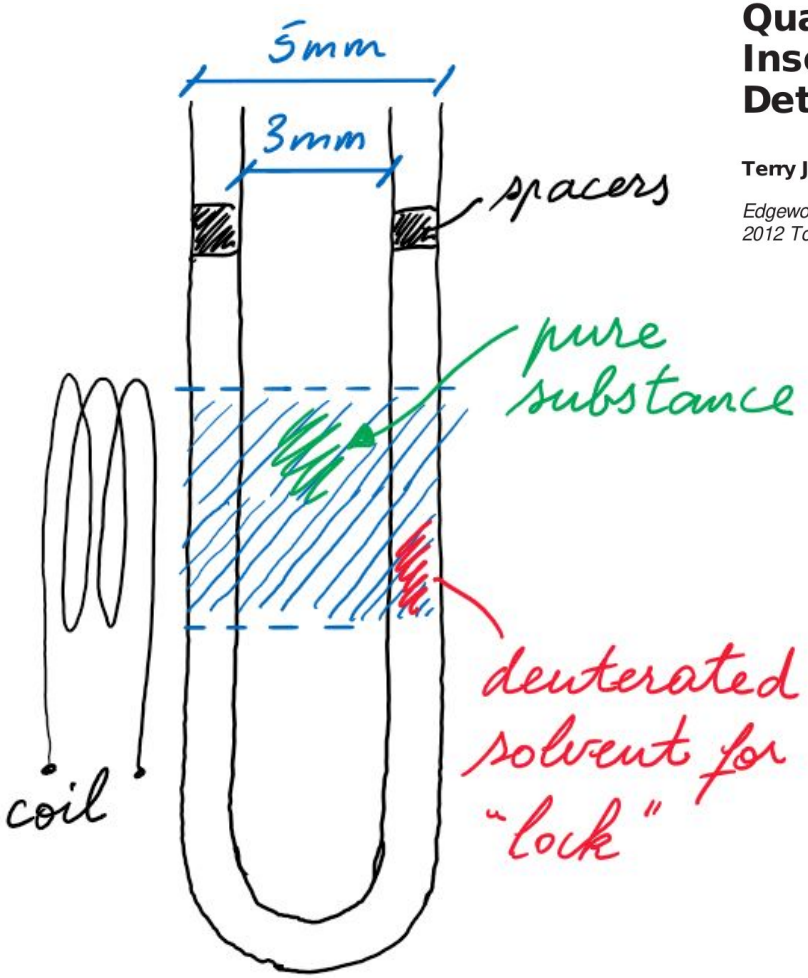
Concentric tubes

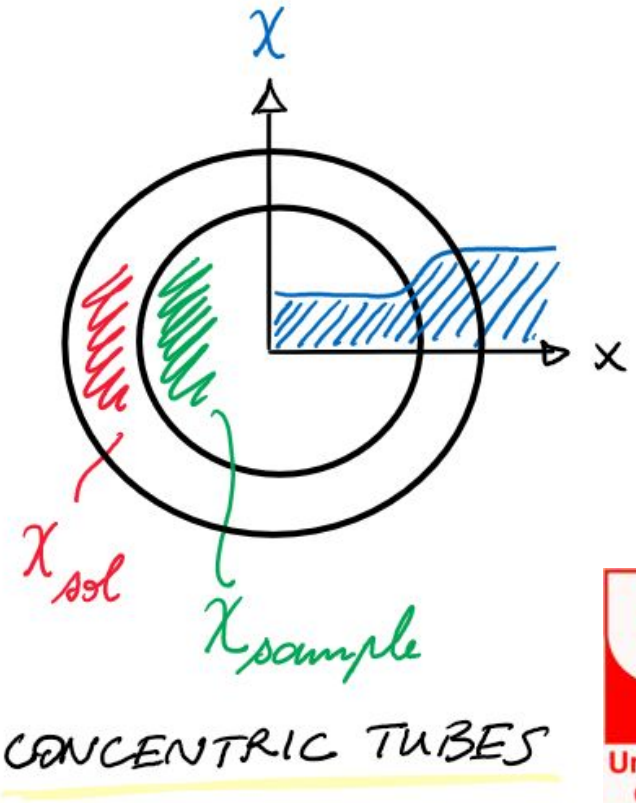
Anal. Chem. **2002,** *74,* 191−198

Quantitative NMR Spectroscopy Using Coaxial Inserts Containing a Reference Standard: Purity Determinations for Military Nerve Agents

Terry J. Henderson*

Edgewood Chemical−Biological Forensic Analytical Center, Battelle Memorial Institute Edgewood Operations, 2012 Tollgate Road, Suite 206, Bel Air, Maryland 21015





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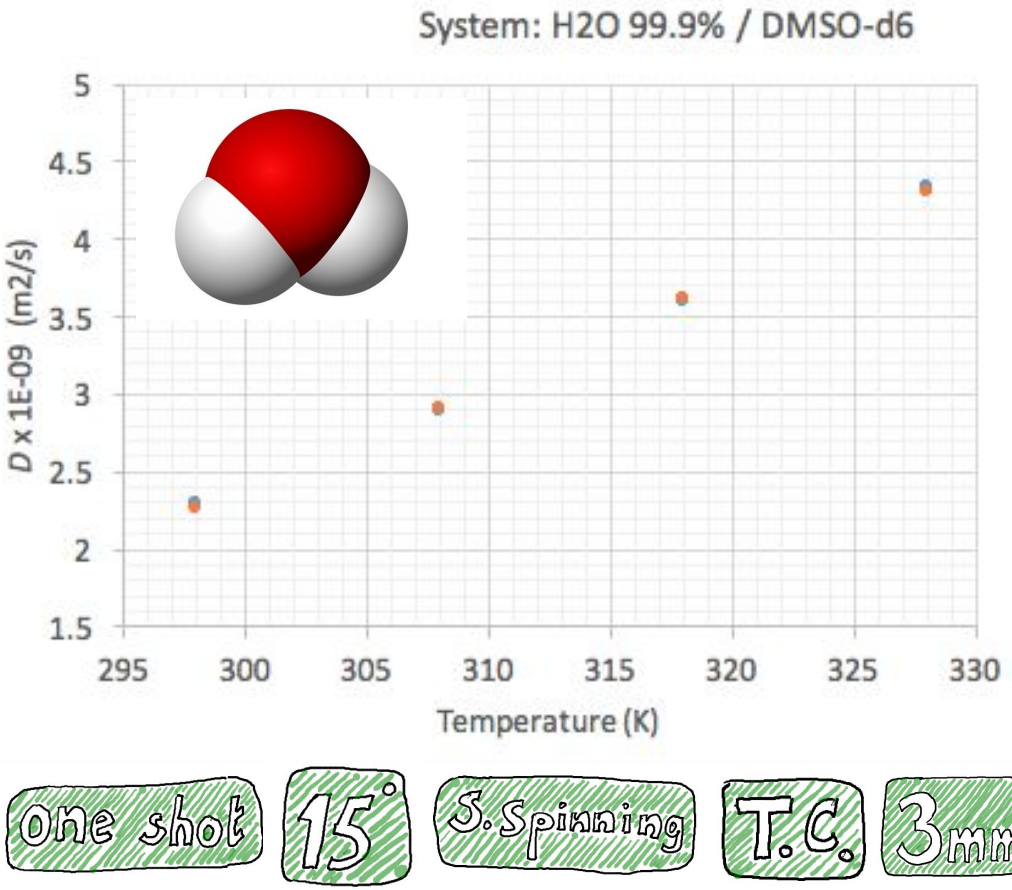
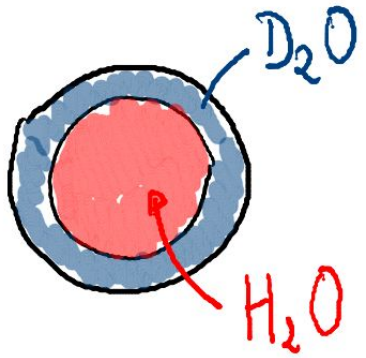
Accurate determination of diffusion of pure water



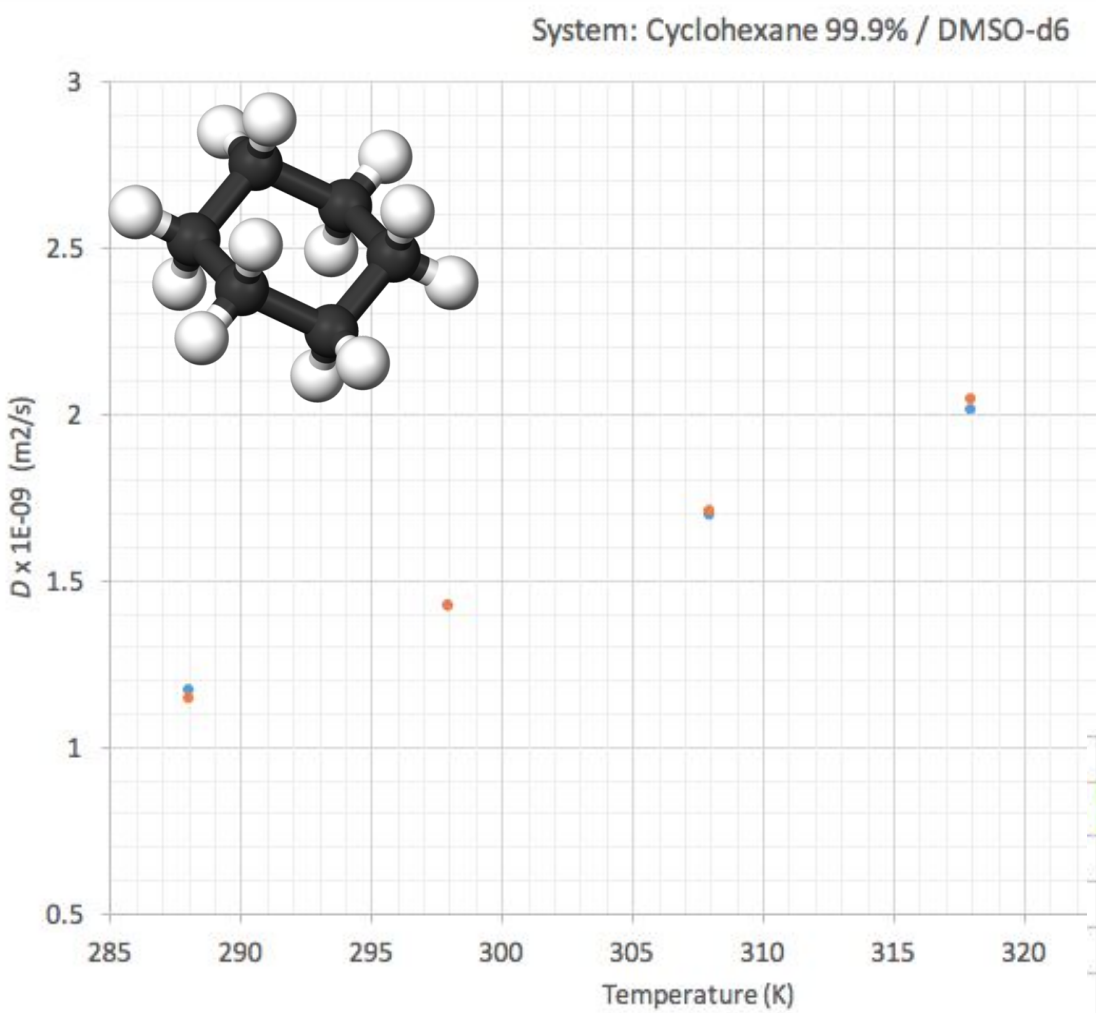


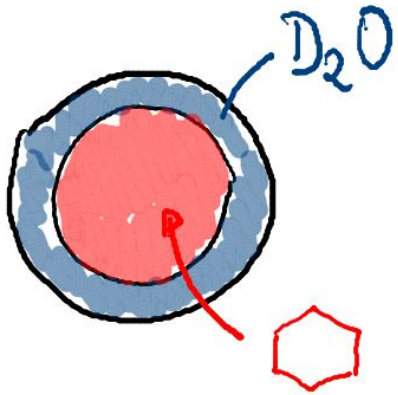
- Holz, 2000
- NMR_coaxial_tube

System: H_2O 99.9%/ DMSO-d_6		
Temperature (K)	D (m^2/s)	% Error
298	2.257	1.83
308	2.900	-0.17
318	3.614	-0.36
328	4.297	0.83

- Holz measured at low field (>RD) with special probe (>convection)

Accurate determination of diffusion of cyclohexane

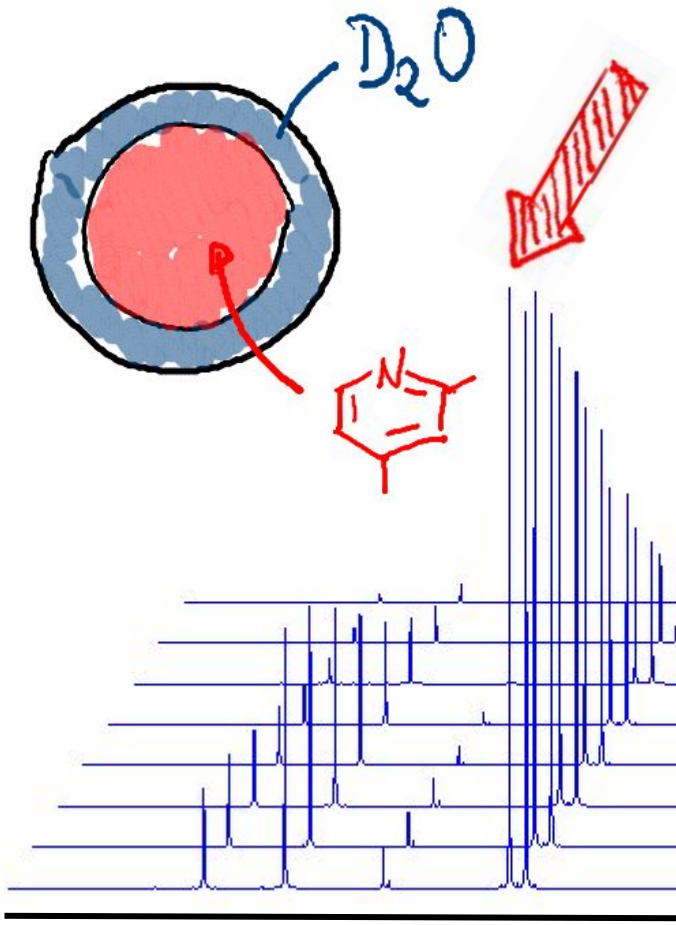




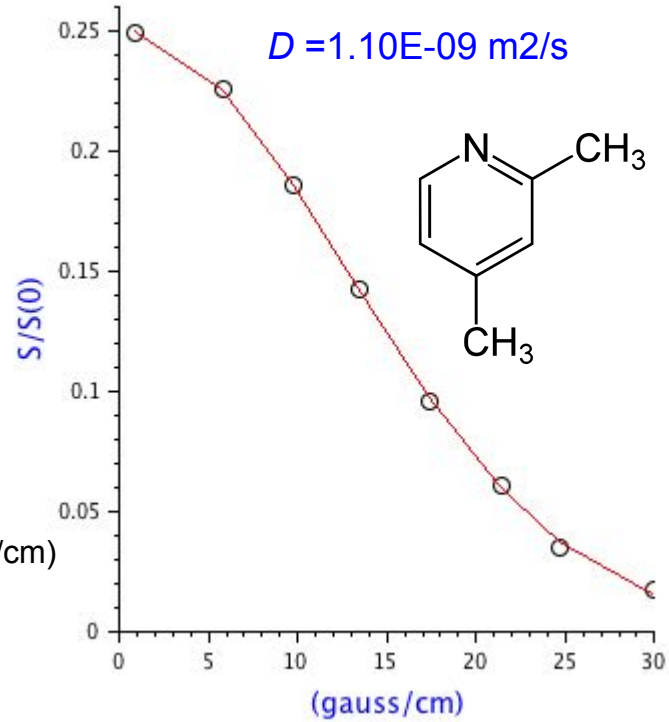
System: Cyclohexane 99.9%/ D2O		
Temperature (K)	D (m^2/s)	% Error
288	1.142	2.39
298	1.421	0.21
308	1.705	-0.65
318	2.044	-1.69
328	2.381	-1.23

One shot | 15° | S.Spinning | T.C. | 3mm

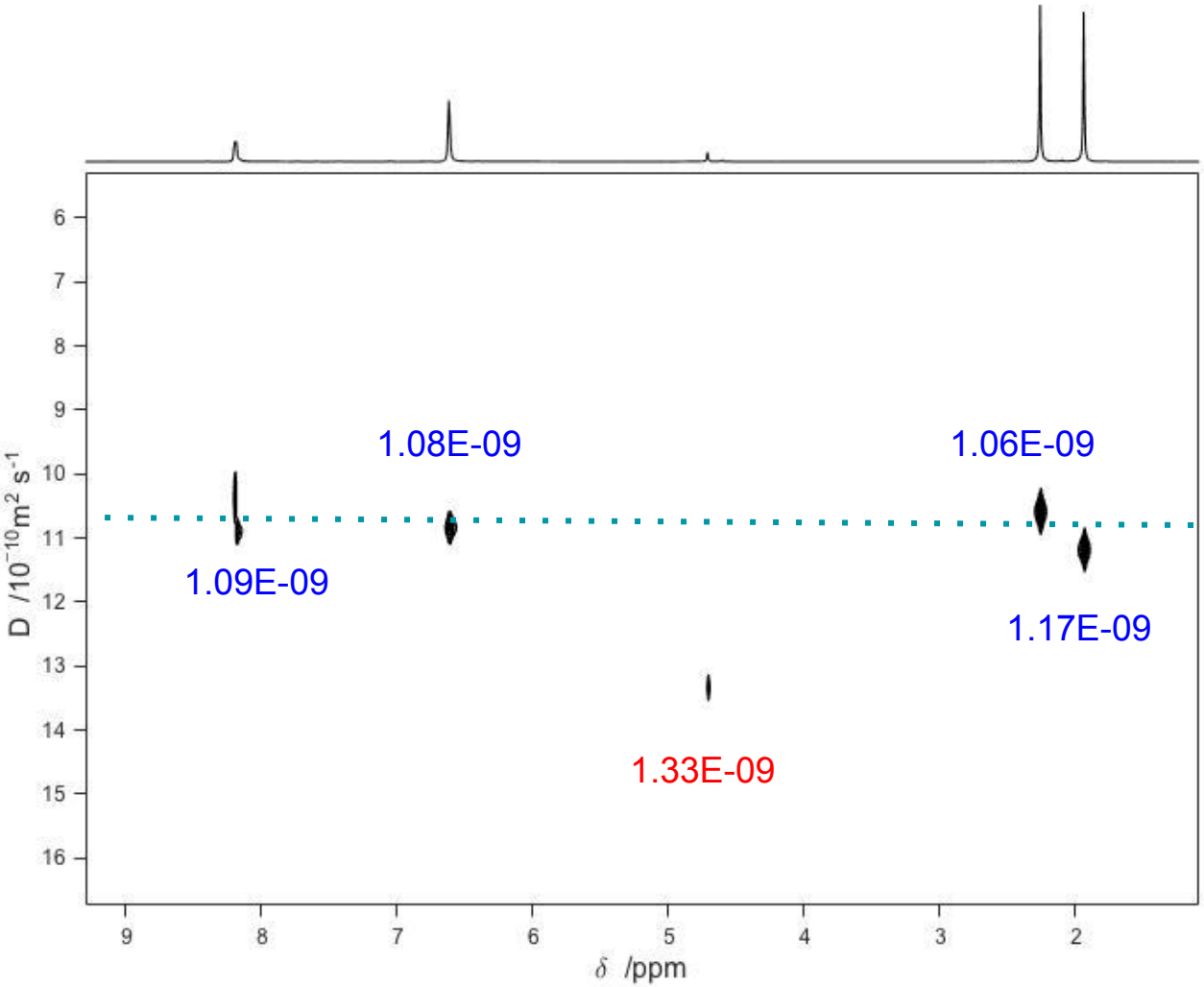
Accurate determination of diffusion of lutidine

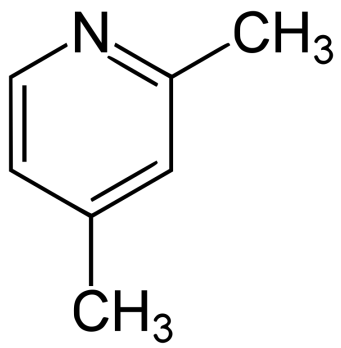


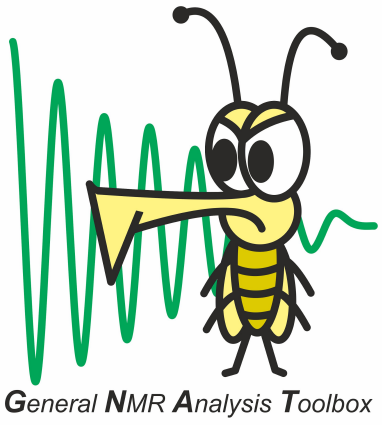
$$\frac{I(g)}{I(0)} = \exp\{-\gamma^2 g^2 \delta^2 [\Delta + \delta(\alpha^2 - 2)/6 + \tau(\alpha^2 - 1)/2]\}$$



DOSY representation of D of lutidine



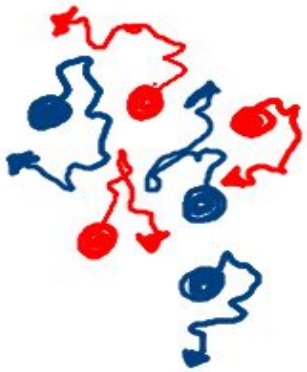




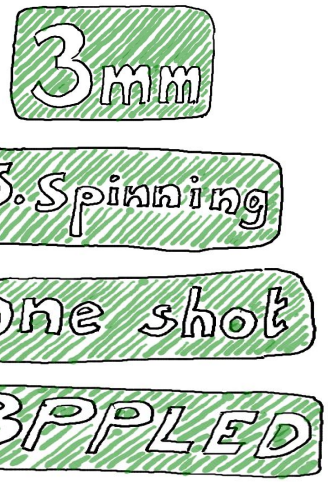
What NMR can tell us about diffusion?

No force applied

self-diffusion



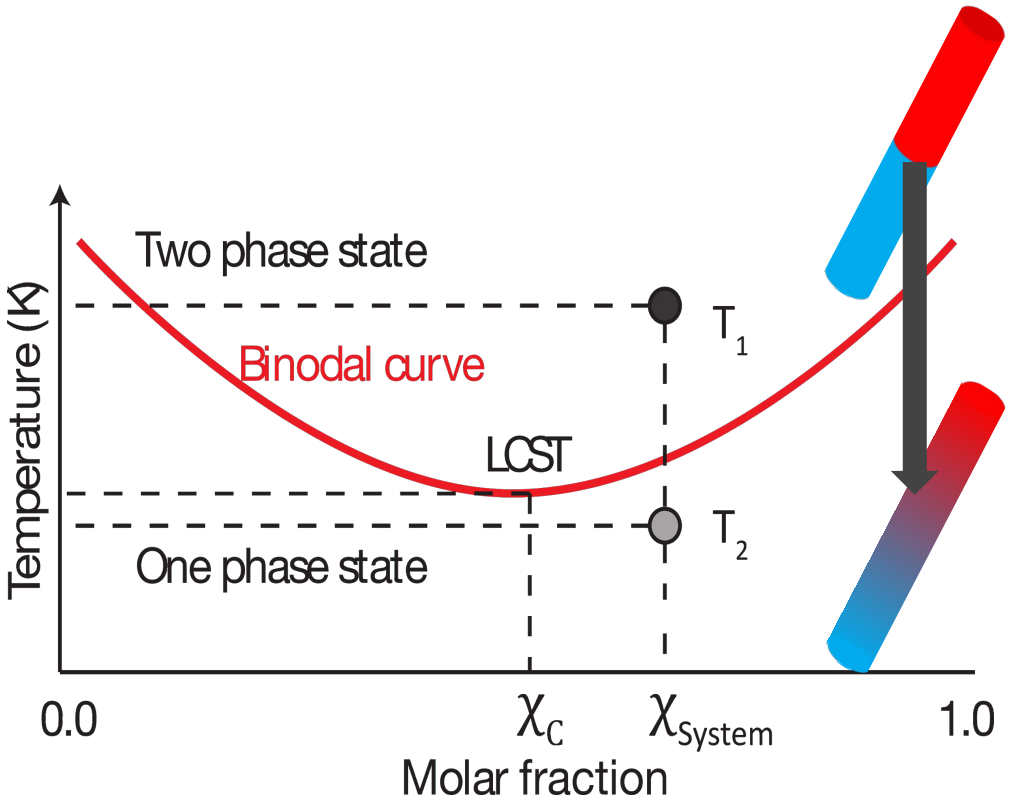
Intra-diffusion



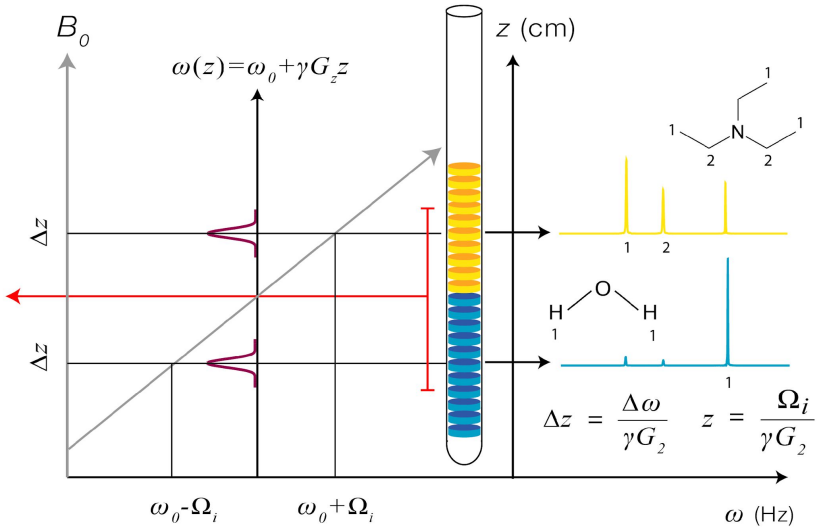
Force is applied

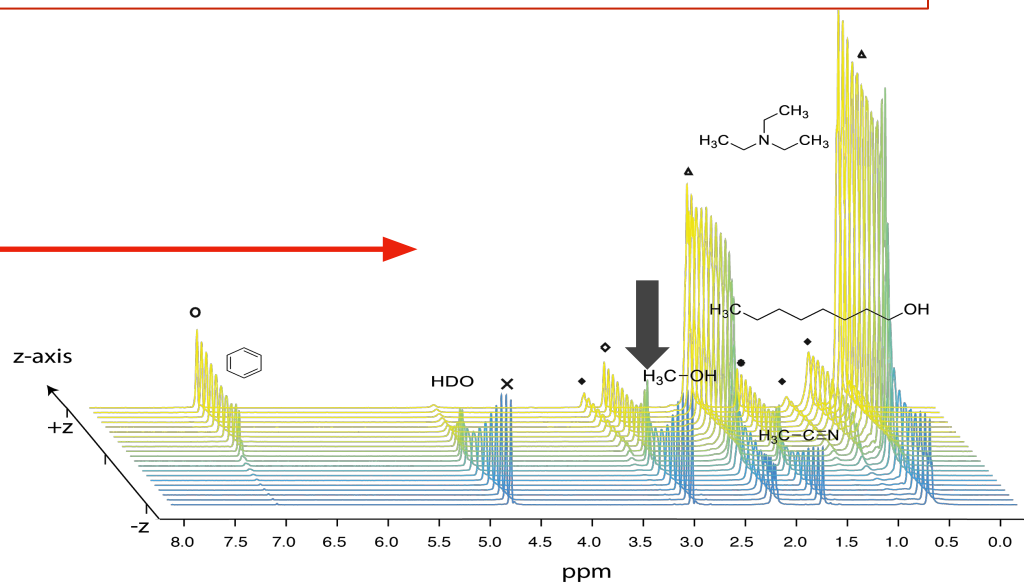
Mutual diffusion

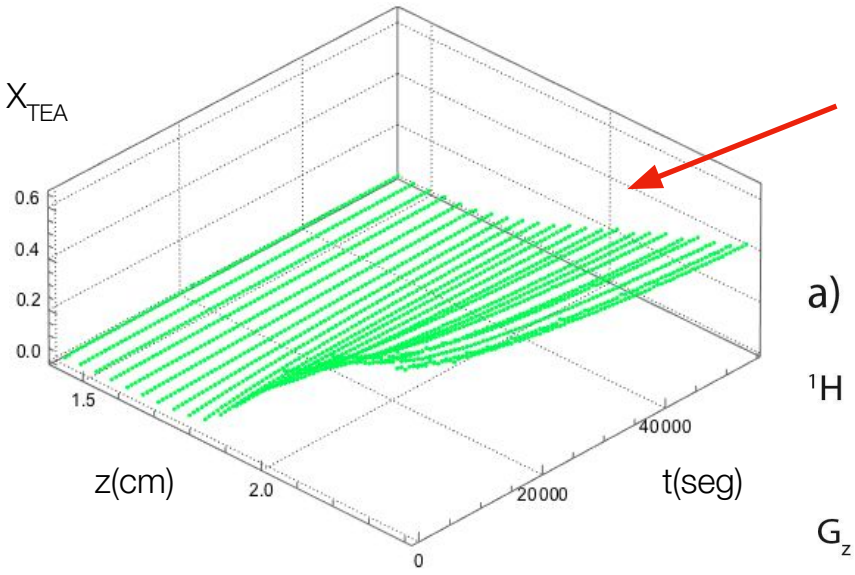
Experimental set-up



Results - time evolution of gradients

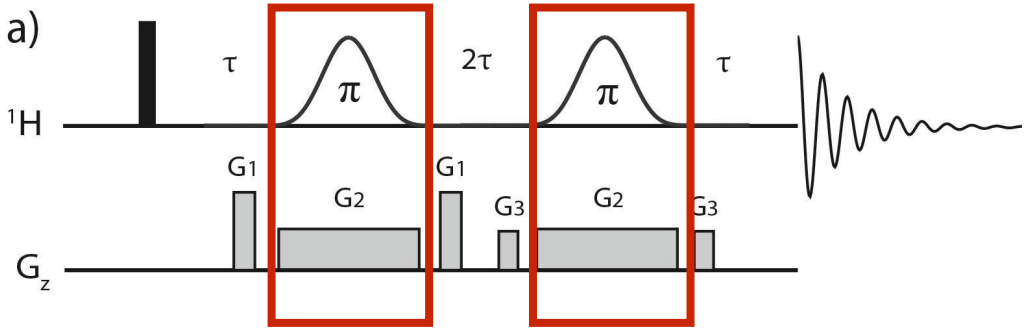




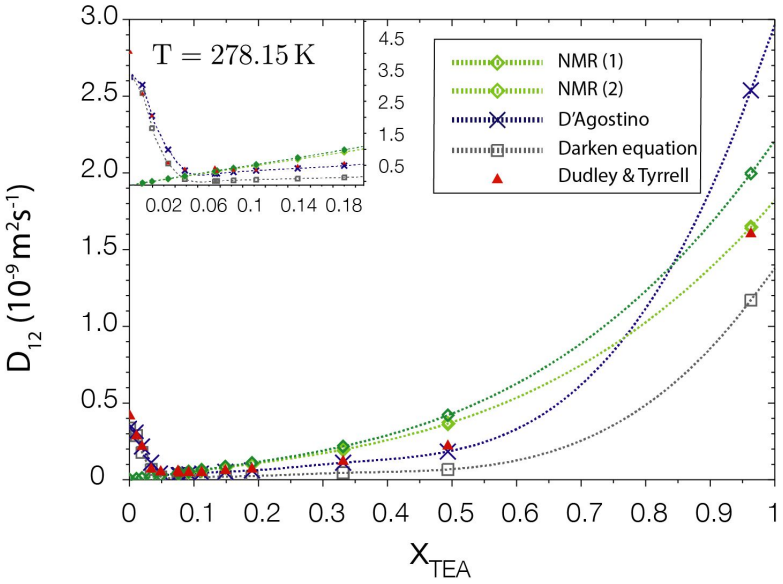


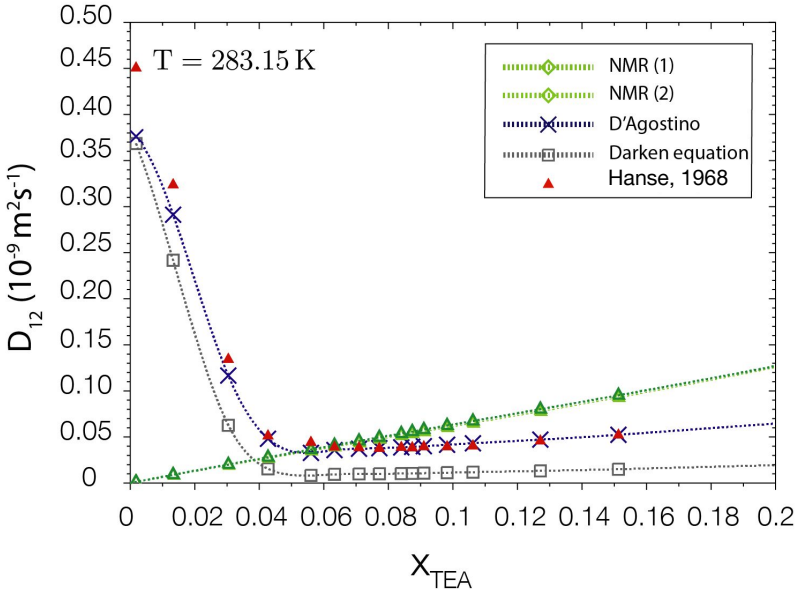
$$x_j = \frac{A_j^{-1} I_j}{\sum_n^{k=1} A_k^{-1} I_k}$$

Molar fraction



Results





Darken-Schneider

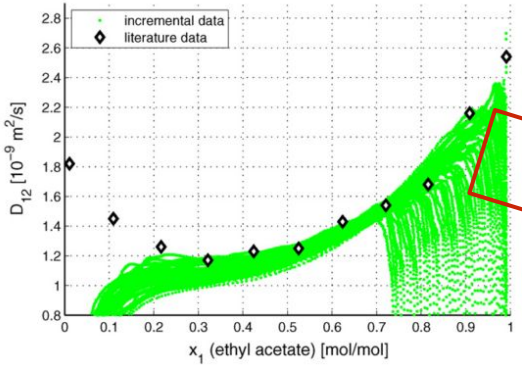
$$D_{12} = (x_2 D_1^* + x_1 D_2^*)\left[1 + \frac{dln\Gamma_1}{dlnx_1}\right]$$

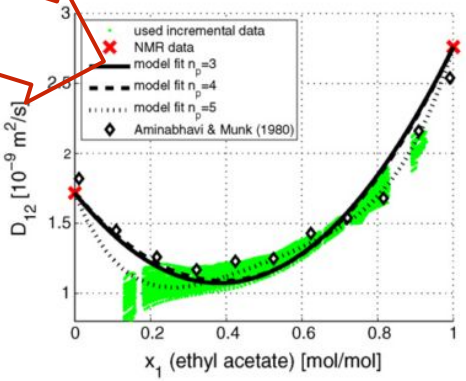
D'Agostino (2012)

$$D_{12} = (x_2 D_1^* + 2x_1 D_2^*)\left[1 + \frac{dln\Gamma_1}{dlnx_1}\right]^{\alpha}$$

dimerization

Clustering factor





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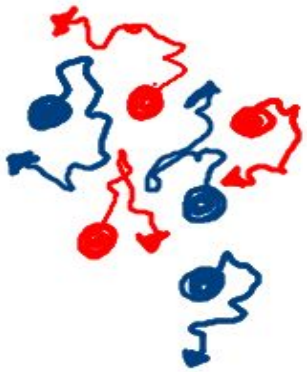
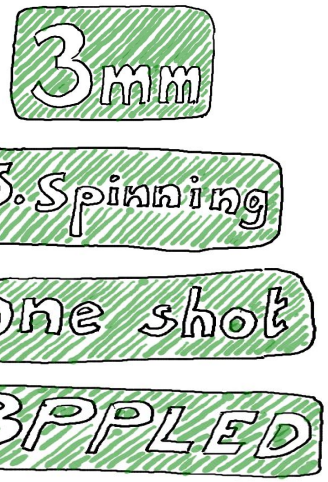


Intra-diffusion



Force is applied

Mutual diffusion

Acknowledgements

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Christian Pantoja

Lorraine Guascar

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The value of universally available raw NMR data for transparency, reproducibility, and integrity in natural product research†

James B. McAlpine, *[a] Shao-Nong Chen, [a] Andrei Kutateladze, [b] John B. MacMillan, [c] Giovanni Appendino, [d] Andersson Barison, [e] Mehdi A. Beniddir, [f] Maique W. Biavatti, [g] Stefan Bluml, [h] Asmaa Boufridi, [i] Mark S. Butler, [j] Robert J. Capon, [j] Young H. Choi, [k] David Coppage, [c] Phillip Crews, [c] Michael T. Crimmins, [l] Marie Csete, [m] Pradeep Dewapriya, [j] Joseph M. Egan, [n] Mary J. Garson, [o] Grégory Genta-Jouve, [p] William H. Gerwick, [qr] Harald Gross, [s] Mary Kay Harper, [t] Precilia Hermanto, [u] James M. Hook, [u] Luke Hunter, [u] Damien Jeannerat, [v] Nai-Yun Ji, [w] Tyler A. Johnson, [c] David G. I. Kingston, [x] Hiroyuki Koshino, [y] Hsiau-Wei Lee, [c] Guy Lewin, [f] Jie Li, [r] Roger G. Linington, [n] Miaomiao Liu, [i] Kerry L. McPhail, [z] Tadeusz F. Molinski, [aa] Bradley S. Moore, [qr] Joo-Won Nam, [ab] Ram P. Neupane, [ac] Matthias Niemitz, [ad] Jean-Marc Nuzillard, [ae] Nicholas H. Oberlies, [af] Fernanda M. M. Ocampos, [e] Guohui Pan, [ag] Ronald J. Quinn, [i] D. Sai Reddy, [b] Jean-Hugues Renault, [ae] José Rivera-Chávez, [ah] Wolfgang Robien, [ai] Carla M. Saunders, [aj] Thomas J. Schmidt, [ak] Christoph Seger, [al] Ben Shen, [ag] Christoph Steinbeck, [am] Hermann Stuppner, [al] Sonja Sturm, [al] Orazio Taglialatela-Scafati, [an] Dean J. Tantillo, [aj] Robert Verpoorte, [k] Bin-Gui Wang, [wao] Craig M. Williams, [o] Philip G. Williams, [ac] Julien Wist, [ap] Jian-Min Yue, [aq] Chen Zhang, [ar] Zhengren Xu, [ag] Charlotte Simmler, [a] David C. Lankin, [a] Jonathan Bisson [a] and Guido F. Pauli *[a]

Received: 22 January 2018 | Revised: 22 February 2018 | Accepted: 25 March 2018
DOI: 10.1002/mrc.4737

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