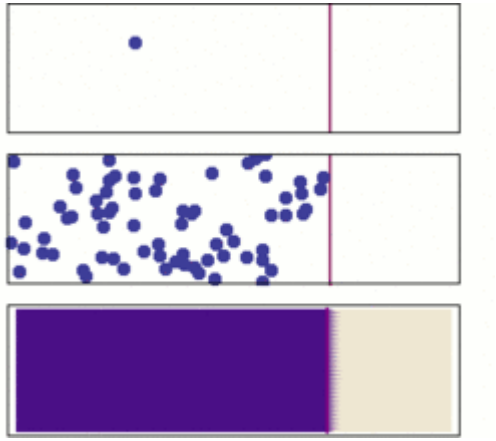
# MOLECULAR DIFFUSION AND DIFFUSION NMR SPECTROSCOPY

**Dissolved molecules can translate (diffuse) through mobile solutions.**

**Mixing two solutions of differing concentrations together will result in equilibration of concentration *via* diffusion.**

- **Higher rate of diffusion from more to less concentrated 'regions' until concentration equilibrates.**
- **Then, molecules will still diffuse, only randomly now that there is no concentration gradient. Analogous to Brownian Motion.**
- **This is SELF-DIFFUSION, and this is what we are interested in.**



**Random (self-) diffusion of molecular species occurs in all mobile solutions.**

- **The rate of random diffusion of a species through a solution is a measurable quantity…**
- **Called the Self-Diffusion Coefficient (*D*), or more commonly, and lazily, the Diffusion Coefficient.**

- **Can be related to molecular size with the Stokes-Einstein equation.**

$$D = \frac{k_B T}{6\pi\eta r s}$$

*$\eta$ = viscosity of the solution*
*$r_S$ = hydrodynamic radius of the sample molecule*

$$D = \frac{k_B T}{6\pi\eta r S}$$

**Looks straightforward…but there are complications.**

- **Principle one is that hydrodynamic radius is defined as the radius of a hard sphere…most molecules are not absolutely spherical!**

**Attempts to 'fix' the Stokes-Einstein equation to accommodate 'real' shaped molecules often involve changing the denominator, 'the frictional factor' reflecting the size and shape of the molecule of interest.**

**Often more appropriate to quote *D* for 'irregular' shaped molecules…polymers, rather than estimate the molecular 'size'.**

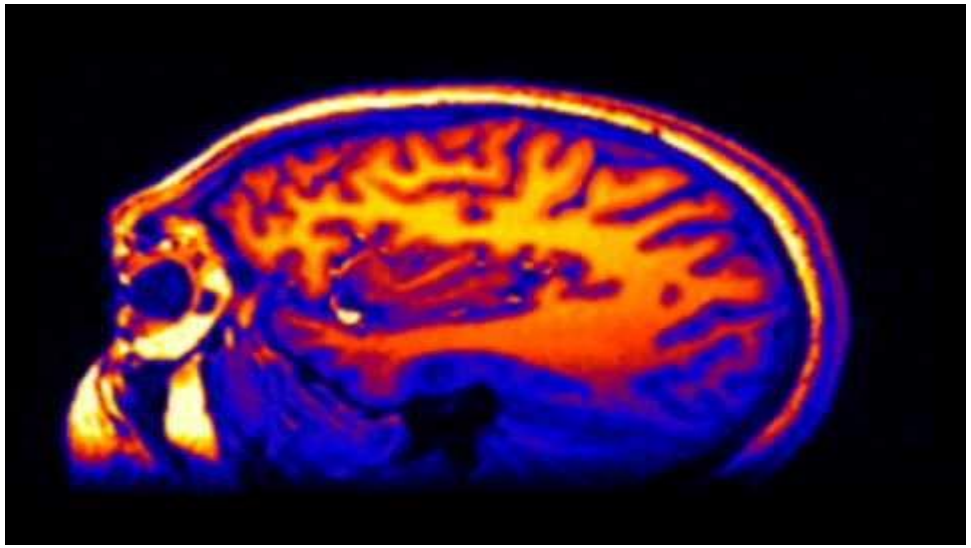
$$\frac{D_{sol}}{D_{ref}} = \sqrt[3]{\frac{M_{ref}}{M_{sol}}}$$

**Rough approximation of molecular weight, *M*, again strictly for spherical molecules only.**

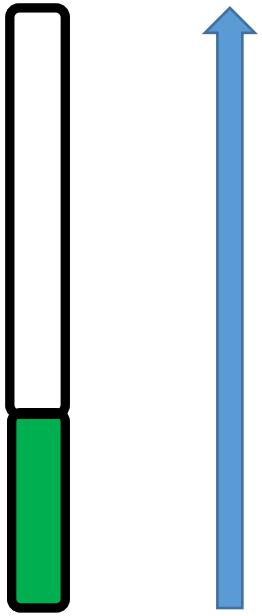
# DIFFUSION-ORDERED SPECTROSCOPY (DOSY)

- **We can study diffusion with NMR spectroscopy…called DOSY.**
- **See SNUG NMR app for a short video tutorial**

**The approach is broadly analogous to that used in MRI (Magnetic Resonance Imaging)…SPACIAL ENCODING.**



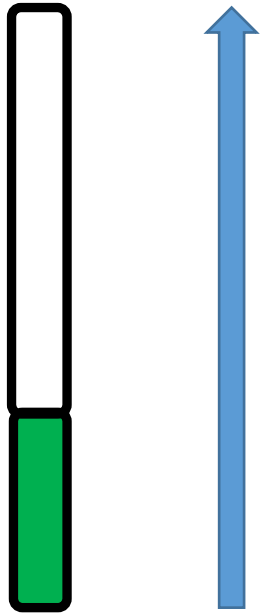
- **Need to be able to label molecules according to their position and track them as they diffuse…PULSED FIELD GRADIENTS**

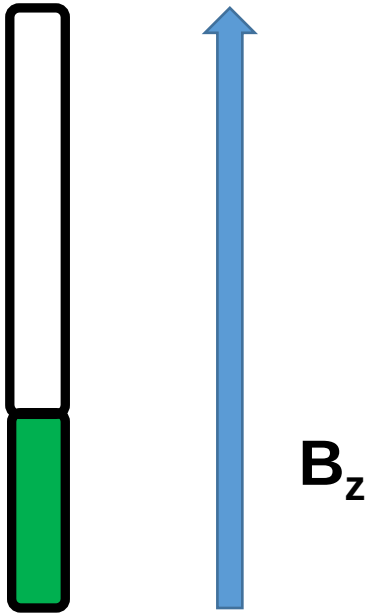


$B_z$

**Classical NMR picture of constant, homogeneous magnetic field in the Cartesian z-axis…called $B_z$**

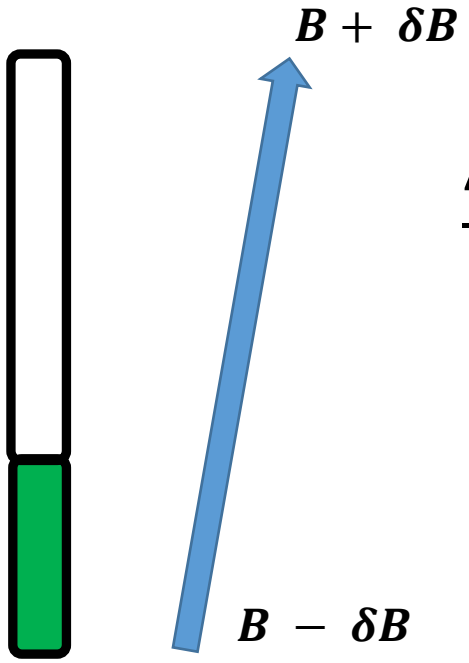
**What would happen if, instead of applying a constant field, we applied a GRADIENT field?**



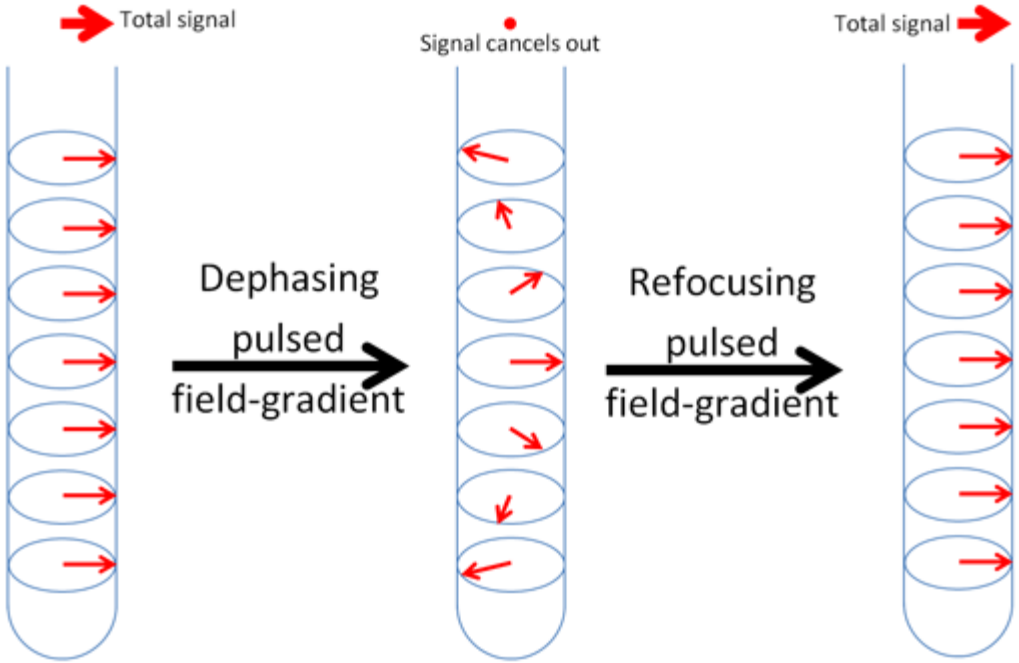



**Classical NMR picture of constant, homogeneous magnetic field in the Cartesian z-axis…called $B_z$**

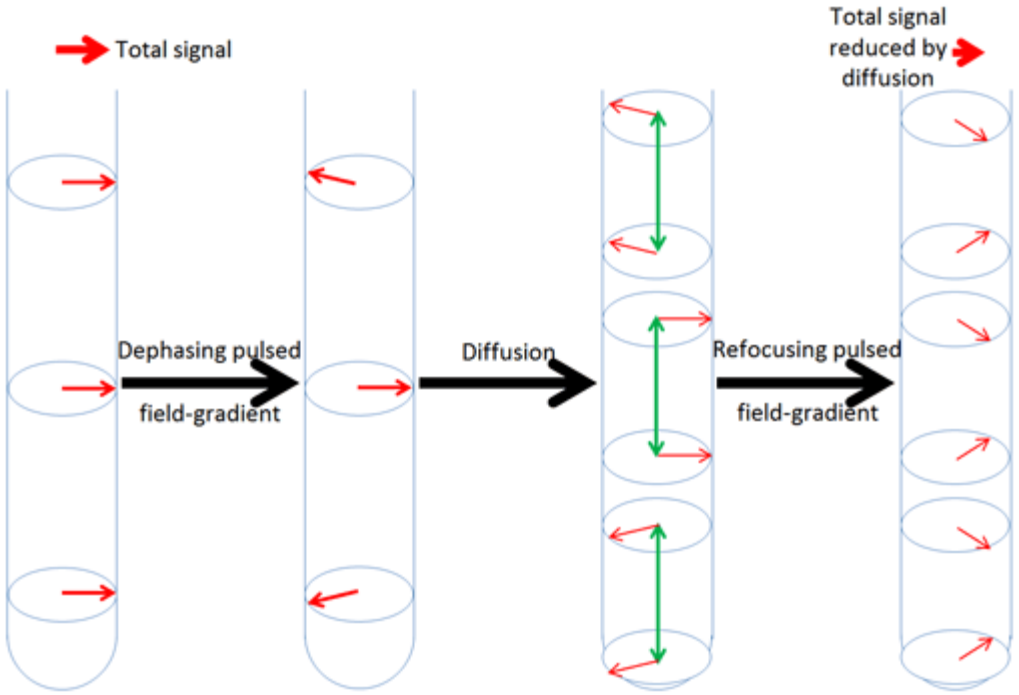
**What would happen if, instead of applying a constant field, we applied a GRADIENT field?**
**Transition frequencies will be slightly higher at the top of the tube.**
**We have LABELLED the spins according to position!**




$$\frac{\Delta E}{h} = \frac{g\beta_N B_z}{h}$$



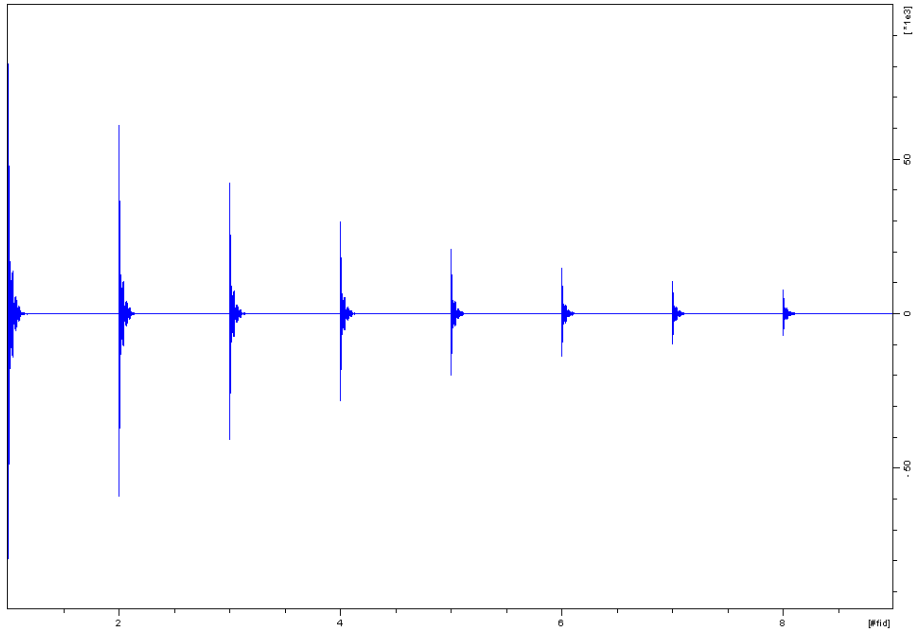

**Diffusion coefficient encoded in this observation, but getting at it has not been straightforward.**



# HOW DOES DOSY WORK?

- **Pseudo-2D experiment.**

**Acquire a series of FIDS, varying ( increasing) only the amplitude of the gradient field each time…produces a set with decreasing signal intensity.**




**Why pseudo-2D experiment?**
**Genuine 2D is a function of two time (frequency) domains, $f(t_1, t_2)$.**
**DOSY is a function of time (frequency) and gradient amplitude (diffusion).**
**Can FT the time dimension…but**
**What about the other one?!**

**Use the Stejskal-Tanner equation.**

$$I_G = IG_{=0}\, exp\left[-(\gamma\delta G)^2\, D\left(\Delta - \frac{3}{2}\right)\right]$$

$I_G$ *intensity of signal at given gradient strength*

$I_{G=0}$ *intensity of signal in the absence of gradient*

$\gamma$ *magnetogyric ratio* $= \frac{\mu}{\rho}$ *where* $\mu$ *is the nuclear magnetic moment and* $\rho$ *the angular momentum*

$\delta$ *gradient pulse duration*

$G$ *gradient amplitude*

$\Delta$ *delay allowed for diffusion*

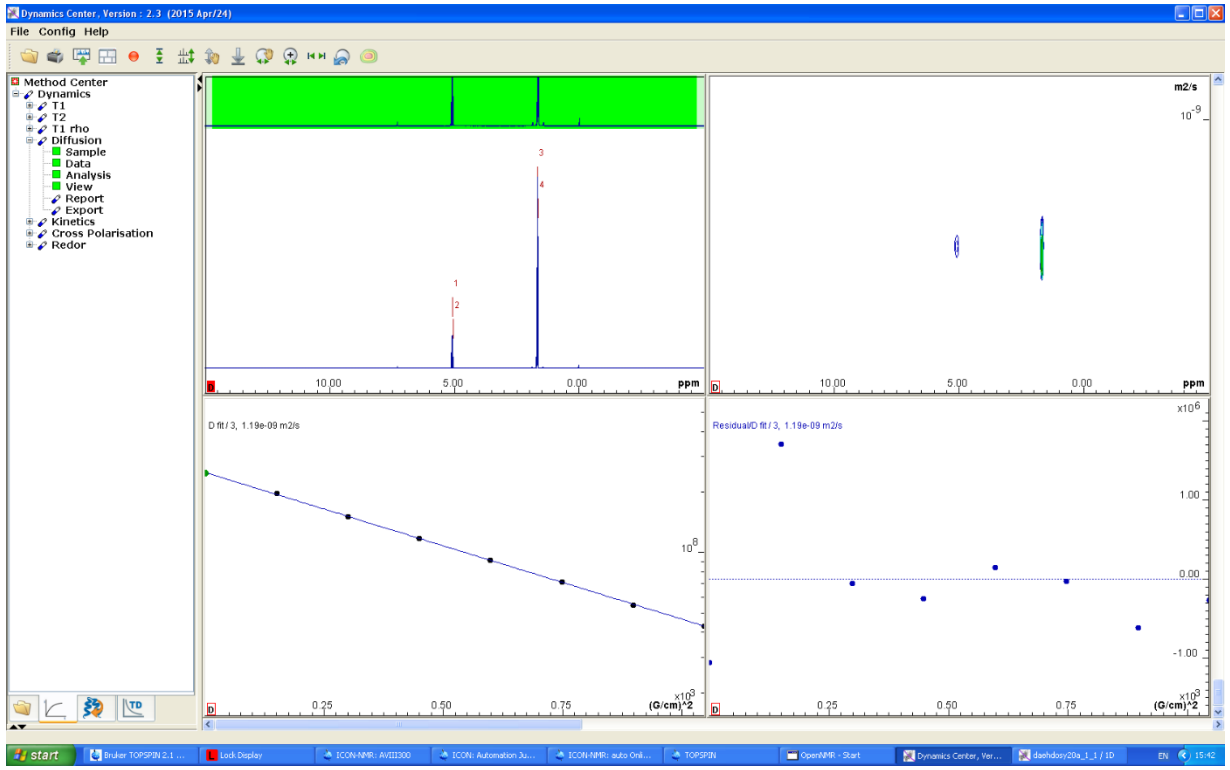
- **Regression plot of *ln* ($I_G/I_{G=0}$) *vs* $G^2$, slope is proportional to $-D$ in a linear, least-squares fit.**

- **Processing software available.**

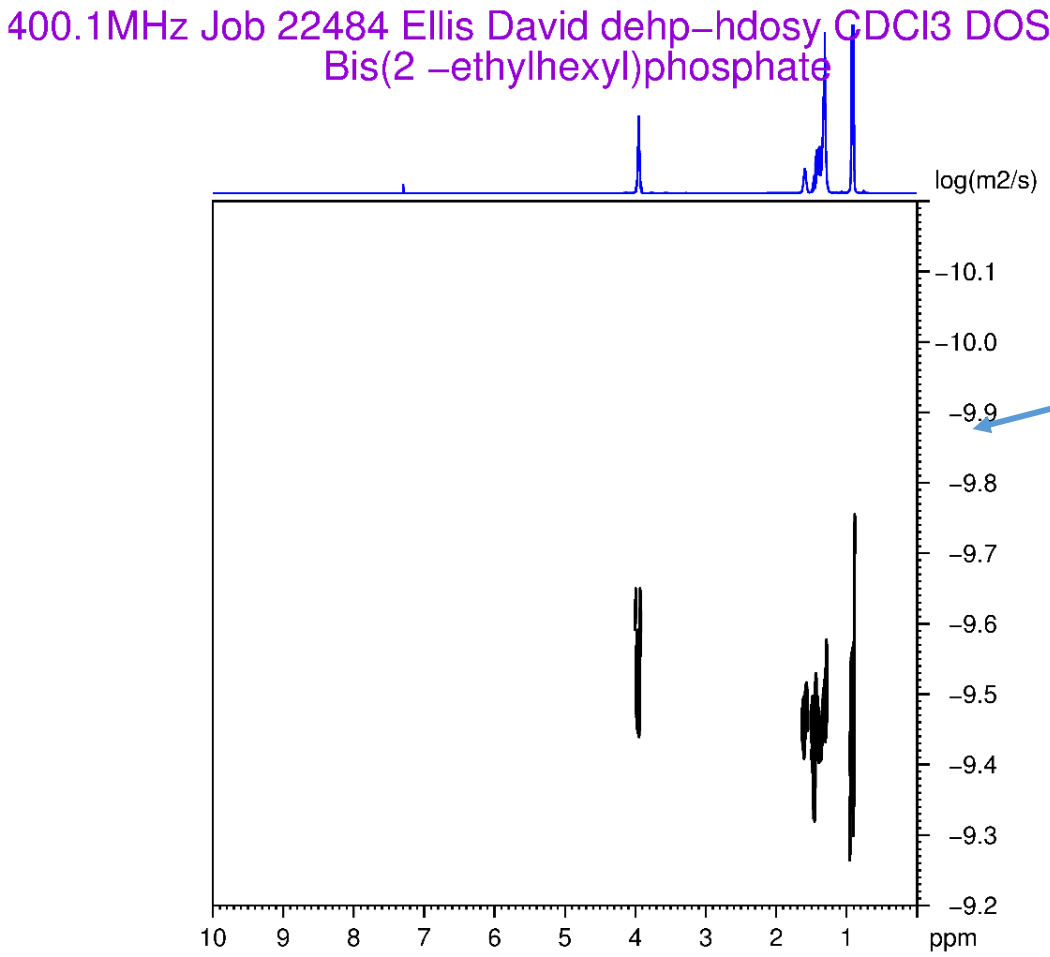
**DOSY Toolbox (now imbedded within GNAT…General NMR Analysis Toolbox at https://nmr.chemistry.manchester.ac.uk/?q=node/430.**

**Bruker ‘Dynamics Centre’.**

**DOSY processing also Implemented in MNova (though not ‘MNova Light’)**



- **Can use the fitting protocol to generate a ‘2D spectrum’.**




**Note that this axis IS NOT a frequency axis, it is the DIFFUSION axis**

- **Reasons to be fearful:**

- **1. Solvent viscosity.**
- **2. Convection…should we rotate the sample tube?**
- **3. Solvent near the boiling point.**
- **4. *D* is temperature dependent…need to know the probe temperature.**
- **5. Signal attenuation through nuclear relaxation.**

## APPLICATIONS

- **Lots but we only have time to consider a few.**

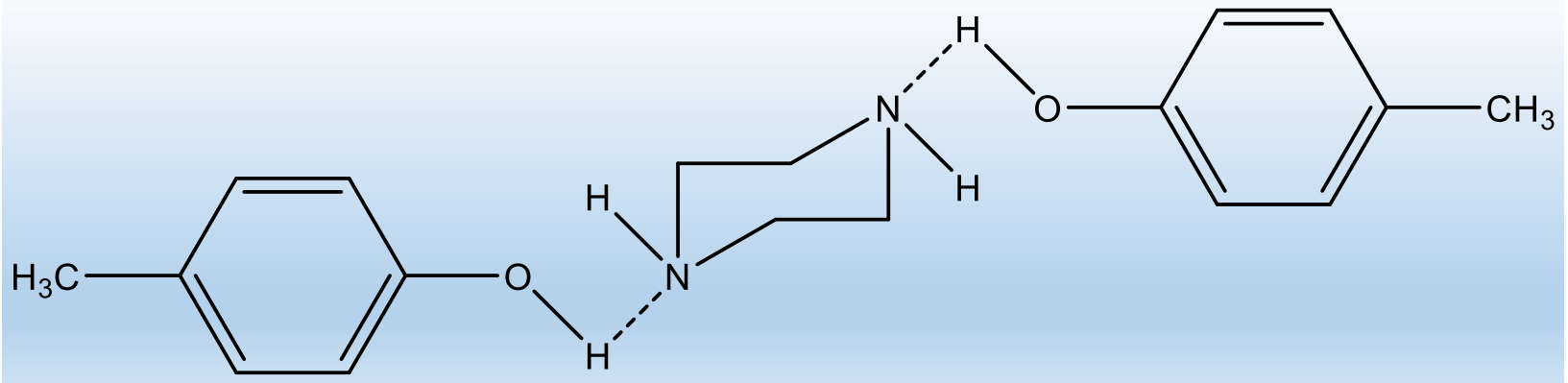
- **1. Hydrogen Bonding.**
- **2. Ion Pairing.**
- **3. Aggregation.**
- **4. Separation of Mixtures.**

## ➢ Hydrogen Bonding.

***p*-Cresol and piperazine form a hydrogen-bonded assembly…in the solid state, we can confirm this by X-ray crystallography.**

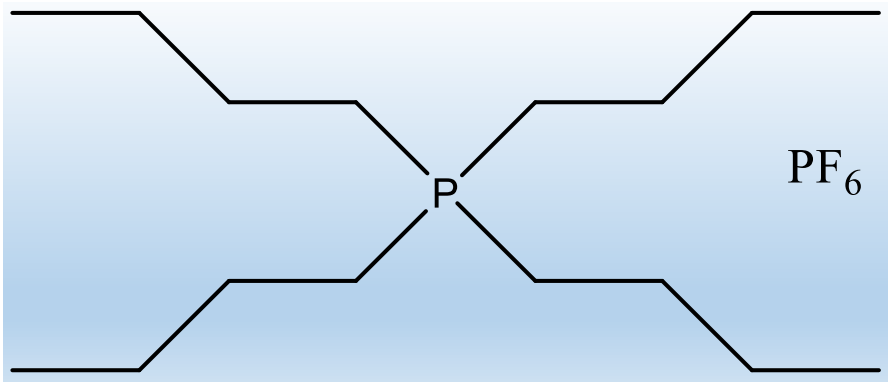
**In solution, we can run DOSY experiments on the two pure components separately, and then on the mixture…all in $CDCl_3$, and look at the values of *D* that we obtain.**

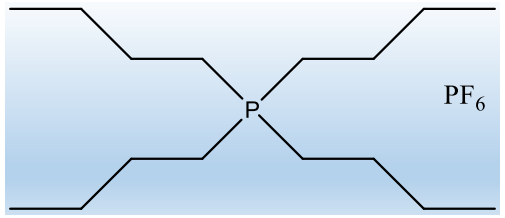
| | *D* - Pure component ($10^{-10} m^2/s$) | *D* - Mixture ($10^{-10}$ $m^2/s$) |
|---|---|---|
| P-Cresol | 16.7 | 9.71 |
| Piperazine | 25.3 | 9.91 |




**Reduced value of *D* for the mixture reflects the presence of the hydrogen-bonded aggregate.**

- **Ion Pairing.**





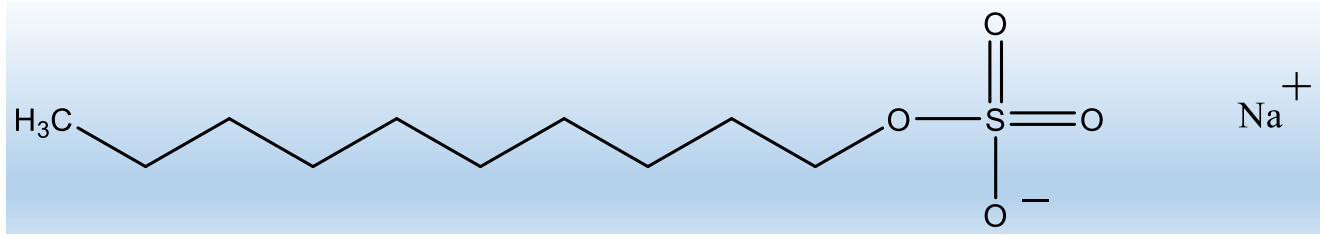

| Nature of analysis | *D* ($10^{-10}$ $m^2/s$) in $CDCl_3$ | *D* ($10^{-10}$ $m^2/s$) in DMSO |
|---|---|---|
| $^{31}P$ cation | 3.8 | 1.7 |
| $^{31}P$ anion | 3.8 | 3.6 |
| | | |
| $^{19}F$ anion | 3.7 | 3.6 |

**One interpretation…the compound behaves as a tight ion-pair in $CDCl_3$ but NOT in DMSO.**

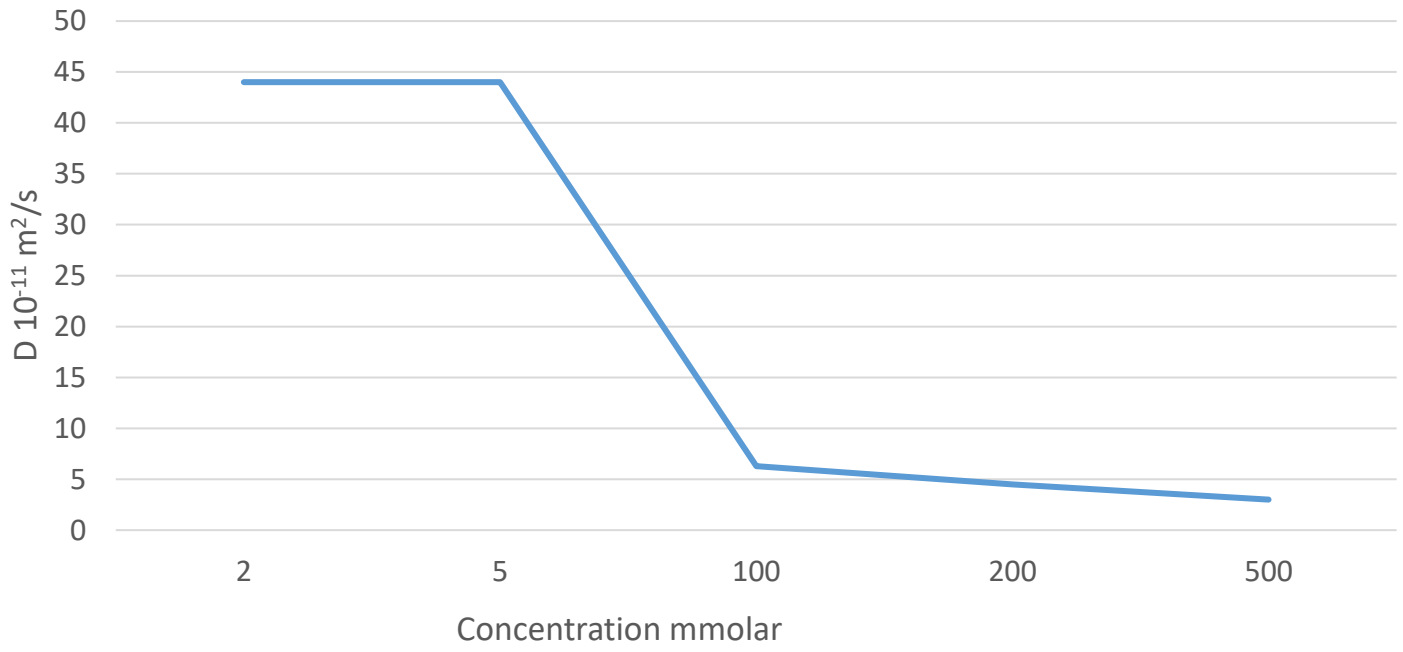
**Note that DOSY is possible with heteronuclei ($^{31}P$, $^{19}F$) not restricted to $^{1}H$.**

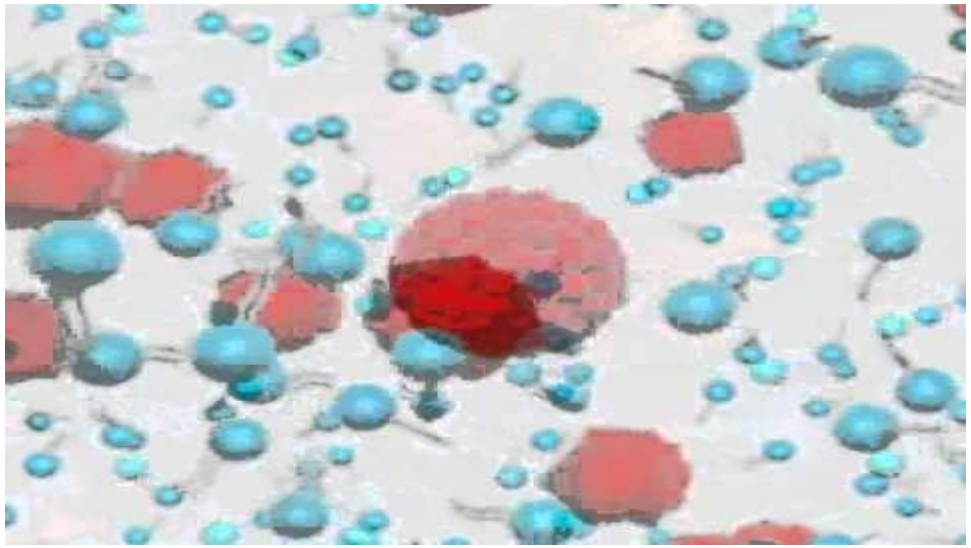
## ➢ Aggregation.

**Dissolve SDS (sodium dodecylsulphate) in $D_2O$…carry out DOSY at different concentrations…what do we observe?**




**Formation of micelles at high concentrations – molecular aggregates which diffuse slowly. Micelles are formed by AMPIPHILIC molecules (display hydrophobic and hydrophilic character).**





**Can determine the Critical Micelle Concentration (CMC) by DOSY.**

- **‘Separation’ of Mixtures.**

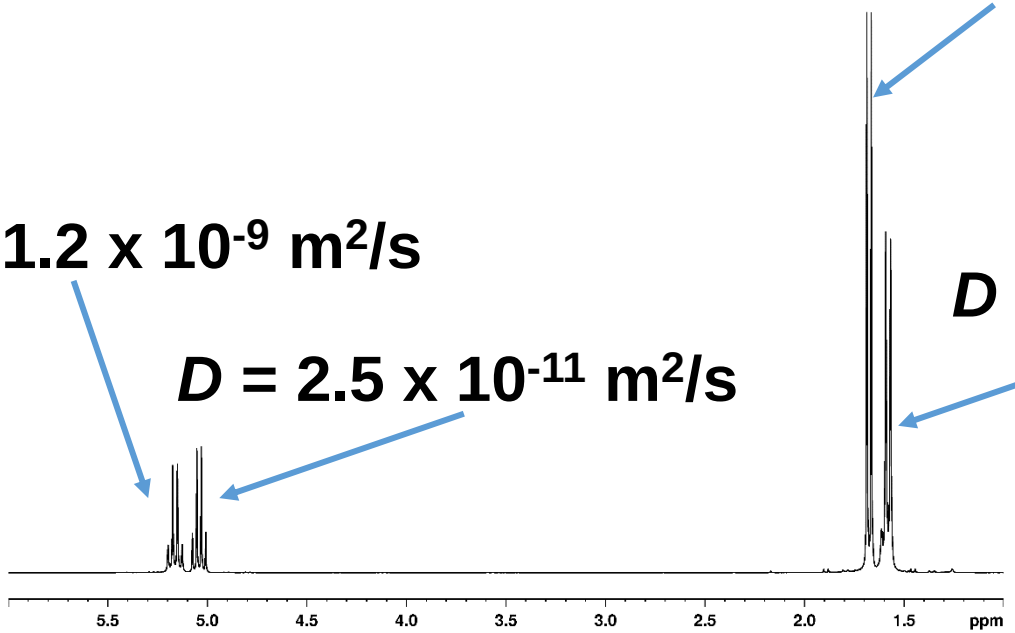
**We have prepared a polymer (polylactic acid) from lactide and we have them both in a crude reaction mix…they have very different molecular weights…we should be able to ‘separate’ them in a DOSY experiment.**

$D = 2.5 \times 10^{-11}$ m²/s

$D = 1.2 \times 10^{-9}$ m²/s

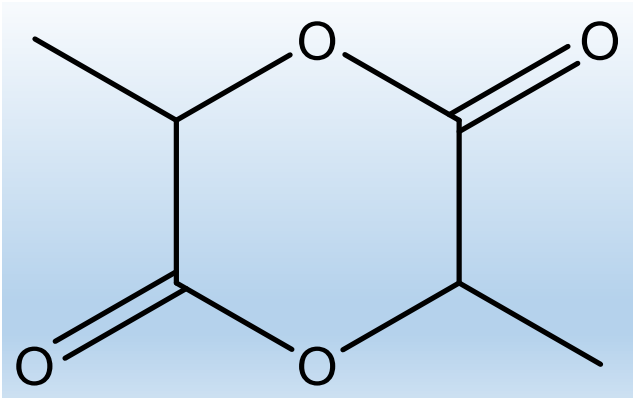
$D = 2.5 \times 10^{-11}$ m²/s

$D = 1.3 \times 10^{-9}$ m²/s




CH region

$CH_3$ region




**Can you explain these observations?**