EXPERIMENT 3 - DETERMINING THE DIFFUSION IN LIQUIDS USING MOLECULAR DYNAMICS SIMULATIONS & NMR

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Objective
Determine the translational diffusion coefficient of a given solute molecule in a relatively dilute liquid mixture. Report the diffusion coefficient and the associated error. Use both Molecular Dynamic (MD) simulations and Nuclear Magnetic Resonance (NMR) spectroscopy to compute a diffusion coefficient of a given (assigned) solute in a solvent of water. One of the great benefits of NMR is that it can resolve many different chemical compounds without the need for chemical separation. Hence, a complex chemical mixture can be provided and the diffusion coefficients of each molecule can be determined. Molecular dynamic (MD) simulations will be performed before the experimental NMR measurements. Compare the results obtained from both computational and experimental methods.

Introduction
Self-diffusion is the random translational motion of atoms, molecules or ions. Translational diffusion is one of the most fundamental forms of motion in liquids and gases, and is responsible for all chemical reactions (since the reacting species must collide before they can react). The diffusion of molecules in a liquid is also closely related to molecular size, as can be seen from the Stokes-Einstein equation [1-3],

\[ D = \frac{kT}{f} \]

where \( k \) is the Boltzmann constant, \( T \) is temperature and \( f \) is the friction coefficient. For the simple case of a spherical particle with an effective hydrodynamic radius \( r_s \) in a solution of viscosity \( \eta \) the friction factor is given by

\[ f = 6\pi r_s \eta \]

So, to first approximation this can be used to estimate the viscosity of a liquid from the measured self-diffusion coefficient.

The experimental data provided for this lab is pulsed field gradient spin echo (PFGSE) NMR spectra. This NMR method is one of the most direct and accurate means of measuring the diffusion coefficient of liquids. The technique was first described by E.O. Stejskal and J.E. Tanner in Journal of Chemical Physics (1965) [4]. The standard PFGSE pulse sequence is shown in Figure 1. The top line labeled 'RF' is the pulses applied to the sample and represent a standard spin echo pulse sequence [5].
Figure 1 – Schematic of a standard pulsed field gradient spin echo pulse sequence. The top line is the RF channel and the second line is the gradient (G). The time between RF pulses is tau (τ), the time of the gradient pulse is δ and the time between gradient pulses is Δ. Lastly, d1 is the time between scans.

The second line is the gradient channel, ∇, and shows two gradient pulses that are turned on between the 90° (π/2) and 180° (π) RF pulses and between the π pulse and acquisition. The length of the two gradient pulses are the same and given by time δ. The time between the two gradient pulses is given by time Δ. The time between the 90° and 180° RF pulses is tau, τ. By repeating this pulse sequence with increasing gradient strength (stronger gradient pulses), the peak intensity of liquid state NMR resonances will decrease because of diffusion in the gradient field. The equation that describes this phenomenon was introduced by Stejskal and Tanner [4] and further explained in numerous scientific papers [6-8].

The derived result of using the pulse sequence shown in figure 1 is

\[
\ln \left( \frac{S(2\tau)}{S(0)} \right) = -γ^2 G' D δ^2 \left( Δ - \frac{δ}{3} \right)
\]

where \( S(2τ) \) is the signal at 2τ, \( S(0) \) is the initial signal, \( γ \) is the magnetogyric ratio, \( G \) is the magnetic field gradient strength, \( D \) is the diffusion coefficient, \( δ \) is the amount of time the gradient pulse is ‘on’ and \( Δ \) is the time between the two gradient pulses. The signal \( S(0) \) is typically determined by running the experiment without any gradient pulse power (G=0%). The signal \( S(2τ) \) is acquired directly in the experiment. Hence, these parameters are determined directly from NMR experiments and corresponding data. The magnetogyric ratio (or gyromagnetic ratio) of a nuclei is a ratio of its magnetic dipole moment to its angular momentum. This is a constant for each nuclear spin isotope [2]. The gradient is controlled by the NMR and is calibrated to provide a known gradient typically expressed in Telsa per meter (T/m) or Gauss per centimeter (G/cm). The timing parameters, \( δ \) and \( Δ \) must be experimentally set. With all these parameters set and/or measured, you will be able to use this equation to determine the diffusion coefficient of a liquid from a set of PSFSE NMR measurements.

**Computational**

One of the focus points of this lab will be on understanding diffusion and computational molecular dynamics (MD) can greatly aid in this process. Hence,
the lab will start with a computational exercise. MD provides a direct measure of diffusion through the mean squared displacement (MSD) of the molecules in the simulation. This is a great molecular level tool for visualizing and understanding diffusion. The MSD of a molecule undergoing translational diffusion is related to the diffusion coefficient by

\[ MSD = 2nDt \]

where \( n \) is the dimensionality of the displacement, \( D \) is the diffusion coefficient and \( t \) is time. Hence, you can calculate a diffusion coefficient using MD and compare this to experiment. The key to accurate MD diffusion coefficients is using a good potential or force field, calculating long enough in time to get an representative MSD and using a big enough simulation box with periodic boundary conditions. While MD is very useful to help visualize complex molecular dynamics such as diffusion, it is difficult to setup and run because of the computational resources required to run a good MD simulation. This becomes a problem in CHM343, because of the computers available in PSH530. A new multi-core workstation is required for reasonable MD simulations. Hence, a representative MD simulation will be done in CHM343 and the large box, long time simulations will be provided to students for analysis. Simulations will be carried out using NAMD and visualized using the software package visual molecular dynamics (VMD).

**Experimental**

A mixture of several compounds will be made and put in an NMR tube for the class. Students will collect NMR data to allow the determination of each compound diffusion coefficient. The data will be collected by students with the help of TA’s that are familiar with the NMR spectrometers. Each student will be assigned a specific resonance or molecular compound to determine the diffusion coefficient. Students will collect the NMR data in the ASU Magnetic Resonance Research Center (MRRC), which is located in ISTB1 (just north of the ASU bookstore) room L2-63 (basement). You need sun-card access to get into this facility. Hence, you will meet in the lobby at the start of class and the TA will take you down to the lab (if you are late, you will need to call 480-965-3613 to have someone come let you in, and I’m sure they won’t be happy about it!). You will be using either an Agilent 500MHz or a Bruker 400 MHz NMR spectrometer to collect the data. Please write down all relevant NMR parameters (90 and 180 degree pulse lengths, gradient values and times, temperature, pulse sequence, NMR probe used, NMR system used and magnetic field strength, rf frequency, filename, number of transients, number of data points, etc.). These are critical to doing the diffusion coefficient calculations. The most critical parameters are the temperature and the value of the gradient pulse and delay between gradient pulses. The value of small delta (\( \delta \), the gradient pulse length) is typically between 1 and 5 ms and has an associated error of 100 ns. The time between gradient pulses, big delta (\( \Delta \)) is typically between 50 and 200 ms and also has an associated error of 100 ns. The raw data consists of free induction decays (FID).
that have been Fourier transformed to spectra. The resulting spectra are saved in ASCII format. By extracting the peak area and/or peak height at various magnetic field gradient strengths, one can use the above Stejskal and Tanner equation and a linear least squared fitting routine to extract the diffusion coefficient, D. The magnetogyric ratio or gyromagnetic ratio (γ) is a constant for all isotopes and can be found in tables of nuclei properties [2,10]. The 1H gyromagnetic ratio (γ) is reported on wikipedia at http://en.wikipedia.org/wiki/Gyromagnetic_ratio. Remember, when using this constant to ensure whether or not you are in angular units, radians. The gradient amplitude on the NMR instruments must be calibrated to provide an accurate gradient strength. Please collect data on several liquids with known diffusion coefficients so that you can accurately determine the gradient strength and use this calibrated gradient strength for your molecular mixture. The NMR gradients are supposed to be linear. The calibration you do on known liquids will also help prove or disprove how linear the gradients are for your NMR probe used in the experiment.

Data Analysis
Determine the diffusion coefficient of the assigned solute in the liquid mixture. An outline of the steps needed to use these NMR spectra and MD data, to calculate the diffusion coefficient is given below:

- Download the MD trajectories from the web.
- Read the data into an analysis package (e.g., plot.ly, Kaleidagraph, Excel, Origin, SigmaPlot, DeltaGraph, Octave, Mathematica, Scilab or Matlab).
- Make a plot of the MSD vs time being careful to use correct units for the axes.
- Use the equation relating MSD to time shown above to calculate the diffusion coefficient of the molecule you have been assigned.
- Download the NMR data from the web.
- Read the data into a data analysis package.
- Make a stacked plot of the spectra (for your report it is common to use a subset of the data to keep the plot clear and not too cluttered).
- Determine the signal intensity for each spectral element, S(2τ) and its associated error (estimation of error). The signal strength can be determined from the area under the peak in the NMR spectrum (or from the height of the NMR peak, but this will have much higher associated error), assuming the linewidth is constant.
- Using the S(2τ) data of the solvent (or calibration standard) and the known self-diffusion coefficient of the solvent or a separate calibration standard sample (typically H2O/D2O, because it’s diffusion rate is so well known), you can convert all gradient amplitude values (e.g., dac units on a Agilent NMR) into an actual magnetic field gradient in T/m or G/cm. This is done using the Stejskal-Tanner equation.
- Looking at data in a linearized fashion can help to determine if any data looks out of place and is suspect of being ‘bad’ data. If so, you should use a Q-test to determine whether the data can be omitted (rejected).
- Now you can use the Stejskal-Tanner equation to determine the diffusion coefficient, D, of the assigned solute (or any peak in the NMR spectrum).
is typically done by plotting the natural log $S(2\tau)$ versus the gradient strength squared ($G^2$). Remember to propagate errors.

- Compare the calculated diffusion coefficients to literature values, if available.
- Done

Safety
Magnetic safety will be discussed immediately before the NMR lab. You will be around high magnetic fields and need to remove all metal. Also, students with pace makers or any electronic devise implanted in their bodies should NOT be near high magnetic fields. I don’t think that computers pose much health risk. However, they can cause mental anxiety.

References