NOESY w/ Exchange
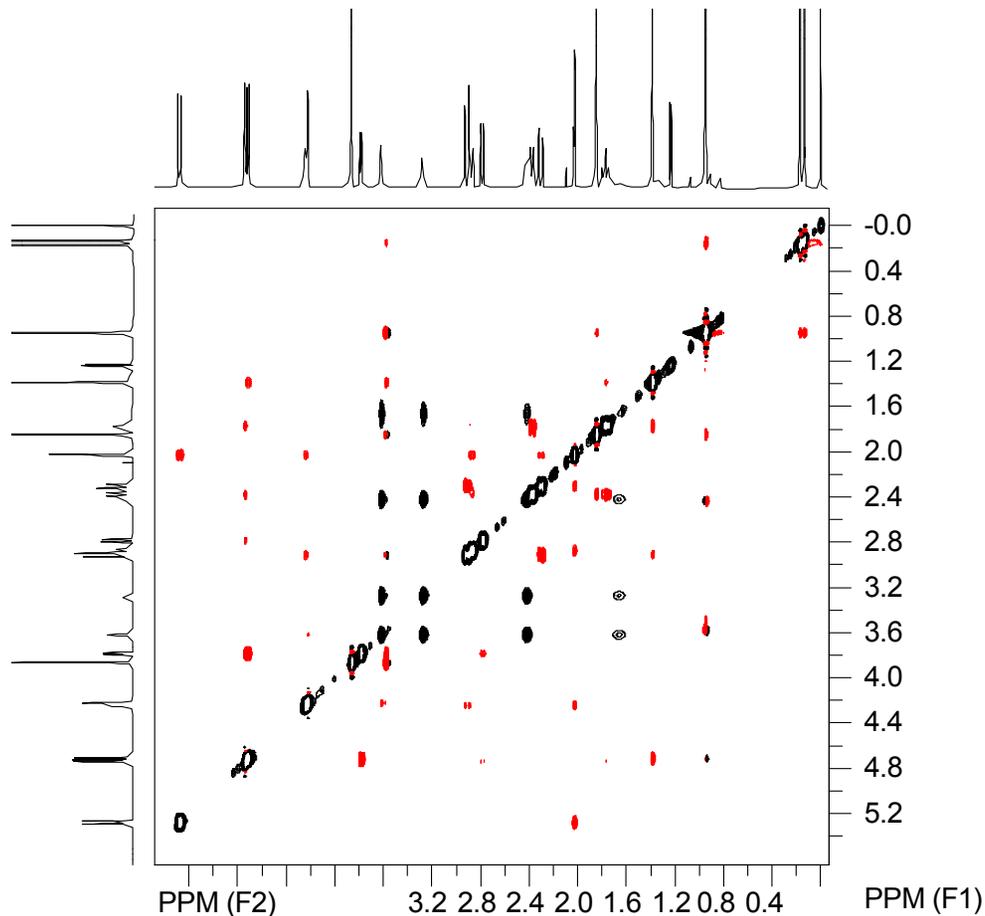

For small molecules :
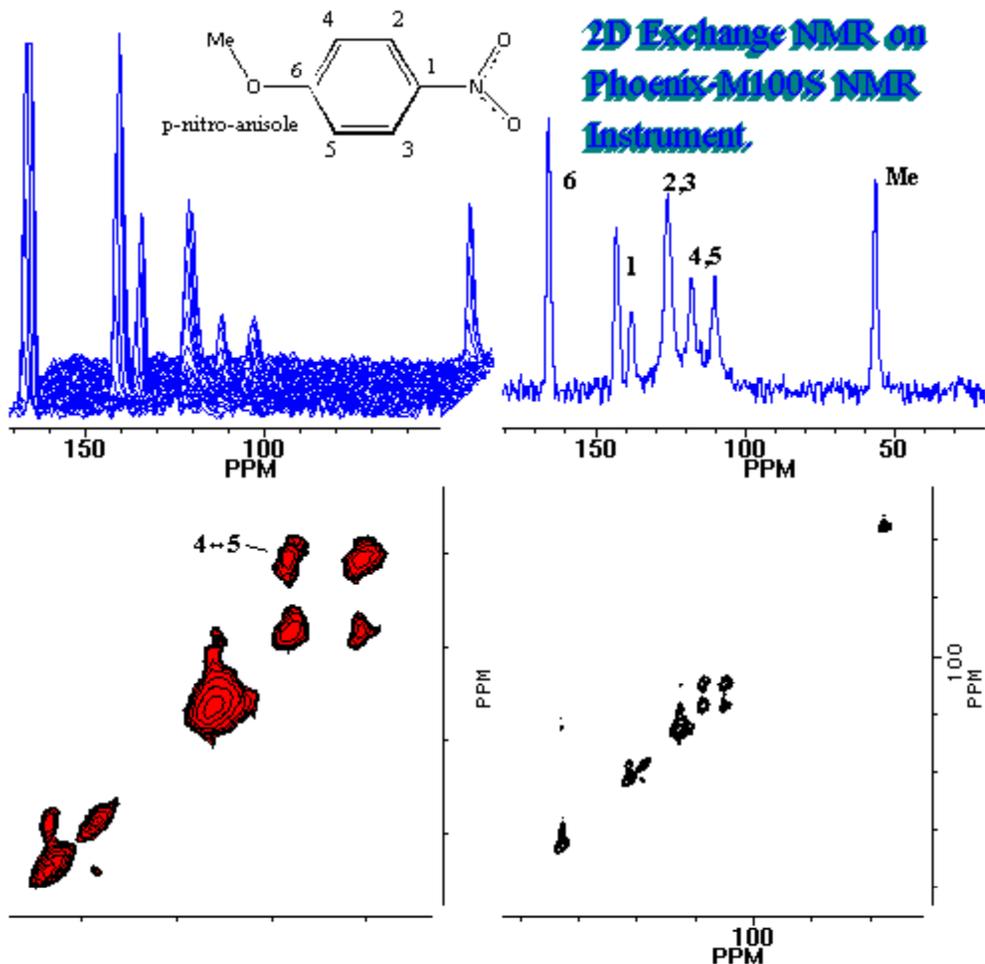
$(\tau_c < 1/\omega_0)$

- NOE cross-peaks have opposite phase vs. the diagonal.
- Exchange Peaks have same phase as the diagonal.

For large molecules:

- NOE & Exchange cross peaks have the same phase
- ROESY can distinguish between NOE/Exchange
- Be careful!

Chemical Exchange NMR (EXCHSY)

2D Exchange NMR on Phoenix-M100S NMR Instrument.

p-nitro-anisole

In this molecule, carbons #4 and #5 have different chemical shifts due to the orientation of the ring relative to the O-Me Group (note this was done in the solid-state, so molecular motion is slower than in solution, where C4 & C5 would be equivalent).

To explain this experiment, consider carbon #5. If, during the time labeled t1 above, the O-Me is oriented as shown above, then this carbon has the chemical shift of Carbon #5 during t1.

If, during the time labeled "Mix", the ring flips relative to the O-Me, then the same carbon atom not takes-on the chemical shift of Carbon #4. So , during the time labeled "t2" this carbon has the chemical shift of position #4.

If this occurs, then you see intensity that has the chemical shift frequency of #5 during t1 (the vertical axis), and the chemical shift of #4 during t2 (the horizontal axis). This is signal appears as the cross-peak connecting peaks #4 & #5 along the diagonal.

Notice that with longer mixing times (Mix) there will be more cross-peak intensity, until everything starts to decay away when T(Mix) starts to become large relative to T1 (T1 relaxation is also occurring during the mixing time).

Analyzing Exchange Data:
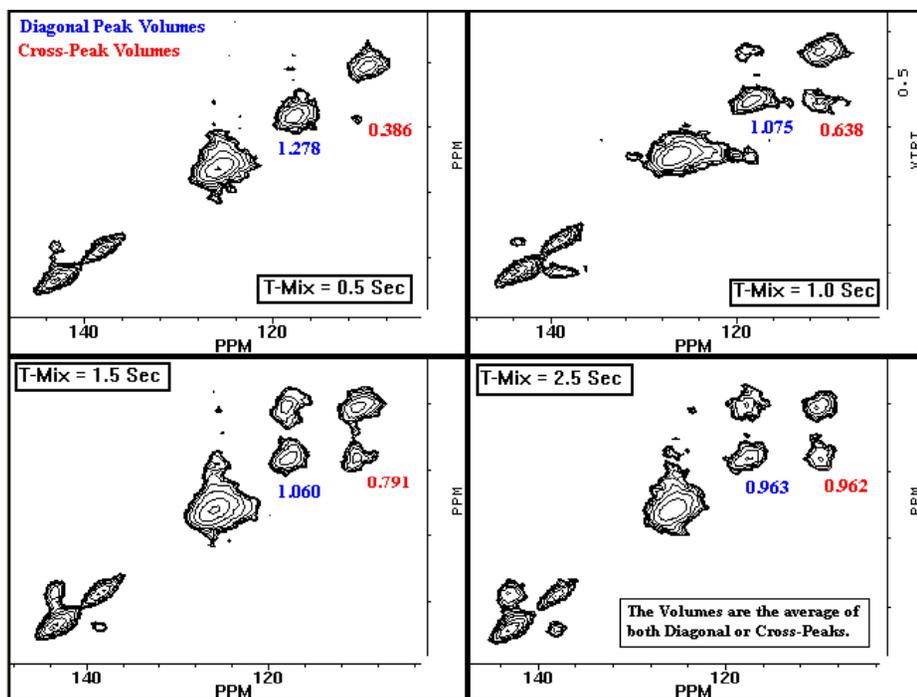
Data Analysis:

The analysis of the build-up data is straightforward if one expresses the cross-peak intensities relative to the diagonal. In terms of Exchange-Rate-Constant (K), mixing-time (Tm), and Spin-Lattice-Relaxation-Time (T1), the intensities of the cross-peaks (Ix) and diagonal peaks (Id) can are given by the following expressions:
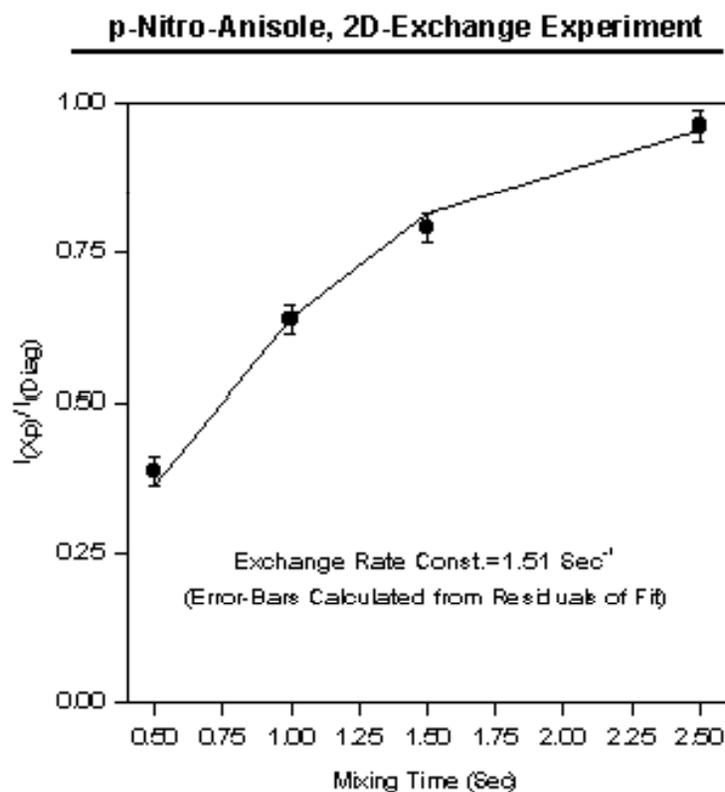
$$Id = 1/4[exp(-Tm/T1)][1+exp(-K\ Tm)]$$
$$and$$
$$Ix = 1/4[exp(-Tm/T1)][1-exp(-K\ Tm)]$$

Therefore, one can fit Ix/Id = [1-exp(-K Tm)]/[1+exp(-K Tm)] using any good curve-fitting program to get excellent results. These data were fit using "Sigma-Plot" (Jandel Scientific), and the results are shown below:

Calculating the Exchange Rate Constant

p-Nitro-Anisole, 2D-Exchange Experiment

Exchange Rate Const.=1.51 Sec^{-1}
(Error-Bars Calculated from Residuals of Fit)

y-axis: $I_{(xp)}/I_{(Diag)}$

x-axis: Mixing Time (Sec)

Therefore, one can fit

$$Ix/Id = [1-exp(-K\ Tm)]/[1+exp(-K\ Tm)]$$

using any good curve-fitting program to get excellent results. These data were fit using "Sigma-Plot" (Jandel Scientific), and the results are shown below:

1D Selective EXCHSY

Performing many 2D-EXCHSY experiments with variable mixing times can require a lot of time. Using selective pulses, one can perform a 1-Dimensional analogue of the 2D-EXCHSY experiment in which one NMR peak (corresponding to the "diagonal" peak in the 2D experiment) is selected, and the peak arising from dynamic exchange will increase (corresponding to the "cross-peak" in the 2D experiment) will appear in increasing intensity vs. Mising Time

Selective pulse applied to this methyl resonance

This peak will appear with Increasing intensity vs. Mixing Time
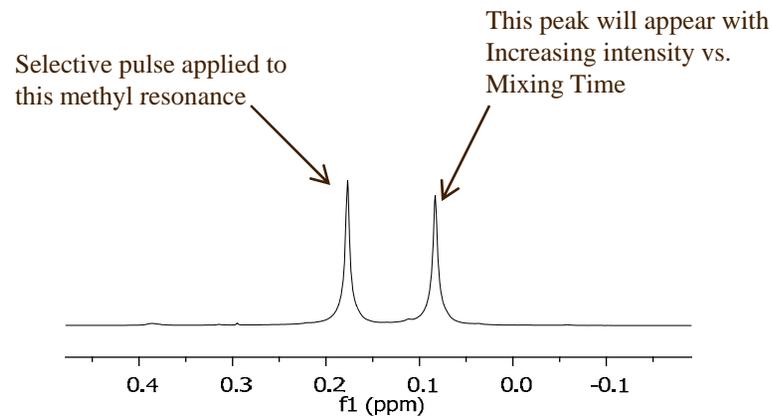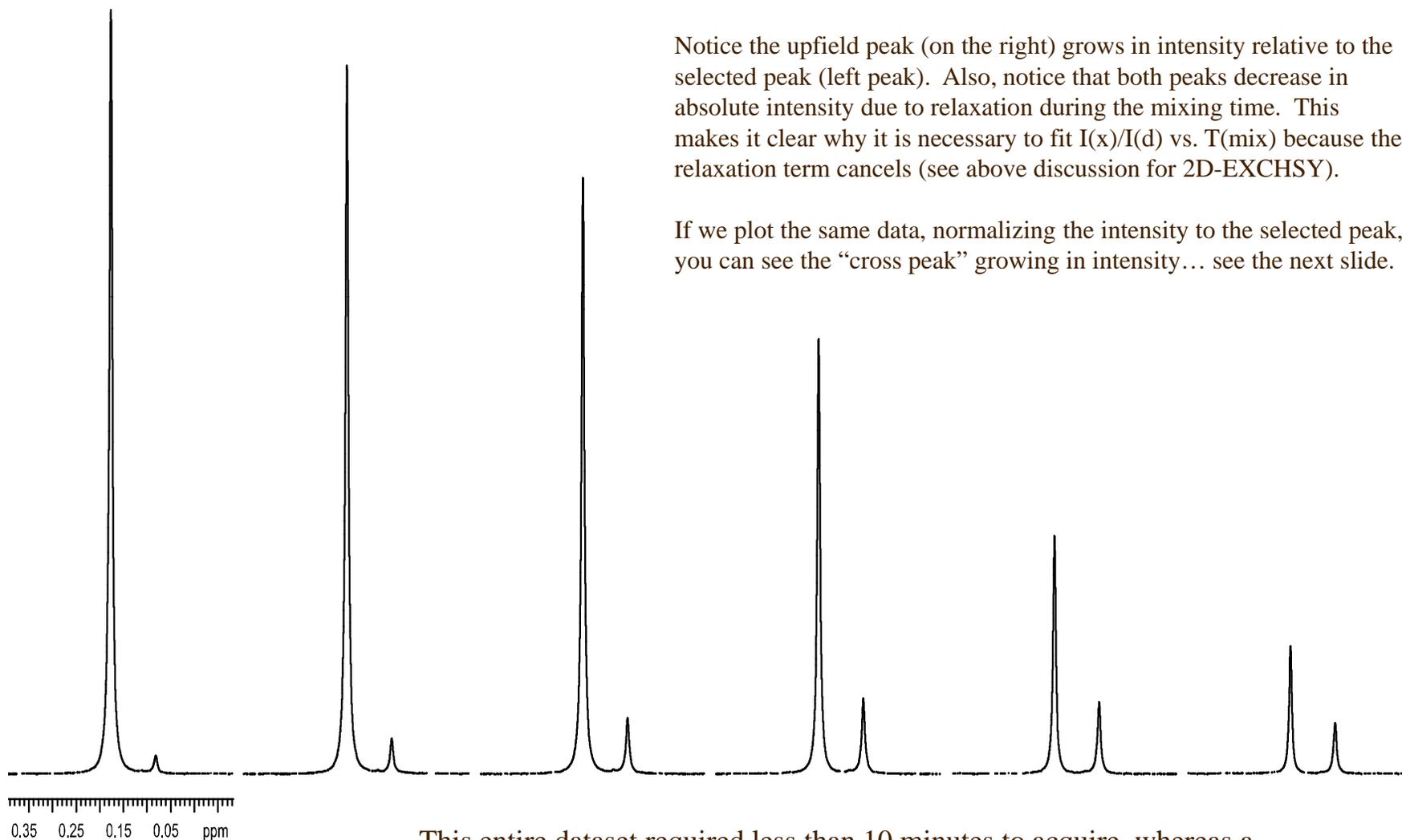

Methyl signals undergo slow exchange at low temperature
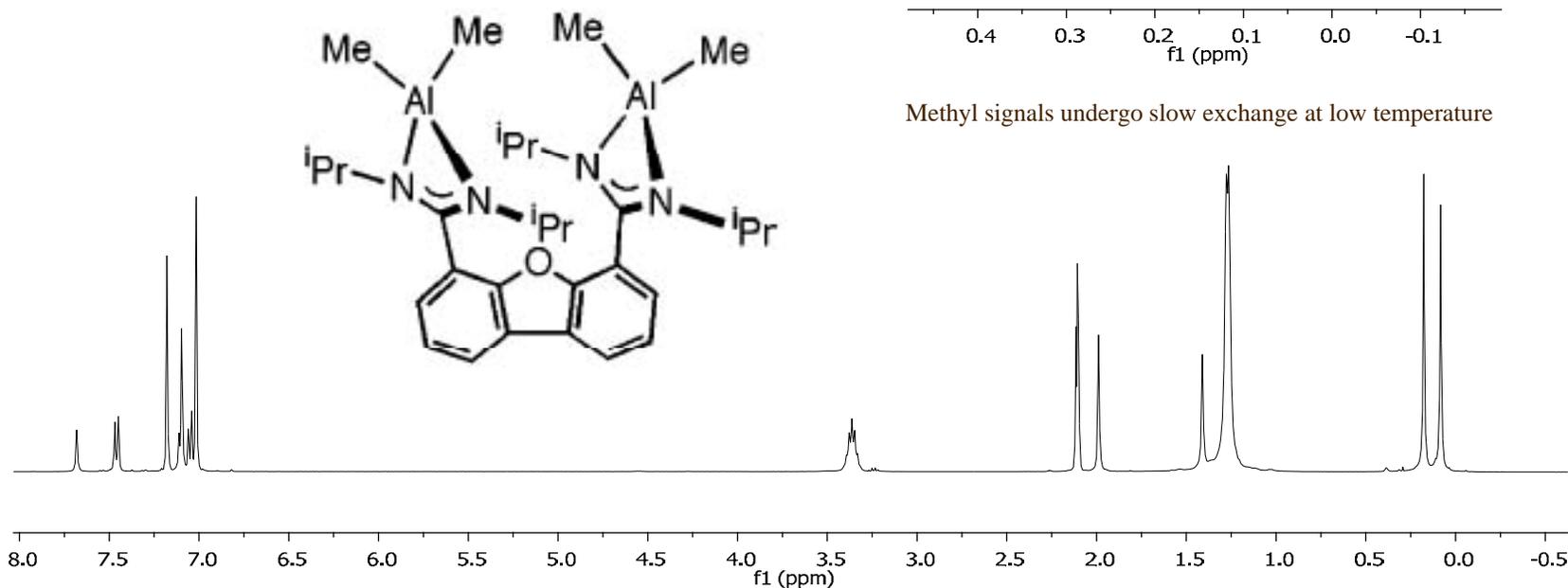
B. Clare, N. Sarker, R. Shoemaker and J. Hagadorn, *Inorganic Chemistry*, **43**, 1159-1166 (2004).
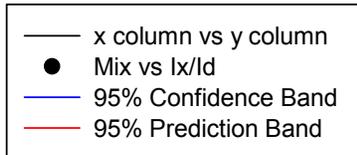
1D Selective EXCHSY

Notice the upfield peak (on the right) grows in intensity relative to the selected peak (left peak). Also, notice that both peaks decrease in absolute intensity due to relaxation during the mixing time. This makes it clear why it is necessary to fit $I(x)/I(d)$ vs. $T(mix)$ because the relaxation term cancels (see above discussion for 2D-EXCHSY).

If we plot the same data, normalizing the intensity to the selected peak, you can see the "cross peak" growing in intensity… see the next slide.
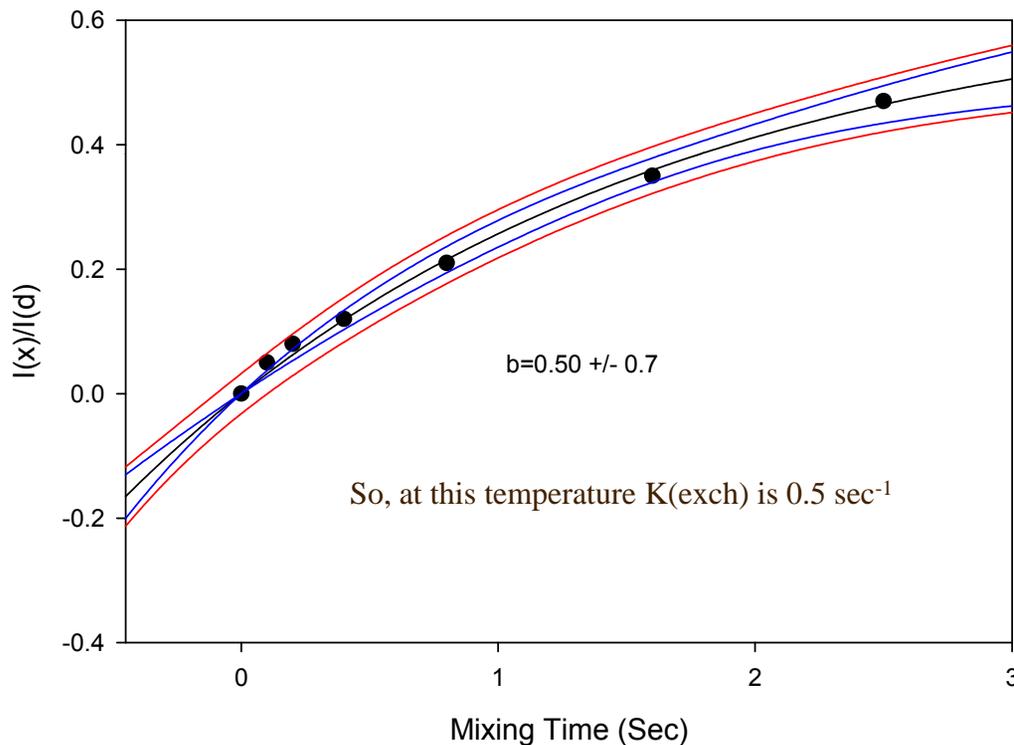
0.35   0.25   0.15   0.05   ppm

This entire dataset required less than 10 minutes to acquire, whereas a full set of 2D-EXCHSY spectra would have been more than 5 hours.

1D Selective EXCHSY

0.35 0.25 0.15 0.05 ppm

T(Mix) = 0.1 Sec   0.2 Sec   0.4 Sec   0.8 Sec.   1.6 Sec   2.5 Sec.
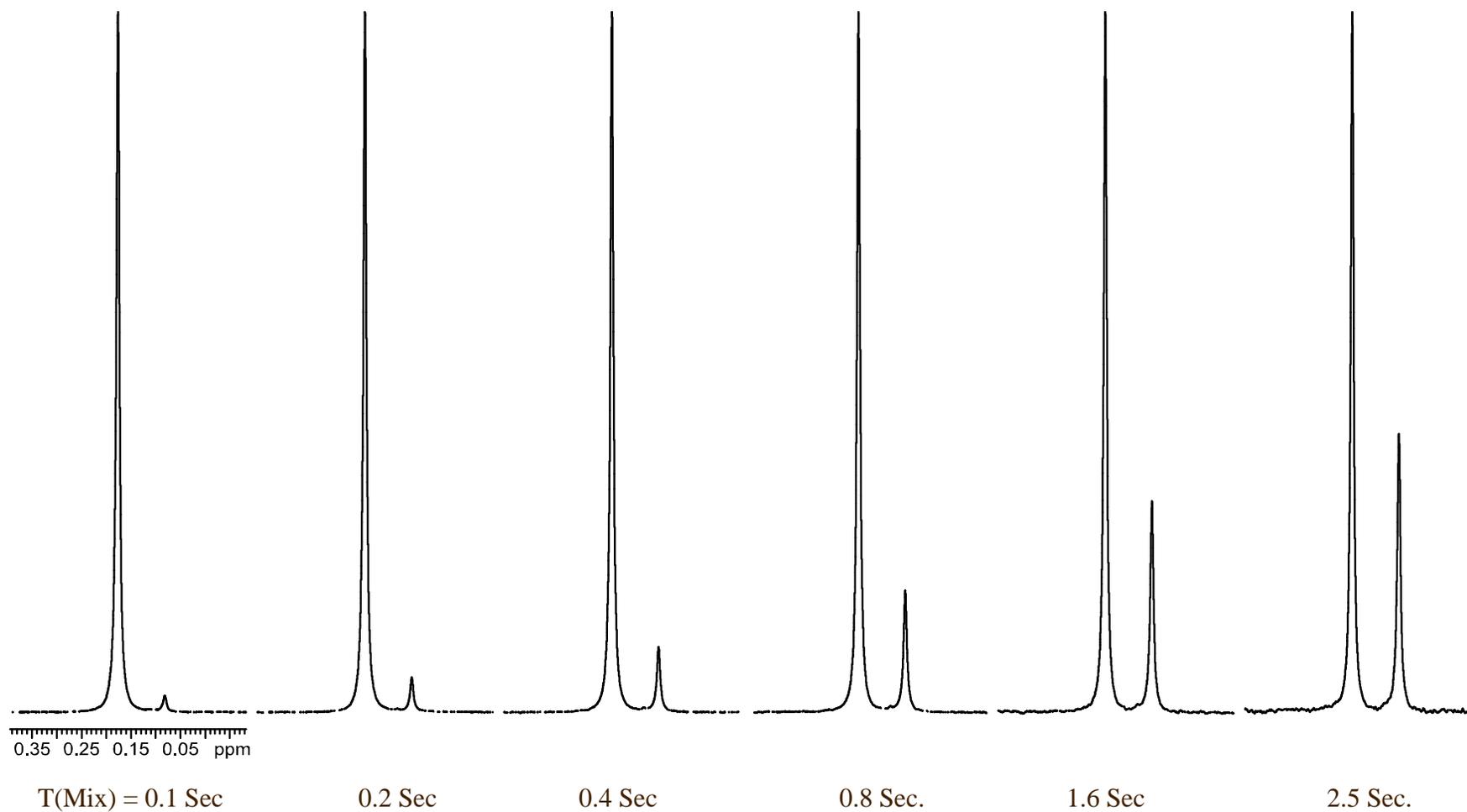
1D Selective EXCHSY… data analysis

1D-EXCHSY Data Fitting Results

Remember, in the 1D-selective experiment, $I(x)/I(d)$ is the Intensity of the selected peak, divided by the intensity of the exchange peak.

b=0.50 +/- 0.7

So, at this temperature K(exch) is 0.5 sec^{-1}

T(Mix)	I(x)/I(d)
0.0000	0.0000
0.1000	0.0500
0.2000	0.0800
0.4000	0.1200
0.8000	0.2100
1.6000	0.3500
2.5000	0.4700

Legend:
— x column vs y column
● Mix vs Ix/Id
— 95% Confidence Band
— 95% Prediction Band