Bloch-McConnell Equations

Kinetics at Equilibrium

Kinetics via NMR

Analogously to other spectroscopic methods, and also to non spectroscopic techniques, either the disappearing of a reagent (A) or the increasing of a product (B) can be followed $A \rightarrow B$

Exclusively by NMR the kinetic constants are determined at equilibrium

$$\boxed{A \leftrightarrow B}$$

Under the usual assumption of a **first order** law.

The main methods are:

- Lineshape analysis
- EXSY (2D)

Parameters to be considered

- R_1
- intrisinc linewidth $\Delta\nu_{1/2} = R_2/\pi$
- shift separation (in $\omega = 2\pi\nu$, field dependent) between the exchangin sites
- k

For $k < R_1$ no effect (the spin system reverted to equilibrium before exchange took place)

For $R_1 < k << \omega_A - \omega_B$ separate signals and cross-peaks in the EXSY 2D spectra

For $R_2 < k << \omega_A - \omega_B$ linebroadening

$$\Delta \nu_{1/2} = \frac{1}{\pi}(R_2 + k)$$

At high magnetic field the system can be in the slow exchange regime since $k << \omega_A - \omega_B$, but exhibits broad lines if k is large

In the simplest case of mutual exchange, the lineshape depends only on:

- frequency difference between the two sites ($\delta\nu$),
- k (or equivalentely on the lifetime in each site t=1/k),
- linewidth in the absence of exchange ($\Delta\nu_{1/2}$)

Simple formulas relate the lineshapes with these parameters

under the assumption that the exchange process is fast compared to T_1

For

$$\boxed{k_c = \frac{\pi\delta\nu}{\sqrt{2}} = 2.22 \cdot \delta\nu}$$

coalescence in the case of mutual exvhange

with $\delta\nu$ shift difference in Hz

signal occurs at $\nu_{av} = p_A\nu_A + p_B\nu_B$

Fast exchange

if k> k_c there is just one broad signal with linewith:

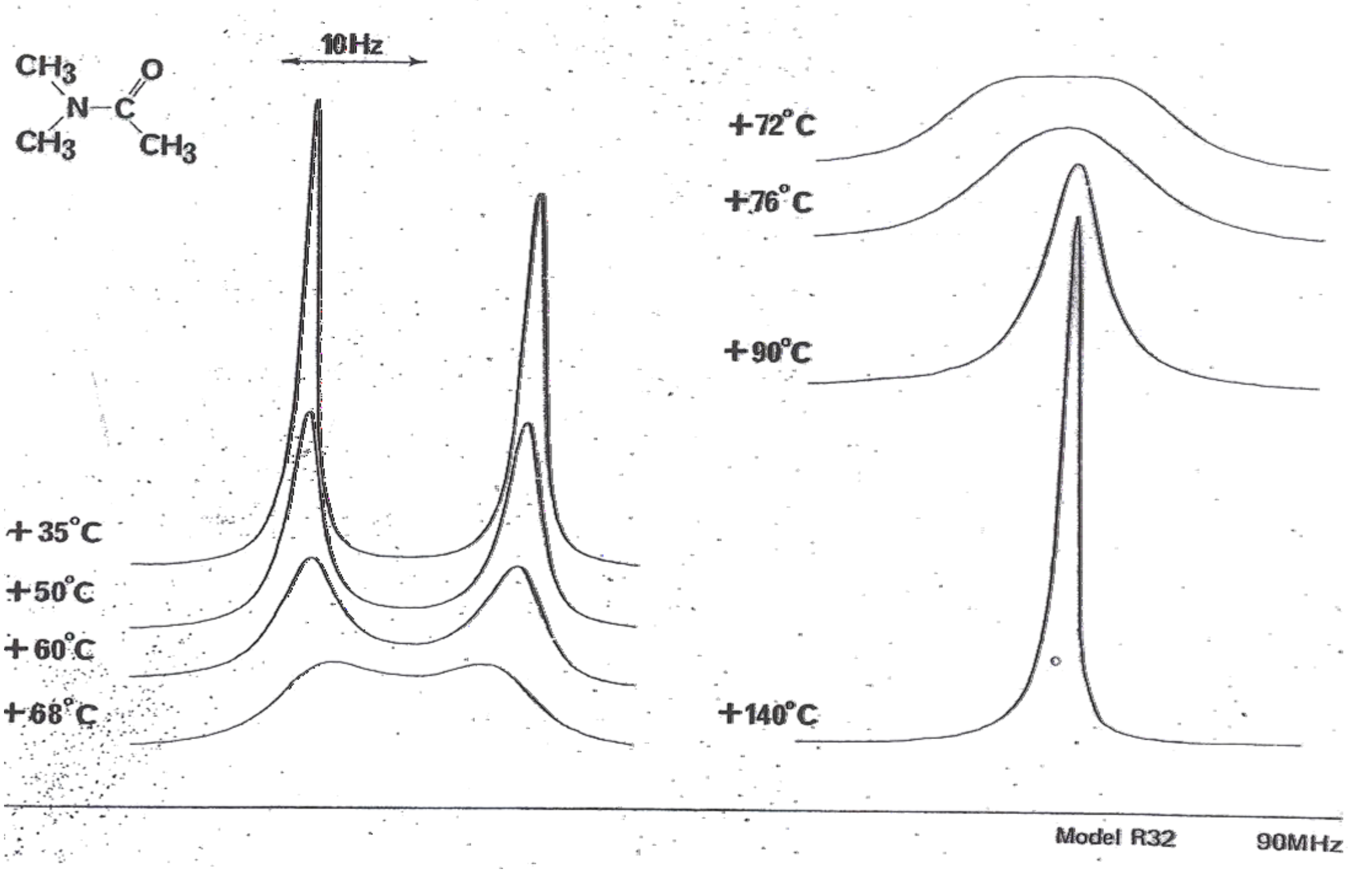
$$\boxed{\Delta\nu_{1/2} = \frac{4\pi p_A p_B (\delta\nu)^2}{k_1 + k_2}}$$

$\Delta\nu_{1/2}$ decreases upon increasing k

For k>> $\delta\nu$ the linewidth is determined by the average of the transverse relaxation rates k depends on temperature according Arrhenius's law

$$k = A\exp\left(-\frac{E_a}{kT}\right)$$

therefore the NMR spectrum changes with temperature



Bloch-McConnell Equations

Let’s consider the Bloch Equations for a system of a single kind of spins, A,

after the pulse,

in a slightly off-resonance rotating frame

$$\frac{dM_{xA}}{dt} = -M_{yA}\Omega_A - \frac{M_{xA}}{T_{2A}}$$

$$\frac{dM_{yA}}{dt} = M_{xA}\Omega_A - \frac{M_{yA}}{T_{2A}}$$

$$\frac{dM_{zA}}{dt} = -\frac{M_{zA} - M_0}{T_{1A}}$$

It is convenient using the complex magnetization M_{+A}

$$M_{+A}=M_{xA}+iM_{yA}$$

Its evolution in the transverse plane is obtained by solving the differential equation

$$\frac{dM_{+A}}{dt}=iM_{+A}\Omega_A-\frac{M_{+A}}{T_{2A}}$$

$$M_{+A}(t)=M_{+A}(0)\exp(i\Omega_A t)\exp(-R_{2A}t)$$

Let’s consider that the molecule with the spin A (which, for simplicity, is not scalarly coupled with any other nucleus) undergoes a reaction with a first order kinetics and the reaction is reversible i.e., it takes part to an equilibrium of the kind: $A \underset{k_2}{\overset{k_1}{\rightleftarrows}} B$

$$K = \frac{k_1}{k_2}$$

$p_A k_1 = p_B k_2$

The differential equations decribing the evolution of transverse magnetization are now coupled

$$\frac{dM_{+A}}{dt} = iM_{+A}\Omega_A - \frac{M_{+A}}{T_{2A}} - k_1 M_{+A} + k_2 M_{+B}$$

$$\frac{dM_{+B}}{dt} = k_1 M_{+A} + iM_{+B}\Omega_B - \frac{M_{+B}}{T_{2B}} - k_2 M_{+B}$$

Matrix Form of Bloch McConnell Equations

$$\frac{d}{dt}\begin{vmatrix} M_{+A} \\ M_{+B} \end{vmatrix} = \begin{vmatrix} i\Omega_A - \frac{1}{T_{2A}} - k_1 & k_2 \\ k_1 & i\Omega_B - \frac{1}{T_{2B}} - k_2 \end{vmatrix} \begin{vmatrix} M_{+A} \\ M_{+B} \end{vmatrix}$$

The solution can be obtained by

- finding two linear combinations of M_{A+} e M_{B+} in which the equations are not coupled any longer
- exponentiating both such linear combination and transforming back to $M(t)_{A+}$ and $M(t)_{B+}$
- summing them, so obtaining the time signal
- Fourier transforming the time signal

In the symmetric case:

$$|\Lambda|=|U|^{-1}|M||U|$$

- $|\Lambda|$ eigenvalues matrix (diagonal),
- $|M|$ starting matrix, to diagonalize
- $|U|$ trasformation matrix (the columns are the eigenvectors)

In the non-symmetric case the diagonalization is more complex

Supplementary material

$$|\Lambda|=|S||M||D|$$

it holds:

$$|S||D|=|D||S|=|1|$$

where: $|1|$= unit matrix (diagonal)

Supplementary material

$$\Lambda_1 = \frac{1}{2}\left\{ i(\Omega_A + \Omega_B) - \frac{1}{T_{2A}} - \frac{1}{T_{2B}} - k_1 - k_2 \right\} - \frac{1}{2} q$$

$$\Lambda_2 = \frac{1}{2}\left\{ i(\Omega_A + \Omega_B) - \frac{1}{T_{2A}} - \frac{1}{T_{2B}} - k_1 - k_2 \right\} + \frac{1}{2} q$$

with:

$$q = \sqrt{\Delta^2 + 4k_1k_2}$$

$$\Delta = i(\Omega_A - \Omega_B) - \frac{1}{T_{2A}} + \frac{1}{T_{2B}} - k_1 + k_2$$

$$|U| = |U|^{-1} = \frac{1}{\sqrt{(q+\Delta)^2 + 4k_1k_2}} \begin{vmatrix} (q+\Delta) & 2k_2 \\ 2k_1 & -(q+\Delta) \end{vmatrix}$$

Peculiarity: |U|=|U|$^{-1}$

The signal in the frequency domain is obtained by the Fourier transform of the signal in the time domain:

$$S(\omega)=\mathrm{Re}\ \mathrm{FT}\{|E||U||e^{Lt}||U|^{-1}|M_{+}(0)|$$

|E| is introduced to make the sum. It is a row matrix with all elements equal to 1. The product of twhis row matrix by a column matrix with the same dimension reults in a matrix of only one element, which is the sum of the elements of the column matrix.

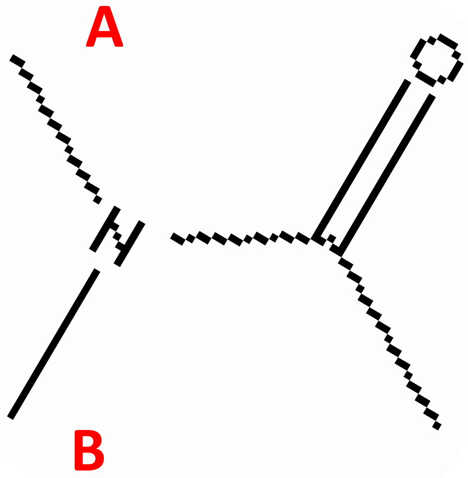
e.g.

$$\begin{vmatrix} 1 & 1 & 1 \end{vmatrix} \begin{vmatrix} a \\ b \\ c \end{vmatrix} = \begin{vmatrix} a+b+c \end{vmatrix}$$

$|M_{+}(0)|$ column matrix of the populations of the two sites at the beginning of acquisition

Signal Analysis in Exchanging Systems

- The simplest case is an exchange that is transferring nuclei between two sites with equal populations and in the absence of scalar coupling
- N,N’-dimethylacetamide is considered a good approximatio this ideal system. The coupling between the two methyls’ protons is small and it can be safely neglected.molto piccolo (trascurabile)



When the exchange is very slow k< $1/T_1$: **no effect on the NMR signal**

For k> $1/T_1$ several regimes occure, according to k and $\delta\nu$ ratios

$$\boxed{\frac{1}{T_1} < k << \Omega_A - \Omega_B}$$

cross peaks in the 2D spectra (EXSY)

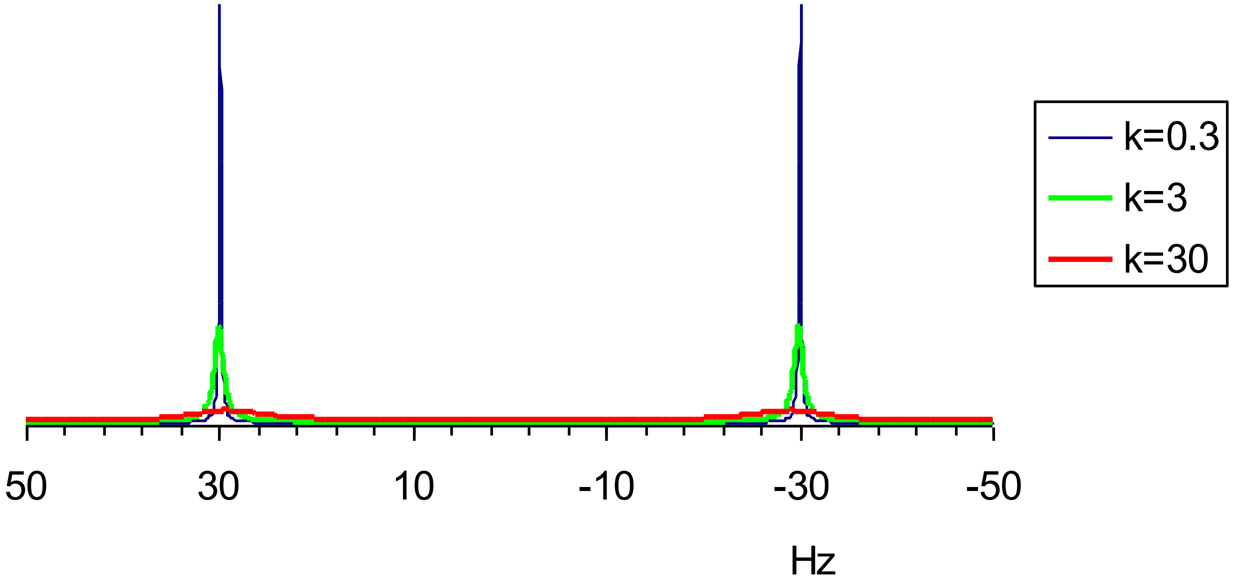
Until k< $1/T_2$ no effect on the linewidth

Lineshape analysis

- When $k > 1/T_2$ the effect on the linewidth is detectable
- The relevant factors for this analysis are:
- the natural linewidth ($\Delta\nu_{1/2}$) and the shift separation (in Hz) between the exchanging sites (A e B)

slow exchange

Ω_A= -30 Hz Ω_B= 30 Hz T_{2A}=T_{2B}= 2 s $1/T_2$= 0.5 s^{-1}

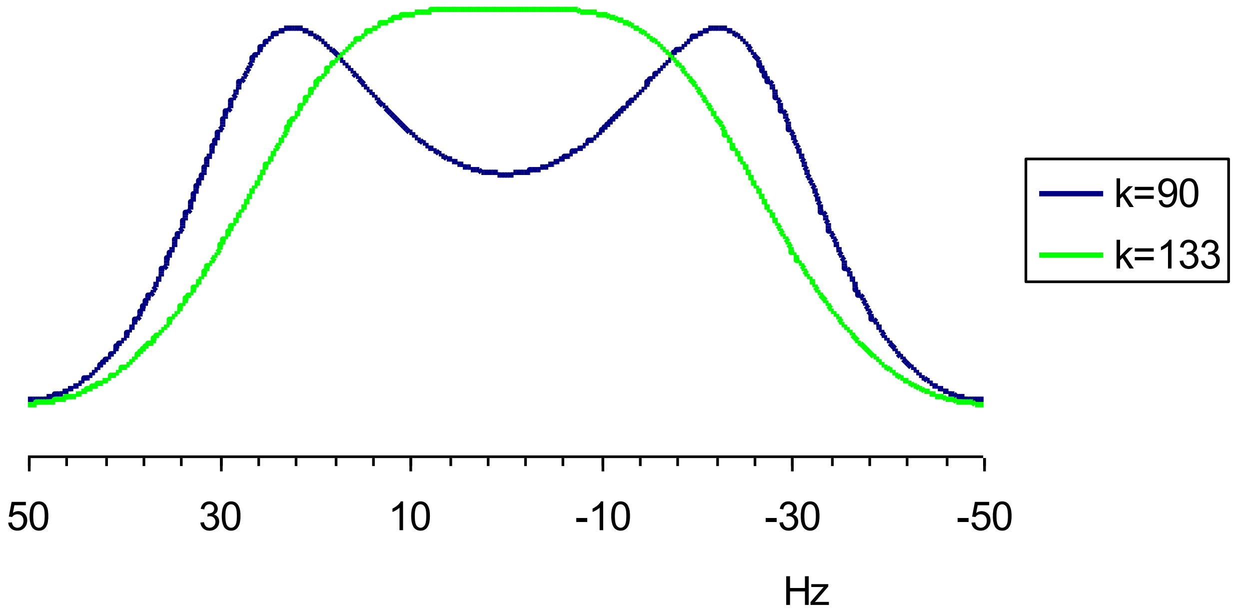


$$\boxed{\Delta \nu_{1/2} = \frac{1}{\pi}\left(\frac{1}{T_2} + k\right)}$$

the linewidth increases with k

in the slow exchange regime at high B_0 (large shift diference) $\Delta\nu_{1/2}$ may be large for large k

Coalescence

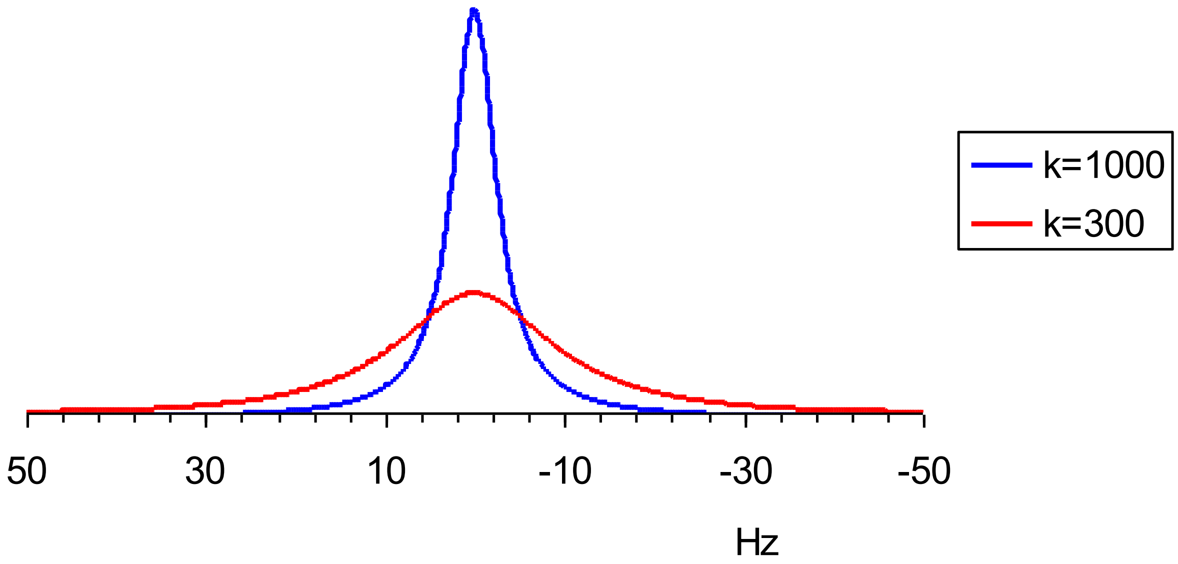


$$k_{coal} = \frac{\pi \delta \nu}{\sqrt{2}}$$

the signal position is the weighted average of the positions of the signals of the two exchanging partners

Fast exchange

$k > k_{coal}$

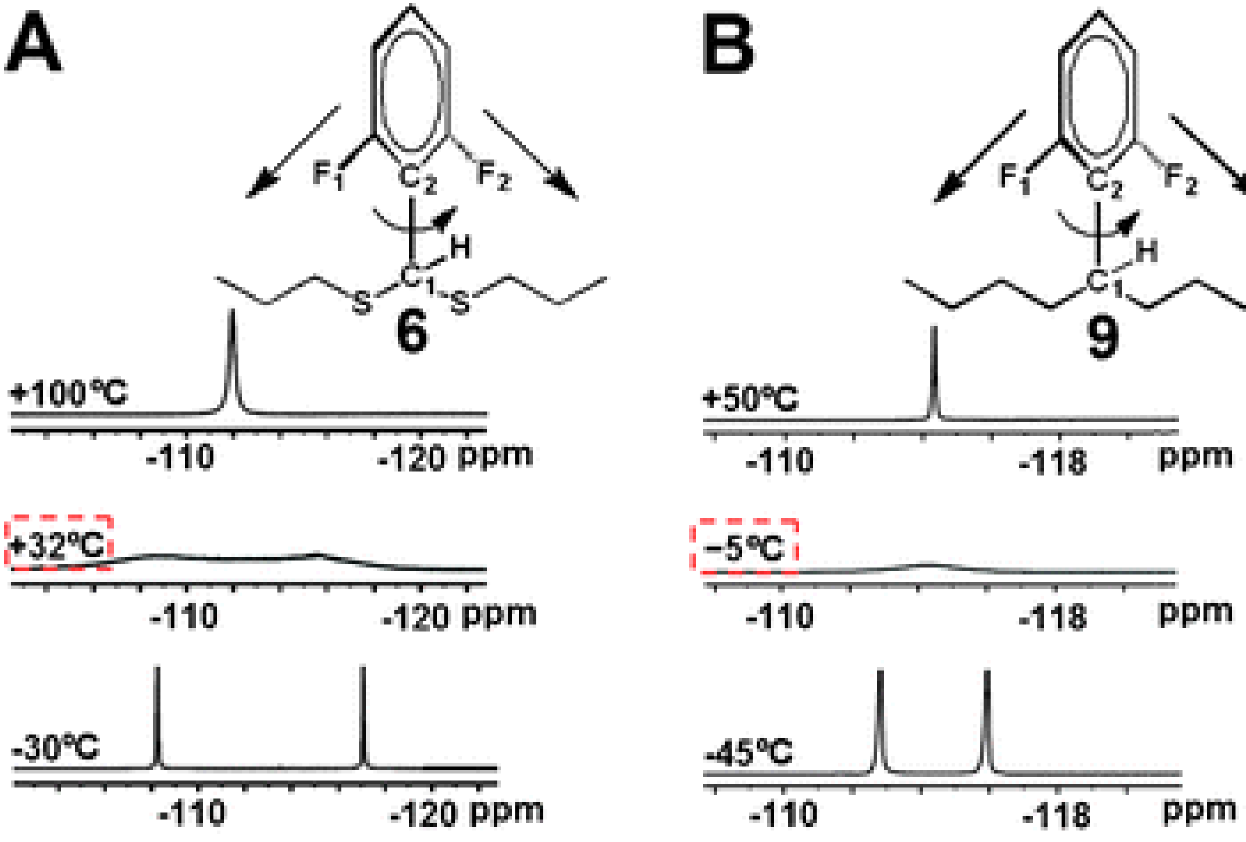


There is just one broad signal with linewidth:

$$\boxed{\Delta\nu = \frac{4\pi p_A p_B (\delta\nu)^2}{k_1 + k_2}}$$

^{19}F NMR

564.6 MHz on Varian Inova-600 spectrometer



F.....S interaction

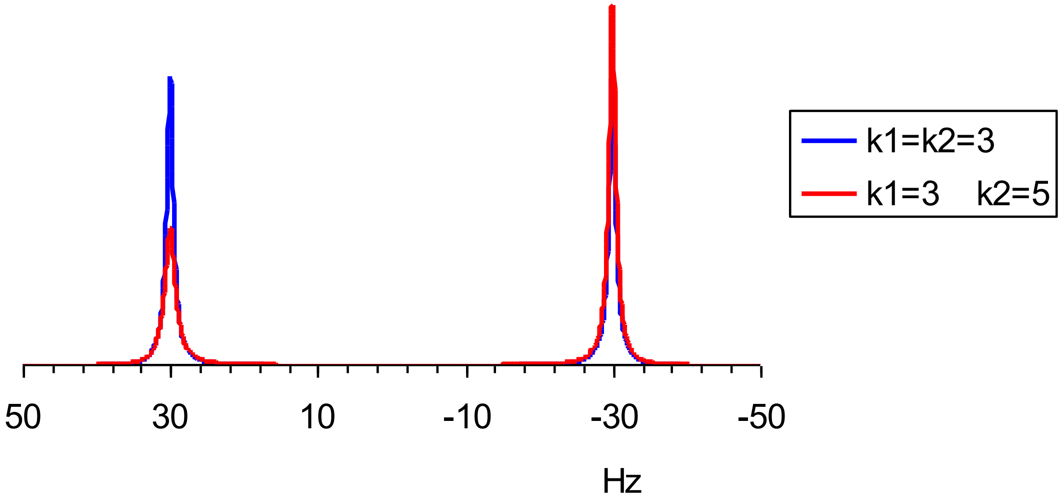
E. Laurini et al. Chem. Commun. 2012, 48, 4284-4286

Non Mutual Exchange

mutual exchange

non mutual exchange: two sites with different populations

$$\boxed{\frac{p_A}{p_B} = \frac{k_2}{k_1}}$$



$$\boxed{p_A = \frac{k_2}{k_1 + k_2}}$$

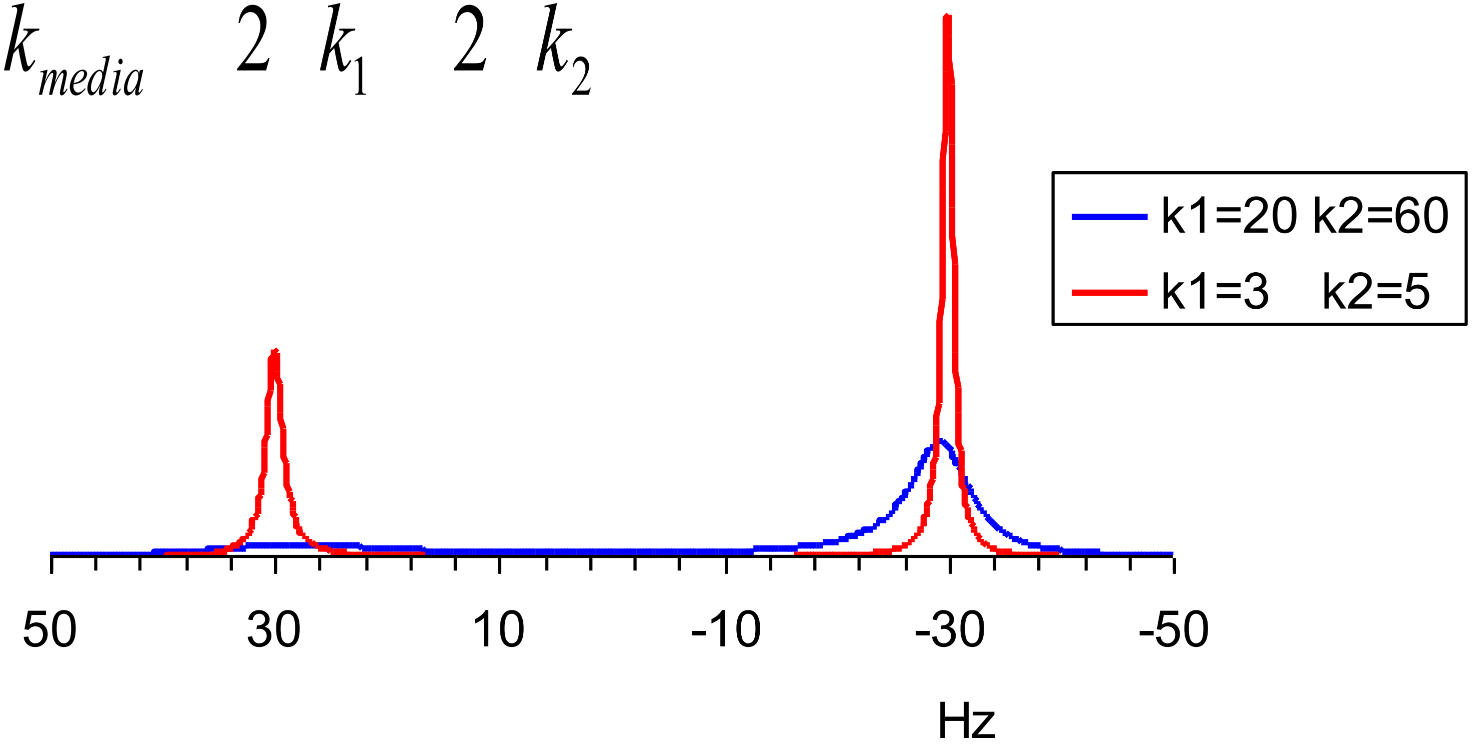
$$\boxed{p_B = \frac{k_1}{k_1 + k_2}}$$

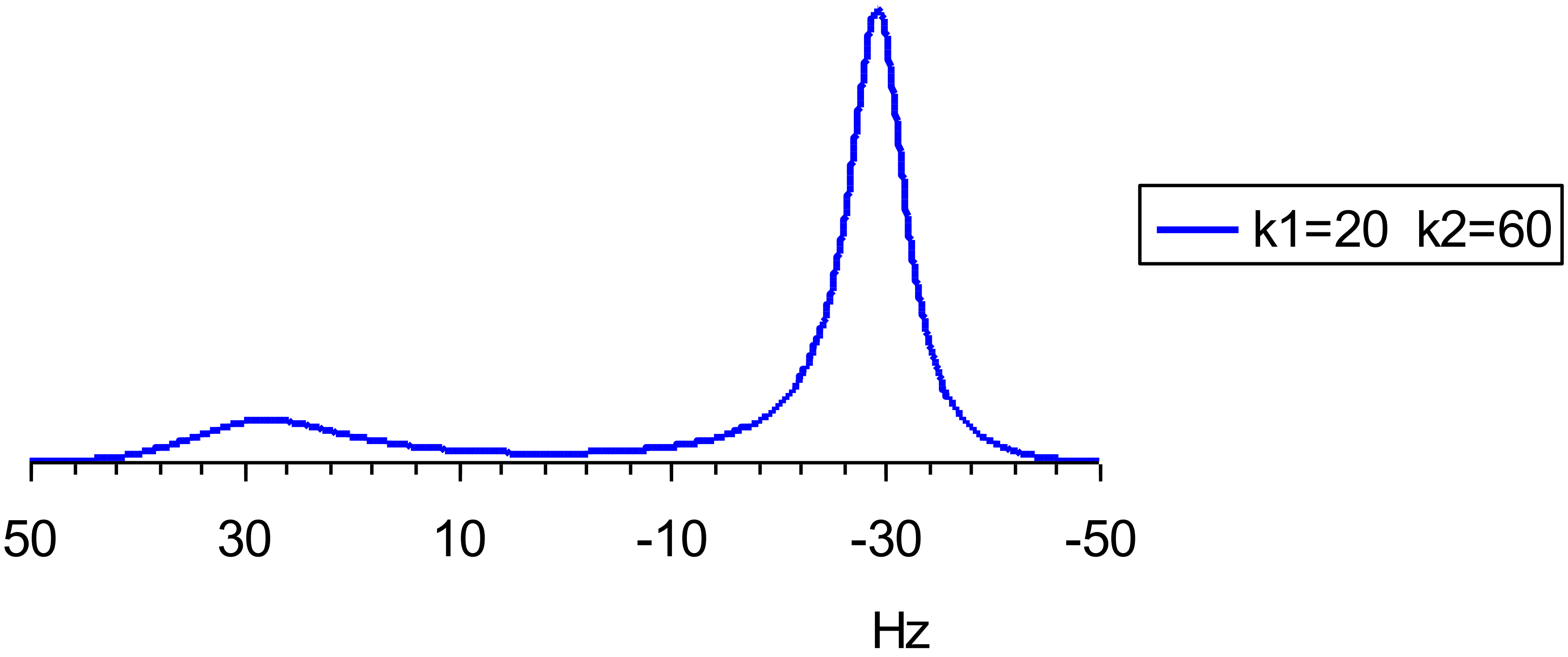
slow exchange

$k_{average}$=3.75

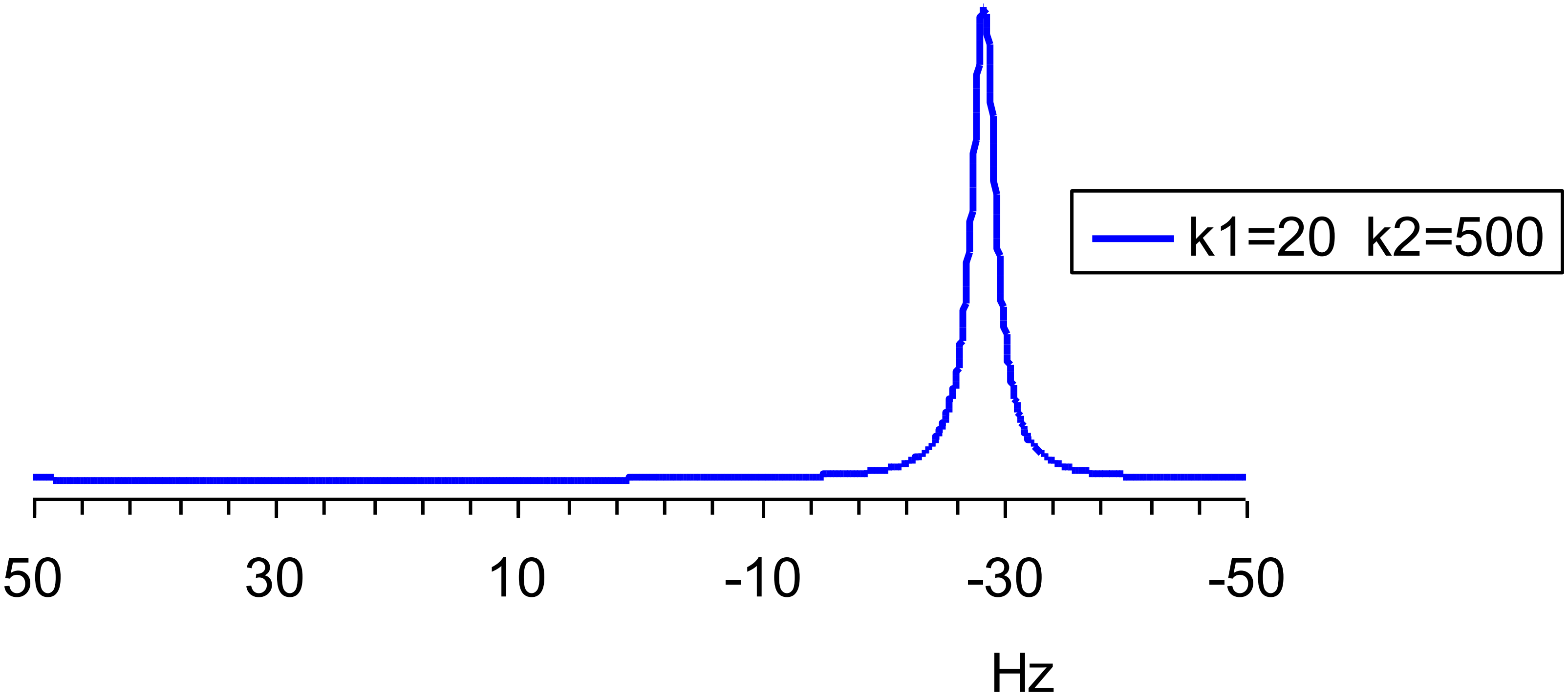
$$k_{media} = p_A k_1 + p_B k_2 = \frac{2k_1 k_2}{k_1 + k_2}$$

$$\frac{1}{k_{media}} = \frac{1}{2} \cdot \frac{1}{k_1} + \frac{1}{2} \cdot \frac{1}{k_2}$$





enlargement of the previous spectrum

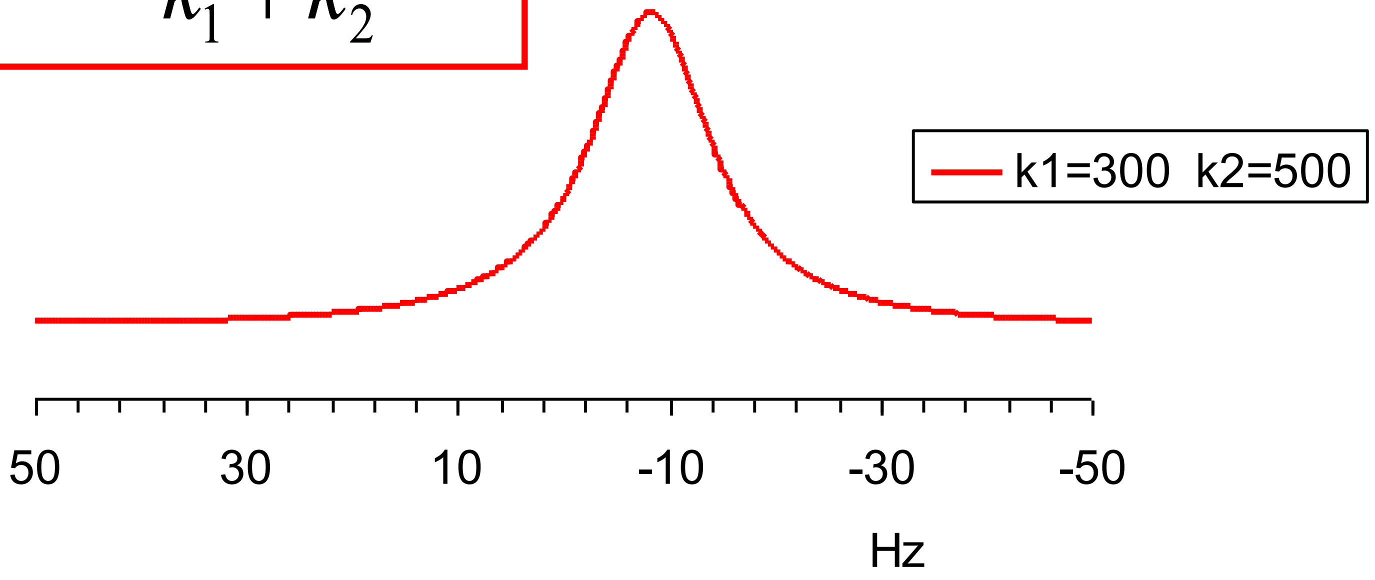


Il segnale di B è impercettibile, ma c’è allargamento del segnale di A

Fast Exchange

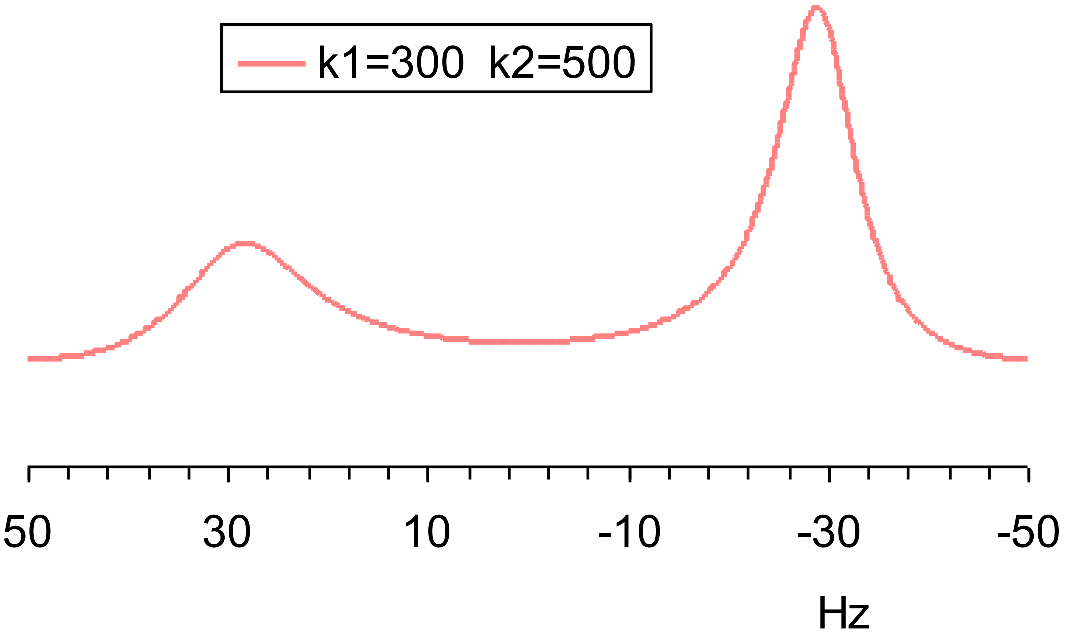
$$\boxed{\Delta\nu = \frac{4\pi p_A p_B (\delta\nu)^2}{k_1 + k_2}}$$

Δν=13



The position of the maximum of the signal is the weigthed average of the shifts of di A and B

Intermediate Rate



The lineshapes are calculated by solving the Bloch-McConnell equations