1) Here you'll show that the tranverse relaxation rate R_2 imposes a limit on the sensitivity and resolution in NMR. After a 90 degree pulse, the NMR signal is a damped oscillation, with the amount of damping depending on the size of R_2. The detected NMR signal takes the form: $S(t) = e^{i\Delta\omega t} e^{-R_2 t}$ with $e^{i\omega t} = \cos\omega t + i\sin\omega t$, $\Delta\omega$ is the resonance offset in the rotating frame due to the chemical shift interaction and R_2 is transverse relaxation rate.

(Bonus) Calculate $S(\omega) = FT[S(t)] = \int_{-\infty}^{\infty} dt S(t)\exp(-i\omega t)$.

It will be useful to write out your answer with a real denominator. Use the identify $(1/z)x(z^*/z^*) = z^*/(a^2+b^2)$ where $z=a+ib$ and $z^*=a-ib$. Note that the NMR signal S(t) is zero for all times less than zero.

Using the result of this calculation, $S(\omega) = \dfrac{\dfrac{1}{R_2}}{1+\left(\dfrac{\Delta\omega-\omega}{R_2}\right)^2}$

a) Sketch the real part of S(ω). This is an NMR spectrum.
b) Show that the intensity of the spectrum is proportional to $1/R_2$.
c) Show that the full width at half the maximal value (FWHM) of Re S(ω) proportional to R_2.
d) Plot an NMR spectrum for $\Delta\omega = 2\pi*500$ rad/sec and $R_2 = 5s^{-1}, 50s^{-1}$ and $5000s^{-1}$ to show how sensitivity and resolution depend on R_2.

2) Provide an explanation for why resonances disappear when stochiometric ligand is added to protein at NMR concentrations of several hundred μM when the Kd is roughly 3μM. You may assume a typical chemical shift change of 50Hz (0.1 ppm for ^1H at 500 MHz) between free and bound forms of protein and an on rate of 10^8 M^{-1} S^{-1}. At approximately what K_d would binding be in fast exchange? Slow exchange? Hint : recall that resonance broaden when $\Delta\omega=k_{ex}$, with $\Delta\omega$ the shift change in rad/s and k_{ex} in s-1. Take fast and slow exchange regimes to be an order of magnitude faster or slower than intermediate.