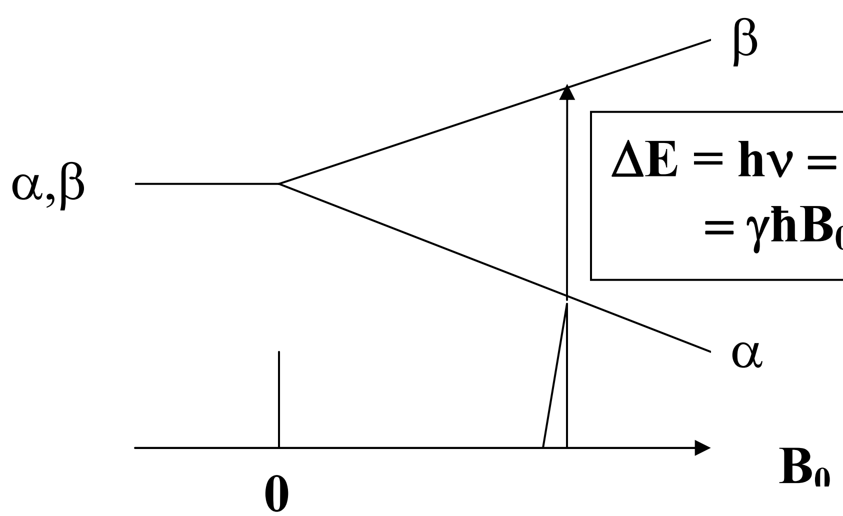
Nuclear Magnetic Resonance (NMR) – 2009 Extra!

NMR is a dominant technique in structural chemistry
Advantage comes from exceptionally narrow linewidths for transitions—result of uncertainty – long lifetime = narrow band , life → weak coupling

Quantum mechanical idea – perturbation
Discussed energy, eigen value of Hamiltonian, *H* op.

$\boldsymbol{H}^0\psi^0 = E^0\psi^0$ Energy and wave/fct in normal state
Perturbation – something added to zero level,
eg field: Electric –***E*** (Stark) or magnetic – ***B*** (Zeeman)

This can shift energy of states or split degenerate states, by
$E^1 = \int\psi^0\, \boldsymbol{H}'\, \psi^0\, dt$ where ***H'*** is perturbing operator



$$\Delta E = h\nu = g_N\beta_N B_0 = \gamma\hbar B_0$$

Spins have degeneracy, α,β same energy states in molecule
But in magnetic field, they have different energies
$\boldsymbol{H}' = -\mu\cdot B_0$ for electrons $\mu_e = g_e\beta \mathbf{S}$, nuclei: $\mu_N = g_N\beta_N I$
Energy - function of applied field, one spin up, one down
Spectra - transition between α and β if excite with magnetic part of the E-M field, $\Delta M_S = \pm1$ or $\Delta M_I = \pm1$

EPR- Electrons in ~3 KG (0.3 T) split of ~9 GHz (μ-wave)

β = eh/2mc = 0.927 x 10^{-20} erg/gauss

NMR - Nuclei less, β_N = eh/2mc = 0.505 x 10^{-23} erg/gauss

~ 5x10^{-27} J/T → 400 MHz ~ 10 T for proteins (big B_0)

Modern spectrometers in radio frequencies (100's MHz)

Spectra: Could scan field (was done for electrons-EPR)

Modern use a pulse method – Fourier Transform NMR

Functionally represent spectra in frequency (Hz)

limited if every ^1H (I = ½) had same resonance ν, B

Same for ^{13}C, ^{19}F, ^{31}P – I=1/2, different g_N → B or ν

Trick: Electrons shield nucleus from the B_0 -diamagnetic

Each peak chemically diagnostic – chemical shielding

$B_{total} = (1-\sigma)B_0$ → resonance $\nu_0 = \gamma B_0(1-\sigma)/2\pi$

so shift from bare nucleus: $\nu = \gamma B_0\sigma/2\pi$

These values depend on field used (or spectrometer design)

Standardize with $\delta = 10^6(\nu - \nu_{ref})/\nu_{ref} \sim 10^6 (\sigma_{ref} - \sigma)$

Chemical shift in ppm, usually from TMS $Si(CH_3)_4$

Diagnostic patterns - types of H's in molecule (or ^{13}C etc.)

amide N-H 7-9, Cα-H ~5, CβH_2~2-3, CH_3 1-2, Aromatics 6-9

Proteins: can trace out types of functional groups, like IR

Next identify multiplet splitting- couple one or more spins

2 spins → 4 states: $\alpha(1)\alpha(2)$, $\alpha(1)\beta(2)$, $\beta(1)\alpha(2)$, $\beta(1)\beta(2)$

Energies: $E = -\gamma B_0\hbar(1-\sigma_1)m_{I_1} - \gamma B_0\hbar(1-\sigma_2)m_{I_2} + hJ_{12}\, m_{I_1}\, m_{I_2}$

Gives characteristic splitting patterns, J_{12} – coupling const.

Energies shift up if same orientation ($\alpha\alpha$ or $\beta\beta$), down- $\alpha\beta$

Can split if not on same nucleus, ex. amide N-H and Cα-H
conformationally sensitive ^3J values – Karplus relation
$^3J = A + B \cos \phi + C \cos 2\phi$ ϕ is dihedral H-C-C-H
3 bond coupling, $\phi = 0$ – *cis*, $\phi = 180$ - *trans*

These interactions trace out coupling through bonds
Multidimensional NMR seen in COSY experiments
couplings of H's on adjacent locations are off-diagonal
And TOCSY (total correlation spec.) – all bonded coupling

Through space couplings also give structural information
Measured with NOESY (2-D) intensity reflect distance
Analogy with FRET, use to restrict possible structure

In biological applications, measure several spectra
with different "pulse patterns" to yield couplings
(COSY, TOCSY, NOESY and variants)
Use results to add to computational modeling program
Constrain fit of structure to model—how?

Molecular mechanics, model bond lengths, angles, torsion,
Each has a potential energy (like harmonic oscillator)
With minimum selected by fitting to known structures
Minimize energy, add constraints, find best structures