Introduction to Nuclear Magnetic Resonance Spectroscopy

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1.1. Introduction to Magnetic Resonance

- Magnetic resonance (MR) is a phenomenon of resonant energy absorption by a system of nuclei (and electrons).
- Nuclear magnetic resonance (NMR) results from the intrinsic magnetic moment of the nuclei of some atoms. Magnetic moments of electrons are exploited in electron spin resonance (ESR).
- Magnetic resonance (MR) generally involves placing a sample in a strong magnetic field (to generate polarisation at a fixed resonant frequency) and detecting signals produced following application of pulsed radio-frequency electromagnetic fields (RF pulses).
- MR is a very powerful method for studying the structure of materials: used in physics, chemistry, biology, medicine etc.

- NMR spectroscopy is used for chemical analysis and for molecular structure determination

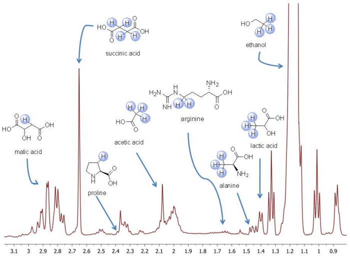


Fig.1: ^{1}H NMR spectrum of a sample of Spanish wine (`http://www.unirioja.es/gsoe/NMR.htm`)

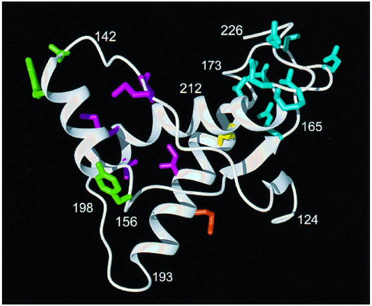


Fig.2: NMR-derived structure of a prion `http://www.pnas.org/content/94/14/7281.full`

1.2. Applications of NMR

- NMR relaxometry can be used to monitor molecular environment

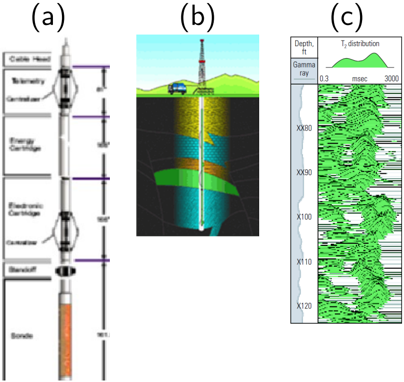


Fig.3: (a) NMR-logging probe, (b) Schematic positioning of the probe in a well, (c) T_2-relaxation profile along the bore. Sources: 1) Allenet al. Oilfield review, Autumn 2000; 2) Coates, Xiao NMR Logging Principles and Applications, Hulliburton

1.2. Applications of NMR

- NMR forms the basis for magnetic resonance imaging (MRI)

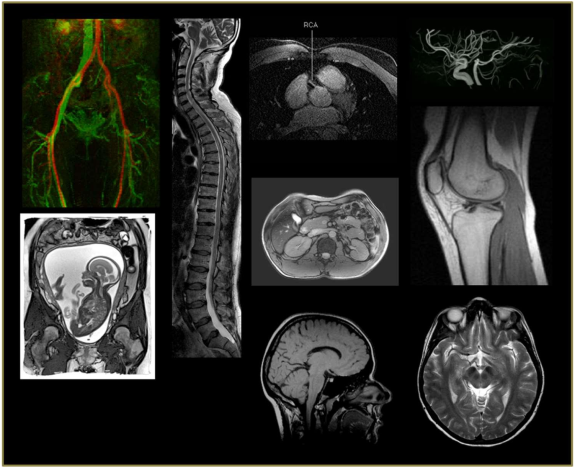


Fig.4: Example magnetic resonance images of blood vessel (in legs), fetus in utero, spine, heart, abdomen, head, blood vessels (in brain), knee, brain (courtesy of Prof. Richard Bowtell)

1.3. Magnetic moments in magnetic field.

- Consider charges moving in a limited volume. The position of a charge $\mathbf{e_n}$ will be given by a vector $\mathbf{r_n}$ and its velocity by $\mathbf{v_n}$. The overall magnetic moment of such a system is defined as:

$$\mathbf{M} = \frac{1}{2} \sum_n e_n \mathbf{r_n} \times \mathbf{v_n} \tag{1}$$

- If all the charges and masses are the same, then $\mathbf{M}$ can be rewritten as:

$$\mathbf{M} = \frac{e}{2m} \sum_n m \mathbf{r_n} \times \mathbf{v_n} = \gamma \mathbf{L}, \tag{2}$$

where

$$\mathbf{L} = \sum_n \mathbf{p_n} \times \mathbf{r_n} \tag{3}$$

is the mechanical angular momentum.

- Gyromagnetic ratio (or magnetogyric):

$$\gamma = \frac{e}{2m} \tag{4}$$

1.3. Magnetic moments in magnetic field.

- When a magnetic moment **M** is placed into an external uniform permanent magnetic field **B**, its energy is given by:

$$E = -\mathbf{M} \cdot \mathbf{B} \tag{5}$$

- The torque acting on the system:

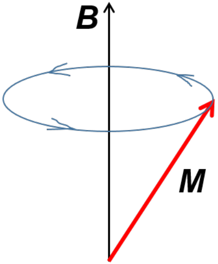
$$\frac{d\mathbf{L}}{dt} = \mathbf{M} \times \mathbf{B} \tag{6}$$

- Now using equation 2 we can obtain the equation describing the motion of vector **M**:

$$\frac{d\mathbf{M}}{dt} = \gamma \mathbf{M} \times \mathbf{B} \tag{7}$$

1.3. Magnetic moments in magnetic field.

- In a uniform magnetic field directed along z-axis $\mathbf{B} = (0, 0, B_0)$, the equation for individual components of $\mathbf{M}$ follow the equations:



$$\frac{dM_x}{dt} = \omega_L M_y$$
$$\frac{dM_y}{dt} = -\omega_L M_x \qquad (8)$$
$$\frac{dM_z}{dt} = 0,$$

where $\omega_L = \gamma B_0$ - Larmor frequency.

- A solution to this system of differential equations with initial values of $M_x(0), M_y(0), M_z(0)$ has the following form:

$$\begin{aligned} M_x(t) &= M_x(0)\cos(\omega_L t) + M_y(0)\sin(\omega_L t) \\ M_y(t) &= -M_y(0)\sin(\omega_L t) + M_y(0)\cos(\omega_L t) \\ M_z(t) &= M_z(0) \end{aligned} \qquad (9)$$

1.4. Orbital angular momentum operator

- In quantum mechanics physical quantity A ise represented by an operator $\hat{A}$. The mechanical angular momentum is replaced by its corresponding operator:

$$\mathbf{L} = \sum_n \mathbf{p_n} \times \mathbf{r_n} \longleftrightarrow \hat{\mathbf{L}} = \frac{1}{\hbar} \sum_n \hat{\mathbf{r}}_\mathbf{n} \times \hat{\mathbf{p}}_\mathbf{n} = -i \sum_n \hat{\mathbf{r}}_\mathbf{n} \times \boldsymbol{\nabla}_\mathbf{n} \quad (10)$$

- Angular momentum operator properties. Commutation:

$$[\hat{L}_y, \hat{L}_z] = i\hat{L}_x, [\hat{L}_z, \hat{L}_x] = i\hat{L}_y, [\hat{L}_x, \hat{L}_y] = i\hat{L}_z \quad (11)$$

- Angular momentum squared, and its commutation properties:

$$\hat{L}^2 = \hat{L}_x^2 + \hat{L}_y^2 + \hat{L}_z^2 \quad (12)$$

$$[\hat{L}^2, \hat{L}_x] = [\hat{L}^2, \hat{L}_y] = [\hat{L}^2, \hat{L}_z] = 0 \quad (13)$$

1.4. Orbital angular momentum operator

- Eigenfunctions of both $\hat{L}^2$ and $\hat{L}_z$ operators can be characterized by integer quantum numbers l and m respectively. These eigen functions will be denoted as $|lm\rangle$. Their eigenvalues are:

$$\hat{L}_z|lm\rangle = m|lm\rangle \tag{14}$$

$$\hat{L}^2|lm\rangle = l(l+1)|lm\rangle \tag{15}$$

- Another useful operator are raising and lowering operators:

$$\hat{L}_+ = \hat{L}_x + i\hat{L}_y, \hat{L}_- = \hat{L}_x - i\hat{L}_y \tag{16}$$

$$\langle lm|\hat{L}_+|l(m-1)\rangle = \langle l(m-1)|\hat{L}_-|lm\rangle = \sqrt{(l+m)(l-m+1)} \tag{17}$$

Problem

Calculate $[\hat{L}_+, \hat{L}_x] =?$, $[\hat{L}_+, \hat{L}_-] =?$

$$[\hat{L}_y, \hat{L}_z] = i\hat{L}_x, [\hat{L}_z, \hat{L}_x] = i\hat{L}_y, [\hat{L}_x, \hat{L}_y] = i\hat{L}_z$$

$$\hat{L}^2 = \hat{L}_x^2 + \hat{L}_y^2 + \hat{L}_z^2$$
$$[\hat{L}^2, \hat{L}_x] = [\hat{L}^2, \hat{L}_y] = [\hat{L}^2, \hat{L}_z] = 0$$
$$\hat{L}_+ = \hat{L}_x + i\hat{L}_y, \hat{L}_- = \hat{L}_x - i\hat{L}_y$$

1.4. Orbital angular momentum operator

- Classical magnetic moment will have its own quantum analogue, the operator of angular momentum:

$$\mathbf{M} = \gamma \mathbf{L} \longleftrightarrow \hat{\boldsymbol{\mu}} = \gamma \hbar \hat{\mathbf{L}} \tag{18}$$

- Given the electron charge $e = 1.6 \cdot 10^{-19}$C, and mass $m = 9.1 \cdot 10^{-31}$kg Bohr magneton:

$$\beta_e = \gamma \hbar = \frac{e\hbar}{2m} \approx 9.27 \cdot 10^{-24} \mathrm{J{\cdot}T}^{-1} \tag{19}$$

- Similarly a nuclear magneton could be calculated for a proton (^{1}H nucleus):

$$\beta = \gamma_N \hbar = \frac{e\hbar}{2m_p} \approx 5.05 \cdot 10^{-27} \mathrm{J{\cdot}T}^{-1} \tag{20}$$

1.5. Spin angular momentum operator

However, real nuclei and electrons have spins (intrinsic magnetic moment). Their z-axis projection m takes integer and half-integer values: $m = \frac{1}{2}, 1, \frac{3}{2}, 2$ etc. Similar to the equation for the orbital angular momentum Eq.18. For nuclei spins we get its magnetic moment as:

$$\hat{\boldsymbol{\mu}}_{\mathbf{N}} = \gamma_N \hbar \hat{\mathbf{I}}, \tag{21}$$

where $\hat{\mathbf{I}}$ stands for the nuclear spin operator. All the properties of angular momentum operators listed in Eqs.11-17 will be true for $\hat{\mathbf{I}}$.

1.5. Spin angular momentum operator

- Many nuclei in the periodic table are magnetic, i.e. have spin $I \neq 0$. Their magnetic moments could be measured in units of β_N:
$$\hat{\boldsymbol{\mu}}_{\mathbf{N}} = \gamma_N \hbar \hat{\mathbf{I}} = g_N \beta_N \hat{\mathbf{I}}, \tag{22}$$
where g_N - dimensionless g-factor.

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Nucleus	Natural abundance %	Nuclear spin (I)	g_N, g-factor	γ_N, Gyromagnetic ratio (10^7 rad/T*s)
^1H	99.98	$\frac{1}{2}$	5.585	26.7519
^2H	$1.5*10^{-2}$	1	0.857	4.1066
^{13}C	1.108	$\frac{1}{2}$	1.405	6.7283
^{14}N	99.635	1	0.403	1.9338
^{15}N	0.365	$\frac{1}{2}$	-0.567	-2.712

- Electron magnetic moments can be measured in units of Bohr magnetons: $\hat{\boldsymbol{\mu}}_{\mathbf{S}} = -\gamma_e \hbar \hat{\mathbf{S}} = -g_e \beta_e \hat{\mathbf{S}}$, and for a free electron spin $g_e \approx 2.0023$.

Summary of Lecture 1

- Applications of NMR: chemistry, biology, medicine, industry ...
- Magnetic moment in magnetic field: Classical description
- Recap of angular momentum operator properties: commutation properties.
- Nuclei have their own nuclear magnetic moment. Described using spin angular momentum operator.

Suggested reading: Harris: 1.1, 1.2, 1.3, 1.4, 1.6, 2.4

1.6. Spin in a magnetic field

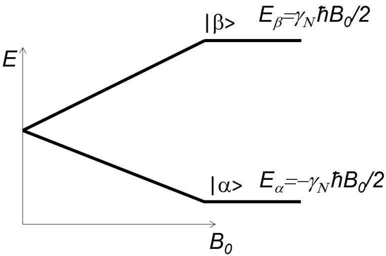
- Let's quantum mechanically describe the system of spins in the magnetic field. Eq. 5 can be rewritten in a form of Hamiltonian:

$$E = -\mathbf{M} \cdot \mathbf{B} \longleftrightarrow \mathcal{H} = -\hat{\boldsymbol{\mu}}_{\mathbf{N}} \cdot \mathbf{B} \tag{23}$$

- when the magnetic field is directed along z-axis $\mathbf{B} = (0, 0, B_0)$:

$$\mathcal{H} = -\hat{\boldsymbol{\mu}}_{\mathbf{N}} \cdot \mathbf{B} = -\gamma_N \hbar B_0 \hat{I}_z \tag{24}$$

- For spin $I = \dfrac{1}{2}$ such Hamiltonian produces a two-level system. Its energy levels corresponding to eigenfunctions $|\alpha\rangle$ and $|\beta\rangle$:



- The transition between the two states requires an energy quantum[1]:

$$h\nu_L = \gamma\hbar B_0, \omega_L = \gamma B_0, \nu_L = \frac{\gamma B_0}{2\pi} \tag{25}$$

ω_L and ν_L is the Larmor frequency (anglular and cyclic respectively)

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Nucleus	Natural abundance %	Nuclear spin (I)	Larmor frequency at 11.744T, MHz	γ_N, Gyro-magnetic ratio (10^7 rad/T*s)
^1H	99.98	$\frac{1}{2}$	500	26.7519
^2H	$1.5*10^{-2}$	1	76.753	4.1066
^{13}C	1.108	$\frac{1}{2}$	125.721	6.7283
^{14}N	99.635	1	36.118	1.9338
^{15}N	0.365	$\frac{1}{2}$	50.664	-2.712

1.7. Equilibrium magnetization

NMR measurements are generally made on bulk samples which contain very large numbers of nuclear spins (e.g. 1 cm^3 contains $N \approx 6.7 \cdot 10^{22}$ ^1H atoms) The measured signals therefore result from the collective effect of a large number of magnetic moments that can be described using a bulk magnetization. At thermal equilibrium, the numbers of nuclei in the $|\alpha\rangle$ state N_α and $|\beta\rangle$ state N_β follow Boltzmann distribution:

$$\frac{N_\alpha}{N_\beta} = e^{-\frac{\gamma B_0}{kT}} \approx (1 - \frac{\gamma B_0}{kT}), \tag{26}$$

when $\gamma B_0 \ll kT$. Overall magnetization then can be calculated as:

$$M_z = N_\alpha(-\frac{1}{2}\gamma\hbar) + N_\beta(\frac{1}{2}\gamma\hbar) = N\frac{\gamma^2\hbar^2 B_0}{4kT} \tag{27}$$

Problem

- What is the value of $\frac{\gamma_N \hbar B_0}{kT}$ for proton nuclei (^{1}H) at 9.4 T magnetic field at 300 K?
- What is the value of $\frac{\gamma_e \hbar B_0}{kT}$ electron (^{1}H) at 9.4 T magnetic field at 4 K?

Electron charge $e = 1.602 \cdot 10^{-19}$C

Electron mass $m_e = 9.109 \cdot 10^{-31}$kg

Proton mass$m_p = 1.673 \cdot 10^{-27}$kg

Plank constant$\hbar = 1.054 \cdot 10^{-34} \frac{\mathrm{J} \cdot \mathrm{s}}{rad}$

Proton g-factor$g_p = 5.585$

Electron g-factor$g_e = 2.0023$

Nuclear magneton$\beta_N = 5.05 \cdot 10^{-27}\mathrm{J} \cdot \mathrm{T}^{-1}$

Bohr magneton$\beta_e = 9.27 \cdot 10^{-24}\mathrm{J} \cdot \mathrm{T}^{-1}$

Proton gyromagnetic ratio$\gamma_N = 26.7519 \cdot 10^7 \frac{\mathrm{rad}}{T \cdot s}$

Electron gyromagnetic ratio$\gamma_e = 1.76 \cdot 10^{11} \frac{\mathrm{rad}}{T \cdot s}$

Boltzmann constant$k = 1.38 \cdot 10^{-23}\mathrm{J} \cdot \mathrm{K}^{-1}$

Avogadro's constant$N_A = 6.023 \cdot 10^{23}\mathrm{mol}^{-1}$

1.8. Resonant energy absoption.

- Let's apply oscillating magnetic field to our system. A spin system Hamiltonian becomes time-dependent and for an oscillation along the x-axis we obtain:

$$\begin{aligned} \mathcal{H}(t) &= -\hat{\boldsymbol{\mu}}(\mathbf{B_0}+\mathbf{B(t)}) = \\ &= -\gamma\hbar\hat{I}_z(B_0+B_1(t)) = \\ &= -\gamma\hbar\hat{I}_z B_0 - \gamma\hbar\hat{I}_x B_1\cos(\omega t), \end{aligned} \tag{28}$$

  where H_1 and ω are the amplitude and the frequency of the oscillating magnetic field.

- According to perturbation theory the transition probability between the initial state $|a\rangle$ and the final state $|b\rangle$ with a time dependent Hamiltonian $\hat{V}(t) = 2\hat{F}\cos(\omega t)$ is (Fermi's golden rule):

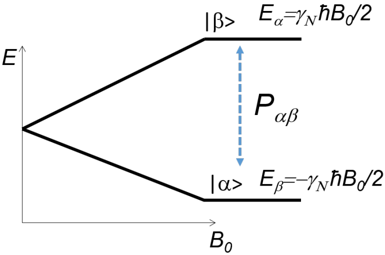
$$P_{ab} = \frac{2\pi}{\hbar}|\langle a|\hat{F}|\rangle b|^2\delta(E_{ab}-\hbar\omega), \tag{29}$$

  where $E_{ab} = E_a - E_b$ is an energy difference between the energies of levels a and b.

1.9. Populations dynamics in two-level system.

- For a two level system described before, the matrix element $\langle\alpha|\hat{I}_x|\beta\rangle = \frac{1}{2}$. The transition probability then becomes:

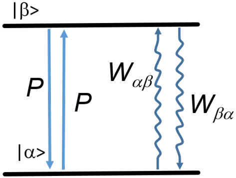
$$P_{\alpha\beta} = \frac{\pi}{2\hbar}(\gamma H_1)^2\delta(E_{\alpha\beta} - \hbar\omega), \tag{30}$$



- **The effect of resonant absorption (and emission) of electromagnetic irradiation at the frequency matching the energy difference in a nuclear system is called Nuclear Magnetic Resonance (NMR).**

1.9. Populations dynamics in two-level system.

- In a two-level system the transition will take place due to the action of external irradiation, but also due to interaction with the environment.



P - the rate of transitions driven by external field, $W_{\alpha\beta}$, $W_{\beta\alpha}$ - rates of spontaneous spin flips due to interaction with environment.

- In thermal equilibrium:

$$N_\alpha^0 W_{\alpha\beta} = N_\beta^0 W_{\beta\alpha}, \text{i.e.} \tag{31}$$

$$\frac{W_{\beta\alpha}}{W_{\alpha\beta}} = exp^{-\frac{\gamma\hbar B_0}{kT}} \approx 1 - \frac{\gamma\beta B_0}{kT} \tag{32}$$

1.9. Populations dynamics in two-level system.

- Equation for populations of levels:

$$\begin{aligned} \frac{dN_\alpha}{dt} &= -N_\alpha(P + W_{\alpha\beta}) + N_\beta(P + W_{\beta\alpha}) \\ \frac{dN_\beta}{dt} &= N_\alpha(P + W_{\alpha\beta}) - N_\beta(P + W_{\beta\alpha}) \end{aligned} \tag{33}$$

- If we introduce the average rate of spontaneous transitions $W = \frac{1}{2}(W_{\alpha\beta} - W_{\beta\alpha})$, then $W_{\alpha\beta} = W(1 + \frac{\gamma\hbar B_0}{2kT})$ and $W_{\beta\alpha} = W(1 - \frac{\gamma\hbar B_0}{2kT})$, the equations can be rewritten:

$$\begin{aligned} \frac{dN_\alpha}{dt} &= (N_\beta - N_\alpha)P + (N_\beta - N_\alpha)W - W\frac{\gamma\beta B_0}{2kT}N \\ \frac{dN_\beta}{dt} &= -(N_\beta - N_\alpha)P - (N_\beta - N_\alpha)W + W\frac{\gamma\beta B_0}{2kT}N \end{aligned} \tag{34}$$

1.9. Populations dynamics in two-level system.

- Denote the population difference as $n = N_\beta - N_\alpha$ and thermal equilibrium population difference $n_0 = N_\beta^0 - N_\alpha^0 \approx N\frac{\gamma\hbar B_0}{2kT}$ the equations can be rewritten as:

$$\frac{dn}{dt} = -2nP - 2nW + 2Wn_0, \tag{35}$$

or

$$\frac{dn}{dt} = -2nP - \frac{(n - n_0)}{T_1}, \tag{36}$$

where $T_1 = \frac{1}{2W}$ is called spin-lattice relaxation time determines how quickly a spin system reaches a thermal equilibrium with environment.

- In equilibrium, when $\frac{dn}{dt} = 0$:

$$n = \frac{n_0}{1 + 2PT_1} \tag{37}$$

when the power is very large $PT_1 \gg 1$, $n \to 0$, i.e. the system is saturated and no signal can be observed.

Summary of Lecture 2

- Spin $I = \frac{1}{2}$ in a magnetic field. Two-level system.
- System of spins in a magnetic field is capable of absorbing radiation at a resonant frequency.
- Population dynamics in a two-level system. Signal as function of radiation power and saturation.

Suggested reading: Harris 1.5, 1.7, Slichter 1.3
Harris 1.20 - CW NMR spectrometer

2.1. Chemical shifts.

- The magnetic fields experienced by nuclei in atoms and molecules are affected by the interaction of the surrounding electrons orbitals with the applied magnetic field B_0.
- This effect slightly shifts the Larmor frequency in a chemical specific manner - this is known as the chemical shift. It allows the identification of chemical species from NMR spectra.
- Classical illustration of diamagnetic chemical shift:

$$\boldsymbol{\omega} = \frac{e}{2m_e}\mathbf{B_0}$$

$$\mathbf{j} = -e[\boldsymbol{\omega} \times \mathbf{r}]\rho_e = -\frac{e^2}{2m_e}[B_0 \times \mathbf{r}]\rho_e$$

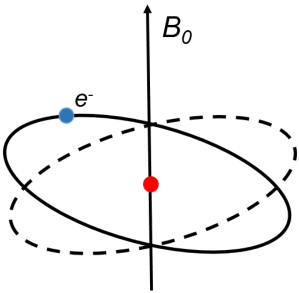
$$d\mathbf{B_i} = \frac{\mu_0}{4\pi r^3}[\mathbf{j} \times \mathbf{r}]dV$$

$$d\mathbf{B_i} = -\frac{\mu_0 e^2}{8\pi m_e r^3}[[\mathbf{B_0} \times \mathbf{r}] \times \mathbf{r}]\rho_e dV$$

$$B_{iz} = -B_0 \frac{\mu_0 e^2}{8\pi m_e}\int \rho_e \frac{x^2+y^2}{r^3}dV$$

Quantum mechanical result:

$$\sigma = -\frac{\mu_0 e^2}{8\pi m_e}\langle\Psi|\frac{x^2+y^2}{r^3}|\Psi\rangle$$



2.1. Chemical shifts.

Let's calculate the effect of ring current in cyclic aromatic molecules. Consider benzene molecule:

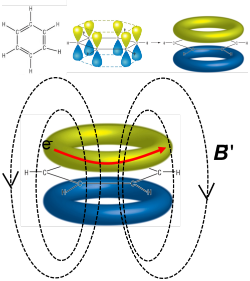


Fig.5: (top) Schematic repsresentation of electron orbitals in a benzene molecule, (bottom) local fields in a benzene molecule produced by electron currents induced by a magnetic field.

- Larmor precession frequency of electrons $\omega_L = \frac{eB_0}{2m_e}$. Current can be calculated as charge $6e$, divided by precession period $\frac{2\pi}{\omega_L}$:

$$i = \frac{3e^2 B_0}{2\pi m_e} \tag{38}$$

- Circular conductor creates a magnetic moment $\mu = i \cdot \pi r^2$, totalling in:

$$\mu = -\frac{3e^2 B_0 r^2}{2m_e} \tag{39}$$

- The magnetic field created by a magnetic moment $\mathbf{B} = \frac{\mu_0}{4\pi}(\frac{\mathbf{r}(\mathbf{mr})}{r^5} - \frac{\mathbf{m}}{r^3})$ reduces to:

$$B_i = -\frac{\mu_0}{4\pi}\frac{m}{r^3} = \frac{3\mu_0 e^2}{8\pi}\frac{r^2}{(r+d)^3}B_0 \tag{40}$$

$$\sigma = - - \frac{\mu_0}{4\pi m_e}\frac{m}{r^3} = \frac{3\mu_0 e^2}{8\pi}\frac{r^2}{(r+d)^3} \tag{41}$$

- Given benzene molecule radius $r = 1.4\mathring{A}$, CH-bond length $d = 1.1\mathring{A}$ we obtain:

$$\sigma \approx -5.3 \cdot 10^{-6}, \sigma_{iso} \approx -1.8 \cdot 10^{-6} \tag{42}$$