Appendix 5
Some Standard Formulae Used in MRS

5.1 BASIC NMR EQUATIONS

5.1.1 The Larmor Equation

$$\omega_0 = \gamma B_0 \tag{5.1}$$

where $\omega_0 = 2\pi\nu_0$ rad s^{-1} is the angular NMR frequency, γ□□ the gyromagnetic ratio, and B_0 the main magnetic field strength.

5.1.2 Flip Angle

$$\alpha = \gamma B_1 \tau \tag{5.2}$$

in radians at a voxel experiencing a square circularly polarized component of the transverse RF pulse of amplitude B_1 and duration τ. For pulses with variable amplitude,

$$\alpha = \gamma \int_0^\tau B_1(t)\mathrm{d}t \tag{5.3}$$

5.1.3 The Bloch Equations

In the laboratory frame of reference, component form:

$$\begin{aligned}
\frac{\mathrm{d}M_x(t)}{\mathrm{d}t} &= \gamma(M_y(t)B_z(t) - M_z(t)B_y(t)) - \frac{M_x(t)}{T_2} \\
\frac{\mathrm{d}M_y(t)}{\mathrm{d}t} &= \gamma(M_z(t)B_x(t) - M_x(t)B_z(t)) - \frac{M_y(t)}{T_2} \\
\frac{\mathrm{d}M_z(t)}{\mathrm{d}t} &= \gamma(M_x(t)B_y(t) - M_y(t)B_x(t)) - \frac{M_z(t) - M_0}{T_1}
\end{aligned} \tag{5.4}$$

Handbook of Magnetic Resonance Spectroscopy In Vivo: MRS Theory, Practice and Applications.
Edited by Paul A. Bottomley and John R. Griffiths,
 ISBN: 978-1-118-99766-6

$\mathbf{M}(t) = (M_x, M_y, M_z)$ is the nuclear magnetization and $\mathbf{B}(t) = (B_x, B_y, B_z)$ is the applied magnetic field in Cartesian coordinates. T_1 and T_2 are the spin–lattice (longitudinal) and spin–spin (transverse) relaxation times.

5.1.4 The Stead-State NMR Response to a Repeated Pulse-and-Acquire Sequence

The NMR pulse sequence comprised of an $\alpha°$ pulse and an intersequence delay of TR with complete dephasing of the transverse magnetization at the end of each TR has a steady-state response,

$$\frac{M_{xy}}{M_0} = \frac{[1 - \exp(-TR/T_1)]\sin\alpha}{1 - \cos\alpha \cdot \exp(-TR/T_1)} \exp(-t/T_2^*) \tag{5.5}$$

where $T_2{}^*$ is the inhomogeneously broadened T_2.

The *Ernst angle* yielding optimum signal-to-noise ratio (SNR) per unit time is

$$\cos\alpha_\mathrm{E} = \exp(-TR/T_1) \tag{5.6}$$

5.1.5 The NMR Response to an Inversion-Recovery (IR) Sequence

The NMR pulse sequence comprised a 180°–inversion time (TI)–90° excitation, starting with equilibrium magnetization $\mathbf{M}(t) = (0, 0, M_0)$ excites a transverse magnetization

$$M_{xy} = M_0[1 - 2\exp(-\mathrm{TI}/T_1)]\exp(-t/T_2^*) \tag{5.7}$$

The magnetization is zero (the 'T_1-null') at $\exp(-TI/T_1) = 1/2$, or, $\mathrm{TI} = 0.693T_1$.

5.1.6 Pulsed Diffusion Experiment

In the pulsed diffusion experiment, comprised of a 90°–180° spin-echo excitation with two pulsed

diffusion gradients, each of duration τ and amplitude G_i applied in the ith direction before and after the 180° pulse, the NMR signal decays as

$$M = M_0 \exp(-b_i D_i)x \text{ with } b_i = \gamma^2 G_i^2 \tau^2 (\text{TD} - \tau/3) \tag{5.8}$$

where D_i is the coefficient of diffusion in the ith direction and TD the time between the start of the two gradient pulses.

5.1.7 The Nuclear Overhauser Enhancement (nOe)

The nuclear Overhauser enhancement (nOe) is

$$\eta = 1 + \gamma_B / 2\gamma_A \tag{5.9}$$

Subscripts denote the NMR nucleus being observed (A) and that being irradiated (B).

5.2 SIGNAL-TO-NOISE RATIO

5.2.1 Absolute SNR

The absolute SNR is

$$\text{SNR} = \frac{\sqrt{2}\omega_0 M B_{10}}{\sqrt{4KTR_L \text{BW}}} \times 10^{-\frac{\text{NF}}{20}} \tag{5.10}$$

where B_{10} is the amplitude of the rotating B_1 field at the signal voxel generated by the detector excited with unit current, T is the absolute temperature of the detector's load R_L, K is Boltzmann's constant, BW is the detector bandwidth, and NF is the system noise figure in decibel. At equilibrium, $M = M_0 = N_{\text{ml}} \nu_0^2 h^2 I(I+1)/3KT = 3.111 \times 10^{-9} \times \text{B}_0$ J T^{-1} ml^{-1} for pure water at 37 °C ($h = 6.626 \times 10^{-34}$ Js is Planck's constant and I is the spin; see Chapter 1).[1]

5.2.2 Intrinsic SNR

The intrinsic SNR is

$$\text{ISNR} = \frac{SNR.10^{\text{NF}/20}}{(1 - Q_L/Q_E)^{1/2}} \tag{5.11}$$

Q_L/Q_E is the ratio of the loaded to the unloaded detector coil quality factors.[2]

5.2.3 SNR Measured from Absorption-Mode MRS Peak Height

The SNR measured from the absorption-mode MRS peak height and the unbiased noise in a portion of the spectrum containing no peaks:

$$\text{SNR} = \frac{\text{(Peak height)-(baseline offset)}}{\text{root-mean square of (noise-baseline offset)}} \tag{5.12}$$

$$\approx 2.5 \frac{\text{[(Peak height)-(baseline offset)]}}{\text{maximum peak-to-peak variation in noise}}$$

The denominator of Equation (5.12) may be replaced by the standard deviation (SD) of the noise after the baseline is fitted and removed.

5.3 SIGNAL PROCESSING

5.3.1 Line Shapes

The *Lorentzian* line-shape function is

$$\text{f}_L(\nu, T_2) = \frac{T_2}{1 + \{2\pi(\nu - \nu_0)T_2\}^2} \tag{5.13}$$

Its full-width at half-maximum (fwhm) spectral width is $\Delta\nu = 1/(\pi T_2)$.

The *Gaussian* line-shape function is

$$\begin{aligned} \text{f}_G(\nu, T_2^*) &= \exp(-[\nu - \nu_0]^2/2\sigma^2) \\ &= \exp(-4\pi[\nu - \nu_0]^2 T_2^{*2}) \end{aligned} \tag{5.14}$$

where $\sigma = 1/\{T_2^* \sqrt{(8\pi)}\}$ is the SD of the Gaussian. Its fwhm is $\Delta\nu_0 = \frac{\sqrt{(\ln 2)/\pi}}{T_2}$.

The *Voigt* line shape is a convolution of Gaussian and Lorentzian profiles typically approximated in MRS by a linear summation of the two profiles adjusted for the same center frequency and fwhm:

$$\text{f}_V(\nu, T_2^*) = a\text{f}_L(\nu, T_2^*) + (1 - a)\text{f}_G(\nu, T_2^*) \tag{5.15}$$

where a is the Lorentzian fraction of the mixed line shape.[3]

5.3.2 Chemical Shift Displacement Artifact

The center of a voxel corresponding to a moiety A with a chemical shift, δ_A ppm, is displaced by a distance

$$\Delta x_i = \frac{(\delta_A - \delta_{\text{pulse}})B_0}{10^6 G_i} \text{meters} \tag{5.16}$$

along the *i*th coordinate axis when excited by a spatially selective pulse with a gradient of strength G_i T/m during at least a central potion of the pulse applied in the *i*th direction and whose excitation frequency is centered at δ_{pulse} ppm.

5.3.3 Spatial Encoding

The MRS signal distribution, $S(x_i)$, is spatially encoded by gradients applied in the x_ith spatial direction that span a k-space of spatial frequency $-k_{\max}/2 \le k \le k_{\max}/2$, such that

$$S(\mathrm{x}_i) = \int_{-k_{\max}/2}^{k_{\max}/2} s(k)\ \exp(2\pi i k x_i)\mathrm{d}k \qquad (5.17)$$

where $s(k)$ is the time domain signal recorded in the presence of the gradient and $I = \sqrt{-1}$. With discrete phase-encoding gradients stepped by $j\Delta k$ and turned off during reception, $S(x_i)$ is discrete and

$$S(x_i) = \Delta k \sum_{j=-N/2}^{(N/2)-1} s(j\Delta k)\exp(2\pi i.j\Delta k.x_i) \qquad (5.18)$$

where j is an integer spanning $\pm N/2$. The nominal spatial resolution is $2/k_{\max}$ (see ***CSI and SENSE CSI***).

5.4 PHYSIOLOGICAL

5.4.1 Concentrations

To convert concentrations in millimole per liter wet tissue volume measured by MRS, to millimole per liter of tissue water (mM), and millimole per kilogram wet weight use:

$$\begin{aligned}[\mathrm{mM}] &= \frac{100[\text{milli-mol/l wet tissue}]\mathrm{SG}}{(\%W)} \\ &= \frac{100[\text{milli-mol/kgwetweight}]}{(\%W)} \\ &[\text{milli-mol/kg wet weight}] \\ &= \frac{\text{milli-mol/l tissue volume}}{\mathrm{SG}}\end{aligned} \qquad (5.19)$$

where square brackets denote soluble metabolite concentrations, SG is the specific gravity and W the water content by mass of the tissue (see Appendix 1).

5.4.2 Proton Density Fat Fraction (PDFF)

Proton density fat fraction (PDFF) is calculated from the T_1- and T_2-corrected areas of the water (s_{W}) and fat (s_{f}) ^{1}H MRS signals (see ***Monitoring Fatty Liver*** and ***Direct Water-Fat Imaging Methods: Chemical Shift-Selective and Chemical Shift-Encoded MRI***):

$$\mathrm{PDFF} = \frac{s_{\mathrm{f}}}{s_{\mathrm{f}} + s_{\mathrm{W}}} \qquad (5.20)$$

5.4.3 Tissue Intracellular pH

The tissue intracellular pH as determined from the chemical shift of the inorganic phosphate (Pi) resonance relative to the phosphocreatine (PCr) resonance (δ_{Pi}, ppm) in ^{31}P spectra, is

$$\mathrm{pH}_i = 6.72 + \log\left(\frac{\delta_{Pi} - 3.17}{5.72 - \delta_{\mathrm{Pi}}}\right) \qquad (5.21)$$

where 6.72 is the p*K*a (negative logarithm of the ionization constant) of Pi at a intracellular free concentration, $[\mathrm{Mg}^{++}]_i$, of 1 mM.[4]

5.4.4 Intracellular Free $[\mathrm{Mg}^{++}]$

Intracellular free $[\mathrm{Mg}^{++}]$ is obtained from the chemical shift difference, $\delta_{\alpha\beta}$, between the α- and β-phosphates of ATP:

$$[\mathrm{Mg}^{++}]_i = K_{\mathrm{D}}^{\mathrm{MgATP}}\left(\frac{\delta_{\alpha\beta}^{\mathrm{ATP}} - \delta_{\alpha\beta}}{\delta_{\alpha\beta} - \delta_{\alpha\beta}^{\mathrm{MgATP}}}\right) \qquad (5.22)$$

where $\delta_{\alpha\beta}^{\mathrm{ATP}}$ and $\delta_{\alpha\beta}^{\mathrm{MgATP}}$ are the chemical shift difference between α- and β-phosphates in a solution of unchelated ATP, and in a solution of ATP saturated with Mg^{++}, respectively.[4] $K_{\mathrm{D}}^{\mathrm{MgATP}}$ is the dissociation constant of MgATP, estimated at 58 µM at pH = 7.2, and adjustable for pH_i via $K_{\mathrm{D}}^{\mathrm{MgATP}} = 58(1+10^{(6.5\text{-pH})})/(1+10^{(6.5-7.2)})$ µM.[5]

5.4.5 Chemical Reaction Rate

For a chemical reaction in which moiety A with equilibrium magnetization M_0^A, observed under control conditions converts to moiety B with magnetization M_0^B at a different chemical shift at a forward rate k_1

and a reverse rate k_{-1}, the forward rate measured by saturating B (denoted by primes) is

$$k_1 = \frac{M_0^A - M_0'^A}{T_1'^A \; M_0^A} \tag{5.23}$$

where $T_1'^A$ is the T_1 of A measured with B fully saturated. At equilibrium, the reverse rate is

$$k_1 \, M_{0n}^A = \; k_{-1} M_{0n}^B \tag{5.24}$$

where subscripts n denote measurements in the absence of saturation (see ***Measuring Biochemical Reaction Rates In Vivo with Magnetization Transfer***).

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REFERENCES

1. C. N. Chen and D. I. Hoult, Biomedical Magnetic Resonance Technology, Bristol, New York: A. Hilger, 1989, p309.
2. W. A. Edelstein, G. H. Glover, C. J. Hardy, and R. W. Redington, *Magn. Reson. Med.*, 1986, **3**, 604–618.
3. I. Marshall, J. Higinbotham, S. Bruce, and A. Freise, *Magn. Reson. Med.*, 1997; **37**, 651.
4. J. C. A. Hopkins, G. K. Radda, R. L. Veech and K. Clarke, *Metab. Eng.*, 2004, **6**, 36.
5. J. P. Headrick, J. C. McKirdy and R. J. Willis, *Am. J. Physiol.*, 1998, **275**, H917.