

## 9.1.

A. Relevant equation:

$$M_{xy}(TR, TE) = M_0(1 - e^{-TR/T_1})e^{-TE/T_2}$$

$$M_0(\text{NAA}) = 308.1$$

$$M_0(\text{creatine}) = 209.6$$

$$M_0(\text{choline}) = 198.4$$

$$M_0(\text{water}) = 27,004$$

## B.

water content (WC) =  $0.4 \times \text{WC}_{\text{CSF}} + 0.5 \times \text{WC}_{\text{GM}} + 0.1 \times \text{WC}_{\text{WM}}$ , or

$$\text{WC} = 0.4 \times 1.0 \times 55.6 + 0.5 \times 0.87 \times 55.6 + 0.1 \times 0.83 \times 55.6 = 51.04 \text{ mol/L.}$$

## C.

1. Correct water integral for difference in number of averages

$$M_0(\text{water}) = 64 \times 27,004 = 1.728 \times 10^6$$

2. Normalize all integrals for the number of protons

$$M_0(\text{NAA}) = 102.7$$

$$M_0(\text{creatine}) = 69.9$$

$$M_0(\text{choline}) = 22.0$$

$$M_0(\text{water}) = 8.641 \times 10^5$$

$$[\text{NAA}] = [\text{water}] \times (M_0(\text{NAA})/M_0(\text{water})) = 6.07 \text{ mM}$$

$$[\text{creatine}] = [\text{water}] \times (M_0(\text{creatine})/M_0(\text{water})) = 4.13 \text{ mM}$$

$$[\text{choline}] = [\text{water}] \times (M_0(\text{choline})/M_0(\text{water})) = 1.30 \text{ mM}$$

D. The volume contains 40% CSF which contains negligible levels of the three metabolites. Therefore, the brain concentration of the three metabolites is 1.667 times higher than calculated under C.

## 9.2.

**A.**  $R = 2.7$  and  $T = 10$  ms give  $M_{xy} = 0.5M_0$  at frequency offsets of  $\pm 135$  Hz.

Using the general expression of a Gaussian excitation profile:

$$M_{xy}(\delta) = M_0 e^{-\text{scale}(\delta - \delta_{\text{water}})^2}$$

gives  $\text{scale} = 1.521$  and  $6.085$  ppm<sup>-2</sup> at 4.7 T and 9.4 T, respectively.

Converting the equation for  $M_{xy}$  to an expression for  $M_z$  (i.e.  $M_z = (1 - M_{xy}^2)^{1/2}$ ) allows the calculation of  $M_z$  after 6 CHESS elements ( $\delta_{\alpha\text{H1glucose}} = 5.216$  ppm, see Table 2.1), which is given by  $0.1711M_0$  and  $0.8871M_0$  at 4.7 T and 9.4 T, respectively. Therefore, CHESS water suppression suppresses 82.89% and 11.29% of the  $\alpha\text{-H1-glucose}$  resonance at 4.7 T and 9.4 T, respectively.

**B.** From Table 2.5 it follows that  $^1J_{\text{HC}} = 169.8$  Hz, such that the satellites appear at {4.792 and 5.641} ppm and {5.004 and 5.428} ppm at 4.7 T and 9.4 T, respectively.

At 4.7 T:

$$M_z(4.792 \text{ ppm}) = 0.000M_0$$

$$M_z(5.216 \text{ ppm}) = 0.1711M_0$$

$$M_z(5.641 \text{ ppm}) = 0.8101M_0$$

At 9.4 T:

$$M_z(5.004 \text{ ppm}) = 0.3071M_0$$

$$M_z(5.216 \text{ ppm}) = 0.8871M_0$$

$$M_z(5.428 \text{ ppm}) = 0.9953M_0$$

For a 50% increment, the theoretical ratio is 0.5 : 1 : 0.5. However, in the presence of partial suppression, the ratio becomes 0 : 1 : 2.37 at 4.7 T and 0.173 : 1 : 0.561 at 9.4 T, respectively.

### C.

At 4.7 T,  $FE = 0.8101 / (0.8101 + 0.1711) \times 100 \% = 82.6 \%$ .

At 9.4 T,  $FE = (0.3071 + 0.9953) / (0.3071 + 0.9953 + 0.8871) \times 100 \% = 59.5 \%$ .

### 9.3.

A. The  $^1\text{H}$  NMR spectrum of aspartic acid consists of three doublets of doublets (Fig. 2.7) making up 12 resonance lines. A completely unconstrained fit would thus require 48 independent parameters (amplitude, line width, frequency and phase for each resonance).

### B.

When full prior knowledge on aspartic acid is used, the spectral fit can be performed with four independent parameters, namely the amplitude, line width, frequency and phase of the entire spectrum. When the spectrum is properly phased prior to the spectral fit, the number of independent parameters can be reduced to three.

The underlying assumptions include:

1. The amplitude of aspartate-H2 and H3/H3' are identical, i.e. water suppression did not affect the aspartate-H2 resonance.
2. Ionic strength, temperature, pH or any other parameter did not lead to different line widths or frequencies for the aspartate-H2 or H3/H3' resonances.
3. The general assumption being that all prior knowledge used is correct.

### C.

Instead of 4 independent parameters, the  $^{13}\text{C}$  POCE difference spectrum of aspartate require 5 independent parameters for a proper spectral fit. Besides the line width, frequency and phase that are identical for all aspartate resonances, the amplitudes for aspartate-H2 and aspartate-H3/H3' need to be independent. This is because aspartate-C2 and aspartate-C3 incorporate the  $^{13}\text{C}$ -label from  $[1-^{13}\text{C}]$ -glucose at different rates, such that their amplitudes do not have to be identical *per se*.

### 9.4.

#### A.

1. Correct lactate and water integrals for  $T_1$  and  $T_2$  relaxation:

$$M_0(\text{lactate}) = 359.9$$

$$M_0(\text{water}) = 8.605 \times 10^5$$

2. Correct lactate integral for editing efficiency:

$$M_0(\text{lactate}) = 438.9$$

3. Correct for number of averages and number of protons:

$$M_0(\text{lactate}) = 146.3$$

$$M_0(\text{water}) = 3.442 \times 10^5$$

From the text the average muscle water content =  $0.78 \times 55.6 \text{ mol/L} = 43.37 \text{ mol/L}$ , which leads to a lactate concentration given by:

$$[\text{lactate}] = [\text{water}] \times (M_0(\text{lactate})/M_0(\text{water})) = 18.4 \text{ mM}$$

**B.** The signal intensity during a general JDE sequence is given by:

$$M_{xy}(\text{TE}) = M_0 [e^{-\text{TE}/T_2} - \cos(\pi J \text{TE}) e^{-\text{TE}/T_2}]$$

The maximum signal intensity can be found by setting the derivative with respect to TE to zero, i.e.  $dM_{xy}/d\text{TE} = 0$ . The optimal echo-time can then be solved as  $\text{TE} = 105.0 \text{ ms}$ . See exercise for the exact expression of the optimal echo-time. This echo-time gives 21.7% more signal than the default echo-time of  $1/J = 144 \text{ ms}$ .

**9.5.** A proton-density-weighted MR image is proportional to the amount of water present in each pixel. This type of image is acquired with a long repetition time and a short echo-time. Potential complications arise from the presence of image inhomogeneity that is not related to the brain structures, such as inhomogeneity in the RF transmit and receive fields. However, provided that RF field inhomogeneity is minimized or measured, proton-density imaging is a simple method to obtain relative water levels. Comparison of intensities to a known concentration, such as pure water in CSF, allows the determination of absolute water levels.

## 9.6.

1. Increasing the echo-time during a non-spatially selective part of a pulse sequence (glutamate + lactate).

Provided that signal modulation due to scalar couplings is taken into account, this method will give an accurate estimate of  $T_2$ . The  $T_2$  relation times may become inaccurate when the signal modulation is a dominant source of signal loss for the majority of echo-times, as is likely the case for glutamate.

2. Increasing the echo-time during a spatially selective part of a pulse sequence (e.g. PRESS, glutamate + lactate).

This method is based on similar arguments as the previous method, but has the additional complication that the signal intensity is affected by spatial displacement artifacts due to difference in chemical shift. While this effect can be taken into account on a homogeneous sample, this method is not advised for high-accuracy  $T_2$  measurements.

3. Increasing the echo-time of a Carr-Purcell-Meiboom-Gill pulse train (glutamate + lactate).

Since glutamate is a strongly-coupled spin-system, the CPMG method will lead to a high degree of signal refocusing, making this method ideal for glutamate  $T_2$  measurements. As lactate is a weakly-coupled spin-system, the benefits of CPMG over a regular spin-echo method are somewhat reduced. However, for both glutamate and lactate the CPMG is expected to provide a measured  $T_2$  that is closer to the inherent  $T_2$  since effects of diffusion are refocused to a higher degree.

4. Increasing the echo-time in a spectrally selective pulse sequence (lactate only).

Since lactate has two well-resolved resonances, a pulse sequence can be devised which selectively refocuses one of the two resonances, thereby completely inhibiting signal modulation due to scalar coupling evolution.

## 9.7.

### A.

Maximum signal would be obtained when the phase of all transients is identical and equal to zero. Maximum signal loss occurs when the signal continuously varies between  $+10^\circ$

and  $-10^\circ$ , such that the dispersive component of the spectrum cancels (i.e.  $\sin(10^\circ) = -\sin(-10^\circ)$ ) and the integral of the absorption spectrum is  $(1 - \cos(10^\circ)) = 1.52\%$  lower than the maximum signal.

**B.**

Experimental duration =  $1,024 \times 1.0 \text{ s} = 1,024 \text{ s}$ . The magnetic field drifts by 2.28 Hz over 1,024 s, such that the resonance broadens by 2.28 Hz. Given that the line width in the absence of a magnetic field drift is 3.18 Hz, the final line width becomes 5.46 Hz.

**C.** Instead of adding all transient together during the experiment, the transients are first stored separately in memory. Then each transient is individual phased and frequency corrected before they are added together. This approach works well, provided that there is enough signal-to-noise to phase and frequency-correct each single-transient spectrum.

**9.8.**

**A.** The expression for the steady-state longitudinal magnetization for this particular sequence is given by:

$$M_z(\omega, TR) = M_0 \frac{1 - e^{-TR/T_1}}{1 + \cos \omega \tau e^{-TR/T_1}}$$

Note the + sign in the denominator which arise from the fact that the  $180^\circ$  spin-echo pulse inverts any residual  $M_z$  following the excitation pulse. The expression for  $M_{xy}$  then becomes:

$$M_{xy}(\omega, TR, TE) = M_0 \frac{(1 - e^{-TR/T_1}) e^{-TE/T_2} \sin \omega \tau}{1 + \cos \omega \tau e^{-TR/T_1}}$$

Note that the nutation angle has a frequency dependence originating from the JR pulse.

From Exercise 9.1 it followed that the  $T_1$  and  $T_2$  corrected metabolite signals are given by:

$$M_0(\text{NAA}) = 308.1$$

$$M_0(\text{creatine}) = 209.6$$

$$M_0(\text{choline}) = 198.4$$

The steady-state metabolite levels obtained with the JR spin-echo sequence ( $\tau = 1/(4 \times 500)$ ) can then be calculated as:

$$M_{xy}(\text{NAA}) = 122.5$$

$$M_{xy}(\text{creatine}) = 50.1$$

$$M_{xy}(\text{choline}) = 45.7$$

**B.** Because of eddy-current-related phase distortion, the JR sequence effectively becomes:

$$90^\circ_{20^\circ} - t - 90^\circ_{180^\circ}$$

The expression for the steady-state  $M_{xy}$  then becomes:

$$M_{xy}(\omega, \text{TR}, \text{TE}) = M_0 \frac{(1 - e^{-\text{TR}/T_1}) e^{-\text{TE}/T_2} \sin(\omega\tau + \pi/9)}{1 + (\cos \omega\tau + \pi/9) e^{-\text{TR}/T_1}}$$

In other words, the additional  $20^\circ$  phase offsets shift the excitation profile  $-1/(18\tau) = -111$  Hz. The steady-state metabolite levels can then be calculated as:

$$M_{xy}(\text{NAA}) = 184.4$$

$$M_{xy}(\text{creatine}) = 85.1$$

$$M_{xy}(\text{choline}) = 81.7$$

### C.

The metabolite and water intensities corrected for  $T_1$ ,  $T_2$  and JR-related signal loss are given by:

$$M_0(\text{NAA}) = 150.4$$

$$M_0(\text{creatine}) = 123.1$$

$$M_0(\text{choline}) = 85.0$$

$$M_0(\text{water}) = 8,111$$

Correct water integral for difference in number of averages

$$M_0(\text{water}) = 5.19 \times 10^5$$

Normalize all integrals for the number of protons

$$M_0(\text{NAA}) = 50.1$$

$$M_0(\text{creatine}) = 41.0$$

$$M_0(\text{choline}) = 9.4$$

$$M_0(\text{water}) = 2.60 \times 10^5$$

Finally:

$$[\text{NAA}] = [\text{water}] \times (M_0(\text{NAA})/M_0(\text{water})) = 7.72 \text{ mM}$$

$$[\text{creatine}] = [\text{water}] \times (M_0(\text{creatine})/M_0(\text{water})) = 6.32 \text{ mM}$$

$$[\text{choline}] = [\text{water}] \times (M_0(\text{choline})/M_0(\text{water})) = 1.46 \text{ mM}$$