

### 7.1.A.

Chemical shift difference =  $3.22 - 2.01 = 1.21$  ppm, which equals 154.5 Hz at 3.0 T.

Spatial displacement =  $154.5/1200 = 0.1287$ , which equals 1.03 cm along the 8 cm side and 0.77 cm along the 6 cm. The 1 cm slice does not have to be considered, as no additional spatial encoding will be performed in that direction.

10 mM NAA corresponds to 30 mM methyl protons and 2 mM choline corresponds to 18 mM methyl protons. Since the middle of the volume does not experience any net spatial displacements, the NAA-to-choline ratio =  $1.667 (= 30/18)$ .

Nominal MRSI volume size =  $1 \times 1$  cm. Since the spatial displacement in one dimension (1.03 cm) is more than 1 MRSI volume side (1.00 cm), the NAA-to-choline ratio in two of the four corners is zero! In a third corner there is no net effect, making the ratio equal to 1.667. Finally, in the fourth corner the volume has shifted by 0.77 cm in one direction, such that the NAA-to-choline ratio becomes  $0.23 \times (30/18) = 0.383$ .

Therefore, even on a homogeneous sample the chemical shift displacement artifact can lead to a wide range of metabolite ratios, which can lead to erroneous interpretation if not accounted for.

**B.** Chemical shift difference =  $3.22 - 2.01 = 1.21$  ppm, which equals 363.0 Hz at 7.05 T.

Spatial displacement =  $363.0/1200 = 0.3025$ , which equals 2.42 cm along the 8 cm side and 1.82 cm along the 6 cm.

Since the chemical shift displacement is more than 1 MRSI volume side in both dimensions, three of the four corners will have a NAA-to-choline ratio of zero. The fourth corner will have a ratio equal to 1.667.

**C.** The ratio does not vary more than 10% when the NAA and choline volumes overlap for  $\geq 90\%$ . In other words,  $(1 - 6x)(1 - 8x) = 0.90$  where  $x$  is the chemical shift difference to RF bandwidth ratio. Solving for  $x$  gives  $x = 0.0073$ , which then results in a

RF bandwidth of 21,087 Hz. This bandwidth can be achieved by shortening the pulse length from 5.0 ms to 0.285 ms, with a corresponding 17.6× increase in RF amplitude.

### 7.2.A.

Since  $TR/T_{1,\text{lipids}} \gg 5$ , the expression for  $M_{z,\text{lipids}}$  will be independent of the TR and can be derived as:

$$M_{z,\text{lipids}} = M_{0,\text{lipids}} (1 - [1 - \cos \alpha] e^{-\Delta/T_{1,\text{lipids}}})$$

where  $\alpha$  and  $\Delta$  are the nutation angle and the delay following the pulse, respectively. Solving for  $\alpha$  when  $M_{z,\text{lipids}} = 0$  gives  $\alpha = 96.04^\circ$  for the first pulse ( $\Delta = 30$  ms) and  $\alpha = 91.94^\circ$  for the second pulse ( $\Delta = 10$  ms).

**B.** In the case of water, the short TR relative to  $T_1$  must be taken into account, leading to the following expression for  $M_{z,\text{water}}$ :

$$M_{z,\text{water}} = M_{0,\text{water}} (1 - [1 - \cos \alpha (1 - e^{-TR/T_{1,\text{water}}})] e^{-\Delta/T_{1,\text{water}}})$$

solving for  $\alpha$  when  $M_{z,\text{water}} = 0$  gives  $\alpha = 91.28^\circ$  for the first pulse ( $\Delta = 30$  ms) and  $\alpha = 90.42^\circ$  for the second pulse ( $\Delta = 10$  ms).

### 7.3.A.

The expression for signal recovery is similar to that derived under exercise 7.2 and is given by:

$$M_z = M_0 (1 - [2 - e^{-TR/T_1}] e^{-TI/T_1})$$

Signal recoveries for compounds with  $T_1 = 1000$ , 1300 and 1600 ms are then given by  $-0.514M_0$ ,  $-0.521M_0$  and  $-0.505M_0$ , respectively.

**B.**

In this case the signal recoveries for compounds with  $T_1 = 1000, 1300$  and  $1600$  ms are then given by  $-0.622M_0, -0.696M_0$  and  $-0.736M_0$ , respectively.

**C.**

While the long-TR experiment provides a higher signal intensity than the short-TR experiment, it also introduces significant  $T_1$ -related signal modulation despite the long TR. The signal variation across the  $T_1$  species is only 3% for TR = 2000 ms, but increases to 17% for TR = 6000 ms. Therefore, for quantitative MRS studies, the TR = 2000 ms experiment does not require a metabolite-specific  $T_1$  correction, whereas the TR = 6000 ms experiment does require a separate  $T_1$  measurement. In this case the shorter TR experiment is more desirable.

**7.4.A.** The imaging bandwidth of the PEPSI method must be 16 times larger than the spectroscopic bandwidth. As a result, the SNR of the PEPSI scan is  $\sqrt{16} = 4$  times lower than the conventional scan, giving SNR = 2.5.

**B.** A modest improvement in temporal resolution can be achieved by:

- circular k-space sampling
- k-space weighting by TR variation
- Using a more sensitive RF coil

**7.5.**

$$TR(k) = -T_1 \ln \left[ 1 - \left( 1 - e^{-TR(0)/T_1} \right) \left( 0.75 + 0.25 \cos \left( \frac{\pi k}{k_{\max}} \right) \right) \right]$$

**7.6.** The ‘half-pixel shift’ can be verified by performing a MRSI experiment on an object that is smaller than half a MRSI pixel. If the ‘half-pixel shift’ is present, then the MRSI dataset must be shifted by half a pixel in order to obtain the highest amount of signal from the desired location. Alternatively, a 3D localization method can select a volume with dimensions smaller than half a MRSI pixel.

**7.7.A.** The two phase-encoded NMR spectra P are given by:

$$P_1 = S_1 e^{+ik_{x,1}x_1} + S_2 e^{+ik_{x,1}x_2}$$

$$P_2 = S_1 e^{+ik_{x,2}x_1} + S_2 e^{+ik_{x,2}x_2}$$

where  $k_{x,1}$  and  $k_{x,2}$  are the k-space coordinates in the first and second experiment, respectively. These two equations are readily solved for the two unknowns,  $S_1$  and  $S_2$ . Note that the y coordinate does not have to be considered, as there is no phase-encoding gradient applied along that direction.

**B.** The two equations derived under A are readily solved for  $S_1$  and  $S_2$ , except when  $x_1 = x_2$  or  $k_1 = k_2$ . In these cases there is not enough information to separate  $S_1$  from  $S_2$ .

**7.8A.** The actual volume of a MRSI pixel derived from a non-weighted k-space grid is circa 18% larger than the nominal voxel size (measured as the FWHM of the real part of the PSF). The k-space-weighting function shown in Fig. 7.7 was calculated for  $T_1 = 1000$  ms, which will give a MRSI voxel that is circa 53% larger than the nominal voxel size. When the k-space weighting function is recalculated for  $T_1 = 2000$  ms, the MRSI voxel size becomes circa 74% larger than the nominal volume size. Note that the exact numbers given here depend on the numerical implementation of the method.

**B.**

Given a weighting function  $W(k)$ , the repetition time TR can be calculated according to:

$$TR(k) = -T_1 \ln[1 - W(k)(1 - e^{-TR(k=0)/T_1})]$$

When the k-space weighting in two dimensions is executed as  $W(k_x, k_y) = W(k_x).W(k_y)$ , the total duration of the experiment can be (numerically) calculated as 687 s. The

standard, non-weighted experiment takes  $32 \times 32 \times 1.5 \text{ s} = 1536 \text{ s}$ . Therefore, the k-space weighted experiment leads to a circa 55% scan time reduction.

**C.** With a Gaussian weighting function the 2D experiment is finished in 219 s, thereby given a circa 85% scan time reduction. However, it should be realized that this particular Gaussian function weighs k-space more heavily than the Hamming function of Exercise B, such that the actual voxel size is larger.

**D.** With a 3D k-space weighted acquisition according to a Hamming function, the scan time is 1847 s. A non-weighted k-space scan would complete in  $32 \times 32 \times 32 \times 1.5 \text{ s} = 6144 \text{ s}$ . Therefore, k-space weighting leads to a circa 70% scan time reduction. Even larger improvements can be achieved with the Gaussian weighting function, again at the expense of larger voxel sizes and thus a lower spatial resolution.

**E.** For the condition that  $\alpha(k=0) = 90^\circ$ , the weighting function is given by:

$$W(\mathbf{k}) = \frac{M_{xy}(\mathbf{k})}{M_{xy}(\mathbf{k} = 0)} = \frac{\sin \alpha}{1 - \cos \alpha e^{-TR/T_1}}$$

Solving for  $\alpha$  is straightforward, although it results in a somewhat complicated function.

## 7.9.

### A.

Mutual  $T_1$  saturation is avoided when none of the three orthogonal slices of volume 1 overlap with volume 2. Therefore, the closest spatial positions in which volume 2 can be placed are given by  $(\pm 2, \pm 2, \pm 2) \text{ cm}$ .

### B.

The overall experimental duration can only remain constant when the number of averages per volume is reduced three-fold, which will lead to a  $\sqrt{3}$  reduction in the S/N of the NAA resonance.

### C.

The  $T_1$ -corrected NAA signal intensities from the non-saturated multi-volume experiment are given by 25.9, 20.7 and 31.1, respectively. When the volumes are positioned such that  $T_1$  saturation occurs, the effective repetition time is reduced to  $5000/3 = 1667$  ms. The NAA signal intensities under these saturating conditions are given by 17.4, 13.9 and 20.9, respectively. In this particular case, the NAA signal intensities under saturating conditions are only slightly higher than those acquired in a sequential, single-volume experiment. It should then be decided if the increase complexity and more limited voxel placement of a multi-volume acquisition justifies the small increase in S/N ratio. This is especially important since the obtain metabolite signals are now heavily  $T_1$ -weighted and most likely require knowledge of the  $T_1$  relaxation time in order to allow for absolute quantification.

### 7.10.

#### A.

The signal-to-noise ratio,  $(S/N)_{SV}$ , of an experiment is proportional to the volume size and the number of scans according to

$$\left(\frac{S}{N}\right)_{SV} = cV_{SV}\sqrt{N_{A,SV}}$$

where  $c$  is a sequence-dependent parameter, holding for example relaxation parameters.

The  $(S/N)$  per unit time,  $P_{SV}$ , is given by:

$$P_{SV} = \frac{cV_{SV}\sqrt{N_{A,SV}}}{\sqrt{T}} = \frac{cV_{SV}\sqrt{N_{A,SV}}}{\sqrt{N_{A,SV}TR}} = \frac{cV_{SV}}{\sqrt{TR}}$$

where  $T$  is the total experimental duration.

**B.**

The volume size of a 3D MRSI experiment is given by

$$V_{\text{MRSI}} = \frac{\text{FOV}_1}{N_1} \cdot \frac{\text{FOV}_2}{N_2} \cdot \frac{\text{FOV}_3}{N_3}$$

The  $(S/N)_{\text{MRSI}}$  is proportional to  $V_{\text{MRSI}}$  according to:

$$\left(\frac{S}{N}\right)_{\text{MRSI}} = cV_{\text{MRSI}} \sqrt{N_1 N_2 N_3 N_{A,\text{MRSI}}}$$

After which the  $(S/N)$  per unit time,  $P_{\text{MRSI}}$ , can be calculated according to:

$$P_{\text{MRSI}} = \frac{cV_{\text{MRSI}} \sqrt{N_1 N_2 N_3 N_{A,\text{MRSI}}}}{\sqrt{T}} = \frac{cV_{\text{MRSI}} \sqrt{N_1 N_2 N_3 N_{A,\text{MRSI}}}}{\sqrt{N_1 N_2 N_3 N_{A,\text{MRSI}}} TR} = \frac{cV_{\text{MRSI}}}{\sqrt{TR}}$$

**C.**

Since  $P_{\text{SV}} = P_{\text{MRSI}}$  for equal voxel sizes ( $V_{\text{SV}} = V_{\text{MRSI}}$ ) and equal sequence parameter ( $c$ ), MRSI does not offer any advantage over single-volume MRS in terms of sensitivity per unit time.

**D.**

However, in the time that it takes single-voxel MRS to acquire one voxel, MRSI can acquire signal from many voxels, such that the information content of MRSI per unit time is much higher than for MRS. As a result, MRSI can provide information from locations not sampled by single-volume MRS.

**7.11.****A.**

This strategy does not lead to scan time reduction for conventional MRSI experiments. It merely provides additional information about the metabolite under investigation by observing them at different echo-times.

When a J-resolved experiment (see Chapter 8) is combined with MRSI, then the acquisition of multiple echoes does lead to a scan time reduction.

## **B.**

This strategy does lead to scan time reduction by a factor equal to the number of echoes that are acquired. Similar to RARE imaging, the obvious disadvantage of this approach is that the latter echoes are more heavily  $T_2$ -weighted, leading to a k-space weighting and ultimately blurring in image space. However, scan time reduction factors of 2 – 4 have been obtained without significant negative effects on the data quality.

## **C.**

For the approach described under A, the presence of scalar coupling is beneficial as it provides additional information about the spin-system under investigation.

The presence of scalar coupling for the method described under B is generally an undesirable complication.