Supporting Background Information

b-matrix

1 Pulse sequence

STEAM acquisition gives rise to different spin coherence pathways (other than the desired stimulated echo) that must be dephased. This is accomplished by an appropriate combination of crusher gradients that selectively preserve the spin coherence of the stimulated echo. Supporting Figure 1 shows the crusher gradients and the phase for each coherence pathway (E1 through E4 in the figure) given by:

$$\begin{cases} \mathrm{E}_1 & = -\phi_1 + \phi_2 \\ \mathrm{E}_2 & = -\phi_1 + \phi_2 + \phi_3 - \phi_4 \\ \mathrm{E}_3 & = -\phi_2 + \phi_3 + \phi_4 \\ \mathrm{E}_4 & = -\phi_1 - \phi_2 - \phi_3 + \phi_4 \\ \mathrm{E}_{1-4} & \neq 0 \\ \mathrm{SE} & = -\phi_1 + \phi_4 \\ \phi_2 & \neq 0 \\ \phi_4 & \neq 0 \end{cases} \tag{1}$$

where ϕ_1 to ϕ_4 refer to the area under the spoiler gradients. The amplitudes of the four spoiler gradients are chosen to satisfy the phase equations given above. The first five equations result in the dephasing of the four coherence pathways (E1-E4) shown in Supporting Figure 1. The last two conditions are to dephase FIDs arising from the second and third 90° RF pulses. The phase evolution of the stimulated echo (STE) is shown in the last line and this phase is refocused as long as the gradients and are balanced.
A schematic of the STEAM pulse sequence diagram is shown in Supporting Figure 2. The slice select spectral spatial (SPSP) RF pulse is applied at time $t = 0$, the second and third RF pulses are both 90° pulses centered on the gradients marked as G'_{sl}.

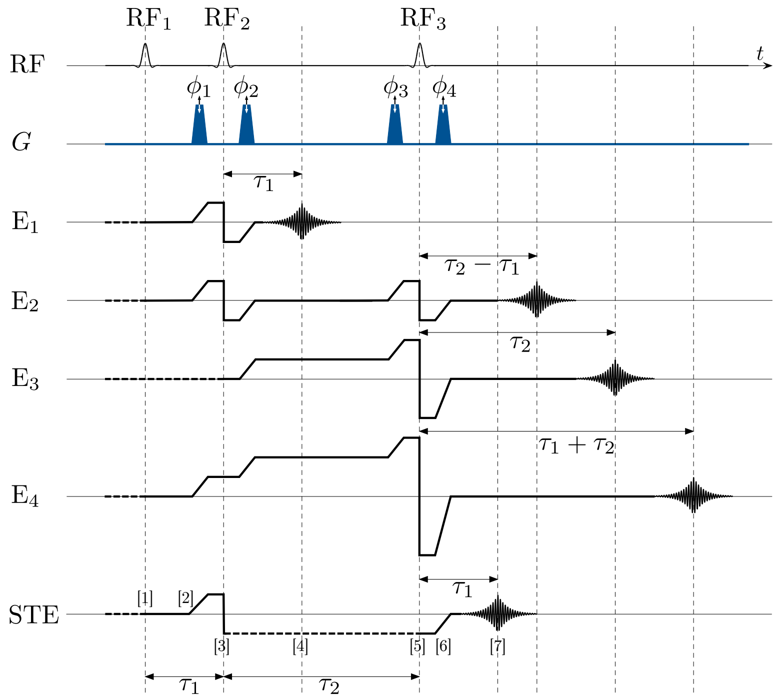
2 Definitions

2.1 Gradients

1. G_{sl} are gradients applied during the spectral spatial (SPSP) RF pulse that selectively excites water;
2. G_{ds}, G_{dr}, G_{dp} are diffusion gradients along the slice select, read and phase encode directions respectively (and corresponding rephasing diffusion gradients);
3. G_{cs}, G_{cr}, G_{cp} are crusher gradients along the slice select, read and phase encode directions respectively (and corresponding rephasing crusher gradients);
4. $G_{sl'}$ are slice select gradient when the second and third RF pulses are applied;
5. G_{rf}, G_{rd}, G_{pdp} are dephasing gradients along the slice select, read and phase encode directions respectively;
6. G_{pe} are phase encode gradients in the EPI readout train;
7. G_{ro} are read out gradients in the EPI readout train.

2.2 Timing parameters

- δ is defined as the time from the start of a gradient to the end of its plateau region
- Δ is the effective diffusion time and is defined as follows:

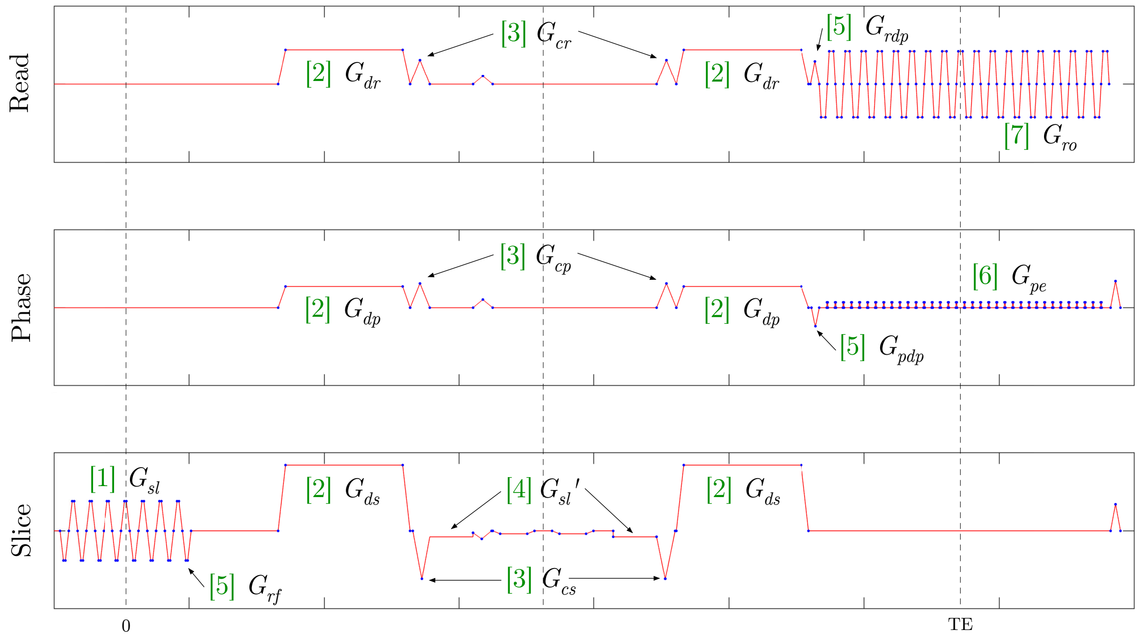


Supporting Figure 1: Spin-phase evolution shown in E1 through E4 are spoiled by the appropriate choice of crusher gradients ϕ_1 through ϕ_4 as explained in the text. The phase coherence pathway for the stimulated echo (STE) is shown in in the last line: RF$_1$ excites magnetization to the transverse plane: [1], phase is accumulated due to gradient ϕ_1: [2], RF$_2$ reverses the phase: [3] and locks magnetization longitudinally: [4], following RF$_3$, magnetization is restored to the transverse plane: [5] and rephased by crusher gradient ϕ_4: [6] to form an echo: [7]. It should be noted that the crusher gradients are not drawn to actual scale; Supporting Figure 2 shows the four crusher gradients designed to meet the phase coherence criteria. Imaging and diffusion gradients are not shown here but the phase from these gradients is zero at the time of the STE.

- Case 1: for a pair of matched gradients (e.g., diffusion, crusher), this is defined as the time between the start time of the first gradient of the pair (t_{g1}) to the start time of the second matching gradient pair (t_{g1}); g stands for diffusion or crusher gradient.
- Case 2: for an unmatched gradient, this is the time between the start of the gradient and the echo time, TE.

3 General analytic form

$$
\begin{aligned}
b_{ij} = \gamma^2 \Big[& G_{1i}G_{1j}\tau_{11} + (G_{1i}G_{2j} + G_{2i}G_{1j})\tau_{12} + (G_{1i}G_{3j} + G_{3i}G_{1j})\tau_{13} + \\
& + (G_{1i}G_{4j} + G_{4i}G_{1j})\tau_{14} + (G_{1i}G_{5j} + G_{5i}G_{1j})\tau_{15} + (G_{1i}G_{6mj} + G_{6mi}G_{1j})\tau_{16m} + \\
& + (G_{1i}G_{71j} + G_{71i}G_{1j})\tau_{171} + G_{2i}G_{2j}\tau_{22} + (G_{2i}G_{3j} + G_{3i}G_{2j})\tau_{23} + \\
& + (G_{2i}G_{4j} + G_{4i}G_{2j})\tau_{24} + (G_{2i}G_{5j} + G_{5i}G_{2j})\tau_{25} + (G_{2i}G_{6mj} + G_{6mi}G_{2j})\tau_{26m} + \\
& + (G_{2i}G_{71j} + G_{71i}G_{2j})\tau_{271} + G_{3i}G_{3j}\tau_{33} + (G_{3i}G_{4j} + G_{4i}G_{3j})\tau_{34} + \\
& + (G_{3i}G_{5j} + G_{5i}G_{3j})\tau_{35} + (G_{3i}G_{6mj} + G_{6mi}G_{3j})\tau_{36m} + (G_{3i}G_{71j} + G_{71i}G_{3j})\tau_{371} + \\
& + G_{4i}G_{4j}\tau_{44} + (G_{4i}G_{5j} + G_{5i}G_{4j})\tau_{45} + (G_{4i}G_{6mj} + G_{6mi}G_{4j})\tau_{46m} + \\
& + (G_{4i}G_{71j} + G_{71i}G_{4j})\tau_{471} + G_{5i}G_{5j}\tau_{55} + (G_{5i}G_{6mj} + G_{6mi}G_{5j})\tau_{56m} + (G_{5i}G_{71j} + G_{71i}G_{5j})\tau_{571} \\
& + G_{6mi}G_{6mj}\tau_{6m6m} + (G_{6i}G_{71j} + G_{71i}G_{6j})\tau_{671} + G_{71i}G_{71j}\tau_{7171} + \\
& + (G_{7mi}G_{7(m+1)j} + G_{7(m+1)i}G_{7mj})\tau_{7m7(m+1)} \Big]
\end{aligned} \tag{2}
$$



Supporting Figure 2: Schematic of the STEAM-DTI pulse sequence with labeled gradients. Numbers in square brackets and green font color denote the index numbers used for gradient and timing terms.

4 Diagonal terms

For the read direction we have:

$$G_1 = 0;\ G_2 = G_{dr};\ G_3 = G_{cr};\ G_4 = 0;\ G_5 = G_{rdp};\ G_6 = 0;\ G_7 = G_{ro}$$

which gives the following for the diagonal readout term:

$$\begin{aligned} b_{rr} = \gamma^2 \Big(& G_{dr}^2 \tau_{22} + 2G_{dr}G_{cr}\tau_{23} + 2G_{dr}G_{rdp}\tau_{25rp} + 2G_{dr}G_{ro}\tau_{271} + G_{cr}^2\tau_{33} + 2G_{cr}G_{rdp}\tau_{35rp} + \\ & + 2G_{cr}G_{ro}\tau_{371} + G_{rdp}^2\tau_{55rp} + 2G_{rdp}G_{ro}\tau_{5rp71} + G_{ro}^2(\tau_{7171} + \tau_{7m7(m+1)})\Big) \end{aligned} \tag{3}$$

taking into account refocused gradient pairs we get:

$$b_{rr} = \gamma^2 \Big(G_{dr}^2 \tau_{22} + 2G_{dr}G_{cr}\tau_{23} + G_{cr}^2\tau_{33} + G_{rdp}^2\tau_{55rp} + 2G_{rdp}G_{ro}\tau_{5rp71} + G_{ro}^2(\tau_{7171} + \tau_{7m7(m+1)})\Big) \tag{4}$$

For the phase direction we have:

$$G_1 = 0;\ G_2 = G_{dp};\ G_3 = G_{cp};\ G_4 = 0;\ G_5 = G_{pdp};\ G_6 = G_{pe};\ G_7 = 0$$

which gives the following for the diagonal phase-encoding

$$\begin{aligned} b_{pp} = \gamma^2 (& G_{dp}^2 \tau_{22} + 2G_{dp}G_{cp}\tau_{23} + 2G_{dp}G_{pdp}\tau_{25rp} + 2G_{dp}G_{pe}\tau_{26m} + G_{cp}^2\tau_{33} + 2G_{cp}G_{pdp}\tau_{35rp} \\ & + G_{cp}G_{pe}\tau_{36m} + G_{pdp}^2\tau_{55rp} + 2G_{pdp}G_{pe}\tau_{5rp6m} + G_{pe}^2\tau_{6m6m}) \end{aligned} \tag{5}$$

taking into account refocused gradient pairs we get:

$$b_{pp} = \gamma^2 (G_{dp}^2 \tau_{22} + 2G_{dp}G_{cp}\tau_{23} + G_{cp}^2\tau_{33} + G_{pdp}^2\tau_{55rp} + 2G_{pdp}G_{pe}\tau_{5rp6m} + G_{pe}^2\tau_{6m6m}) \tag{6}$$

For the slice direction we have: $G_1 = G_{sl}$; $G_2 = G_{ds}$; $G_3 = G_{cs}$; $G_4 = G_{sl}'$; $G_5 = G_{rf}$; $G_6 = 0$; $G_7 = 0$ which gives the following for the diagonal slice-select:

$$
\begin{aligned}
b_{ss} = \gamma^2 \Big(& \frac{14}{3} G_{sl}^2 \tau_{11} + G_{sl} G_{ds} \tau_{12} + G_{sl} G_{cs} \tau_{13} + G_{sl} G'_{sl} \tau_{14} + G_{sl} G_{rf} \tau_{15s} + G_{ds}^2 \tau_{22} + 2 G_{ds} G_{cs} \tau_{23} + \\
& + G_{ds} G'_{sl} \tau_{24} + G_{ds} G_{rf} \tau_{25s} + G_{cs}^2 \tau_{33} + G_{cs} G'_{sl} \tau_{34} + 2 G_{cs} G_{rf} \tau_{35} + G'^2_{sl} \tau_{44} + G'_{sl} G_{rf} \tau_{45s} + \\
& + G_{rf}^2 \tau_{55s} \Big)
\end{aligned} \tag{7}
$$

with refocused gradient pairs one arrives to:

$$
\begin{aligned}
b_{ss} = \gamma^2 \Big(& \frac{14}{3} G_{sl}^2 \tau_{11} + G_{ds}^2 \tau_{22} + 2 G_{ds} G_{cs} \tau_{23} + G_{ds} G'_{sl} \tau_{24} + G_{ds} G_{rf} \tau_{25s} + G_{cs}^2 \tau_{33} + G_{cs} G'_{sl} \tau_{34} + \\
& + 2 G_{cs} G_{rf} \tau_{35s} + \frac{1}{4} G'^2_{sl} \tau_{44} + G'_{sl} G_{rf} \tau_{45s} + \frac{1}{4} G_{rf}^2 \tau_{55s} \Big)
\end{aligned} \tag{8}
$$

5 Off-diagonal terms

Summarizing all gradients together in one place:

$$
\begin{array}{lll}
G_{1r} = 0 & G_{1p} = 0 & G_{1s} = G_{sl} \\
G_{2r} = G_{dr} & G_{2p} = G_{dp} & G_{2s} = G_{ds} \\
G_{3r} = G_{cr} & G_{3p} = G_{cp} & G_{3s} = G_{cs} \\
G_{4r} = 0 & G_{4p} = 0 & G_{4s} = G'_{sl} \\
G_{5r} = G_{rdp} & G_{5p} = G_{pdp} & G_{5s} = G_{rf} \\
G_{6r} = 0 & G_{6p} = G_{pe} & G_{6s} = 0 \\
G_{7r} = G_{ro} & G_{7p} = 0 & G_{7s} = 0
\end{array}
$$

Then starting from the read-out/phase term plugging the gradients G_r and G_p into equation Eq. 2:

$$
\begin{aligned}
b_{rp} = b_{pr} = \gamma^2 \Big(& G_{dr} G_{dp} \tau_{22} + (G_{dr} G_{cp} + G_{cr} G_{dp}) \tau_{23} + (G_{dr} G_{pdp} + G_{rdp} G_{dp}) \tau_{25rp} + G_{dr} G_{pe} \tau_{26m} + \\
& + G_{ro} G_{dp} \tau_{271} + G_{cr} G_{cp} \tau_{33} + (G_{cr} G_{pdp} + G_{rdp} G_{cp}) \tau_{35rp} + G_{cr} G_{pe} \tau_{36m} + G_{ro} G_{cp} \tau_{371} + \\
& + G_{rdp} G_{pdp} \tau_{55rp} + G_{rdp} G_{pe} \tau_{5rp6m} + G_{ro} G_{pdp} \tau_{5rp71} + G_{pe} G_{ro} \tau_{6m71} \Big)
\end{aligned} \tag{9}
$$

taking into account refocused gradient pairs we get:

$$
\begin{aligned}
b_{rp} = b_{pr} = \gamma^2 \Big(& G_{dr} G_{dp} \tau_{22} + (G_{dr} G_{cp} + G_{cr} G_{dp}) \tau_{23} + G_{cr} G_{cp} \tau_{33} + G_{rdp} G_{pdp} \tau_{55rp} + G_{rdp} G_{pe} \tau_{5rp6m} + \\
& + G_{ro} G_{pdp} \tau_{5rp71} + G_{pe} G_{ro} \tau_{6m71} \Big)
\end{aligned} \tag{10}
$$

the read-out/slice select term gives:

$$
\begin{aligned}
b_{rs} = b_{sr} = \gamma^2 \Big(& G_{dr} G_{sl} \tau_{12} + G_{cr} G_{sl} \tau_{13} + G_{rdp} G_{sl} \tau_{15s} + G_{ro} G_{sl} \tau_{171} + G_{dr} G_{ds} \tau_{22} + \\
& + (G_{dr} G_{cs} + G_{cr} G_{ds}) \tau_{23} + \frac{1}{2} G_{dr} G'_{sl} \tau_{24} + (\frac{1}{2} G_{dr} G_{rf} + G_{rdp} G_{ds}) \tau_{25s} + G_{ds} G_{ro} \tau_{271} + \\
& + G_{cr} G_{cs} \tau_{33} + \frac{1}{2} G_{cr} G'_{sl} \tau_{34} + (G_{cr} G_{rf} + \frac{1}{2} G_{rdp} G_{cs}) \tau_{35s} + G_{rdp} G'_{sl} \tau_{45s} + \\
& + G_{ro} G'_{sl} \tau_{471} + \frac{1}{2} G_{rdp} G_{rf} \tau_{55rp} + \frac{1}{2} G_{ro} G_{rf} \tau_{5s71} \Big)
\end{aligned} \tag{11}
$$

again by taking into account refocused gradient pairs the expression simplifies to:

$$
\begin{aligned}
b_{rs} = b_{sr} = \gamma^2 \Big(& (G_{dr} G_{cs} + G_{cr} G_{ds}) \tau_{23} + \frac{1}{2} G_{dr} G'_{sl} \tau_{24} + \frac{1}{2} (G_{dr} G_{rf}) \tau_{25s} + G_{cr} G_{cs} \tau_{33} \\
& + \frac{1}{2} G_{cr} G'_{sl} \tau_{34} + \frac{1}{2} G_{cr} G_{rf} \tau_{35s} + \frac{1}{2} G_{rdp} G_{rf} \tau_{55rp} + \frac{1}{2} G_{ro} G_{rf} \tau_{5s71} \Big)
\end{aligned} \tag{12}
$$

and the last term the phase/slice select:

$$\begin{aligned} b_{sp} = b_{ps} = \gamma^2 \Big(& G_{sl}G_{dp}\tau_{12} + G_{sl}G_{cp}\tau_{13} + G_{sl}G_{pdp}\tau_{15rp} + G_{sl}G_{pe}\tau_{16m} + G_{dp}G_{ds}\tau_{22} + \\ & + (G_{ds}G_{cp} + G_{ds}G_{cp})\tau_{23} + \frac{1}{2}G_{dp}G'_{sl}\tau_{24} + (\frac{1}{2}G_{dp}G_{rf}\tau_{25s} + G_{ds}G_{pdp}\tau_{25rp}) + G_{pe}G_{ds}\tau_{26m} + \\ & + G_{cp}G_{cs}\tau_{33} + \frac{1}{2}G_{cp}G'_{sl}\tau_{34} + (\frac{1}{2}G_{cp}G_{rf} + G_{pdp}G_{cs})\tau_{35s} + G_{pe}G_{cs}\tau_{36m} + G_{pdp}G'_{sl}\tau_{45s} + \\ & + G_{pe}G'_{sl}\tau_{46m} + \frac{1}{2}G_{pdp}G_{rf}\tau_{55rp} + \frac{1}{2}G_{pe}G_{rf}\tau_{5s6m} \Big) \end{aligned} \tag{13}$$

with refocused gradient pairs gives final expression:

$$\begin{aligned} b_{sp} = b_{ps} = \gamma^2 \Big(& G_{dp}G_{ds}\tau_{22} + (G_{ds}G_{cp} + G_{dp}G_{cs})\tau_{23} + \frac{1}{2}G_{dp}G'_{sl}\tau_{24} + \frac{1}{2}G_{dp}G_{rf}\tau_{25s} + G_{cp}G_{cs}\tau_{33} + \\ & + \frac{1}{2}G_{cp}G'_{sl}\tau_{34} + \frac{1}{2}G_{cp}G_{rf}\tau_{35s} + \frac{1}{2}G_{pdp}G_{rf}\tau_{55rp} + \frac{1}{2}G_{pe}G_{rf}\tau_{5s6m} \Big) \end{aligned} \tag{14}$$

6 Timing multipliers

$$\tau_{11} = \delta_1^3 \tag{15}$$

$$\tau_{22} = \delta_2^2 \left(\Delta_2 - \frac{1}{3}\delta_2 \right) + \frac{1}{30}\epsilon_2^3 - \frac{1}{6}\delta_2\epsilon_2^2, \qquad \Delta_2 = t_{22} - t_{21} \tag{16}$$

$$\tau_{23} = \delta_2\delta_3\Delta_3, \qquad \Delta_3 = t_{32} - t_{31} \tag{17}$$

$$\tau_{24} = \delta_2\delta_4\Delta_4, \qquad \Delta_4 = t_{42} - t_{41} \tag{18}$$

$$\tau_{25rp} = \frac{1}{2}\delta_{5rp}\delta_2\Delta_2, \qquad \Delta_2 = t_{22} - t_{21} \tag{19}$$

$$\tau_{25s} = \frac{1}{2}\delta_{5s}\delta_2\Delta_2, \qquad \Delta_2 = t_{22} - t_{21} \tag{20}$$

$$\tau_{33} = \delta_3^2 \left(\Delta_3 - \frac{1}{3}\delta_3 \right) + \frac{1}{30}\epsilon_3^3 - \frac{1}{6}\delta_3\epsilon_3^2, \qquad \Delta_3 = t_{32} - t_{31} \tag{21}$$

$$\tau_{34} = \delta_3\delta_4\Delta_4, \qquad \Delta_4 = t_{42} - t_{41} \tag{22}$$

$$\tau_{35rp} = \frac{1}{2}\delta_{5rp}\delta_3\Delta_3, \qquad \Delta_3 = t_{32} - t_{31} \tag{23}$$

$$\tau_{35s} = \frac{1}{2}\delta_{5s}\delta_3\Delta_3, \qquad \Delta_3 = t_{32} - t_{31} \tag{24}$$

$$\tau_{44} = \delta_4^2 \left(\Delta_4 - \frac{1}{3}\delta_4 \right) + \frac{1}{30}\epsilon_4^3 - \frac{1}{6}\delta_4\epsilon_4^2, \qquad \Delta_4 = t_{42} - t_{41} \tag{25}$$

$$\tau_{45rp} = \frac{1}{2}\delta_{5rp}\delta_4\Delta_4, \qquad \Delta_4 = t_{42} - t_{41} \tag{26}$$

$$\tau_{45s} = \frac{1}{2}\delta_{5s}\delta_4\Delta_4, \qquad \Delta_4 = t_{42} - t_{41} \tag{27}$$

$$\tau_{55rp} = \delta_{5rp}^2 \left(\Delta_{5rp} - \frac{1}{3}\delta_{5rp} \right) + \frac{1}{30}\epsilon_{5rp}^3 - \frac{1}{6}\delta_{5rp}\epsilon_{5rp}^2, \qquad \Delta_{5rp} = \mathrm{TE} - t_{5rp} \tag{28}$$

$$\tau_{55s} = \delta_{5s}^2\left(\Delta_{5s} - \frac{1}{3}\delta_{5s}\right) + \frac{1}{30}\epsilon_{5s}^3 - \frac{1}{6}\delta_{5s}\epsilon_{5s}^2, \qquad \Delta_{5s} = \mathrm{TE} - t_{5s} \tag{29}$$

$$\tau_{5rp6m} = \epsilon_{5rp}\delta_{5rp}\sum_{m=1}^{\mathrm{res}/2}\left(\Delta_{6m} - \epsilon_6\right), \qquad \Delta_{6m} = \mathrm{TE} - t_{6i} \tag{30}$$

$$\tau_{5s6m} = -\epsilon_{5s}\delta_{rf}\sum_{m=1}^{\mathrm{res}/2}\left(\Delta_{6m} - \epsilon_6\right), \qquad \Delta_{6m} = \mathrm{TE} - t_{6i} \tag{31}$$

$$\tau_{5rp71} = \delta_5\left[\delta_7\left(\Delta_{75} - \frac{1}{4}\delta_7\right) + \frac{1}{12}\epsilon_7^2 - \frac{1}{2}\delta_7\epsilon_7\right], \qquad \Delta_{75} = \Delta_{71} = \mathrm{TE} - t_{71} \tag{32}$$

$$\tau_{5s71} = \delta_5\left[\delta_7\left(\Delta_{75} - \frac{1}{4}\delta_7\right) + \frac{1}{12}\epsilon_7^2 - \frac{1}{2}\delta_7\epsilon_7\right], \qquad \Delta_{75} = \Delta_{71} = \mathrm{TE} - t_{71} \tag{33}$$

$$\tau_{6m6m} = \epsilon_6^2\sum_{m=1}^{\mathrm{res}/2}\left[(2m-1)\Delta_{6m} - (m\frac{67}{30} - 1)\epsilon_6\right], \qquad \Delta_{6m} = \mathrm{TE} - t_{6i} \tag{34}$$

$$\tau_{6m71} = \frac{1}{4}\epsilon_6\left(\delta_7\Delta_{71} - \frac{1}{60}\epsilon_7^2\right), \qquad \Delta_{71} = \Delta_{75} = \mathrm{TE} - t_{71} \tag{35}$$

$$\tau_{7171} = \frac{1}{4}\left[\delta_7^2\left(\Delta_{71} - \frac{1}{3}\delta_7\right) + \frac{1}{30}\epsilon_7^3 - \frac{1}{2}\delta_7^2\epsilon_7\right], \qquad \Delta_{71} = \Delta_{75} = \mathrm{TE} - t_{71} \tag{36}$$

$$\tau_{7m7(m+1)} = \left(\frac{\mathrm{res}}{2} - 1\right)\left[\frac{1}{12}\delta_7^3 + \frac{1}{60}\epsilon_7^3 + \frac{1}{4}\delta_7^2\epsilon_7 - \frac{1}{12}\delta_7\epsilon_7^2\right], \qquad \mathrm{res} = 34 \tag{37}$$

Extraction of the timing parameters and gradients from the recorded gradient waveform as well as further calculations of b-matrix were implemented in MATLAB (version R2019b. The MathWorks Inc., Natick, MA) and are publicly available[1].

Microstructure parameters from RPBM

D_0 is a parameter fixed to $D_{\|}$ (average over the values from the long diffusion times).

Directly derived from the fit:

τ	characteristic time scale
ζ	volume fraction

The rest were calculated following [2]:

$$l = \sqrt{D_0 \tau} \qquad \text{diffusion length (effective thickness)} \tag{38}$$

$$\kappa = D_0/2l = \frac{1}{2}\sqrt{\frac{D_0}{\tau}} \qquad \text{permeability (as given by [3])} \tag{39}$$

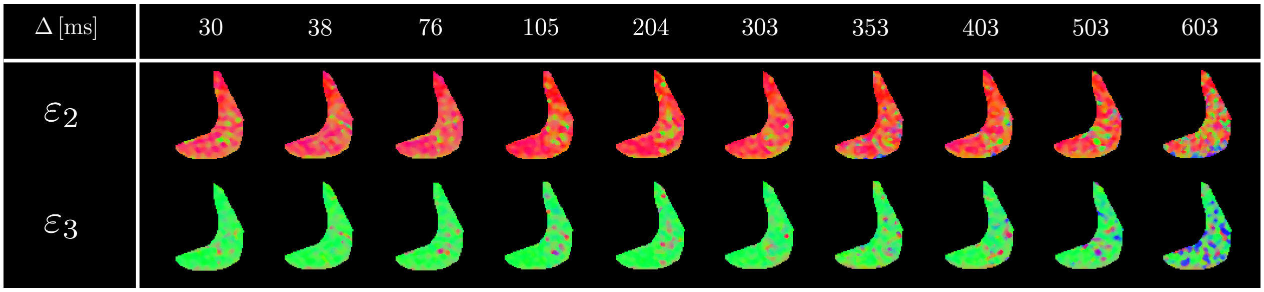
$$S/V = 2\zeta/l = \frac{2\zeta}{\sqrt{D_0 \tau}} \qquad \text{surface to volume ratio} \tag{40}$$

$$a = \beta \frac{V}{S} = \beta \frac{\sqrt{D_0 \tau}}{\zeta} \qquad \text{fiber diameter} \tag{41}$$

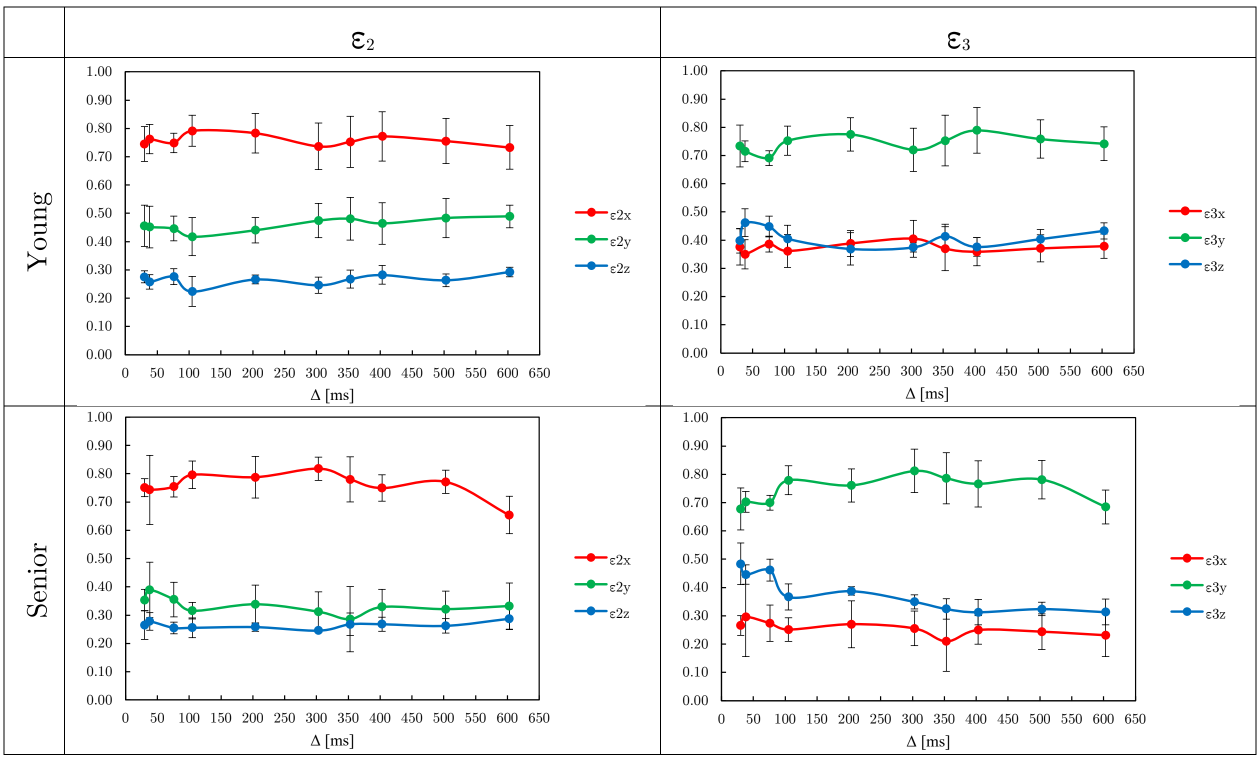
$$\tau_D = a^2/2D_0 = \frac{\beta^2 \tau}{2\zeta^2} \qquad \text{diffusion time} \tag{42}$$

$$\tau_R = a/2\kappa = \frac{\beta \tau}{2\zeta} \qquad \text{residence time} \tag{43}$$

Secondary (ε_2) and tertiary (ε_3) eigenvectors



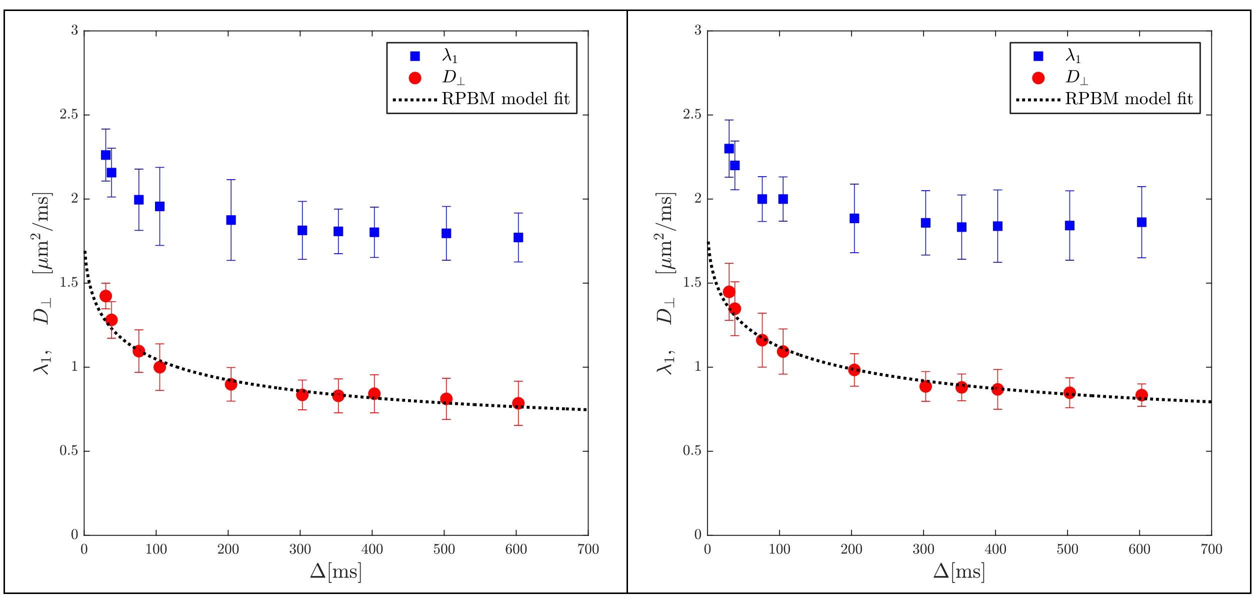
Supporting Figure 3: An example secondary (ε_2) and tertiary (ε_3) eigenvectors colormaps of medial gastrocnemius muscle for one of the volunteers.



Supporting Figure 4: Plots of diffusion-time dependent average secondary (ε_2) and tertiary (ε_3) eigenvectors projections (absolute value) for young and senior subjects.

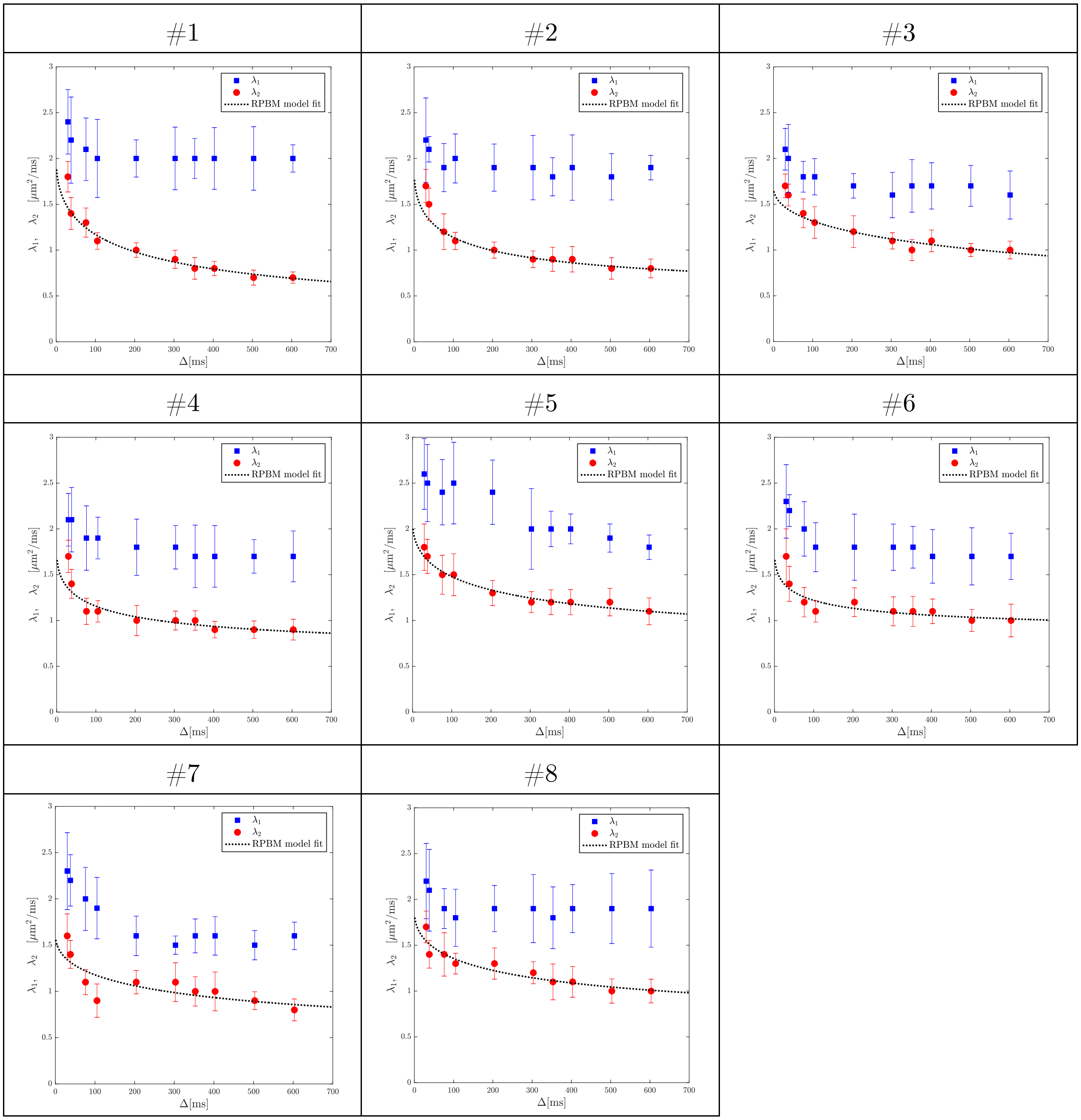
Supporting Table 1: RPBM model fit parameters of tissue microstructure for young and senior participants.

	Young	Senior
D_0 [µm^2/ms] free diffusion	1.83 ± 0.16	1.88 ± 0.18
ζ volume fraction	3.15 ± 1.78	2.86 ± 0.66
S/V [µm^{-1}] surface to volume ratio	0.16 ± 0.03	0.14 ± 0.02
κ [µm/ms] permeability	0.027 ± 0.008	0.024 ± 0.006
a [µm] myofiber diameter	40.71 ± 7.44	45.55 ± 5.33
l [µm] effective thickness	39.59 ± 18.72	41.34 ± 10.46
τ_R [ms] residence time	1389.0 ± 610.0	1601.1 ± 560.1
τ_D [ms] dwell time	1177.3 ± 211.3	1394.9 ± 259.73

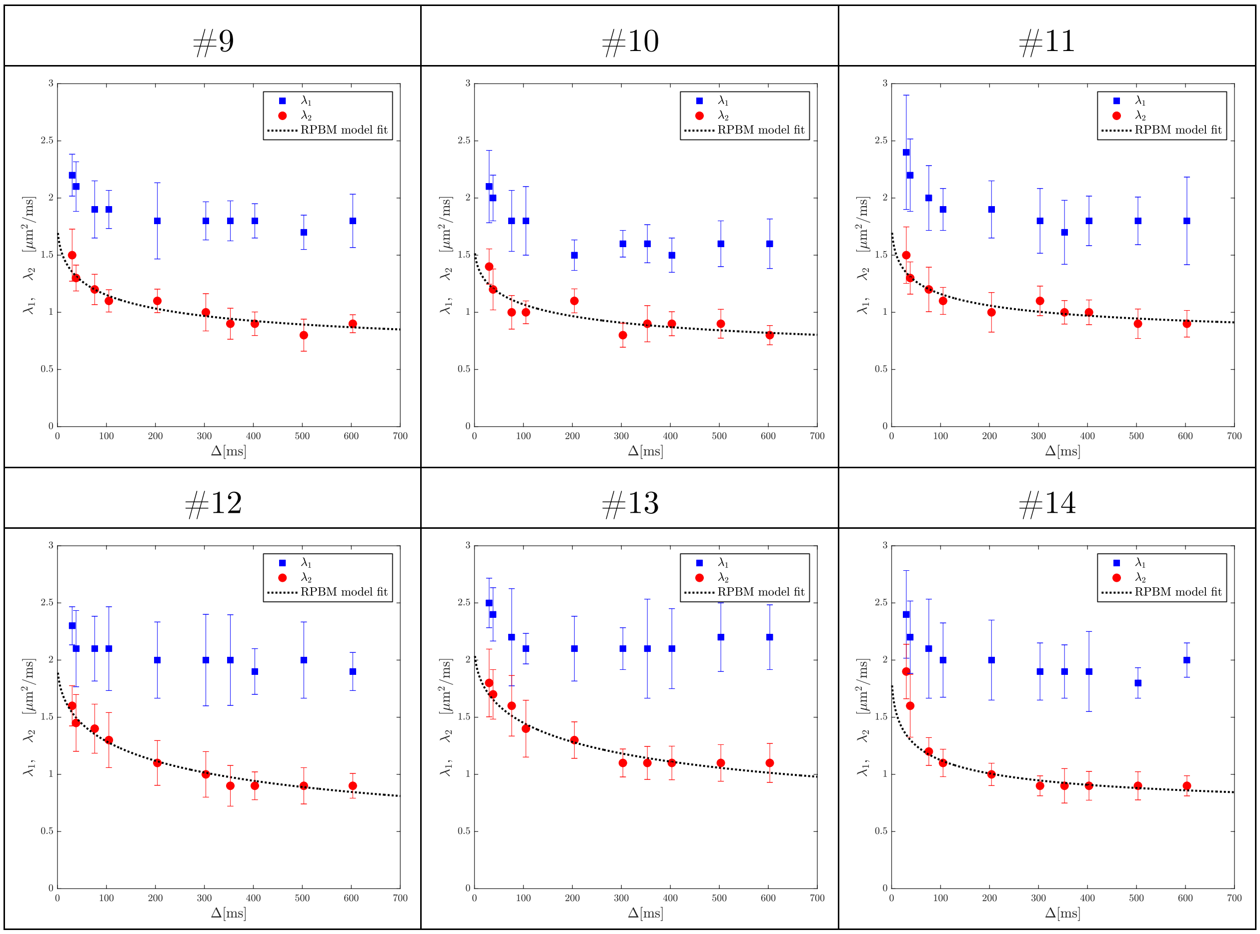


Supporting Figure 5: Average RPBM model fits of $D_\perp(t)$ for the groups of young (a) and senior (b) participants respectively. The points are experimentally determined while the dashed line is the model derived fit. Error bars represent standard deviation of roi-averaged per subject value within the given age group.

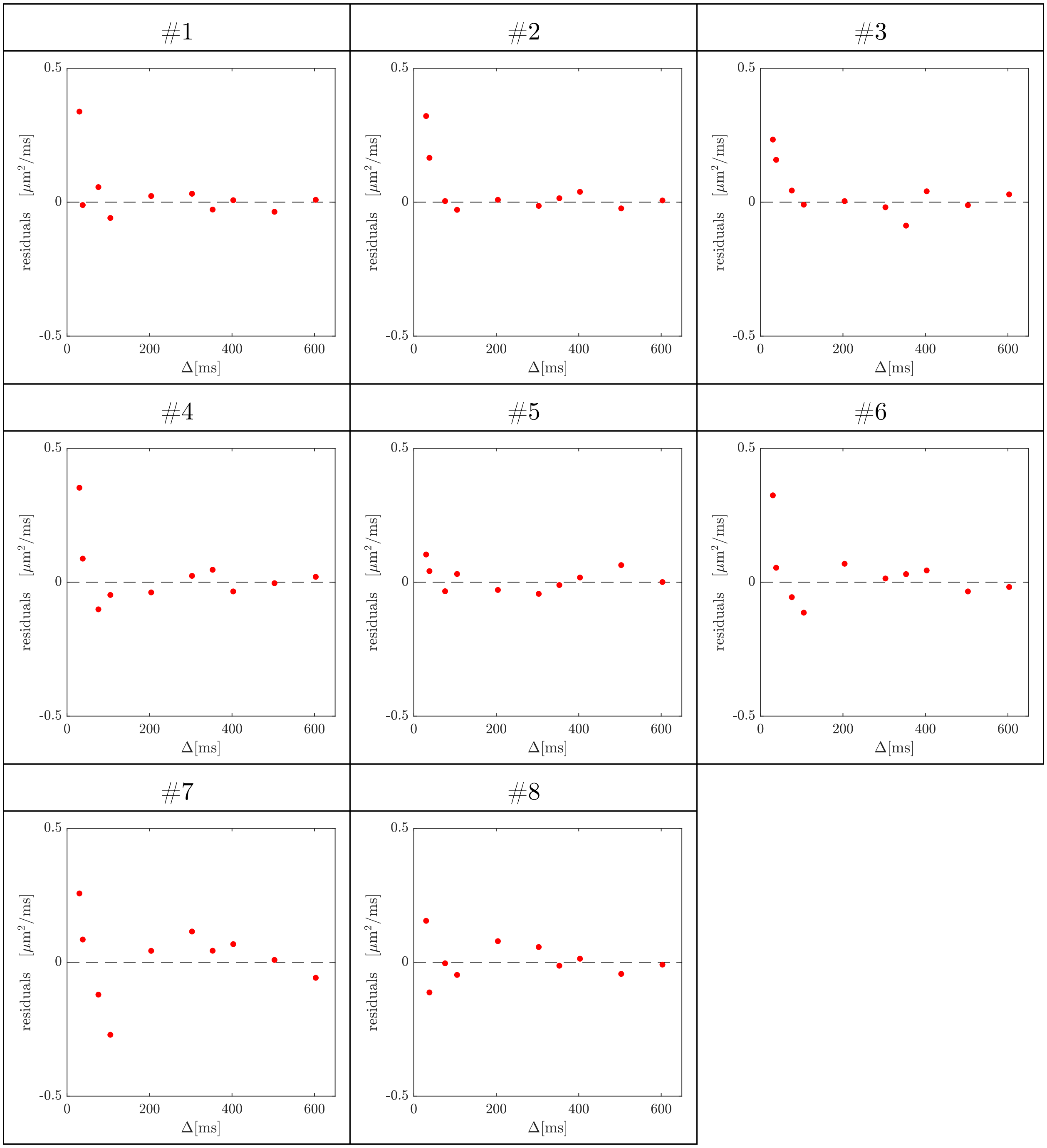
Individual RPBM fits for λ_2



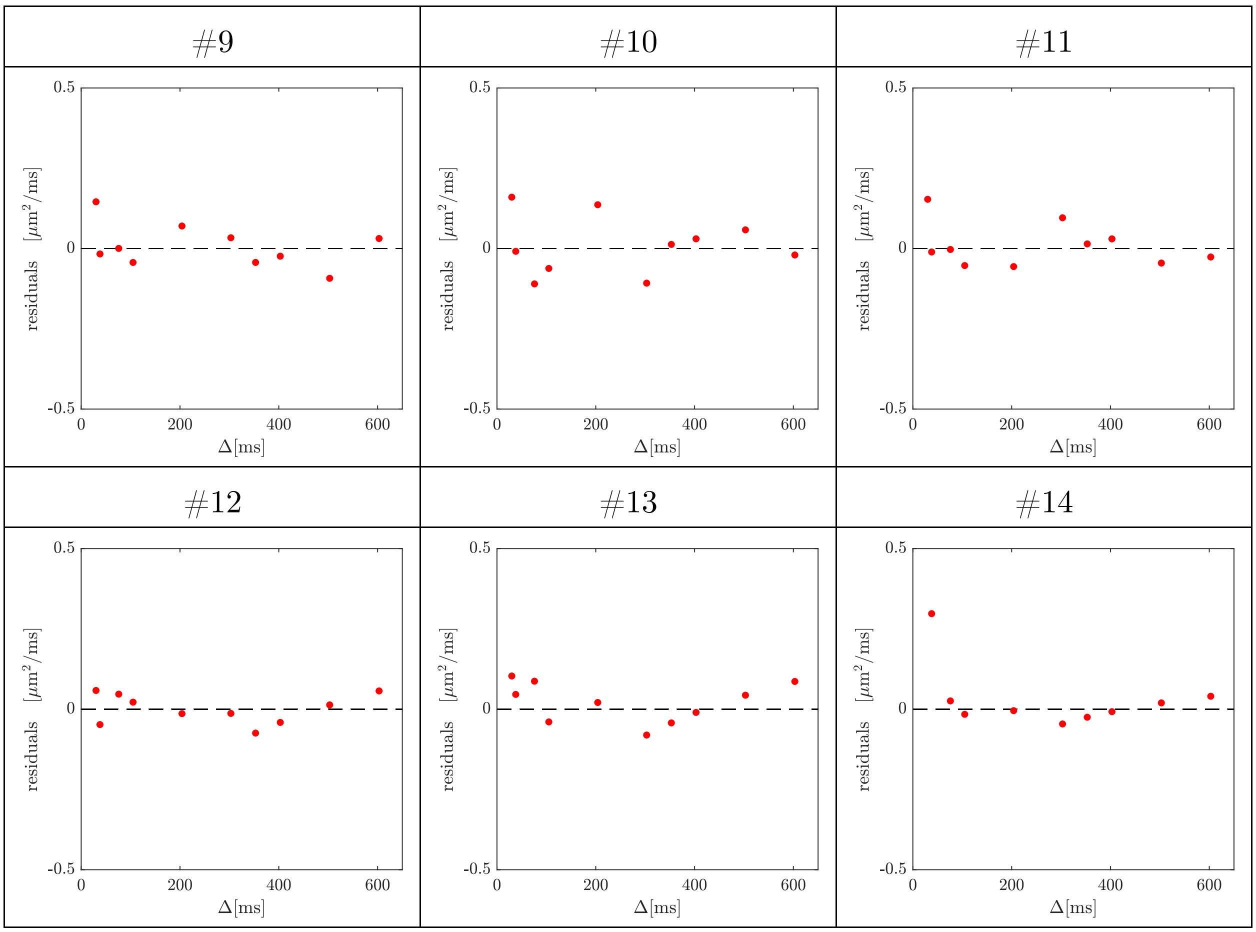
Supporting Figure 6: Individual RPBM fits of all the young participants. Error bars represent standard deviation within the selected region of interest.



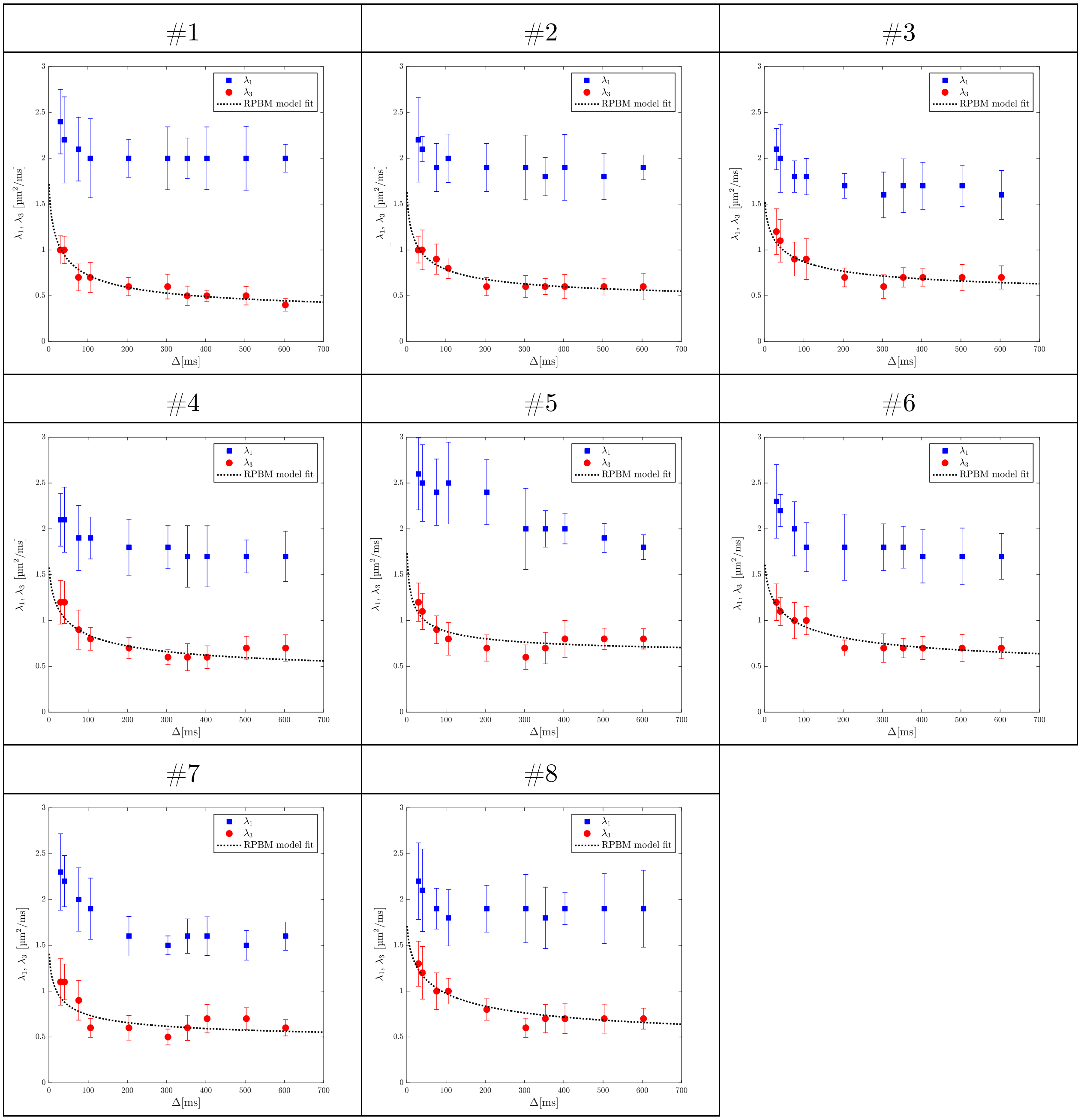
Supporting Figure 7: Individual RPBM fits of all the senior participants. Error bars represent standard deviation within the selected region of interest.



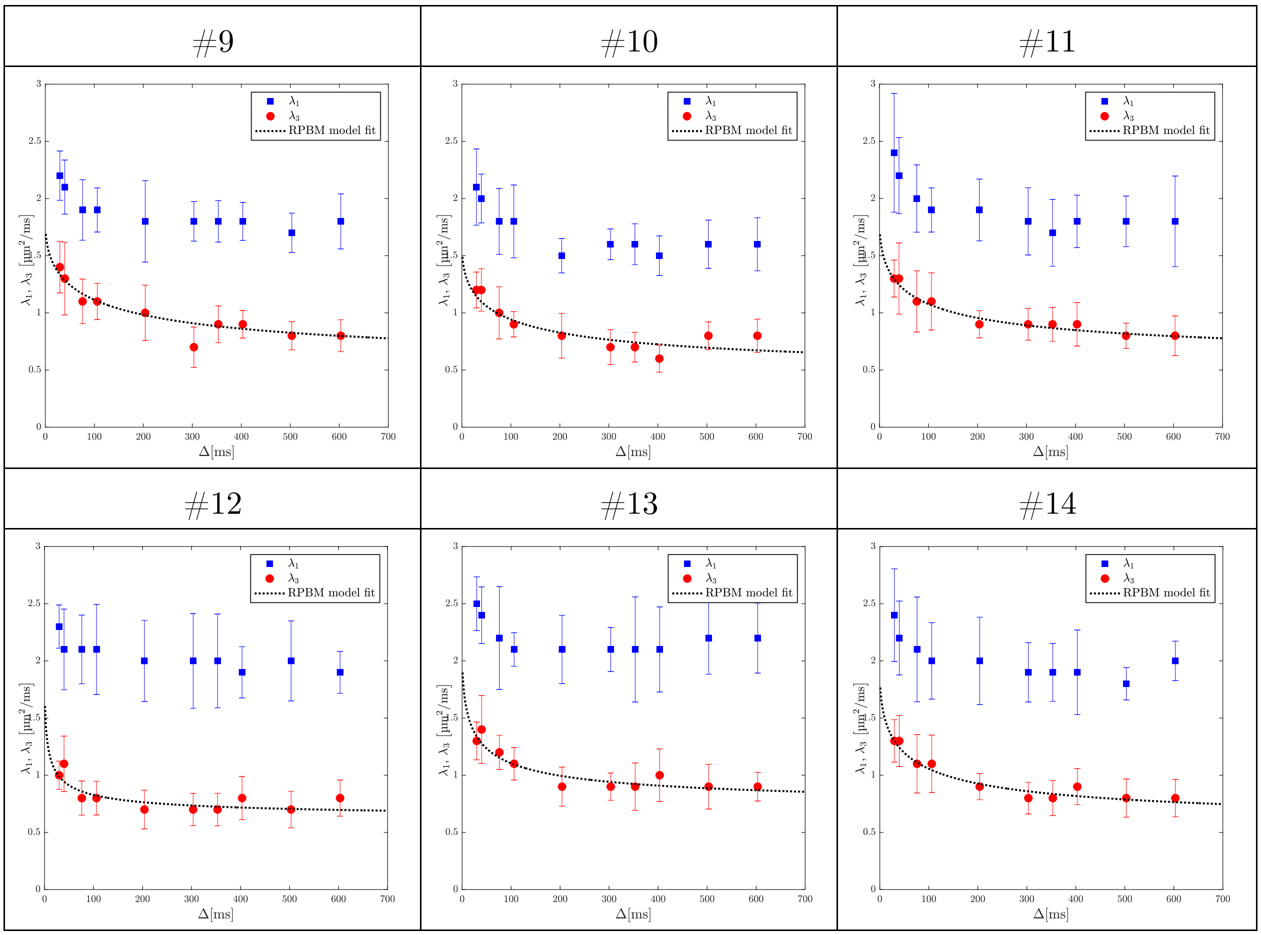
Supporting Figure 8: Individual RPBM fits residuals of all the young participants. The dashed line represents RPBM fit.



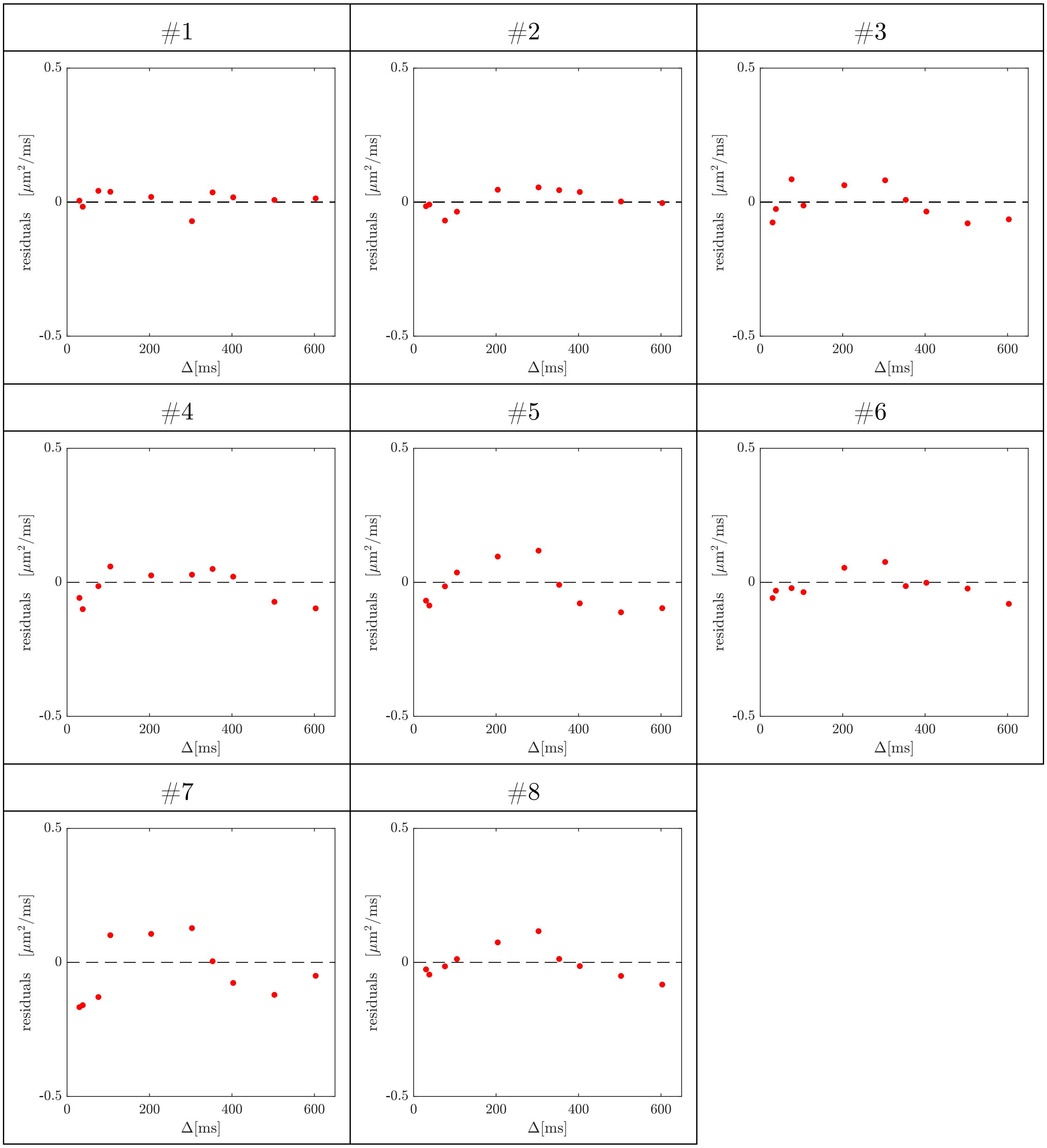
Supporting Figure 9: Individual RPBM fits residuals of all the senior participants. The dashed line represents RPBM fit.



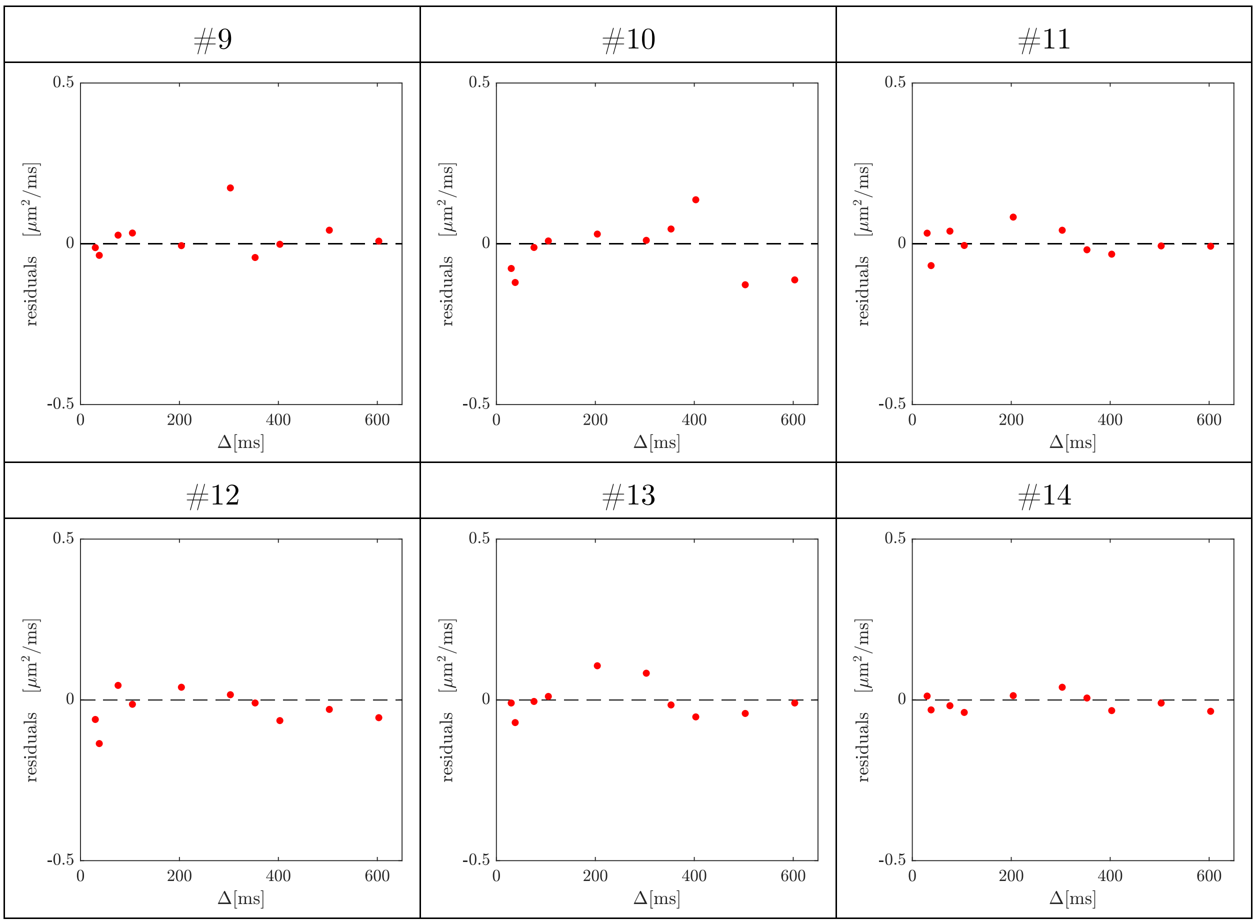
Supporting Figure 10: Individual RPBM fits of all the young participants. Error bars represent standard deviation within the selected region of interest.



Supporting Figure 11: Individual RPBM fits of all the senior participants. Error bars represent standard deviation within the selected region of interest.



Supporting Figure 12: Individual RPBM fits residuals of all the young participants. The dashed line represents RPBM fit.



Supporting Figure 13: Individual RPBM fits residuals of all the senior participants. The dashed line represents RPBM fit.

References

[1] Vadim Malis. *vmalis/bMatrix: with sample gradients wavefroms*. Version 1.01. July 2021. DOI: 10.5281/zenodo.5150023. URL: https://doi.org/10.5281/zenodo.5150023.

[2] Els Fieremans et al. "In vivo measurement of membrane permeability and myofiber size in human muscle using time-dependent diffusion tensor imaging and the random permeable barrier model". In: *NMR in Biomedicine* 30.3 (2017), e3612. DOI: https://doi.org/10.1002/nbm.3612.

[3] Bruno J. Zwolinski, Henry Eyring, and Cecil E. Reese. "Diffusion and Membrane Permeability." In: *The Journal of Physical and Colloid Chemistry* 53.9 (1949), pp. 1426–1453. DOI: 10.1021/j150474a012.