ANISOTROPIC CEREBRAL VASCULATURE CAUSES ORIENTATION DEPENDENCY IN MR SIGNAL

Simulation in the Human Brain

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Declaration of Financial Interests or Relationships

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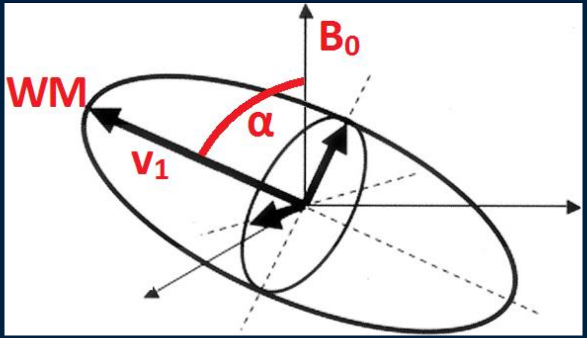
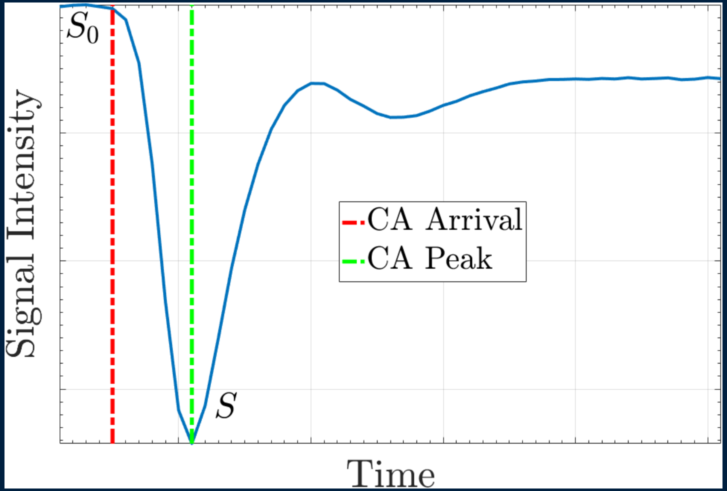
I have no financial interests or relationships to disclose with regard to the subject matter of this presentation.

INTRODUCTION AND MOTIVATION

- Subject Data
  - DTI and Spin Echo DSC scans obtained for 19 healthy subjects
  - WM Fibre orientation angle α determined from DTI data, correlated with change in R_2 with and without CA
  - Change in decay rate ΔR_2 at points S_0 and S can be calculated via:

$$\Delta \mathrm{R}_2 = -\frac{1}{TE}\ln\left(\frac{S}{S_0}\right)$$



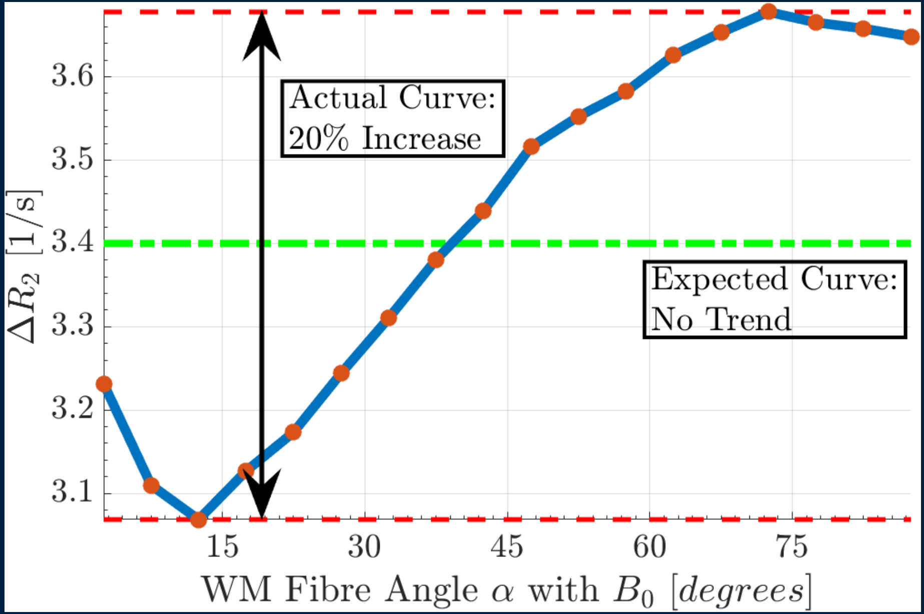


CA: Contrast Agent

INTRODUCTION AND MOTIVATION

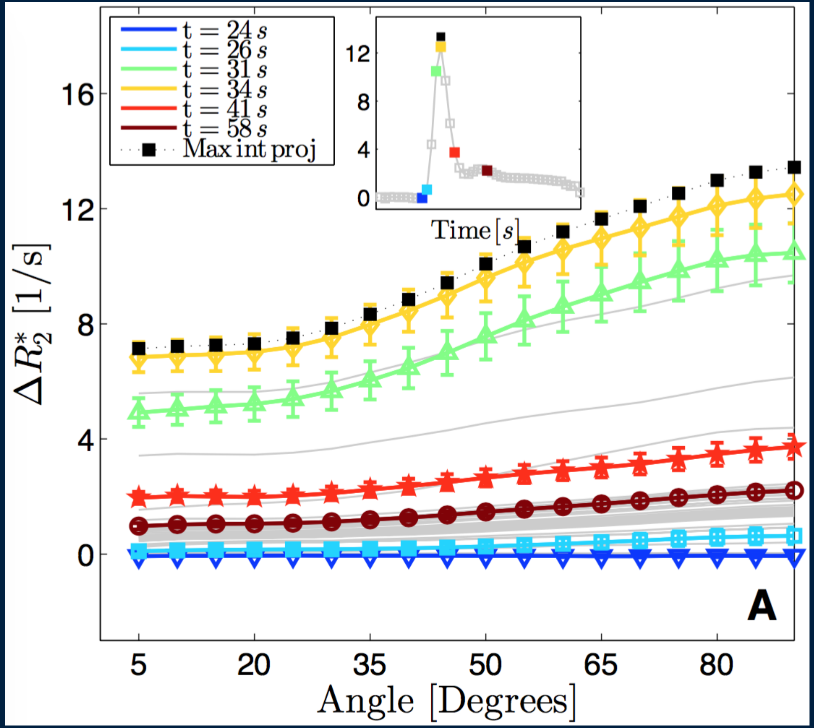
- Expected Spin Echo DSC Signal:
    - SE spins should be refocused by TE
    - Decay should be due <u>only</u> to local (CA dependent) R_2-value
    - Decoherence should be negligible

- Actual Spin Echo DSC Signal:
    - There is extra signal decay!
    - Even more peculiar: <u>**extra decay depends on the local fibre orientation**</u>



INTRODUCTION AND MOTIVATION

- Comparison with Gradient Echo DSC case:
  - Our previous study* showed that orientation dependency is strong in GRE-DSC
- This is *expected* for GRE-DSC
  - For larger angles, the extravascular inhomogeneities occupy larger volume fractions of a voxel
- We now aim to explain why this same effect is present in SE-DSC



*Hernandez-Torres, et al. *JCBFM* (2016)

THE BLOCH EQUATIONS FOR SE-DSC WITH INHOMOGENEITIES

- We start by considering the Bloch Equations:

$$\frac{d\vec{M}}{dt} = \gamma \vec{M} \times \vec{B} - \left(\frac{M_x}{T_2}, \frac{M_y}{T_2}, \frac{M_z}{T_1}\right)$$

- In a rotating frame with constant $\vec{B} = B_0\hat{z}$ and $T_2 \ll T_1$, we have:

$$\frac{d\widetilde{M}_{xy}}{dt} = -\frac{1}{T_2}\widetilde{M}_{xy}$$

- Where we define the <u>complex magnetization:</u>

$$\widetilde{M}_{xy} \coloneqq M_x + iM_y$$

THE BLOCH EQUATIONS FOR SE-DSC WITH INHOMOGENEITIES

- We can add induced field inhomogeneities through incorporating susceptibility changes $\delta\chi$ and using the unit dipole kernel $G(\vec{r})$:

$$\delta\omega(\vec{r}) = \gamma B_0 \cdot (G(\vec{r}) * \delta\chi(\vec{r}))$$

- The resulting differential equation and solution are then:

$$\frac{d\widetilde{M}_{xy}}{dt} = -\big(R_2(\vec{r}) + i\delta\omega(\vec{r})\big) \cdot \widetilde{M}_{xy}$$

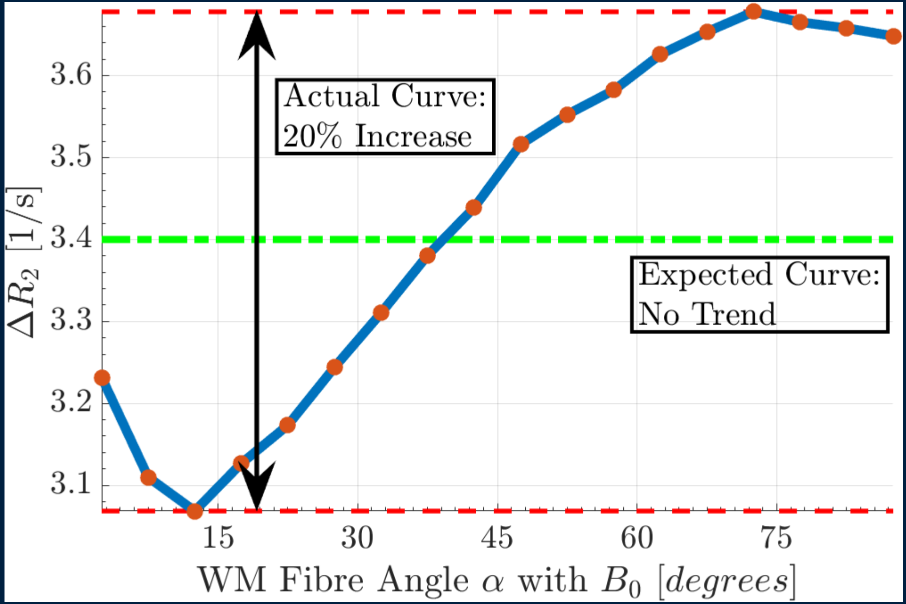
$$\Rightarrow \widetilde{\boldsymbol{M}}_{\boldsymbol{xy}}(\vec{\boldsymbol{r}}, \boldsymbol{t}) = \widetilde{\boldsymbol{M}}_{\boldsymbol{xy}}(\vec{\boldsymbol{r}}, \boldsymbol{0})\boldsymbol{e}^{-(R_2 + i\delta\omega)\boldsymbol{t}}$$

THE BLOCH EQUATIONS FOR SE-DSC WITH INHOMOGENEITIES

- However, this solution can only produce the Expected Curve, not the Actual Curve

- This is because this solution completely refocuses by time TE (as it should for SE!):

$$\widetilde{M}_{xy}(\vec{r}, TE) = \overline{\widetilde{M}_{xy}(\vec{r}, 0)}\, e^{-R_2 \cdot TE}$$



THE BLOCH-TORREY EQUATION FOR SE-DSC

- Remedying this model
  - So far, we have implicitly assumed that all spins are stationary
  - If spins are allowed to move, they will see different local inhomogeneities and will not perfectly rephase – there will be extra decay

- We add diffusion to the equation:

$$\frac{dM}{dt} = D \cdot \nabla^2 M - (R_2 + i\delta\omega) \cdot M$$

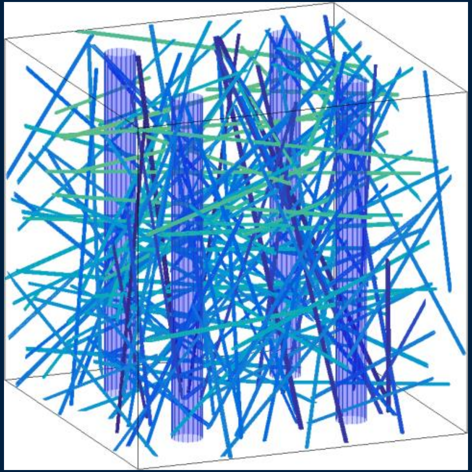
- Where ∇^2 is the 3D Laplacian operator. This is the so-called Bloch-Torrey equation, and has no closed form solution and must be solved numerically

GEOMETRY OF THE SE-DSC PROBLEM

- Now, we consider the geometry of the problem within a single voxel

- The geometry is simulated as follows:
  - Create an isotropic vascular bed of small vessels
  - Add anisotropic large vessels to simulate large vasculature running in parallel to WM tracks*

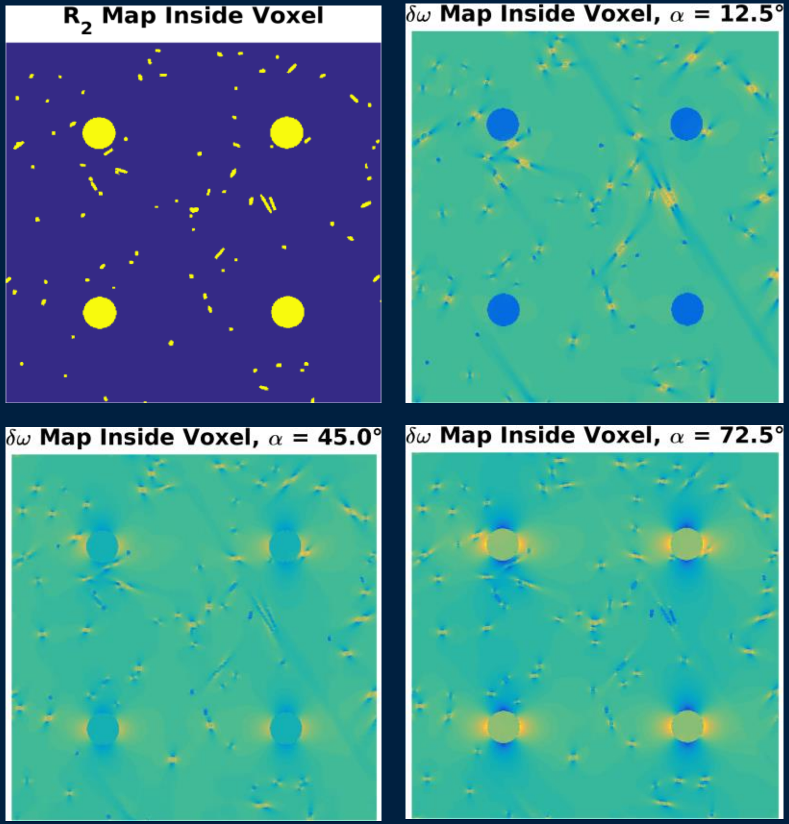
- These large vessels introduce the possibility of angular dependence



*Okudera, et al. *Neuropathology* (1999)

GEOMETRY OF THE SE-DSC PROBLEM

- Given the geometry, we now calculate $R_2(\vec{r})$ and $\delta\chi(\vec{r})$:
    - Each are piecewise constant, taking different values in tissue and in blood
    - Value in blood depends on CA
- Choose a WM fibre angle α relative to $\vec{B}_0$
    - This represents the orientation of the whole voxel
- Calculate the *dephasing*:
    - $\delta\omega_\alpha = \gamma B_0 \cdot (G_\alpha * \delta\chi)$



FORMALIZING THE SE-DSC PROBLEM

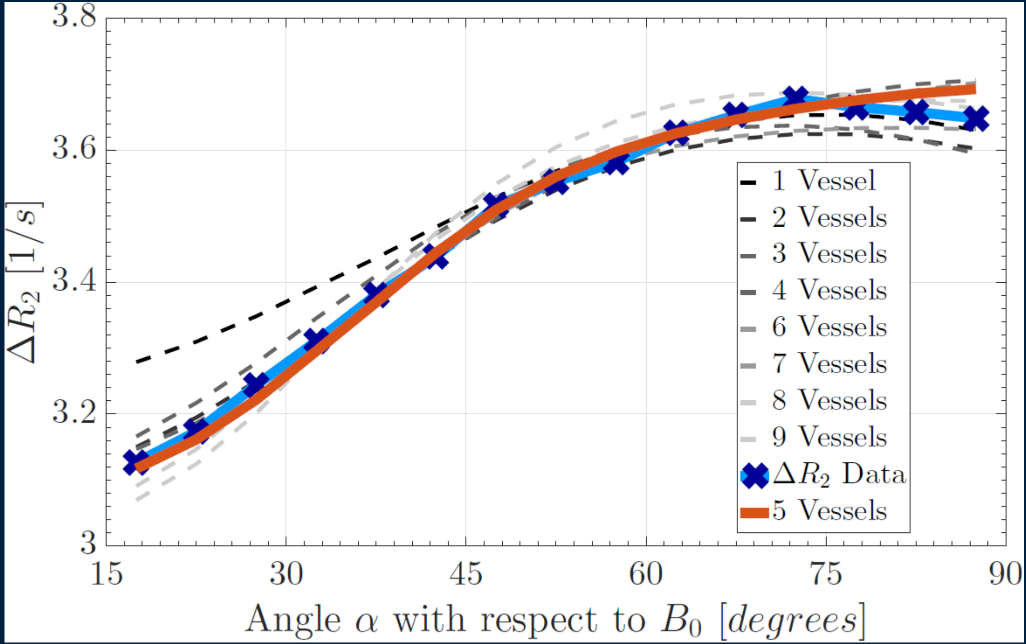
1. ***Initialize***
   - Choose parameters: BVF, iBVF, CA concentration
   - Calculate geometry: $R_2(\vec{r})$ and $\delta\omega_\alpha(\vec{r}) = \gamma B_0 \cdot (G_\alpha * \delta\chi)$
   - Initialize magnetization: $M(\vec{r}, 0) = i$ ($\pi/2$ pulse into xy-plane)
2. ***Propagate***
   - Solve the Bloch-Torrey equation for $M(\vec{r}, TE)$
     - $\frac{dM}{dt} = D \cdot \nabla^2 M - (R_2 + i\delta\omega) \cdot M$
3. ***Sum***
   - The final signal is given by:
     - $S(TE) = \left| \iiint M(\vec{r}, TE) d^3r \right|$

FORMALIZING THE SE-DSC PROBLEM

4. ***Repeat***
   - The simulation is executed for each angle in the range $\{2.5°, 7.5°, \ldots, 87.5°\}$, both **with** and **without** contrast agent
5. ***Fit***
   - Given $S_0(TE)$ and $S(TE)$, calculate $\Delta R_2 = -\frac{1}{TE} \ln S/S_0$ for each angle and compare with observed data
   - If fit is poor, adjust parameters (BVF, iBVF, CA) and go to step 1

SE-DSC SIMULATION RESULTS AND DISCUSSION

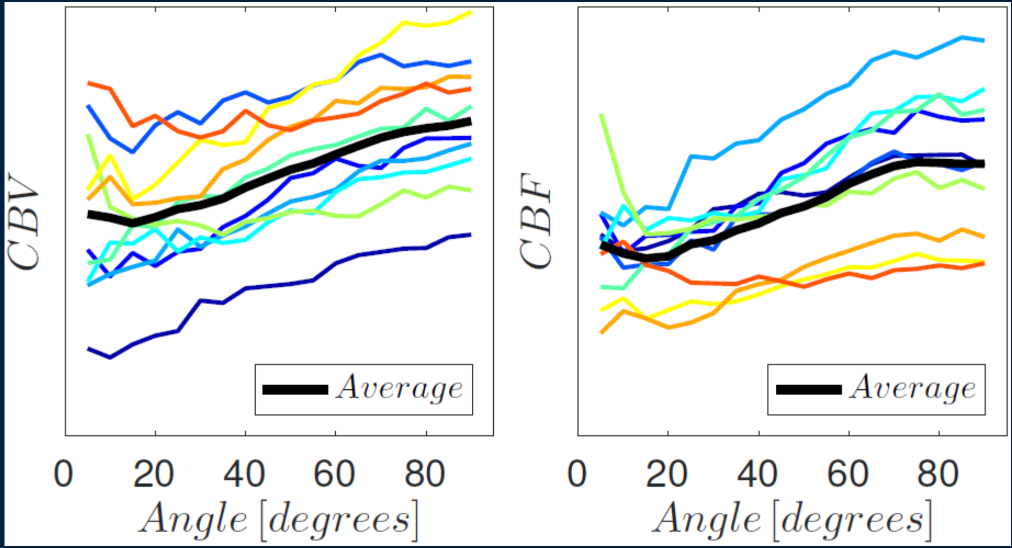
- Simulation matches Actual Curve well
- Simulation was ran for a variable number of large anisotropic vessels
    - Best results occurred for 4-6 anisotropic vessels
    - Corresponding radii of approx. 90 µm, 80 µm, 70 µm
- Resulting Fit Parameters:
    - BVF: 3.49%
    - iBVF: 2.30%
    - CA: 6.23 mM



SE-DSC SIMULATION RESULTS AND DISCUSSION

- Quantities that are derived from R_2 are affected, too!

- Perfusion parameters such as CBV and CBF exhibit orientation dependencies on the order of 20%, similar to R_2



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