# Inferring sizes of compartments using oscillating gradient spin echo magnetic resonance imaging

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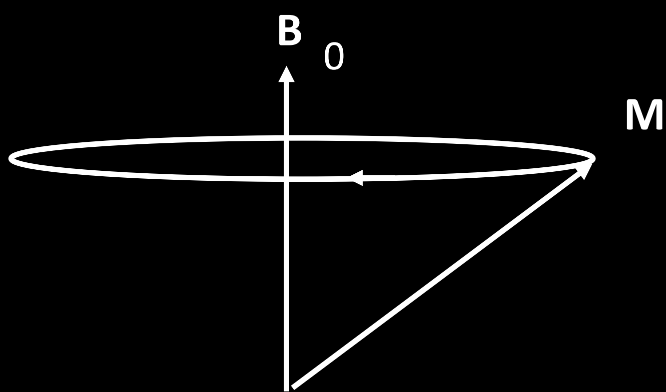
# Outline

- MRI
- Diffusion
- Restricted diffusion
- A model of diffusion to infer cell sizes
- Phantom data
- Simulation data to reduce imaging time

# NMR

$\omega_0 = -\gamma \mathbf{B}_0$

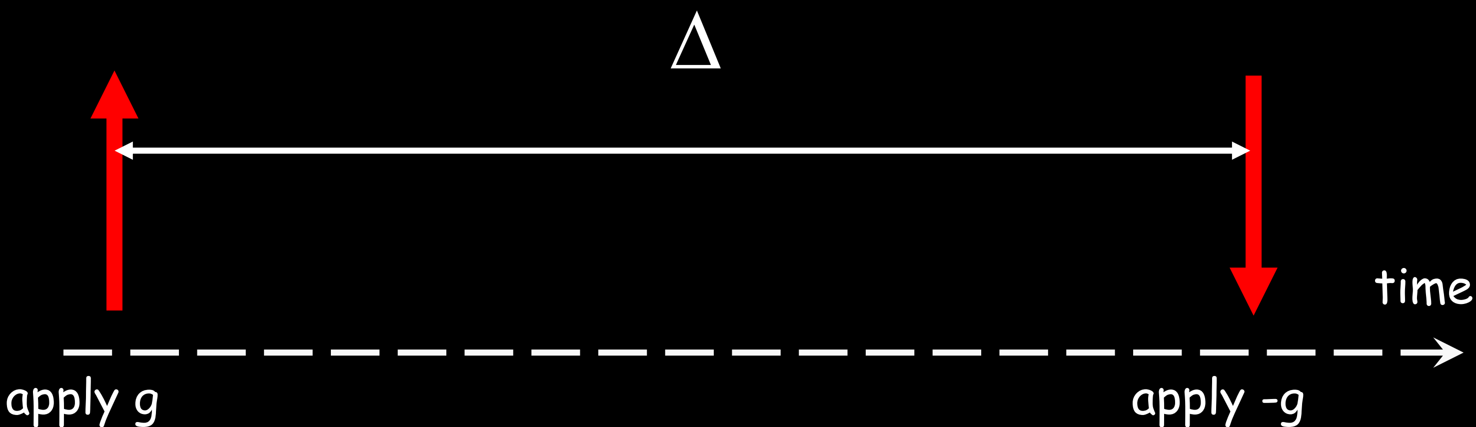



- Nuclear magnetization, **M**, is an ensemble effect
- Angular momentum (spin) means they precess in $\mathbf{B}_0$ field

# Gradients for Measurement of Diffusion

- If the field **B** is uniform then all spins have the same frequency
- If $\mathbf{B} = \mathbf{B}_0 + \boldsymbol{g} \cdot \boldsymbol{x}$ [$\boldsymbol{g}$ = linear gradient] then spins at different positions $x$ have different frequencies ($\Delta\omega = \gamma g x$)
- If spins move along $x$ their NMR frequencies change with time

# Measuring Diffusion Using NMR



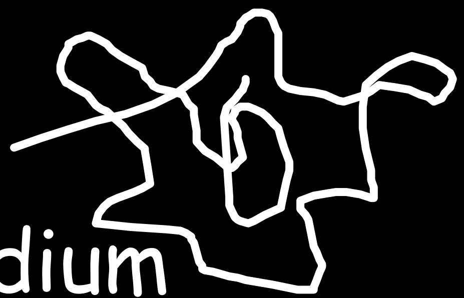

➔ change phase

➔ phase reversal

# Diffusion Coefficient

- Einstein relation

  1D $\langle (x_1 - x_2)^2 \rangle = 2Dt$

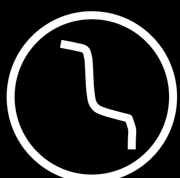


- D is characteristic of medium
- Magnitude of D depends on ease of movement
- $D_{H2O} = 2\ \mu m^2/ms$ at room temperature

# Restricted Diffusion

Diffusion time is $\Delta_{eff}$


- Unrestricted diffusion if $\langle r^2 \rangle \gg 2D_{free}\Delta_{eff}$

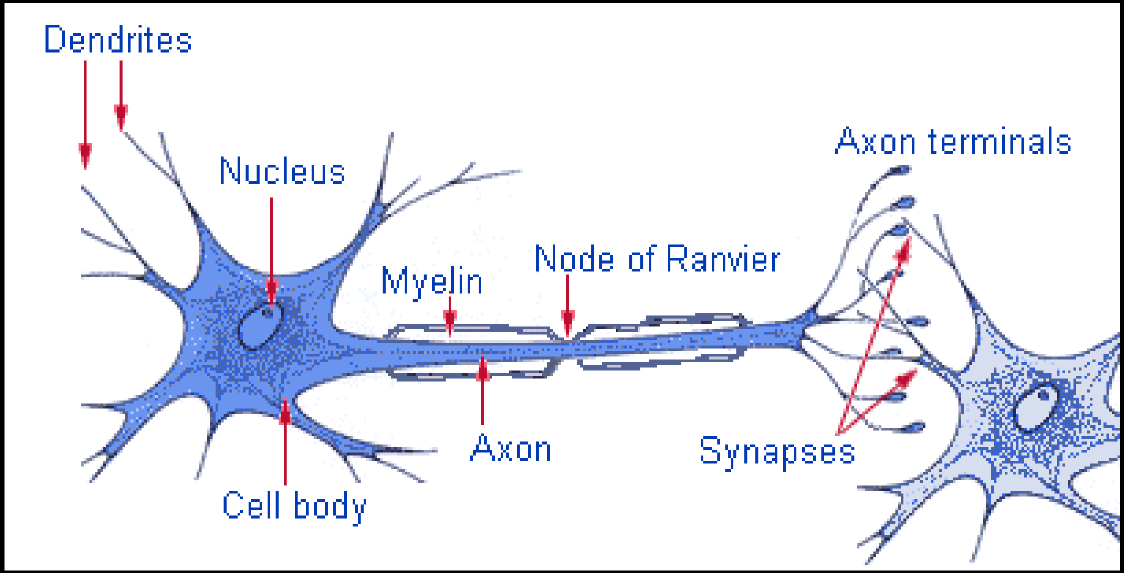


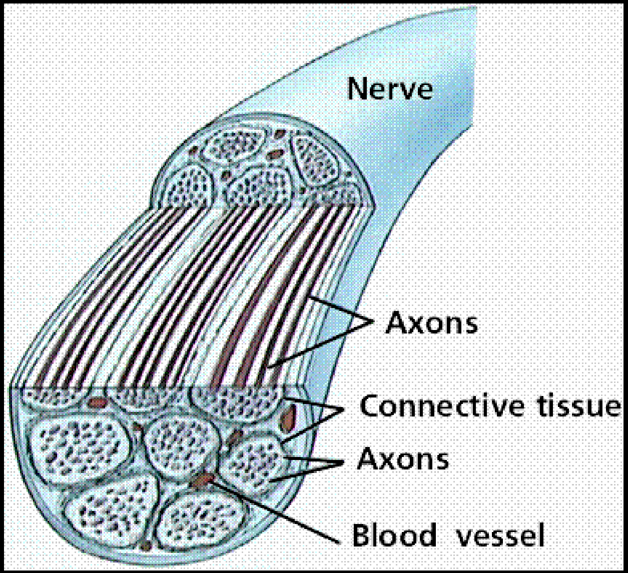
- Hindered diffusion if barriers partially permeable and/or $\langle r^2 \rangle \approx 2D_{free}\Delta_{eff}$

- Restricted diffusion if $\langle r^2 \rangle \ll 2D_{free}\Delta_{eff}$

# Axons

- Part of neurons, or nerve cells in the brain.
- Long, threadlike projections that conduct electrical impulses in nerve cells.
- Transmits information to nerve cells throughout the body.




http://www.biomedresearches.com/root/pages/researches/epilepsy/structure_of_nervous_system.html

# Biological Tissues

- Free water diffuses ≈ 5 μm in 5 ms
- Cells are ≈ 0.1 - 50 μm in size
- Axons in mice are < 1 μm in diameter
- Standard MRI requires ≈ 10 - 100 ms
- Standard MRI cannot measure the transition from restricted to free diffusion
- Standard MRI cannot infer cell sizes

# Measurements at Short $\Delta_{eff}$

- Small displacements → small effects
- Increase sensitivity/accuracy by averaging

or...

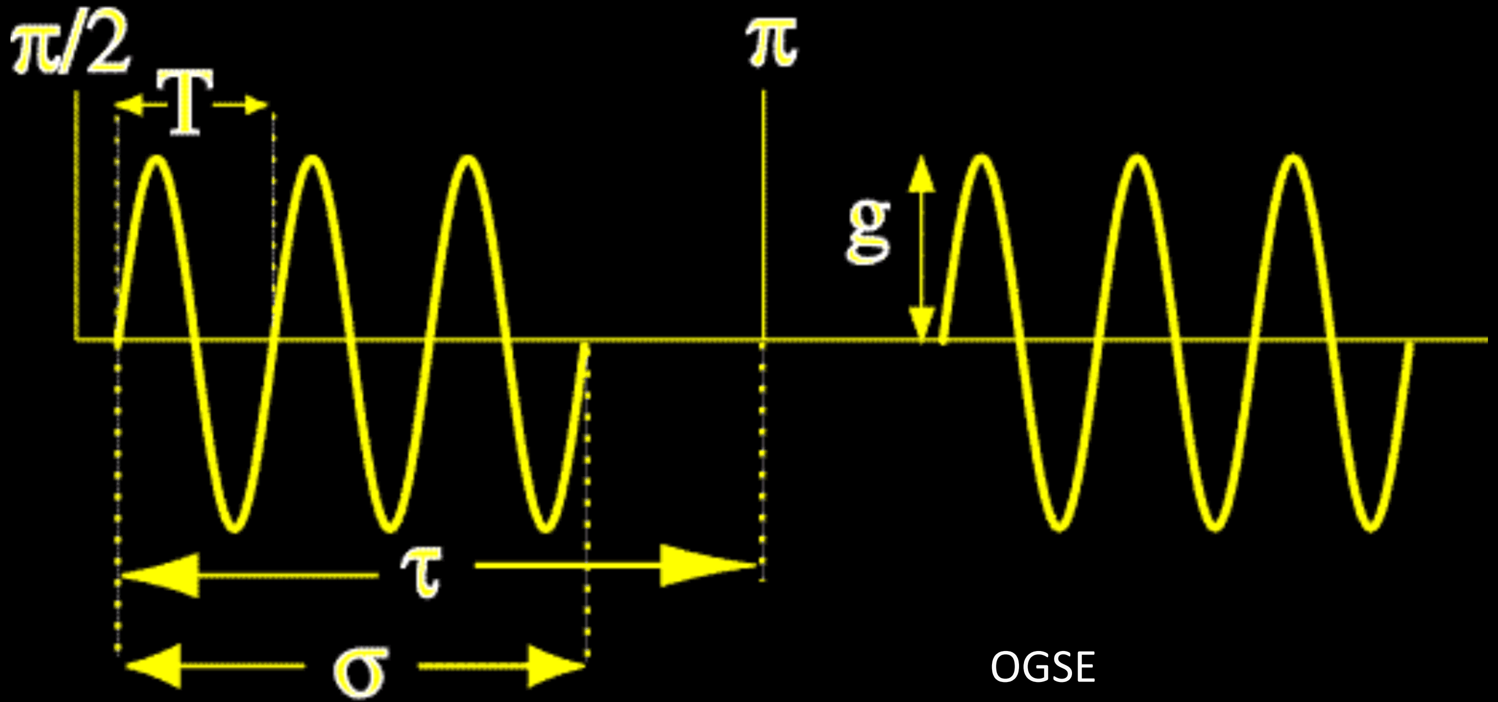
- Increase effect size by using very big g

or...

- Use another method

# Oscillating Gradient Spin Echo Sequence

# OGSE Pulse Sequence




OGSE

Schachter et al, JMR 2000

# Axon diameter distributions (AxCaliber)

- AxCaliber is a model for estimating axon distributions using diffusion MRI
- Model the signal as coming from two compartments:

$$S = (1-f)e^{-bD_h} + f\sum_i \frac{w(r_i,\boldsymbol{\theta})r_i^2 e^{-\beta(r_i,D_i)}}{\sum_k w(r_k,\boldsymbol{\theta})r_k^2}$$

Extracellular signal

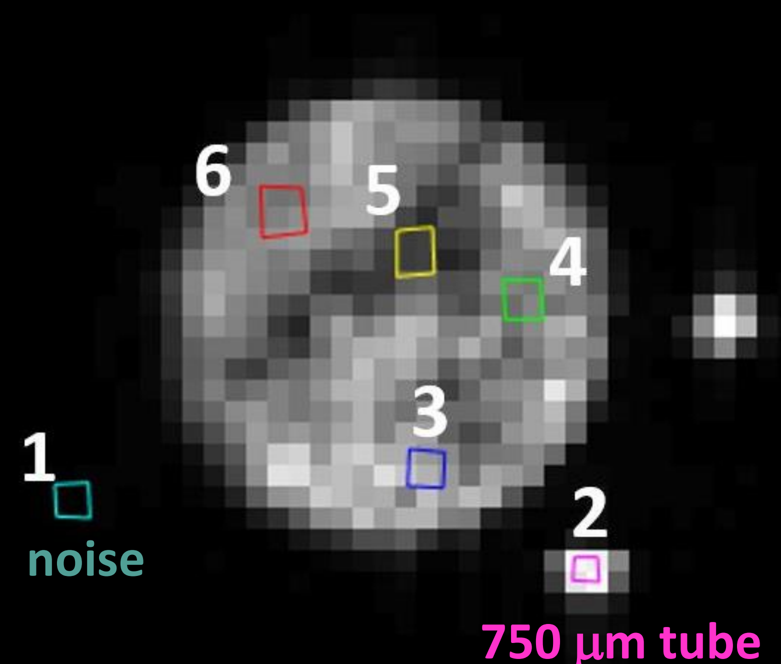
Intracellular signal

  - *f*: volume fraction of intracellular space
  - $D_h$: hindered diffusion coefficient (apparent extracellular diffusion coefficient)
  - $D_i$ : intracellular diffusion coefficient
  - $w(r_i, \theta)$: axon radius distribution (parameterized by $\theta$)
  - $\exp(-\beta(r_i, D_i))$: analytical signal from single cylinder

# Phantom (capillary tubes)

***Capillary tubing*** **(OD ~ 150 μm , ID ~ 2 μm)**

- Soaked in filtered water, packed into centrifuge tubing, ~500 pcs(~2cm)
- Tubing were also filled with water but the volume was not large enough to produce a measurable signal.
- ROIs were created for the noise, within the centrifuge tubing, and a larger capillary tube (ID ~ 750 μm) for comparison.

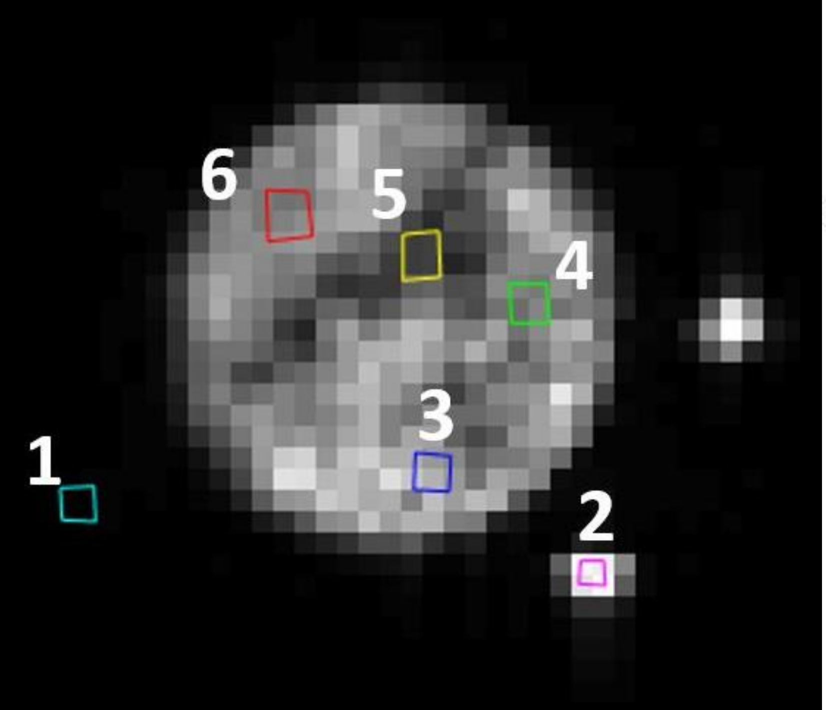


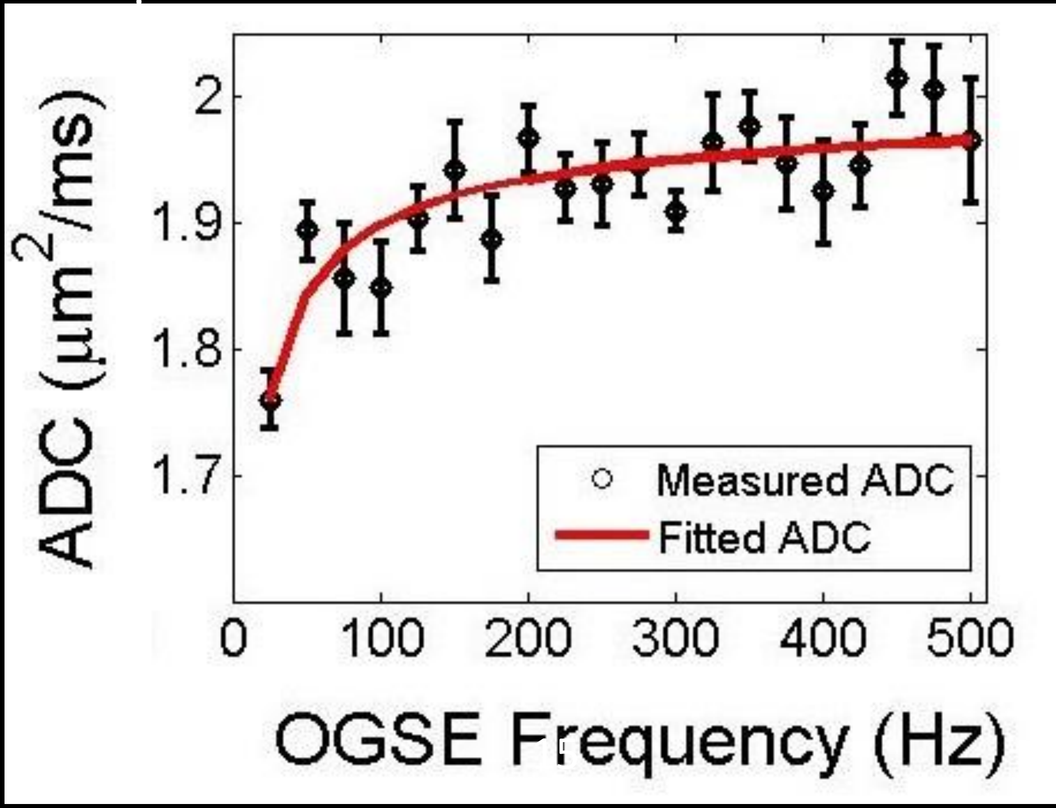
# Phantom (capillary tubes)

- Surface to volume ratio was found to be 0.09 ± 0.01 $\mu m^{-1}$, containing water diffusing at 2.01 ± 0.01 $\mu m^2$/ms.
- Corresponds to tube diameters of 180 ± 30 μm
  (Assuming 80% hexagonal packing)

**Plot for ROI # 4**

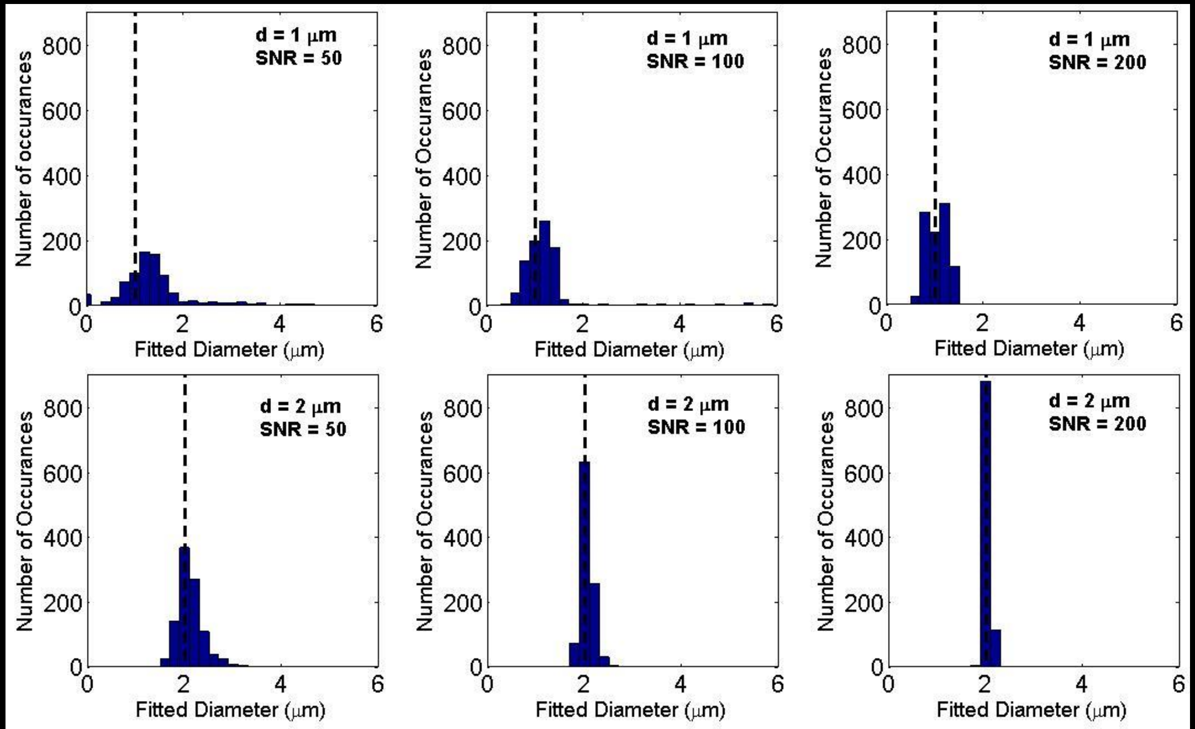
- Actual average outer diameter ~151 μm



# Effects of noise

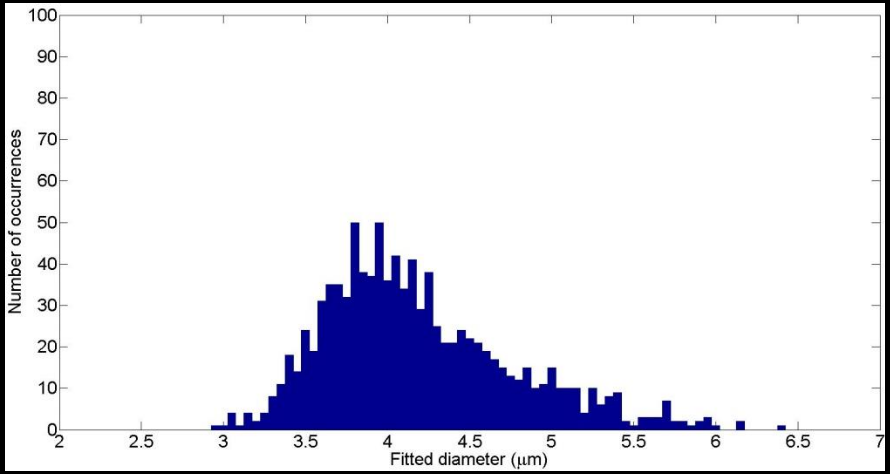
- To see the effects of noise on the parameter estimates, add Gaussian noise to the $M_x$ and $M_y$ components of the simulation results
- For each realization of noise, do the fitting procedure and store the parameter estimates (repeat 1000 times)

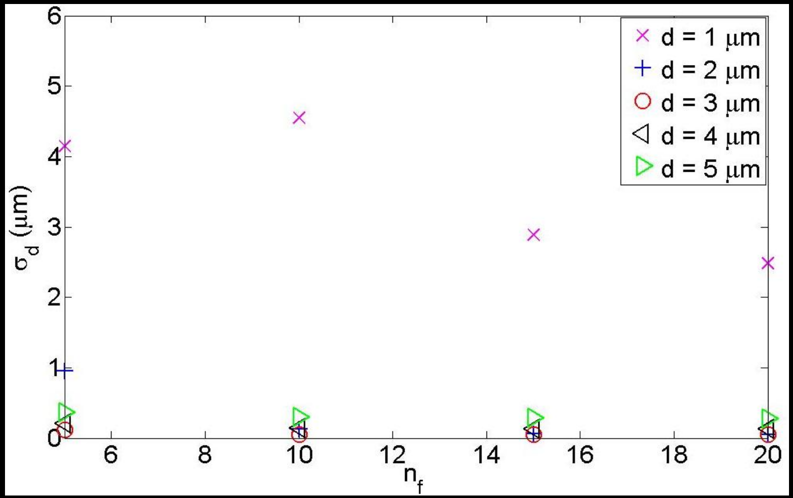



Mercredi et al
MAGMA 2017

# OGSE frequencies

- Want to see how the fitted parameter distributions change when using smaller (or fewer) OGSE frequencies
- Use $n_f$ = {5, 10, 15, 20} frequencies (50 – 250, 500, 750, 1000 Hz)
- For some diameters, $\sigma_d$ change very little

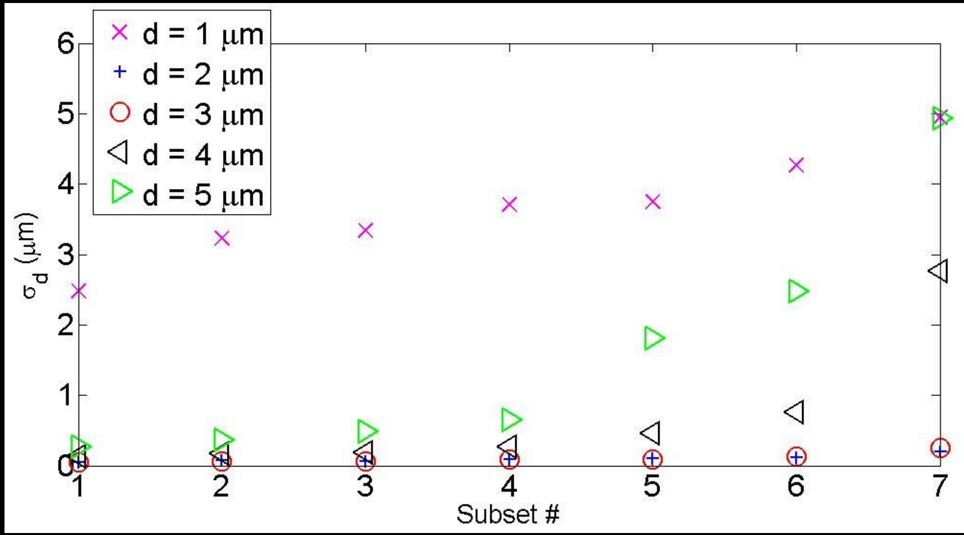


# OGSE gradients

- See how fitted parameter distributions change when using smaller (and fewer) gradients
- $G = \{G_0=0, G_1, \ldots, G_{max} = 900\ mT/m\}$
- Multiple gradients are slightly better than just two
- Two gradients can be better, if the nonzero gradient is big enough

| | |
|---|---|
| #1 | $G_0, G_1, G_2, G_3, G_4$ |
| #2 | $G_0, G_4$ |
| #3 | $G_0, G_1, G_2, G_3$ |
| #4 | $G_0, G_3$ |
| #5 | $G_0, G_1, G_2$ |
| #6 | $G_0, G_2$ |
| #7 | $G_0, G_1$ |




Intra-axonal simulations

# Future studies

- Finding the optimal limited range of frequencies and gradient strengths for expected diameter sizes
- Finding the optimal signal-to-noise ratio for the experiments
- Finding the optimal resolution for the images
- Measurements on brains

# Conclusions

- MRI can infer sizes of structures by measuring water diffusion within the structures
- OGSE sequences can make measurements of micron diameters in biological samples

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