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Modeling Neural Tissue and Membrane Behavior During Far-field Current Injection

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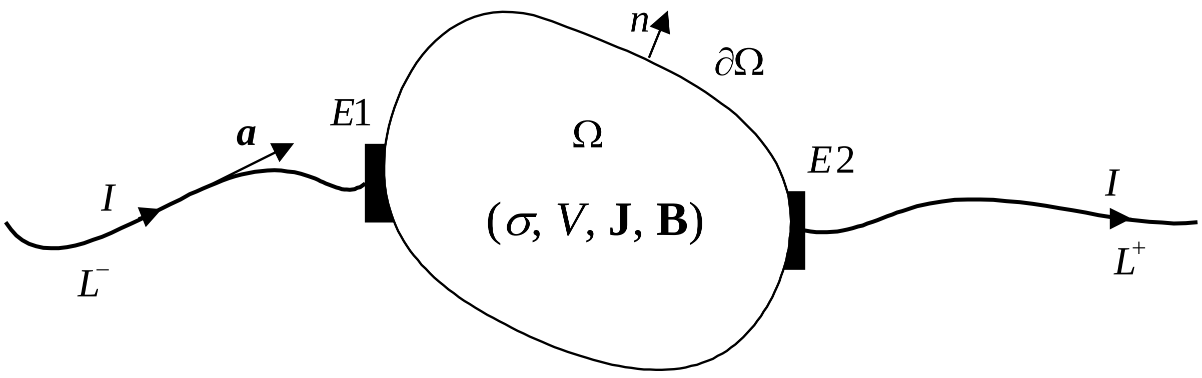
MREIT: From Magnetic Flux Density to conductivity



Material Property : σ : conductivity, $\rho = \dfrac{1}{\sigma}$: resistivity

Neumann Boundary Value Problem :

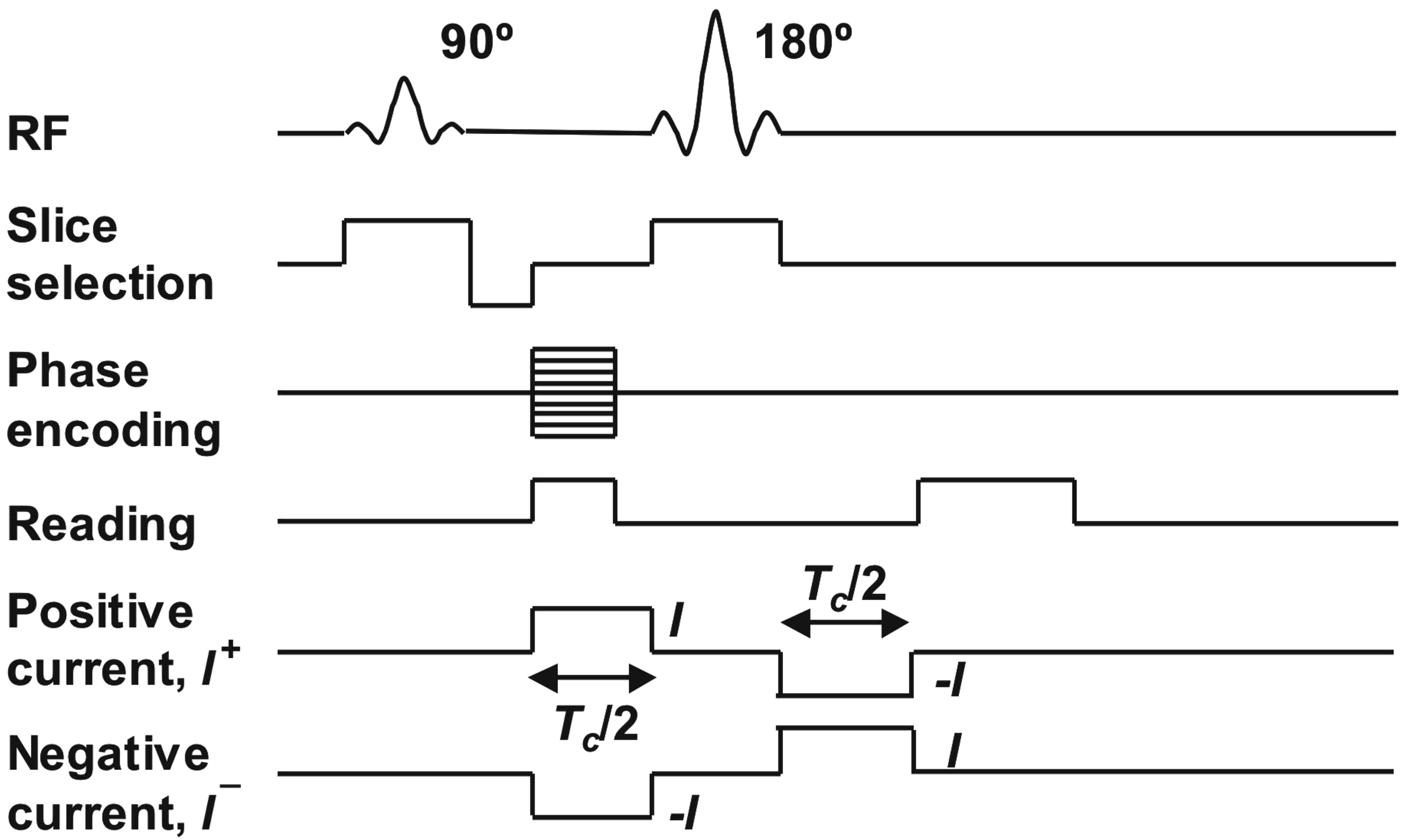
$$\nabla \cdot \left[\sigma(\boldsymbol{r}) \nabla V(\boldsymbol{r}) \right] = 0 \qquad -\sigma \frac{\partial V}{\partial n} = J_n \text{ on } \partial\Omega$$

$$\boldsymbol{J}(\boldsymbol{r}) = -\sigma(\boldsymbol{r}) \nabla V(\boldsymbol{r}) \qquad \nabla \cdot \boldsymbol{J}(\boldsymbol{r}) = 0$$

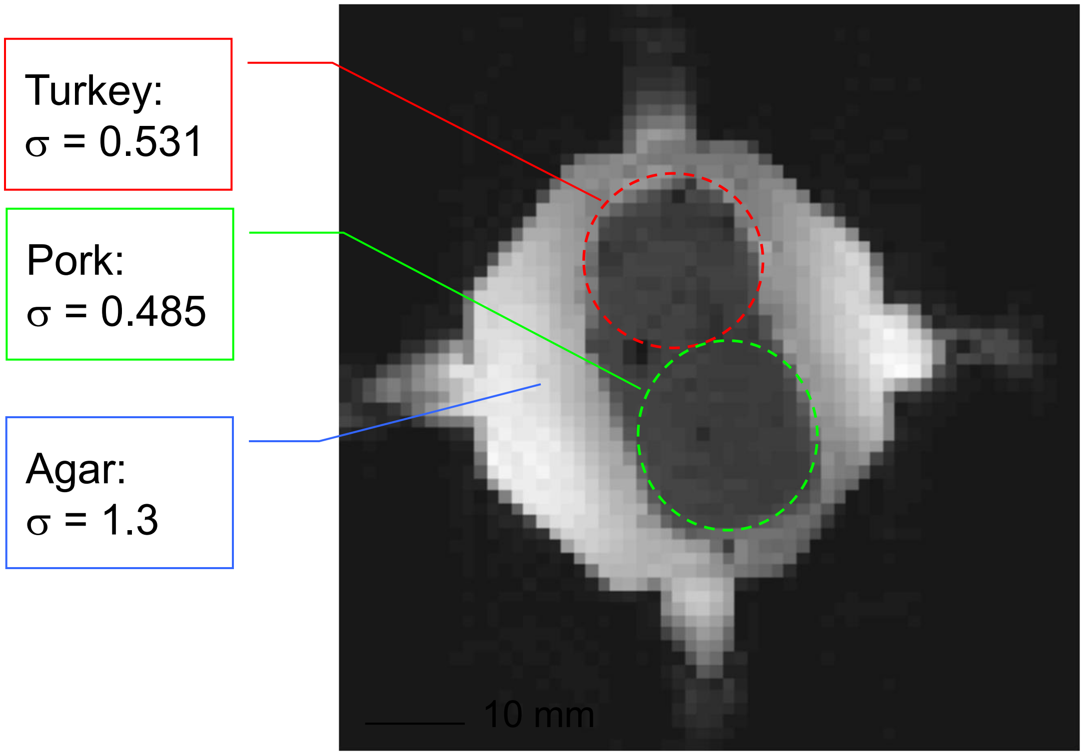
$$\nabla . \mathrm{B} = 0 \Rightarrow \nabla \times \mathrm{J} = -\frac{1}{\mu_o} \nabla^2 \mathrm{B}$$

$$-\frac{1}{\mu_o} \nabla^2 \mathrm{B}_z = \frac{\partial \sigma}{\partial y} \frac{\partial V}{\partial x} - \frac{\partial \sigma}{\partial x} \frac{\partial V}{\partial y}$$

Pulse Sequence (Spin Echo)

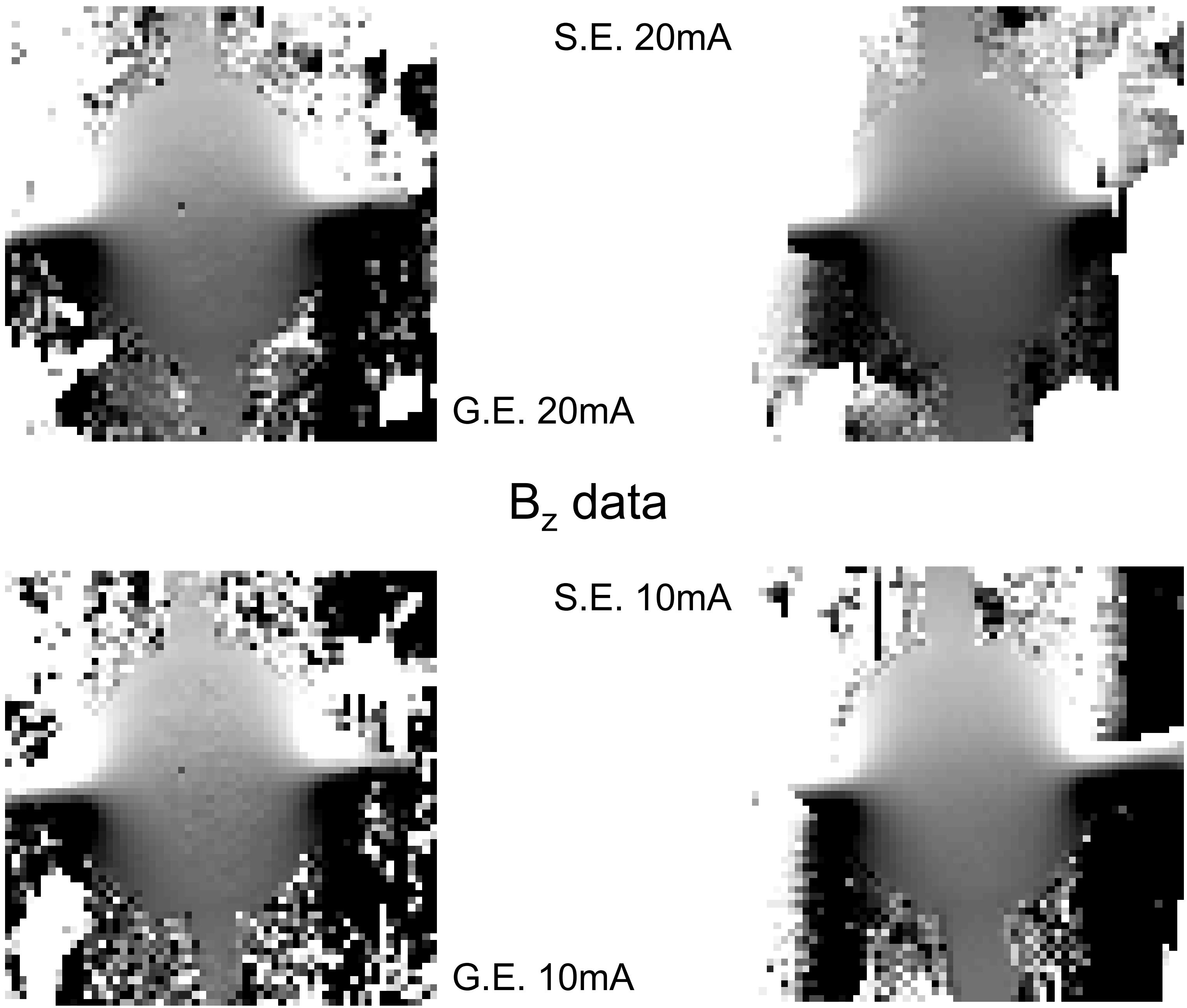


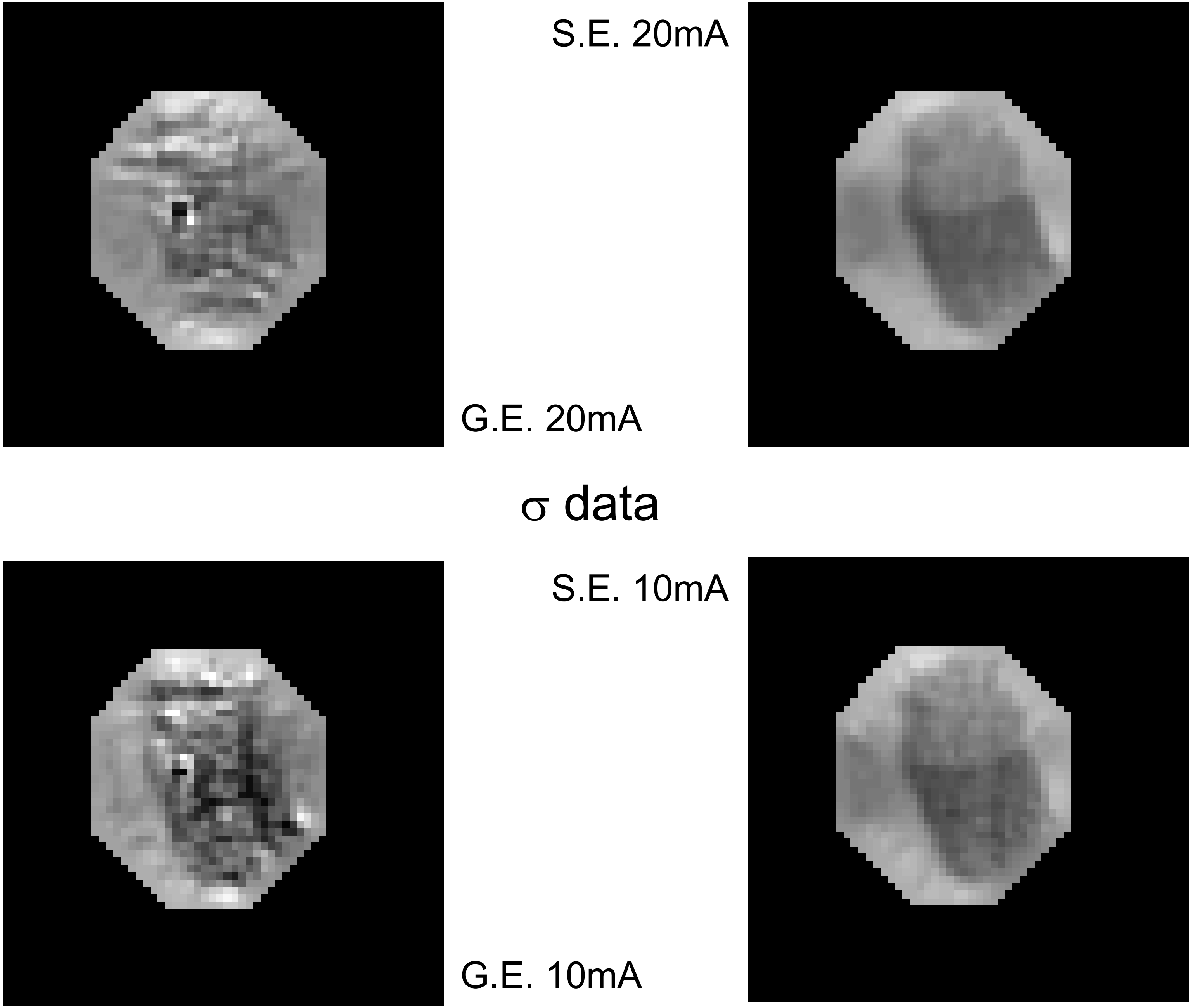
Tissue phantom trials



11 T MR magnitude image

Conductivities in S/m


S.E. 20mA
G.E. 20mA
B_z data
S.E. 10mA
G.E. 10mA



S.E. 20mA
G.E. 20mA
σ data
S.E. 10mA
G.E. 10mA

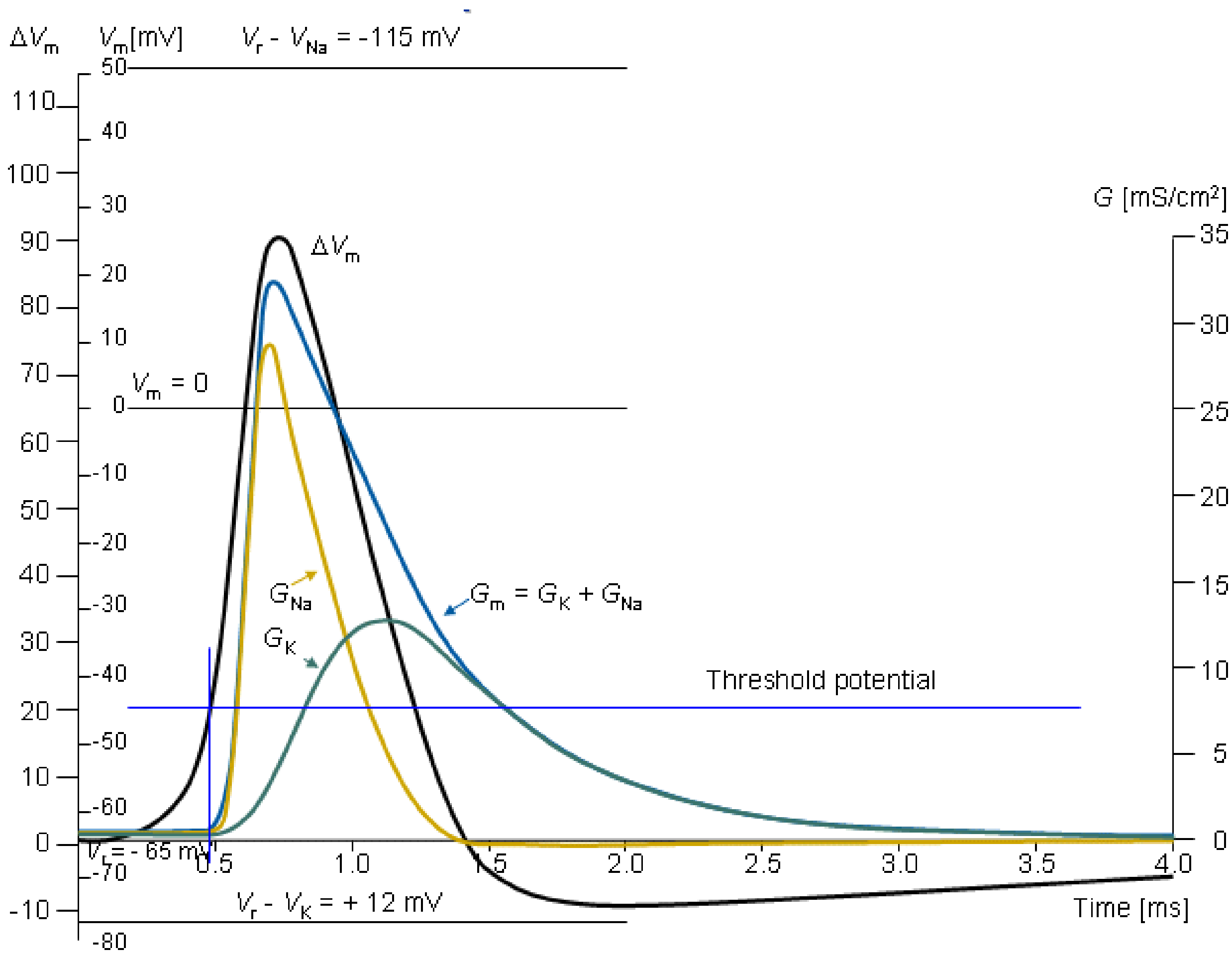
Methods for detecting neural activity

- MEG
- EEG

In MRI

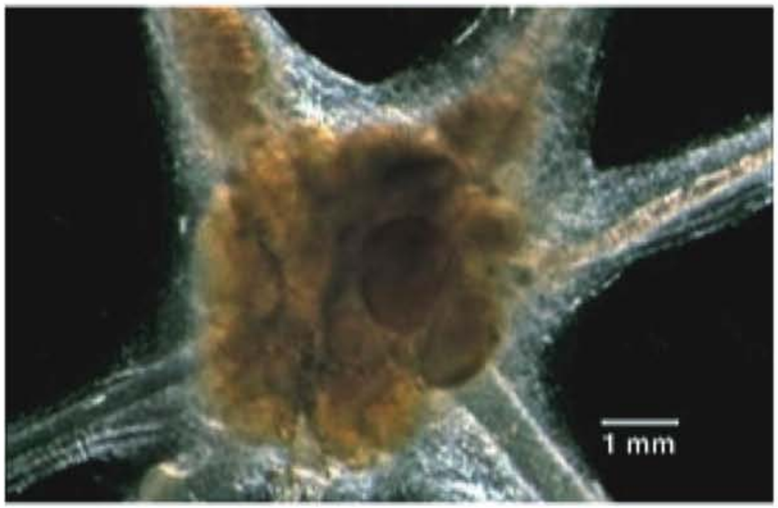
- BOLD contrast (Ogawa and Lee 1990)
- B_o perturbation
  - RF (3T and above) (Bodurka et al. 1999)
  - Low frequency (μHz) (Kraus et al 2008)
- Lorentz effect imaging (Truong et al. 2008)
- Membrane Conductivity Changes (Sadleir et al. 2010)

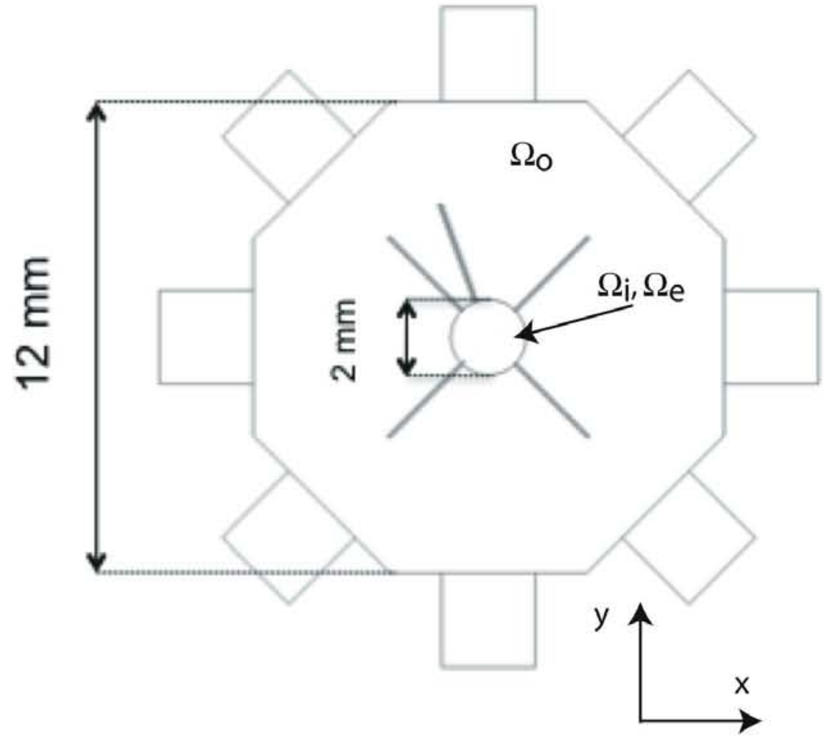
Membrane Conductance variation



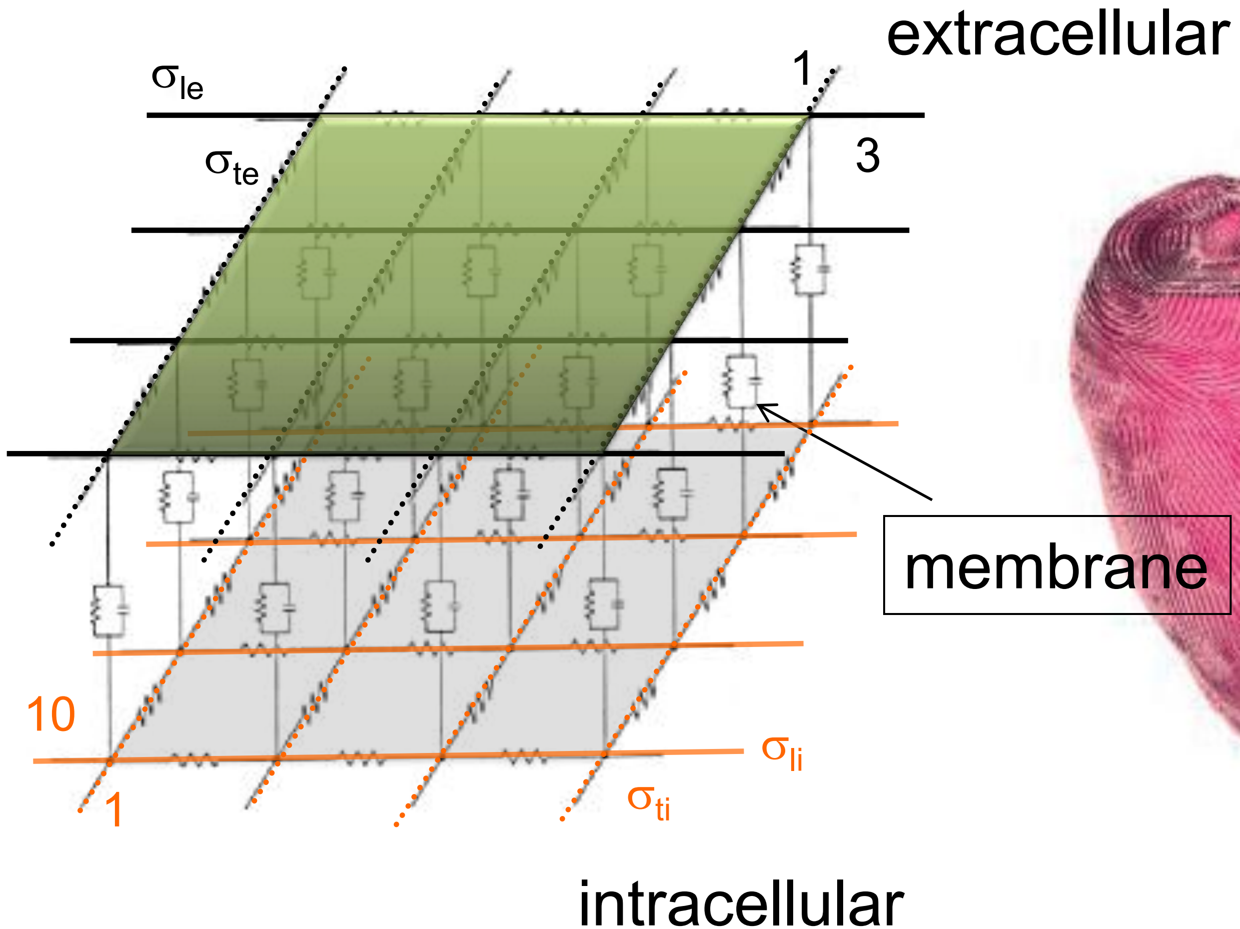
Malmivuo and Plonsey 1995

Aplysia Model



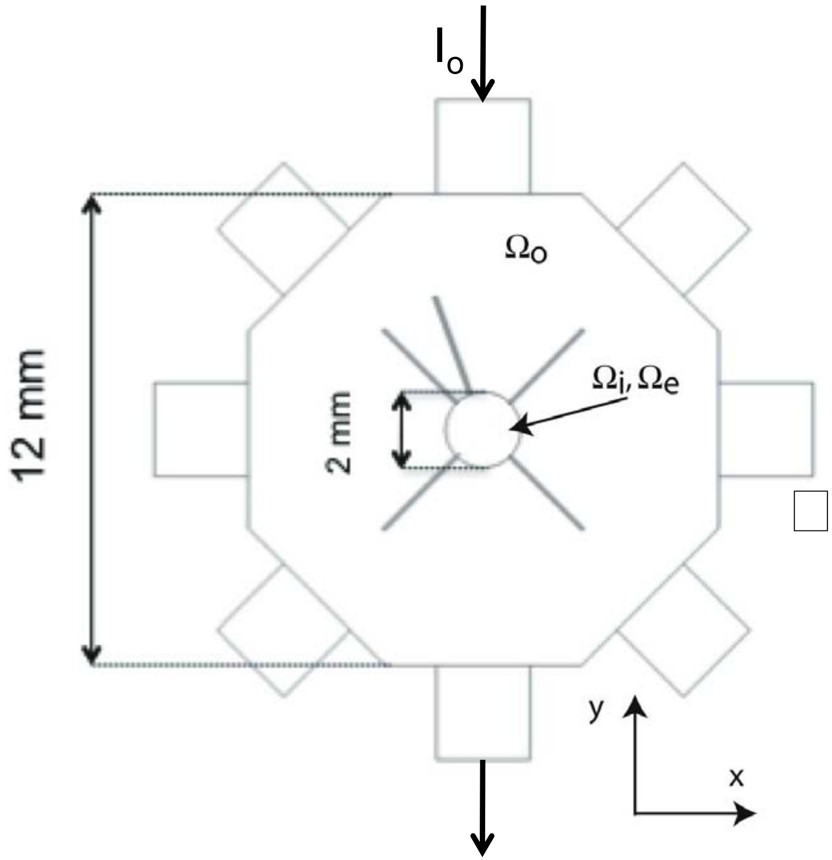


Bidomain conductivity modelling



after Roth (2000)

Bidomain Model



$$\nabla \cdot J_i = -\nabla \cdot J_e = i_m$$

$$V_m = \phi_i - \phi_e \qquad \mathbf{J}_i = -\mathbf{D}_\mathbf{i} \nabla \phi_i$$

$$i_m = \beta G_m V_m \qquad \mathbf{J}_e = -\mathbf{D}_e \nabla \phi_e$$

3 application modes
Vo (bath), Ve and Vi (tissue)
At boundaries: $\frac{\partial \phi_i}{\partial n} = 0$ i.e. insulation

$$V_e = V_o$$

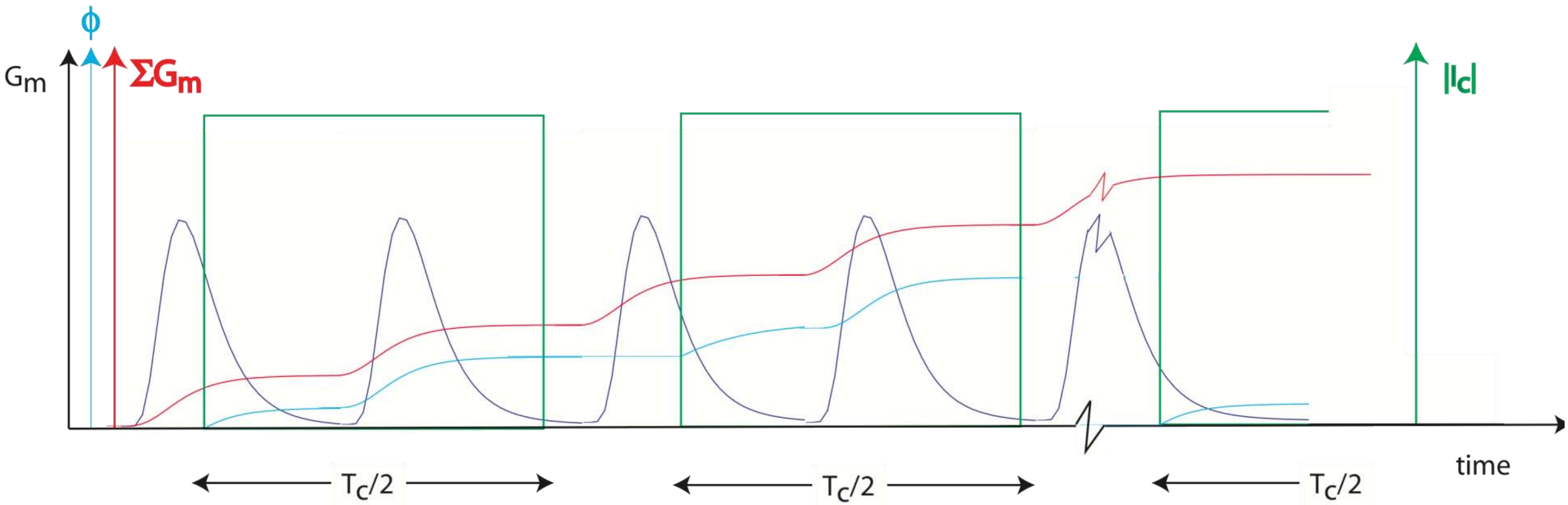
$$\mathbf{D}_{i,e} = \begin{bmatrix} k_{xx} & k_{xy} & k_{xz} \\ k_{xy} & k_{yy} & k_{yz} \\ k_{xz} & k_{yz} & k_{zz} \end{bmatrix}_{i,e}$$

Table 1. Bidomain Parameters and Constants

Parameter	Value	Units	Description
σ_i	3.63	S/m	intracellular conductivity
σ_e	5.07	S/m	extracellular conductivity
σ_o	5.07	S/m	bath conductivity
σ_p	1	S/m	port conductivity
f_i	0.7	-	intracellular filling fraction
β	20 000	m^{-1}	surface to volume ratio
$G_{m,rest}$	6.7	S/m^2	membrane conductivity, rest
$G_{m,active}$	320	S/m^2	membrane conductivity, active

Measurement with MREIT

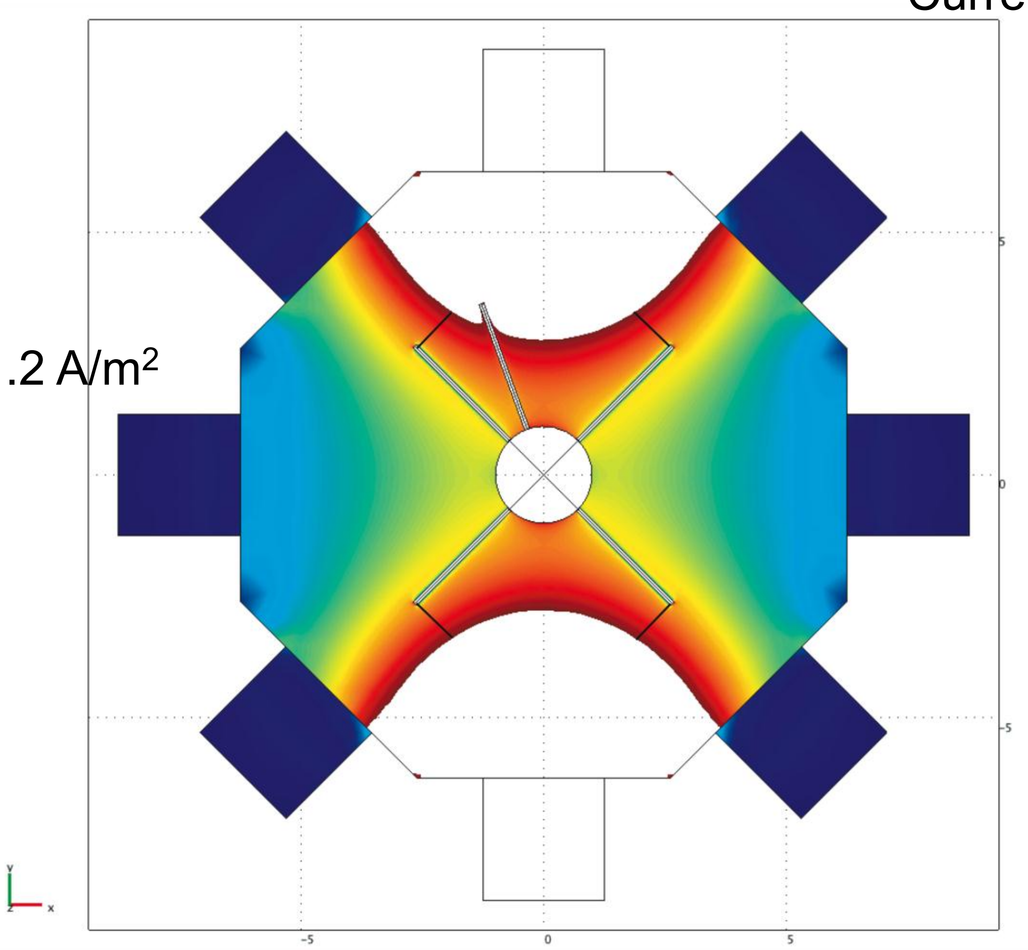
- Detection of changes in B_z (current flow) data as a result of changes in membrane conductance
- Signal size depends on observing membrane conductivity change during application of imaging current



Current Limits

Current Density

90 μA applied
Max scale at 1.2 A/m^2

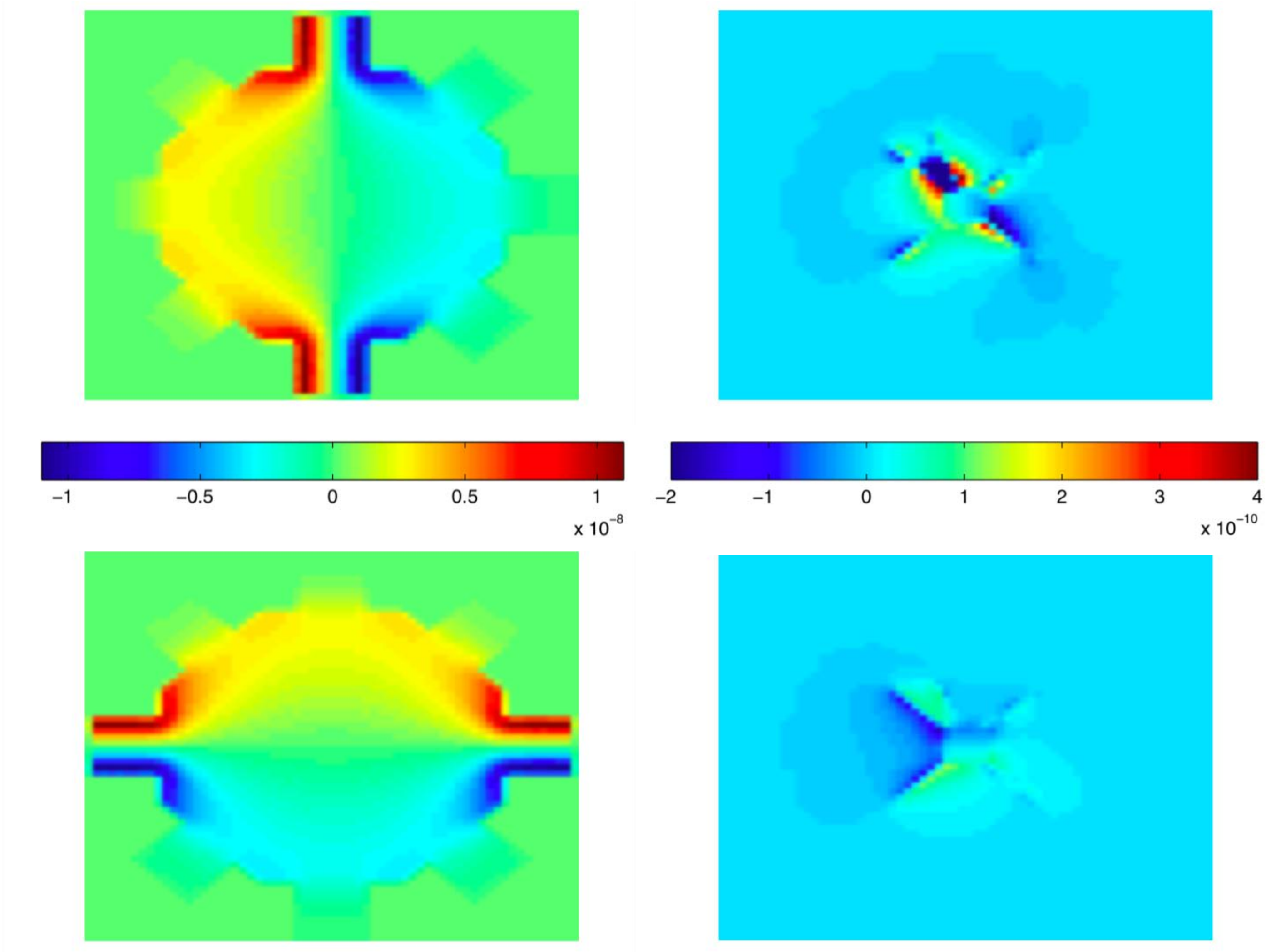


$\Delta x = \Delta y = 281\ \mu m$

$\Delta z = 1\ mm$

B_z and ΔB_z data

Y current direction



90 μA

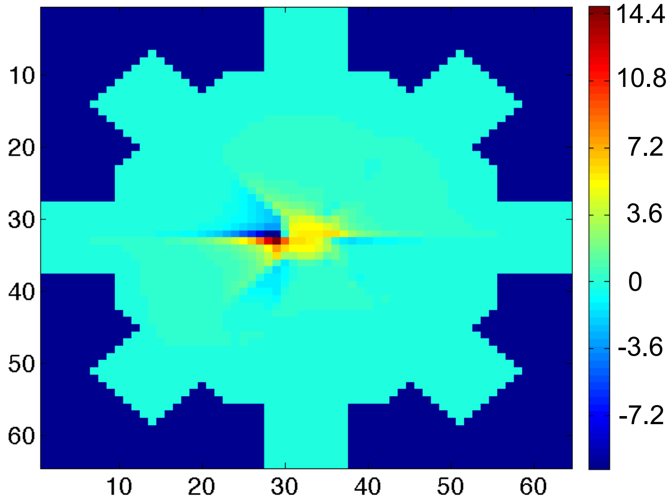
X current direction

B_z

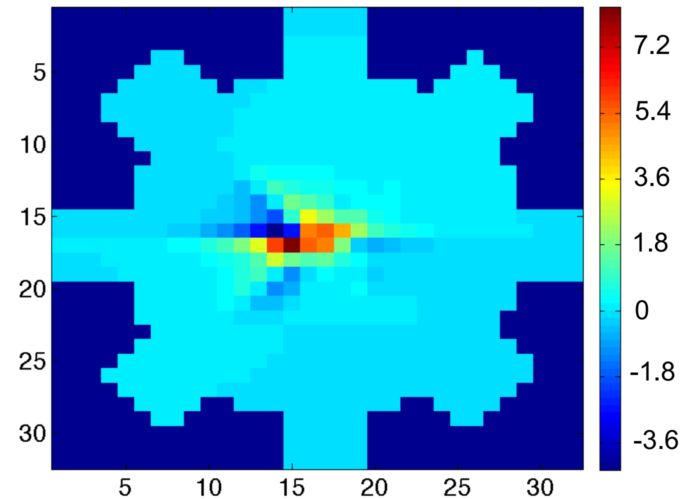
ΔB_z

Percentage Changes

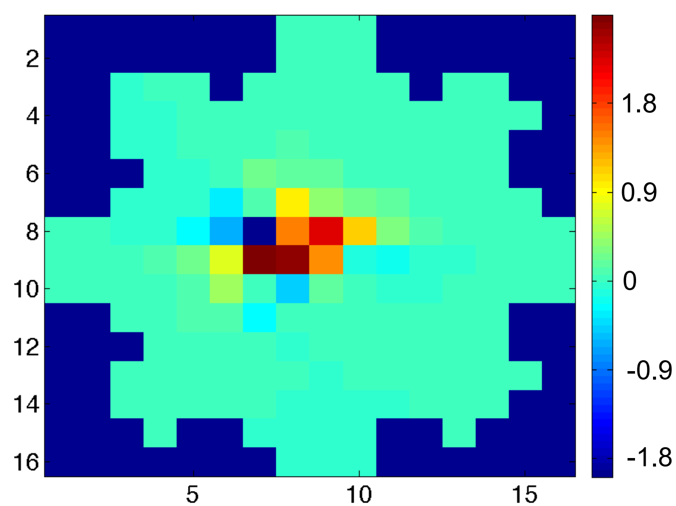
$\Delta x = \Delta y = 281\ \mu m$



$\Delta x = \Delta y = 562\ \mu m$

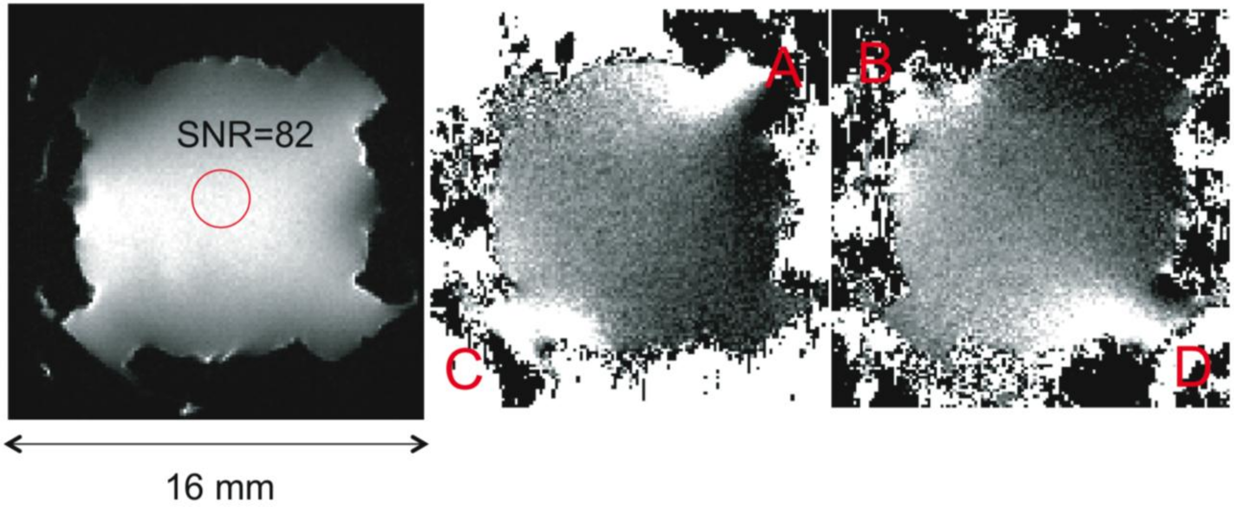


$\Delta x = \Delta y = 1120\ \mu m$



$\Delta z = 1$ mm

SNR at 17.6 T



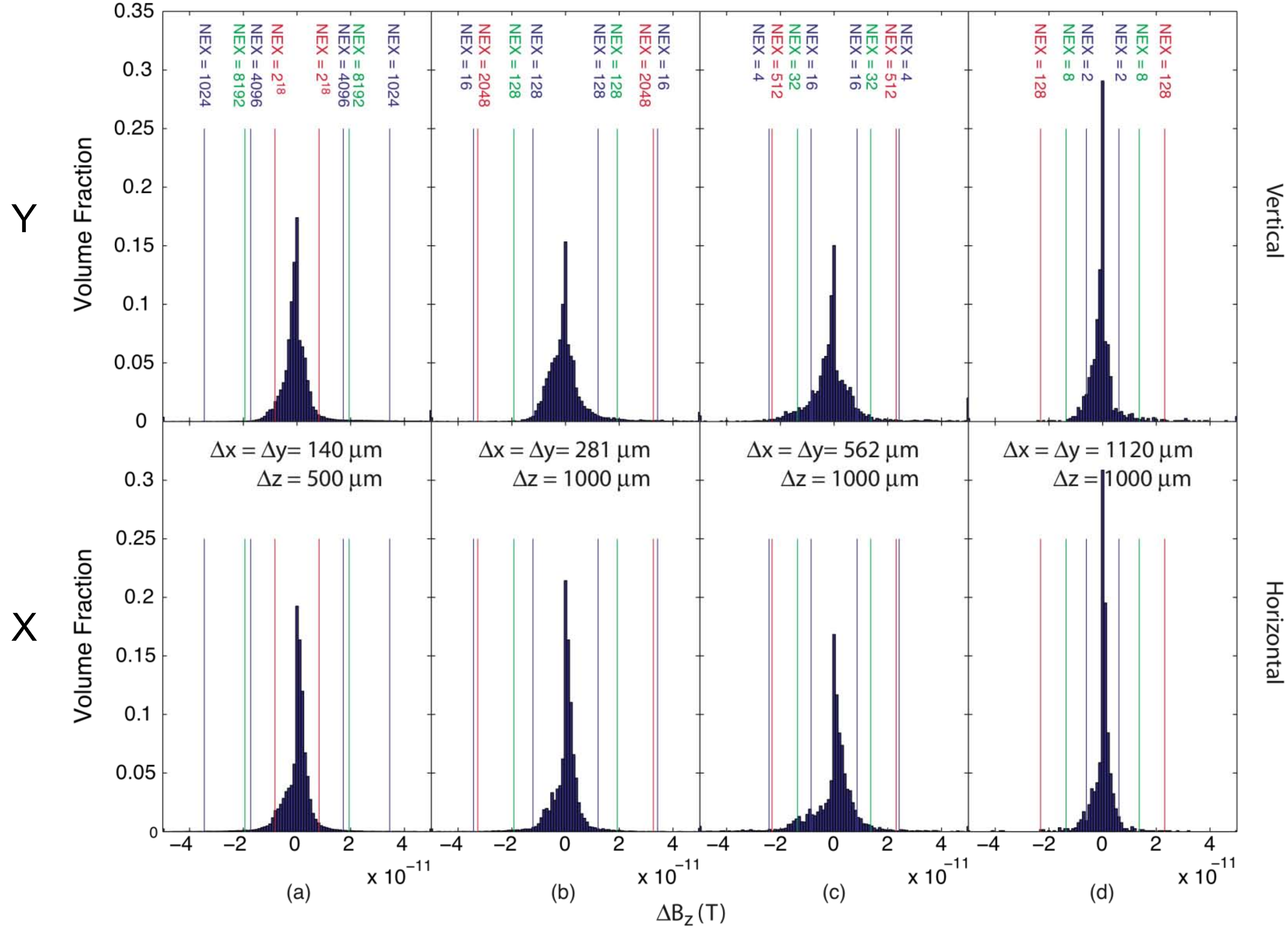
200 μA

Table 2. Expected B_z Noise Levels (T) at different SNR levels in a 17.6 T main field

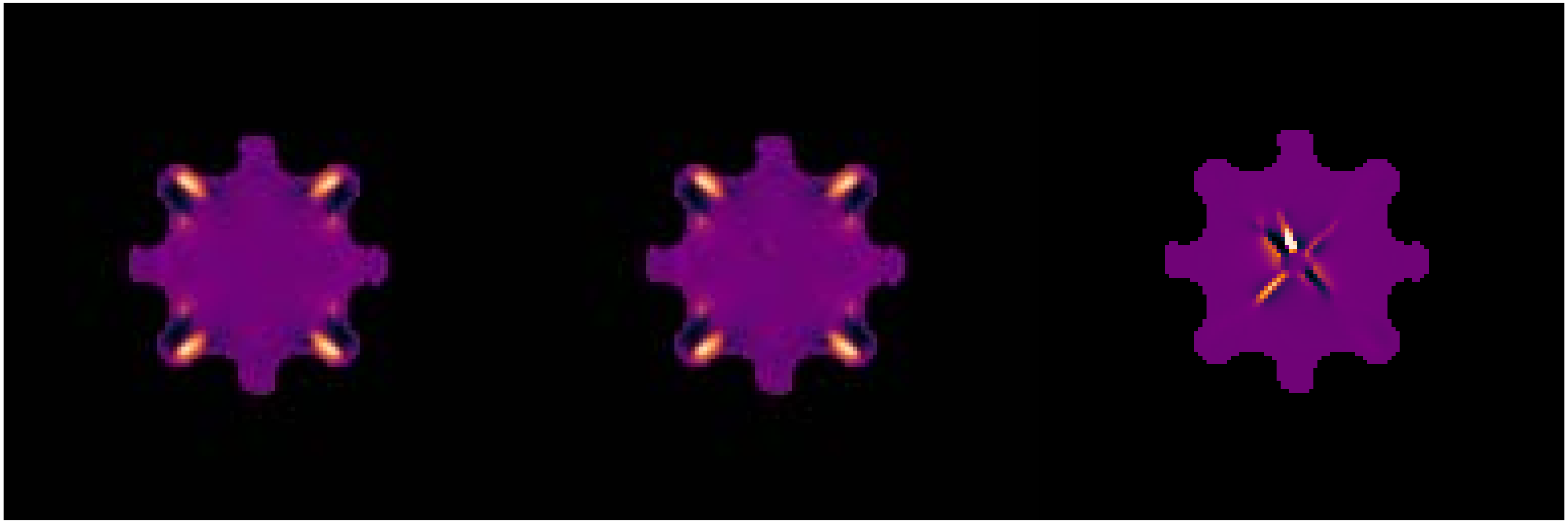
$$sd(B_z) = \frac{1}{\sqrt{2}\gamma T_c Y_M}$$

Resolution	Pixel Size μm	Δz mm	Predicted Noise (T) NEX=2	NEX=1
128 x 128 x 16	140	0.5	8.0×10^{-9}	1.2×10^{-8}
64 x 64 x 8	281	1	2.8×10^{-9}	4.4×10^{-9}
32 x 32 x 8	562	1	1.4×10^{-9}	2.2×10^{-9}
16 x 16 x 8	1120	1	7.0×10^{-10}	1.1×10^{-9}

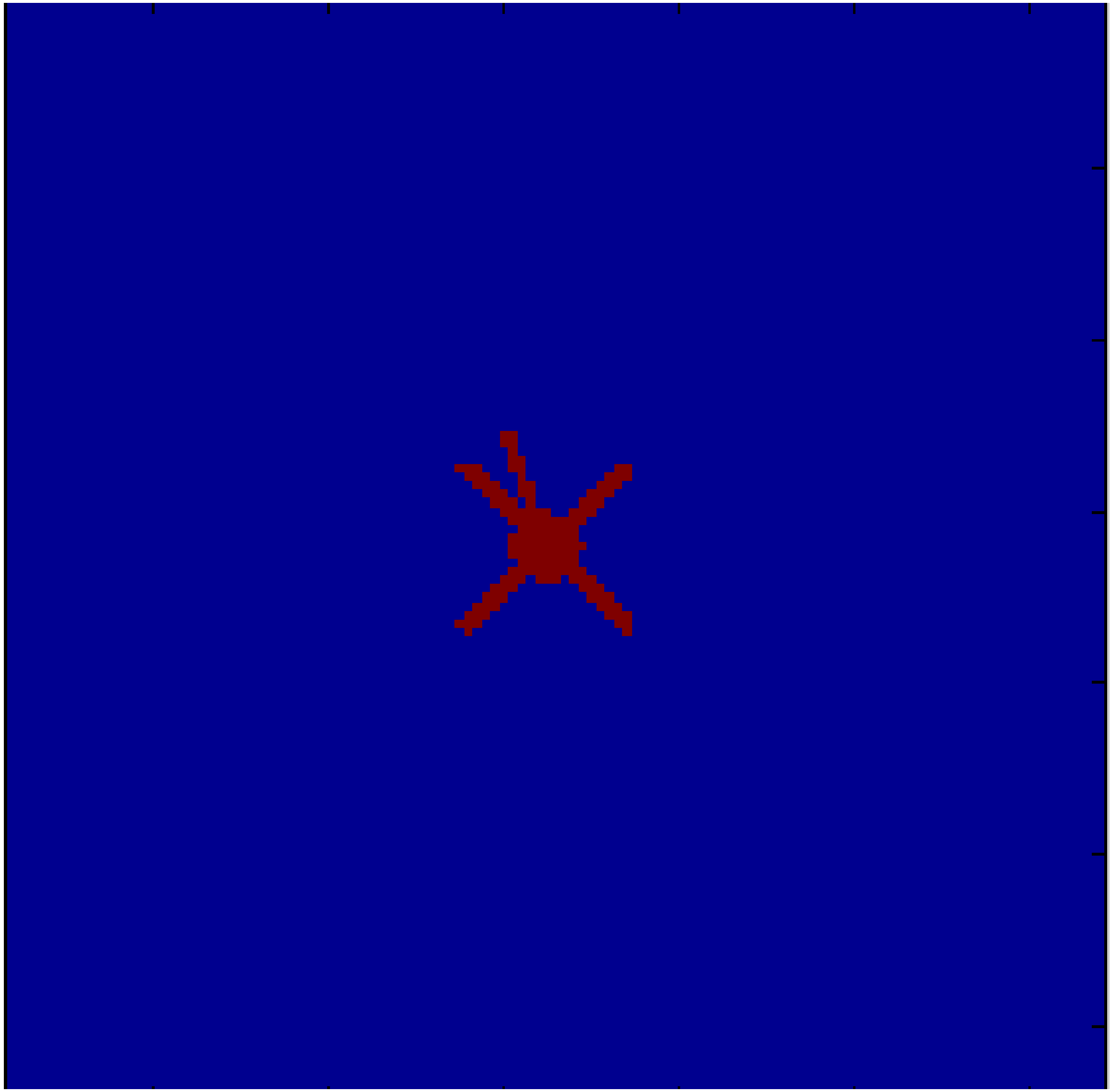
ΔB_z distributions



Rest Active Active-Rest

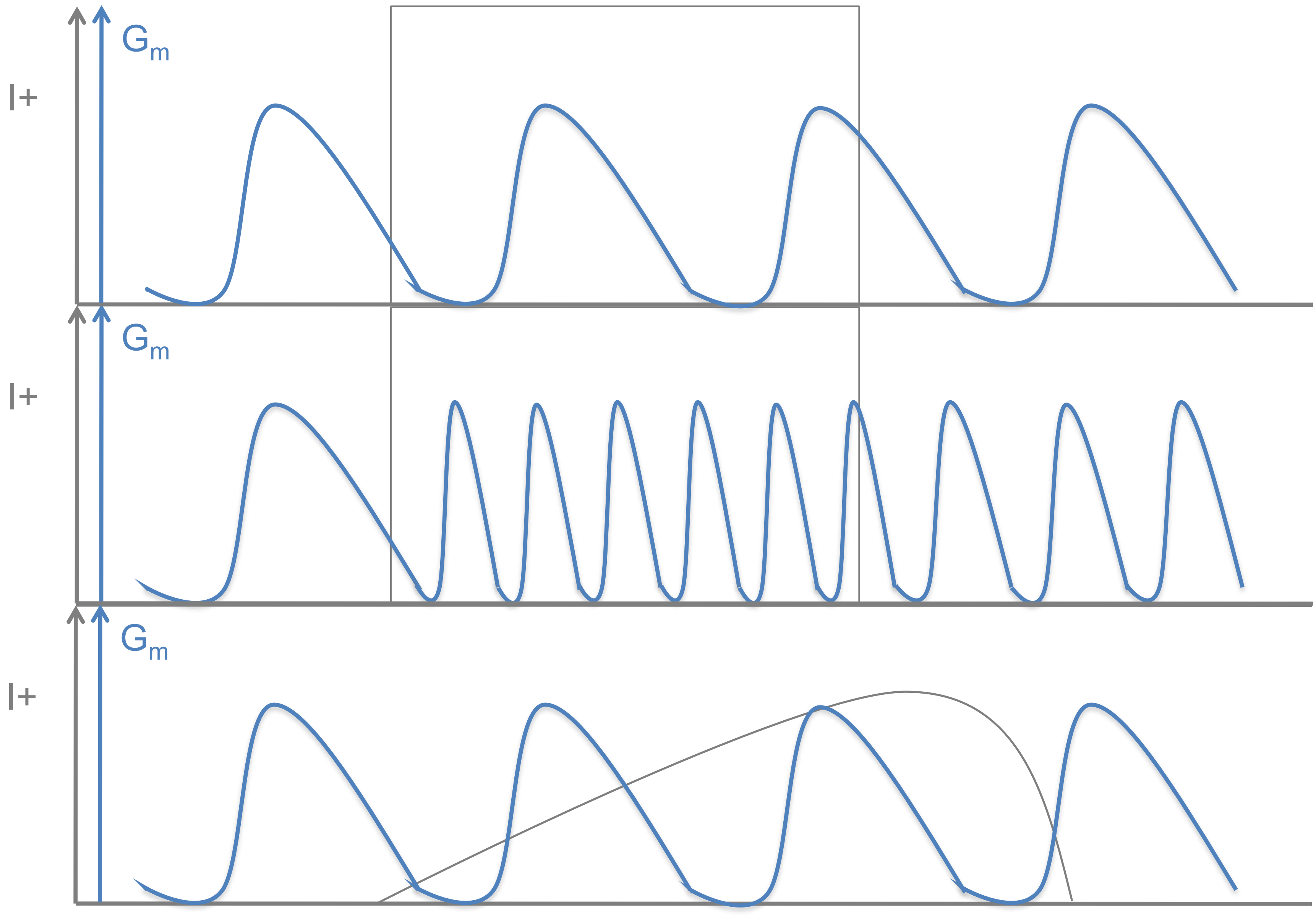


Active-Rest reconstruction



Active Behavior?

- Replace passive membrane with ODE model (e.g. Hodgkin Huxley)
- Helps with dynamic behavior prediction and current pattern design



G_m
I+
G_m
I+
G_m
I+

Bidomain Model

$$V_m = \phi_i - \phi_e$$

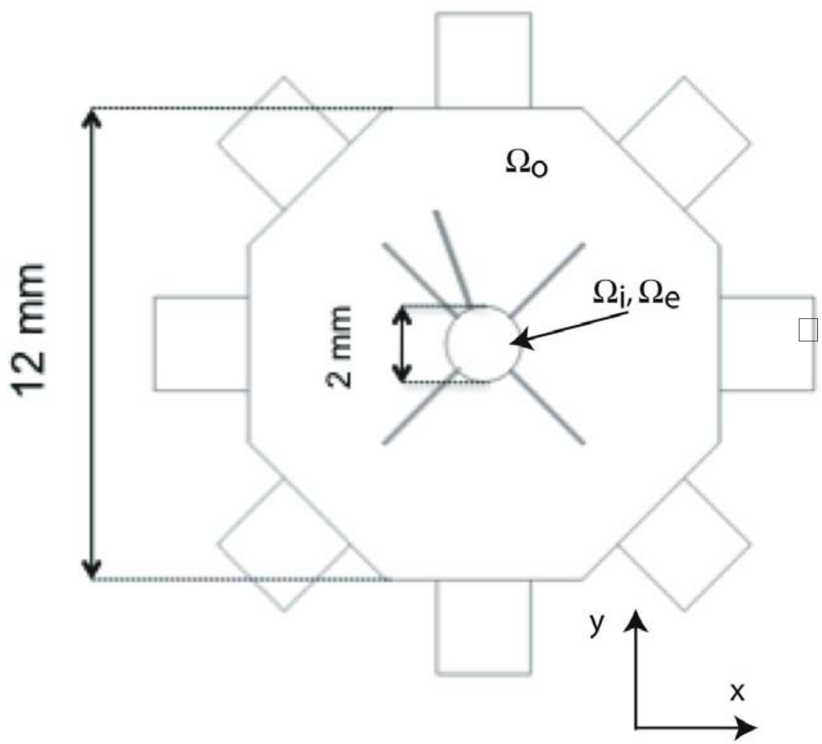
$$\nabla \cdot J_i = -\nabla \cdot J_e = i_m$$

$$i_m = \beta G_m V_m$$

$$i_m = \beta (C_m \frac{dV_m}{dt} + (V_m - V_{Na})G_{Na} + (V_m - V_K)G_K + (V_m - V_L)G_L)$$

$$\mathbf{J}_i = -\mathbf{D}_i \nabla \phi_i$$

$$\mathbf{J}_e = -\mathbf{D}_e \nabla \phi_e$$



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IONIC CONDUCTANCES

Hodgkin Huxley Moel

$$G_{Na} = G_{Na\,max}\, m^3 h$$

$$G_K = G_{K\,max}\, n^4$$

$$G_L = \text{constant}$$

$$\frac{dm}{dt} = \alpha_m(1-m) - \beta_m m$$

$$\frac{dh}{dt} = \alpha_h(1-h) - \beta_h h$$

$$\frac{dn}{dt} = \alpha_n(1-n) - \beta_n n$$

$$i_m = \beta\left(C_m \frac{dV_m}{dt} + (V_m - V_{Na})G_{Na} + (V_m - V_K)G_K + (V_m - V_L)G_L\right)$$

TRANSFER RATE COEFFICIENTS

$$\alpha_m = \frac{0.1\cdot(25 - V')}{e^{(25-V')/10} - 1}\,\frac{1}{\mathrm{ms}} \qquad \beta_m = \frac{4}{e^{(V'/18)}}\,\frac{1}{\mathrm{ms}}$$

$$\alpha_h = \frac{0.07}{e^{V'/20}}\,\frac{1}{\mathrm{ms}} \qquad \beta_h = \frac{1}{e^{(30 - V')/10} + 1}\,\frac{1}{\mathrm{ms}}$$

$$\alpha_n = \frac{0.01(10 - V')}{e^{(10 - V')/10} - 1}\,\frac{1}{\mathrm{ms}} \qquad \beta_n = \frac{0.125}{e^{V'/80}}\,\frac{1}{\mathrm{ms}}$$

CONSTANTS

$V_r - V_{Na} = -115$

$V_r - V_K = +12$

$V_r - V_L = -10.613$ mV

$C_m = 1$ µF/cm²

$G_{Na\,max} = 120$ ms/cm²

$G_{K\,max} = 36$ ms/cm²

$G_L = 0.3$ ms/cm²

Malmivuo and Plonsey 1995

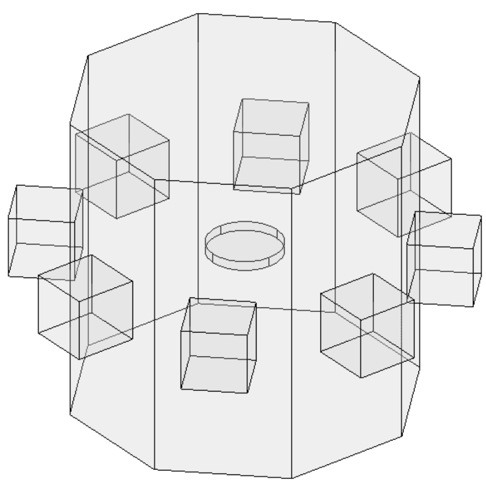
Reduced HH model

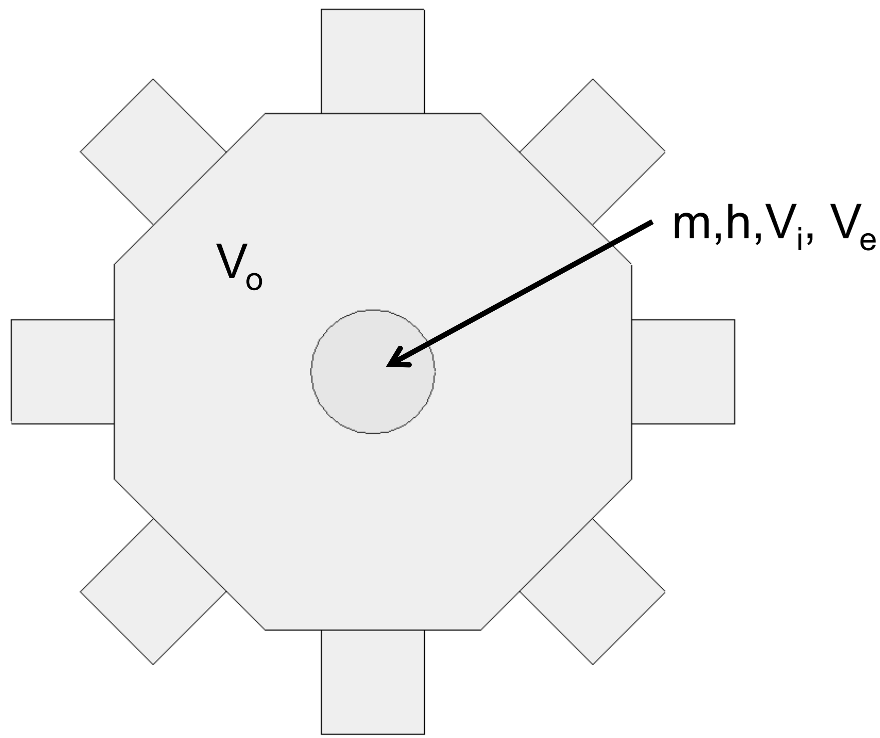
(Kepler, Abott and Marder 1992)

- 2 application modes in HH model (n follows h)

$$\frac{dm}{dt} = k_m \left[\overline{m}(V_m) - m \right]$$

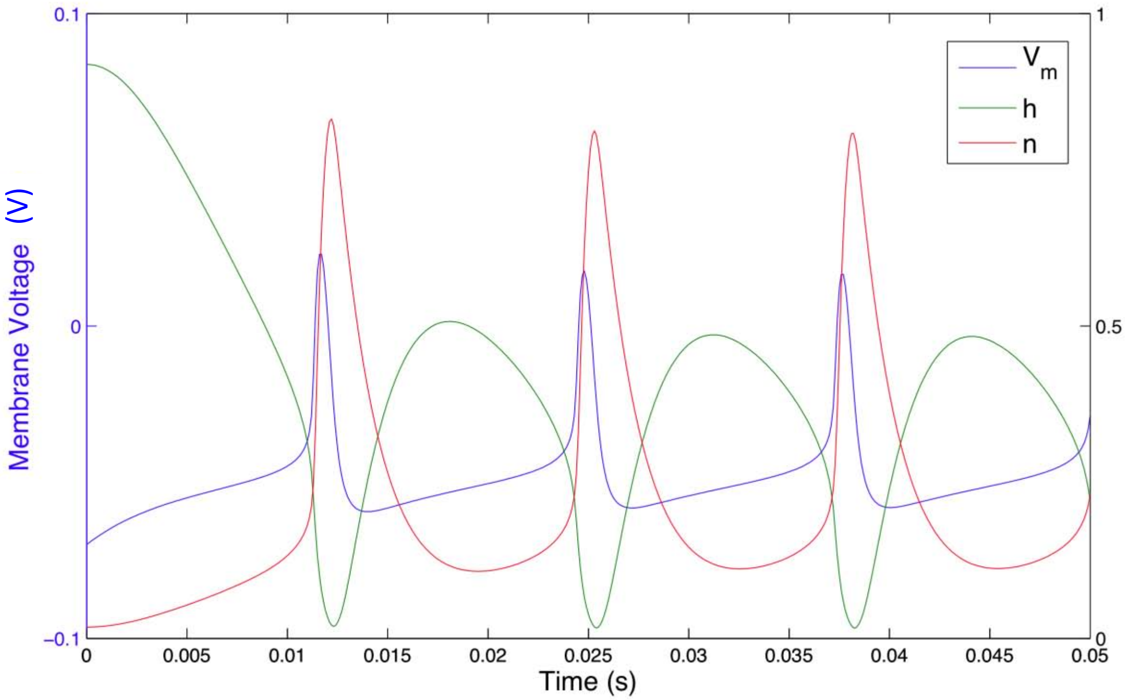
$$\frac{dh}{dt} = k_m \left[\overline{h}(V_m) - h \right]$$



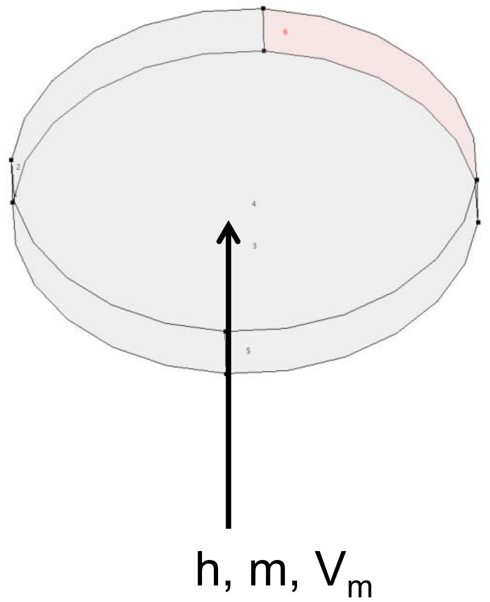


Basic Behavior

- Central cylinder only: 3 App modes (h, m, V_m)
- External <u>constant</u> current i_e = 0.05 A/m^3



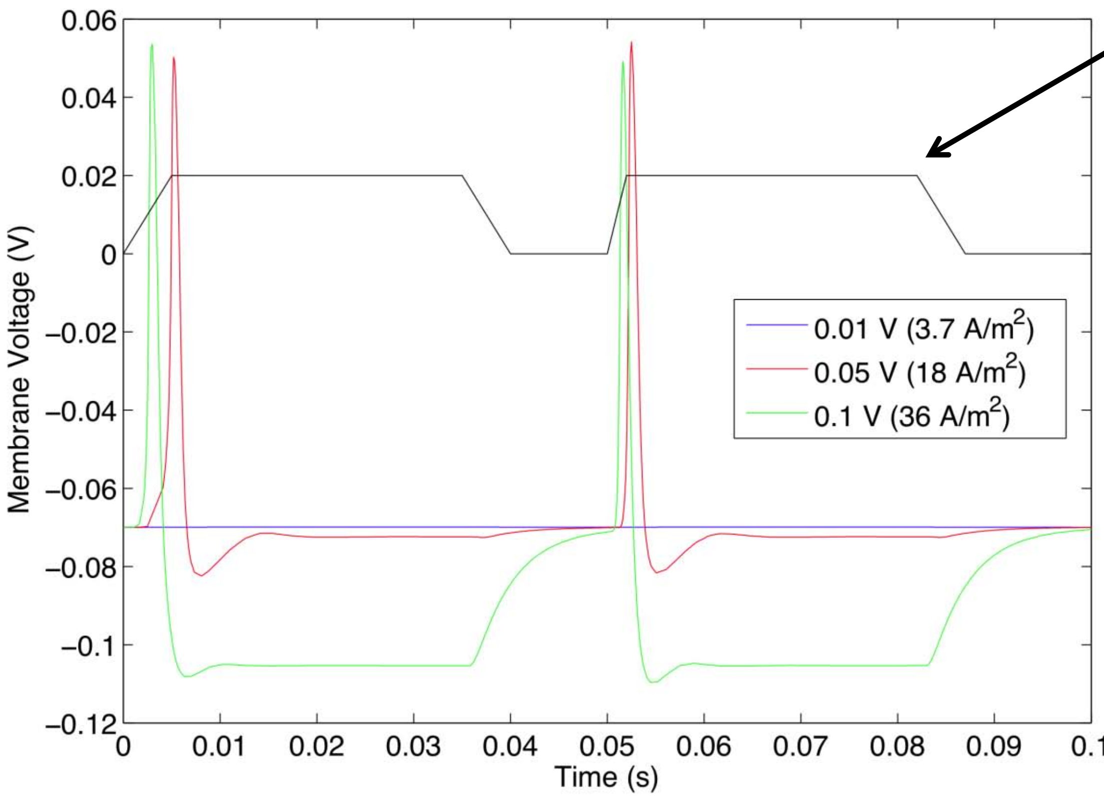
$$\nabla\cdot J_m = i_m + i_e$$

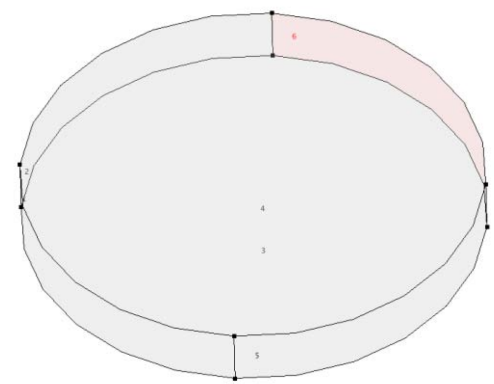


Model 2

- Central cylinder only: 4 App modes (h, m, V_i, V_e)
- Externally Injected Source on opposite sides
- Coupling parameter β = 1 (should be 30000)

Injection pattern (scaled)

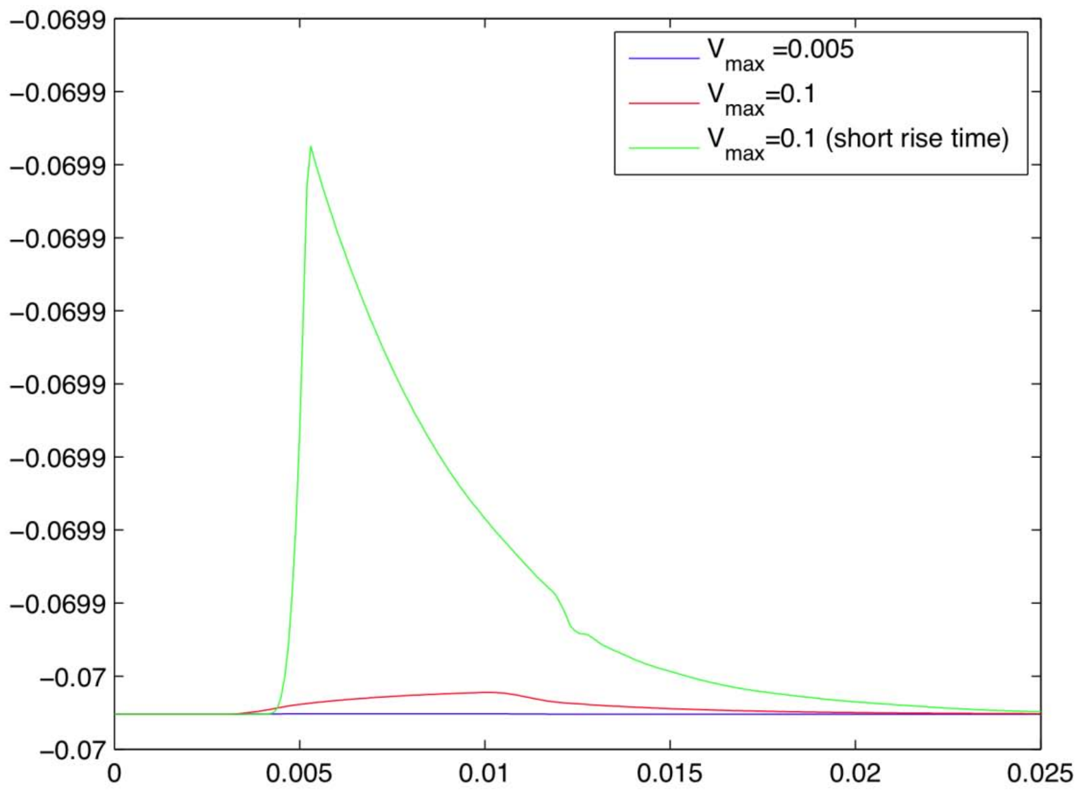




Model 2 dynamic view

Model 3

- Central cylinder + Bath : 5 App modes (h, m, V_i, V_e, V_o)
- Current injected into ports of bath
- Coupling parameter β = 1 (should be 30000)



Conclusions

- Bidomain model is a good way of estimating volume averaged activity
- Results plausibly consistent with others' estimations
- Moderate scale/high field essential to proving concept
- Can be used to explore excitability and/or imaging
- Tweaking of final model is required
  - Solver settings
  - Adding anisotropy

Future Work

- Modelling
  - Active Membrane Model
  - Retinal Ganglion Model
  - Cortical Experiments and Models ?
- MREIT Technology (increased SNR)
  - Pulse Sequences ->
    - reduced current and/or increased injection time/TR
  - Noise reduction
    - In data acquisition
    - In postprocessing
  - Anisotropic Reconstructions
- Technical Considerations
  - Pharmacological manipulation of thresholds