Diffusion MRI simulation of realistic neurons

with SpinDoctor and the Neuron Module

Chengran Fang, Van-Dang Nguyen
Demian Wassermann, Jing-Rebecca Li
Groupe de travail DEFI

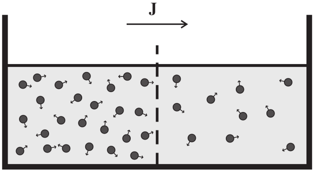
Table of contents

Introduction to Diffusion MRI

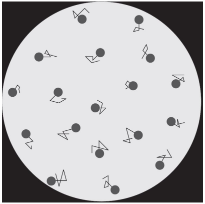
Three main ingredients of dMRI

1. Molecular Diffusion (Wikipedia)

Diffusion is the thermal motion of all (liquid or gas) particles at temperatures above absolute zero.



Diffusion from high concentration regions to low concentration regions

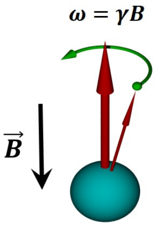


Brownian motion [Johansen 2013]

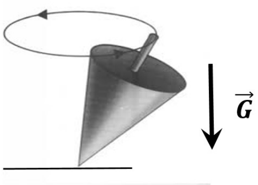
Three main ingredients of dMRI

2. Larmor Precession (Wikipedia)

Larmor precession is the precession of the magnetic moment of an object about an external magnetic field.



Larmor precession of a particle about a magnetic filed



Precession of a rotating cone about a field of gravity

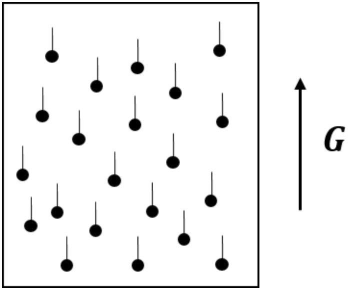
Particles	$\gamma \times 10^6$ $(rad \cdot s^{-1} T^{-1})$
H^1 **(proton)**	**267.522**
He^3	203.789
O^{17}	36.264
C^{13}	67.2828

Table of gyromagnetic ratio γ

Three main ingredients of dMRI

3. Nuclear Magnetic Resonance (NMR) techniques

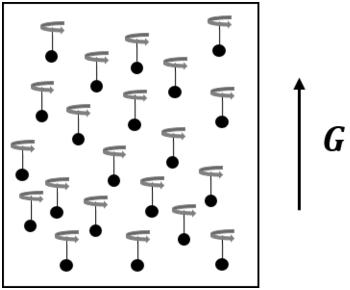
- align the magnetic moment of particles



Three main ingredients of dMRI

3. Nuclear Magnetic Resonance (NMR) techniques

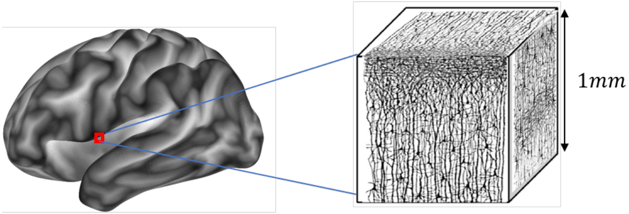
- align the magnetic moment of particles
- synchronize the Larmor precession of particles



Three main ingredients of dMRI

3. Nuclear Magnetic Resonance (NMR) techniques

- align the magnetic moment of particles
- synchronize the Larmor precession of particles
- focus on one dMRI voxel



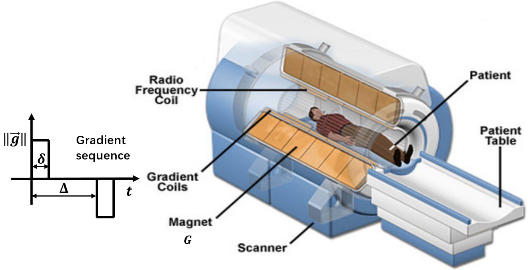
Brain
[M.S. Antonia 2020]

A brain voxel
[Palombo 2020]

Three main ingredients of dMRI

3. Nuclear Magnetic Resonance (NMR) techniques

- align the magnetic moment of particles
- synchronize the Larmor precession of particles
- focus on one dMRI voxel
- measure the dMRI signal, etc.

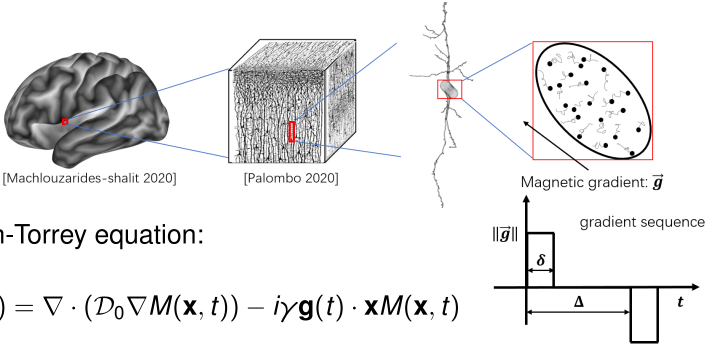


[MagLab 2020]

Principles of Diffusion MRI

Diffusion MRI

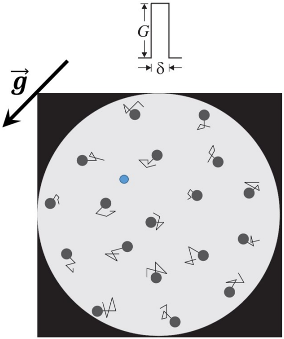
Diffusion MRI is an imaging modality that can be used to probe the tissue microstructure by encoding the diffusion motion of water molecules.



The Bloch-Torrey equation:

$$\frac{\partial}{\partial t}M(\mathbf{x},t) = \nabla \cdot (\mathcal{D}_0 \nabla M(\mathbf{x},t)) - i\gamma \mathbf{g}(t) \cdot \mathbf{x} M(\mathbf{x},t)$$

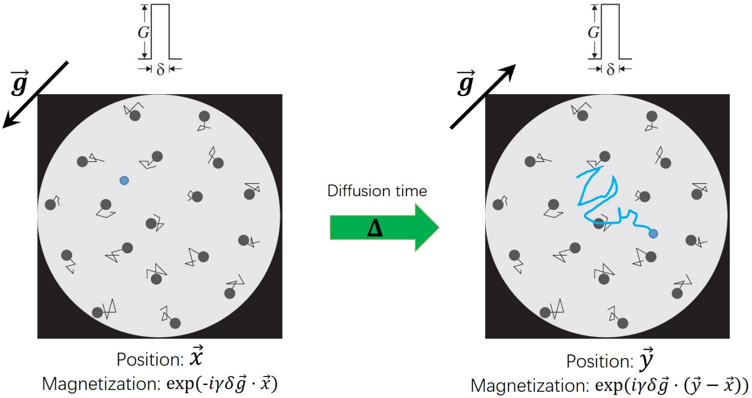
Principles of Diffusion MRI



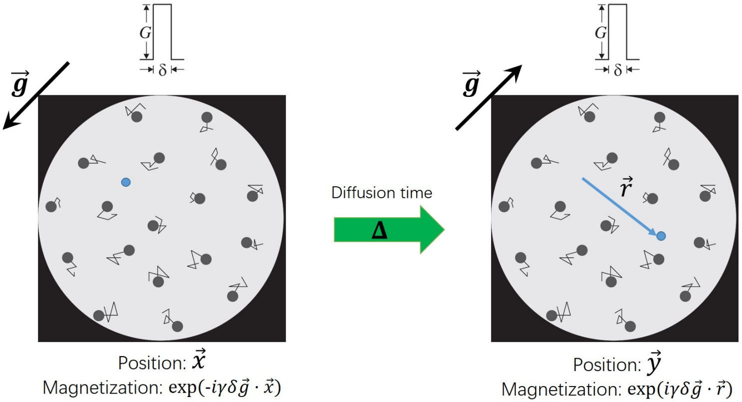
Position: $\vec{x}$

Magnetization: $\exp(-i\gamma\delta\vec{g}\cdot\vec{x})$

Principles of Diffusion MRI

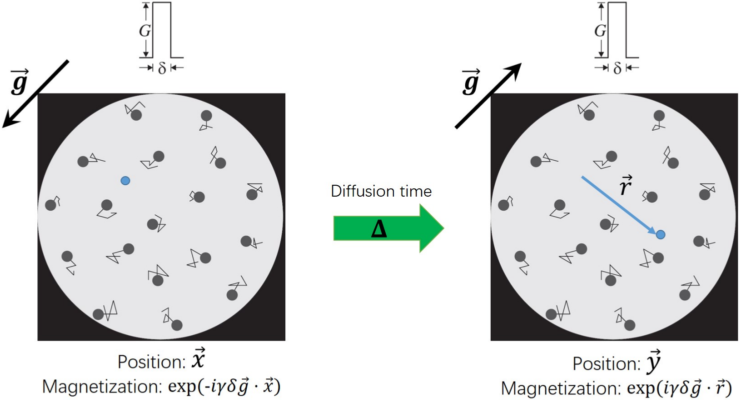


Principles of Diffusion MRI



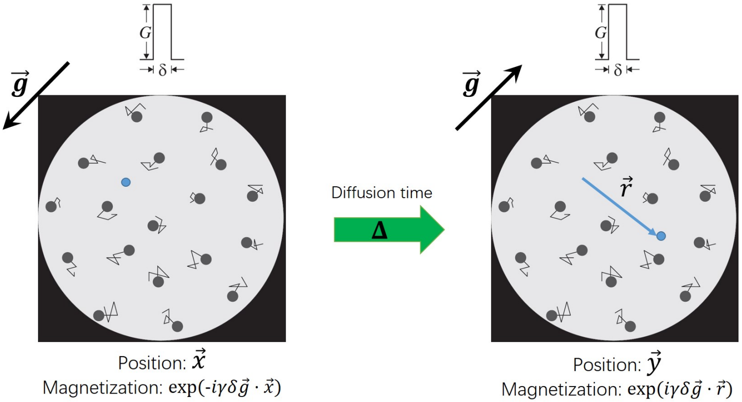
$$S(\vec{g}, \Delta) = \sum_{\vec{r}} n_r \cdot exp(i\gamma\delta\vec{g} \cdot \vec{r})$$

Principles of Diffusion MRI



$$S(\vec{g},\Delta) = \sum_{\vec{r}} N_{total} P(\vec{r},\Delta) exp(i\gamma\delta\vec{g}\cdot\vec{r})$$

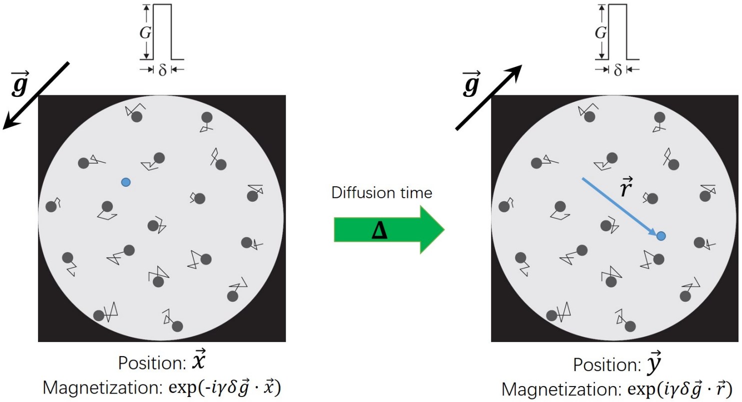
Principles of Diffusion MRI



$$S(\vec{g},\Delta) = \sum_{\vec{r}} N_{total} P(\vec{r},\Delta) exp(i\gamma\delta\vec{g}\cdot\vec{r})$$

$$\vec{q} = \gamma\delta\vec{g}/2\pi$$

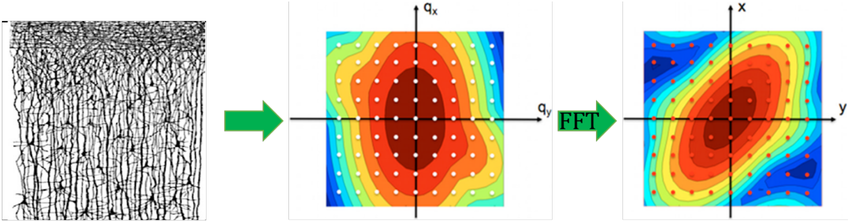
Principles of Diffusion MRI



$$\boldsymbol{S}(\vec{q},\Delta) = N_{total}\sum_{\vec{r}} \boldsymbol{P}(\vec{r},\Delta)exp(2\pi i\vec{q}\cdot\vec{r})$$

Fourier relationship between the measured signal $S(\vec{q},\Delta)$ and the diffusion propagator $P(\vec{r},\Delta)$.

Diffusion Spectrum Imaging (DSI)



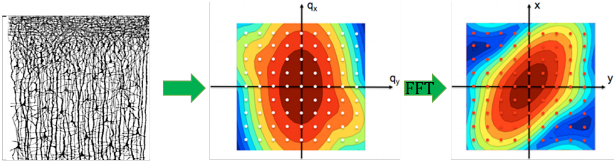
Underlying voxel structure

$S(\vec{q}, \Delta)$

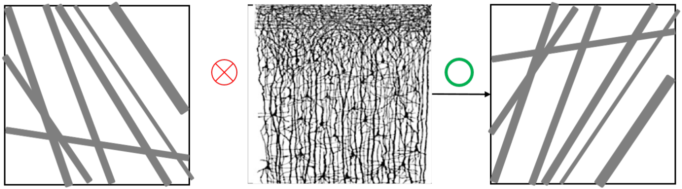
$P(\vec{r}, \Delta)$

[Van 2010]

Diffusion Spectrum Imaging (DSI)



Underlying voxel structure $S(\vec{q}, \Delta)$ $\mathrm{P}(\vec{r}, \Delta)$



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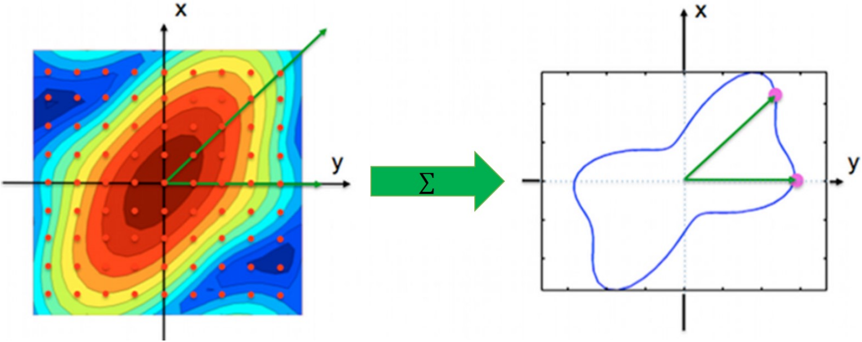
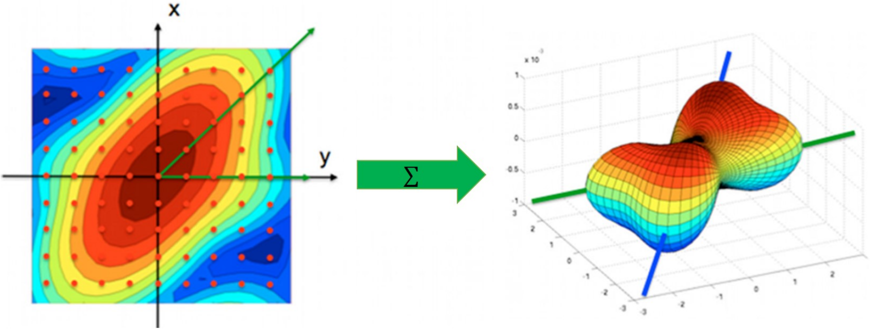


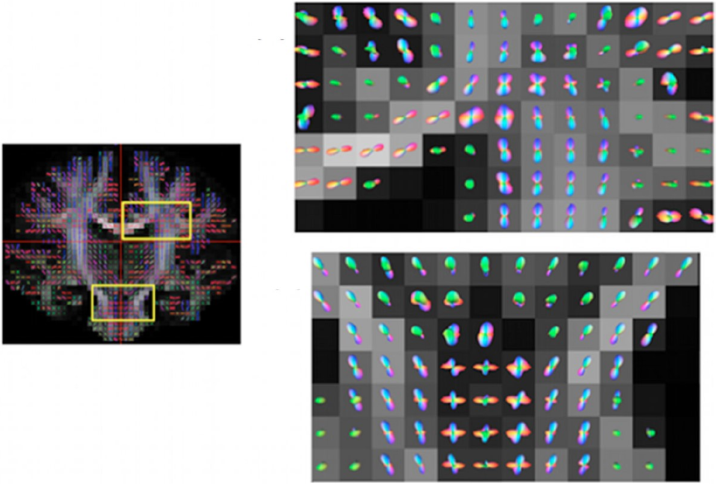
[Van 2010]

Diffusion Spectrum Imaging (DSI)



[Van 2010]

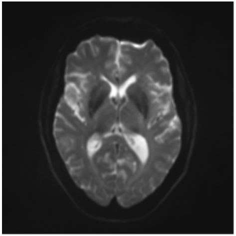
DSI Tractography



[Van 2010]

Model-Independent Diffusion MRI

- Diffusion Spectrum Imaging (DSI)
- Diffusion-Weighted Imaging (DWI) $S(\overrightarrow{q}, \tau) = S_0 \cdot e^{-D_{eff}|\overrightarrow{q}|^2\tau}$
- Diffusion Tensor Imaging (DTI) $S(\overrightarrow{q}, \tau) = S_0 \cdot e^{-\overrightarrow{q}^T \mathbf{D}_{eff} \overrightarrow{q}\tau}$
- Diffusion Kurtosis Imaging (DKI)
- etc.



An example of DWI image
[Radiopaedia.org, rID: 33859]

Model-Independent Diffusion MRI

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- Diffusion Kurtosis Imaging (DKI)
- etc.

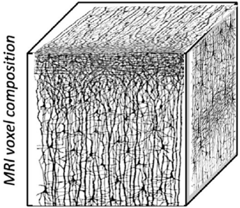
Motivation 1

The understanding of the physical process affects the way of the image reconstruction.
We can take an alternative perspective — Bloch-Torrey equation:

$$\frac{\partial}{\partial t} M(\boldsymbol{x}, t) = -i\gamma \boldsymbol{g} \cdot \boldsymbol{x}\, M(\boldsymbol{x}, t) + \nabla \cdot (\mathcal{D} \nabla M(\boldsymbol{x}, t))$$

Biophysical model based Diffusion MRI

The models of the brain microstructure



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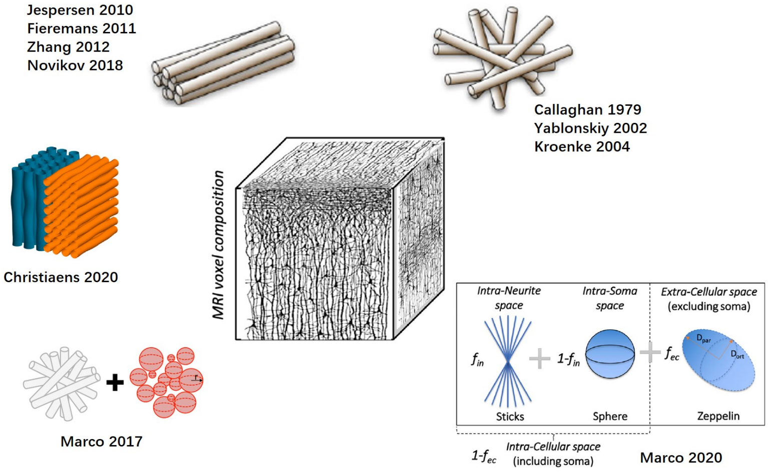

Biophysical model based Diffusion MRI

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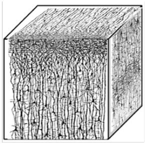

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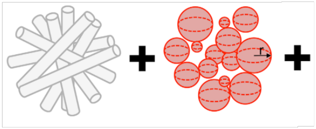

Extracellular space

neurites somas ECS

$$S(b,\xi) = S_0\left[f_n e^{-b.D_n^{\perp} - b.(D_n^{\parallel} - D_n^{\perp})\xi^2} + f_s e^{-bD_s\xi^2} + (1 - f_n - f_s)e^{-bD_{ECS}} \right]$$

Biophysical model based Diffusion MRI

- Neurite Orientation Dispersion and Density Imaging (NODDI)
- White Matter Tract Integrity (WMTI)
- Soma And Neurite Density Imaging (SANDI)
- DIstribution of Anisotropic MicrOstructural eNvironments in Diffusion-compartment imaging (DIAMOND)
- Linearly Estimated Moments provide Orientations of Neurites And their Diffusivities Exactly (LEMONADE)
- etc.

Pros

- Neurite Density
- Dendrites orientation distribution
- Soma size and density

Cons

- Sensitive to the noise
- Failed in the grey matter
- Lack of validation

Biophysical model based Diffusion MRI

- Neurite Orientation Dispersion and Density Imaging (NODDI)
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- Linearly Estimated Moments provide Orientations of Neurites And their Diffusivities Exactly (LEMONADE)
- etc.

Motivation 2

The model of the brain microstructure also matters.
Realistic neuron models should be built and applied for the future research.

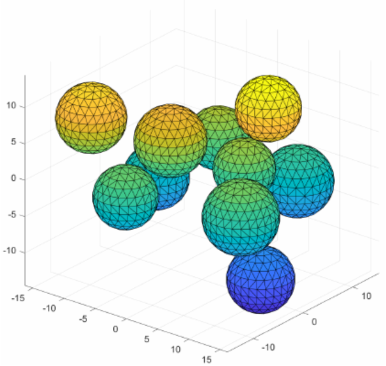
SpinDoctor & Neuron Module

SpinDoctor

SpinDoctor is a Matlab-based dMRI framework which employs the finite element method (FEM) to solve the Bloch-Torrey equation. [Li 2019]
Available on https://github.com/jingrebeccali/SpinDoctor

Features:

- Generate high quality FE meshes



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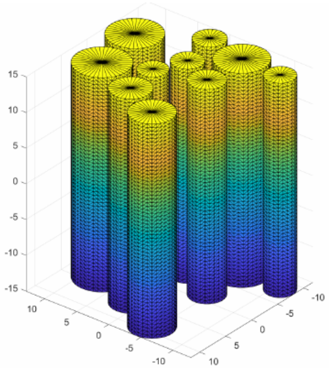

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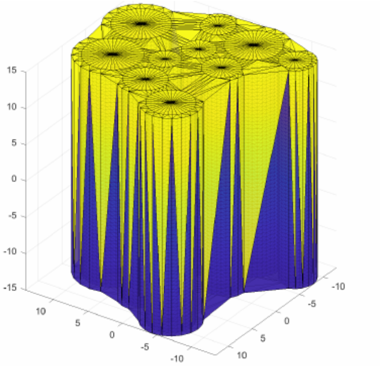

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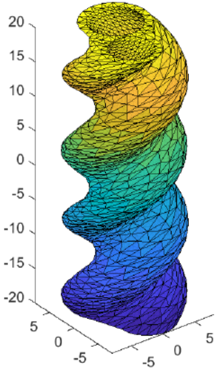

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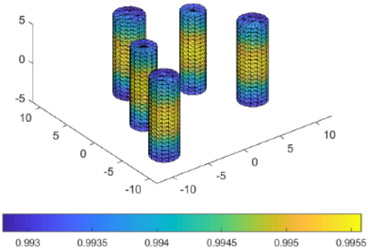
Features:

- Generate high quality FE meshes
- Analyse the compartments individually



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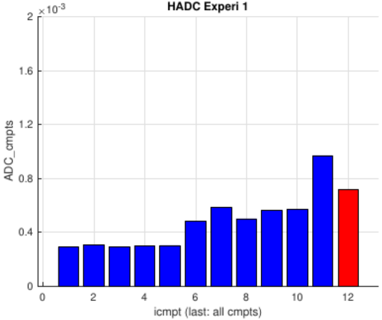

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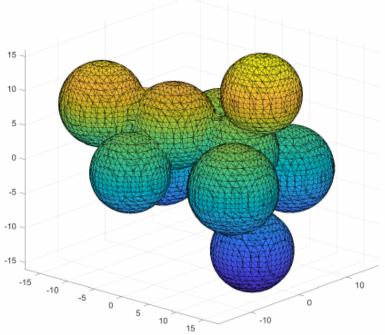
Features:

- Generate high quality FE meshes
- Analyse the compartments individually
- Support permeable interface



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Features:

- Generate high quality FE meshes
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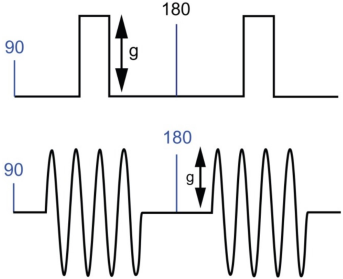
- Support permeable interface
- Support many types of diffusion-encoding pulse sequences



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Features:

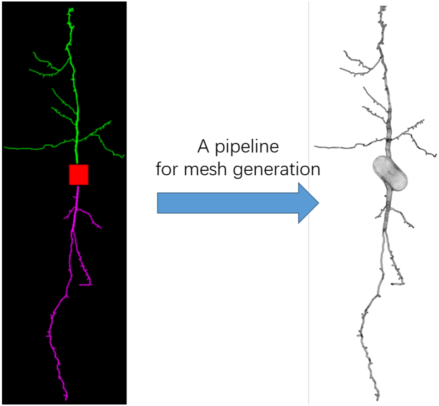
- Generate high quality FE meshes
- Analyse the compartments individually
- Support permeable interface
- Support many types of diffusion-encoding pulse sequences
- 100x faster than the classical Monte-Carlo simulator Camino

Camino logo

Neuron Module

Neuron Module is a new module of SpinDoctor which contains 65 embedded realistic neuron meshes.
The embedded neurons are built from the morphological descriptions published in NeuroMorpho.

NeuroMorpho's morphological descriptions obtained from microscopic measurement.



Neuron Module's meshes which are ready for finite element simulation, Monte-Carlo simulation, etc.

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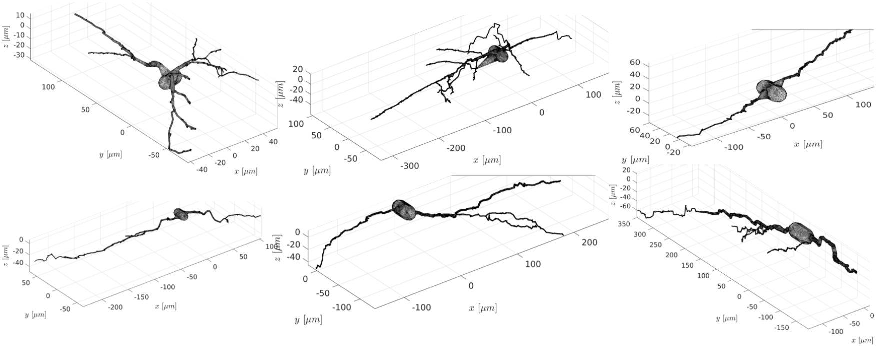

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Features:

- 30x faster than the GPU-based Monte-Carlo simulation

Computational time (s)		neuron	
$\delta = 10ms, \Delta = 43ms$	b	E_{max}	$t\ (s)$
SpinDoctor	1000	0.16	17.1
	4000	0.34	26.0
GPU Monte-Carlo	1000	0.14	537.8
	4000	0.60	1895.9
GPU MC/ SpinDoctor ratio	1000		31
	4000		72

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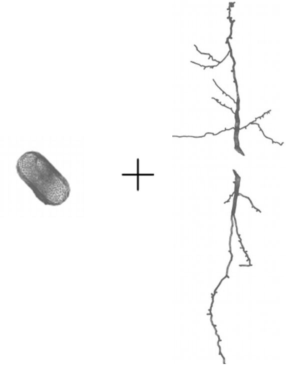
Features:

- 30x faster than the GPU-based Monte-Carlo simulation
- Separated neuron compartments



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Features:

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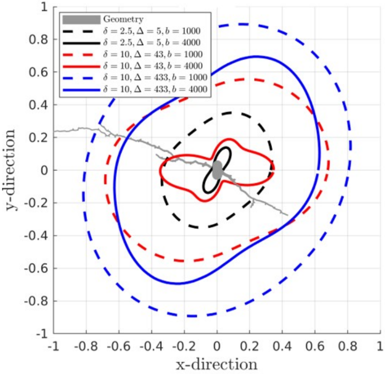
- Separated neuron compartments
- High angular resolution dMRI simulation



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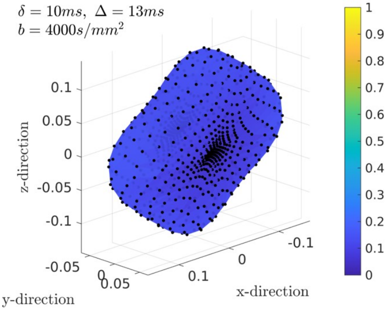
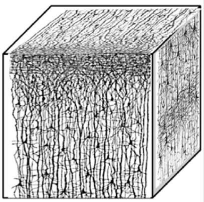


What difference can we make?

Validation of hypotheses



$\sim$

The power law hypothesis

For tubular structures such as cylinders, the diffusion direction averaged signal, $S_{ave}(b)$, is linear in $\frac{1}{\sqrt{b}}$:

$$S_{ave}(b) \equiv \int_{\|\boldsymbol{u_g}\|=1} S_{\boldsymbol{u_g}}(b) d\boldsymbol{u_g} \sim c_0 + c_1 \frac{1}{\sqrt{b}}.$$

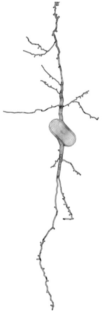
with $b = \gamma^2 \|\boldsymbol{g}\|^2 \delta^2 (\Delta - \delta/3)$ for PGSE sequences.

Validation of the power law

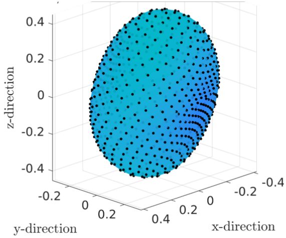
The indispensable Neuron Module features

- Realistic neuron meshes
- Separated neuron compartments
- High angular resolution
- High efficiency

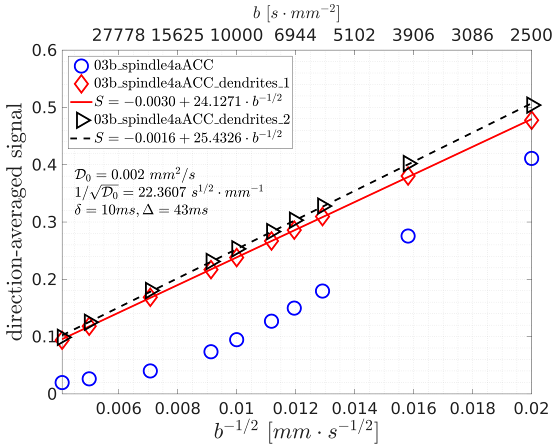
VS



dMRI signal simulated in 720 directions uniformly distributed on a unit sphere



Validation of the power law



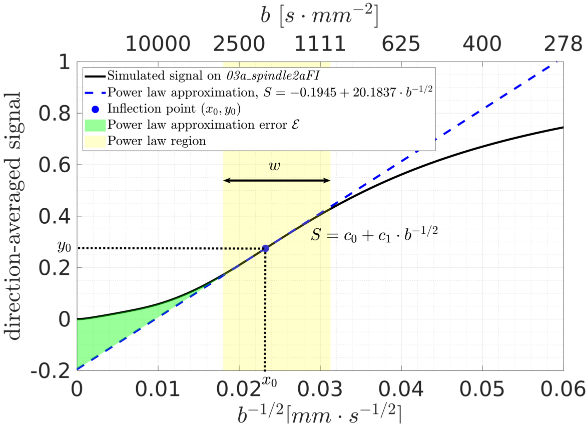
- The power law is valid for dendrite branches.
- Due to the presence of the soma, the power law is no longer valid for the whole neuron.

Potential biomarkers

By leveraging the collection of the realistic neuron meshes, we statistically show the deviation from the power law has the potential to serve as biomarkers for revealing the soma size.

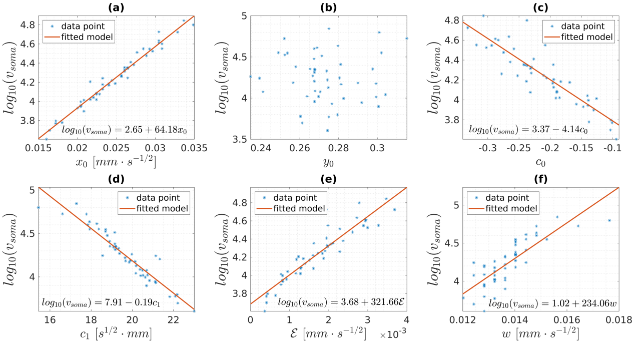
Definition of potential biomarkers

- x_0
- y_0
- c_0
- c_1
- $\mathcal{E}$
- w



Potential biomarkers

We performed a statistical study of the above 6 candidate biomarkers on the collection of the 65 neurons.



- x_0, c_0, c_1, $\mathcal{E}$ and w exhibit exponential relationship with the soma volume v_{soma}.

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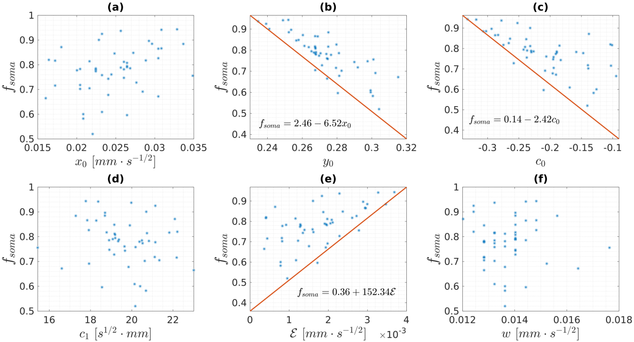

- x_0, c_0, c_1, $\mathcal{E}$ and w exhibit exponential relationship with the soma volume v_{soma}.
- y_0, c_0 and $\mathcal{E}$ seem capable of indicating the lower bound for the soma volume fraction f_{soma}.

Conclusion

Conclusion

- SpinDoctor provides an accurate and fast dMRI simulator for solving the Bloch-Torrey equation.
- Neuron Module which is built on SpinDoctor's FEM solver, allows us to solve the Bloch-Torrey equation on 65 embedded realistic neurons and their compartments.
- The combination of the advanced dMRI simulator and the realistic neuron models enables fast prototype validation and the design for new imaging methods.

Github repo: https://github.com/jingrebeccali/SpinDoctor
Paper: https://doi.org/10.1016/j.neuroimage.2020.117198

Thanks for your attention!

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