Mathematical modelling and numerical simulations applied to cardiac diffusion MRI

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Motivation

Diffusion MRI:

- Measures the diffusion of water molecules in the biological tissues.
- Allows the characterization of the microscopic structure of tissues.
- Provides assistance in the diagnosis of brain, cardiac abnormalities...

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Cardiac diffusion MRI:

Figure: Cardiac motion (Tagged MRI).

Figure: Diffusion-weighted MRI Images of the left ventricle during the cardiac cycle\(^1\).

Tissue motion $\implies$ Signal loss and bad reconstruction of diffusion MRI images.

\(^1\)S. Rapacchi et al. Investigative Radiology, 46(12):751–758 (2011)
Motivation

Diffusion MRI: Bloch-Torrey equation

– The Bloch-Torrey equation is given by:

$$\partial_t M - \text{div}(D \nabla M) + i \gamma x \cdot \mathbf{G}(t) M = 0. \tag{1}$$

$M$ is the magnetization, $D$ is a diffusion tensor of second order, and $\mathbf{G}$ is a diffusion encoding magnetic field gradient.
Motivation

**Diffusion MRI: Bloch-Torrey equation**

- The Bloch-Torrey equation is given by:

\[
\partial_t M - \text{div}(D \nabla M) + i \gamma x \cdot G(t) M = 0.
\]  

(1)

\(M\) is the magnetization, \(D\) is a diffusion tensor of second order, and \(G\) is a diffusion encoding magnetic field gradient.

- The diffusion MRI signal is:

\[
S(t) := \int_V M(x, t)dx.
\]
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PhD work: Numerical analysis of the Bloch-Torrey equation and application to cardiac diffusion MRI

Post-Doc project: In-vivo cardiac diffusion MRI: Simulations and parameters estimation

Motivation

Diffusion MRI: Diffusion measurement

**Figure:** Spin echo (ES) diffusion encoding gradient \((G(t))\).

**Figure:** (Left) Signal without diffusion \(S_0\). (Right) Signal with diffusion \(S\).
Motivation

Diffusion MRI: diffusion measurements

– The diffusion can be estimated at each point of the MRI image by the apparent diffusion coefficient (ADC):

\[
ADC := -\frac{1}{b} \ln \left( \frac{S_b}{S_0} \right).
\]  

(2)

\(S_b\) (resp. \(S_0\)) corresponds to the magnetization \(M\) measured with diffusion encoding gradient \(G(t)\) (resp. without diffusion encoding gradient), and

\[
b = \gamma^2 \int_0^{TE} \left( \int_0^{t'} G(s) ds \right)^2 dt'
\]

is the diffusion weighting factor.

Motivation

Diffusion MRI: diffusion measurements

– The diffusion can be estimated at each point of the MRI image by the *apparent diffusion coefficient* (ADC):

\[
ADC := -\frac{1}{b} \ln \left( \frac{S_b}{S_0} \right). \tag{2}
\]

\(S_b\) (resp. \(S_0\)) corresponds to the magnetization \(M\) measured with diffusion encoding gradient \((G(t))\) (resp. without diffusion encoding gradient), and

\[
b = \gamma^2 \int_0^{TE} \left( \int_0^{t'} G(s)ds \right)^2 dt'.
\]

is the diffusion weighting factor.

– Anisotropic diffusion: \(\ln \left( \frac{S}{S_0} \right) := -\mathbf{B} : \mathbf{D}^A\).

\(\mathbf{D}^A\) is the apparent diffusion tensor. \(\mathbf{B}\) is the diffusion weighted matrix:

\[
\mathbf{B} = \gamma^2 \int_0^{TE} \left( \int_0^{t'} G(s)ds \right) \otimes \left( \int_0^{t'} G(s)ds \right) dt'.
\]
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   1.1 Bloch-Torrey equation with motion
   1.2 Application to cardiac diffusion MRI
   1.3 Diffusion correction using an asymptotic model of the Bloch-Torrey equation with motion

2 Post-Doc project: In-vivo cardiac diffusion MRI: Simulations and parameters estimation
   2.1 Microscopic-scale numerical simulations of cardiac diffusion MRI
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Bloch-Torrey equation with motion: Mathematical model

The Bloch-Torrey equation in the deformed configuration:

$$\frac{\partial}{\partial t} M(X, t) - \text{div} X(D(X) \nabla X M(X, t)) + \text{div} X(M(X, t)v(X, t)) + i \gamma X G(t) M(X, t) = 0,$$

$$X \in \Omega(t), \quad t > 0. \quad (3)$$

The Bloch-Torrey equation in the reference configuration:

$$\frac{\partial}{\partial t} M(x, t) - \text{div} (F - 1(t, x)D(x)F - t(x)) \nabla M(x, t) + i \gamma \phi(x, t) \cdot G(t) M(x, t) = 0,$$

$$x \in \Omega(0), \quad t > 0. \quad (4)$$

$F$ is the Jacobian matrix of $\phi$,

$$F - t = (F - 1) t.$$

$v$ is the velocity field of $\phi$. 

Bloch-Torrey equation with motion: Mathematical model

Figure: Reference and deformed configurations. $\varphi$ is the deformation field.
Bloch-Torrey equation with motion:
Mathematical model

Figure: Reference and deformed configurations. $\varphi$ is the deformation field.

- The Bloch-Torrey equation in the deformed configuration:

$$
\partial_t M(X, t) - \text{div}_X (D(X) \nabla_X M(X, t)) + \text{div}_X (M(X, t)v(X, t)) + i\gamma XG(t)M(X, t) = 0, \quad X \in \Omega(t), \quad t > 0. \quad (3)
$$
Bloch-Torrey equation with motion: Mathematical model

The Bloch-Torrey equation in the deformed configuration:

\[
\partial_t M(X, t) - \text{div}_X (D(X) \nabla_X M(X, t)) + \text{div}_X (M(X, t)v(X, t)) + i\gamma X G(t) M(X, t) = 0, \quad X \in \Omega(t), \quad t > 0.
\] (3)

The Bloch-Torrey equation in the reference configuration:

\[
\partial_t M(x, t) - \text{div}(F^{-1}(t, x) D(x) F^{-t}(t, x) \nabla M(x, t)) + i\gamma \varphi(x, t) \cdot G(t) M(x, t) = 0, \quad x \in \Omega(0), \quad t > 0.
\] (4)

\(F\) is the Jacobian matrix of \(\varphi\), \(F^{-t} = (F^{-1})^t\). \(v\) is the velocity field of \(\varphi\).

Figure: Reference and deformed configurations. \(\varphi\) is the deformation field.
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Application to cardiac diffusion MRI: Analytical cardiac motion model in 2D

The heart deformation function $\varphi$ is given by:

$$\varphi(t, (R_0, \theta_0)) = \begin{cases} 
R(t) = \left( \frac{R_0^2 - R^2_{int}}{\lambda(t)} \right) g(\theta_0) + R_{int}(\theta_0, t)^2 \right)^{1/2} \\
\theta(t) = \theta_0 + \psi(t, R_0) + \chi(t) 
\end{cases}$$

with

$$\lambda(t) = 1 - 0.2S(t)$$

$$R_{int}(\theta_0, t) = R_{int} - (R_{int} - R_{min}) g(\theta_0) S(t)$$

$$g(\theta_0) = 1 + 0.1(\cos(\theta_0 + \pi/4) + 1)$$

$$R_{min} = R_{int} - 5(R_{ext} - R_{int})/6$$

$$\psi(t, R_0) = -(0.2\pi/180) S(t) R_0$$

$$\chi(t) = (10\pi/180) S(t).$$

- The cardiac deformation is controlled by the function $S$.

- The simulated cardiac cycle
  $\sim 1000\text{ms}$, with a systole time
  $\sim 330\text{ms}$ and a diastole time
  $\sim 660\text{ms}$.

**Figure:** Simulated cardiac motion.
Application to cardiac diffusion MRI: Numerical simulations

Unipolar Stimulated Echo (STEAM)
diffusion encoding gradient (G(t)).
Application to cardiac diffusion MRI: Numerical simulations

Unipolar Stimulated Echo (STEAM) diffusion encoding gradient \( G(t) \).

Exact diffusion.
Mathematical modelling and numerical simulations applied to cardiac diffusion MRI

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Application to cardiac diffusion MRI:
Numerical simulations

Unipolar Stimulated Echo (STEAM) diffusion encoding gradient (G(t)).

Exact diffusion.

ADC images at different times of the cardiac cycle.
Application to cardiac diffusion MRI: Numerical simulations

Unipolar Stimulated Echo (STEAM) diffusion encoding gradient \( G(t) \).

ADC images at different times of the cardiac cycle.

Mean ADC during the cardiac cycle.
Application to cardiac diffusion MRI: Comparison with experimental results

Figure: Time curve of mean trace of the diffusion tensor \( \text{tr}(D) \) obtained from a normal subject with a heart rate of approximately 72 bpm and locations of two sweet spots, at mid-systolic and mid-diastolic moments, indicated by the intersections of the curve with \( \langle \text{tr}(D(t)) \rangle_\epsilon \). (Figure extracted from\(^2\)).

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Diffusion correction using an asymptotic model

- Transformation of the Bloch-Torrey equation:

\[ M(x, t) = m(x, t) \exp \left( -i\Phi(x, t) \right) \]  (5)

\[ \Phi(x, t) = \gamma \int_{0}^{t} \varphi(x, t') \cdot G(t') dt' \]
Diffusion correction using an asymptotic model

- Transformation of the Bloch-Torrey equation:

\[ M(x, t) = m(x, t) \exp \left( -i \Phi(x, t) \right) \]  \hspace{1cm} (5)

\[ \Phi(x, t) = \gamma \int_0^t \varphi(x, t') \cdot G(t') dt' \]

- Asymptotic expansion of \( m \):

\[ m = m_0 + \varepsilon m_1 + \cdots \]

\( m \rightarrow m_0 \) formally with \( \varepsilon \), where \( m_0 \) satisfies:

\[ \partial_t m_0(x, t) + (K \nabla \Phi \cdot \nabla \Phi) m_0(x, t) = 0 \text{ in } \Omega \times (0, T) \]

\[ m_0(x, 0) = m^0(x) \text{ on } \Omega \times \{0\}, \]  \hspace{1cm} (6)

\[ K(x, t) = F^{-1}(t, x) D(x) F^{-t}(t, x). \]
**Diffusion correction using an asymptotic model: Diffusion correction formula**

- Then the magnetization $M$ is:

$$M(x, t) \approx m^0(x) \exp \left( - \int_0^t (\nabla \Phi(x, t'))^t K(x, t') \nabla \Phi(x, t') dt' \right) \exp \left( - i \Phi(x, t) \right).$$
Diffusion correction using an asymptotic model: Diffusion correction formula

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– Recovery of the exact diffusion:

We have $K = F^{-1} DF^{-t}$, the diffusion attenuation can be written as:

$$\ln \left( \frac{M(x, TE)}{M(x, TE)|_{G=0}} \right) = - \int_0^{TE} (\nabla \Phi(x, t'))^t K(x, t') \nabla \Phi(x, t') dt'.$$
Diffusion correction using an asymptotic model: Diffusion correction formula

- Then the magnetization $M$ is:

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- Recovery of the exact diffusion:

We have $K = F^{-1}D F^{-t}$, the diffusion attenuation can be written as:

$$\ln \left( \frac{\|M(x, TE)\|}{\|M(x, TE)|_{G=0}\|} \right) = - \int_0^{TE} (\nabla \Phi(x, t'))^t K(x, t') \nabla \Phi(x, t') dt'$$

$$:= \mathbf{B}_\varphi : \mathbf{D}(x)$$

with

$$\mathbf{B}_\varphi = \left( \int_0^{TE} \mathbf{w}(x, t') \otimes \mathbf{w}(x, t') dt' \right)$$

and $\mathbf{w}(x, t) = F^{-t}(x, t) \nabla \Phi(x, t)$, and $\mathbf{D}$ is the exact diffusion tensor.
Diffusion correction using an asymptotic model: Simulations

Figure: ADC images simulated at different times in the cardiac cycle. Before correction (Top). After correction by the asymptotic model (Bottom).

Figure: Exact diffusion.
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Microscopic-scale numerical simulations of cardiac diffusion MRI

Equipe DEFI, INRIA-Saclay:

- Contributing expertise to the project: diffusion MRI, inverse problems, mathematical homogenization.
- Under the supervision of: Jing-Rebecca Li and Houssem Haddar.

Figure: Cardiac microstructure: schematic presentation of heart muscle fibers.
Microscopic-scale numerical simulations of cardiac diffusion MRI

Multiple compartments Bloch-Torrey equation:

Integrate sub-compartments with interface conditions: \( \Omega \subset \mathbb{R}^3 \) a volume of biological tissue.
- \( \Omega \equiv \Omega_i \cup \Omega_e \),
- \( \Omega_e \): extra-cellular space,
- \( \Omega_i \): union biological cells. \( \Gamma \): union of the boundaries of biological cells.
- \( \kappa \): cellular permeability.

\[
\begin{align*}
\frac{\partial}{\partial t} M - \text{div}(F^{-1}DF^{-t}\nabla M) + i\gamma G(t) \cdot \varphi(x, t)M &= 0 \text{ in } \Omega \times (0, T) \\
F^{-1}DF^{-t}\nabla M \cdot n |_{\Gamma} &= \kappa[M] \text{ on } \Gamma \times (0, T) \\
[F^{-1}DF^{-t}\nabla M \cdot n] &= 0 \text{ on } \Gamma \times (0, T) \\
M(x, 0) &= M_{\text{ini}}(x) \text{ on } \Omega \times \{0\}.
\end{align*}
\]

Figure: Example of computational domain \( \Omega \) with intra-cellular space (the cylinders) and extra-cellular space (extra-cylinder region).
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Parameters estimation for cardiac diffusion MRI

Chair of Computational Mathematics and Simulation Science (MCSS), EPFL.

- Contributing expertise to the project: high order and adaptive numerical solution of PDEs, reduced models.
- With: Pr. Jan Hesthaven.

Estimation of macroscopic apparent diffusion coefficient (ADC) after mathematically cancelling the effects of cardiac motion and deformation:

- Data set library from simulations: Generate large number of ADC images in the presence of heart motion at different times of cardiac cycle by solving the Bloch-Torrey equation with prescribed motion to make a library.
- Generate reduced model to map the distorted ADC image to the original ADC image.
Thank you!