Nanoparticle Magnetic Relaxometry for Cancer Detection

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Abstract

Early detection is key to survival for cancer patients. Screening is the best way to catch cancer in its early stages, but for many anatomical sites no screening technique is available. Current screening techniques can often yield false positives or inconclusive results, which lead to unnecessary invasive procedures and treatment. Additionally, even the best methods can only detect tumors as small as 2 mm in diameter, which is already ¿10 million cells. In an effort to provide clinicians with a reliable non-invasive method of detecting cancer in its very early stages, a system that uses the magnetic relaxometry properties of nanoparticles has been developed to detect and count clusters of cancer cells as few as 20,000. For most cancer patients, detection this early could mean the difference between successful and unsuccessful treatment.

Overall Goals: There are many questions to be answered regarding this new system. Below are project goals that are needed to translate this technology into the clinical setting.

1. Develop and calibrate a model for detecting the number and location of nanoparticles in a sample by solving an inverse problem set with known sources.
2. Determine the optimal biokinetic model to describe the nanoparticle interactions with different cell lines.
3. Evaluate the feasibility and resolution limitations of imaging disease with magnetic relaxometry.
4. Differentiate between magnetic relaxometry signals from nanoparticles bound to different targets.

Action Items:

- Develop a mathematical model of the Relaxometry detection system from first principles [Flynn and Bryant(2005)]. The signal relaxation is assumed of the form:

$$F(t) = a_0 + a_1 \ln\left(1 + \frac{a_2}{t}\right) + a_3 \exp\left(-a_4\, t\right)$$

- Acquire Phantom data in 1, 2, 3, 4, 5 point sources. Build a data dictionary of signals from combinatorics of sources and source locations.
  - Apply unsupervised machine learning (clustering algorithms) to classify the signal from 1, 2, 3, 4, or 5 sources at different locations [Fraley(2002), Sebastiani et al.(2003)Sebastiani, Kohane, and Ramoni, Kapp and Tibshirani(2007), Shi et al.(2014)Shi, Horvath, Journal, Statistics, Mar, and Url, Criminisi(2013), Murphy(2012), Bishop(2006), Gelman(200
    Ie how ill-posed is the problem ? which combinations of sources and source locations cluster together ?
- Validate phantom measurements using deterministic quasi-newton curve fit of math model [Fegan et al.(2010)Fegan, Venturini, M
  Adolphi et al.(2010)Adolphi, Huber, Bryant, Monson, Fegan, Lim, Trujillo, Tessier, Lovato, Butler, Provencio, Hathaway, Maj
  Hathaway et al.(2011)Hathaway, Butler, Adolphi, Lovato, Belfon, Fegan, Monson, Trujillo, Tessier, Bryant, Huber, Larson, an
  Tessier and Flynn(2012), Adolphi(2014), Schwindt and Flynn(2013), Shen et al.(2012)Shen, Cai, Wang, Cao, Li, Wang, Guo, Z
  Hajdu et al.(2013)Hajdu, Bodnár, Trencsényi, Márián, Vámosi, Kollár, and Borbély, Paik et al.(2013)Paik, Gordon, Prantner,
  Amiri et al.(2011)Amiri, Mahmoudi, and Lascialfari]. Use initial guess as centroid of machine.
- Compare deterministic inverse problem to advanced methods:
  1. Global optimization using dictionary.
     - in-silico simulate 1, 2, 3, 4, 5 point sources. Build a dictionary of signals from combinatorics of sources and source locations.
     - Code signal forward projection operator as a GPU kernel call from MATLAB
  2. Gaussian Process model [Rasmussen et al.(2006)Rasmussen, Williams, Processes, Press, and Jordan] with phantom data as training data

– Formulate Gaussian Process model within a physics based optimization framework [Constantinescu and Anitescu(2013)], ie constrain the optimization by the physics model
– Solve using MCMC [Liu(2002), Martin and Ghattas(2012), Kaipio and Somersalo(2005), Thanh(2012)]

- Evaluate within the context of a classical statistics framework, ie [Rosner(2010)] Ch 11.

1 Magnetostatics, Hard Ferrormagnets (M given and J=0)

Following Jackson [Jackson(1999)], 'hard' ferromagnets, having a magnetization that is essentially independent of the applied fields may be treated as if they have a fixed magnetization $\vec{M}(x)$. Guass law for magnetism becomes

$$\nabla \cdot \vec{B} = \mu_0 \nabla \cdot (\vec{H} + \vec{M})$$

Given the magnetic scalar potential

$$\nabla \Phi_M \equiv \vec{H}$$

and the effective magnetic-charge density

$$\rho_M \equiv -\nabla \cdot \vec{M}$$

Gauss law reduces to a poisson equation

$$\nabla^2 \Phi_M = \rho_M$$

The Greens function solution to this equation is

$$\Phi_M = \int G(x,y)\rho_M(y)dy \qquad G(x,y) = \frac{1}{4\,\pi\,r}$$

Under the assumption that the effective magnetic-charge density is of the form of the divergence of a point source magnetic dipole, $\vec{\mu} \in \mathbb{R}^3$

$$\rho_M(x) = \nabla_x \cdot \vec{\mu}\delta(x - x_0)$$

The solution must be interpreted in the sense of distributions and reduces to the classical dipole equations

$$\begin{aligned}
\Phi_M &= \int G(x,y)(\nabla_y \cdot \vec{\mu}\delta(y - x_0))dy \\
&= \int \left(\frac{\partial}{\partial y_1} G(x,y)\mu_1\delta(y - x_0) + \frac{\partial}{\partial y_2} G(x,y)\mu_2\delta(y - x_0) + \frac{\partial}{\partial y_3} G(x,y)\mu_3\delta(y - x_0) \right) dy \\
&= \nabla_x G(x, x_0) \cdot \vec{\mu} \\
&= \frac{\vec{r} \cdot \vec{\mu}}{4\,\pi\,r^3}
\end{aligned}$$

$$\vec{B} = \mu_0 \nabla \Phi_M = \frac{\mu_0}{4\pi} \left(\frac{3\vec{r}(\vec{r} \cdot \vec{\mu})}{r^5} - \frac{\vec{\mu}}{r^3} \right)$$

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