Short Note on Diffusion MRI for Physicists

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1 Introduction

Diffusion MRI (dMRI) is a technique that measures how water (typically) molecules move in e.g. biological tissue on a microscopic scale. In tissues such as the brain, water diffusion is affected by obstacles like cell membranes, fibers, and organelles. dMRI exploits the random, thermally driven motion of these molecules to infer information about the tissue microstructure non-invasively.

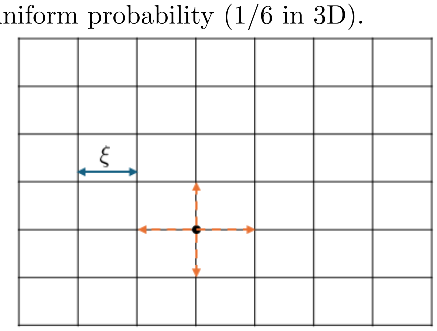
In this note, we will start from the stochastic description of diffusion, derive the diffusion equation in two different ways, and present the MRI signal equation. We will also discuss how to extend this to non-Gaussian diffusion, including the Diffusion Kurtosis Imaging (DKI) model. We will also sketch how to perform Monte Carlo computer simulations of diffusion.

2 Diffusion as a Random Walk

Water molecules undergo random motion due to thermal energy. Consider a particle that at each time step Δt takes a random step of length ξ in each Cartesian direction, independently. The position $\boldsymbol{r}_n$ after $t = n\Delta t$ steps is thus

$$\boldsymbol{r}_n = \boldsymbol{r}_0 + \sum_{m=1}^{n} \xi \boldsymbol{\eta}_m \tag{1}$$

where $\boldsymbol{\eta}$ is a stochastic variable equal to plus or minus one of the unit coordinate vectors, $\pm\hat{\boldsymbol{e}}_j$, with uniform probability (1/6 in 3D).



Let $P(\boldsymbol{r}, t)$ be the probability density of finding a particle at position $\boldsymbol{r}$ at time t. In a simple cubic lattice model, the probability at position $\boldsymbol{r}$ after a short time step becomes:

$$P(\boldsymbol{r}, t+\Delta t) = \frac{1}{6}\sum_{j=1}^{3}\left[P(\boldsymbol{r}+\xi\,\hat{\boldsymbol{e}}_j, t) + P(\boldsymbol{r}-\xi\,\hat{\boldsymbol{e}}_j, t)\right]. \tag{2}$$

This equation simply expresses that the spin can end up at $\boldsymbol{r}$ at time $t+\Delta t$ if it resided at one of the 6 nearest neighbour sites at time t.

Derivation of the diffusion equation

Expanding P in a Taylor series:

$$P(\boldsymbol{r}\pm\xi\,\hat{\boldsymbol{e}}_j, t) = P(\boldsymbol{r}, t) \pm \xi\,\partial_j P + \frac{\xi^2}{2}\partial_j^2 P + \mathcal{O}(\xi^3).$$

where $\partial_j = \partial/\partial r_j$. Summing over $j = 1, 2, 3$, the first-order terms cancel:

$$P(\boldsymbol{r}, t+\Delta t) = P(\boldsymbol{r}, t) + \frac{\xi^2}{2}\nabla^2 P + \mathcal{O}(\xi^3).$$

In the limit $\Delta t \to 0$, $\xi \to 0$ with $\xi^2/2\Delta t = D$ finite, we recover the diffusion equation:

$$\frac{\partial P}{\partial t} = D\nabla^2 P. \tag{3}$$

The constant D is the diffusivity and has units of length squared over time. For water at 37°C, it has a value of $D \approx 3\mu m^2/ms$. To solve the diffusion equation we need to specify initial conditions ($P(\boldsymbol{r}, 0)$) and boundary conditions.

3 Diffusion Equation from Fick's Law and Conservation of Mass

Fick's first law is a phenomenological law that relates the diffusive flux $\boldsymbol{J}(\boldsymbol{r}, t)$ to the gradient of concentration or probability:

$$\boldsymbol{J} = -D\nabla P. \tag{4}$$

It expresses the physical expectation that the current flows so as to even out concentration gradients. Conservation of mass or probability yields:

$$\frac{\partial P}{\partial t} + \nabla\cdot\boldsymbol{J} = 0.$$

Inserting into this Fick's law for **J** gives :

$$\frac{\partial P}{\partial t} = D\nabla^2 P.$$

4 The Propagator

We now define the propagator or Green's function:

$$\mathcal{G}(\boldsymbol{r}, \boldsymbol{r}_0; t) = P(\boldsymbol{r}, t \mid \boldsymbol{r}_0, 0), \quad t > 0 \tag{5}$$

which gives the probability of a particle being at position $\boldsymbol{r}$ at time t given that it started at $\boldsymbol{r}_0$. In other words, it solves the diffusion equation for the initial condition $P(\boldsymbol{r}, 0) = \delta(\boldsymbol{r} - \boldsymbol{r_0})$.

5 Solution for Free Diffusion: Gaussian Propagator

The diffusion equation with this initial equation and "free" boundary conditions ($P \to 0$ when $r \to \infty$) is solved by:

$$\mathcal{G}(\boldsymbol{r}, \boldsymbol{r}_0; t) = \frac{1}{(4\pi D t)^{3/2}} \exp\left(-\frac{|\boldsymbol{r} - \boldsymbol{r}_0|^2}{4Dt}\right), \quad t > 0. \tag{6}$$

This is the fundamental solution describing a Gaussian spreading of probability, and is consistent with the Central Limit theorem for a sum of stochastic variables, Eq. 1.

6 Mean Squared Displacement and Einstein Relation

The mean squared displacement (MSD) for Gaussian diffusion is:

$$\langle |\boldsymbol{r}(t) - \boldsymbol{r}(0)|^2 \rangle = 6Dt. \tag{7}$$

This result is a defining characteristic of (free) diffusion. It can be computed also from the basic random walk picture. First we find $\langle \boldsymbol{\eta} \rangle$ and $\langle \boldsymbol{\eta^2} \rangle$. The mean is clearly 0 as $\hat{\boldsymbol{e}}_j$ and $-\hat{\boldsymbol{e}}_j$ occur with equal probability. For the second moment,

$$\langle \boldsymbol{\eta^2} \rangle = 1/6 \sum_{j=1}^{3} \left((\hat{\boldsymbol{e}}_j)^2 + (-\hat{\boldsymbol{e}}_j)^2 \right) = 1$$

so

$$\langle (\boldsymbol{r}_n - \boldsymbol{r}_0)^2 \rangle = \sum_{m,m'=1}^{n} \xi^2 \langle \boldsymbol{\eta}_m \boldsymbol{\eta}_{m'} \rangle = \sum_{m=1}^{n} \xi^2 \langle \boldsymbol{\eta}_m^2 \rangle = n\xi^2 = (t/\Delta t)\xi^2 \equiv 2Dt \tag{8}$$

using $n\Delta t = t$. For anisotropic diffusion, D becomes a 3 x 3 symmetric, positive definite tensor and

$$\langle (r_i(t) - r_i(0))(r_j(t) - r_j(0)) \rangle = 2D_{ij}t. \tag{9}$$

7 Diffusion and MRI: Phase Accumulation

The xy component (so-called transverse part) of a spin magnetic moment (strictly speaking, its quantum mechanical expectation value) is described by a phase factor, $e^{-i\phi}$, see the note on MRI for physicists. The phase of a spin at position $\boldsymbol{r}(t)$ evolves according to an angular frequency determined by the Larmor equation:

$$\omega(\boldsymbol{r}(t)) = \gamma \delta B_z(\boldsymbol{r}(t), t) \tag{10}$$

where $\delta B_z(\boldsymbol{r}, t) = B_z(\boldsymbol{r}, t) - B_0$ is the deviation from the static magnetic field $B_0 \hat{z}$. The total accumulated phase at time t is then

$$\phi(t) = \int_0^t \omega(\boldsymbol{r}(t'))dt'. \tag{11}$$

The transverse magnetization is as mentioned previously:

$$M_\perp(t) \sim \sum_n \exp(-i\phi_n(t))$$

where the sum is over spins. The MRI signal is proportional to the transverse magnetization, and we write

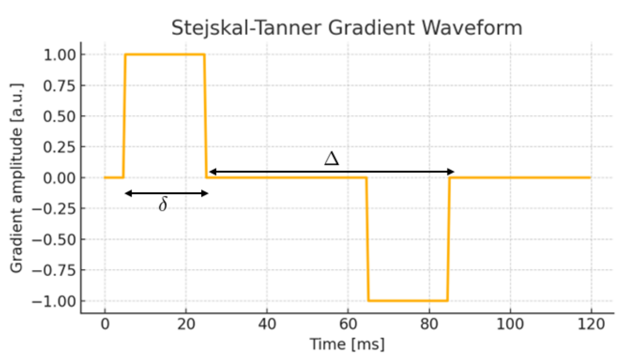
$$S = \left\langle e^{-i\phi} \right\rangle$$

where angular brackets denote average over spins, or equivalently, over the phase distribution.

8 Stejskal-Tanner Sequence

The Stejskal-Tanner sequence uses two gradient pulses:

$$\delta B_z(\boldsymbol{r}, t) = \begin{cases} \boldsymbol{G} \cdot \boldsymbol{r}, & t \in [0, \delta], \\ -\boldsymbol{G} \cdot \boldsymbol{r}, & t \in [\Delta, \Delta + \delta]. \end{cases}$$



Note that the gradients here are gradients of the magnetic field's z-component, i.e., $\boldsymbol{G} = \nabla B_z$. A static spin would thus accumulate zero net phase, as the effect of the two gradients cancel, but diffusing (or moving) spins acquire a net phase dependent on their displacement. Given the Larmor equation, it's convenient to write it in terms of the Larmor frequency

$$\delta\omega(\boldsymbol{r}, t) = \begin{cases} \boldsymbol{g} \cdot \boldsymbol{r} & t \in [0, \delta], \\ -\boldsymbol{g} \cdot \boldsymbol{r}, & t \in [\Delta, \Delta + \delta]. \end{cases}$$

where $\boldsymbol{g} = \gamma \boldsymbol{G}$ is the Larmor frequency gradient.

9 Signal in Terms of the Propagator

Under the Stejskal-Tanner sequence, if we ignore diffusion during the gradient application δ (infinitely narrow pulses), each spin's phase becomes $\phi(t) = \delta \cdot \boldsymbol{g} \cdot (\boldsymbol{r}(t) - \boldsymbol{r}(0))$ upon renaming $\Delta \to t$. Introducing the diffusion wave vector with $\boldsymbol{q} = \gamma\delta\boldsymbol{G} = \delta\boldsymbol{g}$, we then have

$$S = \left\langle e^{-i\phi} \right\rangle = \left\langle e^{-i\boldsymbol{q}\cdot(\boldsymbol{r}(t)-\boldsymbol{r}(0))} \right\rangle$$

The average over spins can be rewritten as an average over trajectories leading to

$$S = \int d^3\boldsymbol{r}_0 P(\boldsymbol{r}_0, 0) \int d^3\boldsymbol{r}\, \mathcal{G}(\boldsymbol{r}, \boldsymbol{r}_0; t) \exp\left(-i\boldsymbol{q} \cdot (\boldsymbol{r} - \boldsymbol{r}_0)\right) \tag{12}$$

Often, the initial spin density is uniform, $P(\boldsymbol{r}_0, 0) = 1/V$ with V the volume of the system.

10 Gaussian Diffusion Signal

For free diffusion, combing Eqs. 6 and 12, we find

$$S = \exp(-bD), \tag{13}$$

where

$$b = (\gamma G\delta)^2(\Delta - \delta/3) = q^2(\Delta - \delta/3).$$

is the diffusion weighting (b-value), with dimensions of inverse diffusivity. Equation 13 is often a good approximation for b-values below $1ms/\mu m^2$. When diffusion is anisotropic, we find (implying summation over repeated indices)

$$S = \exp(-b_{ij}D_{ij}), \tag{14}$$

and

$$b_{ij} = (\gamma\delta)^2 G_i G_j(\Delta - \delta/3) = q_i q_j(\Delta - \delta/3)$$

11 Diffusion Kurtosis Imaging (DKI)

Real biological tissues do not feature perfectly Gaussian diffusion. The cumulant expansion is a Taylor series of the log of the signal as function of b or q around $b = 0$:

$$\ln S = -bD + \frac{1}{6}b^2 D^2 K + \cdots .$$

Here, K is the **kurtosis** describing the leading deviation from Gaussianity. Terminating the series with this term comprises the so-called diffusion kurtosis imaging (DKI). When diffusion is anisotropic, the kurtosis term becomes $\frac{1}{6} b_{ij} b_{kl} \operatorname{Tr}(D)^2 W_{ijkl}$, where W is the kurtosis tensor, a rank-4 fully symmetric tensor (81 elements but only 15 independent).

12 Time Dependent Diffusion Coefficient $D(t)$ via MSD

For general (non-Gaussian) diffusion we define the time dependent diffusivity $D(t)$ by analogy to the MSD for free diffusion:

$$D(t) \equiv \frac{1}{6t} \langle |\boldsymbol{r}(t) - \boldsymbol{r}(0)|^2 \rangle.$$

Thus, for free diffusion, this gives the constant D, but in general media, $D(t)$ becomes time-dependent. For example, if spins are confined, $\langle |\boldsymbol{r}(t) - \boldsymbol{r}(0)|^2 \rangle$ is bounded and the diffusivity eventually falls off as $\sim 1/t$.

13 Monte Carlo Simulation of Diffusion MRI

A simple Monte Carlo approach:

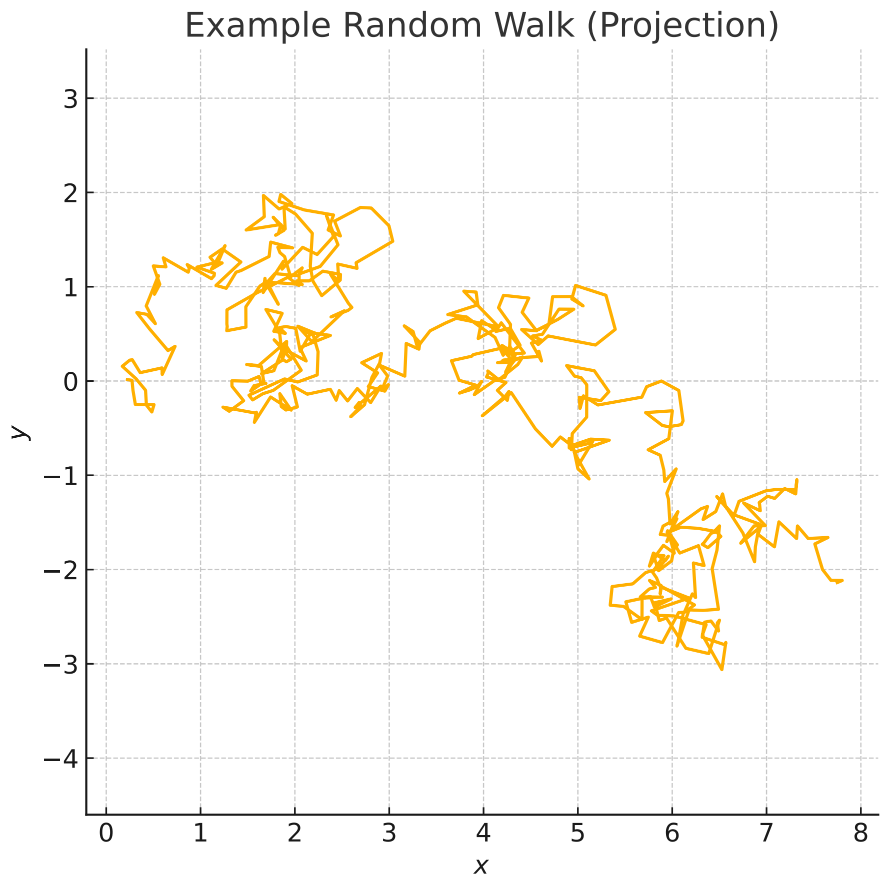
1. Simulate random walks for N particles.
2. Accumulate phase:
$$\phi_n = \int_0^T \boldsymbol{g}(t) \cdot \boldsymbol{r}_n(t) dt$$
3. Compute $S = \frac{1}{N} \sum_n e^{-i\phi_n}$

This method can handle arbitrary geometries and non-Gaussian effects naturally. In more detail:

Algorithm 1 Monte Carlo Simulation of Diffusion MRI Signal

Require: Number of particles N, total experiment time T, time step dt, diffusion coefficient D, gyromagnetic ratio γ, gradient waveform $\boldsymbol{G}(t)$

for each particle $n = 1$ to N **do**
  Set initial positions $\boldsymbol{r}_n$, typically uniformly in simulation volume.
  Set accumulated phase $\phi_n = 0$
end for
for each particle $n = 1$ to N **do**
  for time t from 0 to T in steps of dt **do**
    for each direction $i \in \{x, y, z\}$ **do**
      Update the position: $r_n[i] \leftarrow r_n[i] + \mathcal{N}(0, \sqrt{2Ddt})$. Account for boundary conditions, e.g. reflecting walls.
    end for
    Update the phase: $\phi_n \leftarrow \phi_n + \gamma \boldsymbol{G}(t) \cdot \boldsymbol{r}_n dt$
  end for
  Compute transverse magnetization: $M_n \leftarrow e^{-i\phi_n}$
end for
Compute the signal: $S(T) = \frac{1}{N} \sum_{n=1}^{N} M_n$


Example Random Walk (Projection)
3
2
1
0
−1
−2
−3
−4
y
0
1
2
3
4
5
6
7
8
x