On the problem of an additional phase term in diffusion MRI in anisotropic media

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Introduction: The Bloch-Torrey equation has been used to analyze the diffusion MR signal for anisotropic media where theoretical analysis yields the term $\nabla\cdot[D(\mathbf{r},t)\nabla\int_0^t \Delta B(\mathbf{r},\tau)d\tau] \equiv \Omega(\mathbf{r},t)/\gamma$ where B is the magnetic field and $D(\mathbf{r},t)$ the diffusion tensor. The factor $\Omega(\mathbf{r},t)/\gamma$ has units of magnetic field and characterises the influence of magnetic field gradient $\nabla(\Delta B)$ on diffusion tensor $D(\mathbf{r},t)$ of the anisotropic media. Under the influence of this term, spins precess with a frequency of $\Omega(\mathbf{r},t)$ in addition to the Larmour frequency $\omega_0 = \gamma B_0$ and this induces an additional phase $\int_0^t \Omega(\mathbf{r},\tau)d\tau$ in the MR signal. In this work, the additional phase was estimated for diffusion MRI. The result indicates that the additional phase can be neglected in the conventional diffusion MR measurement, but should be considered in high b-value and high spatial resolution diffusion MRI.

Theory: The motion of an isochromatic magnetization vector $\boldsymbol{M}(\mathbf{r}, t)$, representing the magnetization in a volume element, dv, of the sample at location $\mathbf{r}$, can be described by Bloch-Torrey equation [1-3]. T_1 and T_2 are the longitudinal and transverse relaxation times, B the applied magnetic field, γ the gyromagnetic ratio, D the diffusion tensor, and $\boldsymbol{M} = (M_x, M_y, M_z)$ the net nuclear magnetization vector. M_0 is the equilibrium magnetization. We introduce the complex-valued transverse magnetization $m(\mathbf{r},t) = M_x(\mathbf{r},t) + iM_y(\mathbf{r},t)$ and consider that the applied magnetic field is in the z-direction $\mathbf{B}(\mathbf{r},t) = \mathbf{B}_0 + \Delta\mathbf{B}(\mathbf{r},t) = [0, 0, B_0 + \Delta B(\mathbf{r},t)]^T$.

Using $\gamma B_0 = \omega_0$ and the notations of ref.[3], we have:

$$\frac{\partial m(\mathbf{r},t)}{\partial t} = -i\gamma\omega_0 m(\mathbf{r},t) - \frac{m(\mathbf{r},t)}{T_2} - i\gamma\Delta B(\mathbf{r},t)m(\mathbf{r},t) + \nabla\cdot\left[D(\mathbf{r},t)\nabla m(\mathbf{r},t)\right], \qquad (1)$$

Substituting $m(\mathbf{r},t) = \psi(\mathbf{r},t)\exp\left[-\left(i\omega_0 + 1/T_2\right)t\right]$ into eqn. (1), gives eqn.(2) as

$$\frac{\partial \psi(\mathbf{r},t)}{\partial t} = -i\gamma\Delta B(\mathbf{r},t)\psi(\mathbf{r},t) + \nabla\cdot\left[D(\mathbf{r},t)\nabla\psi(\mathbf{r},t)\right]. \qquad (2)$$

Thus, we eliminate the attenuation due to transverse relaxation and signal modulation by the Larmour precession. $\psi(\mathbf{r},t)$ describes the precessing magnetization untenanted by relaxation. Note that $\nabla\cdot\left[D(\mathbf{r},t)\nabla m(\mathbf{r},t)\right] = D\nabla^2 m$ is only valid for spatially uniform media, but invalid to spatially non-uniform, anisotropic media.

Taking $\psi(\mathbf{r},t) = Y(t)\exp\left(-i\gamma\int_0^t \Delta B(\mathbf{r},\tau)d\tau\right)$ into eqn.(2) and using the formula $\nabla\cdot(f\mathbf{u}) = \nabla f\cdot\mathbf{u} + f\nabla\cdot\mathbf{u}$, we obtain

$$\frac{dY(t)}{dt} = -\gamma^2 Y(t)\left\{\nabla\int_0^t \Delta B(\mathbf{r},\tau)d\tau\cdot D(\mathbf{r},t)\nabla\left[\int_0^t \Delta B(\mathbf{r},\tau)d\tau\right]\right\} - i\gamma Y(t)\nabla\cdot\left\{D(\mathbf{r},t)\nabla\left[\int_0^t \Delta B(\mathbf{r},\tau)d\tau\right]\right\}, \qquad (3)$$

where $Y(t)$ is the amplitude of the precessing magnetization unattenuated by $\Delta B(\mathbf{r},t)$. The term $\nabla\cdot[D(\mathbf{r},t)\nabla\int_0^t \Delta B(\mathbf{r},\tau)d\tau]$ has the units of magnetic field. Using the definitions $\mathbf{k}(\mathbf{r},t) \equiv \nabla[\int_0^t \Delta B(\mathbf{r},\tau)d\tau]$ and $\Omega(\mathbf{r},t) \equiv \gamma\nabla\cdot[D(\mathbf{r},t)\nabla\int_0^t \Delta B(\mathbf{r},\tau)d\tau] = \gamma\nabla\cdot[D(\mathbf{r},t)\mathbf{k}(\mathbf{r},t)]$, eqn.(2) can be simplified and its solution can be obtained as

$$\frac{dY(t)}{Y(t)} = \left[-\gamma^2\mathbf{k}(\mathbf{r},t)\cdot D(\mathbf{r},t)\cdot\mathbf{k}(\mathbf{r},t) - i\Omega(\mathbf{r},t)\right]dt \quad \text{and} \quad \frac{Y(t)}{Y_0} = \exp\left[\gamma^2\int_0^t\left[-\mathbf{k}(\mathbf{r},t)\cdot D(\mathbf{r},t)\cdot\mathbf{k}(\mathbf{r},t)\right]d\tau\right]\cdot\exp\left[-i\int_0^t \Omega(\mathbf{r},\tau)d\tau\right] \qquad (4)$$

where the initial value $Y(t_0) = Y_0$ has been imposed. The term, $\exp\left[-i\int_0^t \Omega(\mathbf{r},\tau)d\tau\right]$, induces an additional phase in the diffusion MR signal.

Results and discussions: For a given diffusion gradient $\boldsymbol{G}$, we have $\Delta B = \mathbf{G}\cdot\mathbf{r}$ and $\mathbf{k} = \nabla\int_0^t (\Delta B)d\tau = \int_0^t \mathbf{G}d\tau$. Therefore, we obtain the simplified expression $\Omega(\mathbf{r},\tau)/\gamma = \sum_{i=1,2,3}\sum_{j=1,2,3}[k_j(\partial D_{ij}/\partial x_i)]$ and $b = \left[\gamma^2\int_0^t\left[-\mathbf{k}(\mathbf{r},t)\cdot\mathbf{k}(\mathbf{r},t)\right]d\tau\right]$. For a given voxel at the location $\mathbf{r}$, different directions of the diffusion gradient induce different frequencies $\Omega(\mathbf{r},\tau)$ and an additional phase $\left[\int_0^t \Omega(\mathbf{r},\tau)d\tau\right]$. The additional phase depends not only on $D(\mathbf{r},t)$, but also on the magnitude of diffusion gradient and its direction. In the continuous tensor field approximation, $\partial D_{ij}/\partial x_i$ could be used to characterise the curving or twisting feature of the triad of eigenvectors in imaging [4]. . A special case is that of a uniform medium with isotropic diffusion properties such as water, $\Omega = 0$ and no additional phase.

From the expression of $\Omega(\mathbf{r},\tau)$, it is easy to estimate the additional phase for a diffusion MR measurement. Take the border between grey matter and white matter in human brain as an example. Assume the eigenvalues of diffusion tensor are (0.7, 0.7, 0.7) for grey matter and (1.4, 0.35, 0.35) for white matter (units: 10^{-3} mm^2/s). **(1)** For a conventional diffusion MR measurement of b = 1000 s/mm^2 and echo time TE = 80ms, we have $\partial D_{11}/\partial x_1 \approx \Delta D_{11}/\Delta x_1 = 7\times10^{-4}\,mm/s$ for the voxel size of the order $1mm$. From $b = \left[\gamma^2\int_0^t\left[-\mathbf{k}(\mathbf{r},t)\cdot\mathbf{k}(\mathbf{r},t)\right]d\tau\right] \approx \gamma^2 k_1^2 TE$, we get $\gamma k_1 \approx \sqrt{b/TE} \approx 110/mm$ and $\Omega = \sum\sum(\gamma k_i \partial D_{ij}/\partial x_j) \approx \gamma k_1 \partial D_{11}/\partial x_1 = 7.7\times10^{-4}/s$. The additional phase is $\Omega\cdot TE \approx 6.2\times10^{-3}\,circles = 2.2°$ for a conventional diffusion MR measurement. **(2)** However, for a high b-value and high spatial-resolution (for example, voxel size of the order of $\Delta x = 0.1mm$), b=17000s/mm^2 and TE=32ms[5], the estimation gives $\gamma k_1 \approx \sqrt{b/TE} \approx 730/mm$, $\partial D_{11}/\partial x_1 \approx 7\times10^{-3}\,mm/s$ and $\Omega \approx \gamma k_1 \partial D_{11}/\partial x_1 = 5/s$. Therefore, the additional phase is $\Omega\cdot TE \approx 57°$ which cannot be neglected.

In conclusion, according to a theoretical analysis of the Bloch-Torrey equation, an additional phase is obtained in diffusion MR signal of anisotropic meida. For a given diffusion gradient direction, the additional phase for different voxels is not same and will cause image distortion. Different diffusion gradient directions induce different additional phases for the same image and could introduce errors in the diffusion coefficient calculation. The analysis indicates that the additional phase is negligible in conventional diffusion MR measurements, but should be considered for the case of high spatial resolution and high b-value.

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