27 Angular variations: The shape of diffusion

27.1 Sensitizing in Arbitrary Directions

We have now demonstrated how diffusion in the presence of a bipolar gradient effects the MR signal. We consider the one-dimensional case not only because of its simplicity, but also because, as we discovered earlier, only the diffusion *along* the gradient direction has an effect on the signal, and the single bipolar gradient we examined is only along a single direction, by definition. Of course, the distribution of particles that is evolving in time (according to the simple Gaussian model, for example), is distributed in 3-dimensions, and because it can be anisotropic, we need a way to sensitize to diffusion in arbitrary direction. In this section we make a very important generalization, but with very little effort, by recalling a simple result from Chapter 16: gradients add like vectors, as shown in Figure **??**. We can immediately conclude then that this will also be true for bipolar gradients applied along different axes, as shown in Figure **??**. Although we've shown an example of 2-dimensions, we can obviously extend this to 3-dimensions by adding a gradient along the $\hat{z}$ direction (which we'll do later). This means that the 1-dimensional analysis we have performed above can be along *any* direction. It is still a 1 (spatial) dimensional problem, however. But at this point where we're headed should be clear: We have a 3D anisotropic spatial distribution of spins that will give a signal that will depend upon the spatial direction along which we measure. And we know now that we can measure along any directions we choose. So, by measuring, along several different directions and observing the variation in signal with direction, can we infer the underlying distribution of spins? Yes (or you wouldn't be reading this book).

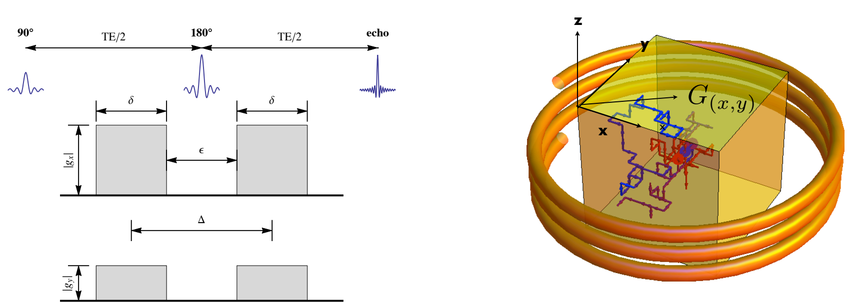


Figure 27.1 Diffusion sensitization along any direction can be achieved by suitable combinations of bipolar diffusion weighting gradients.

However, although it is a simple step to extend our ability to sensitize the experiment to diffusion along any direction and we can do this in the presence of a 3D distribution, the form of the signal becomes significantly more complicated to describe. Fortunately, you already have learned all the methods necessary to do so. Formally, the complication is describing how the signal measured along arbitrary directions represents the underlying distribution of spins (an anisotropic 3D Gaussian, for example). Conceptually, there is an often more difficult problem: what can be thought of as the "shape" of the diffusion weighted signal as we gather together our samples along several directions. So first we will do the "formal" mathematics part by analyzing the 3D Gaussian distribution, and then we will consider this problem of the shape of diffusion.

27.2 3D Gaussian diffusion in a bipolar gradient

We now consider the problem of applying a diffusion weighted gradient along an arbitrary direction in 3D in the presence of a 3D Gaussian distribution described by:

$$p(\bar{\boldsymbol{r}}, \tau) = \frac{1}{\sqrt{|\boldsymbol{D}|\,(4\pi\tau)^3}} e^{-\bar{\boldsymbol{r}}^t \boldsymbol{D}^{-1} \bar{\boldsymbol{r}}/(4\tau)} = N(0, 2\boldsymbol{D}\tau) \tag{27.1}$$

where $\tau = \Delta - \delta/3$. Substituting this into Eqn 25.23 gives the signal

$$\mathfrak{s}(q, \Delta) = \frac{1}{\sqrt{|\boldsymbol{D}|\,(4\pi\tau)^3}} \int e^{-\bar{\boldsymbol{r}}^t \boldsymbol{D}^{-1} \bar{\boldsymbol{r}}/(4\tau)} e^{-i\boldsymbol{q}\cdot\bar{\boldsymbol{r}}}\, d\bar{\boldsymbol{r}} \tag{27.2}$$

can be done analytically (Appendix C), giving a signal from diffusion weighting gradients along an arbitrary direction applied to a 3D Gaussian distribution as

$$s(\boldsymbol{q}, \tau) = s(0) e^{-\boldsymbol{b}\boldsymbol{D}} + \eta(\boldsymbol{q}) \tag{27.3}$$

where again the assumption has been made that the noise $eta(\boldsymbol{q})$ is additive. The first term on the right hand side can be written in component form as

$$s(\boldsymbol{q}, \tau) = s(0) \exp\left(-\sum_{i=1}^{3} \sum_{j=1}^{3} b_{ij} D_{ij} \right) \tag{27.4}$$

where

$$\boldsymbol{D} = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix} \quad , \quad \boldsymbol{b} = \begin{pmatrix} q_x^2 & q_x q_y & q_x q_z \\ q_y q_x & q_y^2 & q_y q_z \\ q_z q_x & q_z q_y & q_z^2 \end{pmatrix} \tau \tag{27.5}$$

and the diffusion tensor is symmetric: $\boldsymbol{D}^t = \boldsymbol{D}$ and its elements are real: $D_{ij} \in \Re$. Note that even though we are applying *three* different sets of diffusion weighting gradients (corresponding to the three lab coordinate axes $\{x, y, z\}$), the b-matrix involves terms only constructed from *pairs* of gradients. Note that Eqn 27.6 can be written in the form

$$\boldsymbol{b}\boldsymbol{D} = \tau \boldsymbol{q}^t \cdot \boldsymbol{D} \cdot \boldsymbol{q} \tag{27.6}$$

so Eqn 27.3 can be written

$$s(\boldsymbol{q}, \tau) = s(0) e^{-\tau \boldsymbol{q}^t \cdot \boldsymbol{D} \cdot \boldsymbol{q}} + \eta(\boldsymbol{q}) \tag{27.7}$$

This form is very useful both computationally and for seeing geometrically what the signal looks like.

$$\boldsymbol{bD} = \tau \boldsymbol{q}^t \cdot \boldsymbol{D} \cdot \boldsymbol{q} = q^2 \tau \underbrace{\hat{\boldsymbol{q}}^t \cdot \boldsymbol{D} \cdot \hat{\boldsymbol{q}}}_{\tilde{\boldsymbol{D}}} \tag{27.8}$$

where the *q-vector* is given by $\boldsymbol{q} = q\hat{\boldsymbol{q}}$ where $q = |\boldsymbol{q}|$ is the magnitude of q-vector and $\hat{\boldsymbol{q}} = \boldsymbol{q}/q$ is the unit vector in direction of q-vector. Therefore the signal can be written

$$s(\boldsymbol{q}, \tau) = s_o e^{-\boldsymbol{bD}} = s_o e^{-b\tilde{D}} + \eta(\boldsymbol{q}) \tag{27.9}$$

where

$$\tilde{D} = \hat{\boldsymbol{q}}^t \cdot \boldsymbol{D} \cdot \hat{\boldsymbol{q}} \tag{27.10a}$$

$$b = -q^2 \tau \tag{27.10b}$$

This is the same form as Eqn 25.33 except in three-dimensions: The signal decays in an exponential fashion along the direction of the gradient, as defined by $\boldsymbol{q}$. The diffusion coefficient along that direction is $\tilde{D}$. The form Eqn 27.10 is very useful when calculating the *nominal* b-value for an experiment. However, it assumes ideal gradients, thus allowing the amplitudes and directions to be disassociated. However, in practice, the imaging gradients interfere with the diffusion encoding gradients and this ideality is not realized. So, in practice, it is more useful to keep this in the form $\boldsymbol{bD}$ and speak of the *b-matrix* $\boldsymbol{b}$:

$$b_{ij}(\tau) = \int_0^\tau q_i(t) q_j(t)\, dt \tag{27.11a}$$

$$\text{where} \quad q_i = \int_0^\tau g_i(t)\, dt \tag{27.11b}$$

For constant gradients, these become

$$b_{ij} = q_i q_j \tau \qquad \text{where} \qquad \begin{cases} q_i = g_i \tau \\ \tau = \Delta - \delta/3 \end{cases} \tag{27.12}$$

This form allows the individual $\boldsymbol{q}$ values to be calculated. One therefore speaks of “calculating the b-matrix” when performing an actual DTI experiments so as to account for the actual gradients values applied. The diffusion tensor can then be calculated (as we discuss in the next chapter) by fitting the signal equation Eqn 27.9. But note that this equation is a function of both b-value magnitude (i.e., for different magnitudes of q) and the direction so the fitting is more complicated (and more subtle) than in the case of the diffusion coefficient in Section 25.6.

27.3 The orientation of the diffusion tensor

We have found that for 3D Gaussian diffusion our signal is

$$\mathfrak{s}(q) = e^{-b\tilde{D}} + \eta(\boldsymbol{q}) \tag{27.13}$$

Now recall from Section **??** that the diffusion tensor $\boldsymbol{D}$ in the Gaussian model of diffusion is a real, symmetric 3×3 matrix and so can be diagonalized by a similarity transformation with rotation matrices (Section **??**). In other words, it can be written in the form

$$\boldsymbol{D} = \boldsymbol{R}^t \, \boldsymbol{D}_\Lambda \, \boldsymbol{R} \tag{27.14}$$

where $\boldsymbol{D}_\Lambda$ is the diagonal matrix with the elements along the diagonal that are the diffusion coefficients along the principal axes (the coordinate axes in the reference frame of $\boldsymbol{D}$). Substituting this into Eqn 27.10 gives

$$\tilde{D} = \hat{\boldsymbol{u}}^t \, \boldsymbol{D}_\Lambda \, \hat{\boldsymbol{u}} \tag{27.15}$$

where

$$\hat{\boldsymbol{u}} = \boldsymbol{R}\hat{\boldsymbol{q}} \tag{27.16}$$

is the gradient direction vector rotated into the eigencoordinates of the diffusion tensor. Eqn 28.3 and Eqn 27.15 are two equivalent but different representations that are useful intuitively. Eqn 28.3 shows that in the lab frame we apply the gradients along the direction $\hat{\boldsymbol{q}}$ and the resulting signal decay depends upon the projection of the diffusion tensor $\boldsymbol{D}$, which is oriented in some arbitrary direction, along that direction. Eqn 27.15, on the other hand, shows that in the reference frame (i.e., eigencoordinates) of the diffusion tensor, where it is diagonal, i.e. $\boldsymbol{D}_\Lambda$, the measured signal is seen as being produced by the projection of $\boldsymbol{D}_\Lambda$ along the direction $\boldsymbol{u}$, the applied gradient $\boldsymbol{q}$ rotated into the eigencoordinates of the diffusion tensor. That is,

$$\tilde{D} = \hat{\boldsymbol{u}}^t \cdot \boldsymbol{D}_{\boldsymbol{\Lambda}} \cdot \hat{\boldsymbol{u}} \tag{27.17}$$

If the measurements are made along the principal axes, ie, in the coordinate system in which the diffusion tensor is diagonal, and the applied diffusion encoding gradients $\hat{\boldsymbol{u}}$ are in the direction of the eigenvectors of $\boldsymbol{D}$.

$$\hat{\boldsymbol{u}} = \begin{pmatrix} u_1 \\ u_2 \\ u_3 \end{pmatrix} \quad , \quad \boldsymbol{D}_\Lambda = \begin{pmatrix} d_1 & 0 & 0 \\ 0 & d_2 & 0 \\ 0 & 0 & d_3 \end{pmatrix} \tag{27.18}$$

where the eigenvalues are the *principal diffusivities* $\{d_1, d_2, d_3\}$. Generally, however, this principal axis coordinate system is not known. The applied diffusion encoding gradients $\hat{\boldsymbol{v}}$ are therefore not coincident with the principal axis system, but are related to it by a rotation $\boldsymbol{R}$:

$$\hat{\boldsymbol{u}} = \boldsymbol{R}\,\hat{\boldsymbol{q}} \tag{27.19}$$

where $\hat{\boldsymbol{v}}$ is a unit vector in direction of diffusion encoding. Thus, one usually wants to infer the principal diffusivities and the rotation R. From these can be determined the diffusion properties, such as the anisotropy, and the fiber directions. The rotation R is defined within the coordinate system shown in Figure **??**. The two angles that define the direction in this coordinate system are the *polar* angle $\theta \in [0, \pi]$ which is defined as the angle between the vector and the *positive* z-axis, and the *azimuthal* angle $\phi \in [0, 2\pi)$, which is defined as the angle in the $x - y$ plane relative to the positive x axis. It is also common to use the *elevation* angle $\delta = 90° - \theta$, which is the angle between the vector and the $x - y$ plane. This is often denoted by ϕ, however (e.g. (**?**)). We will retain the standard physics usage, depicted in Figure **??**, where (θ, ϕ) denote the polar and azimuthal angles, respectively. It often useful to use the shorthand notation $\Omega \equiv (\theta, \phi)$. The angles (θ, ϕ) are two of the Euler angles used to described rotations in 3-dimensional coordinates that we studied in Section **??** where there we called them by (α, β, γ) where α is the azimuthal rotation angle, β is the polar rotation angle, and γ is a rotation about the new axis defined by the rotation through (α, β). For the description of a single point (i.e., a measurement) on a sphere, as is the case in this paper, rotations about the final (radial) axis are unimportant, so the rotations can be described by the two angles (α, β). It is common in this case to denote these (θ, ϕ).

The gradient direction vectors in the two coordinate systems are related by a rotation ((?))

$$\boldsymbol{R} = \begin{pmatrix} \sin\phi & -\cos\phi & 0 \\ \cos\phi\cos\theta & \sin\phi\cos\theta & -\sin\theta \\ \cos\phi\sin\theta & \sin\phi\sin\theta & \cos\theta \end{pmatrix} \tag{27.20}$$

The apparent diffusion coefficient for an arbitrary gradient direction $\hat{\boldsymbol{q}}$ can thus be written ((?))

$$\tilde{D} = \hat{\boldsymbol{q}}^t \cdot \boldsymbol{D} \cdot \hat{\boldsymbol{q}} \tag{27.21}$$

where

$$\boldsymbol{D} \equiv \boldsymbol{R}^t\, \boldsymbol{D}_\Lambda\, \boldsymbol{R} \tag{27.22}$$

Eqn 27.22 defines the diffusion tensor $\boldsymbol{D}$ in a rotated coordinate system. For any *symmetric* matrix $\boldsymbol{D}$, such as the diffusion tensor, the product $\boldsymbol{x}^t\boldsymbol{D}\boldsymbol{x}$ is a pure quadratic form (?). The rotation of the tensor relates the orientation of the fiber coordinate system relative to the laboratory system wherein the eigenvalues determine the diffusivities. Since $\boldsymbol{D}$ is positive definite, it can be written in the form of Eqn 27.22 where $\boldsymbol{D}_\Lambda$ is diagonal and the unit eigenvectors of $\boldsymbol{D}$ are the columns of $\boldsymbol{R}$. The rotation $\boldsymbol{u} = \boldsymbol{R}\hat{\boldsymbol{q}}$ produces the sum of squares

$$\hat{\boldsymbol{q}}^t\boldsymbol{D}\hat{\boldsymbol{q}} = \hat{\boldsymbol{q}}^t\boldsymbol{R}\boldsymbol{D}_\Lambda\boldsymbol{R}^t\hat{\boldsymbol{q}} = \boldsymbol{u}^t\boldsymbol{D}_\Lambda\boldsymbol{u} = \sum_i^n \lambda_i\, y_i^2 \tag{27.23}$$

As we saw in Section 8.2, the equation $\hat{\boldsymbol{q}}^t\boldsymbol{D}\hat{\boldsymbol{q}} = 1$ describes an ellipsoid whose axes end at the points where $\lambda_i y_i^2 = 1$ and where the remaining y components are zero. Undoing the rotation, these points are in the directions of the eigenvectors and the axes have half length $1/\sqrt{\lambda_i}$. It is important to emphasize, however, that the ellipsoid that describes the eigenspace of the diffusion tensor is *not* a description of the shape of the measured local diffusion (?). Of course, in an experiment the eigenvalues and the angles that determine the tensor orientation are not known, and are, in fact, what we want to determine. How to do that is the subject of the next chapter. But now let's turn to the question of the "shape" of diffusion.

27.4 The Shape of Diffusion

Let's return to the signal Eqn 27.9 where b is given by Eqn 27.10 and $\tilde{D}$ is given by Eqn 27.10 and $\boldsymbol{u}$ is the measurement direction [1]. And for clarify we will assume here that there is no noise, $\eta(\boldsymbol{q}) = 0$. The geometry of $\tilde{D}$ is illustrated in Figure 27.2. and we see the importance of $\tilde{D}$: it is *the projection of the diffusion ellipsoid onto the diffusion sensitized direction* $\boldsymbol{u}$. Therefore the *measured* signal is the projection of the diffusion weighted signal along $\boldsymbol{u}$. Since the elements of the diffusion tensor are the covariances of the 3D gaussian distribution, we see that

The measured diffusion coefficient along an arbitrary direction is proportional to the variance of the projection of the spin displacement onto the measurement axis.

[1] Get the hat's straight! Either make the unit vector $\boldsymbol{u}$ or $\hat{\boldsymbol{u}}$ - you have both now!

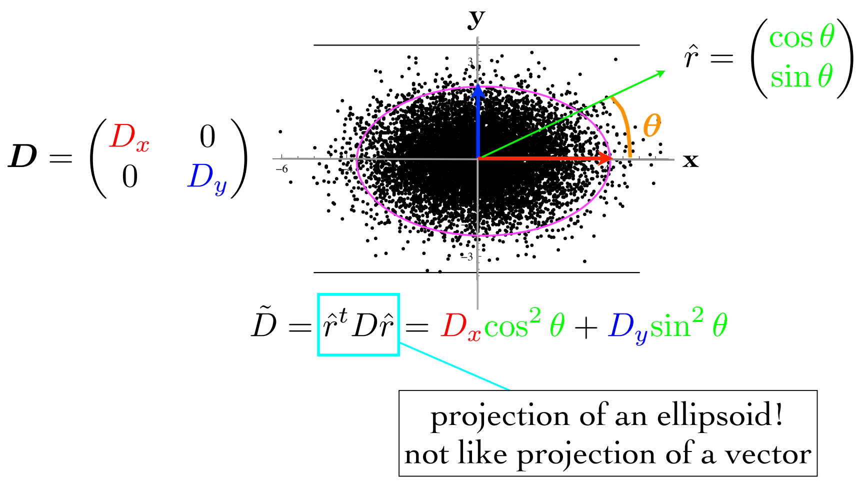


Figure 27.2 The geometry of $\tilde{D}$.

Let's look at the sampling vector in the 2D case first.

$$\boldsymbol{u} = \boldsymbol{R}\boldsymbol{v} \tag{27.24}$$

where

$$\boldsymbol{R} = \begin{pmatrix} \cos\theta & -\sin\theta \\ \sin\theta & \cos\theta \end{pmatrix} \quad , \quad \boldsymbol{v} = \begin{pmatrix} 1 \\ 0 \end{pmatrix} \quad \Rightarrow \quad \boldsymbol{u} = \begin{pmatrix} \cos\theta \\ \sin\theta \end{pmatrix} \tag{27.25}$$

Sampling at equally spaced angular increments would thus give sampling vectors as shown in Figure 27.3. We can now construct $\tilde{D}$ using

$$\boldsymbol{u}^t = (\cos\theta, \sin\theta) \quad , \quad \boldsymbol{D} = \begin{pmatrix} D_x & 0 \\ 0 & D_y \end{pmatrix} \quad , \quad \boldsymbol{u} = \begin{pmatrix} \cos\theta \\ \sin\theta \end{pmatrix} \tag{27.26}$$

so that

$$\tilde{D}(\theta) = \boldsymbol{u}^t \boldsymbol{D} \boldsymbol{u} = D_x \cos^2\theta + D_y \sin^2\theta \tag{27.27}$$

The measured signal is thus, from Eqn 27.28,

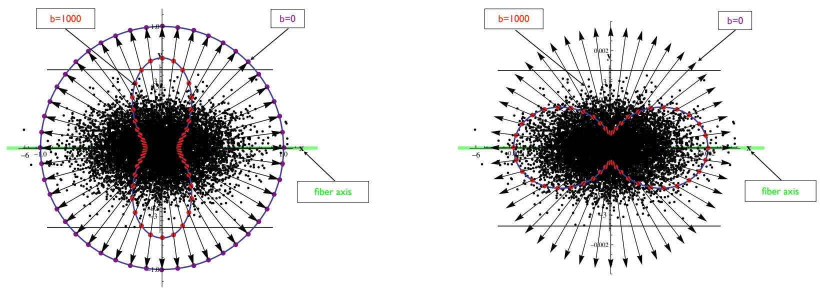
$$s(b) = s_o e^{-b\left(D_x \cos^2\theta + D_y \sin^2\theta\right)} \tag{27.28}$$

Consider the case that the diffusion is anisotropic and $D_x = 10D_y$. The signal for measurements made at equilangular increments is shown in Figure 27.3a. The measured, or *apparent* diffusion coefficient D_{app}, found by solving Eqn 27.28 for D (we're ignoring noise!), is given by

$$D_{app}(\theta) = -\frac{1}{b} \log\left(\frac{s_b}{s_o}\right) \tag{27.29}$$

and this is shown in Figure 27.3b.

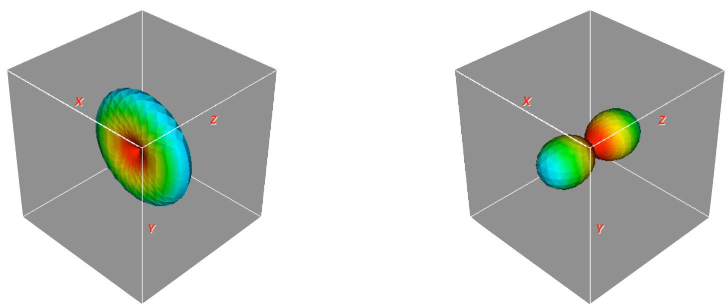
This can be extended to 3D by exactly the same steps we just followed, except using the 3D rotation matrices, as shown in Figure 27.4. The shape depends on the ratio of the diffusion



(a) The signal $S(b,\theta) = S(0)e^{-bD(\theta)}$ where $D(\theta) = D_x \cos^2\theta + D_y \sin^2\theta$.

(b) The apparent diffusion coefficient $D_{app}(\theta) = -\frac{1}{b}\log\left(\frac{S_b}{S_0}\right)$

Figure 27.3 The signal and the apparent diffusion coefficient for $D_{xx} : D_{yy} : D_{zz} = 1 : 1 : 10$ and $b = 1000 s/mm^2$.

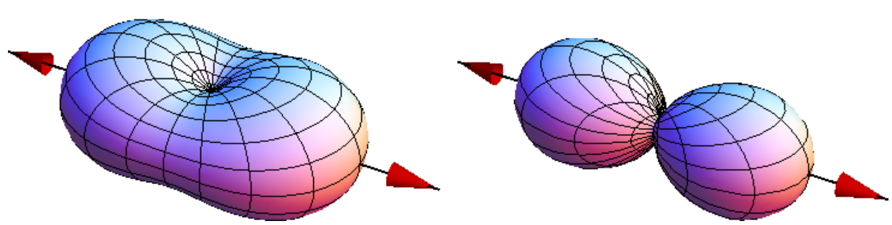


(a) Measured signal.

(b) Apparent diffusion coefficient

Figure 27.4 Equiangular sampling of 3D Gaussian diffusion with $D_{xx} : D_{yy} : D_{zz} = 1 : 1 : 10$ and $b = 1000 s/mm^2$.

along the different directions. If none of the values are equal, the shape is no longer rotationally symmetric about any of the principal axes, as shown in Figure 27.5. We have only consider here



(a) $D_{xx} : D_{yy} : D_{zz} = 5 : 3 : 1$.

(b) $D_{xx} : D_{yy} : D_{zz} = 10 : 1 : 1$.

Figure 27.5 The shape of the apparent diffusion coefficient depends upon the values of the diffusion along the principal axes.

Figure needed

Figure 27.6 Signal as a function of b for 3D Gaussian diffusion. For a known $\boldsymbol{D}$, the contours of constant level, where the signal $s(\hat{\boldsymbol{u}}, b)$ as a function of gradient direction ($\hat{\boldsymbol{u}}$, the angular component) and b (the radial component) is $e^{-1/2}$ its maximum value, is shown for three different b-values $b = \{1000, 2000, 3000\}$ for $\lambda = \{.001, .002, .003\}$.

the angular variations, for a constant b-value. For multiple b-values, the magnitude of the signal changes, but the shapes do not as shown in Eqn 27.6

Suggested reading