Supplementary Materials: Supplementary Material: " Fractional Diffusion with Geometric Constraints: Application to Signal Decay in Magnetic Resonance Imaging (MRI)"

Here, we start the results of applying the model to describe the behavior of the experimental data provided in Refs. [23,24] for the cases $\Delta = 10\,ms$ and $\Delta = 20\,ms$. The experimental data are represented by the symbols (circle and square) and the model by the lines (red and green) as in the manuscript. Figure S1 shows the behavior for $\Delta = 10\,ms$ and Figure S2 shows the model and the experimental data for the case $\Delta = 20\,ms$. In both cases, we have an agreement between the model and the experimental data for the bovine optic nerve.

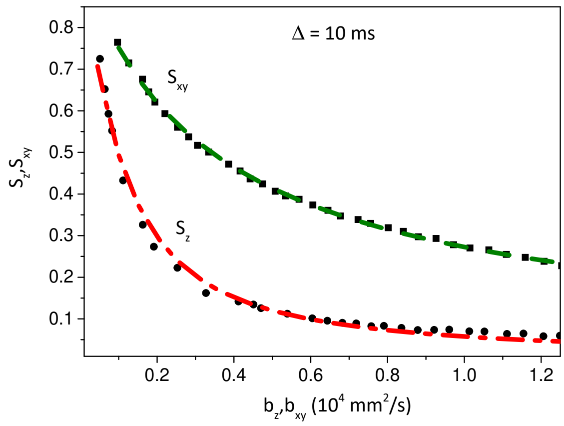

Figure S1. Behavior of the model (lines green and red) and the experimental data (symbols square and circles) for the bovine optic nerve. The parameter values obtained in the fitting process by using the function NonlinearModelFit present in the software Mathematica for each case are $\mu_{xy}/2 = 0.86$, $l_z = 5.5 \times 10^{-2} mm$, $\overline{\eta}_{xy} = 0.36$, $D'_{xy} = 2.07 \times 10^{-4}\ mm^2/s$, $l_z = 2.6 \times 10^{-2}\ mm$, error $= 2.32 \times 10^{-4}$ (estimated variance) for S_{xy} and $\eta_z = 0.64$, $D'_z = 7.46 \times 10^{-4}\ mm^2/s$, error $= 3.32 \times 10^{-4}$ (estimated variance) for S_z. By using the scaling argument (see Ref. [10] for details), it is possible to obtain the behavior of the mean square displacement for each case and show that $\sigma^2_{xy} \propto t^{0.41}$ and $\sigma^2_z \propto t^{0.64}$.

Now, we present and discuss other models used to analyze the experimental data obtained from the MRI technique. One of these models is the bi-exponential, with the attenuation function given by

$$S(b) = S_0\left(fe^{-b\mathcal{D}_{slow}} + (1-f)e^{-b\mathcal{D}_{fast}}\right), \quad (1)$$

where $\mathcal{D}_{slow}$ and $\mathcal{D}_{fast}$ are the diffusion constants for the slow and fast diffusion compartments, respectively, f is the volume fraction of the slow compartment, and $(1-f)$ the volume fraction of the fast compartment (for details, see Ref. [27]). Tables S1 and S2 show the parameters obtained from using the biexponential model to fit the experimental data. We evaluate the error, i.e., the estimated variance, as performed for the comb-model by using the function NonlinearModelFit that is available in the software Mathematica for the parameters present in these tables. We also use this function to evaluate the estimated variance for the parameter values obtained for the other models.

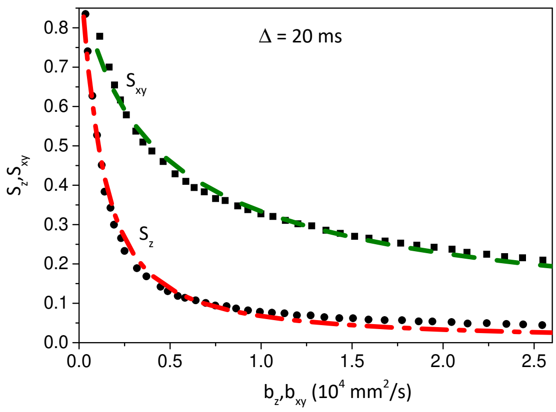

Figure S2. Behavior of the model (lines green and red) and the experimental data (symbols square and circles) for the bovine optic nerve. The parameters values obtained in the fitting process by using the function NonlinearModelFit present in the software Mathematica for each case are $\mu_{xy}/2 = 0.71$, $\overline{\eta}_{xy} = 0.41$, $D'_{xy} = 1.52 \times 10^{-4}\ mm^2/s$, $l_z = 8.1 \times 10^{-2}\ mm$, error $= 2.76 \times 10^{-4}$ (estimated variance) for S_{xy} and $\eta_z = 0.59$, $D'_z = 7.04 \times 10^{-4}\ mm^2/s$, error $= 4.35 \times 10^{-4}$ (estimated variance) for S_z. By using the scaling argument (see Ref. [10] for details), it is possible to obtain the behavior of the mean square displacement for each case and show that $\sigma^2_{xy} \propto t^{0.65}$ and $\sigma^2_z \propto t^{0.59}$.

Table S1. Parameters used to fit the experimental data present in Refs. [23,24] with Eq. (1) for different values of Δ for the perpendicular direction. The values presented in this table, for the parameters D_{slow}, D_{fast}, and f present in Eq. (1), were also obtained from the data in Ref. [27].

$\Delta(\times 10^{-3}\,s)$	$D_{slow}(\times 10^{-4}\,mm^2/s)$	$D_{fast}(\times 10^{-4}\,mm^2/s)$	f	error$(\times 10^{-4})$
30	0.23	4.15	0.41	0.63
20	0.28	4.13	0.42	0.18
10	0.70	5.86	0.55	0.10
8	1.09	7.70	0.63	0.31

Table S2. Parameters used to fit the experimental data present in Refs. [23,24] with Eq. (1) for different values of Δ for the parallel direction.The values presented in this table, for the parameters D_{slow}, D_{fast}, and f present in Eq. (1), were also obtained from the data in Ref. [27].

$\Delta(\times 10^{-3}\,s)$	$D_{slow}(\times 10^{-4}\,mm^2/s)$	$D_{fast}(\times 10^{-4}\,mm^2/s)$	f	error$(\times 10^{-4})$
30	0.43	8.18	0.13	2.12
20	0.46	7.75	0.13	1.09
10	0.75	8.71	0.15	1.28
8	1.10	8.58	0.15	1.14

The bi-exponential model has two diffusion coefficients and, consequently, two relaxation processes for each direction in addition to the relative size of the two compartments specified by the additional parameter f. This feature implies in an additional parameter and function is used to describe the behavior of the experimental data. In this sense, the comb-model could be extended in order to present different relaxation processes by incorporating a different term in the diffusion equation.

Another model used to describe the experimental data is an extension of the relaxation equation for the attenuation by considering a variable diffusion coefficient. It considers the equation

$$\frac{d}{db}S(b) = -D(b)S(b)\,, \tag{2}$$

where $D(b)$ is an arbitrary function of b. The solution of this equation can be formally found and is given by

$$S(b) = S_0 \exp\left(-\int_0^b db' D(b')\right) . \tag{3}$$

In Ref. [24,27] this equation has been applied to the bovine optical nerve by considering some particular cases of $D(b)$. Similar to the bi-exponential model, the different choices for $D(b)$ are fit to the experimental data to provide a suitable description of the experimental behavior. One of the choices employed a stretched exponential decay rate given by

$$D(b) = \alpha D_0 (bD_1)^{\alpha-1} e^{-(bD_1)^\alpha} \tag{4}$$

yielding

$$S(b) = S_0 \exp\left[-\frac{D_0}{D_1}\left(1 - e^{-(bD_1)^\alpha}\right)\right] . \tag{5}$$

Tables S3 and S4 show the parameters obtained from Eq. (5) to fit the experimental data presented in Refs.[23,24] for the bovine optical nerve for the perpendicular and vertical direction.

Table S3. Parameters used to fit the experimental data present in Refs. [23,24] with Eq. (5) for different values of Δ for the perpendicular direction. The values presented in this table, for the parameters D, α, and β present in Eq. (1), were obtained from the data provided in Ref. [27].

$\Delta(\times 10^{-3}\, s)$	$D_0(\times 10^{-4}\, mm^2/s)$	$D_1(\times 10^{-4}\, mm^2/s)$	α	error$(\times 10^{-4})$
30	1.83	1.09	0.80	1.75
20	2.05	1.27	0.84	1.01
10	2.09	1.04	0.83	0.28
8	1.65	0.48	0.77	1.08

Table S4. Parameters used to fit the experimental data present in Refs. [23,24] with Eq. (5) for different values of Δ for the parallel direction.The values presented in this table, for the parameters D_0, D_1, and α present in Eq. (1), were obtained from the data provided in Ref. [27].

$\Delta(\times 10^{-3}\, s)$	$D_0(\times 10^{-4}\, mm^2/s)$	$D_1(\times 10^{-4}\, mm^2/s)$	α	error$(\times 10^{-4})$
30	7.93	2.69	1.01	2.99
20	8.01	2.87	1.08	1.79
10	9.20	3.47	1.11	1.37
8	9.28	3.19	1.12	0.92

Another choice for $D(b)$ is

$$D(b) = D_0 \frac{\alpha (bD_1)^{\alpha-1}}{1 + (bD_1)^\alpha} \tag{6}$$

yielding

$$S(b) = S_0 \exp\left[-\frac{D_0}{D_1} \ln(1 + (bD_1)^\alpha)\right] . \tag{7}$$

Tables S5 and S6 show the parameters obtained from using Eq. (7) to fit the experimental data presented in Refs. [23,24] for the bovine optical nerve for the perpendicular and vertical direction.

Table S5. Parameters used to fit the experimental data present in Refs. [23,24] with Eq. (7) for different values of Δ for the perpendicular direction. The values presented in this table, for the parameters D_0, D_1, and α, were also obtained from the data in Ref. [27].

$\Delta(\times 10^{-3}\, s)$	$D_0(\times 10^{-4}\, mm^2/s)$	$D_1(\times 10^{-4}\, mm^2/s)$	α	error$(\times 10^{-4})$
30	3.50	11.09	1.42	0.14
20	2.85	12.08	1.91	0.10
10	3.27	4.06	0.99	0.20
8	2.26	1.07	0.81	0.47

Table S6. Parameters used to fit the experimental data present in Refs. [23,24] with Eq. (1) for different values of Δ for the parallel direction.The values presented in this table, for the parameters D_0, D_1, and α, were also obtained from the data in Ref. [27].

$\Delta(\times 10^{-3}\, s)$	$D_0(\times 10^{-4}\, mm^2/s)$	$D_1(\times 10^{-4}\, mm^2/s)$	f	error$(\times 10^{-4})$
30	4.94	24.31	3.95	0.70
20	8.57	19.86	1.98	1.03
10	8.11	22.10	2.39	0.24
8	9.98	14.49	1.67	0.38

Equation (2) has also been extended by incorporation of a fractional derivatives as discussed in Ref. [24], i.e.,

$$\frac{d^\alpha}{db^\alpha} S(b) = -D(b)S(b)\;, \tag{8}$$

where the fractional derivative is of the Caputo type and the $D(b) = \mathcal{D}b^\beta$. The solution for this case is

$$S(b) = S_0 E_{\alpha,1+\frac{\beta}{\alpha},\frac{\beta}{\alpha}}\left(-(\mathcal{D}b)^{\alpha+\beta}\right)\;, \tag{9}$$

where $E_{\alpha,m,l}(x)$ is the Kilba-Saigo function, which is defined as follows:

$$E_{\alpha,m,l}(x) = 1 + \sum_{n=1}^{\infty} \prod_{j}^{n-1} \frac{\Gamma(1+\alpha(jm+l))}{\Gamma(1+\alpha(jm+l+1))} x^n\;. \tag{10}$$

Table S7. Parameters used to fit the experimental data present in Refs. [23,24] with Eq. (9) for diferent values of Δ for the perpendicular direction. The values presented in this table, for the parameters D, α, and β present in Eq. (9), were obtained from the data provided in the Ref. [27].

$\Delta(\times 10^{-3}\, s)$	$D(\times 10^{-4}\, mm^2/s)$	α	β	error$(\times 10^{-4})$
30	1.95	0.38	0.31	5.60
20	2.05	0.42	0.27	3.06
10	2.72	0.38	0.46	0.30
8	2.75	0.62	0.20	0.53

Table S8. Parameters used to fit the experimental data present in Refs. [23,24] with Eq. (9) for different values of Δ for the parallel direction.The values presented in this table, for the parameters D, α, and β present in Eq. (9), were obtained from the data provided in the Ref. [27].

$\Delta(\times 10^{-3}\, s)$	$D(\times 10^{-4}\, mm^2/s)$	α	β	error$(\times 10^{-4})$
30	7.19	0.76	0.06	6.40
20	7.14	0.75	0.14	6.35
10	8.86	0.64	0.33	3.91
8	8.74	0.74	0.26	1.84

All of these models, as well as the comb-model, have the objective of describing the experimental data by taking into account the characteristics of the system. It is worth mentioning that, except for the logarithmic S(b) case, each model fits the data quite well with errors that decrease with the diffusion time. That is, as expected, anomalous diffusion is more pronounced when the water has a longer time (e.g., 30 ms versus 8 ms) to explore the tissue structure. Hence, "goodness" of fit alone can not be used to favor one model over another.