

Apparent Diffusivity and Anisotropic Dispersion of Water in Diffusion Tensor Magnetic Resonance Imaging of Biological Tissues

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Abstract

A physical theory explaining the anisotropic dispersion of water in biological tissues observed in so-called diffusion-weighted imaging (DWI) or diffusion-tensor magnetic resonance imaging (DTMRI) is introduced based on the phenomena of Taylor dispersion, in which highly diffusive solutes cycle between flowing and stagnant regions in the tissue, enhancing dispersion in the direction of microvascular flow. Failure to account for flow-mediated dispersion in vascular tissues has led to misinterpretations of imaging data and significant overestimates of directional bias in molecular diffusivity in biological tissues. An effective diffusion equation is derived, for which the coefficient of dispersion in the axial direction (direction of capillary orientation) depends on the molecular diffusion coefficient, tissue perfusion, and theory suggests a means of obtaining quantitative functional information on capillary vessel density from measurements of dispersion coefficients. It is shown that a measurement of the ratio of axial to transverse diffusivity –obtained by DTMRI–may be combined with an independent measurement of perfusion to provide an estimate of capillary vessel density in the tissue.

Background

- **Diffusion-weighted imaging (DWI) and diffusion-tensor magnetic resonance imaging (DTMRI) are used to map the structure and function of brain and other tissues in vivo.**

- **It is found the apparent diffusivity of water is largely reduced during cerebral ischemia.**
 - The reduction in overall diffusivity is coincident with reduction in flow.

 - The anisotropic reduction of the diffusivity in the direction that coincides with the greatest diffusivity or largest eigenvalue of the diffusion matrix

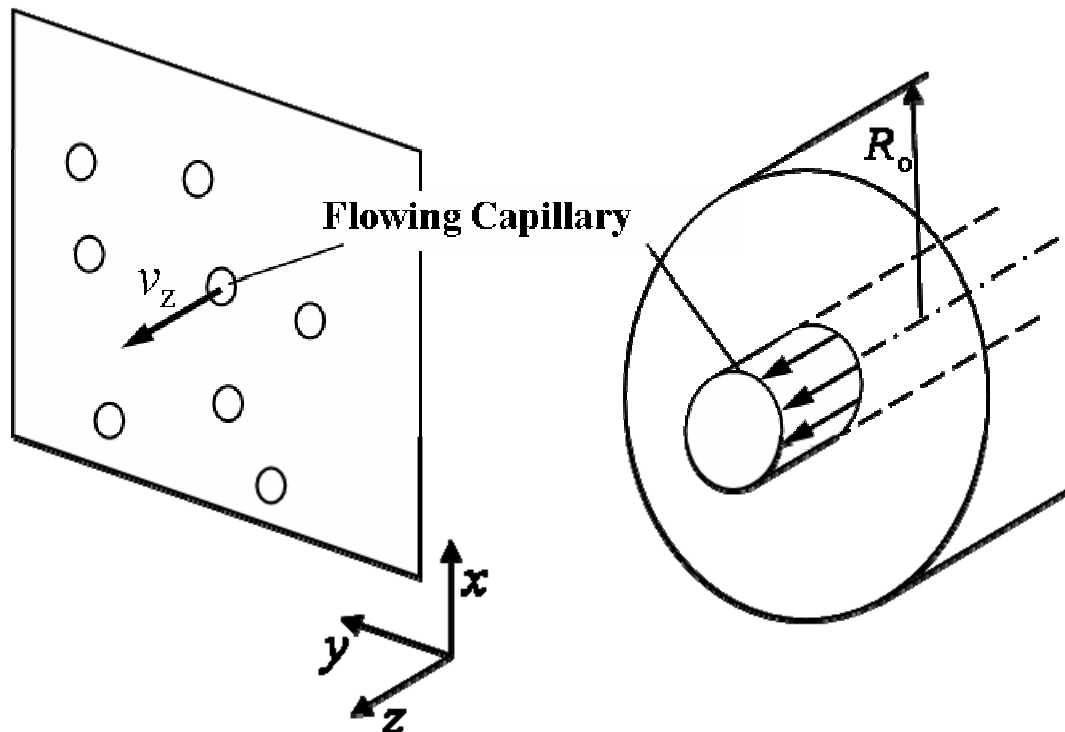
- **What causes the anisotropic reduction?**
 - A conventional explanation is that local edema changes microscopic geometry of the brain during ischemia.

 - There is no certain physical link between edema and the reduction of overall diffusivity.

 - Taylor dispersion in capillary beds may be used to partially explain the observed phenomenon.

Model

- **An idealized model with Krogh cylinder geometry**



- **Simplifications and assumptions:**
 - Capillary exchange vessels are oriented in the axial direction and distributed with a fixed density.
 - Each capillary along with a portion of its surrounding tissue is modeled using an idealized radial geometry, or Krogh cylinder.
 - Vessel velocities are randomly distributed with Gaussian probability distribution.

Governing Equations

- **Advection-diffusion equation:**

$$\frac{\partial C}{\partial t} + v(r) \frac{\partial C}{\partial z} = D \nabla^2 C, \quad (1)$$

where C is the solute concentration, $v(r)$ is the fluid velocity in the axial direction, and D is the molecular diffusion coefficient.

- **Introducing the coordinate frame $z^* = z - Flt$, Equation (1) is simplified:**

$$D \frac{1}{r} \frac{\partial}{\partial r} r \frac{\partial}{\partial r} C(r, z^*) = (v(r) - Fl) \frac{\partial C}{\partial z^*}. \quad (2)$$

- **The fluid velocity is specified:**

$$v(r) = \begin{cases} v_z, & 0 < r < R_i \\ 0, & R_i < r < R_o \end{cases}. \quad (3)$$

- R_i and R_o - radii of the vessel and the stagnant tissue, respectively
- v_z is the constant velocity in the capillary.
- The outer radius of the Krogh cylinder, $R_o = 1/\sqrt{\pi\rho}$.

Solutions

• **Boundary conditions:**

$$C(r, z^*) \Big|_{r=R_i, 0 < r < R_i} = C(r, z^*) \Big|_{r=R_i, R_i < r < R_o} \quad (4)$$

$$\frac{\partial C(r, z^*)}{\partial r} \Big|_{r=R_i, 0 < r < R_i} = \frac{\partial C(r, z^*)}{\partial r} \Big|_{r=R_i, R_i < r < R_o} \quad (5)$$

• **Concentration profile:**

$$C(r, z^*) = \begin{cases} \left[\frac{r^2(v_z - Fl)}{4D} + \frac{R_o^4 Fl - R_i^4 v_z + 4R_i^2 R_o^2 v_z \ln(R_i / R_o)}{8DR_o^2} \right] \frac{\partial C_{av}}{\partial z^*} \\ \qquad \qquad \qquad + C_{av}(z^*) , & 0 < r < R_i \\ \\ \left[-\frac{r^2 Fl}{4D} + \frac{2R_i^2 R_o^2 v_z - R_i^4 v_z + R_o^4 Fl}{8DR_o^2} + \frac{R_i^2 v_z \ln(r / R_o)}{2D} \right] \frac{\partial C_{av}}{\partial z^*} \\ \qquad \qquad \qquad + C_{av}(z^*) , & R_i < r < R_o \end{cases} \quad (6)$$

where $C_{av}(z^*)$ is the average concentration at position z^* :

$$C_{av}(z^*) = \frac{\int_0^{R_i} dr \cdot 2\pi r \cdot C(r, z^*) \Big|_{0 < r < R_i} + \int_{R_i}^{R_o} dr \cdot 2\pi r \cdot C(r, z^*) \Big|_{R_i < r < R_o}}{\int_0^{R_o} dr \cdot 2\pi r} \quad (7)$$

Taylor Dispersion Coefficient

- **Assuming the vessel velocities are distributed with:**

$$P(v_z) = e^{-(v_z - \bar{v})^2 / 2\sigma_v^2} / \sqrt{2\pi}\sigma_v. \quad (8)$$

- **The continuity equation for $C_{av}(z^*)$ is:**

$$\frac{\partial C_{av}}{\partial t} = -\frac{1}{\pi R_o^2} \int_0^{R_o} \int_{-\infty}^{+\infty} P(v_z) v(r) \frac{\partial}{\partial z^*} C(r, z^*) dv_z 2\pi r dr. \quad (9)$$

- **Evaluating the integrals in Equation (5) yields:**

$$\frac{\partial C_{av}}{\partial t} = \tilde{D} \frac{\partial^2 C_{av}}{(\partial z^*)^2}. \quad (10)$$

- **The Taylor dispersion coefficient \tilde{D} is computed:**

$$\tilde{D} = \frac{F^2 l^2}{8 \pi \rho D} \left[(\pi \rho R_i^2 - 1)(\theta^2 + 2) - 4(\theta^2 + 1) \ln(R_i \sqrt{\pi \rho}) \right]. \quad (11)$$

where $\bar{v} = Fl R_o^2 / R_i^2$, $\theta = \sigma_v / \bar{v}$, and $R_o = 1 / \sqrt{\pi \rho}$.

Total Dispersion Coefficient

- **The total effective dispersion coefficient is expressed:**

$$D_z = D + \tilde{D}. \quad (12)$$

- D – Molecular diffusion coefficient
 - \tilde{D} – Taylor dispersion coefficient
 - D_z is an explicit function of D , Fl , ρ , R_i , and θ .
- **If the microvascular flows are uniform, then $\theta = 0$ and the Taylor dispersion coefficient reduces to**

$$\tilde{D} = \frac{F^2 l^2}{4 D} \left[R_i^2 - R_o^2 - 2 R_o^2 \ln(R_i / R_o) \right]. \quad (13)$$

- **When there exists a finite permeability across the vessel wall, the Taylor dispersion coefficient is expressed:**

$$\begin{aligned} \tilde{D} = \frac{F^2 l^2}{8 \pi \rho D} & \left[(\pi \rho R_i^2 - 1)(\theta^2 + 2) - 4(\theta^2 + 1) \ln(R_i \sqrt{\pi \rho}) \right] \\ & - \frac{F^2 l^2}{2 \pi \rho R_i p} (\pi \rho R_i^2 - 1)(\theta^2 - \pi \rho R_i^2 + 1). \end{aligned} \quad (14)$$

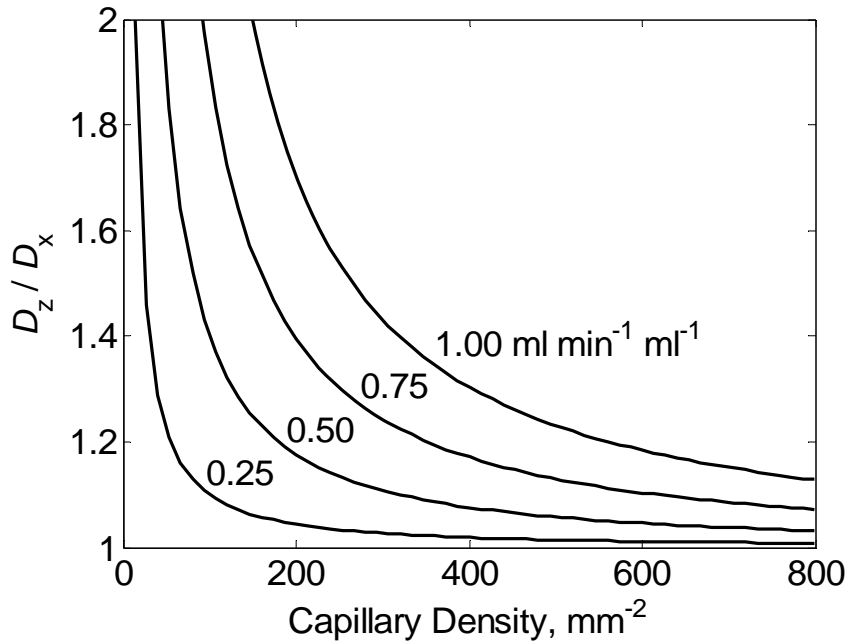
where p is the permeability of the vessel wall.

Results

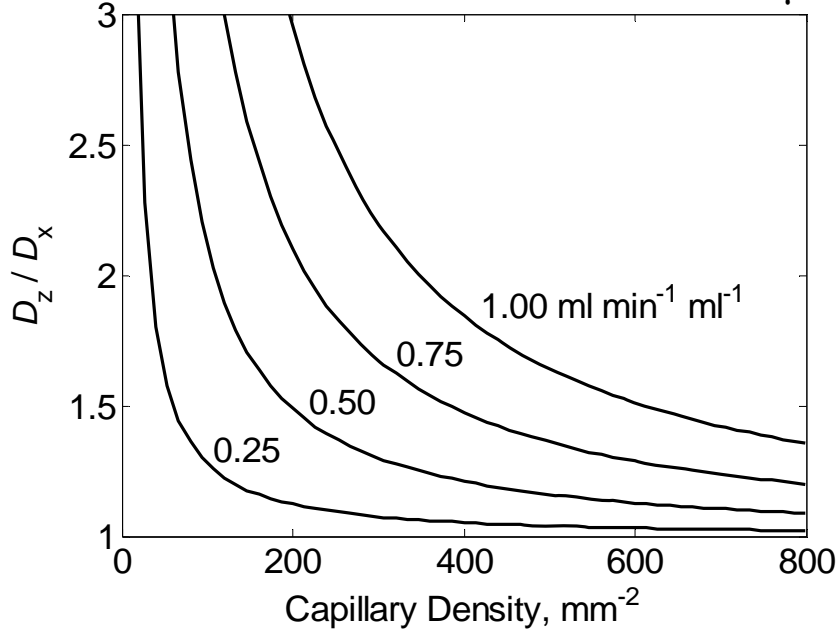
- **Theoretical predictions:**

- $R_i = 2.0 \mu\text{m}$; $l = 1000 \mu\text{m}$; $\sigma_v = 0.5\bar{v}$

- $D = D_x$ is assumed to have a value of $1000 \mu\text{m}^2 \text{sec}^{-1}$.

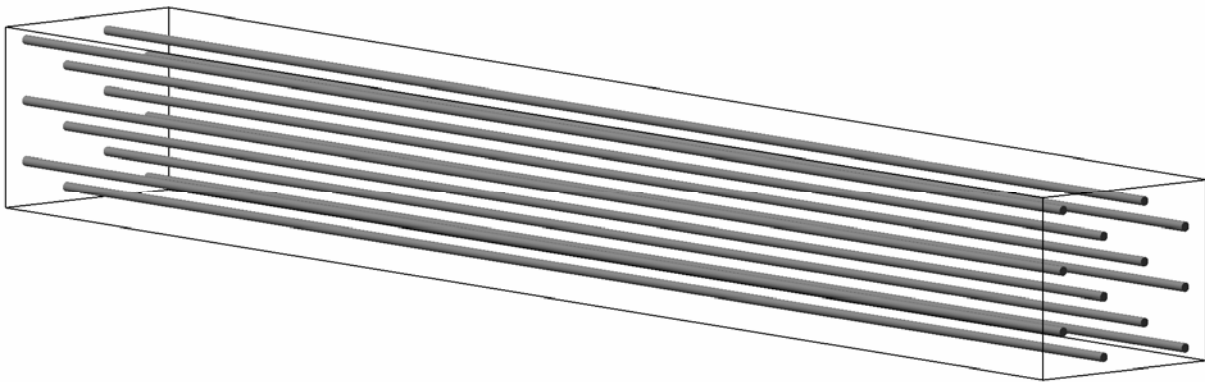


- $D = D_x$ is assumed to have a value of $600 \mu\text{m}^2 \text{sec}^{-1}$.

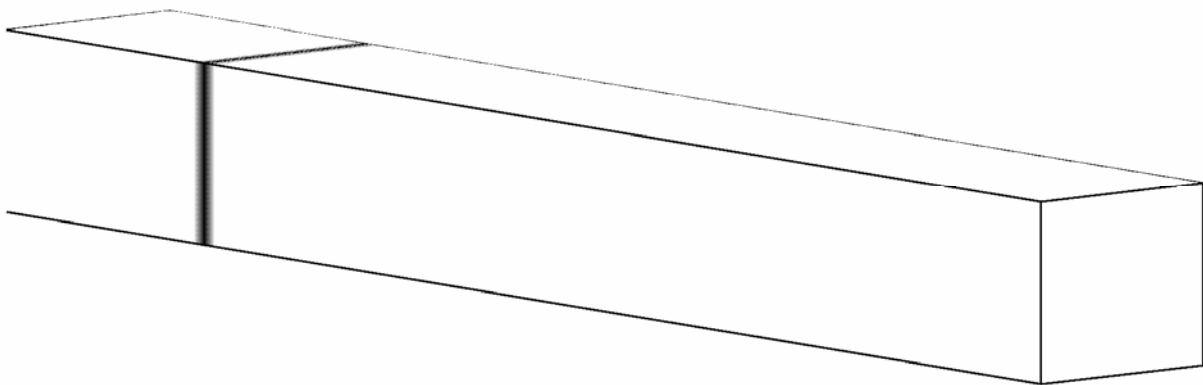


Numerical Validation

- **A three-dimensional model (Beard, 2001) for transport simulation**
 - $132 \times 114 \times 1000 \mu\text{m}$ region; 12 parallel capillaries; total $F = 2 \text{ ml min}^{-1} \text{ ml}^{-1}$.

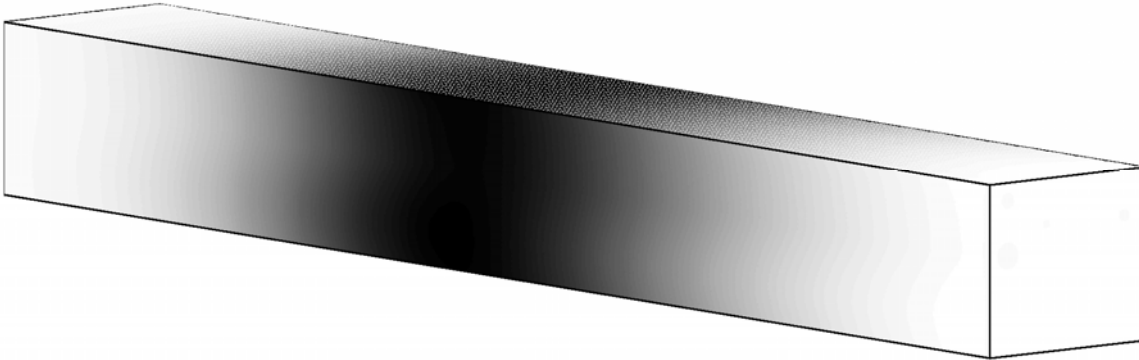


- The tissue is initially labeled with tracer solute at the $z = 200 \mu\text{m}$ location.

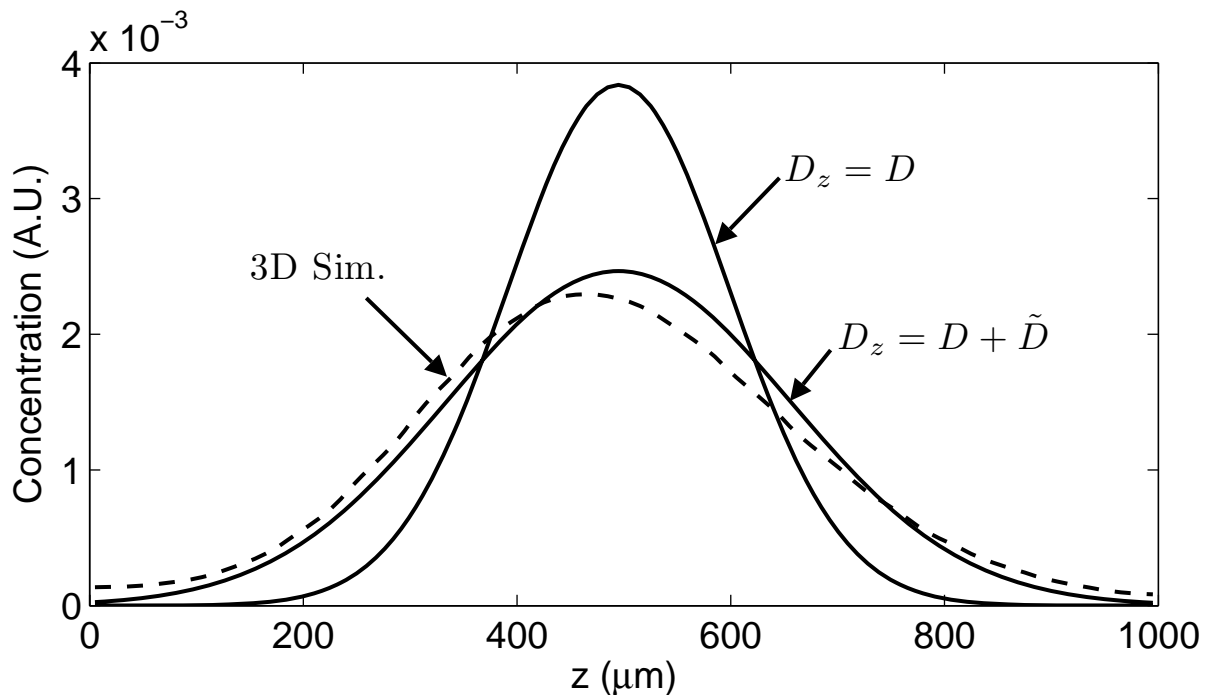


Numerical Validation (Continued)

- The simulated solute concentration profile after 9 seconds of simulation time



- Comparison between theoretical prediction and numerical simulation results



Conclusion

- Taylor dispersion represents a reasonable and plausible explanation for dispersion anisotropy observed in diffusion weighted MRI and diffusion tensor MRI.
- Given independent measures of D_z , D , and F , it is possible to invert Eqs. 11 or 14 to provide a measurement of vessel density ρ .
- The theory presented here is particularly suited to using diffusion tensor MRI to measure capillary vessel density *in vivo* in tissues with parallel microvascular morphometry.
- Treatment of molecular diffusivity as isotropic in tissue represents an assumption that is not a fundamental requirement of the above analysis and may readily be revised.
- It may be possible to reduce the complexity of blood-tissue exchange model by accounting for Taylor dispersion in the direction of capillary flow.

Acknowledgements

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References

- Beard, D. A.** (2001). "Computational framework for generating transport models from databases of microvascular anatomy." *Ann Biomed Eng* 29(10): 837-43.
- Goresky, C. A.** (1963). "A linear method for determining liver sinusoidal and extravascular volumes." *Am J Physiol* 204: 626-40.
- Hrabe, J., S. Hrabetova, et al.** (2004). "A model of effective diffusion and tortuosity in the extracellular space of the brain." *Biophys J* 87(3): 1606-17.
- Krogh, A.** (1919). "The number and distribution of capillaries in muscle with calculations of the oxygen pressure head necessary for supplying the tissue." *J. Physiol. (Lond.)* 52: 409-415.
- Maas, L. C., P. Mukherjee, et al.** (2004). "Early laminar organization of the human cerebrum demonstrated with diffusion tensor imaging in extremely premature infants." *Neuroimage* 22(3): 1134-40.
- Minematsu, K., L. Li, et al.** (1992). "Diffusion-weighted magnetic resonance imaging: rapid and quantitative detection of focal brain ischemia." *Neurology* 42(1): 235-40.
- Moseley, M. E., J. Kucharczyk, et al.** (1990). "Diffusion-weighted MR imaging of acute stroke: correlation with T2-weighted and magnetic susceptibility-enhanced MR imaging in cats." *AJNR Am J Neuroradiol* 11(3): 423-9.
- Partridge, S. C., P. Mukherjee, et al.** (2004). "Diffusion tensor imaging: serial quantitation of white matter tract maturity in premature newborns." *Neuroimage* 22(3): 1302-14.
- Scollan, D. F., A. Holmes, et al.** (2000). "Reconstruction of cardiac ventricular geometry and fiber orientation using magnetic resonance imaging." *Ann Biomed Eng* 28(8): 934-44.
- Secomb, T. W. and R. Hsu** (1994). "Simulation of O₂ transport in skeletal muscle: diffusive exchange between arterioles and capillaries." *Am J Physiol* 267(3 Pt 2): H1214-21.
- Sotak, C. H.** (2002). "The role of diffusion tensor imaging in the evaluation of ischemic brain injury - a review." *NMR Biomed* 15(7-8): 561-9.
- Taylor, G. I.** (1953). "Dispersion of solute matter in solvent flowing slowly through a tube." *Proc. Roy. Soc. (London), Series A* 219: 186-203.