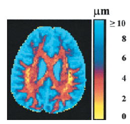
Computational MR Imaging: From Diffusion to Microstructural Tissue Characterization



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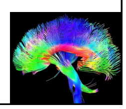
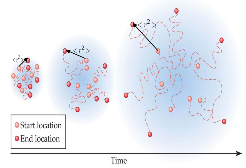
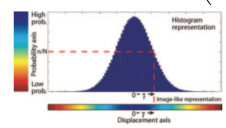


Isotropic Case

In the isotropic case, the probability *P* of displacement vector ***R*** at a time *t* of a water molecule is a Gaussian distribution:

$$P(X,t) = \frac{1}{\sqrt{6D\pi t}} \exp\left(-\frac{\vec{R}^2}{6Dt}\right)$$





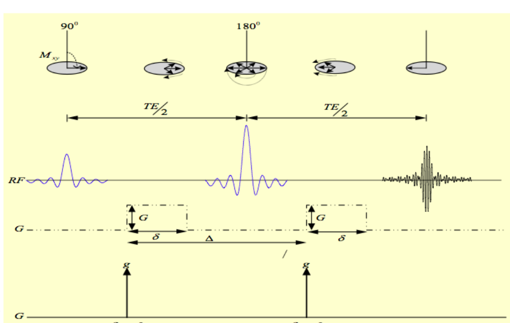
The mean square displacement of the molecule in time t is given by:

$$< \vec{R}^2 >= \int_{-\infty}^{\infty} R^2 P(\vec{R},t) d\vec{R} = 6Dt$$

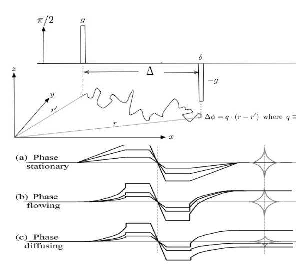
Diffusion Imaging

PGSE

q-space



How can Diffusion Affect the MRI Signal ?



a) Stationary spins are refocused to form an echo.

b) Spins in bulk motion are refocused with a net phase shift.

c) Diffusing spins experience differing phase shifts

Stejskal-Tanner diffusion sequence (1965)

Bloch-Torrey NMR/Diffusion Equation

- Extension of the NMR Bloch Equation to include effects of diffusion on transverse magnetization

$$\frac{\partial M_{xy}}{\partial t} = -i\omega_0 M_{xy} - \frac{M_{xy}}{T_2} - i\gamma(\vec{G}\cdot\vec{r})M_{xy} + D\nabla^2 M_{xy}$$

- For a magnetic field gradient along a single direction, M_{xy} becomes:

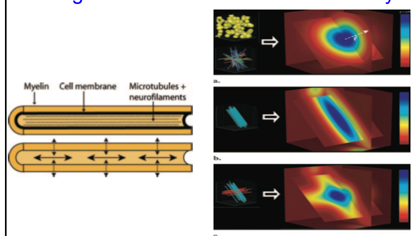
$$M_{xy} = A_0 e^{-bD} e^{-ik(t)\cdot\vec{r}} e^{-i\omega_0\cdot t} e^{-t/T_2}$$

- For a balanced gradient at echo time TE:

$$M_{xy}(TE,b) = gA_0 e^{-bD} e^{-i\omega_0\cdot t} e^{-TE/T_2}$$

Random Walks and Anisotropy

Biological structures exhibit directionality in diffusion properties



- ***D*** is a **3 x 3** rank-2 tensor

$$D = \begin{pmatrix} D_{xx} & D_{xy} & D_{xz} \\ D_{yx} & D_{yy} & D_{yz} \\ D_{zx} & D_{zy} & D_{zz} \end{pmatrix}$$

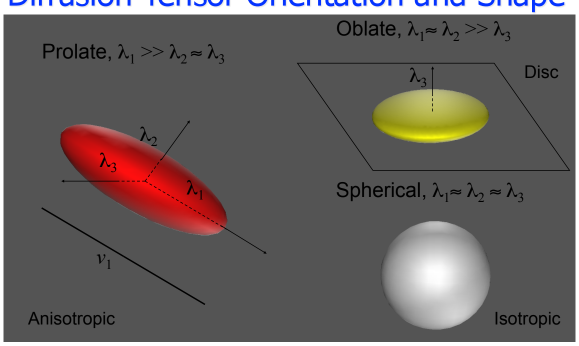
Principal Axes ⟷ Eigenvectors of D

Principal Diffusivities ⟷ Eigenvalues of D

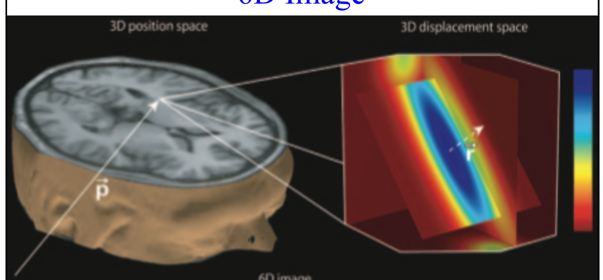
- For uncharged molecules such as water, ***D*** is symmetric: $D_{ij}=D_{ji}$

$$\{D_{xx}, D_{yy}, D_{zz}, D_{xy}, D_{xz}, D_{yz}\}$$

Diffusion Tensor Orientation and Shape



6D Image

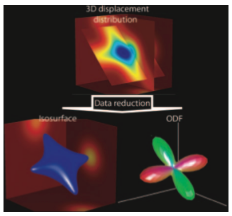


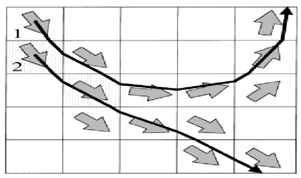
Standard Image versus 3D Displacement Image

Streamline Tractography

Attempt to 'connect' voxels on basis of directional similarity of coincident eigenvectors

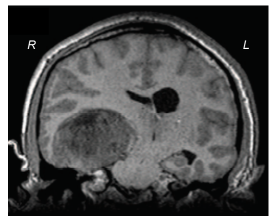
Fiber tracking simplifies the diffusion tensor to the vector field of the principal eigenvector

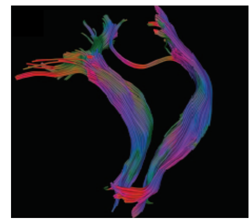




Mori et al., Ann Neurol 1999

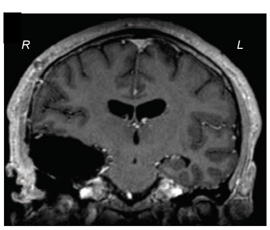
Glioma: Pre-op

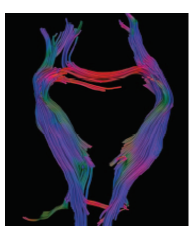




Nimsky et al. Neuroscience 2005

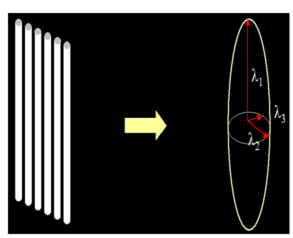
Glioma: Post-op

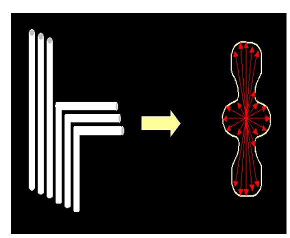




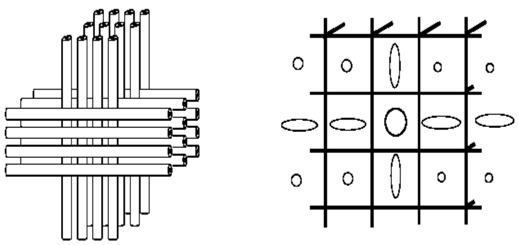
Nimsky et al. Neuroscience 2005

Fiber Tracking: High Angular Deviations



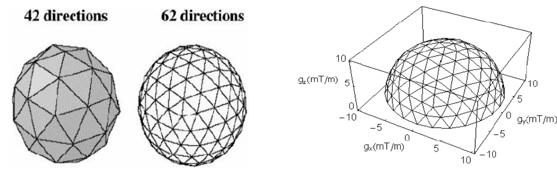


Resolving Tensor Directions: Partial Volume Effects



Lack of resolvability of fine underlying structures

Gradient Tensor Sampling



- High angular resolution DTI: Spherical Tessellations of an icosahedron
- Spherical surface is uniformly divided by the diffusion encoding gradients
- High gradient sampling: more uniform and less bias to any particular direction.

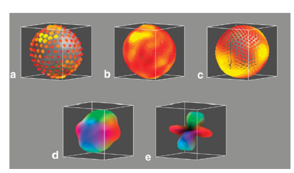
Diffusion Spectrum Imaging: Tractography

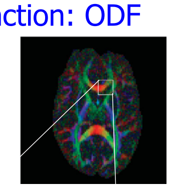
- High angular resolution diffusion imaging to resolve ambiguities high field multi-channel systems
- In q-space imaging, high Gradient strength (δ --> 0) to measure incoherent self-diffusion without Gaussian assumption.

$$S(q) = \int \rho(r_0) P(\vec{R}, t_d) \exp(i2\pi q \cdot \vec{R}) d\vec{R}, \;\; q = \gamma\delta/2\pi g$$

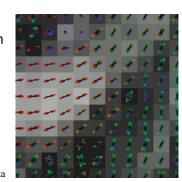
- Diffusion Spectrum Imaging (DSI) is a compromise using very high b-values (b=15 X 10^9 sm^{-2})
- Challenges of implementation on clinical scanners

Orientation Distribution Function: ODF

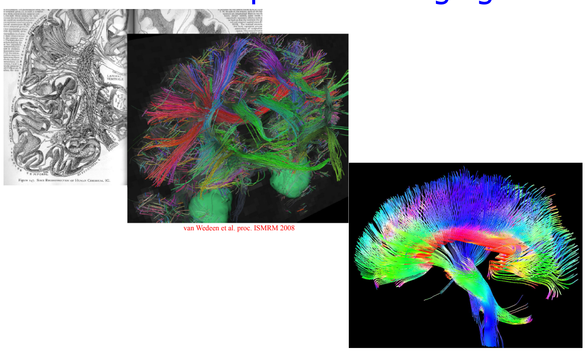




a) Diffusion signal sampled on tessellated icosahedron
c) Regridding of diffusion signal
e) Diffusion ODF using Fourier Analysis
g) Color-coded spherical polar plot rendering of ODF
e) Min-Max normalized ODF



Diffusion Spectrum Imaging



van Wedeen et al. proc. ISMRM 2008

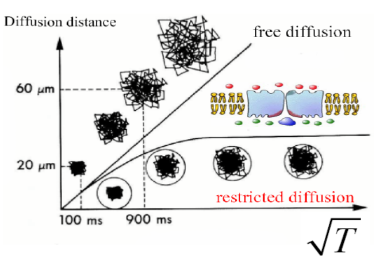
Temporal Evolution the Diffusion Tensor

Time Dependence of Diffusivity

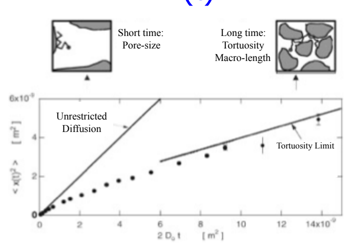
Diffusion distances

~ 3 um²/ms – Body temperature in water (CSF)
~ 2.1 um²/ms – Body temperature in axoplasm

- *In isotropic case, an average water molecule will diffuse a distance of* $\sqrt{2Dt}$ *in a time t, and D is the scalar apparent diffusion coefficient.*



Temporal Evolution of the Diffusion Tensor D(t)



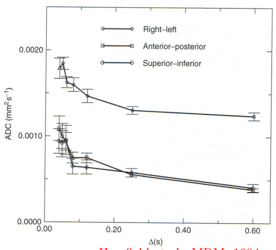
P. Sen, Phys. Rev. B. 47, (1993)

Confining geometry encoded in the mean-square displacements as a function of time

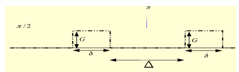
Implications of Temporal Diffusion Changes

τ: interval between molecular collision with boundary

Δ: is the diffusion observation time



Horsfield et al., MRM, 1994



$\Delta << \tau \rightarrow$ unrestricted diffusion D_{free}

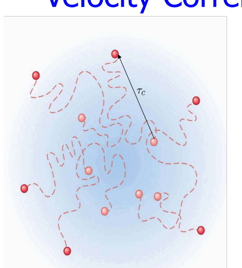
$\Delta >> \tau \rightarrow$ restricted diffusion $D_{restricted}$

Deviates from linearity when:

$D_{free} \rightarrow D_{restricted}$ with increasing Δ

Diffusion Process in the Spectral Domain

Velocity Correlation Viewpoint



- τ_c is the particle diffusion jump time
- The rms jump length is of the order $\upsilon_z\tau_c$
- The velocity correlation is thus given by:

$$\overline{v_z(0)v_z(t)} = \overline{v_z^2}e^{-t/\tau_c}$$

-The spectrum of the velocity correlation function is the diffusion tensor:

$$D_{zz}(\omega) = \int_0^\infty \overline{v_z(0)v_z(t)}\exp(i\omega t)dt$$

where $D_{zz}(0) = \overline{v_z^2}\tau_c$

-For free diffusion, velocity correlation time is very short

-For restricted diffusion, τ_c is long, hence longer time correlations exist:

Spectral Interpretation of Diffusion

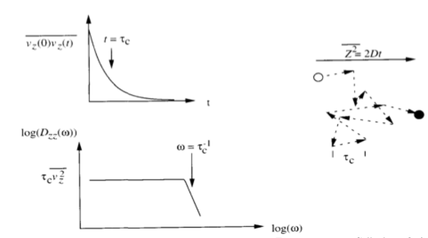
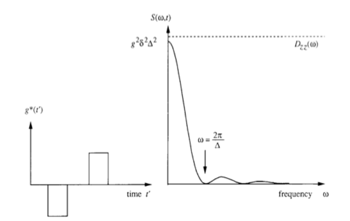


Fig. 6.3, pp. 337 Callaghan, Oxford Press (1991)

- Diffusion is thus characterized by a spectrum of frequencies
- In the brain, this spectrum spans frequencies from DC-3 KHz
- PGSE NMR is an aggregate weighting of all components of diffusion from DC to some cut-off $1/\tau_c$

Spectral Viewpoint: PGSE Case



- Diffusion signal in MR is given by:

$$M_{xy}(t) = M_0 e^{-bD} = M_0 e^{-\alpha(t)}$$

- In the PGSE case:

$$\alpha(\Delta) = \underbrace{\gamma^2 \delta^2 g^2 (\Delta - \delta/3)}_{b} D$$

- In the spectral domain:

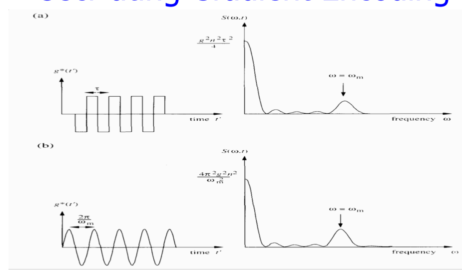
$$\alpha(t) = \frac{1}{2\pi}\gamma^2 \int_{-\infty}^{\infty} D(\omega) S(\omega, t) d\omega$$

-PGSE gradient is dominated by a zero frequency lobe with $BW = \Delta^{-1}$

-Gradient spectrum is a filter of underlying diffusion spectrum

- PGSE is unsuitable for extracting high frequency information in $D(\omega)$

Oscillating Gradient Encoding



- Oscillating gradients allow the probing of high frequency components in D(t)
- Offers possibility of investigating rapid motions over long evolution times
- Segregation of diffusion time constants to probe specific dynamics

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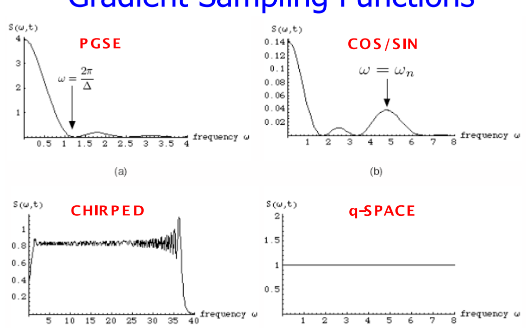
Gradient Sampling Functions



Kiruluta et al. JMR, 2008

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Can One hear the shape of a drum ?
Kac, 1966

Mark Kac. "Can one hear the shape of a drum?" Amer. Math. Monthly, 73, 1966.

Is a Riemannian Manifold (possibly with a boundary) determined by its spectrum ?

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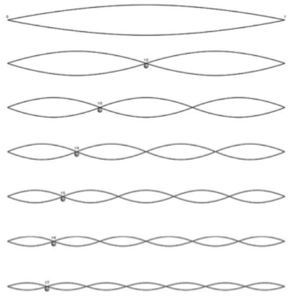
Analogy with Vibrating String



The fundamental harmonic is given by:

$$f = \frac{v}{2L} = \frac{1}{2L}\sqrt{\frac{T}{\mu}}$$

T: is the tension in the string
μ: is the linear mass
L: is the length of the string

- The shorter the string, the higher the note
- The higher the tension, the higher the note
- The lighter the string, the higher the note

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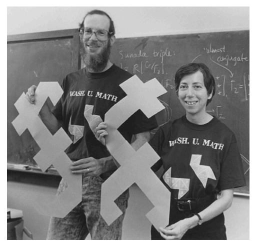
You Can't Always Hear the Shape of a Drum



Webb and Carolyn Gordon, former faculty at Washington University in St. Louis, with paper models of a pair of "sound-alike" drums.

- 1991 Carolyn Gordon, David Webb, and Scott Wolpert found examples of distinct plane "drums" which "sound" the same
- There is one case, however, in which we can tell the exact shape of the drum, and the problem remains solvable. This is the case of a circle.
- Kac showed that both the **area** of a drum's membrane and the length of its **perimeter** affect short-time behavior eigenspectrum.
- In other words, one can "hear" a drum's **area** and **perimeter**

C. Gordon, D. Webb, and S. Wolpert. "One cannot hear the shape of a drum." Bull. Amer. Math. Soc., 27:134-138, 1992.

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Time-dependent Diffusion Coefficient: A Summary

- At short times D(t) determines:

$$D(t) \sim S/V_p, \kappa$$

$\longrightarrow$ Surface area to total internal cell volume (S/V_p) & cell wall permeability κ

$\longrightarrow$ S/V_p analogous to the perimeter of a drum

- At long times:

$$D(t \longrightarrow) = \frac{D_0}{\alpha} = \frac{D_0}{F\phi}$$

$\longrightarrow$ Tortuosity α characteristic of confining geometry (F) and porosity (ϕ)

Sen, Concepts in NMR, 2004, Kiruluta et al., Chem Phys, 2008

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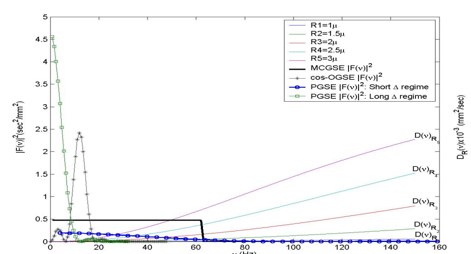
Spectral Sampling Experiments with Cylindrically Bound Spins



Kiruluta et al. J. Chem Phy. 2008

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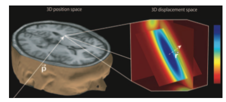
Comparison of q-space and Chirp-Space for Diffusion Encoding

Dynamic Microscopy

MR Imaging Equation:

$$S(\vec{k}) = \int \rho(\vec{r}) \exp(i2\pi \vec{k}\cdot\vec{r}) d\vec{r}$$



6D Image

Combined Static and q-space Imaging:

$$S(\vec{k},\vec{q}) = \int \rho(\vec{r}) \exp(i2\pi \vec{k}\cdot\vec{r}) d\vec{r} \int P(\vec{r}|r',t') \exp(i2\pi \vec{q}_{t'}\cdot(r'-\vec{r}))dr'$$

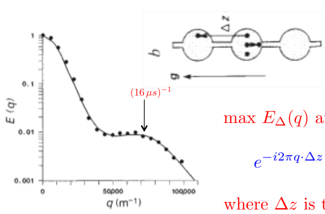
where $q = \frac{\gamma}{2\pi} g\delta$

Combined Static and Chirp based Encoding:

$$S(\vec{k},\vec{q}_{t'}) = \int \rho(\vec{r}) \exp(i2\pi \vec{k}\cdot\vec{r}) d\vec{r} \int P(\vec{r}|r',t') \exp(i2\pi \vec{q}_{t'}\cdot(r'-\vec{r}))dr'$$

where $q_{t'} = \frac{\gamma}{2\pi} g t'$ is the wavelength for a given step in the chirp encoding

Echo Intensity $E_\Delta(q)$ versus Gradient Wave Vector q



Callaghan, Nature, 351 (1991)

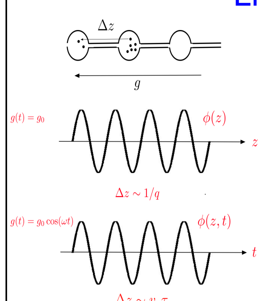
max $E_\Delta(q)$ at $|q| = (\Delta z)^{-1}$ so that

$$e^{-i2\pi q\cdot\Delta z} \sim e^{-i2\pi} \longrightarrow q \sim \frac{1}{\Delta z}$$

where Δz is the restricting pore spacing

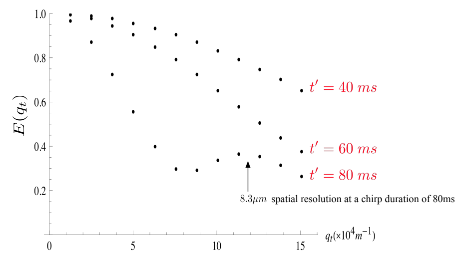
Optimum diffusion evolution time is thus $\Delta \approx (\Delta z)^2/2D_{eff}$

Spatial-Spectral Displacement Encoding



- Oscillatory Gradient:
  $G(t) = g\cos(2\pi f_{osc} t)$
  $k(t) = g\sin(2\pi f_{osc} t)$
- Resolvability on time scale of diffusion jump:
  $$e^{-i2\pi f_{osc}\cdot\tau_c} \sim e^{-i2\pi} \longrightarrow f_{osc} \sim \frac{1}{\tau_c}$$
- Linear Gradient:
  $G(t) = g \longrightarrow k(t) \sim gt$
- Resolvability of displacement on the scale:
  $$e^{-i2\pi q\cdot\Delta z} \sim e^{-i2\pi} \longrightarrow q \sim \frac{1}{\Delta z}$$
  For $16\,\mu m$, $q = (2\pi)^{-1}\gamma g\delta = 60,000$!

Echo duration versus Chirp Duration



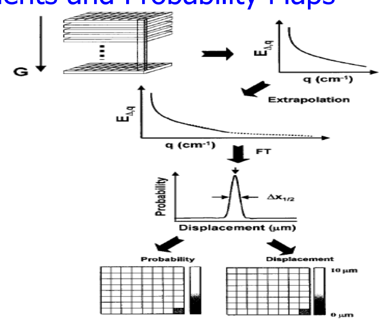
- Restrictive morphology consisting of a packed bead phantom with a porosity of 40%

- At both t′ = 60 ms and 40 ms, the resulting wave vector is beyond the resolvability of the packed bead phantom but asymptotically approaches it as $1/q_t' \longrightarrow 8.3\ \mu m.$

Displacements and Probability Maps

$$E_\Delta(q) = \int P(R,\Delta) e^{i2\pi q\cdot R} dR$$

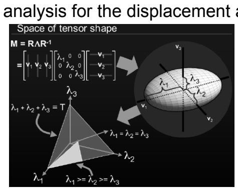
$$E_\Delta(q) \underset{\longleftrightarrow}{\mathfrak{F}} P(\vec{R},\Delta)$$



-Repeat for all $\vec{G} = \{xy, xz, yz, -xy, -xz, y - z\}$

Tensor Analysis

- Calculate displacement and probability images for the six directions
- Perform a tensor analysis for the displacement and probability indices



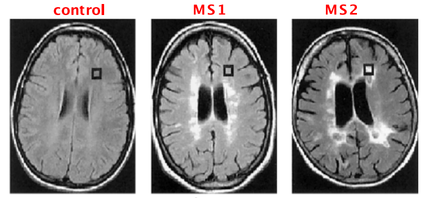
Principal Axes ⟷ Eigenvectors of M

Principal Diffusivities ⟷ Eigenvalues of M

- For the displacement tensor, the smallest eigenvalue was chosen: displacement perpendicular to the long axis of neuronal fibers
- For the probability of zero displacement, the largest eigenvalue was used

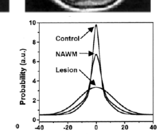
Application to an MS Case

control MS1 MS2



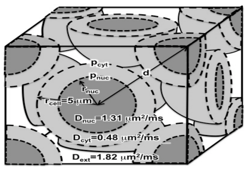
FLAIR

Assaf et al. MRM 44:713-722, 2000

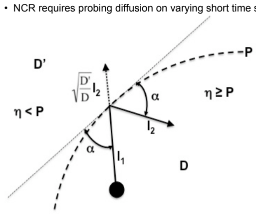


TR/TE = 1500/160 ms
$\Delta/\delta = 80/100\ ms$
256 x 256, NEX = 4
T_{acq} = 12 min

Diffusion & Permeability in Cancer Cells



- Use DTI to discriminate tumor grades
- Change in cell-volume-fraction (CVF) not a reliable indicator
- Nucleus-to-cell volume (NCR) is a better indicator
- NCR requires probing diffusion on varying short time scales



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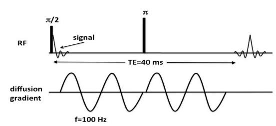
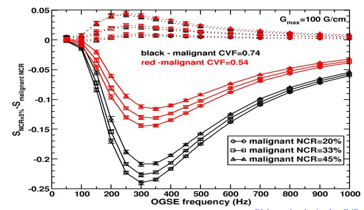
Diffusion Sensitivity to Changes in NCR


Prof Jae Kim, Thunder Bay Regional Research Institute





Blake et al. submitted to JMR

Summary

Temporal evolution of the restricted diffusion coefficient can be used to extract:

1. Fluid types (diffusion relaxation parameters)
2. S/V_p and cell wall permeability κ (short-time D(t))
3. Macrolength and tortuosity α (long-time D(t))
4. q-space imaging with chirped gradients can detect small lesions in MS & tumor morphology characterizations

Future Work:

1. Disentangling the complexity due to the combined effects of disorder, diffusion and relaxation time constants
2. Adequate chirp-space sampling to resolve complexity
3. Implementation on clinical scanners for in-vivo evaluation work is on-going

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