Diffusion-limited diffusion MRI and a universal optimum b-value

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Introduction: A basic objective of diffusion MRI is to resolve the probability density function (PDF) of spin displacements as a marker for the structure of the spin-accessible micro-environment of the tissue: "the container" as David Cory termed it. Let us model diffusion MRI as an effort to image this container. In this case, the diffusion can be considered to inflict on the image of this underlying structure a spatial "blurring". This process has no closed-form model in tissue, but initially diffusion should blur local structure according to its displacement kernel, repeating iteratively in each time interval.

Approach: If we accept this ansatz, then the resolution of the *q*-space diffusion image is defined by 2 factors, the resolution of the "camera" which is the diffusion encoding $1/q_{max}$, and the blurring due to the diffusion kernel over the experimental timescale, $\sqrt{(2Dt)}$, where D is the diffusivity of the material, and $t = \Delta$, the diffusion encoding time. At fixed gradient intensity, these factors are simply coupled, for if one tries to increase camera resolution $1/q_{max}$, then at a given gradient strength one must increase the diffusion encoding time Δ, counteracting this by broadening the diffusion kernel $\sqrt{(2Dt)}$.

Making this explicit, define the diffusion resolution for underlying tissue R_{eff} Then

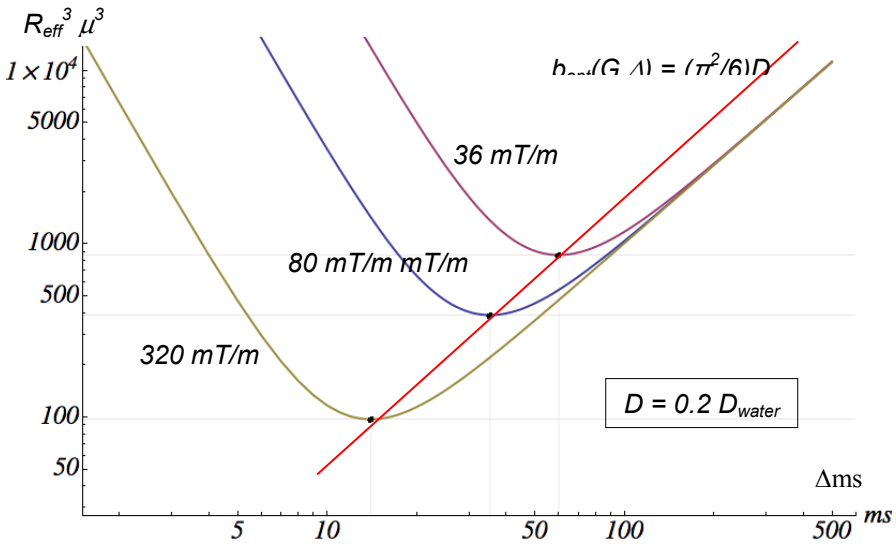
$$R_{eff}^2 = QSI\ encoding\ resolution^2 + diffusion\ blurr^2 = q^{-2} + 2Dt$$

Then for the best possible R_{eff}, in DWI/QSI, setting $t = \Delta = \delta$ and $q = \gamma G t$, we require

$$d/dt[(\gamma G t)^{-2} + 2Dt] = 0$$

Solving, we find diffusion encoding parameters for the best possible structural resolution

- *the optimal encoding time is……* $t_{opt} = (D(\gamma G)^2)^{-1/3}$
- *the optimal b is……* $b_{opt} = (\pi^2/6)\, D^{-1}$
- *the best resolution possible is……* $R_{min} = 3^{1/2}\,(D/\gamma G)^{1/3}$



Results: Let us consider the implications of these results. First, the best possible resolution of the only technical variable that affects the resolution of the underlying structure is maximum gradient strength G. Second, no matter the gradient, the optimum b-value is always simply $b_{opt} = \pi^2/6\ D^{-1}$. This sounds rather odd, but what it means is that the best possible resolution for tissue with diffusivity D is always achieved at this same b-value. If gradients are more powerful, resolution improves at this constant b-value as a result of shorter encoding time, and reduced blurring due to diffusion, but $b > b_{opt}$ doesn't help; it hurts. These relations are illustrated in the following diagram, of resolution as a function of mixing time Δ at several gradient levels in wide use, for a material with $D \geq 0.2D_{water}$. Note that all minima are achieved along the straight line of constant $b = b_{opt}$.

Discussion: For living tissue, if we take a rough minimum of mean diffusivity of $0.2D_{water}$, then the optimum b-value for in vivo imaging should be $b_{opt} \approx 18{,}000$ s/mm^2. Ex vivo, we find empirically little improvement in DSI resolution of tissue structure ex vivo for $b > 40{,}000$ s/mm^2, consistent with an ex-vivo diffusivity ≈ ½ of the in vivo diffusivity. This analysis has 2 limitations. First, it may be difficult to determine the true minimum diffusivity present in tissue, and therefore difficulty to be absolutely certain that an experiment with higher b might not disclose more detail. Recent evidence from temporal diffusion spectroscopy suggests that highly restricted components may indeed be present in vivo, and observable at short time scales [1]. Second, this analysis omits the effects of noise, which will tend to reduce the ideal b-value below its theoretical noise-free value. Thus, this analysis indicates that gradient strength is critical, should motivate the hardware community to facilitate diffusion MRI through improved gradient performance.

[1] Gore JC, Xu J, Colvin DC, Yankeelov TE, Parsons EC, Does MD. NMR Biomed. 2010 Aug;23(7):745-56.