Exact results for diffusion weighted MR on branched structures

N. Buhl[1,2], and S. Jespersen[2]
[1]Physics and Astronomy, University of Aarhus, Aarhus, Denmark, [2]CFIN, University of Aarhus, Aarhus, Denmark

Introduction: Branched structures are found in many biological systems, including plant roots, neural networks, and respiratory systems. Diffusion-weighted MRI (DWI) employing long diffusion times can provide information on connectivity and topology in such systems, a prime example being the measurement of hyperpolarized ^{3}He gas diffusion in human lungs. In emphysema, tissue destruction creates collateral pathways between the lung alveoli. The effects of such connectivity changes on DWI have previously been analyzed using numerical simulations [1]. Here we present an exact result for the diffusion propagator on a large class of metric networks (graphs) and derive an analytical expression for the signal attenuation in a PGSE diffusion experiment. It is demonstrated that the return to origin probability is explicitly independent of embedding in three-dimensional space, in contrast to the diffusion signal. We apply these results to a simple acinar model and examine the sensitivity of DWI to collateral pathways.

Theory: In order to derive the diffusion propagator, we introduced the following notation: Let $G = (V,E)$ be a simple graph, i.e. V is a set of vertices and E is a set of edges that connects pairs of distinct vertices. For a given edge e connecting the vertices $v,w \in V$, there are two directed edges given by the ordered pairs (v,w) and (w,v). For each edge $e \in E$ we select one of these pairs and denote it by $dir(e)$. If $d = dir(e)$, an interval $[0,L_e]$ can be associated with e by letting 0 and L_e correspond to the first and last vertex of d respectively. L_e is the length of e. The structure obtained in this way is called a metric graph. It allows one to specify the position of a point on a graph in terms of the edge it lays on and the coordinate x along the interval associated with this edge (Fig. 1). (The theory below is independent of the choice of direction).By considering the eigenvalue problem for the Laplace operator on each edge subject to continuous Neumann boundary conditions at the vertices, the diffusion propagator $[p_t(x_0,x)]_{e,e'}$ may be written down as a sum of weighted Gauss functions parameterized in terms of all the walks connecting e and e' [2]. Here a walk from e to e' is defined as an ordered sequence of edges forming a path between e and e'. $[pt(x_0,x)]_{e,e'}$ gives the probability for a diffusing particle initially at $x_0 \in [0,Le]$ on e to have moved to $x \in [0,L_{e'}]$ on e' after a time t. If all edges are restricted to have the same length L, the sum can be expressed in a simple way as ***Eq. 1***, using powers of the matrix $U_{dd'}=U_{(v)(mw)}=\delta_{lm}(2/deg(l)-\delta_{vw})$, which has as indices all the directed edges which can be formed from edges in E. deg(l) is the number of edges having l as one of their ends.

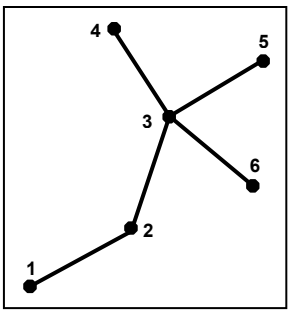

Fig. 1: Simple graph (network) with 6 labeled vertices and 5 edges.

$$\left[p_t(x_0,x)\right]_{e,e'} = \delta_{e,e'}g_t(x_0-x)+\sum_{n=1}^{\infty}\left(U^n_{d,d'}g_t(-x_0+nL+x)+U^n_{d,\hat{d}'}g_t(-x_0+(n+1)L-x)+U^n_{\hat{d},d'}g_t(x_0+(n-1)L+x)+U^n_{\hat{d},\hat{d}'}g_t(x_0+nL-x)\right) \quad \textbf{[Eq. 1]}$$

where $g_t(u):=(4\pi Dt)^{-1/2}\exp(-u^2/4Dt)$, d = dir(e) and d' = dir(e'). $\hat{d}$ and $\hat{d}'$ are the corresponding inverted directed edges formed by swapping the vertices in d and d' respectively. The series converges rapidly and may typically be truncated when $nL/(2Dt)^{1/2} \sim 5$. Based on an embedding (coordinates for the vertices) and Eq. 1, the signal attenuation in a PGSE experiment with short gradient duration can be obtained by integrating $p_t(x_0, x)$ times the phase shift over the whole structure.

Calculations: The calculations were based on a 2D lung acinar model (Fig. 2). Starting with the leftmost, each edge had 2 daughter edges with inplane angles of ±34° with respect to the parent edge. Calculation of $pt(x_0,x)$ for the acinar model (without collateral paths) was done together with a random walk simulation with 6×10^6 particles starting at x_0, each taking 4000 steps. Edges are 30 steps long. (A vertex which has only one connection constitute a reflecting boundary). Fig. 3 shows the excellent agreement between the calculated $[pt(x_0,x)]_{e,e'}$ and the random walk simulation of the same quantity. The signal attenuation was then calculated for a PGSE experiment comparing the case with no collaterals and the cases with 5 and 10 collateral pathways (see Fig. 2). Each edge had a length of 1mm [3], $D = 0.88cm^2/s$ and diffusion time = $10ms$. Fig. 4 shows the effect of increasing collateral paths on the calculated signal attenuation.

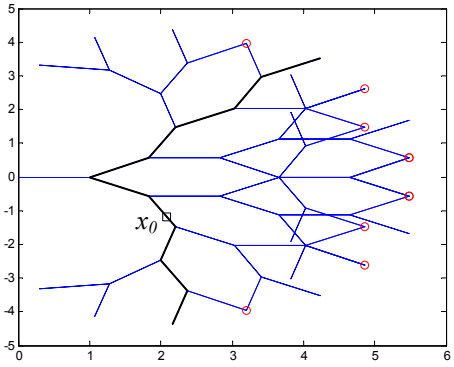

Fig. 2: A 2D acinar model. Due to the regular design, some vertices and edges overlap. Collateral paths were created by connecting the terminal vertices (red circles), which affect only the connectivity. x_0 and the points along the highlighted path are respectively the start and end points used in the calculation/simulation in Fig. 3.

Conclusion: We have outlined an exact mathematical framework for DWI in branched structures and applied it to a simple model of human pulmonary archini, showing the effect of increasing collateral paths in the calculated DWI signal attenuation. An application of the theory to a full lung model with realistic geometry is underway, which should allow us to further investigate the long diffusion time regime (seconds). These results are important for understanding the role of airway connectivity in DWI of lungs and supplement models addressing microstructural sensitivity [4]. In addition, our expressions may be useful for the design and optimization of pulse sequences. Finally, it contributes to the very limited number of systems for which the diffusion signal can be calculated exactly, and may therefore prove valuable as a test case scenario for new DWI techniques as well as simulations.

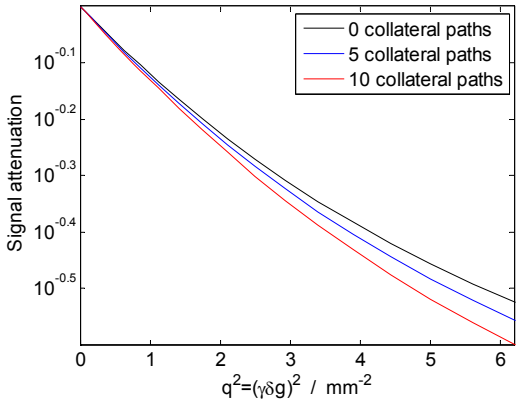

Fig. 4: Signal attenuation calculated via the theory for a PGSE experiment with spins diffusing in the acinar model (Fig. 2) with and without collateral paths.

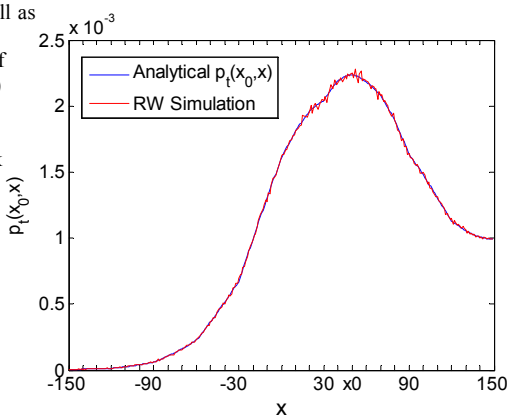

Fig. 3: Comparison of the calculated $pt(x_0,x)$ for the acinar model (without collaterals) with the random walk simulation, showing good agreement.

References: [1] Grebenkov (2007) J. Magn. Reson. 184, 143-156; [2] Kostrykin (2007) Amer. Math. Soc. 447, 175-198; [3] Haefeli-Bleuer (1987) Anatomical Record 220, 401-414 [4] Yablonskiy et al. (2002) PNAS 99.