# Maximal entropy tractography

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**Introduction** A problem of significant interest is the determination of neural pathways from diffusion tensor imaging (DTI) data. Current fiber tractography methods generally fall into two categories: 1) deterministic methods, typically based on some form of streamline construction [1] or 2) probabilistic methods, typically also based on streamline construction, but with the most likely principal diffusion direction drawn from a sample of the posterior distribution of principal diffusion directions, thus equating the probability of a tract with the frequency it is reconstructed by a Monte Carlo random walk governed by properties of the diffusion tensor (e.g., [2]). These algorithms are thus probabilistic in the local (spatial) sense and hence determining any globally optimal path from them is problematic. Here we present a truly global method that defines and constructs an optimal path between two user defined regions, and thus can be used to quantitatively assess the probability of connection between brain regions. The method is based upon the maximal entropy random walk [3] which is used to construct the pathway of maximal entropy regions in a 3D diffusion tensor field. The computational method is surprisingly simple and straightforward to implement.

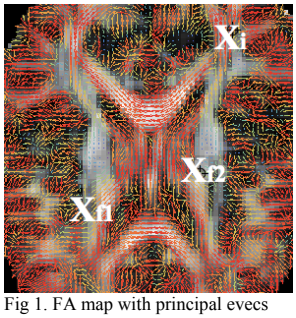

Fig 1. FA map with principal evecs

**Theory** The DTI data are assumed to be on a finite, connected, 3D regular lattice (i.e., all nodes have the same degree) defined by the symmetric adjacency matrix $\boldsymbol{A}$ with elements $A_{ij} = 1$ if $i$ and $j$ are neighboring nodes, and $A_{ij} = 0$ if they are not. A particle hops between nodes in a discrete time Markov fashion, from node $i$ at time $t$ to neighboring node $j$ at time $t+1$ with probability $P_{ij}$, independent of its past history. If two nodes are not linked ($A_{ij} = 0$) then $P_{ij} = 0$ and at each node $\Sigma_j P_{ij}=1$. The probability $\pi_i(t)$ of finding a particle at node $i$ at time $t$ is found recursively from $\pi_i(t)= \Sigma_j \pi_j(t-1) P_{ji}$. Thus the probability $P(\sigma[i_0,i_t])$ of generating a trajectory $\sigma[i_0,i_t]$ of length $t$ passing through the nodes $(i_0, i_1,..., i_{t-1},i_t)$ is $P(\sigma[i_0,i_t])= P_{0,1}P_{1,2}...P_{t-1,t}$. The maximally random trajectories are those that are equiprobable for a given length $t$ and endpoints $(i_0,i_t)$ and maximize entropy production rate $s =-\Sigma_i \pi_i^* \Sigma_j P_{ij} \ln P_{ij}$. The transition probability $P_{ij}$ results in a unique stationary state $\pi_i^*$ that satisfies $\pi_i^* = \Sigma_j \pi_j^* P_{ji}$. For the generic random walk (GRW) $P_{ij} = A_{ij} /k_i$ where $k_i = \Sigma_j A_{ij}$ is the degree of node $i$ for which $\pi_i^* = k_i / \Sigma_j k_j$ so that $P(\sigma[i_0,i_t])=1/(k_{0,1} k_{1,2} ...k_{t-1,t})$. With this form of $P_{ij}$ trajectories of equal length $t$ and equal endpoints are not equiprobable except on a $k$-regular graph. The transition probability that is equiprobable for trajectories of equal length $t$ and equal endpoints is $P_{ij} =(A_{ij} / \lambda)(\psi_i / \psi_j)$ where $\psi_i$ is the normalized ($\Sigma_i \psi_i^2=1$) principal eigenvector (i.e., corresponding to the largest eigenvalue $\lambda$) of the adjacency matrix $A$ [3]. This defines the maximum entropy random walk (MERW) distribution, for which $\pi_i^* =\psi_i^2$. The key fact is that the local transition probabilities between nodes depend on the *global* structure of the graph through the eigenvector $\psi_i$. The GRW and MERW are the same on k-regular graphs but differ dramatically on graphs with unequal node weights: the $\pi_i^*$ of MERW localizes in the largest Lifshitz sphere. For tractography, 3D lattice node weights are defined by a coupling coefficient $\alpha_{ij} = (FA)_i (FA)_j \mathbf{e}_i \cdot \mathbf{e}_j$ between neighboring nodes $(i,j)$ where $(FA)_i$ and $\mathbf{e}_i$ are the fractional anisotropy and principal eigenvector of the diffusion tensor at node $i$. To construct the maximum entropy trajectory $\sigma_s$ between two *specified* points, rather than $\pi_i^*$, a "test" distribution of particles is placed at a user defined seed point. The largest Lipshitz sphere to which the stationary distribution will concentrate is of little interest in this problem; rather, we construct the largest Lipshitz sphere at the user defined trajectory endpoint in order to force this to be the location of the final (stationary) distribution. From the initial distribution $\pi_i(0)$ at node $i$ and time 0, this trajectory can be generated by computing each time step $\pi_i(t+1)= \Sigma_j \pi_j(t) P_{ji}$ where $P_{ji}$ is the MERW generated by $\boldsymbol{A}$ constructed from the coupling coefficients.

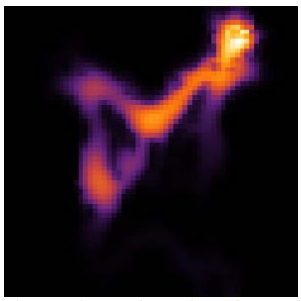
Fig 2. Trajectory from Xi to Xf1.

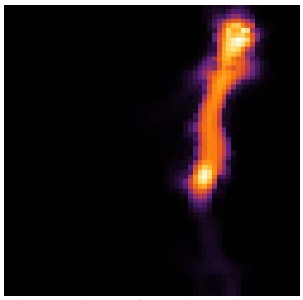
Fig 3. Trajectory from Xi to Xf2.

**Results** DTI data were collected on a GE Signa 3T scanner with a clinical dual spin echo EPI acquisition with $b=1000s/mm^2$ and 61 gradient directions. A composite map of FA overlayed with the principal eigenvectors is shown for a single slice in Fig 1. Diffusion tensors were computed using AFNI, and the coupling coefficients were calculated at each node. A threshold was applied to generate a sparse matrix representation of the white matter volume and from this was computed the adjacency matrix $\boldsymbol{A}$. The principal eigenvector and eigenvalue of $\boldsymbol{A}$ were computed using Arnoldi's method. For clarity we show 2D results. A small distribution $\pi_i(0)$ of particles is placed at a user defined initial point (Xi). At a user defined termination point (Xf) a small sphere ($r=3$ voxels) was created within the adjacency matrix. $\pi_i(t)$ was then iteratively computed and at each time step the distribution of particles follows the maximum entropy trajectory and these values are stored. The final trajectory is visualized by combining the particle distributions for all time steps. Examples are shown in Fig 2 and Fig 3.

**Conclusion** We have developed a fiber tractography method that computes the maximum entropy trajectories between locations and depends upon the global structure of the diffusion tensor field. Computation of the pathways requires only solving a simple (albeit large) eigenvector problem for which efficient numerical routines exist, and a simple iterative computation. This method has potential significance for a wide range of applications, including studies of brain connectivity.

**References** [1] Basser, et. al., IEICE Trans. Inf. Sys. **E85**(1):2002, [2] Behrens, et. al, Neuroimage **34**:2007. [3] Burda et. al. Phys. Rev. Let. **102** (16):2009.
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