A Path Integral Approach to White Matter Tractography

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Introduction

The so-called white matter tractography problem of finding the white matter anatomic pathways from diffusion MRI has generated a fair share of interest recently due to the promise the approach holds for providing models of anatomic connectivity. The most popular solution to the tractography problem is the principal eigenvector streamline method which, motivated by the heuristic notion that the fiber paths should follow the direction of maximal diffusion, simply integrates over the diffusion tensor principal eigenvector field (1-3). The streamline solutions tend to suffer, however, from numerous practical weaknesses including high noise sensitivity and dependence on the particular choice of interpolation scheme. More fundamentally, the streamline approach lacks an explicit mechanical picture of the tracts; cannot handle distributed fiber orientations; does not allow for interactions between tracts; and, perhaps most significantly, is not amenable to probabilistic interpretations of the tract solutions. Prompted by the above concerns, it is reasonable to ask: How do the tract solutions behave in the presence of fiber crossing, divergence, twist, etc.? How sensitive is the solution to the true mechanical properties of white matter? What is the mechanical influence of other tracts on the tract of interest? What is the probability associated with a particular tract solution? Here, we show how the above concerns can be addressed through a path integral approach.

Theory

The path integral method has enjoyed tremendous success for describing the behavior of a random manifold in an external potential, a classical problem in condensed matter and statistical physics (4). Examples of such problems are numerous but the one most germane to the discussion here is the configuration of a polymer in a potential; hence, most of the following is analogous to the polymer problem.

We wish to describe the trajectory of the tract $\mathbf{x}(s)$ as a function of the curvilinear coordinate s along the tract. The Lagrangian for the tract is written as $\mathcal{L} = T - V$ where $T = \frac{1}{2a}\dot{\mathbf{x}}^2$ is the Wiener measure, a is the step or Kuhn length, and $V = V_\psi + V_K + V_w$ is the potential energy of the tract which is comprised of, respectively, the empirical potential V_ψ derived from the diffusion data, the elastic potential energy V_K, and the excluded volume potential V_w which arises from interactions between tracts.

Expressions for the individual potentials can be derived as follows. The empirical potential is related to the fiber orientation distribution function (ODF) $\psi(\mathbf{n})$, which gives the probability distribution for finding a fiber within a differential solid angle around $\mathbf{n}$ where $\mathbf{n} = \dot{\mathbf{x}}/|\dot{\mathbf{x}}|$ is the bulk direction of the fiber, also referred to as the material director. If the fiber is drawn from a Gibbs ensemble then the empirical potential can be written as $V_\psi = -kT \log \psi$ where kT is the thermal energy. Note that the principal eigenvector streamline solution implicitly takes $V_\psi = \delta(\mathbf{n}(\mathbf{x}) - \mathbf{e}_1(\mathbf{x}))$ where $\mathbf{e}_1$ is the principal eigenvector of the diffusion tensor and is thus incapable of handling anatomic phenomena such as fiber crossing and divergence which have been observed under more complete sampling of q-space than is required for tensor imaging (5).

For the elastic potential of the tract, we employ, as an ansatz, the Frank free energy

$$\mathcal{H}_K = K_1(\nabla \cdot \mathbf{n})^2 + K_2(\mathbf{n} \cdot \nabla \times \mathbf{n})^2 + K_3(\mathbf{n} \times \nabla \times \mathbf{n})^2 \quad (1)$$

where the individual terms represent the bend, twist, and splay elastic energies and the coefficients the corresponding elastic moduli. Bend refers to the simple bending of tracts, twist to the shearing of planes of fibers with respect to each other, and splay to the divergence of tracts, which is of particular significance at the radiation of fibers from the compact stems.

Neglecting for a moment the excluded volume interaction, the equation of motion for the tract can be obtained by substitution of the Lagrangian with the above potentials into the Euler-Lagrange equation. The excluded volume interaction can be included by introducing

$$V_w = \frac{w}{2} \int dt \delta(\mathbf{x}(s) - \mathbf{x}(t)) \quad (2)$$

where w is the strength of the excluded volume interaction (6). The partition function for the fiber can then be expressed in terms of the path integral

$$Z(\mathbf{x}, L) = \int \mathcal{D}\mathbf{x}(s) \exp\left\{-\beta \int_0^L ds \mathcal{H}\right\} \quad (3)$$

where $\mathcal{D}\mathbf{x}(s)$ represents the integral over all possible fiber paths, $\mathcal{H} = T + V$ is the Hamiltonian and $\beta \equiv 1/kT$, from which the probability of a particular fiber can be readily calculated. The above integral is referred to as the Edwards' path integral when the excluded volume interaction is included (6). The partition function for the tract solutions can be determined in practice by solving the imaginary-time Schrodinger equation with the Hamiltonian developed above (4).

Discussion

The path integral approach to the white matter tractography problem has the advantages over the streamline method of a specific mechanical representation of the tracts, a probabilistic interpretation of the tract solutions, and the inclusion of excluded volume interactions. The experimental task of determining the correct mechanical model for white matter along with the associated moduli, as well at the mechanical forces between tracts, remains to be conducted. The most pressing open theoretical problem is how to derive the fiber ODF from the diffusion data, a project which will undoubtedly benefit from three-dimensional q-space imaging beyond the tensor model.

References 1. T.E. Conturo, *et. al.* *PNAS* **96,** 10422-10427, 1999. 2. S. Mori, *et. al.* *Ann. Neurol.* **45,** 265-269, 1999. 3. V.J. Wedeen, *et. al.* Int. Conf. Human Brain Map. **2,** 1996. 4. H. Kleinert. *Path integrals in quantum mechanics, statistics and polymer physics* (Singapore, World Scientific, 1995). 5. D.S. Tuch, *et. al.* Proc. ISMRM. **7,** 1999. 6. S.F. Edwards. *Proc. Phys. Soc.* **85,** 613, 1965.