NeuroData Design 1
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Paper Information:

Title: Diffusion MRI fiber tractography of the brain
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Key Common Terms:

Diffusion MRI (dMRI) – MRI sequence that is able to detect the diffusion of water molecules. Useful for mapping brain fibers due to the directional dependence along the fibers.
Tractography – Virtual characterization the global fiber trajectories of a brain from a set of data that relate indirectly to nerve fibers.
Connectome – Comprehensive map of neural connections in the brain. (Brain wiring)
White matter fibers – Brain matter composed of myelinated nerve fibers (white) that are packed into bundles and connect different regions of the brain.
Voxel – "Spatial" pixel, represents a point in a 3-D space.

Summary:
Fiber tracking from dMRI data allows quantitative analysis of white matter for tractography, an essential part of building maps of the brain for a greater understanding of the brain and many practical applications such as surgical planning.

Key Assumptions of Fiber Tractography:

- Is a virtual entity that indirectly relates to actual white matter fibers
- Each imaging voxel is characterized by a single predominant fiber orientation
- Nerve fibers align themselves along a common orientation and diffusion will be hindered across it rather than along it.
- Local orientations at each voxel are pieced together into a global fiber trajectory

Steps of Fiber Tractography:

- Local Fiber Orientation Estimation
    - Relate raw dMRI to local fiber orientations using average diffusion pattern of water
    - Common Models
        - Diffusion Tensor Imaging (DTI)
            - Can only measure one fiber population per voxel
            - Pros: Low computational and data requirements, Cons: Poor estimator of underlying fiber orientation
        - Higher Order Models: Fiber Orientation Distribution Function (fODF)
            - Can measure multiple fiber orientations per voxel

                - Pros: Better estimation of underlying fiber orientation, Cons: Low adoption
- Integration Methods
    - Form long-range fiber trajectories
    - Start at a seed point and step-wise integrate (Eulers or Runge-Kutta integration)
        - Seeds are determined by user
            - Seed points from ROIs (e.g defined by Atlases, cortical activation maps, users)
            - Whole brain tractography – seed points from around the brain
- Interpolation Methods
    - Relate local fiber orientations in an arbitrary position in space to voxel spatial grid
    - Most Common Method: Trilinear Interpolation
        - Calculated as a weighted (dependent on distance) sum from 8 nearest voxels to point of interest
    - Other Methods: nearest-neighbor
- Termination Criteria
    - Local Fiber Orientation Probability
        - fODF: falls below a threshold prob.
        - DTI: when fractional anisotrophy (FA) falls below a threshold
    - Curvature
        - Maximum local curvature imposed on tracks
    - Other acceptance/rejection criteria
        - Minimal track length, reject short tracks, anatomical priors, termination in cerebrospinal fluid, and etc…
- Fiber Tracking Algorithms
    - “Process of following the path of least hindrance to diffusion”
    - General Limitations:
        - Diffusion
        - Dependence on stepwise progression from initial seeds (dependent on seed location)
        - Quantification
            - Integration errors accumulate
            - Methods tend to create short, straight tracks (can be partially mitigated by biologically realistic priors)
    - Deterministic vs. Probabilistic Approaches
        - Deterministic
            - Assumes unique fiber orientation in each voxel
            - Cons: Subjectable to imaging noise and artifacts, local model inaccuracies, streamline integration errors
        - Probabilistic

- Generates a distribution of possible trajectories (orientation distribution function (ODF)) from each seed points. Built on deterministic approaches.
    - Uncertainty ODF
        - Assume discrete fiber orientations
        - Takes into account noise and model uncertainty
        - Focus on statistical uncertainty
    - Fiber ODF
        - Assume continuous distribution of fiber orientations
        - Ignore noise and model uncertainty
        - Focus on anatomical distribution and dispersion

- Local vs. Global Approaches
    - Local
        - Tracking via small successive integration steps following a previous model
        - Pros: Fast, common
        - Cons: Local errors accumulate, poor predictor of dMRI data
    - Global
        - Reconstruct all tracks simultaneously and optimize for best fit.
            - Pros: More resistant to noise and imaging artifacts, better agreement with dMRI data
            - Cons: Stochastic optimization does not always converge, reliant on prior knowledge that can skew the chosen tracks
- Slippery Slope of Quantification
    - Limitations in the tract reconstruction prohibit straightforward quantification of fiber tracking results.
    - Method 1: Voxel-wise Track Counts
        - Track count mapping or track density imaging (TDI)
            - Count tracks passing through each voxel.
            - Limitations
                - Sensitive to noise, accumulation of noise-induced errors, and model imperfections
                - Bias towards simple fiber trajectories
                - Seeding procedures overrepresent long fiber tracks and under represent short fiber tracks
    - Method 2: Connection Strength
        - Connection strength estimated from the proportion of white matter fibers connecting different regions
            - Limitations
                - Bias towards simple fiber trajectories

        - For connectomics, long connections will have been overrepresented by seeding
        - Limitations in probabilistic approaches assumptions

Current Challenges:

- Ambiguous Local Geometries
    - Complex and distinctly different local fiber geometries are impossible to distinguish
        - Crossing, kissing, bending, fanning, and etc…
    - Global tracking has potential but currently isn't superior to ambiguous geometries
- Near Cortex Tracking
    - Difficult to map within cortex with complex folds
        - Large modeling errors when near grey matter
        - Multi-shell scheme developed as a solution
            - Acquires multiple b-values (diffusion weighting strengths from multiple scan distances)
            - Additional B-values provide more information on tissue types and microstructures
- Spatial Resolution
    - Tractography is limited by resolution of dMRI
        - Typical 96x96 dMRI = 0.009 megapixels.
        - Need equipment/methods to improve to increase speed and resolution
- False Positives
    - The non-specificity within a single voxel can be the result of multiple plausible fiber configurations.
    - How to find and screen for false positives?
- Sheetography
    - Recent literature suggests that there are sheet structures.
    - Models could try use models for areas with these sheet structure.