Representing Neural Connectivity in the Foundational Model of Anatomy Ontology

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1. Summary

• Our current effort focuses on representing neural connectivity relationships between gray matter and white matter structures in the Foundational Model of Anatomy Ontology (FMA)[1] from the scale of synapses to long-range fiber tracts.

• The FMA contains a number of terms that imply either structural or functional connectivity, such as sends_output_to or receives_input_from, but the semantics of their structural connectivity relationships were not yet made formally explicit.

• To formalize structural connectivity relationships in the FMA we developed a set of definitions to disambiguate and clarify the terminologies describing the types of connectivity relationships that exist between gray matter and white matter structures at different levels of granularity.

• Connectivity relations vary in scale from long-range association, commissural, and projection fibers at the mesoscopic scale to synaptic junctions at the microscopic scale.

• This work focused on generating a representation of connectivity at the mesoscopic scale, which aims to facilitate the annotation and integration of open-access neuroimaging datasets - including structural MRI (sMRI), functional MRI (fMRI), and diffusion tensor imaging (DTI).

2. Methodology

• The FMA is a reference ontology for the domain of anatomy that symbolically represents the phenotypic organization of the human body at all levels of granularity.

• In this study we applied FMA principles to the represent structural connectivity properties of gray matter and white matter neural structures using the principle of Anatomical Structural Abstraction (ASA).

• *Connectivity*, in addition to *Location* and *Orientation*, is one of the three components of the ASA Spatial Association Network (SAn). We focused on explicitly representing connectivity properties between white matter and gray matter neural entities at the mesoscopic scale (Figure 1).

• **Gray Matter Properties**
- *has_projection* and *receives_projection* are properties that connect "gray matter structure of origin" and "gray matter structure of termination," respectively with the same white matter fibers.
  - 'Brodmann area 39 of inferior parietal lobule' has_projection 'Superior longitudinal fasciculus proper'
  - 'Brodmann area 6 of inferior frontal gyrus' *receives_projection* from 'Superior longitudinal fasciculus proper'

• **White Matter Properties**
- *projects_from* and *projects_to* are properties that connect white matter tract fibers to "gray matter structure of origin" and "gray matter structure of termination (target)," respectively.
  - 'Superior longitudinal fasciculus proper' *projects_from* 'Brodmann area 39 of inferior parietal lobule'
  - 'Superior longitudinal fasciculus proper' *projects_to* 'Brodmann area 6 of inferior frontal gyrus'

3. Example of a Connectivity Relation

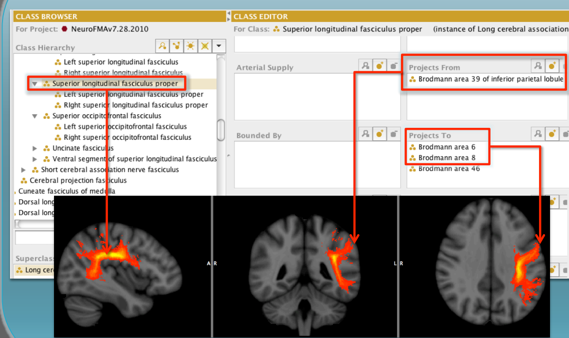

Figure 1. Demonstration of FMA white matter and gray matter classes that relate to the JHU DTI-81[2] atlas probability distribution of the left superior longitudinal fasciculus.

4. Relate Tract and Region Based Atlases

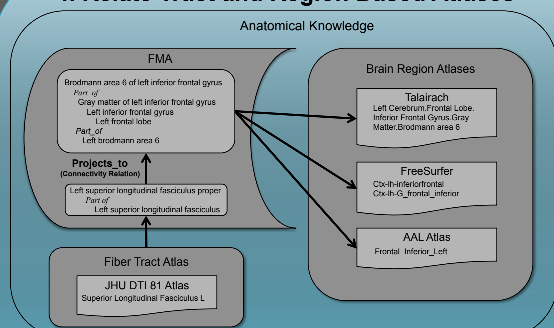

Figure 2. Labels are used to annotate white matter structures in the JHU-DTI-81[2] fiber tract atlas and grey matter structures in atlases based on brain regions. The FMA can be used to reconcile the different parcellation schemas by modeling the relationships between labels.

5. Sub-property Hierarchy and Definitions

Sub-property Hierarchy

Connectivity Hierarchy

- connected_to
  - attached_to*
    - innervates
    - projects_to*
  - receives_attachment_from*
    - innervated_by
    - receives_projection _from*
  - continuous_with*
    - has_projection*
    - projects_from*
  - synapse_with*
  - has pathway
    - has efferent pathway
      - sends_output_to*
    - has afferent pathway
      - receives_input_from*

Figure 3. Connectivity properties arranged in a hierarchy in the Spatial Association Network (SAn) of the FMA (above). Definitions for properties implemented in the FMA* (right).

Term	Definition
Connected_to	Structural anatomical property which holds between each anatomical structure of type A and some anatomical structure of type B such that each structure shares some part of its bona fide anatomical surface with that of the other.
Continuous_with	Connected_to property which holds between each anatomical entity of type A and some anatomical entity of type B such that there is no bona fide boundary between their contiguous constitutional parts.
Synapse_with	Connected_to property where there is apposition between the presynaptic membrane of a neurite of one neuron and the postsynaptic membrane of one or more neurites of another neuron or a region of a muscle cell or a gland cell and some form of neurotransmission is evident between them.
Projects_to*	Attached_to property where individual axons comprising a fiber tract originating from one or more brain regions synapse_with neurites or somas of a collection of neurons located in one or more other brain regions. This relation may be synonymous with '*terminates_in*'.
Projects_from*	Continuous_with property where individual axons comprising a fiber tract are parts of a collection of neurons located in one or more brain regions. This relation may be synonymous with '*originates_from*'.
Sends_output_to*	Efferent pathway property consisting of relations where A has_projection B and B projects_to C, and where neuro-mission is sent from A to C.
Receives_input_from*	Afferent pathway property consisting of relations where A receives_projection_from B and B projects_from C, and where neurotransmission is received by A from C.

6. Future Work

• Extend previous[3,4] work by demonstrating the utility of connectivity relations in the FMA for knowledge discovery by integrating region-based annotations from sMRI and fMRI datasets with tract-based annotations from DTI datasets (Figure 2).

•Continue developing the FMA representation of connectivity at the mesoscopic scale and implement additional connectivity relations at finer levels of granularity (Figure 3).

• Develop a more rich representation of the Brodmann Area parcellation schema by explicitly defining cytoarchitectonic, regional, and long-range connectivity properties.

• Determine how new knowledge about neural connectivity from the Human Connectome Project and related structural and functional connectivity research can can be incorporated into the FMA ontology.

Acknowledgements

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