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INTEGRATING INFORMATION FROM PATHOLOGICAL BRAIN MRI INTO AN ANATOMO-FUNCTIONAL MODEL

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ABSTRACT
This paper presents a contribution to a large problematic in medicine and neuroscience which consists in integrating information extracted from medical images (MRI) into a global framework (such as electronic patient records or anatomo-functional databases). In this work, we focus on (1) the construction of an anatomo-functional model based on an Attributed Relational Hypergraph representation and (2) the integration into this model of information extracted from cerebral imaging scans, via several segmentation procedures. This model, including information on anatomical structures and their spatial relations, is able to cope with the complexity of anatomy and of MRI data.

KEY WORDS
Brain, MRI, Segmentation, Anatomo-functional model, Hypergraph, Knowledge Representation.

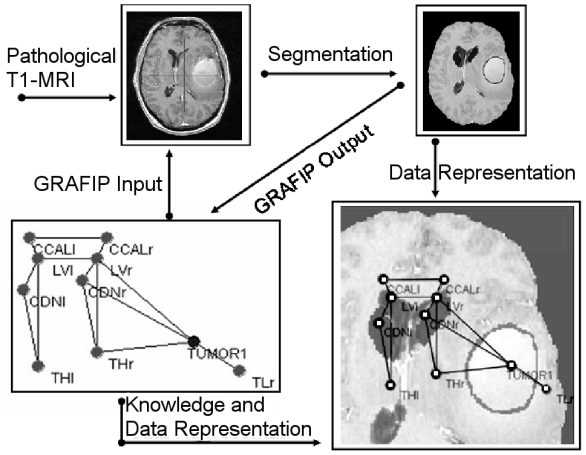


Figure 1. Overview of the system integrating information from pathological brain MRI into an anatomo-functional model.

1 Introduction

This paper focuses on brain images and neurological pathologies. Correlation of image-based information with clinical data (e.g. anamnesis, neurological examination, neuropsychological tests) and its functional interpretation are essential for clinicians and neuroscientists. To assist this task, we propose a methodology for modeling healthy and pathological cerebral anatomy (Figure 1). The brain model developed by our group consists of a Graph of Representation of Anatomical and Functional data for Individual patients including Pathologies (GRAFIP). The generic model includes both anatomical and functional knowledge. The instantiation of the generic model for an individual patient is based on anatomical information extracted from standard brain MRI exams (including T1, T2 and FLAIR protocols).

The brain model provides a descriptive framework in which we can integrate pathology localization, type, anatomical and functional positioning, segmentation results, description of the surrounding structures, and their spatial relationships.

Other graph-based approaches have been proposed in the literature, in particular for the cortex, among which a model of sulco-gyral anatomy for the healthy human brain [1], or a random graph approach for automatic labeling of sulci [2]. These studies focus on the inter-individual variability of the sulco-gyral anatomy and do not take into account pathology. To our knowledge, no graph-based model including pathologies has been proposed so far.

The descriptive framework GRAFIP includes spatial knowledge guiding segmentation. Other graph-based approaches for the segmentation process can be found e.g. in [3, 4].

This paper is organized as follows. In Section 2, we present our generic anatomo-functional brain model and we show that the hypergraph structure is well suited for the description of normal and pathological cerebral knowledge. We introduce the GRAFIP descriptive framework and motivate the necessity to follow a "pathology-dependent" paradigm. In Section 3, we present our contribution for encoding the proposed brain model, using resources based on the XML language: (i) A GraphML [5] file (an easy-to-use file format for graphs), that provides a comprehensive representation of cerebral data, (ii) a XML Schema Description (XSD) file that describes our data structure and knowledge representation. In Section 4 we illustrate on an example how the visualization of the GRAFIP descriptive framework on the MRI data set offers new perspectives to expert clinicians. Finally we discuss future applications of the proposed framework.

2 Modeling normal and pathological brain anatomy with hypergraphs

The proposed modeling framework allows the integration of generic anatomical and functional knowledge on normal human brains as well as specific anatomical information extracted from brain MRI exams, for a detailed description of the cerebral pathology and its impact on the brain anatomy.

2.1 GRAFIP descriptive framework

The cerebral model developed in this project is a Graph of Representation of Anatomical and Functional data for an Individual patient including Pathologies (GRAFIP). The proposed framework enables the modification of generic anatomical knowledge to adapt the model to a specific clinical case and includes pathological areas. Modification of the generic model is performed via the integration of information extracted via the segmentation of brain MRI exams. A detailed description of the segmentation procedures for tumors and normal brain structures falls outside the scope of this paper. The tumor segmentation method is described in [6] and the segmentation of normal cerebral structures guided by anatomical knowledge is described in [7].

2.2 Model description: Attributed Relational Hypergraph

The GRAFIP framework is based on an Attributed Relational Graph (ARG) representation. An ARG is a 4-uple $G = (N, E, \sigma, \delta)$ graph where N is the set of vertices, E is the set of edges, σ is the vertex interpreter and δ is the edge interpreter. Attribute values are assigned to vertices and edges.

The GRAFIP has a hypergraph structure, where edges between two vertices are replaced by hyperedges describing a relation between an arbitrary number of vertices.

In the GRAFIP framework, **graph vertices** represent cerebral structures. According to the pre-identified needs from a group of collaborating clinicians, we selected 622 cerebral structures. The structural cerebral anatomy is composed of two symmetric hemispheres, leading to a duplication of the majority of brain structures into left and right components (e.g. left thalamus and right thalamus). A synthetic list of cerebral structures used in our anatomical model is provided in Table 1.

Vertex attributes are defined as follows:

1. **ID_NODE** An acronym to identify the vertex into the graph (for instance: *THr* for the *right thalamus*). Each acronym is unique.

2. **Num_NODE** An internal vertex number.

3. **NATURE_NODE or Matter Concept** This attribute labels the vertex according to the main categories of normal cerebral matter and taking account the pathological tissues (Table 2).

Table 1. List of Cerebral Structures used in the brain model

Structure Type	# of Structures
Hindbrain	25
Midbrain	25
Internal structures	44
Ventricle	12
Frontal Lobe	92
Temporal Lobe	46
Parietal Lobe	52
Occipital Lobe	58
Limbic Lobe	64
Insula	28
White Matter	60
Miscellaneous	116

Table 2. **NATURE_NODE**

GRAY_MATTER
WHITE_MATTER
CSF
NERVE
VESSEL
PATHOLOGY

These types of matter can be further specified according to anatomical characteristics. We detail here the case of *gray matter* and *white matter*. *CSF*, *nerve* and *vessel* are anatomically simpler and do not need further categorization for our purpose. The case of pathological tissues is left for future work.

- **GRAY_MATTER** Inside the brain, the gray matter is clustered into groups called nuclei. On the periphery, the cortex is a multi-layered cover of gray matter, on both hemispheres. Possible values of the structure type are: $CORTEX$ and $NUCLEUS$.
- **WHITE_MATTER** The white matter fibers are classified according to tract characteristics. *Association fibers* connect different regions of the cerebral cortex within the same cerebral hemisphere and are involved in cognitive tasks such as language. *Commissural fibers* cross through the midline of the brain to connect cortical regions in both left and right hemispheres, thereby coordinating the activity of the two cerebral hemispheres. *Projection fibers* connect the cerebral cortex with subcortical structures such as the thalamus and the spinal cord. Possible values of the structure type are: $ASSOCIATION\_FIBERS$, $COMMISSURAL\_FIBERS$, $PROJECTION\_FIBERS$.

4. **MESH** MeSH Identifier (for instance: $A08.186.211.730.385.826$ for the *thalamus*). MeSH

is the National Library of Medicine's controlled vocabulary thesaurus [8]. It consists of sets of terms naming descriptors in a hierarchical structure that allows the exploration of the cerebral model at various levels of specificity.

5. **NAME** and **Synonymous** according to the major brain thesauruses and atlases (for instance: *Middle frontal gyrus* is also known as *F2* and *intermediate frontal gyrus*).

6. **Unpaired** Attribute to identify several cerebral structures which do not duplicate into right and left components (e.g. *pineal body*).

7. **Structure_SURFACE** A semantic attribute describing a cerebral structure surface according to anatomical axes. Possible values are *INFERIOR_SURFACE, SUPERIOR_SURFACE, LATERAL_SURFACE, MEDIAL_SURFACE*.

8. **BA** Each possible value corresponds to a Brodmann's area according to the cytoarchitectonic referential [9].

9. **Domain** Each possible value corresponds to a cognitive sector according to anatomo-functional knowledge.

10. **Volume** and **surface** are quantitative attributes describing cerebral structures and depending on inter-subject variability and pathology impact.

Edges represent relations between vertices. Our model includes major types of anatomical relations according to the normal cerebral anatomy (at a large scale and at a finer scale) as well as the pathological anatomy.

The anatomical relations are essentially descriptive and correspond to a grouping of elements according to the principal types of organization of the central nervous system. A set of 651 relations was encoded to model anatomical links between the various cerebral structures. These relations are divided into taxonomical and spatial relations, according to prior anatomical descriptions (see Section 2.3).

Edge attributes are defined as follows:

1. **Syntactic_ATTRIBUTE_EDGE** This attribute labels the edge according to the previously mentioned distinction between taxonomical and spatial relations. The type **SPATIAL_RELATION** is defined through its possible values: *UpOf, Down, InFrontOf, Behind, Left, Right, IncludedIn, AdjacentTo, Along, Between*.

2. **References_EDGE** This attribute offers the possibility to mark the source knowledge (for instance: *Neuronames Brain Hierarchy* [10]). It is based on references from the literature (providing generic information, and generally qualitative attributes values) or segmentation results (providing more specific information on the particular case under study).

2.3 Normal and pathological cerebral anatomy and function

The brain has a complex and hierarchical organization, characterized by a modular organization repeated across a spatial scale. From this point of view, the majority of brain thesauruses (Neuronames Brain Hierarchy (NBH) for instance) [10] describe the cerebral anatomy and its structural organization in a hierarchical way.

The *thalamus* for instance can be viewed as an individual structure involved in both the sensory and the motor systems or, at a more detailed scale, as a nuclear mass and a set of subnuclei (Figure 2). In a graph representation, edges can describe details of a particular cerebral structure.

Our anatomical model includes 596 **taxonomical relationships**, based on the NBH [10].

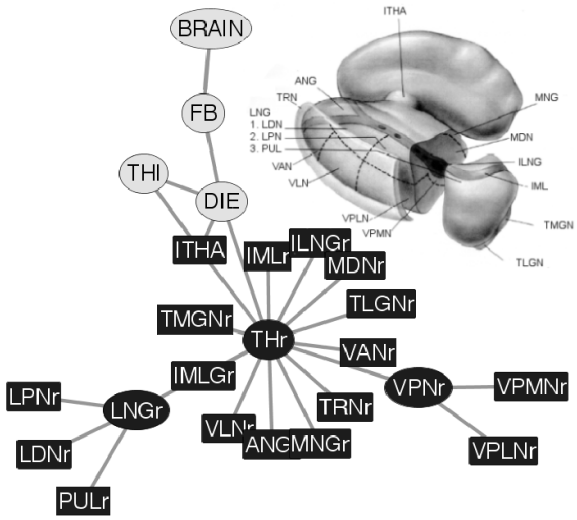


Figure 2. Anatomy of the thalamus and its subdivision into subnuclei (from [11]) and its graph description.

Spatial relationships complement the descriptive graph, enabling anatomy-guided spatial navigation within the data for automatic segmentation. Currently, our anatomical model contains 55 spatial relationships: 33 between internal structures derived from [12] and 12 describing the macro-organization of the cortex derived from Duvernoy's atlas [13]. Each cerebral structure involves spatial relations with surrounding structures. For example, the putamen is *along* the globus pallidus (Figure 3). Hypergraphs are particulary interesting when dealing with complex spatial relations involving more than two structures. For instance, the posterior limb of the internal capsule *separates* the putamen from the thalamus (Figure 3).

The whole human brain **functional architecture** is strongly conditioned by the anatomical relationships between brain regions. Brain functions are dependent on the interactions between specialized regions of the cortex that process information within local and global networks. For example, the *arcuate fasciculus* is well-known in aphasia

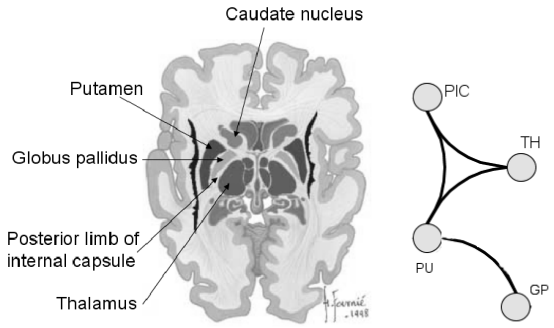


Figure 3. Spatial organization of internal cerebral structures (from [14]). The putamen (PU) is *along* the globus pallidus (GP) (edge of cardinality 2). The posterior limb of internal capsule (PIC) *separates* the putamen from the thalamus (TH) (hyperedge linking three nodes).

(deficiency of the language).

Hypergraphs are also interesting for the description of the anatomo-functional brain organization. A hyperdege can be used to link a set of anatomical vertices involved into a cognitive function according to a cognitive model (as for the language for instance [15], Figure 4). If a lesion impacts one of the vertices shown in this figure, a functional impairment hypothesis can then be made.

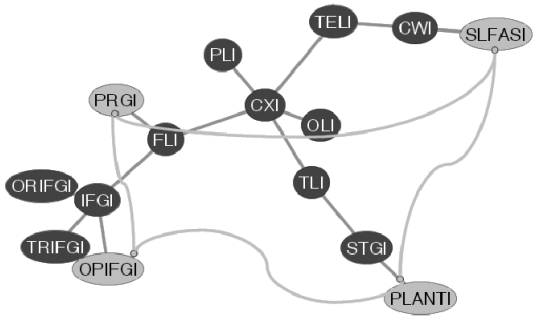
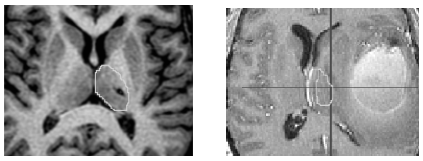


Figure 4. Hyperedge linking the vertices (PLANTl) *Wernicke's Area*, (OPIFGl) *Broca's Area*, (PRGl) *Motor cortex* and (SLFASl) *Arcuate fascicle* according to the *Wernicke-Geschwind model of language "Repeating a spoken word*" [15].

The proposed cerebral graph model needs to adapt to different types of **pathologies** and the modifications they may induce. Figure 5 illustrates a thalamic lesion after a stroke and a cerebral subcortical tumor modifying the location of internal structures.

These different neurological cases illustrate the need for a "pathology-dependent" paradigm:

- Lesion pathology: Cerebral structures and tissues are impacted and functional impairment is suspected. Lesional volume and surface must be measured (e.g. ratio: $thalamus\ volume/lesion\ volume$).



(a) (b)

Figure 5. (a) Lesion impacting the thalamus. (b) A tumor localized in the temporal lobe, modifying the location of the thalamus.

- Tumoral pathology: Cerebral structures and tissues are not impacted and consequently no functional impairment is suspected. However the presence of a brain tumor modifies the local cerebral organization and the characteristics of the surrounding structures. These structures should therefore be characterized by their potential degrees of deformation and infiltration, and new spatial coordinates are necessary. Volume measurements are thus of prime importance.

The paradigm proposed in our approach is to encode in the graph model the pathological impact based on MRI segmentation results, using two procedures (Figure 6): (i) adding a vertex *pathology* linked with the surrounding cerebral structures, and (ii) updating the affected vertex and edge attributes.

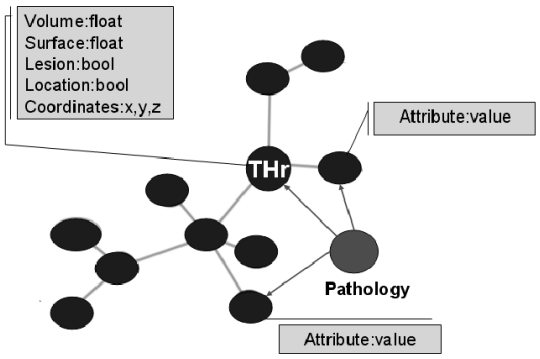


Figure 6. Pathological graph according to information extracted from the image. A vertex *Pathology* is added and linked to the concerned cerebral structures. Attribute values of corresponding vertices and edges are updated.

3 Encoding the Anatomo-Functional Brain Model

3.1 Hypergraph encoding in XML Format

Implementation of the GRAFIP anatomical model involves a GraphML [5] file based on the XML standard. This file structure is a comprehensive and easy-to-use file format for graphs, based on the XML standard. The GraphML syntax is defined by the GraphML Schema [16]. We used this file structure to encode our anatomo-functional cerebral model, stored into an **XML file**.

3.2 Extensions of the GraphML format

GraphML is designed to be easily extensible. To handle more complex data structures one has to define, by an XML Schema, new attributes or new elements. The Schema which defines such extensions is the eXtended Schema Description (XSD) language.

We need to extend the GraphML schema for two reasons: (i) as mentioned earlier, the high complexity of the brain anatomy requires elaborated node attributes, (ii) interaction with the image segmentation module requires specific data structures.

We add *elements* and *attributes* in our schema into an **XSD file** as follows:

- A GraphML *element*: ***nodeInternalInformation*** and a set of associated attributes describing a vertex (Section 2.2) (for instance the attribute: *NATURE_NODE* is added to the new element *nodeInternalInformation*).
- A set of attributes describing an edge (Section 2.2) (for instance the attribute: Syntactic_Attribute_EDGE is added to the standard Graphml element *Edge*).
- **Additional constraints** to attribute values (as defined in vertex interpreter or edge interpreter of the ARG). Restrictions are encoded in the attribute section (for instance, *GRAY_MATTER* is an authorized value for the vertex attribute *NATURE_NODE*, according to Table 2).

We used this schema to encode 622 nodes and 651 relations (Section 2.2) as illustrated in Figure 7 into an XML file.

```
<node id="THr">
    <data key="ninf">
        <nodeInternalInformation
            Num_NODE="167"
            Name="THALAMUS(r)"
            NATURE_NODE="GRAY_MATTER">
    </data>
</node>

<hyperedge
    Syntactic_ATTRIBUTE_EDGE="spatialRelation.UpOf"
     References_EDGE="[Colliot, 2003]">
            <endpoint node="THr" directed="source"/>
            <endpoint node="CDNr" directed="dest"/>
</hyperedge>
```

Figure 7. Encoding the cerebral structure *Thalamus* in the XML file and the spatial relation *UpOf* between two vertices (*Thalamus* and *Caudate Nucleus*) into an edge. Different attributes (*Name, NATURE_NODE*) are associated to the *nodeInternalInformation* element.

4 Data visualization

While the previous format is well adapted to knowledge representation and manipulation of structural information, other tasks such as visualization are easier to implement using a different format. Therefore, we developed an interface between the previous descriptive framework and a Java library based on the Java Universal Network Graph (JUNG) [17] framework for graph analysis and visualization tools.

This allows storing, handling and displaying neurological MRI exams along with information extracted from data segmentation and anatomical models. The aim is to tool up medical experts with a user-friendly GUI for interactivity and visualization of the GRAFIP content.

The physician can interactively select a specific slice within the MRI volume. Each corresponding 2D view will be automatically changed. In addition to the usual functionalities (e.g. zoom in/out), it is possible to visualize simultaneously the associated 3D segmented lesions or its intersection with the current slice by overlying its 3D information onto the MRI images. A 3D viewer has also been developed and allows the user to navigate around the segmented structures. The GRAFIP components can be viewed as a single entity or as an overlay onto 2D MRI slices. For such display, the GRAFIP graph nodes are locally attached to specific MRI slices. Some functionalities for interacting with the graph are also available.

An illustrative example is shown in Figure 8, where information extracted from a clinical MRI brain exam with a tumor is provided. A subset of structures and attributes were extracted to illustrate the general scheme. We illustrate the following functionalities of the system: image visualization, visualization of the GRAFIP on the MRI data, visualization of the information associated to a particular anatomical structure (i.e. graph node).

5 Conclusion

The proposed GRAFIP framework includes original features, combining generic knowledge representation, specific patient's information extracted from medical images, including pathologies, attributes of anatomical structures and of the spatial relations they share. The developed coding methods allow for easy updating, manipulation and vi-

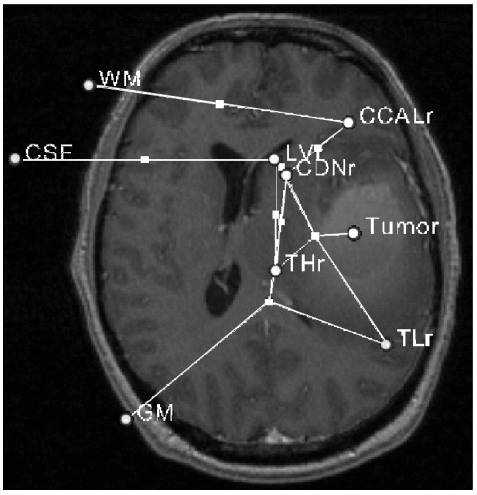


Figure 8. Visualization of an image and a part of the associated GRAFIP.

sualization.

From preliminaries experiments with medical experts from several hospitals, it appears that the proposed framework is well adapted to provide a quick and structured overview of the image content, to focus on the region around the pathology and understand its impact on the surrounding structures and the brain functional organization.

Future work includes reasoning on the proposed graph representation and matching of different graphs, that will lead to powerful tools to assist therapeutic patient follow up (for instance by comparing different objects by means of graph matching algorithms), to perform diagnosis and surgery planning, to facilitate the comprehension of cognitive functions and their neural basis, and to help in education.

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