

An Object Oriented Neuroanatomic Atlas

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Abstract

This report describes the design and development of a knowledge based object-oriented system called the NeuroAnatomic Atlas (NAA). The NAA serves as the core of the Anatomic Localization Algorithm (ALA) and encodes gross and macroscopic structures. *Methods:* A prototype atlas has been implemented using the Common Lisp Object System and consists of over 1100 objects including arteries, cortical regions, basal ganglia, brainstem nuclei, dermatomes, dorsal root ganglia, and white matter tracts. The atlas has been associated with a three-dimensional brain model for display of structures. *Results:* Using a query language, the atlas provides a mechanism for mapping from symptoms to anatomic pathways and from pathways to vascular structures. Fundamental localization algorithms have shown accuracy in finding structural lesions. *Keywords:* artificial intelligence, object oriented design, neurology, expert systems, computer graphics.

Introduction

This paper describes the design and development of the NeuroAnatomic Atlas (NAA). NAA employs object-oriented knowledge-based techniques to represent structures of the human central nervous system.

Several neurology expert systems have been implemented using artificial intelligence (AI) techniques. The SCAN system [1] and INKBLOT [2] represented the nervous system using a hierarchy of cubes. Algorithms were developed to reason about disease by analyzing geometric relationships between cubes. Smeets [3] developed a system to prescribe anti-epileptic drugs with the conclusion "the system was at least as good in prescribing as individual neurologists." A system called NEUREX [4] diagnosed neurogenic diseases of the lower limbs and helped to assist users in planning electrophysiology tests.

We have addressed the knowledge representation of neuroanatomy from an object-oriented perspective [5] which we consider an innovation. This technology uses classes, methods, and inheritance algorithms to organize data and has been applied to complex problems including Hubble Space Telescope scheduling ([6] and [7]). Our object-oriented model will be comprehensive in its knowledge of macroscopic structures in the central nervous system.

Project Goals

The goals of this development effort are listed here: (1) Design and create the NeuroAnatomic Atlas (NAA) that, once complete, may function as a knowledge resource. (2) Write a set of functions that encode the Anatomic Localization Algorithm (ALA). (3) Create a three dimensional Brain Model that illustrates the anatomic structures in the atlas. (4) Test the atlas by analyzing correctness and potential for use in an expert system (described briefly below).

The SYNAPS Expert System

Software called the **System for Neurologic Analysis of Patient Symptoms** (SYNAPS) is in the early stages of design and development. SYNAPS will be a medical expert system focusing on neurologic diagnoses and will accept, as input, patient signs, symptoms, laboratory values, etc. A hypothesis-driven rule system will produce a set of diagnostic possibilities ranked by confidence.

SYNAPS will employ two key modules: NAA and the **Anatomic Localization Algorithm** (ALA). ALA consists of a set of functions that compute the location of nervous tissue injury. These functions query the atlas knowledge base and via heuristics derive localization.

Other potential applications for the atlas include teaching systems, simulation, and model analysis.

Anatomy Terms. Terms important to this report are defined briefly here. The *neuron* is a cell that functions as an information processing unit. A *nucleus* is a collection of neuron cell bodies grouped by location and function. An *axon* is a fiber-like neuron component that extends beyond the neuron's body to communicate with other neurons or with muscle tissue. A *synapse* is a region of chemical communication between two neurons. A *ganglion* is a collection of neuron cell bodies usually found outside of the central nervous system. The *dermatome* is a region of skin innervated by a spinal nerve. For more details, refer to [8], [9], and [10].

Concepts for the Atlas

To design the atlas required definition of a set of concepts that are described below.

Conceptual Threshold Based on Size. A key decision was setting the smallest size for structures to be included. Only structures above this size threshold are defined. If an inappropriate threshold is selected, the number of objects to be defined would be too large for the initial phase of work. Our threshold, at present, is on the scale of millimeters and includes basal ganglia, brainstem nuclei, thalamic nuclei, sensory tracts, motor tracts, cortical regions (e.g., calcarine sulcus), Brodmann's areas, dorsal root ganglia, etc. Microscopic structures below the size threshold include organelles, dendrites, individual axons, neurotransmitter receptors, and synaptic vesicles.

CNS-Structures. We begin model creation with the definition of *cns-structure*, a discrete unit of excitable tissue possessing a specific biologic function (see [10]). A common *cns-structure* is the *nucleus* but others include *cortical gyri*, *sulci*, *areas*, and *lobes*. Subclasses of the nucleus include *thalamic nuclei* and the *basal ganglia*. Each structure should be assigned *arterial* supply.

Brodmanns-Areas. This concept is a template for *Brodmann's areas* that divide the cerebral cortex into discrete regions. Area 17 (the visual cortex) is an example.

Connections. The second key concept, the *connection*, represents the axonal fibers between *cns-structures*. Examples of *cns-structures* would be the *C5 dorsal root ganglion* and the *nucleus cuneatus*. The connection between these structures represents the set of axons with source cell bodies in the dorsal root ganglion and destination synapses in the nucleus cuneatus. The class *connection* includes a *source* *cns-structure*, a *destination* *cns-structure*, and one or more *fiber tracts* within which the axons of the source are found. Generally, the *cns-structure* is either a nucleus, a ganglion, spinal cord gray matter region, or a cortical area.

For example, a *cortical motor neuron* whose body lies in the *C5 motor area* of the *precentral gyrus* projects a long axon to the contralateral *ventral horn* of the *spinal cord*. To represent this intercellular communication, three objects are instantiated: (1) the motor area of the cortex (corresponding to the C5 spinal segment), (2) the ventral horn (at a specific spinal level C5), and (3) the connection between them (with source motor area C5 and destination C5 ventral horn).

Subpathways. At the next level of complexity, we define the concept of the *subpathway*. This class consists of structures and connections of a similar nature (e.g., sensory), associated with a specific spinal cord level (e.g., 4th cervical level, C4). The organization of the spinal cord dictates the requirement for this concept and the description is appropriate for sensory and motor tracts. Attributes include *modality* (the physiologic function), *connections* (a list of connection objects), *spinal cord level*, and *laterality* (left or right). The *Left C4 Touch Subpathway* is an example.

Processing of sensory signals in the dorsal horn, cuneate nucleus, thalamic ventral posterolateral (VPL) nucleus, and sensory cortex is physiologically complex [10]. We will, in our initial phase, implement a system that maintains spinal cord sensory subpathways (e.g. C4) discretely from dermatome to cortex. This is a heuristic to support phased project completion. Later project phases should address the integrative processing known to occur in the sensory pathways.

Pathways. Composed of subpathways, the *pathway* concept defines a higher level nervous system complex. The pathway is a set of *cns-structures* and connections that share a specific functionality such as the sensation of temperature. Multiple spinal cord levels are included within one pathway and a pathway is unilateral. The definition of a pathway includes the major CNS structures that compose the pathway.

For example, the *Left Corticospinal System* (which connects the left motor cortex with the contralateral spinal cord ventral horn) has a definition that includes the left motor cortex, left internal capsule, left crus cerebri, corticospinal decussation, right lateral corticospinal tract, and the right ventral horn. Other pathways include the *Right Dorsal Column Medial Lemniscus Pathway (DCML)* and the *Left Anterolateral Pathway*.

Systems. The concept *system* encompasses a set of two pathways (left and right). The semantic difference between a pathway and a system is merely that the system defines the biologic function for both sides of the body. For example, the dorsal column medial lemniscus (DCML) system encompasses sensations of touch and vibration throughout the entire body (not including that served by cranial nerves).

Arteries. The class *artery* encodes components of the vascular supply to nervous tissue. Knowledge about blood vessels is crucial to analysis of CNS disease processes. Our initial phase excludes veins and venous sinuses. The attribute *branches* includes pointers to the branches of the artery instance (e.g., the internal carotid artery is a branch of the common carotid artery). Ultimately, every CNS structure will be assigned arterial supply.

System Mapping Tables. Possessing definitions of a system such as the DCML and the spinal cord level subpathway definitions, we define *dermatome sensory mappings*. To adequately convert a symptom (e.g., paresthesia) to a clinical diagnosis requires assignment of function to the various systems, structures, and connections already described. Our model accomplishes this by supporting explicit definitions of an association between an input and a subpathway. For example, an input would include the *modality* (e.g., touch), *location* (e.g., the C5 dermatome), and the side (e.g., left). The associated subpathway is the C5-touch-subpathway-left. This subpathway is a component of both the touch pathway and of the DCML system.

Each of the concepts described above is associated with a software class encoded using the Common Lisp Object System.

CNS Object Table. The atlas requires a *CNS Object Table* that, for each entry, stores a unique key (i.e., the structure's symbolic identifier) and an object (that is an instance of a class).

Knowledge Base Definition Rules. NAA definition adheres to these rules: (a) Definitions are coded in files and utilize functional specifications. (b) Definitions use unique symbolic identifiers for CNS structures. (c) Each definition produces object instantiation and placement into the CNS Object Table. (d) Once definitions are complete, a function is executed that traverses all objects and converts symbolic references to memory pointers by table lookup.

Nomenclature and Laterality. The NAA uses the following naming convention. All symbols must be unique. Most identifiers must include a laterality suffix, "right" or "left." Names usually follow this example: The identifier "dermatome-C6-temperature.left" (representing the index finger), is composed of "dermatome" (a skin region), "C6" (the spinal cord level), "temperature" (the modality), and "left" (the side). When subpathways cross the midline, the side designation is chosen based on the side of the body where sensation of motor activity occurs.

NeuroAnatomic Atlas Functions

Given the conceptual framework described above, a set of functions has been written to embody these ideas. Two large groups, definition functions and query functions, are described below.

Definition Functions

Define-Nucleus creates a nucleus object. *Define-Connection* specifies the axonal connection between a *source* structure and a *destination* structure via a *fiber path*. *Define-artery* creates an artery object with a list of branch identifiers. *Define-cns-structure* creates an object of class *cns-structure*.

Define-sensory-subpathway creates an object with an associated set of connection identifiers.

Sensory-Subpathway: Light Touch

The following function defines the C4 touch sensory subpathway. The side effect of this function is the creation of multiple objects in memory each of which is cached by symbolic identifier into the CNS Object Table. An example follows.

```
(define-sensory-subpathway
 :id 'c4-touch.left
 :component-of 'dorsal-column-medial-
   lemniscus-system.left
 :modality 'touch
 :connections '(c1 c2 c3 c4))

(define-connection :id 'c1
 :source 'dermatome-c4-touch.left
 :destination 'drg-c4-touch.left)
(define-connection :id 'c2
 :source 'drg-c4-touch.left
 :destination 'cuneate-nucleus-c4-
   touch.left
 :tract 'dorsal-root-c4.left)
(define-connection :id 'c3
 :source 'cuneate-nucleus-c4-touch.left
 :destination 'vpl-c4-touch.right
 :tract '(internal-arcuate-fibers
   medial-lemniscus.right))
(define-connection :id 'c4
 :source 'vpl-c4-touch.right
 :destination 'sensory-area-1-c4.right
 :tract 'posterior-limb-internal-
   capsule.right)

(define-dermatome
 'dermatome-c4-touch.left)
(define-drg 'drg-c4-touch.left)
(define-nucleus 'cuneate-nucleus-c4-
   touch.left)
(define-tract 'medial-lemniscus.right
 :arteries '(paramedian-rami.right))
(define-nucleus 'vpl-c4-touch.right)
(define-area 'sensory-area-1-c4.right)
(define-artery
 'lateral-striate-artery.left)
(define-artery 'paramedian-rami.right)
```

Modality Table. The modality table is a vehicle to associate specific nerve modalities such as touch with a subpathway. The table then provides a mechanism to obtain an anatomic system from symptom information. We define a function *associate-symptom* that populates the table. This example creates the association of the sensory modality of *pain* in the *V1-face* distribution (forehead) of cranial nerve 5 (the trigeminal nerve) with the subpathway *v1-pain-pathway*.

```
(associate-symptom
 :sign 'pain :region 'v1-face
 :modality 'face-v1-pain
 :pathway 'v1-pain-pathway)
```

A second example defines a mapping from the C7 dermatome for the sensory modality vibration to the specific pathway for this which is called *c7-vibration*.

```
(associate-symptom
 :sign 'vibration :region 'c7
 :modality 'vibration
 :pathway 'c7-vibration)
```

Query Functions

To access the atlas, a set of functions to query the knowledge base is defined.

Vessels-Of. Let *vessels-of* be a function definition that employs knowledge in the digital atlas to map from a structure to its arterial supply. The function returns a list of lists. Each inner list contains the artery to the structure and recursively the parent arteries. So for any given artery (e.g. the lateral striate artery) we obtain the arterial path back to the aorta. The algorithm follows:

```
LET Newlist = nil
LET Artery = artery-of (Cns-Structure)
LOOP
  SET Parent = parent-artery (Artery)
  IF Parent == nil THEN exit LOOP
  ELSE push (Parent, Newlist)
  SET Artery = Parent
END-LOOP
RETURN reverse (Newlist)
```

An example follows:

```
(vessels-of 'internal-capsule.left) =>
((<ARTERY lateral striate artery.left>
 <ARTERY middle cerebral artery.left>
 <ARTERY internal carotid artery.left>
 <ARTERY common carotid artery.left>
 <ARTERY aorta>))

(vessels-of 'area-17.right) =>
((<ARTERY calcarine artery.right>
 <ARTERY internal occipital artery.right>
 <ARTERY posterior cerebral artery.right>
 <ARTERY basilar artery>
 <ARTERY vertebral artery.right>
 <ARTERY subclavian artery.right>))
```

```
<ARTERY brachiocephalic trunk.right>
<ARTERY aorta>))
```

Lookup-Pathway. An operator *Lookup_Pathway* (modality body-region) is defined to use the modality table. This operator takes as input a symptom modality (e.g., pain) and a body region (e.g., V1-face) and produces an object that is the pathway (e.g., V1-pain-pathway) stored. This is the first step in the mapping from symptom to anatomic structure.

Sign-To-Path-And-Arteries. The function *sign-to-path-and-arteries* provides important behavior for the automation of the diagnostic process by querying the atlas, converting a symptom to a subpathway, examining all connections, fiber tracts, and associated arterial supply. This function has the following behavior:

```
P = lookup-pathway (Modality Level Side)
LET ArteryList = nil
LOOP C over connections-of (P)
  ArteryPath = vessels-of (C)
  PUSH (ArteryPath, ArteryList)
END-LOOP
RETURN ArteryList
```

Subpathway Traversal

Using the NAA and query functions, two examples of pathway traversal and analysis are demonstrated.

Subpathway: C4-Touch

We may now trace the subpathway in logical steps. Consider the example where the patient has loss of the sensation of touch in the C4 dermatome on the left side of the body.

```
(sign-to-path-and-arteries
'touch 'c4 :side 'left)
```

Via the modality table, we obtain the subpathway for this dermatome and the list of connection objects for this object.

```
<SENSORY-SUBPATHWAY c4 touch.left>
CONNECTIONS: (C1 C2 C3 C4)
```

Each connection is analyzed to obtain artery information:

Process the first connection:

```
<Connection C1>
Source: <Dermatome C4 Left>
Destination: <GANGLION C4 Touch Left>
;; No artery information is available
```

Process the second connection:

```
<Connection C2>:
Source: <GANGLION-MODALITY C4 Touch Left>
Destination: <CUNEATE-NUCLEUS-C4-
TOUCH.LEFT>
Tract: <DORSAL-ROOT dorsal root c4.left>
;; No artery information is available
```

Process the third connection:

```
<Connection C3>
Source: <NUCLEUS CUNEATE-NUCLEUS-C4-
TOUCH.LEFT>
Destination: <NUCLEUS VPL-C4-TOUCH.RIGHT>
Tracts:
(<DECUSSATION internal arcuate fibers>
<SENSORY-TRACT medial lemniscus.right>)
;; Fibers cross to contralateral side.
```

The function *vessels-of* reveals that there are two arteries that supply the medial lemniscus:

```
((<ARTERY paramedian rami.right>
<ARTERY basilar artery>
<ARTERY vertebral artery.right>
<ARTERY subclavian artery.right>
<ARTERY brachiocephalic trunk.right>
<ARTERY aorta>)
(<ARTERY anterior spinal artery.right>
<ARTERY vertebral artery.right> ...))
```

Process the fourth connection:

```
<Connection C4>
Source: <NUCLEUS VPL-C4-TOUCH.RIGHT>
Destination:
<AREA Sensory Area-1 C4.RIGHT>
Tract: <CAPSULE posterior limb internal
capsule.right>
```

Arteries of the internal capsule:

```
((<ARTERY lateral striate artery.right> <ARTERY middle cerebral artery.right> ...))
```

Subpathway: Pupillary Constriction

The *pupillary reflex* subpathway is described here. The retina can be divided reasonably into four quadrants. We trace the connections of the left upper quadrant of one retina to the *mesencephalic nucleus* controlling this reflex and the motor path to the constricting muscles of the pupil.

```
<SENSORY-SUBPATHWAY pupillary nasal upper quadl.right>
There are two connections:
(<Connection CS1> <Connection CS2>)
```

Process the first sensory connection:

```
<Connection CS1>
SOURCE: <RETINA-NASAL-UPPER-
QUADRANT.RIGHT>
DESTINATION: <NUCLEUS PRETECTAL-
NUCLEUS.LEFT>
TRACT: (OPTIC-NERVE.RIGHT OPTIC-CHIASM
OPTIC-TRACT.LEFT
BRACHIUM-OF-SUPERIOR-COLLICULUS.LEFT)
```

The arteries can be obtained via query.

Process the second sensory connection:

```
<Connection CS2>
Source: <NUCLEUS PRETECTAL-NUCLEUS.LEFT>
Destination: <EDINGER-WESTPHAL-
NUCLEUS.LEFT>
```

Arteries of the Eninger Westphal Nucleus:

```
((<ARTERY paramedian rami.left>
<ARTERY basilar artery> ...))
```

The Eninger-Westphal nucleus reacts to retinal light signals by producing pupillary constriction. There are two connections in the motor segment of this reflex:

```
<MOTOR-SUBPATHWAY
pupillary constriction.left>
CONNECTIONS:
(<Connection CM1> < Connection CM2>)
```

Process the first motor connection:

```
<Connection M1>
Source:<NUCLEUS edinger westphal
nucleus.left>
Destination: <GANGLION ciliary-
ganglion.left>
TRACT: <OCULOMOTOR-NERVE.LEFT>
```

Process the second motor connection:

```
<Connection CM2>
Source: <GANGLION CILIARY-GANGLION.LEFT>
Destination: <MUSCLE IRIS-SPHINCTER-
MUSCLE.LEFT>
```

This concludes traversal of the entire reflex path.

Algorithms for Localization

We propose a **calculus of disease localization** that is based on the notion that central nervous system functional units may be geometrically adjacent only in certain regions. If two nearby units are adversely affected, a disease process (tumor or stroke) may have occurred in the containing structure. An example is the *lateral medullary syndrome* wherein a stroke of the lateral medulla can be diagnosed by findings that include ipsilateral sympathetic dysfunction and contralateral loss of pain and temperature sense.

We have designed two techniques of localization: (1) *the common arterial supply algorithm* and (2) *the common parent structure algorithm*. They are defined below.

Common Arterial Supply Algorithm

We define a function *common-artery* that maps from symptoms to common arteries. Recall our function *vessels-of* that processes a structure argument and returns a list of arteries. Let S1 and S2 be symptom variables.

```
Define-function Common-Artery (S1 S2)
intersection
(vessels-of (symptoms-to-structure (S1)),
vessels-of (symptoms-to-structure (S2)))
```

The resulting set of arteries should be ones that supply the structures associated with the two different symptoms. The computed vessels returned may represent an area of vascular dysfunction. That is, if the common vessels are disrupted (by injury or occlusion), their associated anatomic structures will be injured (by lack of oxygen), and the normal function of those structures will be altered resulting in the symptoms experienced by the patient.

Common Parent Structure Algorithm

This algorithm requires a function *adjacent-structure* that returns true if its argument structures are anatomically adjacent. The function *component-of*(X, Y) returns true if structure X is an anatomic part of structure Y. This example predicate *component-of*(*nucleus cuneatus*, *medulla*) is true. The diagnostic heuristic *common-parent-structure* is defined here:

```
Let S1, S2, and PS be structures
Define-Function
Common-Parent-Structure (S1, S2, PS)
IF AND (adjacent-structures (S1, S2),
component-of (S1, PS),
component-of (S2, PS))
THEN RETURN true
```

If dysfunction of S1 and S2 is found then the parent structure PS may be injured as well.

Visualization of Structures

User interface design for the atlas includes brain visualization in 3D and with virtual reality.

Scanned Human Brain Specimen

A human brain specimen (supplied by the West Virginia University Department of Anatomy) was scanned using the Minolta VIVID 700 Scanner. The resulting brain model was exported and manipulated using 3D software. An illustration is included in this report.

Brain Region Table. We have defined a table that supports a mapping from an NAA object (“left face area of primary somatosensory cortex”) to a predefined area on the 3D Brain Model. An area is defined using interactive tools to select polygons on the model. The set of polygons is stored by area name for later recall. A limited number of areas have been defined and these include the *somatosensory cortex* and the *primary motor cortex*.

Results and Discussion

The object-oriented NeuroAnatomic Atlas has been partially implemented and includes over 1100 objects. As a knowledge resource, this atlas should support the SYNAPS expert system that is currently in the design phase. The atlas functions as a model and as a knowledge base of CNS structures. The core knowledge is sufficient to peruse the object network and to execute basic deductive analysis of nervous system pathology.

Future Work

The System for Neurological Analysis of Patient Symptoms (SYNAPS) is in the design phase now. The prototype NAA will provide (1) core anatomic knowledge, (2) 3D visualization of structures, (3) a framework for adding new paths and systems to the atlas, and (4) the core of teaching software. We plan to augment the atlas with new structures, connections, and mappings to areas on the 3D Brain Model. A natural language software module [11] will be used to convert free text information to expert system input data.

References

- [1] Banks, Gordon, and Bruce Weimer, 1983. Symbolic coordinate anatomy for neurology (SCAN), in *Proceedings of the Symposium on Computer Applications in Medical Care 7* (1983), 828-830.
 - [2] Citro, G., G. Banks, G. Cooper, 1997. INKBLOT: A neurological diagnostic decision support system integrating causal and anatomical knowledge, *Artificial Intelligence in Medicine 10* (1997) 257-267.
 - [3] Smeets R, Talmon J, Meinardi H, Hasman A, 1999. Validating a decision support system for anti-epileptic drug treatment. Part I: initiating anti-epileptic drug treatment *Int J Med Inf* 1999 Nov;55(3):189-98.
 - [4] Starita A, Majidi D, Giordano A, Battaglia M, Cioni R., 1995. NEUREX: a tutorial expert system for the diagnosis of neurogenic diseases of the lower limbs, *Artif Intell Med*. 1995 Feb;7(1):25-36.
 - [5] Keene, Sonya, 1989. *Object-Oriented Programming in Common Lisp: A Programmer's Guide to CLOS*, Addison-Wesley, Reading.
 - [6] Johnston, Mark, Glenn Miller, Jeff Sponsler, Shon Vick, 1990. Spike: Artificial intelligence scheduling for Hubble Space Telescope. *Proc of Fifth Conf on Artificial Intelligence for Space Applications* (Huntsville, May22, 1990), pp 11-18.
 - [7] Sponsler, Jeffrey L., 1994. A Criterion Autoscheduler for Long Range Planning, *Proc. of the 1994 Goddard Conference on Space Applications of Artificial Intelligence* (Greenbelt, Md).
 - [8] Adams, Victor, Ropper, 1997. *Principles of Neurology, 6th Edition*. McGraw-Hill, New York.
 - [9] Carpenter, Malcolm, 1991. *Core Text of Neuroanatomy 4th Edition*, Williams & Wilkins, Baltimore.
 - [10] Haines, Duane, 1997. *Fundamental Neuroscience*, Churchill Livingstone, New York.
 - [11] Sponsler, Jeffrey L. 2001. HPARSER: Extracting formal patient data from free text history and physical reports using natural language processing software. *Proceedings of the American Medical Informatics Association Annual Symposium*, Washington DC, Nov 3-11, 2001.
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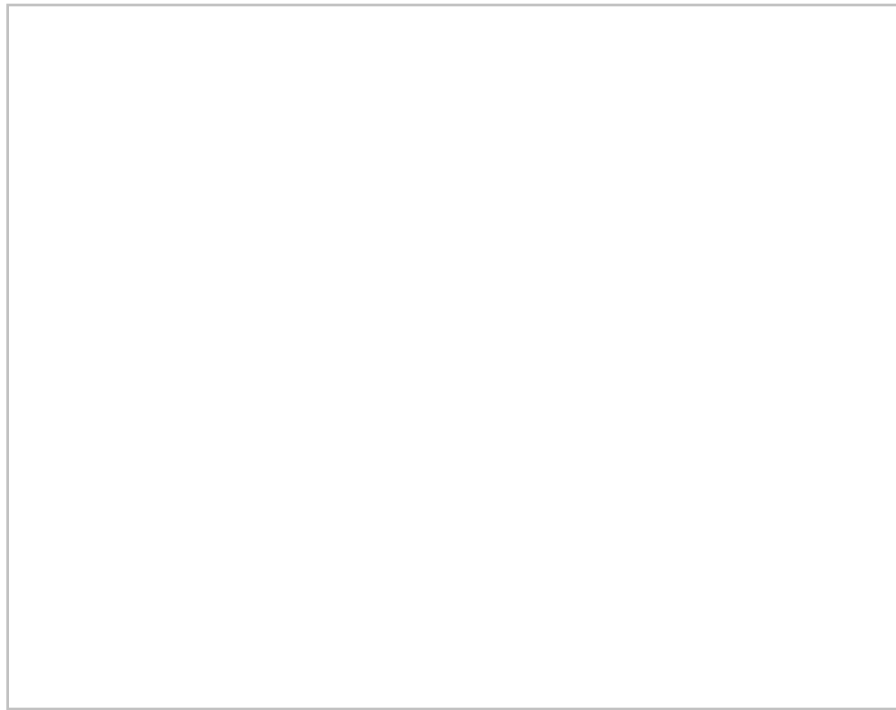


Figure 1. Image of the Neuroanatomic Atlas 3D Brain Model (from scanned specimen).