Original Article

Neuroanatomical Affiliation Visualization-Interface System

Olivier Palombi,[*,1,2] *Jae-Won Shin,*[1] *Charles Watson,*[3] *and George Paxinos*[1]

[1]POWMRI, The University of New South Wales, Randwick NSW, Australia; [2]GRAVIR, Josephe Fourier University, Grenoble, France; and [3]Division of Health Sciences, Curtin University of Technology, Perth, Australia

Abstract

A number of knowledge management systems have been developed to allow users to have access to large quantity of neuroanatomical data. The advent of three-dimensional (3D) visualization techniques allows users to interact with complex 3D object. In order to better understand the structural and functional organization of the brain, we present Neuroanatomical Affiliations Visualization-Interface System (NAVIS) as the original software to see brain structures and neuroanatomical affiliations in 3D.

This version of NAVIS has made use of the fifth edition of "The Rat Brain in Stereotaxic coordinates" (Paxinos and Watson, 2005). The NAVIS development environment was based on the scripting language name Python, using visualization toolkit (VTK) as 3D-library and wxPython for the graphic user interface. The following manuscript is focused on the nucleus of the solitary tract (Sol) and the set of affiliated structures in the brain to illustrate the functionality of NAVIS. The nucleus of the Sol is the primary relay center of visceral and taste information, and consists of 14 distinct subnuclei that differ in cytoarchitecture, chemoarchitecture, connections, and function. In the present study, neuroanatomical projection data of the rat Sol were collected from selected literature in PubMed since 1975. Forty-nine identified projection data of Sol were inserted in NAVIS. The standard XML format used as an input for affiliation data allows NAVIS to update data online and/or allows users to manually change or update affiliation data. NAVIS can be extended to nuclei other than Sol.

Index Entries: 3D visualization; data entry process; digital atlas; functional anatomy; nucleus of the solitary tract; knowledge management system.

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*Author to whom all correspondence and reprint requests should be addressed.
E-mail: olivier.palombi@imag.fr

Introduction

Functional activity of the central nervous system is based, interalia, on a complex connectivity network among its anatomical structures. Both conventional and novel pathway-tracing techniques have led to discovery of a large number of neuroanatomical connections (Vercelli et al., 2000; Leergaard et al., 2003; Boldogkoi et al., 2004). However, because of the vastness of available connectivity data it is difficult to display and disseminate them. Therefore, considerable efforts have been made to develop an effective means of communicating currently available neuroanatomical affiliation data. A number of knowledge management systems have been developed, i.e., Collations of Connectivity Data on the Macaque Brain (CoCoMAC) (Bowden and Dubach, 2003), NeuroNames (Bowden and Dubach, 2003), and Brain Architecture Management System (BAMS) (Bota et al., 2005) to allow users to have an access to a large quantity of neuroanatomical data. However, current knowledge management systems provide users with a type of information that still requires them to investigate what it means *in situ* by consulting hard copies of neuroanatomical atlases.

The advent of three-dimensional (3D) visualization techniques in computer science allows investigators to reconstruct a real-life 3D object and to view it on computer screen from different points of view. Therefore, 3D-visualization techniques provide a powerful means of communication of neuroanatomical information. A number of studies have developed 3D-digital atlases (Toga et al., 1989; Funka-Lea and Schwaber, 1994; Toga et al., 1995; Brevik et al., 2001) in order to better understand the structural organization of the brain. However current 3D-atlases lack information about a connectivity network of the central nervous system and only serve as a morphological reference. The reason is that the interaction between 3D-atlases and current knowledge

management systems has been relatively scarce, especially when it comes to communicating neuroanatomical affiliation data. Therefore, a system that integrates information from knowledge management systems and that from 3D-neuroanatomical atlases needs to be developed to depict neuroanatomical affiliation information within a digital 3D-atlas. This will provide an effective and fast means of information communication by synchronizing of neuroanatomical information with its graphical representation.

To address this issue, the present study constructed a graphical user interface (GUI)-based system named "Neuroanatomical Affiliation Visualization-Interface System" (NAVIS), for retrieving, synthesizing, and visualizing neuroanatomical structures and affiliations in a digital 3D-atlas.

Methods and Materials

NAVIS Development Environment

The main programming language used to create NAVIS was Python 2.3.3 (http://www.python.org/), an interpreted, object-oriented programming language, which is a suitable choice for applications that require portability across different machine architectures. The visualization environment of NAVIS was built using Visualization ToolKit (VTK 2.4.2: http://public.kitware.com/VTK/). This open source C++ library for 3D-computer graphics and visualization is available with a specific Python interface layer. The GUI of NAVIS was built using wxPython 2.4.1.2 (http://www.wxpython.org/), which is an extension module that wraps the wxWidgets, which is a cross platform GUI library (http://www.wxwidgets.org/). The XML parser was based on the python module, PyXML 0.8.4 (http://pyxml.sourceforge.net/), to read XML description files. NAVIS was designed and implemented using an object-oriented design with extensibility in mind.
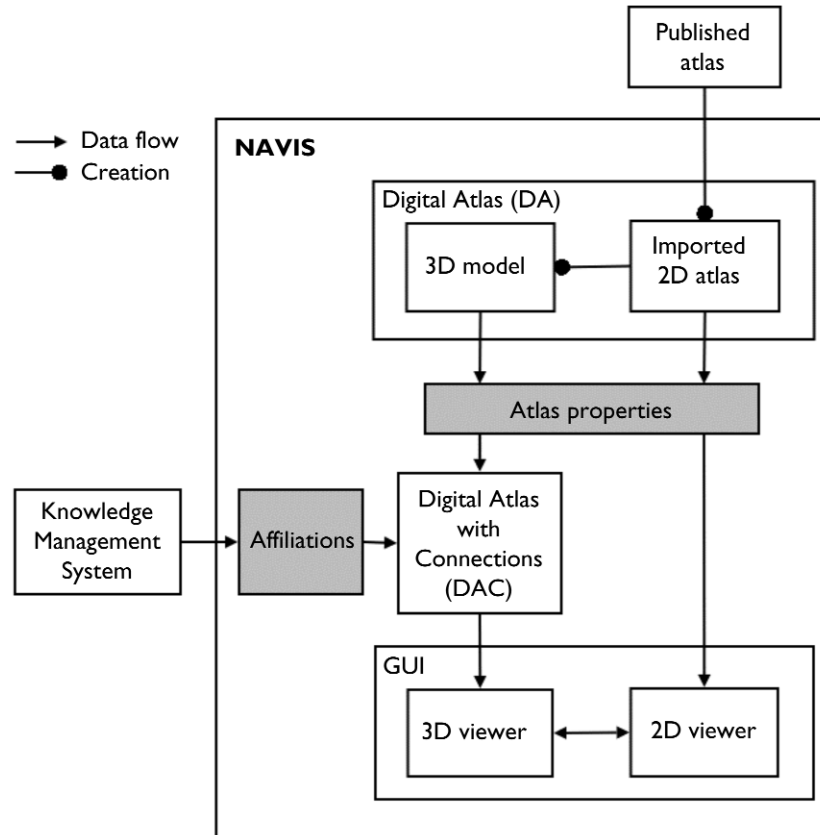
Fig. 1. General organization and data flow of NAVIS.

The General Structure of NAVIS

The current version of NAVIS was constructed at two levels: an intrinsic level, which involves retrieving and processing of neuroanatomical data, and an output level as GUI where these data are visualized. The general structure of NAVIS is illustrated in Fig. 1. The intrinsic level of NAVIS consists of two modules: *Digital Atlas* (DA) and *DA with Connections* (DAC). The DA module contains two-dimensional (2D) spatial information and 3D-models of neuroanatomical structures. The DAC module is derived from the DA module and neuroanatomical connection data registered into NAVIS. The derivation of the DAC module is mediated by metadata, which describe specific formats of data organization to be used in NAVIS:

1. *Atlas properties* metadata organize information retrieved from the DA module into structural hierarchy inherent in neural organs,
2. *Affiliations* metadata is an entry point for neuroanatomical affiliation data. The output from the DAC module is used to visually represent neuroanatomical structures and affiliations in GUI.

At an output level of NAVIS, GUI has 2D- and 3D-viewer components. Both components interact with each other to allow users to navigate neuroanatomical information about a nucleus of interest that users choose before running the program.

The "Digital Atlas" Module

The present study used a standard atlas, The Rat Brain in Stereotaxic Coordinates 5th
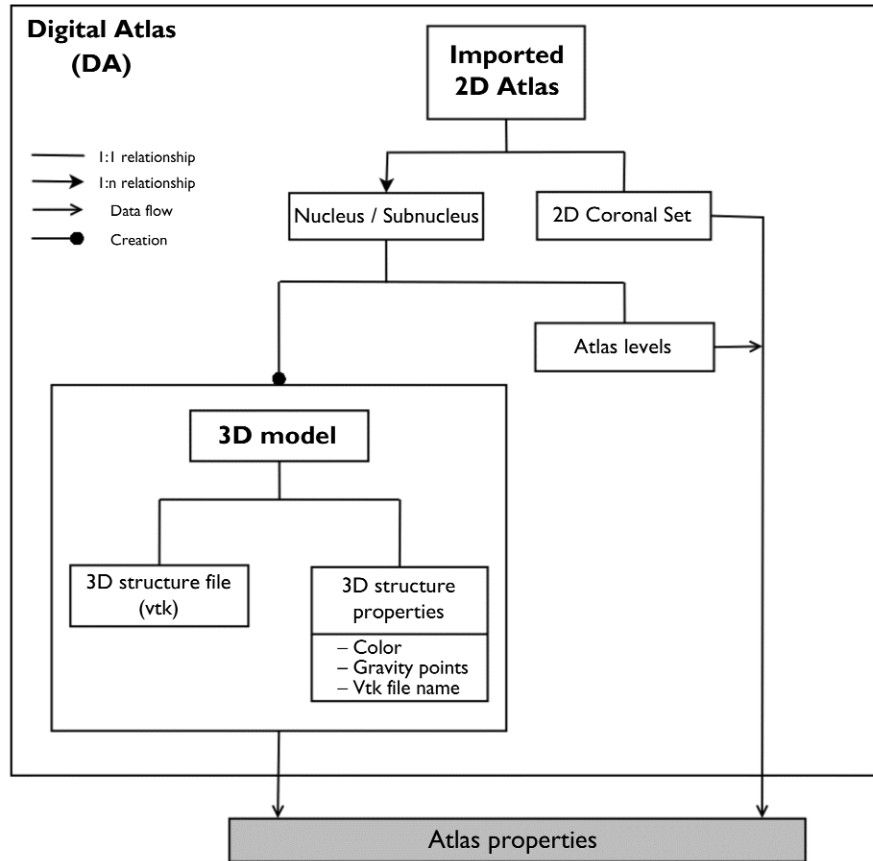
Fig. 2. Organization of the DA module.

Edition (RBSC5) (Paxinos and Watson, 2004) to create the DA module (Fig. 2). In the DA module, 2D-spatial information of neuroanatomical structures was derived from RBSC5 directly, whereas 3D-models of nuclei and subnuclei were created from delineations in the coronal set of RBSC5. This was done for the nucleus of the solitary tract (Sol) and nuclei with which it is affiliated. Beyond this, the outline of the brain was included as well as the orientation plane, axes, and stereotaxic box.

RBSC5 contains a coronal set of 161 sections from a single rat brain at regular 120-μm intervals. The 2D-digital set of diagrams contains free-hand delineation of nuclei and subnuclei, and is available in encapsulated postscript format in the accompanying CD-ROM of RBSC5. The drawings on histologically prepared

tissues in RBSC5 were performed only on the right side of each section and the outline of structures on the left side was derived from using mirror image construction. This principle was also maintained in 3D-model reconstruction. In importing RBSC5 into the DA module, the coronal set was colored to assign each nucleus or subnucleus with its unique color.

For each nucleus or subnucleus a *3D-model* object was created. The "3D-model" object consists of *3D-structure file* and *3D-structure properties* attributes. 3D-structure files in a VTK format were constructed by computational 3D-reconstruction methods and each 3D-model was assigned a set of properties including a color, a pair of gravity centers, and a file name of the 3D-model.

The 3D-Reconstruction Process

3D-models of the nucleus of interest and its affiliates were reconstructed using a sequence of 2D-planar anatomical delineation in RBSC5. The stereotaxic reference system was used to perform the 3D-reconstruction using the surrounding rectangle as reference. The 3D-reconstruction process consisted of three phases. The first phase was to convert and transform the 2D-digital set of diagrams to prepare contour extraction. The second phase was to extract the contour of each identified neuroanatomical structure. The third phase was to rebuild the 3D-surface model of each structure from a set of contours.

Phase I

In RBSC5 structures in outline were drawn in continuous and/or broken lines. All the outlines in a digital diagram were converted to continuous lines to get closed areas. All features except the outlines and the surrounding rectangle were excluded in the 3D-reconstruction process. The set of 161 encapsulated postscript files were then converted to portable network graphics format. Each nucleus or subnucleus on each section was colored manually with reference to a color lookup table. In the lookup table a color (red, green, and blue) was assigned to each nucleus or subnucleus.

Phase II

A distance map approach was used in the contour extraction process. In implementing this approach, a discrete distance called Chanfer distance was used (Borgefors, 1986). The Chanfer distance allows a fast distance map computation. The Rosenfeld method was used to locate the nearest background pixel for each pixel in the image (Rosenfeld and Platz, 1966). Two filter passes on the image allow the distance information to be propagated to all pixels. After filtering, the generated contour was a set of pixels with the smallest distance from the background. The polygonization of this set of pixels creates a nonintersecting polygonal contour. The polygonization method was based on Vittone's recognition algorithm for the decomposition of a discrete boundary into discrete 2D-line segments (Vittone, 1999).

Phase III

The surface reconstruction of 3D-objects from contour datasets was performed using the Delaunay triangulation method. The 3D-surface models were created from these datasets using a set of software tools (Nuages) developed by Bernard Geiger (Geiger, 1993). In the process of reconstruction vertices were added on or inside contours to generate a compact tetrahedrization. The nearest neighbor connection was detected using the medial axis of the contours. This approach is suitable for branching structures. The resulting set of surface models was a 3D connection of contours preserving an original delineation in RBSC5. The set of triangles produced was directly converted to a VTK file format (vtkUnstructuredGrid). The set of 3D-triangular models then underwent a smoothing process described in the VTK pipeline design as shown in Fig. 3.

Metadata: Extensible Markup Language

Metadata is structured data that describes a specific data organization used in a system. One of the universal formats of metadata used in informatics is eXtensible Markup Language (XML, http://www.w3.org/XML/) developed by the World Wide Web consortium (http://www.w3.org/). Two important characteristics of XML distinguish itself from other formats of metadata. Its ability to organize data structurally and hierarchically allows users to describe a complex biological system in a simple manner. In addition, universality of XML lets users design a single data structure to interact with different types of documents and other systems. To take advantage of these characteristics, two XML description files were used in
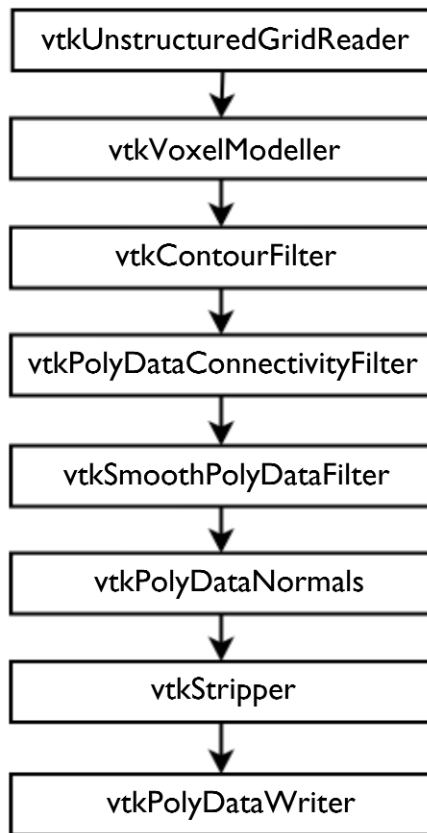
```
┌──────────────────────────────┐
│   vtkUnstructuredGridReader   │
└──────────────────────────────┘
                │
                ▼
┌──────────────────────────────┐
│       vtkVoxelModeller        │
└──────────────────────────────┘
                │
                ▼
┌──────────────────────────────┐
│       vtkContourFilter        │
└──────────────────────────────┘
                │
                ▼
┌──────────────────────────────┐
│ vtkPolyDataConnectivityFilter │
└──────────────────────────────┘
                │
                ▼
┌──────────────────────────────┐
│    vtkSmoothPolyDataFilter    │
└──────────────────────────────┘
                │
                ▼
┌──────────────────────────────┐
│      vtkPolyDataNormals       │
└──────────────────────────────┘
                │
                ▼
┌──────────────────────────────┐
│         vtkStripper           │
└──────────────────────────────┘
                │
                ▼
┌──────────────────────────────┐
│      vtkPolyDataWriter        │
└──────────────────────────────┘
```

Fig. 3. The VTK pipeline for smoothing 3D-models of neuroanatomical structures, vtkVoxelModeller, is a filter that converts an arbitrary data set to a structured voxel representation. vtkContourFilter takes any dataset as an input and generates an isosurface. VtkPolyDataConnectivityFilter removes an unnecessary isosurface that can be created when a 3D-model possesses concave features. vtkSmoothPolyDataFilter adjusts point coordinates using Laplacian smoothing. vtkPolyDataNormals computes point normals for a polygonal mesh. vtkStripper generates a triangle strip from the polygonal mesh. The VTK filters used to build this pipeline are available in Visualization ToolKit (VTK 2.4.2: http://public.kitware.com/VTK/).

NAVIS, one as a means of mediating data flow *(Atlas properties)* and the other for data retrieval *(Affiliations)*.

"Atlas properties" XML mediates data flow by organizing the content in the DA module into neuroanatomical hierarchy. As shown in Fig. 4A, the most upper level of hierarchy is "atlas", which represents the whole organ on which an atlas was based. It is characterized by attributes including species, organ, information about the atlas, and properties of 3D-model of the organ. "Atlas" and "nucleus" elements are in a 1:n relation (one to many) as there are many nuclei identified in the atlas. Each "nucleus" element has a "panel" tag and attributes including "longname" and 3D-model properties. The "panel" tag consists of the range of atlas levels and coordinates of the bounding box at which the nucleus can be identified. The relationship between "nucleus" and "subnucleus" elements can vary, depending on the number of subnuclei identified in each nuclei. The "subnucleus" element has attributes such as "partname" and 3D-model properties. All the values for attributes of elements in "Atlas properties" XML are retrieved from the DA module.

"Affiliations" XML was written primarily to take advantage of universality of XML for retrieval of neuroanatomical projection data from currently available on-line knowledge management systems and other forms of knowledge representation such as published papers. The "Affiliations" XML description file consists of a set of "affiliation" elements as shown in Fig. 4B. Each element has attributes including origin of projection, target of projection, type of connection, strength of projection, and database/reference from which affiliation data were retrieved. Neuroanatomical affiliation data can be appended to each "affiliation" element of the XML description file either m anually by users or automatically by developing a module, which allows registration of connectivity data retrieved from database. The present study used the former method of data entry.

The "Digital Atlas With Connections" Module

Every component of the DAC module was implemented as an individual Python class,

A

```
<?xml version="1.0" ?>
<!-- /NAVIS version 1.0 / -->
- <atlas_properties>
  - <atlas species="Rat" organ="Brain" title="The Rat Brain in Stereotaxic Coordinates 5th Edition" authors="Paxinos, G. and Watson, C." year="2004"
      color="0, 255, 0" vtk_file="Brain.vtk">
    - <nuclei>
      - <nucleus name="Sol" longname="Nucleus of the solitary tract" color="250, 250, 255" gravity_center_right="-0.109, 0.524, 0.317">
          <memo>The nucleus of the solitary tract (Sol) is the primary visceral and taste information relay center.</memo>
          <panel firstsection="125" lastsection="161" frame="0,1220,440,1510" />
          <subnucleus name="sol" partname="Solitary tract" color="209, 0, 178" gravity_center_right="-0.169, 0.526, 0.341" vtk_file="sol_t.vtk" />
          <subnucleus name="SolDL" partname="Dorsolateral" color="121, 208, 97" gravity_center_right="-0.093, 0.542, 0.265" vtk_file="SolDL.vtk" />
          ::
          <subnucleus name="SolRL" partname="Rostroclateral" color="245, 130, 95" gravity_center_right="-0.295, 0.472, 0.562" vtk_file="SolRL.vtk" />
          <subnucleus name="SolRC" partname="Rostrocentral" color="242, 255, 0" gravity_center_right="-0.201, 0.496, 0.469" vtk_file="SolRC.vtk" />
        </nucleus>
        ::
      - <nucleus name="AP" longname="Area Postrema" color="64, 216, 214" gravity_center_right="-0.001, 0.567, 0.255" vtk_file="AP.vtk">
          <panel firstsection="147" lastsection="152" frame="0,1200,225,1350" />
        </nucleus>
        <nucleus name="KF" longname="Kolliker-Fuse nucleus" color="45, 139, 70" gravity_center_right="-0.352, 0.545, 0.879" vtk_file="KF.vtk" />
      </nuclei>
    </atlas>
  </atlas_properties>
```

B

```
<?xml version="1.0" ?>
<!-- // -->
- <affiliation_data>
  - <affiliations species="rat">
      <!-- /Sol/ -->
      <affiliation origin="Sol" target="Amb" />
      <affiliation origin="Sol" target="10N" strength_of_projection="strong" />
      <affiliation origin="Ce" target="SolM" />
      <affiliation origin="LPB" target="SolM" connection_type="I" database="PubMed" />
      ::
      <affiliation origin="SolM" target="LPBE" />
      <affiliation origin="SolM" target="LPBC" />
    </affiliations>
  </affiliation_data>
```

Fig. 4. The data structure of **(A)** "Atlas properties" and **(B)** "Affiliations" described in XML format.

the basic unit of the object-oriented program, permitting an easy implementation of hierarchical data structure described in XML metadata and subsequently allowing visual representation of each neuroanatomical entity and connectivity on computer screen. In NAVIS, neuroanatomical structure was modelled at three levels—organ, nucleus, and subnucleus—based the levels of structural hierarchy at which the original atlas identifies neuroanatomical entities. As shown in Fig. 5, the "NeuroSubnucleus" class inherits from the
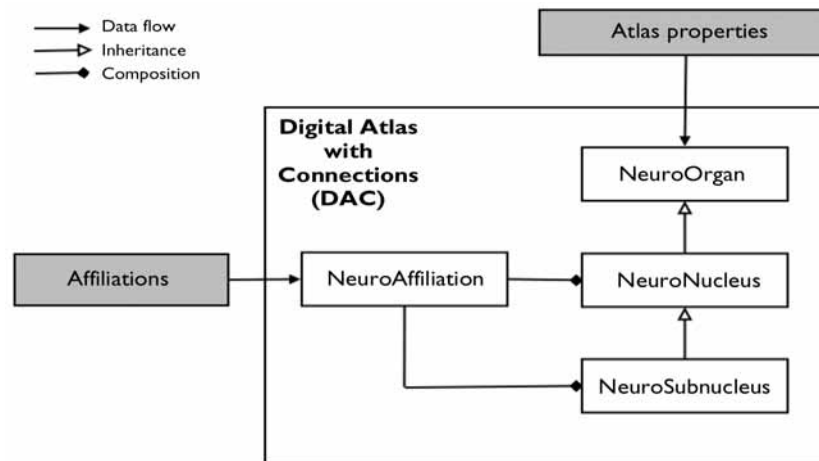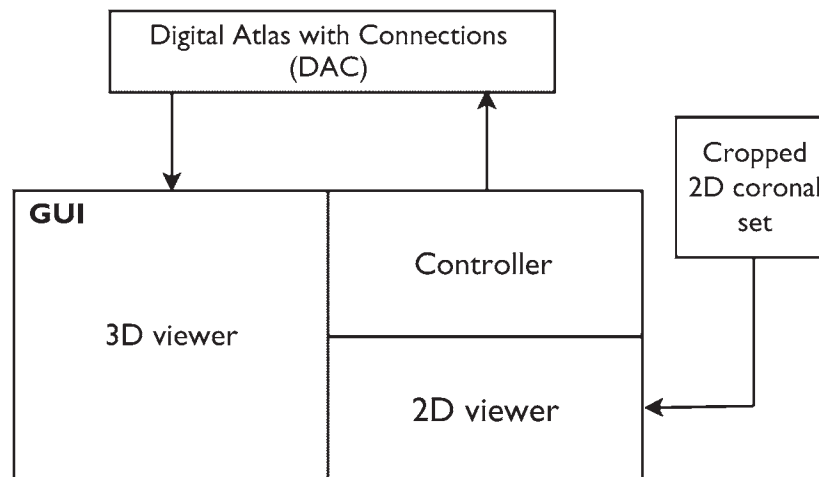
Fig. 5. Organization of the DAC module.

Fig. 6. General structure of NAVIS GUI.

"NeuroNucleus" class, which in turn inherits from the "NeuroOrgan" class. These classes were prepared to represent each neuroanatomical hierarchical unit used in NAVIS. The "NeuroAffiliation" class was prepared to represent affiliation data retrieved from the "Affiliations" XML description file. As the classes in the DAC module were prepared to implement data structure described in "Atlas properties" and "Affiliations" XML files, their attributes conform the attributes of relevant elements in the XML files.

Each piece of affiliation data from "Affiliations" XML is registered into an appropriate object represented by "NeuroNucleus" or "Neuro Subnucleus" class, based on values assigned in its "origin" and "target" attributes (Fig. 5). After data registration from the XML description files is completed, the objects represented by "NeuroOrgan," "NeuroNucleus" and "NeuroSubnucleus" classes are registered into NAVIS GUI to make themselves available for visualization.

GUI in NAVIS

The GUI in NAVIS consists of three components (Fig. 6).

1. 3D-viewer, which depicts nuclei/subnuclei structures and projections in a 3D-space;
2. 2D-viewer, which shows a 2D-coronal set of a nucleus/subnucleus of interest in focus; and
3. Controller, which allows users to selectively visualize the structure and affiliations of a nucleus/subnucleus of interest.

The 3D-viewer panel was implemented by using a set of VTK and wxPython classes. Each object created from the DAC module is assigned a 3D-model in a VTK file format, which was created during the 3D-reconstruction process. VTK files are read and displayed in the 3D-viewer using the standard VTK visualization pipeline (Schroeder et al., 2004). In retrieving data from a 2D-coronal set, NAVIS retrieves atlas levels and bounding box coordinates of a nucleus of interest selected by users, from the "panel" tag of the "nucleus" element in "Atlas properties" XML. Then it crops an original coronal image from RBSC5 to show the nucleus of interest and its surrounding structures in focus. This cropped image set is registered into the 2D-viewer panel for user navigation.

The controller panel interacts with the DAC module to manipulate visualization of neuroanatomical structures and affiliations in the 3D-viewer on the user's request. Python programming language has a built-in data type called "dictionary," which is a collection of data that are indexed and retrieved by keys. Therefore, in selecting a set of neuroanatomical structures and affiliations for display, the controller retrieves and utilizes a dictionary from the DAC module, which is a collection of the objects that are indexed by abbreviations of neuroanatomical structures.

Visualization of Neuroanatomical Affiliation in 3D

The current first version of NAVIS depicts three types of projection information in the 3D-viewer, including connectivity type, connectivity strength, and projection direction. To depict neuroanatomical projections in 3D, lines were created by joining gravity centers of the 3D-model of a nucleus or subnucleus of interest with those of its affiliated structures. In NAVIS, there are four types of connection: ipsilateral, contralateral, bilateral, and unknown. In joining gravity centers, different combinations of line connections were implemented to visualize different types of connections (Fig. 7). Visual representation of information on connectivity strength was based on qualitative criteria consisted of four levels: lower, medium, strong, and unknown. In depicting connectivity strength, color intensity variation was used. Strongest connectivity was signified by brightest intensity. In addition, a first letter representing each level of connectivity strength ("L," "M," "S," and "U") was inserted in the midpoint of each line. After creating lines, cone animation was built along each line to show the direction of projections (Fig. 8). The color of each line was assigned to conform to that of a nucleus or subnucleus of interest.

Data Insertion and Construction

To demonstrate an application of using NAVIS, the nucleus of Sol was selected as an example. Sol is the brain's primary visceral and gustatory relay center, which consists of 14 subnuclei, according to a cytoarchitectonic criteria by Paxinos and Watson (2004), with a lot of information on its connections (Paxinos, 2004). Paxinos and Watson (2005) did not commit themselves on the borders of all subnuclei of Sol in their published atlas. For the purpose of this study they completed these borders and this permitted 3D-reconstruction of all subnuclei.

In the present study, neuroanatomical projection data of the rat Sol were collected from selected literature in PubMed since 1975. Forty-nine identified projection data of Sol were inserted in the "Affiliations" XML description file. 3D-models were reconstructed from RBSC5 for all subnuclei of Sol and their affiliated structures, resulting in the total of 45 rat brain nuclei and subnuclei with 3D-representation.
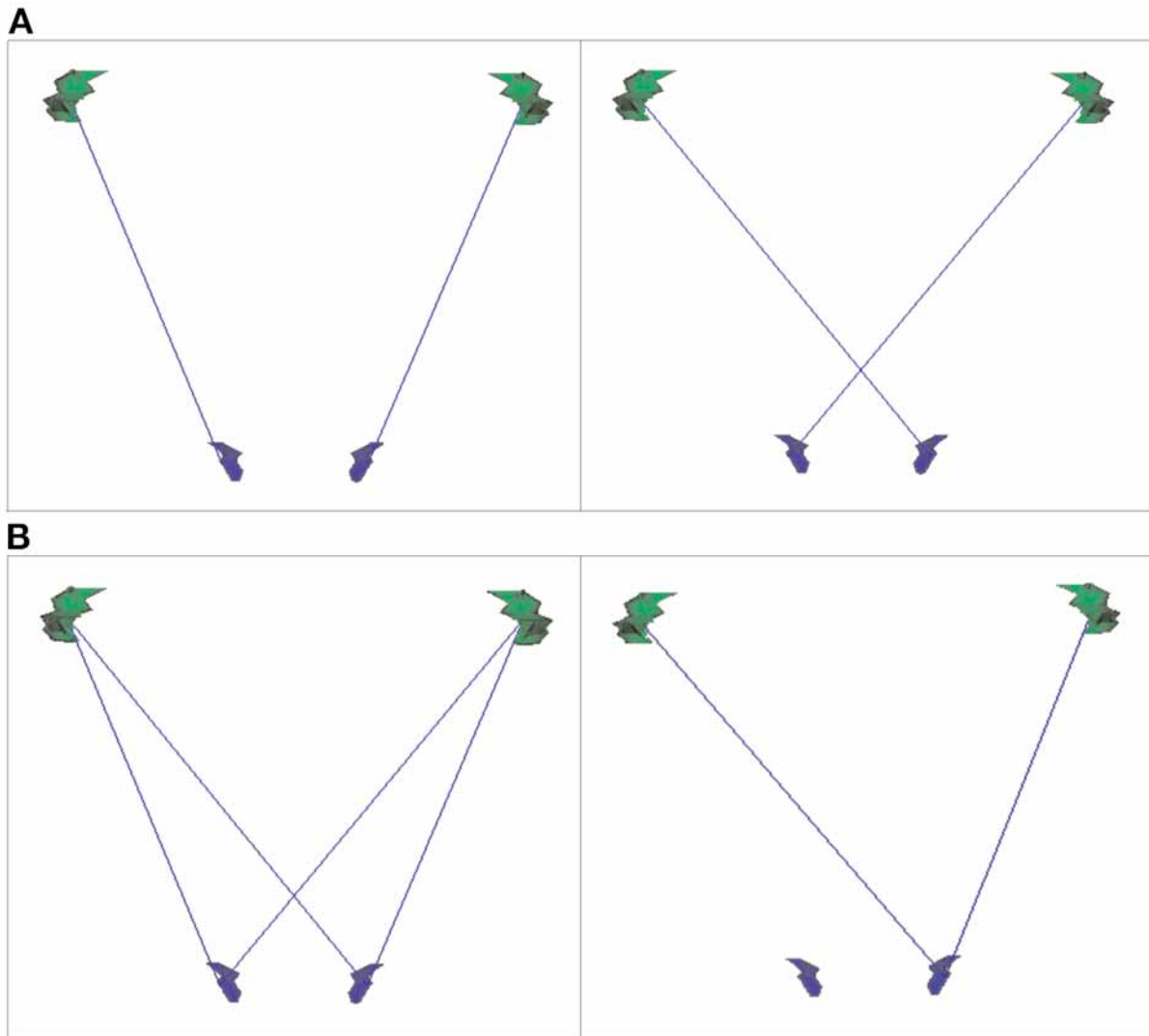
Fig. 7. Depiction of different connection types in 3D. Each structure has a pair of gravity points. **(A)** Ipsilateral connection is depicted by connecting the gravity centers of the same side. **(B)** Contralateral connection is shown by connecting the gravity centers of the opposite side. **(C)** Bilateral connection was shown by joining each gravity center from the nucleus/subnucleus of interest with both gravity centers of each affiliated structure. **(D)** 'Unknown' type of connection was displayed by joining one gravity center from the nucleus/subnucleus of interest with both gravity centers of each affiliated structure.

Results

NAVIS is characterized by its ability to interactively display neuroanatomical structures in 2D- and 3D-spaces, its facility to depict neuroanatomical affiliations directly onto 3D-atlases, and its power to coordinate different forms of neuroanatomical affiliation information.

Initial Setting Module in NAVIS

In starting NAVIS, users are presented with the NAVIS main controller frame (Fig. 9). Three decisions have to be made before starting the
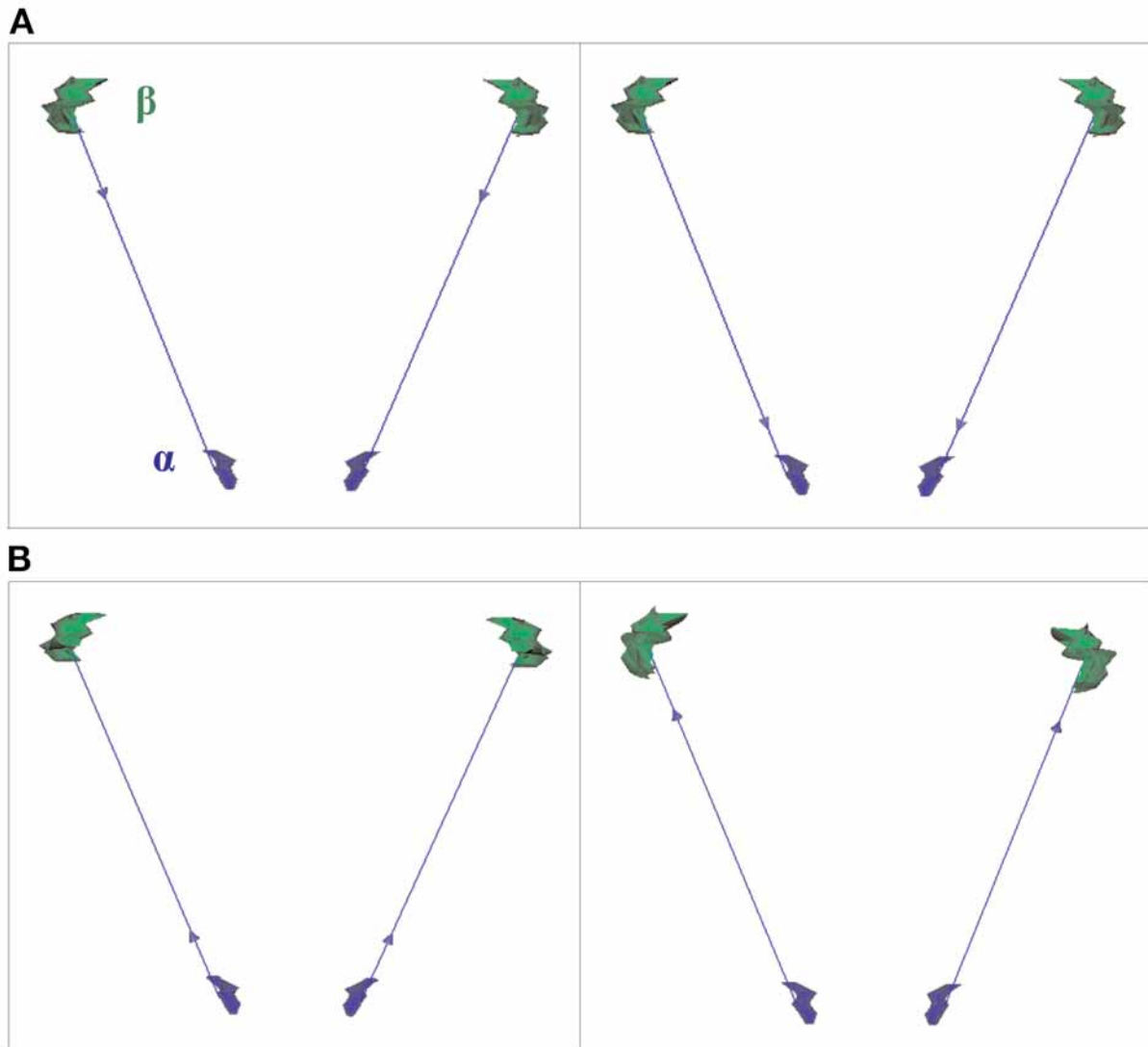
Fig. 8. Animation showing **(A)** afferent and **(B)** efferent projections. Structure α is the nucleus/subnucleus of interest and structure β is its affiliated structure.

NAVIS GUI: *Atlas, Affiliation data, and Nucleus*. "Atlas" refers to a choice among published atlases that offer a digitalized 2D-coronal set and a 3D-surface reconstruction model of neuroanatomical entities identified in an atlas. Only RBSC5 is available in the current version of NAVIS. "Affiliation data" refers to an XML description file through which NAVIS retrieves neuroanatomical affiliation data. Users can choose any XML description file by clicking on the "Load" button, if it conforms to the "Affiliations" XML used in NAVIS. "Nucleus" allows users to choose nucleus of interest in which NAVIS GUI will display as the point of view. Users can get further information of each option by clicking on the "Details" button next to each drop-down menu. Users can then proceed with NAVIS GUI by clicking on the "Viewer" button.
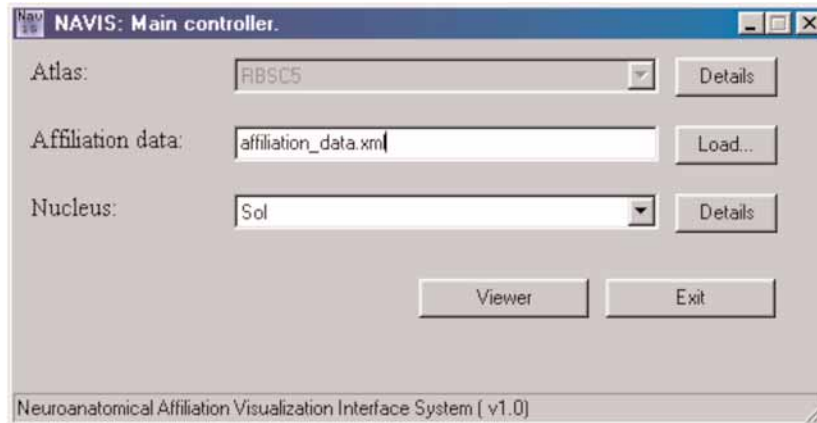
Fig. 9. Before running NAVIS GUI, users can choose an atlas, an XML file containing affiliation data and a nucleus of interest to be viewed as a point of view.

Display of Neuroanatomical Structures in NAVIS

There are generally two types of structural information displayed in the 3D-viewer panel of NAVIS GUI. One type is the nucleus of interest and all of its subnuclei if present, which are displayed as different colors registered in the lookup table. NAVIS GUI starts by displaying the nucleus of interest. There are two types of nuclei—the one with subnuclei and the other with no substructure. Whereas the latter type of nucleus is displayed as a single structure, the former type is displayed as a group of its subnuclei, all with the identical color, which changes on clicking to signify that there is a further cytoarchitectonic classification of this nucleus. In starting NAVIS GUI, a button is generated for each nucleus of interest and its subnuclei on the upper right panel. An example of 3D-models displayed and a set of buttons created for Sol and its subdivisions is shown in Fig. 10A and B. Users can click on a button to selectively display a nucleus of interest or its subnuclei. The other type of neuroanatomical structures displayed in 3D is a set of affiliated structures of the nucleus of interest. Unlike the nucleus of interest, they are not assigned a button, because their display will depend on the user's choice of afferent/efferent display settings in the controller panel.

The 3D-viewer panel allows users to interactively view 3D-structures on display using the mouse. In the 3D-viewer, users can access functions offered by VTK. 3D-structures can be viewed at different camera angles by left click and drag in the direction to which users want to rotate 3D-models. Right click and drag allows users to zoom in and out 3D-models. Users can also relocate the whole displayed structures to adjust the viewpoint by middle click and drag. In addition, users can choose a type of 3D-representation of structures displayed in the viewer by pressing "w" key to view the wire frame model and "s" to view the surface model.

The 2D-viewer panel shows a set of coronal section images of the nucleus of interest, its subnuclei, and their surrounding structures as shown in Fig. 10C. Each nucleus/subnucleus is labeled and assigned a color corresponding to that of its 3D-model and button. Users can navigate through a coronal image set by moving a slider or clicking an arrow next to the text showing an atlas number with reference to RBSC5. The location of the current coronal section is also indicated by a line on the sagittal-section plan displayed next to a coronal image.
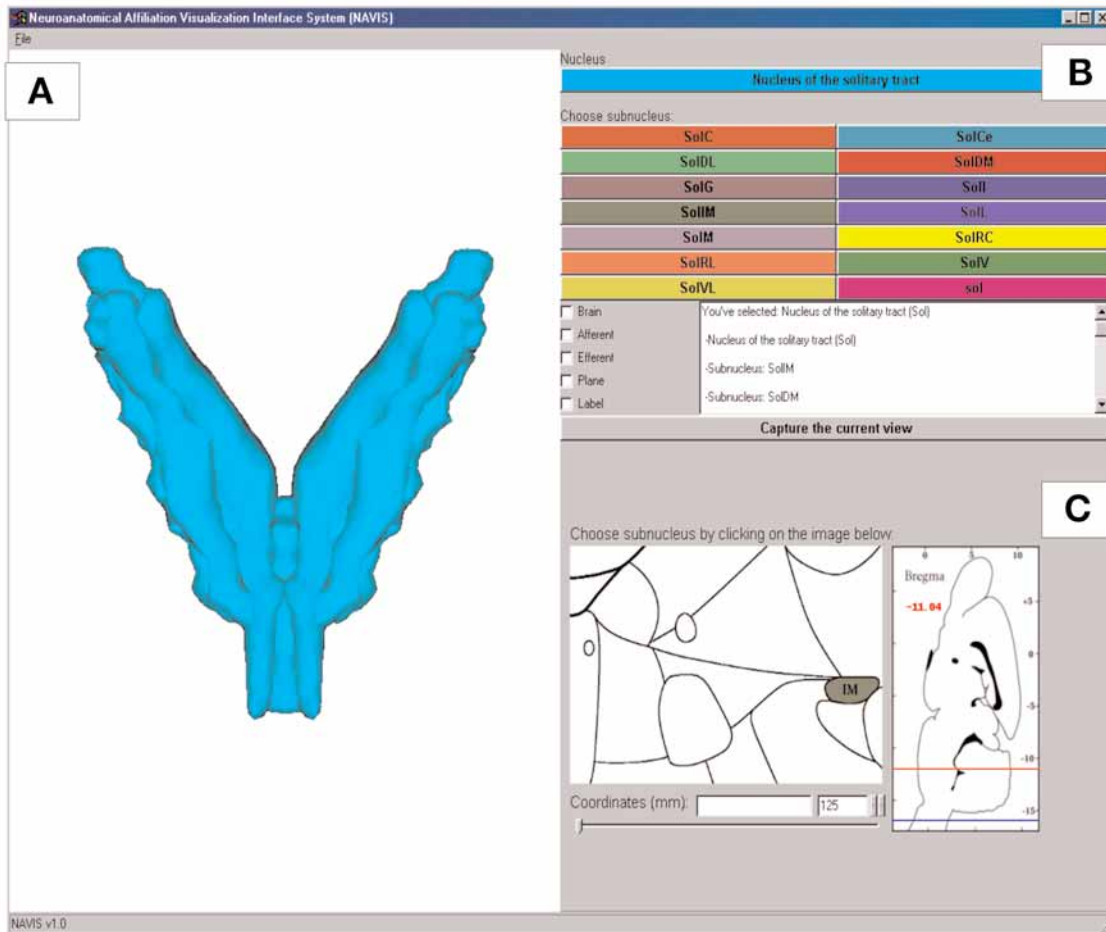
Fig. 10. NAVIS GUI showing Sol as the nucleus of interest (ventral view). GUI consists of **(A)** the 3D-viewer panel (left), **(B)** the controller panel (upper right), and **(C)** the 2D-viewer panel (lower right).

Display of Neuroanatomical Affiliations in NAVIS

3D-visualization output of projection data can be retrieved using any combination of two selections: affiliation data and direction of projections. On selecting a nucleus of interest by checking an "Afferent" or "Efferent" box in the controller panel, users can view the structures and projecting lines that connect with the nucleus of interest as well as with its subnuclei. Figure 11A depicts all afferent and efferent projection data of Sol and those of its subnuclei that have been entered into DAC. This simultaneous depiction allows users to observe a general pattern of

afferent and/or efferent projections of a nucleus of interest. Users can dissect this general pattern by clicking a button assigned for each subnucleus and subsequently viewing its projections selectively as shown in Fig. 11B. Therefore, in viewing projections of each subnucleus, users can observe the contribution of each subnucleus in forming the general projection pattern of the nucleus of interest.

Coordination of Neuroanatomical Information in NAVIS

NAVIS coordinates different types of neuroanatomical information, presented in text,
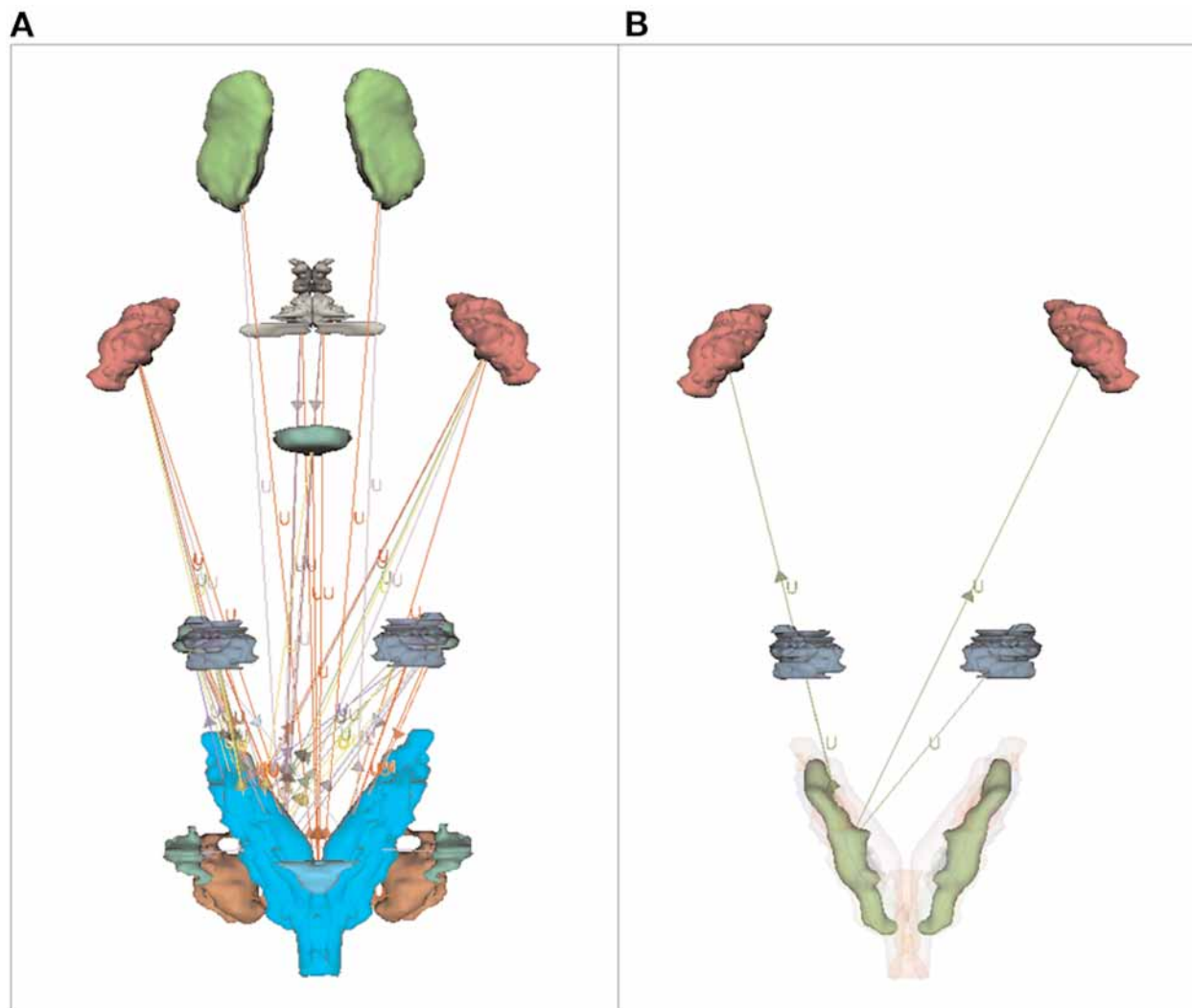
Fig. 11. The 3D-visualization output of affiliation data of Sol (dorsal view). **(A)** Afferent and efferent projections of Sol and its subnuclei. Users can view all projections of a nucleus of interest and those of its subnuclei at the same time in a single 3D-space to observe a general pattern of afferent/efferent projections. **(B)** Afferent and efferent projections of the ventral part of Sol. Users can view projections of each subnucleus selectively.

2D- and 3D-graphical formats, which are synchronously displayed on the user's request. Hence users can retrieve these types of information at the same time, promoting a fast and effective communication of neuroanatomical information. Figure 12 demonstrates coordination of information between the 2D- and 3D-viewers. In ticking a "Plane" check box and choosing an atlas level by the slider located below the coronal image set, users cannot only observe a different coronal diagram in 2D, but also view in 3D which atlas level they have chosen (Fig. 12A). After choosing an atlas level of interest, users can select an individual nucleus/subnucleus by left-clicking on a coronal image (Fig. 12B). On clicking, the 3D-viewer immediately responds by selectively displaying a 3D-model of the chosen nucleus/subnucleus. At the same
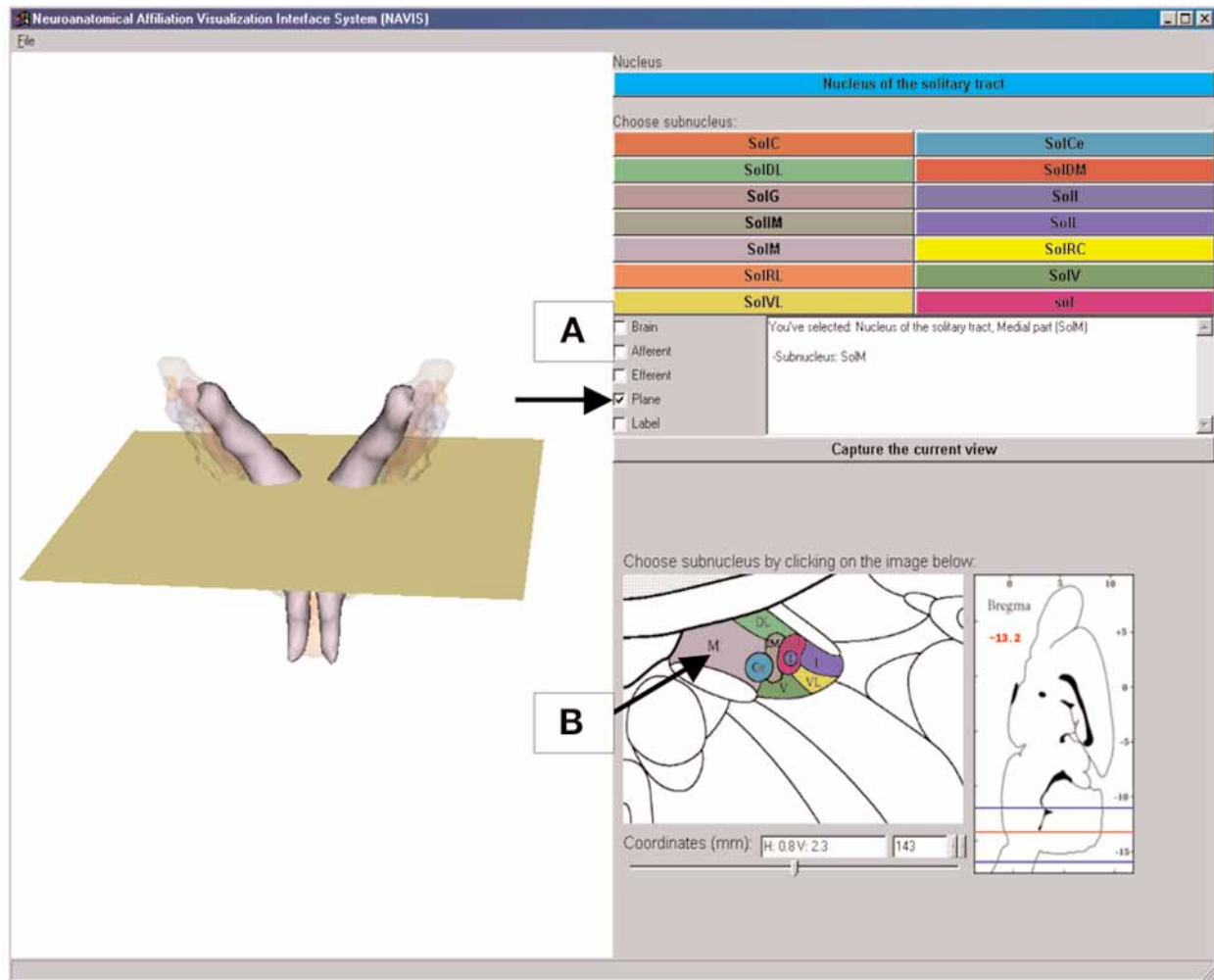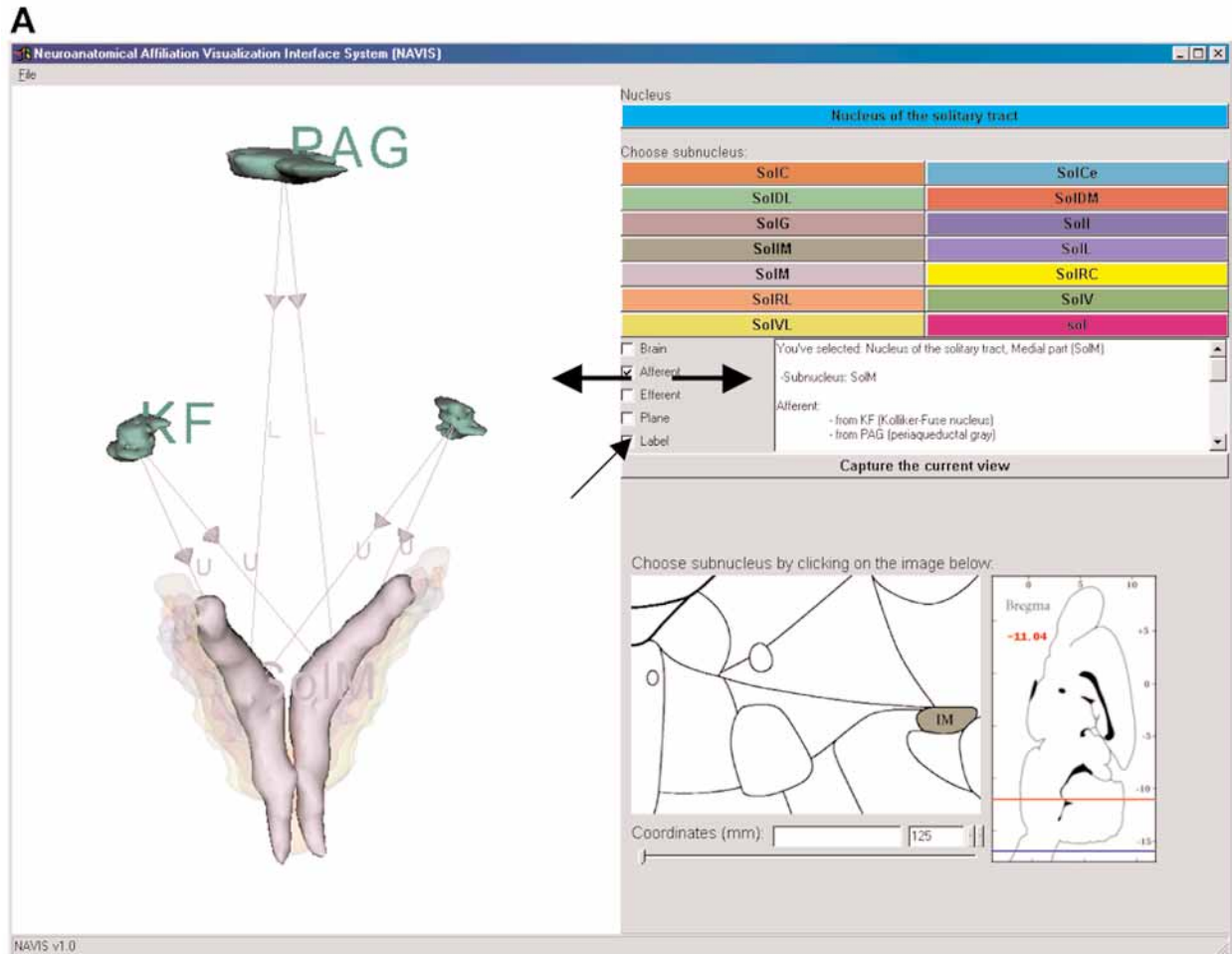
Fig. 12. Coordination of 2D- and 3D-information in NAVIS GUI. **(A)** Clicking on the "Plane" check box (indicated by an arrow) allows users to view a coronal plane in the 3D-viewer with displayed structures. The plane in 3D moves along the atlas levels of the structure of interest when the user navigates through a coronal set in the 2D-viewer panel. **(B)** Users can choose a nucleus/subnucleus of interest by clicking on a coronal section. In clicking the medial part of Sol (SolM; indicated by an arrow), the 3D-viewer selectively displays the 3D-model of SolM.

time, users can also retrieve 3D-stereotaxic coordinates of the clicked point from the 2D-viewer panel.

To observe in 3D where structures exist within the brain, users can click on the "Brain" check box at the controller panel to view the 3D brain outline with the structures on display. In addition, users can add the 3D stereotaxic frame and axes to the 3D-viewer by clicking on the "Stereo-frame" check box. As shown in Fig. 13A,

in checking a "Label" box, nomenclature abbreviations appear adjacent to 3D structures displayed in the 3D-viewer panel. Although each neuroanatomical structure can be identified by its unique color assigned in the lookup table, simultaneous visualization of a 3D-model with its abbreviations allows an immediate identification of structures.

After dissecting the general projection pattern of a nucleus of interest by selectively viewing

A

B

You've selected: Nucleus of the solitary tract, Medial part (SolM)

 -Subnucleus: SolM

Afferent:
        - from KF (Kolliker-Fuse nucleus)
        - from PAG (periaqueductal gray)

1. KF to SolM
        Type of connection: Bilateral
        Strength of projection: Unknown
        DataBase: Not documented

2. PAG to SolM
        Type of connection: Ipsilateral
        Strength of projection: light
        DataBase: Not documented

projections of its subnuclei, users can get information about individual projection data from the information text box located in the controller panel under buttons (Fig. 13A). Therefore, in checking the "Afferent" or "Efferent" box, users are presented not only with visual depiction of projection data, but also with detailed information of individual projection data as shown in Fig. 13B. Conversely, projection data presented in the information box can be identified in 3D using a combination of structure abbreviation, direction of projection, type of connection, and strength of projection.

Image Capture of 3D-Visualization Data

NAVIS provides a saving function to store in a 2D-image format any combination of neuroanatomical structure and affiliation data displayed in the 3D-viewer. Users can capture the contents displayed in the 3D-viewer by clicking on the "Capture the current view" button located under the information text box. The output of image capture is saved as a joint photographic experts group format.

Discussion

In the present study we have described the construction, organization, and features of NAVIS, which were designed as a framework to depict functional networks of the central nervous system in a 3D-space. The current version of NAVIS uses a digital rat brain atlas derived from the atlas of Paxinos and Watson (2005). The atlas of the rat brain in RBSC5 (Paxinos and Watson, 2005), presents in a three-dimensional

coordinate system, free-hand drawings of the neuroanatomical structures based on cytoarchitectural, and standardized nomenclature. However, in a book form, the special organization of the brain can only be viewed as a series of 2D-diagrams. In visualizing the connectivity networks among nuclei/subnuclei, a 3D-digital atlas is required because of the difficulty in following a projection in 2D. It would be even more difficult to visualize in a series of 2D-diagrams the spatial representation of many affiliation data at the same time.

The modular organization of NAVIS allows an integration of any kind of a 2D-histological atlas of any species including human. In the first current version of NAVIS, a digital atlas is embedded internally, and the "Atlas properties" XML description file is used to associate structural properties of each neuroanatomical entity identified in the atlas, with a set of VTK files for the 3D-representation. Future development of NAVIS will focus on simplifying and automating annotation and 3D-modeling of structures identified in different atlases.

Our digital model of the brain is oriented to depict *in situ* affiliations between structures. In the graphic user interface of NAVIS, the 3D-viewer is connected to the 2D-viewer where diagrams are displayed. This relation between 3D-models and 2D-sections is fundamental to maintain references to the 2D-atlas routinely used by researchers.

NAVIS receives an input file (XML format), which contains a concise and structured description of affiliations. This formatted file

Fig. 13. *(Opposite page)* Coordination of affiliation information of the medial part of Sol (SolM). **(A)** In clicking on the "Label" check box (indicated by a smaller arrow), an abbreviation of SolM and that of its affiliated structures are displayed in the 3D-viewer. On clicking on the "Afferent" check box , 3D-visualization of SolM afferent projection data and detailed information about the data are presented simultaneously in the 3D-viewer and the information text box, respectively (indicated by a pair of larger arrows). **(B)** The details of afferent projection data of SolM displayed in the information box.

can be written manually or automatically generated by database research engines. Therefore, different researchers can exchange this XML affiliation file as a medium of communication to update and retrieve neuroanatomical projection data. For example, in BAMS, there is the "Connections" module, which contains detailed reports on neuroanatomical projections that are defined as relations between pairs of the brain structures (Bota et al., 2005). Hence managers of knowledge management system will only have to connect an appropriate module of their system with the "Affiliations" XML description file to have an access to NAVIS.

Connectivity networks are central to information processing in the brain. To depict the structural network NAVIS uses line segments between structures. Morphology of anatomical pathways is usually unknown. However from a functional point of view, morphology of pathways is less relevant than actual connections between anatomical structures. Therefore, straight-line segments in 3D allow depiction of complex affiliations involving a multitude of structures.

As NAVIS offers a user-friendly 3D-interface, it can be used by teachers or investigators to illustrate functional network or to depict their results or hypothesis to general audiences. NAVIS offers a functionality extension to currently available on-line knowledge management systems. On-line systems can communicate with NAVIS simply by generating an XML description file with the appropriate format to be read by NAVIS. By attaching NAVIS as an add-on function, users can take advantage of viewing their queries about neuroanatomical structures and affiliations in 3D. We invite members involved in developing on-line neuroanatomical knowledge management systems to test NAVIS (http://www-evasion.imag.fr/Membres/Olivier.Palombi/) and to

participate in our effort to create a specific module inside NAVIS to efficiently and automatically interact with on-line systems.

NAVIS Software

Description and download page for NAVIS 1.0 is available at the URL: http://www-evasion.imag.fr/Membres/Olivier.Palombi/.

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