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Study of the brain connectivity in an Immersive Space

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ABSTRACT

Virtual reality is a powerful tool for scientific visualization. When the amount and complexity of the visualized data grows, standard visualization applications on desktop computers become inefficient. In this paper we present the use of a CAVE like VR facility in a neuroscientific context. The aim is to have a better understanding of the brain connectivity. Both anatomical and functional data are attached to a mesh representing the brain surface. Specific tools developed for this study and the way we used them are presented below, emphasizing drawbacks and advantages of virtual reality in a scientific visualization context.

Index Terms: I.3.7 [Computer Graphics]: Three-Dimensional Graphics and Realism—Virtual reality; J.3 [Computer Applications]: Life and medical sciences— [H.5.2]: Information Systems—Information interfaces and presentation

1 INTRODUCTION

Surface mesh is an ergonomic tool to visualize scientific data [9]. It allows the modeling of complex 3D surfaces carrying values coming from scientific analyses. Immersive environments offer users the experience of being submerged in a virtual space transcending the boundary between the real and the virtual world. The integration of meshes carrying scientific data in an immersive space allows the user to analyze the scientific results in an innovative way. The user has a multitude of options: he can go in the object, see it from the bottom, or from the top. This allows him to easily compare and contrast confront values of the data in order to have a better understanding of them.

In this paper, we state the experience of the visualization of brain meshes in an immersive space for the specific study of brain connectivity.

Brain connectivity is both anatomical and functional. The brain is composed of several layers. The white matter (WM) is in the center of the brain and is composed of fibers. It is surrounded by the gray matter, also called the cortex, which contains the neurons. Different areas of the cortex are anatomically connected by the fibers of the white matter, this is what we call the anatomical connectivity. Additionally, regions of the cortex are sequentially and/or simultaneously activated during a cognitive process, allowing the subject to carry out functions such as talking, learning, moving, seeing ... These cortical areas are functionally connected.

It is generally assumed that cortical areas which are functionally connected are also anatomically connected, but we do not always known how this occurs. What is the pathway of connection? How does the brain manage a damaged anatomical connection? One of the most important challenges in neuroscience is to understand the relationship, not always obvious, between functional and anatomical connectivity.

To have a better understanding of the relationship between structure and function in the brain in a non invasive way, neuroscientists extract information from both anatomical and functional modalities of medical imaging. So there is a need to synthesize information coming from several modalities. This is why, adding data to brain meshes is a relevant way to work with only one object which carries information extracted from different imaging modalities.

We consider that each vertex of the mesh of the cortex represents a set of similar neurons. This vertex is called a source. Multiple values, resulting from the analysis of different modalities, can be attached to each source.

Let us remark that we need to manage massive amount of data which also have to be visualized in 3 dimension. This can be a significants problem It often becomes a real problem for neuroscientists: average computers are not able to handle the whole scene at once and even with a subset of the scene, navigation and interaction are rather complicated on a desktop computer due to the inherent complexity of the dataset.

Visualization of brain meshes in an immersive space is very useful tool in the study of brain connectivity. The brain is a complex volume, within which there are a huge number of fibers. In order to respect the topology of the cortex, the number of sources (thus of vertices) of the cortical mesh needs to be at least to 10 000. We need an ergonomic space of representation of the fibers and the cortical mesh in order to perform our study on brain connectivity.

This paper presents a brain connectivity study in the Gouraud-Phong immersive space. We visualize both fibers of the white matter and other data attached to the cortical mesh. We develop tools which allow us to color the surface meshes reflecting data values with a greater precision. A graphical user interface (GUI) integrated in the 3D scene rendered in the cave helps analyzing data with ergonomics. The specification of visualization functions following the different nature of data allows us to have a better understanding of results and a more general view of the structure-function relationship in the brain.

2 NEUROSCIENTIFIC CONTEXT

Understanding the relationship between structure and function is a necessary major challenge in neuroscience. Cerebral organization is determined by segregated and integrated regions both functionally and anatomically. These cerebral networks are the foundation for the execution of cognitive processes. Information about both the structure of the white matter and the functionality of networks is needed to understand the connectivity in the brain [3], [1].

The non invasive study of cerebral networks is based on the analysis of both functional and anatomical imaging modalities. In this study of a human brain, we use the diffusion magnetic resonance imaging, dMRI, and the T1 weighted magnetic resonance imaging, T1 weighted MRI, to obtain anatomical information concerning the subject. Additionally, we use magneto-electroencephalography, MEG, to obtain functional information. These modalities will be described in this section as well as the various data which result from their analysis.

2.1 Brain surface meshes extraction

Magnetic resonance imaging (MRI) is a medical imaging technique used in radiology to visualize internal structures of the body in detail. MRI makes use of the property of nuclear magnetic resonance (NMR) to image nuclei of atoms inside the body.

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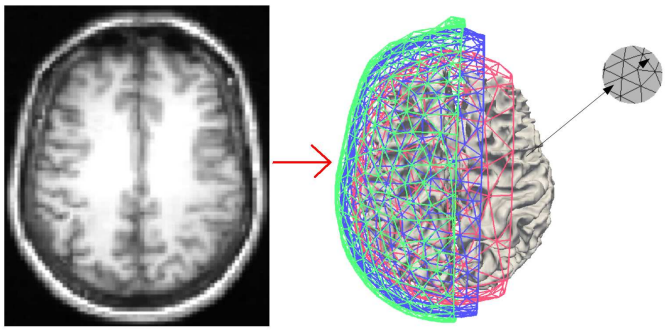


Figure 1: Extraction of brain surfaces from an anatomical MRI (image with the black bottom). Surface meshes: inner skull (pink), outer skull (violet), skin surface (green), cortical mesh (gray). Focus on a part of the cortical mesh where a source is represented by an arrow on a vertex of the mesh.

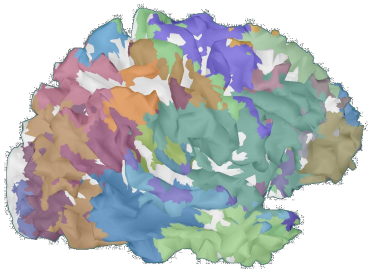


Figure 2: We associated to each source of the cortical mesh a number corresponding to areas of the Brodmann'atlas registered on the anatomical MRI.

The T1 weighted MRI is an anatomical MRI which allows the differentiation of the different surfaces of the brain: the white matter appears lighter than the cortex, the cerebrospinal fluid, located between the cortex and the skull, appears like the darkest shell of the brain. Thus, from a T1 weighted MRI, we extract the different surface meshes corresponding to the cortex, the inner skull, the outer skull and the skin (these four nested shells are illustrated in Fig 1). The surface extraction is performed with the software Freesurfer[1]. All surface meshes are converted with the software Slicer3D[2] into a *Visualization Toolkit* VTK[3] format.

The choice of this format is relevant for different reasons. First, fibers of the WM are reconstructed in the .fib format which is a VTK format. Thus, using the VTK format is the easiest way have both surface meshes and WM fibers. Secondly, it is used by the main medical imaging visualization softwares. Finally, the VTK library [4] allows to deal with a lot of functions: for example decimation of meshes, intersection between two meshes, or the association of data to a mesh either on vertices or triangles. Thus, we develop a VTK function which allows us to add data to each vertex of a surface mesh. This VTK function allows to store several data on the same mesh. We illustrate the integration of this function in our work in box A of the Fig 3.

In our study, we consider that each vertex of the cortical mesh is the location of a source representing a group of similar neurons. This choice allows us to associate to each cortical source data values coming from several analysis. This process is described in box A of the Fig 3.

Brodmann's atlas-based data [2] is also added to the cortical mesh. Each source of the cortical mesh is thus associated to its corresponding Brodmann areas, see Fig 2.

2.2 Diffusion data

The diffusion magnetic resonance imaging (dMRI) is the only non invasive modality allowing access to the WM fibers, and consequently to the anatomical connectivity of the brain [6]. The analysis of diffusion imaging of brain connectivity is performed using tractography algorithms. In this study, we used two tractography methods and obtain two different types of results.

Firstly, deterministic tractography methods allow us to reconstruct fibers of the WM in order to obtain all WM fibers of a specific

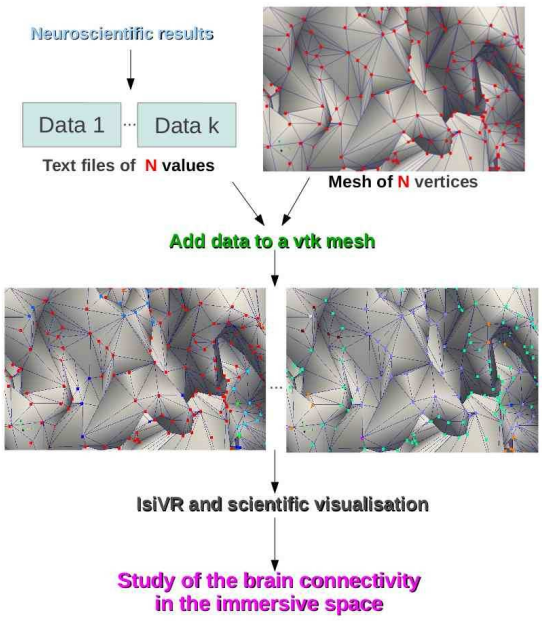


Figure 3: Illustration of the proceeding to integrate neuroscientific results in a immersive space

[1] http://surfer.nmr.mgh.harvard.edu/
[2] http://www.slicer.org/
[3] http://www.vtk.org/
[4] http://www.vtk.org/doc/

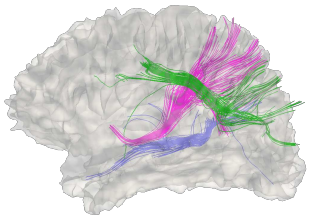


Figure 4: WM fibers are clustered into bundles, here is the example of three bundles.

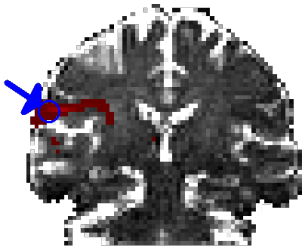


Figure 5: Image of connectivity of the source (in blue): probabilistic tractography allows to have access to the degree of connectivity of a seed, here we chose a cortical source, to all voxels of the WM.

subject. Then, we used an automatic clustering alogorithm of WM fibers into bundles [8] to group similar fibers, as illustrated with the visualization of three WM fiber bundles on Fig 4.

Secondly, probabilistic tractography methods allow a quantification of connectivity degree from of a seed to all voxels of the WM. The result of probabilistic tractography is an image of connectivity, see Fig 5. Thus, we obtain an image of connectivity for each cortical source, taking each one of the vertices of the cortical mesh as a seed for the probabilistic tractography. Then, we cluster all of the cortical sources via reduction of dimensionality applied on their images of connectivity, [4] [5]. Thus we obtain cortex parcellation-based data. We add this data to the cortical mesh following the proceeding illustrated by the box A of the Fig 3. An example of cortex parcellation via probabilistic tractography-based analysis is available on Fig 10.

2.3 Sources reconstruction data

Several modalities of functional medical imaging exists, one of whose is the magneto-electroencephalography (MEG). It is a non invasive modality allowing us to access the magnetic field produced by neurons of the cortex when they are activated. The magnetic field is measured by sensors positioned outside of the brain. The MEG inverse problem allows to reconstruct the signal at source level but it is an ill-posed problem because the number of cortical sources is much larger that the number of sensors.

We include in this study results of a new method for the MEG inverse problem which is actually in publication. This method is based on the use of cortex parcellation via diffusion data as a prior knowledge for the MEG inverse problem. It is an example of analysis merging an anatomical and a functional imaging modality.

Thus, we simulated active sources to obtain synthetic MEG measures. We reconstruct cortical sources from the noised synthetic MEG measurements with our innovative method for MEG inverse problem as well as with classical methods for MEG inverse problems. Thus, for each method used, we associated to each source located on the cortical mesh a value of magnetic field. We add these different data coming from the different methods for MEG inverse problem on the same cortical mesh following the proceeding illustrated by the box A of the Fig 3. So, visualization of the different data allows to compare our new method with classical methods. An example of results of this comparative study is available on Fig 6.

Several medical imaging visualization softwares are available to visualize meshes of WM fibers and brain surface meshes. But any of them allow to visualize several data attached to a same mesh. *Paraview*, the graphical interface of VTK, allows to read data on a mesh but is not suitable for specific needs of medical images analysis.

3 Hardware and Software considerations

The experimentation described in this paper took place in the *Gouraud Phong*[5] immersive space in Sophia Antipolis (Fig. 7). It benefited from both its hardware infrastructure and its software platform.

3.1 Hardware setup

The *Gouraud Phong* immersive space contains three workspaces: a space composed of consumer equipment (3D TV), an image wall (CadWall) and an immersive cube (iSpace) allowing immersion of very high quality.

- TV3D: Composed of a FullHD 3D TV (50”, 1920x1200 pixels) and systems monitoring user position (Microsoft Kinect, Asus Xtion, Nintendo Wii, ...), this space allows to assess this type of equipment for professional use and also facilitate the transfer of our virtual reality applications to a wider audience.

- CADWall:The image wall is a 4.1x1.4m screen displaying 3528 x 1200 pixels. Images are generated by two blended video projectors. Due to its size, this device is particularly suitable for group work. Due to its geometry, it is very easy to use. In fact, any standard application can directly run on CADWall. With some modifications in their code (supporting stereoscopic rendering and taking into account the tracking informations), users will benefit from a first approach of immersive virtual reality.

- ISpace: This workspace is a 4 sided CAVE-like equipment (3 vertical screens and the floor). Each screen is 3.2x2.4m and has an associated projector displaying a stereoscopic 3D image of 1600x1200 pixels. Thanks to the tracking, screens disappear: the user is immersed in a digital world. The sense of presence is maximum. Two sources can be used to generate images and sound in the cube:

  - A computer with a sound card and enough graphics card is sufficient to generate alone the virtual environment,
  - When the need for computing power is required, a mini cluster made of a master managing interaction and synchronization, 4 slaves, each dedicated to a graphical display and a PC dedicated to sound generation is available. This mini cluster is interconnected with an InfiniBand network offering high throughput and low latency.

All of these workspaces benefit from spatialized sound rendering and target tracking.

3.2 isiVR, scalable and immersive Virtual Reality

isiVR is a software platform developed at Inria Sophia Antipolis - Meditérannée. It supports several kind of virtual reality display (from a simple laptop to a clustered CAVE-like environment via high resolution power walls). The aim of isiVR is to ease the

[5]http://www.inria.fr/centre/sophia/mediacenter/plateforme-gouraud-phong

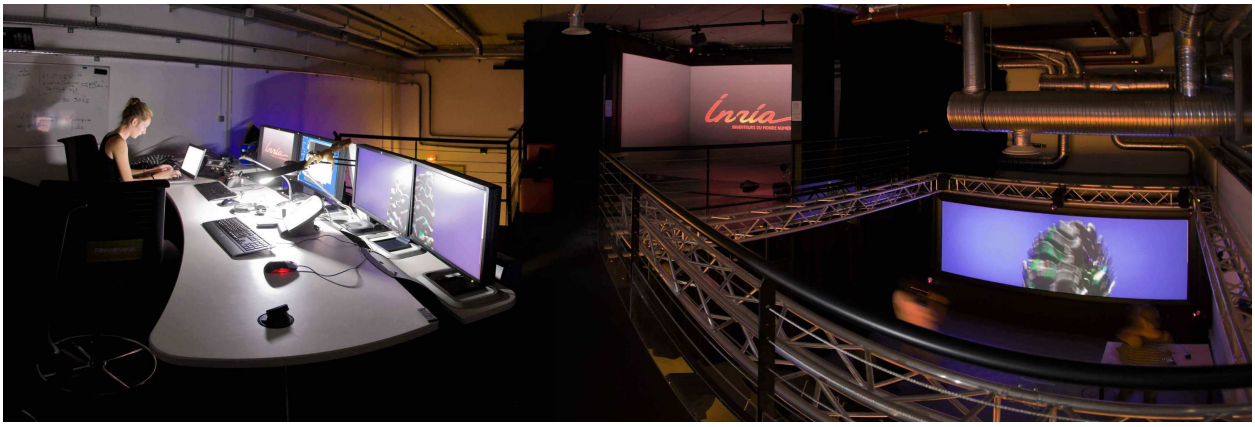


Figure 7: The *Gouraud Phong* immersive space

development of virtual reality application by handling low level tasks such as head tracking and clustering issues (distribution, synchronization, etc.). *isiVR* is mainly based on *OpenSceneGraph*[6][7] (OSG) for the scene graph management and the rendering, on *Open MPI*[7] for the distribution and *Qt*[8] for the 2D user interface.

isiVR provides abstractions for the main concepts in a virtual reality context (mainly Application, Viewer, Device, Behavior, Gui and Events) and lower level tools to handle settings (either global or host dependent), time, etc. It is highly customizable through three mechanisms:

- Plugins. They are useful either to load specific data format (OpenSceneGraph's plugins[9]) or to implement specific versions of isiVR's concepts. Devices and Behavior are typical plugins.

- Callbacks and Events. OpenSceneGraph's callbacks allow to trigger specific code during the scene graph's traversals. isiVR extend this mechanism to trigger callback during the main application phases (namely, during initialization, before each simulation step, after the communication is performed and before the rendering occurs, after the rendering, and when the application exits) and when specific events occurs (ie upon user interaction through the devices). Users are allowed to define their own kind of events and associated handlers. isiVR will ensure the event distribution while running in cluster mode and trigger handlers on the viewers.

- Inheritance. isiVR is a C++ SDK relying on well known design patterns. Although it is rarely needed, developers with a fair understanding of isiVR internal mechanisms might replace any isiVR class with their own implementation.

isiVR is under the process of being released as an open source project and should soon be available from the Inria Forge site[10].

3.3 isiVR and scientific visualization

3.3.1 From VTK to OSG

As stated earlier in this paper and as in many scientific communities dealing with data visualization, VTK is the natural data format in the neuroscience community. To ease the acceptation of virtual reality in these communities, we have to respect their habits. Unfortunately, VTK and its pipeline strategy for rendering is not suitable for virtual reality applications where the rendering must occur at regular time interval to allow the user immersion.

We wrote an OpenSceneGraph data loader plugin to to automatically convert VTK data to an OSG scene graph. This work is based on previous work by Michael Gronager[11]. VTK's PolyData are mapped to osg::Geometry, associated data are stored as Uniforms.

3.3.2 Representing information through color mapping

The scientific visualization implies several constraints:

- input data must not be modified by our rendering (value or position)

- every shown color must match a corresponding data value (no color interpolation)

- color ramps chosen to represent a physical entity must be consistent between datasets to allow the comparison between them

In this study we have two very different kind of data to map on the geometry. Although both are scalar values, one depict a scalar field on the surface (the MEG inverse problem solution) and the other describes labels associated to the mesh vertices. In the first case, values should be interpolated between the neighboring vertices just as with a classical Gouraud shading. In the second case, the information is a local label, not a continuous field discretization. Thus, values must not be interpolated across triangles.

Our general process to render scalar informations mapped as color on a mesh is the following. We first read values stored as uniforms on the geometry and process them, according to their type, to produce per vertex values stored as vertex arrays. We then use shaders to affect colors to values.

3.3.3 Rendering simulated MEG fields

One of the goals of this study is to compare various numerical methods to solve the MEG inverse problem. Is is mandatory that produced images are coherent between datasets. The computed values are either negative, null or positive. The first step is to globally normalize the datasets. Uniforms corresponding to these fields are read and global maximal absolute value of the field is computed. Each dataset is then scaled to a [-1,+1] range according to this maximum

[6] http://www.openscenegraph.org/
[7] http://www.open-mpi.org/
[8] http://qt.nokia.com/
[9] http://www.openscenegraph.org/projects/osg/wiki/Support/UserGuides/Plugins
[10] http://gforge.inria.fr
[11] http://www.openscenegraph.org/projects/osg/wiki/Community/NodeKits

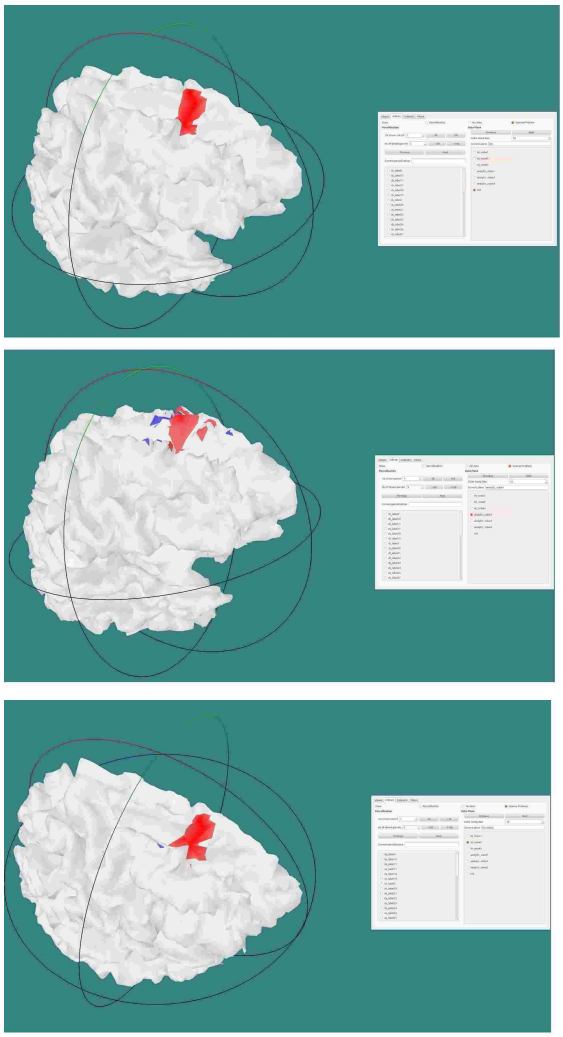


Figure 6: Illustration of our study to compare methods for MEG inverse problem. The first image corresponds to the synthetic sources, the second one to the sources reconstruction with a classical method MEG inverse problem, the third image corresponds to the sources reconstruction with the method for MEG inverse problem informed by prior knowledge via cortical parcellation.

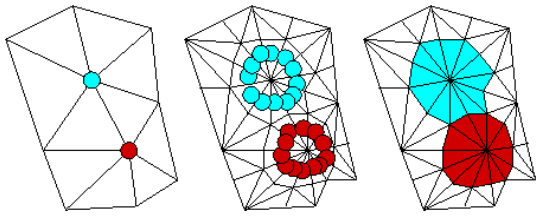


Figure 8: Mesh subdivision: original data per vertex, (middle) triangle subdivision with data per triangle, (right) final rendering

and given to the shader as a vertex attribute array. The maximum value is obviously stored to be able to compute the actual field value from a vertex attribute value.

To allow the neuroscientist to have a fine control over the rendering we wrote a specific algorithm (implemented as a fragment shader) to select the exact color mapped on each field value instead of using a standard 1D texture mapping using field value as a texture coordinate. Parameters provided to control the rendering are:

- `MinCol` A color corresponding to the minimal field value
- `MaxCol` A color corresponding to the maximal field value
- `NulCol` A color corresponding to the null value
- `Epsilon` A constant defining a tolerance around the null value to handle numerical errors issued from the inverse problem resolution
- `Steps` A number of generated color strips allowing to go through a continuous color interpolation to isovalue rendering

Given `x` an input field value for a given fragment, the fragment color `gl_FragColor` is as follow (`shadeColor` is the color component reflecting the lighting and the original object color).

```
vec3 color = (x > Epsilon) ? MaxCol
           : (x <-Epsilon) ? MinCol
           : NulCol;
float alpha = 0.5
    + 0.5*abs(floor(x*Steps)/Steps);

gl_FragColor = vec4(
    mix(shadeColor, color, alpha),
    1.0);
```

3.3.4 Rendering cortex parcellation

In this case, the input data are labels attached to vertices. Labels are arbitrary numbers. During the first step we compute a map to establish a match between these labels and the first n integers. These continuous integer labels are stored on vertices as attribute.

The difficulty in this case is to prevent the rendering from interpolating colors and thus producing unknown labels. Flat shading is not an option. Flat shading keeps a constant value over a triangle, and in our case, values are attached to vertices which represents neurons end points. Our coloring algorithm should render a given color to a zone around a specific vertex. The straight forward way of achieving this effect is to refine the mesh to create triangle homogeneous according to the label and use flat shading. We implemented this thanks to a geometry shader. Each triangle is replaced by 6 new triangles linking the center of the triangle, the middle of each edge and the corresponding vertex. Each newly generated triangle has only one vertex from the original mesh and thus can be easily labeled (Fig. 8. The fact that we do this treatment as a geometry

shader and not on the CPU minimize the impact on the frame rate but requires an OpenGL 3 compatible GPU.
Colors are affected to each label thanks to a 1D texture. The texture was generated using the CMC(I:c) color differencing algorithm to ensure that neighboring pixels are visually-distinguishable[12].

3.4 User interaction

We firstly use classical VR interaction paradigms to allow the neuroscientist to navigate its various datasets (ie using a Wand to point and click on the cortex surface, wand's buttons to cycle through the various datasets) but it was inefficient. Too much parameters have to be handled.
On the desktop version of this application, we built a *Qt* graphical use interface (GUI) to solve this problem. Several tab widgets are used respectively to choose which datasets are shown and to set the corresponding rendering parameters. This prove to be efficient, everyone knows how to interact with a classical 2D GUI.

Our objective is to have an easy interaction with the application while in immersion. The ideal solution should merge a classical 2D GUI with 3D co-located interaction with the data. The 2D GUI should not break the sensation of immersion and thus be integrated in the 3D scene.

We achieved this by rendering the 2D GUI as a texture mapped on a 3D quad in the scene. Interaction is performed with the wand. The intersection between the wand and the quad is computed at each frame. If an intersection occurs, the 3D coordinates of the intersection point is converted into texture space and a 2D event is generated (either a hover event or a mouse button even depending on the status of the wand buttons). We have to pay attention to multi threading issues: the event is generated in the rendering thread while the 2D GUI leaves in its own thread. Thus, the generated 2D event is not fed directly to the 2D GUI but piled on a event stack shared between threads. The GUI thread is responsible for popping and handling the events.

This mechanism is very powerful and easy to use. The user have an access to a rich 2D interface in the virtual world, while in immersion. The GUI is a standard one and can easily be produced with standard tools such as *Qt*'s *designer*. There is no restriction on the used widget. The only limitation is that the wand only simulate a mouse, not a keyboard.

4 Immersive study of the brain connectivity

In this work, we use the Gouraud-Phong immersive space (mainly the ISpace) to study the connectivity in the brain combining and merging information coming from structural and functional medical imaging. We visualize both WM fibers and all the data attached to the cortical mesh and described in previous section. Let us remind the 2 natures of data associated to the same mesh of the cortex: the cortex parcellation-based data (from Brodmann's atlas or diffusion analysis) and sources reconstruction-based data (from the different methods for the MEG inverse problem).

We develop a GUI usable inside the cave to facilitate the analysis and the comparison of data. For the representation of different data on the mesh, we particularly pay attention of the automatic coloration of surfaces considering in a specifically way each nature of data. The GUI allows to navigate between the different data associated to the cortical mesh. A picture of the GUI is available on Fig 11. A tab is dedicated to the parcellation data, an other tab is dedicated to the functional data, that is to say sources reconstruction resulting from the different methods of MEG inverse problem, and a last tab is dedicated to manage with the WM fibers bundles and the whole brain deterministic tractography, see 9.

This separation of data into tabs following the nature of data allows to compare the different data having the same nature like the comparison between the methods for MEG inverse problem or the visualization of 1 or more WM fibers bundles. In the case of the comparison between different parcellations or the visualization of a specific parcellation, we develop in the GUI a specific way to manage with the huge number of parcels (from few ten to several hundred). Within each parcellation-based data of the whole cortical mesh, the interface gives the possibility to see each parcel one by one, two by two, ten by ten or more, see Fig 10. This tool is very practical to understand, validate and use the results of parcellation.

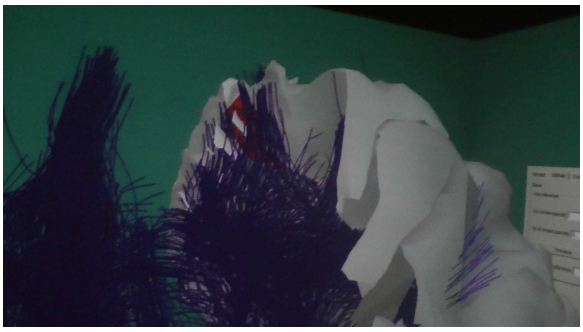


Figure 9: Whole brain deterministic tractography in the left hemisphere of the cortical mesh.

Besides, this separation in tabs allows to merge data having different nature.. For example the immersive space allow to understand the relationship between the parcellation via probabilistic tractography and the WM fibers bundles coming from deterministic tractography, that is to say we can compare probabilistic and deterministic tractographies. An other example of the ability that an Immersive Space offer for the merging of data of different modalities is the option to analyze the fibers pathways passing through activated sources and so predict the next activated sources following these fibers. This type of work is one of the most important challenge in neurosciences and become easier in an Immersive Space. This type of visualization allows to researchers to develop others simulations of networks, to see with a better precision the pathways taken by the signal to activate different regions of the brain because they can have a better and a more general view of the reality.

An important advantage of the study in an Immersive Space, comparatively to a study on a classical screen, is the simplification of the visualization of data. In an immersive space, the space of visualization is enough large to distinguish all fibers of the WM, their intersections with the cortical mesh.Additionally, we can easily differentiate each parcel of a parcellation of the cortex to perform a quicker and a more precise work. Because we are able to have a precision of visualization allowing to have access to the value of each source while seeing all the cortical mesh, we can evaluate results with a more accurate way than with a 2D screen. With a classical workspace, we have to zoom in a part of the mesh to examine its values and we can not visualize at the same time others regions of the cortical mesh. Though in the study of connectivity in the brain we do need to examine different regions of the cortex at the same time, without to focus on one and after on an other. Besides, because we are studying the connectivity of several regions, we need to have an easy access to all their data: parcellation of these regions, WM fibers which connect them, their values of magnetic field when they are activated. An immersive space is suitable to perform this type of study whereas a classical screen is very limited.

5 Conclusion and future works

Working sessions in the immersive space allow to validate with a precise way the results. Then, we easily can compare data between

[12] http://phrogz.net/css/distinct-colors.html

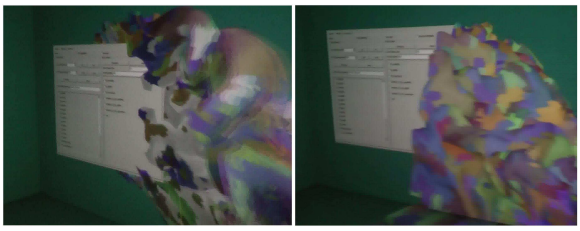


Figure 10: We can see as much as parcels we want and switch them by group, the number of parcel permuting together being fixed by the user.

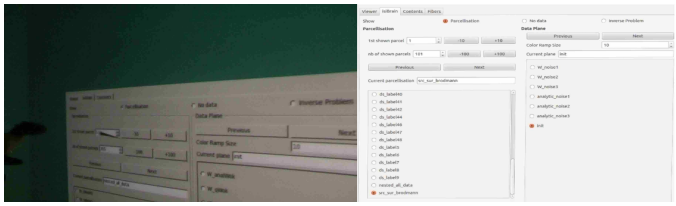


Figure 11: The GUI in the Gouraud-Phong immersive space allowing to manage differently data having different natures: WM fibers bundles, cortex parcellation data or sources reconstruction data.

the different tractography methods as well as between methods for MEG inverse problem. Visualization of WM fibers allow to have a better understanding of the dynamic activation of sources which is generally hard to study.

We develop tools for the visualization of the study of brain connectivity in the immersive space with the idea that needs could evolve. Other tabs of the interface could be associated to data resulting from future works: integration of data on the cortical mesh coming from an other modality of medical imaging or coming from the intersection between fibers and the cortical mesh. Several future software enhancement are planed. The first one will be to add a tab int he embedded GUI to allow the neuroscientist to access to the original values of the visualized data. The second one will consist to develop the possibility to select an area of a mesh to see its attached data, thus we will be able to understand the specification of two connected regions with ergonomics and have a better knowledge of the structure-function relationship in the brain.

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