INTERACTIVE VISUALIZATION OF COMPLEX NETWORKS DYNAMICS: A NEUROSCIENCE TEST CASE

Layout of a Simulated Environment Based on Connectome Dataset

David Cabrera Dalmazzo

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Supervisor: Alberto Betella (SPECS) Director: Prof. Dr. Paul Verschure



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Abstract

Simulated interactive layouts can play a key role in the understanding of hidden patterns in large datasets, especially the information related to connection weights. In this study, we investigated the role of physical simulations applied to an immersive 3D visualization of a complex network. As a test case, we used a 3D interactive visualization of the dataset of the human brain connections called connectome, in the immersive space "eXperience Induction Machine (XIM)". We conducted an empirical validation where 10 subjects were asked to visualize different simulation principles to compare the information from the anatomical structure against the structure formed after 10 seconds of simulation, and subsequently we tested their understanding of the dataset. As a comparative validation of the new version, we systematically measured participants' understanding and visual memory of the connectomic structure, pointing to the areas of more connectivity as well to the clusters as a consequence of the simulation showing groups of nodes made of different brain areas. The hypothesis presents the idea that real-time particle systems simulations, highlight information that is not only related to strength connections but also to areas of higher connectivity in the brain. It is appropriated to simulate attraction-repulsion forces using the values stored in the dataset, to reorganise the structure over the network, and finally create clusters that can identify where the most important hubs are located and which nodes are more directly related to them. This comparison between anatomic vs cluster formations can bring new insights about how the structure of the brain is organised. Another advantage of such an immersive visualization is that human cognitions is enhanced when interactive manipulation are available; deconstruct and reconstruct the information also affect the experience by enhancing the analysis and comprehension[9].

Keywords: XIM; Data Visualization; Connectome; Neuroscience Application, Real-Time simulation, Particle Systems, Time.

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1. Introduction

1.1 Data Deluge.

With the apparition of the computer in our society, the era of Data Deluge or "Big Data" (BD) has started. The quantity of information in the world is arising; mankind created 150 exabytes (billion gigabytes) of data in 2005, and in 2014 it will be created and stored more than 1.200 exabytes of data. The development of computational mechanism to store this amount of information in bits is a complex task. However, to analyse this information, to discover patterns and extract useful meanings is a contemporary challenge. This tendency empowered by enhanced computer memory management and big data centres. increases in the field of economics, but is also present in a vast range of disciplines. Hence, data deluge already started to transform business, governments, science and everyday life. For instance, in 2013 the total amount of traffic generated through the internet reached almost 2.5 exabytes of data, and that number is doubling every 40 months. In other words, every second stored nowadays in terms of memory sizes are bigger that the entire information used on internet 20 years ago [16]. Databases are treated not only as a source of information but as a valuable entity. "Data is the new Oil" is an analogy that resonates pointing into the direction that data powers the information's economy as oil does in industrial economy. Scientists behind BD discipline claim to bring future solutions and deeper understanding in many research fields.[15] [35].

In the field of bioinformatics, it is estimated that human genome DNA contains around 200 Gigabytes. In addition, after X-ray structure measurements of DNA proteins, the data volume required expands dramatically to several Petabytes, as an example. In the Sanger Institute, the Data Centre hosts more than 20 terabytes of key genomic information [44].

In the field of astronomy, scientific experiments to create 'virtual observatories' contain astronomical data at many different wavelengths. This projects are being conducted in USA [50], in Europe [51] and the UK [52]. It is estimated that The Astrophysical Virtual Observatory (AVO) project in USA has stored around 500 Terabytes per year since 2004.

In the neuroscience field, relevant projects are conducted in USA and Europe to make advances on mapping the human brain complexity, it is said that the amount of neurons in the human brain is equivalent to stars in the Milky Way Galaxy, cerebral cortex alone contains at least 88⁹ neurons linked by 10¹⁵ synaptic connections. Each neuron may be connected to up to 10.000 other neurons.

In the Particle Physics field, Large Hadron Collider (LHC) at CERN in Geneva began to

generate collision data in late 2006 [54]. These experiments are then storing, accessing and processing around 10 Petabytes per year which require a very powerful computers to process around of 200 Teraflop/s of information. By 2015, particle physicists will be using Exabytes of storage and Petaflop/s of computation. This studies present one of the biggest challenge for scientist to analyse and extract information from the datasets. The discovery of Higg's Boson is one of the relevant consequences but they claim that it will start a new era of quantum discoveries [55].

1.2 Data Visualization and The Human Connectome Project.

The amount of data generated nowadays overflows human capacity to analyse it, leading to an urgent need for a new generation of computational theories and tools to assist humans in extracting useful conclusions [24]. More than a solution these computational tools open new possibilities to animate, simulate and represent the data, which enhance the practice of interpret, analyse and extract useful meanings, in other words, they allow experts to manipulate the information. To develop a computer-supported interactive representation of abstract data, it is recommended to follow a methodology that works mainly in two areas: a) technical approach about how to acquire information and develop graphic representations that run in real-time; b) the aesthetic design and the interaction principles, that enhance the representations and the user experience. As a consequence, these techniques can have a relevant influence on how the information can be reorganised into new associative elements, allowing the discovering of patterns and meanings within complex datasets (Betella et al [8]).

On this framework, The Human Connectome Project has started on 2010. It provides a compilation of neural data and an interface. It has the goal to open new opportunities to conduct research on the human brain, also propose new perspectives on how we experience the information. With it, it is possible to navigate through major brain pathways, compare essential circuits, zoom into a region to explore they connectivity, and formulate hypothesis about how this complex networks functions.

HCP is being carried out in two phases: a) Development of equipment and techniques to scan the human brain using custom MRI hardware to create a local coordinate system for nodes and connections. During this first phase data acquisition and analysis methods were optimised during the first two years of the project. b) Visualization of the information. During the second phase, different methodologies are applied to visualize this information stored on databases (information available in the following link: <u>http://humanconnectome.org</u>)

The term 'connectome' was proposed independently and simultaneously by Dr. Patric Hagmann (Indiana University) and Dr. Olaf Sporns (Laussane University) in 2005. It refers to the human brain map and its neuronal connections [43][30].



Figure 1. Connectome Visualization taken from the url: http:// theconnecto.me

In The Synthetic Perceptive, Emotive and Cognitive Systems group SPECS at the Universitat Pompeu Fabra (UPF) in Barcelona, an interactive visualization of the Connectome dataset has been developed. This software receives the name of BrainX³ and It was incorporated into an immersive environment for virtual reality applications called The eXperience Induction Machine (XIM) to conduct research studies (See section 2.1).

Furthermore, the contributions of this study are the optimisation of the $BrainX^3$ in terms of real-time rendering techniques, on one hand, and the addition of particle physic simulations, on the other.

First, optimisation on rendering allows the computer application to be prepared for new layouts of how the information is presented and also how the interaction design can be

improved. After the optimisation, the addition of physical simulations to add a layer of dynamical reorganisation of the nodes, is possible to program. These simulations use values already stored in the dataset, and they visualize in a new perspective how the forces within connections can be experienced in terms of movement, attraction and repulsion.

1.3 Problem Statement

Electrically speaking, observing how a program uses the computer resources, we can visualize a 3D model of how RAM memory, CPU and GPU are connected when this program is executed. That could constitute a complex visualization, and a challenge if we want to understand which particular software is running at this specific moment, even though, very difficult to know what independent functions it has and how they are interconnected. Taking into account similar situation but observing the brain connections, first we have to clarify that it has a different biological architecture, but it is, in a similar way, a serious challenge.

Visualizing the connectome, several studies are being conducted to understand the complex functionality of the microscopic, mesoscopic and macroscopic network of the brain. Also, it is needed specify the complex functionality of the multi layered bio mechanisms and decipher the interconnected self contained architecture. In neuroscience, this journey has started but it full comprehension is still a mystery [3].

In the connectome there are clear and well-known pathways [3] [4], but most of the biological functionalities are still not known.

To map brain activity, MRI systems use graph theory such as vertex segregation and edge ordering, to detect which nodes in the cortical network are related [20], therefore, another relevant question to the problem is, taking into account that this datasets are built by mapping the activity of the brain using such techniques, what is then, the role played by the Corpus Callosum, and the Cerebellum? Hesslow proposes in the Simulation Hypothesis, that the brain is understood as a machine that predicts behaviour, simulates perception and runs anticipations, pointing into some Brain areas that run those functions, for instance, including Cerebellum as an area that has a key role on anticipating or even inhibit motor actions [32]. A complete visualization of this three main regions of the brain interconnected is crucial to have at least the big picture. However, this modern graph theory provides powerful quantitative tools and measures for the analysis of complex biological networks, used in a broad range of research areas including proteomics, cellular signaling, metabolism, among others. Network analyses of brain connectivity have begun

to bring important insights into brain organization of humans. Graph measures allow the characterisation of network structure by identifying local contributions of individual nodes and connections, as well as the network's general capacity to integrate information, and its tendency to form interconnected communities or modules.[6][48]. Graph theory has already proven to be applicable to a considerable diversity of complex systems, including markets, ecosystems, computer circuits, or gene-gene interactomes [18].

To resolve these problems, as a step forward, this research proposes a work in collaboration with software developers and neuroscientists to develop a dynamic interactive visualization tool, programmed in C# - Unity 3D that is an enhanced version of Brain χ^3 [9].

1.4 State of the Art

In the paper "*The future of the human connectome*" (2012) [45] authors propose that the recognitions of the brain areas are being discovered and mapped, first starting with the general picture, and then exploring the details, making an analogy to cartography (figure 2).



Figure 2. From the paper [45] Revolutions in cartography of the earth's surface (left) and the human brain (right).

In 2012, a methodology was presented as a novel technique for the mapping and visualization of population-level and individual human connectomics via an intuitive twodimensional circular representation [33]. The methodology combines MRI/DTI data acquisition and automatic image segmentation. Using it, authors generate detailed representations of regional geometry and connectivity for each individual to assess and examine their statistical properties, making visible their similitudes and differences in terms of connections (Figure 3).





In 2013, *VisNEST* application, Large-scale simulations serve this purpose of visualize complex neuronal network dataset by representing neurons and synapses using reduced sets of dynamic equations and connecting them to form structured networks, that can be displayed in different scales (Figure 4). [36]



Figure 4: (Image and text from VisNEST) Left: Comparison of structural and functional connectivity for a simulation with transient input to V1. A strong structural connection exists from area V1 to V2. Centre and Right: The *flux view* reveals a transient increase of the transmission from V1 to V2, in line with the anatomy.

Inside SPECS and framed by CEEDS (The Collective Experience of Empathic Data Systems) [49], there are relevant research studies that have been conducted within the same framework. In 2012 [8], researchers have developed an interactive 3D visualization and navigation system in the mixed-reality immersive space called *The eXperience Induction Machine* (XIM more information in section 2.1) to represent the connectivity of complex neuronal networks. They evaluated an application empirically measuring the users' level of understanding of the neuronal data presented with 3 different navigation mappings.

The system was programmed using IQR which is a multi-level neuronal simulation environment that allows to graphically design complex neuronal models, and to visualize and analyze their properties in real-time. The 3D game engine Unity3D (Figure 5) was used to graph the architectonical structures. The results show that different navigation mappings affect the structural understanding of the system.



Figure 5: Taken from [8] A complex neuronal network in iqr converted into a 3D representation using Unity3D.



Figure 6: Taken from [31] Frontal view screenshot of the connectome within the XIM dynamical simulation environment.

Subsequently, researches took anatomical structures and linked them to the *iqr* neuronal simulator, to point in which areas of the brain this activations are occurring and also to display the node's connections triggered by a simulation of activity [3]. All the system was tested in XIM. The results show that large-scale temporal activity mapped across directionally connected brain structures are directly informative of brain-wide neural circuit mechanisms. Being able to predict these maps by implementing realistic biophysical dynamics, aimed to identifying the neural correlates of cognitive function.

Using the interactive software $BrainX^3$ [9], a custom system determines the user's cognitive workload and arousal; consequently adapt the visualization at the same time to avoid information overload and boost the exploration process.

As part of the interaction design, different sensors were included into the system.

The use of gloves (Figure 7) that measure the user's arousal as well gestures. Eyetracker (figure 8) that allows the system not only to know where the user is addressing the attention, but also to recollect the spatial information related to the projection of the pupil movement to measure the user's attention; it addresses

the emotive feedback in conjunctions with the data received from the sensing glove. It provides audio feedback by a synthetic voice that guides the user on the actions performed. The application allows the user to change the level of complexity, ask a "Sentient Agent" for assistance, reset or remove selected brain-node's areas, activate a pathway of neuronal connection, and navigate trough all the 3D simulation to search for interesting



Fingertip electrodes measuring electrodermal response (EDR)

Figure 7: Taken from [9] Sensing glove with its main components.

patterns. Full body immersive interaction with the representation of the dataset, helps human perception and intuition to explore the meanings of this complex neuronal network. In a further development [10], it was added a layer of information to read user's heart rate, skin conductance and pupil size. This version of the application within XIM, allows the subjects to literally grab the areas of interest and visualize a simulation of the activations path through the neuronal network.

Another approach to BrainX³ was the incorporation of an auditive feedback of information [39] to support the 3D graphical navigation of the connectome dataset. In this case, audio was playing a key role to bring to the surface hidden information about node connectivity in brain areas that have been touched during navigation-interaction. This discipline of present





Figure 8: Taken from [10] Sensing glove with its main components. eye-tracker and its components: (A) inertial measurement unit to obtain head position, (B) camera capturing the pupil position and size, and (C) mirror.

auditorial information is called Auditory Display. The main idea behind the sonification is to represent auditory feedback to the users at the moment they interact with the application. It gives information to the user about where they are virtually placed in the brain areas and how dense those areas are in terms of connection weights.



Figure 9: Image taken from [7]. It explanation: *The Illustration shows the system in the eXperience Induction Machine (XIM)*. In sections from b) to g) Modes of node activation and connectivity pathways.

In the next version of BrainX^3 [7], the application shows the entire system and paint the nodes that are being touched by the user, making evident the region of interest with it subsequently area of connectivity in the neuronal network (Figure 9).

To allow the user to navigate through the entire visualization in the XIM, an infrared camera tracks the user position, which is translated into a virtual position. Taking into account the XIM is 25 m² and the brain area is approximately 14cm Width and 17cm Length, the navigation follows a scale of 166:1, if you move 1.66m in the XIM you navigate 1cm through the brain.

After this overview over BrianX³ project, the proposal of this Master thesis is a continuation into the analysis of the connectome data using interactive experiences.

1.5 Visualization of Complex Network Dynamics

During the process of development of this study, we present new layouts of the connectome visualization by adding different layers of colour representations related to node activity and connectivity. Then a particle systems simulations based on Newtonian laws was incorporated.

As an observation, we can argue that the brain is active mostly all the time, different functions are running constantly, therefor, the information stored in the dataset is taken from a process that happens intrinsically related to time. Part of the data also reflects this particular time momentum, which is a value that represents a range of connection's strengths, in other words, how high is the activity among specific regions. Grounded on this concept, we impulse one of the main ideas of this project, which is to add four real-time simulations using weights values to reorganise nodes's position, velocity,

acceleration, subsequently attraction and repulsion. These simulations form clusters, structures and centres of interest that does not conflict with the original dataset in terms of connectivity and forces, but add a new spacial organization that can be compared to the anatomical structure. To extract meaning from the comparison of anatomical and cluster formation, further analysis has to be conducted.

New layouts of dynamical networks propose parallel perspectives directly mapped from the dataset that show the nature of the connections from a temporal simulated point of view, which is intended to help researchers to comprehend the connectome connection's nature. The cluster formations are a consequence of the simulations and they change depending on how long the simulations are performed; these simulations are the first step towards the visualization of multilayered processes that are present in the brain functions creating parallel spatial regions of higher activity, physically reorganising the nodes its three dimension.

Our main goal is to program an application that allows visualizations of the connectome in different scales, comparing anatomical structures with new simulated clusters.

2. Methods

2.1 The eXperience Induction Machine

The Collective Experience of Empathic Data Systems (CEEDS) project englobes the studies conducted in the *eXperience Induction Machine*. It has the goal of develop novel, integrated technologies, to efficiently support human experience, analysis, exploration and understanding of large complex datasets.

The XIM is an immersive space equipped with a variety of body sensors (sensing-glove, eye tracker, infrared camera for overhead tracking, floor pressure sensors) and effectors (8 Projectors, 16 loudspeakers, 4 Projection screens, 72 RGB coloured neon lights in Floor tiles) constructed to conduct empirical studies on human behavior in ecologically valid situations in full body interactions in a mixed reality environment (Figure 10) [11].



Figure 10: Schematic illustration of the eXperience Induction Machine (XIM). The space covers an area of 25m2 and is equipped with a number of sensors (labeled in red) and effectors (labeled in blue). Taken from [11]

2.2 BrainX³

The computer application uses multimodal input and output and permits full body interaction. The dataset is available on the following link http://www.cmtk.org/viewer/ datasets/[31]. It is composed by 998 regions of interest (ROIs), 28000 bidirectional connections and 66 anatomical subregions in the left and right hemisphere of the human brain, as well as node anatomical 3D space correlation and weights of strength connections among nodes.

In this study, we started from the previous version of the application, as detailed in the SoA, to facilitate the process of composition and simulation. The programming of the new layouts are based on:

- Control of the amount of connections presented, based on a threshold that follows strength connections values (weights). It filters the information painting only the connections with more weights and therefor clear the visualization to focus the attention. The parameter is reversible allowing the system to draw the stronger or weaker connections.
- 2. Control of the amount of names of the nodes displayed controlled by a threshold which is the value of weight's strength.
- Control of the independent colour of brain lobes vs a range of colour from low to hight (blue to red) that shows node activity.
- 4. Based on Shiffman's method [42] addition of attraction, repulsion functions controlling positions, velocity and acceleration of the nodes.
- 5. Different mathematical approaches (Monte Carlo optimisation) [42] to generate clusters, adding perlin noise to the system.
- 6. Implement rendering optimisation based on Craig Reynolds methods.[40]
- 7. New layouts were made using a dataset that simulate deactivation (or lesions) in nodes, furthermore a visualization of the brain connections and the subsequent alteration in the network (manuscript under development).

2.3 Development Process

The development process was divided in 7 main states, the very first step was to learn Unity3D and C#. To do so, a number of book and online tutorials were needed. [13]

The following step consisted in testing previously existing examples (originally developed in processing) under the Unity 3D environment, and compare code architecture and then test their differences in performance.

Unity 3D presents an assets store which includes a large number of assets for a wide range of features or game implementations. For this study, we tested various assets, such as Flocking behaviour simulations.

After playing with different versions we realised that the system based on the Connectome dataset will not allow a Flocking Simulation due to the amount of nodes (998) when the Unity3D simulations only allow around 100 particles simulated in a 3D environment.

For the next step, we used a desktop version of BrainX³, to avoid redundant development specially related to the extraction and parsing of the GraphML dataset.

Ben Fry is one of the co-founders of *Processing* computer language; as well a very known programmer working in the intersection field between art and science. He has developed a well known methodology followed by artists, scientist or software developers; precise enough to focus on the principal steps when an interactive data visualization software is needed. We followed Fry's methodology which is divided in seven steps [29], explained bellow:

- 1. Acquire: The connectome dataset is available online in the following link. http:// www.cmtk.org/viewer/datasets/
- Parse: The format of the connectome dataset is GraphML. It is an XML-based version for graphs. It provides structure for the data's meaning, and orders it into categories. There are mainly two elements, one that carries the node information and the edges that carry the connection's information:
- Each node in the system includes information of its connections in terms of from-node id to-node id.
- Each node has multiple array of connections.
- Each connection has a weight (force of the connection).
- Each Node has a value that is the sum of the total connections' weights which is the "Total weight".
- Each Node has a *mass* made by the sum of simple connections which is called *Degree*.
- Each node has four vectors: simulated position, anatomical position, velocity and acceleration.

- 3. **Filter**: The weight of the connections are filtered by a threshold to control the amount of connections and names are displayed in the application.
- 4. **Mine**: In this process, is needed to apply methods from statistics or data mining as a way to discern patterns or place the data in mathematical context. For instance, each node carries gravitational forces to simulate attractions or repulsions based on the weights and masses they individual have. Gravity is determined by the result of the distance between two nodes, then the strength is limited to avoid extreme reactions, having a s a formula:

magnitude = (G * mass1 * mass2) / (distance * distance). (see Annex I)

Finally, a Monte Carlo algorithm along with perlin noise is added to the positional vector, to make the node moves in a random way and furthermore find the strongest area of attraction in the system.

- 5. **Represent**: In this process a rendering optimisation was applied. it was then possible to navigate trough the system in an frame rate approximately to 30fps in a MacBook Pro (mid 2009), Core2Duo, 8GB Ram Memory.
- Each Node is painted as a 4 point mesh made of two triangles, then textured with a image png that contain an ellipse (Fig.10). It cause the sensation of a spherical node placed in a 3D environment.
- The connections are rendered with a LineRenderer object that is part of Unity3D engine which also a billboarded 2D plane.

 Text is painted into textMesh Unity3D object that follows the same principle of facing the virtual camera object.



Figure 10. Diagram shows a state of the art visualization after translating the game Objects spheres into 2D planes textured with ellipse png images (Billboard planes)

- The different weights and masses are graphically represented by different nodes and connections sizes. This way, it is very easy for the human eye to discriminate areas of strong connections and to notice the differences.
- Refine: New algorithms were implemented to represent the nodes activities and therefore the connections in a range of colours from blue to red, mapping values from 0.0 to 150.0 (mean frequency rate activation) graph explained in the point 2.6. For figures refer to annex II.
- Interact: The process of interaction is divided in two areas, navigation and simulation (see Section 2.4):
- Navigation. The first version use a Logitech DualPad Game Controller to allow the subjects to control pitch, roll, rotation and zoom of the system.
- Paint/Erase connections
- Paint/Erase names of interest.
- Show Lobes areas.

- Show node activity.
- Simulate particle system based on weights.
- Simulate particle system based on *degrees*.
- Show closest distances among nodes.
- Compare anatomical structure vs simulated network structure.

2.4 **Simulation**: Shiffman [42] describes from basics to advanced concepts how to simulate graphically natural systems using the computer language Processing, which is a high level programming language based on java, design to simplify the programming process and facilitate the drawing process.

The first basic step on the simulation is to add vectors to the nodes with the aim to make them move randomly. For that, creating a random vector for velocity and acceleration and then add this vectors to the node position makes the anatomical structure to break updating their position in every frame. In principle it follows the first Newton's law.

- First law: When viewed in an inertial reference frame, an object either remains at rest or continues to move at a constant velocity, unless acted upon by an external force.
- Second law: F = ma. The vector sum of the forces 'F' on an object is equal to the mass 'm' of that object multiplied by the acceleration vector 'a' of the object.
- Third law: When one body exerts a force on a second body, the second body simultaneously exerts a force equal in magnitude and opposite in direction on the first body.

```
velocity = velocity + acceleration
position = position + velocity
```

2.5 Attraction.

Adding forces to nodes to simulate attraction-repulsion.

Now simply taking in account the second law of newton. F = M × A

Force equals mass times acceleration

Acceleration is directly proportional to force and inversely proportional to mass:

- The mass of an object is a measure of the amount of matter in the object. This value is mapped to the connectome using the sum of the connections per node.
- Weight, though often mistaken for mass, is technically the force of gravity on an object. From Newton's second law, we can calculate it as mass times the acceleration of gravity (w = m * g). In this case the gravity weight is directly mapper to the connection weight in a scale of 1:1. That means the simulation will follow a direct representation of the dataset changing weight connection to weight attraction.



Figure 12. Dynamic simulated network in the intersection of visualization of the connectome and a particle system simulation.

• Density is defined as the amount of mass per unit of volume.

Synthetic textures using Perlin noise are often used in computer graphics to make computer-generated visual elements – such as fire, smoke, or clouds – by imitating the controlled random appearance of textures in nature. This algorithm was added to the velocity vector of the nodes. The purpose of this noise is to program a Monte Carlo optimisation which increases the probability that nodes will find the most efficient attraction centre.

The intersection between connectome visualization and particle system is the main proposal of this study (Figure 12).

2.6 Coding Connections and Nodes

An additional method was applied to draw the node's connections following the structure of the Connectome dataset. Each of the nodes has information internally stored, part of this data is a list of connections that counts one by one the connection to other nodes, and the strength of this particular connection. Then in the system a line is painted with a colour that corresponds to the strength of the connections. For that, a range from 0.0 to 150.0 being 0 a very weak force against 150 that is the strongest force (mean of the frequency rate of the neuronal activity). The colours are mapped using a gradient scale in Blue from 0 to 100, in green from 25 to 125 and in Red from 50 to 150.

The scale is made by a simulated activation made in MATLAB based on the original values from the Connectome dataset.

During this process of redraw lines instead of tubes, used in the previous version of BrainX³; the amount of cycles of process was reduced considerably, from 2248 draw calls (polygons) to 1146 draw calls in the new version. It also simplify the code allowing easier implementations for further development.

After this implementation a set of 48 different images were generated to show how all the network is affected after simulating injuries in specific nodes (manuscript in preparation).

2.7 Experimental Design within subjects

Four Particle Physics Simulations were design. Two Based on weight forces and two in mass value (sum of connections per node).

- Simulation 1 weight based (simple)
- Simulation 2 weight based (Montecarlo Optimisation)
- Simulation 3 mass based (Montecarlo Optimisation)
- Simulation 4 mass based (simple)

10 subjects (6 females, mean age 30, SD+- 5) were asked to visualize in random order 4 simulations:

Paired - samples design: A questionnaire was given to the subjects. They were asked for structural understanding making comparisons among anatomical vs post-simulated structures. They were also asked about how accurate were the clusters formations after the simulations, in relation of the most connected areas in the anatomical structure.

Behavioural data was recorded from the Game Pad, having total activity, buttons pressed, movements of the navigation pads, to analyse in which simulations subjects performed more activity and more comparisons among structures.

Independent variable: Four simulations (1.5 min each) where presented in random order to avoid bias on the data related to the first navigation, which is the moment users are learning how the system works.

Dependent variable: Spatial understanding Questionnaire 1. An online version of the questionnaire were given to the participants after they experienced the simulations.

Before the experiment, all participants received a document explaining concepts of *weight* and *mass,* and experienced the application for 5 minutes to learn how the navigation works.

The experiment has a duration of 15 minutes.

3. Results

3.1 **Benchmark** (Frame Rate difference between versions).

For the optimisation test a MacBook Pro (Mid 2009). Processor of 2.8 GHz Intel Core 2 Duo. RAM 8GB 13333 MHz DDR3. OS X 10.9.3. Unity3D Version 4.5.0f6.

After having simplified the polygons rendered using Billboarding technique, the versions showing 998 nodes and 14000 connections, the figure 6.1 (optimisation) shows 35.1 FPS. And 3D polygons version runs up to 9.8 FPS (Fig 6.2). The simulation runs in real-time up to 26.8 FPS.

It is disabled the Sphere Collider Unity3D engine parameter to reduce extra calculations. In consequence the optimised version runs 262,64% faster than the original.

| | Original Version | Optimised Version | | |
|-------------------------|------------------------|----------------------|--|--|
| Frame Per Seconds (FPS) | 9.8(102.0ms) | 26.8 (28.5ms) | | |
| Main Thread | 102.0ms Render: 32.4ms | 26.8ms Render:15.9ms | | |
| Draw Calls | 2248 | 1146 | | |
| Used Textures | 8 - 13.8KB | 6 - 32.1 KB | | |
| Screen | 1027x424 - 5.0MB | 1082x460 - 5.7MB | | |

Table 1. Benchmark of the optimisation model to enhance real-time performance



Figure 12. Diagram shows the cluster formation after an attraction simulation based on weights values on strong node's connections. Forming around of 9 clusters.

3.2 Simulation results

After the simulations, the first result is a cluster formation. Those clusters show, in the case of the Monte Carlo optimised version, the areas of higher activity, forming groups of nodes that are more connected specially in terms of weight. The functional relation will require a further analysis and it will be necessary to expand the dataset to allow for a better semantical or functional interpretation of the cluster formations. Hence, the first conclusion is that clusters can be analysed mathematically, the formations are not arbitrary and show the groups of nodes more directly related at least in terms of strength (Fig 12).

Different dataset of connections were applied to generate new clusters formations and visualize areas of the brain that the activity was diminished after disable nodes in the network.

3.3 Relevance of the simulations

Simulations are not only applied to the particle systems. External data was added to the connectome dataset to generate new states, after visualize deactivation in specific nodes, the results show how the connections' forces are distributed in the network (see annex II) and how simulated lesions or low node activity affects the whole system.

The new layers of information allow the application to simulate patterns of activity that run in real-time following the paths of the most direct nodes connection inside the network, bringing to the user a better idea about how the activity is propagated.

For further implementations it will be interesting to investigate the GPU Shader implementation to increase the amount of nodes and connections, releasing the CPU from the task of process graphical information, enhancing the performance in terms of rendering. In the reference [41] it is explained how an extension library called GLM (OpenGL Mathematics) is very optimised to run parallel systems and vectors in 3D, directly storing the vectors into the Graphic Card.

3.4 Experiment Results

Besides, a comparison among old and new version of BrainX³ is exposed in the benchmark results. The goal of the study is to offer an update using optimisation methods exposed before.

In table 2, it is shown how the subjects performed more comparisons among the anatomical and cluster's structures. These comparisons where required to answer the questions if the cluster are directly related to the areas of the brain that shows more activity. It is important to clarify that simulation 1 and simulation 2 are based on *weight* values, being the second (simulation 2) more precise in terms of cluster formation around most connected brain areas (Monte Carlo optimisation version). The simulation 3 and simulation 4 on the other hand, are based on *degree* (can be understood as node *mass*, it is the sum of the individual connections in each node). It is important to clarify that simulation 4 has a high value as a threshold for *degree* to perform the attraction among the nodes; the result was a unique single cluster that groups all nodes, which simply means, all node are internally connected. From these observations, subjects didn't

compare structure formations in the same proportion of the other three simulations



Table 2.1. Comparison of structural formations between anatomical version against each of four different simulations p<0.5

| | | \sim | ۰. | | L. |
|---|---|--------|----|---|----|
| А | N | U | ν | P | ٤ |
| | | ~ | | | ٠ |

| Simulation_Activity | | | | | | | |
|---------------------|-------------------|----|-------------|-------|------|--|--|
| | Sum of Squares | df | Mean Square | F | Sig. | | |
| Between Groups | 83.300 | 3 | 27.767 | 2.748 | .057 | | |
| Within Groups | 363.800 | 36 | 10.106 | | | | |
| Total | 447.100 | 39 | | | | | |

(p<0.05).

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Table 3 shows how related were both structures (anatomical vs. cluster post simulation), in other words, how close in the anatomical space are the cluster generated to those areas of strongest connectivity. The anatomical version shows in different colour and size where the highest values were located.



Bar charts showing the level of closeness between the anatomical visualization and the cluster simulated results on a scale from 1 to 7, where 7 indicates the highest similarity

Table 4 shows the mean absolute error. The questionnaire asked for number of clusters formed after the simulations, giving a range of options around a scale of 7 values (That means, the most distant error is close to 3). My explanation to the Graph is that the first simulation (sim1) has the biggest number of clusters, increasing the probability of an error.



the four simulations.

The new version of the application developed on this study, serves to generate large-scale brain activity visualizations. With them, it was possible to observe the consequences of nodes deactivation in the brain circuits, but it also allows for an intuitive identification and analysis of patterns in the data (Figure 13). For this purpose, 48 different images were generated (see Annex II) and added to a manuscript that is under development. Furthermore, this platform constitutes a step forward on the development of an interactive program that combines computational power with human intuition in the study of the brain-circuits and its functions.



Figure 13. Four simulation runs within $BrainX^3$ showing dynamics of the resting state network at the stable attractor point. The simulation are generated with a given noise amplitude ((A) 0.01, (B) 0.05, (C) 0.07 and (D) 0.1).

4. Discussion & Conclusions

To visualize the connectome dataset, this study opened new observations, simulated layouts of the same information that compares anatomical structures against self organised clusters to highlight the nature of the weights in one hand and open possibilities to draw this information in new structural organizations on the other. Considering that the goal was to develop a custom software that supports researchers to explore, manipulate the data and extract new interpretations, this study brings a clear method to improve the performance and the experience through the interaction design. The objective of this study was also to develop a tool to teach an audience or students about the nature of the brain in an immersive environment as the XIM.

Through the application of optimisation methods such as Reinold's it will be possible to simulate more complex behaviours in different scales.

The billboard technique does not reduce the quality of the representations and it proves to be an optimal methodology to reduce the amount of calculations. It has an evident repercussion on how reactive the system is, enhancing the interaction and the experience.

The results of the experiment show that subjects understood the cluster formations as a parallel visualization that surely represent the same data that compose the anatomical version. Cluster formation gives a second lecture about how the connections' strength are distributed in the network and it simplifies the observation of the groups of nodes that are more directly related, specially in the case of the Monte Carlo optimised version. However, extract meaning from those cluster formations, a deeper mathematical approach is needed.

The connectome dataset has 998 nodes related to Cortical areas; it is necessary to have an equivalent of the Corpus Callosum and the Cerebellum, to develop and formulate more complete visualizations and hypothesis of the brain architecture.

From the technical point of view, Unity3D presents some limitations, specially drawing connections dynamically. It was not possible in the computer application to run in real-time the particle system simulations and draw the edges at the same time.

4.2 Further Development

- To continue developing the app BrainX³, the original connectome dataset is being complemented with other datasets that can affect the nodes' information, in that way the simulations and visualizations react in concordance with it, allowing new formulations and hypothesis.
- It is necessary for further development to implement OpenGL Shading Language. This will allow the system to process a part of the information using the Graphics Processing Units.
- Unity3D is a framework oriented to game development, which simplifies many of the problems a software developer can encounter while programming. However, it has some architectural limitations when it is needed to create and erase dynamically thousand of "Game-objects".

- A flocking simulation based on CPU running around 30FPS, Unity3D handle at least 100 particles, while the same system in C++ OpenGL, can handle around of 1000 particles.
 For this reason, the next step will consist in testing a C++ version to compare both cases.
- XIM full body interaction implementation for further research projects.
- Desktop application downloadable form the official web side of \mbox{BrainX}^3

Annex I

Code of the C# version of the particle simulation:

```
public void update (){
if (AllowPerlin) {
  findPerlin ();
  velocity += perlin; //adding perlin noise to the system
  velocity += acceleration;
  newPosition += velocity;
  acceleration *= 0.0f;
  }
  public void applyForce (Vector3 force){
  Vector3 f = (force / massForce);
  acceleration += f;
  }
  redice f ending
```

The attraction function:

```
public Vector3 attract (Node m){
Vector3 force = newPosition - m.newPosition;// Calculate direction
of force
float distance = force.magnitude;// Distance between objects
// Limiting the distance to eliminate "extreme" results for very
close or very far objects
distance = Mathf.Clamp (distance * 0.5f, 5.0f, 50.0f);
force = force.normalized;// Normalize vector (vector for direction)
float strength = (g * massForce * m.massForce) / (distance *
distance); // Calculate gravitational force magnitude
force *= strength;// Get force vector --> magnitude * direction
return force;
}
```

Perlin Noise code:

```
public void findPerlin (){
float xyRads = getRads (newPosition.x, newPosition.z, 40.0f,
50.0f):
float yRads = getRads (newPosition.x, newPosition.y, 40.0f, 50.0f);
perlin = new Vector3 (Mathf.Cos (xyRads), -Mathf.Sin (yRads),
Mathf.Sin (xyRads));
perlin *= 0.0025f; //scale the output to nodes size
//Get radians Function
float getRads (float val1, float val2, float mult, float div){
float xCoord = val1 / div * mult;
float yCoord = val2 / div * mult;
float rads = Mathf.PerlinNoise (xCoord, yCoord);
if (rads < minNoise)minNoise = rads:</pre>
if (rads > maxNoise)maxNoise = rads;
rads -= minNoise:
rads *= 1.0f / (maxNoise - minNoise);
return rads * mult;
ļ
```

code translated from Hodgin's Particle System [19]

Annex II

This pictures were made to map the activity on brain areas and compare their distribution after simulate lesions on specific groups of nodes (manuscript under development).



Figure 1 Annex II. Simulation runs within $BrainX^3$ showing dynamics of the resting state network at the stable attractor point. This is a healthy version with a noise amplitude of 0.01.



Figure 3 Annex II. Simulation runs within $BrainX^3$ showing dynamics of a focal lesion in the parietal lobe, with a given noise amplitude of 0.01



Figure 2 Annex II. Lateral view. Simulation runs within BrainX³ showing dynamics of the resting state network at the stable attractor point. This is a healthy version with a noise amplitude of 0.01.

Firing rate (Hz)



Figure 4 Annex II. Simulation runs within BrainX^3 showing dynamics of a focal lesion in the parietal lobe, with a given noise amplitude of 0.01

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