THE DYNAMIC CONNECTOME: A TOOL FOR LARGE-SCALE 3D RECONSTRUCTION OF BRAIN ACTIVITY IN REAL-TIME

Xerxes D. Arsiwalla[1,*], Alberto Betella[1], Enrique Martinez[1],
Pedro Omedas[1], Riccardo Zucca[1], Paul F.M.J. Verschure[1,2]
(All authors have contributed equally to this work)

[1]*Synthetic Perceptive Emotive and Cognitive Systems Lab,*
Universitat Pompeu Fabra, Roc Boronat 138, 08018, Barcelona, Spain
[2]*Institució Catalana de Recerca i Estudis Avançats (ICREA), Barcelona, Spain*
*email: x.d.arsiwalla@gmail.com

KEYWORDS

Human connectome; 3D reconstruction; Virtual reality; Neural dynamics

ABSTRACT

We present a large-scale simulation tool for real-time 3D reconstruction of brain activity in a virtual reality environment. The 3D interactive visualization of the human cortex connectome in virtual reality is achieved by using a gaming engine (Unity 3D). Further, the visualization is bi-directionally interfaced with a real-time neuronal simulator, `iqr`. As a result, by stimulating populations of neurons with external input currents, we are able to reconstruct neural activity propagating in 3D and in real-time. We explicitly demonstrate causal activity propagation in the parietal lobe, indicative of visuo-motor integration. This is a first step to simulating and mapping large-scale brain activity.

INTRODUCTION

Recent interest in whole-brain structural and functional connectivity has given rise to the notion of the human connectome (Hagmann 2005; Sporns et al. 2005). Analogous to the genome, that maps the complete genetic sequence of an organism, the connectome is supposed to map the complete neuronal circuitry of the brain (in the most ambitious interpretation of the term). The organization of these circuits can be physiologically probed at different scales: microscopic, mesoscopic and macroscopic. However, determining the exhaustive array of biophysical mechanisms, that intertwine these scales into one functional architecture, remains a major challenge in neuroscience. Hence, the operational assumption that is often made is that brain organization is hierarchical with respect to scales, such that only ensemble aggregates of lower scales (along with their stochastic fluctuations) are fed as inputs to higher scales (Zhou et al. 2006). For instance, even though the macroscopic scale is dominated by neuronal population dynamics and large-scale structural connectivity, a thorough description of population activity still requires knowledge about synaptic dynamics residing at a microscopic scale. This interplay between population and synaptic dynamics can be described by mean-field models (Wong and Wang 2006). In principle, coupling structural connectivity data with detailed enough population dynamics should be sufficient in predicting functional correlations and large-scale activity patterns. In fact, large-scale interactions across brain regions have recently been touted as the 'fingerprints' of neuronal computations underlying cognitive processes (Siegel et al. 2012).

In this paper, we present a virtual reality based dynamic simulation tool that reproduces activity propagation upon excitation of any chosen brain region. The challenge here is threefold: to implement dynamics pertinent at the macroscopic scale, to construct tools that allow for 3D visualization, and finally perform real-time analysis of neural activity generated from large datasets. The structural connectivity data is obtained from (Hagmann et al. 2008), which is Diffusion Spectrum Imaging (DSI) data. Each node of the connectivity matrix corresponds to a population of neurons. In our simulation, we model the dynamics of this population by a linear-threshold filter, which sums up all the input signals to a population module from various dendrites (within a fixed time window) and fires an output signal to neighboring modules only if the summed inputs cross a designated threshold. Additionally each neuronal population module is stochastic, having Gaussian noise.

In addition to the problem of connecting the different levels of neuronal dynamics, researchers need tools to explore complex data sets such as those deployed in the connectome. For this reason, we adapted our so called, eXperience Induction Machine (XIM), to the immersion and exploration of complex neuroscience data sets

Proceedings 27th European Conference on Modelling and Simulation ©ECMS Webjørn Rekdalsbakken, Robin T. Bye, Houxiang Zhang (Editors)
ISBN: 978-0-9564944-6-7 / ISBN: 978-0-9564944-7-4 (CD)

by human users. The XIM is a virtual/mixed reality environment, which enables user-immersion within the data reconstruction, giving an inside-out perspective of the connections in the brain and allowing the user to 'walk' through pathways in the brain.

In order to understand the relationship between structural connectivity data and neural dynamics and function, we set-up a bi-directional mapping of structural data unto a large-scale real-time neural simulator, `iqr`. Using natural gestures, the user can then inject a current to excite any region of the network and watch real-time neuronal activity propagate through the connectome network. The system allows simultaneous activation as well. This opens out the possibility of analyzing real-time activity propagation due to causal dynamics. Compared to functional correlations, dynamical analysis of causal activity serve as a more powerful tool to unravel mechanisms of large-scale neural circuits. The dynamic connectome tool, that we present in this paper, is a first step in that direction.

METHODS

The connectome we build is based on structural data taken from the human cortex connectivity dataset (Hagmann et al. 2008). This dataset includes DSI recordings of 5 subjects in the resting state (one subject has been scanned twice). The set contains 998 voxels (nodes) and approximately 14000 bi-directional connections for each subject. The 998 Regions Of Interest (ROIs) have an average size of 1.5 cm^2. Each ROI is associated with $\{x, y, z\}$ coordinates as per the Talairach coordinates of ROIs (Talairach et al. 1998). The connection strengths between ROIs is based on white matter fibre tracts from the DSI dataset we used. The network data of interest to us, is stored in the GraphML format, which is based on the XML format and is convenient for representing network data.

The virtual reality environment we create, to visualize the connectome, runs in the eXperience Induction Machine (XIM) (Bernardet et al. 2008; Bernardet et al. 2010). The XIM is a multi-user mixed/virtual reality space with a 5.6x5.4 m^2 surface area and 3.6 m height (Fig. 1). It is equipped with 3 cameras, 3 microphones, 8 steerable theater lights, 4 steerable color cameras, 16 speakers. The space is surrounded by 4 projection screens and 8 video projectors are used to display graphical content. The floor consists of 72 custom-built tiles, each of which is equipped with pressure sensors and can display a color by means of a built-in computer controlled RGB light source (Delbrück et al. 2007). Real-time location of a user can be tracked with the floor sensors, enabling the user to navigate through the mixed/virtual reality environment.

The processing architecture of the XIM integrates external data with the visualization engine (Fig. 2). 3D graphical content is programmed in C# using the Unity

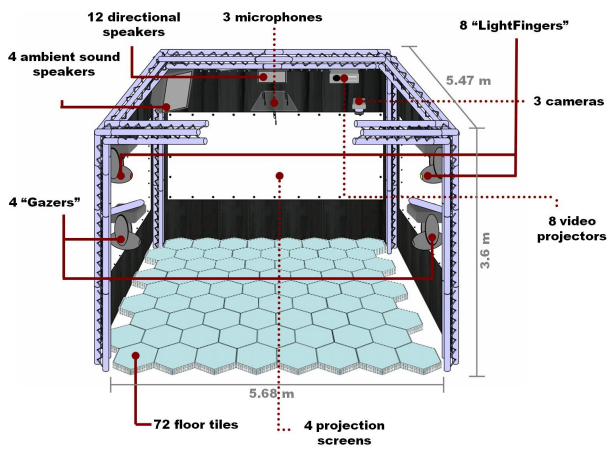

Fig. 1: Schematic illustration of the eXperience Induction Machine (XIM).

3D (http://unity3d.com/) gaming engine. XML data of structural connectivity is read and parsed in Unity and then reconstructed using the Talairach coordinate system of ROIs.

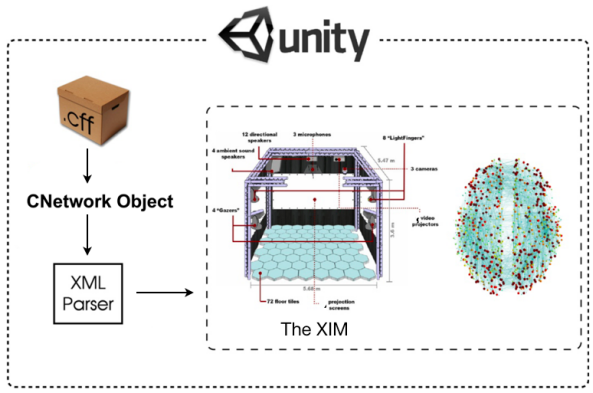

Fig. 2: Processing architecture of the XIM (figure courtesy: Wipawee Kongsantad).

To introduce dynamics into the visualization, the large-scale multi-level neural networks simulator, `iqr` (http://iqr.sourceforge.net/), is bi-directionally interfaced to Unity. (Bernardet and Verschure 2010). `iqr` allows the user to design complex neuronal models through a graphical interface and to visualize, analyze and modify the model's parameters online. The architecture of `iqr` is modular, providing the possibility to define custom neurons and synapses. `iqr` can simulate large neuronal systems up to 500k neurons and connections and can be directly interfaced to external sensors and effectors. In order to enable real-time user interaction with the reconstructed data, user input from Unity is sent to `iqr`. `iqr` computes the processes and broadcasts the output of the simulation back to the Unity engine in the XIM. The simulation runs continuously in real-time, with `iqr` receiving commands through Unity at any time during the simulation. The

simulator transmits activity from each neuronal module back to Unity every 500 ms. The activity has a normalized value between 0 and 1, and is the average activity per group. Gaussian noise of standard deviation 0.1 in introduced in all neuronal modules of the system. Upon receiving input from `iqr`, Unity updates the network reconstruction. Moreover, the user can also stimulate a neuronal group by a natural gesture corresponding to injecting an external excitatory current into the network. Gesture-based signaling within the XIM is supported via the Social Signal Interpretation (SSI) framework (Wagner et al. 2011).

As a proof of principle, the XIM has been previously been tested for visualization and analysis of artificially generated networks (Betella et al. 2012). The system transforms neuronal systems designed with `iqr` into three-dimensional representations of neuronal processes, groups and connections. While exploring the neuronal simulation, users are presented with a visualization of network configurations and associated activity. They can manipulate parameters of the system to perform specific computations. Fig. 3 shows a user exploring a neural network whilst navigating in the XIM. The screen on the left shows output of network activity from `iqr`.

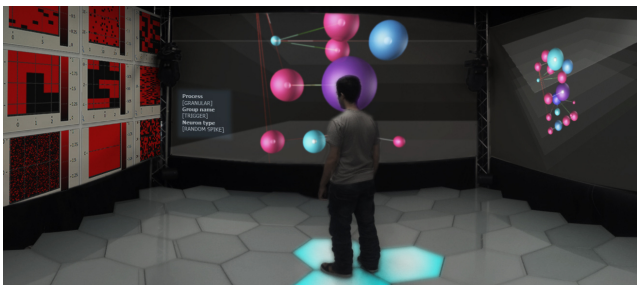

Fig. 3: Neural network 3D reconstruction in the XIM.

With the connectome data, we now push the limits of the XIM for dynamical simulation and analysis of real-world complex networks. This was done by optimizing the Unity engine to improve real-time visualization and interaction with the system. Our results are shown below.

RESULTS

Fig. 4 shows the frontal view of the connectome simulation, when the user is positioned afar from the screen. When the user moves sideways, parallel to the screen, the network will rotate (in the opposite direction to the user's movement) and reveal its side-view. On the other hand, when the user moves directly towards the screen, the visualization becomes immersive Fig. 5, placing the user "within" the 3D network.

Coupling the visualization of the data with `iqr` now allows the user to selectively perturb the system. What

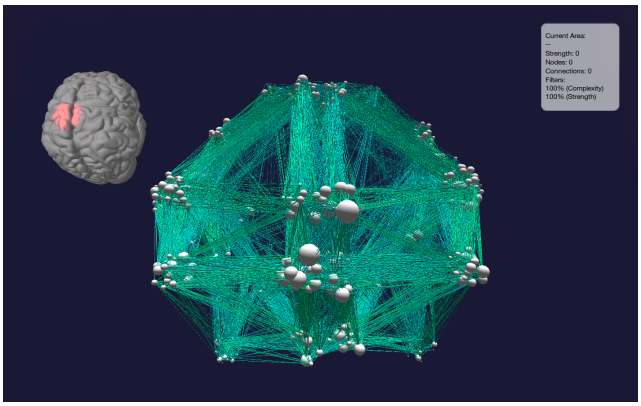

Fig. 4: Frontal view screenshot of the connectome within the XIM dynamical simulation environment.

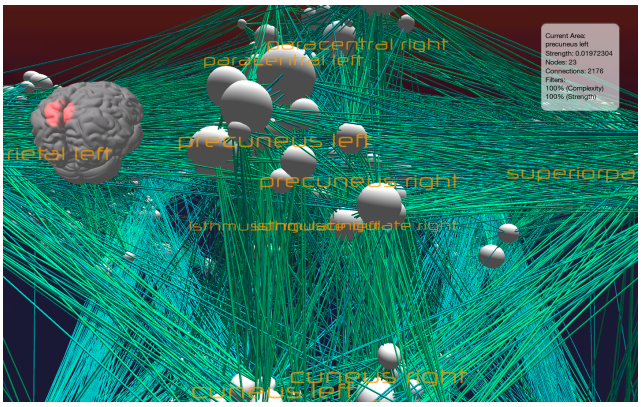

Fig. 5: User-immersed visualization of the connectome within the XIM.

can we learn from these perturbations about causal activity sequences in underlying neural circuits? In the example here, we excite two brain regions (not simultaneously), the left superior parietal (lSP) area and the right superior parietal (rSP) area, by injecting them with an external current. These regions are marked in bold in the cortical atlas provided in Fig. 6. The other regions marked in the atlas are those through which ensuing activity propagates. Causal propagation of activity is shown in Fig. 7. Seven areas are activated in each hemisphere during the sequence following SP stimulation. Column A of Fig. 7 shows stimulation and activity in the left hemisphere, whereas column B shows the same for the right hemisphere. T1 to T6 denote six time-points. T1 is 1 seconds before stimulation. T2 is when stimulation of the two SP areas begin. T3 is 0.5 seconds after stimulation onset. T4 is 5 seconds after onset and this is when stimulation of SP is stopped. T5 shows surviving activity 10.5 seconds after onset and the network returns to its initial state at T6 11.5 seconds after stimulation onset. Persistent activation after stimulation removal is stronger in the right hemisphere. The network shows low levels of default activity even before stimulation, due to Gaussian noise in each module. Specifically regions with more recurrent con-

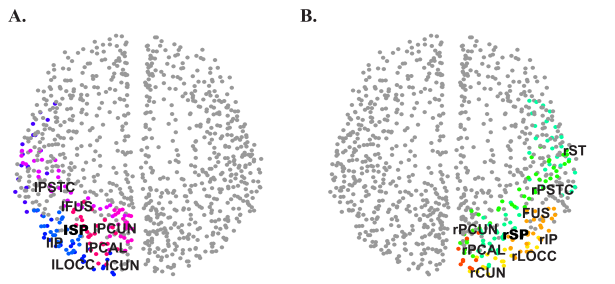

Fig. 6: Atlas of brain areas activated by stimulation of the left (A) and right (B) superior parietal region. Bold labels identify the stimulation site.

nections, show greater default activity and also greater post-stimulation persistent activity.

The superior parietal region is known to primarily control visual guidance of movements of the hands, fingers, limbs, head, and eyes (Wolbers et al. 2003). This region has expanded in humans to include regions controlling not only the actual manipulation of objects but also the mental manipulation of objects. Our simulation predicts that exciting SP leads to persistent activation in regions ST (superior temporal cortex, which is associated to perception of motion), LOCC (lateral occipital complex plays a role in object recognition), pCUN (precuneus is involved in visuo-spatial imagery) and CUN (cuneus is involved in visual processing). All these regions are indeed associated to visuo-motor functions. Hence the causal activation sequence we observe in the parietal lobe is indicative of visuo-motor integration.

DISCUSSION

As techniques of quantitative analysis and measurement devices in neuroscience make improvements, it is becoming more evident that the role of large-scale dynamics and brain-wide quantitative measures cannot be ignored. Local two-point correlations in functional data do not capture these features. Large-scale temporal activity maps across directionally connected brain structures are directly informative of brain-wide neural circuit mechanisms. Moreover, being able to predict these maps by implementing realistic biophysical dynamics brings us a small step closer to identifying the neural correlates of cognitive function.

The dynamic connectome tool, we present in this paper, is a first step in this direction. It opens the possibility of analyzing real-time activity propagation due to causal dynamics. Being immersive, it gives a completely different anatomical perspective, than a standard brain atlas would. As possible applications of this technology, we foresee online user-interaction with simulations as a step toward virtual brain surgery, enabling a surgeon to try out several procedures and assessing their impact by analyzing resulting activity. In our results, we notice a sequence of causal activations in regions that represent cognitively related functions.

As further improvements to this work, we are in the process of implementing more realistic biophysical dynamics, that will enable a finer comparison between empirical data and simulation.

ACKNOWLEDGMENTS

This work was performed within the framework of the "Collective Experience of Empathic Data Systems" (CEEDS) (FP7-ICT-2009-5, project number: 258749).

REFERENCES

[1] Bernardet, U.; Bermudez i Badia, S.; Duff, A.; Inderbitzin, M.; Le Groux, S.; Manzolli, J.; Mathews, Z.; Mura, A.; and Verschure, P.F.M.J. 2010. "The eXperience Induction Machine: A New Paradigm for Mixed-Reality Interaction Design and Psychological Experimentation". In E. Dubois, P. Gray, L. Nigay (Eds.), *The Engineering of Mixed Reality Systems* (pp. 357-379). London: Springer London.

[2] Bernardet, U.; Inderbitzin, M.; Wierenga, S.; Väljamäe, A.; Mura, A.; and Verschure. P.F.M.J. 2008. "Validating Presence by Relying on Recollection: Human Experience and Performance in the Mixed Reality System XIM". In L. G. Anna Spagnolli, editor, 11th Annual International Workshop on Presence, Padova Italy, volume 54.

[3] Bernardet, U.; Verschure, P. 2010. "`iqr`: A Tool for the Construction of Multi-level Simulations of Brain and Behaviour". *Neuroinformatics*, 8(2): 113-134.

[4] Betella, A.; Carvalho, R.; Sanchez-Palencia, J.; Bernardet, U.; Verschure, P.F.M.J. 2012. "Embodied Interaction with Complex Neuronal Data in Mixed-Reality". In proceedings of the 2012 Virtual Reality International Conference, p3, ACM.

[5] Delbrück, T.; Whatley, A.M.; Douglas, R.; Eng, K.; Hepp, K.; Verschure, P.F.M.J. 2007. "A Tactile Luminous Floor for an Interactive Autonomous Space". *Robotics and Autonomous Systems* 55(6): 433-443.

[6] Hagmann, P. 2005. "From Diffusion MRI to Brain Connectomics" [PhD Thesis]. Lausanne: École Polytechnique Fédérale de Lausanne (EPFL).

[7] Hagmann, P.; Cammoun, L.; Gigandet, X.; Meuli, R.; Honey, C.J.; Wadeen, V.J.; Sporns, O. 2008. "Mapping the Structural Core of Human Cerebral Cortex". *PLoS Biol* 6(7): e159.

[8] Siegel, M.; Donner, T.H.; Engel, A.K. 2012. "Spectral Fingerprints of Large-scale Neuronal Interactions". *Nature Reviews Neuroscience* 13: 121-34.

[9] Sporns, O.; Tononi, G.; Kötter, R. 2005. "The Human Connectome: A Structural Description of the Human Brain". *PLoS Comput Biol* 1: 245-251.

[10] Talairach, J.; Tournoux, P. 1998. "Co-planar Stereotaxic Atlas of the Human Brain: 3-Dimensional Proportional System - an Approach to Cerebral Imaging". Thieme Medical Publishers, New York.

[11] Wagner, J.; Lingenfelser, F.; André, E. 2011. "The Social Signal Interpretation Framework (SSI) for Real Time Signal Processing and Recognition". *Proceedings of Interspeech 2011*, Florence, Italy.

[12] Wolbers, T.; Weiller, C.; and Büchel, C. 2003. "Contralateral Coding of Imagined Body Parts in the Superior Parietal Lobe". *Cereb. Cortex*, 13 (4): 392-399.

[13] Wong, K.F.; Wang, X.J. 2006. "A Recurrent Network Mechanism of Time Integration in Perceptual Decisions". *Journal of Neuroscience*, 26(4):1314-1328

[14] Zhou, C.; Zemanova, L. ; Zamora, G.; Hilgetag, C.C.; Kurths, J. 2006. "Hierarchical Organization Unveiled by Functional Connectivity in Complex Brain Networks". *Physical Review Letters*, 97, 238103.

The biographies of the authors are listed on the SPECS webpage: http://specs.upf.edu/people

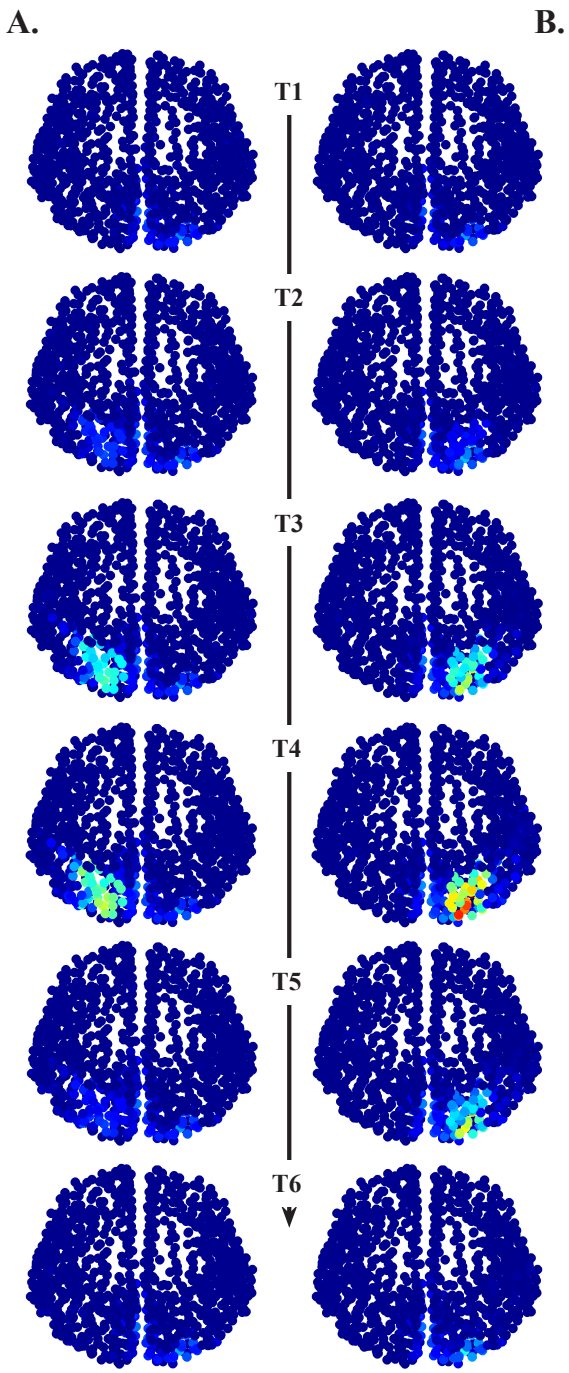

Fig. 7: Activation sequences of the cortical network following stimulation of the left (A) and right (B) superior parietal regions. Stimulation is applied at T2 and released at T4. Warmer colors indicate higher neuronal activity.