A computational framework for the investigation of large-scale brain organisation

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Abstract

Understanding large-scale brain organisation is a challenging task due to the complexity of the cortex and the unclear criteria for considering a brain region a separate functional unit. Several principles and mechanisms have been proposed to explain large-scale brain organisation, such as the free energy principle (Friston, 2010) and the principal gradient of connectivity (Margulies, et al., 2016). This project presents a framework that may be used to model the emergence of large-scale organisation from such primary principles. The Self-Organising Map (SOM) algorithm (Kohonen, 1980) is used to simulate how cortical structure or activity might develop and change as a result of fulfilling cognitive tasks. The resulting models of brain organisation are compared with neuroimaging data and discussed in relation to theory of brain structure and function. Finally, suggestions for further research utilizing this framework are discussed.

Introduction

The human brain is characterized by incredible complexity that makes constructing useful models of brain organization and function a challenging task. This is illustrated by the fact that one of the central debates in cognitive neuroscience concerns functional specialization (Genon, et al., 2018). The tendency of researchers to come up with simplified narratives for the function of brain regions has even led Uttal (2001) to compare cognitive neuroscience to the pseudo-scientific discipline of phrenology and challenge the assumption that the functional specialization of a brain region can at all be described. However, the brain is far from an undifferentiated mass as its regions vary in terms of their blood-oxygen-level dependent (BOLD) response in functional magnetic resonance imaging experiments (fMRI) (Glasser, 2016), anatomy (Haines, 1983), cytoarchitecture (Brodmann, 1909) and the cognitive impairments arising from damage to different regions (Shallice, 1988). It is therefore a major challenge for neuroscience to construct meaningful explanations for how such segregation occurs.

One of the approaches to this problem could be to aggregate data across many experiments by conducting meta-analyses of fMRI studies and then conducting a systematic mapping of brain regions to the semantic labels used to describe them such as “working memory” or “visual perception” (Yarkoni and Poldrack, 2016). However, such neuroinformatics projects still rely on the assumption that the function of a brain region can be defined in relation to the behavioural tasks that elicit activation in the region in fMRI studies. A different method for solving this problem may be to look for primary principles of brain organization that are unrelated to a particular cognitive task, such as the gradient of functional connectivity identified by Margulies, et al. (2016) using resting-state MRI. Resting state functional connectivity is calculated by computing the BOLD signal correlations between all voxels in the brain, while the participant is not instructed to perform any task. This study found a whole-brain gradient that extended from the primary cortices at one end to regions and networks that are responsible for the most abstract cognitive functions (such as mind-wandering) in the other. These regions were not only the most different in terms of their connectivity pattern, but also the most topologically distant from the primary cortices. This has led Huntenburg, Bazin and Margulies (2017) to suggest that the gradient is a fundamental structural constraint that determines brain connectivity and leads to the emergence of a global functional hierarchy similar to that observed within primary cortices.

The validity of such a theoretical account of large-scale organization could be supported if the developmental mechanisms leading to the emergence of this structure were described. A candidate mechanism that could form the basis for such an explanation is self-organisation. Self-organisation is a mechanism by which large-scale order can emerge from the local interaction of units and has been widely used to describe how learning is implemented in neural circuits. For example, neural networks could learn to make accurate predictions about the environment following a winner-take-all mechanism in which the neuron that best matched the input to the network won and has the synaptic connections to it are reinforced (Chen, 2017). However, the principle is rarely applied to the study of large-scale cortical structure, possibly because of its simplicity.

While self-organisation is a simple mechanism that seems unlikely to explain the incredibly complex large-scale structure of the brain in its entirety, there are reasons to believe It might be useful in explaining aspects of large-scale development. According to the influential free energy principle (Friston, 2010) biological systems maintain life by minimizing the amount of error in their predictions about the environment. This is observed at multiple levels in the brain, from individual neuron to the large-scale network level. If there is such a fundamental constraint on development at all resolutions, then it might be possible that large-scale structure is determined by a mechanism that is similar to the self-organisation observed in neural circuits. In order to investigate this possibility, this project has used an algorithm that has been widely used to study neuronal networks, the Kohonen Self-Organising Map (1980) to model the emergence of large-scale brain organization.

This report outlines a framework in which cognitive tasks could be described as vectors and presented to a modified version of the SOM that can be visualized on a cortical surface. This allows any researcher to create models of the emergence of large-scale organization. The key principles of the SOM algorithm are explained, the framework for creating vectors and projecting the map onto the cortex is described, and then multiple simulations of cortical self-organization with different parameters are provided. A method for evaluating the model in relation to real neuroimaging data is presented, and it is demonstrated that this framework can be used to make predictions for future neuroimaging experiments. The goal of this project is to provide a new way for researchers to model and think of large-scale organization and functional specialization in the brain.

Methods

The Kohonen Self-Organising Map

This project utilized the Self-Organising Map algorithm to model cortical self-organisation. The SOM algorithm developed by Teuvo Kohnonen is a way to project multi-dimensional data onto a low-dimensional display, usually a 2-dimensional grid of nodes (Kohonen, 1980). The SOM can be thought of as producing a type of abstraction, where some complex relationships in the data are captured as simple geometric relationships in a grid. This algorithm was chosen because of its relative simplicity and because it has already been successfully used to model neural self-organization at lower scales. It is worth discussing how the SOM works as that may be relevant to understanding the forces that drive self-organisation in this framework.

The first step of the algorithm is defining a set of input variables $[E_i]$ as real vectors $x = [E_1, E_2,\dots E_n] \in R^n$. These are used to train the SOM. The map itself is set up as an array where each element is associated with a parametric real vector $m_i = [\mu_{i1}, \mu_{i2},\dots,\mu_{in}]^T \in R^n$, which we call a model. This is usually visualised as a rectangular or hexagonal grid (see figure 1). There are various ways of choosing the initial values of m_i, but this project utilises the simplest - determining them by random.

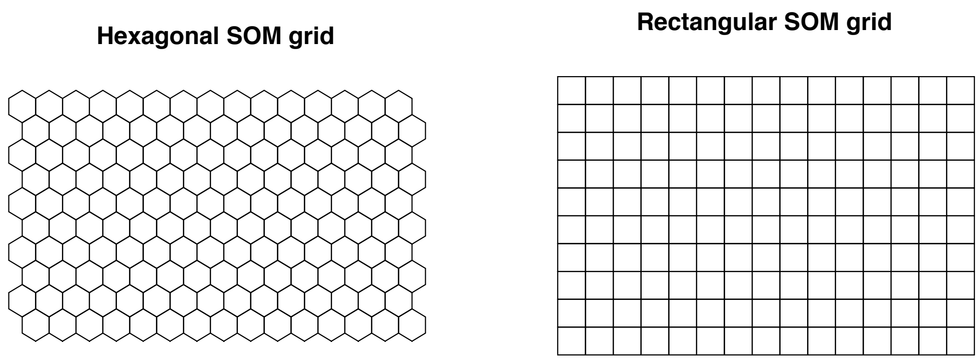

Figure 1. The SOM grid can be hexagonal or rectangular. Each element in the grid has a model mi associated with it. Following training, the mi values or the Euclidean distance between adjacent units can be visualized.

The next step of the algorithm is “training” this network of nodes using the input data and adjusting the values of the units that best match the input. In order to do that a general measure of distance between each input vector and the units in the grid is calculated, denoted as $d(x_i,m_i)$. This is used to find the best matching unit (BMU) for an input E_n by minimizing the distance function:

$$C = \arg\min [d(x,m_i)]$$

Once the BMU has been determined, the algorithm considers a “neighbourhood” N_i that involves all units in a certain radius from the winning unit m_i (see figure 2) and adjusts the values of all units in this neighbourhood to make them more similar to the BMU. The new value of each m_i at the next time step of the algorithm t+1 is determined by adding to it the difference between the input vector xi and the winning unit, multiplied by the learning rate α (ai-junkie.com, 2018):

$$m_i(t+1) = mi\ (t) + \alpha(t) * (x_i(t) - m_i(t))$$

The learning rate α is used to control how much the SOM changes its values in response to training and was set to the commonly used value of 0.05 in the present simulations.

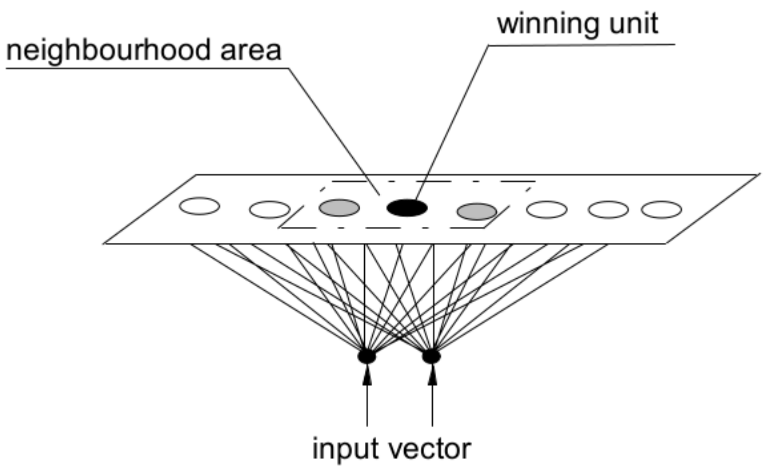

Figure 2. An illustration of a part of the SOM, showing the winning unit and the surrounding neighbourhood (https://en.proft.me/2016/11/29/modeling-self-organising-maps-r)

The modified area of the SOM will now be more likely to “win” in the next iteration of the algorithm if the input is similar to x_i. Over many iterations, clusters tend to appear in the SOM that are most responsive to a particular type of input.

This makes the SOM a useful tool for the classification of complex data, such as for example decoding which letter is being said by a speaker from the acoustic spectra of pronounced phonemes (see figure 3).

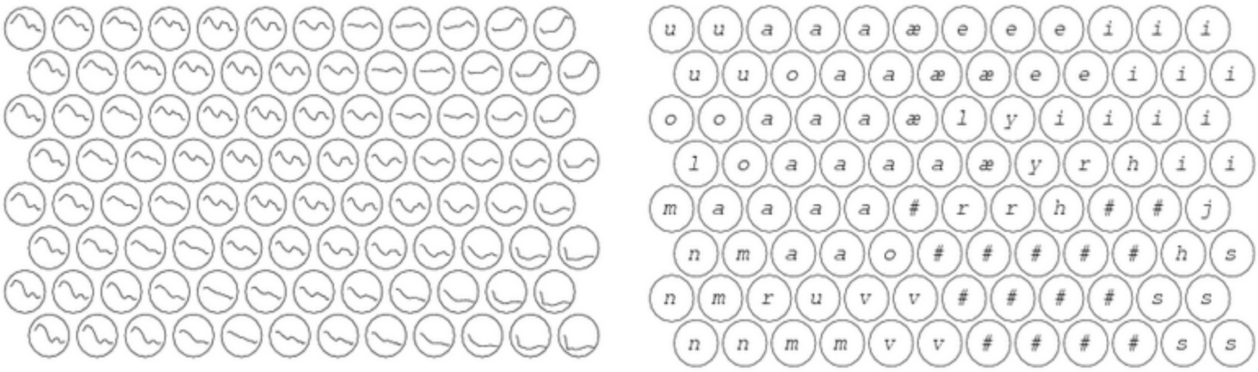

Figure 3. An example of the SOM being applied to classify the acoustic spectra of Finnish phonemes (left) into the letters that are being pronounced. The algorithm can transform continuous data into discrete categories. (http://www.scholarpedia.org/article/Kohonen_network)

As more similar inputs are presented to the algorithm, this class of inputs will also occupy a larger proportion of the map. This self-organisation mechanism is similar to how undifferentiated populations of neurons may develop to respond to particular types of input (Singer, 1982) and has made the SOM algorithm a good candidate for modelling the emergence of organization in neural systems at the large scale as well. This project has utilized a modified version of the SOM algorithm that is described below (Alhoniemi, et al., 2000).

Establishing a connection between the SOM and the cortex

In order to study large-scale brain organization a relationship was established between the SOM and a standardized cortical surface, which was obtained from the Freesurfer image analysis suite (Fischl, 2012). Freesurfer is a set of tools for the study of cortical anatomy and includes a cortical surface-based atlas representing the average folding pattern of the human brain (Fischl, Sereno and Dale, 1999). This atlas was calculated by identifiying the grey matter surface of many different brains, inflating them to a sphere (which allows the sulci to be visualized as well as the gyri) and then matching the local curvature between different individuals to obtain a standardized surface-based coordinate system (see figure 4).

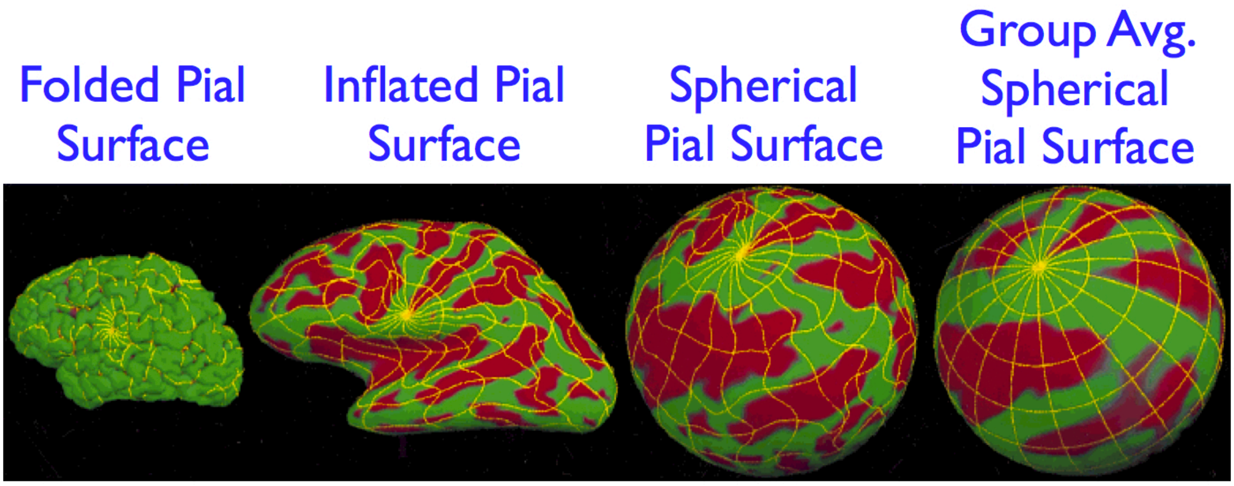

Figure 4. An illustration of the procedure that is used to obtain the spherical surface of the average brain in Freesurfer. The pial surface (a thin membrane resting on top of white matter) of an individual's brain is inflated and its curvature is matched to the average sphere (http://ielvis.pbworks.com/w/page/117733770/Mapping%20Electrode%20Locations%20to%20Average%20Brains).

The vertex coordinates and faces from this atlas were read into MATLAB using the read_surf function (Fischl, 2013) and then downsampled to an icosahedron with 1002 vertices (see figure 5) using delaunay triangulation. This was necessary in order to reduce the size of the corresponding SOM and ensure that it can develop in a manageable amount of iterations. This framework allowed to use both left and right hemisphere as a model, but only the right hemisphere is discussed throughout this report for simplicity.

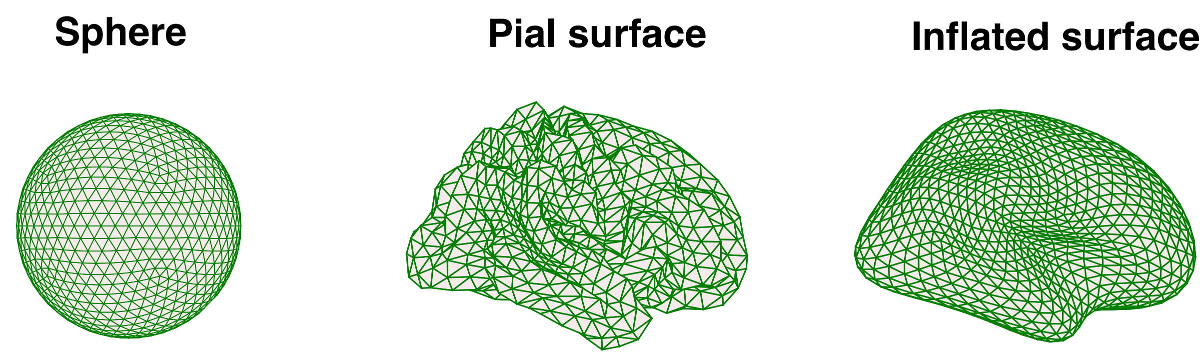

Figure 5. The average freesurfer sphere was downsampled to the icosahedron shown above. It could then be visualized as a sphere, a pial or an inflated surface.

The coordinate data from Freesurfer were then used when creating the topological structure of the SOM to ensure the faces that are adjacent in the icosahedron model of the brain surface correspond to adjacent units in the SOM array.

Modifying the SOM to allow for prewiring

The algorithm was modified to allow for the "prewiring" of some areas of the SOM. The coordinates of the primary cortices were obtained from Freesurfer, identified in the icosahedron and the corresponding values of the SOM fixed for every iteration of the algorithm (see figure 6).

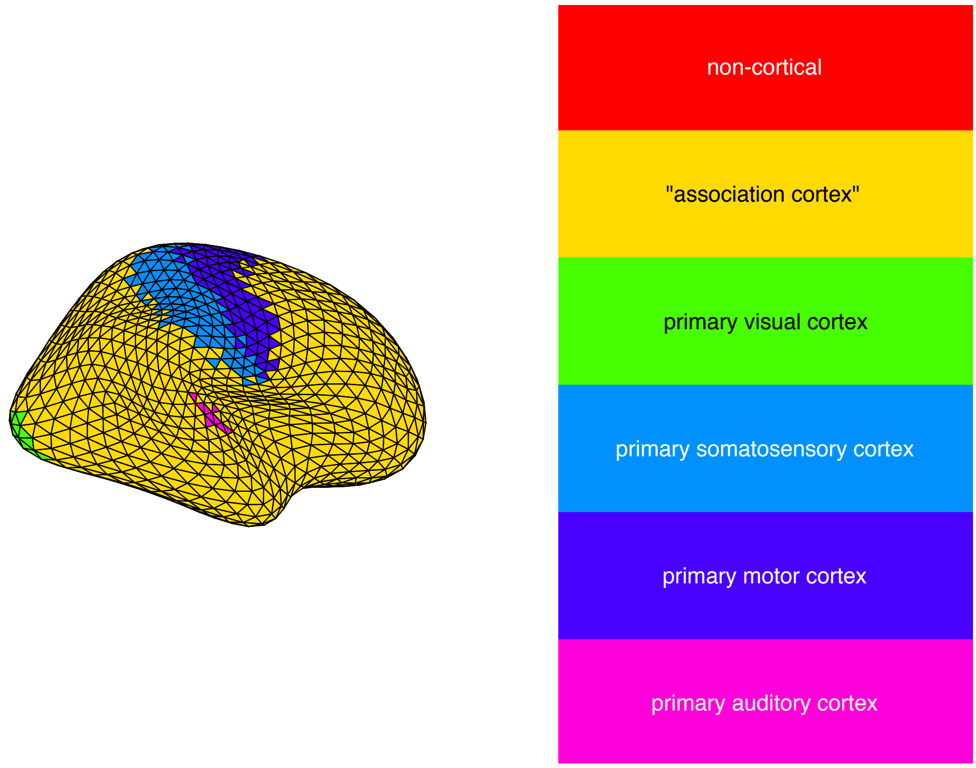

Figure 6. The coordinates of the primary cortices were obtained from Freesurfer and used to prewire the corresponding area of the map before training

This operation biased some units in the SOM to respond to vectors representing one of the primary cognitive tasks, which provided initial points from which the model cortex could develop and self-organise. This appeared necessary as without this feature the SOM would develop randomly and would not provide a good model of the cortex. This set of regions was chosen because these are the parts of the brain most likely to be present early in development, facilitating the most basic cognitive tasks and they also comprise the less abstract end of the principal gradient from Margulies, et al. (2016). A different set of initial regions could be chosen for the simulation if necessary.

<u>Generating vectors describing cognitive tasks</u>

The cognitive tasks that the developing brain must carry out that would eventually lead to self-organization were represented by vectors. For example, in a basic simulation involving vision, audition, somatosensation and motion each of those cognitive functions could be represented by a 4x1 vector with a 1 coding for the type of task (e.g. [0 1 0 0] for audition). Multimodal tasks could be represented in the framework using the same notation (e.g. [0 0 1 1] would stand for a sensorimotor task). The simulation also allowed for training involving a disproportionate number of tasks in different modalities, for example three times as more vectors representing vision than audition. Another property called "order" was introduced allowing to specify the degree of abstraction involved in a cognitive task. This accounted for the possibility that simply combining tasks involving primary cortices was not enough to demonstrate emergence, by biasing the algorithm when heteromodal, higher order cognitive tasks were involved. When the task involved more than 1 modality and/or the "order" property, the vectors were normalized so that the magnitude of each vector was equal to 1. This is important in order for some components of the input not to dominate the SOM (Kohonen, 2001). For every simulation, the vectors representing cognitive tasks were compiled into a matrix, which was then used to train the SOM (see figure 7).

Cognitive task	**Task components**				
	Order	Visual	Auditory	Somatosensory	Motor
Visual	0	1	0	0	0
Auditory	0	0	1	0	0
Somatosensory	0	0	0	1	0
Motor	0	0	0	0	1
Audiovisual	0.5	1	1	0	0
Sensorimotor	0.5	0	0	1	1

Visuomotor	0.5	1	0	0	1
Multimodal	0.75	1	1	1	1

Figure 7. An example of the task representation matrix showing the cognitive tasks that could be used to train the map and the components they could be made of.

<u>Training and visualisation</u>

After the matrix of vectors representing the cognitive tasks involved in each simulation was created, it was used to train the modified SOM algorithm. The initial radius was set to 4, the final radius to 1 and the alpha value to 0.05. The training length was varied between the simulations to illustrate the progress of self-organisation in the model brain. Following training, the m_i values stored in the SOM codebook were extracted. These values corresponded to each of the 1002 units of the SOM and each component of the task representation matrix. The codebook values could then be visualized directly on the icosahedron model of the cortex or interpreted using statistical tests. In this model, higher values in the SOM can be interpreted as higher activation in response to a cognitive task, or a greater role for a region of the brain in facilitating this cognitive task.

Results

The framework outlined above was used to conduct multiple simulations of cortical self-organisation in order to illustrate the possible uses of this model, discuss the emergent properties of training that could be seen in the map and the relevance of the SOM algorithm to understanding large-scale organization.

<u>Training the SOM on vectors representing basic cognitive tasks</u>

The simplest type of model that could be generated in this framework involved creating a matrix representation of the cognitive tasks associated with the primary cortices using simple vectors (such as [0 0 1 0] for somatosensation) and training the SOM on this data. The codebook values associated with each unit and cognitive task could then be extracted and visualized on the icosahedron surface. Comparing the structure of the map at various stages of training shows the process of self-organisation (see figure 8). The prewiring of the primary visual cortex ensures that the winning SOM units are more likely to be located within the prewired area. As the neighbourhood surrounding the winning units is adjusted to be more responsive to this type of input vector, units that are more distant from the primary cortex have an increased probability of winning. As the vectors are presented to the algorithm, these units take on higher values “colonizing” more of the SOM.

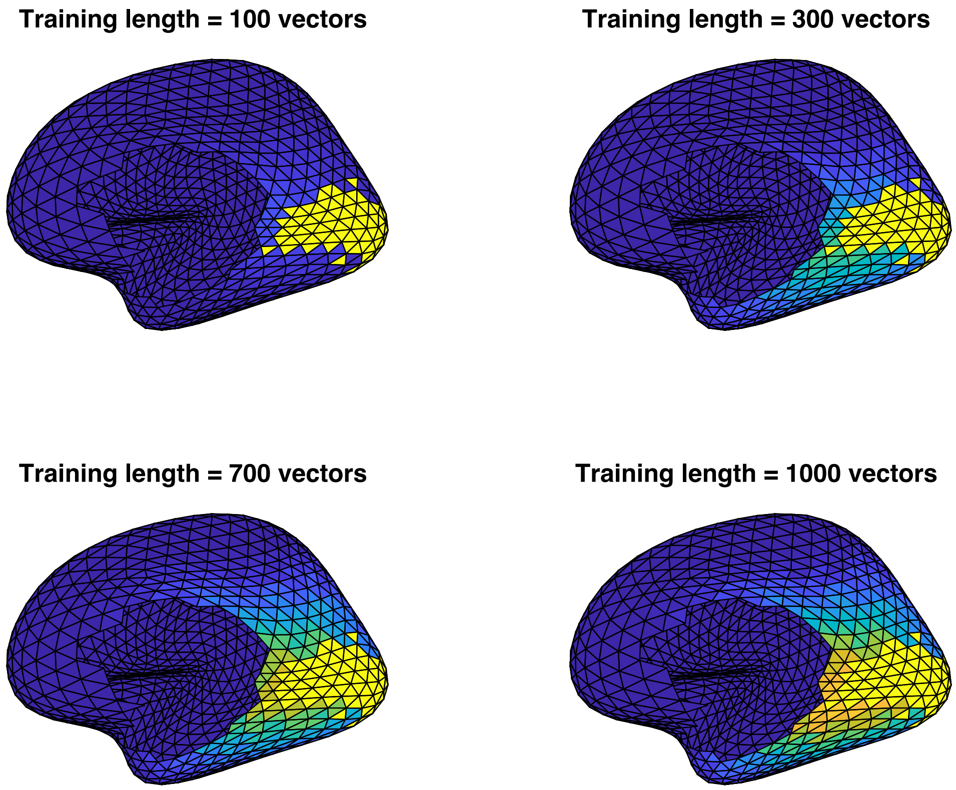

Figure 8. Medial view of the model cortical surface for right hemisphere at various stages of being trained on vectors representing vision. Here, and in the following figures, hotter colours indicate higher SOM values.

This pattern could be seen for all the basic cognitive tasks introduced in this model (see figure 9). Training the SOM on vectors representing basic cognitive tasks resulted in the “activation” gradually expanding beyond the corresponding primary cortices. These patterns resemble processing hierarchies that have been observed in the human cerebral cortex in fMRI. For example, a gradient similar to the one seen in the auditory simulation has been observed in the primate brain (Rauschecker & Scott, 2009) and in fMRI studies of the human temporal cortex (Visser, et al., 2012). This simulation may illustrate how such gradients arise as a consequence of learning and development. The similarity could be further evaluated by comparing the result of the simulation to neuroimaging data or another theoretical model (this possibility is illustrated later in the report).

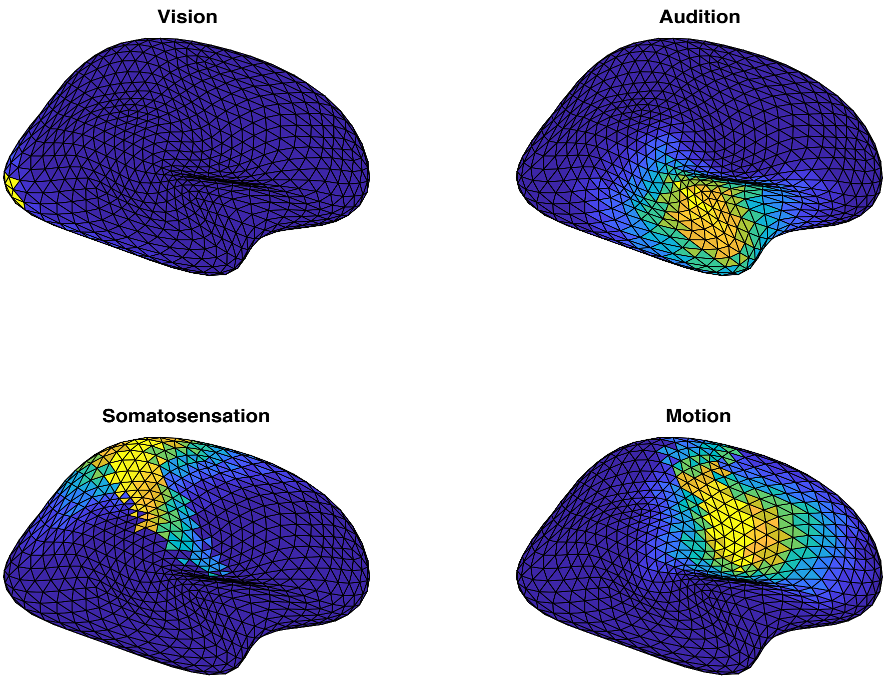

Figure 9. Lateral view of the model cortical surface after the SOM has been trained on 1000 vectors representing primary sensory and motor functions.

<u>Introducing multimodal cognitive tasks</u>

This framework also allowed for simulations involving multimodal tasks. For example, an audiovisual task could be represented as [1 1 0 0] and a visuomotor task as [1 0 0 1] and these vectors then used to train the SOM. However, since directly visualizing codebook values could only be used to interpret the organization of the SOM in relation to a single component of the task (such as vision or audition) a measure of overall brain "activation" in response to a cognitive task was obtained by calculating a measure of cosine similarity between a multimodal task vector and every vector m_i associated with the SOM units after training using the cosine similarity formula:

$$\text{similarity} = \frac{x_i \bullet m_i}{\|x_i\| \bullet \|m_i\|}$$

This resulted in a matrix of scalar values that could be visualized on the icosahedron and interpreted as a measure of which parts of the model cortex would be most involved in dealing with the presented cognitive task. For example, training the SOM on a matrix of vectors representing basic cognitive tasks as well as a multimodal visuomotor task produced this “activation” pattern (see figure 10). In this case it was also necessary to normalize the vectors so that the magnitude of each is equal to 1 and a valid comparison could be made between them. For example, the visuomotor task was represented as [0.7071 0 0 0,7071].

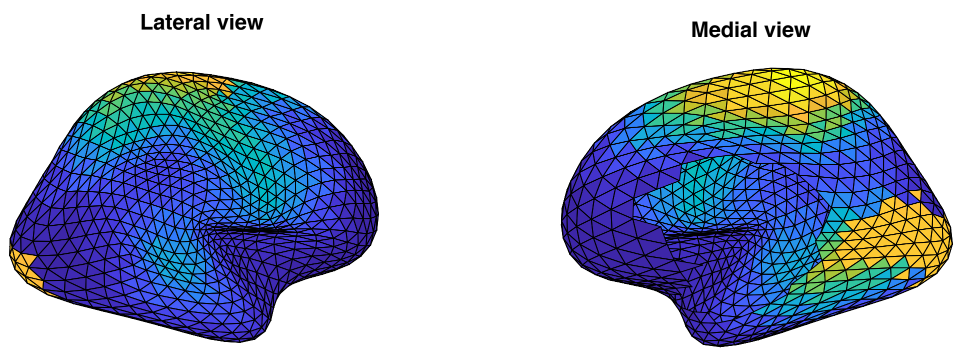

Figure 10. The SOM after being trained on a matrix of vectors including those representing visual, motor and visuomotor tasks for 1000 iterations. The values shown in this figure have been calculated using the cosine similarity formula.

This visualization of the SOM shows regions that would be involved in carrying out a task that involved both vision and motion. The resulting pattern of organization doesn't seem to illustrate any emergent properties beyond that observed in the simpler simulation. This may reflect a limitation of this model as the only constraints on self-organisation in this case are the locations and prewired values of the primary cortices. It may be possible to overcome this with the introduction of the "order" property that is discussed further in this report.

<u>Training the SOM on matrices involving a disproportionate amount of some type of task vector</u>

A cognitive task may have components that disproportionally recruit some part of the brain. For example, a behavioural task that involves choosing between visual stimuli and indicating the choice with a button press might involve a high amount of visual and motor processing, and only minor amounts of auditory processing (if background noise is not controlled for). This could be reflected in the modelling framework by training the SOM on task representation matrix with three times as many visual, motor and visuomotor vectors as any other vectors. It is then possible to compare the result with a different SOM that was trained on an equal number of vectors representing various cognitive tasks (see figure 11). This may be achieved by calculating the cosine similarity between the SOMs and a vector taken to represent general cognitive activity (which in this example was [0.5 0.5 0.5 0.5]).

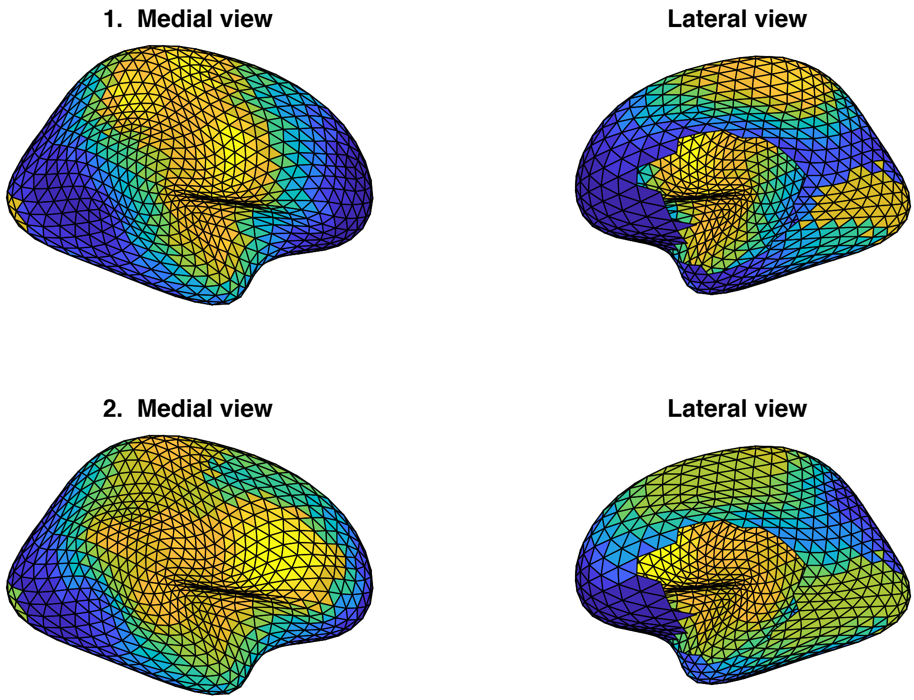

Figure 11. 1. The activation in the model brain in response to a normalized multimodal vector [0.5 0.5 0.5 0.5] calculated using cosine similarity. 2. The activation in the model brain after the SOM has been trained on a task vector matrix involving three times as much visual, motor and visuomotor vectors. The peak of activation appears to be expanding towards the prefrontal cortex.

In this simulation, the increased amount of visuomotor vectors seems to have resulted in the peak of peak of activation shifting towards the anterior part of the brain (corresponding to the prefrontal cortex). This may suggest that this area of the cortex is more specialized for the processing of visuomotor tasks, or that it is more likely to show activation in an experiment with an increased proportion of such tasks.

Adding the “order” property to the model

It may be the case that training the SOM on task vectors representing combinations of the basic functions of vision, audition, somatosensation and motion is insufficient to effectively model large-scale brain organization. For example, in one of the above simulations (see figure 10) the map doesn't seem to expand far beyond the primary motor and visual cortex, even though we would expect much more distributed activation in response to a visuomotor task in the real brain. This can potentially be alleviated by introducing "order" – a property that indicates how abstract a cognitive task is and biases the algorithm to expand further from the primary cortices. This can result in more realistic multimodal "hubs" being created (see figure 12). The order property may be useful when constructing more accurate models of the cortex but might undermine the biological plausibility of this model. This is discussed further in this report.

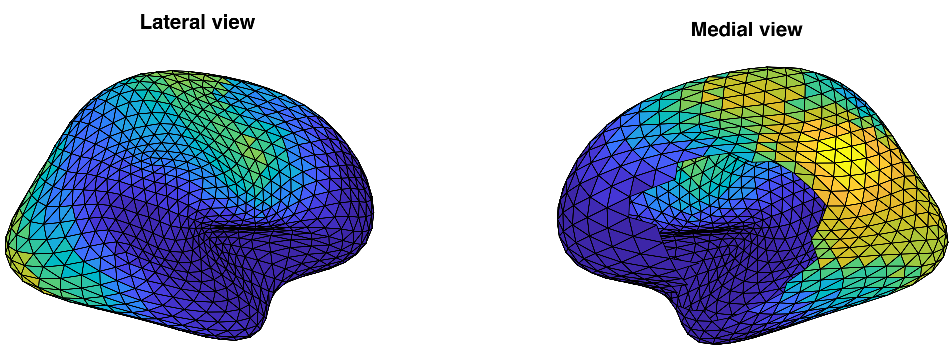

Figure 12. The activation in the model brain in response to a vector representing a visuomotor task calculated using cosine similarity. In this simulation, multimodal vectors were assigned order 0.5 and unimodal vectors 0. This leads to the peak of activation expanding beyond the primary cortices, generating a heteromodal hub that appears half-way between the primary visual and motor cortex.

<u>Comparing the model to experimental data</u>

An important feature of this framework is that resulting models of large-scale organisation may be compared to data from real neuroimaging experiments to test the validity and explanatory power of the model. To illustrate this, neuroimaging data were downloaded from neurosynth.org (source), a database of neuroimaging studies. The dataset used in this example was obtained from an automated meta-analysis of 97 fMRI studies involving the term “audiovisual”. This was an unthresholded z-statistic map computed using neurosynth’s default processing stream. The map was based on reverse inference, meaning it only included regions that were preferentially reported in studies that had the word “audiovisual” in the abstract over those that did not (for further information please visit http://neurosynth.org/analyses/terms/audiovisual). The data in NIFTI format were then transformed into the average Freesurfer (Fischl, 2012) space using the mri_vol2vol command and projected onto the icosahedron surface. The SOM was trained on vectors representing the basic unimodal tasks as well as audiovisual vectors and the results visualized on the icosahedron surface alongside the neuroimaging data (see figure 13).

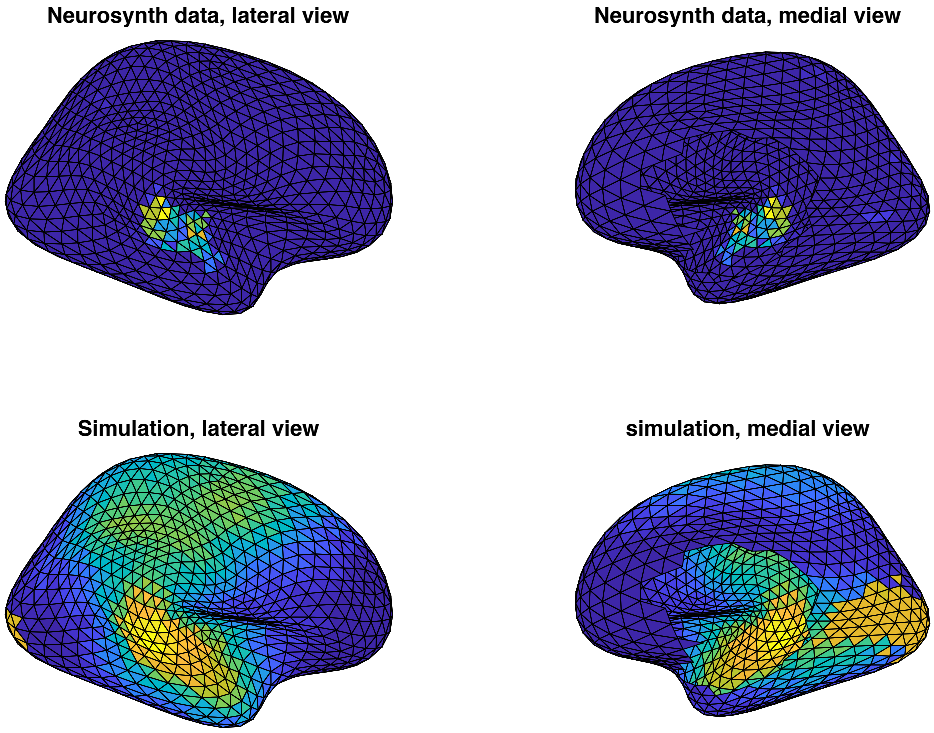

Figure 13. Data from a neurosynth.org meta-analysis of audiovisual experiments compared to the activation in response to an audiovisual task in the model brain. The peak of activation in the model appears to correspond to the neuroimaging data but involves regions that were not highlighted as significant in the meta-analysis.

The model appears to correctly predict some proportion of the activation observed in fMRI experiments. To evaluate this similarity the correlation between the SOM values and the z scores from the neuroimaging meta-analysis was computed ($R^2 = 0.10$). Calculating the R^2 statistic for the two sets of values can be used to compare the accuracy of different models in this framework. For example, a model of brain organisation obtained in a simulation involving just vectors representing vision explains much less of the data from this meta-analysis ($R^2 = 0.01$).

Examining the principal gradient of connectivity in this framework

The models of large-scale brain organisation obtained in this framework can also be used to evaluate other theoretical accounts of brain function and structure. For example, it may be possible to demonstrate the emergence of the principal gradient of functional connectivity identified by Margulies, et al. (2016). The gradient was identified using a dimensionality reduction technique called diffusion embedding that bears some similarity to the SOM algorithm. The principal gradient is an axis that explains the most variance in resting state functional connectivity data. It appears to correspond to measures of topological distance from the primary cortices, which suggests that the SOM may be able to demonstrate its emergence given the correct training data. In order to do that, the gradient values expressed as z-scores were downloaded from the Google Drive of the Mind-wandering lab at the University of York and projected onto the icosahedron following the same procedure that was used for the meta-analysis in the previous section. The SOM was then trained on a task representation matrix involving basic and multimodal vectors and the activation values computed using cosine similarity and visualized alongside the gradient data (see figure 14). The colour scheme was inverted for the simulation values, as the areas of the SOM that were least responsive to the multimodal vector seemed to correspond to the gradient more closely.

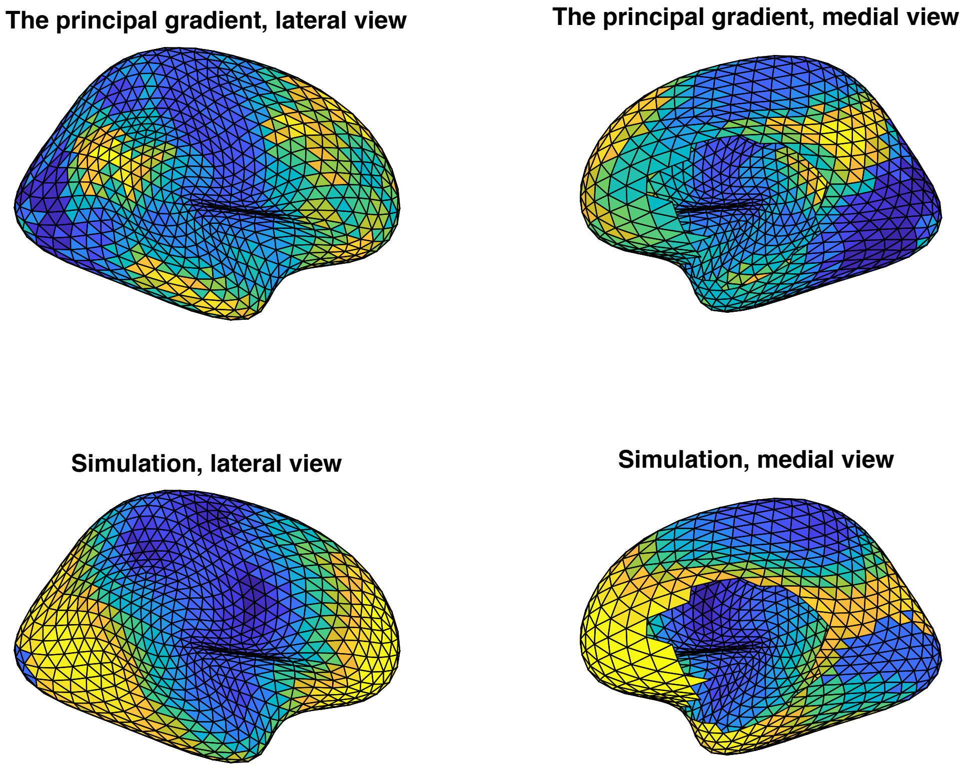

Figure 14. The principal gradient of connectivity compared to activation in the model brain in response to a vector representing a multimodal task. There appears to be some correspondence, but not enough to consider the model accurate.

In this example, the model appears to capture some aspects of the distribution of gradient values, such as the extensive involvement of the prefrontal cortex (PFC) and the anterior temporal lobe (ATL). The statistical similarity between the data appears to be higher than in the previously discussed model involving audiovisual activity (R^2 = 0.16). However, the model doesn't seem to capture the highly specific connectivity structure seen in the principal gradient. An alternative way to simulate resting state activity that could have produced better results would be to generate the task representation matrix by random from the set of available unimodal and multimodal vector. However, implementing that has produced a similar result (see figure 15).

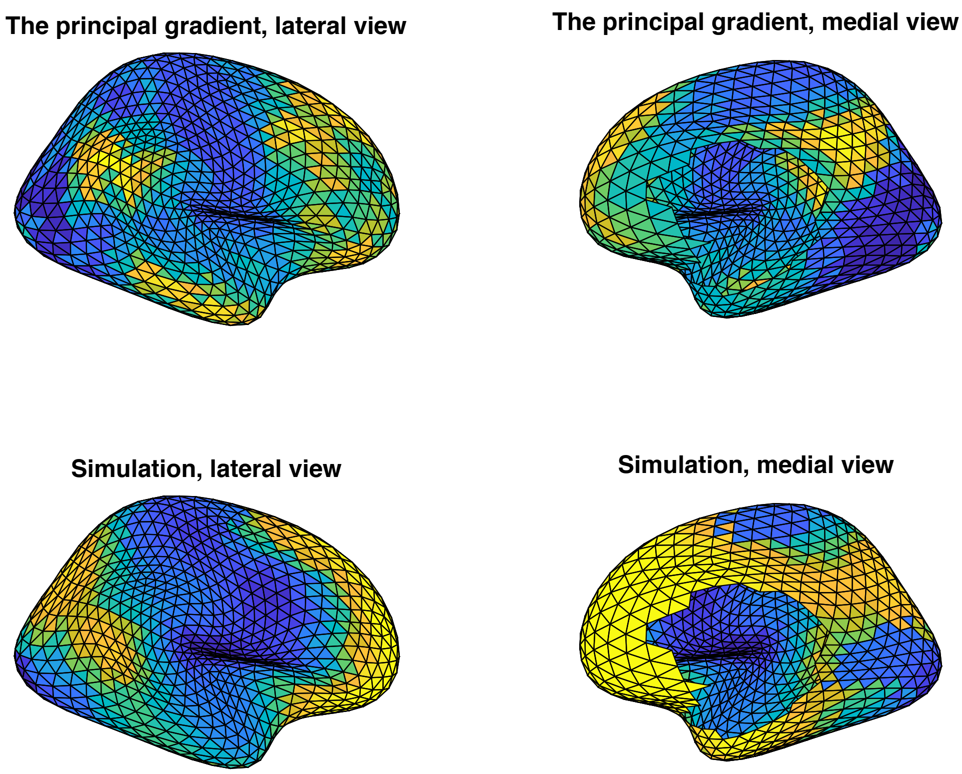

Figure 15. The gradient compared to activation in the model brain that was trained on random unimodal and multimodal vectors

The resulting pattern of activation seems to involve the PFC and ATL, but also seems to more accurately capture the involvement of the area around the angular gyrus (AG). These regions have been identified by Margulies, et al. (2016) as some of the more distinct peaks of the abstract end of the principal gradient. This model also explained a larger proportion of the variance in the data (R^2 = 0.23). However, it still falls short of capturing the full pattern of the distribution and a more refined model may be necessary to achieve this.

<u>Generating predictions for future fMRI experiments</u>

This framework may also be used to generate predictions for future fMRI experiments, testing the validity of this computational model of self-organisation or the experiment. For example, it can be used to generate a prediction for a neuroimaging experiment involving an auditory alternative-choice task where the participant lies in a scanner and indicates responses with a button press. This may be achieved by training the network on vectors representing the full range of cognitive tasks (as a participant's cortex would) and then calculating the cosine similarity between the SOM units and the normalised audiomotor vector [0 0.7071 0 0.7071]. The resulting activation pattern (see figure 16) could be compared to data obtained in an fMRI experiment and used to refine the experiment design, or the model.

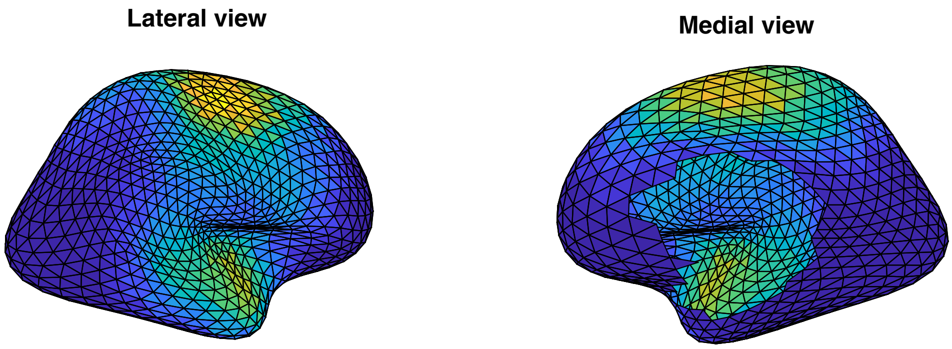

Figure 16. Activation in the model brain in response to a vector representing audiomotor activity. It can be hypothesized that activation in a behavioural experiment involving listening to auditory instructions and pressing buttons will involve the brain regions seen in this visualisation.

Discussion

The modelling framework presented in this project allows to simulate the process of self-organisation in the human cortex at a large scale. The simulations described in this report have demonstrated that it is possible to train the SOM on vectors representing cognitive tasks and obtain maps that can be interpreted as patterns of activation or cortical specialization. These maps show various emergent structures that can also be seen in the human cortex. For example, the gradual expansion of the SOM away from the primary cortices as a result of training resembles the multiple processing hierarchies observed in the brain. Training the network on vectors representing vision has resulted in gradients expanding dorsally and ventrally from V1. This corresponds to the widely accepted account that visual processing occurs in two streams of visual processing (Goodale and Milner, 1992). Another gradient that could be seen in the SOM following training on auditory vectors appears similar to the auditory processing hierarchies observed in the superior temporal gyrus (STG) (Visser, et al. 2012). These results suggest that self-organisation may be a key factor in the development of such gradients in the brain.

The application of the SOM algorithm to studying large-scale neural structures may also provide a solution to the puzzle of functional specialisation. Instead of assigning discrete functions to parts of the cortex, the SOM values can be used to provide a quantitative estimate of the contribution of a brain region to fulfilling a cognitive task. For example, in the aforementioned simulation of visual activity the regions that were closest to V1 took on higher values in the SOM and could be interpreted as more essential to visual processing. At the same time, a region that is located further in the association cortex may have a less immediate contribution, but to a broader range of cognitive processes. The emergence of such heteromodal hubs in the brain could be demonstrated in this framework due to the possibility of representing unimodal and multimodal tasks using the same syntax. For example, one of the simulations that involved training the network on vectors representing visuomotor tasks resulted in the SOM taking on higher values in a region that appears half-way between the primary visual and motor cortices. This means that the algorithm can be used to model the development of key neural structures that are involved in processing highly abstract information such as the ATL (Ralph, et al., 2016). This may allow researchers to define and discuss the function of brain regions in terms of their role in distributed networks and in relation to developmental principles that lead to their position in information processing hierarchies.

In addition to providing a novel theoretical model of the development of large-scale organization this computational framework can be seen as a tool for testing the validity of other theories of brain function. It appears especially appropriate for the examination of large-scale gradients discussed by Huntenburg, et al. (2017). A key feature of their theory is that the topological distance of a brain region from primary cortices plays an important role in determining its function. The SOM provides a great way to test that, as the map is a topological structure and the algorithm relies on the calculation of distances in order to determine the winning units. Training the SOM on vectors representing basic cognitive tasks can show precisely how the regions that are furthest away from the primary cortices develop to facilitate the most abstract cognitive functions, such as mind-wandering or autobiographical memory. The simulations in this report were not precise enough to arrive at the exact structure of the principal gradient. However, they still successfully illustrated the overall principle that may lead the topologically remote regions such as ATL and PFC. A more refined model could possibly provide further support for the idea of a principal gradient of large-scale organization.

While this computational framework appears well-suited to capture some principles of learning and development, its core limitation is that is unclear how biologically plausible the SOM algorithm is for explaining organization at the large scale. In order to determine which properties of the SOM might be essential to understanding self-organisation in the brain, the models produced in this framework need to be validated at the algorithmic and implementational level of analysis (Marr & Poggio, 1976) by examining the primary neural structures that might determine and constrain developmental processes. This is especially true if the "order" property is used in the simulation, as it does not have a clear potential neural substrate. This might be addressed by expanding the framework to include subcortical structures. Brain regions such as the hippocampus and the basal ganglia play a key conjunctive and modulatory roles in learning (Atallah, Frank & O'Reilly, 2004). Including those structures in models of large-scale cortical organisaton may explain how the brain is capable of forming truly abstract, higher-order representations.

Given the incredible complexity of the brain it is unlikely that a model relying on a simple algorithm such as the SOM will be able to explain all of its large-scale structure. However, the strength of this framework is that it allows models of the cortex to be easily compared with results from neuroimaging studies and evaluate the proportion of variance in the data that is explained by the model. This would allow future researchers to investigate what kind of properties of the model contribute to an increase in its ability to predict activation in fMRI studies. This may be achieved by creating more elaborate task representation structures involving higher-order cognitive tasks, increasing the complexity of prewire patterns (e.g. by adding retinotopic, somatotopic maps to the primary cortices) or determining a systematic way of creating task vectors from real experimental paradigms. Determining the initial parameters that maximise the predictive power of models in this framework may lead to a better understanding of the essential developmental constraints that determine large-scale organization of the brain.

In conclusion, a computational framework for studying large-scale brain organization has been presented in this project. It has utilized the SOM algorithm that has been extensively used to study neural networks at lower resolutions to investigate the emergence of large-scale structure. The algorithm has been shown to be useful for explaining aspects of large-scale brain organization such as gradients and heteromodal hubs, discussing theories of brain structure such as the principal gradient identified by Margulies, et al. (2016) and making predictions for neuroimaging experiments. Further research using this framework could focus on creating more elaborate models of self-organisation that would involve higher-order tasks or factor in subcortical influences and should aim to predict fMRI data with the highest possible accuracy. Applying algorithms such as the SOM to the study of large-scale brain organization could shed light on the complex problem of functional specialisation in the cortex.

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