Understanding the Human Brain Via its Spatio-temporal Properties (Vision Paper)

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ABSTRACT

The human brain is probably the most complex object in the universe, and also one of the least understood. For example, how the brain produces the mind and consciousness is a complete mystery. Nevertheless, the brain is amenable to measurements of various kinds that produce lots of data. It is a spatial object residing in the skull; it is also temporal in the sense that neurons communicate by signals that take traverse the brain network over time. In this paper we ask whether spatio-temporal data analysis can contribute to its understanding. Toward this goal we propose several research directions that are inspired by GIS work. However, these are just examples, and other work on moving objects in space or on networks is applicable.

CCS CONCEPTS

• Bioinformatics • Computational Biology

KEYWORDS

Data mining; Connectomics; Transportation; Mobile Data Analytics; Brain Applications of Mobile Data

1. INTRODUCTION

1.1 Background

The human brain is probably the most complex object in the universe. It is also one of the least understood. For example, even for a basic activity such as sleep there is no consensus concerning its purpose and how the purpose is achieved. Higher level functions such as imagination, creativity, aggressiveness, and more generally consciousness are highly controversial. To some scientists consciousness is in some sense a fundamental (but still mysterious) element, whereas to others it is an emergent property resulting from neural computation and coding (see [14]). In this paper we argue that spatio-temporal data analysis can shed a light on such issues.

Recently, brain research has received a boost from the BRAIN initiative of the Obama administration ([1]). A number of disciplines are involved in this research, including neuroscientists, psychiatrists, physicists, philosophers, computer scientists, and psychologists. The data management community has also become interested in the subject, emphasizing graph mining (e.g. [3]), and the performance improvement of database operations (e.g. [4]).

Although the spatial-information community has not addressed the topic, the brain is fundamentally a spatial object. It has on the order of 100 billion neurons, each of which is connected (via synapses) to about 1,000 other neurons on average ([9]). Each neuron has a location in 3D space which is indexed using a common coordinate system, e.g. Talairach or MNI ([6]). Such a coordinate system is independent of individual differences between humans.

The structure of the brain can be represented by a graph $G = (V, E)$, where V is a set of nodes representing neurons and E is a set of edges representing synapses between these neurons. This graph is called the *Structural Connectome* (SC). Furthermore, the brain also has a temporal component in the sense that the neurons communicate by sending signals that travel from neuron to neuron, across the synapses, at a certain speed. To some extent this is analogous to vehicles traveling along the road network, although some models of the brain communication allow a vehicle to "split" at an intersection and travel along multiple paths (the parallel-communication model [15]); similarly, signals from multiple sources can be merged by a neuron into a single one. Although individual signals currently cannot be identified and tracked, signals clearly often travel from sources to destinations. For example, signals travel from the brain to a muscle to activate it.

The set of signals communicated in the brain changes dynamically depending on the mental task, or the function, performed by a person; for example, it differs depending on whether the person is at rest, or solving a problem, or sleeping. Thus this set is referred to as the *Functional Connectome* (FC).

Currently, limitations of brain imaging technology do not allow capturing the SC at the level of individual neurons. Similarly, the FC cannot yet capture the movement of individual signals; instead, aggregate movement is inferred from the level of activity of distinct brain regions. This is in contrast to common practice in the mobile data community, where mobile units (vehicles or pedestrians) are tracked by, for example, GPS receivers. Nevertheless, as we show in this paper, important questions in brain research can be addressed even when the available SC and FC data is at a coarse level of granularity. Furthermore, human brain mapping is advancing at a rapid pace, and animal studies already produce brain data at a much finer level of granularity ([5, 28]).

1.2 Current construction of the connectome

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Although neuronal- and signal-level SC and FC cannot be obtained using existing technology, some approximations can; furthermore, the data and software for producing these are in the public domain. In this subsection we discuss these approximations.

Brain connectivity information is typically acquired via Diffusion Tensor Imaging (DTI) [10]. This technique produces neural tract images that are analyzed to calculate the number of fiber tracts that connect regions in the brain (see [11]). Using the DTI images, each of which may contain millions of voxels, the SC is produced as a weighted undirected graph. In this graph the nodes are brain regions, or parcels, formed by aggregating voxels of the image. And a weighted edge in the SC specifies the strength of a connection between two brain parcels. The strength may represent both, the number of fiber tracts and their length. The SC graph is may have hundreds or thousands of nodes, and is incomplete in the sense that not every pair of regions is connected.

Signal activity information is gathered using fMRI, which is a method of functional brain imaging. It is used to evaluate interactions between brain parcels that occur when a subject is at rest or performing an explicit task [10]. This brain activity is observed through changes in blood flow. These changes generate a Blood-Oxygen-Level Dependent (BOLD) time series for each parcel. The BOLD signal time-series data is used to produce the FC which is a square matrix, or a complete graph. Each element F_{ij} denotes the cross correlation between the time-series of parcel i and parcel j. The correlation is often used as a proxy metric for the magnitude of signal-communication between parcels i and j; the higher the absolute value of the correlation, the higher the traffic.

Presently, data and software tools that are necessary to produce the SC and FC at an aggregate level, for varying levels of aggregation, have recently become available in the public domain ([7, 20, 21, 27]). A notable example is the Human Connectome Project (HCP) ([7]). In HCP the brains of over a thousand people have been imaged extensively. According to [8]: "The goal of the Human Connectome Project is to build a "network map" (connectome) that will shed light on the anatomical and functional connectivity within the healthy human brain, as well as to produce a body of data that will facilitate research into brain disorders such as dyslexia, autism, Alzheimer's disease, and schizophrenia".

Observe that better understanding of the brain has implications that go beyond medicine, biology, and philosophy. The Artificial Neural Network is a transformative computational paradigm inspired by the brain, but its applicability seems limited to pattern recognition. Better understanding of the brain's generation of common sense, understanding, and emotion can inform novel computational and communication paradigms (see [26]).

Connectomics studies the whole brain as a network, aiming to understand its organizational properties. For this purpose neuroscientists have recently turned their attention specifically to GIS functionality (see e.g. [12]), and we feel that the Spatio-Temporal Information research community can play an important role in better understanding the brain. Most existing work in connectomics, particularly in data mining (see [3]), address either the Functional or the Structural connectome, but not both. As demonstrated in this paper, the GIS community has expertise that puts it in a unique position to study the combination of the brain structure and dynamics. A preliminary spatio-temporal approach was published by the author jointly with neuroscientists ([13, 25]).

The rest of the paper is organized as follows. In sec. 2 we discuss a spatial approach to understanding the modularity of the brain. In sec. 3 we discuss spatio-temporal objective functions for analyzing the brain; and in sec. 4 we conclude and discuss challenges.

2. MODULARITY OF THE BRAIN

This section discusses spatial analysis of the brain. An important step in understanding the brain is finding its salient components or modules. Existing connectomics work focuses on parcellations of the brain based on an atlas of anatomically defined structures such as the hippocampus. This means that spatially adjacent brain imaging voxels are aggregated into parcels [15] according to a fixed and restricted number of options. Moreover, there is no consensus parcellation. However, many topological objective functions used in neuroscience, e.g. network efficiency (defined as the average reciprocal of the distance, or weight, between a pair of nodes) and betweenness centrality [15], depend on the parcellation.

Indeed, the optimal parcellation depends on the objective function. For example, the PLACE-function maximizes inter-parcel path lengths and minimizes intra-parcel path lengths [16]. In other words, it finds an aggregation of the voxels into parcels that maximizes the ratio between the average inter-parcel and intra-parcel path lengths. However, the optimal PLACE-parcellation is found by a heuristic algorithm that does not guarantee optimality.

Other objective functions are optimized by different parcellations. In general, given n brain voxels the number of parcellations is $O(n^n)$ [17]. Furthermore, even under simplifying assumptions the problem of finding the optimal parcellation is NP-complete [17].

Fortunately, analyzing the modularity search space is similar to a problem that was studied in economics, AI, and transportation, namely Coalition-Structure Generation (CSG) [18]. The CSG problem is to partition a set of agents (e.g. the travelers issuing origin-destination ride-requests in Manhattan between 10:00am and 10:01am) into coalitions (of taxi ridesharing partners) such that some objective function (the total mileage saved by ridesharing compared to solo-travel) is optimized.

Furthermore, some existing CSG work is applicable. One approach that has proved useful is an anytime algorithm [19]. This approach starts with an approximation of the optimal solution, and then improves it. The larger the computation time allowed for improvement, the closer the algorithm gets to the optimum.

Another promising approach is incremental processing, which we discuss for the rest of this section. The value of an objective function for a parcellation depends on the SC, or the FC, or both. However, the generation of the connectomes based on brain imaging data may take hours of computing time for a single parcellation [20, 21]. Then the exploration of a large number of parcellations may become infeasible even using CSG techniques.

However, consider two parcellations P_1 and P_2 that are identical, except that two neighboring parcels a and b of P_1 have been coalesced into a single parcel c to obtain P_2. Rather than computing SC(P_2) from scratch, incremental processing would take advantage of the fact that SC(P_1) has already been computed in order to reduce the time of computing SC(P_2) from $O(n^2)$ to $O(n)$. This can be done by computing the SC(P_2) matrix entries (c, i) for every node i in P_2; the rest of the SC(P_2) entries are identical to their corresponding entries in SC(P_1). Furthermore, even the entries (c, i) can probably be machine learned based on the SC(P_1) entries (a, i), (b, i), rather than recomputed. What is the error introduced by doing so?

3. GIS-INSPIRED BRAIN ANALYSIS

In this section we discuss two spatio-temporal objective functions, anarchy-gap and discovery-network-confirmation, that are rooted in Intelligent Transportation. Intuitively, the motivation is that dynamic signals in the brain travel along the SC in the same sense that vehicles travel on the road network; and the FC translates into the demand (by signals) for mobility, whereas the SC translates into the supply (of fibers) designed to meet the demand (see Fig. 1).

The anarchy-gap and discovery-network-confirmation functions translate the insights of transportation networks to understanding communication dynamics in brain networks. The two functions represent two methodologies to bring intelligent transportation to bear on brain networks. Each one is applied for a different purpose.

One purpose is to determine if brain networks satisfy certain properties, or are in certain mathematically defined states. Subsec. **a** does so by calibrating transportation networks to match the brain, and then evaluates the function to determine the state.

The other purpose, addressed in subsec. **b**, is to determine whether brain networks perform some tasks that are analogous to tasks performed on transportation networks; for example, whether they search for resources in the way, for example, a taxi driver would search for customers. Here the proposed methodology is to use increasingly accurate algorithms for search execution, and determine whether the results of these algorithms on brain networks become increasingly close to the ground truth.

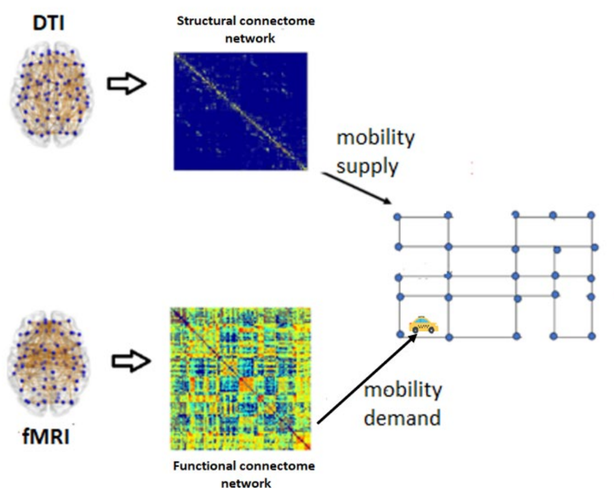

Figure 1: The brain as a mobility supply/demand system

The objective functions discussed in this section serve as a demonstration as to how GIS research can shed light on understanding the brain. Other GIS approaches used to mine urban data such as taxi-trajectories, pollution, bike-sharing, may prove successful in opening up research directions for understanding the brain, and how evolution shaped its efficiency.

a. Anarchy-gap objective function

In transportation one distinguishes between the concepts of equilibrium and optimum. An anarchical system, i.e. one in which each traveler behaves selfishly with the purpose of minimizing her own travel time, settles into a User equilibrium (UE) state. In contrast, if the system is centrally controlled, then the total travel time of all the vehicles can be reduced, leading to a System optimum (SO) state. It has been established that equilibrium and optimum states may differ significantly (see Braess paradox [22]).

In this analogy, one asks the following fundamental control problem: If the brain is centrally controlled, then its “traffic” assignment will give rise to an SO assignment of the signals on the structural connectome, such that the total expected travel times of the signals is minimized. Alternatively, if the brain is not centrally controlled, it is “anarchical” in the sense that each signal acts as an independent agent. In this case, traffic assignment will settle into UE, i.e., a state in which no signal can unilaterally reduce its own travel time. From a neural perspective, a UE assignment represents a system that is slower due to increased signal interference. Such interference (or congestion) in the brain is discussed in ([13, 15]).

Initial steps towards determining whether the brain is in a UE or SO state were reported [13]. There, surprisingly we have found that the SO flows per region are closer to the actual measured brain activity. Therefore, it is more likely that the true signal transport activity within the brain is closer to System Optimum than to User Equilibrium. If the result withstands scrutiny (see rest of subsection), it begs the question what are the mechanisms by which optimality is achieved. Could consciousness be involved? Otherwise, if evolution is responsible for the optimization, what are the mechanisms it uses? In transportation, tolling is a mechanism authorities use for converting UE to SO. If something similar occurs in the brain, where are the traffic control points (toll roads)?

The SO-favorability result was obtained for a particular parcellation, and for healthy subjects. However, it may turn out that the result depends on the parcellation. Another important question is whether the parcellation that produces the maximum gap is similar to known anatomical or functional parcellations. For addressing this question it is necessary to define a measure of similarity between parcellations. This definition could be similar to the edit-distance between strings of symbols in the following sense: the edit distance is the minimum number of voxels that need to be moved to transform one parcel into another.

Another research direction has diagnostic implications. Specifically, the SO-favorability result was obtained for healthy subjects. For depressed subjects, |SO-flow – Actual-flow| was statistically not significantly different than |UE-flow – Actual-flow|. Does this point towards a biomarker for detecting depression? Another possible future research question will ask whether the results hold for the parallel-communication model.

b. Discovery net objective function

An important field of brain research is neural coding [24]. It stipulates that each human experience has a neural code, i.e. a set of neurons that by firing simultaneously produce the experience. However, how such simultaneous firing occurs is unknown. Could neural coding be explained by a process similar to a search in a transportation network? In this subsection we address this vision. And, again, the discussion constitutes the demonstration of an idea that may be more widely applicable.

More specifically, the hypothesis is that the SC and FC are consistent with a Resource Discovery Network (RDN). A RDN is a probabilistic network in which agents follow paths in the graph, searching for resources. Practically, a RDN can be viewed as the road network along with searching agents, e.g. taxi/Uber-drivers searching for customers. Each edge in the network has a traversal cost, and a probability of finding the resource on it. The objective of an agent is to find a resource at minimum (expected) cost. In the brain, the agents are communication signals, and a resource may be a subgraph of the connectome with a certain level/pattern of activity, or a similar object. To test the hypothesis, one can use the structural connectome to construct the RDN, with a traversal cost on each edge. Then use the functional connectome to generate the probability of each edge. Intuitively, this means that we interpret the FC-correlation between two neighbors in the SC as an indication of the probability that a search finds the resource along the edge between the two neighbors.

Now assume that signals in the brain indeed conduct a resource search. Then one would expect that millions of years of evolution would make this search more efficient than, for example, a random walk. Efficiency can be measured in various ways, but all of them would take into consideration edge costs and probabilities. If so, and if indeed the brain conducts a search, then one would expect the traffic generated by an algorithm that takes into consideration the edge costs and probabilities in order to do the search to be closer to the traffic measured by the FC than the traffic generated by a Random Walk algorithm. Thus, to test the RDN hypothesis we evaluate the error of four increasingly efficient search algorithms, starting with a Random Walk and ending with the decision-theory based Expected Cost Minimization (ECM) algorithm (see [23]).

The error of a search algorithm SA for a parcellation P can be computed as follows. For each pair of nodes v and w that are not necessarily neighbors, compute $f(v, w, P)$ which is the probability that a search using SA and starting from v ends at w. Then, assuming P has n nodes, the error of SA is the average difference $|f(v, w, P) - |FC(v, w, P)||$ over all pairs of nodes v and w, where $FC(v, w, P)$ is the value of the functional connectome matrix entry (v, w) for the parcellation P. Formally, $ErrorSA(P) = \frac{2(\sum_{v,w}|f(v,w) - |FC(v,w)||)}{n(n-1)}$. In other words, using the FC as the ground truth, compute the error of SA (the pairs of FC nodes used in the generation of the RDN can be excluded in computing the error).

Then the hypothesis is supported if the error decreases as the efficiency of the search algorithm increases. More precisely, denote by SA_i, $i = 1 \ldots 4$ four search algorithms in order of increasing efficiency, with SA_1 being Random Walk and SA_4 being ECM. Let the Discovery-network-confirmation function be defined for parcellation P as $Dnc(P) = \sum_2^4 (ErrorSA_i(P) - ErrorSA_{i-1}(P))$. So the Dnc function is the sum of the error improvement as the algorithm efficiency improves. Obviously, $Dnc(P)$ may be negative, in which case the hypothesis is refuted for P. And if $Dnc(P_1) > Dnc(P_2)$, then parcellation P_1 confirms the hypothesis more than P_2.

In this case $Dnc(P)$ serves as the objective function. What are the maximum and minimum of this function over the possible parcellations? Does the parcellation that optimizes the Dnc function correspond to a known one? Observe that even if $Dnc(P)$ is positive for all parcellations, it doesn't yet confirm that the brain is a RDN; it only indicates that further investigation is warranted.

4. CONCLUSION

In this paper we proposed a vision of exploring the human brain as a spatio-temporal object, using spatio-temporal information analysis tools. We also pointed out some possible directions and approaches to do so. More specifically, we pointed towards spatial aggregation into parcellations of the brain, and the integration of brain structure and dynamics.

The connectomics field is in its infancy. Decoding the connectome at the cellular level is a significantly more difficult task than sequencing the human genome, and the field of connectomics is currently at the level of genomics in the 80's. This presents both challenges and opportunities. This paper focused on the opportunities for the spatio-temporal research community.

The challenges are several. First is that although the brain is still very poorly understood, there exists a lot of work on connectomics ([15]) and new results have to be put in context. Second is that often collaboration with neuroscientists may be necessary in order to ensure that the questions addressed are relevant and that the results are reasonable; nevertheless, the whole neuroscience approach to understanding the brain has recently been challenged [2], and the problem is ripe for new perspectives. Third is that the GIS community often considers moving objects that can be individually tracked, whereas in connectomics structure and dynamics are currently only available in aggregate. Finally, computer networking approaches may also need to inform the GIS work.
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