A Postulate: Connectome Development is the Driving Factor of Brain Growth

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***Abstract*—We postulate that the consensus architecture inherent in the Common Model of Cognition (CMC) not only captures decades of progress in cognitive science and modeling human and human-like intelligence, but that the CMC also connects and strengthens the idea that brain growth is directly correlated to connectome development. In this paper, we show how these relationships are driven by the development of the communication links, the synapses, between the axon and the dendrite, hence providing interneuronal communication, in essence, we show how these are driven by the connectome development. We provide a mathematical means for defining brain growth of the grey matter layers, lobes and the white matter pathways.**

***Keywords*—connectomes; fetal brain development; artificial intelligence.**

I. Introduction

We postulate that, because it is commonly accepted that common sense in humans and animals requires priori and posterior knowledge [1], if one were to synthesize a mechanism to store priori and posterior knowledge, one would need to mathematically emulate steps in neuroscience that map the development of the fetal brain from conception to two years of age. This mapping will include, but is not limited to i) emulating how the directionality of brain signals in the white matter of the brain form a plurality of synaptic pathways [2], that enable a flow of information between distant gray matter regions [3], ii) presenting a modular network topology in the brain from the first days of life [4] [5], and iii) adhering to the recent mapping of the human connectome [6] [7].

Herein, we postulate the ability of tracking infantile brain development over time. Using data collected from the baby connectome project [8], we will derive the growth rates and accelerations of the brain regions of grey matter and the pathways of the white matter. The resulting growth rates and accelerations along with their time of occurrence provide us with a sequence of events in the infantile brain development. The resulting sequences are then utilized as a script for the brain model development, defining which Regions of Interest (ROI), layers and pathways are deployed, when and where. Accordingly, we present the first step towards building a developing model reflecting the infant human brain development. This model provides the physical structure of the brain's development, laying out which structures are available to learn functionality over time. Thus, the functionality can only be learned if the physical structure exists and the actual neurons are trained with posterior experience leading to knowledge. Because we are limited by the data available, the specific experiences over time from conception to two years of age are not available. Hence, our model is limited to physical growth until experiential data is tracked for subjects.

The rest of this paper is structured as follows. In section II, we discuss brain development. In section III, we explain our dynamic modeling of brain growth. In section IV, we discretize growth into solvable problems. In section V, we present our conclusion and future work.

II. Brain Development

Recent research in brain development centers on how a first set of neurons that become grey matter grow radially outward before a second set of neurons that will form white matter pathways, grow tangentially underneath the first set of neurons and consequently pushes it outward [9] [10] [11] [12]. In the first six months of fetal growth the brain is driven by genetic influences [11] including developments in the womb that are more priori than posteriori. Zollei *et al.* [13] found myelin accumulation was critical in the development in the fetus brain, that included 14 white matter pathways, increased fractional anisotropy (FA), and decreased mean diffusivity (MD). After the first six months, the brain continues to develop its white matter pathways up the 42 known bundles [14] in the adult.

A. Recent Brain Atlas Research

In order to appreciate our contribution to optimizing brain atlas research we review the state-of-the-art in this field. In building a more efficient and accurate pediatric brain atlas we model the lobe and pathway development from instantiation through 2 years of age by leveraging 4D surfaces introduced by Li *et al.* [15] where separate surfaces were created for various intervals of time from birth to 24 months of age. Our model is unique from Li *et al.*'s 4D surfaces because we include pathways and their connections in our model. We note that Maffei *et al.* [14] developed a pathway atlas they integrated it into their `TRACULA`; however, our model is unique from Maffei *et al.*'s work as we are particularly interested in the neurological growth from conception to two years of age. Our age range inherent in the mapping of our model also

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differentiates us from work performed by Maier *et al.* [16] who refined pathway definitions from several researchers to produce ground truth for the fiber bundles. To effectively model the brain's growth, as alluded to above, we have differentiated space and time in order to observe the *rate and acceleration* of growth. Here, our model focused on keeping track of how the fetal brain grows. Fetal neuronal growth is complex and in order to effectively track said growth, the resulting system needs to track how the fetal brain produces 250,000 nerve cells every minute from conception to birth [11] that form pathways and six distinct compartments that become lobes. Our system tracks the brain lobes as they move through the brain. More so it will also track the new lobes appearance and their subsequent motion to their destination and track the pathways appearance and growth as they connect the lobes.

B. Recent Common Model of Cognition Research

The Common Model of Cognition (CMC) not only captures decades of progress in cognitive science and modeling human and human-like intelligence as proposed by Stocco *et al.* , [17], but, as described in their paper, the CMC also connects and strengthens the idea that brain growth is directly correlated to connectome development. This view that the fetal brain's network develops in conjunction with the connectomes is well-supported by large-scale analysis of the human functional connectome. This paper adds to this concept because we show that it is commonly accepted that common sense in humans and animals requires priori and posterior knowledge which means that if one were to synthesize a mechanism to store priori and posterior knowledge, one would need to mathematically emulate steps in neuroscience that map the development of the fetal brain from conception to two years of age.

The CMC proposed by Laird *et al.*, [18] is comprised of a set of principles that summarize the similarities of multiple cognitive architectures that were developed over the course of five decades in the fields of cognitive psychology, artificial intelligence, and robotics [17]. The CMC has been used to design cognitive agents because agents exhibiting human-like intelligence share five functional components: a feature-based declarative long-term memory, a buffer-based working memory, a system for the pattern-directed invocation of actions represented in procedural memory, and dedicated perception and action systems. Importantly, the CMC has been used as a basis in computational neuroscience in robotics' AI system and artificial neural networks including but not limited to DeepMind's AlphaGo [17], look-ahead search, working memory and procedural memory, in addition to dedicated systems for perception and action [19] and the Differentiable Neural Computer [20]. Therefore, the cross-correlation between the CMC connecting robotics and the fetal brain deems it as a critical resource in validating connectomic perturbations and fetal brain growth,

III. Dynamic modeling of Brain Growth

As mentioned above, we model the brain's growth by differentiating by space and time. Here, the space differentiation shall consider three differing structures, called 'spaces' of the brain, i) the grey matter, ii) the white matter and the iii) intersecting matter. In each space separate entities will be called out. For the grey matter space the entity distinction shall be the name of the brain lobe or layer. For the white matter space the entity distinction shall be the white matter pathway. For the intersecting matter the entity distinction shall be the combined pathway-lobe pair. Additionally, the intersecting matter represents the neuronal pathways terminating into grey matter lobes, a definite intermingling of volumes that shall be better defined by future research. We provide a location and volume description for each lobe in the grey space, each pathway in the white space, and each pathway-lobe pair in the intersecting matter, for each time instance, if the entity exist at that time. Additionally the pathway entities include the set of streamline definitions that comprise that particular pathway. The streamline definition includes the coordinates of each axonal segment found by MRI. With the longitudinal data of position and volume over time, Curve fittings shall provide the functions for individual entity volume growth and positional movement. These functions shall be integrated into a differential equation representing the position movement and a differential equation representing the volume growth for each of the lobes, pathways, and pathway-lobe pair. Further refinement of these spaces may be possible in the future.

IV. Discretizing Growth into Solvable Problems

Our goal is to mathematically model the growth of the brain. There are quite a few facets to consider. The brain starts by building the layers of the grey matter and then builds the white matter connections underneath them. The layers of the grey matter development is different from the white matter development. Separate models will be developed and then combined. Both developments contribute to the brain volume growth. The grey matter development might take into consideration several factors including the neuronal growth, the movement towards the skull, the changes in density of the separate layer and the insertion of white matter pathway connections. The white matter development starts after the grey matter development. The white matter development is different from the grey matter development due the oligodendrocytes, glial cells, that excrete the myelin around the axons, producing the white. For each layer and for each pathway, a model will be developed as data becomes available from the connectome project. Several measures are currently used to describe the brain such as Fractional Anisotropy (FA), Mean Diffusivity (MD) [13], Cortical Thickness, surface area, gyrification, and position [15]. Therefore, longitudinal parameter and data values representing brain structure with collected data over time, are candidates for the same analysis we propose.

For instance, given the volume measurements collected over time, we can plot the volume over time and curve fit to

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produce a function for volume over time. The challenge is locating the method for curve fitting is finding the method that minimizes error. With the function *VolumeOverTime*, we then take the first and second derivatives to give the growth rate and acceleration. This same approach can be applied to any brain measurements that have been collected. Myelination over time should be included for the white matter model. The sum of these functions provide the brain development model. There will be intersecting variables in these functions that will need to be resolved. Volume is dependent on density, which is dependent on the growth rate of the skull and its volume. First we have the total brain volume over time as the sum of the volumes of the grey matter layers volume and the sum of the white matter pathway volumes.

$$TV(t) = \sum(GLV_{t,i}, i = 1..14 + \sum(WPV_{t,j}, j1.. = 42) \quad (1)$$

where GLV is the grey matter layer volume for each of the fourteen grey matter layers and WPV is the white matter volume for each of the 42 white matter pathways. We take the derivative of both sides.

$$TV'(t) = \sum(GLV'_{t,i}, i = 1..14 + \sum(WPV'_{t,j}, j = 1..42) \quad (2)$$

where we now have GLV' as the growth rate of grey matter layers over time and WPV' as growth rate of the white matter pathways over time. These growth rates give the rates at which these distinguishable brain regions shall grow in our synthesis of the infantile brain development. We now take the second derivative.

$$TV''(t) = \sum(GLV''_{t,i}, i = 1..14 + \sum(WPV''_{t,j}, j = 1..42) \quad (3)$$

where we now have GLV" as the acceleration of grey matter layer growth over time and WPV" as acceleration of the white matter pathway growth over time. These accelerations give the time at which these distinguishable brain regions grow in our synthesis of the infantile brain development. From [10] [11] we know that these individual regions of interest develop in an almost prescribed order with certain functions taking precedence, such as vision and auditory. What we have defined here is a means to quantify the mathematical order of growth by using the accelerations and growth rates.

A region of interest or pathway starts growth with an acceleration of growth, from no existence to growth. When the growth is completed the acceleration and the growth rate falls back to zero. Therefore, we can determine the ordering over time of the infantile brain development. We show an example of the difference in growth between two regions of interest in Figure 1. In order to test our hypothesis, we generated random sample data to reflect differing rates of growth; the red region shows the volume difference of the two regions over time. If the curve fitting provides a mathematically twice differentiable function then a differential equation can be developed for the growth of a specific region over time. This will lead to the investigation of any patterns of development.

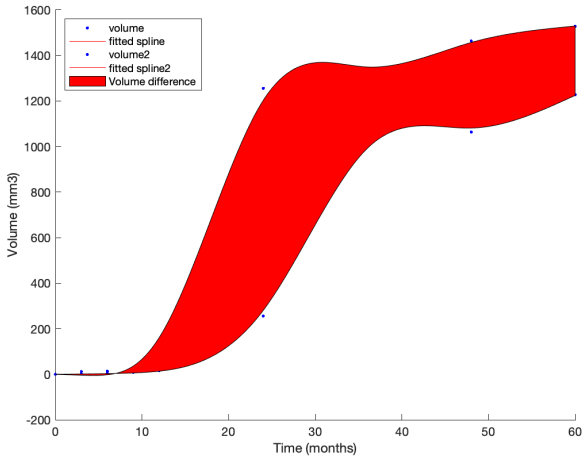

Fig. 1. The difference between two brain regions volume over time.

We show the growth rate and acceleration in Figure 2. The growth rate and acceleration must be positive going from no volume to the identified region. Our example used spline curve fitting which probably produced a piece-wise function that would not be friendly to differentiation for pattern investigation. This process could be expanded from conception to two years of age to death, possibly identifying the negative growth in dementia.

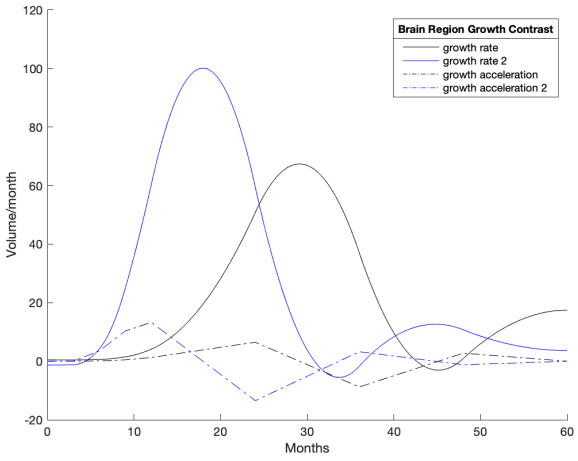

Fig. 2. The growth rate and acceleration between two brain regions over time.

V. Conclusion and Future Work

We have described how the brain growth model is inherently linked to connectome growth. It is generally accepted that Rapid cortical Gyrification Index (GI) and Local Gyrification Index (LGI) growth in the early postnatal period is related to 1) an increase of dendritic arborization [21] [10] and 2) growth of the terminal axon arborization, synaptogenesis [21]. We can logically determine that because all of the aforementioned

occurs inside of the fetal brain's connectome development, that these connectomes are therefore a major factor in determining fetal brain development *per se*. We therefore deduce that it will be interesting to investigate how the cortical LGI relates to the underlying WM connectivity. Lastly, while relationships have been established between several factors, it is our hypothesis that neuronal proliferation, and the glial proliferation providing the myelination for the axons, to protect their signals, are a contributing force in brain growth. The connectome model will contribute a means to efficiently define and predict brain growth not seen before. Furthermore, a second subset of our hypothesis is the aforementioned moves existing structures away from their origin to their predestined position in the brain.

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