Introducing and Applying Newtonian Blurring: An Augmented Dataset of 126,000 Human Connectomes at braingraph.org

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Abstract

Gaussian blurring is a well-established method for image data augmentation: it may generate a large set of images from a small set of pictures for training and testing purposes for Artificial Intelligence (AI) applications. When we apply AI for non-imagelike biological data, hardly any related method exists. Here we introduce the “Newtonian blurring” in human braingraph (or connectome) augmentation: Started from a dataset of 1053 subjects, we first repeat a probabilistic weighted braingraph construction algorithm 10 times for describing the connections of distinct cerebral areas, then take 7 repetitions in every possible way, delete the lower and upper extremes, and average the remaining 7-2=5 edge-weights for the data of each subject. This way we augment the 1053 graph-set to 120 x 1053 = 126,360 graphs. In augmentation techniques, it is an important requirement that no artificial additions should be introduced into the dataset. Gaussian blurring and also this Newtonian blurring satisfy this goal. The resulting dataset of 126,360 graphs, each in 5 resolutions (i.e., 631,800 graphs in total), is freely available at the site \url{https://braingraph.org/cms/download-pit-group-connectomes/}. Augmenting with Newtonian blurring may also be applicable in other non-image related fields, where probabilistic processing and data averaging are implemented.

Introduction

Gaussian blur operations (Mair et al., 1996; Cho and Don, 1991; Erdem and Tekalp, 1990) are standard tools in image processing for different purposes. In
Artificial Intelligence (AI), it is widely used for image-data augmentation, i.e., increasing the size of the training and testing image databases by blurring some parts of the original images and adding the resulting pictures to the dataset (Talukdar et al., 2018; Andriyanov and Andriyanov, 2020; Lands et al., 2020). The augmented dataset is applicable for pattern recognition tasks with AI tools, and — since no new objects were artificially introduced, just some parts of the images blurred — the integrity and the validity of the image-set will not be hurt. Additionally, in many applications in pattern recognition, the positive or negative identification of patterns is desirable even when some noise (i.e., blurring) is present in the images.

In non-image datasets, and especially biological datasets, similar augmenting techniques are generally missing. In the present contribution, we describe an augmenting method, which is called “Newtonian blurring”, paying tribute to Isaac Newton’s Binomial Theorem and binomial coefficients (Newton, 1687). The Newtonian blurring is introduced and first applied here for augmenting a set of human braingraphs.

**Human braingraphs**

Human braingraphs (or connectomes) describe the cerebral connections between the anatomically identified areas of the human brain. Human brain, in a simplified setting, consists of gray matter and white matter. Gray matter is – again, with simplifications – formed from the bodies (or somas) of the neurons, and the white matter from the axonal fibers of the neurons: these fibers connect the somas of the neurons. The white matter also contains myelin covers of these fibers, providing electrical insulation of the axonal fibers. The gray matter is situated on the outer surface (the cortex) of the brain, and also in some subcortical regions; the white matter can be found under the cortex, in the internal parts of the brain.

It is a very interesting question to map the neuronal level connections of the brain: in this mapping, a graph is defined, where the nodes correspond to neurons, and an edge connects two neurons if the axon of one of them is connected to the other’s dendrite. Unfortunately, no such graph can be measured for the human brain, which has 80 billion neurons: we simply do not have methods for discovering all the connections of such a great number of vertices. The nematode worm *Caenorhabditis elegans* is the only developed organism, for which such a graph is described (White et al., 1986), but it has only 203 neurons. Very recently, it is announced that the neuronal level connectome of the fruit fly *Drosophila melanogaster* (Zheng et al., 2018) is within our reach in one or two years, but today only the connections between some 25,000 neurons are available from the total of 100,000 neurons of the flybrain, i.e., the brain of the fruit fly (et al., 2020).

The connectome (or the braingraph) of humans can be described today in a coarse resolution: the vertices correspond to around 1000 anatomically identified areas (called ROIs, Regions of Interests) of the gray matter. We write here “areas” instead of “volumes”, since, in the cortex, the gray matter is relatively thin, typically 1-3 mm thick. The edges of the graph connect those pairs of
vertices, between which a magnetic resonance imaging (MRI) workflow discovers axonal fibers (Hagmann et al., 2008; Cammoun et al., 2012). More exactly, diffusion MRI is capable of identifying the directional distribution of the water molecules in the neurons of the brain. This distribution is isotropic in the large body (soma) of the neurons, but it has a definitive direction (i.e., it is anisotropic) in the thin and long, tunnel-like axon of the neuron. Therefore, axonal fibers can be discovered in the white matter of the brain, and one can construct brain graphs (or connectomes) as follows: two vertices, corresponding to two ROIs, are connected by an edge if at least one axonal fiber is discovered between them. The number of fibers detected is assigned as weights to the edges. For more details, we refer to (Hagmann et al., 2008; Kerepesi et al., 2017; Szalkai et al., 2019; Varga and Grolmusz).

As a result of a large, NIH-funded research project, the Human Connectome Project (HCP) (McNab et al., 2013), high-quality diffusion MRI data were published from hundreds of healthy, young adults. Applying this resource, together with an integrated toolset (Daducci et al., 2012) for computing brain graphs from the MRI data, our research group successfully introduced numerous mathematical and graph-theoretical techniques into the analysis of the human brain graphs (Szalkai et al., 2015a,b; Kerepesi et al., 2016, 2017; Szalkai et al., 2017a, 2016; Kerepesi et al., 2018a,b; Szalkai et al., 2019, 2017b; Fellner et al., 2019, 2020a,b,c).

We have also published the brain graphs, computed by us at the site https://braingraph.org. First, we had made available several graph-sets, based on the HCP 500 Subjects Release (Szalkai et al., 2019; Kerepesi et al., 2017, 2016), later we have published 1064 human connectomes, each in five resolutions (Varga and Grolmusz), which were based on the 1200 Subjects Release of the Human Connectome Project. For each set and each resolution, the edges of the graphs are weighted by the fiber-numbers detected between their endpoints.

The 1064 brain graphs, described in (Varga and Grolmusz), were computed by using probabilistic algorithms, and typically, any two runs on the same input yielded slightly different outputs. For increasing the robustness, and the reproducibility, we have applied an averaging and extreme-value deleting strategy, as follows:

**Basic Averaging Strategy**

- For all subjects, the tractography step of the processing, which determined the axonal fibers, connecting the ROIs of the brain, was computed 10 times;

- For each subject and each resolution (i.e., 83, 129, 234, 463, and 1015 nodes), the brain graph of the subject was computed, and ten interim weights were assigned for each edge. The ten interim weights corresponded to the number of fibers detected in the 10 tractography runs, respectively;

- Those edges, which appeared with 0 fibers in at least one of the 10 tractography runs, were deleted;
• For the remaining edges, the maximum and minimum edge-weights were deleted, and the remaining eight weights were averaged (by simple arithmetic mean). This value was assigned to the edge as its (final, non-interim) weight.

In (Varga and Grolmusz) the particular choice of 10 repetitions is analyzed and explained in detail.

In the present contribution, we modify the averaging strategy above and define the Newtonian blurring for braingraphs.

We remark that the averaging process called Basic Averaging Strategy (Varga and Grolmusz) clearly increased the robustness of the results and decreased the variance of the graph weights due to the probabilistic processing.

In the introduction of the Newtonian blurring, we also focus on robustness, and we do not intend to add any artifacts to the data: we just slightly perturb the error-correcting, averaging steps of the real, unmodified data.

We also note that even in the augmented graphs, we have used averaging error correction for increasing robustness.

Discussion and Results

Newtonian Blurring

Here, we describe the new Newtonian Blurring method as a modification of the Basic Averaging Strategy for braingraphs.

• For all subjects, the tractography step of the processing, which determined the axonal fibers, connecting the ROIs of the brain, is computed 10 times;

• For each subject and each resolution, the braingraph of the subject is computed, and ten interim weights were assigned for each edge;

• Those edges, which appeared with 0 fibers in at least one of the 10 tractography runs, are deleted;

• For each subject and each resolution, 7 graphs from the 10 repeatedly computed graphs are chosen in every possible way (i.e., \( \binom{10}{7} = 120 \) ways). Now, for each edge, the maximum and minimum edge-weights out of the 7 are deleted, and the remaining five weights are averaged (by simple arithmetic mean). This value is assigned to the edge as its (final, non-interim) weight.

This way, we augment the starting braingraph-set to a 120-times larger set. The augmented braingraphs do not contain any artificial components: they even contain strict error correction by deleting the extremal edge weights and averaging the remaining five weights.
On the deviation of the augmented graphs

The following is a natural question: How diverse are the augmented graphs, compared to the starting ones? Clearly, one needs certain diversity in the augmented set for the applications in artificial intelligence since simply repeating the starting graph several times is useless. However, as in the Gaussian blurring, where the blurred images are very similar to the original ones, here we can also find a similar situation: the Newtonian-blurred graphs are also similar to the starting one.

For a distance measure, we apply Jaccard-distance for the edges $E(G)$ of graphs $G$:

$$J(G_1, G_2) = \frac{|(E(G_1) \cup E(G_2)) - (E(G_1) \cap E(G_2))|}{|E(G_1) \cup E(G_2)|}$$

The Jaccard-distance of any two graphs is a non-negative number between 0 and 1; it describes the fraction of edges in which the graphs differ.

Figure 1 depicts the distribution of the Jaccard-distances of all the pairs formed from the 120 augmented graphs of the two closest (in Jaccard-distance) graphs from 1053, the graphs No. 101915 and 654350.

From the $120+120=240$ graphs we can form $\binom{240}{2} = 28680$ pairs. The pairs are partitioned in three classes in Figure 1:

- Red class: both members of the pair belong to subject 101915;
- Blue class: both members of the pair belong to subject 654350;
- Green class: one member belong to subject 101915, the other to 654350.

On the x-axis, the Jaccard distance is given; on the y-axis, the count of the pairs of graphs with the given Jaccard-distance (it is a histogram).

In the figure, one can observe that the red, blue, and green classes form Gaussian distributions. Additionally, the expectation of the fraction of the different edges within the 120 graphs of the same origins are a little larger than 2%, while the expectation of the Jaccard-distance in the green class is more than 0.14, i.e., at least 14% of the edges differ.

Therefore, typically, more than 2% of the edges differ in the graphs of the same subject, and in more than 14% in graphs of different subjects.
Figure 1: The distribution of the Jaccard-distances of all the pairs formed from the 120 augmented graphs of the two closest (measured in Jaccard-distance) graphs from the 1053 ones: the graphs No. 101915 and 654350. From the 120+120=240 augmented graphs, we can form 28680 pairs. The pairs are partitioned into three classes: Red class: both members of the pair belong to subject 101915; Blue class: both members of the pair belong to subject 654350; Green class: one member belongs to subject 101915, the other to 654350. On the x-axis, the Jaccard distance is given; on the y-axis, the count of the pairs of graphs with the given Jaccard-distance is shown (it is a histogram).

Conclusions

We have introduced a new augmenting method for non-image data, called Newtonian blurring. With the new method, we have prepared 631,800 augmented braingraphs for artificial intelligence applications (training and testing) and made the set publicly available at the https://braingraph.org/cms/download-pit-group-connectomes/. One important feature of the Newtonian blurring that it would not introduce any artifacts, any artificial perturbation into the data, and, still, it is capable of considerable augmenting for AI applications.

Data availability

The data source of this work is published at the Human Connectome Project’s website at http://www.humanconnectome.org McNab et al. (2013). The parcellation data, containing the anatomically labeled ROIs, is listed in the CMTK nypipe GitHub repository https://github.com/LTS5/cmp_nipype/blob/master/cmtklib/data/parcellation/lausanne2008/ParcellationLausanne2008.xls.
The braingraphs, computed by us, can be accessed at the http://braingraph.org/cms/download-pit-group-connectomes/ site. For each resolution, a compressed archive is available, containing 126,360 graphs. Technical remark: uncompressed an archive containing that number of files takes several minutes, even on fast systems.

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Conflict of Interest: The authors declare no conflicts of interest.

**Author Contribution**

LK and ES invented the novel Newtonian blurring method for braingraphs, BV invented the Basic Averaging Strategy, constructed the image processing system, computed the augmented braingraphs, analyzed the deviation of the braingraphs and prepared the figures, VG has secured funding, analyzed data, and wrote the paper.

**References**

B. A. Mair, D. C. Wilson, and Z. Reti. Deblurring the discrete gaussian blur. In *Proc. Workshop Mathematical Methods in Biomedical Image Analysis*, pages 273–277, 1996.

C.-. Cho and H.-. Don. Blur identification and image restoration using a multi-layer neural network. In *Proc. / 1991 IEEE Int. Joint Conf. Neural Networks /*, pages 2558–2563 vol.3, 1991.

A. T. Erdem and A. M. Tekalp. Blur identification using bispectrum. In *Proc. and Signal Processing Int. Conf. Acoustics, Speech*, pages 1961–1964 vol.4, 1990.
J. Talukdar, A. Biswas, and S. Gupta. Data augmentation on synthetic images for transfer learning using deep cnns. In Proc. 5th Int. Conf. Signal Processing and Integrated Networks (SPIN), pages 215–219, 2018.

N. Andriyanov and D. Andriyanov. Pattern recognition on radar images using augmentation. In Proc. Radioelectronics and Information Technology (US-BEREIT) 2020 Ural Symp. Biomedical Engineering, pages 0289–0291, 2020.

A. Lands, A. J. Kottarathil, A. Biju, E. M. Jacob, and S. Thomas. Implementation of deep learning based algorithms for diabetic retinopathy classification from fundus images. In Proc. 4th Int. Conf. Trends in Electronics and Informatics (ICOEI)(48184), pages 1028–1032, 2020.

Isaac Newton. Philosophiae naturalis principia mathematica, first edition. 1687.

JG White, E Southgate, JN Thomson, and S Brenner. The structure of the nervous system of the nematode caenorhabditis elegans: the mind of a worm. Phil. Trans. R. Soc. Lond, 314:1–340, 1986.

Zhihao Zheng, J Scott Lauritzen, Eric Perlman, Camenzind G Robinson, Matthew Nichols, Daniel Milkie, Omar Torrens, John Price, Corey B Fisher, Nadiya Sharifi, Steven A Calle-Schuler, Lucia Kmeecova, Iqbal J Ali, Bill Karsh, Eric T Trautman, John A Bogovic, Philipp Hanslovsky, Gregory S X E Jefferis, Michael Kazhdan, Khaled Khairy, Stephan Saalfeld, Richard D Fetter, and Davi D Bock. A complete electron microscopy volume of the brain of adult drosophila melanogaster. Cell, 174:730–743.e22, July 2018. ISSN 1097-4172. doi: 10.1016/j.cell.2018.06.019.

C.S. Xu et al. A connectome of the adult drosophila central brain. bioRxiv preprint, 2020. doi: 10.1101/2020.01.21.911859. URL https://doi.org/10.1101/2020.01.21.911859.

Patric Hagmann, Leila Cammoun, Xavier Gigandet, Reto Meuli, Christopher J. Honey, Van J. Wedeen, and Olaf Sporns. Mapping the structural core of human cerebral cortex. PLoS Biol, 6(7):e159, Jul 2008. doi: 10.1371/journal.pbio.0060159. URL http://dx.doi.org/10.1371/journal.pbio.0060159.

Leila Cammoun, Xavier Gigandet, Djalel Meskaldji, Jean Philippe Thiran, Olaf Sporns, Kim Q. Do, Philippe Maeder, Reto Meuli, and Patric Hagmann. Mapping the human connectome at multiple scales with diffusion spectrum mri. J Neurosci Methods, 203(2):386–397, Jan 2012. doi: 10.1016/j.jneumeth.2011.09.031. URL http://dx.doi.org/10.1016/j.jneumeth.2011.09.031.

Csaba Kerepesi, Balazs Szalkai, Balint Varga, and Vince Grolmusz. The braingraph.org database of high resolution structural connectomes and the brain graph tools. Cognitive Neurodynamics, 11(5):483–486, 2017.

Balazs Szalkai, Csaba Kerepesi, Balint Varga, and Vince Grolmusz. High-resolution directed human connectomes and the consensus connectome dynamics. PLoS ONE, 14(4):e0215473, September 2019. URL https://doi.org/10.1371/journal.pone.0215473.
Balint Varga and Vince Grolmusz. The braingraph.org database with more than 1000 robust human structural connectomes in five resolutions. *arXiv preprint arXiv:2008.13273*, (2008.13273).

Jennifer A. McNab, Brian L. Edlow, Thomas Witzel, Susie Y. Huang, Himanshu Bhat, Keith Heberlein, Thorsten Feiweier, Kecheng Liu, Boris Keil, Julien Cohen-Adad, M Dylan Tisdall, Rebecca D. Folkerth, Hannah C. Kinney, and Lawrence L. Wald. The Human Connectome Project and beyond: initial applications of 300 mT/m gradients. *Neuroimage*, 80:234–245, Oct 2013. doi: 10.1016/j.neuroimage.2013.05.074. URL http://dx.doi.org/10.1016/j.neuroimage.2013.05.074.

Alessandro Daducci, Stephan Gerhard, Alessandra Griffa, Alia Lemkaddem, Leila Cammoun, Xavier Gigandet, Reto Meuli, Patric Hagmann, and Jean-Philippe Thiran. The connectome mapper: an open-source processing pipeline to map connectomes with MRI. *PLoS One*, 7(12):e48121, 2012. doi: 10.1371/journal.pone.0048121. URL http://dx.doi.org/10.1371/journal.pone.0048121.

Balázs Szalkai, Csaba Kerepesi, Bálint Varga, and Vince Grolmusz. The Budapest Reference Connectome Server v2. 0. *Neuroscience Letters*, 595:60–62, 2015a.

Balázs Szalkai, Bálint Varga, and Vince Grolmusz. Graph theoretical analysis reveals: Women’s brains are better connected than men’s. *PLoS One*, 10(7):e0130045, 2015b. doi: 10.1371/journal.pone.0130045. URL http://dx.doi.org/10.1371/journal.pone.0130045.

Csaba Kerepesi, Balázs Szalkai, Bálint Varga, and Vince Grolmusz. How to direct the edges of the connectomes: Dynamics of the consensus connectomes and the development of the connections in the human brain. *PLOS One*, 11(6):e0158680, June 2016. URL http://dx.doi.org/10.1371/journal.pone.0158680.

Balazs Szalkai, Csaba Kerepesi, Balint Varga, and Vince Grolmusz. Parameterizable consensus connectomes from the Human Connectome Project: The Budapest Reference Connectome Server v3.0. *Cognitive Neurodynamics*, 11 (1):113–116, feb 2017a. doi: http://dx.doi.org/10.1007/s11571-016-9407-z.

Balázs Szalkai, Bálint Varga, and Vince Grolmusz. The graph of our mind. *arXiv preprint arXiv:1603.00904*, 2016.

Csaba Kerepesi, Balázs Szalkai, Bálint Varga, and Vince Grolmusz. Comparative connectomics: Mapping the inter-individual variability of connections within the regions of the human brain. *Neuroscience Letters*, 662(1):17–21, 2018a. doi: 10.1016/j.neulet.2017.10.003.

Csaba Kerepesi, Balint Varga, Balazs Szalkai, and Vince Grolmusz. The dorsal striatum and the dynamics of the consensus connectomes in the frontal lobe
of the human brain. *Neuroscience Letters*, 673:51–55, March 2018b. doi: 10.1016/j.neulet.2018.02.052.

Balázs Szalkai, Bálint Varga, and Vince Grolmusz. The robustness and the doubly-preferential attachment simulation of the consensus connectome dynamics of the human brain. *Scientific Reports*, 7(16118), 2017b. doi: 10.1038/s41598-017-16326-0.

Mate Fellner, Balint Varga, and Vince Grolmusz. The frequent subgraphs of the connectome of the human brain. *Cognitive Neurodynamics*, 13(5):453–460, 2019. URL https://doi.org/10.1007/s11571-019-09535-y.

Mate Fellner, Balint Varga, and Vince Grolmusz. The frequent network neighborhood mapping of the human hippocampus shows much more frequent neighbor sets in males than in females. *PLOS One*, 15(1):e0227910, 2020a. URL https://doi.org/10.1371/journal.pone.0227910.

Máté Fellner, Bálint Varga, and Vince Grolmusz. The frequent complete subgraphs in the human connectome. *PloS One*, 15(8):e0236883, 2020b. URL https://doi.org/10.1371/journal.pone.0236883.

Mate Fellner, Balint Varga, and Vince Grolmusz. Good neighbors, bad neighbors: The frequent network neighborhood mapping of the hippocampus enlightens several structural factors of the human intelligence on a 414-subject cohort. *Scientific Reports*, 10(11967), 2020c. URL https://doi.org/10.1038/s41598-020-68914-2.