A model of brain folding based on strong local and weak long-range connectivity requirements

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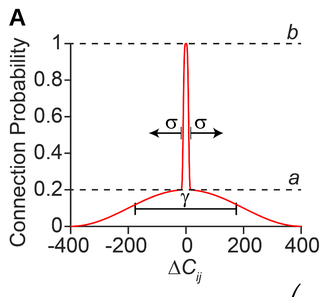
1. Abstract

Throughout the animal kingdom, the structure of the central nervous system varies widely from distributed ganglia in worms to compact brains with **varying degrees of folding in mammals**. The differences in structure may indicate a fundamentally different circuit organisation. However, the folded brain most likely is a direct result of mechanical forces when considering that a larger surface area of cortex packs into the restricted volume provided by the skull. Here, we introduce a computational model that instead of modelling mechanical forces relies on dimension reduction methods to **place neurons according to specific connectivity requirements**.

- Model uses simplified **strong local and weak long-range connectivity**.
- Model predicts a **transition** from separate ganglia through smooth brain structures to heavily folded brains.
- Our model suggests that mechanical forces that are known to lead to cortical folding may synergistically contribute to arrangements that reduce wiring.
- We **reproduce experimentally determined relationships** between metrics of cortical folding.
- Our model provides a unified conceptual understanding of gyrification linking cellular connectivity and macroscopic structures in large-scale neural network models of the brain.

2. Methods



The model cortex is organized into cortical columns *C* labeled form one to n. Each column contains the same number of neurons which are represented by points, with all points of the same colour belonging to the same Column.
A: Connection probability *p* with cyclical topological distance between columns ΔC_{ij}. The spatial reach of the strong local connectivity is set by the variance σ of a Gaussian function. The weaker global connectivity is limited by the exponent γ of a cosine function. The relative strengths of the local and global connectivity are set by *b* and *a*, respectively.

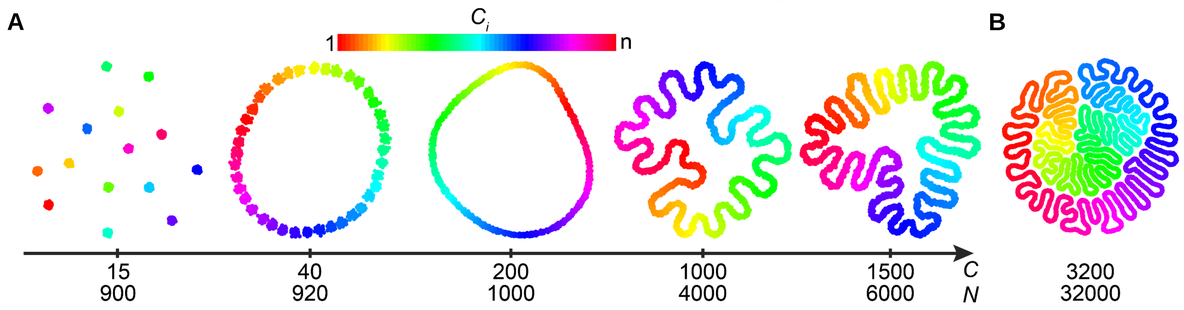
$$p_{k,l} = a\left(\frac{\cos\left(\Delta C_{ij}\cdot {}^{\pi}/_{C}\right)+1}{2}\right)^{\gamma} + (b-a)\cdot exp\left(-\frac{\left(\Delta C_{ij}\cdot {}^{\pi}/_{C}\right)^{4}}{2\pi\sigma/_{C^4}\cdot 10^6}\right)$$

We use a variant of a method that we previously applied to predict relative neuronal positions using ordinal multidimensional scaling (oMDS) (Weigand et al. 2017) to find neuronal arrangements for a given connectivity. Here we use (t-SNE) (van der Maaten and Hinton 2008) instead of oMDS (Borg and Groenen 2005) to predict the positions of neurons based on their connection dissimilarities.

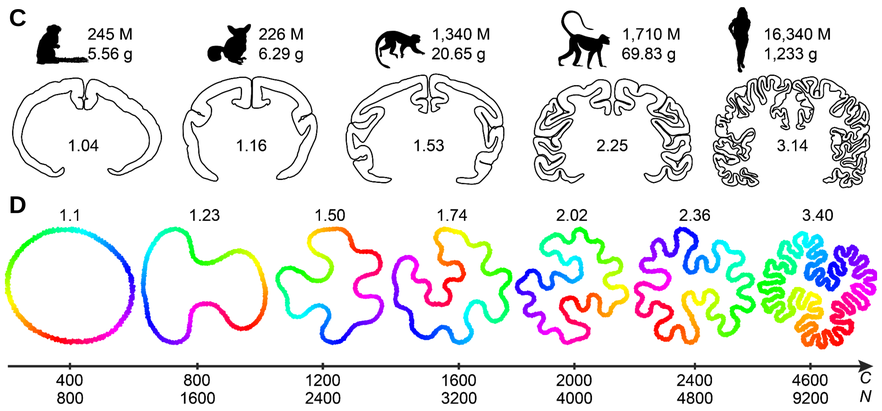
To quantify the morphological features of the modelled folding patterns, we implemented different measurements, the most important of which is the folding index *F*. *F* is the ratio between the exposed circumference A_E and the total circumference A_T.

$$F = \frac{A_T}{A_E}$$

3. Strong local and weak global connectivity predicts a transition in folding patterns

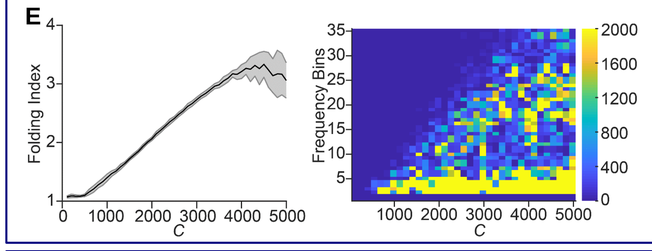


A: Strong local vs. weak global connectivity requirements show that the ratio between the number of neurons *N* and the number of columns *C* determines the extent of folding. We see a transitions from ganglia like structures through lissencephalic cortices to highly convoluted ones while the other connectivity parameters are fixed.
B: Adjusting the connectivity parameters in the right way extreme levels of gyrification can be achieved.



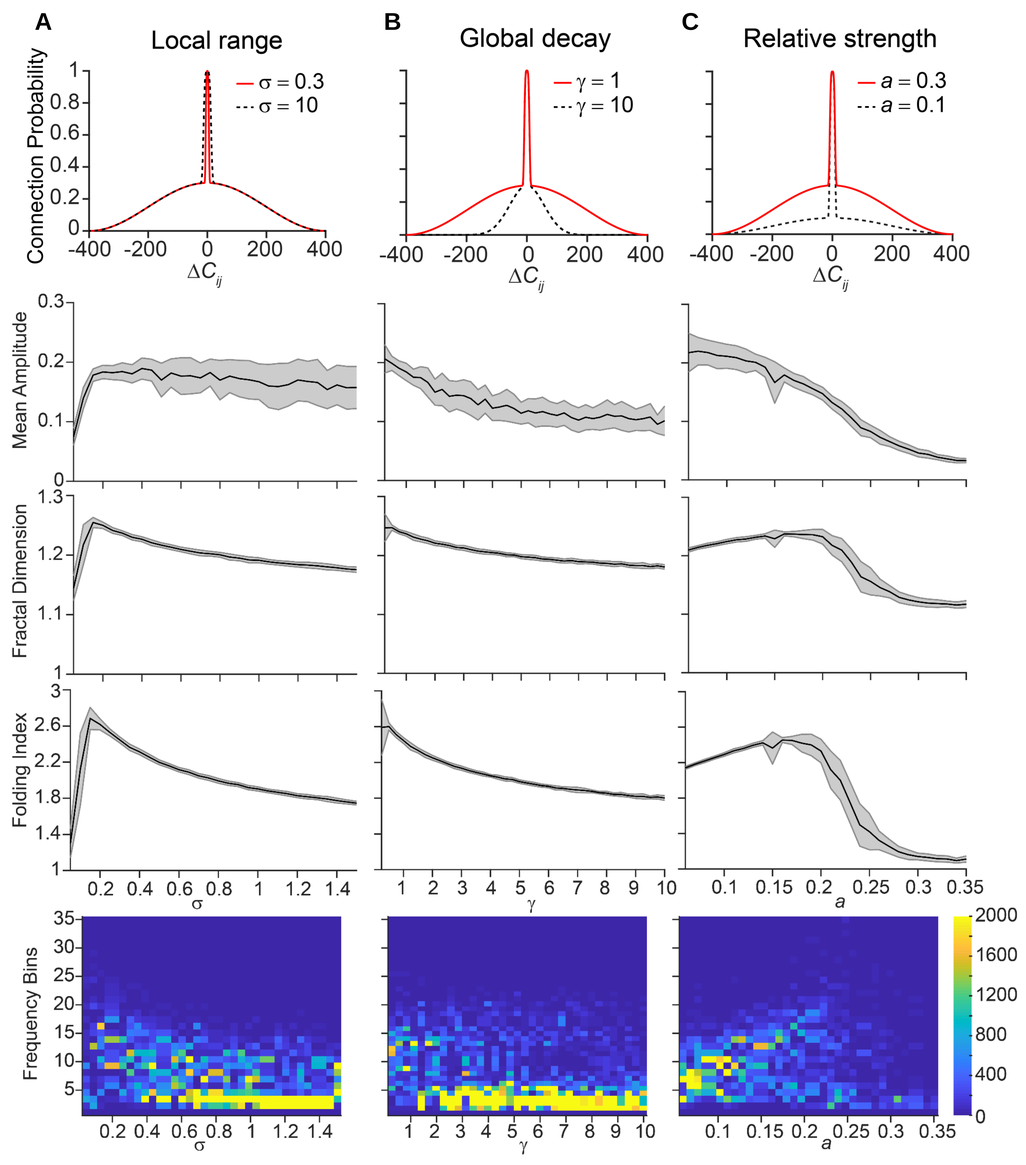
C: Folding degree in coronal sections with folding index of different primates with increasing brain size (from *left* to *right*: marmoset, galago, squirrel monkey, macaque, and human). Gyrification in primate brains increases with brain size.

D: Cortical layouts for different *C*s, with the number of neurons per column *M* and the connectivity fixed. Calculated folding index above each layout; Folding in the model increases with brain size (*C* corresponds to brain size in the model) similarly to primates.

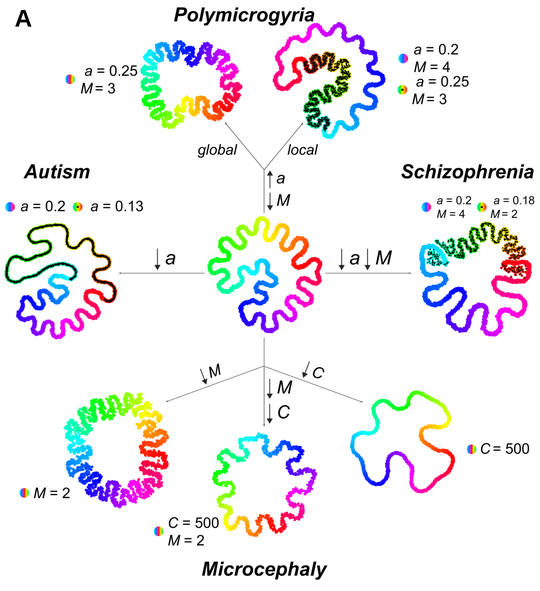


E: Quantification of two different properties of folding patterns for a large range of *C* (same parameters as in (**D**))**.** The mean folding index (*left*) and the frequency spectrum (*right*) with amplitudes of different frequency bins indicated by different colours. Higher frequencies emerge on top of lower ones.

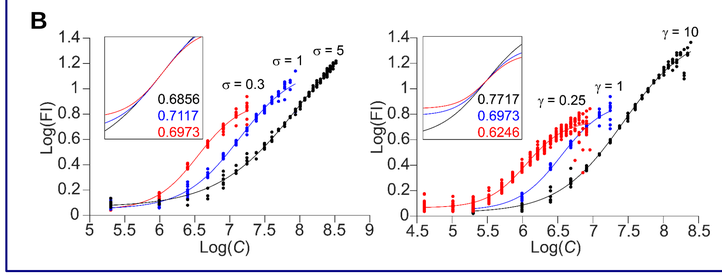
4. Connectivity determines the shape of the folding pattern



5. Predictions for brain disorders and folding scaling behavior



A: The model reproduces pathological changes of the cortical folding pattern in humans. This is done by altering the connectivity parameters in specific sections of the model cortex similar to the changes we find in human brains with certain disorders. (*middle*) Presumptive normal cortical folding pattern in a healthy brain. (*left*) Lowering the strength of global connectivity *a* → deeper folds in that segment similar to changes in the frontal lobe of patients with autism spectrum disorder. (*right*) Schizophrenic patients exhibit increased depth of the superior temporal sulcus and an increased folding frequency in the superior temporal gyrus. Decreasing strength of the global connectivity *a* and the number of neurons per column *M* → model shows a similar change in folding. (*top*) The smaller folds more frequent folds in polymicrogyria could be reproduced by decreasing *M* and increasing *a*. (*bottom*) Microcephaly can be modelled using a lower *C*, *M* or both.



B: The degree of folding scales differentially with brain size between mammalian orders (Pillay and Manger 2007; Zilles et al. 2013; Mota and Herculano-Houzel 2015). In our model changing the range of local connectivity had no impact on the scaling of gyrification. Changing the decay of global connectivity however had a marked effect.

6. Conclusions

- Our model reproduces relationships between folding metrics observed in biology.
- **Strong local vs. weak global connectivity** predicts a transition from ganglia like structures, through smooth to highly convoluted cortices
- Increasing brain size leads to more gyrification
  - ➢ The model explains the **different scaling behavior of folding** with brain size between different mammalian orders by altering the **decay of global connectivity**
- Varying connectivity continuously instead of column numbers also alters amount of folding.
- Stereotypic folding patterns follow local variations of connectivity parameters.
- Model explains pathological changes in the folding pattern including lissencephaly.

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