Modelling the development of cortical networks

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Abstract

The brain shows a highly specific organization also in terms of neural connectivity. How may genetic determination or self-organization influence the layout of cortical systems connectivity? We present a computational model of neural network growth to investigate the necessary factors yielding similar density and clustering as in cortical networks of cat and macaque. Three factors were found. First, growth of the network has to be spatially limited. Second, the position of the initial nodes determines the spatio-temporal gradients of network growth. Third, synaptic formation limited to a certain time window is necessary for homogenous spatial density.

Key words: Cortical connectivity; Development; Network growth; Preferential attachment

1 Summary

The brain shows remarkable differentiation in structure and function. In terms of cytoarchitecture, different areas as well as classes of neurons can be distinguished. Further, neurons and areas exhibit different functions relating to their incoming and outgoing connections and internal processing. The variety in function is also represented by the cortical systems connectivity. Regions with similar function are located near to each other, tend to be connected and to have similar afferent and efferent connections. Looking at the structure of cortical connectivity, the question remains how much is determined genetically and how much is due to self-organization. We used a computational model to investigate the factors being necessary for cortical development.

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We simulated mechanisms of spatial growth so that connections to nearby nodes were more probable than to spatially distant nodes [9]. This could be due to the concentration of unspecific factors for axon guidance decaying exponentially with the distance to the source [6]. The probability that an edge between a new node u and an existing node v was established was

$$P(u,v) = \beta \; \mathrm{e}^{-\alpha \; d(u,v)} \tag{1}$$

with $d(u,v)$ being the distance between the nodes and α and β being scaling coefficients. Nodes that did not establish connections were disregarded. The resulting networks should meet two essential cortical properties. First, distinct structural and functional clusters, as found in the organization of cat and macaque monkey cortical connectivity [7, 3, 10], should arise. Second, the clustering coefficient, that is the percentage of neighbors of a node that are connected with each other [8], should be similar to the value for biological cortical networks.

Only limited growth, giving an area in which new nodes could be formed, yielded network properties similar to cortical networks. The limits could represent internal restrictions of growth (e.g., by apoptosis [5]) as well as external factors (e.g., skull borders). When two initial network nodes were positioned at medio-posterior coordinates, only growth in lateral and anterior direction occurred representing the spatio-temporal gradients found during cortical development [2, 4].

In contrast to real cortical networks, however, the spatial density was larger for developmentally older regions. In accordance with the timing of synaptic formation and myelination in the brain [4], the time in which existing nodes could attract connections from new nodes was limited, that means, the probability of edge formation was decreasing with the age of the existing node

$$P(u,v) \sim age^{-1} \tag{2}$$

Using growth and preferential attachment (BA-model [1]) also yielded similar density and clustering coefficient. However, the scale-free networks resulting from preferential attachment consisted of only one main cluster, in contrast to cortical networks with multiple clusters [3].

This simple model can be extended for future developmental studies and used to test hypotheses of brain development and determine essential factors. For example, we found that spatial borders are required to produce network properties comparable to the real brain. Importantly, the characteristic properties

of networks in the current study could be generated without assuming specific growth factors and receptors. Therefore, simple self-organizing growth mechanisms may be sufficient to create essential network parameters without genetic predetermination. A general understanding of the principles by which cortical connections are formed and a comparison with known anatomical connections of the macaque monkey may also lead to predictions of currently unknown cortical connections in the human brain. With accompanying experimental studies these computational development studies may clarify key mechanisms of brain development.

References

[1] A-L. Barabási and Reka Albert. Emergence of scaling in random networks. *Science*, 286:509–512, 1999.

[2] Harry T. Chugani, Micheal E. Phelps, and John C. Mazziotta. Positron emission tomography study of human brain functional development. *Annals of Neurology*, 22:487–497, 1987.

[3] C. Hilgetag, G. A. P. C. Burns, M. A. ONeill, J. W. Scannell, and M. P. Young. Anatomical connectivity defines the organization of clusters of cortical areas in the macaque monkey and the cat. *Philos. Trans. R. Soc. Lond. B*, 355:91–110, 2000.

[4] Mark H. Johnson. Functional brain development in humans. *Nature Reviews Neuroscience*, 2:475–483, 2001.

[5] K. Kuida, T. F. Haydar, C. Y. Kuan, Y. Gu, C. Taya, H. Karasuyama, M. S. Su, P. Rakic, and R. A. Flavell. Reduced apoptosis and cytochrome c-mediated caspase activation in mice lacking caspase. *Cell*, 94(3):325–337, 1998.

[6] James D. Murray. *Mathematical Biology*. Springer, Heidelberg, 1990.

[7] JW Scannell, C Blakemore, and MP. Young. Analysis of connectivity in the cat cerebral cortex. *Journal of Neuroscience*, 15(2):1463–1483, 1995.

[8] D. J. Watts and S. H. Strogatz. Collective dynamics of 'small-world' networks. *Nature*, 393:440–442, 1998.

[9] B. M. Waxman. Routing of multipoint connections. *IEEE Journal of Selected Areas of Communication*, 6(9):1617–1622, 1988.

[10] M. P. Young. The organization of neural systems in the primate cerebral cortex. *Philosophical Transactions of the Royal Society*, 252:13–18, 1993.