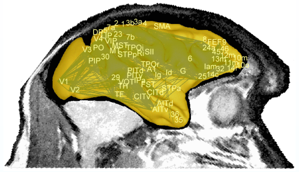


Clustered cortical architecture: Development and Robustness

Marcus Kaiser* & Claus C. Hilgetag
*m.kaiser@iu-bremen.de, International University Bremen, 28759 Bremen, Germany

IUB International University Bremen

Clustered cortical architecture

The brain shows a highly specific organization, also in terms of neural connectivity (Sporns et al., 2004; Kaiser & Hilgetag, 2004c). Our approach is to establish the organization of cortical wiring in the rhesus monkey brain and then use computational modeling to try and identify essential developmental factors that influence the large-scale connectivity of cortical areas.

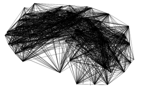
The simulated networks should meet two essential cortical properties. First, distinct structural and functional *clusters* should arise, as found in the organization of cat and Macaque monkey cortical connectivity (Hilgetag et al., 2000; Young, 1993). Second, global network properties, as characterized by the clustering coefficient and the ASP, should be similar to the ones for biological cortical networks. The *clustering coefficient* is the percentage of neighbors of a node that are directly connected with each other (Watts & Strogatz, 1998). The *average shortest path* (ASP) is the smallest number of edges that, on average, have to be passed to travel from any one node to another.

In addition we demonstrate that the cortical topology possess particular robustness after elimination of fiber tracts or areas.

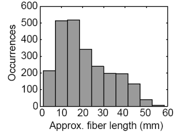
Macaque wiring organization

We analyzed the wiring organization of the macaque cortical network. Average spatial positions of areas were derived from CARET (Van Essen lab - http://stp.wustl.edu/caret.html), and connections between areas were extracted from CoCoMac (http://www.cocomac.org) merging connection data of three articles (Carmichael & Price, J. Comp. Neurol. 346:366,1994; Felleman & Van Essen, Cereb. Cortex, 1:1, 1991; Lewis & Van Essen, J. Comp. Neurol. 428:79, 2000).

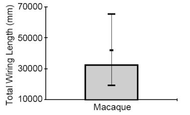
Many long distance connections were found (e.g., V1 – A46). The total length of all connections was between that for a randomly wired network and a network with shortest possible connections. However, while the cortical network uses more wire it has a lower ASP than the minimally wired network.



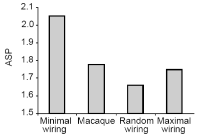
2D-projection of the macaque cortical wiring.



The distribution of approximated fiber length shows a preference for short-distance connections. Nonetheless, quite many long-range connections do exist



The total wiring length of the macaque is greater than that of minimally wired networks (lower mark) but lower than random wiring (middle mark) and longest-possible wiring (upper mark).



For ASP, the cortical network had lower values than networks with minimal wiring. This is explained by the existence of short-cuts linking distant nodes.

Development

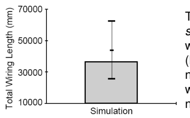
We simulated *spatial network growth*, in which connections were more likely formed to nearby nodes than to spatially distant nodes. This was motivated by the fact that concentrations of growth factors for axon guidance decay exponentially with distance to their source. The probability that an edge was established between a new node *u* and an existing node *v* was

$$P(u,v) = P_{dist}(u,v) = c * \exp(-a\, d(u,v))$$

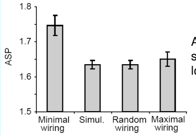
($d(u,v)$ distance between nodes; a, c scaling coefficients)

Nodes that did not establish connections were disregarded (Kaiser & Hilgetag, 2004a).

Our simulations showed that without spatial borders it was impossible to generate brain-like networks (Kaiser & Hilgetag, 2004b). Interestingly, global properties could be generated without involving cortical activity. Also experimental results agree with this outcome (Verhage et al., 2000).



The total wiring length of the *simulated* spatial-growth network was between that for minimally (lower mark) and randomly wired networks (middle mark). This was also true for the macaque network (see left column).



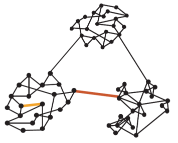
Also, the ASP of the *simulated* spatial-growth networks was lower than for minimal wiring.

How does network structure influence robustness?

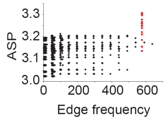
We studied the effect of eliminating edges or nodes in the macaque cortical network. The resulting damage was defined as the increase in the average-shortest path (*ASP*).

Edges between clusters are most vulnerable

Edge frequency (EF), a measure similar to 'edge betweenness' (Girvan and Newman 2002), indicates how many times a particular edge appears in all pairs shortest paths of the network. Among various tested measures it was the best predictor of damage after edge elimination in biological networks. The linear correlation between EF and damage was r = 0.84 for the macaque connectivity network. Interestingly, edges between highly-connected nodes do not seem to correlate with high damage (r = 0.1).



Schematic drawing of network with three clusters. Edges between clusters (red) are more important than within clusters (yellow) as fewer alternative pathways do exist



Elimination of edges between clusters (red) result in a larger ASP. In addition, their edge frequency is highest.

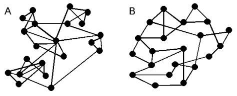
In order to find out where the most vulnerable edges are, we generated 20 test networks with three clusters each and defined inter-cluster connections in analogy to clustered cortical networks (schematic drawing on the left). The plot shows the EF and the resulting damage after edge removal (right). Inter-cluster connections (red) were more vulnerable showing a larger increase in ASP after edge elimination. In addition, these edges also showed a higher edge frequency.

→ Inter-cluster connections are most vulnerable

→ This could explain why some fibers are more critical than others concerning lesions

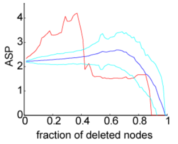
Low vulnerability for random node lesions

In the macaque brain some areas are highly-connected such as LIP or the Amygdala. Highly connected nodes also occur in scale-free networks which are generated by growth and preferential attachment (Barabási & Albert, 1999). We tested whether also behaves like a scale-free network concerning elimination of nodes (Martin et al., 2001; Kaiser et al. 2004).



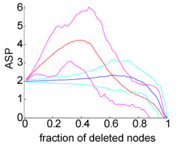
Scale-free networks (**A**) exhibit highly-connected nodes (hubs, here shown at the center) which are improbable in randomly wired networks (**B**).

Nodes were removed one after another either randomly (blue curves) or ranked by node degree, that means, eliminating highly-connected nodes first (cf. Albert et al., 2000). The resulting ASP values of the macaque cortical networks are similar to scale-free benchmark networks but different from random or small-world networks (generated by rewiring a regular network, cf. Watts & Strogatz, 1998).



Macaque cortical network

A large increase in ASP after eliminating highly connected areas first (red) but lower effect for random elimination (blue with standard deviation over 50 trials, cyan)



Scale-free benchmark network

The network was generated by growth and preferential attachment and had similar density and clustering coefficient as the macaque cortical network. For eliminating highly-connected nodes (red, standard deviation in purple) peak value as well as fraction at which the peak occurs is similar to the cortical network.

→ Lesions of highly connected areas can have a great effect

→ On average, however, damage after area lesions (by random elimination) is low

Spatial growth with time windows

In addition to distance dependence, we examined time windows for corticogenesis (Rakic, 2002) as a factor during development. The formation of many cortical areas overlaps in time but ends at different time points with highly differentiated sensory areas (e.g., area 17) finishing last. Therefore, we used a wiring rule by which network nodes were connected if they developed during the same time window.

Algorithm for network development

(1) We used three seed nodes for development. New nodes were placed randomly in space. The time window of the new node was the same to that of the nearest seed node as it was assumed to originate from this node.

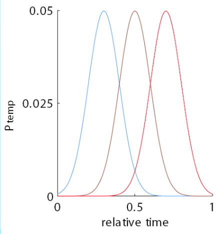
(2) The new node *u* established a connection with an existing node *v* with probability

$$P(u,v) = P_{temp}(u) * P_{temp}(v) * P_{dist}(u,v)$$

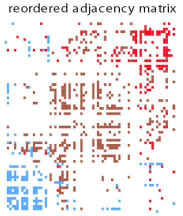
(P_{temp} shown in the figure directly to the right; P_{dist} as for the previous spatial growth model).

(3) If no connections were established, the node was removed from the network

The algorithm was able to yield multiple clusters where the size of clusters and the connectivity between clusters depended on the width or overlap of the time windows.



Different time windows were used for influencing the probability P_{temp} of edge formation. The relative time is normalized to total duration of development (0:start; 1: end).



The reordered matrix represents the connectivity network in such a way that nodes with similar connectivity were placed nearby in the adjacency matrix.

Summary

Cortical networks feature long-distance connections, functional and structural clusters as well as highly connected nodes. Whereas at first long wires appear to be a waste of resources, such short-cuts help to minimize the ASP and therefore enhance the probability for synchronous processing that is unaffected by further intermediate areas.

A developmental algorithm based on spatial distance and multiple time windows for synaptogenesis yielded networks which were similar to cortical networks.

Network topology also relates to robustness. Whereas most edges are within clusters, the few edges between clusters are especially vulnerable. Similarly, in most cases lesions of cortical areas can be compensated quite well. However, removing one of the few highly-connected areas results in higher damage.

Future work

Development of cortical networks: Which factors influence the cortical topology, esp. layer structure and functional specialization?
Structure-Function relationships: How can the function of nodes or similarity between nodes be inferred from the structure of the network. Is this similarity relevant to functional compensation?
System dynamics: How does the topology influence processing or activity spreading as, for example, during epileptic seizures?

References

Albert R, Jeong H, Barabási A-L (2000) Error and attack tolerance of complex networks. *Nature* 406:378–382

Barabási A-L, Albert R (1999) Emergence of scaling in random networks. *Science* 286:509–512

Girvan M, Newman MEJ (2002) Community structure in social and biological networks. *Proc Natl Acad Sci* 99:7821–7826

Hilgetag, C., Burns, G.A.P.C., O'Neill, M.A., Scannell, J.W. & Young, M.P. (2000) *Philos. Trans. R. Soc. B* **355**:91–110.

Kaiser M, Hilgetag CC. (2004a) Spatial growth of real-world networks. *Physical Review E* **69**:036103.

Kaiser M, Hilgetag CC. (2004b) Modelling the development of cortical networks. *Neurocomputing* **58-60**:297-302.

Kaiser M, Hilgetag CC. (2004c) Edge vulnerability in cortical and biochemical networks. *Biological Cybernetics* **90**:311-317.

Kaiser M, Martin R, Andras P, Young MP (2004) Structural robustness of cortical networks (submitted)

Kuida, K. et al. (1998). Reduced apoptosis and cytochrome c-mediated caspase activation in mice lacking caspase. *Cell* **94,** 325–337.

Martin R, Kaiser M, Andras P, Young MP (2001) Is the brain a sale-free network? *Soc. Neurosci. Abstr.*

Rakic P (2002) Neurogenesis in Adult Primate Neocortex: An Evaluation of the Evidence. *Nature Rev. Neurosci.* **3**:65-71.

Sporns O, Chialvo DR, Kaiser M, Hilgetag CC. (2004) Organization, Development and Function of Complex Brain Networks. *Trends in Cognitive Sciences* 8:418-425.

Verhage et al. (2000) Synaptic Assembly of the Brain in the Absence of Neurotransmitter Secretion. Nature 287:864-869

Watts, D. J. & Strogatz, S. H. (1998). Collective dynamics of 'small-world' networks. *Nature*, **393**:440–442.

Young, M. P. (1993). The organization of neural systems in the primate cerebral cortex. *Philos. Trans. R. Soc. B*, **252**:13–18.

M.K. acknowledges financial support by the German National Academic Foundation. Reprints are available at http://www.biological-networks.org/