Modelling Human Cortical Network in Real Brain Space *

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Highly specific structural organization is of great significance in the topology of cortical networks. We introduce a human cortical network model, taking the specific cortical structure into account, in which nodes are brain sites placed in the actual positions of cerebral cortex and the establishment of edges depends on the spatial path length rather than the linear distance. The resulting network exhibits the essential features of cortical connectivity, properties of small-world networks and multiple clusters structure. Additionally, assortative mixing is also found in this model. All of these findings may be attributed to the specific cortical architecture.

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Real-world complex systems are composed of interacting entities with nontrivial dynamical behaviour and complicated interaction topology.[1] Networks have been extensively applied to the descriptions of complex systems for a long time,[2,3] and some models have been proposed. As landmarks, Watts and Strogatz (WS)[4] constructed the small-world model by random rewiring on lattice which may greatly reduce the average-shortest path (ASP), while keeping the clustering coefficient relatively large. Barabási and Albert (BA)[5] suggested that the two mechanisms, growth and preferential attachment, may result in the scale-free property represented by the power-law degree distribution. While the WS and BA models have successfully described the topological properties of many real-life complex networks, some other associated factors must be taken into account when modelling the real systems, such as the distance in spatial networks.

The cortical system network is a representative spatial network, in which connection probabilities depend on the distance between nodes, and long-distance connections are rare, partially because the concentration of diffusible signalling and growth factors decays with distance.[6] Accounting for this constraint, Kaiser and Hilgetag[7,8] presented a spatial growth model in which a new node position is chosen randomly in two-dimensional space, and the establishment of connections from a new node u to one of the existing nodes v depends on the distance $d(u,v)$ between nodes, that is, $P(u,v) = \sigma e^{-\lambda d(u,v)}$. Note that the model does not adopt the power-law edge probability due to its disability to yield the small-world networks. This spatial growth mechanism in the limit of spatial border can produce network properties comparable to those in real cortical systems.[9,10] However, the highly specific organization of cortical systems is not only in its connectivity, but also in its spatial structure, i.e. the spatial arrangement of the neurons. Therefore, the specific cortical structure should be considered in modelling cortical networks.

Accordingly, we present a human cortical network model constructed in the real brain space. Concretely, the nodes in our model are the brain sites, in dimensions $2 \times 2 \times 2\,\mathrm{mm}^3$, placed in their actual position in human cerebral cortex, labelled in the Montreal Neurological Institute (MNI) space.[11] The probability for establishing a connection between two nodes u and v is set as

$$P(u,v) = \beta L^{-\alpha}(u,v), \tag{1}$$

where $L(u,v)$ is the spatial path length (SPL) between the node positions, i.e. the geographical distance, rather than the Euclidean distance; α and β are the scaling coefficients shaping the connection probability, which serve to regulate the dependence of edge formation on the SPL between nodes and to adjust the general probability of edge formation, respectively. The connection probabilities are calculated for all the pairs of nodes, and those larger than one are set to one.

It is well known that there is extensive folding in cerebral cortex, which makes linear distance a dubious parameter. Therefore, we calculate the SPL instead of the Euclidean distance. By the automated anatomical labelling (AAL),[12] human brain is partitioned into 90 regions by the main sulci. Accordingly, the SPL is computed in three cases. First, if two nodes are in the same region, the SPL is estimated by the linear distance, i.e.

$$L(u,v) = d(u,v) = \sqrt{(x(u)-x(v))^2 + (y(u)-y(v))^2 + (z(u)-z(v))^2}, \tag{2}$$

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where x, y and z denote the coordinates of nodes. Second, when two nodes in the same hemisphere but in different regions, they must stride over the obstructive sulci to establish a connection. Therefore, the SPL is set as

$$L(u,v) = d(u,v) + deep(u) + deep(v), \qquad (3)$$

in which $d(u,v)$ is the linear distance between the nodes, and $deep(x)$ denotes the distance between the node x and the bottom of neighbouring sulcus. Due to the complexity of cortical architecture, $deep(x)$ for all the nodes is hardly fixed. For simplicity but no influence on the statistical results, $deep(x)$ is set as a stochastic number between zero and the depth of neighbouring sulcus. It was reported that the average depth of different sulci are different, varying from 15 mm to 20 mm.[13−15] We choose 15 mm as the uniform depth of all the sulci in this model. Third, if two nodes lie in different hemispheres, the SPL is simply calculated by

$$L(u,v) = d(u,0) + d(v,0), \qquad (4)$$

where 0 is the origin of the cerebral space.

According to the above description, the edges in the resulting networks can be primarily classified into two kinds: intra-region and inter-region. Hence, the influence of parameters α and β on the networks can be investigated from local and global aspects.

In the local subnets, investigations focus on the clustering coefficient, the percentage of neighbours of a node that are connected with each other,[4] and the ASP, that is, the number of links that have to be crossed, on average, to go from one node of the network to another. Typically, in a small-world network, we expect the ratio $C_{ratio} = C_{net}/C_{ran} > 1$ and the ratio $\mathrm{ASP}_{ratio} = \mathrm{ASP}_{net}/\mathrm{ASP}_{ran} \sim 1$,[4] where C_{ran} and ASP_{ran} respectively denote the clustering coefficient and the ASP of a comparable random network. A scalar summary of small-worldness is therefore the ratio $C_{ratio}/\mathrm{ASP}_{ratio}$, which is typically larger than 1.[16] As shown in Fig. 1(a), in large parameter ranges $\alpha \in [3;5]$ and $\beta \in [5;50]$, the subnets in left supplemental motor area show the small-world property.

Although it is a local property, the small-world topology of subnets can influence the global dynamics. A previous study on structural and functional clusters of cortical networks in macroscopic scale indicates that the underlying small-world subnets can lead to the formation of diverse dynamic clusters corresponding to different brain functions such as vision and hearing, whereas random connections result in one major cluster, which corresponds to abnormal synchronous activity of large neuronal assembles, for example, during epileptic seizures.[1] Note that in two-dimensional spatial growth model, power-law edge probability is unable to yield small-world networks.[7] We conclude that the small-world properties of the local networks are induced by the specific architecture of human cerebral cortex.

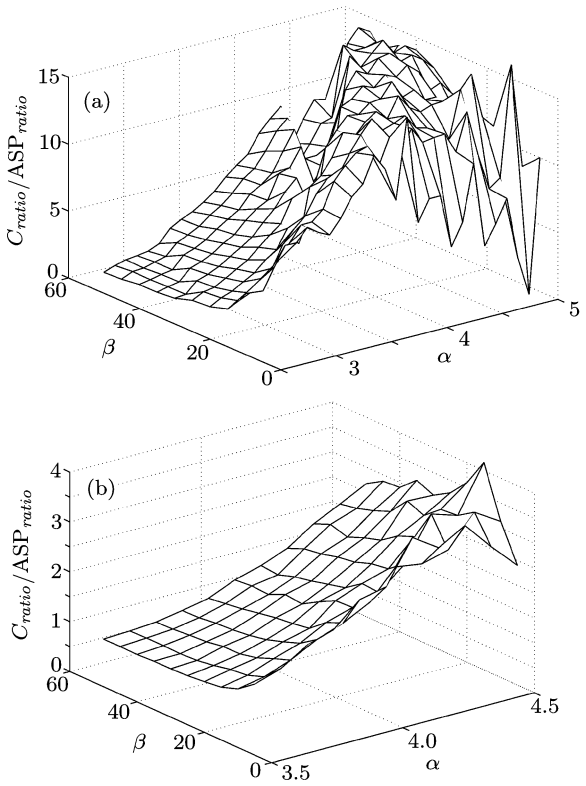

Fig. 1. Ratio of C_{ratio} to ASP_{ratio}, a scalar summary of small-worldness, (a) in the subnets in left supplemental motor area and (b) in the LSCN. A ratio larger than one indicates the small-world property.

The global investigation of the model network focuses on the relationship of different regions, by virtue of large-scale cortical networks (LSCN) abstracted from the original networks. Nodes in LSCN are the regions in cerebral cortex corresponding to the subnets in the original networks, and the edges are established if there are connections between the regions in the original networks. Previous studies on anatomical and functional connectivity have demonstrated that the cortical networks have small-world topology at a macroscopic (regional) scale.[9,17−20] As shown in Fig. 1(b), in a small interval of intermediate values for α around 4, the LSCN exhibits the properties of small-world networks, indicated by the ratio of C_{ratio} to ASP_{ratio} to be larger than 1. Note that the LSCN are fully connected networks at $\alpha < 3.5$, while they are split into fragmentary ones at $\alpha > 4.5$.

The small-world properties reflect the need of the cortical network to simultaneously satisfy the opposing demands of local and global processing.[6,21] On the one hand, the clustering coefficient is a good approximation of the local efficiency, which shows how

efficient the communication is between the first neighbours of a node when it is removed.[22] This implies that cortical networks with high clustering are robust in local information processing even if some neurons languish or suffer attack. Moreover, high clustering promotes functional overlap of densely connected neuronal elements, which are functionally segregated from one another and constitute building blocks (topological modules) of the cortical architecture.[21] On the other hand, a low ASP is of significance in avoiding the additional noise and shortening the signalling delay.[8] In addition, long-range connections are indispensable to synchronous processing over the entire cortical network.

Multiple distinct network clusters, as an essential feature of cortical connectivity, are also investigated. Theoretically, the definitions of connection probability and the SPL would lead to the fact that nodes connect preferentially to the intra-regional ones and selectively to those in other regions. Then multiple clusters structure emerges and the anatomical regions are the distinct clusters. In numerical modelling, modularity[23] is introduced to evaluate the strength of cluster structure in the network. First an $n\times n$ symmetric matrix $\boldsymbol{e}$ is defined for a network divided into n clusters, whose element e_{ij} is the fraction of all edges in the network that link nodes in cluster i to nodes in cluster j. Then, the modularity can be measured by

$$Q = \sum_i e_{ii} - \|e^2\|, \tag{5}$$

where $\|x\|$ indicate the sum of the elements of the matrix $\boldsymbol{x}$. If the number of within-cluster edges is not better than random, we can obtain $Q = 0$. Values approaching 1, which is the maximum, indicate networks with strong cluster structure. In this model, we consider the 90 clusters analysed above. Due to its little influence on the modularity, here β is fixed at 50. The modularity Q of the resulting networks increases with α, varying from 0.6 to 0.95, whereas in practice values of Q for generic networks typically fall in the range from about 0.3 to 0.7.[23] The large values of modularity Q indicate the strong cluster structure that regions are densely intra-connected but sparsely interconnected, which promotes the specialized or modular processing in local neighbourhoods, e.g. somatic motor information processing in the pre-central gyrus. However, considering distributed or integrated processing over the entire network, there should be adequate inter-regional edges. Otherwise, the synchronization of cortical networks would be suppressed or even destroyed.[24] In this model, a small α is appropriate to the cortical networks.

Besides the small-world properties and multiple clusters structure, we also study the hierarchy of the modelling cortical network ($\alpha = 4$ and $\beta = 25$) by the clustering and assortative mixing.[25] Clustering, found in many cases to scale as $C(k) \sim k^{-\lambda}$, is an indication of hierarchical organization in which low-degree nodes belong to well interconnected clusters (with a high clustering coefficient), while hubs connect many nodes that are not directly connected (with a small clustering coefficient).[26] As shown in Fig. 2(a), there is only a weak dependence of clustering from degree in the model network. On the other hand, a network is said to show assortative mixing if a highly connected node tends to connect with other well connected nodes. In the model network, a positive correlation between the degrees of adjacent nodes is found (see Fig. 2(b)), with the Pearson correlation coefficient of the degrees being 0.467. We speculate that the assortative mixing may result from the unequal distribution of cerebral cortex.[27] In the central and dense regions, nodes always have large degree and they connect each other, while in the marginal and sparse regions, nodes link to each other with small degree.

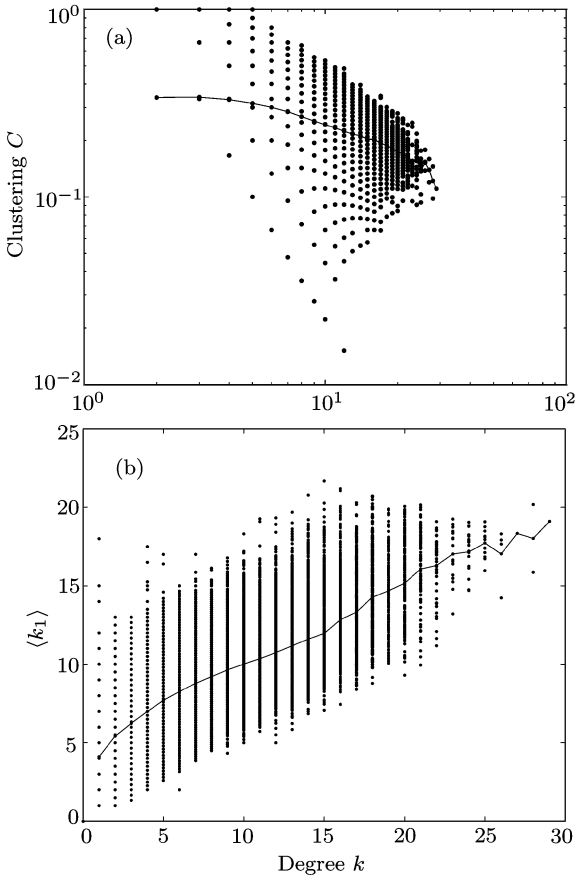

Fig. 2. (a) Plot of clustering C versus degree k. (b) Plot of the average nearest-neighbour degree versus degree. Symbols represent individual data and the lines the average values for nodes with the same degree (using $\alpha = 4$ and $\beta = 25$).

In this model, the remarkable features are the introduction of the specific cortical architecture and the

spatial path length between nodes. Compared with the previous study,[7] the local model networks with power-law edge probability exhibit the small-world effect, which can be only attributed to the specific cortical architecture. On the other hand, the SPL depicts the actual connection length in brain space, leading to the phenomenon that the nodes preferentially connect with those in the same region and rarely link to other regions, resulting in the multiple distinct network clusters. As to the nontrivial assortative mixing in the cortical model network, we speculate that it may result from the unequal distribution of the cerebral cortex.[27]

In summary, we have presented a model network of human cerebral cortex constructed in the real-life brain space. Whether nodes connect to others depends on the geographical distance rather than linear distance. The model networks exhibit properties of small-world networks and multiple clusters structure, which are the essential features of cortical connectivity. In addition, assortative mixing is also found in this model. We speculate that these features of the cortical networks may result from the specific cortical architecture.

References

[1] Zemanová L, Zhou C and Kurths J 2006 *Physica* D **224** 202
[2] Newman M E J 2003 *SIAM Rev.* **45** 167
[3] Albert R and Barabási A L 2002 *Rev. Mod. Phys.* **74** 47
[4] Watts D J and Strogatz S H 1998 *Nature* **393** 440
[5] Barabási A L and Albert R 1999 *Science* **286** 509
[6] Sporn O, Chialvo D R, Kaiser M and Hilgetag C C 2004 *Trends Cogn. Sci.* **8** 418
[7] Kaiser M and Hilgetag C C 2004 *Phys. Rev.* E **69** 036103
[8] Kaiser M and Hilgetag C C 2004 *Neurocomputing* **58-60** 297
[9] Hilgetag C C, Burns G A, O'Neill M A, Scannell J W and Young M P 2000 *Philos. Trans. Roy. Soc.* London B **355** 91
[10] Scannell J W, Blakemore C and Young M P 1995 *J. Neurosci.* **15** 1463
[11] Collins C L, Neelin P, Peters T M and Evans A C 1994 *J. Comput. Assist. Tomogr* **18** 192
[12] Tzourio-Mazoyer N, Landeau B, Papathanassiou D, Crivello F, Etard O, Delcroix N, Mazoyer B and Joliot M 2002 *NeuroImage* **15** 273
[13] Hummel T,Damm M,Vent J,Schmidt M,Theissen P,Larsson M andKlussmann J P 2003 *Brain Res.* **975** 85
[14] Savel'ev V I 1984 *Neurosci. Behav. Physiol.* **14** 60
[15] Ebeling U and Steinmetz H 1995 *Acta Neurochir. Wien* **136** 8
[16] Humphries M D, Gurney K and Prescott T J 2006 *Proc. R. Soc.* B **273** 503
[17] Stephan K E, Hilgetag C C, Burns G A, O'Neill M A, Young M P and Kötter R 2000 *Philos. Trans. Roy. Soc.* London B **355** 111
[18] Stam C J 2004 *Neurosci. Lett.* **355** 25
[19] Salvador R, Suckling J, Coleman M, Pickard J D, Menon D K and Bullmore E 2005 *Cereb. Cortex* **15** 1332
[20] Achard S, Salvador R, Whitcher B, Suckling J and Bullmore E 2006 *J. Neurosci.* **26** 63
[21] Sporns O and Zwi J D 2004 *Neuroinformatics* **2** 145
[22] Latora V and Marchiori M 2001 *Phys. Rev. Lett.* **87** 198701
[23] Newman M E J and Girvan M 2004 *Phys. Rev.* E **69** 026113
[24] Huang L, Park K, Lai Y C, Yang L and Yang K Q 2006 *Phys. Rev. Lett.* **97** 164101
[25] Newman M E J 2002 *Phys. Rev. Lett.* **89** 208701
[26] VHazquez A, Pastor-Satorras R and Vespignani A 2002 *Phys. Rev.* E **65** 066130
[27] Jones S E, Buchbinder B R and Aharon I 2000 *Hum. Brain Mapp.* **11** 12