Spatial and modular organisation of brain networks prevents large-scale activation

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http://www.biological-networks.org
Network Science

Rapidly expanding field:

Modelling of SARS spreading over the airline network
(Hufnagel, *PNAS*, 2004)

Identity and Search in Social Networks
(Watts et al., *Science*, 2002)

The Large-Scale Organization of Metabolic Networks.
(Jeong et al., *Nature*, 2000)
Types of neural/cortical connectivity

- **Structural / Anatomical (connection):** two regions are connected by a fibre tract
- **Functional (correlation):** two regions are active at the same time
- **Effective (causation):** region A causes activity in region B

Cortical networks

Nodes: cortical areas

Edges: fiber tracts between areas

Human cortical areas (after Brodmann, 1909)
Cortical networks

Visual pathways

Visual system
Structure and Function in Neural Systems

- Multiple clusters
- Small-world architecture
- Scale-free organisation
- Spatial arrangement

- Development of spatial networks
- Hierarchy and critical activation
Cat cortical network

Multiple clusters/communities

| AREAS | 5Al | 5m | 5Am | SII | SSAI | SIV | SSAo | 4g | 6l | 5Bl | 6m | 5Bm | 6m | 5Bm | 1 | 2 | 4 | 3a | 3b | 7 | AES | PFCL | pSb | 35 | 36 | Amyg | 2b | Sb | Enr | RS | IA | PFCMd | CGA | IG | CGP | PFCMII | EPp | P | AAF | AI | VP(ctx) | All | Tem | Hipp | ALLS | DLS | PLLS | 17 | 18 | 19 | AMLS | 2a | 21a | 21b | VLS | PMLS | PS |
|--------|------|----|-----|-----|------|-----|------|----|----|-----|----|-----|----|-----|----|----|----|----|----|-----|-------|------|-----|-----|------|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|-----|

**SENSORY-MOTOR**

**FRONTO-LIMBIC**

**AUDITORY**

**VISUAL**

Reconstructing connectivity

Macaque visual cortex (31 nodes)

Green: **correct** prediction

Red: **wrong** prediction

Yellow: prediction of **untested** connectivity

Small-world architecture
Small-world features

- Average clustering coefficient

Path length \( \sim 2 \)  
One degree of separation
Scale-free organization
Scale-free networks

(Barabasi & Albert, Science, 1999)  
(Liljeros, Nature, 2001)
Is the brain similar to scale-free networks?
Sequential node removal

randomly = irrespective of degree

targeted = highly-connected nodes first

Spatial arrangement
Reducing neural wiring costs

- Minimizing total wire length reduces metabolic costs for connection establishment and signal propagation.
- Every alternative arrangement of network nodes will lead to a higher total wiring length. (Component Placement Optimization, CPO) (Cherniak, *J. Neurosci.*., 1994)

![Diagram showing rearrangement of nodes A and D]
Previous results supporting CPO

- **Macaque**: layout of cortical prefrontal areas
  (Klyachko & Stevens, *PNAS*, 2003)

- **C. elegans**: layout of ganglia
  (Cherniak, *J. Neurosci.*, 1994)
Rhesus monkey cortical network

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**C. elegans** neural network

Global level (277 neurons with 2105 connections)

Local level (rostral ganglia, 131 neurons, 764 connections)

(White et al., 1986; Choe et al., 2004)
Wiring length distribution

A. Macaque
B. *C. elegans* (local)
C. *C. elegans* (global)

![Histograms showing wiring length distribution](image)

- **Y-axis**: Occurrences
- **X-axis**: Approximated projection length [mm]
Reduced wiring length for alternative placements

Fewer long-distance projections for optimized placement
Networks without long-distance connections

Original network

Minimal wiring

same number of connections preference for short-distance
Why are there long-distance connections?

![Bar chart showing the comparison between original and minimal for Macaque and C. elegans local and global networks.](chart.png)
Benefits of fewer processing steps

- Synchrony of near and distant regions
- Reduced transmission delays
- Less (cross-modal) interference
- Higher reliability of transmission
Altered Connectivity in Alzheimer patients

EEG synchronization Network

Stam et al. (2007) Cerebral Cortex, 17:92
Path length and task performance

Mini Mental State Examination (attention, memory, language)

Diamonds: Alzheimer patients

Empty squares: Control
Development
Real-world networks extend in space!

References

Topological and spatial organization

(1) Preference for short-distance connections
(2) Existence of long-distance connections
(3) Small-world properties
(4) Spatial and topological clusters

Spatial growth

Time windows
Distance dependence

Global connectivity (between areas)
Kaiser & Hilgetag, 2004

Macaque
(one hemisphere)

Local connectivity
Braitenberg & Schuez, 1998
Hellwig, 2000

Rat visual cortex
(layers 2, 3)
Spatial growth

Edge formation probability depends on spatial distance $d$ between nodes $u$ and $v$

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

Kaiser & Hilgetag, Physical Review E, 2004
Resulting network topology

- German highway system
- Yeast Protein-Protein Interaction Network

Cortical Networks
Spatial growth and time windows

**Spatial component:**

\[ P_{\text{dist}}(u,v) = c \cdot e^{-a \cdot d(u,v)} \]

**Time-window dependance:**

\[ P(u,v) = P_{\text{temp}}(u) \cdot P_{\text{temp}}(v) \cdot P_{\text{dist}}(u,v) \]
Development of Clusters

Robustness of small-world properties

Is this model implemented in the brain?

Experimentally testable predictions:

(1) A small overlap of the time windows of two regions should result in fewer fibre tracts between those regions.

(2) Regions with wider time windows should (a) have a larger number of connections and (b) be part of a larger cluster.

(3) Older regions should get more connections than newer regions.
Hierarchy and critical activation

One degree of separation
Critical range of cortical function

High level of activation

Epileptic seizure

Low activation
Standard model:
Balance between inhibition and excitation

Excitatory population

- 

Inhibitory population

+ 

Topological model: Hierarchical modular network

- clusters of sub-clusters of nodes
Spatial self-similarity

Neuron

Cortical network

Box counting dimension:
1.5-1.7

Binzegger et al. (2005), Cerebral Cortex

Box counting dimension:
1.39-1.42

(Kaiser, unpublished)
Hierarchical cluster network model

- 1,000 nodes; 12,000 bidirectional connections
- Activation threshold: >6 presynaptic neurons, stochastic deactivation, $p=0.3$
Comparison networks

- hierarchical cluster
- random
- small-world
Example activation behaviour

- 30 runs
- 100 (10%) randomly activated initial nodes
Robustness for starting parameters

Robustness for spreading parameters

k: activation threshold
v: deactivation probability
Robustness for node exhaustion
Dependence on inter-cluster connectivity

Sustained activity in three clusters for reduced inter-cluster connectivity

Do epilepsy patients have larger inter-cluster connections?
Outlook: Hierarchies and activity spreading

- Subsubcluster activation
  - Spatially near nodes
  - Rapid feedback
  - Rapid oscillation

- Cluster activation
  - Spatially near and distant nodes
  - Slower feedback
  - Slower oscillation
Partial seizure

Xiang and Kaiser, unpublished
£4.5M e-science project started in Oct 2006

4-year PhD Programme:
‘Systems Neuroscience: From Networks to Behaviour’
starting October 2008

Newcastle:
Prof. Colin Ingram,
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Dr Stuart Baker,
Dr Marcus Kaiser,
Dr Phil Lord,
Dr Evelyne Sernagor,
Dr Tom Smulders,
Prof. Miles Whittington

York:
Prof. Jim Austin

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Sheffield:
Dr Kevin Gurney,
Dr Paul Overton

Plymouth:
Prof. Roman Borisyuk

Warwick:
Prof. Jianfeng Feng

Imperial College:
Dr Simon Schultz
Summary

- Cortical networks show properties of small-world and scale-free networks and have a modular organization (clusters).

- Neural systems are optimized for fast processing rather than for saving energy.

- Spatial growth with time windows generates modular small-world networks.

- Hierarchical modules enable robust sustained activity without inhibition or external inputs.
Collaborators

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