Simulation of Biological Neuronal Networks

Cortical networks: Background and simple models

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Outline

Biological background: Cortex structure

Some graph-theoretical concepts

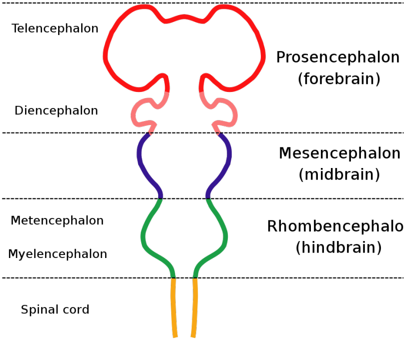
Random networks

The balanced-random-network model (Brunel, 2000)

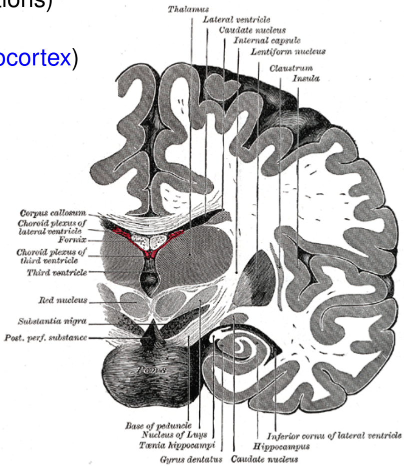
Literature

Macroscopic structure

- forebrain (anterior part of the brain):
  - diencephalon, e.g. thalamus and hypothalamus
  - telencephalon (cerebrum)
    - basal ganglia (motor control, cognition, emotions, learning)
    - limbic system, e.g. amygdala (emotions)
    - olfactory bulb (smell)
    - cerebral cortex (archeocortex + neocortex)

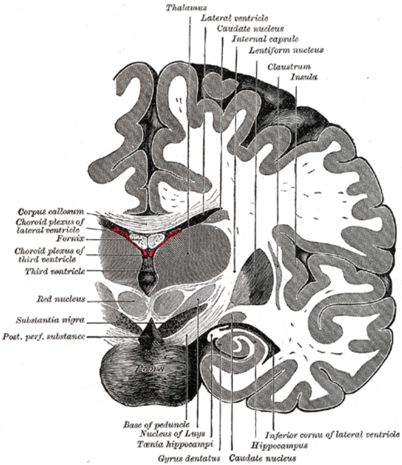


(embryonic vertebrate brain)



Macroscopic structure: Cortex folds

- neocortex = surface of the mammalian brain (gray matter)
- strongly folded in ’higher’ mammals
  - large surface (relatively to skull volume)
  - efficient wiring between cortical areas through white matter



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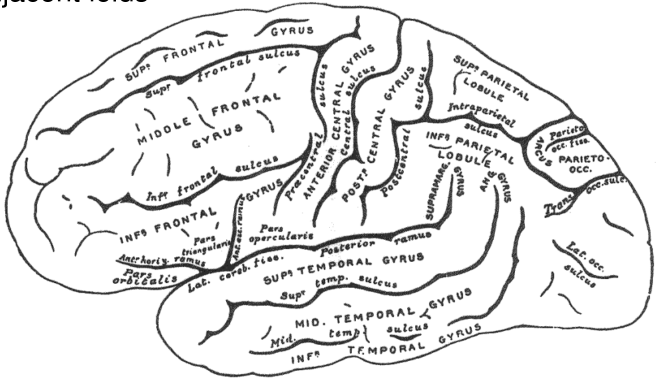
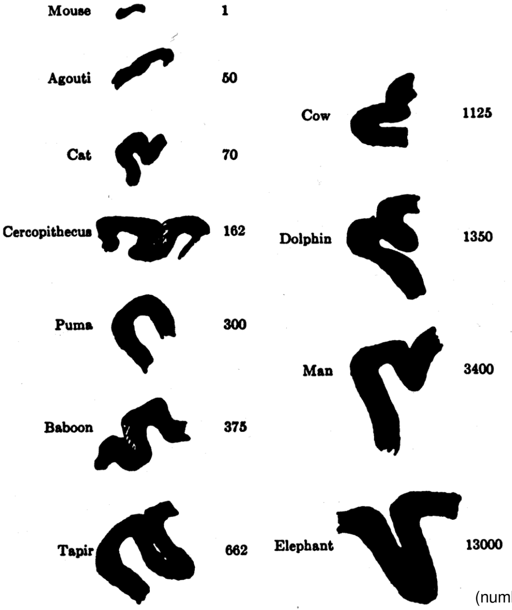
- folds = 'sulci'
- region between adjacent folds = 'gyrus'
- location of (deep) sulci is consistent across individuals of the same species



Macroscopic structure: Cortex thickness



(numbers represent brain mass)

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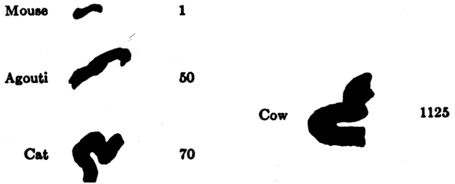
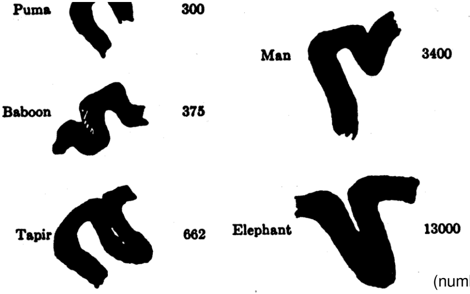


Evolution increased mainly the surface of the cortex. Its vertical organisation (thickness, cortex layers, cell proportions, etc.) remained relatively constant.



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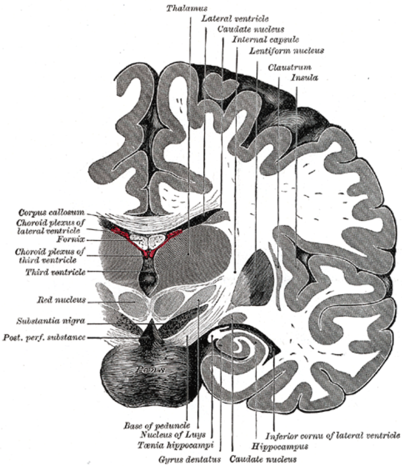
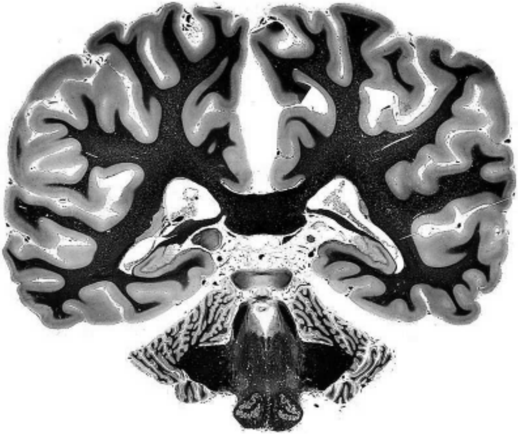
Macroscopic structure: Cerebral hemispheres

- two mirror-symmetric cerebral hemispheres
- interconnected via the Corpus callosum (white matter)





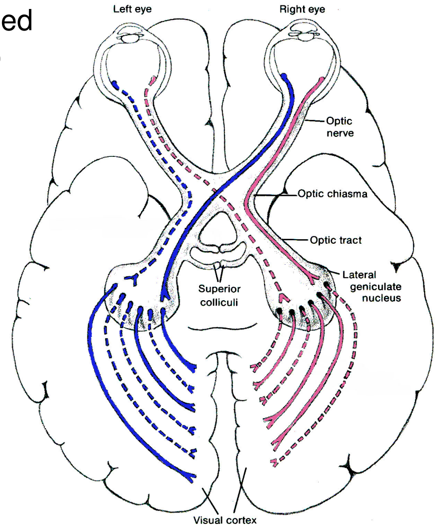
Macroscopic structure: Cerebral hemispheres

- two mirror-symmetric cerebral hemispheres
- interconnected via the Corpus callosum (white matter)
- brain function is sometimes lateralised (i.e. preference for one hemisphere)
- in general, however, involvement of both hemispheres

  e.g. visual processing:

  each hemisphere receives information from both eyes

  however, preference of input from left part of the visual field for right hemisphere (and vice versa)



Cortical areas

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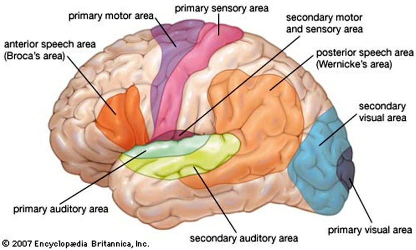
  - functional properties



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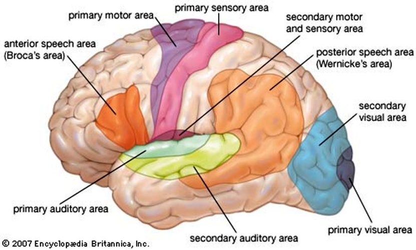
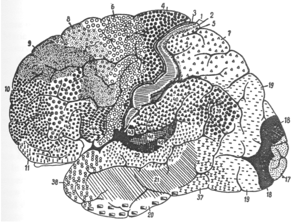
  - histo-anatomical features (cytoarchitecture, e.g. Brodman areas)





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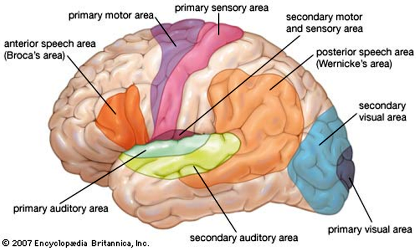
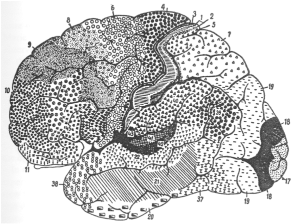
- frequent coincidence of both definitions
  e.g. primary visual cortex (V1)
  = Brodman area 17





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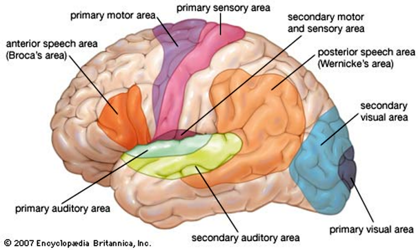
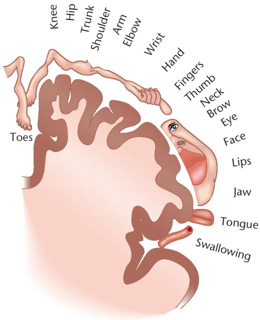
- further segmentation of cortical areas into functional subdomains





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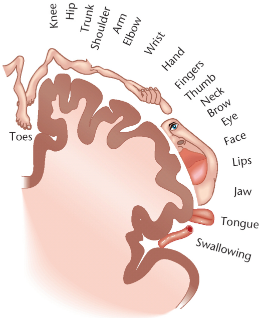

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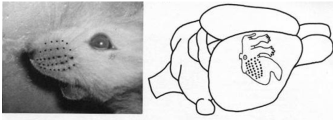
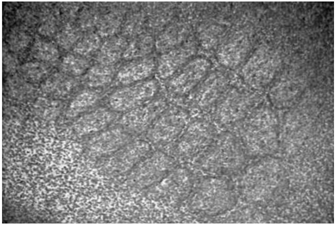
  e.g. rat 'barrel' cortex





Microscopic structure: Cell types

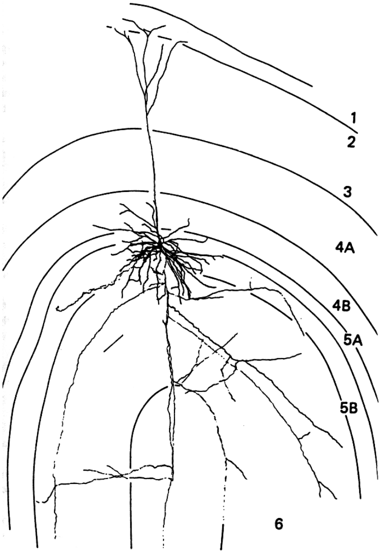
- cortical tissue is mainly composed of two cell types:
  - **neuroglia (glia)**:
    - important role in development of the brain
    - metabolic supportive role
    - control ionic composition of extracellular space
    - form myelin sheath around axons of neurons
    - do not take part in interaction between neurons on a millisecond scale (however, may play a role in slow modulations)
  - **nerve cells (neurons)**:
    - carry out information processing and storage in the brain

Microscopic structure: Neuron types

- pyramidal cell:
  - dendrites covered with spines
  - axon leaves cortex into white matter but has numerous branches close to cell body
  - axons makes excitatory synapses
  - cell receives input from inhibitory cells mainly at the soma and from excitatory cells at the basal and apical dendrite

Microscopic structure: Neuron types

Pyramidal cell



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- spiny stellate cell:
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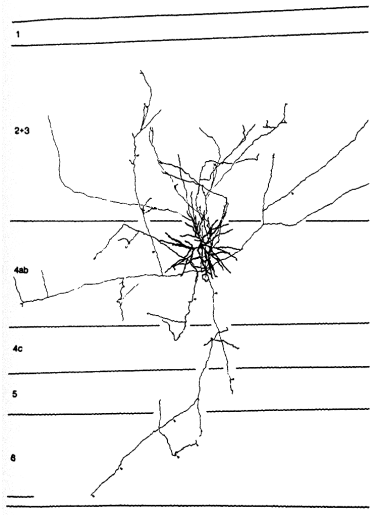
Microscopic structure: Neuron types

Spiny stellate cell



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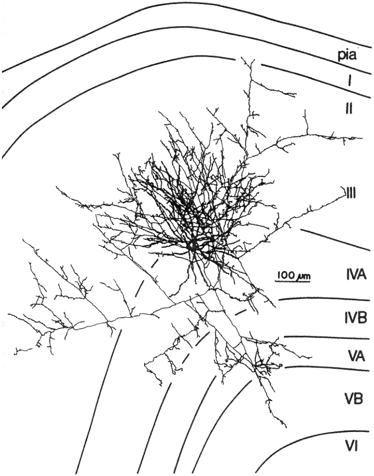
  - axon branches out within the cortex (rarely leaves the cortex)
  - axons makes excitatory synapses
  - soma receives exclusively inhibitory and dendrites mostly excitatory inputs
- smooth stellate cell (e.g. basket cell):
  - axon branches out only in the cortex
  - axons makes inhibitory synapses (GABA)
  - both the soma and the dendrites receive a mixture of excitatory and inhibitory inputs

Microscopic structure: Neuron types

Smooth stellate cell



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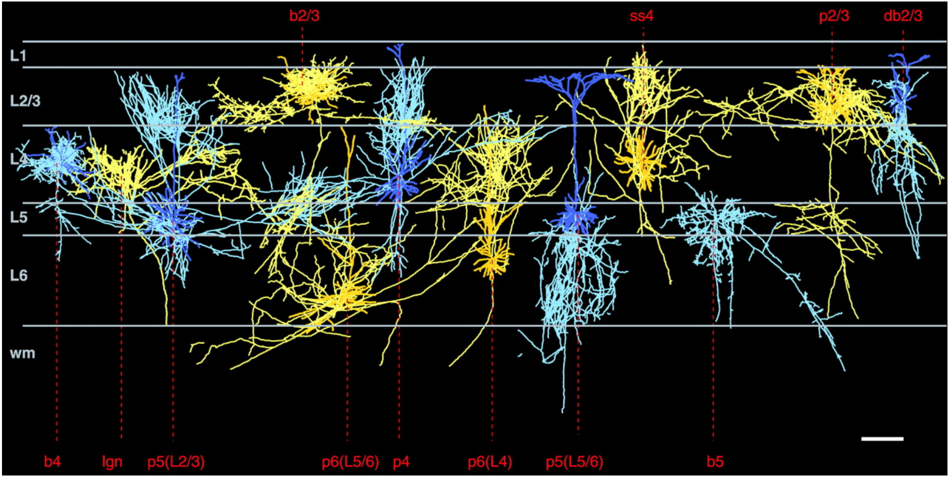
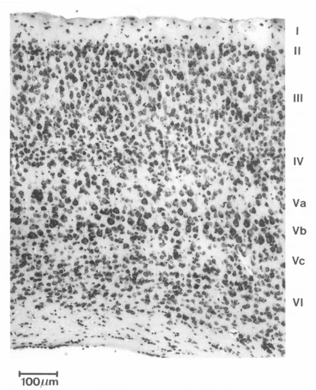
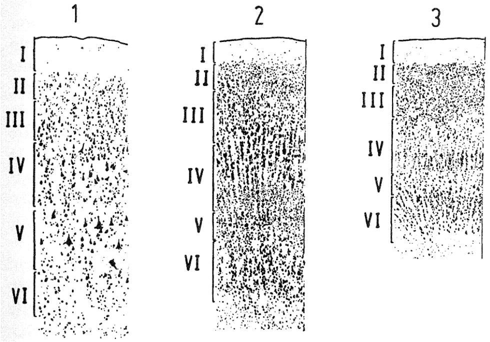


(Binzegger et al., 2004)

Microscopic structure: Cortex layers

- subdivision of neocortex into 6 (or 5) layers
  - layer I: very few neurons, only dendrites and mesh of horizontal axons
  - layer II/III: small pyramidal cells
  - layer IV: small and medium-size pyramidal cells and stellate cells in layer IVA, almost exclusively stellate cells in IVB
  - layer V: all cell types, very large pyramidal cells dominate
  - layer VI: small and medium-size pyramidal cells



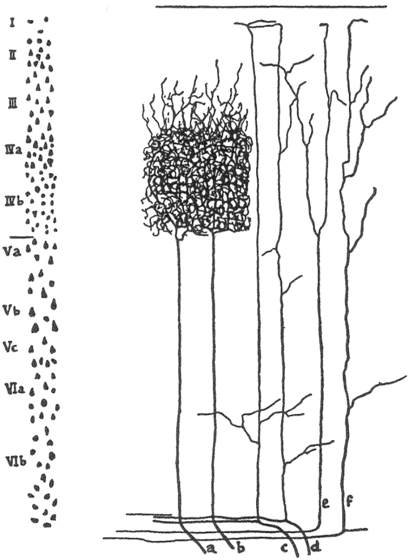


primary motor area

primary sensory area

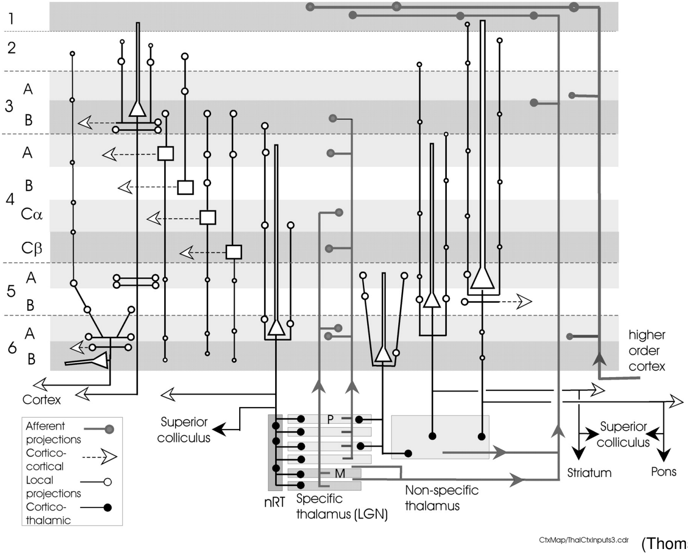
Cortex connectivity: Afferent connections

- external (non-local) input from
  - thalamus
    (thalamo-cortical afferents)
    mainly to layer IV
  - other cortical areas
    (cortico-cortical afferents)
    via white matter
    mostly to superficial layers
- input from cortical neurons
  in the local vicinity



Cortex connectivity: Vertical connectivity

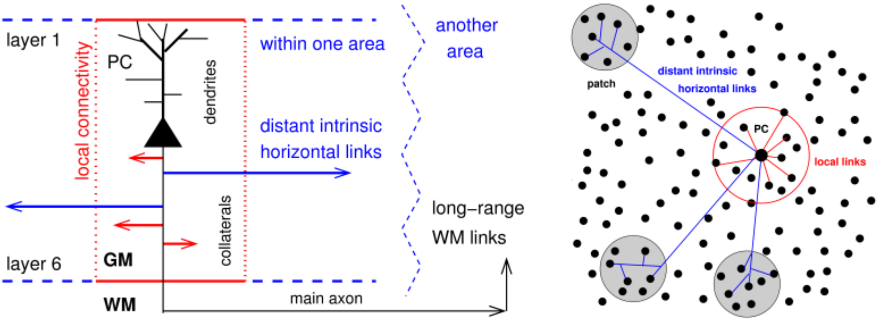
- layer- and cell-type specific local connections



(Thomson et al., 2003)

Cortex connectivity: Horizontal connectivity

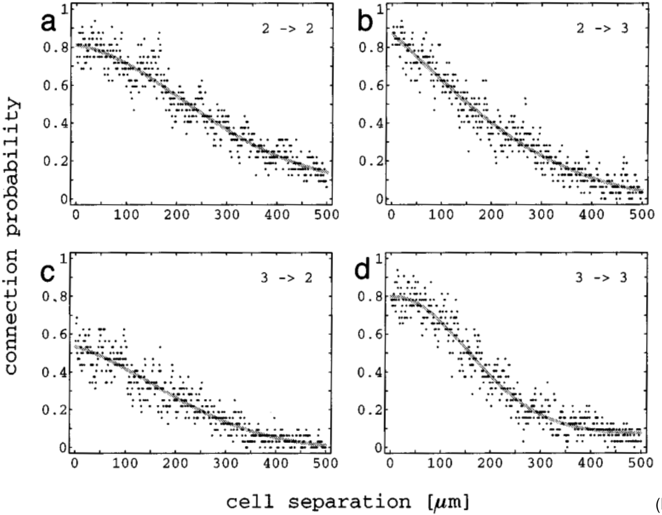
- local synapses established by local axon collaterals arborizing within ~ 0.5 mm (all neuron types)
- intrinsic horizontal long-range connections of pyramidal cells over distances up to several millimeter (within gray matter)
- extrinsic long-range connections of pyramidal cells through white matter



(Voges et al., 2007)

Cortex connectivity: Local connectivity

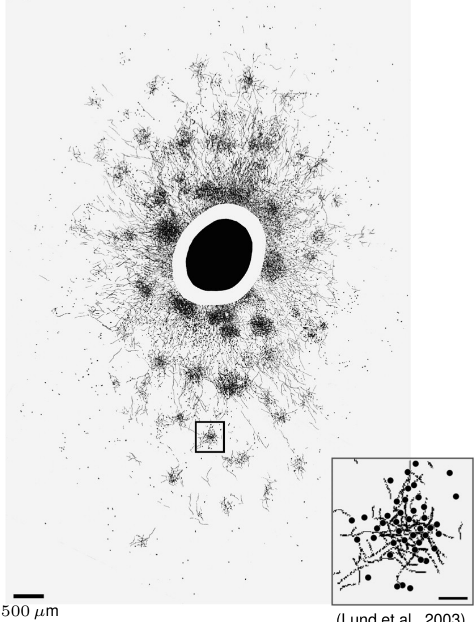
- probability of synaptic connection between adjacent cortical neurons decays to zero within a horizontal distance of $\sim 0.5\,\mathrm{mm}$



(Hellwig, 2000)

Cortex connectivity: Long-range connectivity

- intrinsic long-range connections form 'patchy' projection patterns, i.e. pyramidal cells project to distant clusters of target cells



(Lund et al., 2003)

Cortex connectivity: Summary - some numbers

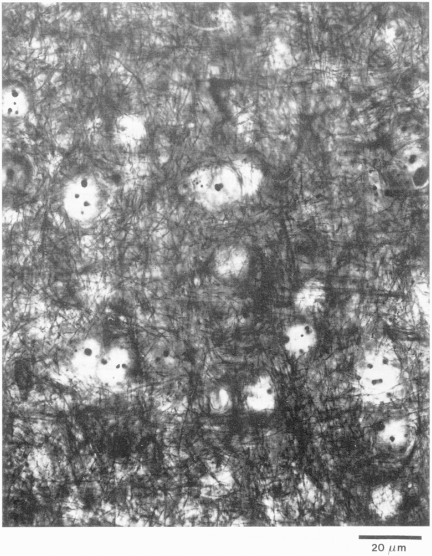


Table 1.5.1. *Densities of neurons in the cortex (thousands per cubic millimeter)*

A		B		C	
Animal	Density	Region	Density	Layer	Density
Mouse	142.5	Visual	106	I	20
Rat	105.0	Somatosensory	60	II	82
Guinea pig	52.5	Auditory	43	III	62
Rabbit	43.8	Motor	30	IV	67
Cat	30.8			V	61
Dog	24.5			VI	77
Monkey	21.5				
Human	10.5				
Elephant	6.9				
Whale	6.8				

Table 1.5.4. *Typical compositions of cortical tissues*

Variable	Value
Neuronal density	40,000/mm^3
Neuronal composition:	
Pyramidal	75%
Smooth stellate	15%
Spiny stellate	10%
Synaptic density	$8 \cdot 10^8$/mm^3
Axonal length density	3,200 m/mm^3
Dendritic length density	400 m/mm^3
Synapses per neuron	20,000
Inhibitory synapses per neuron	2,000
Excitatory synapses from remote sources per neuron	9,000
Excitatory synapses from local sources per neuron	9,000
Dendritic length per neuron	10 mm

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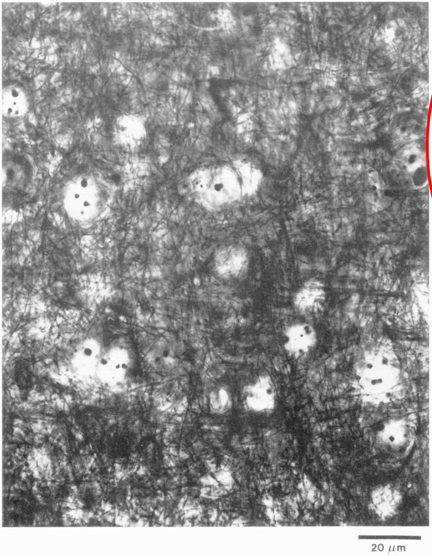

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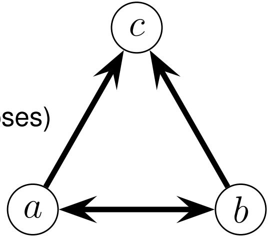
Some graph-theoretical concepts

- Graph: $G := (V, E)$

  V: set of 'vertices' (neurons)
  E: set of (ordered) pairs of vertices $\curvearrowright$ 'edges' (synapses)

  example:
  $V = \{a, b, c\}$, $E = \{\{a, b\}, \{b, a\}, \{b, c\}, \{a, c\}\}$



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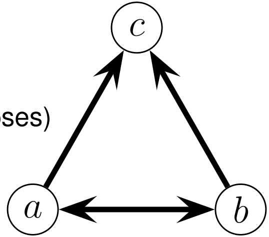

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  adjacency matrix $A = \begin{array}{cc} \text{presynaptic} & \\ \begin{pmatrix} 0 & 1 & 0 \\ 1 & 0 & 0 \\ 1 & 1 & 0 \end{pmatrix} & \text{postsynaptic} \end{array}$ (columns=axons, rows=dendrites)

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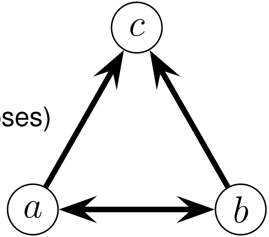

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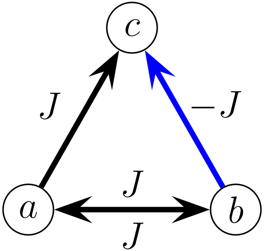
  weight matrix $W = \begin{pmatrix} 0 & J & 0 \\ J & 0 & 0 \\ J & -J & 0 \end{pmatrix}$

  (for weighted graphs)



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  example: linear firing-rate network model (Wilson-Cowan model)

$$\tau \frac{dy}{dt} = -y + Wy$$

with firing rates $y(t) = [y_1(t), \ldots, y_N(t)]^{\mathsf{T}}$ of neurons $1, \ldots, N$

$\curvearrowright$ stability of fixed point determined by eigenvalue spectrum of $W - 1$

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- popular random networks in Computational Neuroscience:
  - Erdös-Renyi graphs:
    - Each possible connection is randomly and independently drawn with probability ϵ.

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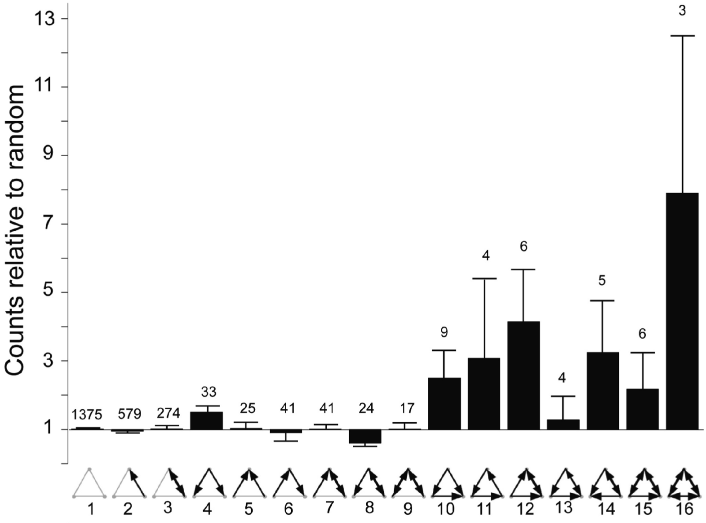

Song et al. (2005), Highly Nonrandom Features of Synaptic Connectivity in Local Cortical Circuits

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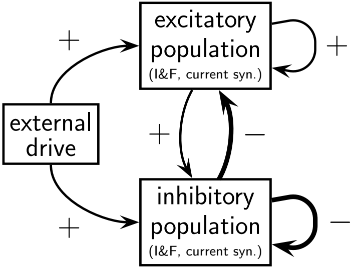
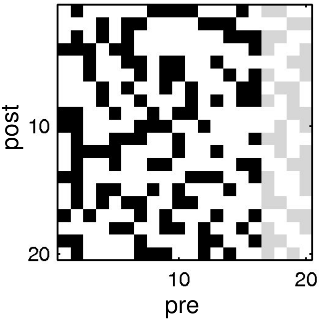
  - ... and infinitely many more

The balanced-random-network model (Brunel, 2000)

Simple model of a local cortex volume ($\sim 1\mathrm{mm}^3$, $\sim 10^{4\ldots5}$ neurons)



Connection matrix $J = \{J_{ij}\}$



- N_E excitatory, N_I inhibitory neurons, $N = N_\mathsf{E} + N_\mathsf{I} \sim 10^{4\ldots5}$
- random Dale-conform connectivity with fixed in-degrees $K_{\mathsf{E/I}} = N_{\mathsf{E/I}}/10$

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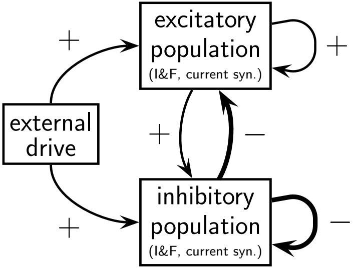

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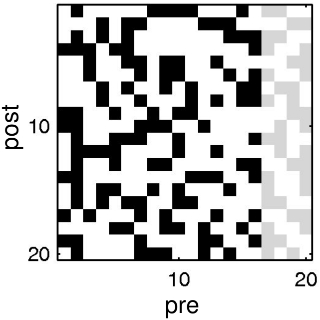

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- LIF dynamics with current synapses:

$$\tau_\mathsf{m}\dot{v}_i = -v_i(t) + RI_i^\mathsf{net}(t) + RI^\mathsf{ext}(t) \quad (i \in \{1,\ldots,N\})$$

$$I_i^\mathsf{net}(t) = \textstyle\sum_j (h_{ij} * s_j)(t)$$ (with postsynaptic current kernel $h_{ij}(t) = J_{ij} \cdot h(t)$)

if $v_i(t_{i,k}) \geq \theta$: spike at time $t_{i,k}$, reset $v_i(t_{i,k}^+) = 0$

spike train: $s_i(t) = \sum_k \delta(t - t_{i,k})$

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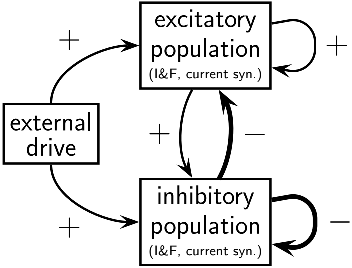
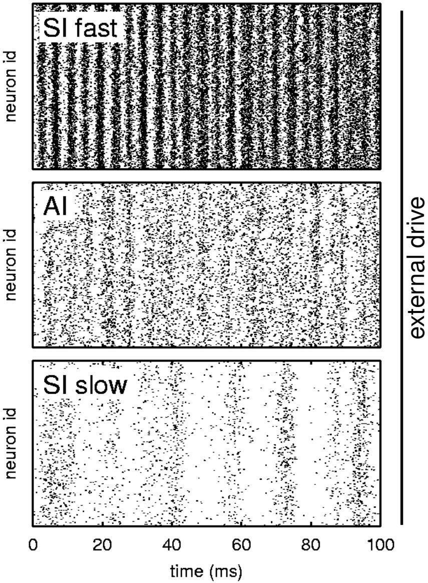


Activity states



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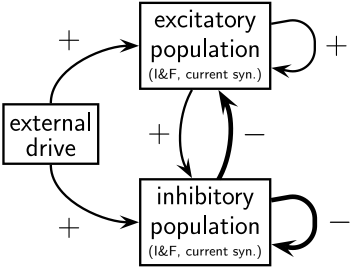
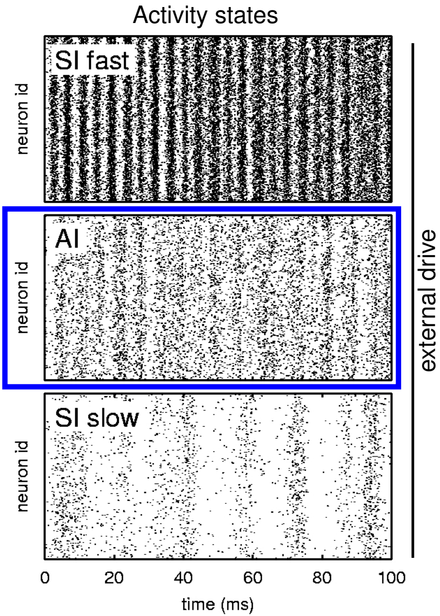


- in-vivo like activity
  - large membrane potential fluctuations
  - low firing rates
  - irregular spiking
- global oscillatory modes in various frequency bands



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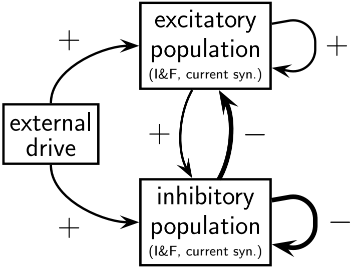
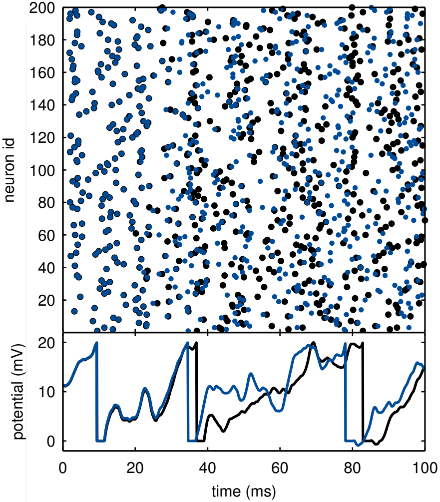


- in-vivo like activity
  - large membrane potential fluctuations
  - low firing rates
  - irregular spiking
- global oscillatory modes in various frequency bands
- chaotic spiking (high sensitivity)

Chaos in random networks



Simulation of two identical networks ($N \sim 10000$), slight perturbation of initial membrane potential of one neuron ($\Delta V = 0.1$ mV)

Activity regimes

- analysis of network dynamics in diffusion approximation (small synaptic weights, high firing rates, small correlations) (see Brunel, 2000)

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SR:	synchronous regular
AI:	asynchronous irregular
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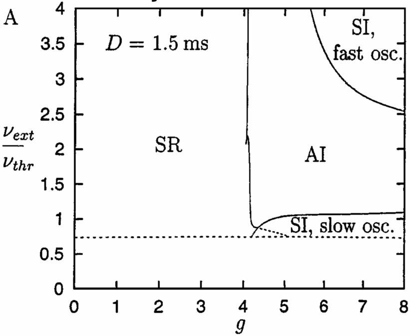
theory



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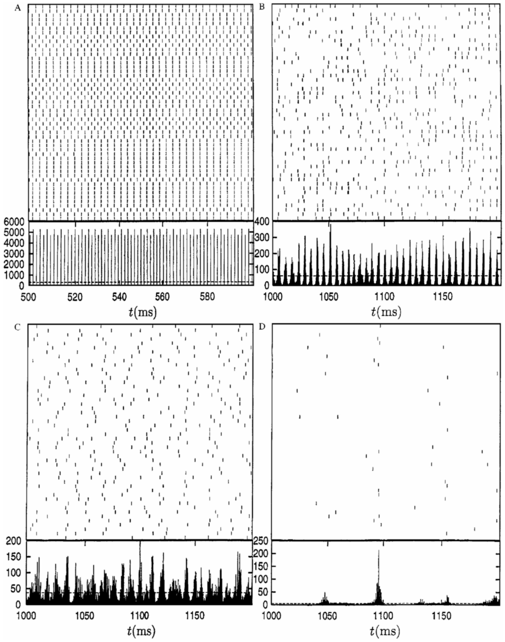

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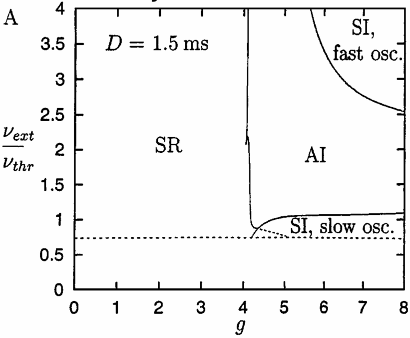
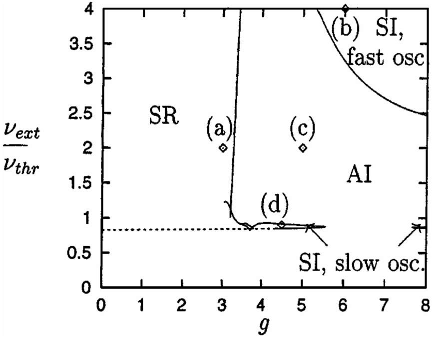


simulation



(Brunel, 2000)

Literature: Cortex anatomy

- Abeles,
  Corticonics: Neural Circuits of the Cerebral Cortex,
  Cambridge University Press, 1991
- Braitenberg & Schüz,
  Cortex: Statistics and Geometry of Neuronal Connectivity,
  Springer, 2nd edition, 1998

- Thomson & Bannister (2003), Interlaminar Connections in the neocortex, Cerebral Cortex 13:5–14
- Binzegger et al. (2004), A Quantitative Map of the Circuit of Cat Primary Visual Cortex, J Neurosci 39(24):8441–8453
- Hellwig (2000), A quantitative analysis of the local connectivity between pyramidal neurons in layers 2/3 of the rat visual cortex, Biological Cybernetics 82:111–121
- Lund et al. (2003), Anatomical Substrates for Functional Columns in Macaque Monkey Primary Visual Cortex, Cerebral Cortex 13:15–24
- Voges et al. (2010), A modeler's view on the spatial structure of intrinsic horizontal connectivity in the neocortex, Progress in Neurobiology 92(3):277–292
- Song et al. (2005), Highly nonrandom features of synaptic connectivity in local cortical circuits, PLoS Biology 3(3):0507–0519

Literature: Spiking random-network models

Random matrices:

1. ML Mehta, *Random matrices*, 3rd edition, Elsevier Ltd., 2004

Recurrent-network dynamics:

2. LF Abbott, C van Vreeswijk, Asynchronous states in a network of pulse-coupled oscillators, Phys Rev E 48:1483–1490, 1993
3. N Brunel, Dynamics of sparsely connected networks of excitatory and inhibitory spiking neurons, J Comput Neurosci 8:183–208, 2000
4. A Renart, N Brunel, XJ Wang, Mean-field theory of irregularly spiking neuronal populations and working memory in recurrent cortical networks, in *Computational neuroscience – A comprehensive approach*, J Feng (ed.), Chapman & Hall/CRC, London, 2003