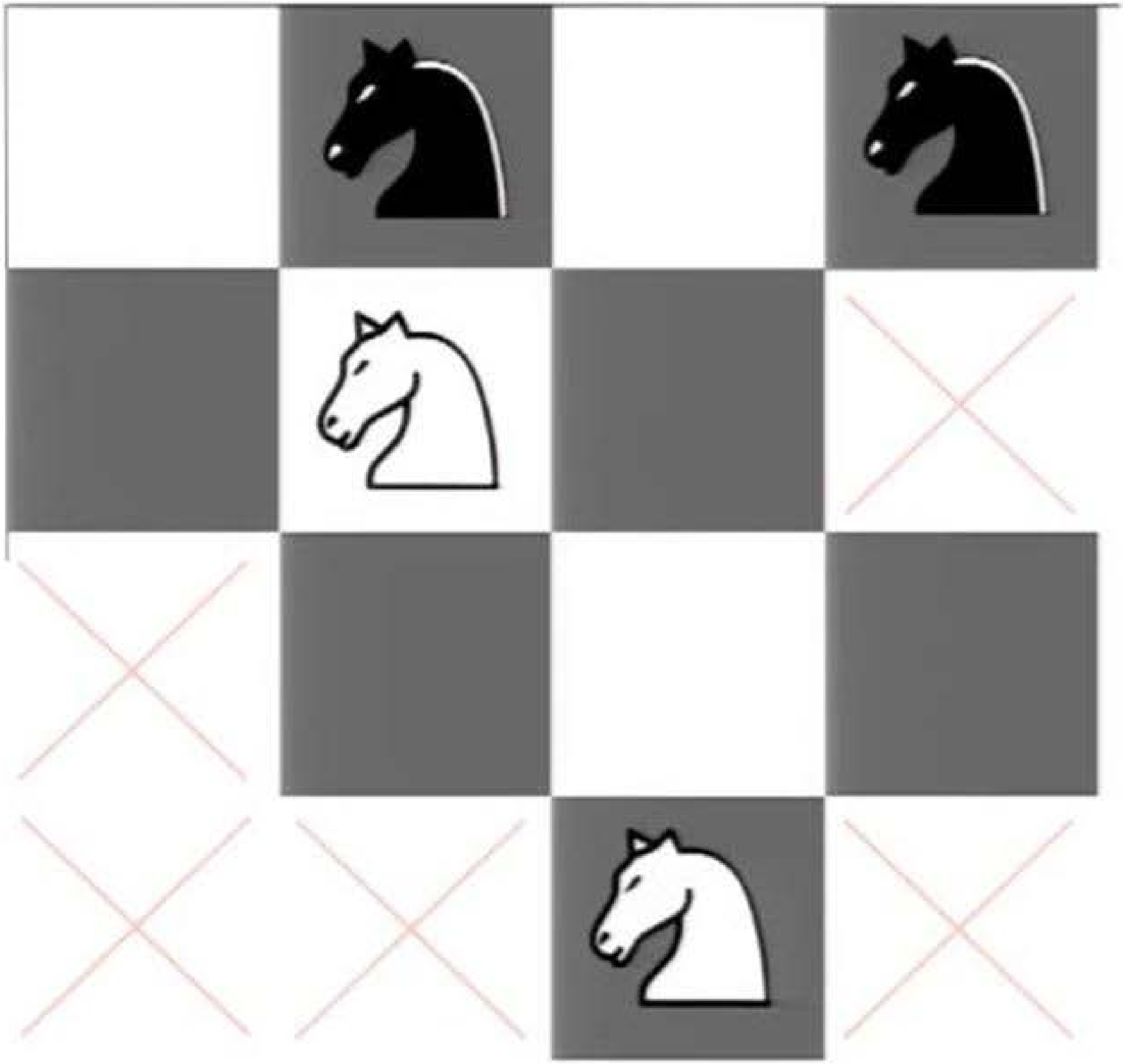
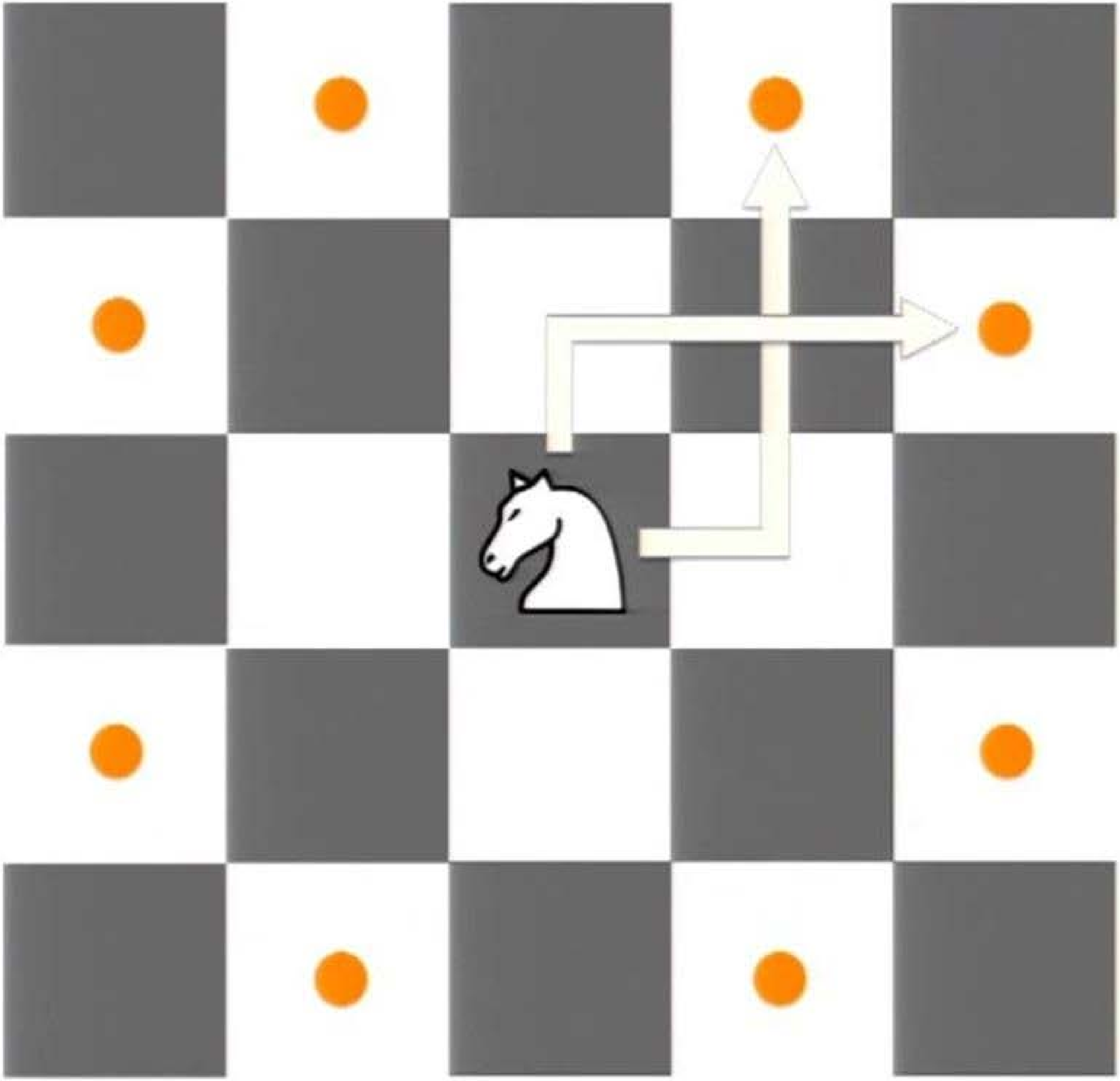
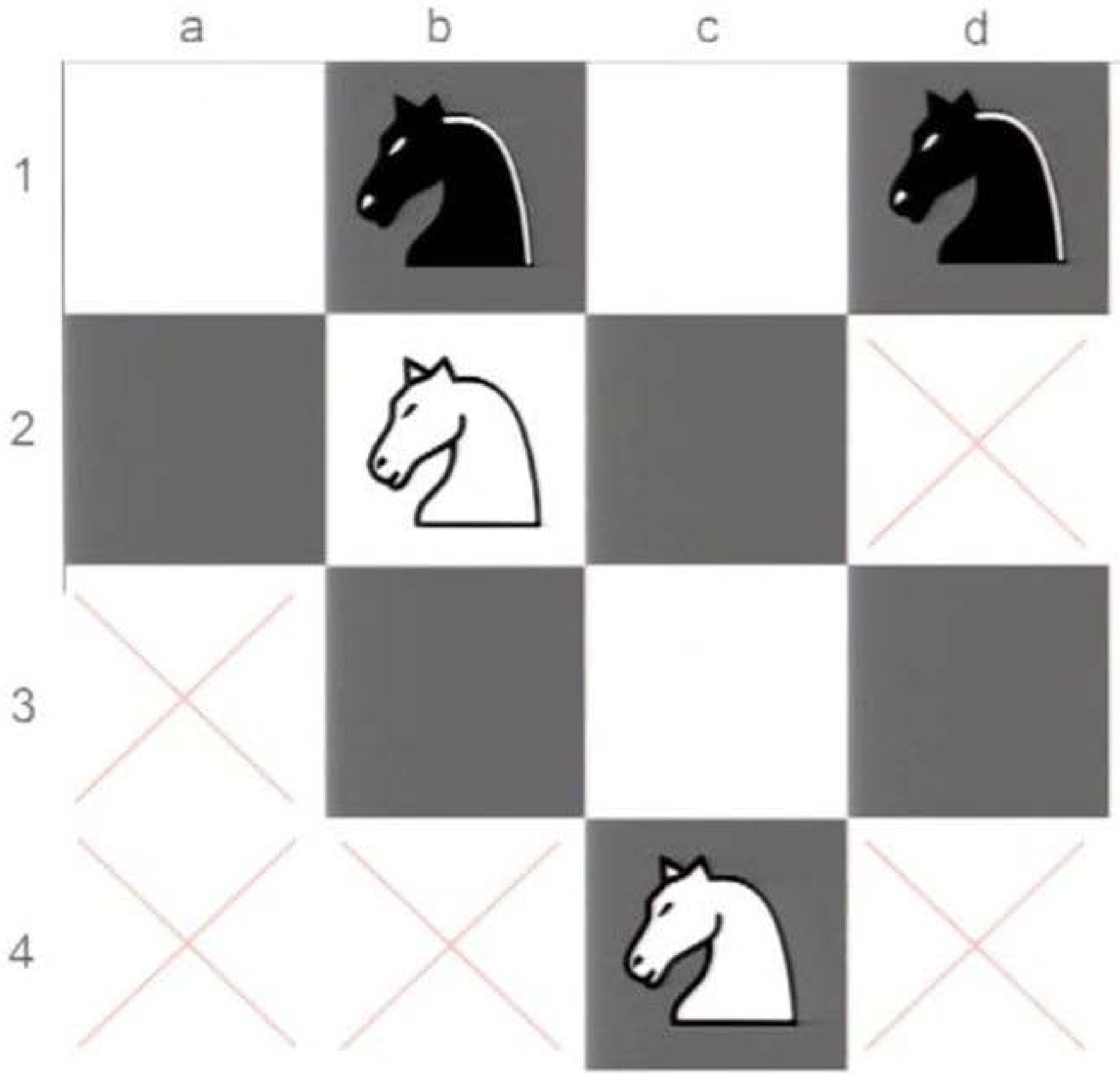
Chess Puzzle: Swap the positions of white knights with those of the black knights



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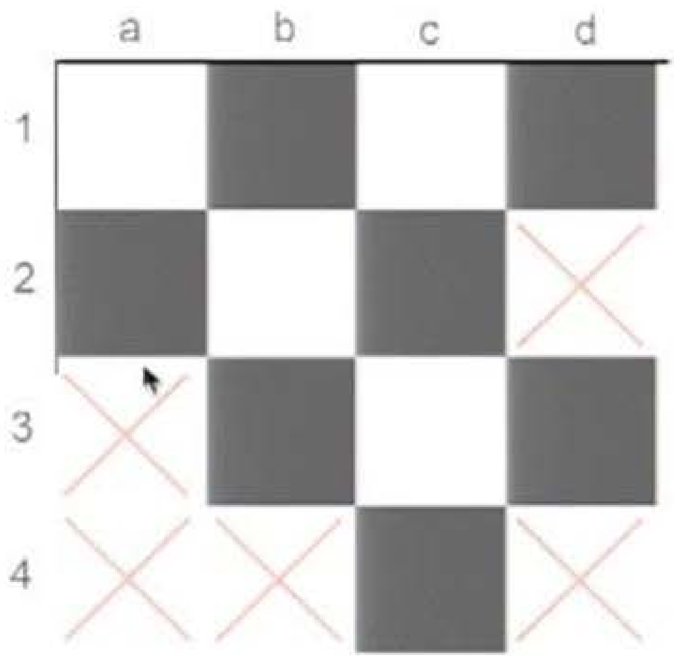
2
3
4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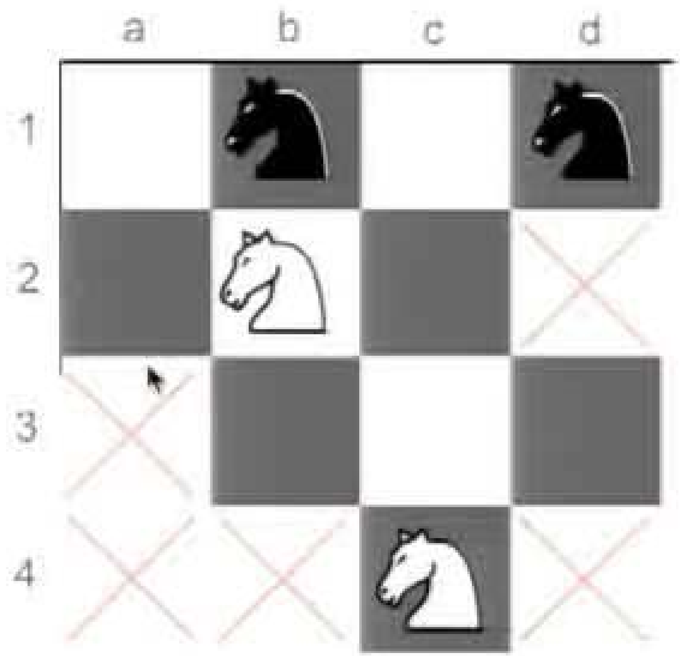
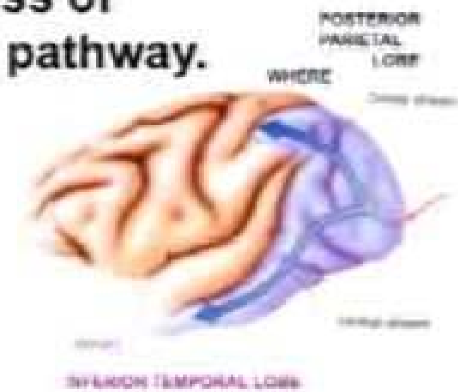
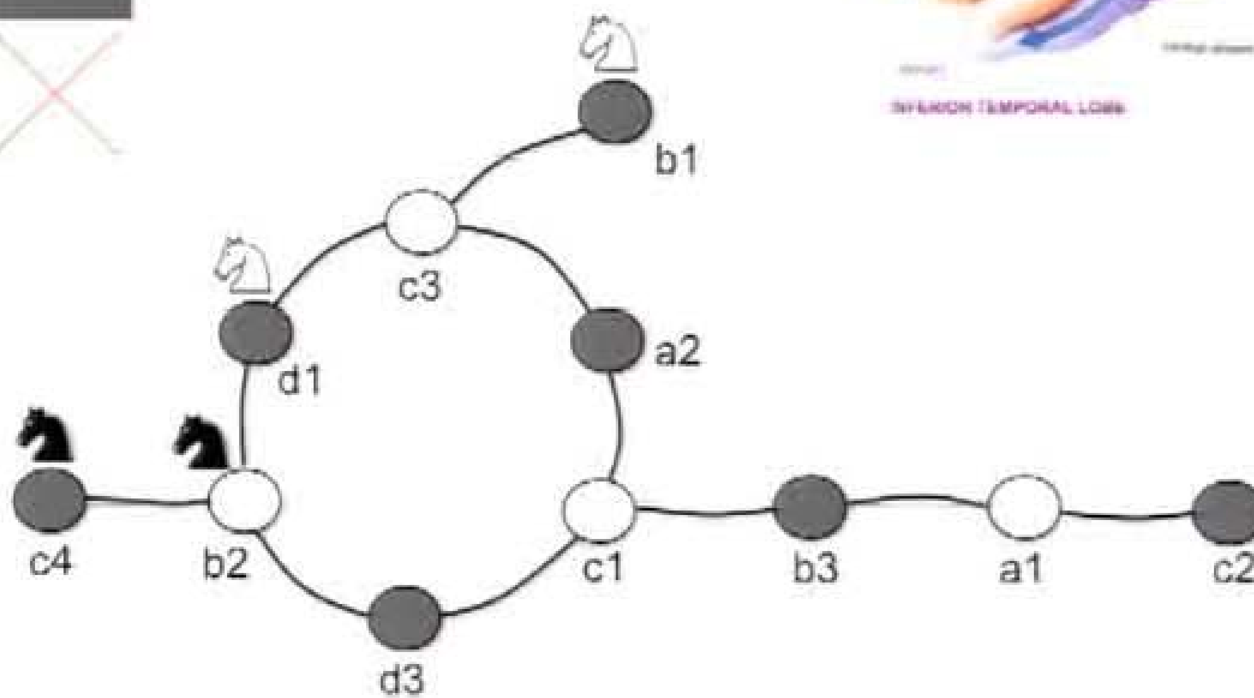
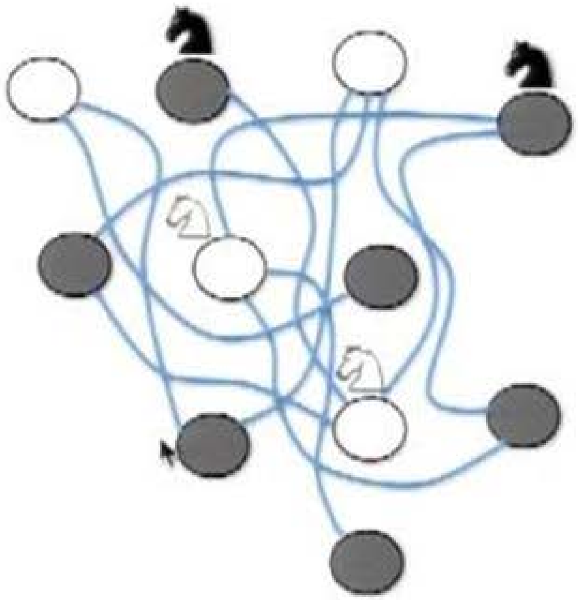


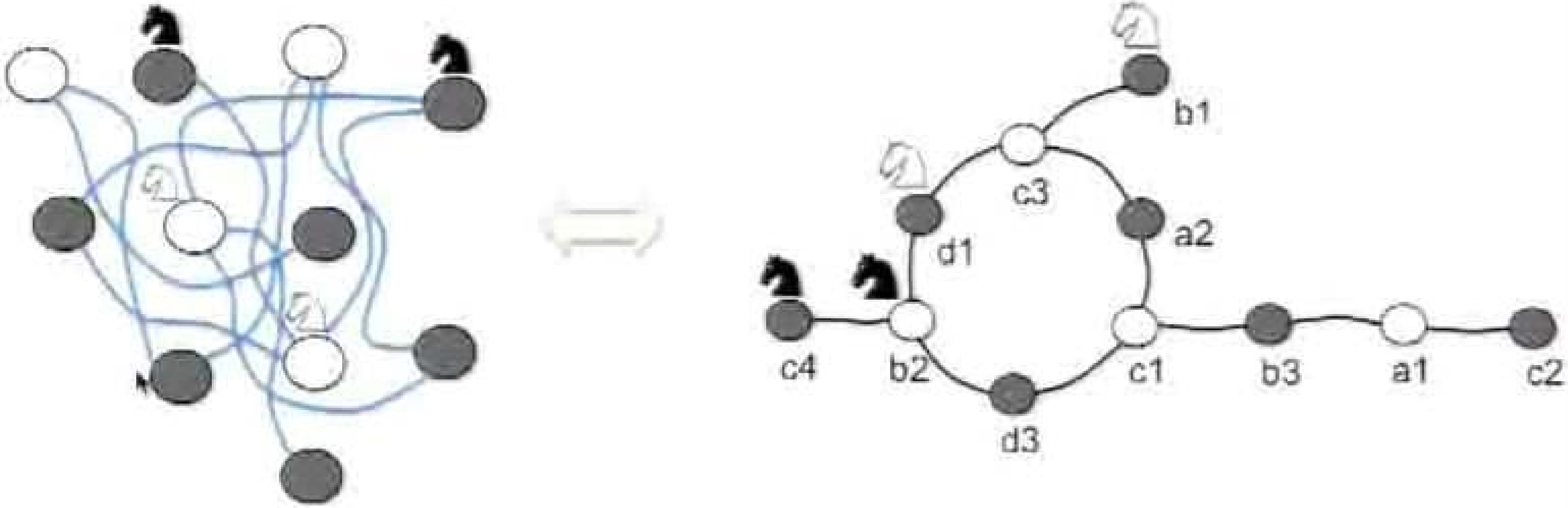
I. Network representation

II. Redirected the process of thought to the "where" pathway.









Not optimal: it only respects the relationships.

Optimized layout: minimal edge crossings, minimal wire length.

This representation allows us to infer **GLOBAL** information quickly

- In the brain, the pulses/firing signals do not encode information as in packet-switching networks (Internet).
- Instead, information is encoded by Collectives of Pulses, their patterns.

The wiring is part of the algorithm!

What is the structure? Does it have features that are universal across all mammals?

The Physical Brain

With:

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Henry Kennedy — Stem Cell and Brain Research Inst, INSERM U846 Lyon, France
Kenneth Knoblauch — Université de Lyon, France
Nikola Markov
etc.

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DARPA
AFOSR
FA9550-12-1-0405

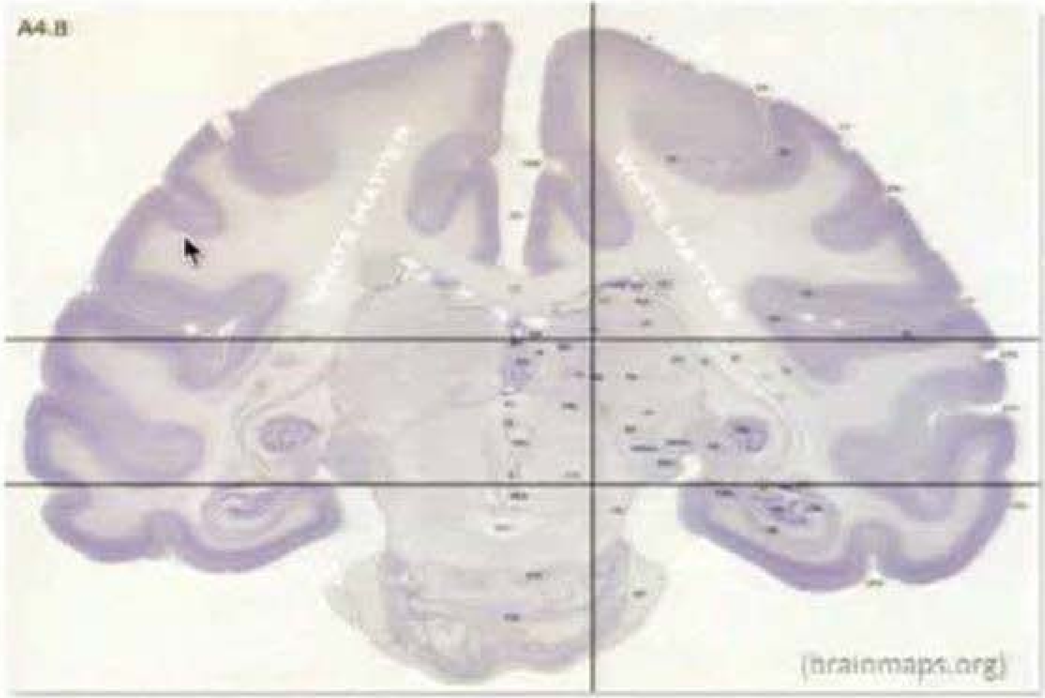
European Commission
FP6-2005 IST-1583
FP7-2007 ICT-216593
FP7-PEOPLE-2011-IIF-299915

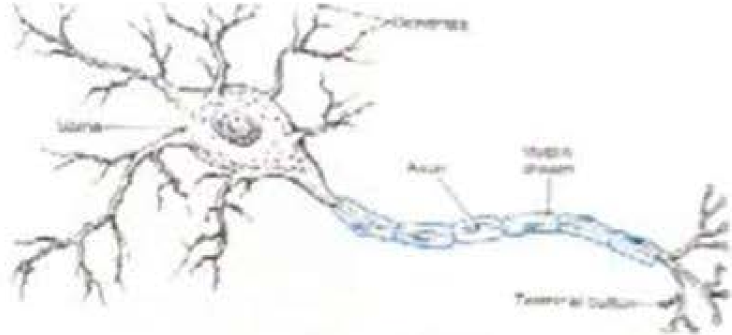
ANR
ANR-11-BSV4-501
ANR-11-LABX-0042

National Institutes of Health
R01 MH60974

The cerebral cortex

THE NEURON





An adult human brain: 86 billion (8.6×10^{10}) neurons.

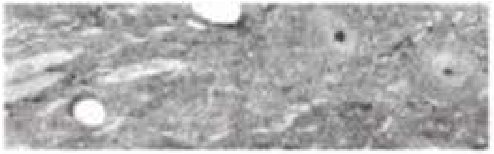
16 billion in the cortex → 3.2 billion white matter neurons

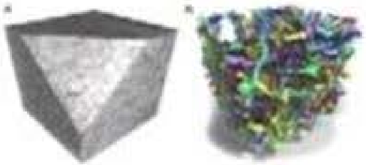
More than 100 trillion (10^{14}) connections (links).

This network simply too large to be genetically encoded synapse by synapse.

Has randomness, modified during learning: Information encoding emerges at all (larger?) scales.

A brave project: Connectomics (S. Seung, MIT): a slice-by-slice reconstruction to track all features.





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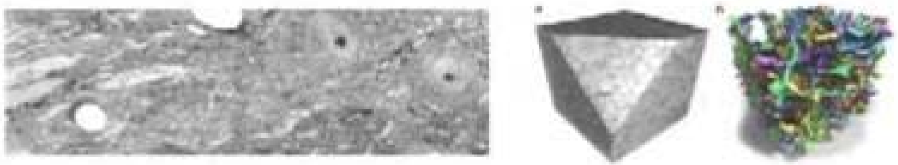


A more natural method is **a TOP-DOWN approach: Functional Decomposition.**

The brain's interactions with the environment is through functional modalities (vision, hearing, sensing/taste, etc.).

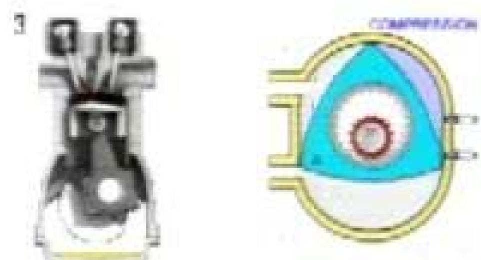
Many of these form well localized brain regions (areas).

Such *large-scale features* should be more robust and *universal/comparable across species.*

Ex: understanding the workings of a car from a top-down perspective:

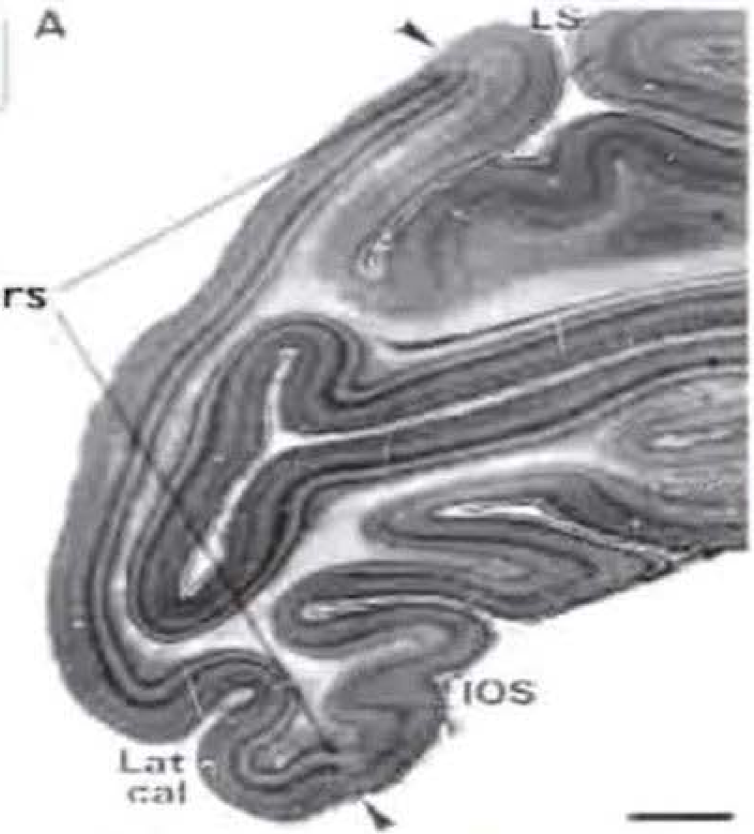
Design variability appears with increasing resolution:

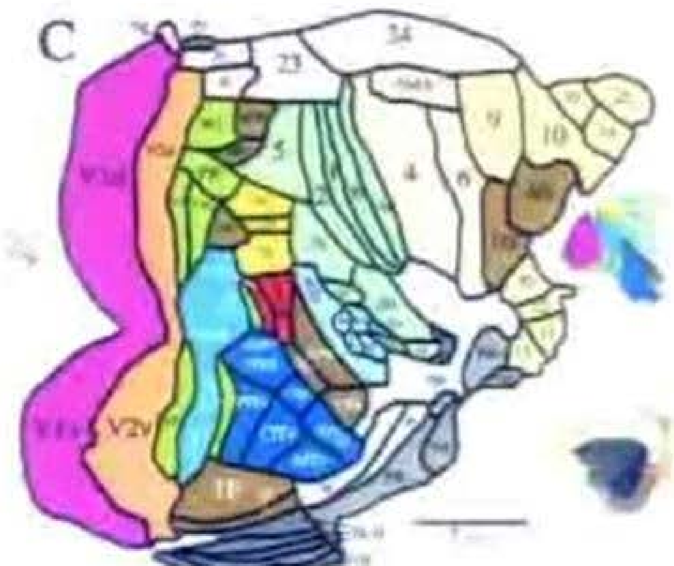
- Same function
- Varying implementations



Functional areas of the cortex

Garey LJ. *Brodmann's Localisation in the Cerebral Cortex*. New York Springer, 2006





Segmentation based on histological criteria. Cytoarchitectonic details.

Macaque cortex: 91 areas

Experiments: Retrograde Tracing

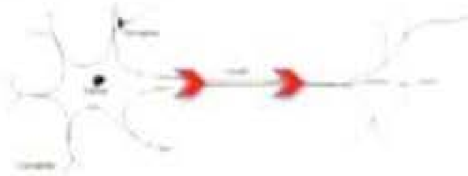
Kennedy team (Lyon):

(80 man-years work!)

Retrograde tracing uncovers DIRECT inter-areal connectivity.

Tracers: Fast Blue (FsB), Diamino Yellow (Dy)

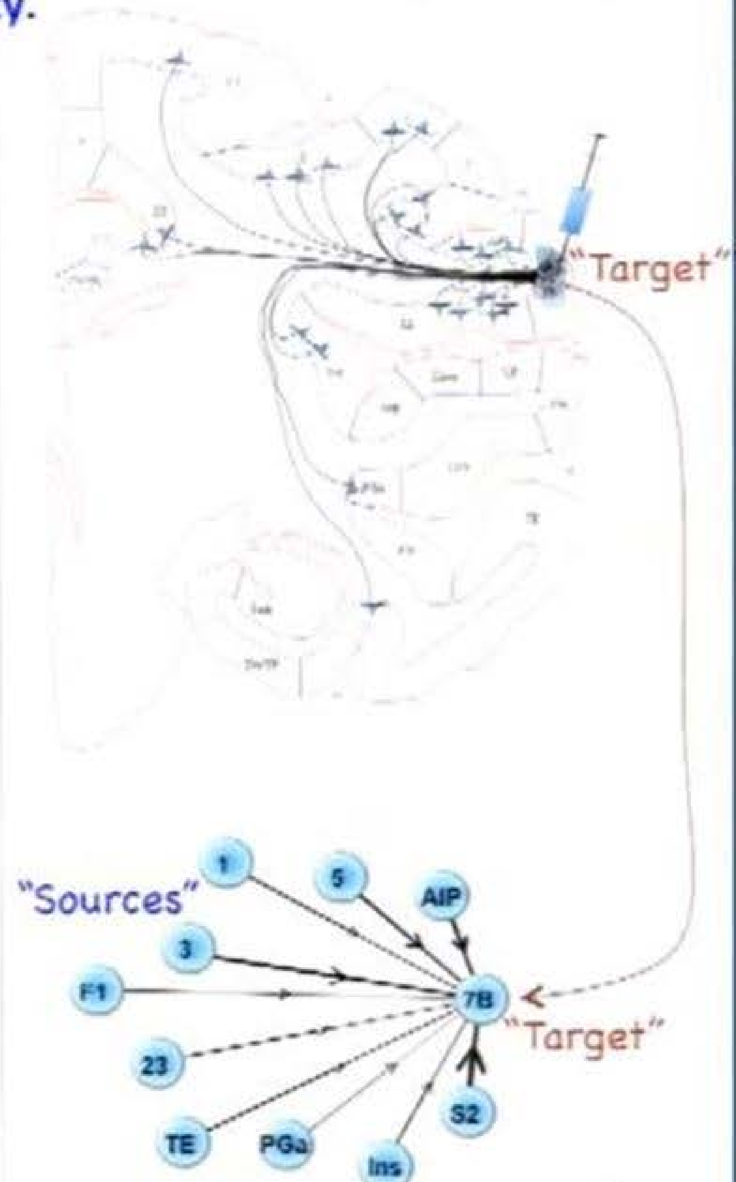
A neuron is a directed element



NO secondary labeling (of pre-synaptic neurons)!

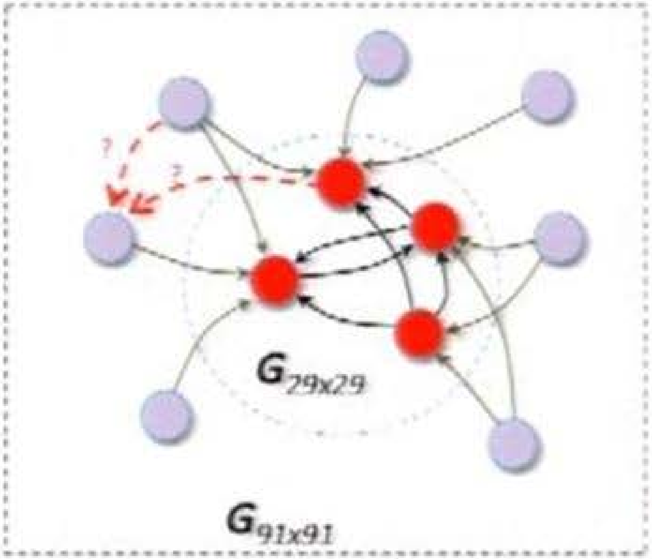
Measurements:

- **number of labeled neurons** in source areas
- **projection lengths** through the white matter



Network properties

- directed
- weighted
- spatially embedded



Network properties

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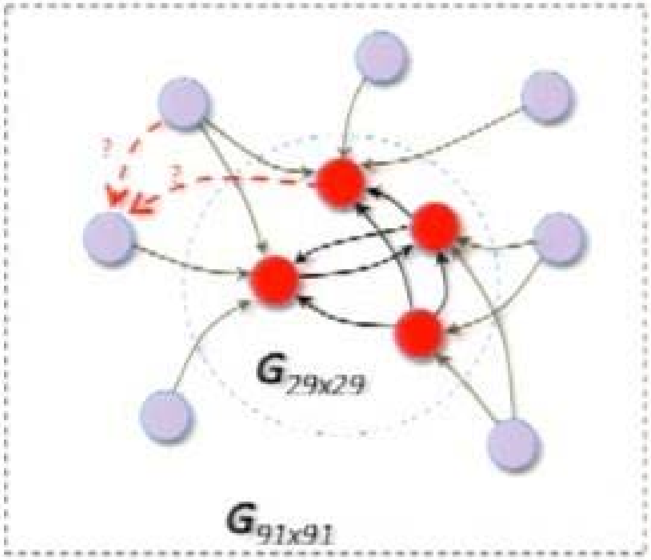


- 29 injected nodes
- all 91 nodes projecting into the set of 29
- found **total** of 1615 directed edges/projections
- there are M=536 edges between the 26 nodes

⇨ The graph amongst the 29 nodes forms G_{29x29}

which is an ***edge-complete*** sub-graph of G_{91x91} (FIN)

Density of G_{29x29}: $\rho_{29\times 29} = \frac{M}{N(N-1)} = \frac{536}{812} = 0.66$

It is very dense! 66%

At such high densities, the density of the graph is a chief determining factor for its "binary" properties:

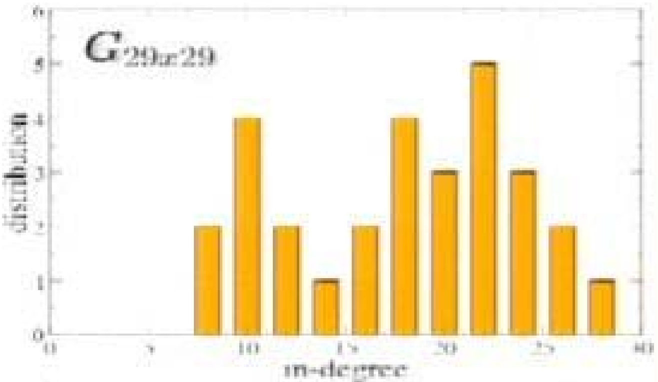
Necessarily it will have:

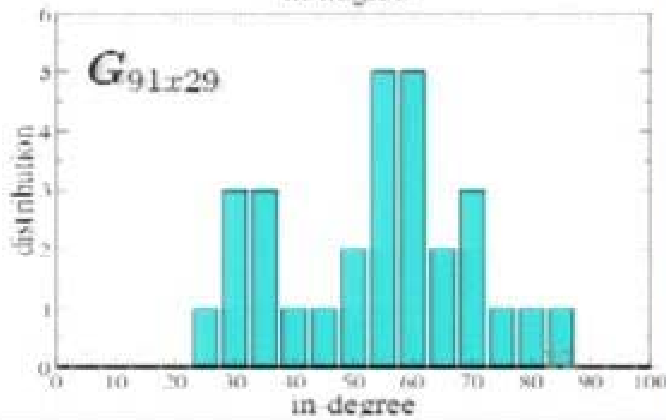
-short average path length (= 1.34 for G_{29x29})

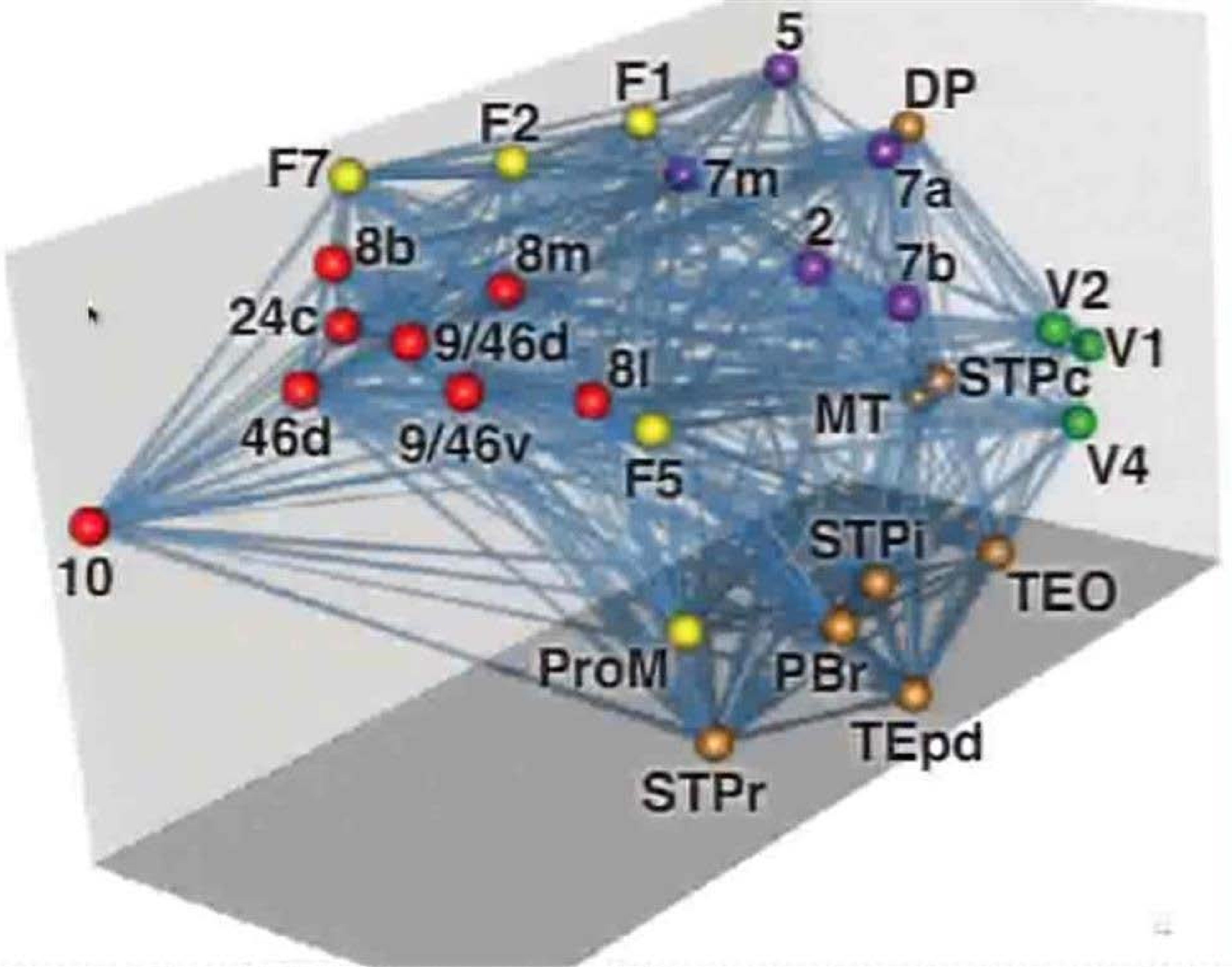
-small diameter (= 2)

-high clustering coefficient (= 0.87).

○ degree distributions are not too telling.






5
F1
DP
F2
F7
7m
7a
8b
8m
2
7b
V2
24c
9/46d
V1
8l
STPc
46d
9/46v
MT
F5
V4
10
STPi
TEO
ProM
PBr
TEpd
STPr

Is there some sort of global structure/regularity in the interareal network?

The Exponential Distance Rule (EDR)

Clues from *analysis of the weight and the spatial embedding properties* of the network.

Is there some sort of global structure/regularity in the interareal network?

The Exponential Distance Rule (EDR)

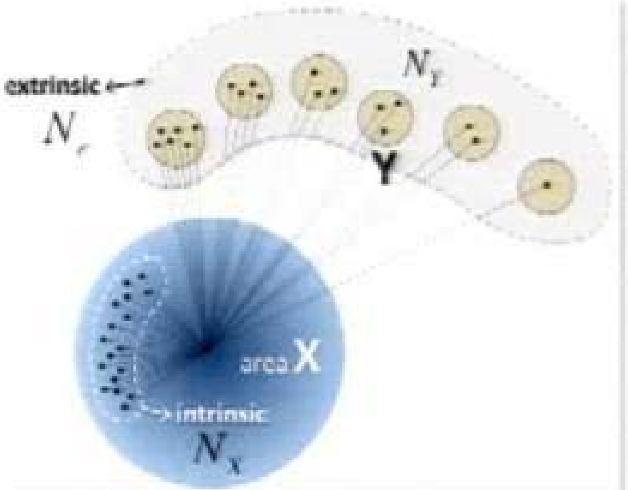
Clues from *analysis of the weight and the spatial embedding properties* of the network.

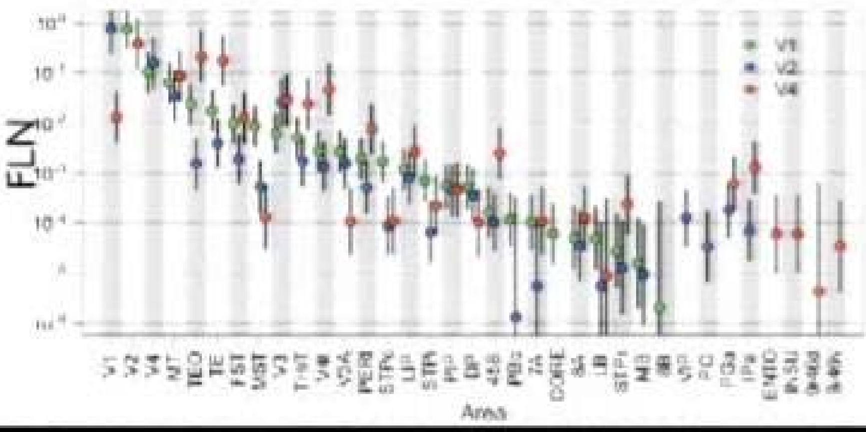
Projection/Link weight: **Fraction of Labeled Neurons (FLN)**

Assume that an injection was performed in area X.

Define: $$\mathrm{FLN}(X \leftarrow Y) = \frac{N_Y}{N_e}$$

- the "**probability**" that ***an extrinsic*** labeled neuron is projecting into X from Y.





- Varies over 5 orders of magnitude!

- This heterogeneity is a signature of functional organization.

The FLN (link weight) distribution

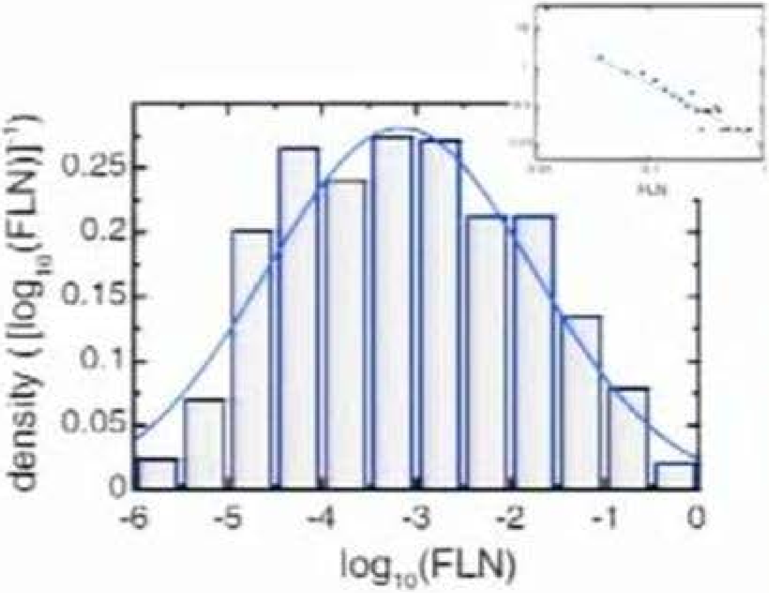
Conforms to a **lognormal**.

$f \equiv FLN$

$$\frac{1}{\beta\sqrt{2\pi}}\frac{1}{f}e^{-\frac{1}{2\beta^2}(\log f - \alpha)^2}$$

= the distribution of log(f) is Gaussian (normal).

- **Strong heterogeneity in weight distribution.**
- **Heavy Tail**



What about the network? How strongly is the network constrained by the EDR and geometry?

Two Random Graph models (Maximum Entropy based):

Constant distance rule (CDR): $p(d) = constant$ (null-model)

Exponential distance rule (EDR): $p(d) = c\, e^{-\lambda d}$

Using the matrix of distances $D = \{d_{ij}\}$ between the areas (geometry):

- We generate random networks by generating connections with probability *p(d)* between two area pairs. We stop when we have as many pairs connected as in the data.
- Repeat pairs are allowed → generates their weight.

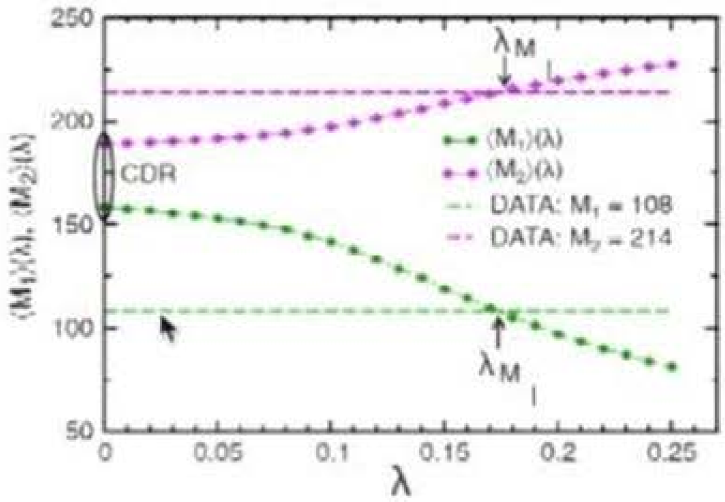
The models are **Random, spatially embedded, weighted directed networks.**

Comparison between model networks and the brain network:

While changing λ compare network measures between model and data.

If the model is a strong descriptor of the data network then there will be agreement for all measures at a λ value that is close to the one from projection length measurements.

From physical wire lengths: $\lambda_d = 0.188\, mm^{-1}$



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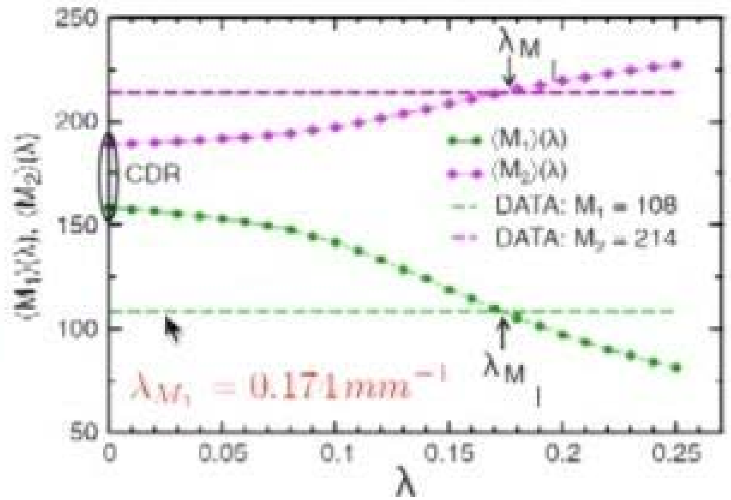
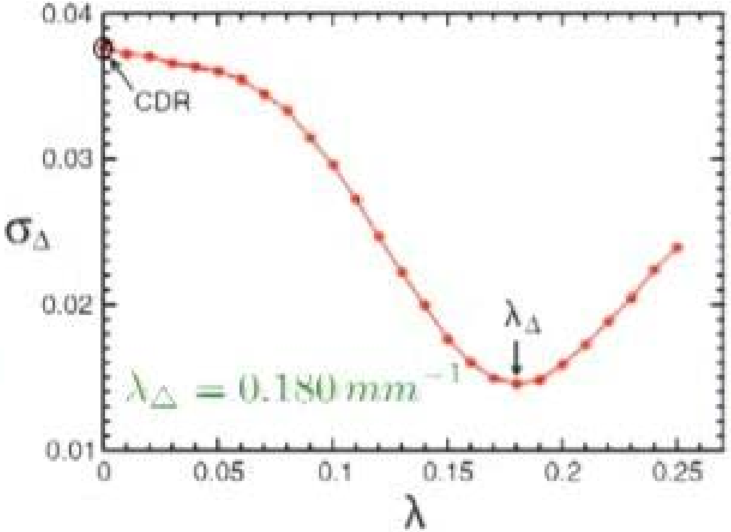
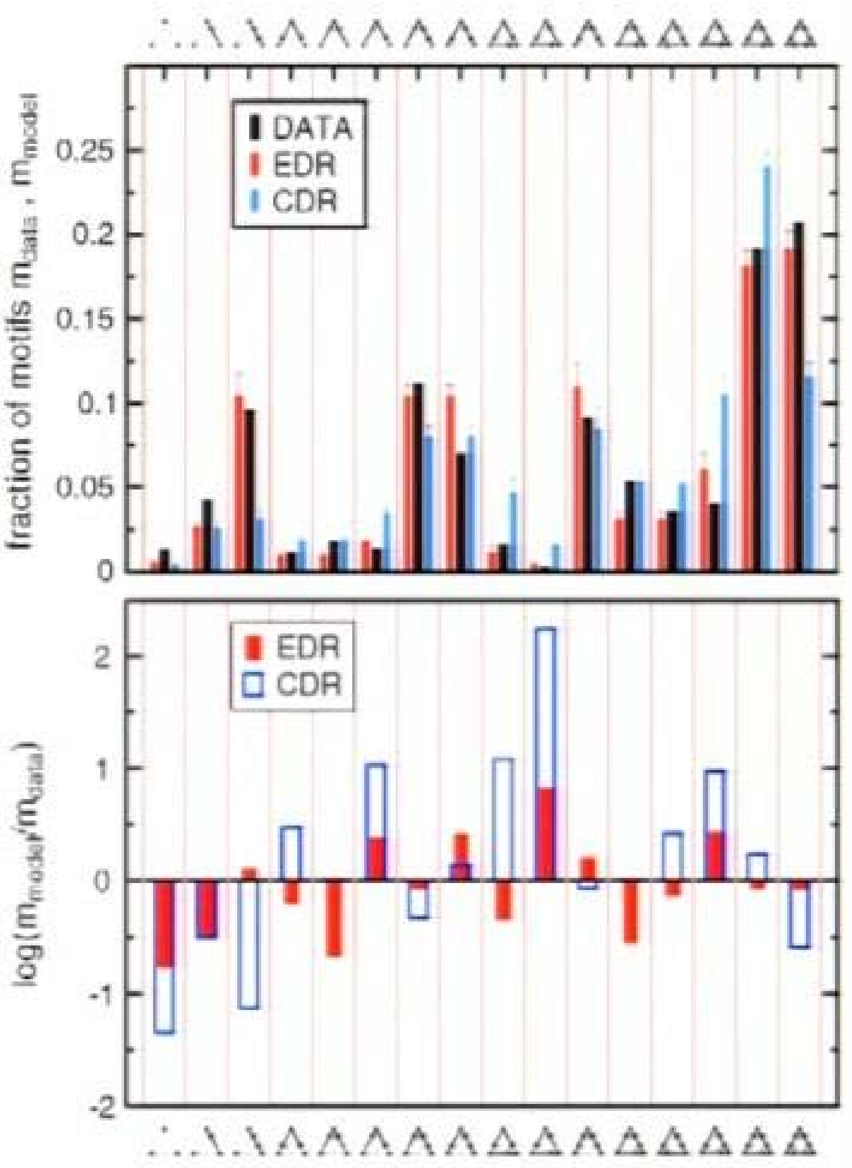






$$q_i = \log\left[\frac{m_{mod}(i)}{m_{dat}(i)}\right] \;,\; i = 1, \ldots, 16$$

$$\sigma_\Delta = \mathrm{stdev}(\boldsymbol{q})$$

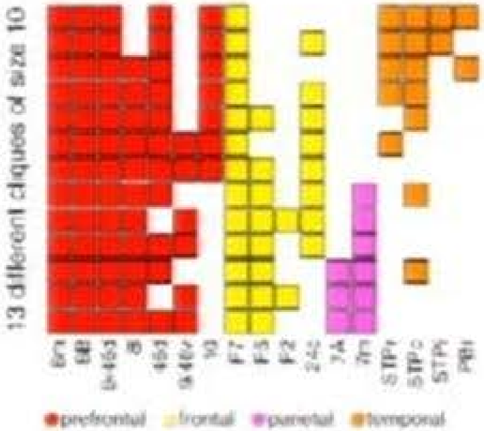
The EDR reproduces:

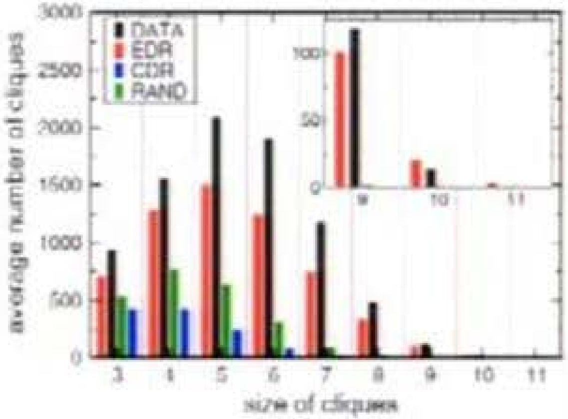
Core-Periphery structure:

- ❑ Core density: $\rho_{c-c} = 0.92$
- ❑ Periphery density: $\rho_{p-p} = 0.49$

Probability by chance: 4.52×10^{-17}

Core: dominated by prefrontal areas





N.T. Markov, M. Ercsey-Ravasz, D.C. Van Essen, K. Knoblauch, Z. Toroczkai and H. Kennedy. *Science* **342**(6158), 1238406 (2013).

Optimal Placement

The cortical network is embedded in 3D space.

Is the layout optimal to ***minimize total wire length***?

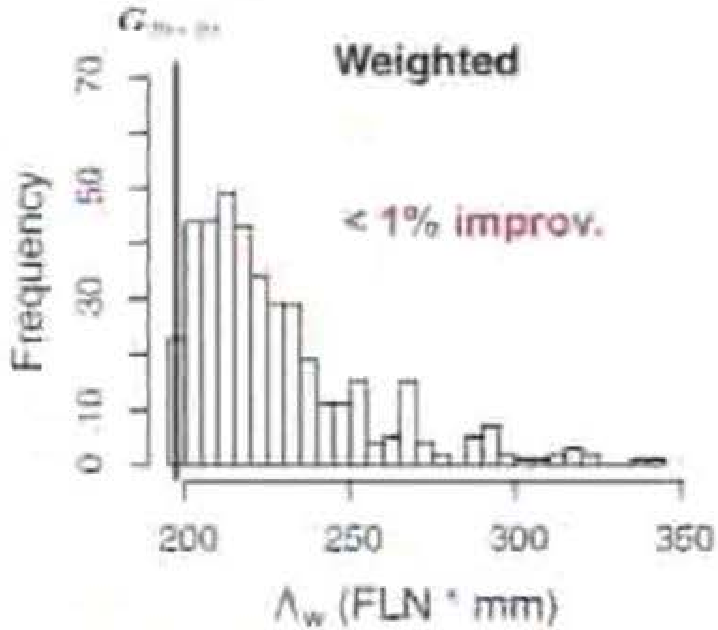
Total wire length depends on the relative positions of the nodes and on the nr of links.

TOTAL wire length: sum the (length × density) of all connections.

Testing for optimality:

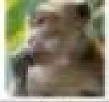
Permute the positions of nodes while keeping connectivity.

The cortical network does have an optimal placement to minimize total wire.



The EDR networks also show this property.

Macaque



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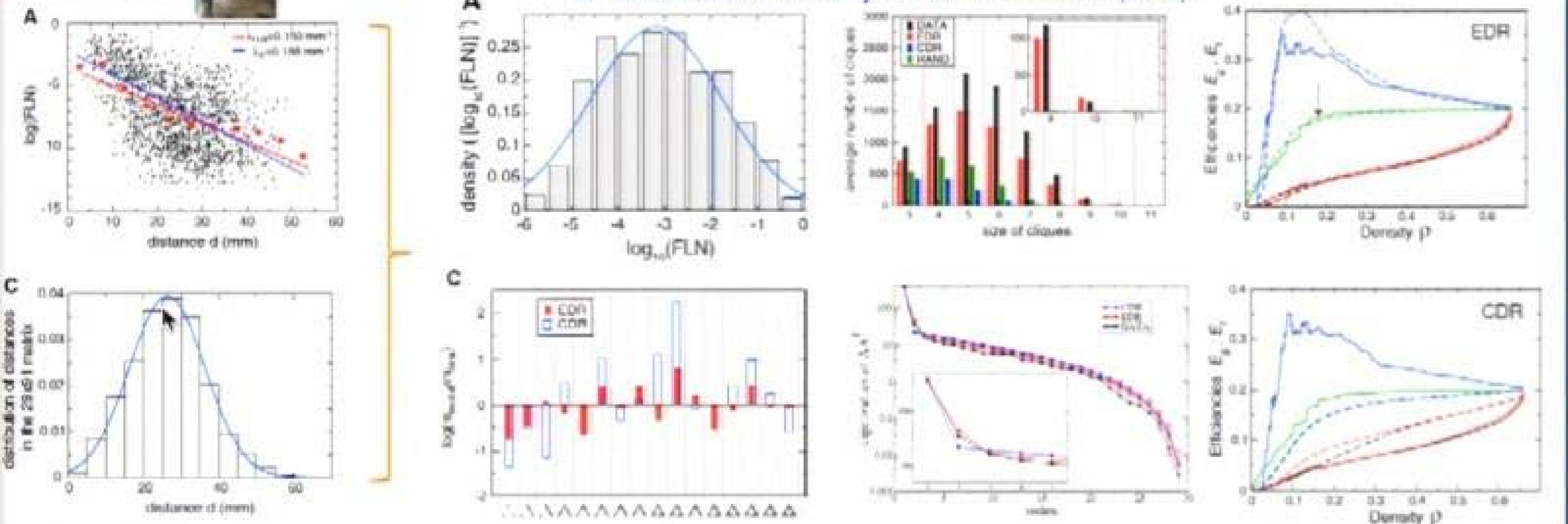
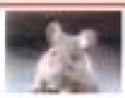
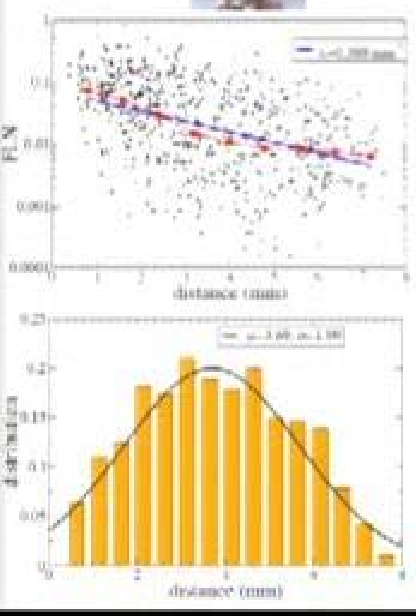
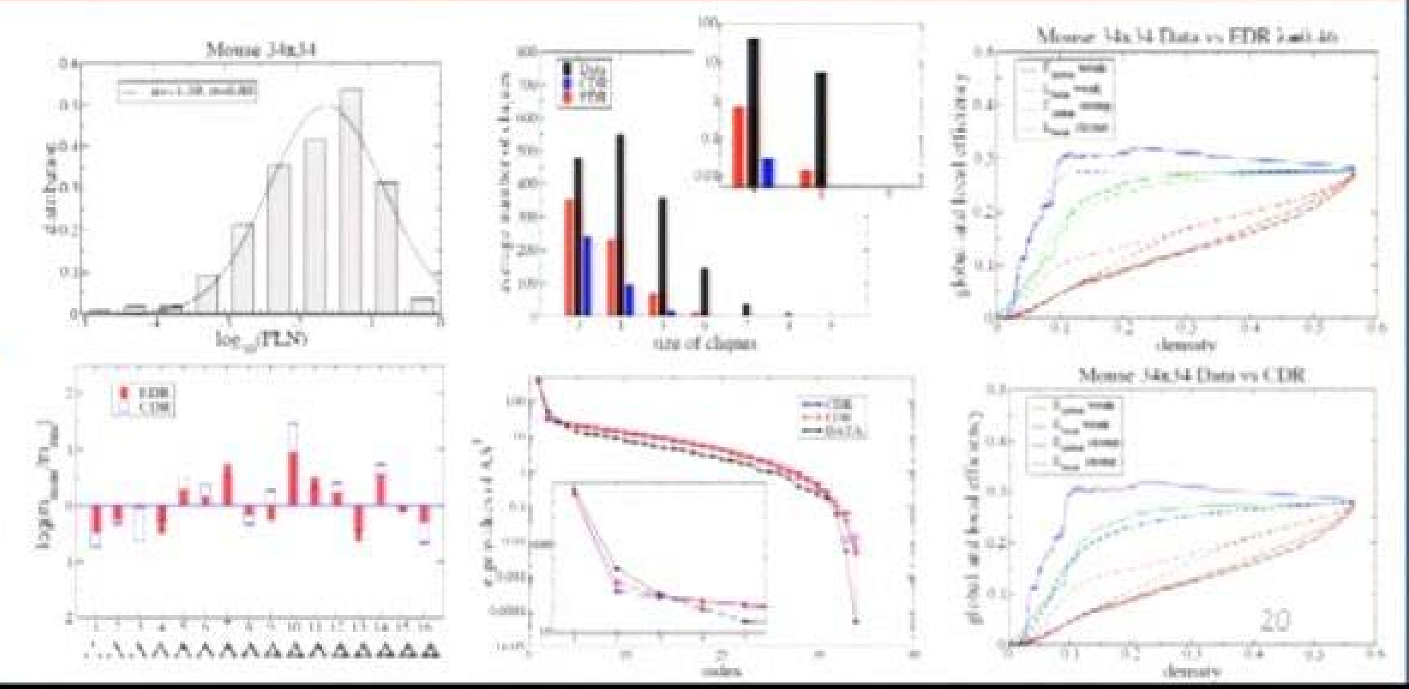


Mouse



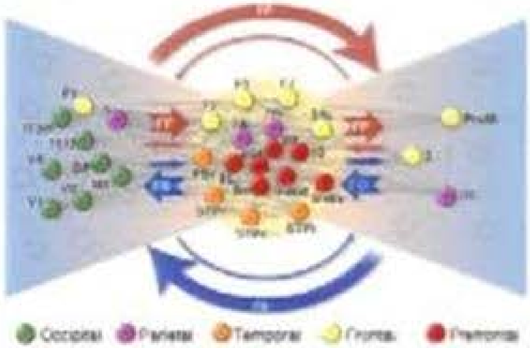




Summary, Discussion

- Wire minimization is an important design constraint of the cortex.
- The **EDR network model is predictive and** captures the binary and weighted properties of the interareal network. Its determinants are:
  - Physics: Exponential cost of wire
  - Geometry: positioning, cortical surface shape


- The interareal network is very dense: diameter of 2, high clustering. → there must be a filtering mechanism to avoid cacophony: implemented by weights.



Exploiting the laminar distributions of the connections, the network is naturally organized into a *bow-tie* structure, similar to many other functional networks, biological and man-made.

A. Broder et al. *Web. Comput. Netw.* **33**, 309 (2000).
N.T. Markov et al. *Science* **342**(6158), 1238406 (2013).

- When cognitive demands are low, the functional networks reconfigure to a more modular structure [Kitzbichler et al., 2011]. The EDR naturally allows for this economical reconfiguration of the activity. When long-range links are not in use, local processing is highly efficient (local efficiency).

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