The brain as a spatially embedded network

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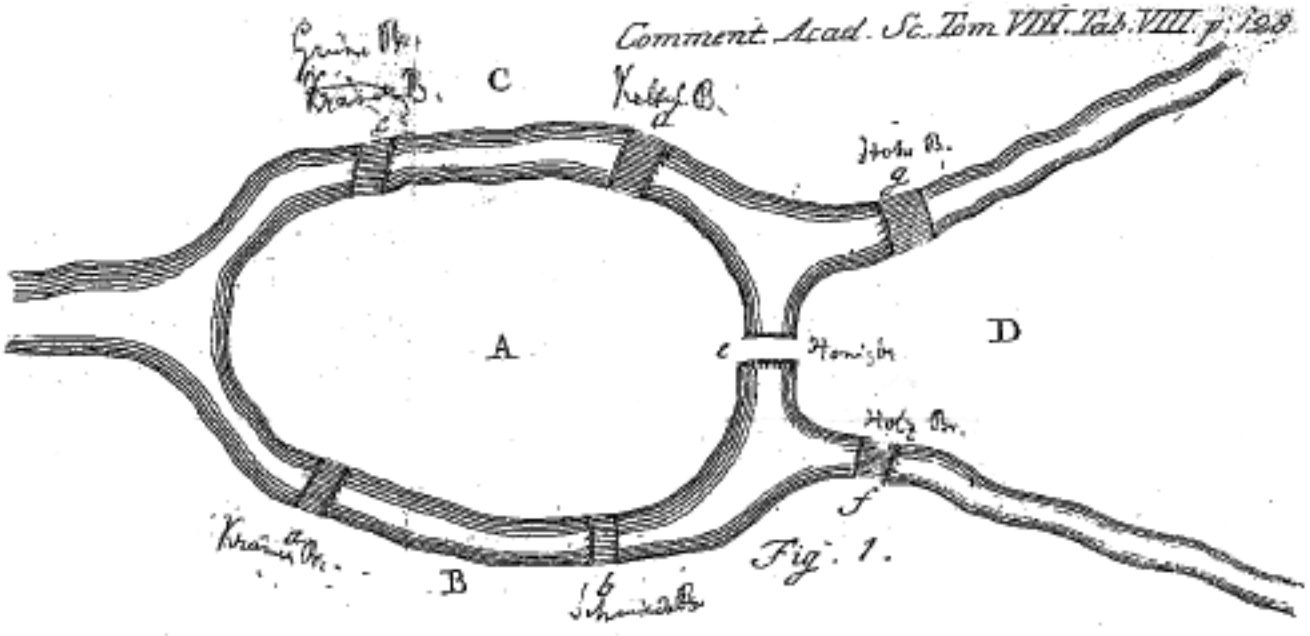
What is a network?

Introduction to graph theory and network science

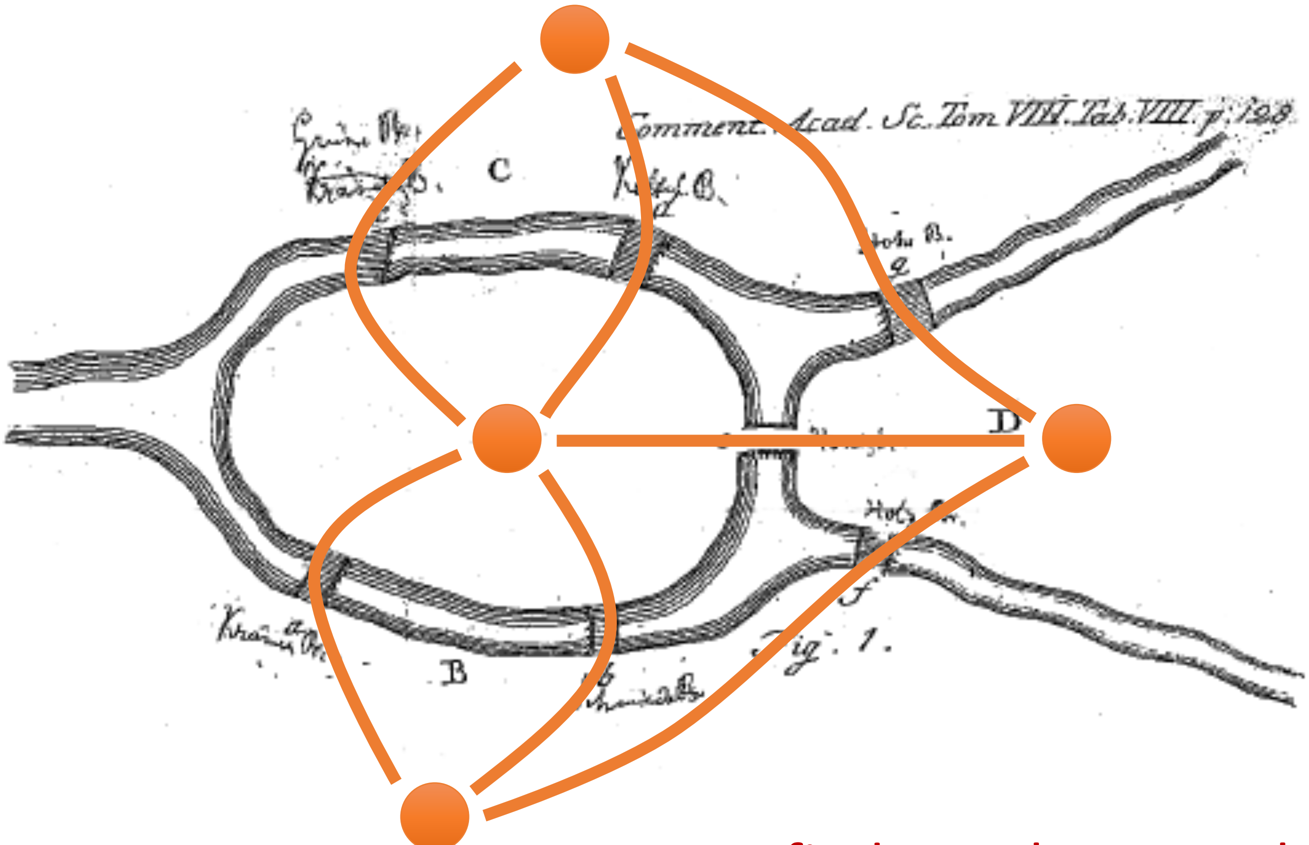
The bridges of Königsberg



Leonhard Euler, 1736

Can you find a path across the city that crosses each bridge exactly once?

The bridges of Königsberg



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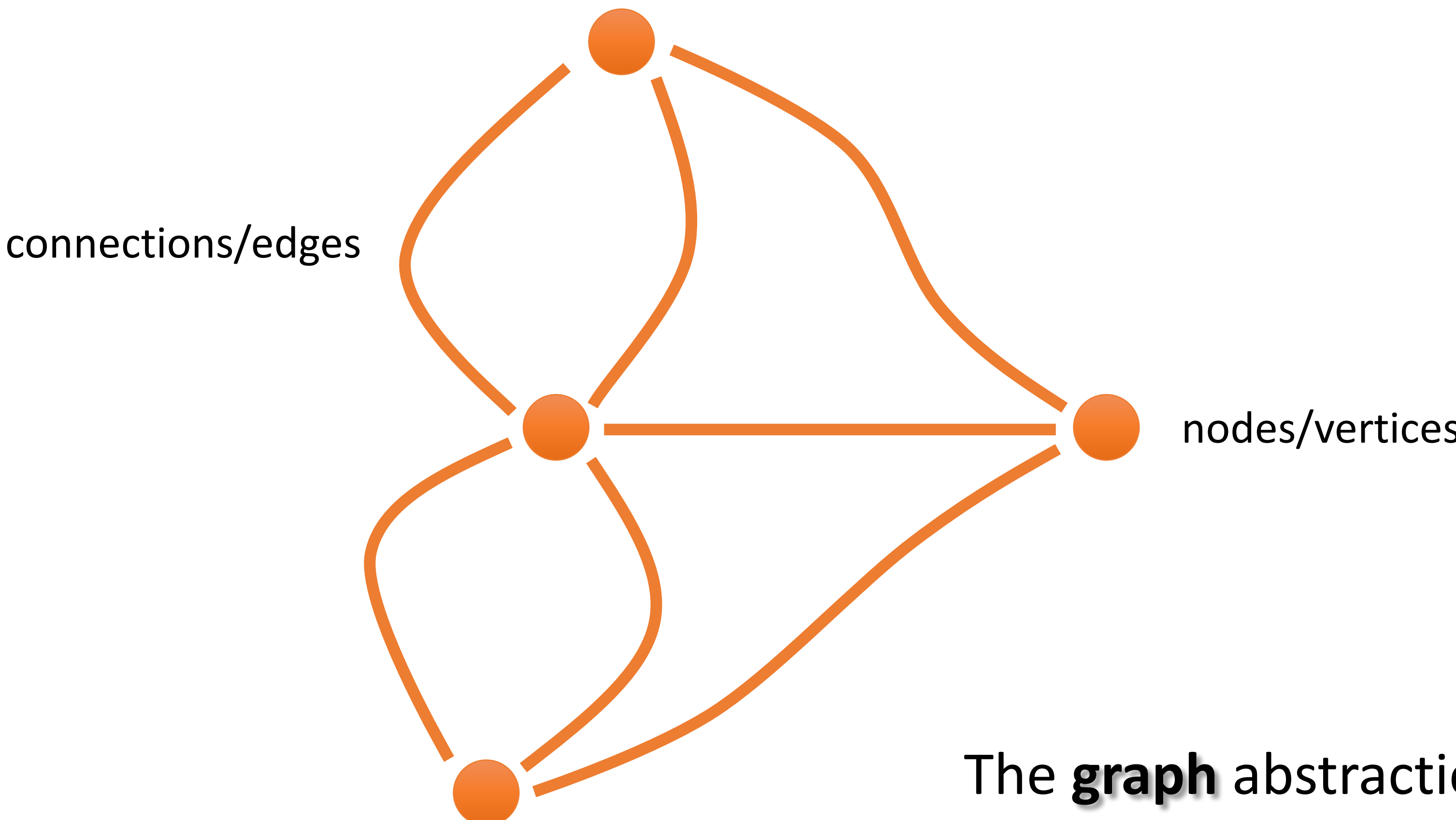
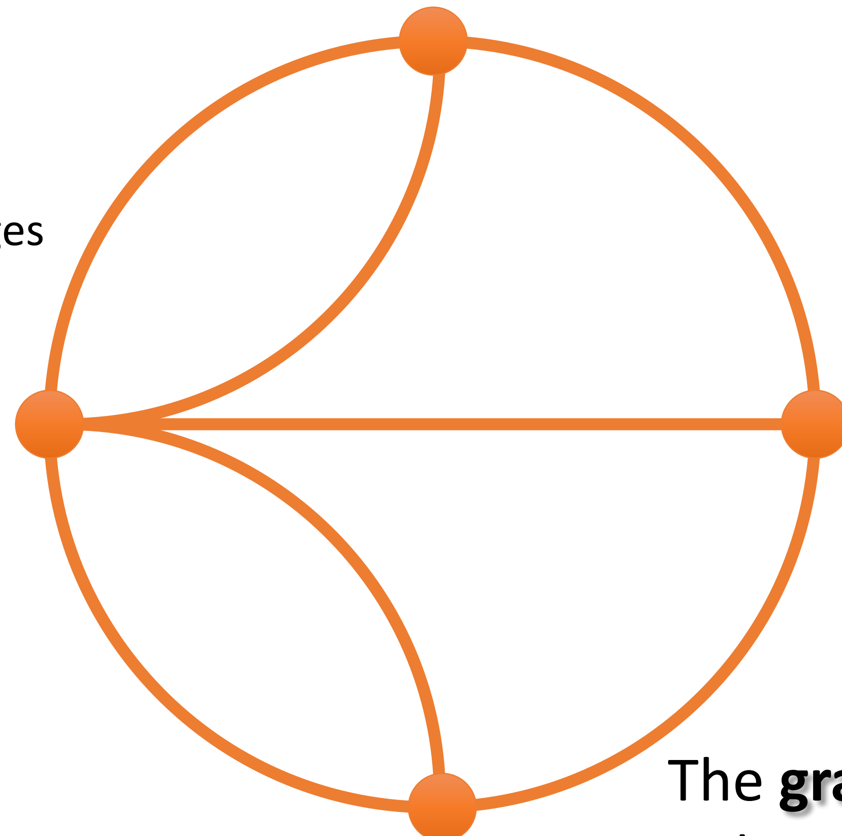


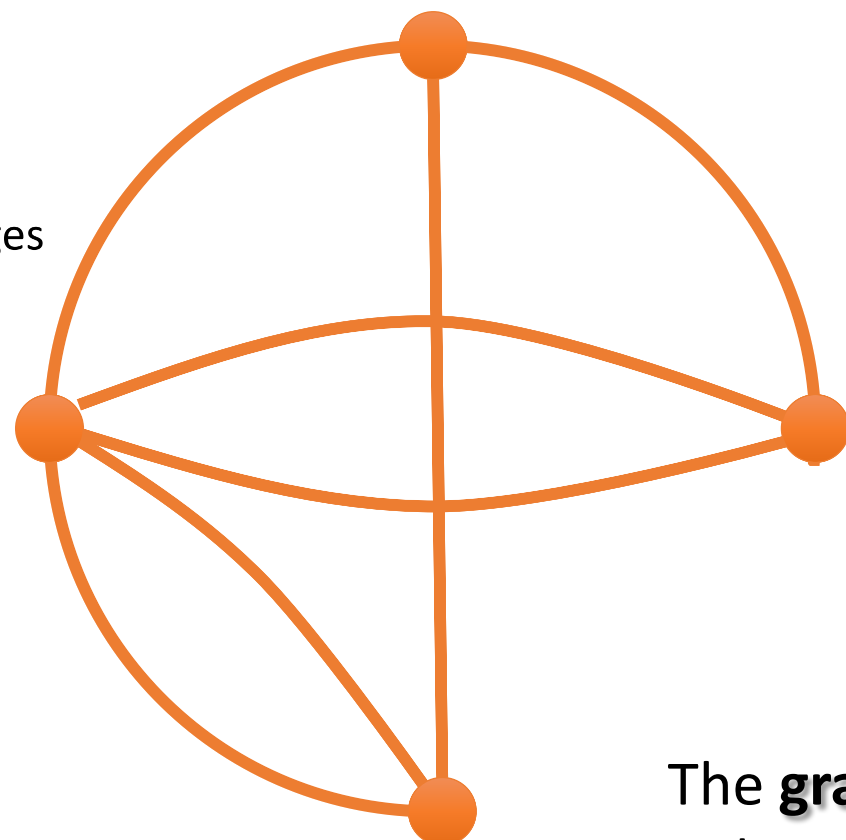
The **graph** abstraction:
only *connections* matter

The bridges of Königsberg



The **graph** abstraction:
only *connections* matter
(not e.g. locations)

The bridges of Königsberg



The **graph** abstraction:
only *connections* matter
(not e.g. locations)

What is a network?

- A **graph** is a mathematical abstraction: connections between entities

- In the context of *network science*, a **network** is a graph with a non-trivial structure that is used to model a real system.

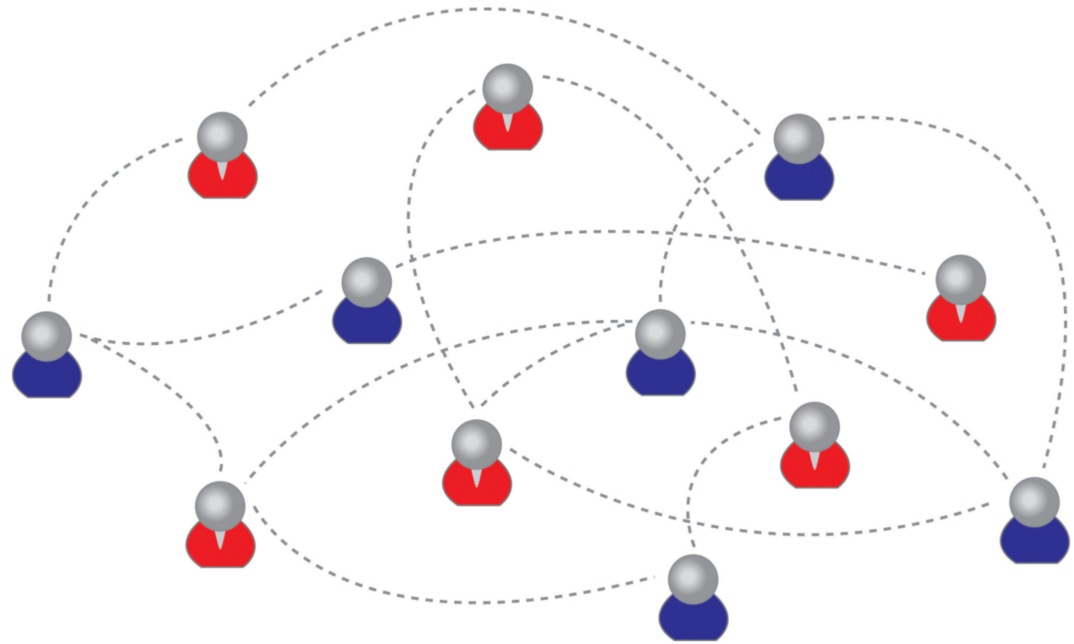
“Social” networks

vertices:
people

edges:
acquaintance relationships

Examples:

friendship network,
collaboration networks
(e.g. scientific), etc.

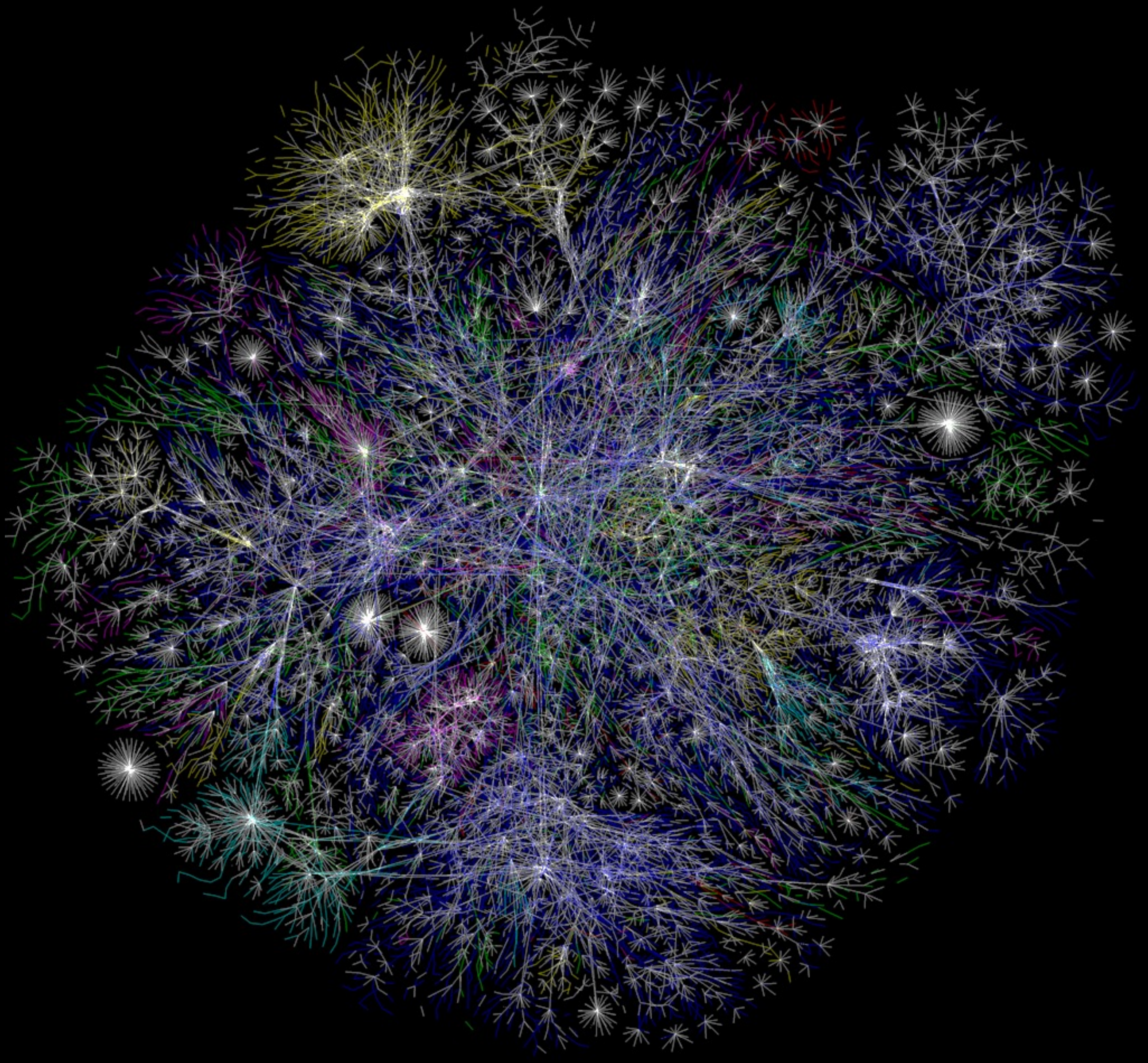


Information networks

Example:

vertices:
webpages

edges:
hyperlinks



Map of the World Wide Web (opte.org)

Transportation networks

The network of transportation routes between destinations, e.g. network of roads / train lines, network of airline / ship routes, etc.

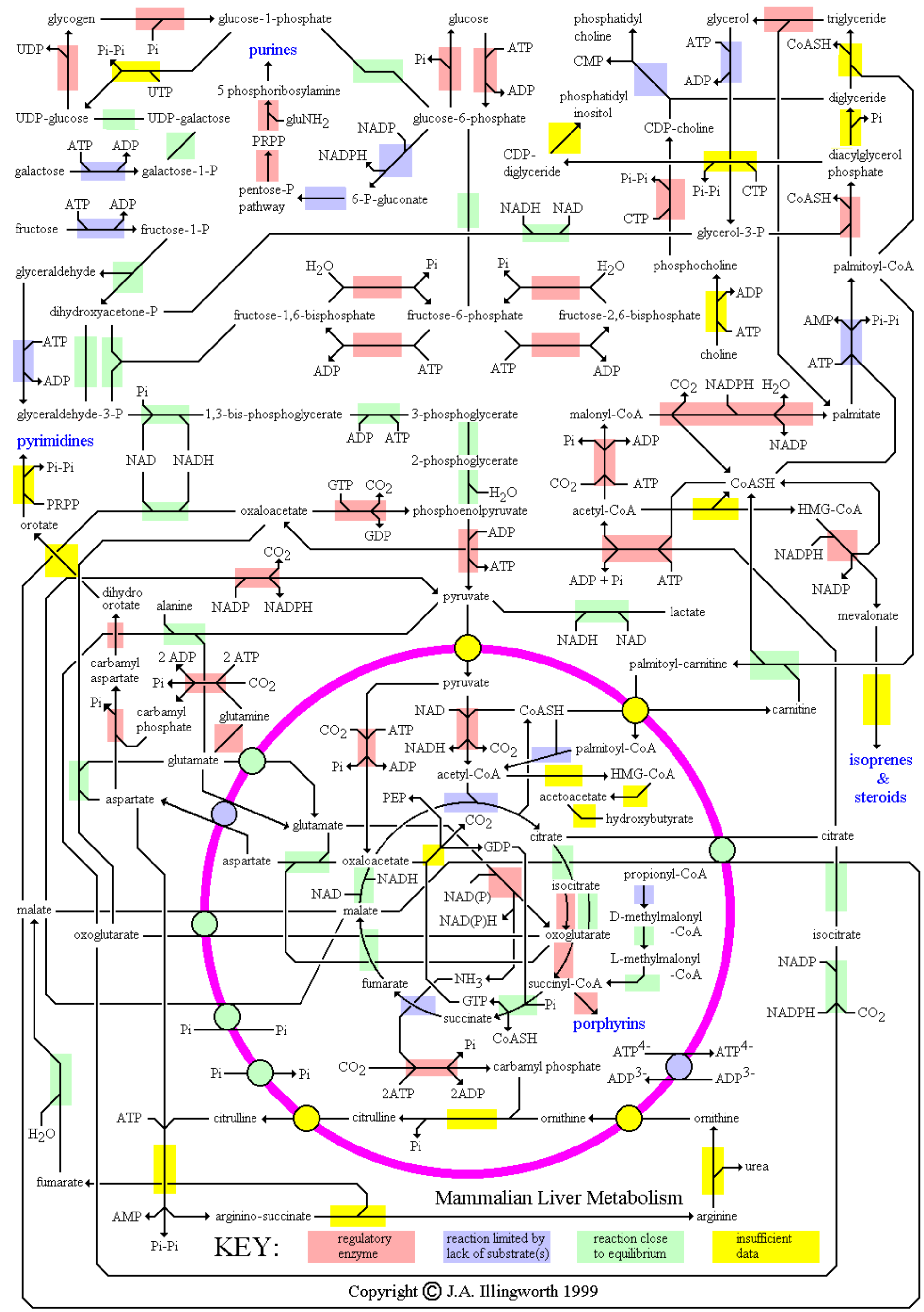
Map of word wide airline routes

Biological networks

Examples:

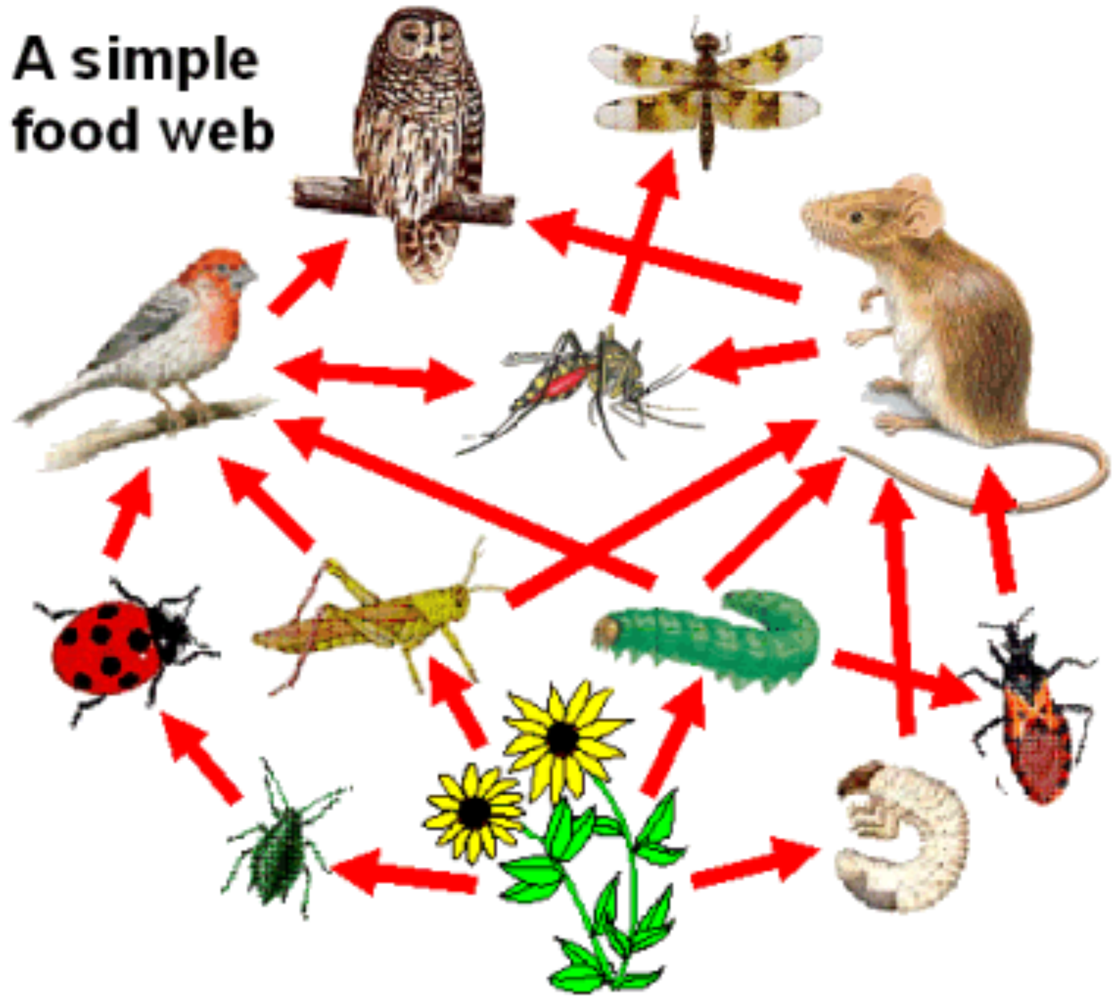
metabolic pathways:
cell constituents and their interactions

genetic regulatory network



Food webs

The network of predator-prey relationships in an ecosystem



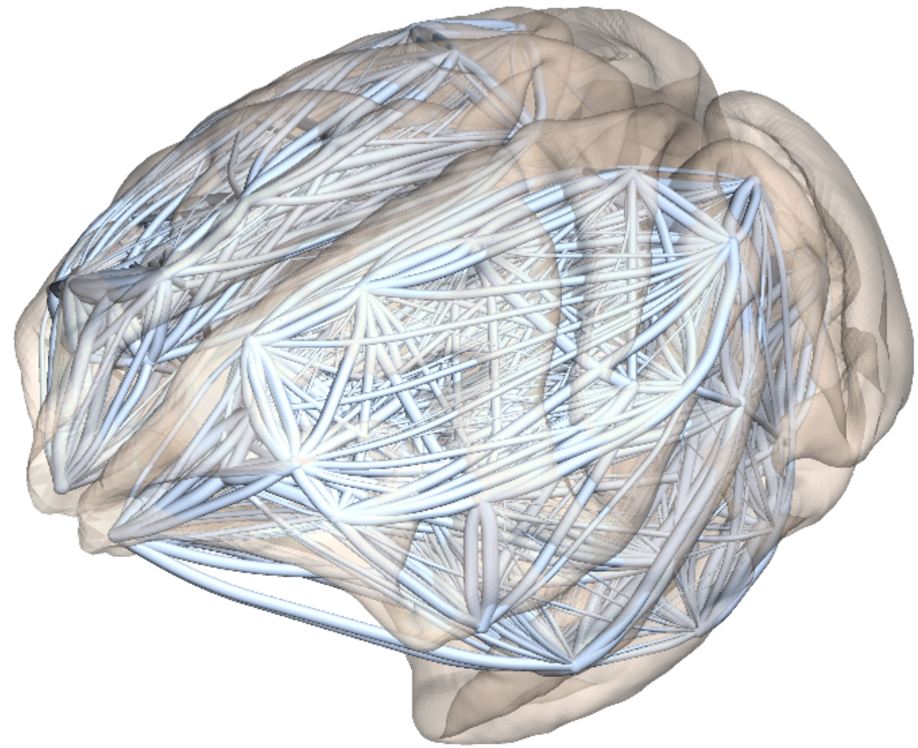
Brain networks

vertices:

- neurons
- brain regions

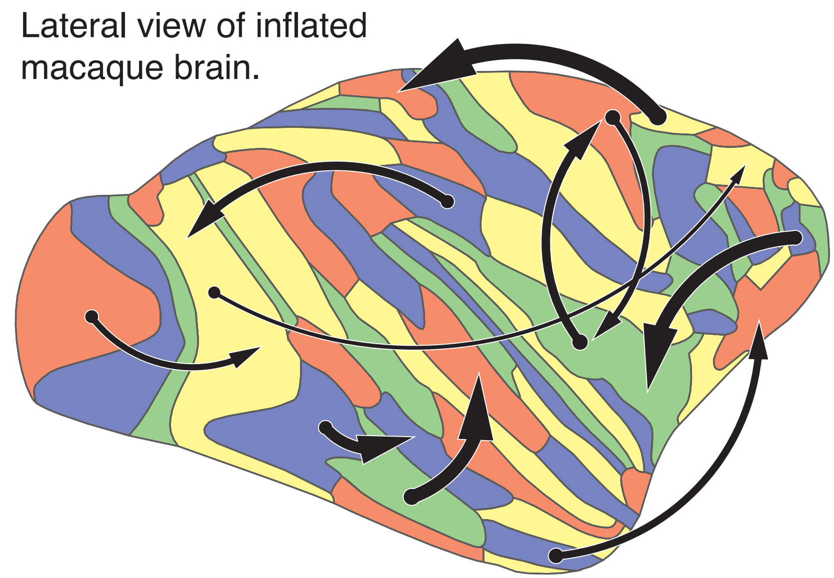
edges:

- anatomical (synaptic) connections
- functional connectivity (correlation between activity)

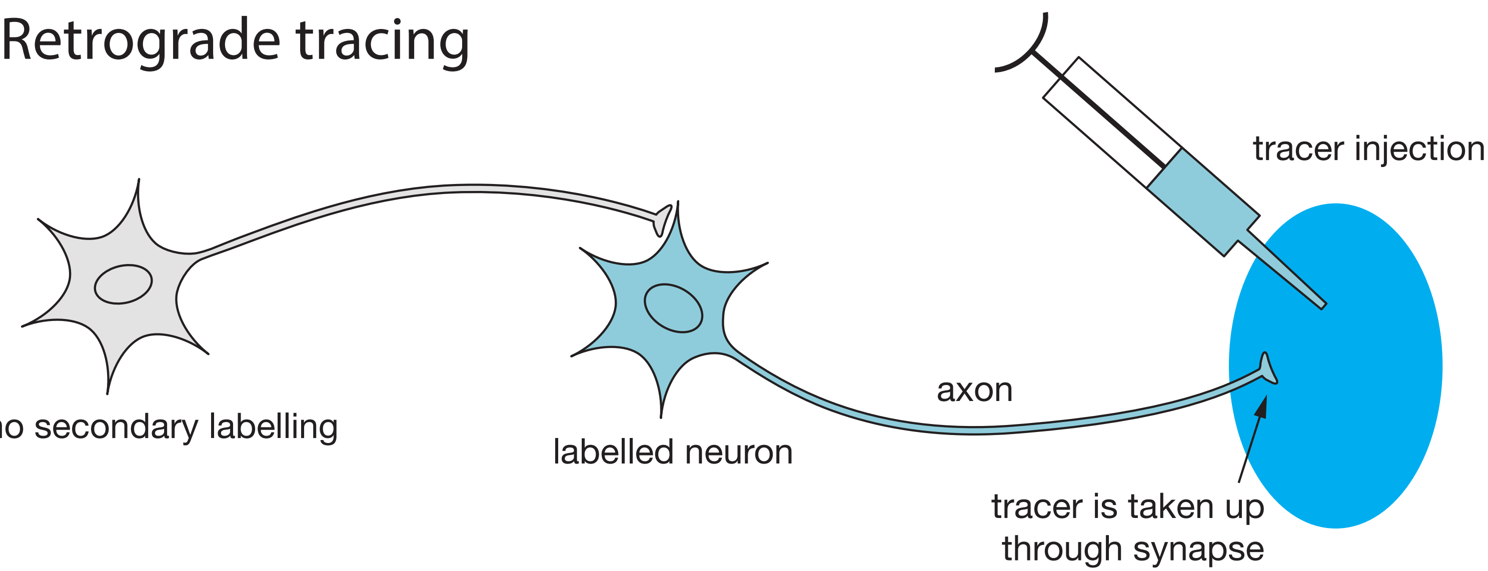


Mapping anatomical connections in the brain

Brain networks (connectomes)

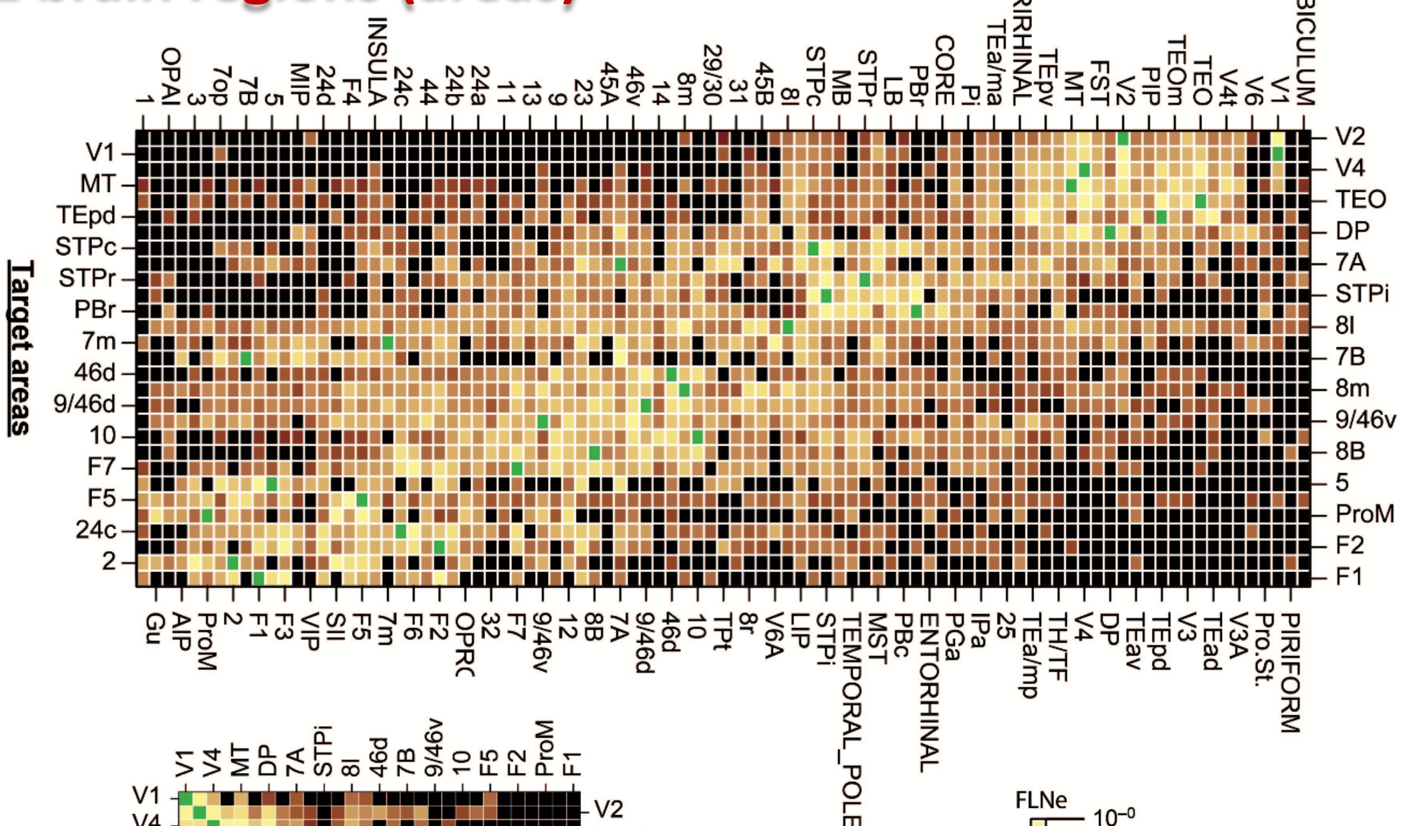


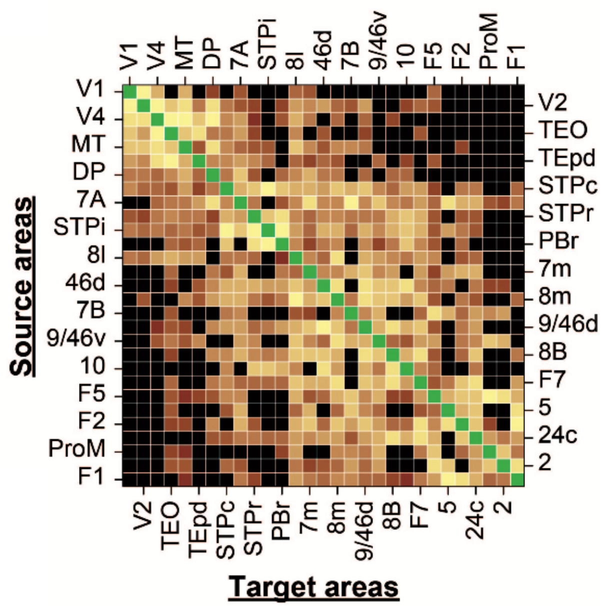
Retrograde tracing

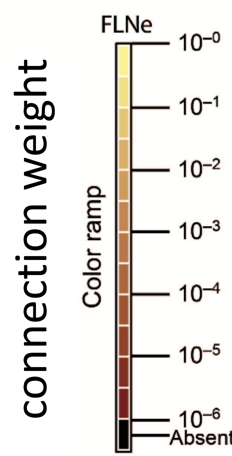


The macaque cortex

91 brain regions (areas)







Markov, N. T. *et al. Cereb. Cortex* **24,** 17–36 (2012).

The macaque cortex

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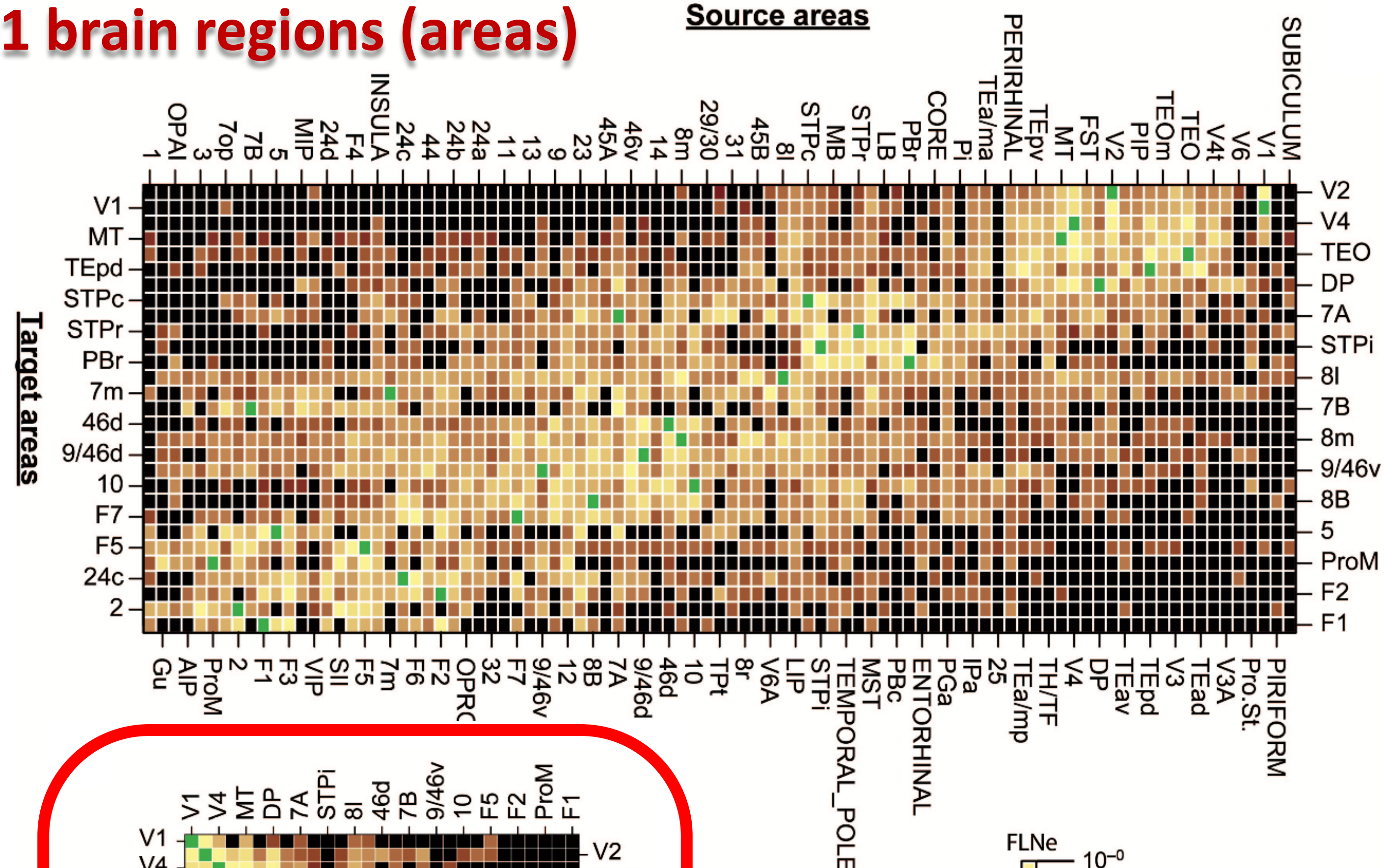
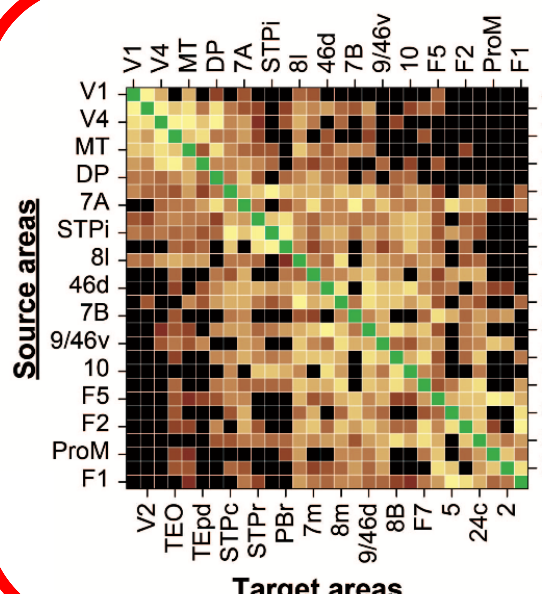
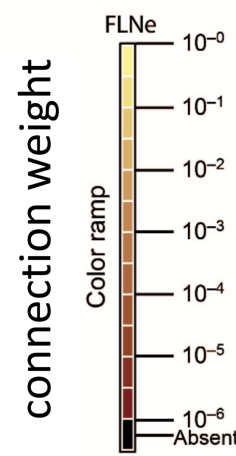




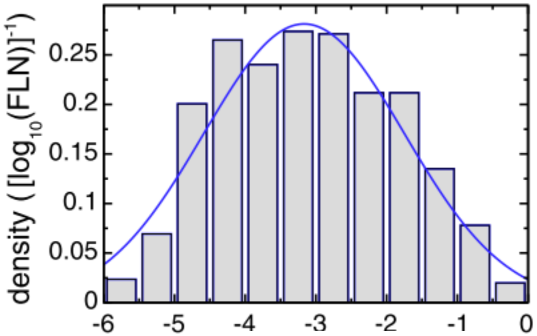


29×29 edge-complete

Properties of the cortical network

- Directed: $i \rightarrow j$ distinct from $j \rightarrow i$
- Weighted: connections have a strength.
  Strengths span 5 orders
  of magnitude.

log-normal weight distribution



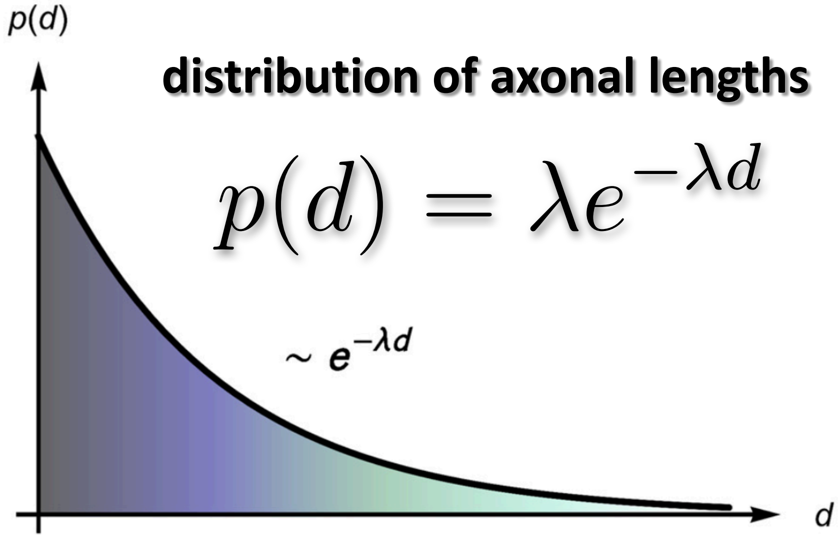
log - weight

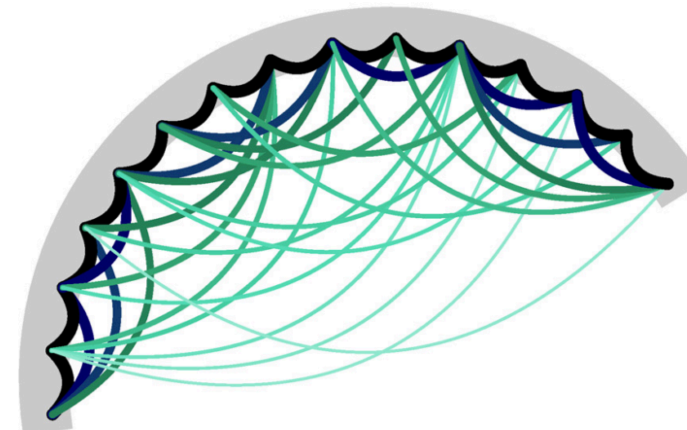
- Dense: 66% density in macaque
- Spatially embedded:
  The cortical regions have physical locations.
  Is there a connectivity–distance relationship?

The Exponential Distance Rule (EDR)

distribution of axonal lengths

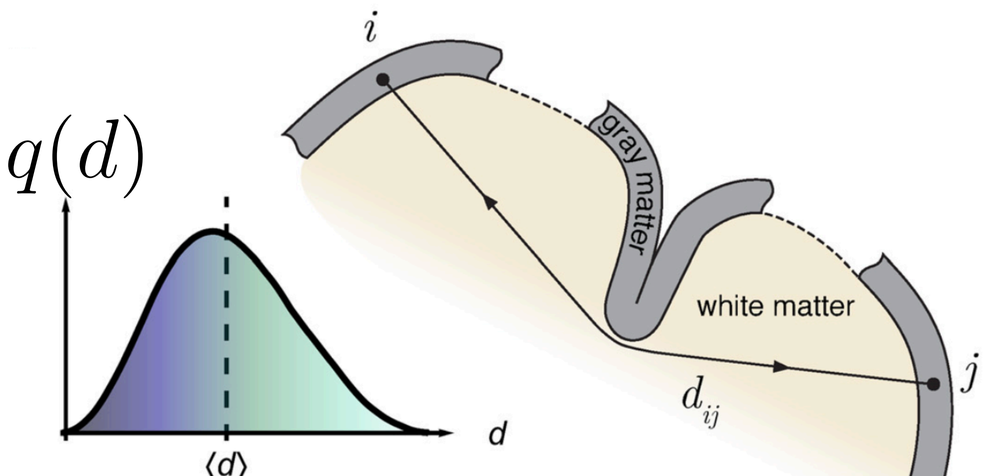
$$p(d) = \lambda e^{-\lambda d}$$





inter-areal connections

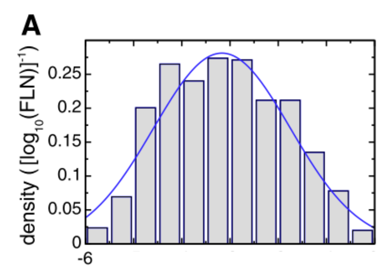
black – strong
green – weak



inter-areal distances through white matter

approximate axon lengths

EDR explains weight heterogeneity



log - weight

The Exponential Distance Rule (EDR)

macaque (*Macaca fascicularis*)

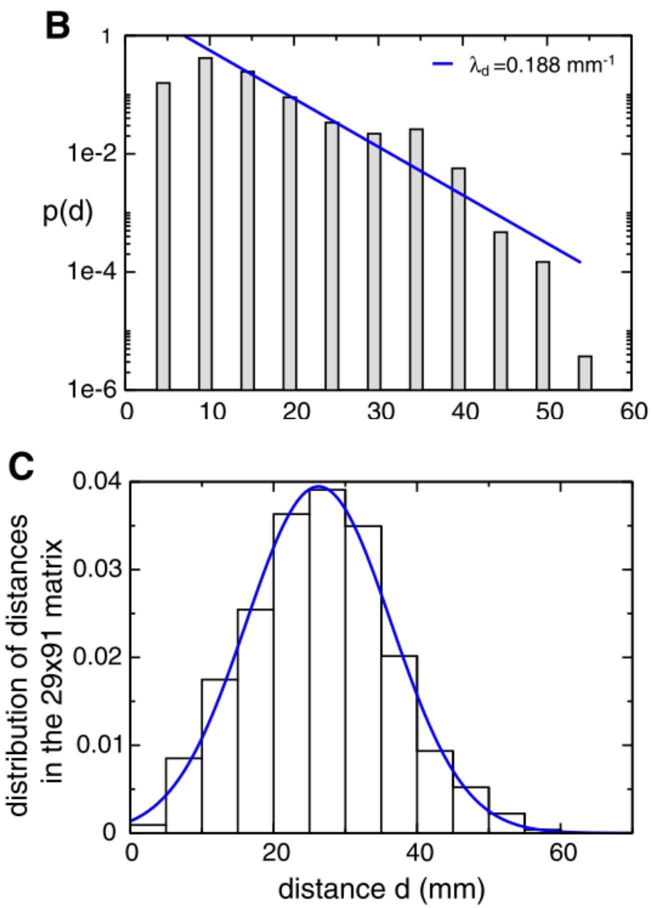
$\lambda = 0.19\ \mathrm{mm}^{-1}$, from 29 injections

mouse (*Mus musculus*)

$\lambda = 0.78\ \mathrm{mm}^{-1}$, from 13 injections

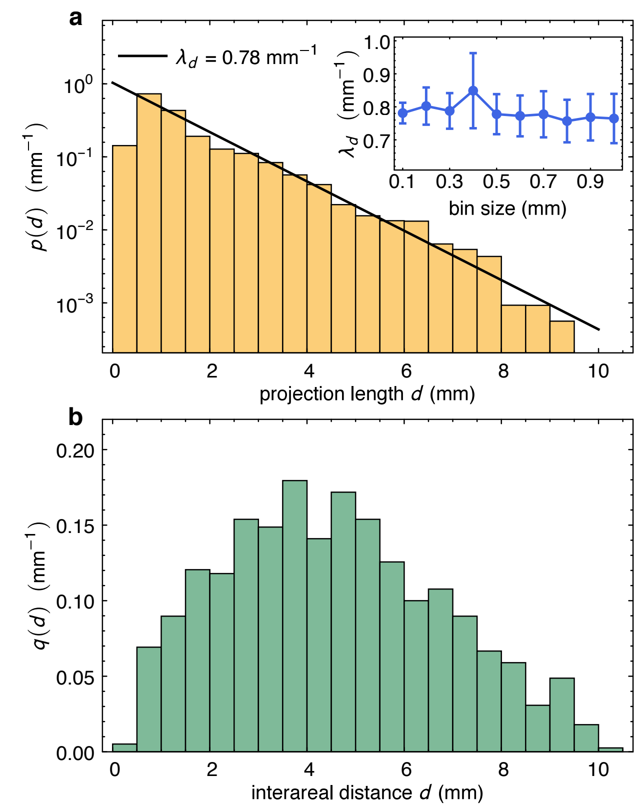
axon length distr. $p(d)$

inter-areal dist. distr. $q(d)$



Ercsey-Ravasz, M. *et al.* *Neuron* **80,** 184–97 (2013).

EDR in mouse, from 2 million labelled neurons



Horvát, Sz. *et al.* *PLOS Biol.* **14,** e1002512 (2016).

An EDR-based random graph model

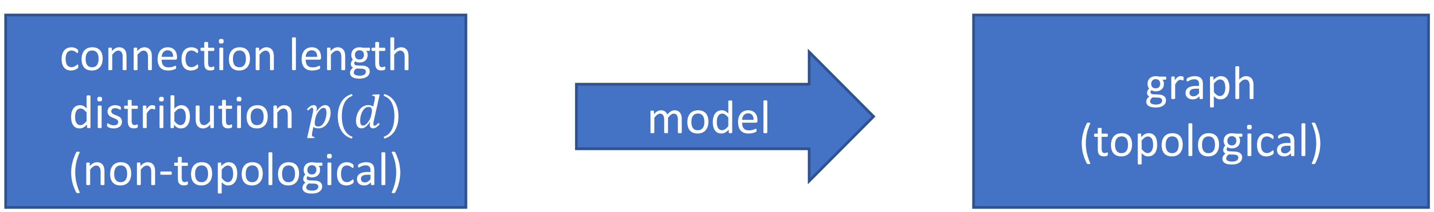
Maximum entropy principle
"most random" graphs still consistent with EDR

Generative model

Repeat:
1. Draw a random distance d from $p(d) \sim e^{-\lambda d}$
2. Pick a random ordered area pair (i, j) with separation d (within some tolerance)
3. Insert connections $i \rightarrow j$

Multiple connection between i and j are allowed → **weight**
Stop when reaching the desired *binary* density (to match with measurements)

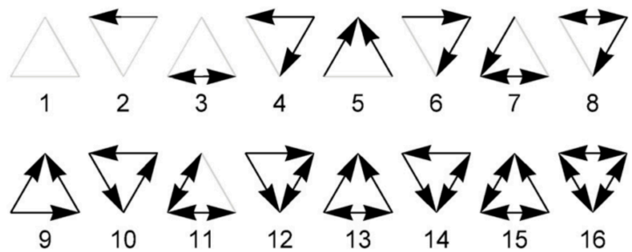
Random, spatially embedded, weighted, directed networks.



Model fitting

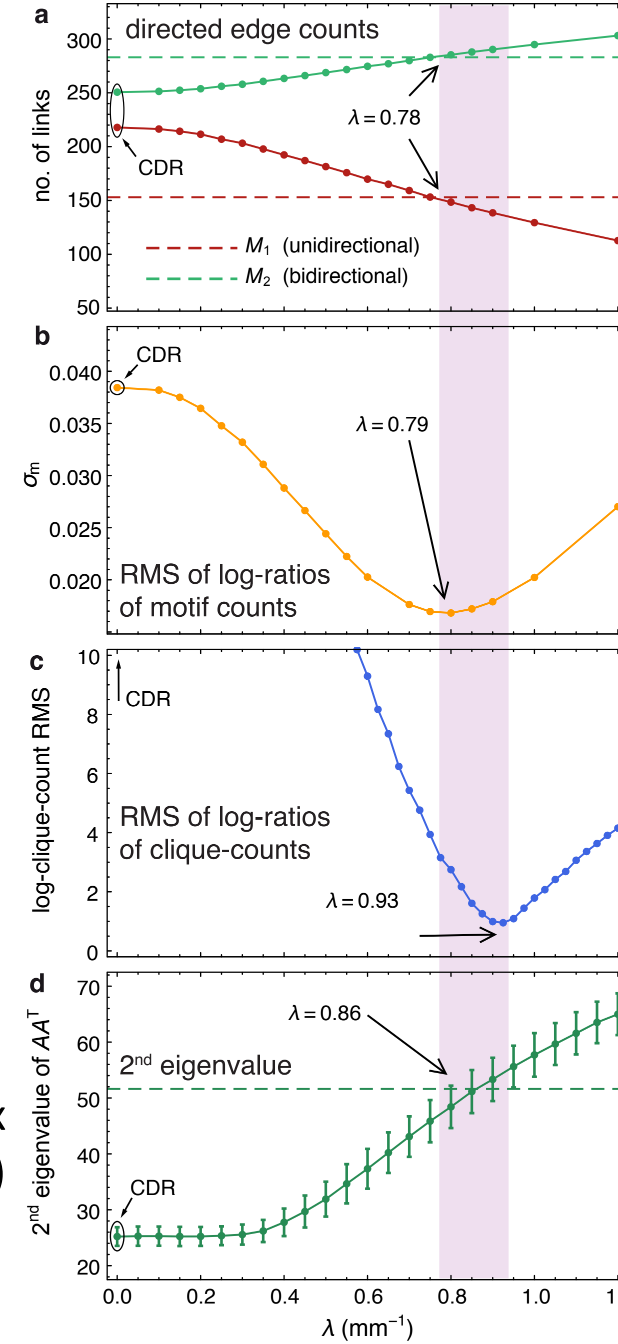
unidirectional edges
bidirectional edges

graph motif counts



size distribution of cliques (complete subgraphs)

2^{nd} eigenvalue of AA^T matrix (A = adjacency matrix)



mouse $\lambda\ (\mathrm{mm}^{-1})$

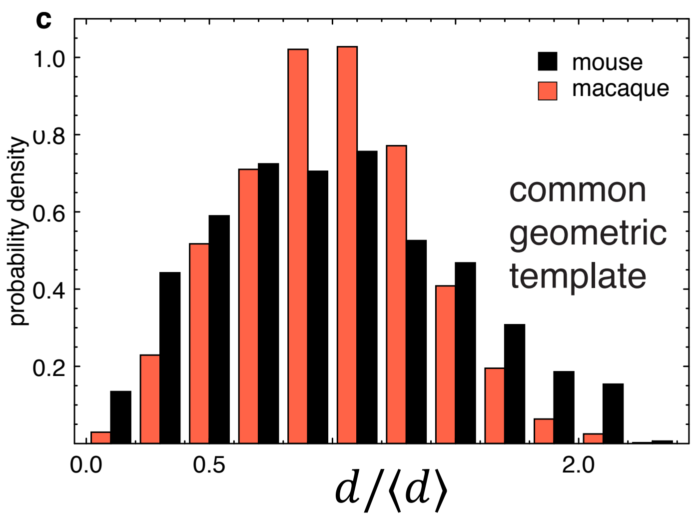
Comparing networks through *global graph properties*

- good model-data agreement
- determine λ from known topology

Comparing macaque vs mouse cortices

Common geometric template

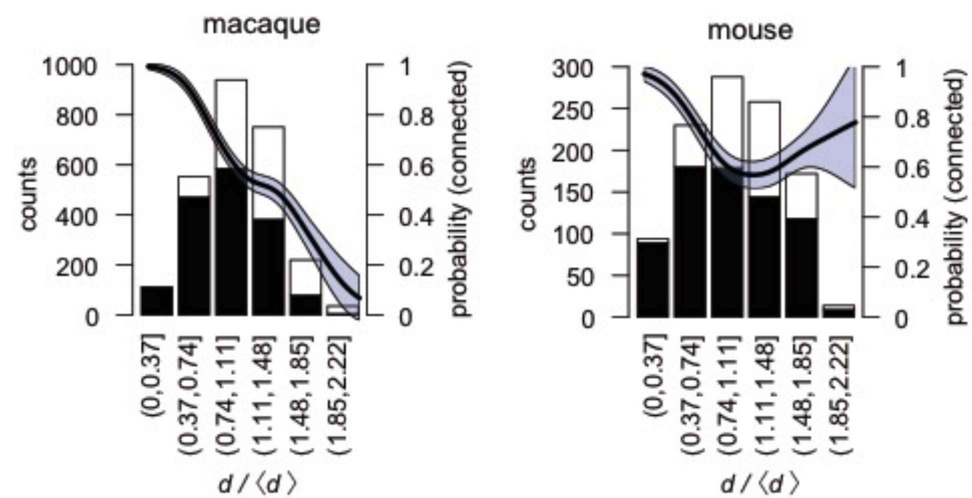
Normalize by avg. inter-areal distance $\langle d \rangle$



Normalized interareal distance distributions in macaque and mouse are similar

normalized (size-relative) EDR decay rates

$(\lambda\langle d \rangle)_{\text{macaque}} = 5.0$ $(\lambda\langle d \rangle)_{\text{macaque}} = 3.5$



Fraction of connected area-pairs vs. normalized distance: more long-distance connections in mouse

- the EDR leads to a decrease in the strength of long-range connections in macaque compared to mouse
  - expectedly even more emphasized in the human brain
  - increased susceptibility to disconnection syndromes (Alzheimer, schizophrenia)

Summary

- The connectivity (topological) structure is important in many real-world systems, including biological ones.
  → **Borrow concepts from graph theory.**
- **Exponential Distance Rule (EDR)** is valid across mammalian brains of different sizes (tested for macaque, mouse)
- *Global properties* of the anatomical ***connectivity*** of the cerebral cortex is well described by *the simplest EDR-based random graph model.*
- EDR provides a framework for cross-species comparison, possible extrapolation for larger (human) brains.