Bottleneck Capacity of Random Graphs for Connectomics

Lav R. Varshney

University of Illinois at Urbana-Champaign

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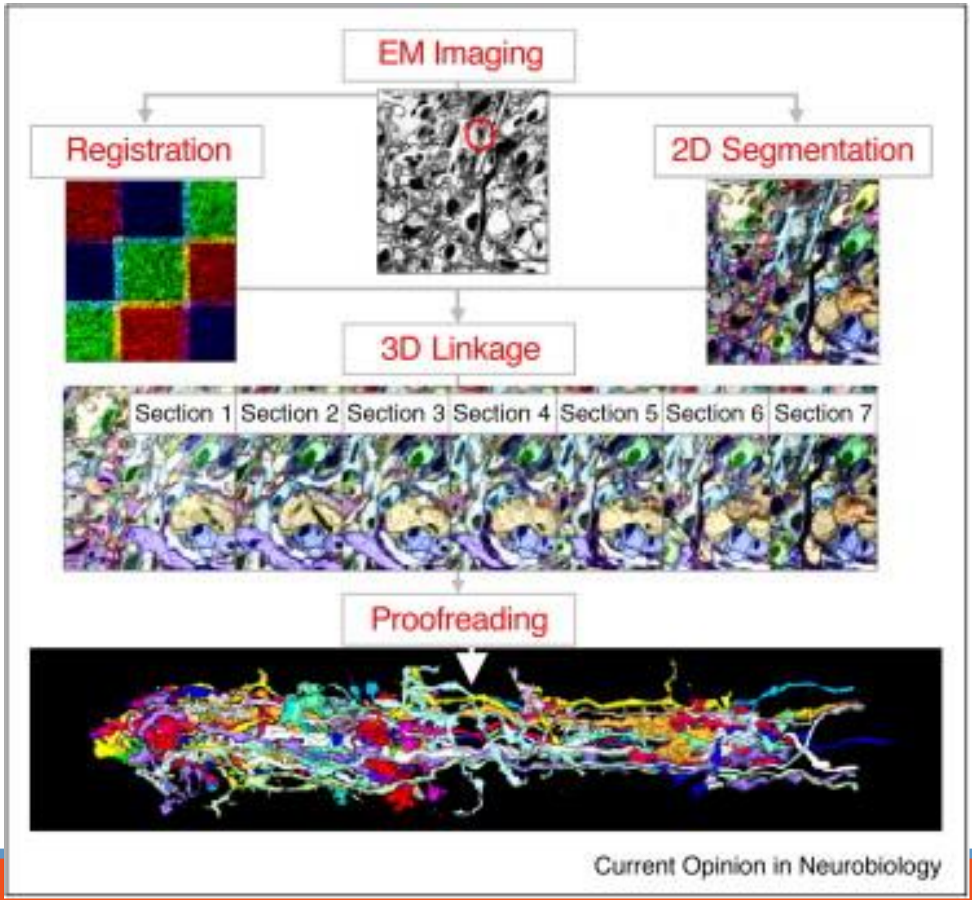
Connectomics

- A connectome is a comprehensive map of neural connections in the brain, its wiring diagram
- The full anatomical connectome at the level of individual neurons and synapses has been mapped for only one organism: the nematode *Caenorhabditis elegans* [White et al., 1986; Varshney et al., 2011]
- Partial connectomes of mouse retina [Briggman et al., 2011], mouse primary visual cortex [Bock et al., 2011], *Drosophila* lamina [Rivera-Alba et al., 2011] and *Drosophila* medulla [Takemura et al., 2013] have also been successfully reconstructed at the level of individual neurons and synapses

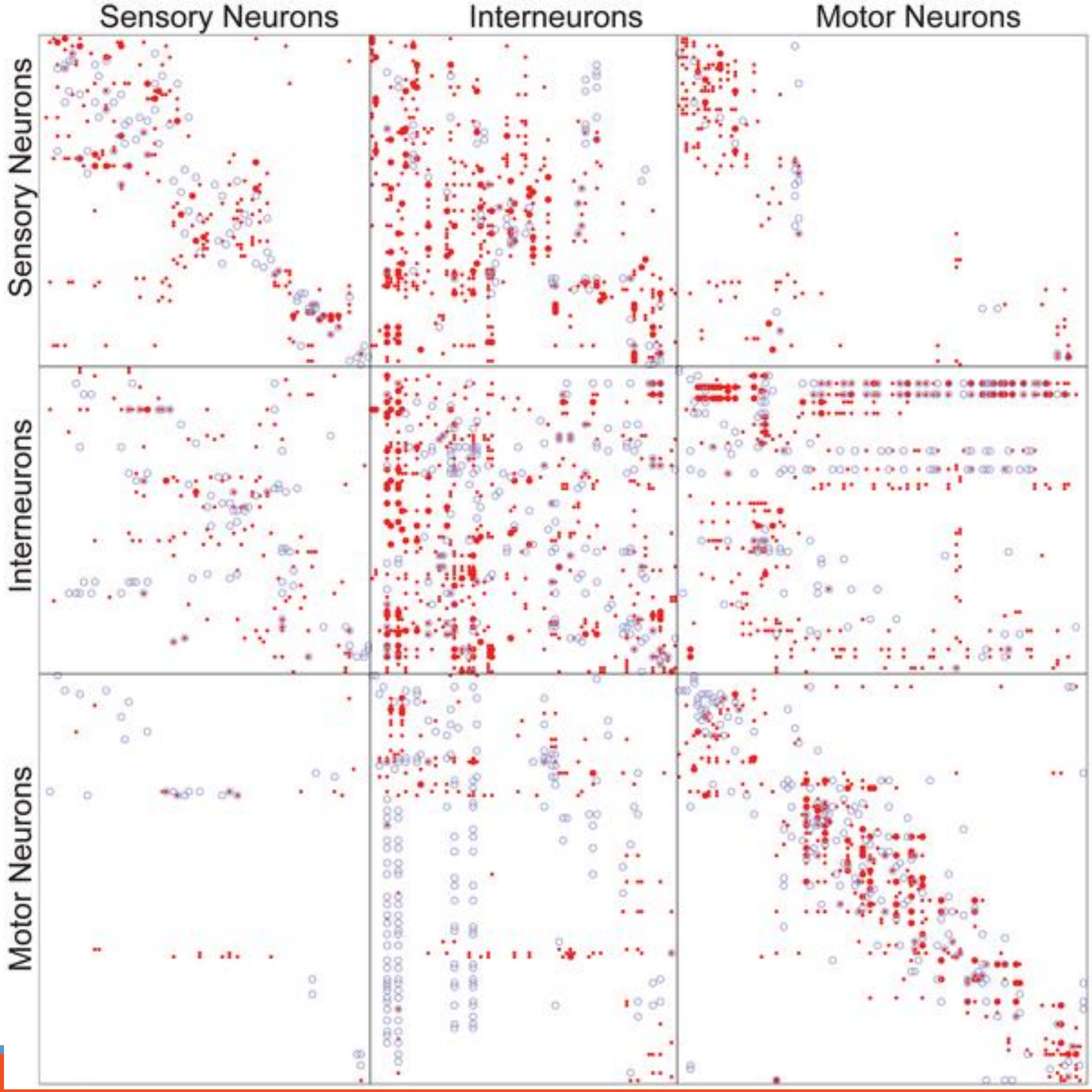
Connectomics

- Connectome reconstruction from serial-section transmission electron micrographs (ssTEM) is a difficult image processing problem, relying on machine learning and crowdsourcing



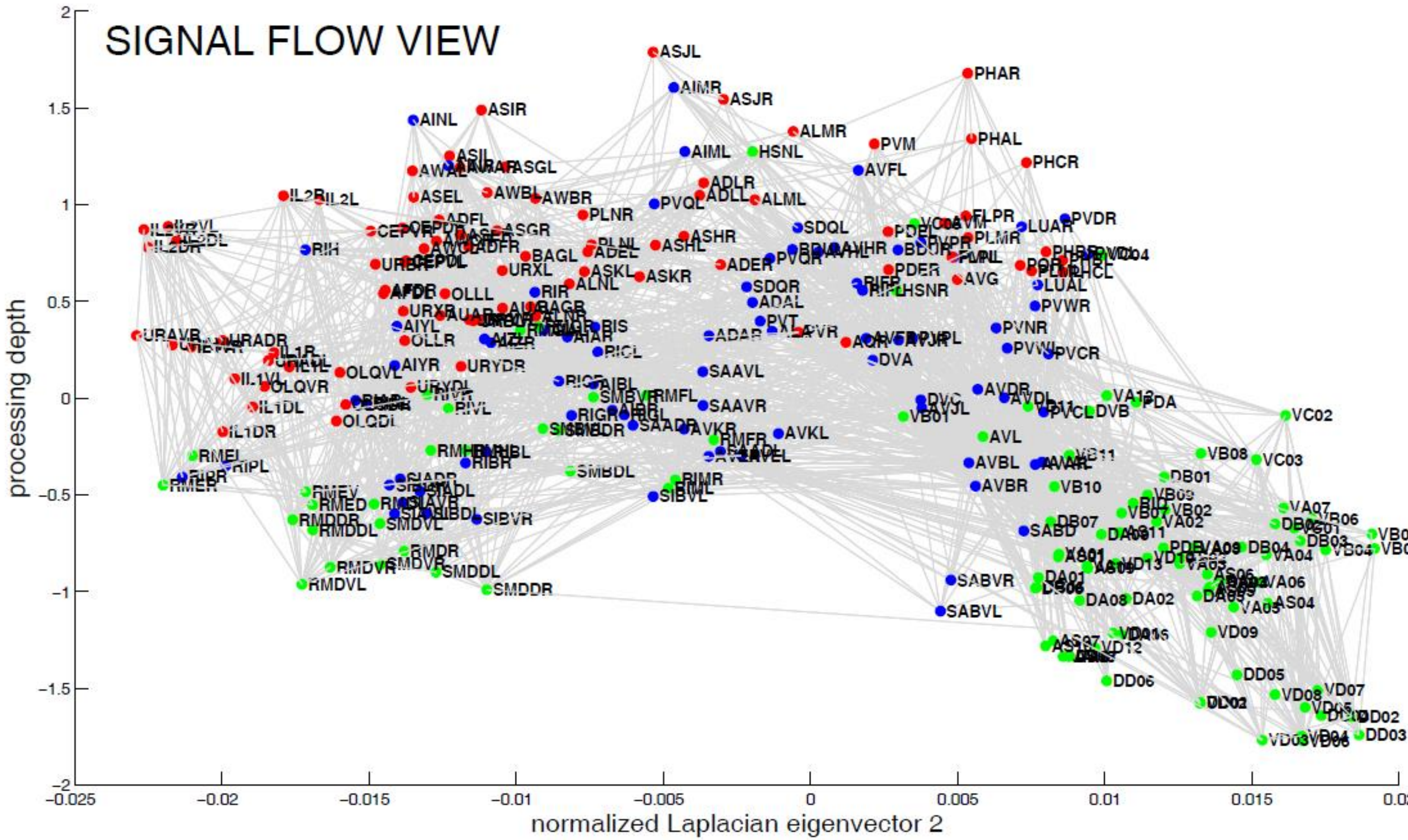
The semi-automated reconstruction pipeline for ssTEM images deployed at HHMI Janelia Farm [Chklovskii et al., 2010]

C. elegans Connectome



Adjacency matrices for the gap junction network (blue circles) and the chemical synapse network (red points) with neurons grouped by category [Varshney et al., 2011]

C. elegans Connectome



The wiring diagram arranged so the direction of signal flow is mostly downward. Neurons are identifiable, with sensory neurons (red); interneurons (blue); motorneurons (green) [Varshney et al., 2011]

Connectomics

- Experimental connectomics has been advancing, but how can we advance theoretical neuroscience?

Understand relationships between structure and function in the brain

Connectomics

- Experimental connectomics has been advancing, but how can we advance theoretical neuroscience?

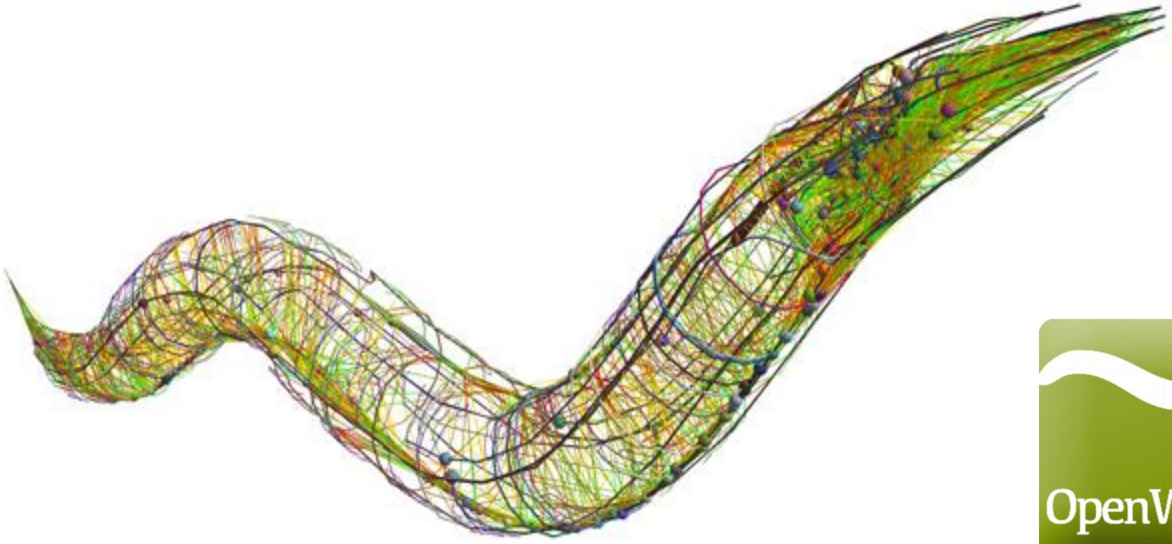
Understand relationships between structure and function in the brain

- One approach to analysis is discovery-oriented
- Simultaneously screen for several features of the anatomical network that may be associated with cognitive, behavioral, and psychiatric phenotype differences between nervous systems
- Connectome-wide association study (CWAS)

Connectomics

- Another approach is hypothesis-driven

- Detailed simulation



OpenWorm

Connectomics: A Theoretical Approach

- Use a hypothesis-driven approach to study a particular information-theoretic network functional that may provide insight into neural function
- Neural efficiency hypotheses of intelligence argue that information flows better in the nervous systems of bright individuals
- We have previously argued that information-theoretic capacity limits on information flow are predictive of behavioral speed [Varshney and Shah, 2011]
  - bottleneck capacity of the network emerges from a pipelining model of information flow

Connectomics: A Theoretical Approach

- Here we ask whether the bottleneck capacity of the *C. elegans* neuronal network is significantly different from random graphs from ensembles that match other network functionals
- Is the network non-random in allowing behavior that is faster or slower than other networks?

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- (Restrict attention to gap junction network. Note that it is a weighted network since there may be more than one gap junction between two neurons. We previously found Shannon capacity of a gap junction, but that is just a scaling factor here.)

Bottleneck Capacity from Pipelining Model of Information Flow

- Think of a neuronal network as a communication network where neurons are nodes and synapses are capacitated links
- Information must go over a single route rather than being split over several routes to be recombined by the destination [Pollack, 1960; Hu, 1961]
  - Different from max-flow/min-cut [Ford-Fulkerson, 1956; Elias-Feinstein-Shannon, 1956]

Definition Let $G = (V, E)$ be a weighted graph. Then the *bottleneck distance* between nodes $s, t \in V$ is denoted $d_B(s, t)$ and is the number of edges connecting s and t, scaled by the weight of the maximum-weight edge, in the path with the smallest total scaled weight between them.

Bottleneck Capacity from Pipelining Model of Information Flow

Lemma Let $d_G(s,t)$ be the geodesic distance and $d_W(s,t)$ be the weighted distance in a graph. Then:

$$d_W(s,t) \leq d_B(s,t) \leq d_G(s,t)$$

- The all-pairs geodesic distance and weighted distance are easy to compute, and can be used for bounding. Bottleneck distance can also be computed using a maximum spanning tree algorithm
- Geodesic distance and weighted distance are metrics, whereas bottleneck distance is an ultrametric (non-Archimedean metric) [Rammal et al, 1986]

Bottleneck Capacity from Pipelining Model of Information Flow

Definition The graph *diameter* is

$$D = \max_{s,t \in V} d(s,t)$$

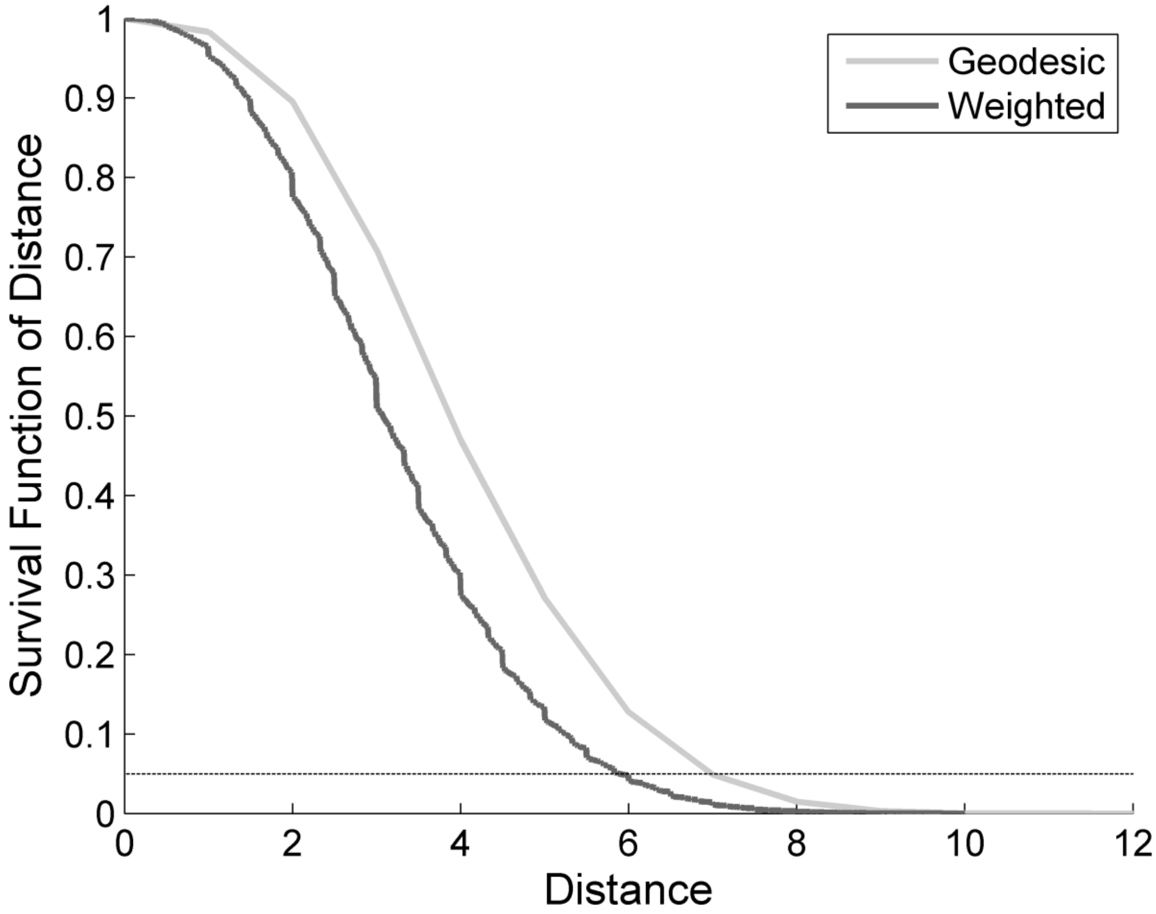
Definition For a network of size n, let $F(x)$ be the empirical cdf of the distances of all $\binom{n}{2}$ distinct node pairs. Then the *effective diameter* is:

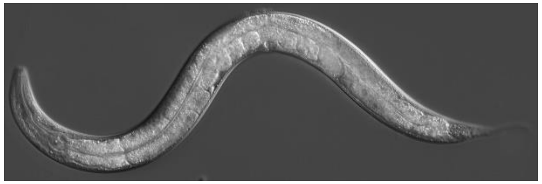
$$D_e = Q(0.95)$$

where $Q(p) = \inf\{x \in \mathbb{R} | p < F(x)\}$ is corresponding quantile function (Defining constant is tighter than others in literature [Leskovec-Kleinberg-Faloutsos, 2007])

Bottleneck capacity inversely proportional to diameter
(in the sequel we restrict to the giant component)

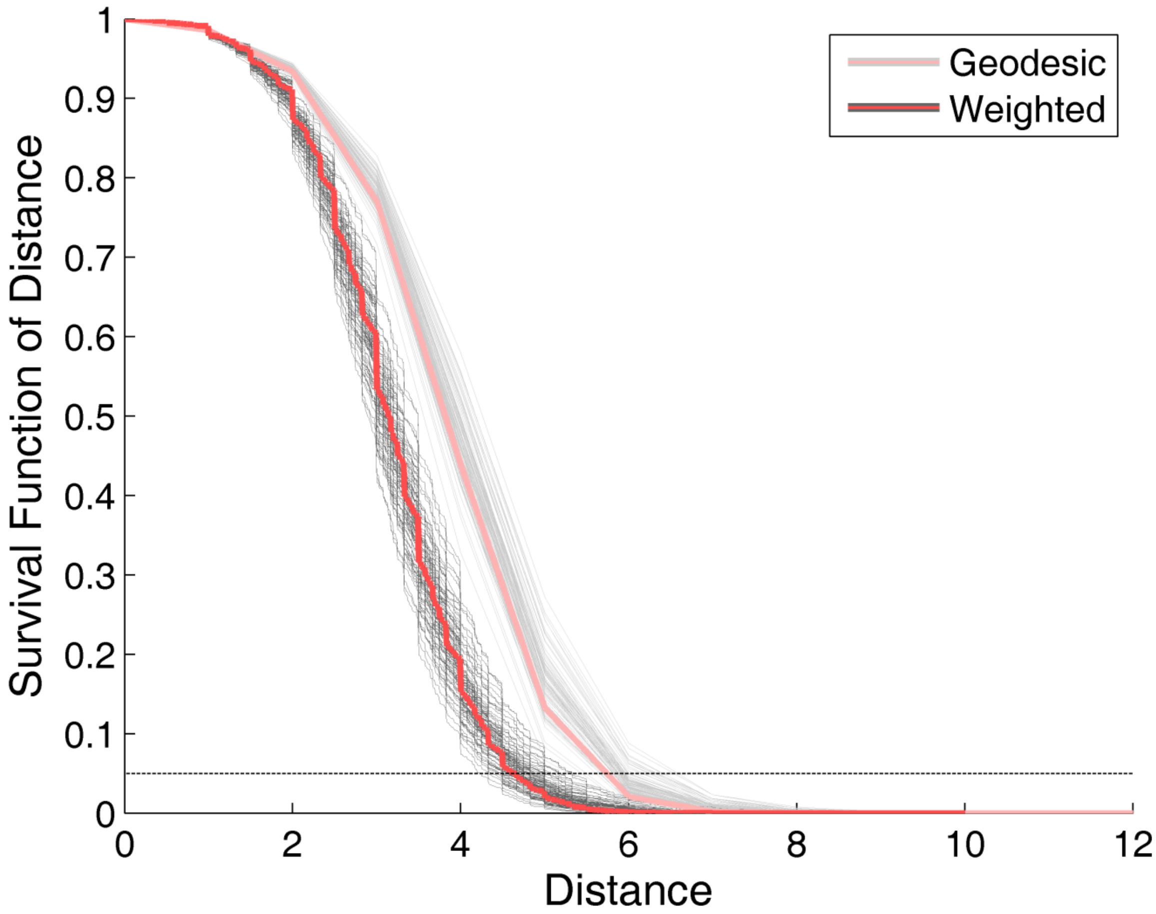
Bottleneck Capacity of *C. elegans*

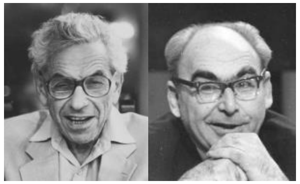




Bottleneck diameter effectively between 6 and 7

Bottleneck Capacity of Weighted Erdos-Renyi Random Graphs

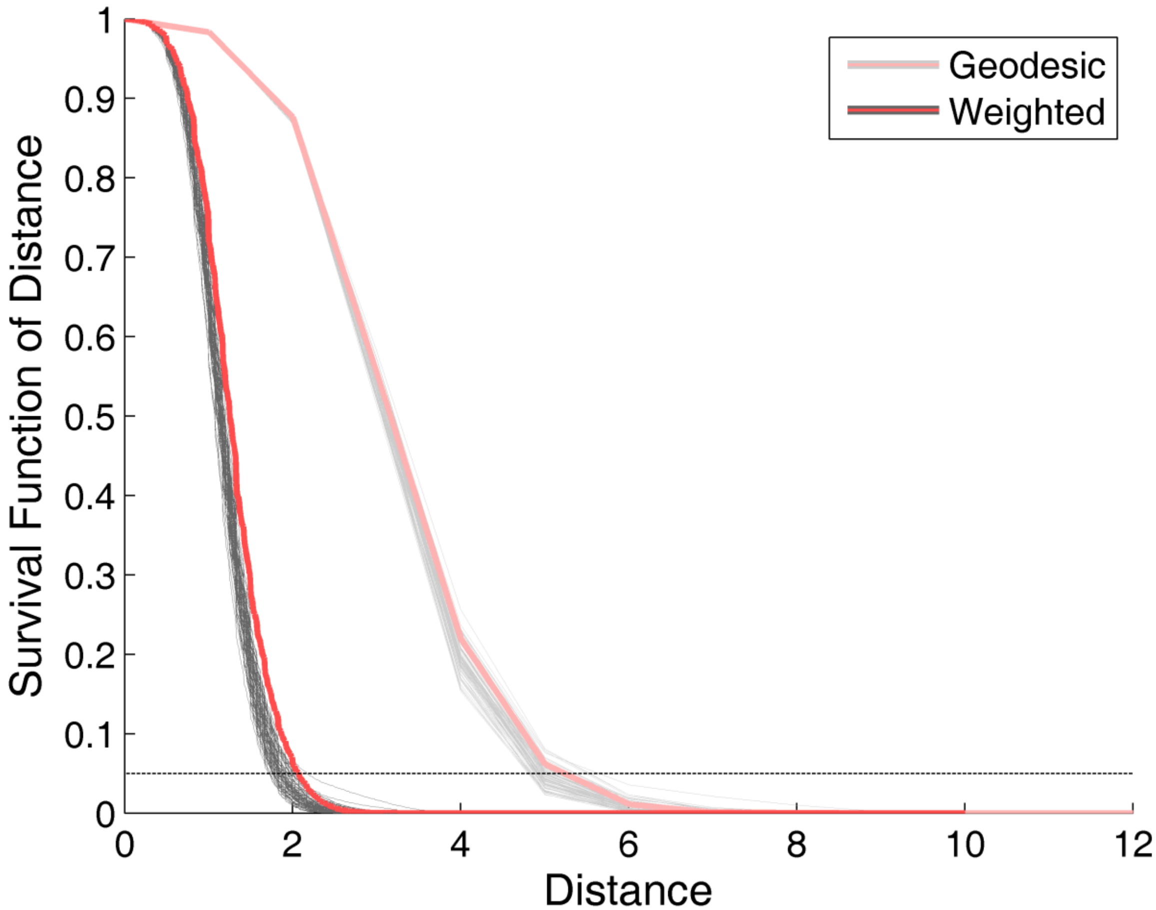


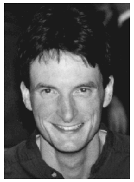


Consider random ensemble where structure is Erdos-Renyi with probability of connection between two neurons matching *C. elegans*, $p = 0.0133$. Multiplicity of connections matches *C. elegans*, which is well-modeled as a power-law with parameter 2.76.

Bottleneck diameter effectively between 5 and 6

Bottleneck Capacity of Degree-Matched Random Graphs

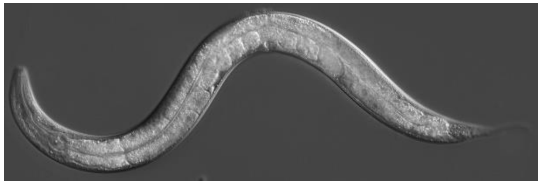
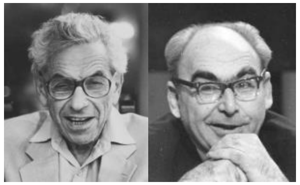




Consider random ensemble where structure is degree-matched to *C. elegans* using random rewiring. Multiplicity of connections matches *C. elegans*, which is well-modeled as a power-law with parameter 2.76.

Bottleneck diameter effectively between 2 and 5

Main Result: Bottleneck Capacity Comparison

 <  < 

- There is a surprising nonrandom feature in synaptic connectivity of the *C. elegans* gap junction network
- The network has a nonrandomly *worse* bottleneck capacity compared to basic random graph ensembles
- It enables globally *slower* behavioral speed than similar random networks

Making Sense of Things

- The *C. elegans* neuronal network enables globally slower behavioral speed than similar random networks
- In contrast, we had previously found that at the micro-level of small functional sub-circuits, the *C. elegans* gap junction network has several hub-and-spoke structures, which are optimal from an information flow perspective [Varshney and Shah, 2011]
- There is a need for greater nuance in stating efficient information flow hypotheses in neuroscience

Conclusion

- In terms of neural organization, smaller sub-circuits within the larger neuronal network are responsible for specific functional reactions, and these should have fast information flow (to quickly achieve the computational objective of that circuit, such as chemotaxis)
- Behavioral speed of the global network may not be biologically relevant
- Screen for individual behavioral phenotype differences to test experimentally