Wiring Optimization

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Wiring Optimization of the Neural Circuit

"After the many shapes assumed by neurons, we are now in a position to ask whether this diversity ... has been left to chance and is insignificant, or whether it is tightly regulated and provides an advantage to the organism. ... we realized that all of the various conformations of the neuron and its various components are simply morphological adaptations governed by laws of conservation for time, space, and material." *Ramon y Cajal*

Given the high convergence and divergence of a neuron, it is a highly challenging task how the nervous system might wire itself to save time, space and material. Below, we will perform a few thought experiments and to argue that the existence of dendrites and axons, as well as the presence of dendritic spines could be a consequence of wiring up a large highly connected neuronal network in an allotted volume. We will also show that the actual lengths of axons and dendrites are close to the minimum length for a given interconnectivity.

Consider that we are wiring up a neuronal network with N neurons . This network may be a cortical column, which is thought as a basic functional unit for brain computation. Within a cortical column, all neurons can potentially make a synapse with each other. We ask: what could be the design that might minimize the total wiring volume?

Design I: Point-to-Point Axons

In the first and the simplest design, a synaptic connection between any pair of neurons requires a dedicated axon, which I call a point-to-point axon. To estimate the total volume of the wiring, we could use a scaling argument. The typical length of an axon that is dedicated to make one connection should be proportional to the linear dimension of the wiring volume R. Let's denote d as the diameter of the axon, we have

$$R^3 \sim Nld^2.$$

Substituting $l \sim NR$ in the above equation, we obtain

$$R \sim Nd. \tag{1}$$

A cortical column of a mouse brain contains $N = 10^5$ neurons, and the typical diameter of an axon is $d = 0.3\mu m$. Substituting these numbers, we found that $R \sim 3$ cm, which is much larger than the actual ~ 1 mm size of a cortical column.

Design II: Axons with *en passant* synapses

Next, we calculate the volume with branching axons, or axons that make *en passant* synapses. In such as design, the axons can make a synapse with every cell body of a neuron it bypasses. Thus the total length of an axon is given by the number of neurons, N, times the typical interneuron distance. Assume uniform distribution of neurons, the typical interneuron distance is given by $R/N^{1/3}$, and thus we have

$$l \sim N^{2/3}R,$$

and the total volume of the neuropil is

$$R^3 \sim Nld^2 \sim N^{5/3}Rd^2.$$

Rewrite this equation, we obtain

$$R \sim N^{5/6}d. \tag{2}$$

Clearly, in the large limit of N, having an *en passant* design is better than point-to-point axon design, as the leading power over N is smaller. Plugging $N = 10^5$ into the Equation 2, we found that $R \sim 4.4mm$. However, this is still much larger than the size of a cortical column.

Design III: Axons and Dendrites

In the axon-only network, each axon has to make its way to every cell body. Rather than integrating the signal at the cell body, a smarter strategy is to introduce another process, which we will call dendrites and to meet the axon halfway. Below we shall calculate the probability that one neuron's axons could meet the other neuron's dendrites.

Axons and dendrites could meet each other if the processes are closer than segment diameter $\sim d$. In other words, if the dendritic and axonal segments could occupy the same voxel with a volume $\sim d^3$, then they can make a synapse with each other. The probability that axon and dendrites will occupy the same voxel is given by the product of axonal and dendritic volume filling factor $\rho_{a,d}$:

$$P = \rho_a \rho_d,$$

where by symmetry

$$\rho_a = \rho_d = \frac{ld^2}{R^3}.$$

The total number of voxels in the volume is given by $(R/d)^3$, and the total number of contacts between axons and dendrites $n = P(R/d)^3$, and our constraint imposes $n \sim 1$. Putting the above equation together, we have

$$\frac{l^2 d}{R^3} \sim 1. \tag{3}$$

Now by combining the above equation with $R^3 \sim Nld^2$ and excluding l, we found

$$R \sim N^{2/3} d. \tag{4}$$

Comparing equation 4 with the equation 2, the scaling exponent on N is further reduced.

Design IV: Branching Axons and Spiny Dendrites

Design III may be further reduced by the addition of dendritic spines, which expand the reach of the dendrites without increasing their length. Spine has a typical length of 2 μm. However, spine has a very narrow spine neck, and its volume is much smaller than a dendrite with the same length. If we include spines, then Equation 3 becomes

$$\frac{l^2 s}{R^3} \sim 1 \tag{5}$$

Now the size of the neural network become

$$R \sim N^{2/3} \frac{d^{4/3}}{s^{1/3}}. \tag{6}$$

Optimality of the design

Plug Equation 4 back into Equation potential synapse constraint with spine, we found that the length of the process is given by

$$l \sim N \frac{d^2}{s} \tag{7}$$

Indeed, this is the minimum length of the axon/dendrite we could achieve. No other design could reduce the length of the process by order of magnitude.