Have brains evolved to wiring economy configurations?

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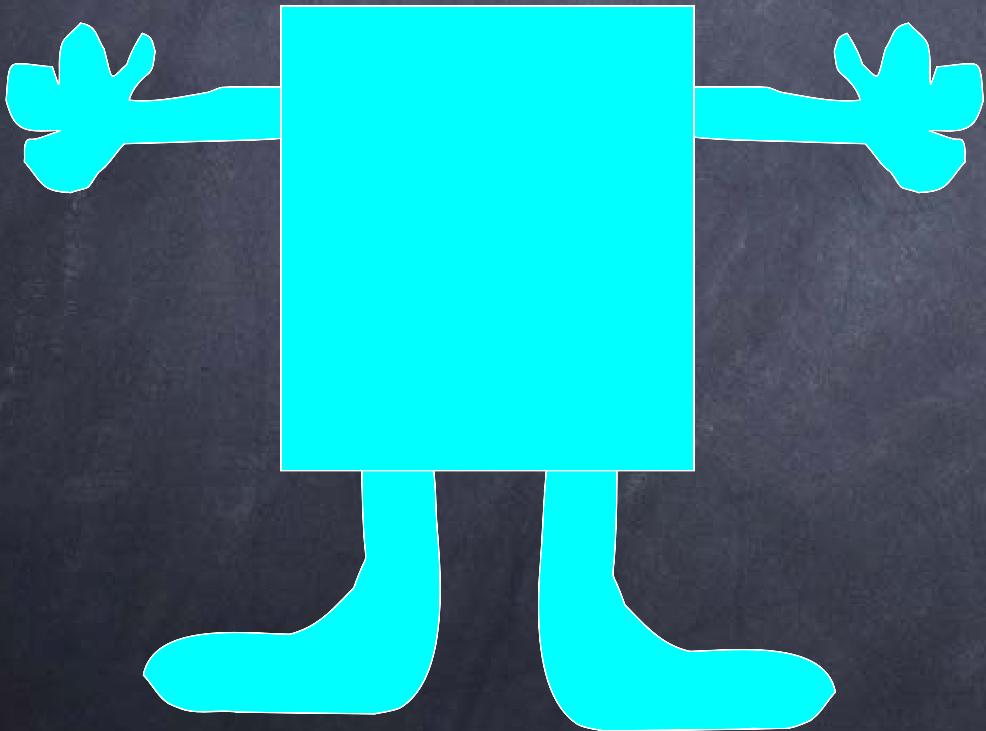
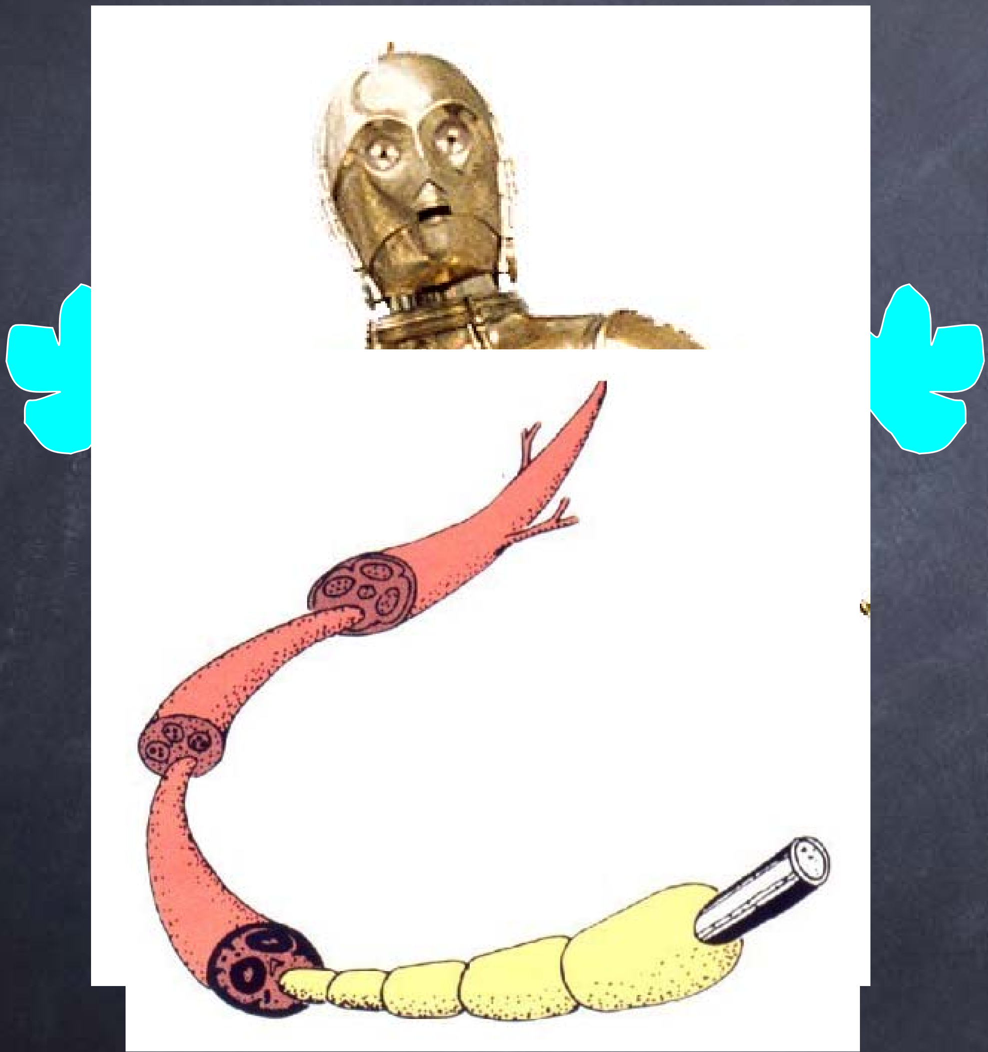
Why is the brain in the head?

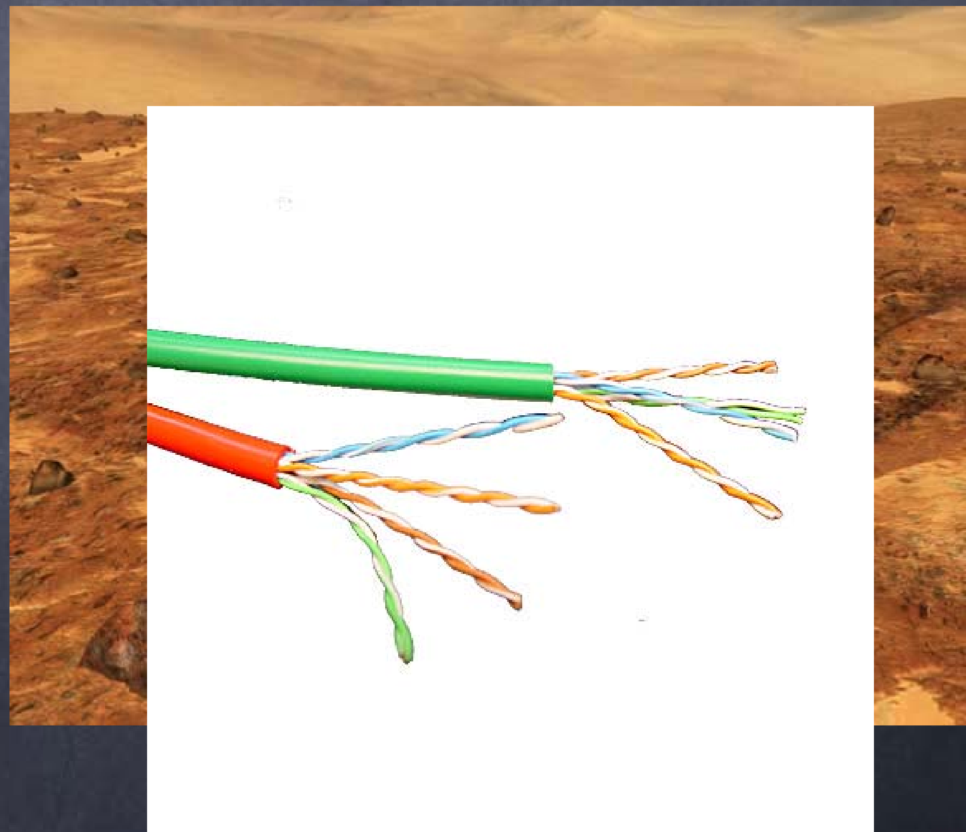


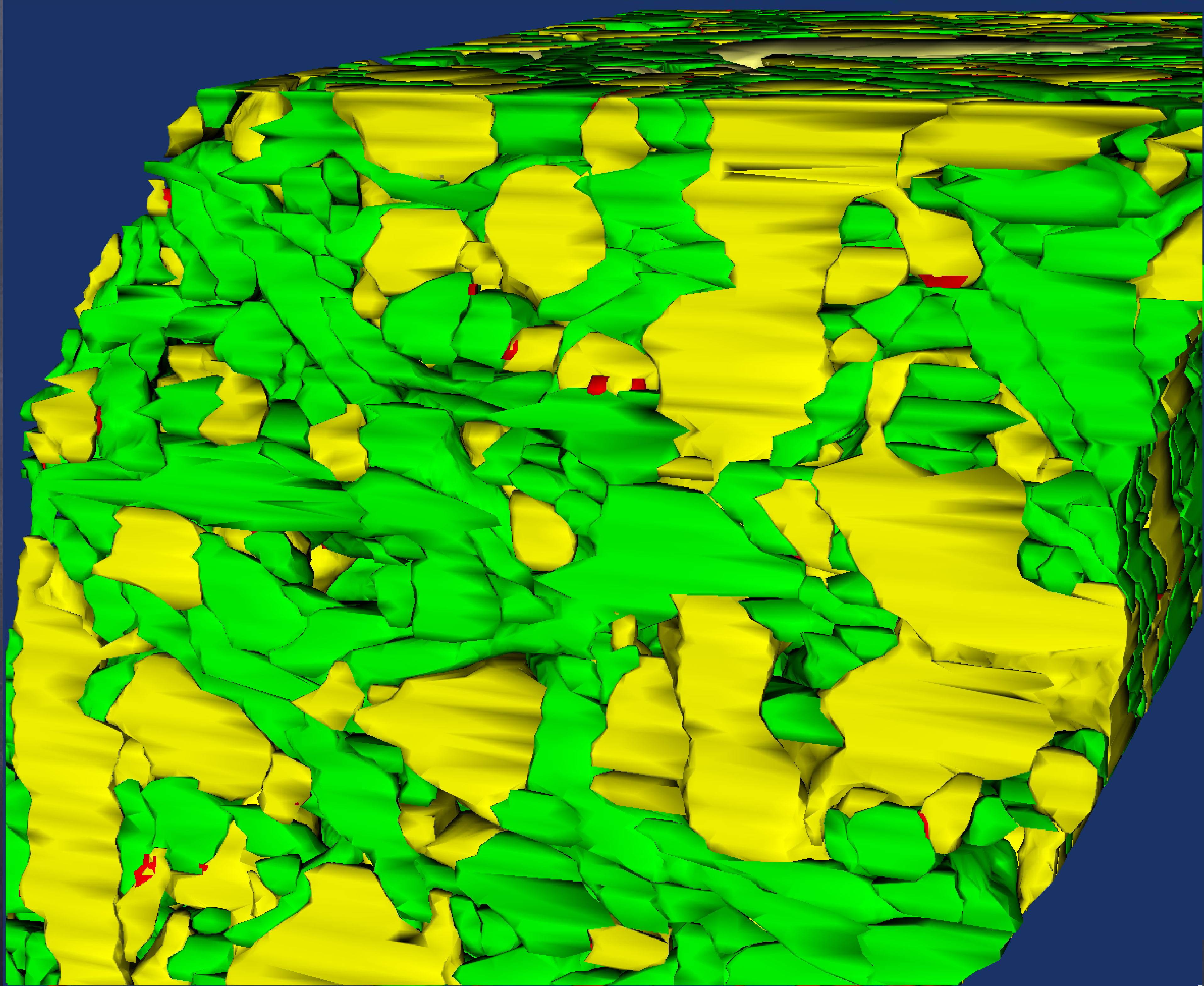
Head: Movable part that hosts

fragile

Why is the brain in the head?







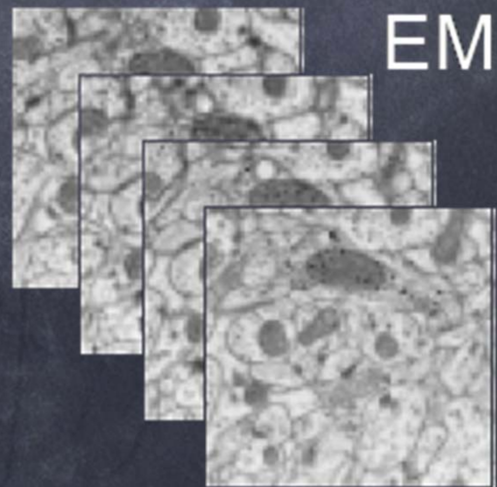
Wiring optimization

Neuroanatomy is governed by the laws of conservation of time, space and material

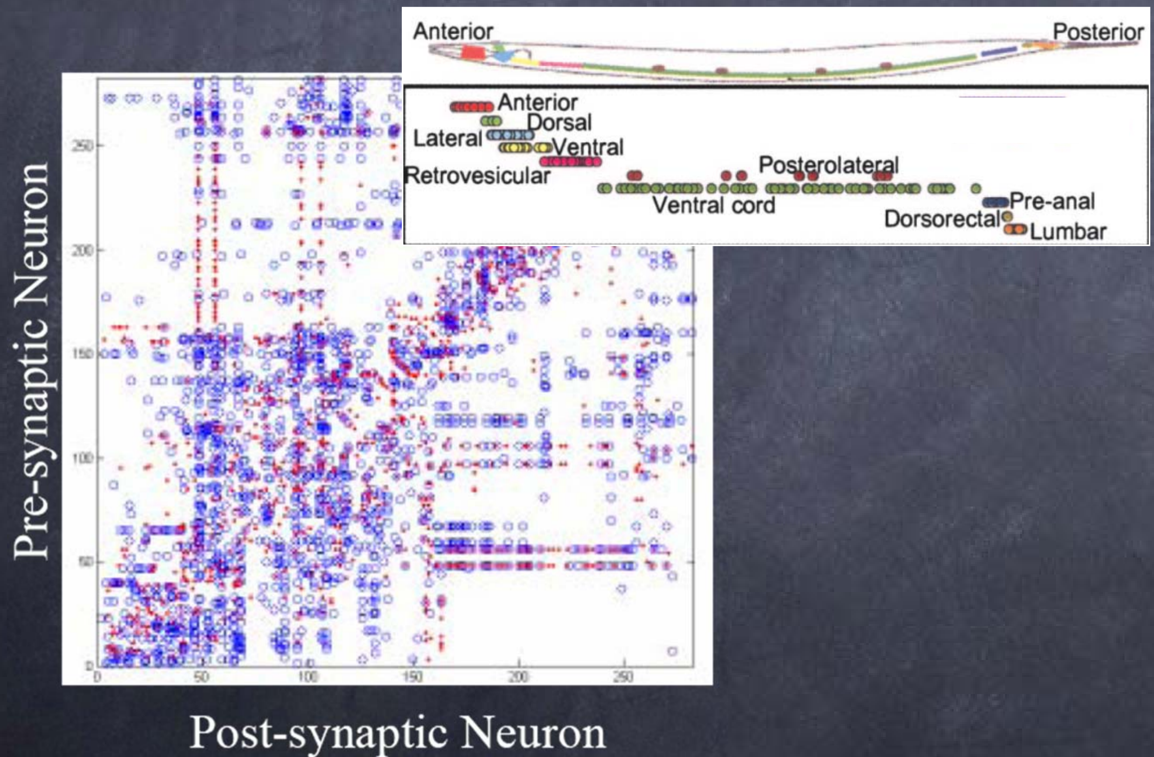
Ramón y Cajal, S. (1899) ***Texture of the nervous system of man and the vertebrates***

Caenorhabditis elegans

- It is a worm (nematode)
- ~ 300 neurons



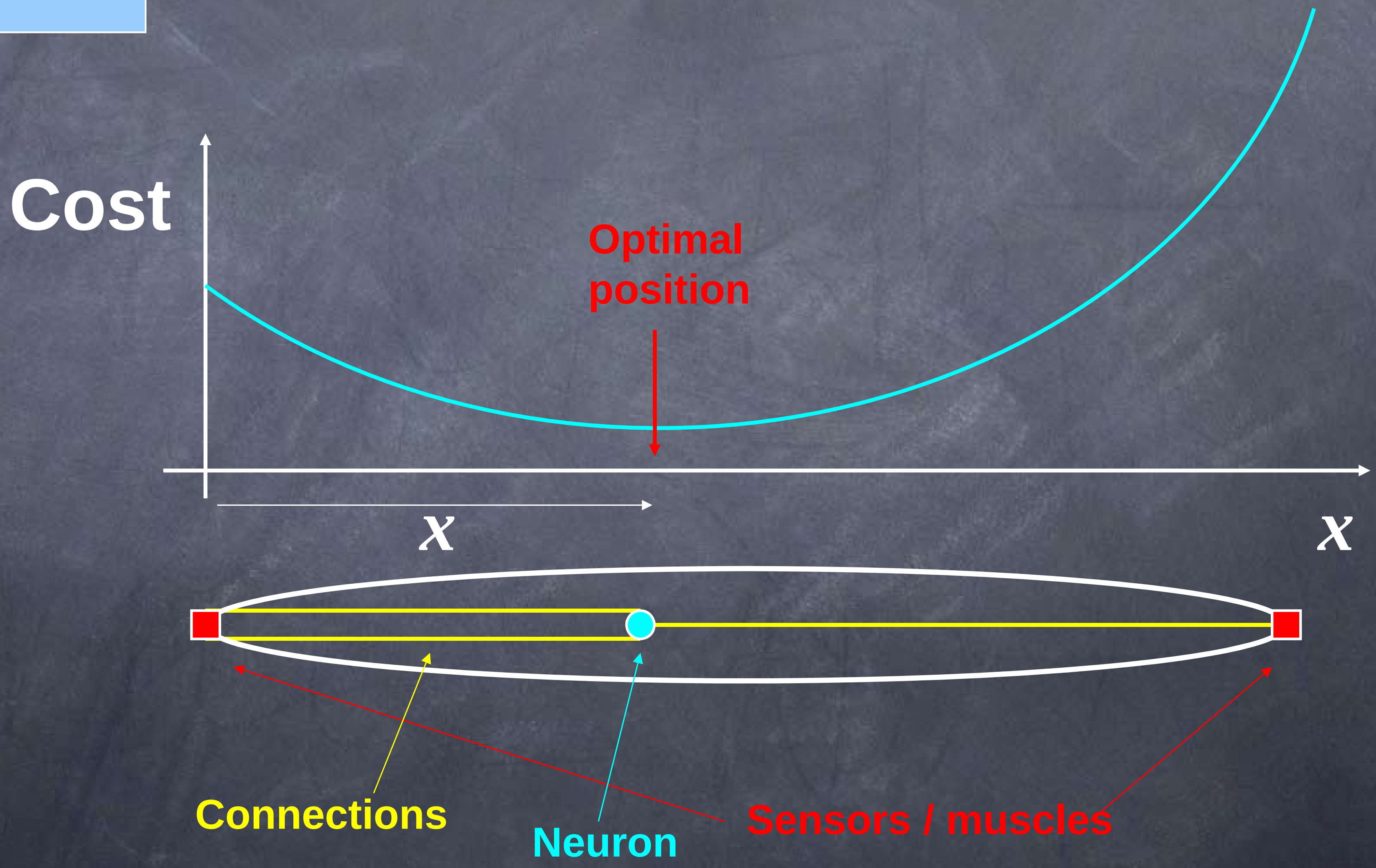
EM



White *et al.* (1986) *Philos. Trans. R. Soc., London Ser. B* 314:1-340
Chen, Hall, Chklovskii (2006) *PNAS* 103(12):4723-4728

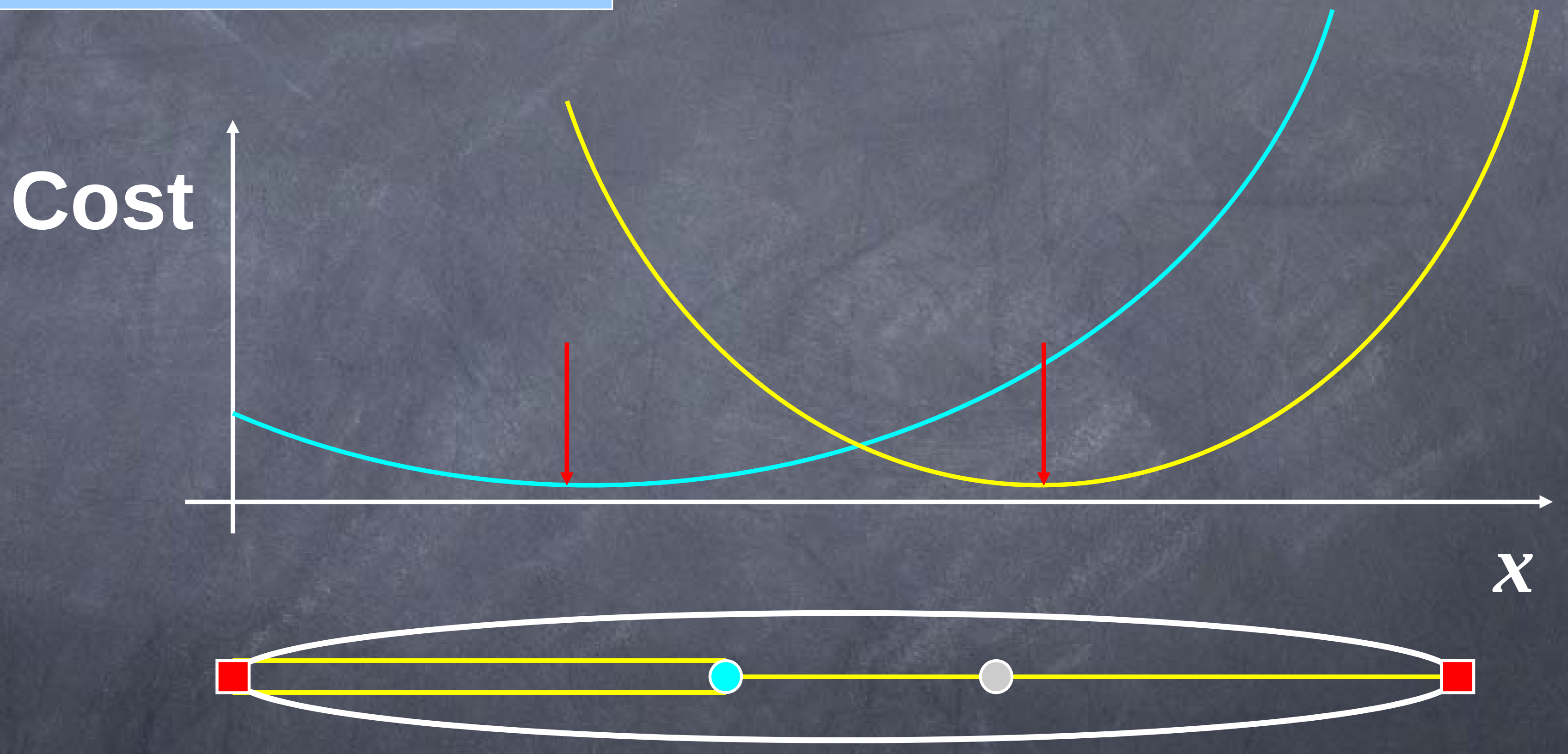
Prediction of neuroanatomy

$$C = \sum_{j=1}^{2} B_{i,j}(x - s_j)^2$$

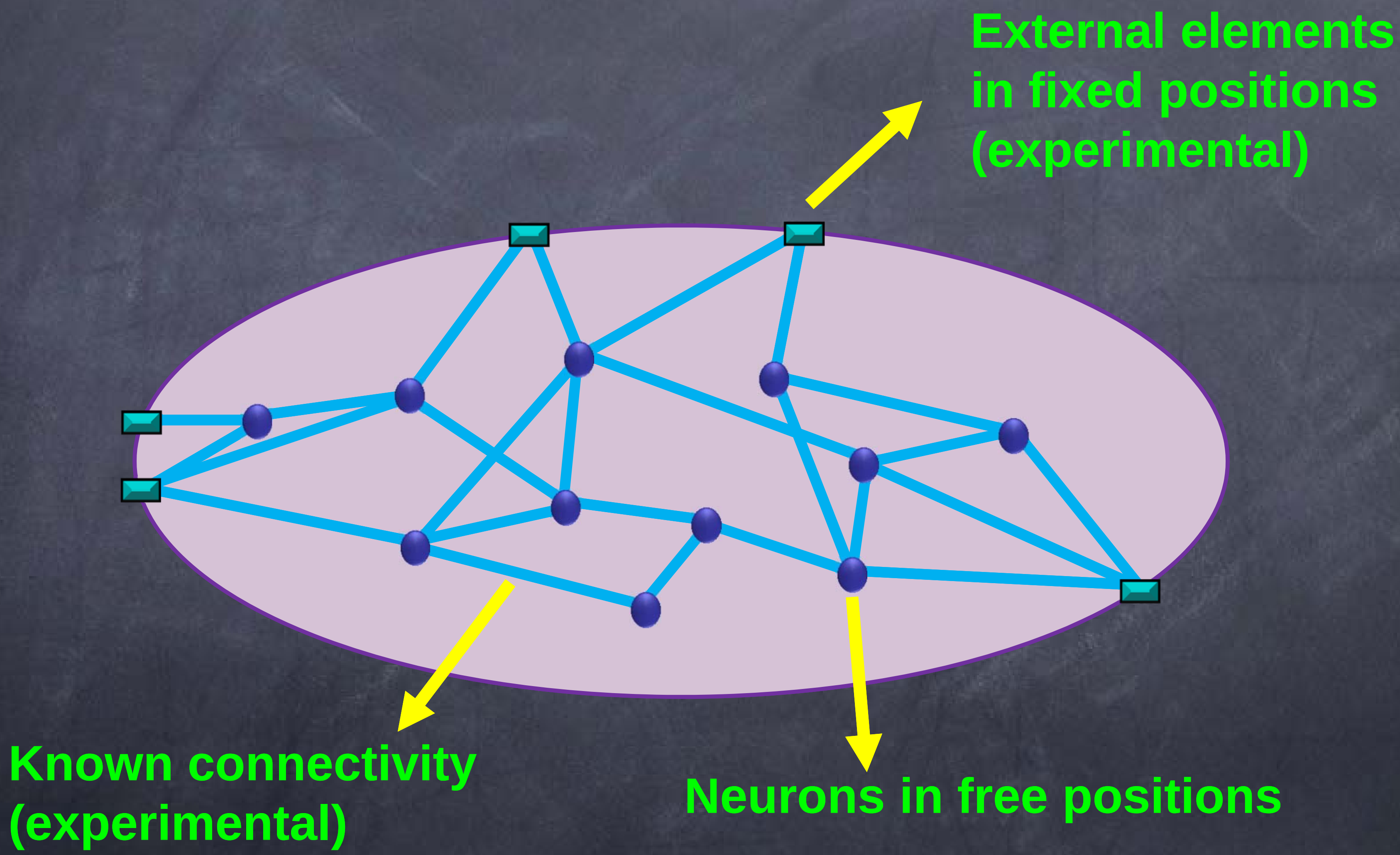


Prediction of neuroanatomy

$$C = \sum_{i,j=1}^{2,2} B_{i,j}(x_i - s_j)^2 + \sum_{i,j=1}^{2,2} A_{i,j}(x_i - x_j)^2$$



The problem


External elements
in fixed positions
(experimental)
Known connectivity
(experimental)
Neurons in free positions

Assume quadratic cost for a general model

$$W = \frac{1}{2}\alpha \sum_{i,j=1}^{N} A_{ij} \left| x_i - x_j \right|^{\xi} + \sum_{i,k=1}^{N,S} B_{ik} \left| x_i - s_k \right|^{\xi} + \beta \sum_{i,l=1}^{N,M} C_{il} \left| x_i - m_l \right|^{\xi}$$

Cost of neuron-neuron connection

Cost of neuron-sensor connection

Cost of neuron-muscle connection

For quadratic cost, the solution has closed form

$$W = \frac{1}{2}\alpha\sum_{i,j=1}^{N} A_{ij}\left|x_i - x_j\right|^{\xi} + \sum_{i,k=1}^{N,S} B_{ik}\left|x_i - s_k\right|^{\xi} + \beta\sum_{i,l=1}^{N,M} C_{il}\left|x_i - m_l\right|^{\xi}$$

$$\vec{x} = Q^{-1}\left[B\vec{s} + \beta C\vec{m}\right]$$

$$Q_{ip} = \delta_{ij}\left(\alpha\sum_{j=1}^{N} A_{ij} + \sum_{k=1}^{S} B_{ik} + \beta\sum_{l=1}^{M} C_{il}\right) - \alpha A_{ip}$$

In the following we give for completeness a very explicit derivation of Eq. (2). Equivalent derivations based on a heavier use of matrix properties can be found in (Hall, 1970) or (Chklovskii, 2004). When cost increases quadratically with wire length, total cost is given by Eq. (1) with $\xi = 2$,

$$W = \frac{1}{2}\alpha \sum_{i,j=1}^{N} A_{ij}(x_i - x_j)^2 + \sum_{i,k=1}^{N,S} B_{ik}(x_i - s_k)^2 + \beta \sum_{i,l=1}^{N,M} C_{ik}(x_i - m_l)^2 .$$

This function has a minimum where partial derivatives with respect to the positions of all neurons are zero, $\frac{\partial W}{\partial x_p} = 0$ for all p=1,…,N, with

$$\frac{\partial W}{\partial x_p} = \frac{\alpha}{2}\sum_{i,j=1}^{N} A_{ij}\left[2\delta_{ip}(x_i - x_j) - 2\delta_{jp}(x_i - x_j)\right] + \sum_{i,k=1}^{N,S} B_{ik} 2\delta_{ip}(x_i - s_k) + \beta\sum_{i,l=1}^{N,M} C_{il} 2\delta_{ip}(x_i - m_l),$$

and δ_{ij} the Kronecker delta (δ_{ij} =1 when i=j and 0 otherwise). Because of the Kronecker delta functions, most terms vanish. However, we keep most of them for later convenience. After regrouping terms and removing some of the vanishing terms, we get

$$\alpha\sum_{i,j=1}^{N} A_{ij}\delta_{ip}(x_p - x_j) + \alpha\sum_{i,j=1}^{N} A_{ij}\delta_{jp}(x_j - x_i) + 2\sum_{i,k=1}^{N,S} B_{ik}\delta_{ip}x_i + 2\beta\sum_{i,l=1}^{N,M} C_{il}\delta_{ip}x_i = 2\sum_{k=1}^{S} B_{pk}s_k + 2\beta\sum_{l=1}^{M} C_{pl}m_l .$$

As the matrix A is symmetric, the first and second terms are identical, giving

$$\alpha\sum_{i,j=1}^{N} A_{ij}\delta_{ip}(x_p - x_j) + \sum_{i,k=1}^{N,S} B_{ik}\delta_{ip}x_i + \beta\sum_{i,l=1}^{N,M} C_{il}\delta_{ip}x_i = \sum_{k=1}^{S} B_{pk}s_k + \beta\sum_{l=1}^{M} C_{pl}m_l .$$

Regrouping terms we obtain

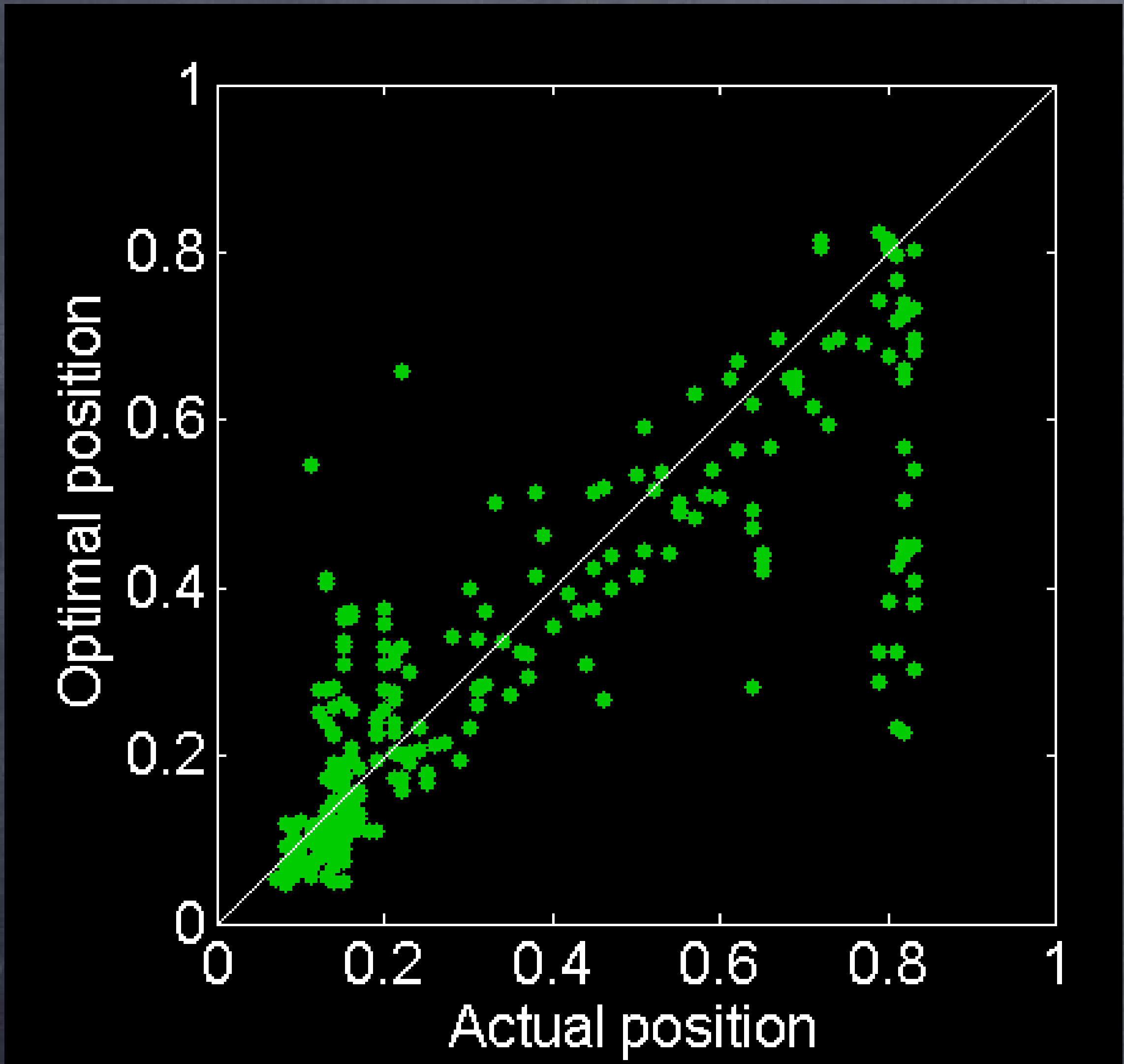
$$\sum_{i=1}^{N}\delta_{pk}\left(\alpha\sum_{j=1}^{N} A_{pj} + \sum_{k=1}^{S} B_{ik} + \beta\sum_{l=1}^{M} C_{pl}\right)x_p - \alpha\sum_{j=1}^{N} A_{pj}x_i = \sum_{k=1}^{S} B_{ik}s_k + \beta\sum_{l=1}^{M} C_{pl}m_l ,$$

where we have eliminated vanishing terms in the second term. Renaming the summation index j for i in the second term, and using the definition of Q in Eq. (2b), we can write

$$\sum_{i=1}^{N} Q_{ip} x_p = \sum_{k=1}^{S} B_{pk} s_k + \beta \sum_{l=1}^{M} C_{pl} m_l; \quad p = 1 \ldots N$$

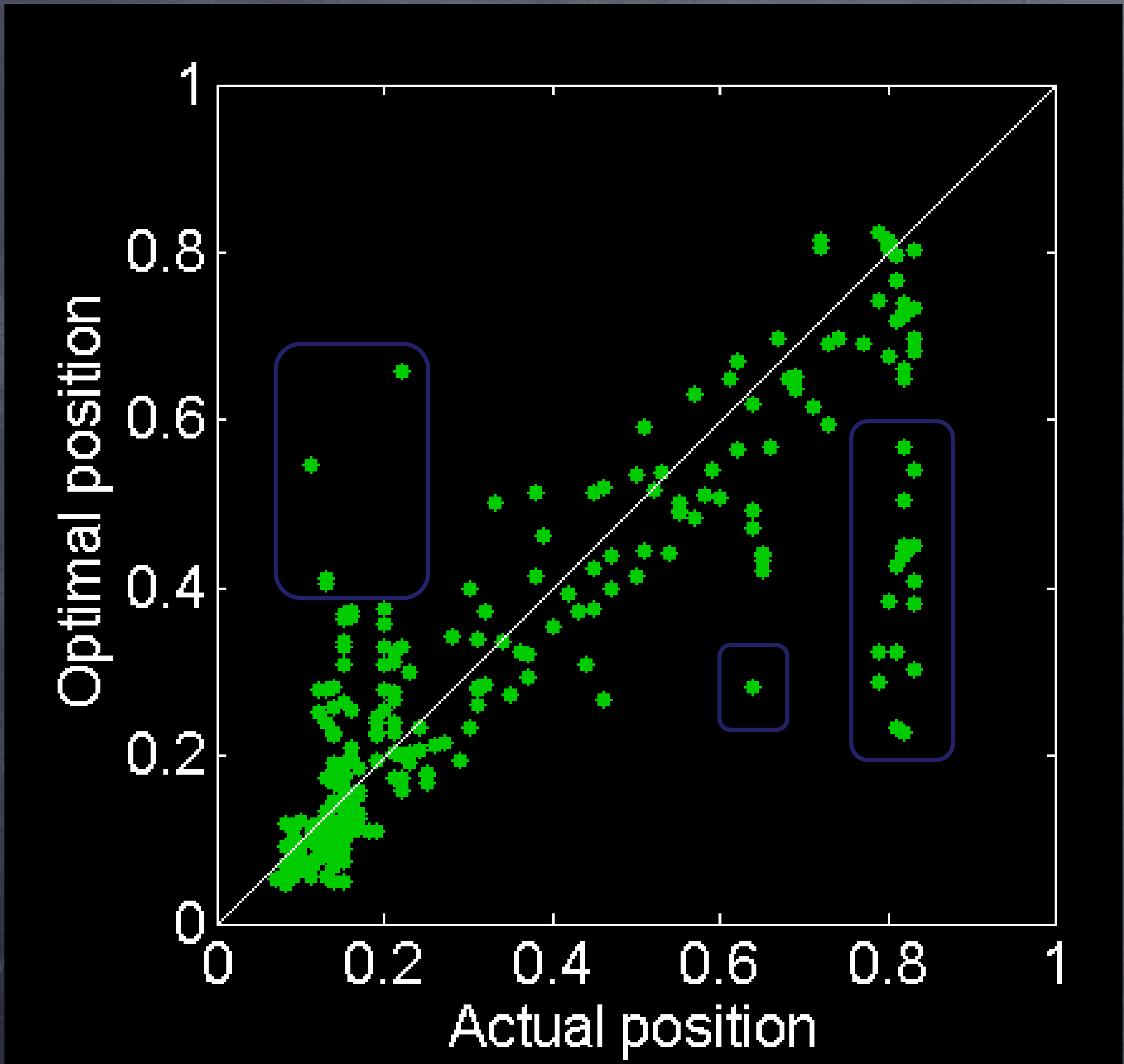
This is a system of N equations with the soma positions x_i as the N unknowns. In matrix notation we can write it as $Q\vec{x} = B\vec{s} + \beta C\vec{m}$, where $\vec{x}$, $\vec{s}$ and $\vec{m}$ are column vectors that store the positions of all neurons, sensors and muscles, respectively. Multiplying from the left by Q^{-1} both members of the matrix equation, we obtain the solution $\vec{x} = Q^{-1}\left[B\vec{s} + \beta C\vec{m}\right]$, as given in Eq. (2a).

C. elegans nearly minimizes wiring cost



Chen, Hall, Chklovskii (2006) *PNAS* 103(12):4723-4728
Pérez-Escudero, de Polavieja (2007)*PNAS* 104(43):17180-17185

C. elegans nearly minimizes wiring cost



Why deviations?

- Developmental constraints?
- Experimental error?
    - Missing connections?
- Unknown functions?
- Local neuromodulation?

Chen, Hall, Chklovskii (2006) *PNAS* 103(12):4723-4728
Pérez-Escudero, de Polavieja (2007)*PNAS* 104(43):17180-17185

We must expect deviations

Evolution is not optimization

- System is not isolated
- Objective function misidentified
- Phylogenetic constraints
- No guarantee of selecting the fittest
- Insufficient time
- …

Gould, Lewontin (1979) *Proc R Soc London Ser B* 205:581–598

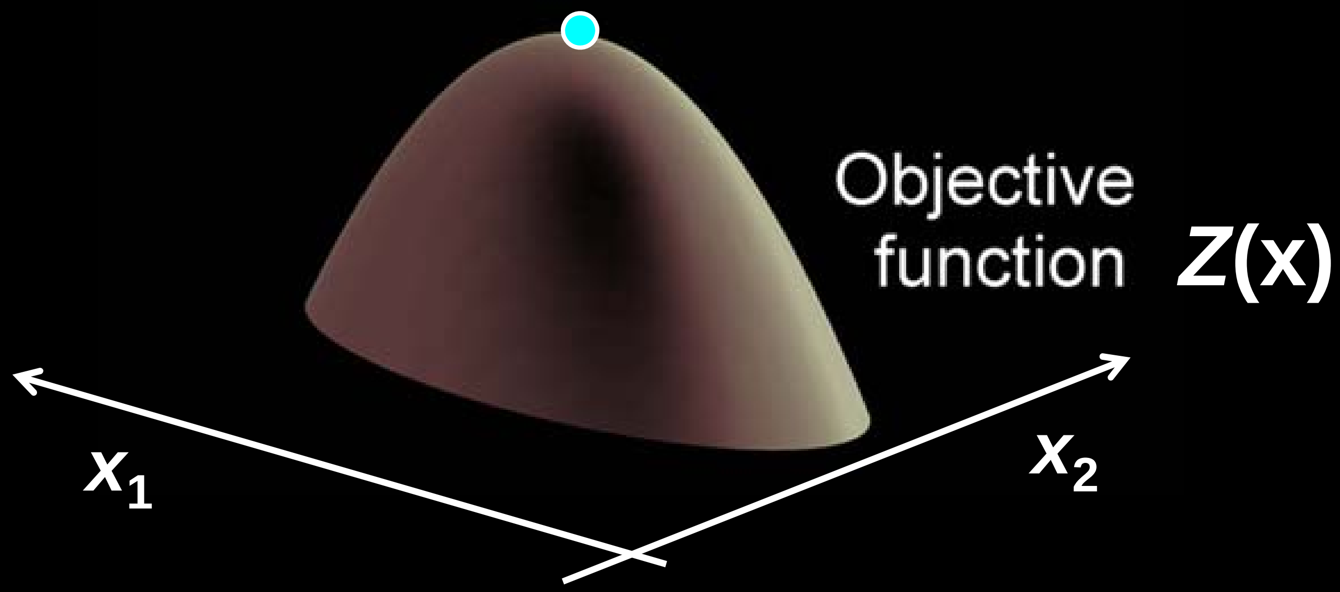

Real System

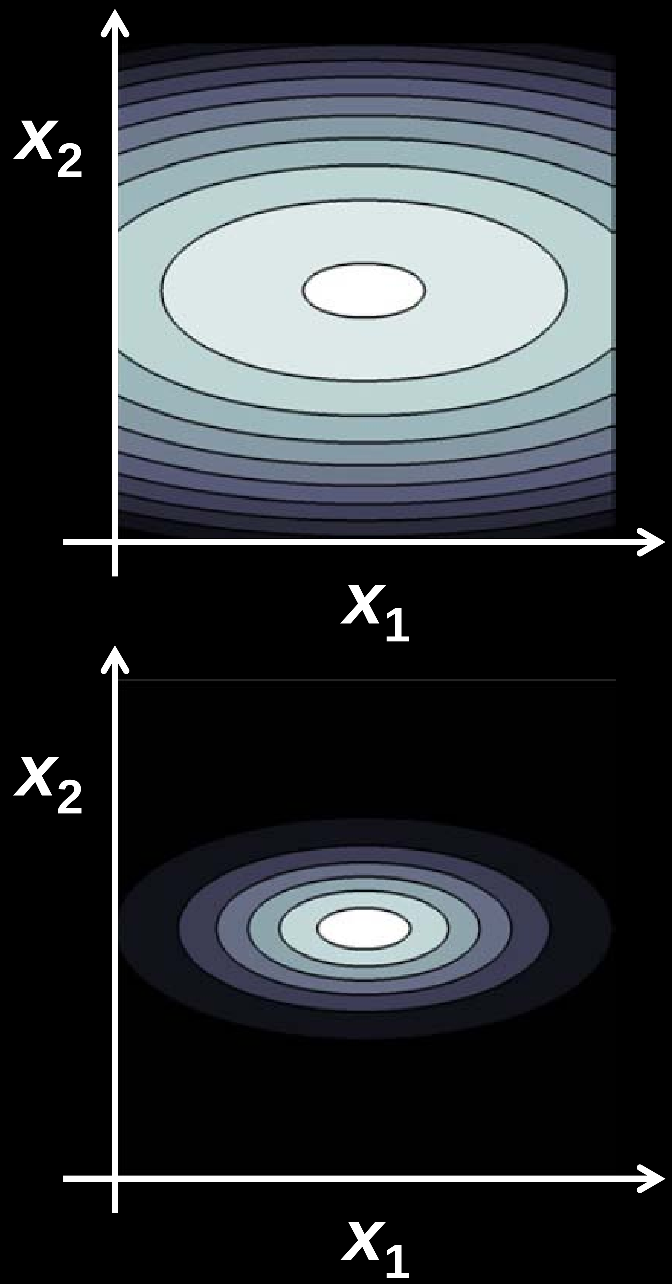
OPTIMAL **RANDOM**

Natural Selection ***Stochactic factors***

Real systems have evolved under adaptative forces and random factors

$$P(x) = f(Z(x))$$

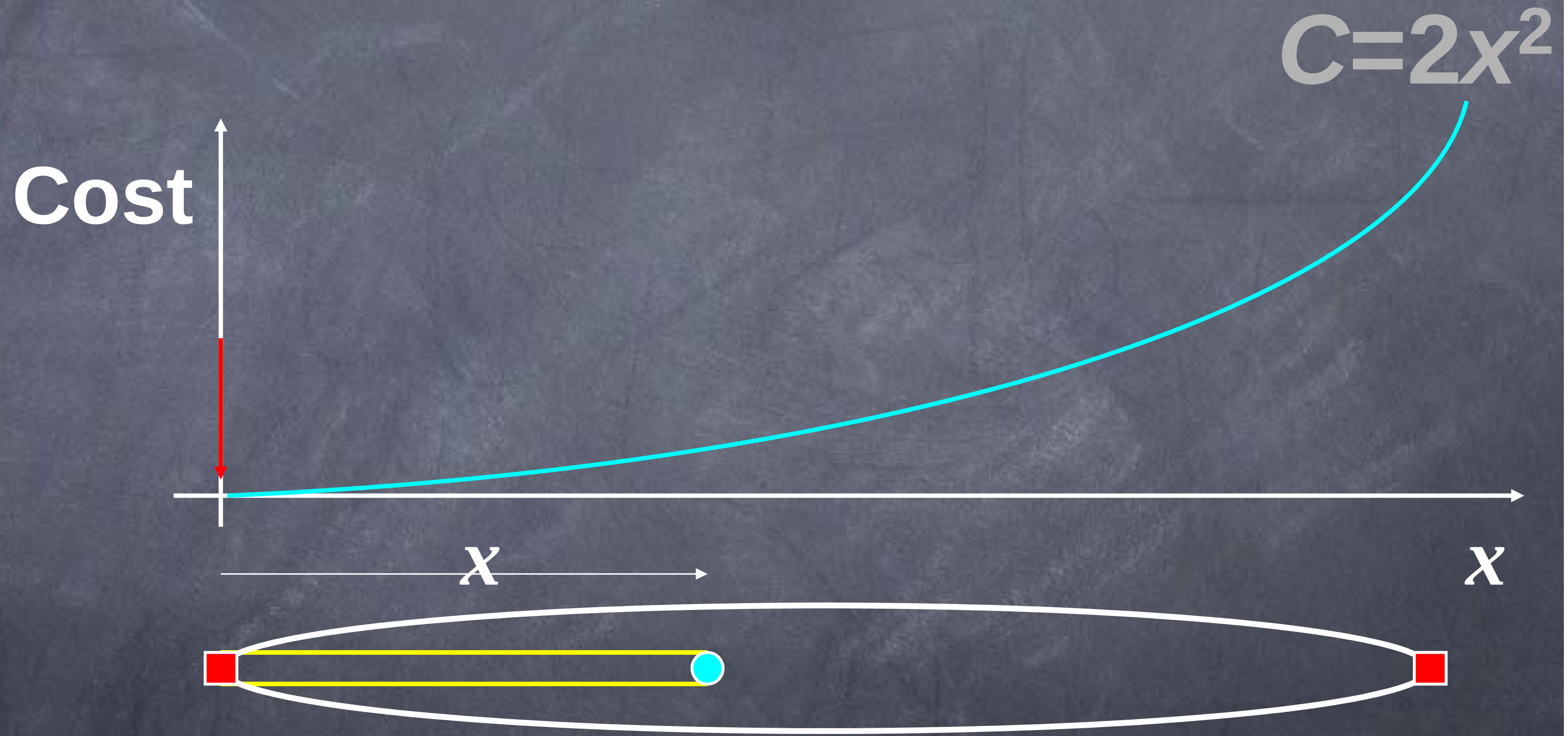




Pérez-Escudero, Rivera-Alba, de Polavieja (2009) *PNAS* 106(48):20544-20549

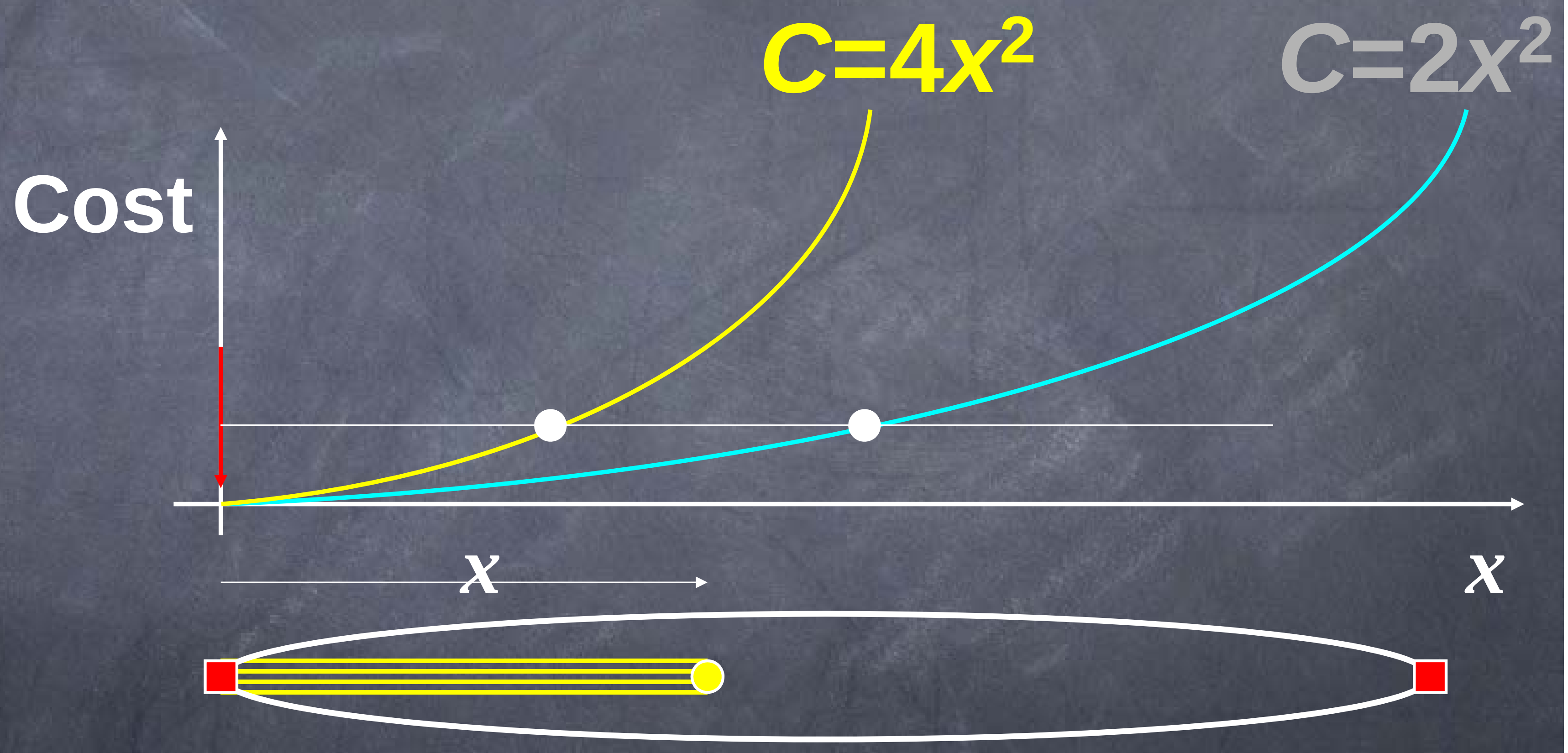
Cost for each neuron

Neuron with 2 connections

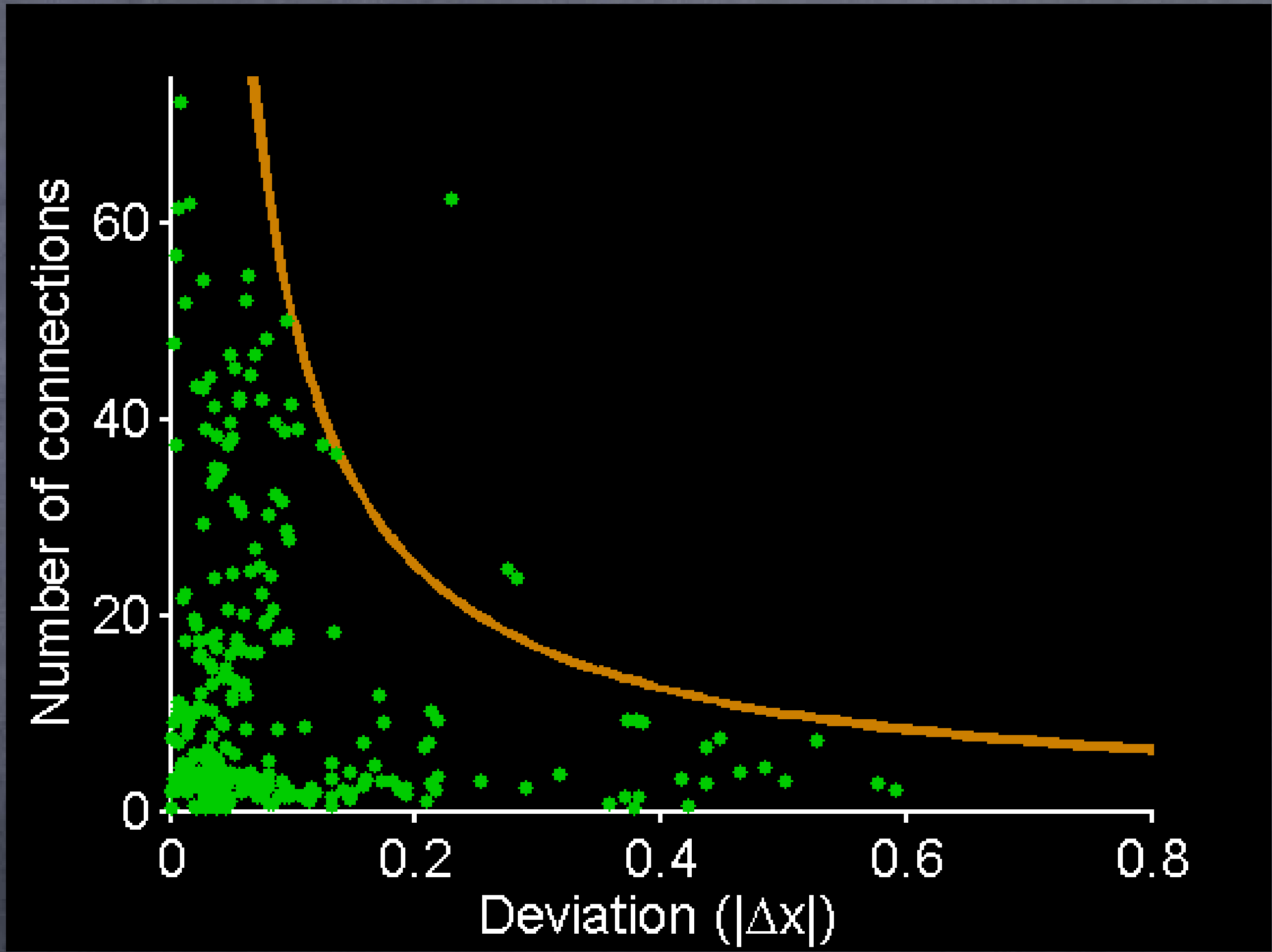


Cost for each neuron

Neuron with 4 connections

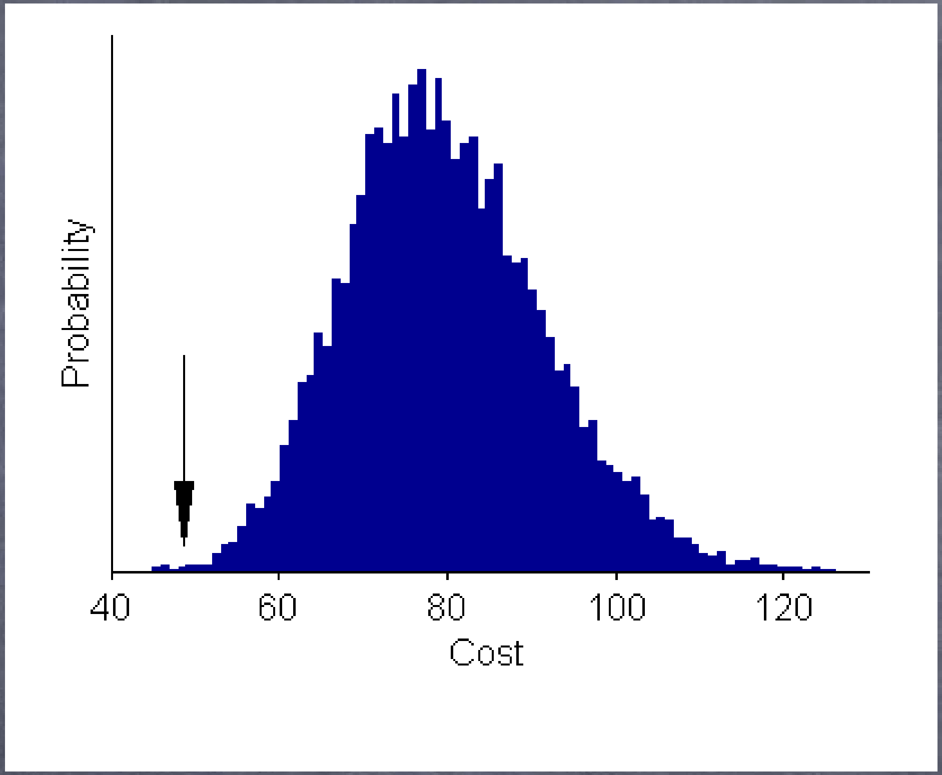


Deviations are consistent with theory



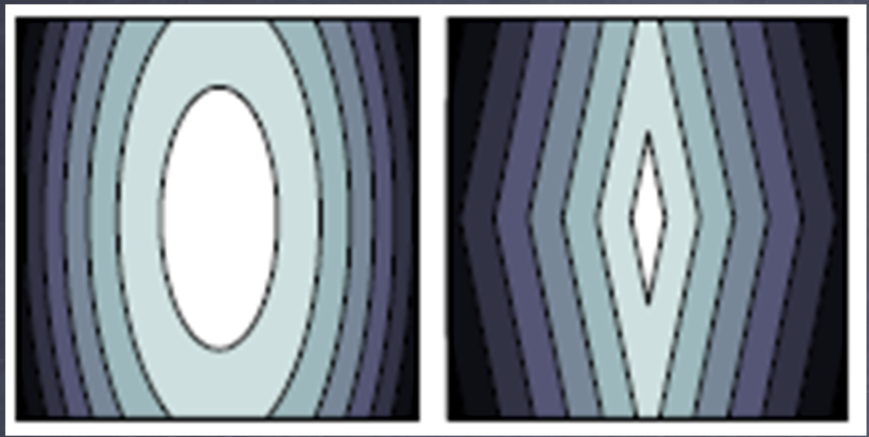
Pérez-Escudero, Rivera-Alba, de Polavieja (2009) *PNAS* 106(48):20544-20549

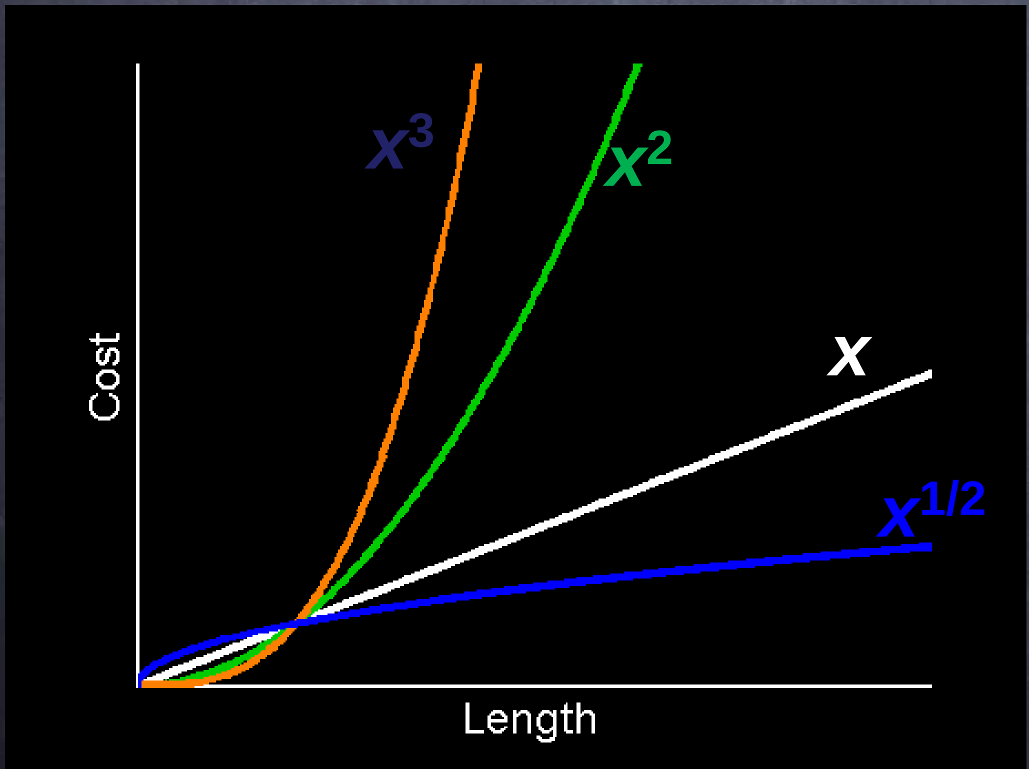
Significance test

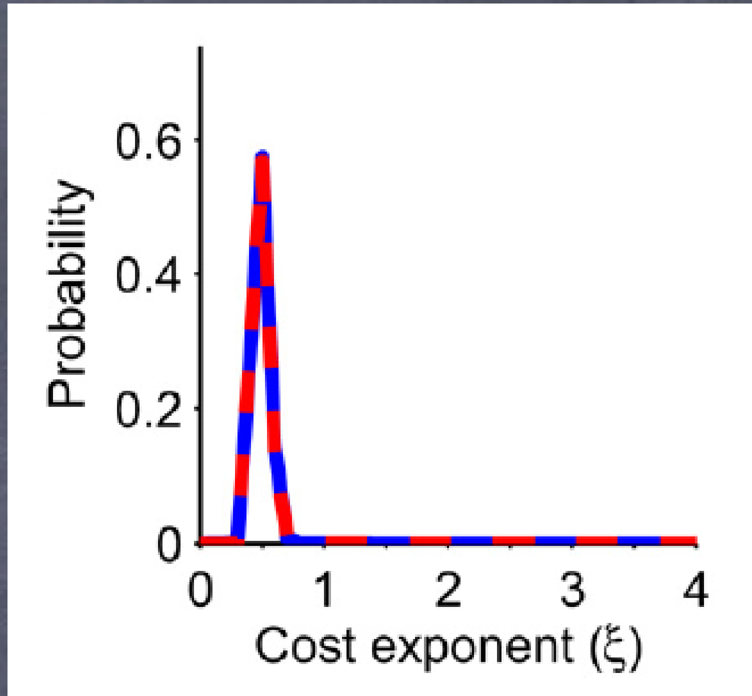


99.999999999% of configurations with same deviations (but randomly distributted among neurons) would use more wire

We can use deviations to explore the objective function





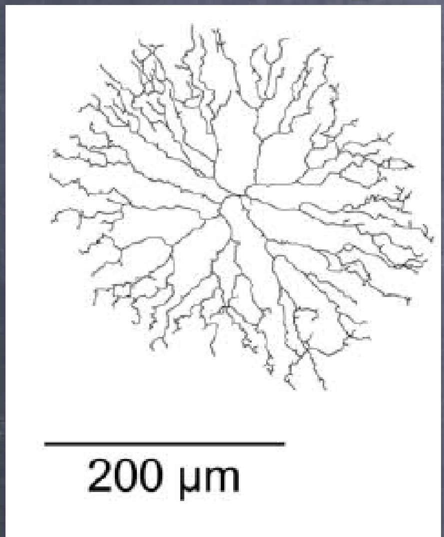


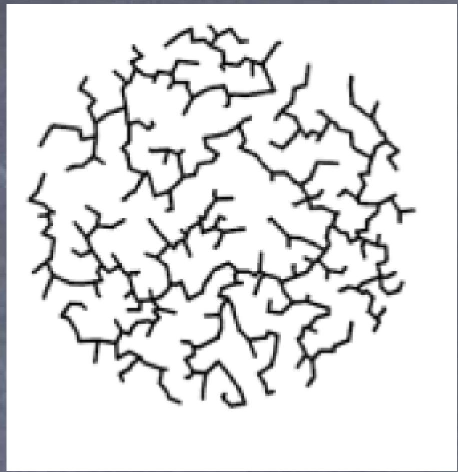
Sublinear cost!

Economy of scale and distance

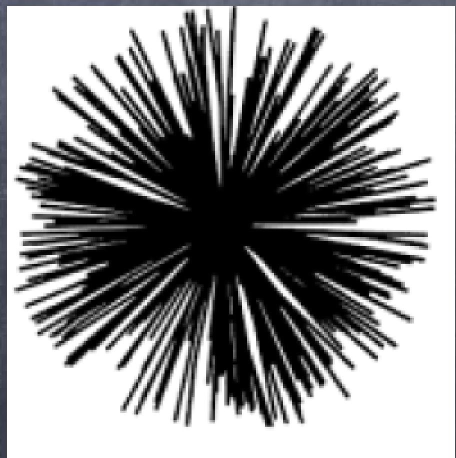
Pérez-Escudero, Rivera-Alba, de Polavieja (2009) *PNAS* 106(48):20544-20549

Is the structure of neurons at an optimum?





Minimum wiring length
(large conduction time to soma)

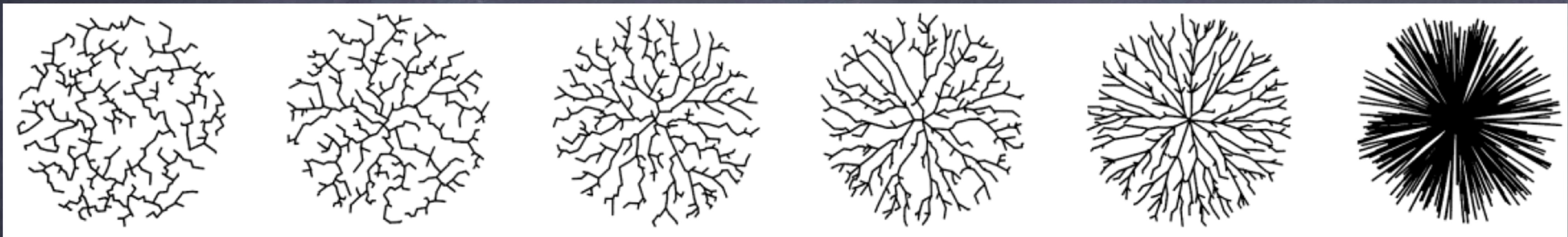


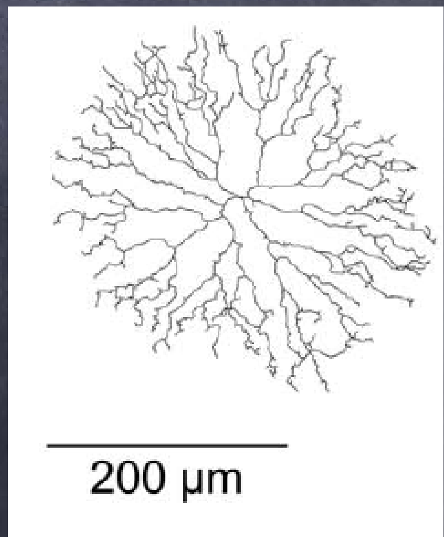
Minimum conduction time
(large total wiring length)

Cuntz H, Forstner F, Borst A, Häusser M (2010) PLoS Comput Biol 6(8): e1000877.

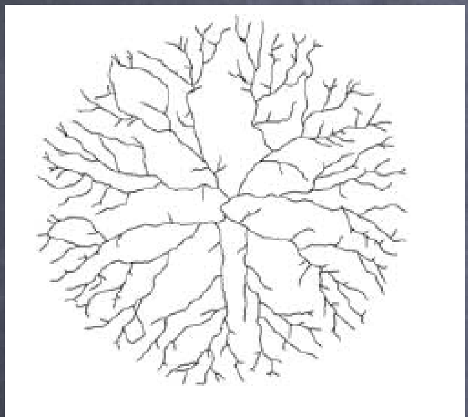
What about a balance of the two principles?

Minimum (total wiring length + λ path length to soma)

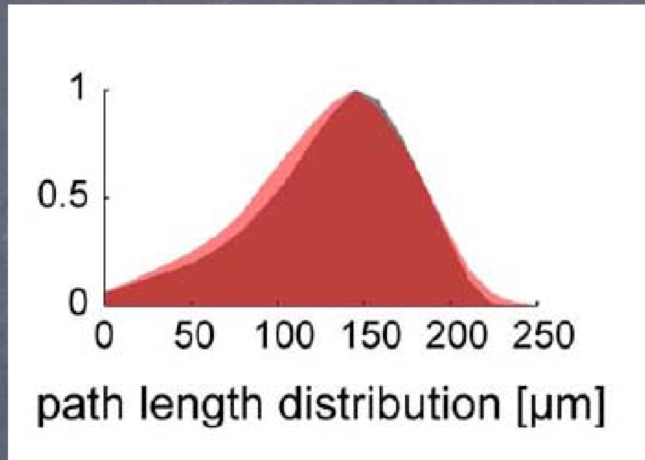


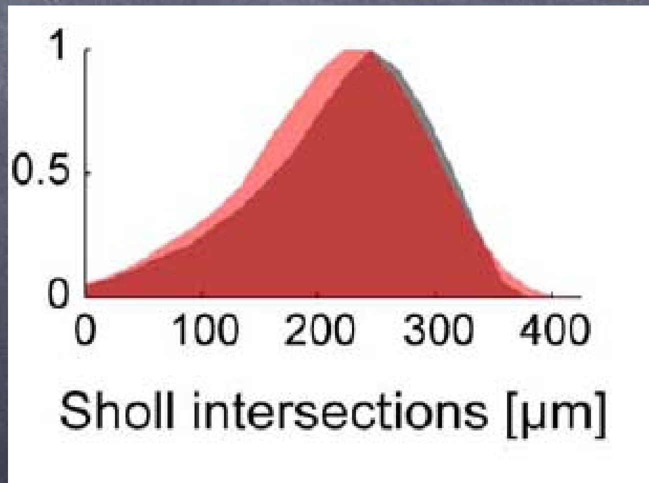


The combination of these two principles corresponds well to data



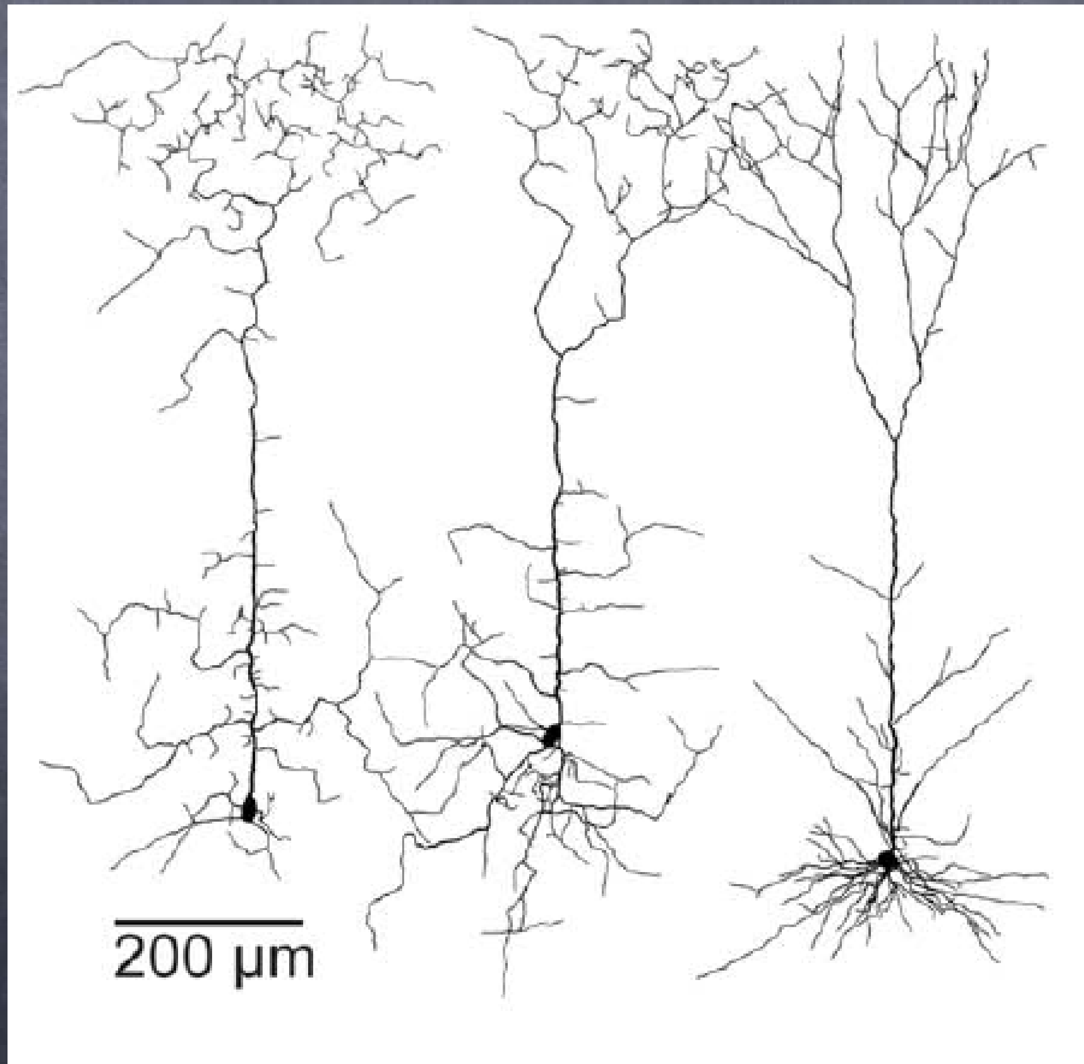
λ=0.6



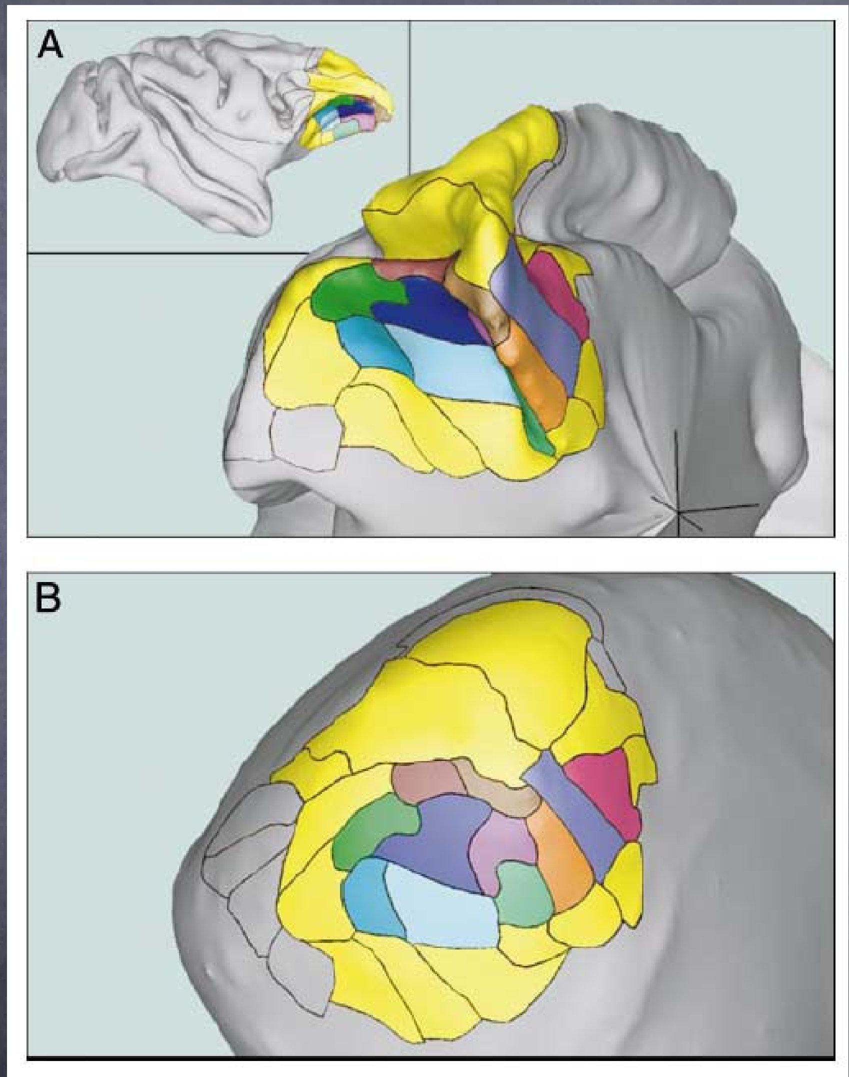


Seems to work well for many neuronal types

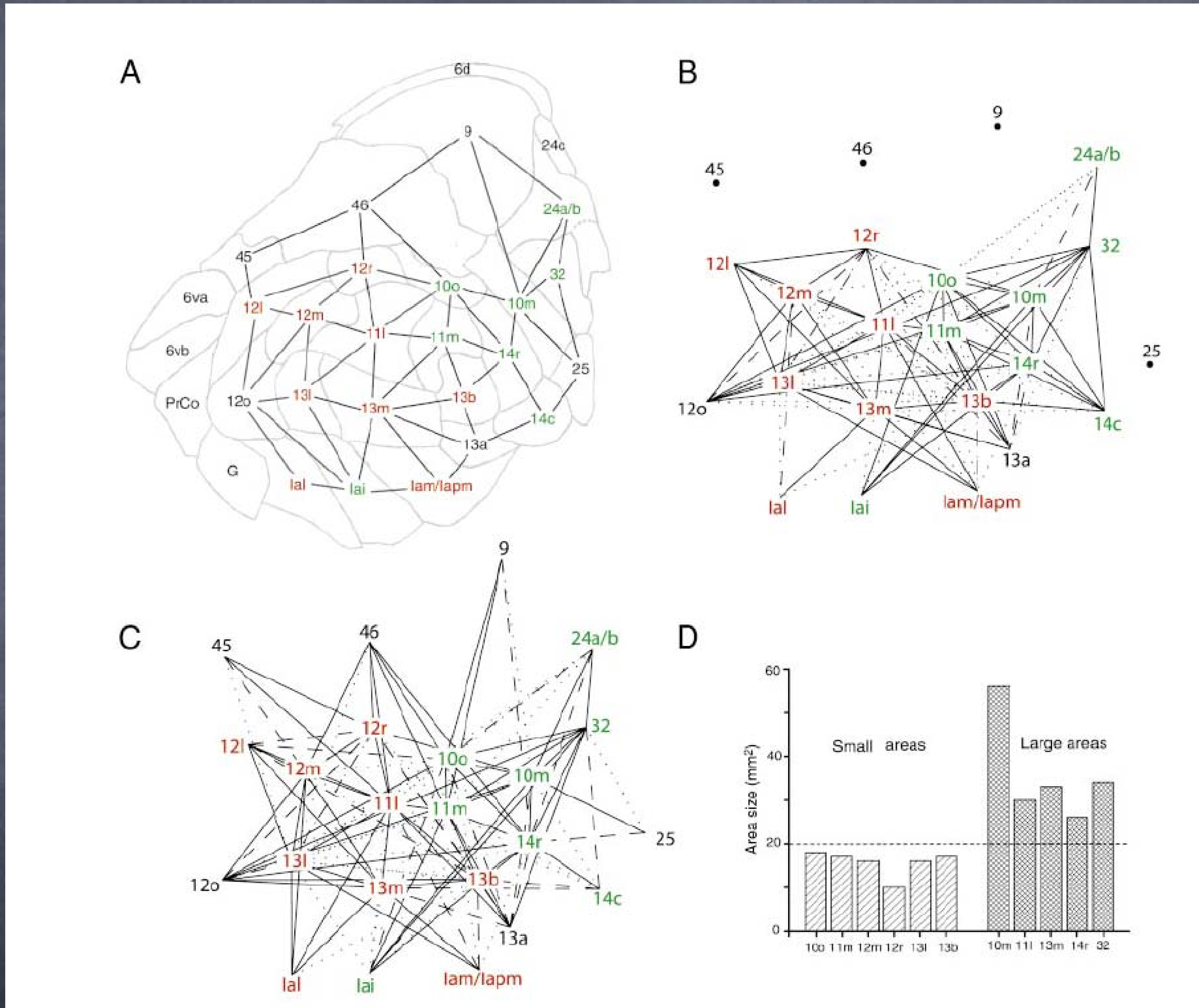
λ=0 λ=0.2 λ=0.7



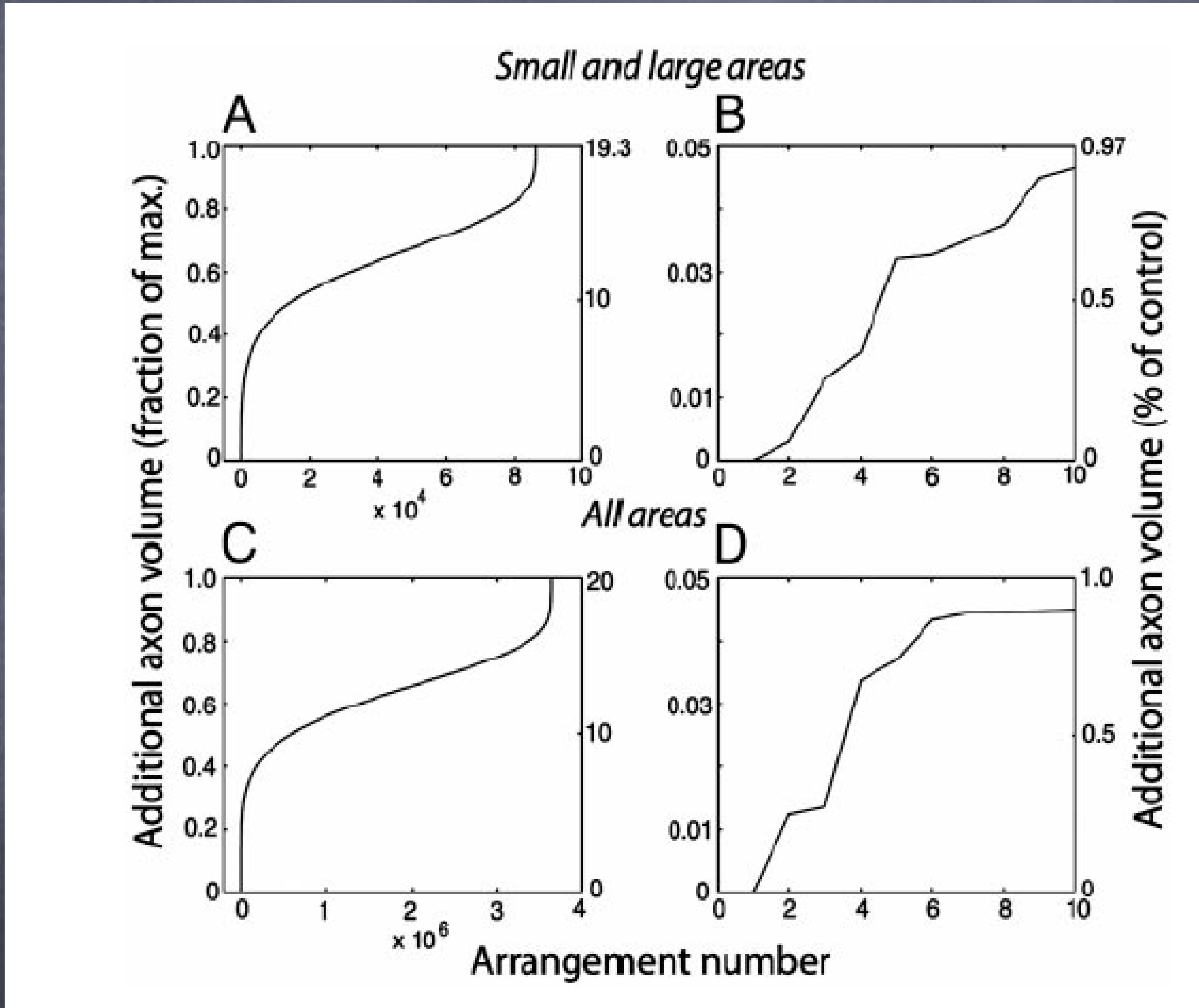
Are positions of cortical areas at minimum wiring?



Connectivity



Wiring length



What about the diameter of neuronal cylinders?

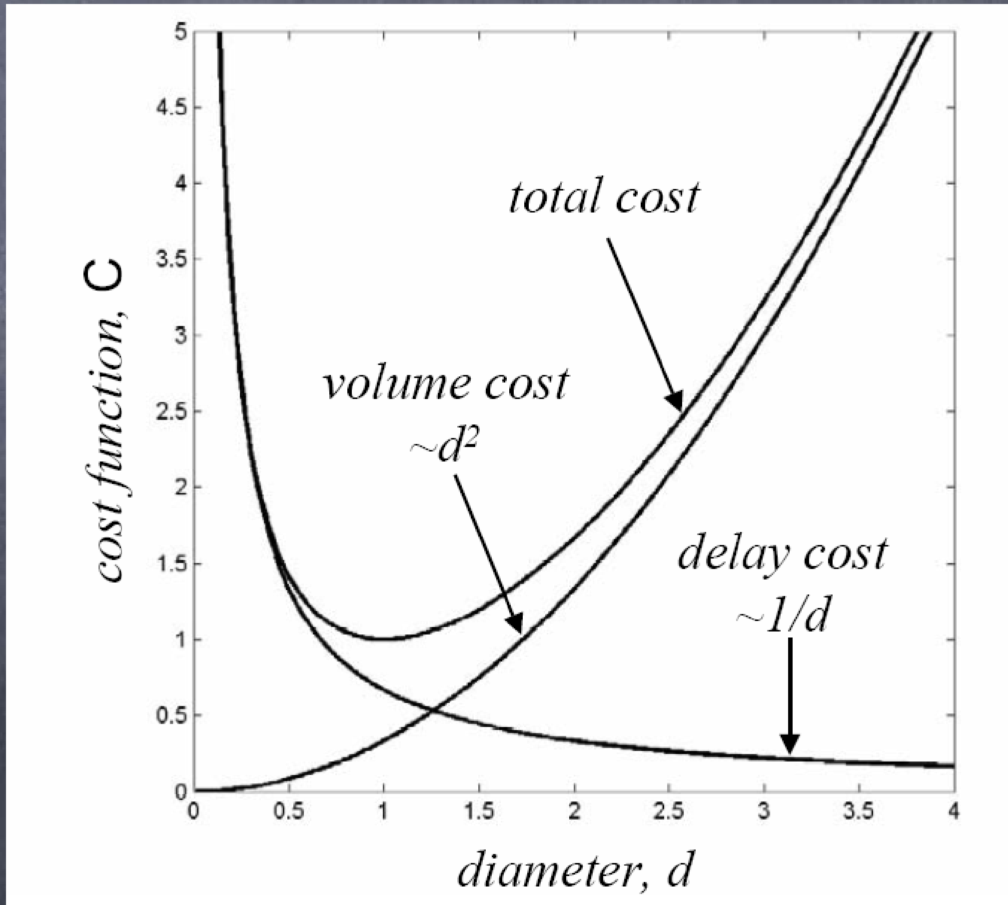
$$\mathfrak{C} = \alpha T + \beta V.$$ with $$T = \frac{L}{s}$$ and $$V = \frac{\pi}{4} L d^2$$

Conduction time and volume

$$s = kd$$

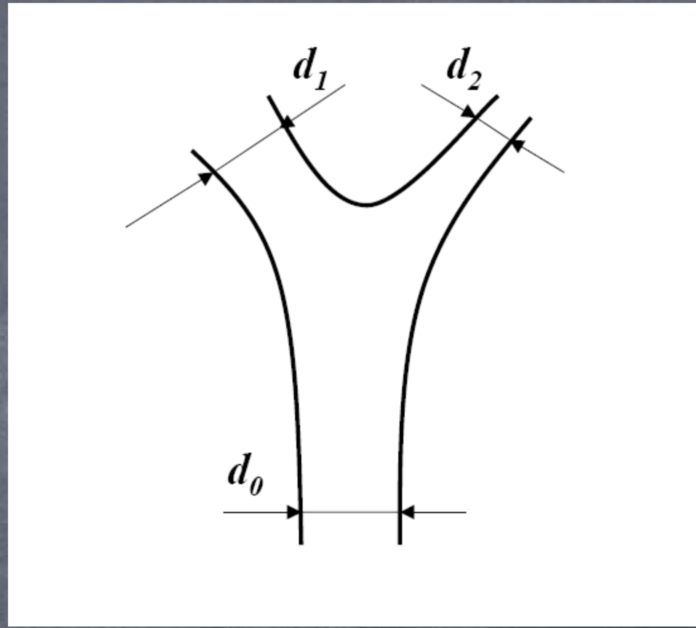
Explicitly

$$\mathfrak{C} = \alpha \frac{L}{s} + \beta L \frac{\pi}{4} d^2 = L\left(\frac{\alpha}{kd} + \frac{\beta\pi}{4} d^2 \right).$$



$$\frac{\partial \mathfrak{C}}{\partial d} = 0$$ gives $$d = \left(\frac{2\alpha}{\pi k \beta} \right)^{1/3}$$

At bifurcation:



$$\mathfrak{C} = \alpha_1 (t_0 + t_1) + \alpha_2 (t_0 + t_2) + \beta (V_0 + V_1 + V_2)$$

or

$$\mathfrak{C} = [(\alpha_1 + \alpha_2)\, t_0 + \beta V_0] + [\alpha_1 t_1 + \beta V_1] + [\alpha_2 t_2 + \beta V_2]$$

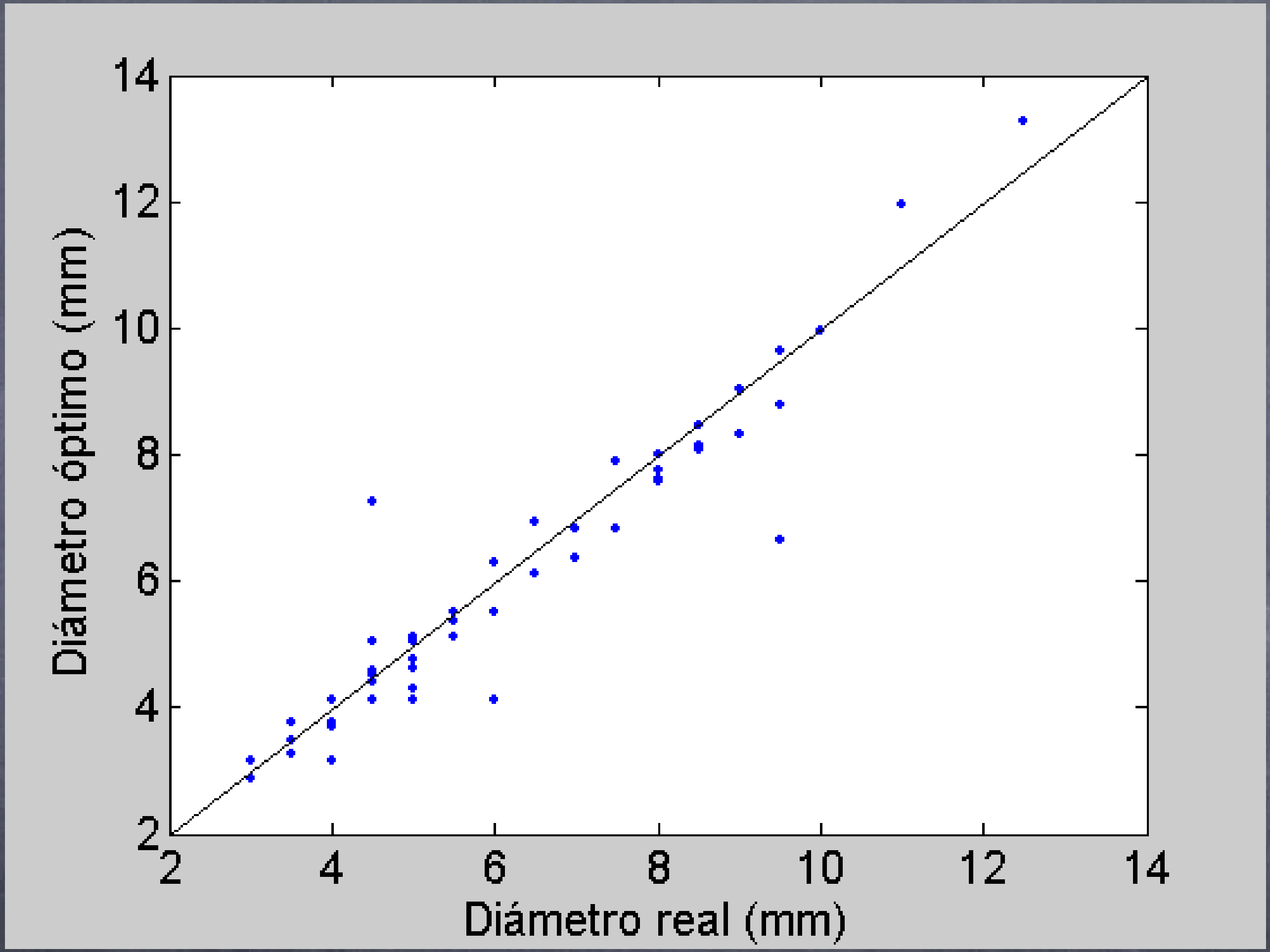
$$\frac{\partial \mathfrak{C}}{\partial d} = 0$$ gives

$$d_0 = \left(\frac{2(\alpha_1 + \alpha_2)}{k\beta\pi} \right)^{1/3}, \quad d_1 = \left(\frac{2\alpha_1}{k\beta\pi} \right)^{1/3}, \quad d_2 = \left(\frac{2\alpha_2}{k\beta\pi} \right)^{1/3}$$

or

$$\boxed{d_0^3 = d_1^3 + d_2^3}$$

Theory *vs* data



Summary

1. Optimization theory is a fruitful method to understand neurobiological systems (works well with very few parameters)

2. Wiring optimization explains neuroanatomy (position of neurons, shape of neurons, position of cortical areas, structure of bifurcations, etc)

3. Evolution does not imply that systems are optimized. Test for the structure of deviations.