ENERGY AND THE DESIGNS OF BRAINS

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zoology cambridge

The circuit busters' creed

1. There are no neural circuits without anatomy (but information lives without membra
2. There are identified neurons (fortunately)
3. One needs to combine the range of the LM (whole neurons)
   with the resolution of the EM (synapses and synaptic complexes)
4. Not all morphological synapses are functional synapses
5. Many factors modulate synaptic transmission
6. Not all neurons are electrically compact
7. Neuron geometry and ion channel distribution can play roles
8. *More useful stuff can happen in extracellular space than you might think*
9. NS's are opportunistic (only a few have read Kandel and Schwartz).
10. To identify a connection in a network (synaptic or otherwise) you must
    drive the source and observe the signal in the receiver.
11. Networks operate at many levels, from the molecular upwards
12. To fully understand a circuit you must know all of its inputs and outputs
    (a strategic synapse or better still, a neuromodulator, can have a big effect)

13. *Beware of sub-optimal preps*
    (struggling to adjust to trauma; insufficiently nourished, improper milieu,
    running down = dying)
14. Wherever possible use intact preps in awake behaving animals
15. Circuits only make proper sense in the context of natural behaviour
16. *Describe and strive to use natural stimuli*
    (don’t test bat echolocation with white noise)
17. *Describe and strive to use natural behaviour*
18. *Strive to discover how the NS connects natural stimuli to natural behaviour*
19. *There is a place for artificial stimuli (probing and describing interactions)*
    but the artificial must be related to natural
20. To discover how circuits contribute to behaviour you must perturb the circuit
    and observe the effect on behaviour
21. To understand this test you will usually need models.
    Circuits are often too complicated to intuit their actions.
22. Circuits are versatile and adaptable because cells are versatile and adaptable

23. **Laughlin’s Rule**

Don’t a make rule unless you know why
cells cannot break it

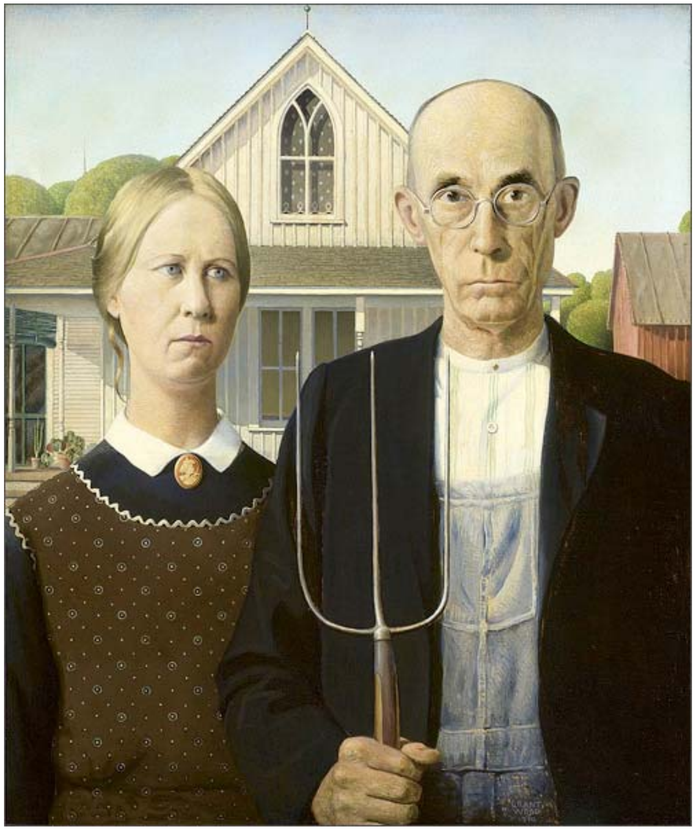
.

The buster’s dilemma - t**here are no solved circuits.**
Is this because they will never be?

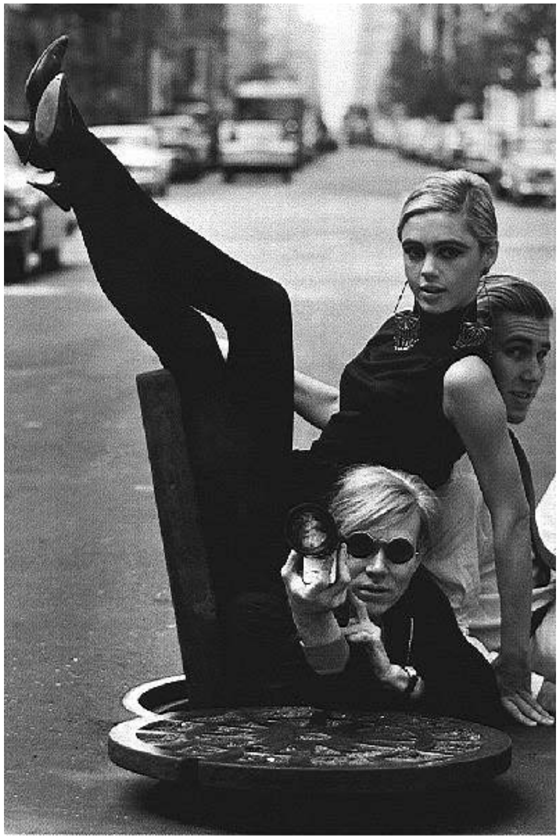
Plenty of examples of bits of circuits doing important stuff
(producing a rhythm, adapting behaviour to experience)
but all of these accounts are incomplete

Constraints

Physics



Biology



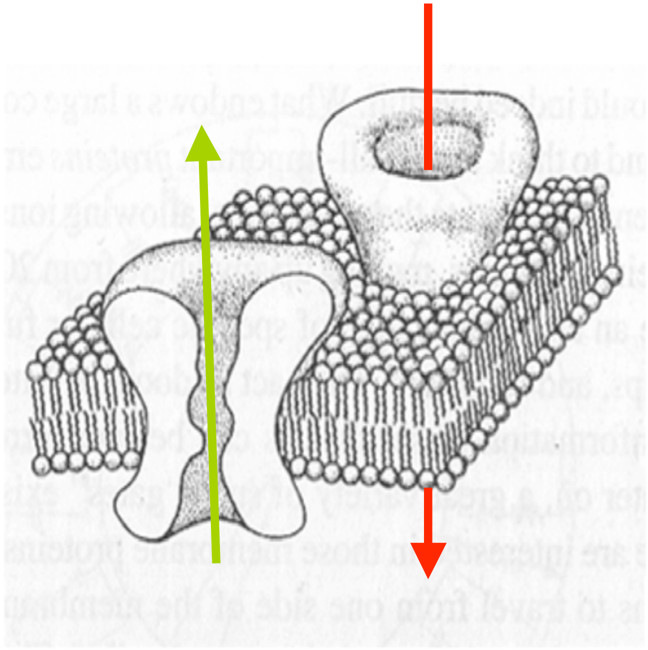
Principles, what principles?

- Design Principles
  - – Wiring economy
  - – Efficient communication (chemical synapse, action potential, myelin)
  - – Efficient and effective signal processing (redundancy reduction - lateral inhibition, c.p.g.’s - Szekely’s disinhibitory ring)
  - – Effective operations etc
  - – There will be lots of principles, lots to be done and lots to do it with!

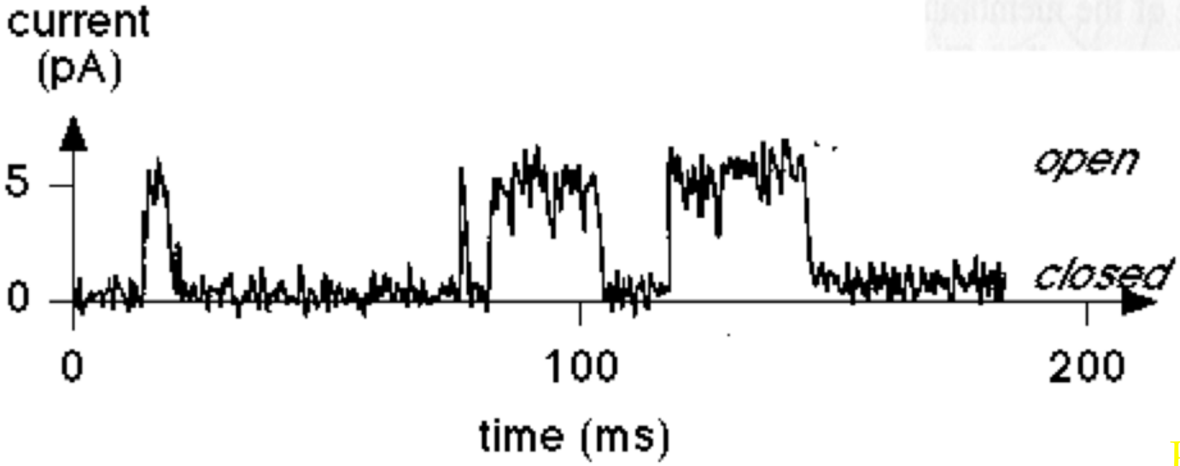
What is design?

- Task
  - – Specifications; performance, size, cost, energy consumption *etc*
- Operations
  - – set of interacting processes that will implement the task
- Components
  - – Mechanisms that will perform the operations

Neurons use ion channels to generate electrical signals

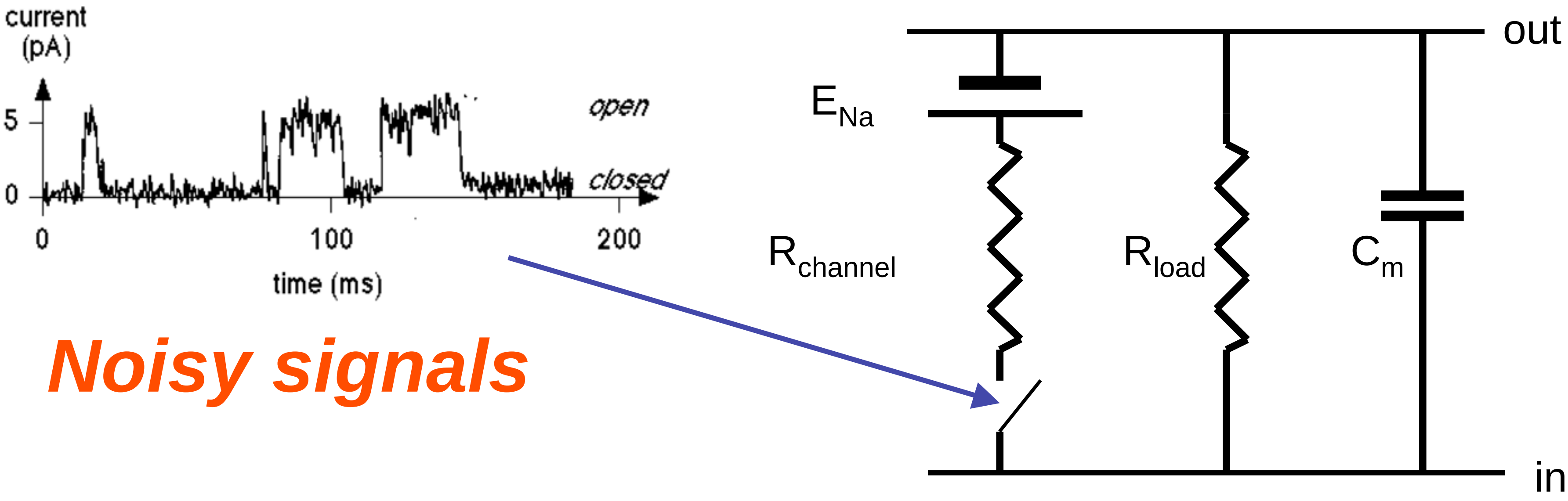


Channels open and
close to regulate
current flow
across the nerve cell
membrane



Hille (1992)

Basic biophysics of ion channels and membranes determine signal quality



Noisy signals

$R_{channel} = 10^{11}$ Ohms

$E = 10^{-1}$ V

$R_{load} = 10^{9}$ Ohms

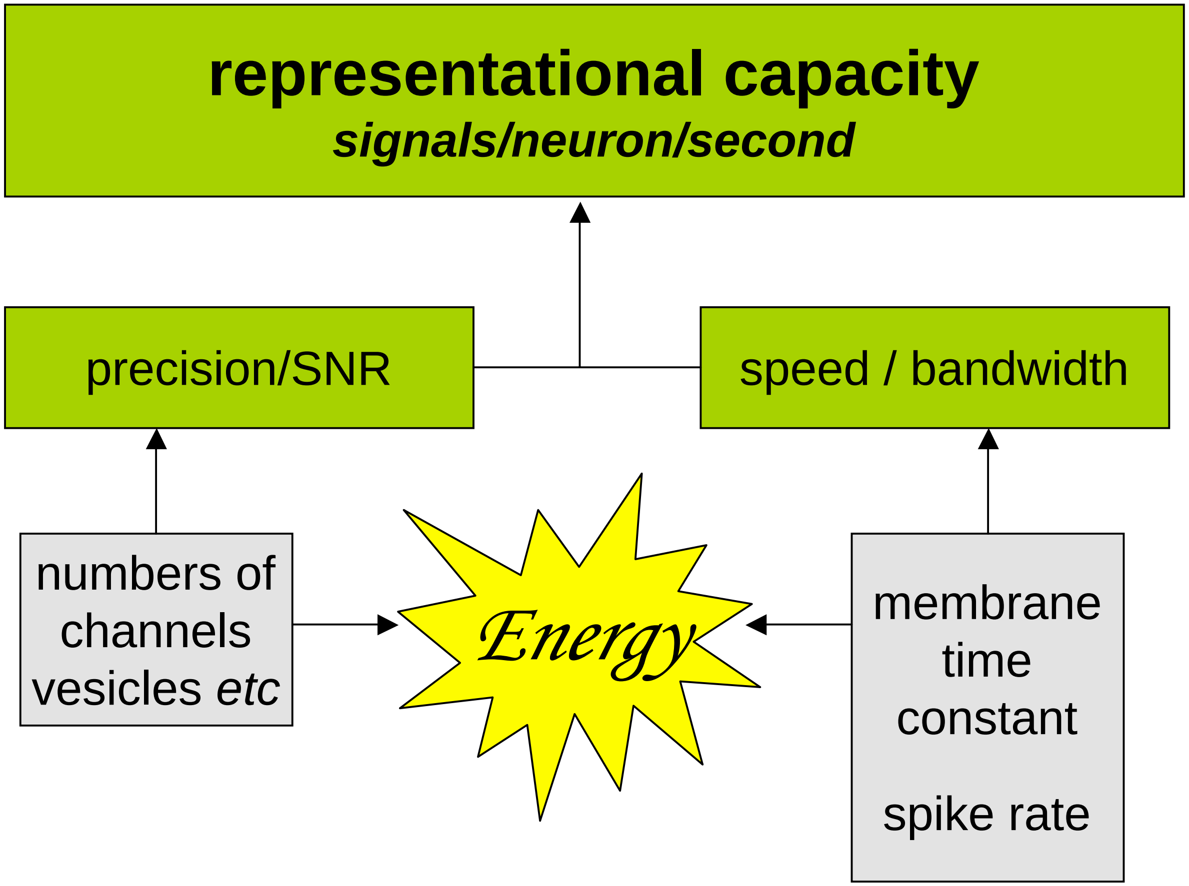
Small signals

$\tau = R_m C_m$

C_m is significant

R_m is high

Slow signals



representational capacity
signals/neuron/second

precision/SNR

speed / bandwidth

numbers of channels vesicles *etc*

Energy

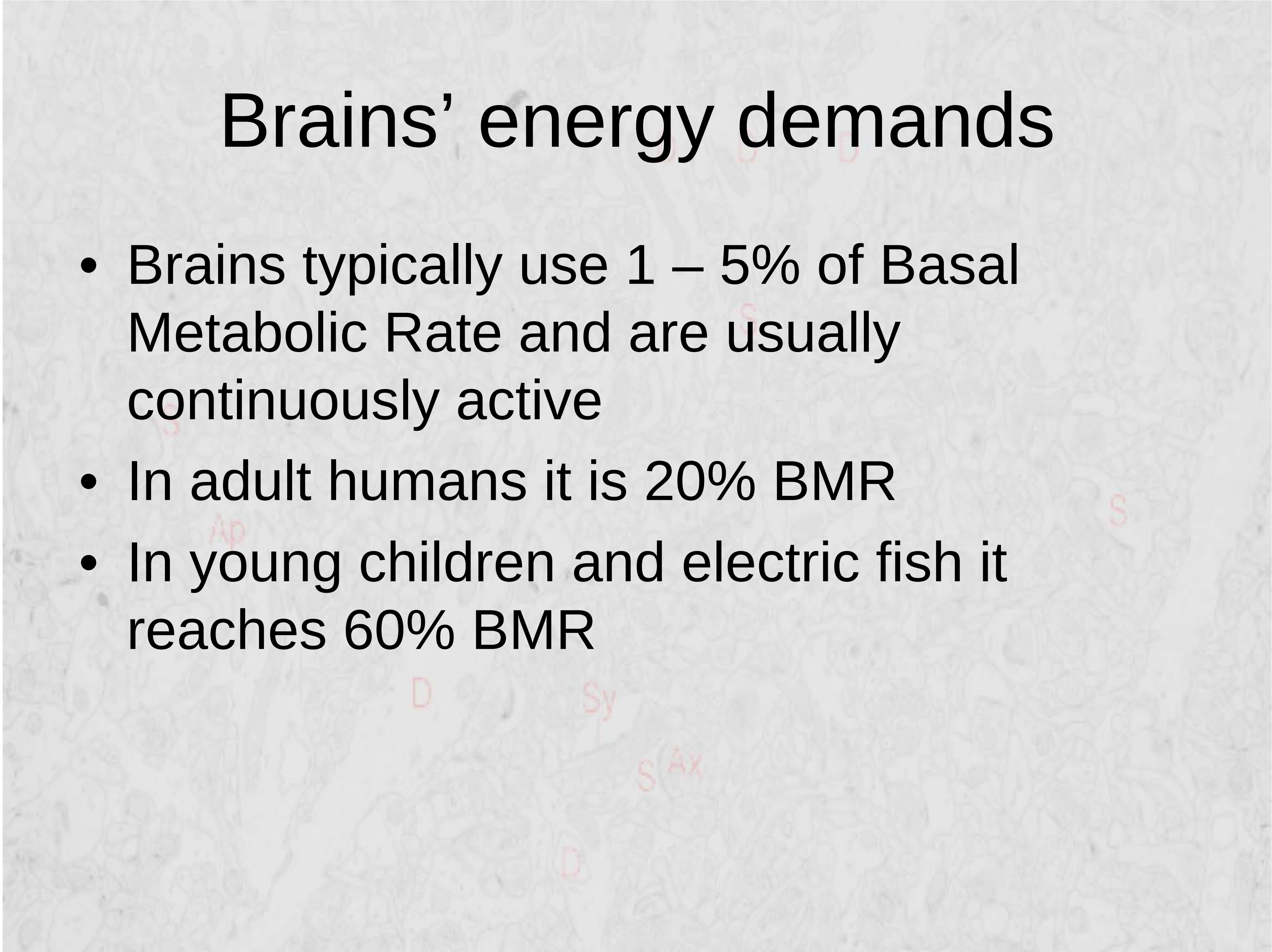
membrane time constant

spike rate

Noise and time constant limit representational capacity

Energy is required to ease these limits

Is energy consumption relevant ?



Brains’ energy demands

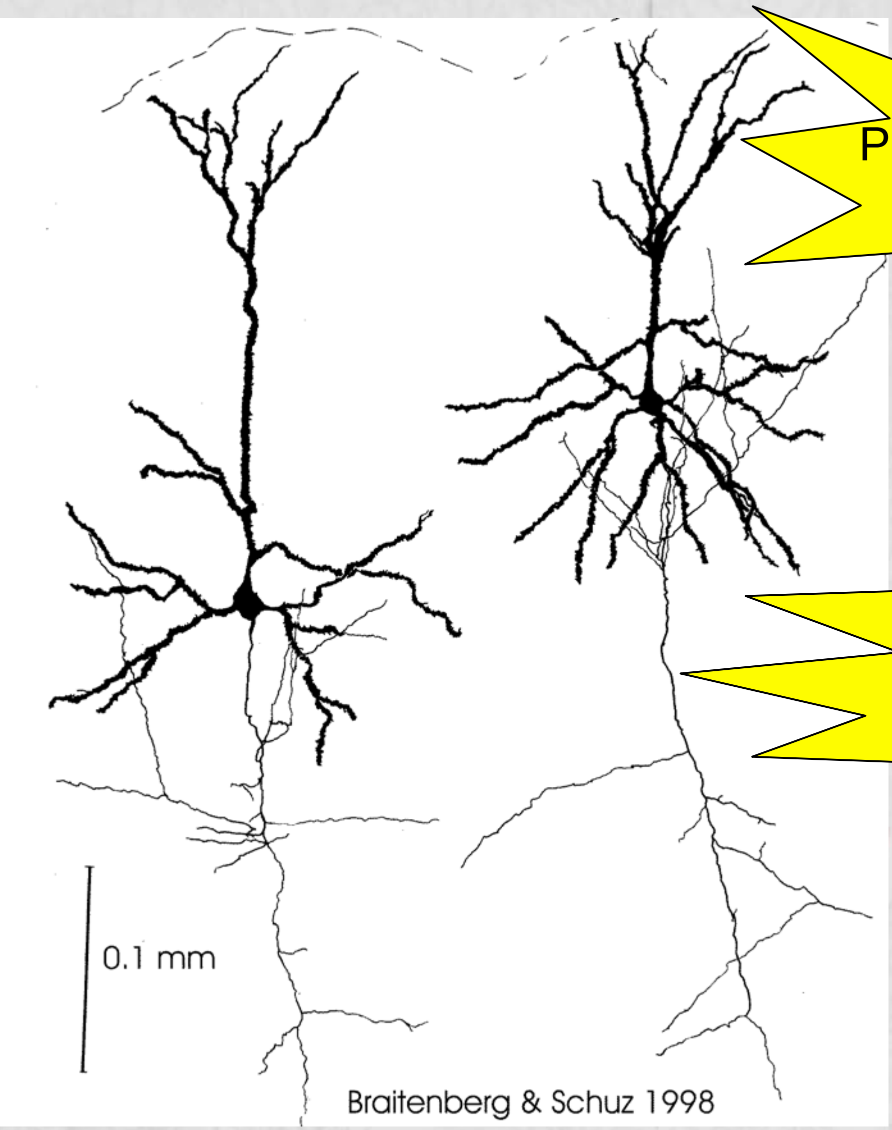
- Brains typically use 1 – 5% of Basal Metabolic Rate and are usually continuously active
- In adult humans it is 20% BMR
- In young children and electric fish it reaches 60% BMR

Where does a brain's energy go?

- Generating the signals that transmit, process and store information
- Maintenance
  - Turnover of macromolecules
  - Proton leak
  - Intracellular transport
  - Neuronal and glial resting potentials
  - Communication for maintenance

Bottom up energy budgets indicate the magnitudes of these demands

Energy usage in rodent grey matter, % total



Braitenberg & Schuz 1998

Post-synaptic current
25%

r.p.'s
neurons, glia
10%

Action potentials
35%

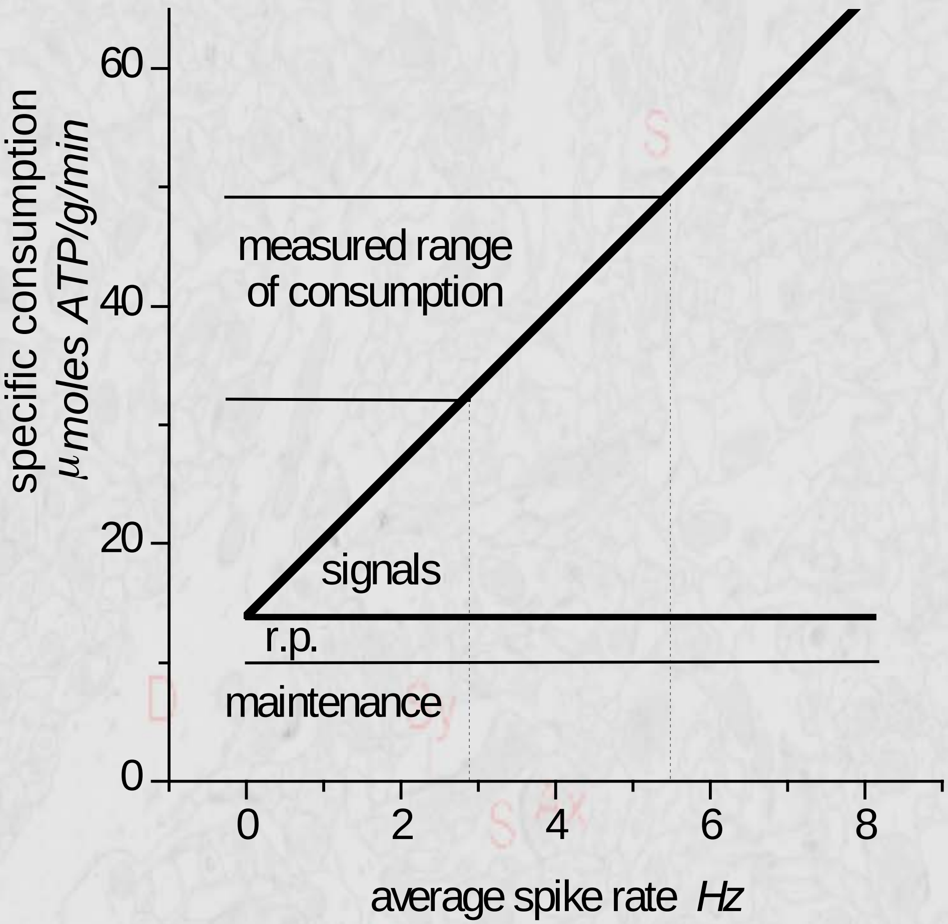
Pre-synaptic **5%**

Maintenance
25%

Attwell & Laughlin, J Cereb Blood Flow Metabolism 2001

Energy cost *vs* signalling rate

cortical grey matter - rodent



From Attwell & Laughlin 2001

Conclusions from bottom up budgets

Energy usage by neurons in cortical grey matter

- Electrical signals take 65% energy
  - Fast synaptic processing
  - Fast transmission over relatively long distances
- Chemical signalling is an order of magnitude less expensive than electrical
- Grey matter uses energy to make numerous long range connections
- Energy usage limits representational capacity
  - *Energy efficient designs*

Energy efficient designs

- Minimise wiring costs (maps, circuit layout)
  - reduces a.p. transmission costs
- Reduce redundancy (opponent responses, adaptation, synaptic plasticity)
  - reduces signal traffic
- Implement efficient codes
- **Hybrid architecture**
- **Miniaturise components**
- **Arrange components in efficient circuits**

Hybrid architecture

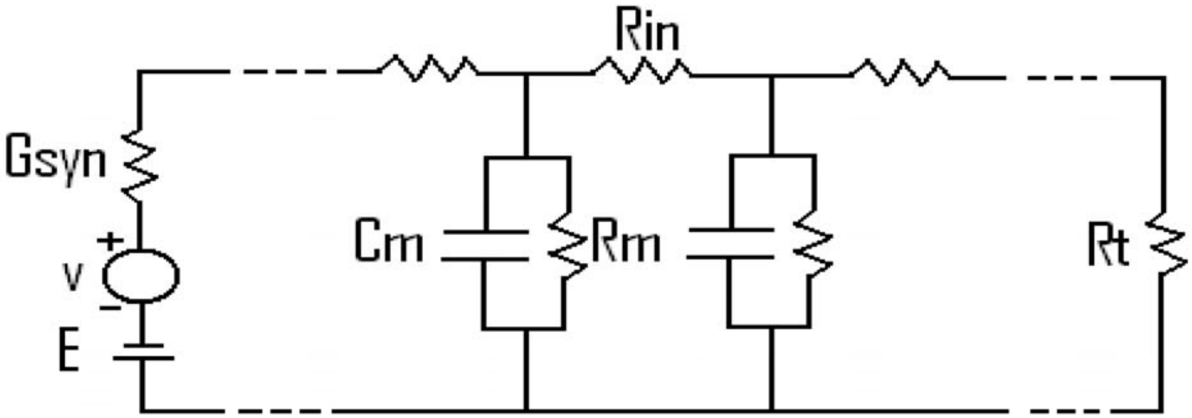
Rahul Sarpeshkar, 1998

Neural Computation 10, 1601 (1998)

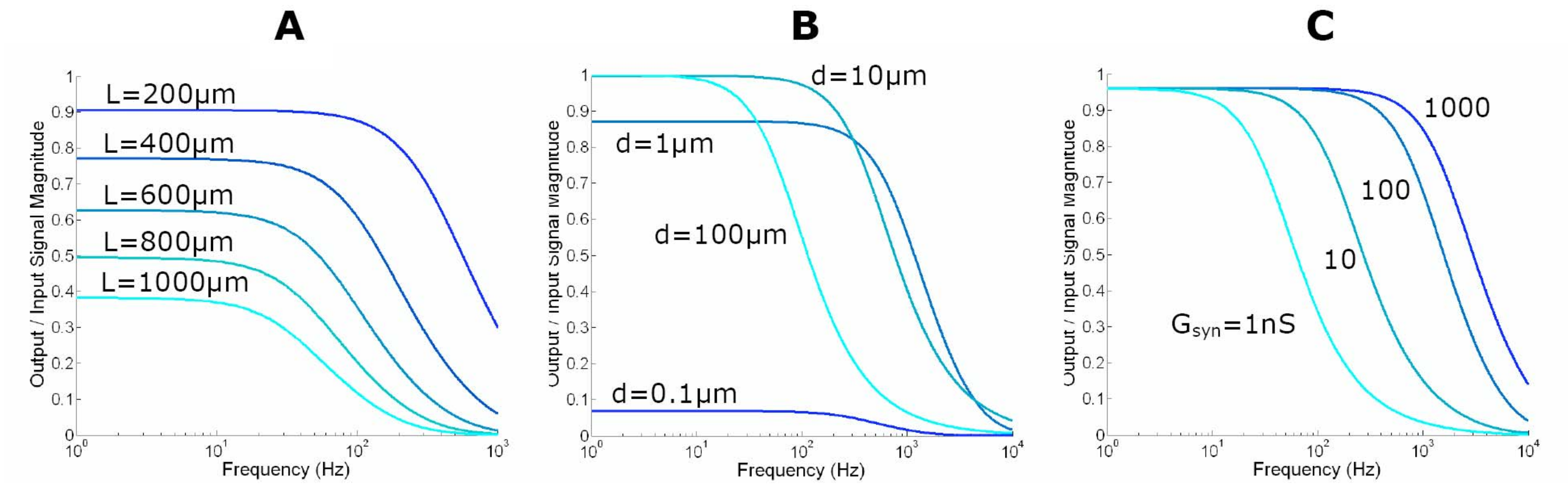
Energy efficiency of analogue and spike transmission of information along axons

Mark Scott, Engineering, Cambridge

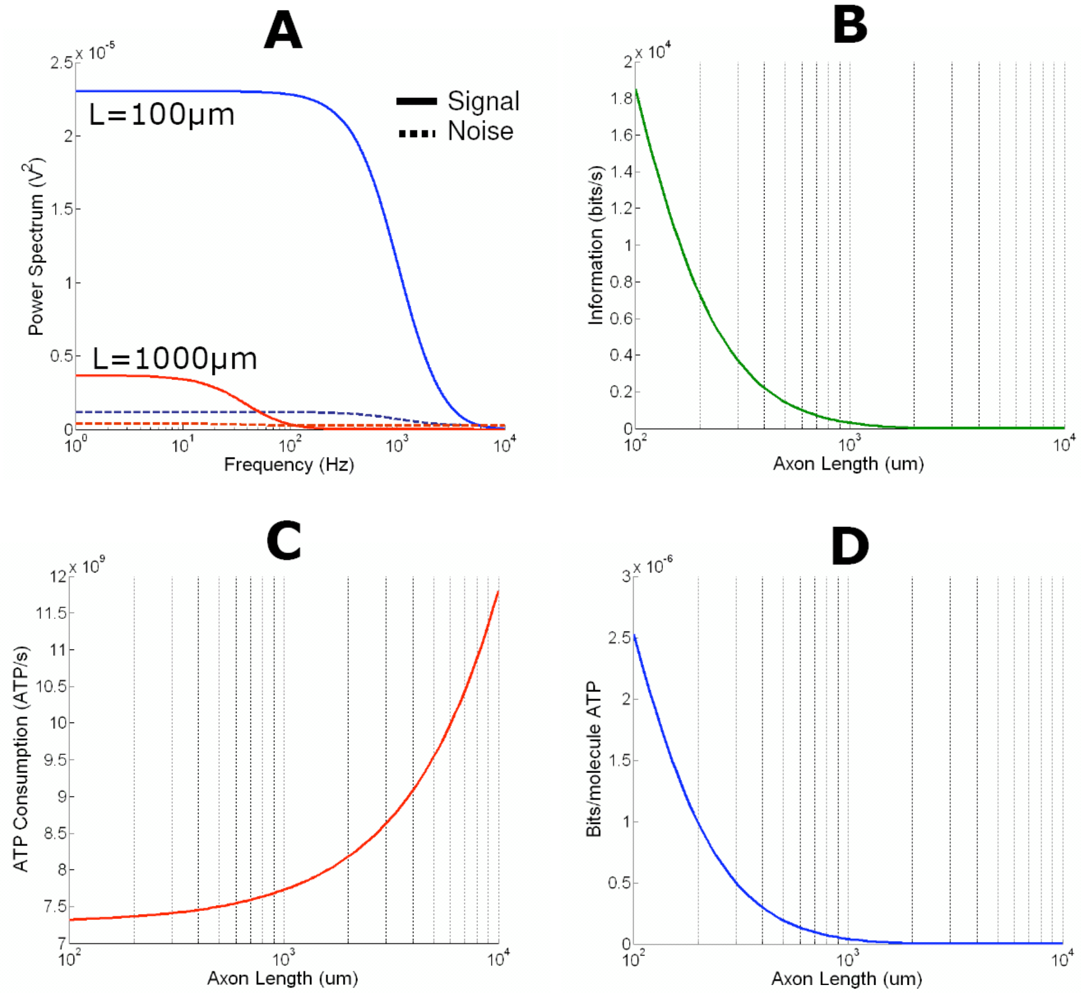
with Jorge Goncalvez and Simon Laughlin



Axon frequency response depends on length, diameter and driving conductance

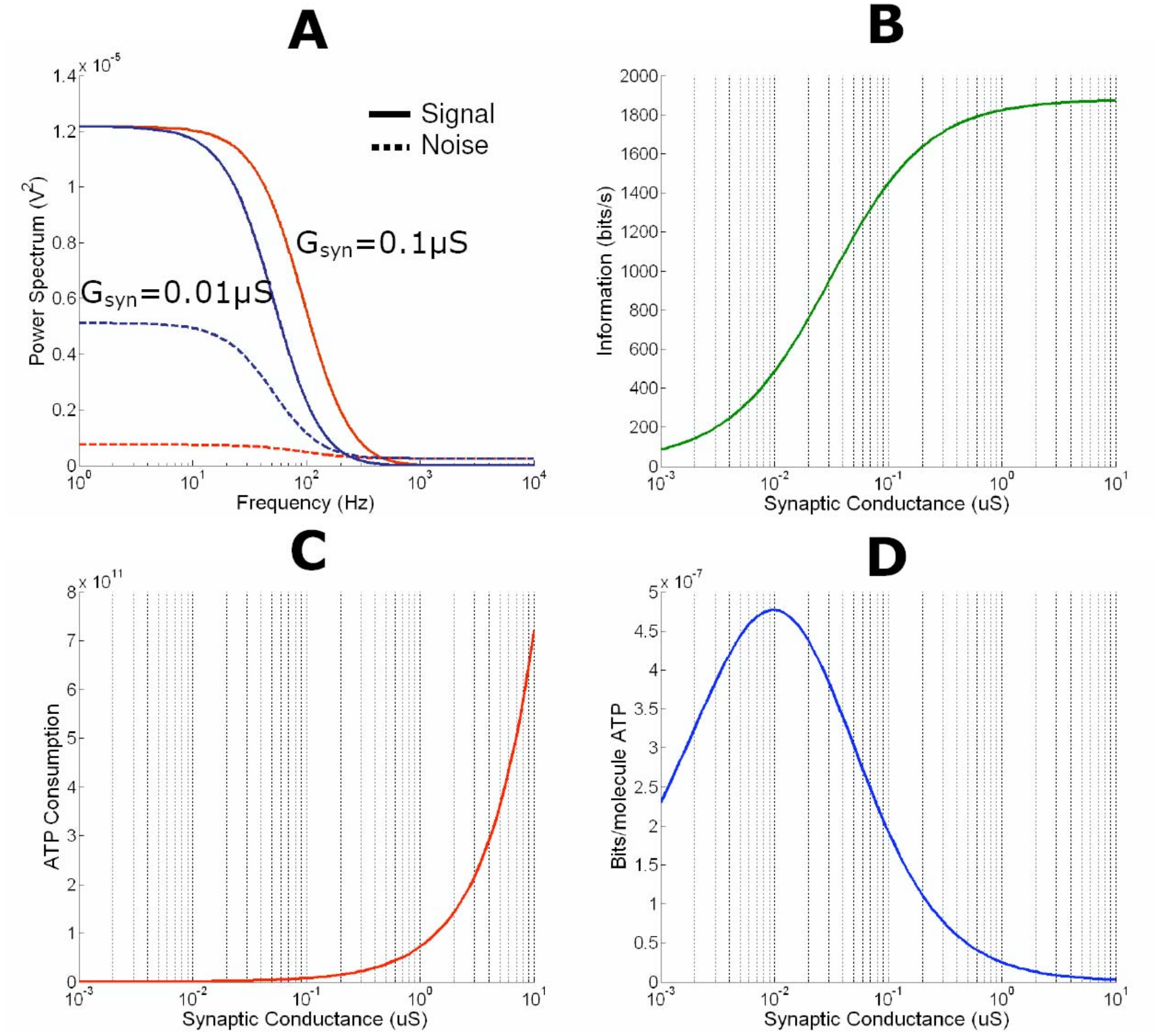


Effects of axon length, at constant dia. and driving conductance

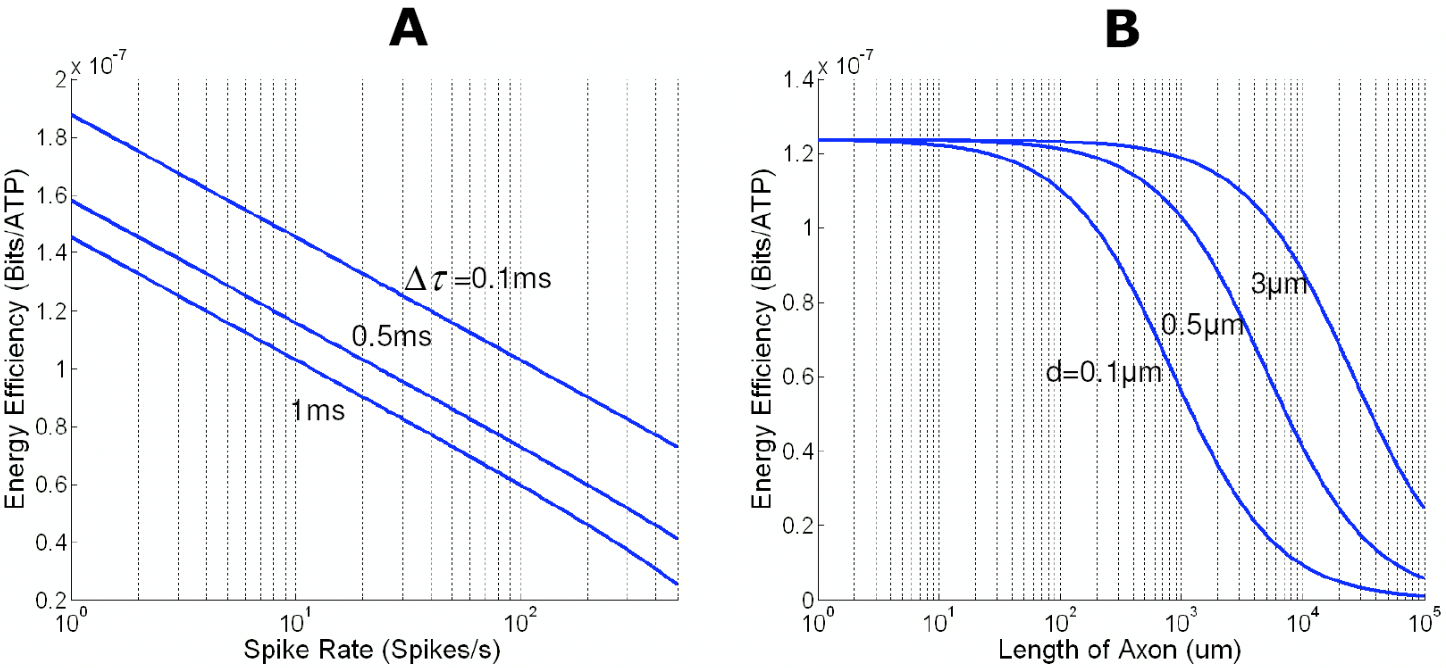


Mark Scott, MEng Report

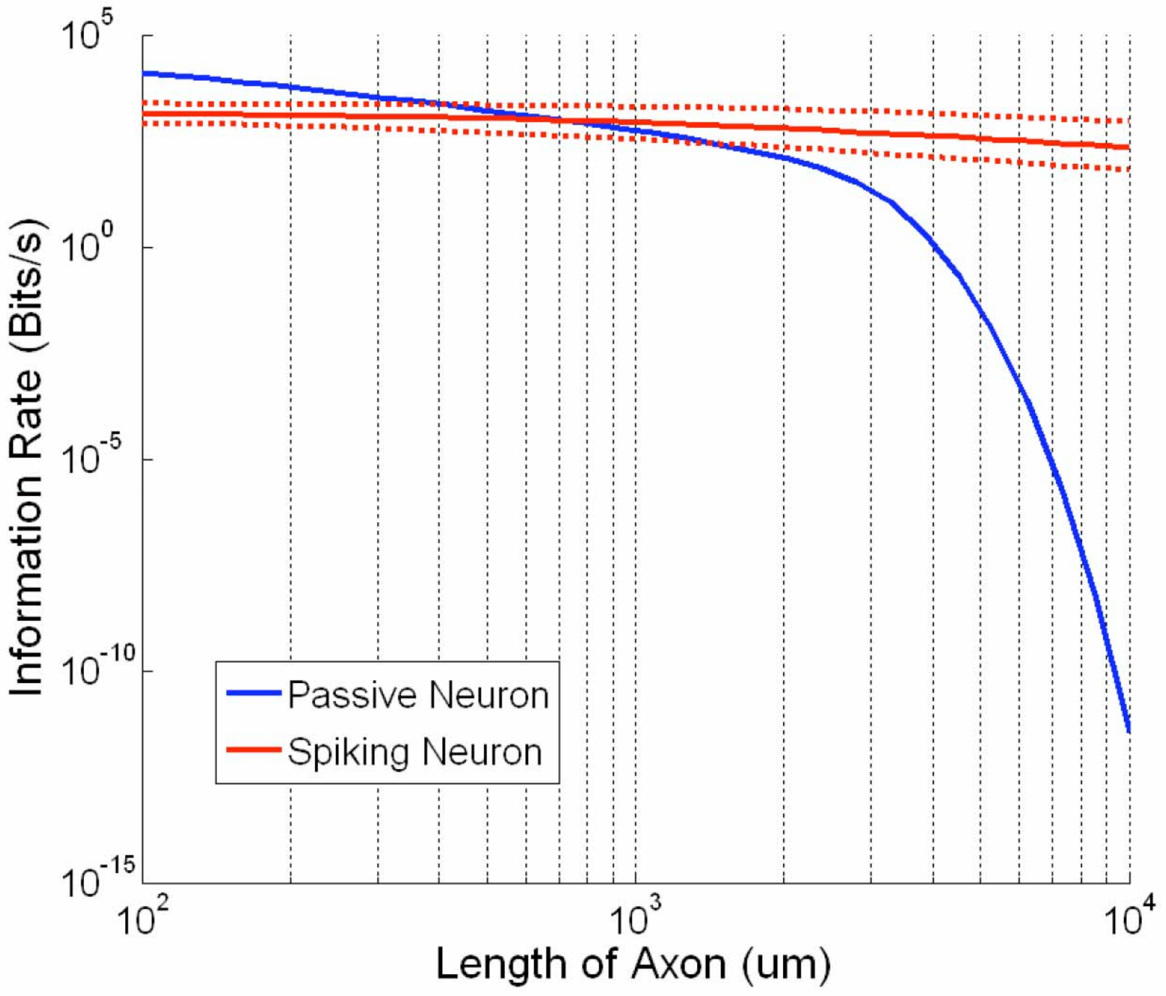
Effect of driving conductance on frequency response, noise spectrum, information rate, energy consumption and efficiency



Energy efficiency of spiking neuron



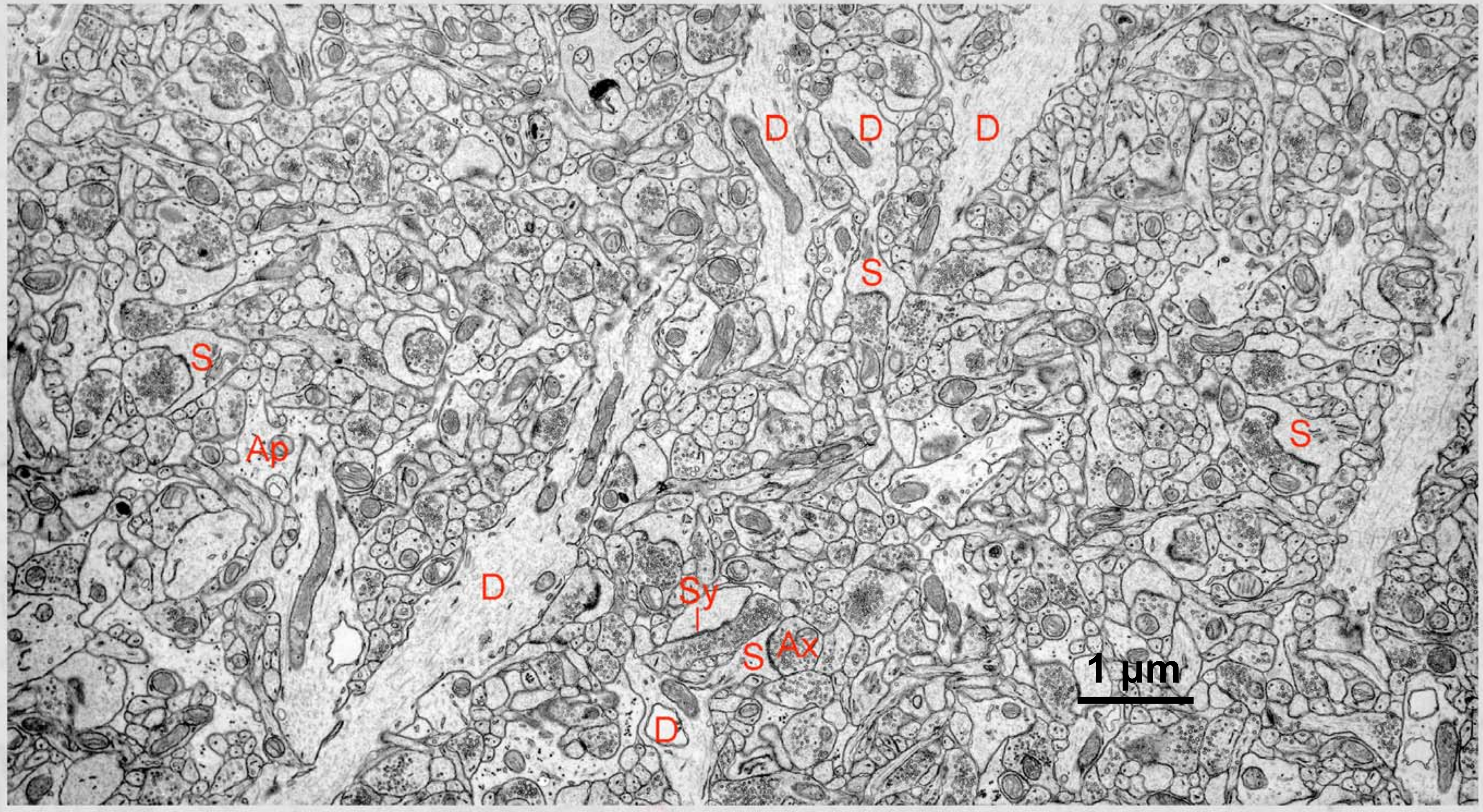
Information rate achieved with a given expenditure of energy, as a function of axon length



miniaturisation

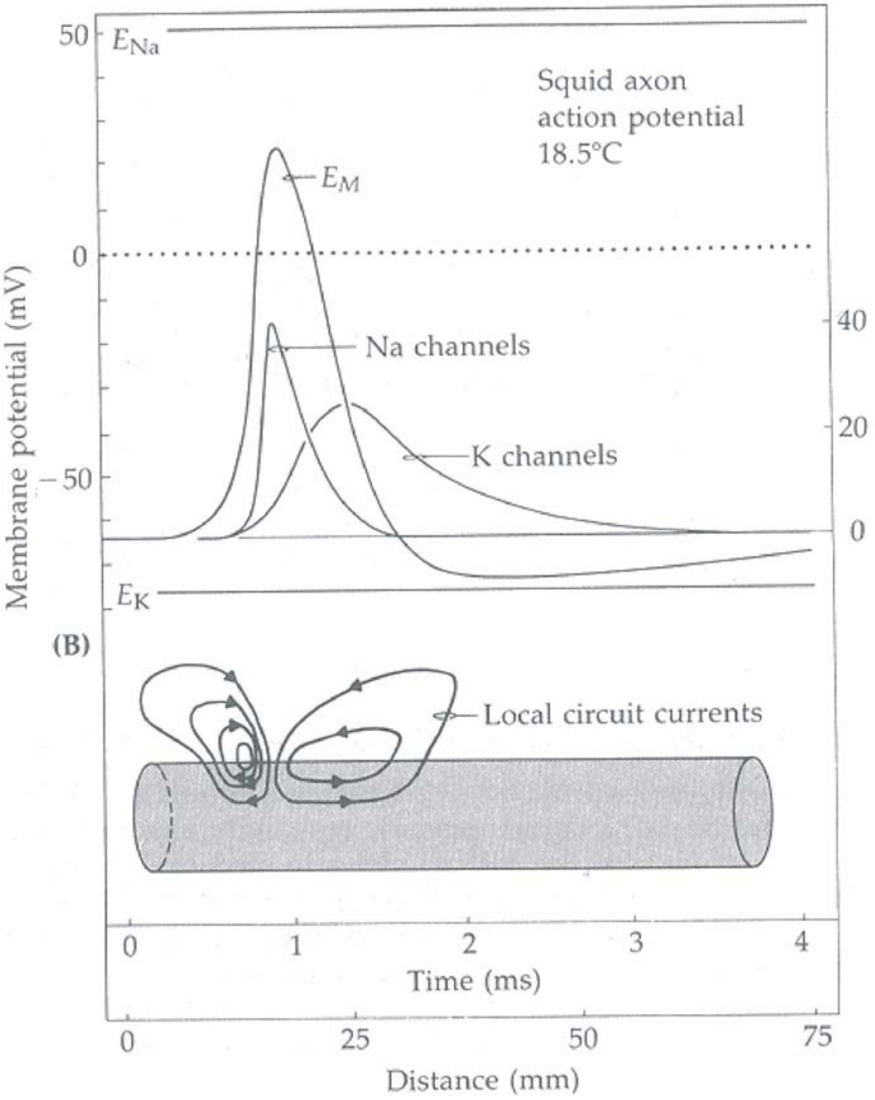
Noise limits to the miniaturisation of axons

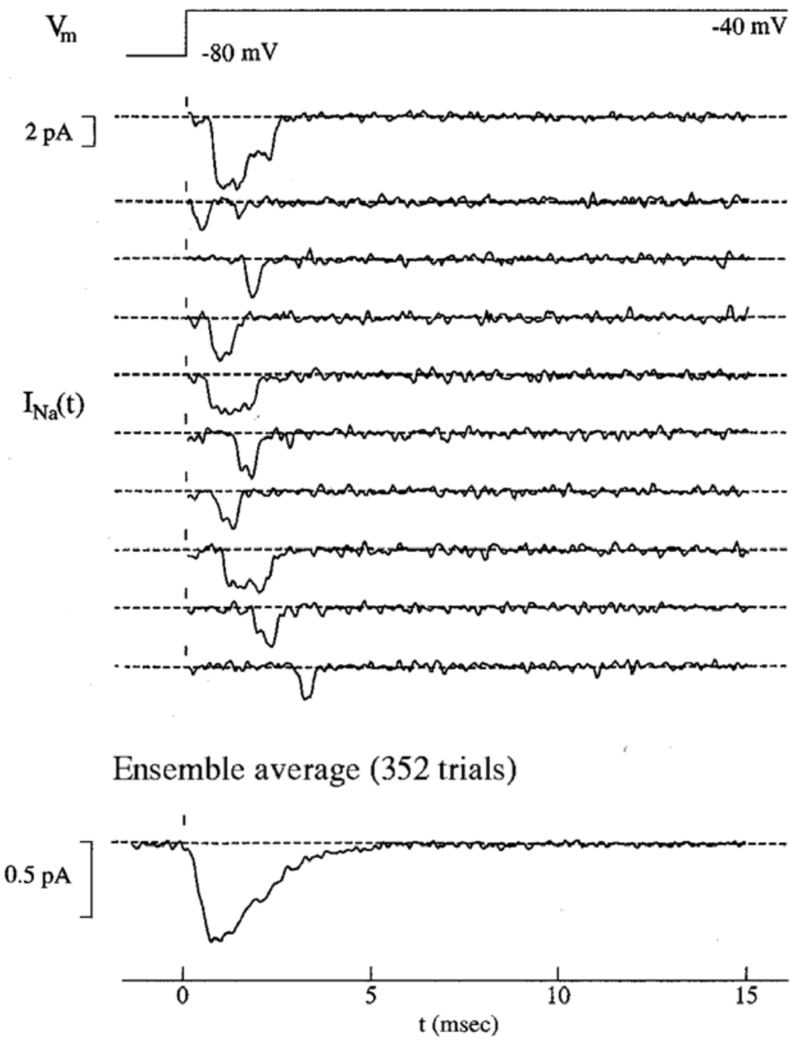
Aldo Faisal John White Simon Laughlin



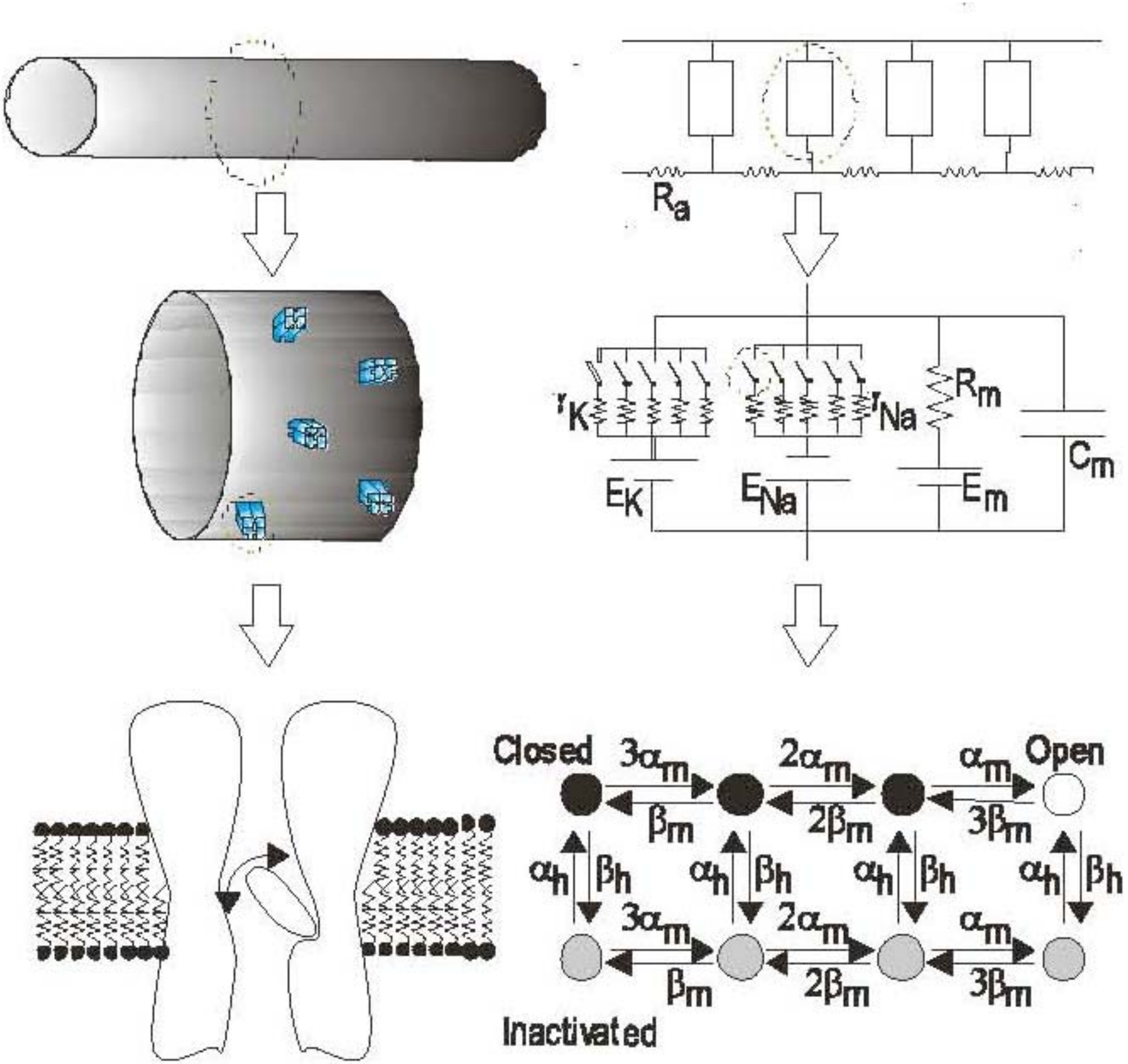
Dendrites (D) of CA1 pyramidal cells – EM section by Dr J. Spacek, Charles Univ Czech Rep. Visit Synapse Web http://synapses.mcg.edu for more details

Action potential channel noise

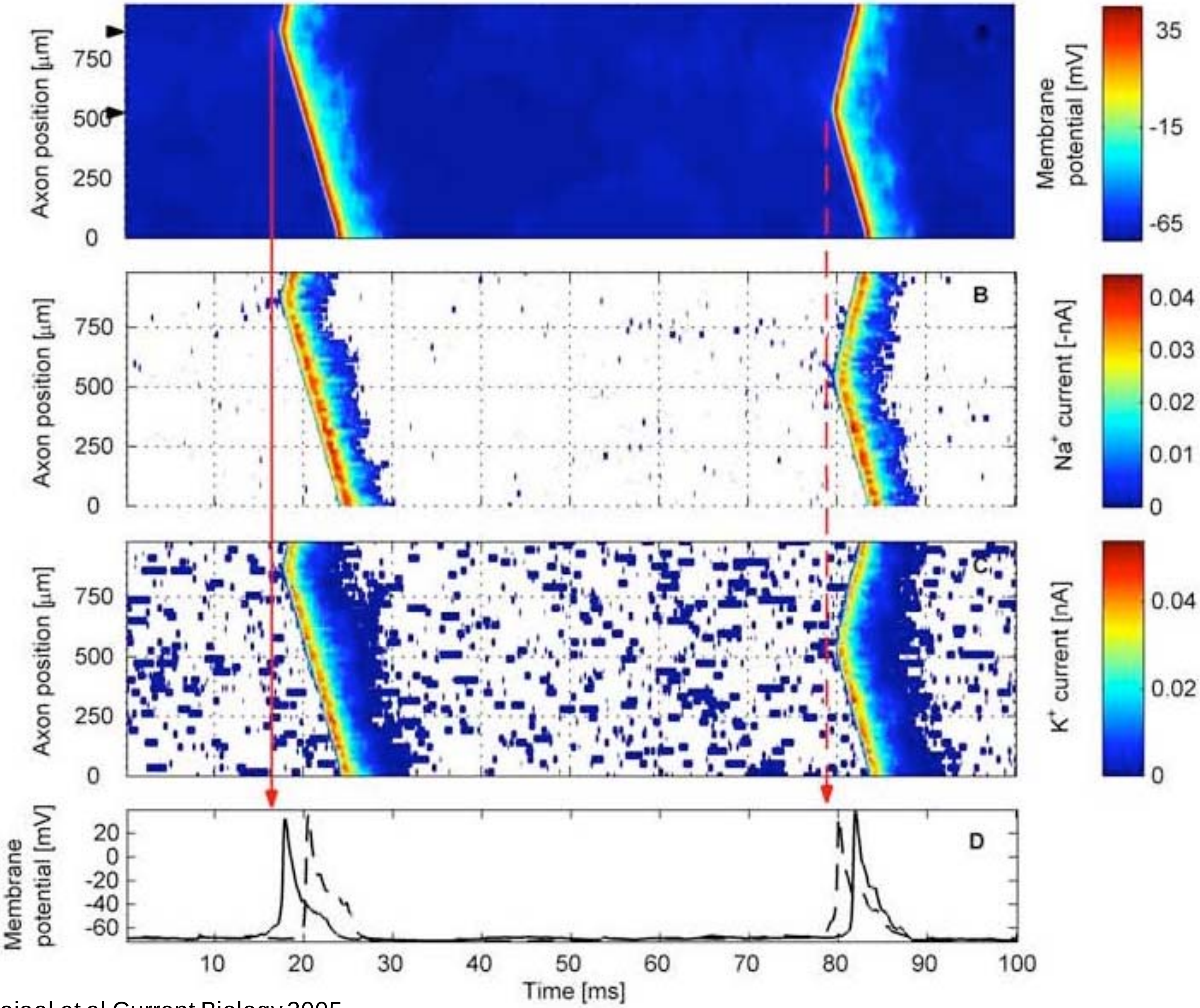




Hille(1992), Patlak & Ortitz (1986)

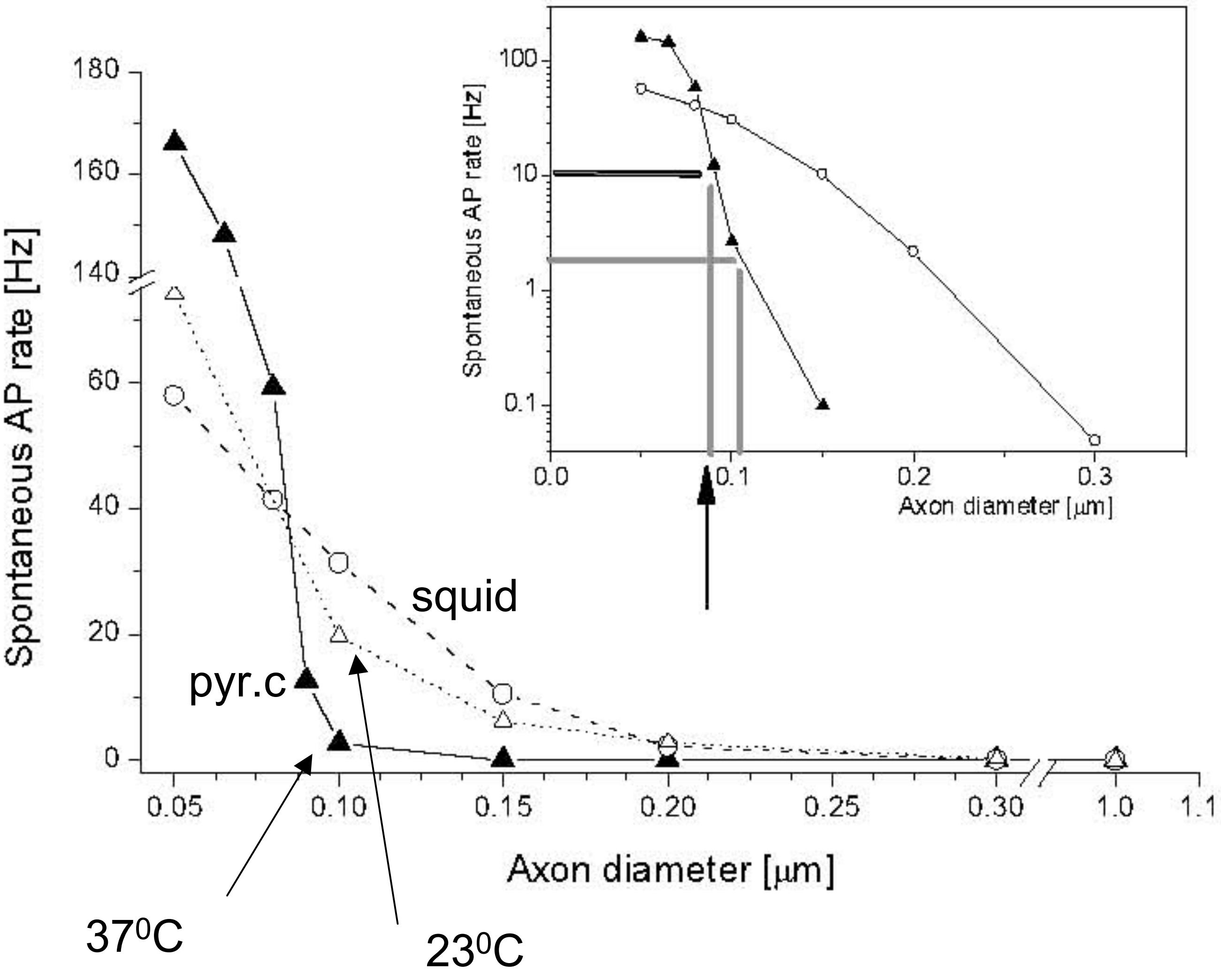


Faisal, White & Laughlin, Current Biology 2005; Faisal & Laughlin, PLoS Comput. Biol. 2007



Faisal et al Current Biology 2005

Spontaneous rate increases rapidly with decreasing diameter, below 0.2 μm



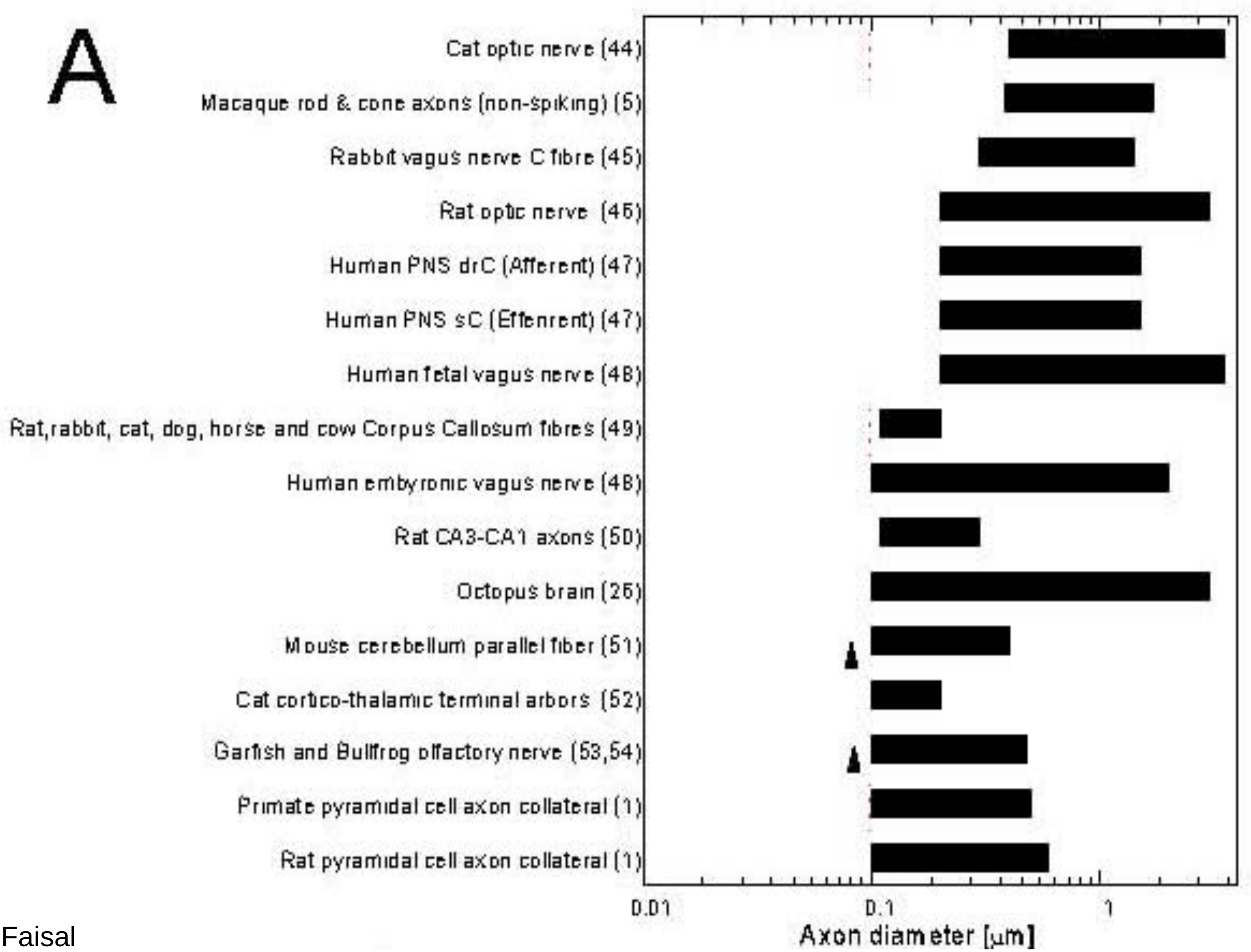
squid

pyr.c

37^0C

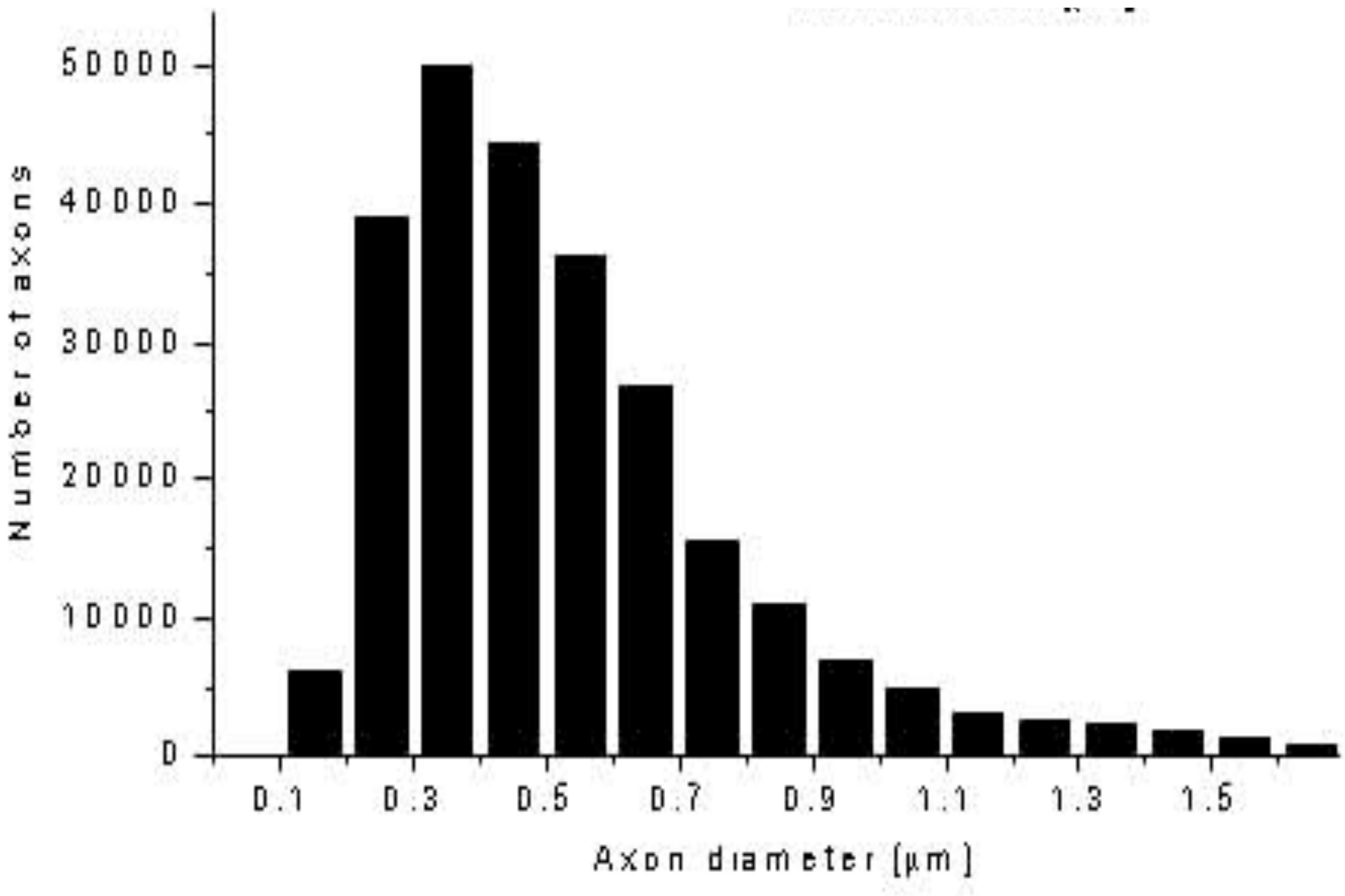
23^0C

Range of axon diameters in a variety of peripheral nerves and CNS regions



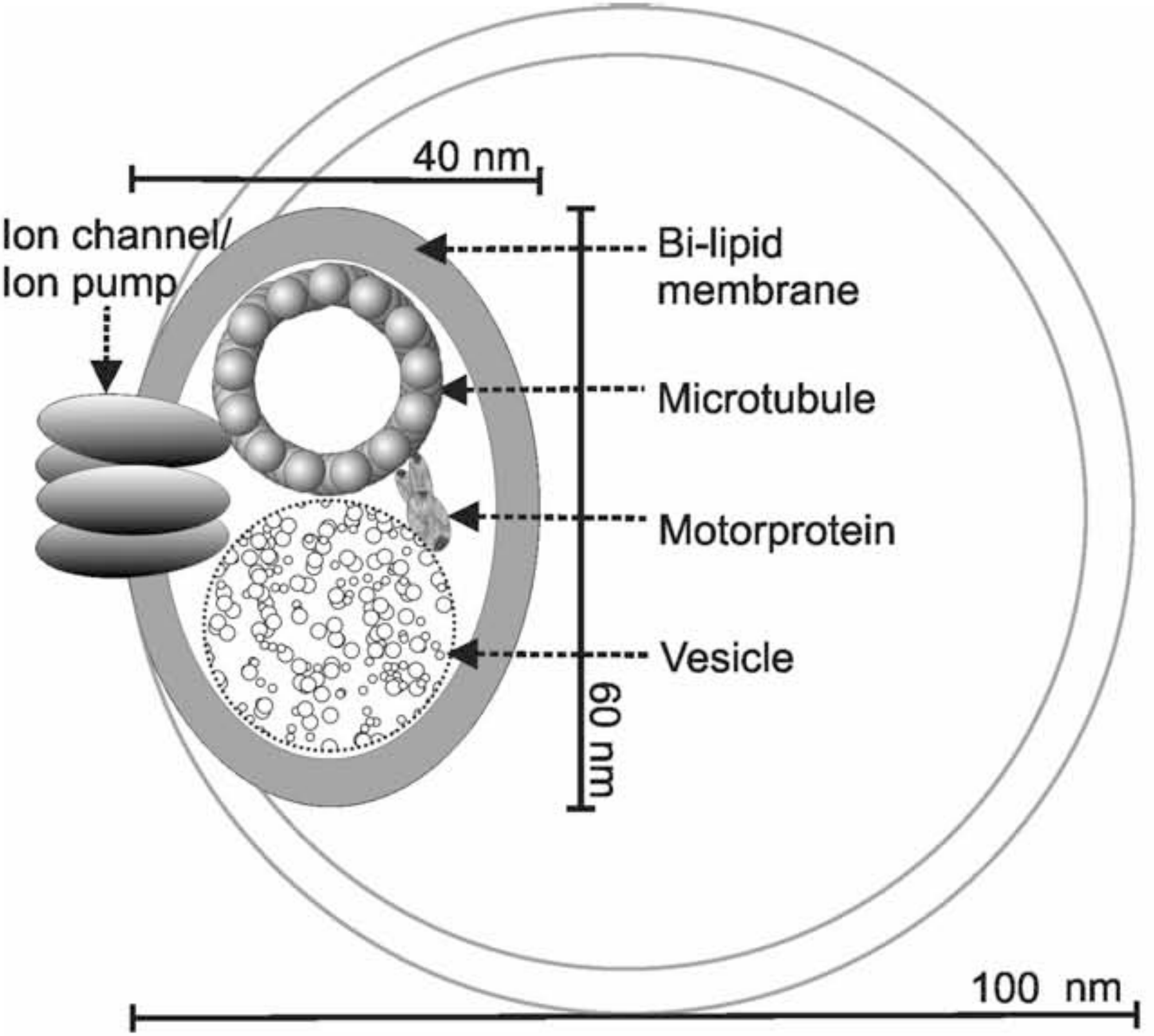
Aldo Faisal

Distribution of fibre diameters in octopus brain
plotted from data collected by ***J-P Camm,***

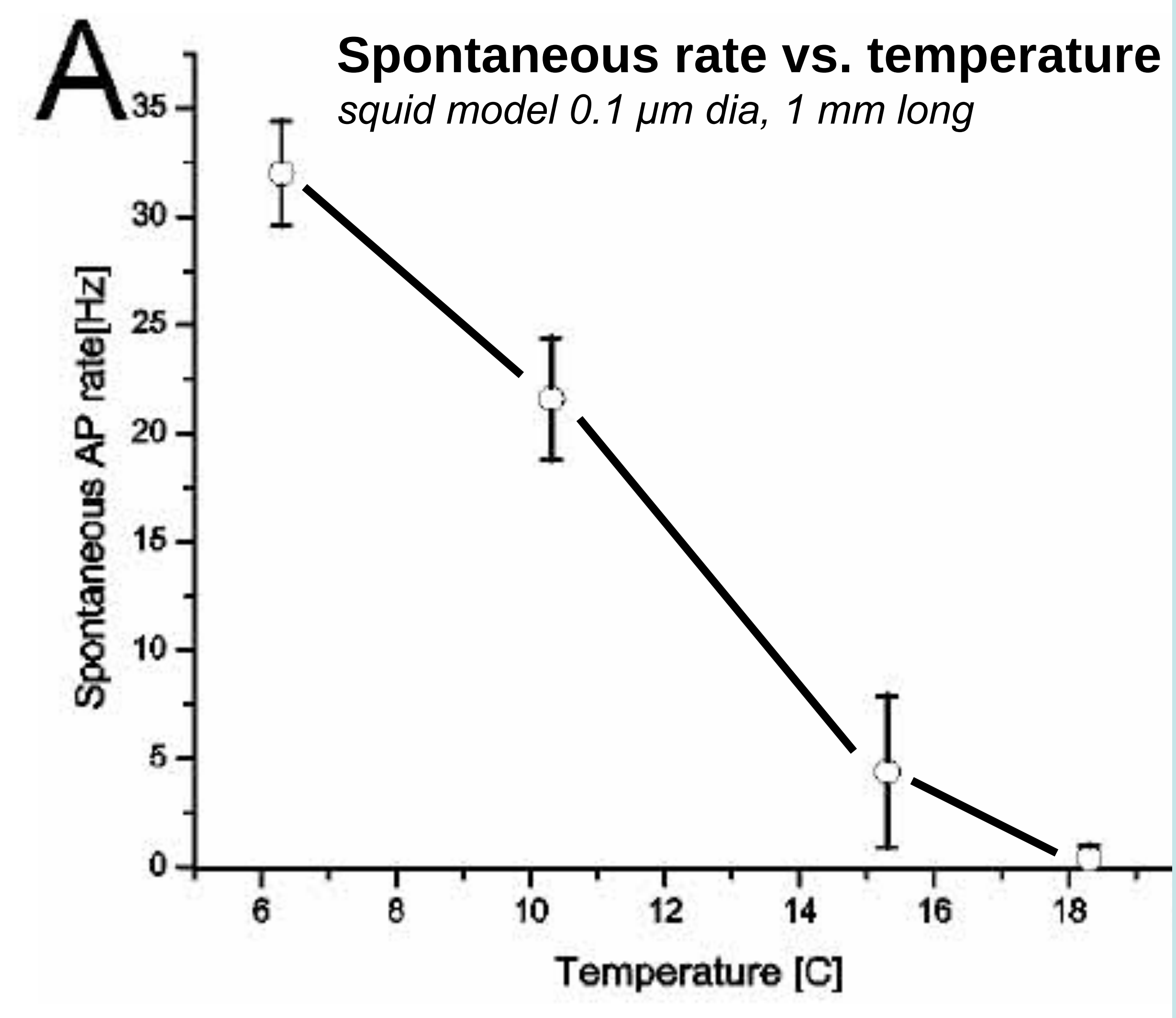


Aldo Faisal

Camm, J.-P. The chromatophore lobes and their connections in octopus. Ph D Thesis, University of Sheffield, U.K. (1986)


40 nm
Ion channel/
Ion pump
Bi-lipid
membrane
Microtubule
Motorprotein
Vesicle
60 nm
100 nm

Hot heads are more reliable



Spontaneous rate vs. temperature

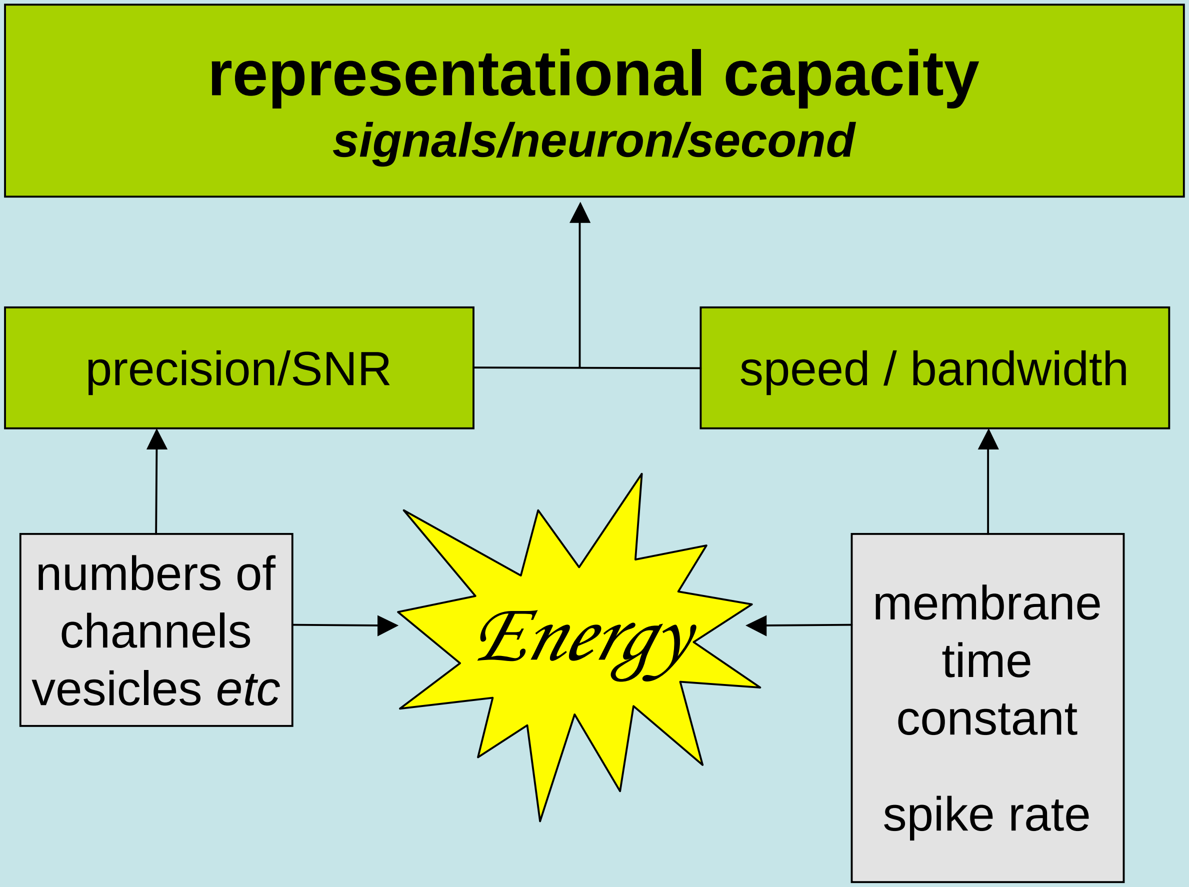
squid model 0.1 µm dia, 1 mm long

Conclusions from stochastic modelling

- Channel noise sets a lower limit to axon diameter
- Many nervous systems work down to this limit
- Cortical wiring operates close to this limit
  - to minimise costs?
- Raising body temperature eases the noise limit (also reduces conduction delays)

Energy efficient circuit design

- Pre-synaptic inhibition, sensory receptor output synapses
  - Olfactory bulb (*Nawroth et al, 2007)*
  - Insect and vertebrate photoreceptors
- Selecting components
  - How does performance scale with energy usage?



representational capacity

signals/neuron/second

precision/SNR

speed / bandwidth

numbers of channels vesicles *etc*

Energy

membrane time constant

spike rate

Noise and time constant limit representational capacity

Energy is required to ease these limits

What's the trade-off between energy and capacity?

How do energy costs vary with representational capacity?

Compare energy costs of neurons that perform the same task but have different capacities

Like comparing petrol consumption in cars with different top-speeds

John Anderson

Rob de Ruyter van Steveninck

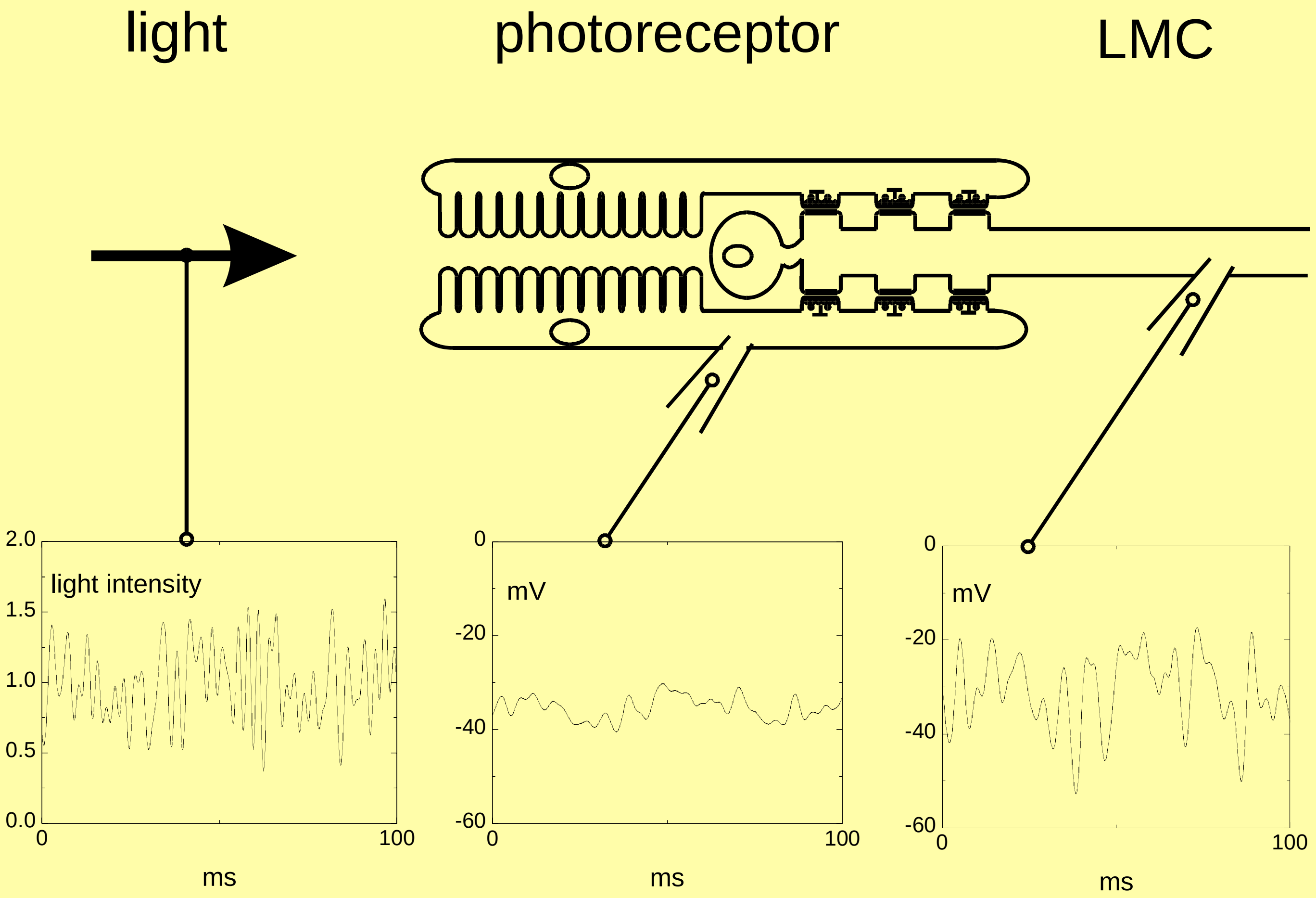
MEASURING THE RELATIONSHIP BETWEEN ENERGY AND INFORMATION IN THE BLOWFLY COMPOUND EYE

Laughlin et al, Nature Neurosci 1998

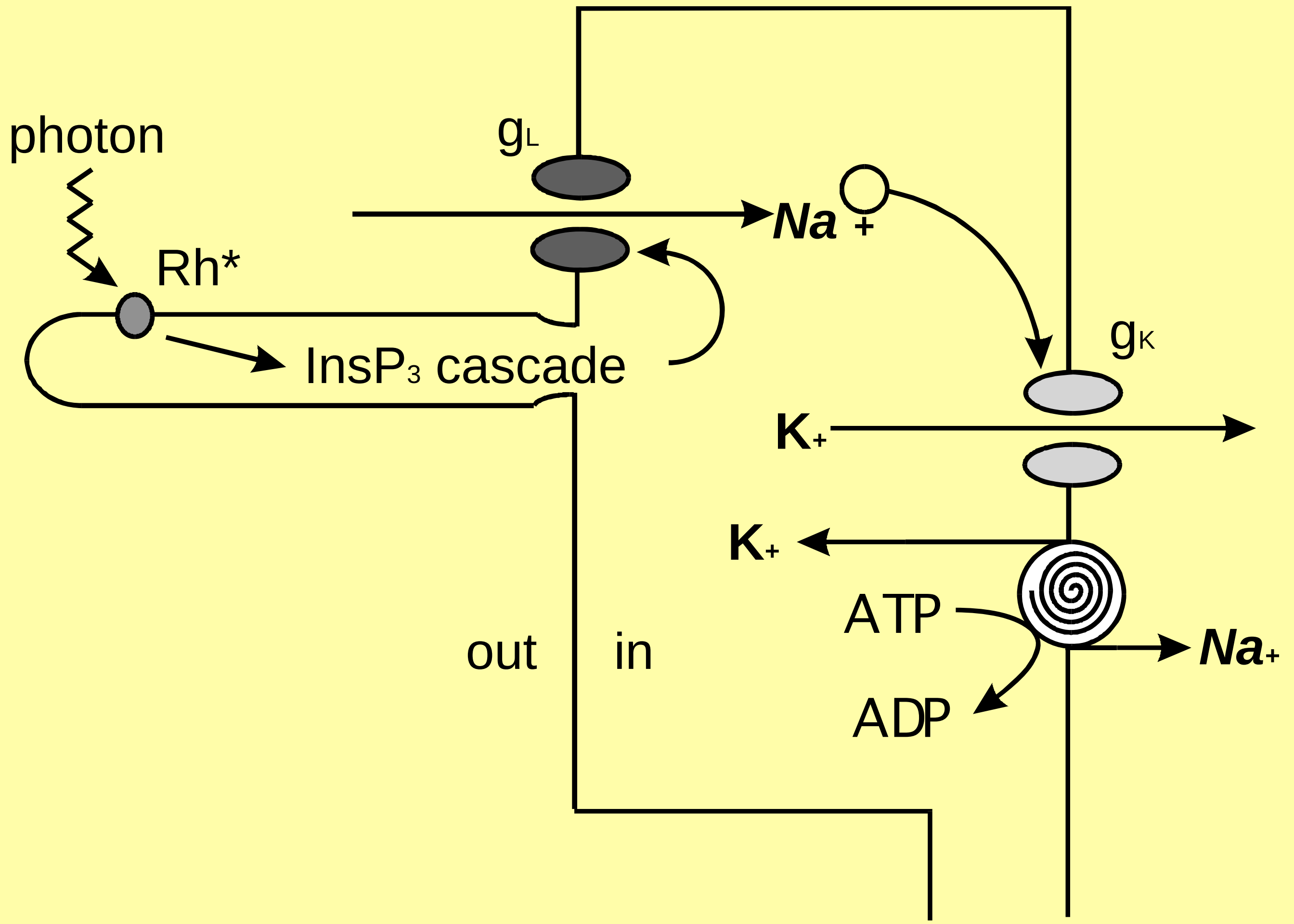
Facets are pixels

NO!

MEASURE INFORMATION

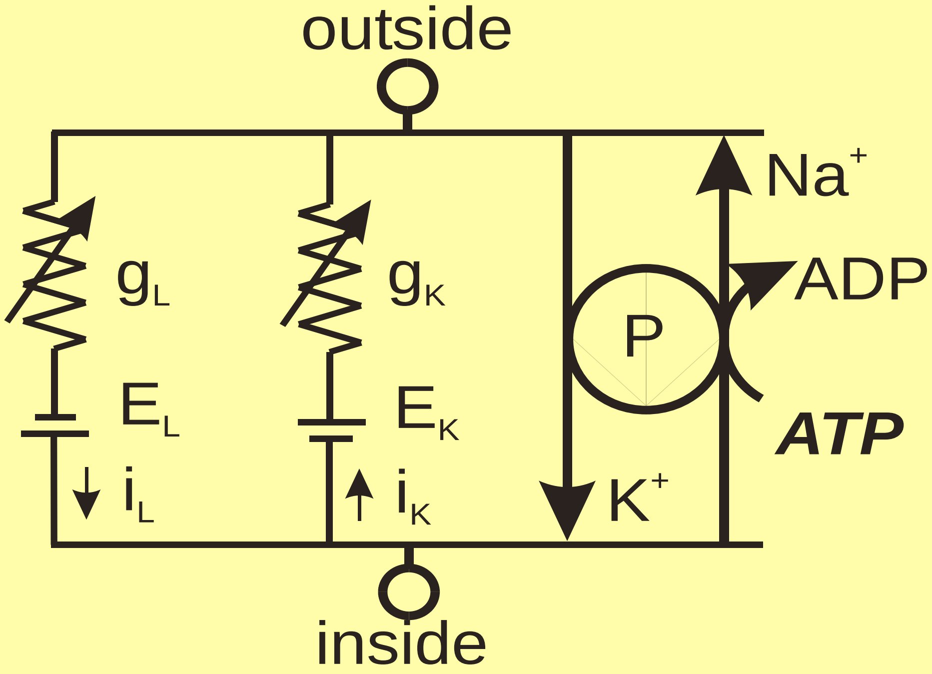


transduction uses energy



Calculate energy costs

photoreceptor



A tale of four flies

Jeremy Niven, John Anderson and Simon Laughlin

Sarcophaga carnaria

Calliphora vicina

Drosophila melanogaster

Drosophila virilis

Niven et al., PLoS Biology (2007)

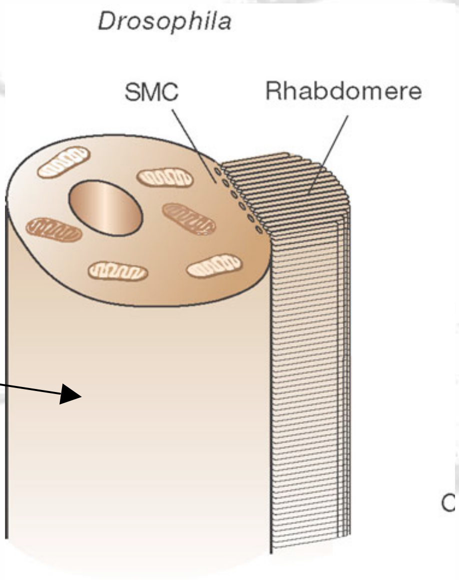
Structure of R1-6 photoreceptors

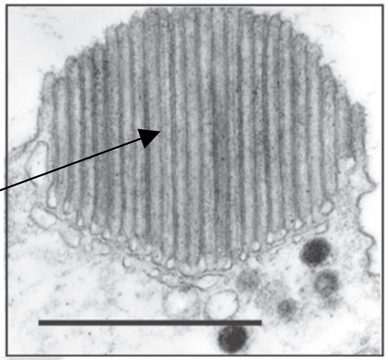
Cross-section of ommatidium

Cell Body

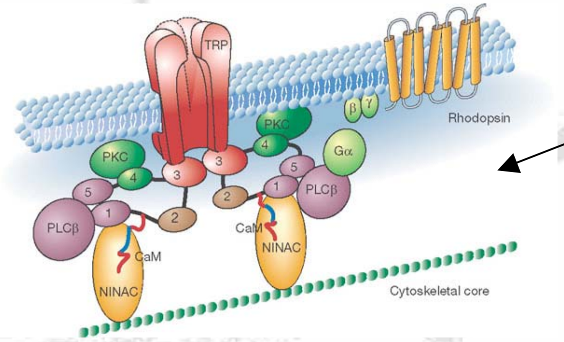
Rhabdome

Microvillus



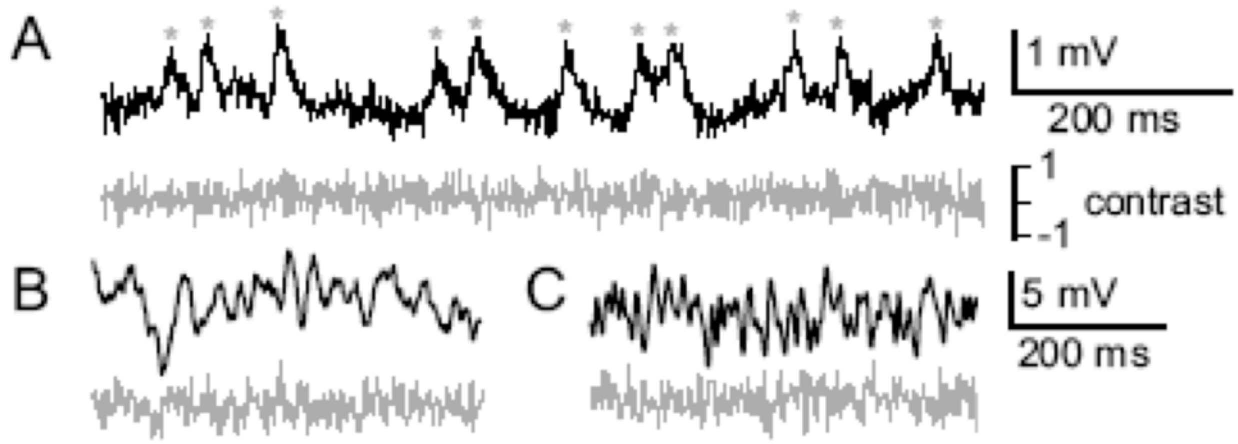


1 micron



(Hardie & Raghu, 2001)

Photoreceptor recordings



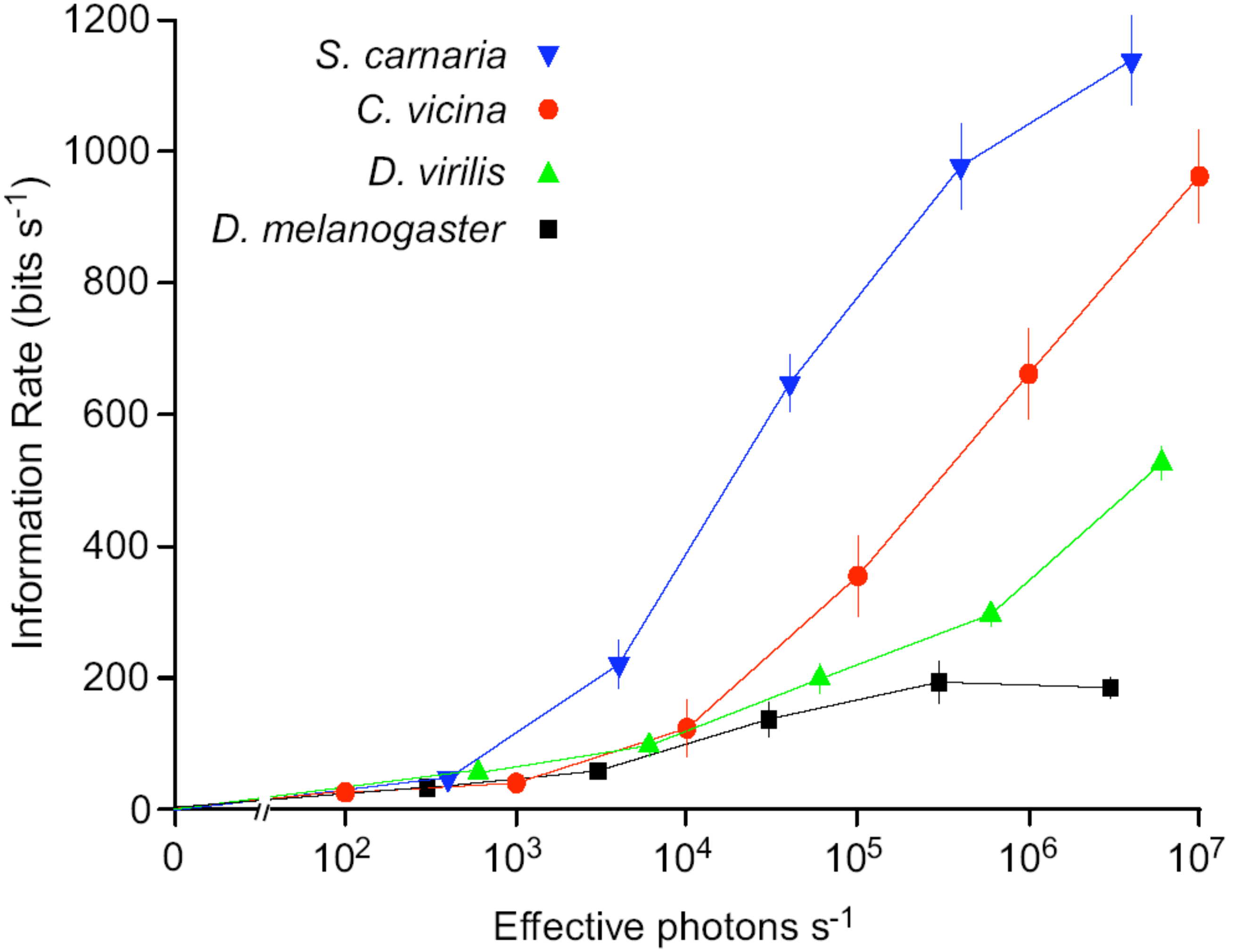
Quantum
bumps

Response to
white noise
modulation

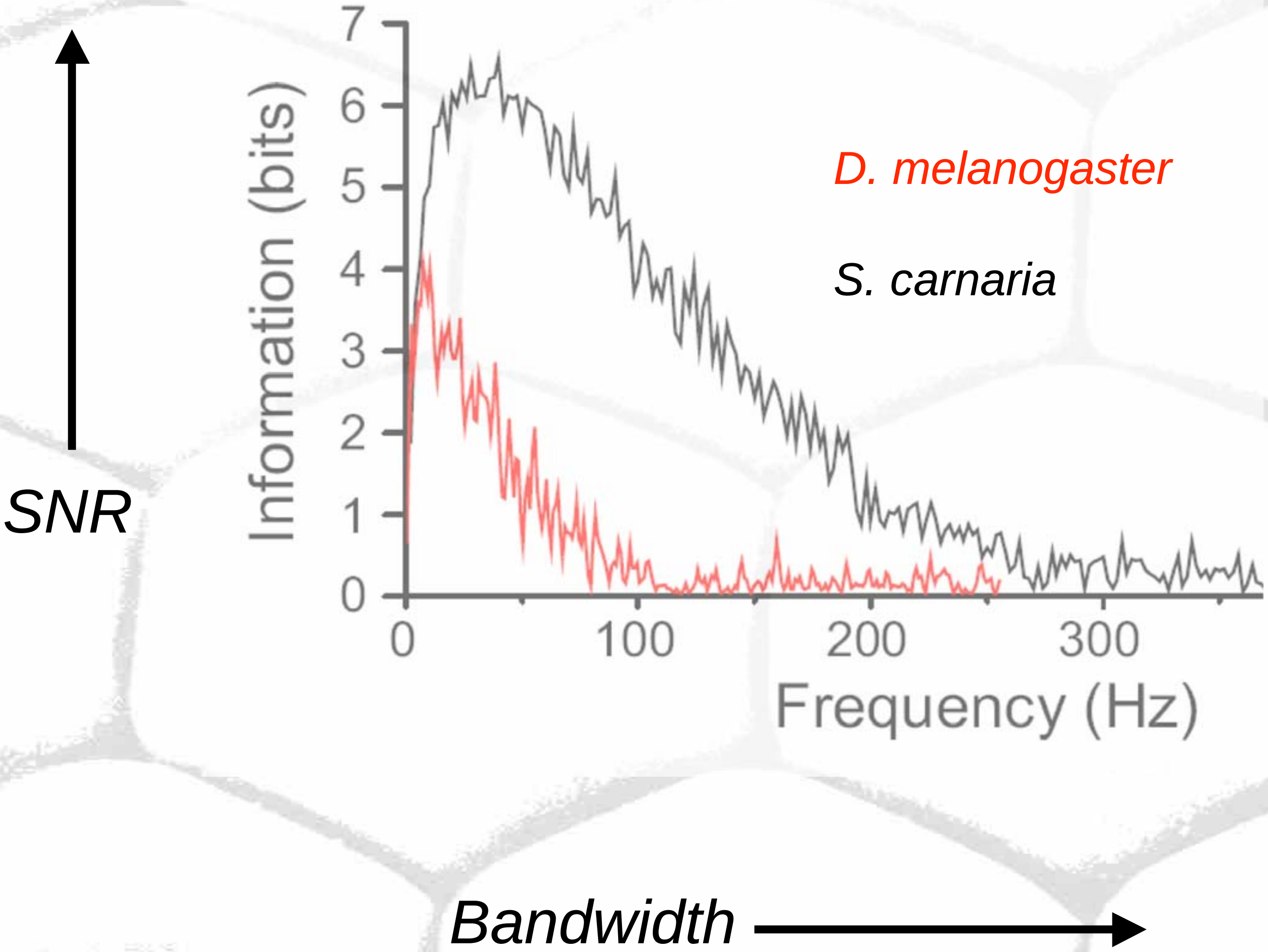
D. melanogaster *Sarcophaga carnaria*

Different levels of performance

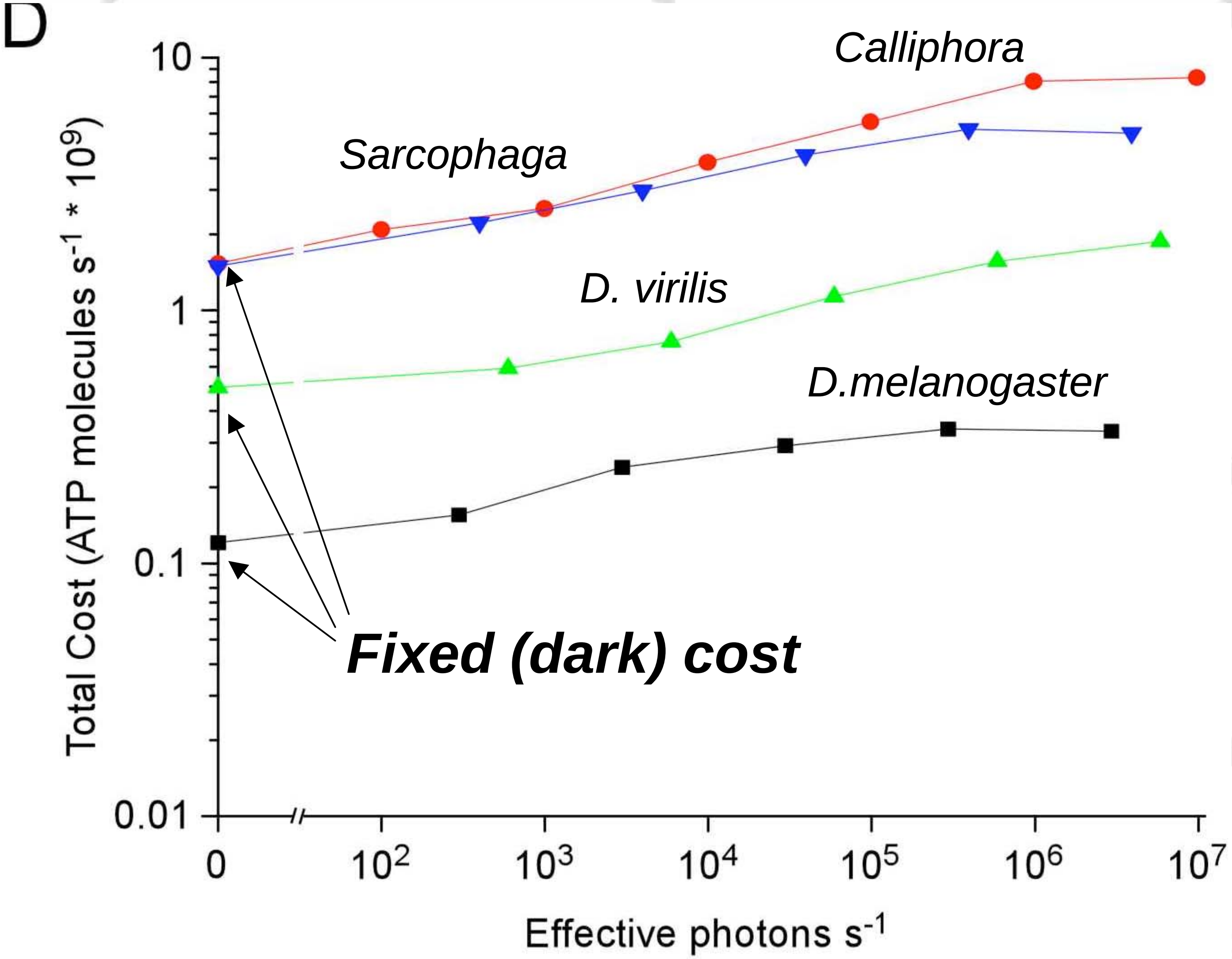
photoreceptor information rates



S. carnaria performs better than *D. melanogaster* because it has a better SNR and wider bandwidth



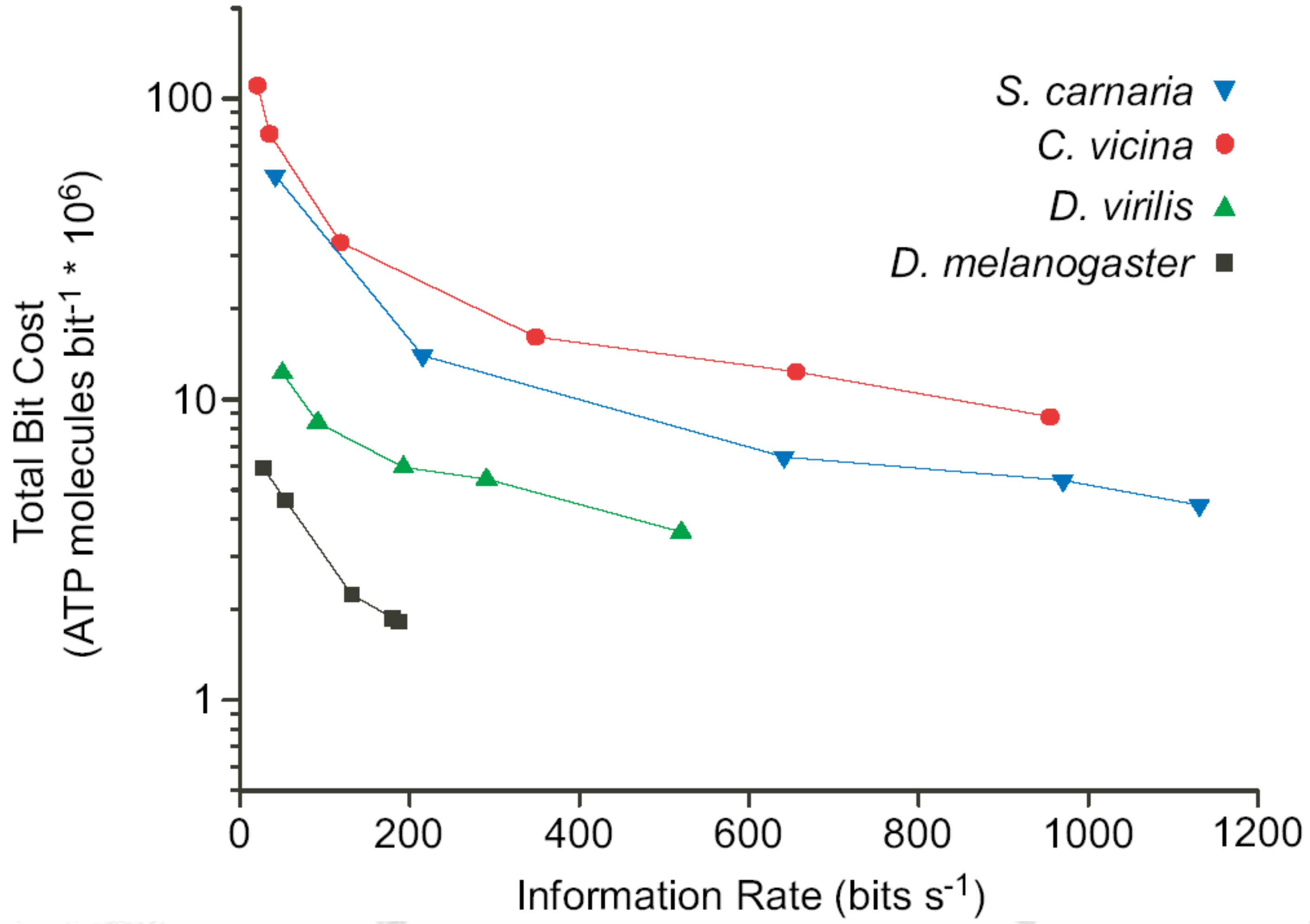
Larger, higher performance cells use more energy



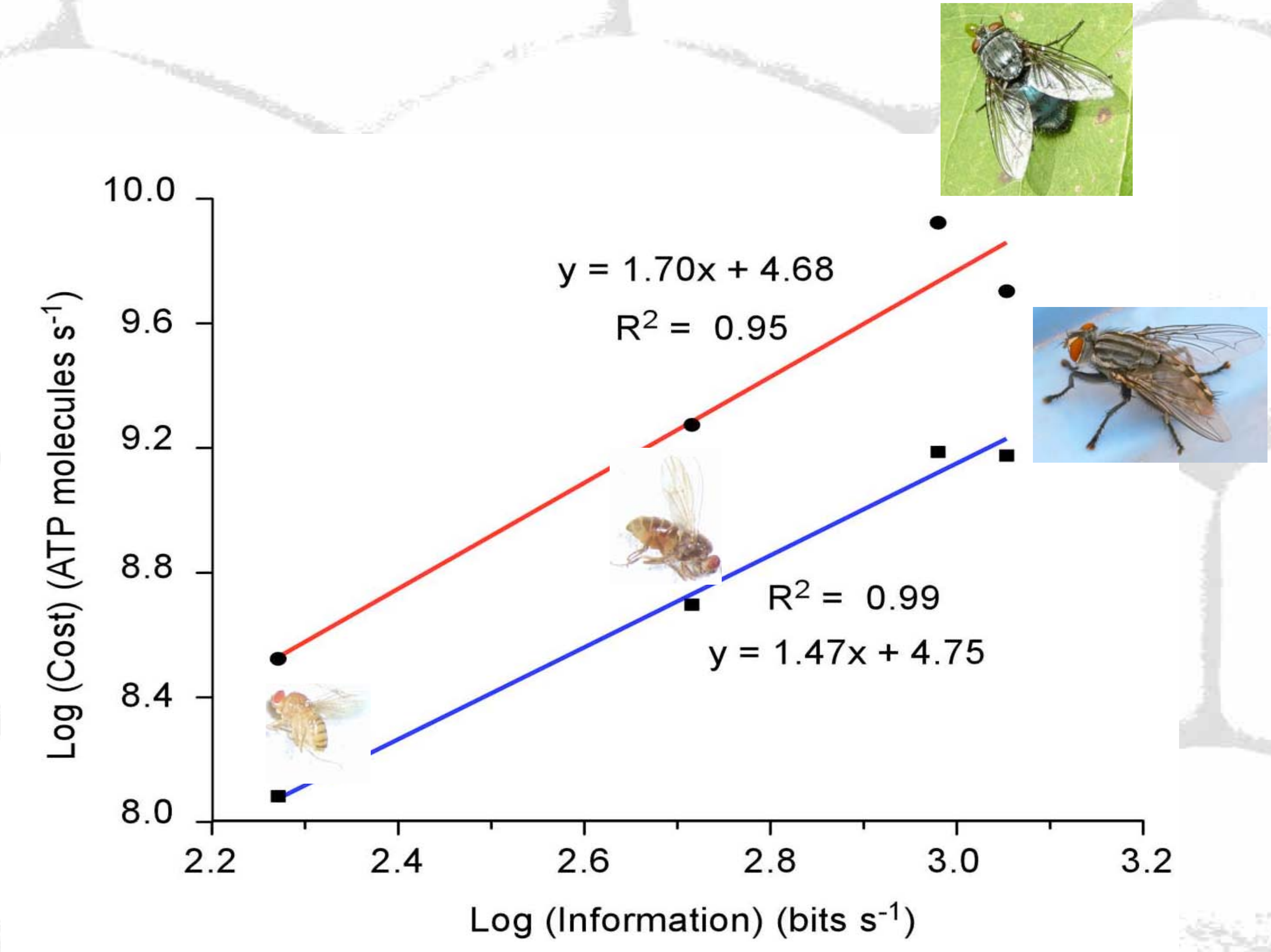
Fixed (dark) cost

Information is cheaper in lower performance cells

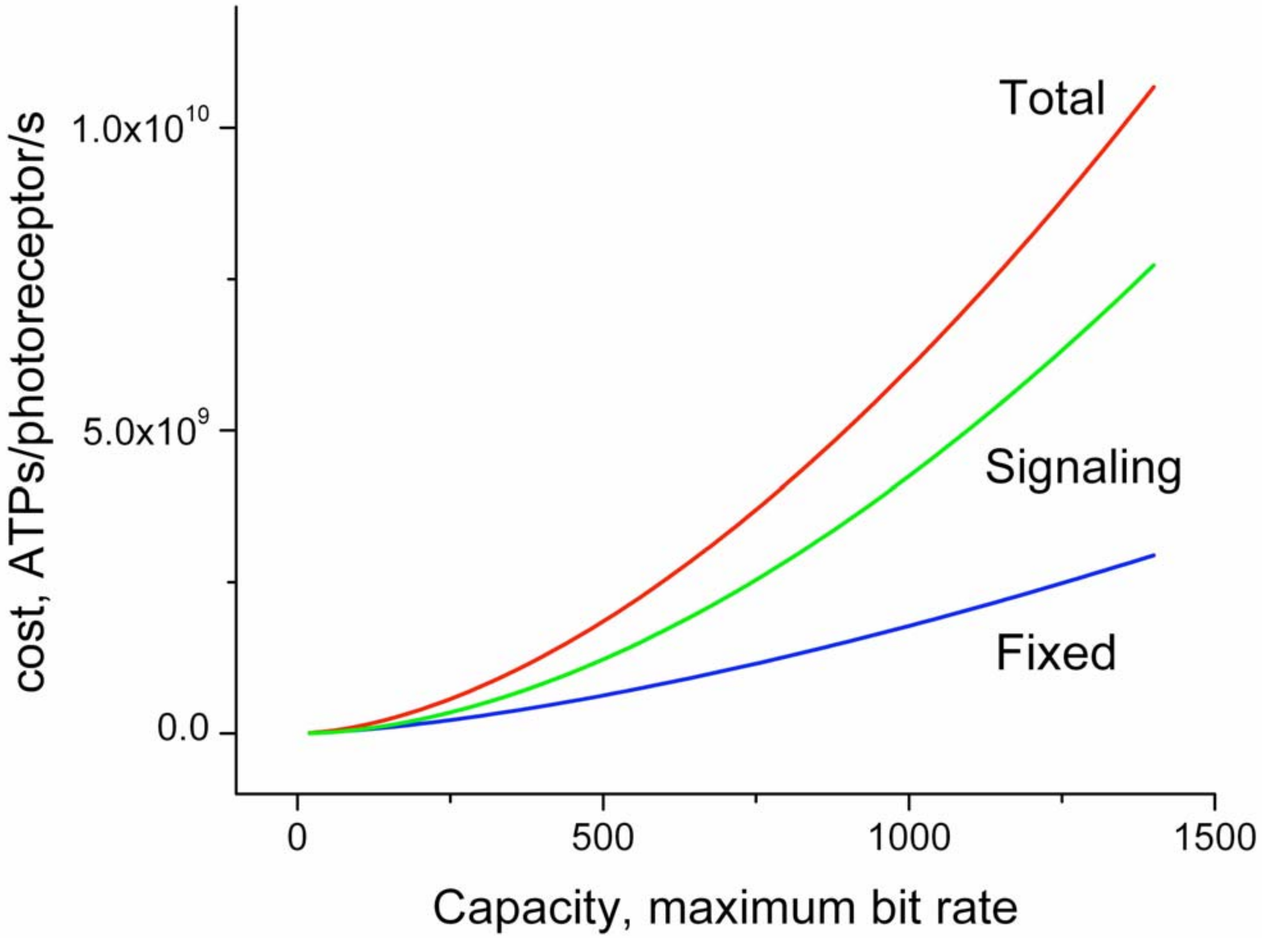
Costs per bit for R1-6 photoreceptors of 4 spp



The scaling of costs with capacity from R1-6s of 4 *spp*



The Law of Diminishing Returns



Sarcophaga R1-6

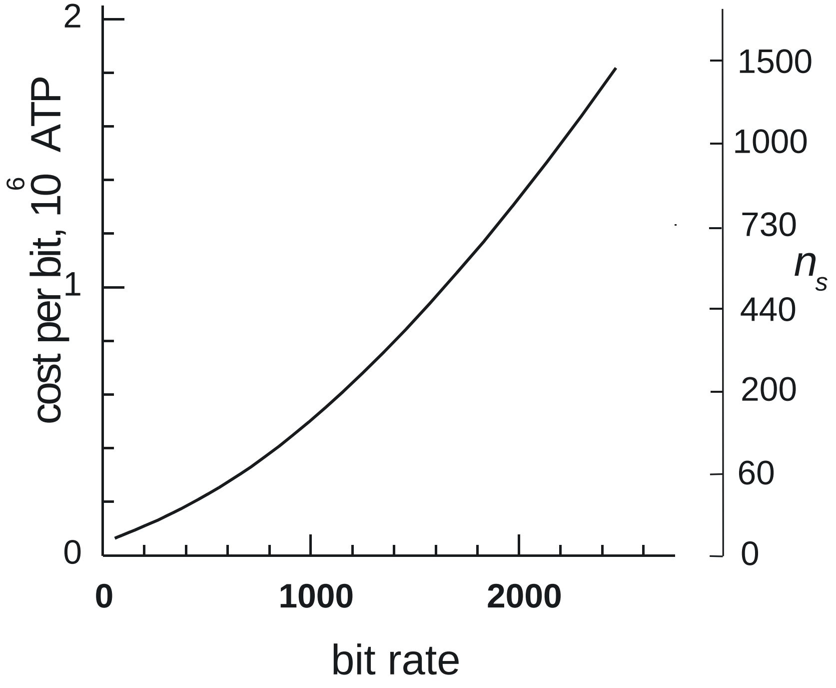
Drosophila R1-6

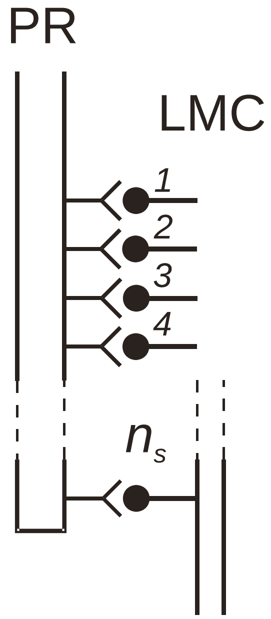
Photoreceptors are like cars

An efficient brain will minimise the use it makes of two expensive commodities

speed and precision

Cost/capacity scaling applies to synaptic events and to spikes





Bit rate and cost per bit rise with number of parallel synapses
Fly Photoreceptor-LMC synapses
(Laughlin, Anderson & de Ruyter van Steveninck, Nat Nsci 1998)

NN77 Fig. 4
Laughlin

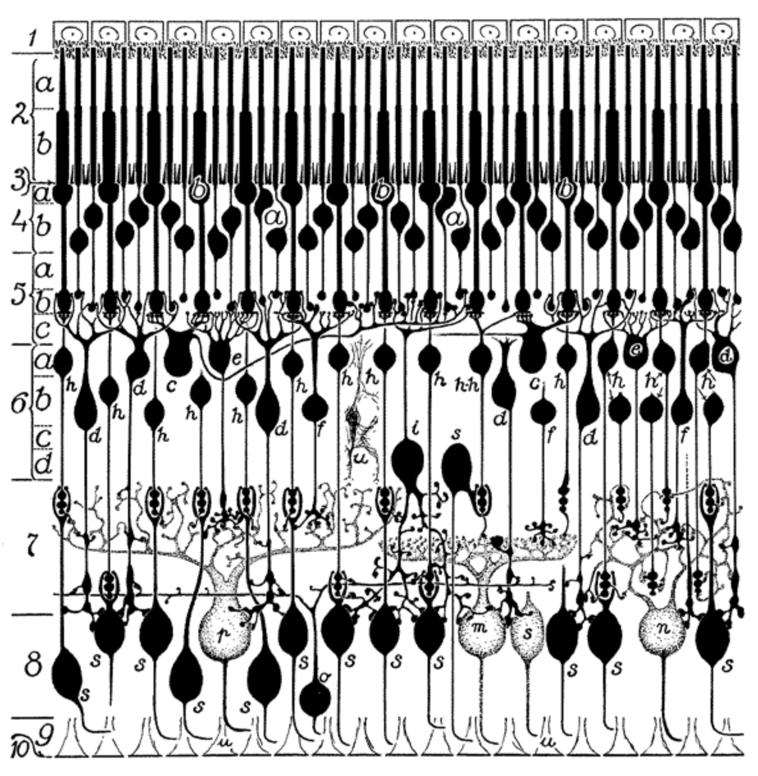
Brisk and sluggish retinal ganglion cells in guinea pig retina

Kristin Koch, Judith McLean, Ronen Segev, Michael A. Freed, Michael J. Berry II, Vijay Balasubramanian, and Peter Sterling Curr Biol 2006

850,000 bits/s along optic nerve

64% by sluggish cells (W)

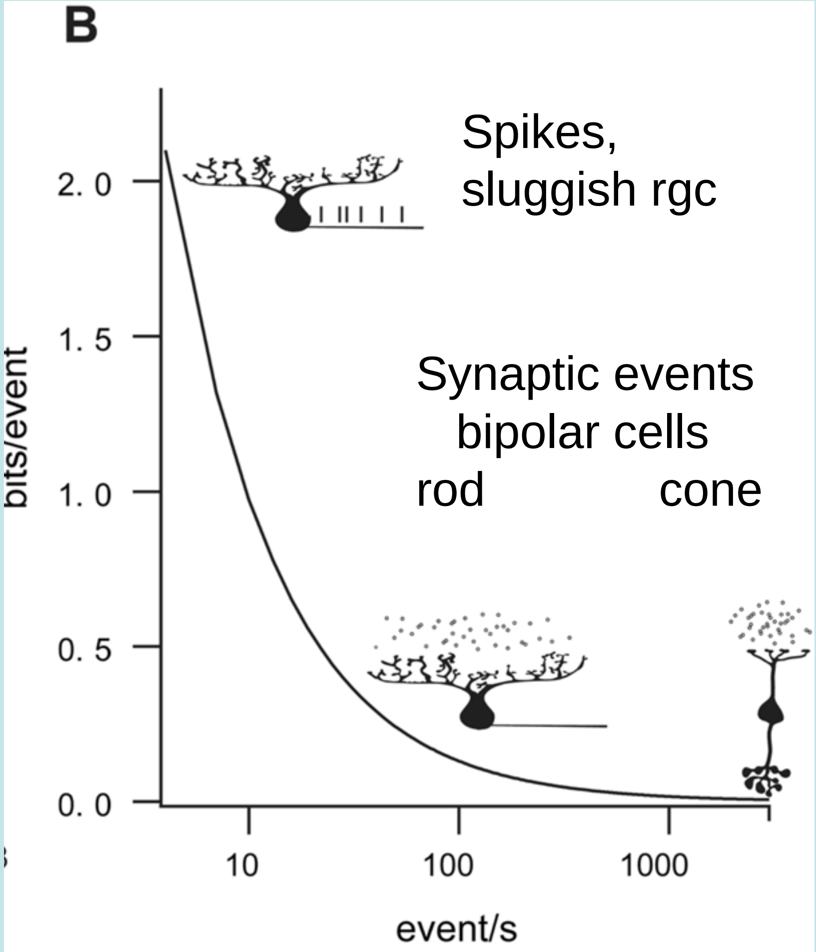
36% by brisk cells (X,Y,P,M/M,P)



Sluggish cells	3 bits/spike	20 bits/s
Brisk cells	1 bit/spike	40 bits/s

Bits/event vs event rate mammalian retina

Sterling and Freed Vis Neurosci 2007



Spikes,
sluggish rgc

Synaptic events
bipolar cells
rod cone

Design Principle

Reduce capacity to improve efficiency

- Fly photoreceptors
- Bipolar cells and ganglion cells in mammalian retina
  - *More examples?*

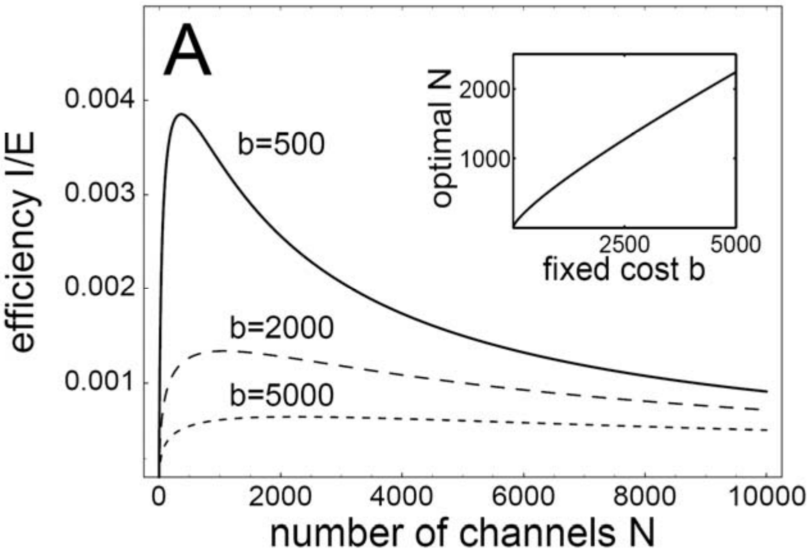
Design Principle

- Match capacities
  - Low drives low, high drives high
  - An added bonus for coding in parallel pathways?

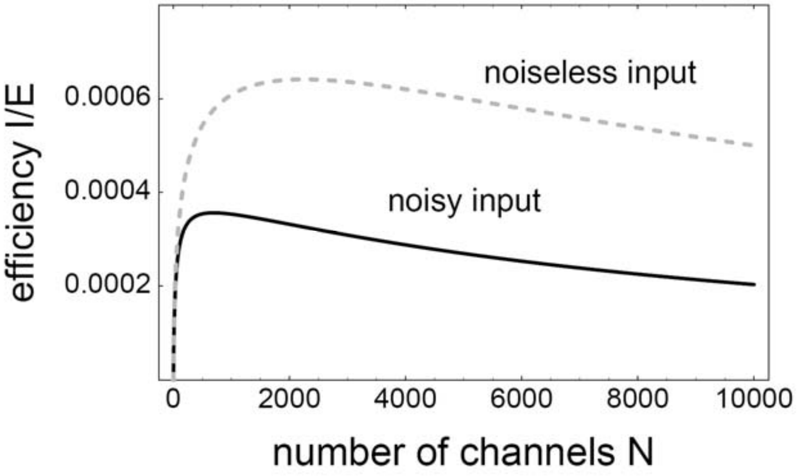
Matching works in theory

Optimum number of stochastic channels (events) depends on

fixed cost



input SNR

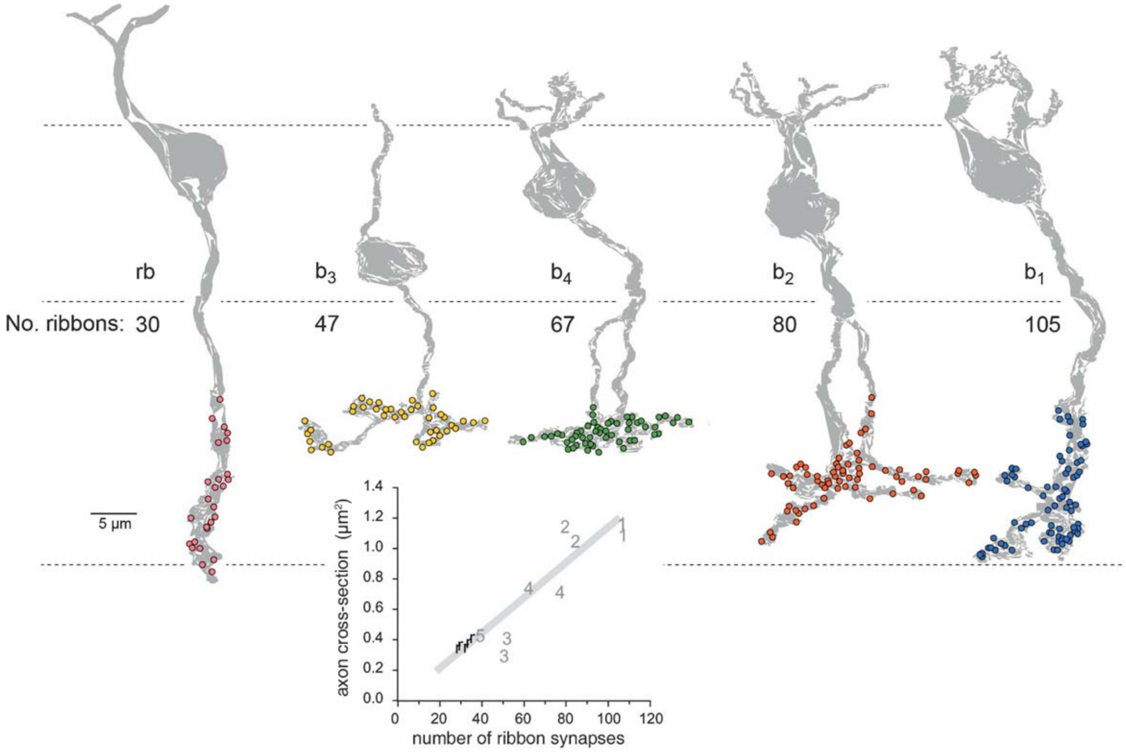


Schreiber, Machens, Herz & Laughlin, Neural Comput 2002

In practice, do circuits match?

Output synaptic ribbons in different classes of cat bipolar cell
Sterling and Freed, 2007 *How robust is a neural circuit?*

to rod rgc   to sluggish   to brisk



Versatility adaptability and efficiency

- Connecting levels
- Reaching around to tweak the design
- Helps make brains energy efficient

IBM Blue Gene/L 478 teraflops = 5.10^{14} flops s^{-1} ***>6 MW***

Dan the (IBM) Man, 10^{15} sops s^{-1} (neocortex alone) ***12 W***