Scale:
Biology

Two kinds of theories/points of view:

Mechanistic (underlying physical laws)

Teleological (design principles)

cf: Tinbergen’s program: A trait must be understood from four perspectives:

Mechanistic
Developmental
Evolutionary
Functional (i.e from a design perspective)

Scale in physics:

(1) Overarching laws: i.e. those that transcend scale:
Conservation laws (e.g. mass-energy is conserved)
Symmetry principles (e.g. translational symmetry in space-time)

(2) Renormalisation “group” flow:

Effective Hamiltonian with scale dependent parameters: H[g(L)]

a) Scale hiding: microscopic details hidden at macroscopic scales;
b) Scale invariance: system looks the same at different scales.
c) On the whole: fairly homogeneous (sometimes with anomalous scaling).

Scale in Biology:

Heterarchy of scales: structure looks different at different scales (at least superficially).
[Molecules – cells – organisms – ecosystems]

How to tie the scales together?

The naïve reductionist program (e.g. derive everything from one microscopic theory) seems to be doomed to fundamental intractability. There is too much heterogeniety and too many orders of magnitude.

Are there laws that span scales?

Idea:

There are principles in biology that span scales;
These would be the analogs of conservation laws/ symmetry principles.

These are design laws that are not domain or scale specific. Examples may be chosen from controls, including distributed controls/game theory, communication theory, computation.

(The laundry list approach)
Choose those principles that are applicable to biological systems at different scales. Conjecture: there is a relatively short list, or the 80-20 rule.

Caveat: reject the philosopher's stone approach, the TOI principle.

Example:

Function: asymptotic tracking (or perfect adaptation)

Design rule: Integral feedback.

Cellular scale example: Bacterial chemotaxis.

Neural system scale example: Vestibular-Ocular reflex.

A different perspective about scale in biology

"self organisation" from a microscopic rule:

Random point mutations + selection = phylogenetic diversity

Local learning rule in neural network + experience = brain ("tabula rasa learning")

(no interesting set of general design principles beyond that stated above)

… don't think this is the case …

Metabolic Cost of Readiness

PPM

Rahul Sarpeshkar (MIT)
John Doyle (Caltech)

"There is in electrical engineering a split which is known in Germany as the split between the technique of strong current and the technique of weak currents, and which we now know as the distinction between power and communication engineering. … Actually, communication engineering can deal with currents of any size whatever … what distinguishes it from power Engineering is that its main interest is not economy of energy but the accurate reproduction of a signal."

Norbert Wiener: Cybernetics, Ch.2 (Newtonian and Bergsonian Time).

… but as any laptop or cellphone user, or biological organism knows, metabolic resources are scarce: can one really divorce energy resources from communications/control? (No …)

Salient observation (Laughlin et al):

Brain tissue is metabolically expensive
(~10x other tissue)

e.g. in humans brains:
Fraction of basal metabolic rate ~ 20%
Fraction of body weight ~ 2%

Caveat: Muscle metabolic rate rises to these levels when running fast; dynamic range of muscle metabolic rate ~10 times brain. Brain fraction of total metabolic load is small when running.

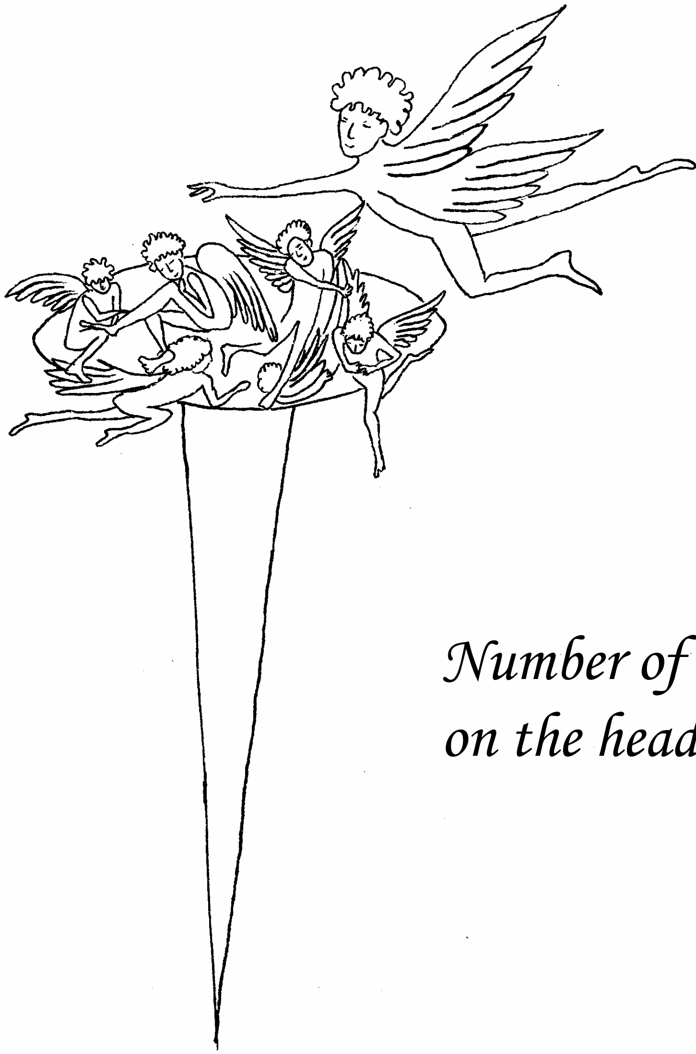
A prevalent explanation:

“information is metabolically costly”

Laughlin, SB, de Ruyter van Steveninck, RR & Anderson, JC (1998)
The **metabolic cost** of neural **information**, Nature Neuroscience 1: 36 - 41

Argument: require large number of ATP/bit.

$$\#bits / ATP = \frac{\#bits / spike}{\# ATP / spike}$$



$$\text{Number of angels on the head of a pin} = \frac{\text{Number of angels}}{\text{Number of pins}}$$

Right explanation

Wrong explanation

Nonsense (conceptually ill-formed)
(e.g.: The country to the East of the North Pole)

Associating a certain #(bits) with each spike in the brain sounds nice, but is conceptually ill formed …

Many problems:

- Longer axons will consume more power. However, this has nothing to do with sending more information. (cf: long haul optical fiber transmission: amplifiers extend system length, so that Dissipation ~ Reach; But capacity i.e. #bits/pulse, does not scale up with dissipation)

- Even in the sensory periphery, where one might expect communication capacity to be a sensible concept, there are problems (cf: Toby Berger). Channel coding does not apply: as opposed to communication systems (given channel, choose code) – given inputs, optimise channel. Channel capacity in usual sense is meaningless.
- It is nonsensical to speak of pacemaker cells in pattern generators or regularly firing cells as carrying "bits/spike". Cf: cardiac neurons.

We offer an alternative point of view:

“the ability to respond rapidly is metabolically costly”

For an active system, keeping accuracy fixed,

$$\text{Metabolic cost} \sim (\text{latency})^{-1}$$

Underlying agenda:

Engineering perspective is critical; however,
the “laundry list” of relevant engineering subjects need to be reordered

Emphasise the role of feedback control theory
in brain function

De-emphasise communications/information theory

[Motor vs sensory, in some sense …]

Cell phone example

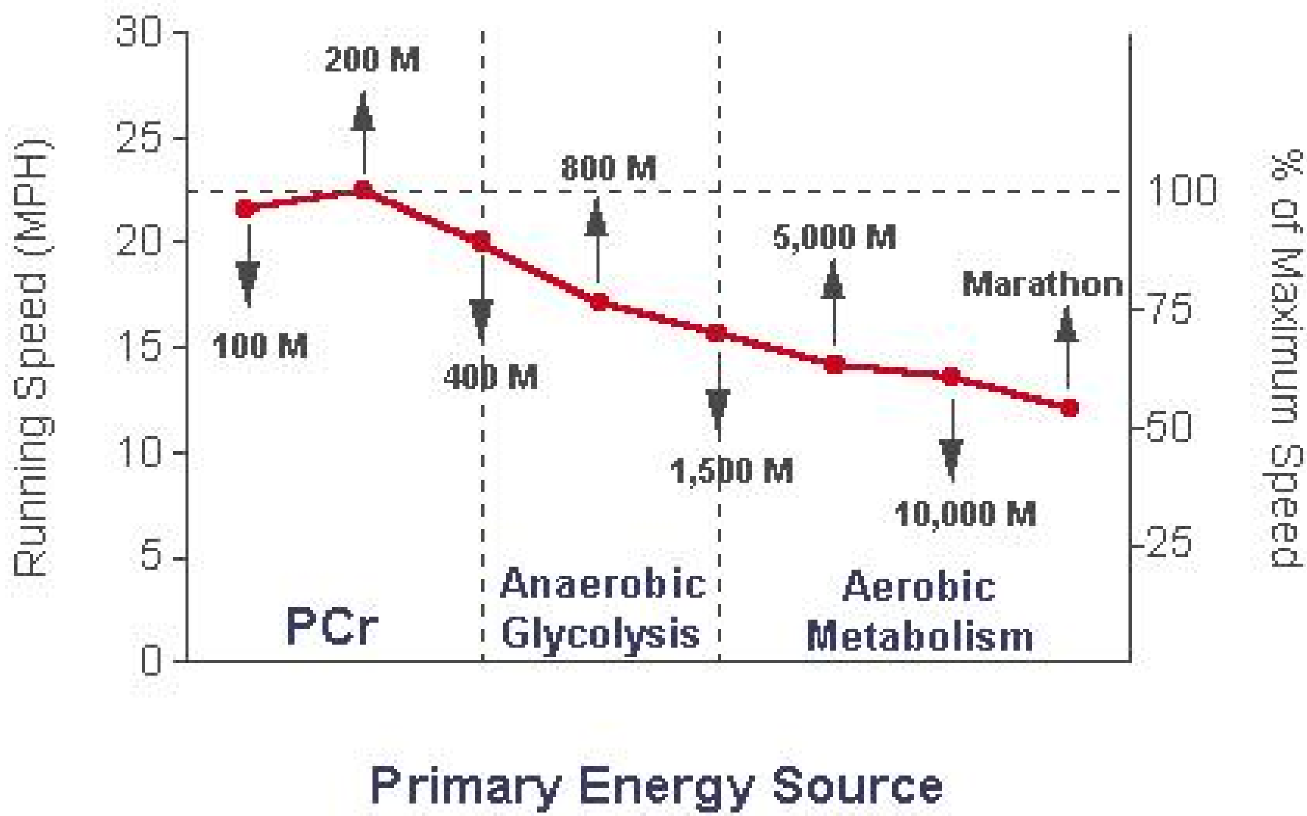
- Static power dissipation – waiting for calls
- Two hypothetical scenarios for getting messages:
- High dissipation, low latency
- Low dissipation, high latency

Car example

- Dissipation latency tradeoffs: for fixed cruising speed, static power dissipation goes up with ability to accelarate (hence the inefficiency of sports cars)
- How hybrid cars ameliorate the problem using two technologies (brain analogy?)

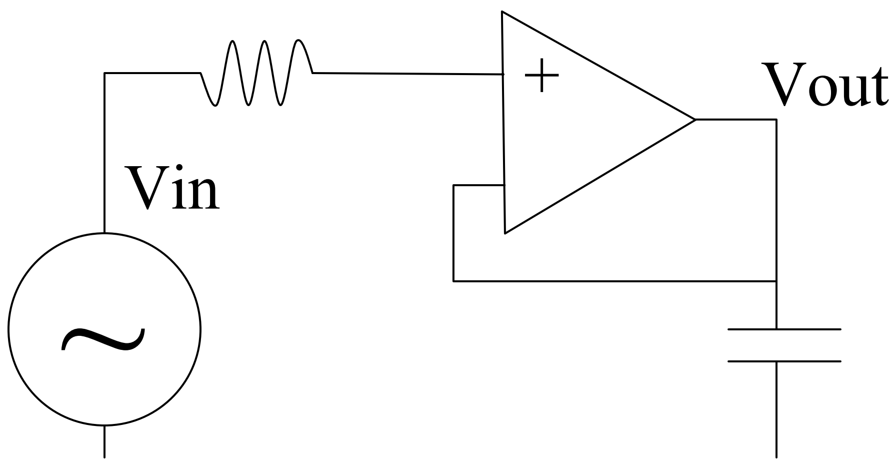
Athletics example

Aerobic metabolism: slow; efficient.
Anaerobic metabolism: fast, inefficient.
Dissipation/latency tradeoff …



Active Voltage buffer

Common in preamplifier circuits;
building block circuit in consumer electronics.

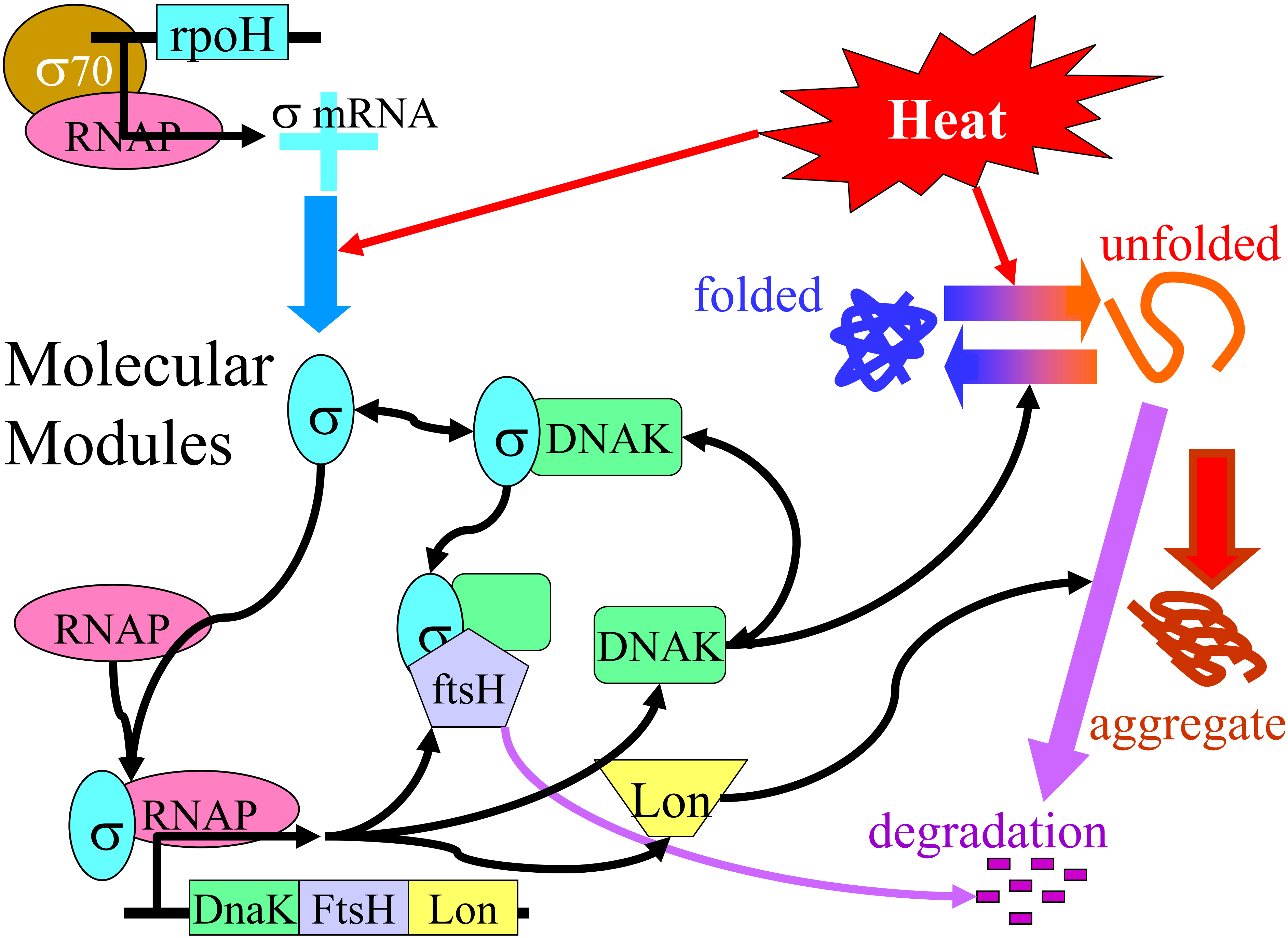


$$\tau = \frac{C}{G_m} \propto \frac{1}{P}$$

Latency between Vin and Vout is given by τ, the time constant of the buffer; this scales with the output impedance. This leads to an inverse dependence on the power dissipated in the amplifier.

Heat shock example (John Doyle):

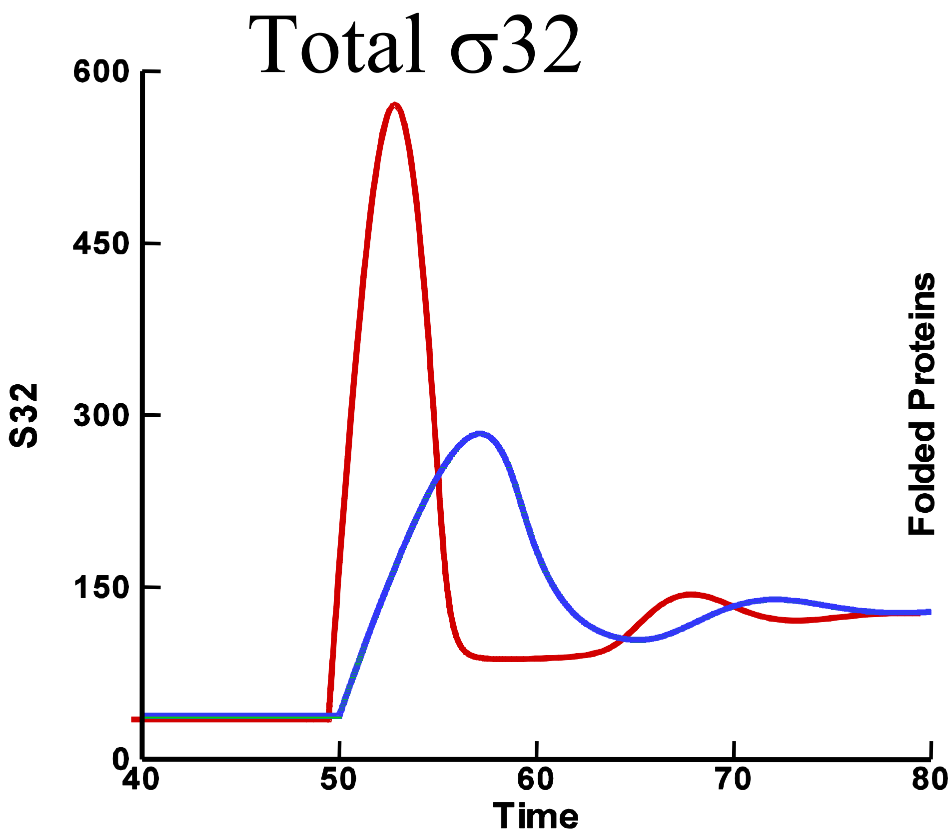
[contains “futile cycle”]

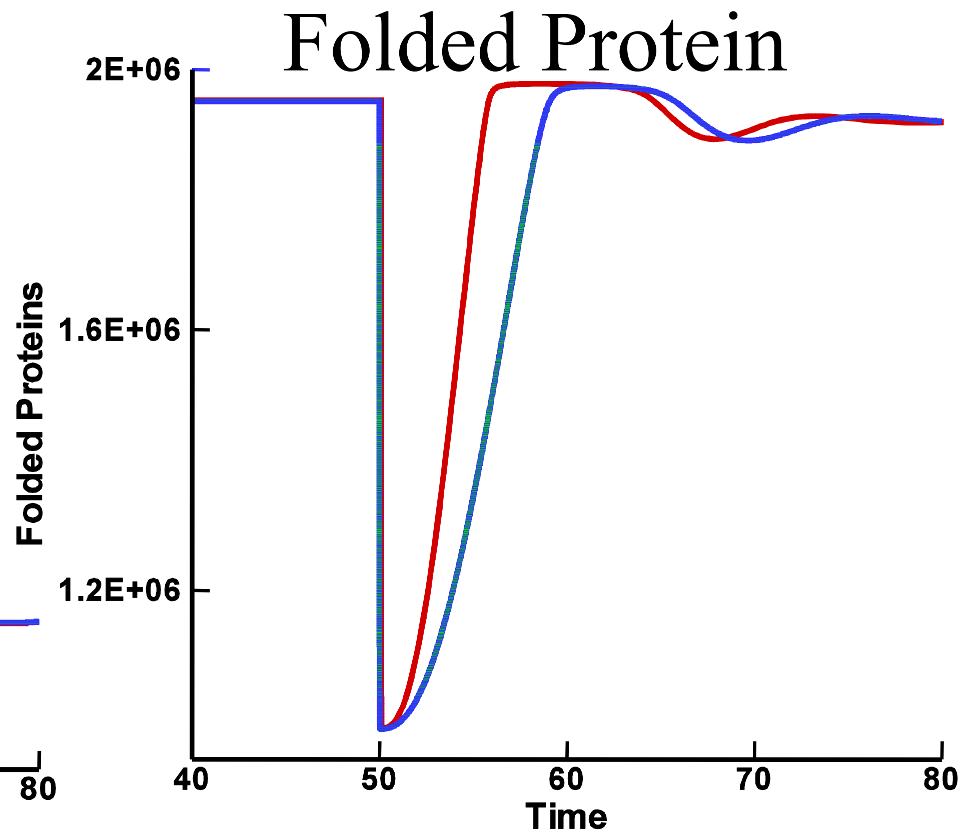


rpoH
σ70
RNAP
σ mRNA
Heat
unfolded
folded
Molecular
Modules
σ
σ
DNAK
RNAP
σ
ftsH
DNAK
aggregate
σ
RNAP
Lon
degradation
DnaK
FtsH
Lon

Wild type

Without "amplifier"





Heuristics: push-pull mechanism

Response rate: $$\frac{dx}{dt} = K(\text{"}create\text{"} - \text{"}destroy\text{"})$$

Dissipation rate: $$\frac{dP}{dt} \propto K(\text{"}create\text{"} + \text{"}destroy\text{"})$$

K ↑

Response rate ↑

Dissipation rate ↑

Disambiguating Bandwidth from Latency:

Gaussian channel example

$y(t) = x(t) + n(t)$

$C = B \log(1 + S/N)$

Add latency: $x(t) \rightarrow x(t-\tau)$

$y(t) = x(t-\tau) + n(t)$

$X(f) \rightarrow X(f)e^{2i\pi\tau}$

$S' = E[|X(f)|^2] = S$

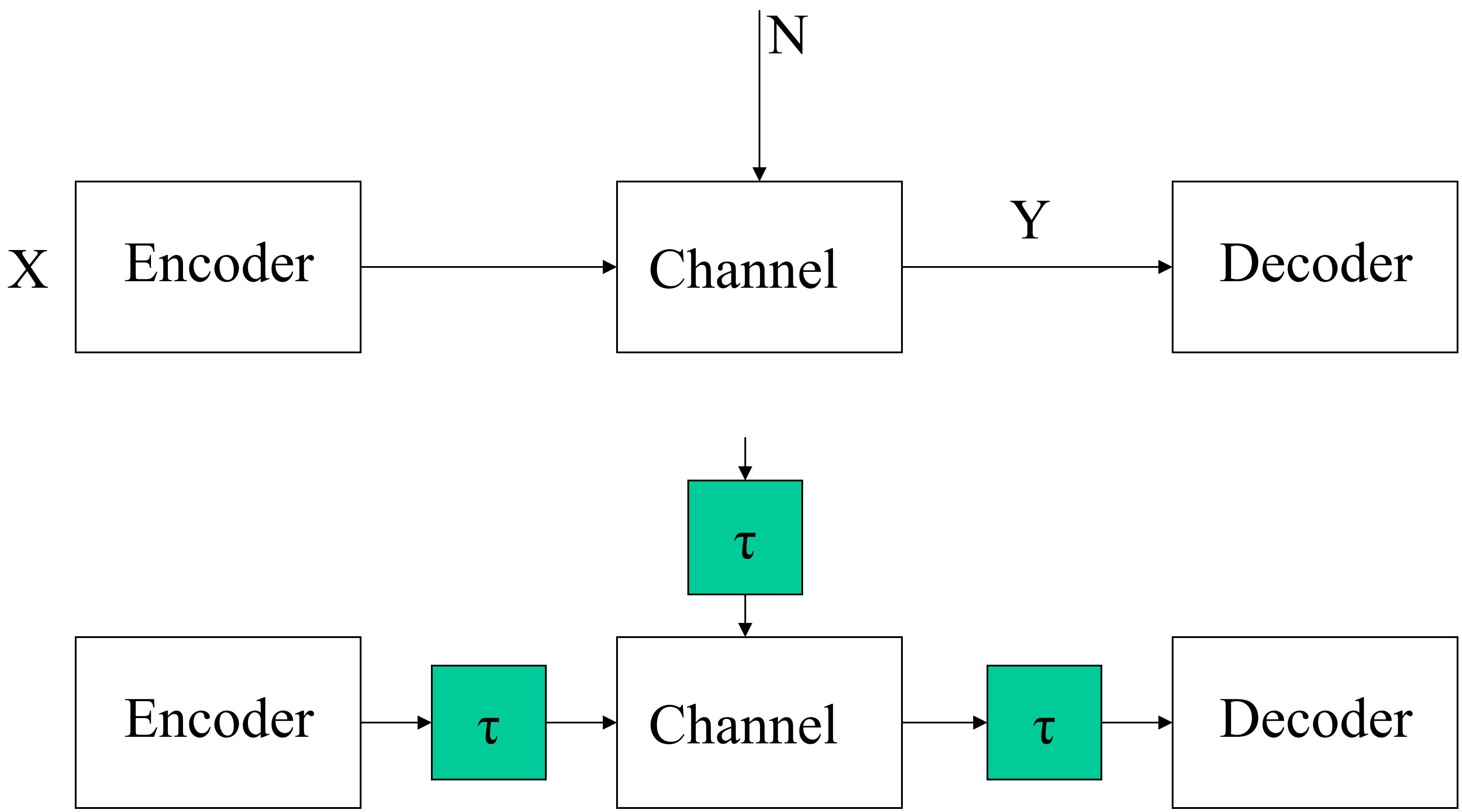
$C' = C$

Adding a latency does not change the channel capacity …

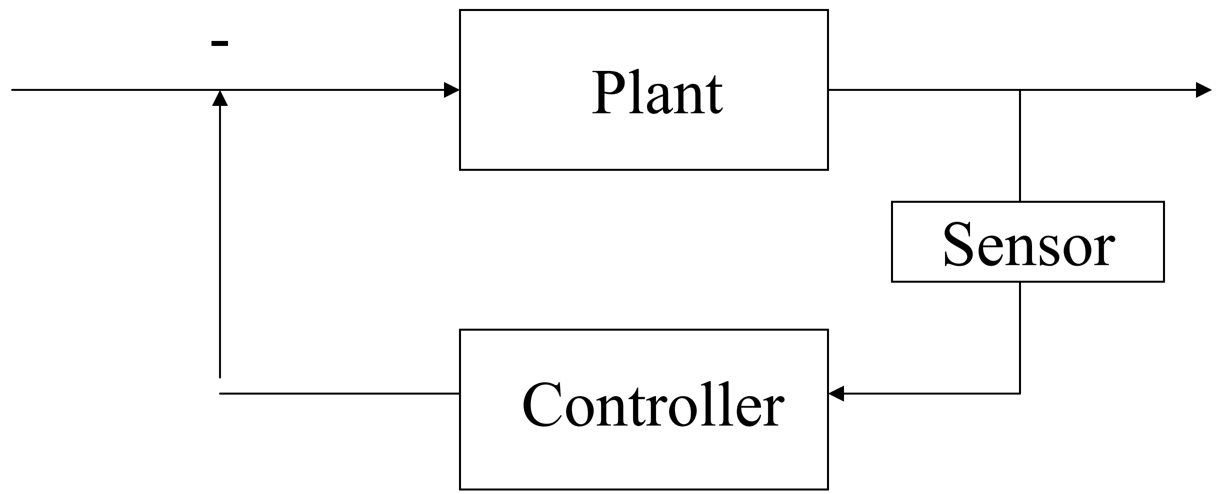
Axon potential speed

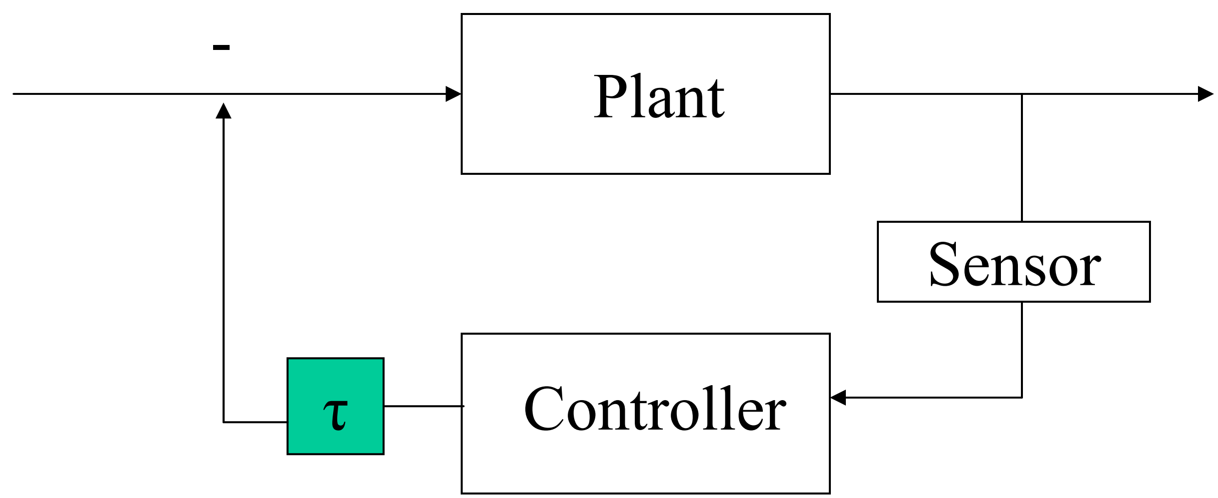
- Speed and bandwidth can be manipulated separately and hence disambiguated:
- Speed goes up on increasing Na channel density per unit length (with higher metabolic cost); bandwidth depends on the inactivation (through the refractory period), and hence remains the same.

Latency has no role in a simple communication channel,
but has a fundamental role in the simplest feedback controller …

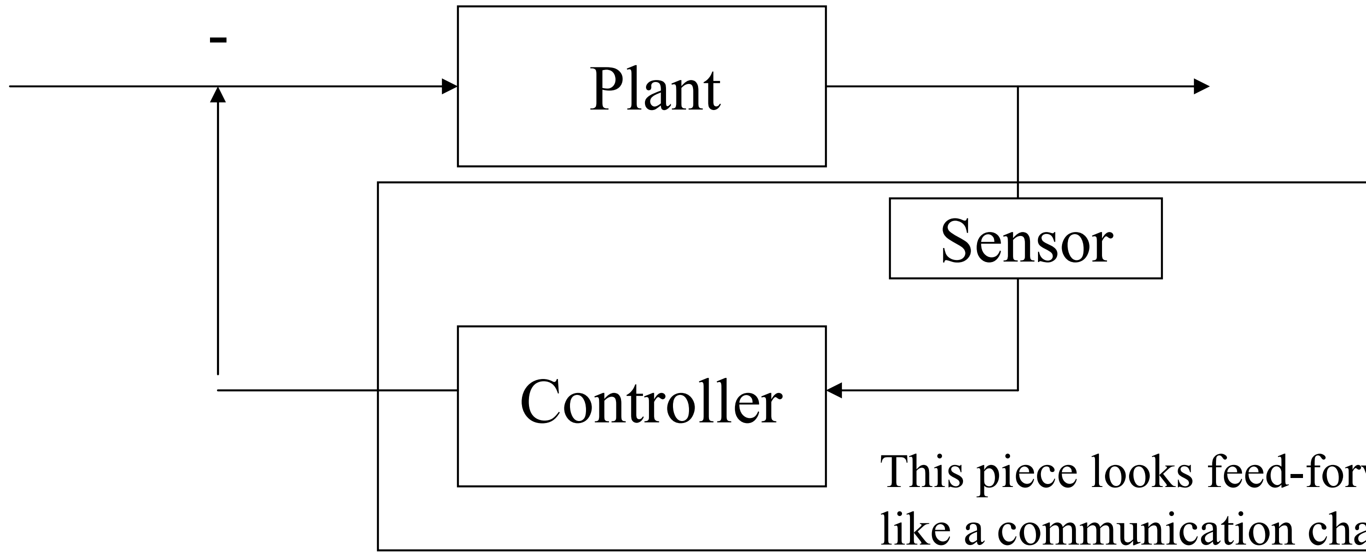


Channel capacities independent of the latencies

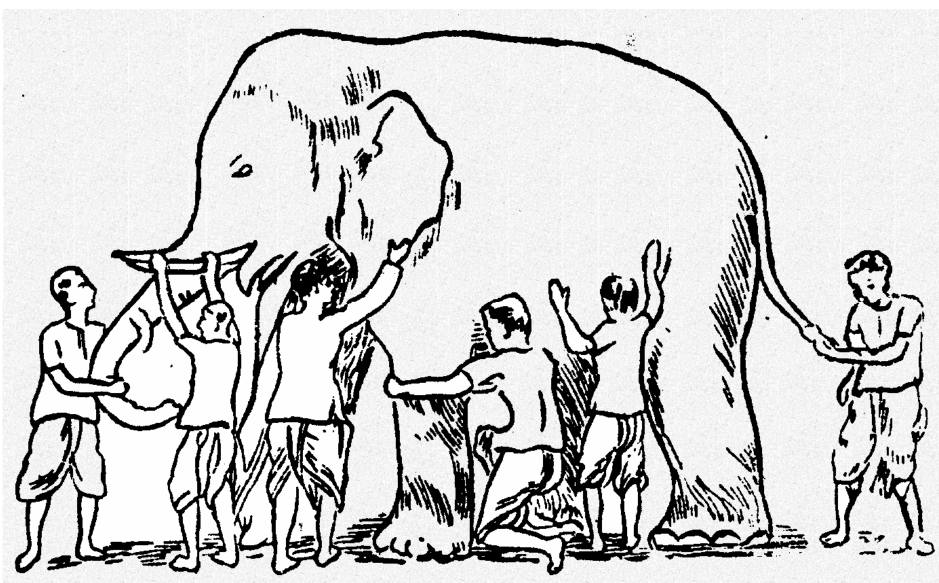




Inserting a latency into the controller can fundamentally alter the operation – for example, can cause a stable loop to oscillate.



This piece looks feed-forward
like a communication channel –
Hence focus on information theory
in sensory neuroscience

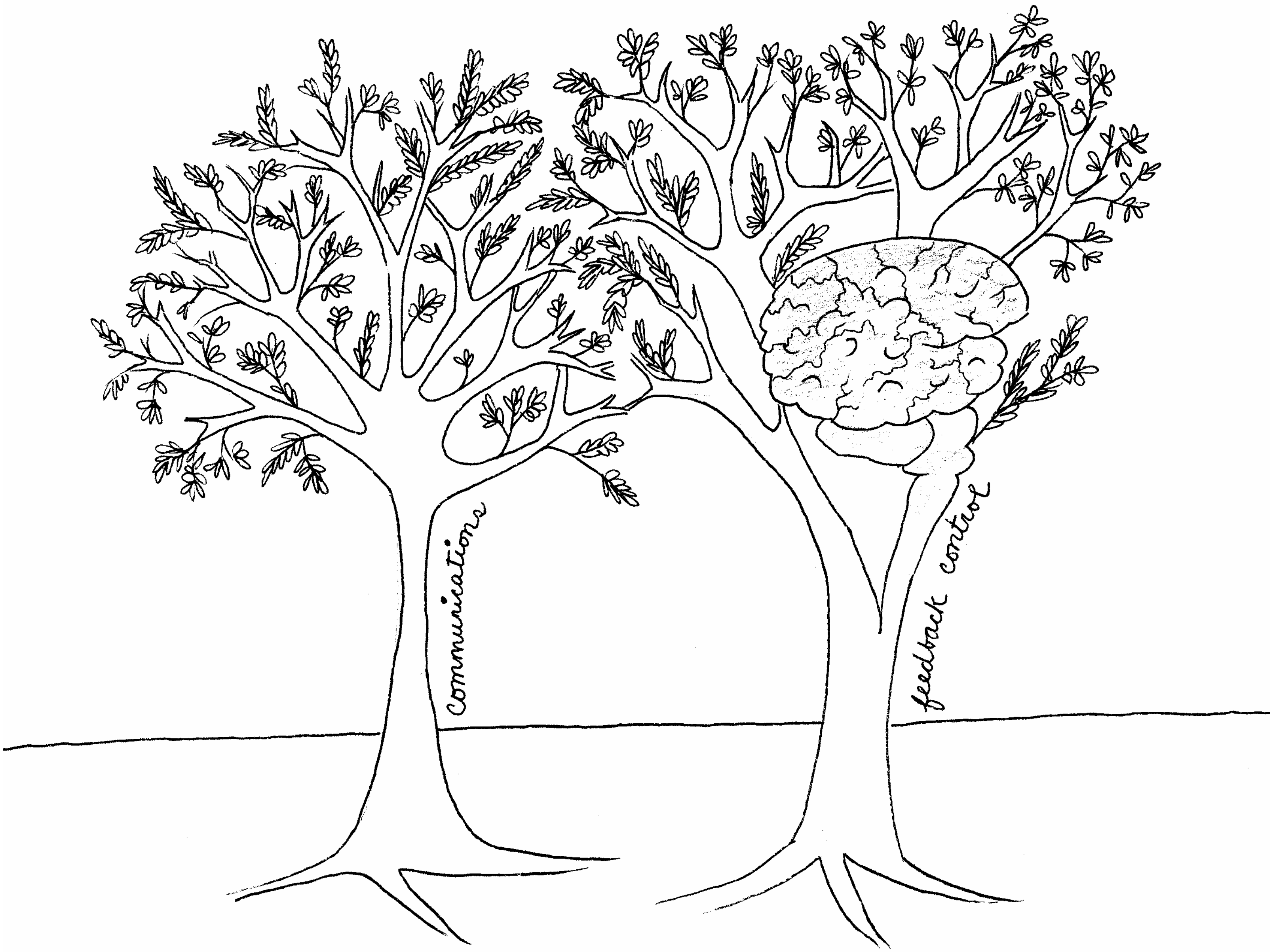


Cf: famous Indian parable …

"It will be noted that our point of view considerably transcended that current among neurophysiologists. The central nervous system no longer appears as a self contained organ, receiving inputs from the senses and discharging into the muscles. On the contrary, some of its most characteristic activities are explicable only as circular processes, emerging from the nervous system into the muscles, and re-entering the nervous system through the sense organs, whether they be proprioceptors or organs of the special senses. This seemed to us to mark a new step in the study of that part of neurophysiology which concerns not solely the elementary processes of nerves and synapses but the performance of the nervous system as an integrated whole."

Norbert Wiener, Cybernetics (introduction) ;1948.

The wrong tree?



Course+workshop : Design Principles in Biological Systems

Will span scales from cells to organisms: have people who
work on bacteria talk to people who work on nervous systems, in the
context of engineering theories …