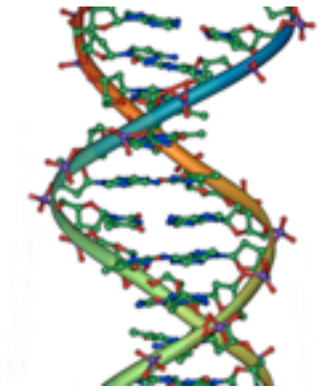
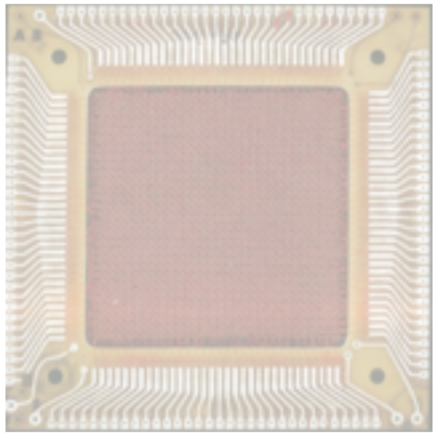
THE EVOLUTION OF COGNITIVE SYSTEMS

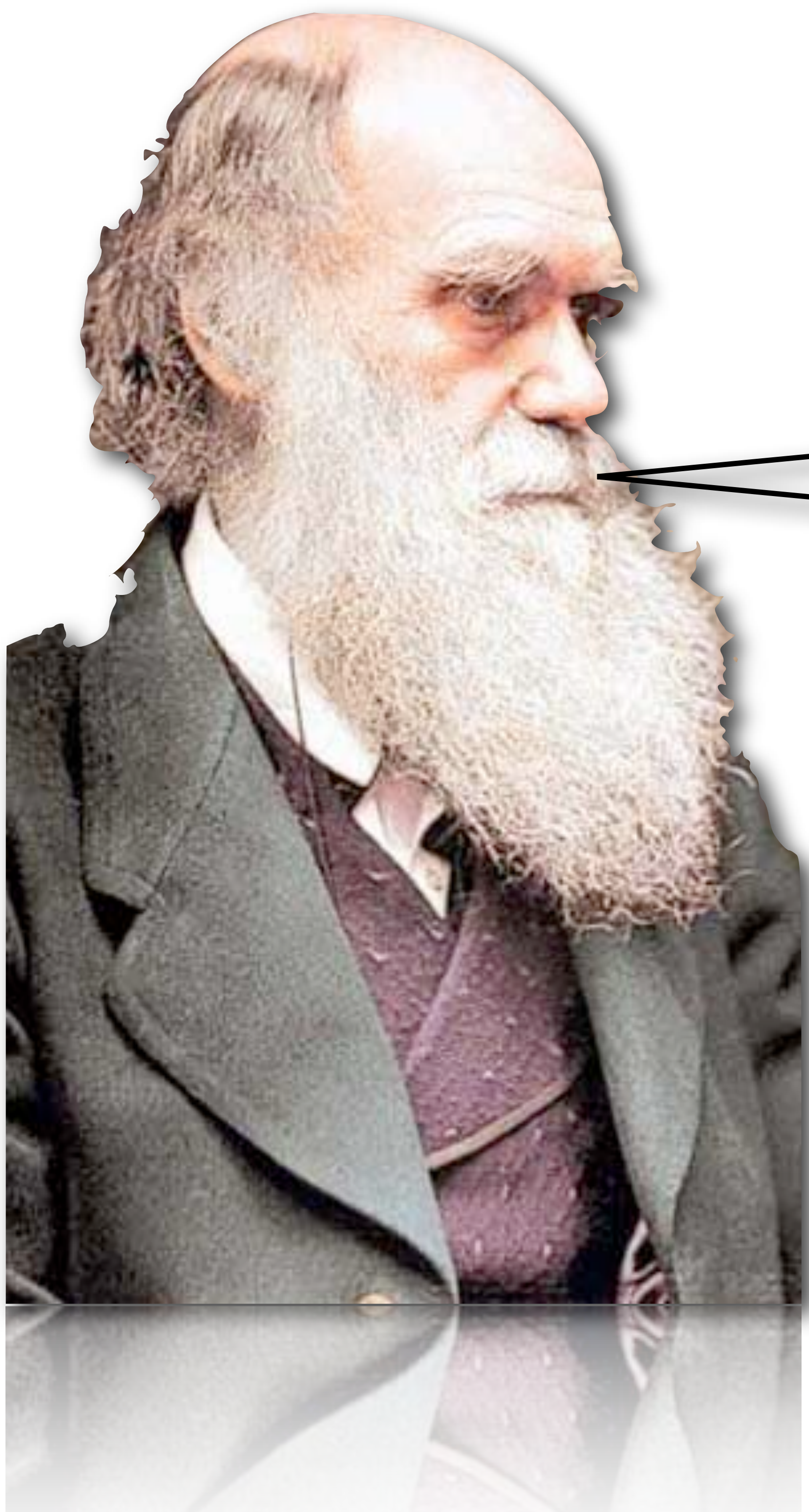
David Krakauer ©
Santa Fe Institute



3 Perspectives

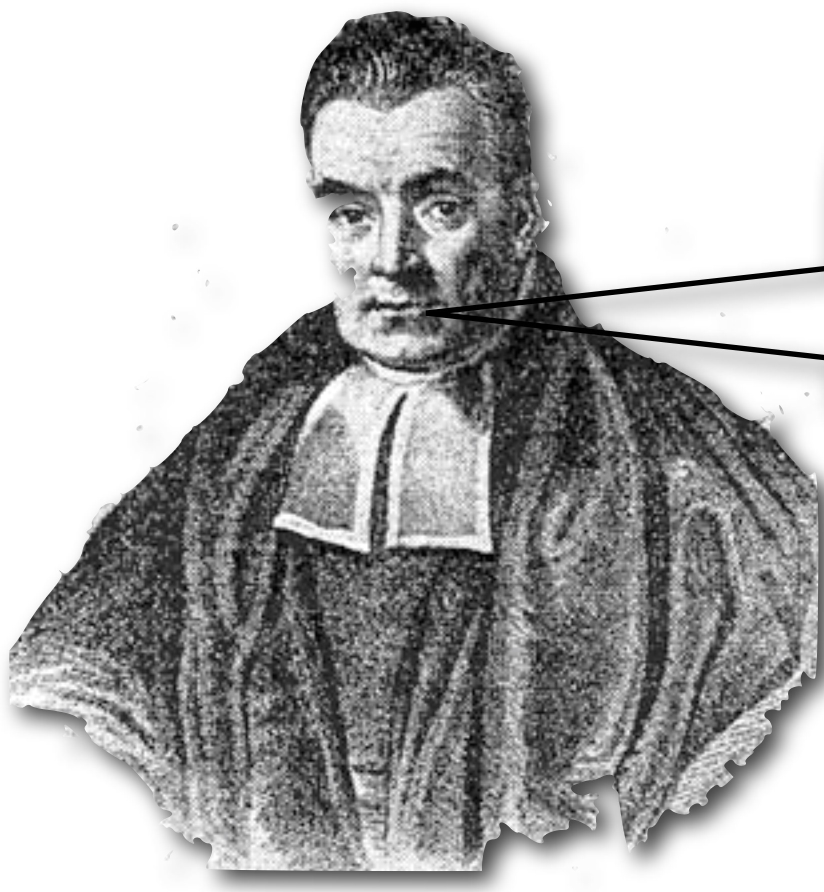
- Brains and cognition have evolved much the way, hair, hands and eyes have evolved -- to solve problems in the world
- Evolution and cognition are fundamentally similar processes using different mechanics
- Cognition is ubiquitous - not restricted to brains - and this is required for brains to have evolved.



"In the struggle for survival, the fittest win out at the expense of their rivals because they succeed in adapting themselves best to their environment."

"I have called this principle, by which each slight variation, if useful, is preserved, by the term Natural Selection"

$$\frac{\Delta g_i(t)}{\Delta t} = g_i(t-1)(r_i(\mathbf{g}) - \bar{f})$$

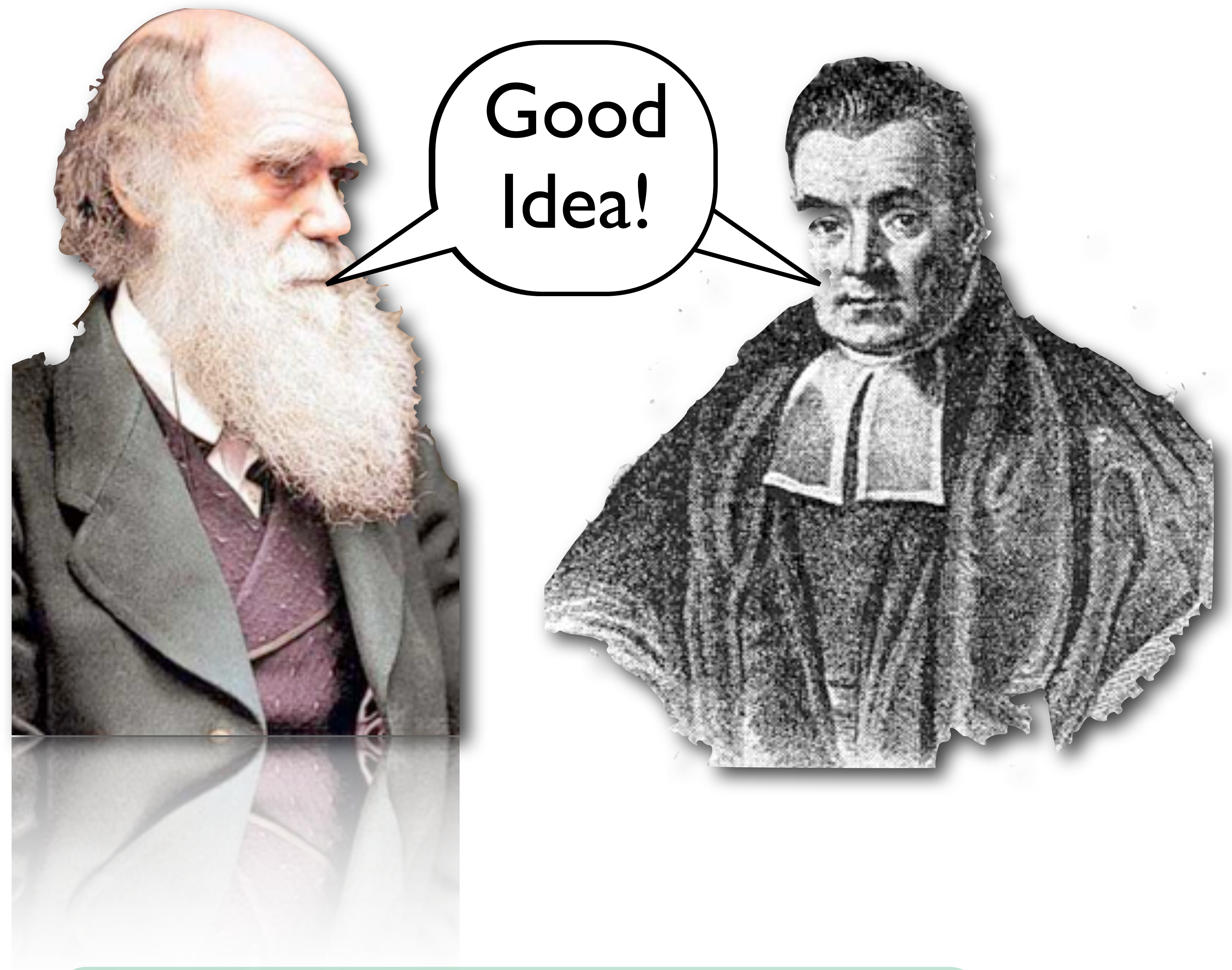


$$P(H|E) = P(H)\frac{P(E|H)}{P(E)}$$

$$P(H|E) = P(H)\frac{L_H}{\bar{L}}$$

$$P_X(t) = P_X(t-1)\frac{L_X}{\bar{L}}$$

$$\bar{L} = P(E) = \sum_{x \in \omega} P(E|H)P(H)$$



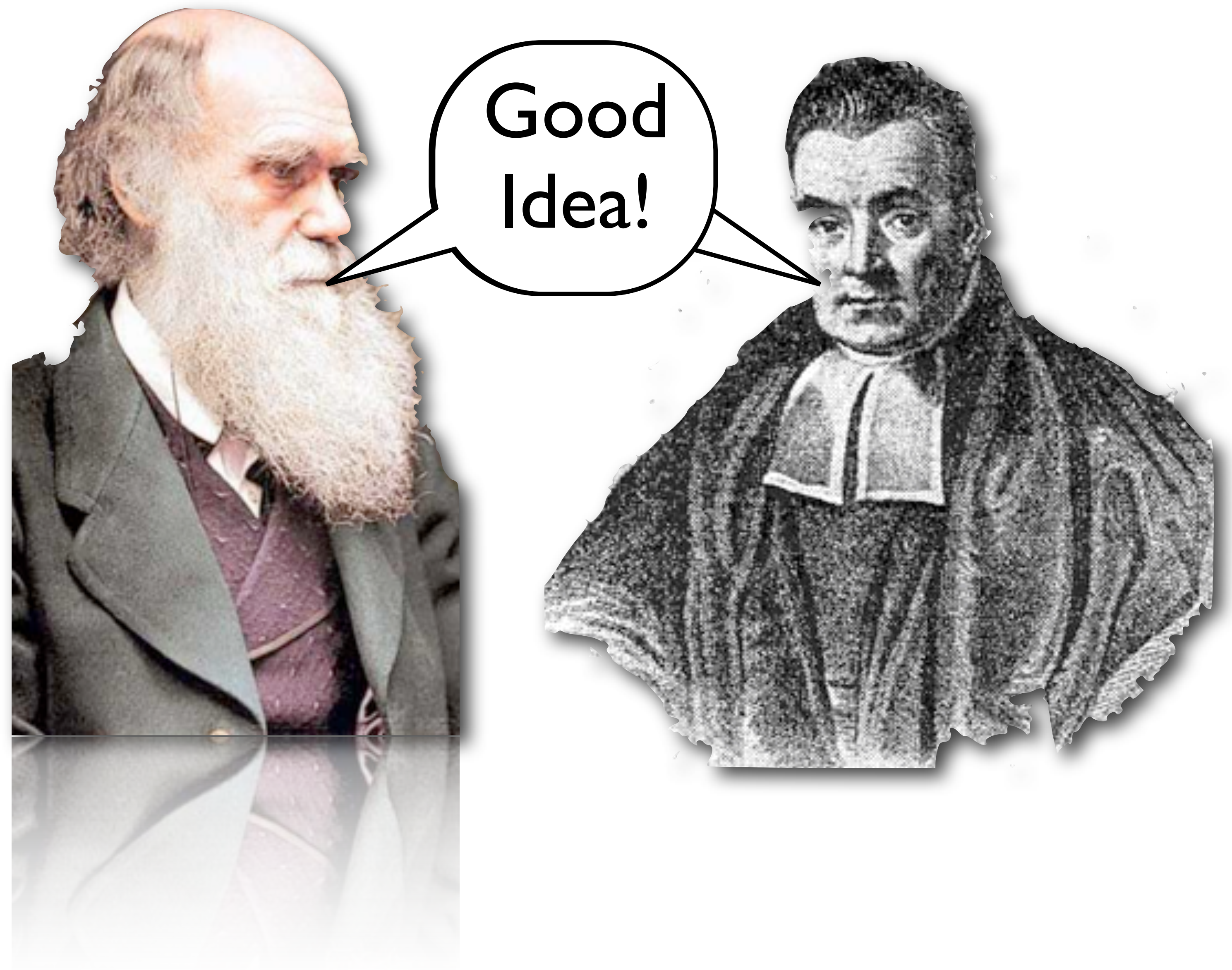
replicator equation

$$\frac{\Delta g_i(t)}{\Delta t} = g_i(t-1)(r_i(\mathbf{g}) - \bar{f})$$

Baye's Rule

$$\Delta P_X(t) = P_X(t-1)(f_t - \bar{f}), \quad \text{where} \quad f_t = L_X/\bar{L}$$

see: Cosma Shalizi CMU statistics.



"Biological offspring are the hypotheses of their parents, formulated through the success of their ancestors predicting the future state of the world"

The Implications & Requirements of Inference

Adaptive System

Cognitive System

Sensation/Perception (P)
& feedback from Environment (E)

Noisy Production of Behavior/Phenotype

Representation and Noisy Transmission of Memory

SELECTION

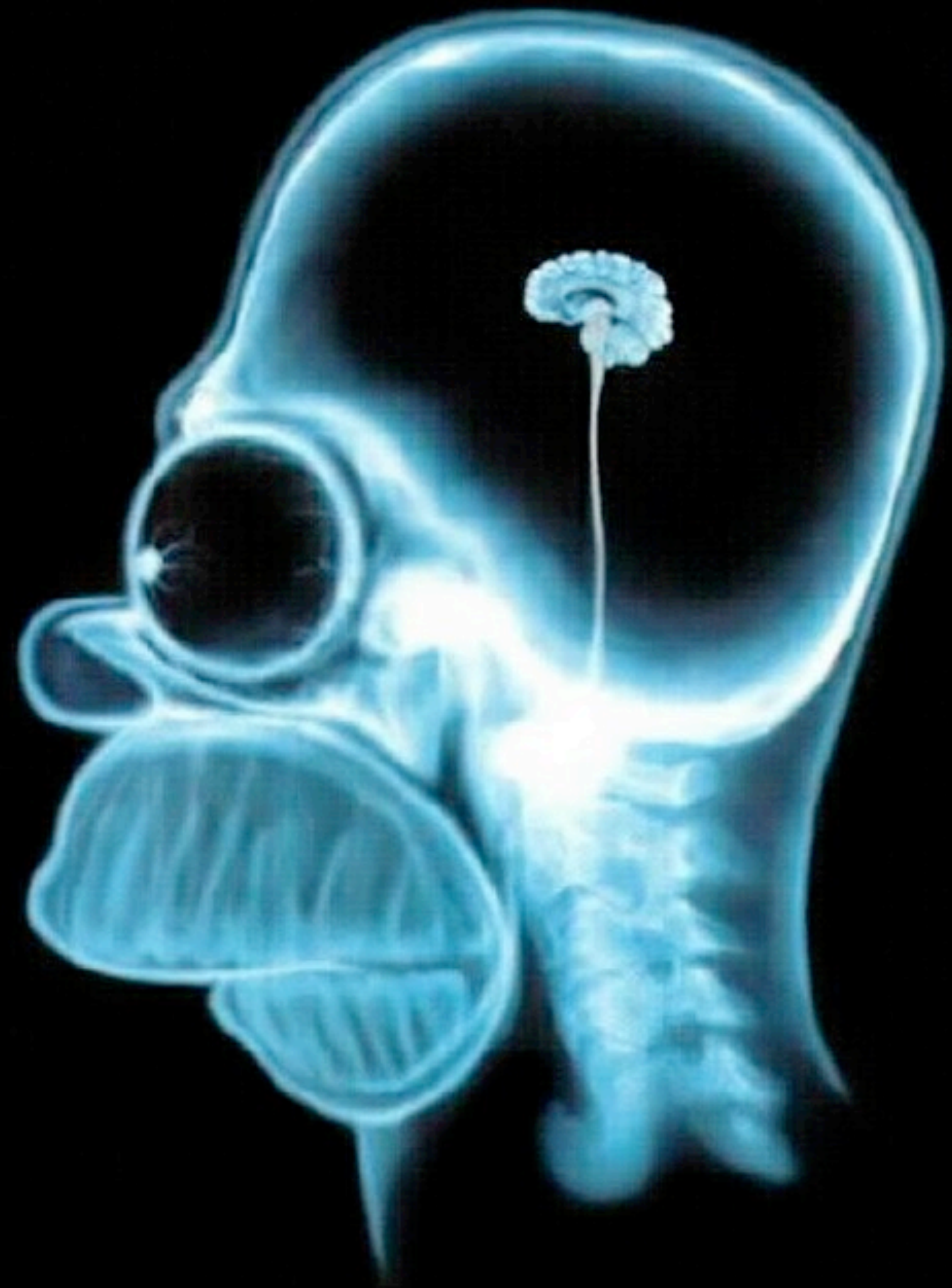
DEVELOPMEN

HEREDITY

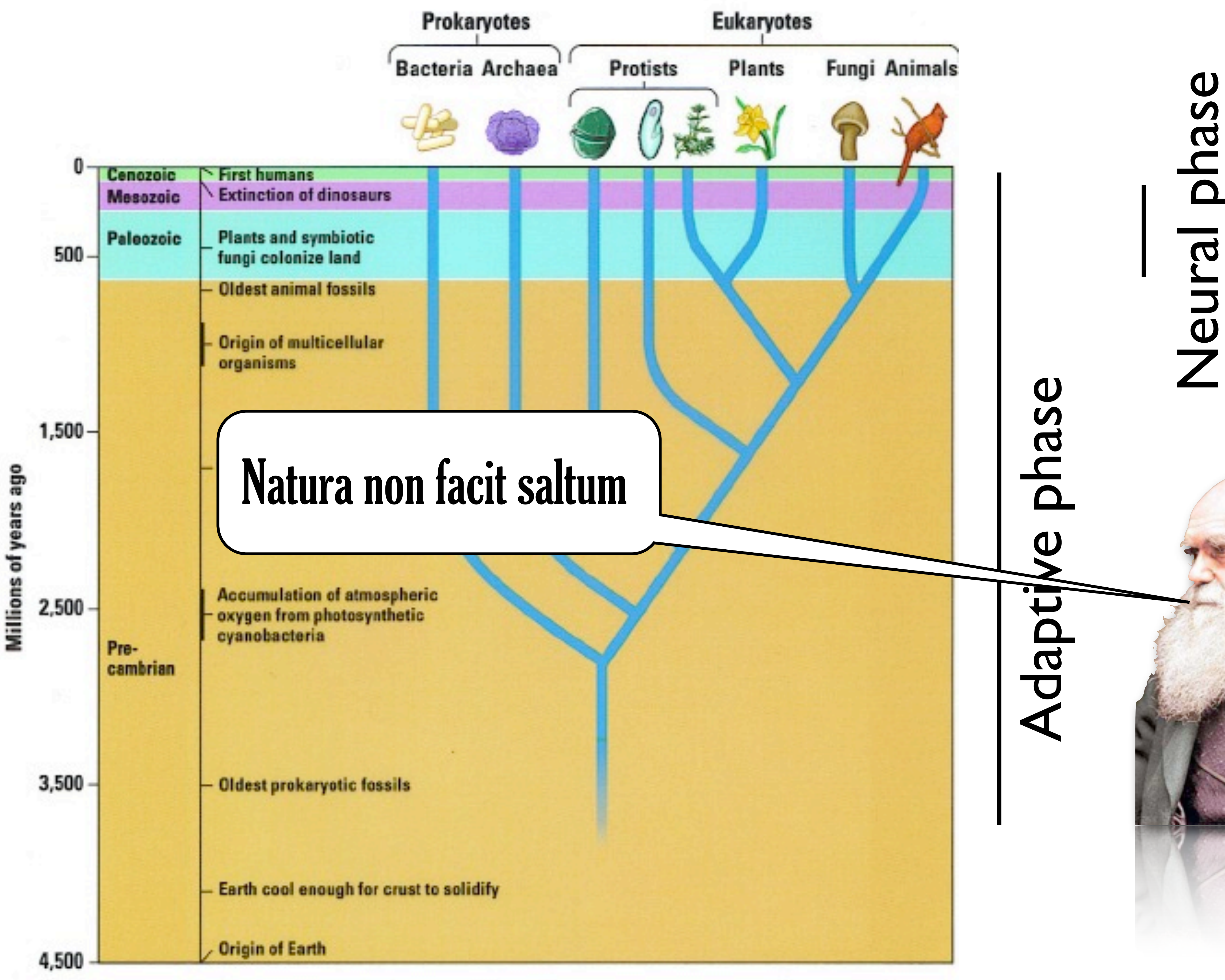
Use of P & M for Prediction in Variable Environments

Fast Learning of Different Environments
(new Ms for new Ps)

“The only cognitive system is the nervous system”

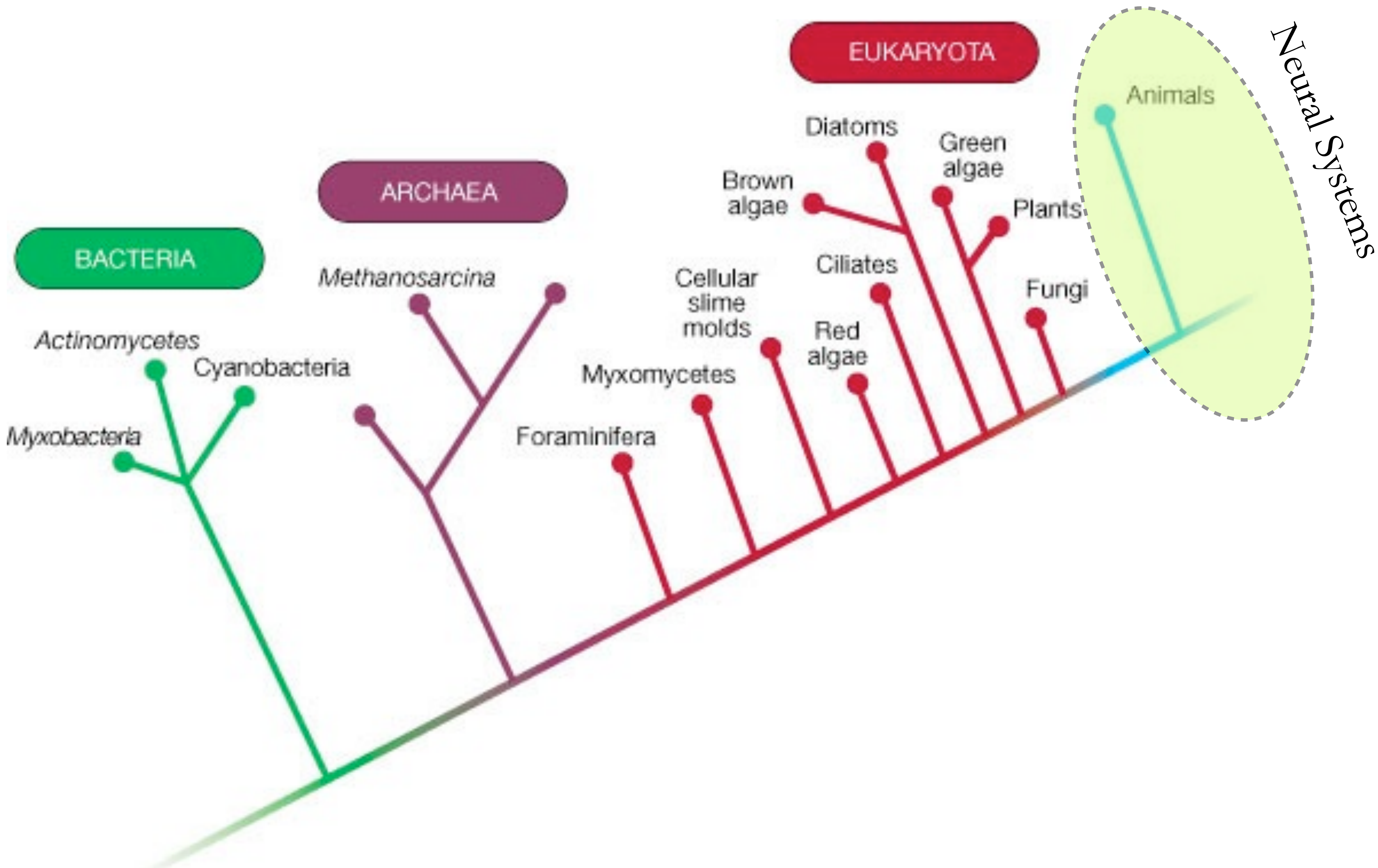


An Evolutionary Limitation of the Neural Bias.


Prokaryotes
Eukaryotes
Bacteria Archaea
Protists
Plants
Fungi Animals
Millions of years ago
0
500
1,500
2,500
3,500
4,500
Cenozoic
Mesozoic
Paleozoic
Pre-
cambrian
First humans
Extinction of dinosaurs
Plants and symbiotic
fungi colonize land
Oldest animal fossils
Origin of multicellular
organisms
Accumulation of atmospheric
oxygen from photosynthetic
cyanobacteria
Oldest prokaryotic fossils
Earth cool enough for crust to solidify
Origin of Earth
Natura non facit saltum
Adaptive phase
Neural phase

The Multicellular Argument

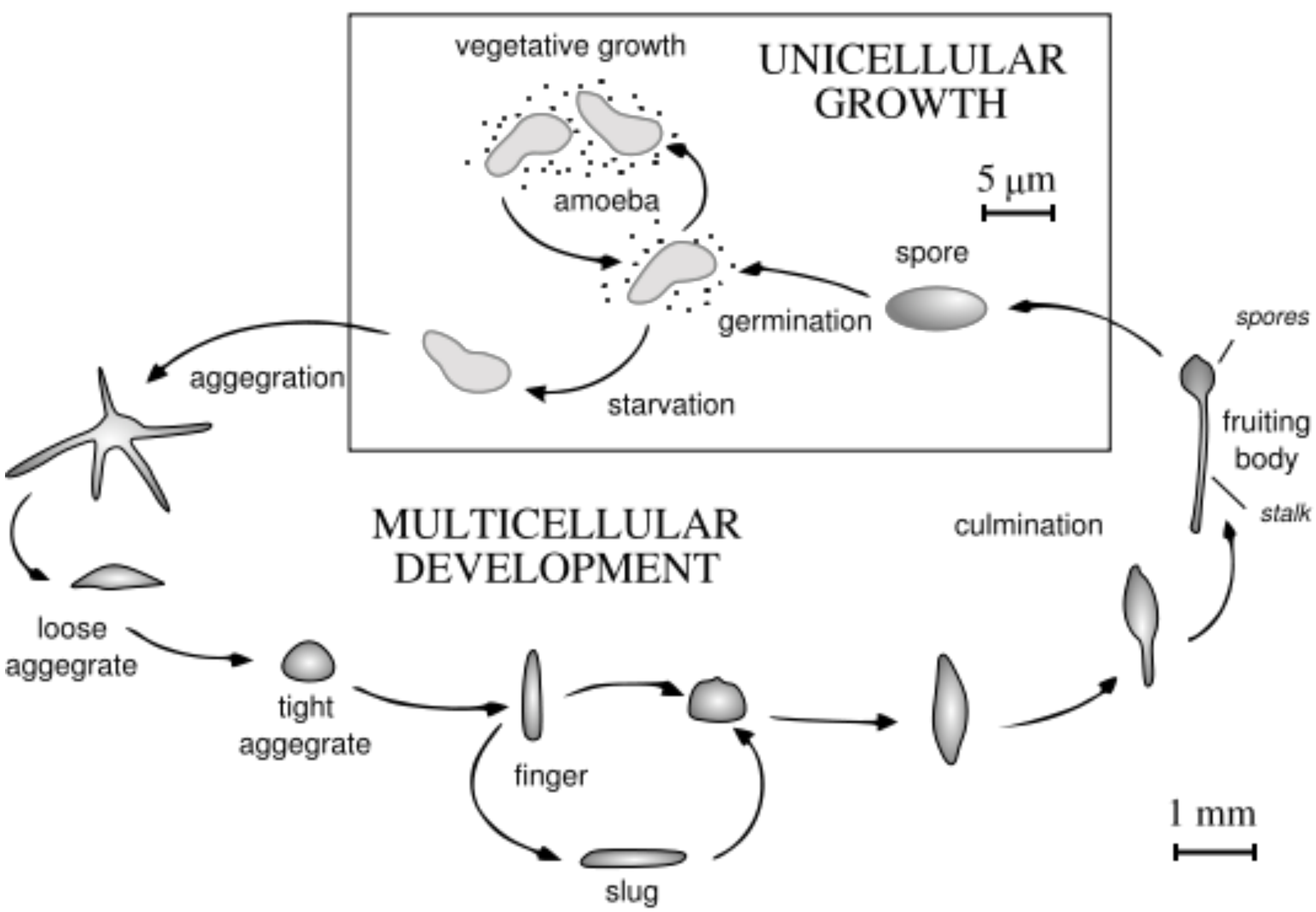
Multiple, independent origins of multicellularity

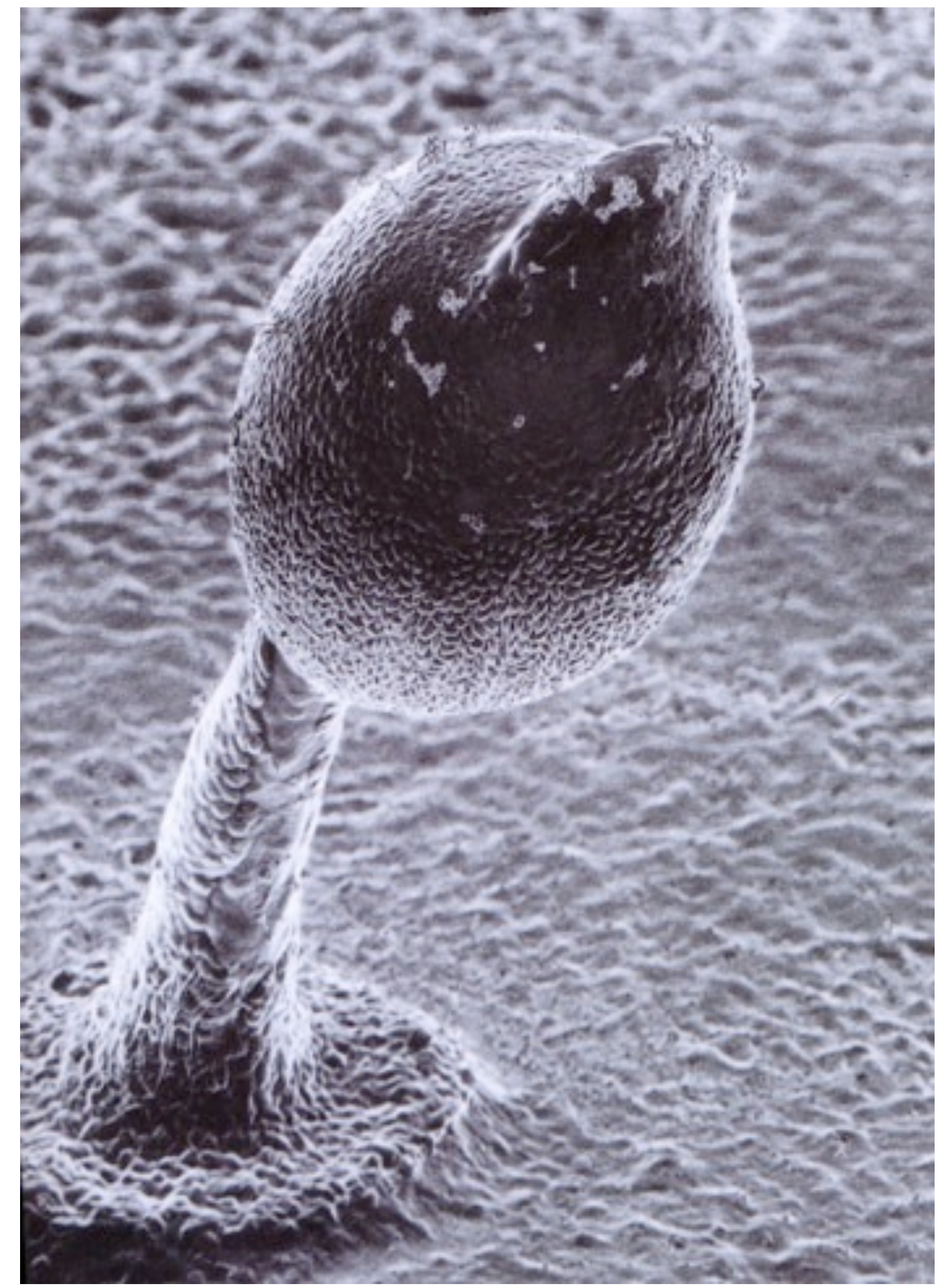


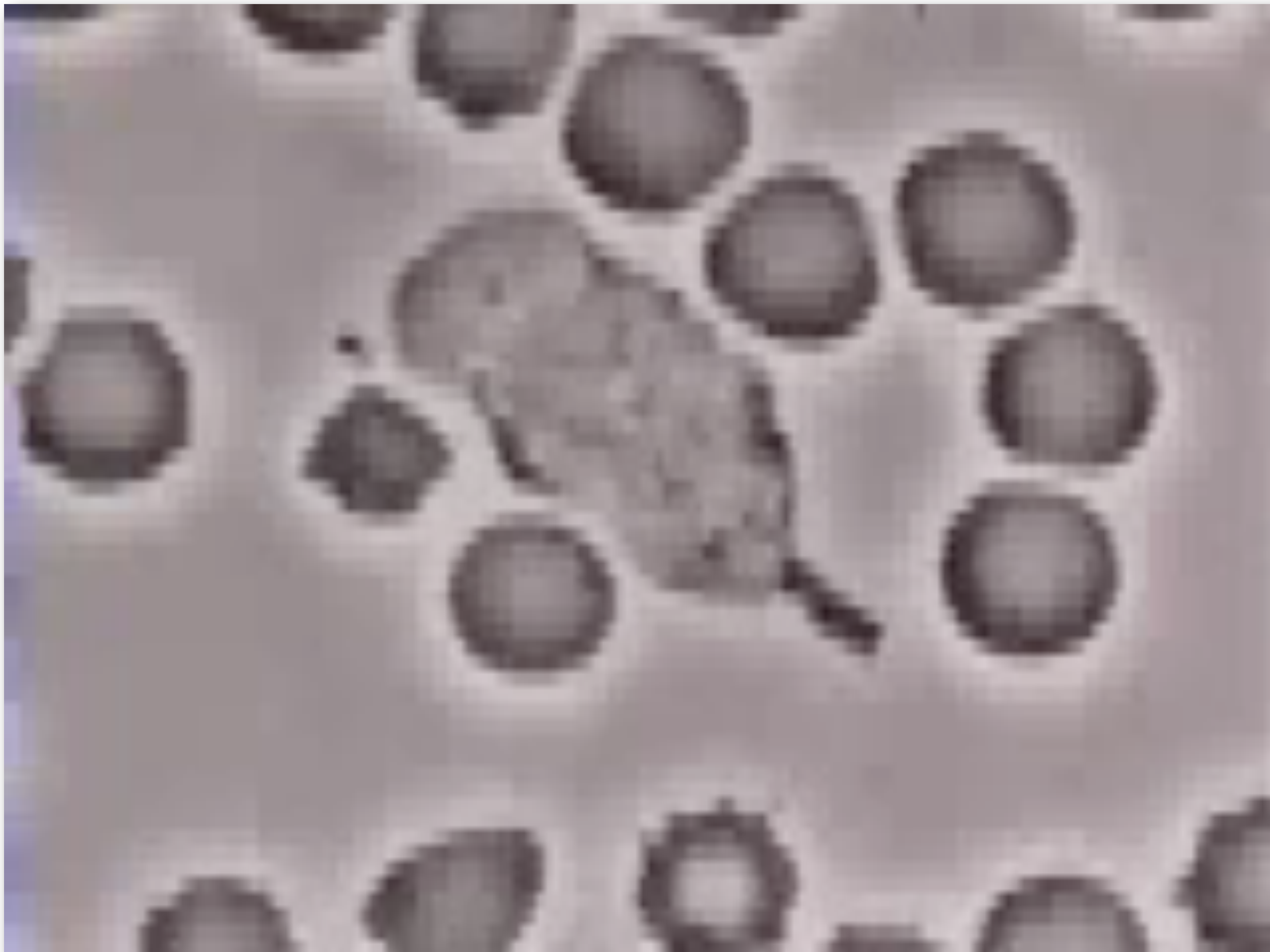
Pre-Neural Cinema

"In Life Cognition is Everywhere"

- Georgio LUCAs (Last Universal Common Ancestor(s))

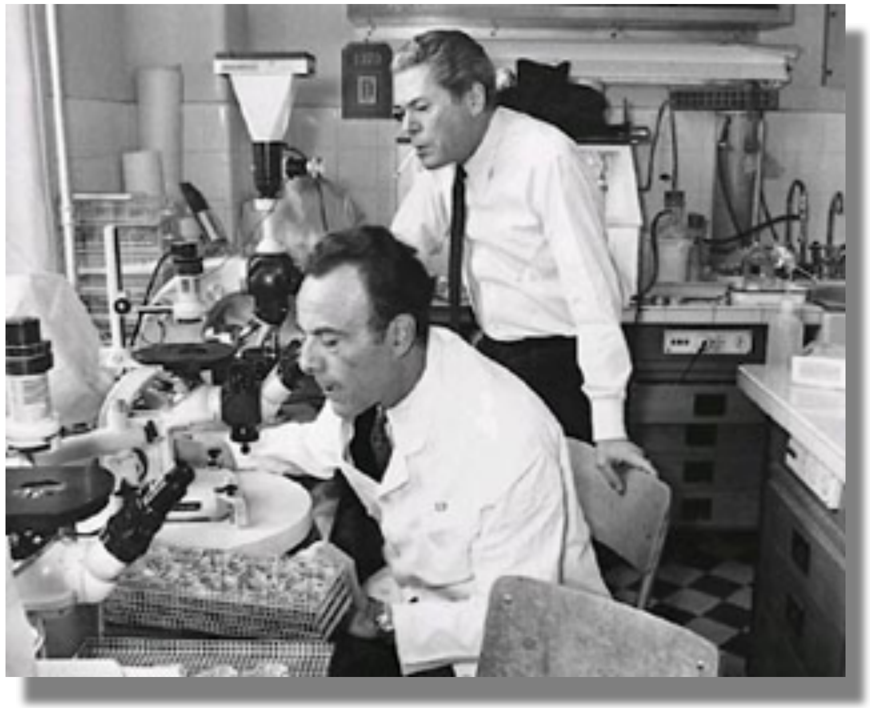

vegetative growth
UNICELLULAR GROWTH
amoeba
5 μm
spore
germination
spores
aggegration
starvation
fruiting body
stalk
culmination
MULTICELLULAR DEVELOPMENT
loose aggregate
tight aggregate
finger
slug
1 mm

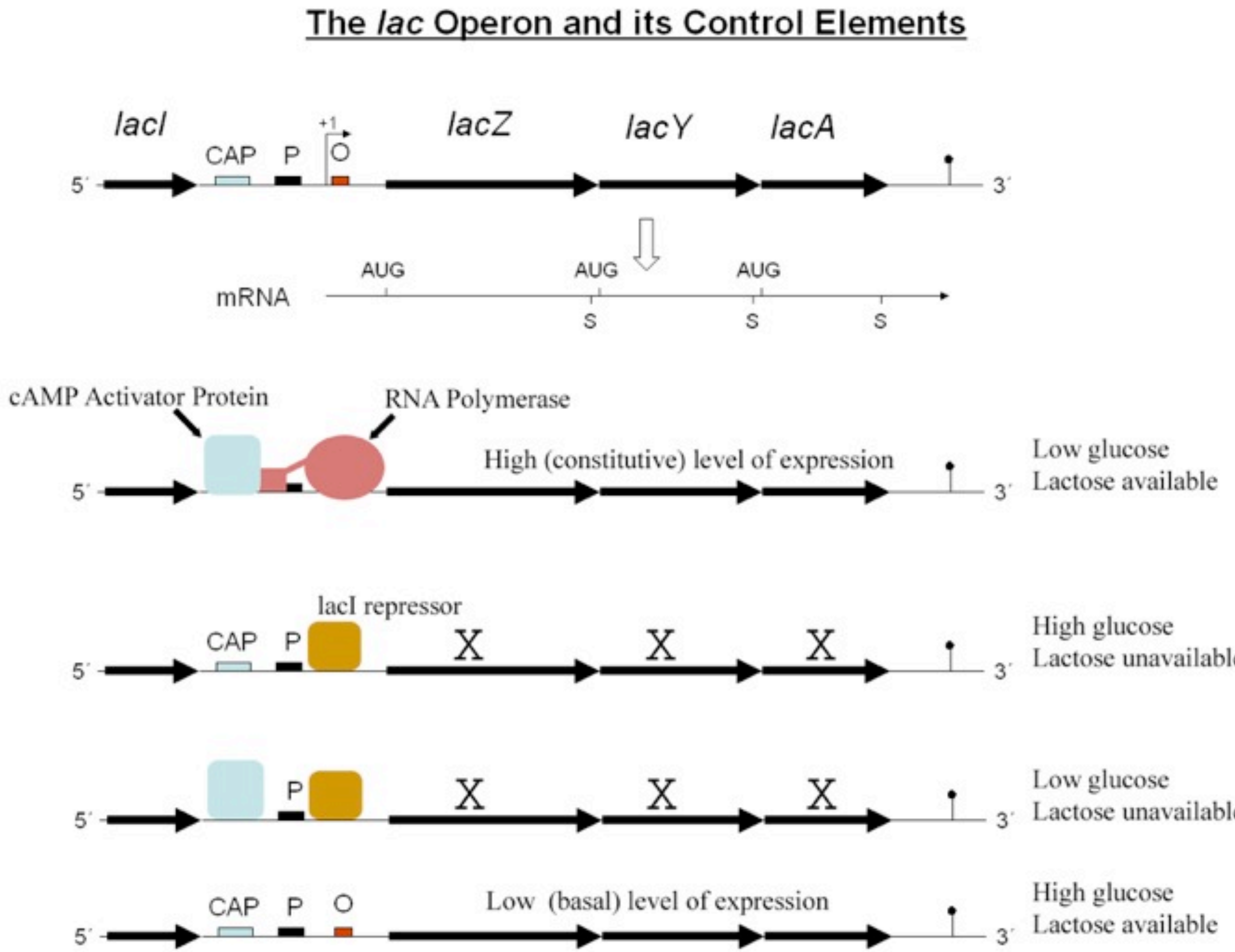


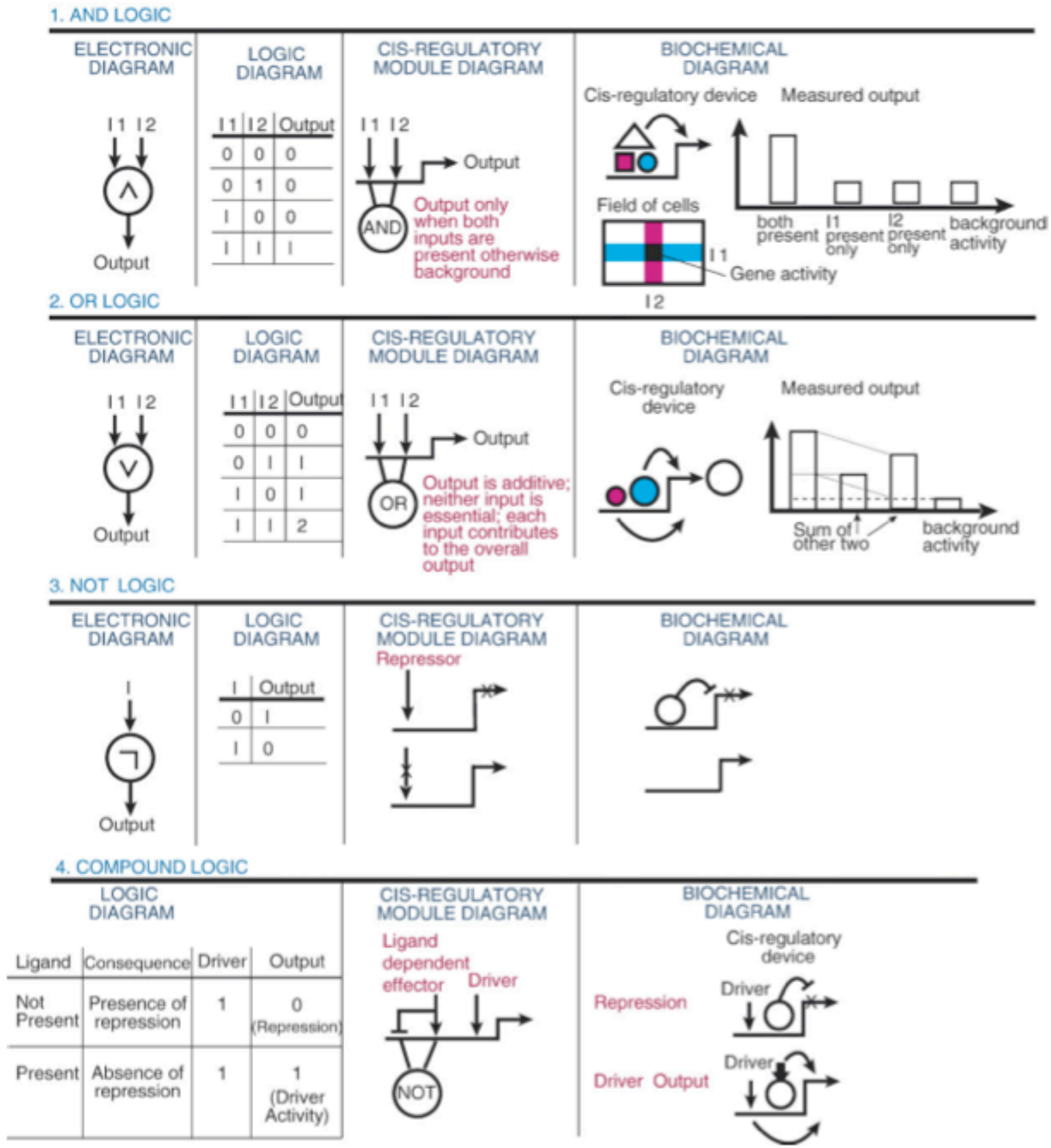


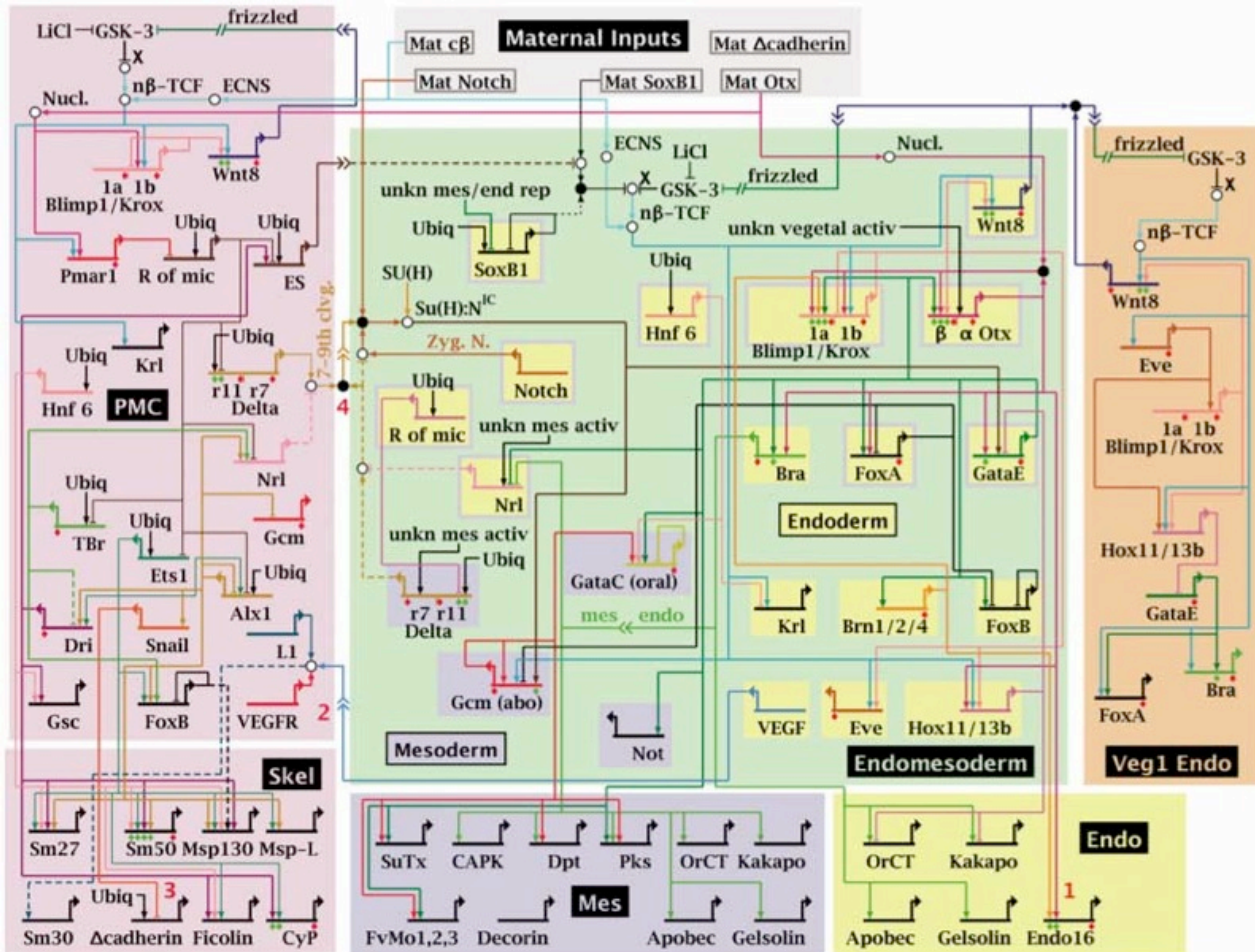
Part 1: Genomic Cognition

- Genetic sensation and programmed adaptive behavior - *operon to GRN*
- Efficient Representation of genetic memory - *compression*
- Limitations of genomic cognition - *evolutionary information storage law*




The lac Operon and its Control Elements
lacI
CAP
P
+1
O
lacZ
lacY
lacA
5´
3´
mRNA
AUG
AUG
AUG
S
S
S
cAMP Activator Protein
RNA Polymerase
High (constitutive) level of expression
Low glucose
Lactose available
lacI repressor
CAP
P
X
X
X
High glucose
Lactose unavailable
P
X
X
X
Low glucose
Lactose unavailable
CAP
P
O
Low (basal) level of expression
High glucose
Lactose available


1. AND LOGIC
ELECTRONIC DIAGRAM
I1 I2
Output
LOGIC DIAGRAM
I1 I2 Output
0 0 0
0 1 0
1 0 0
1 1 1
CIS-REGULATORY MODULE DIAGRAM
I1 I2
Output
AND
Output only when both inputs are present otherwise background
BIOCHEMICAL DIAGRAM
Cis-regulatory device
Measured output
Field of cells
I1
I2
Gene activity
both present
I1 present only
I2 present only
background activity
2. OR LOGIC
ELECTRONIC DIAGRAM
I1 I2
Output
LOGIC DIAGRAM
I1 I2 Output
0 0 0
0 1 1
1 0 1
1 1 2
CIS-REGULATORY MODULE DIAGRAM
I1 I2
Output
OR
Output is additive; neither input is essential; each input contributes to the overall output
BIOCHEMICAL DIAGRAM
Cis-regulatory device
Measured output
Sum of other two
background activity
3. NOT LOGIC
ELECTRONIC DIAGRAM
I
Output
LOGIC DIAGRAM
I Output
0 1
1 0
CIS-REGULATORY MODULE DIAGRAM
Repressor
BIOCHEMICAL DIAGRAM
4. COMPOUND LOGIC
LOGIC DIAGRAM
Ligand | Consequence | Driver | Output
Not Present | Presence of repression | 1 | 0 (Repression)
Present | Absence of repression | 1 | 1 (Driver Activity)
CIS-REGULATORY MODULE DIAGRAM
Ligand dependent effector
Driver
NOT
BIOCHEMICAL DIAGRAM
Cis-regulatory device
Repression
Driver
Driver Output
Driver



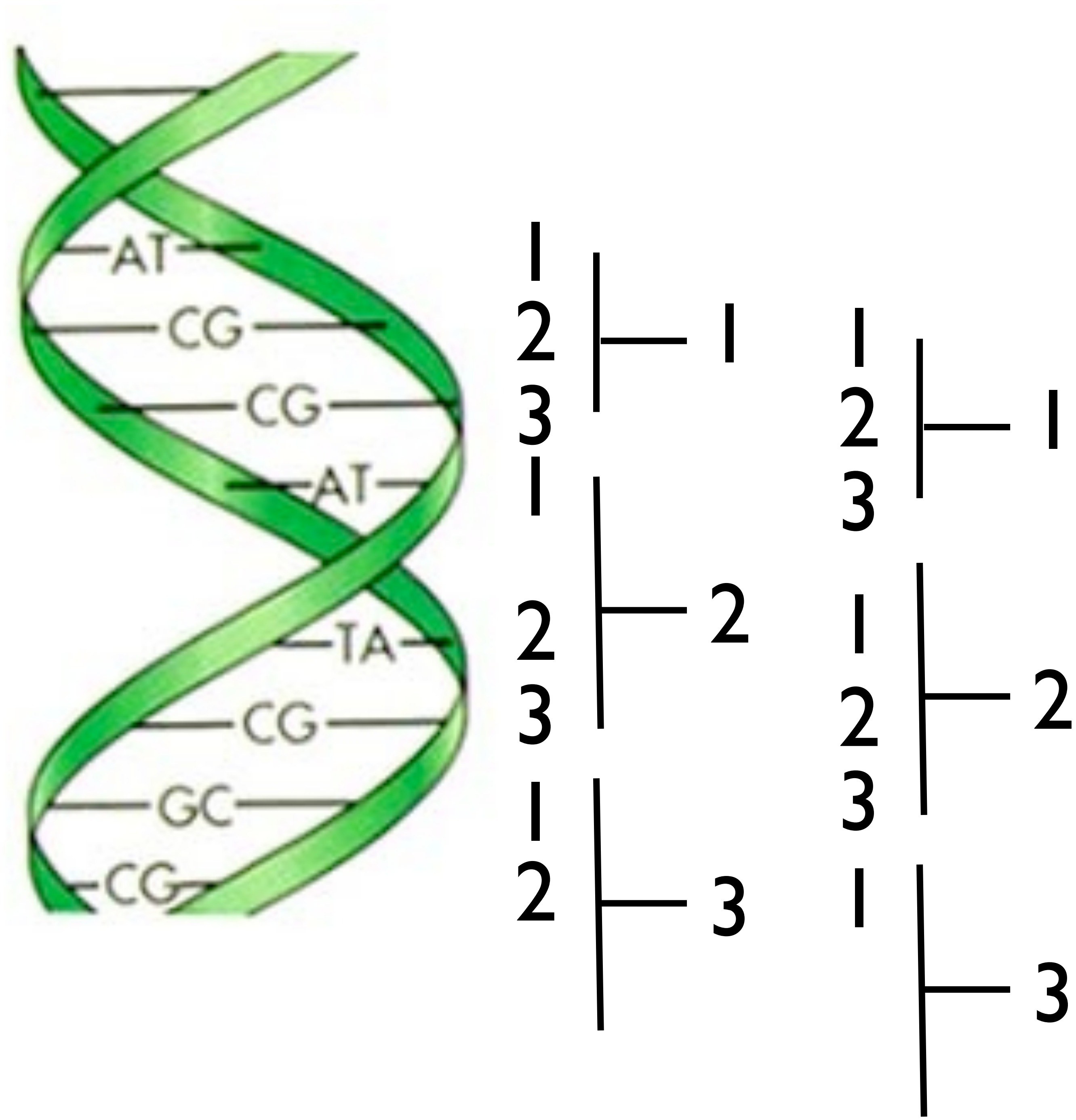
Ubiq=ubiquitous; Mat = maternal; activ = activator; rep = repressor;
unkn = unknown; Nucl. = nuclearization; χ = β-catenin source;
nβ-TCF = nuclearized b-β-catenin-Tcf1; ES = early signal;
ECNS = early cytoplasmic nuclearization system; Zyg. N. = zygotic Notch

Genomic Representation

The Ingenuity & Ambiguity of the "gene"

The Genetic Code

First letter	Second letter: U	Second letter: C	Second letter: A	Second letter: G	Third letter
U	UUU, UUC: Phe UUA, UUG: Leu	UCU, UCC, UCA, UCG: Ser	UAU, UAC: Tyr UAA: Stop UAG: Stop	UGU, UGC: Cys UGA: Stop UGG: Trp	U C A G
C	CUU, CUC, CUA, CUG: Leu	CCU, CCC, CCA, CCG: Pro	CAU, CAC: His CAA, CAG: Gln	CGU, CGC, CGA, CGG: Arg	U C A G
A	AUU, AUC, AUA: Ile AUG: Met	ACU, ACC, ACA, ACG: Thr	AAU, AAC: Asn AAA, AAG: Lys	AGU, AGC: Ser AGA, AGG: Arg	U C A G
G	GUU, GUC, GUA, GUG: Val	GCU, GCC, GCA, GCG: Ala	GAU, GAC: Asp GAA, GAG: Glu	GGU, GGC, GGA, GGG: Gly	U C A G


AT
CG
CG
AT
TA
CG
GC
CG
1
2
3
1
2
3
1
2
1
2
3
1
2
3
1
2
3
1
2
3
1
2
3

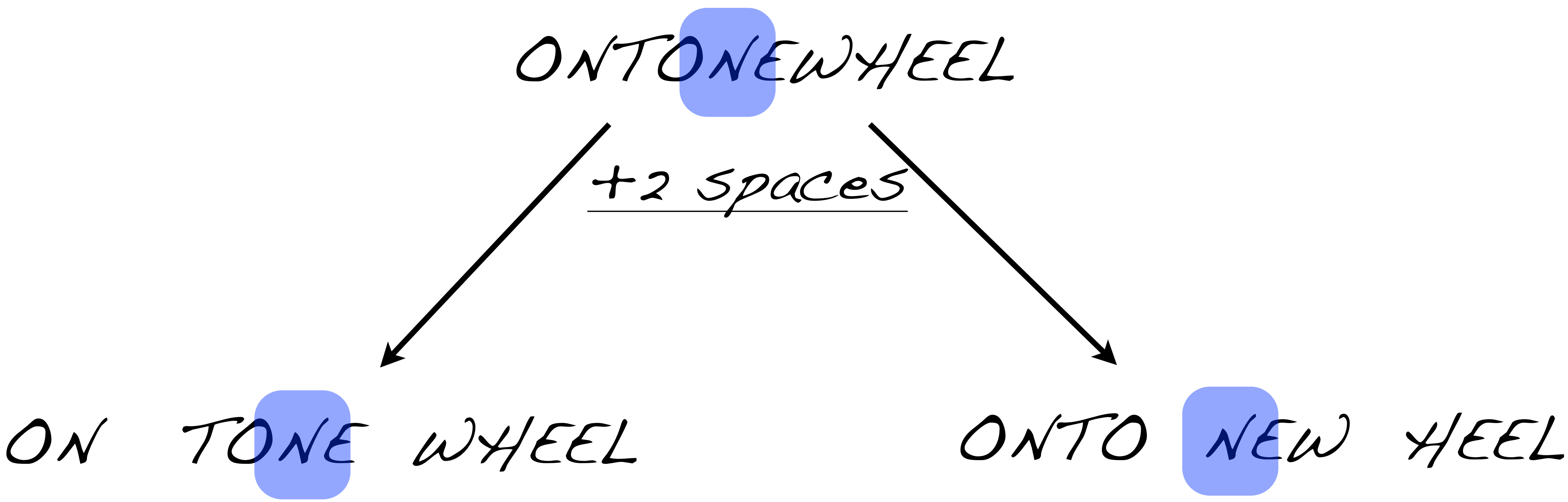
The Archimedes Palimpsest

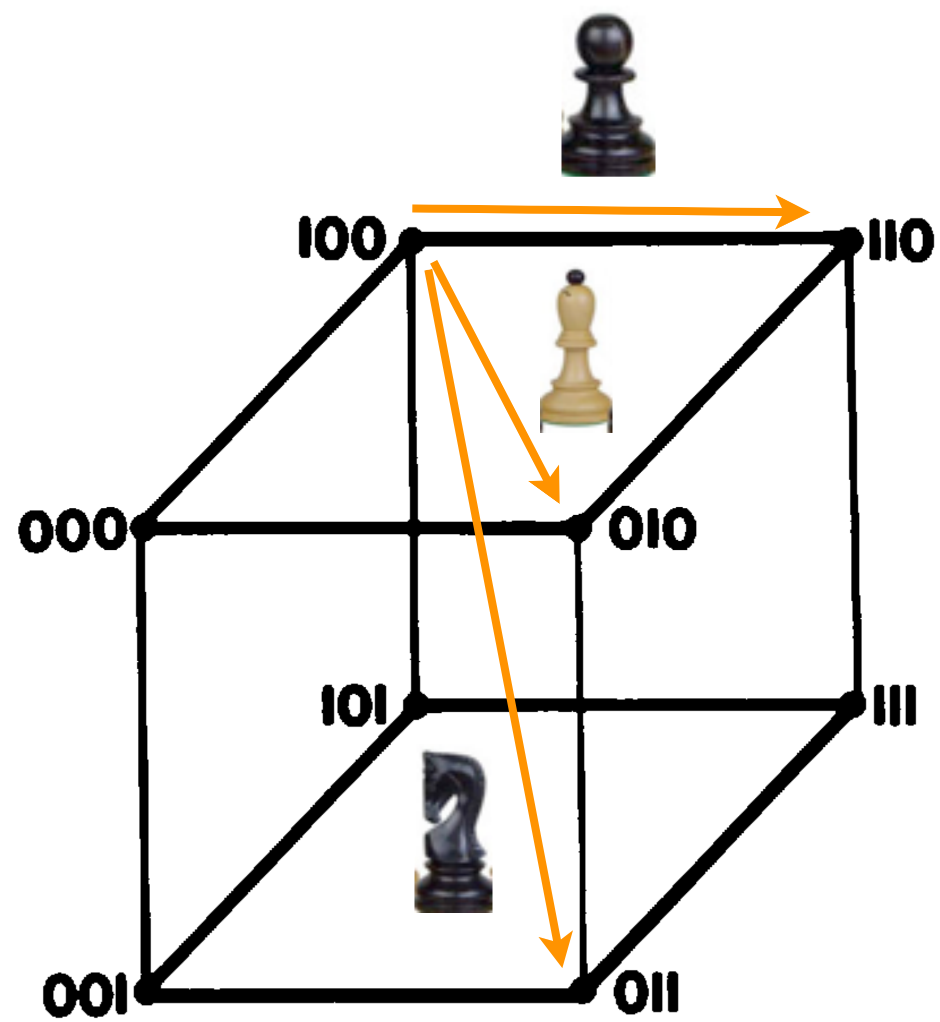
THE GENETIC PALIMPSEST

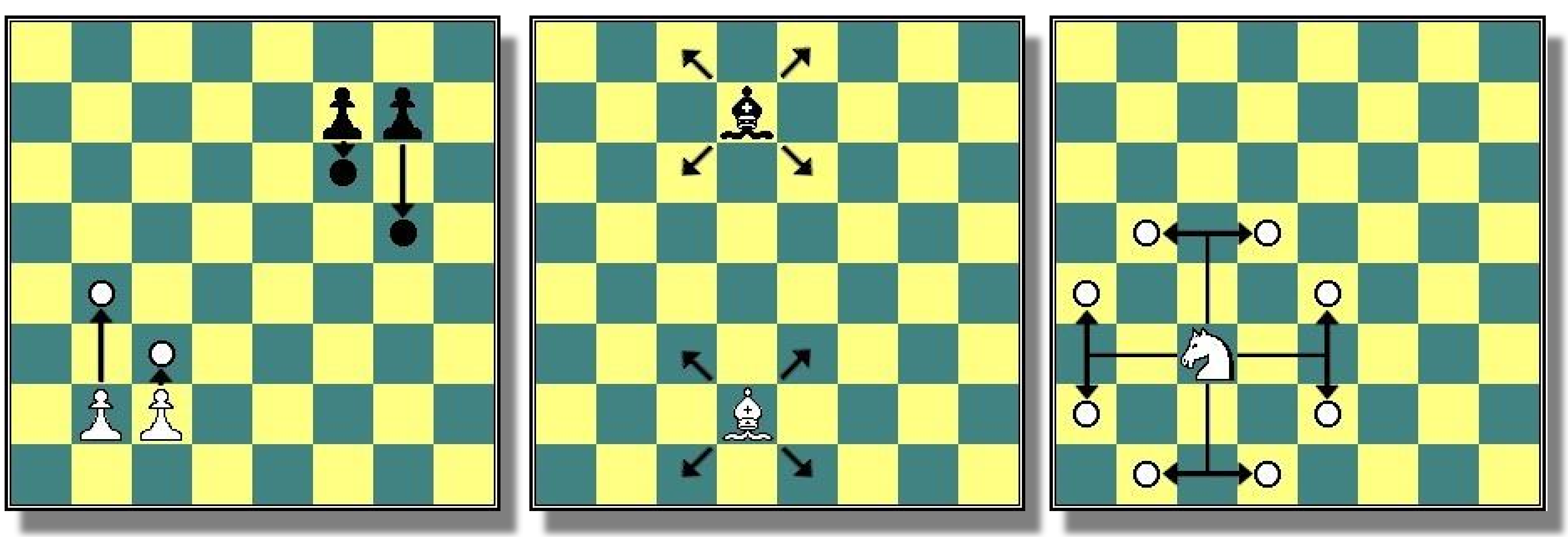
Phase	Alignment
−2	321321321321321321321
	321321321321321321321
	321321321321321321321
0	123123123123123123123
	123123123123123123123
2	123123123123123123123

1 sequence ⟶ 6 messages (proteins)

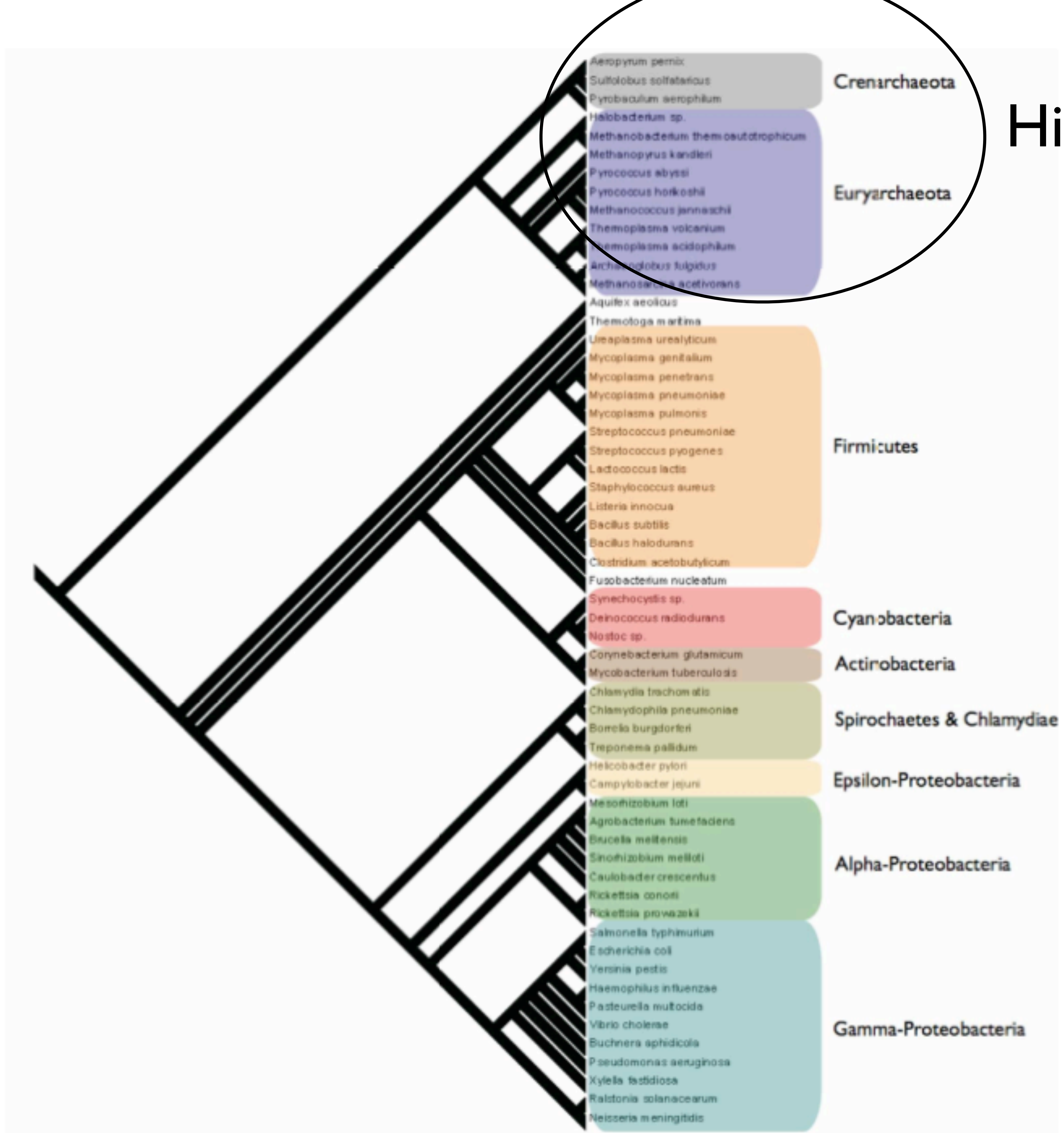
A LINGUISTIC PALIMPSEST




100
110
000
010
101
111
001
011



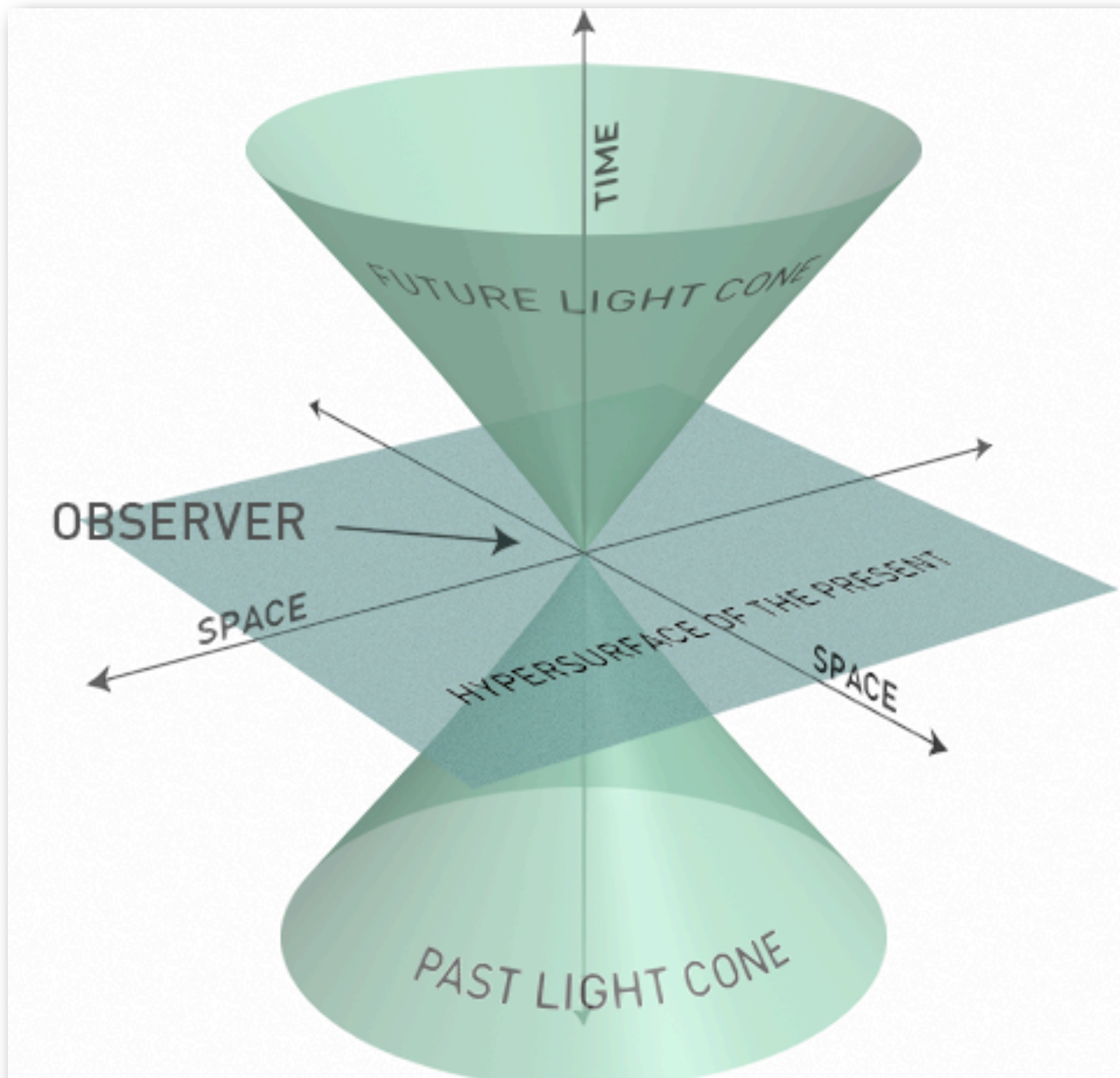
High temperatures



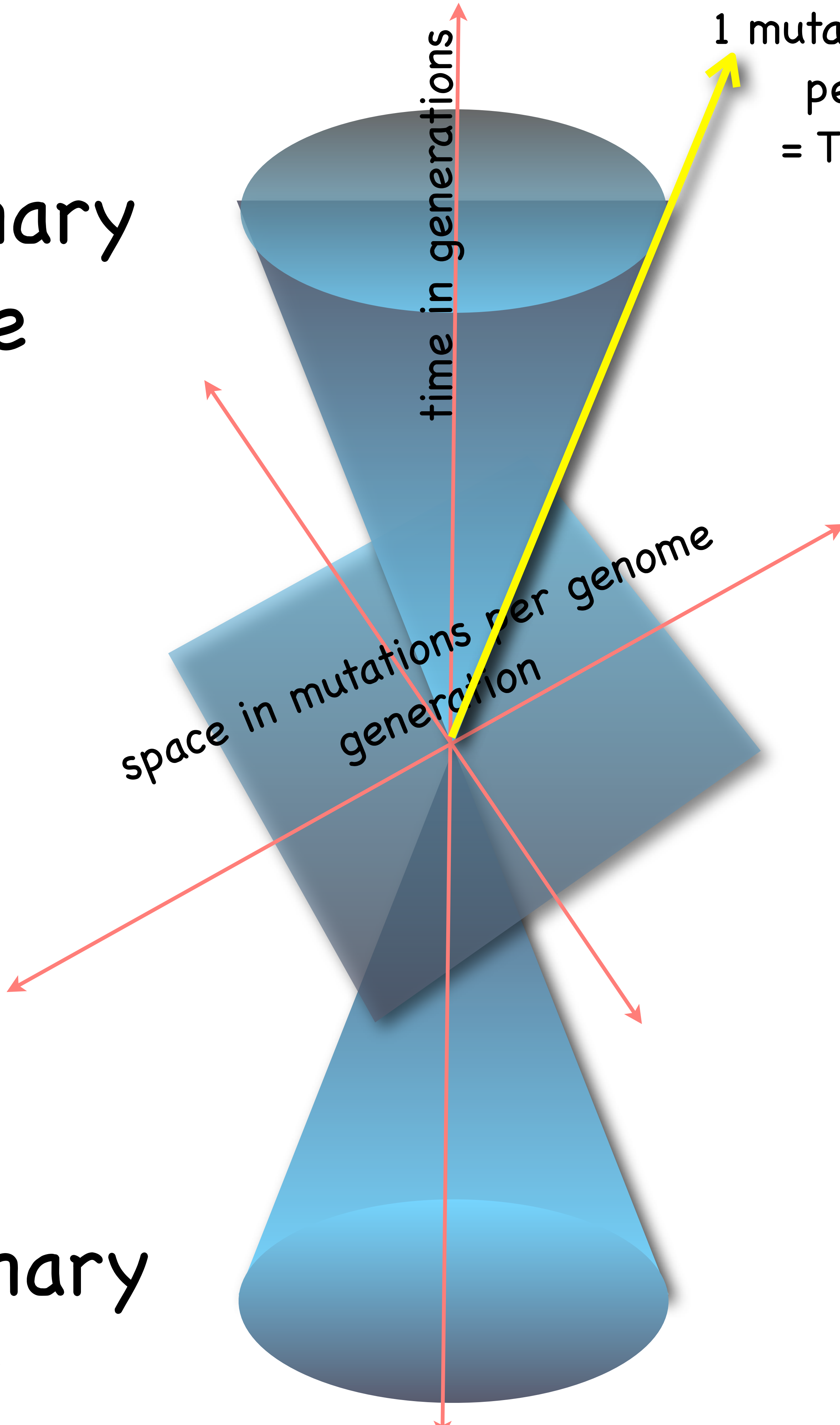
Computational Limitations of Genomes

The Constraint of Evolutionary Light Speed

Fundamental Constraints in Physics



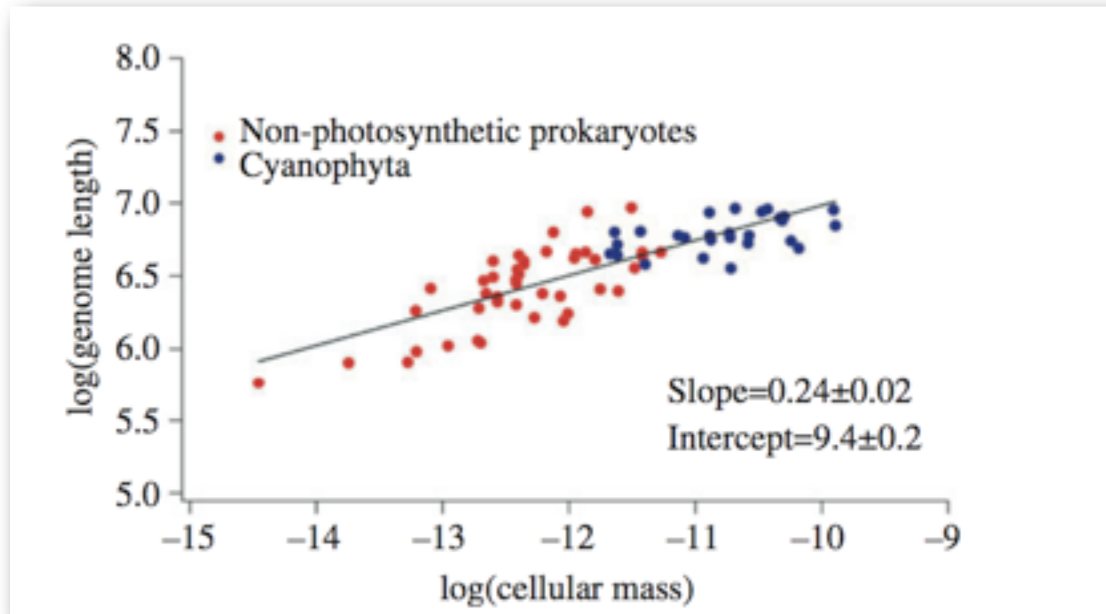
The evolutionary future



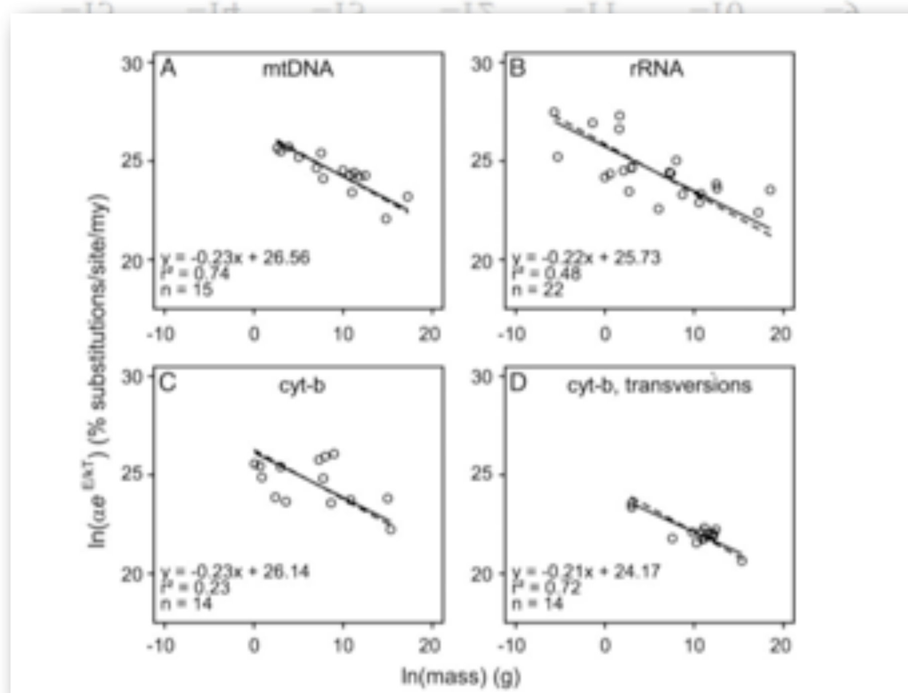
$$\mu = \frac{1}{L}$$

The evolutionary past

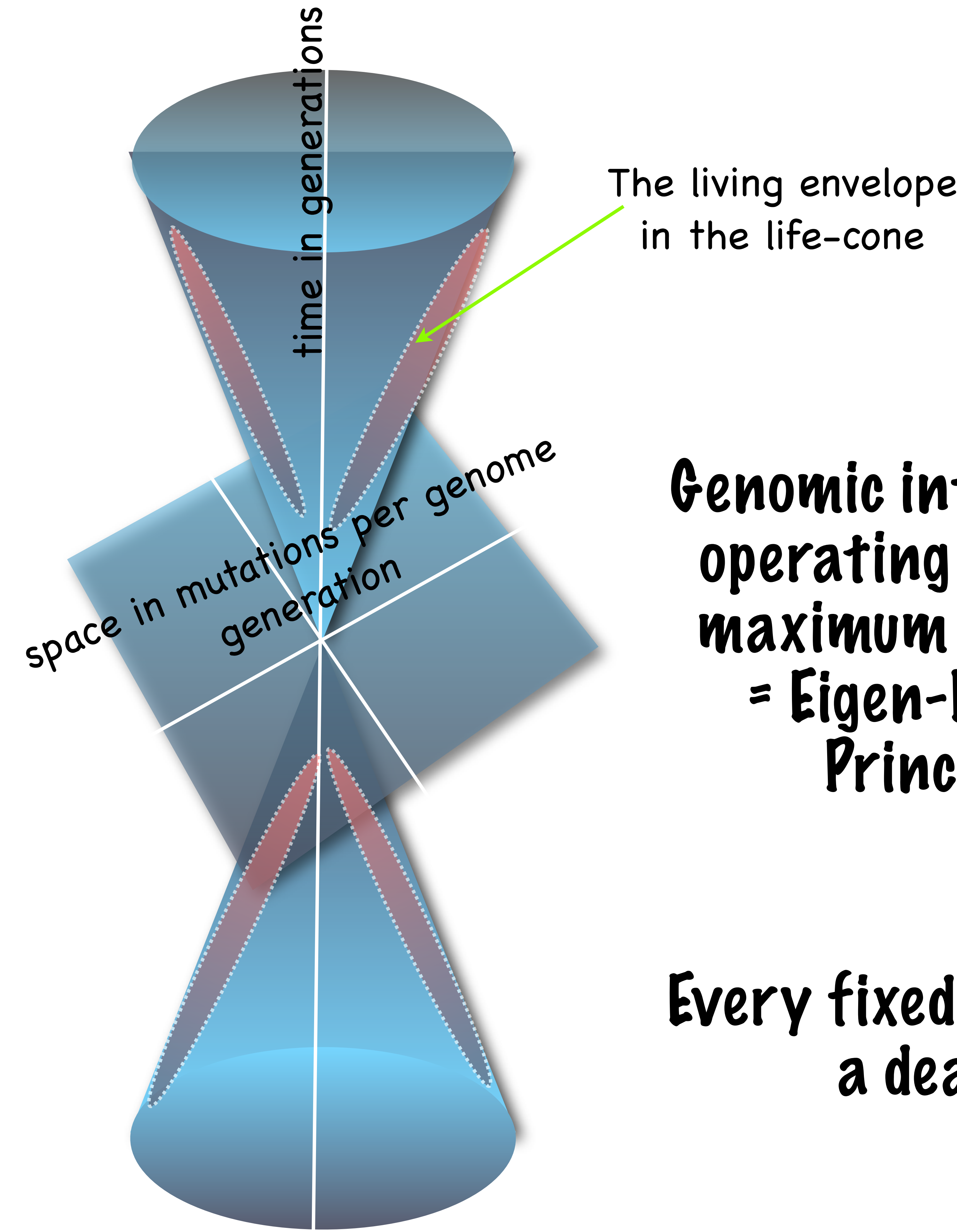
$$L = km^{\frac{1}{4}}$$



$$\mu = km^{-\frac{1}{4}}$$

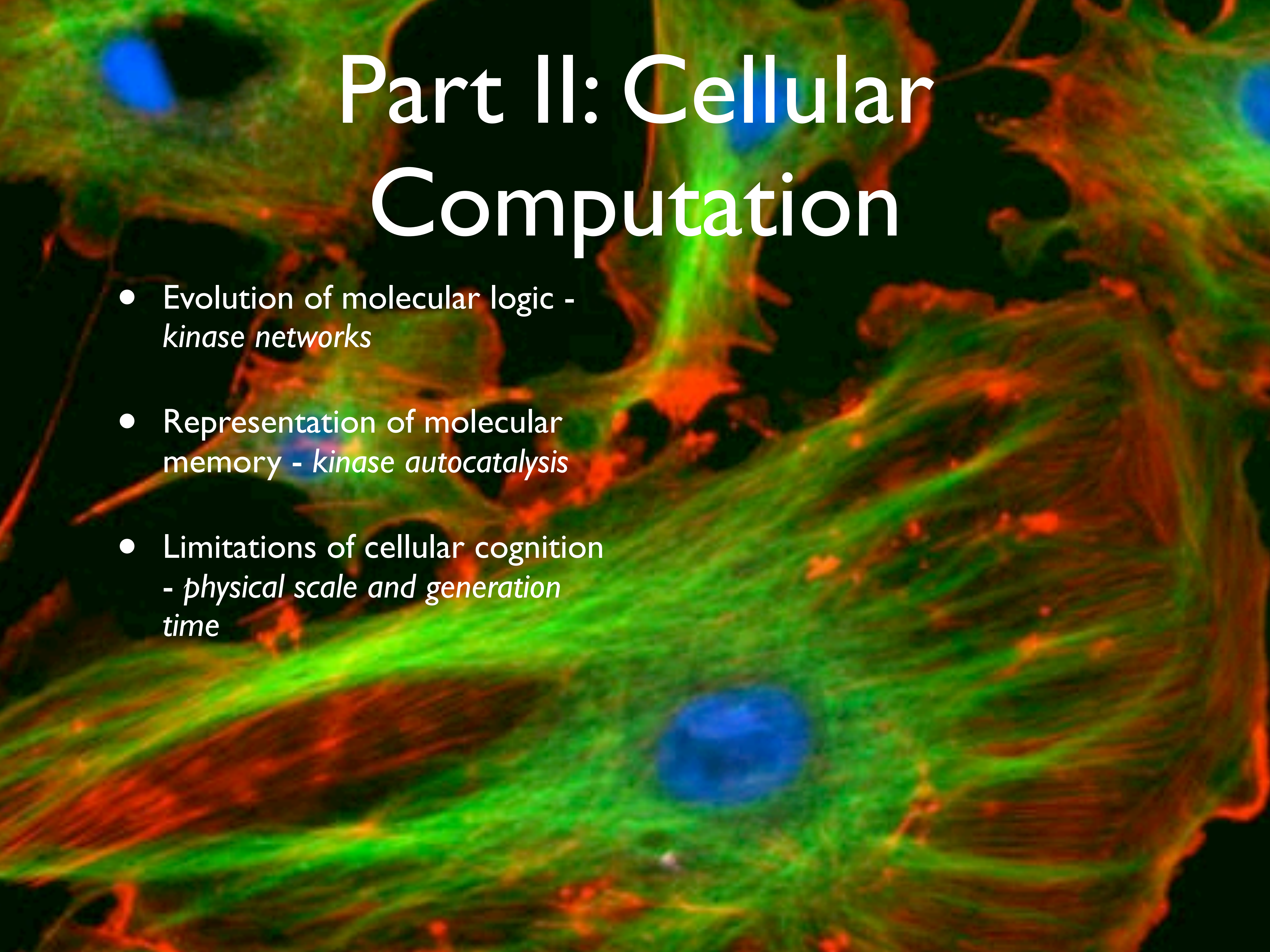


$$\mu = \frac{1}{L}$$



Genomic inference is operating near its maximum velocity = Eigen-Muller Principle

Every fixed bit needs a death

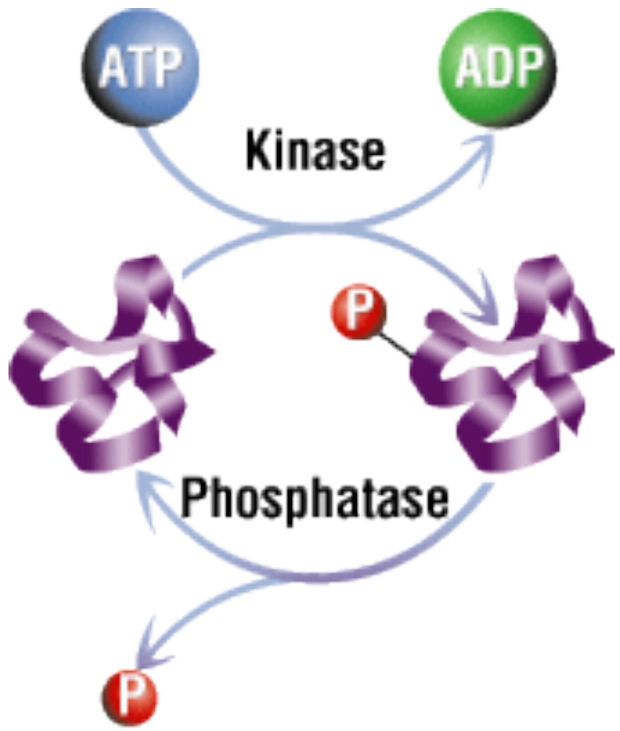


Part II: Cellular Computation

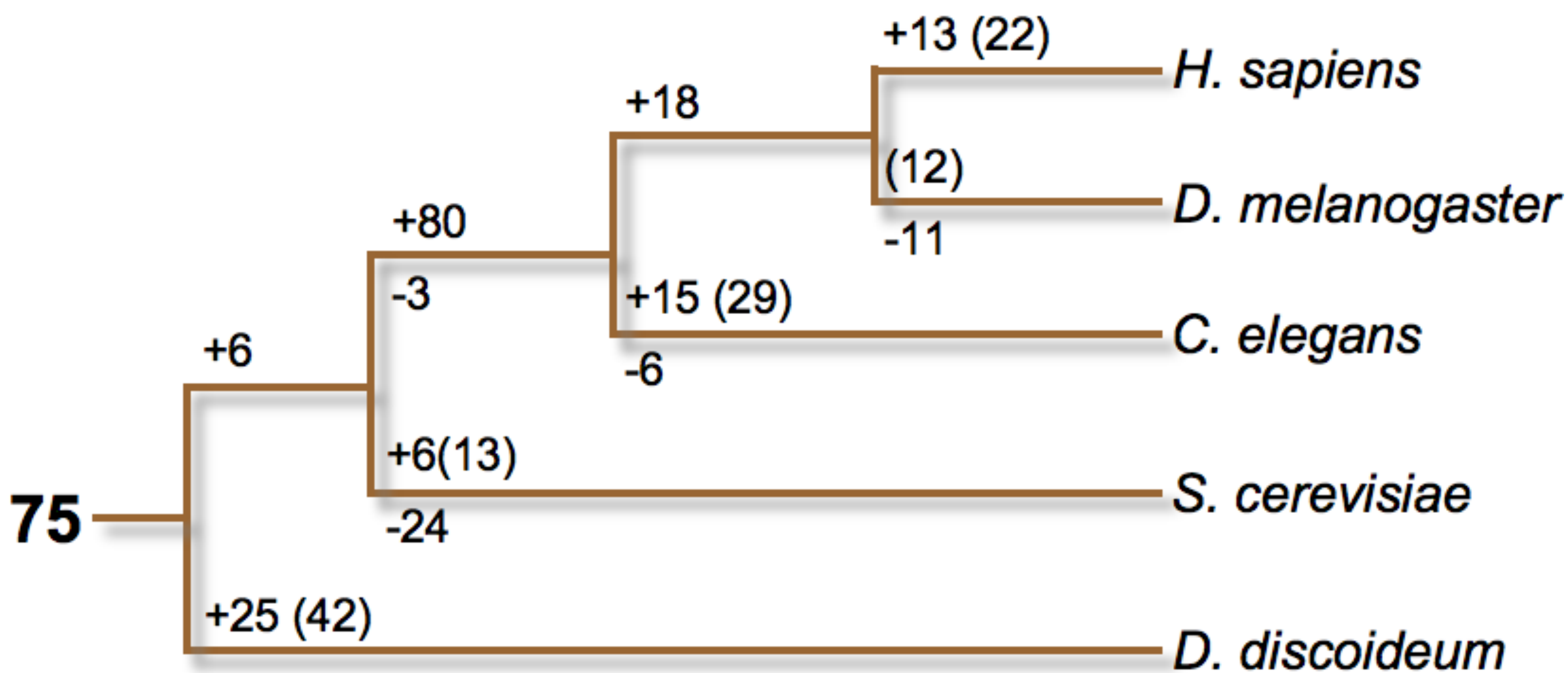
- Evolution of molecular logic - *kinase networks*
- Representation of molecular memory - *kinase autocatalysis*
- Limitations of cellular cognition - *physical scale and generation time*

Phosphorylation:

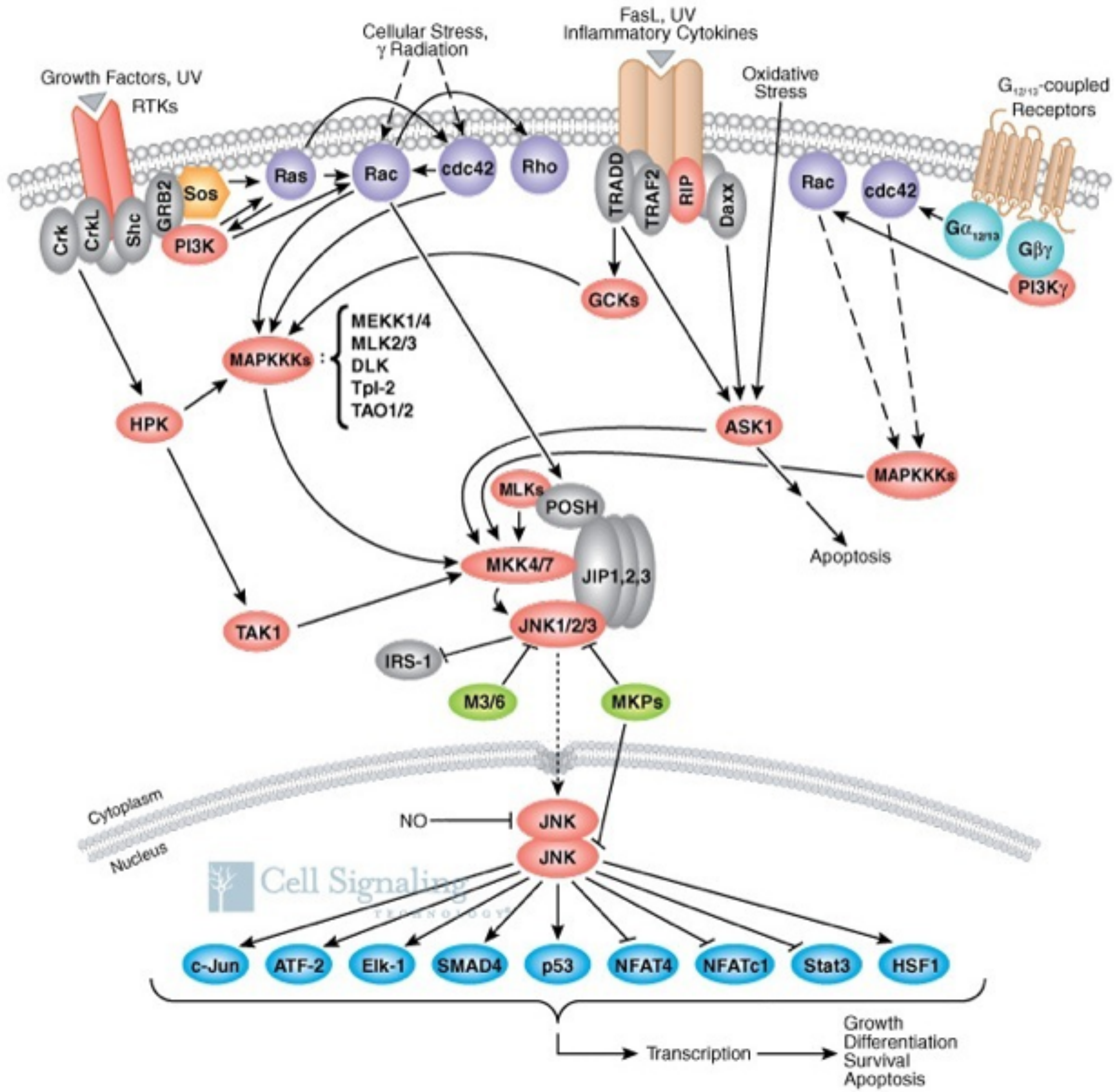
Modulation of Protein Function



Kinases ~ 2% genes (kinome)
Phosphorylate around 30% proteins

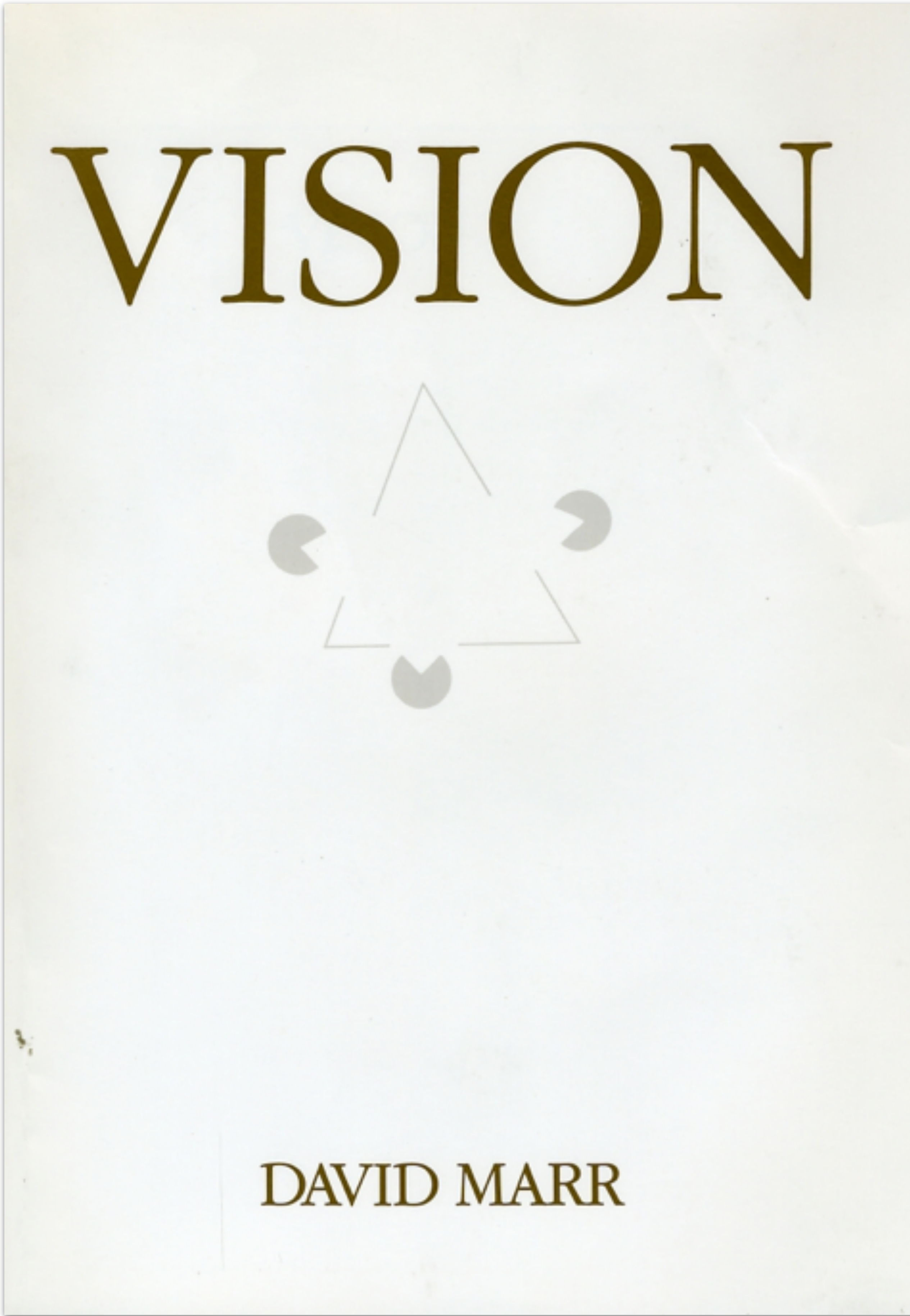


From Goldberg et al. PLoS (2006)



Cell Signaling Technology 2002

Computations, Algorithms
Mechanisms



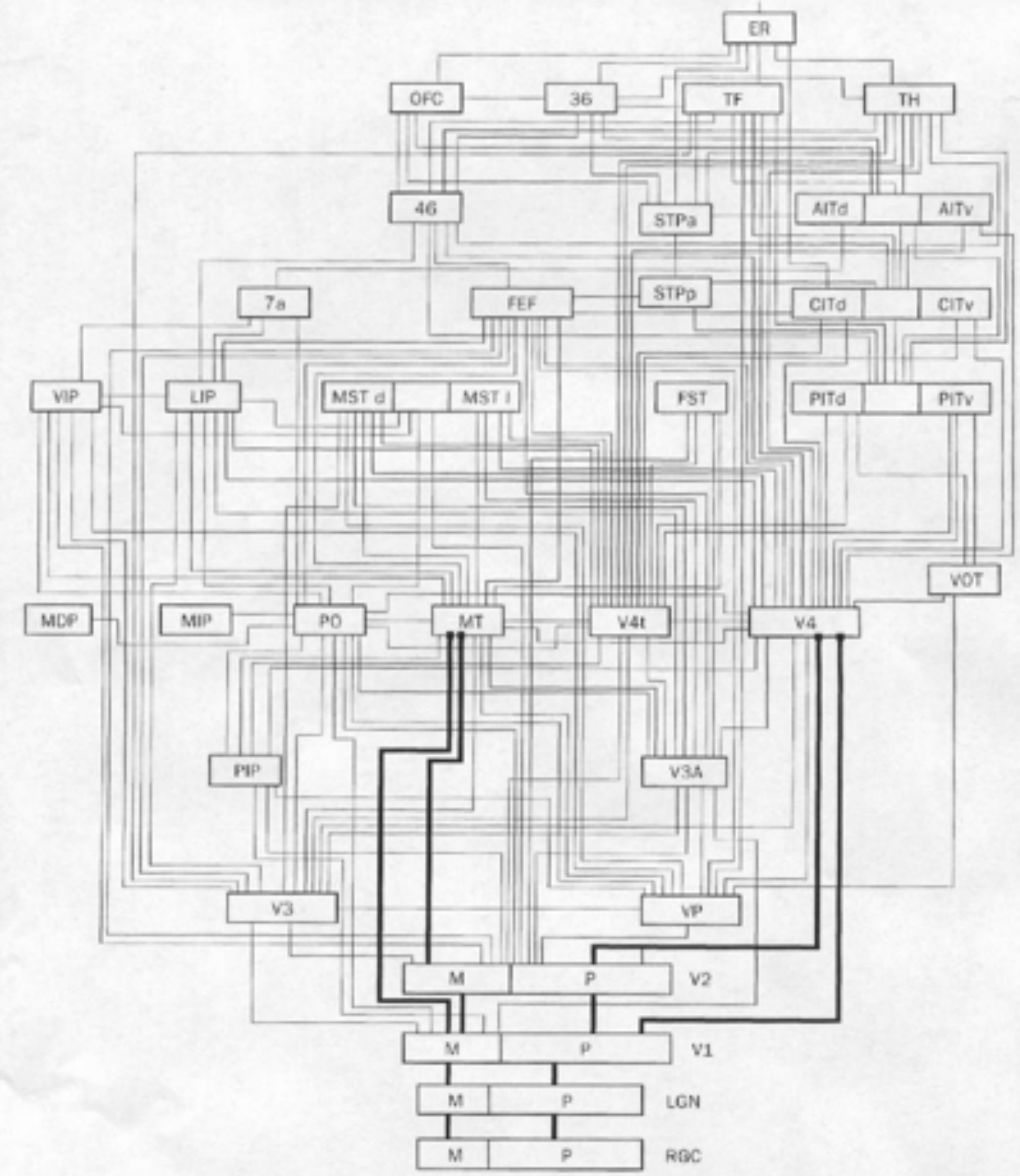


FIGURE 4.15 Diagram showing the hierarchical arrangement of visual processing stages, starting with the retina (bottom of diagram) and moving up through the multiple visual areas of the brain. The bold lines show the P and M pathways discussed in the text. (Adapted from Felleman and Van Essen, 1991.)

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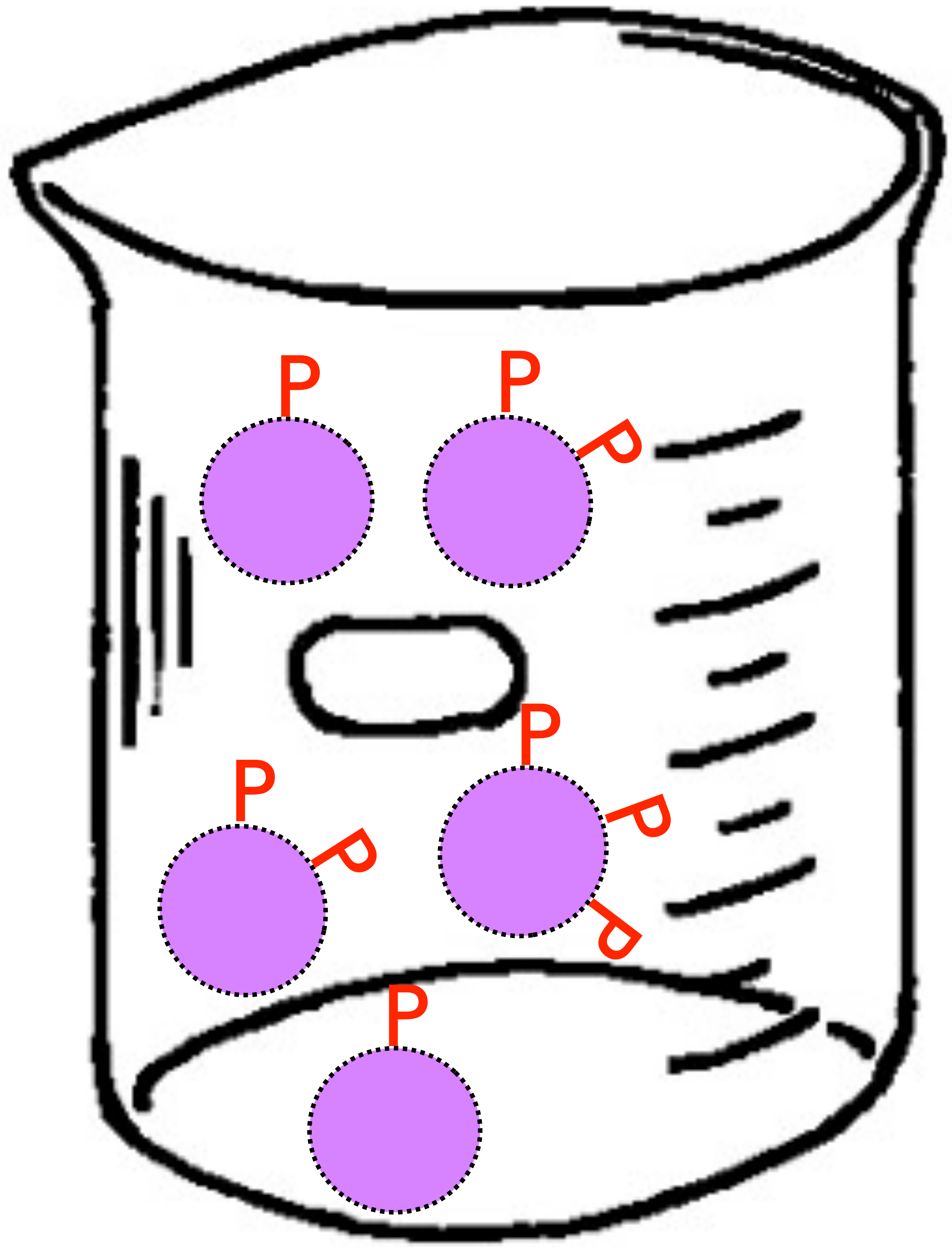
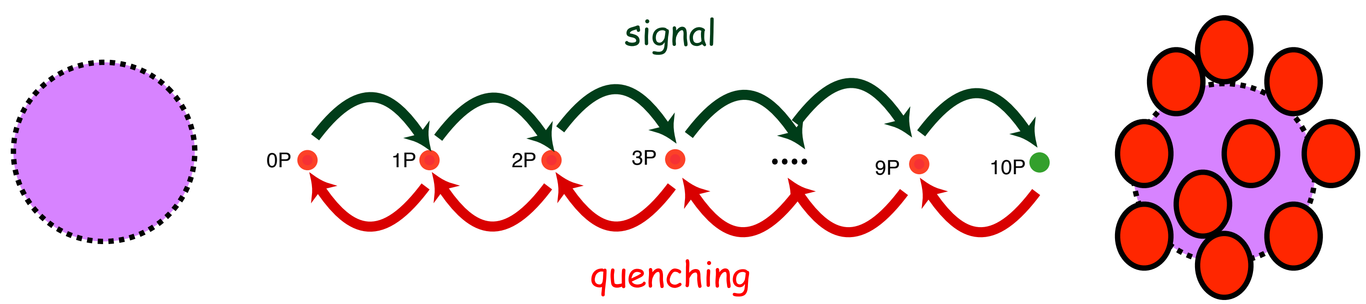
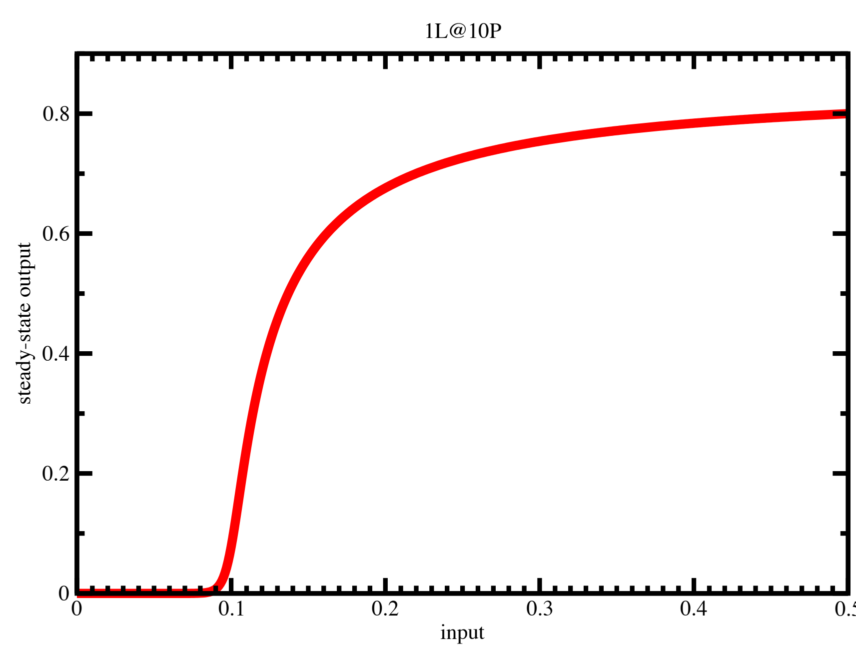
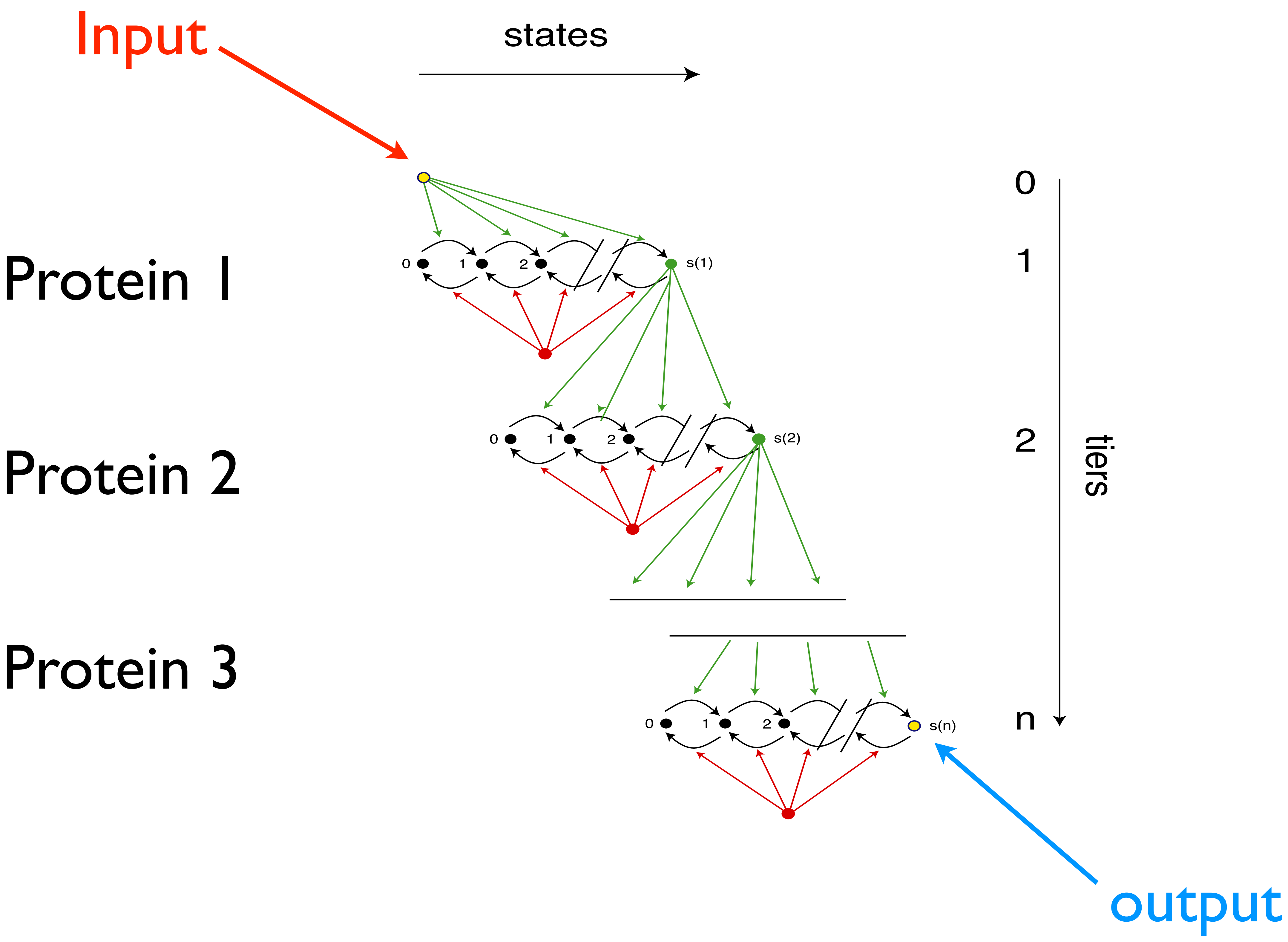
Kinase computations and algorithms



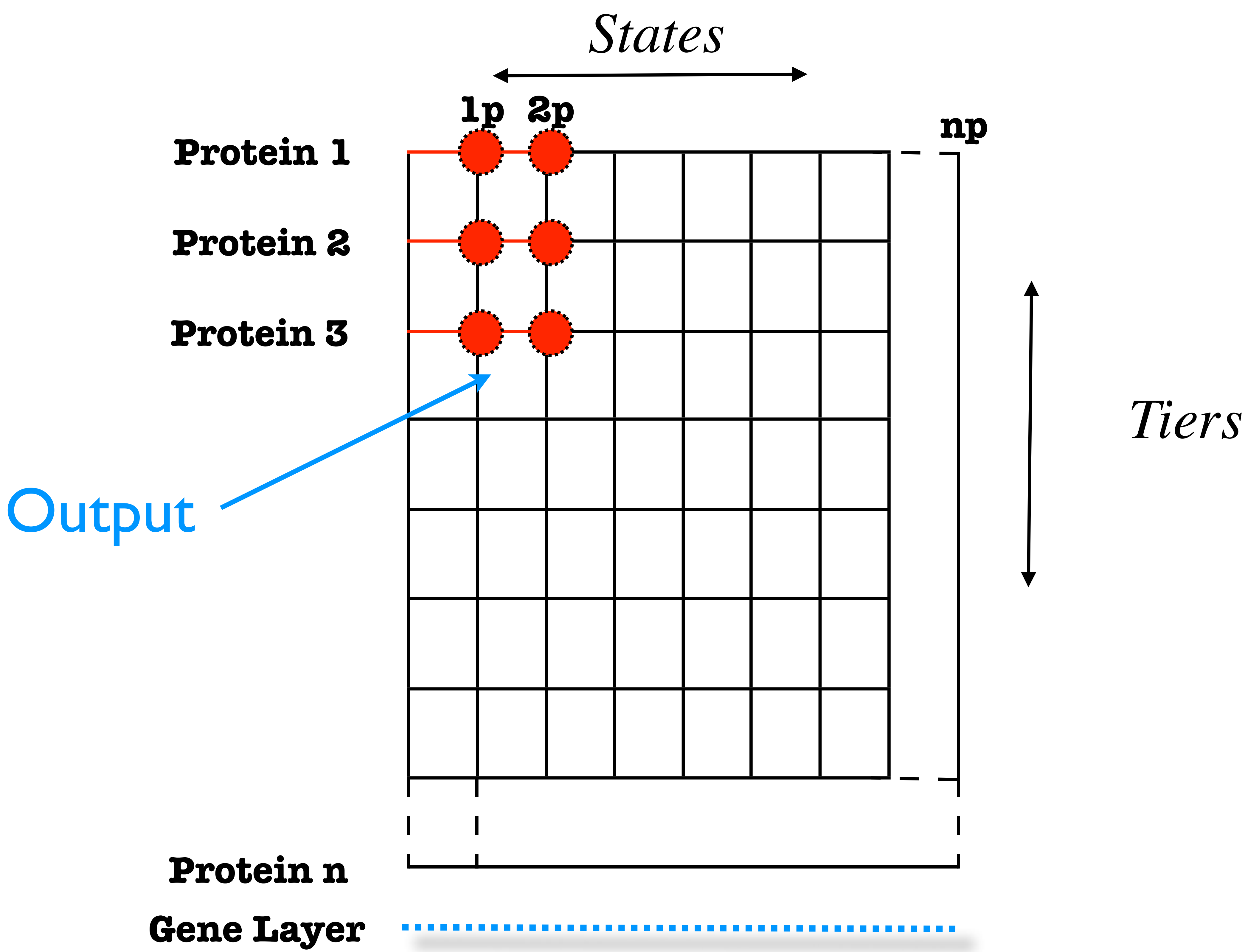


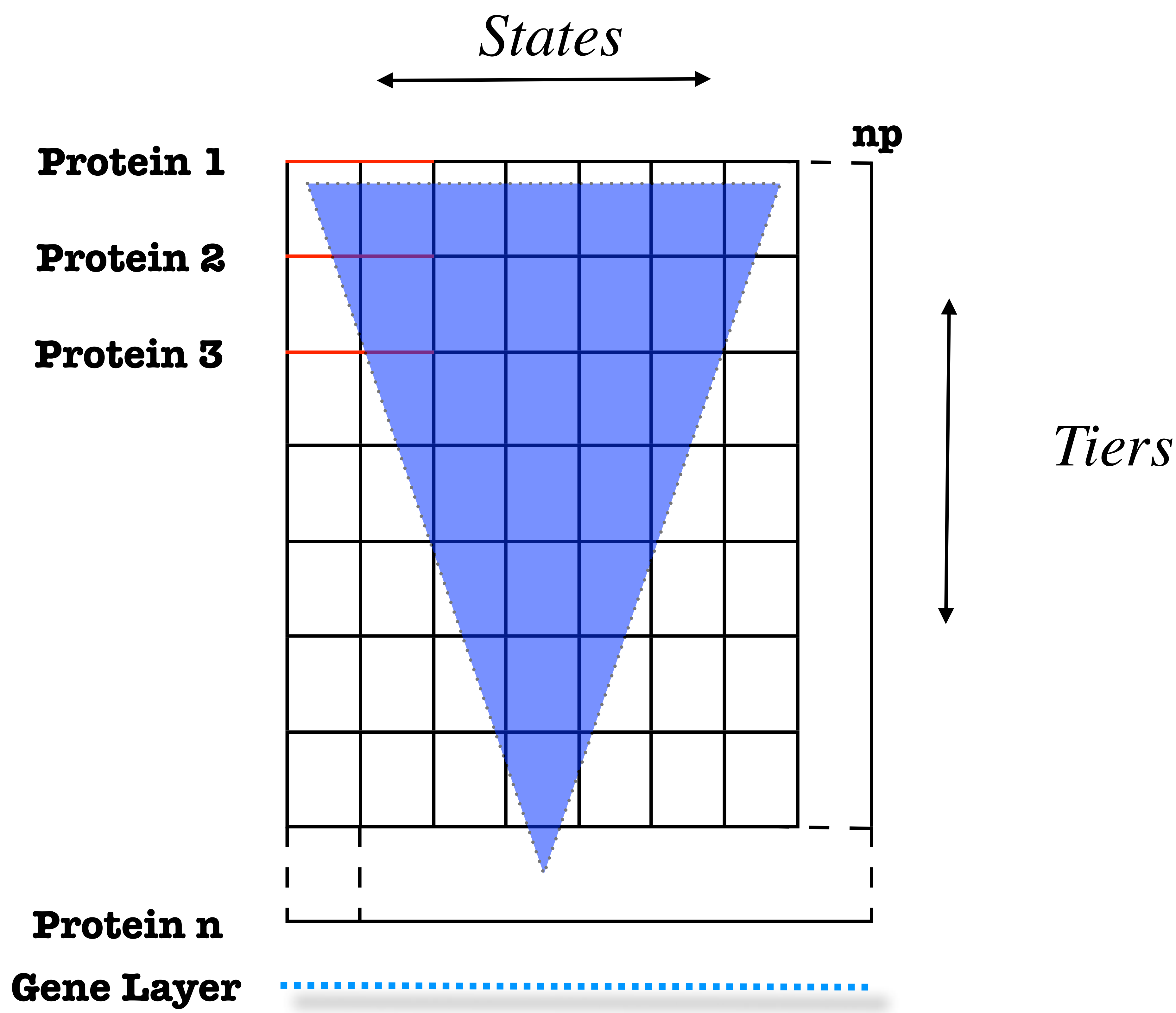


hypersensitivity



Input
states
Protein 1
Protein 2
Protein 3
0
1
2
n
tiers
s(1)
s(2)
s(n)
output

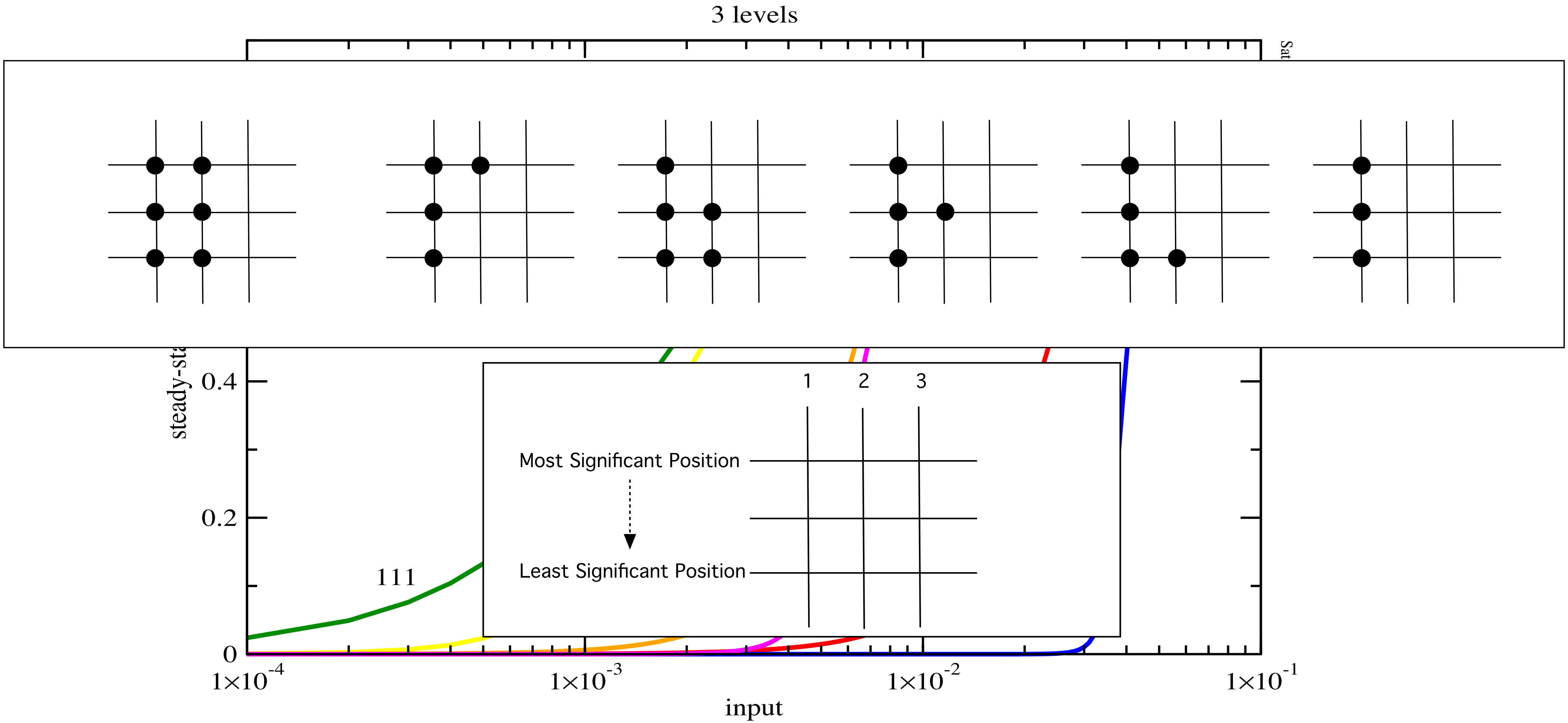

States
1p
2p
np
Protein 1
Protein 2
Protein 3
Tiers
Output
Protein n
Gene Layer



Phosphobase. ELM

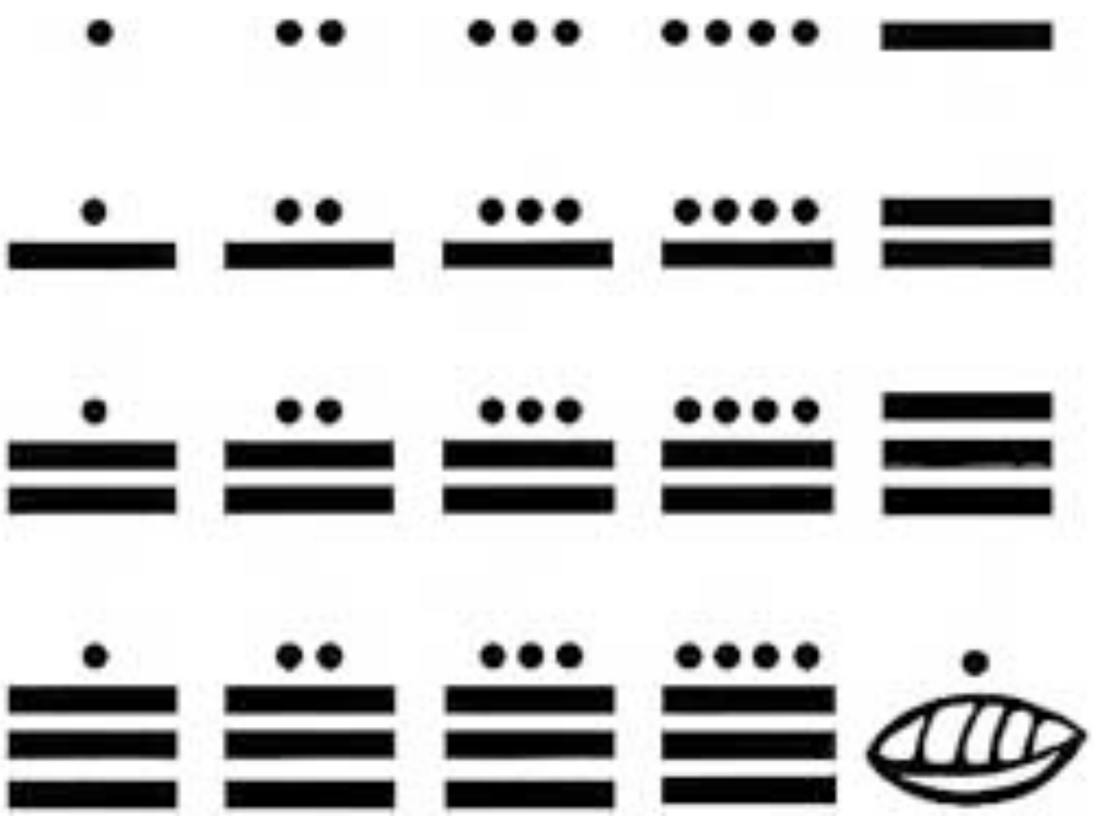
THE MOLECULAR ABACUS

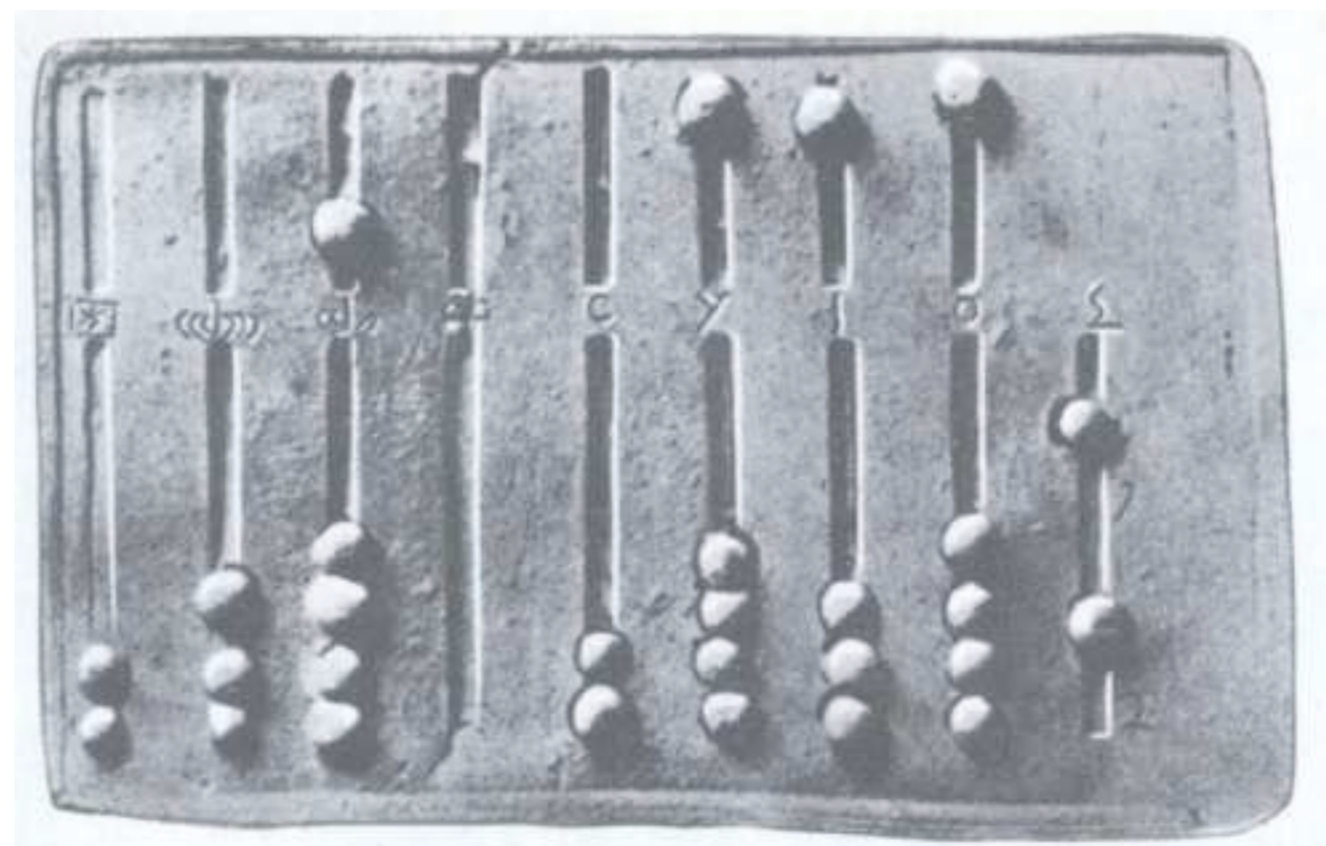
Third Tier Concentrations



I(222) > I(211)> I(122)>I(121)>I(112)>I(111)

Place Value-based Number Systems






Problems of Time Scales

Communication

Persistent Protein Kinase Activation in the Maintenance Phase of Long-term Potentiation*

(Received for publication, September 12, 1991)

Eric Klann, Shu-Jen Chen, and J. David Sweatt

From the Division of Neuroscience, Baylor College of Medicine, Houston, Texas 77030

Long-term potentiation (LTP) of synaptic transmission in the hippocampus is a robust form of synaptic plasticity that may contribute to mammalian memory formation. A variety of pharmacological evidence suggests that persistent kinase activation contributes to the maintenance of LTP. To determine whether persistent activation of protein kinases was associated with the maintenance phase of LTP, protein kinase activity was measured in control and LTP samples using exogenous protein kinase substrates in an *in vitro* assay of homogenates of the CA1 region of rat hippocampal slices. After LTP, protein kinase activity was persistently increased, and the induction of this effect was blocked by the *N*-methyl-D-aspartate receptor antagonist DL-2-amino-5-phosphonovaleric acid. The increased protein kinase activity was found to be significantly attenuated by $PKC_{(19-36)}$, a selective peptide inhibitor of protein kinase C. Thus, LTP is associated with an *N*-methyl-D-aspartate receptor-mediated generation of a persistently activated form of protein kinase C. These data lend strong support to the model that persistent protein kinase activation contributes to the maintenance of LTP.

The Journal of Neuroscience, June 15, 2000, 20(12):4497–4505

Presynaptic Protein Kinase Activity Supports Long-Term Potentiation at Synapses Between Individual Hippocampal Neurons

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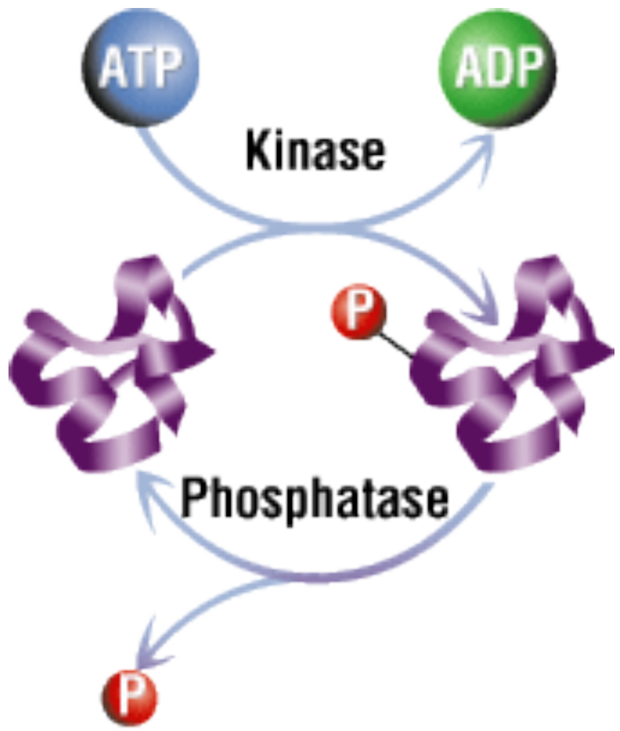
Department of Molecular and Cellular Physiology, Stanford University School of Medicine, Stanford, California 94305-5345

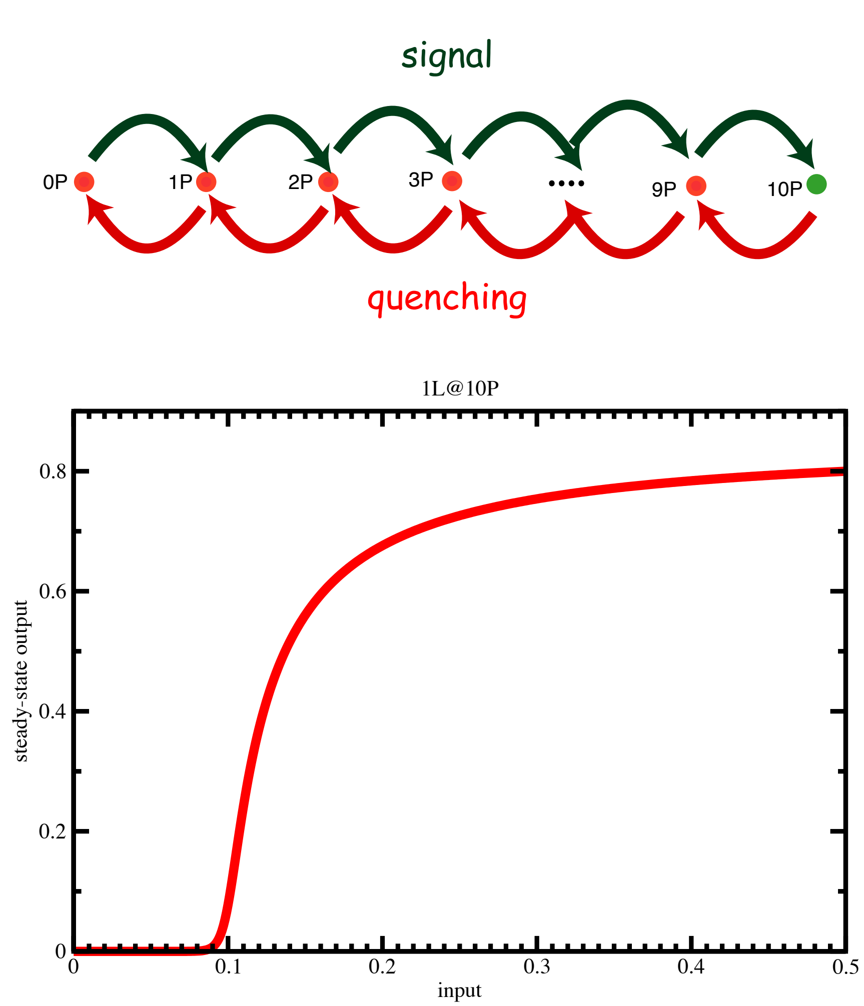
Simultaneous microelectrode recording from two individual synaptically connected neurons enables the direct analysis of synaptic transmission and plasticity at a minimal synaptic connection. We have recorded from pairs of CA3 pyramidal neurons in organotypic hippocampal slices to examine the properties of long-term potentiation (LTP) at such minimal connections. LTP in minimal connections was found to be identical to the NMDA-dependent LTP expressed by CA3–CA1 synapses, demonstrating this system provides a good model for the study of the mechanisms of LTP expression. The LTP at minimal synaptic connections does not behave as a simple increase in transmitter release probability, because the amplitude of unitary EPSCs can increase several-fold, unlike what is observed when release probability is increased by raising extracellular calcium. Taking advantage of the relatively short axon connecting neighboring CA3 neurons, we found it feasible to introduce pharmacological agents to the interior of presynaptic terminals by injection into the presynaptic soma and have used this technique to investigate presynaptic effects on basal transmission and LTP. Presynaptic injection of nicotinamide reduced basal transmission, but LTP in these pairs was essentially normal. In contrast, presynaptic injection of H-7 significantly depressed LTP but not basal transmission, indicating a specific role of presynaptic protein kinases in LTP. These results demonstrate that pharmacological agents can be directly introduced into the presynaptic cell and that a purely presynaptic perturbation can alter this plasticity.

Key words: long-term potentiation; presynaptic; protein kinase; hippocampus; electrophysiology; synaptic transmission

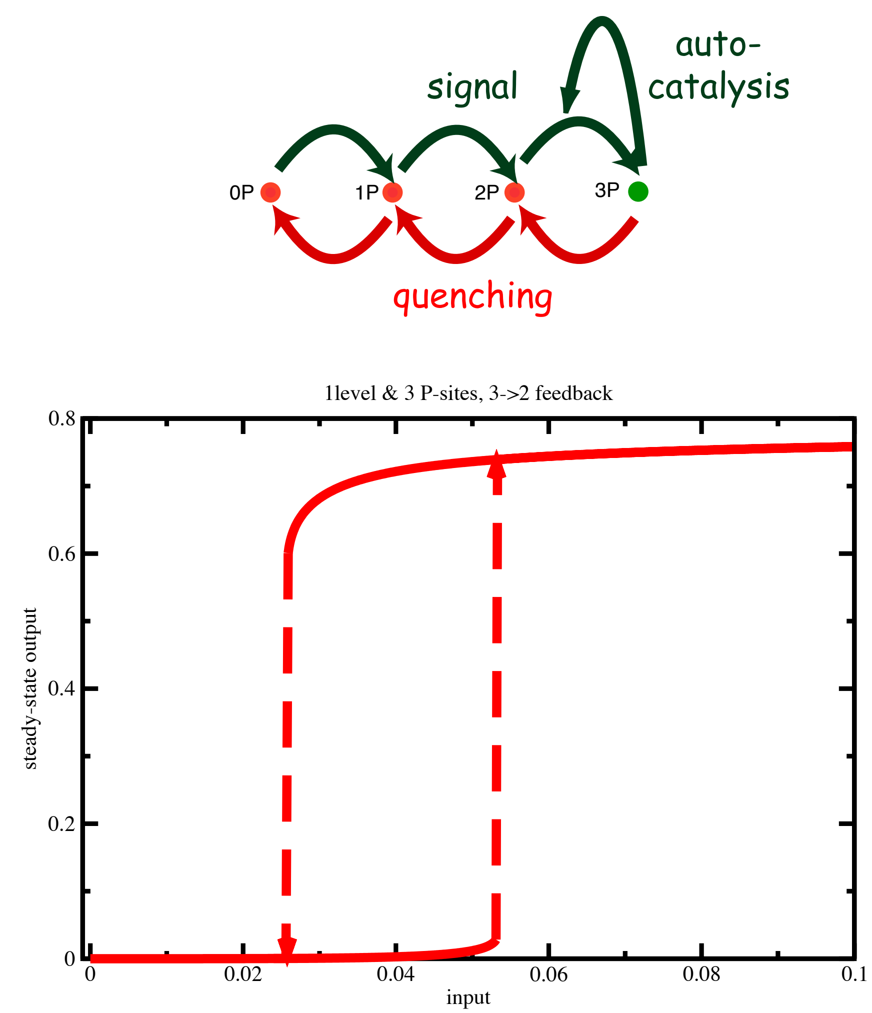
Phosphorylation:

Modulation of Protein Function

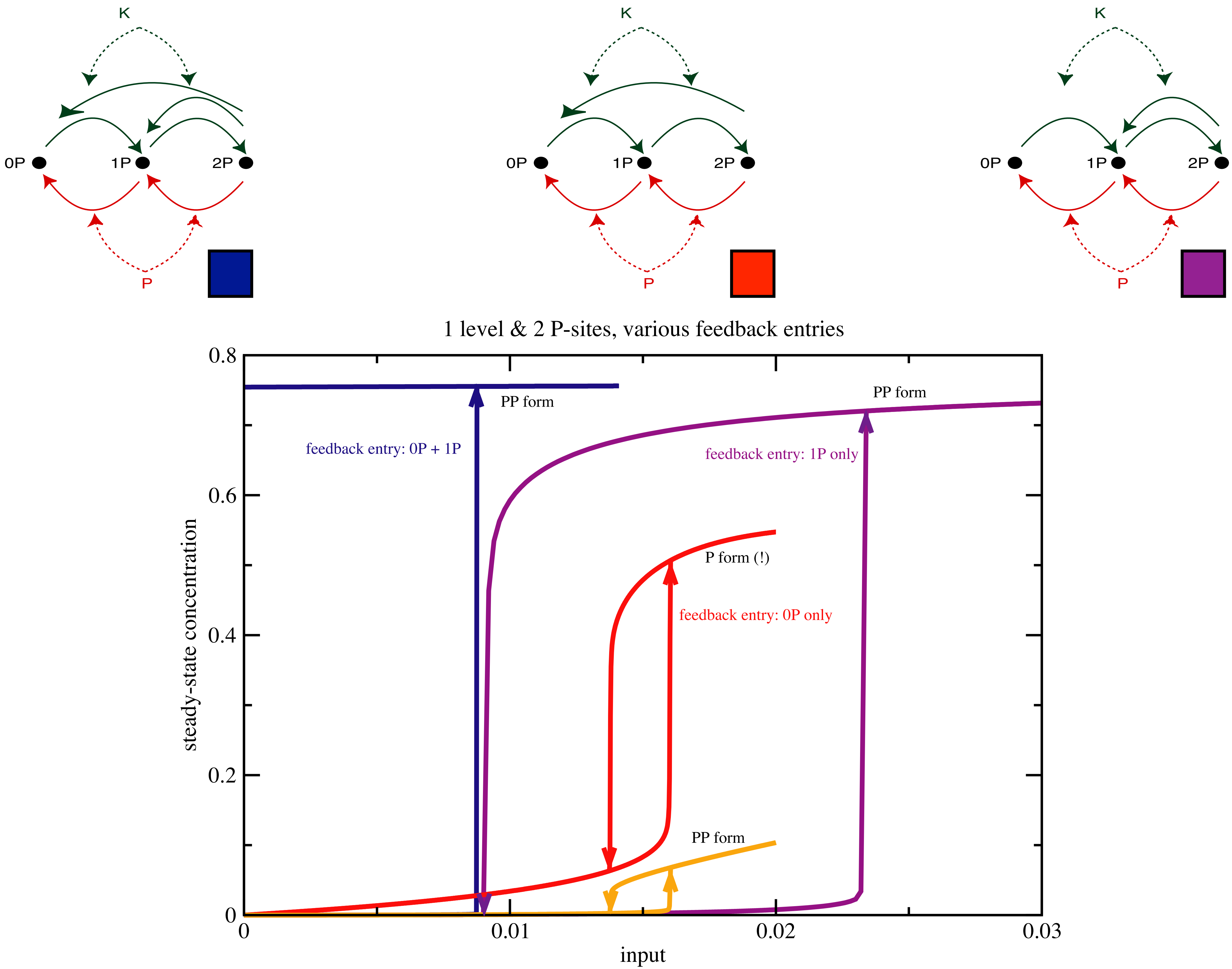




hypersensitivity

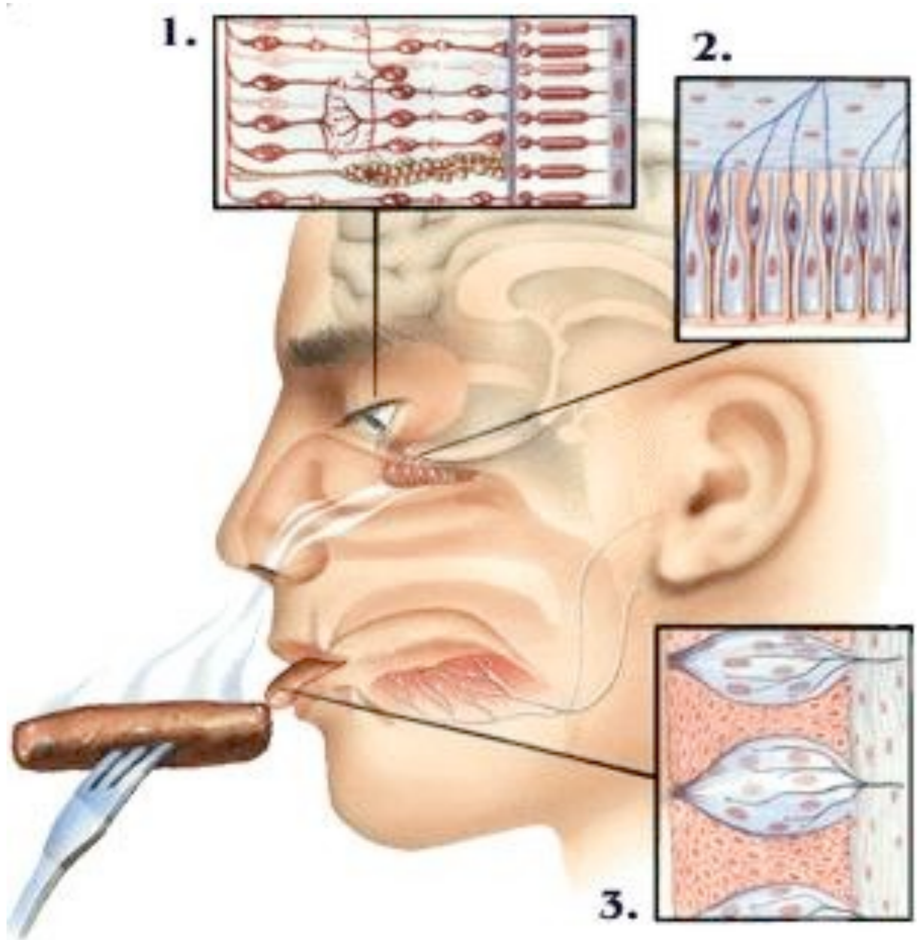


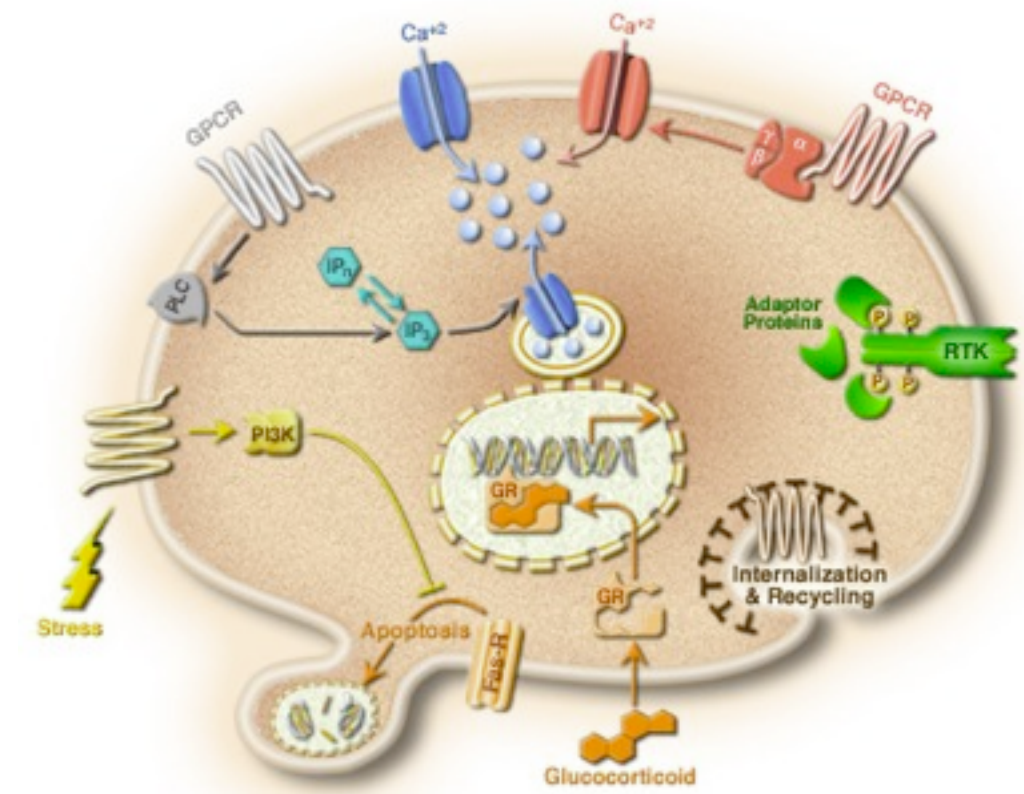
switch


K
0P
1P
2P
P
1 level & 2 P-sites, various feedback entries
0.8
0.6
0.4
0.2
0
0.01
0.02
0.03
steady-state concentration
input
PP form
feedback entry: 0P + 1P
PP form
feedback entry: 1P only
P form (!)
feedback entry: 0P only
PP form

Fundamental Limitations of Cells

The Search for an Eigen-Muller Style Principle for the Cell





	Connectivity	Connectivity Density	Dynamics	Differentiation (connection & function)
Nervous system	Physical & Chemical = short & long-range	High	Variable time Constants & global	By Activity & Connection
Cell	Chemical - short-range	Sparse	Generally Rapid & localised	By sequence

Summary - *things to consider*

- Evolution and cognition are both inferential processes
- Cognitive molecular devices are ubiquitous
- Much as we can consider mechanism, algorithm and function for brains we can do so for cells (e.g. molecular abacus)
- Genomes are inferentially limited by the Muller-Eigen principle
- Cells (receptor & protein networks) multiply genetic states, and introduce new integration and temporal functions
- The seeds of neural cognition (representation, logic-switches and memory) reside in genomic and cellular cognition (smaller and smaller elephants much of the way down..)

A Few more (biased) References

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