Universal laws and architecture 4:
Layering, learning, and decentralized control

John Doyle

John G Braun Professor

Control and Dynamical Systems, EE, BE

Caltech

Outline: Laws and architectures

- Motivating case studies
  - Brains
  - Computers, networks
  - Cells
  - Physiology
- Layered architecture of the cell
  - replication, transcription, translation
  - metabolism, signaling, chemotaxis
  - 2CST and cross layer control

Compute

Turing

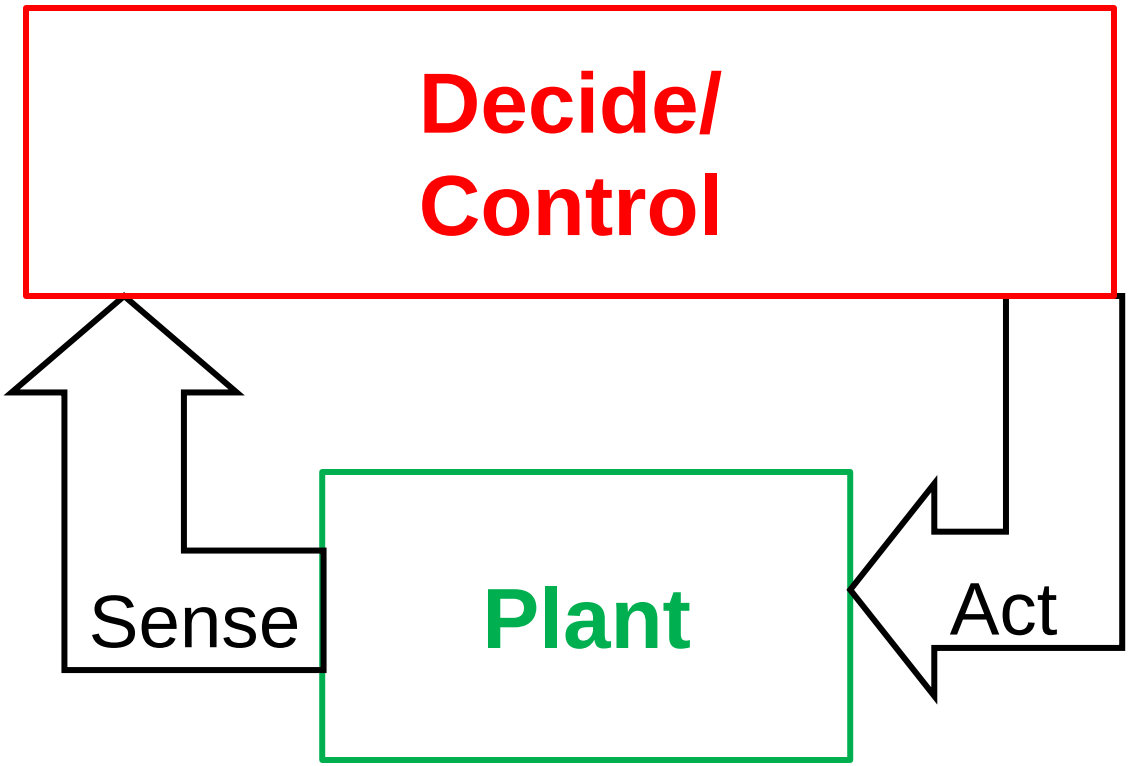
Delay is *most* important

Bode

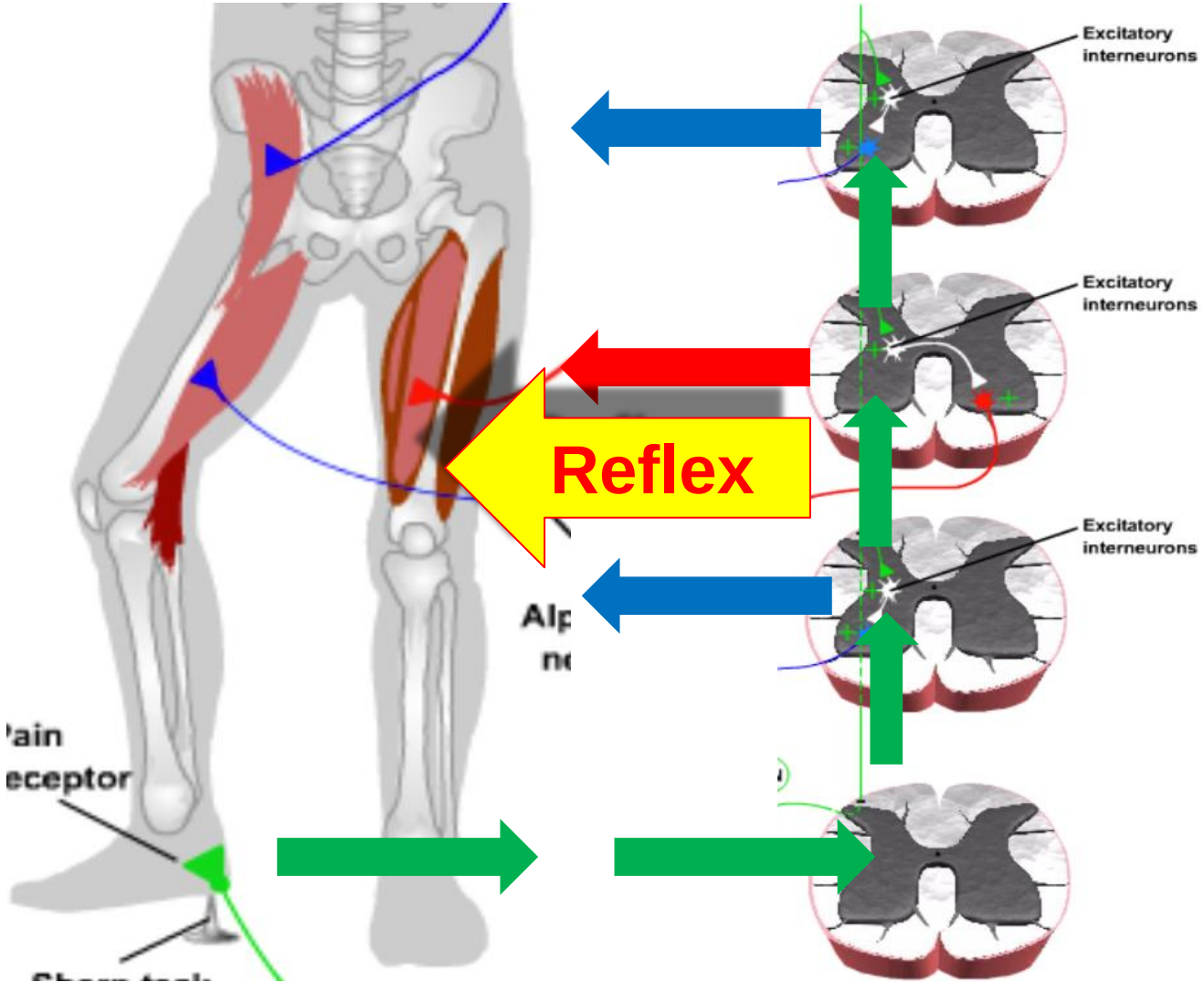
Control

Closing the loop

- On the “plant”
- On the “story”

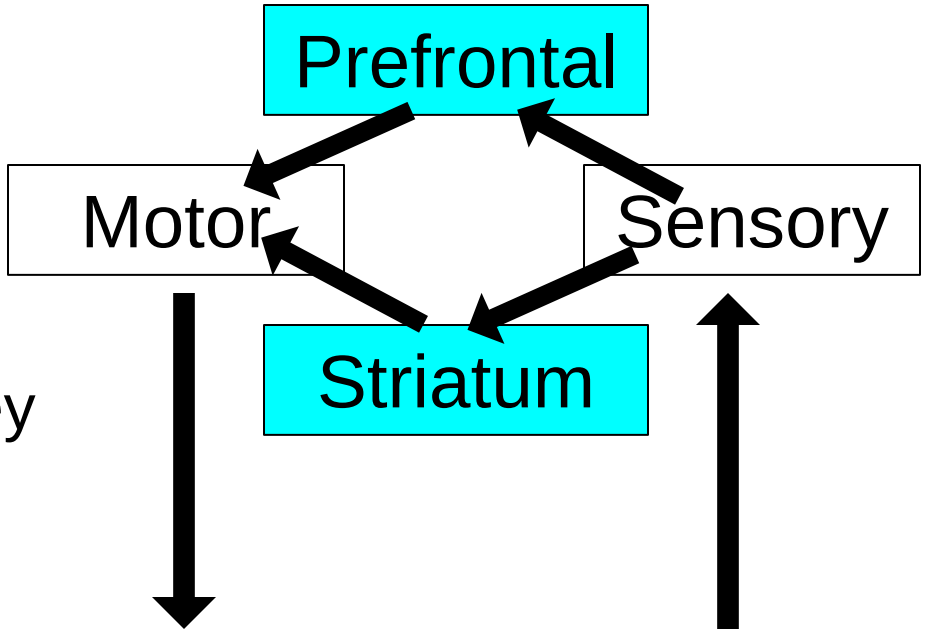


Neuro motivation



Fast
Inflexible

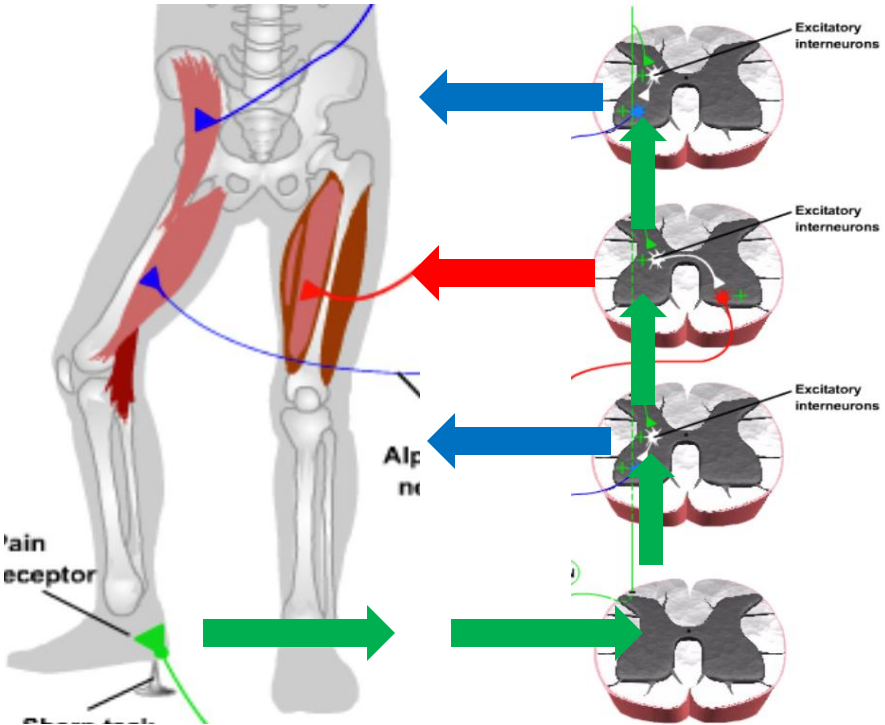
Slow Flexible



Learning

Ashby & Crossley

- **Acquire**
- Translate/ integrate
- Automate



Thanks to Bassett & Grafton

Slow Flexible

Prefrontal

Motor

Sensory

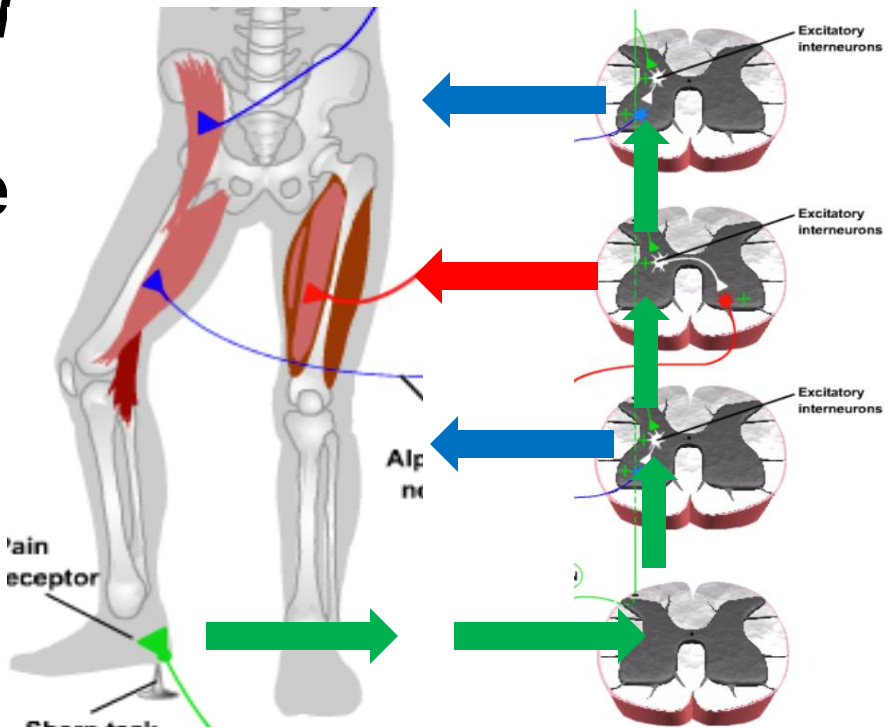
Striatum

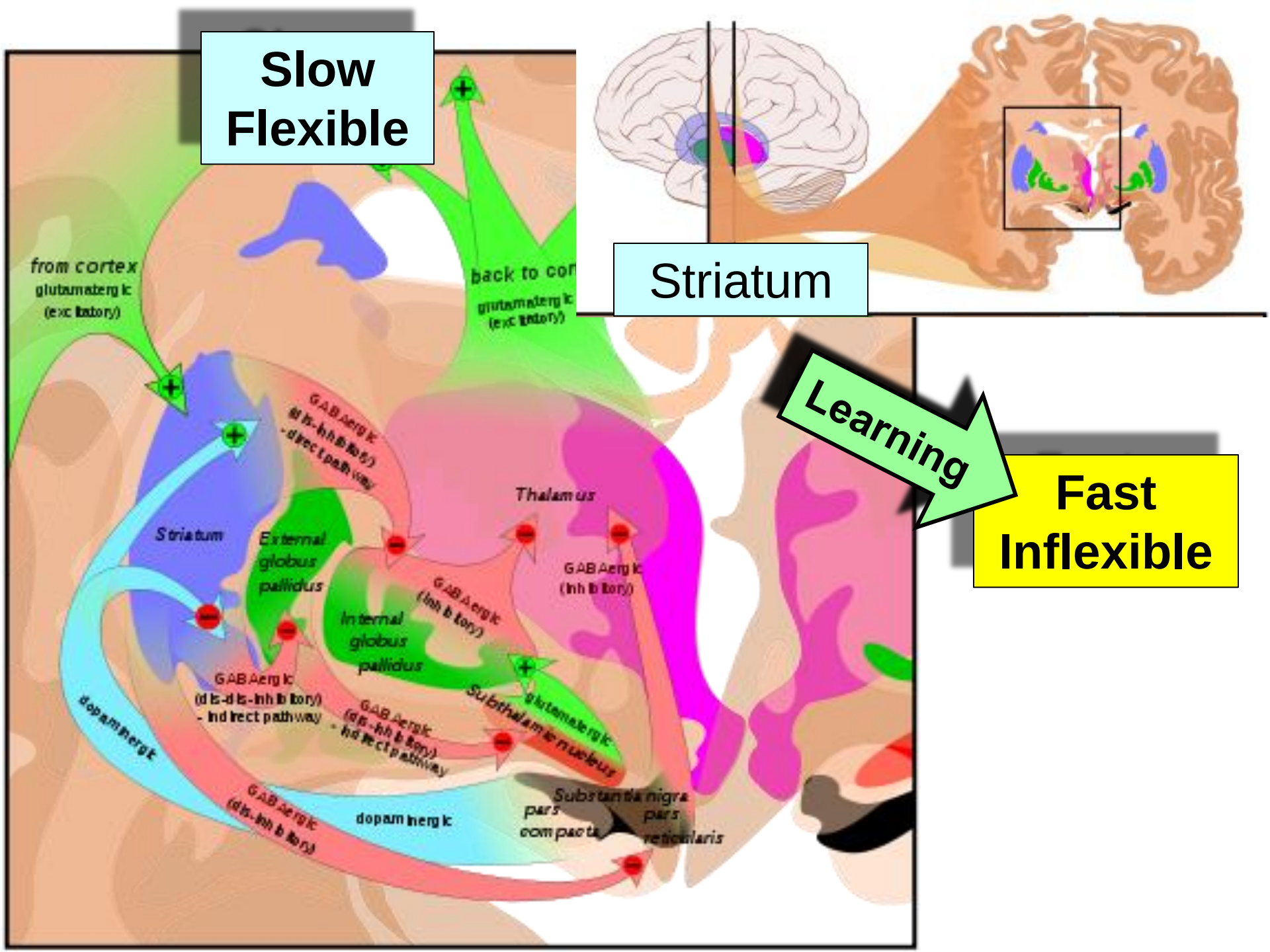
Learning

Fast Inflexible

Ashby & Crossley

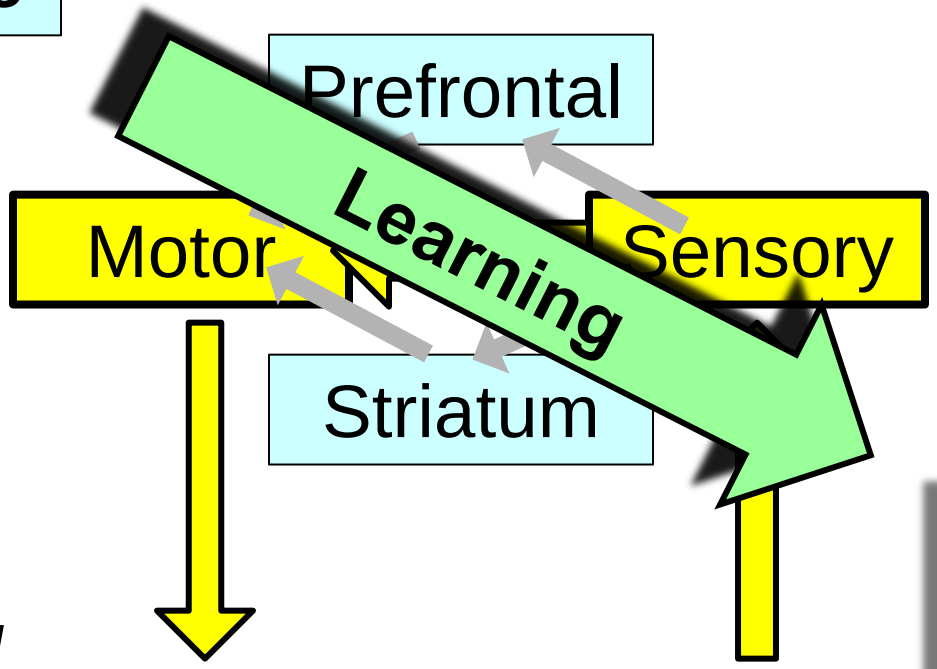
- Acquire
- **Translate/ integrate**
- **Automate**




Slow
Flexible
from cortex
glutamatergic
(excitatory)
back to cor
glutamatergic
(excitatory)
Striatum
Learning
Fast
Inflexible
Striatum
External
globus
pallidus
Internal
globus
pallidus
Thalamus
GABAergic
(inhibitory)
GABAergic
(inhibitory)
GABAergic
(dis-inhibitory)
- direct pathway
GABAergic
(dis-dis-inhibitory)
- indirect pathway
GABAergic
(dis-inhibitory)
- indirect pathway
Subthalamic nucleus
glutamatergic
dopaminergic
GABAergic
(dis-inhibitory)
dopaminergic
Substantia nigra
pars
compacta
pars
reticularis

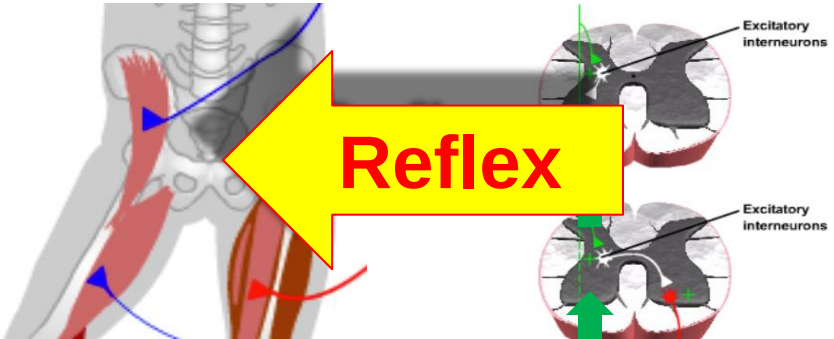
Build on Turing to show what is *necessary* to make this work.

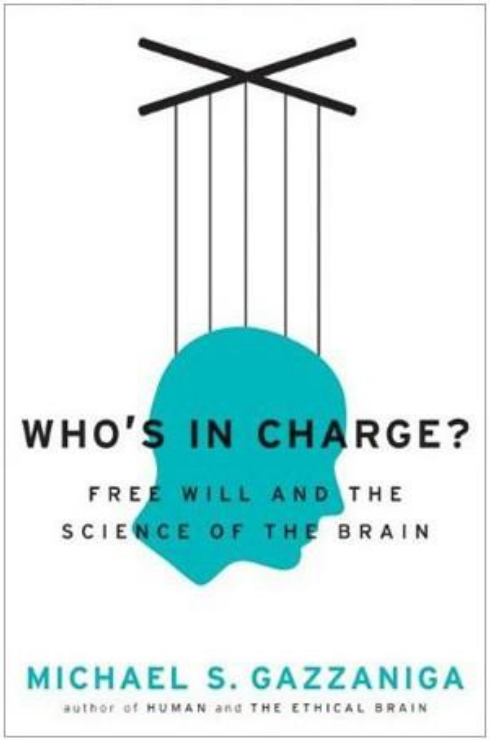
Slow Flexible

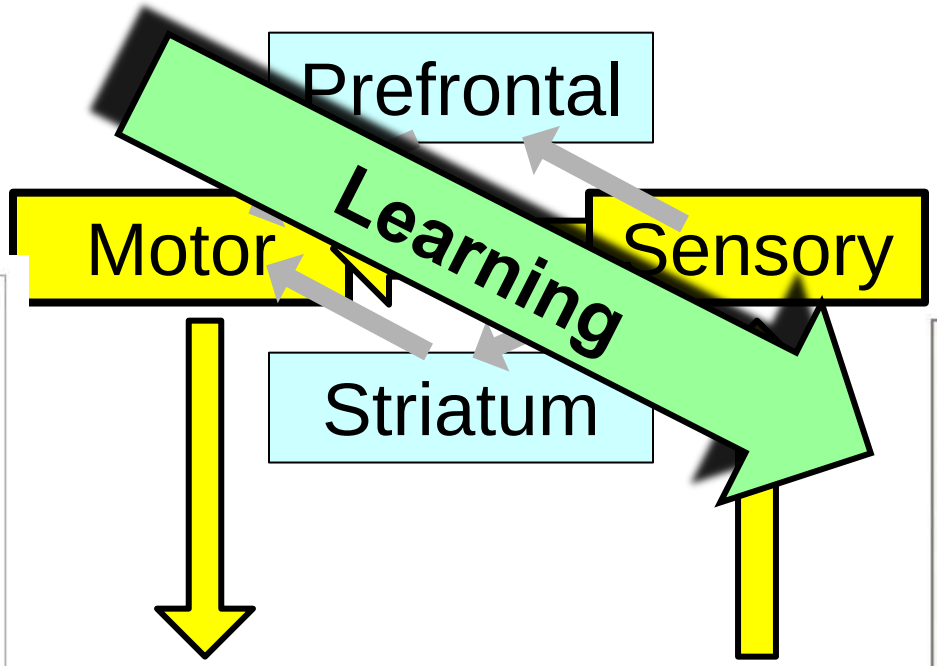


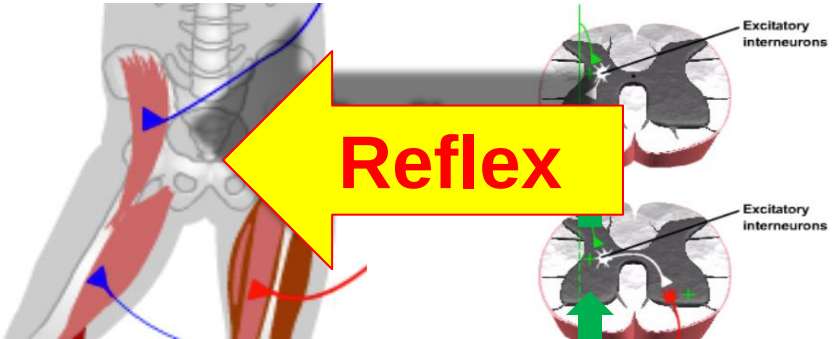
Fast Inflexible

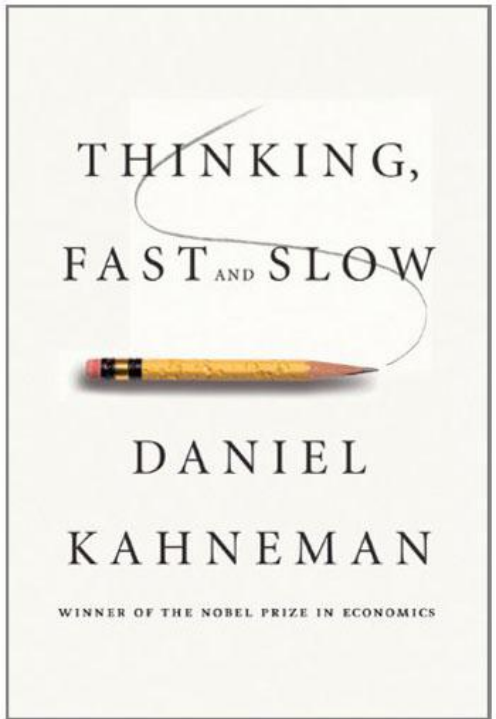
- **Acquire**
- **Translate/ integrate**
- **Automate**

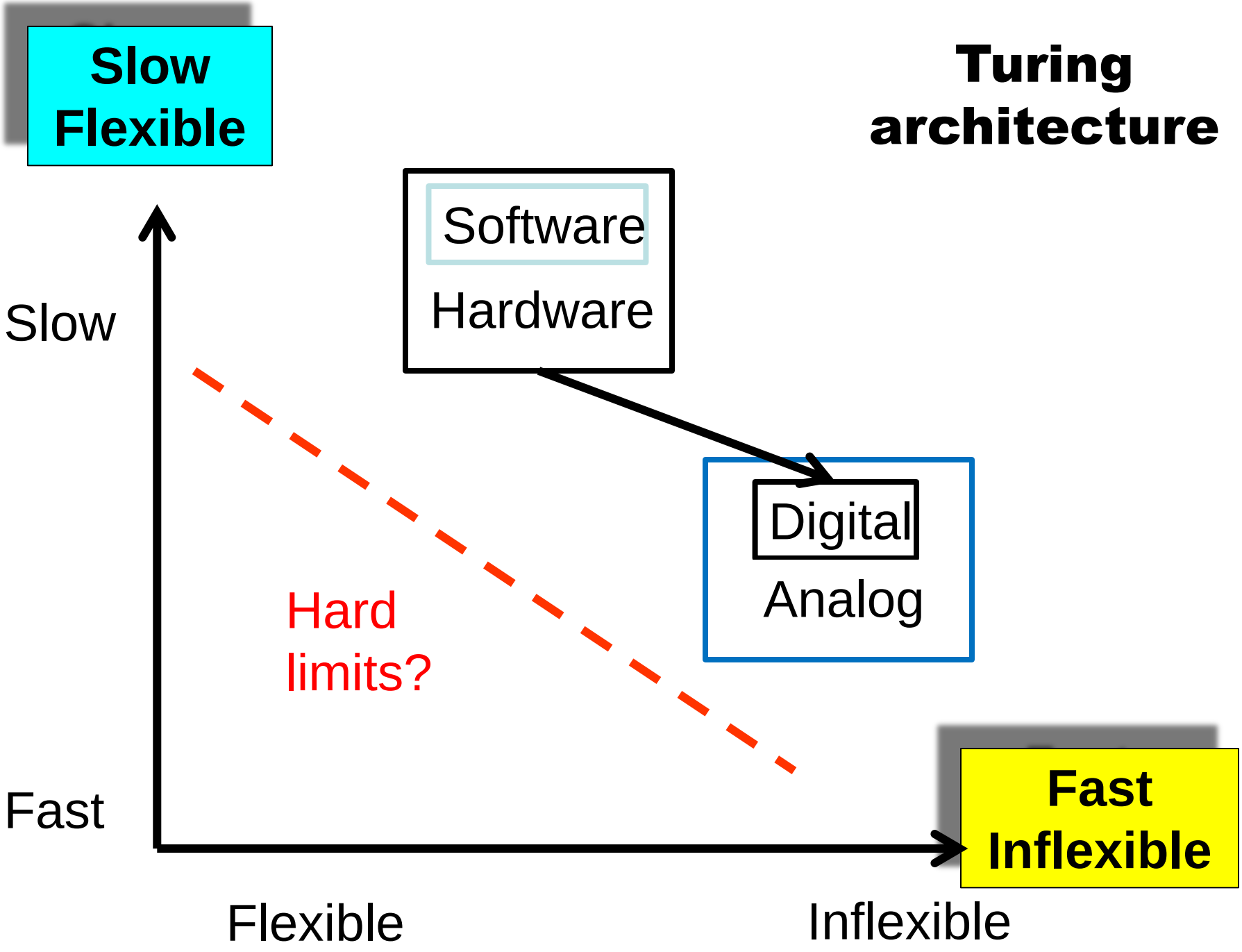



WHO'S IN CHARGE?
FREE WILL AND THE SCIENCE OF THE BRAIN
MICHAEL S. GAZZANIGA
author of HUMAN and THE ETHICAL BRAIN


Prefrontal
Motor
Sensory
Striatum
Learning


Reflex
Excitatory interneurons
Excitatory interneurons


THINKING, FAST AND SLOW
DANIEL KAHNEMAN
WINNER OF THE NOBEL PRIZE IN ECONOMICS

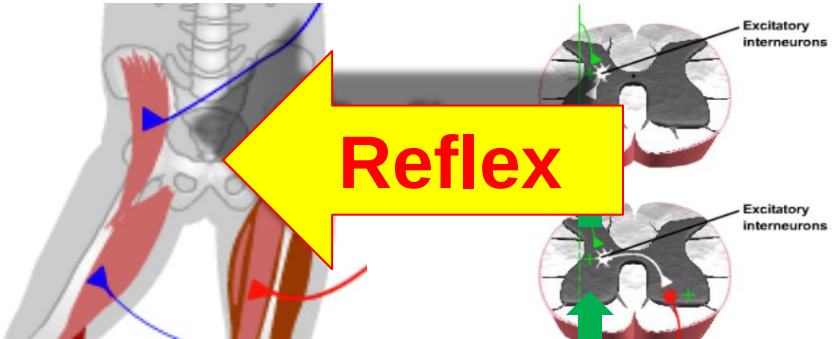

Slow
Flexible
Turing
architecture
Software
Hardware
Slow
Digital
Analog
Hard
limits?
Fast
Fast
Inflexible
Flexible
Inflexible

Wolpert, Grafton, etc

robust

Brain as ~~optimal~~ controller

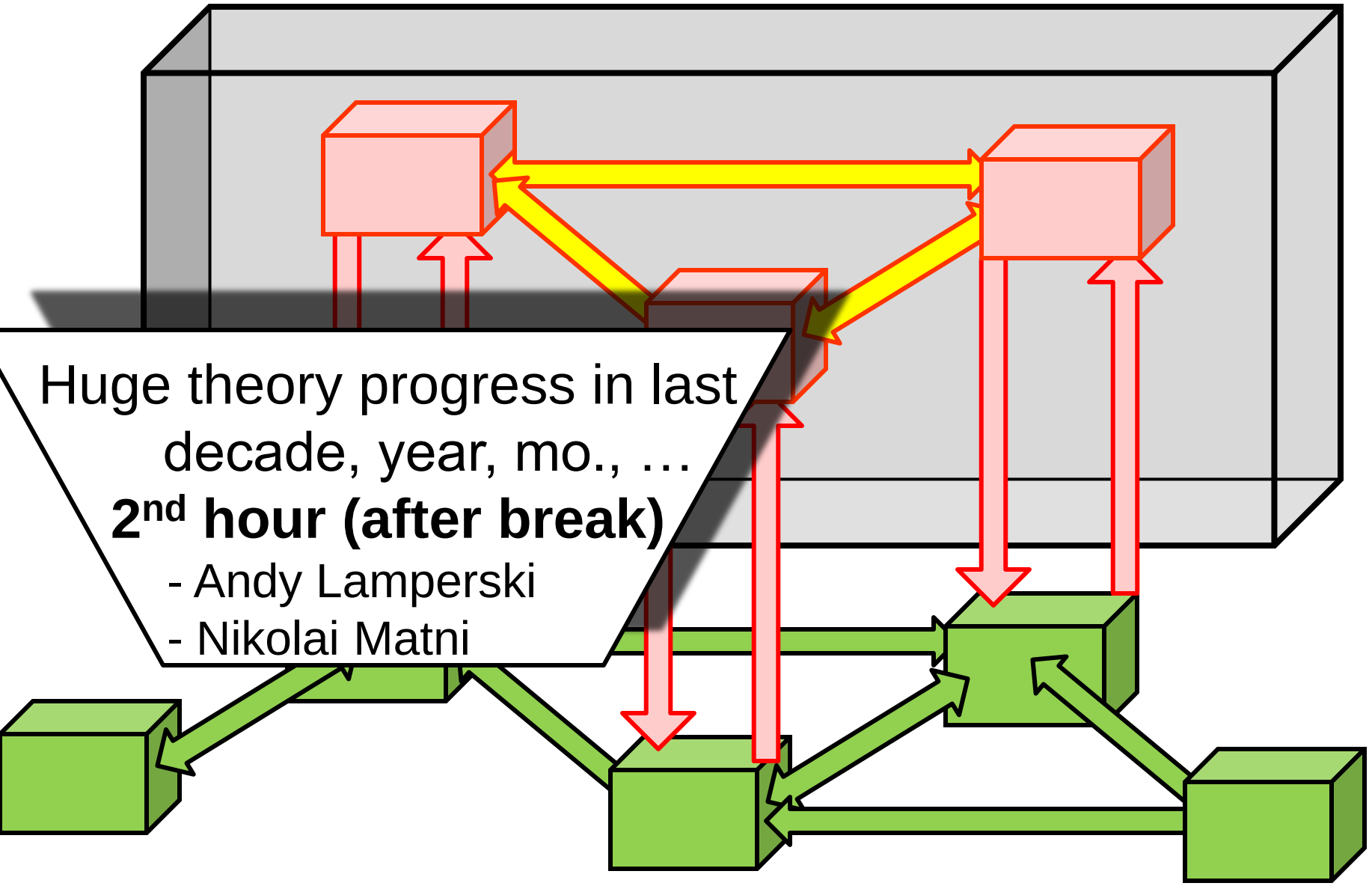
- Acquire
- Translate/ integrate
- **Automate**



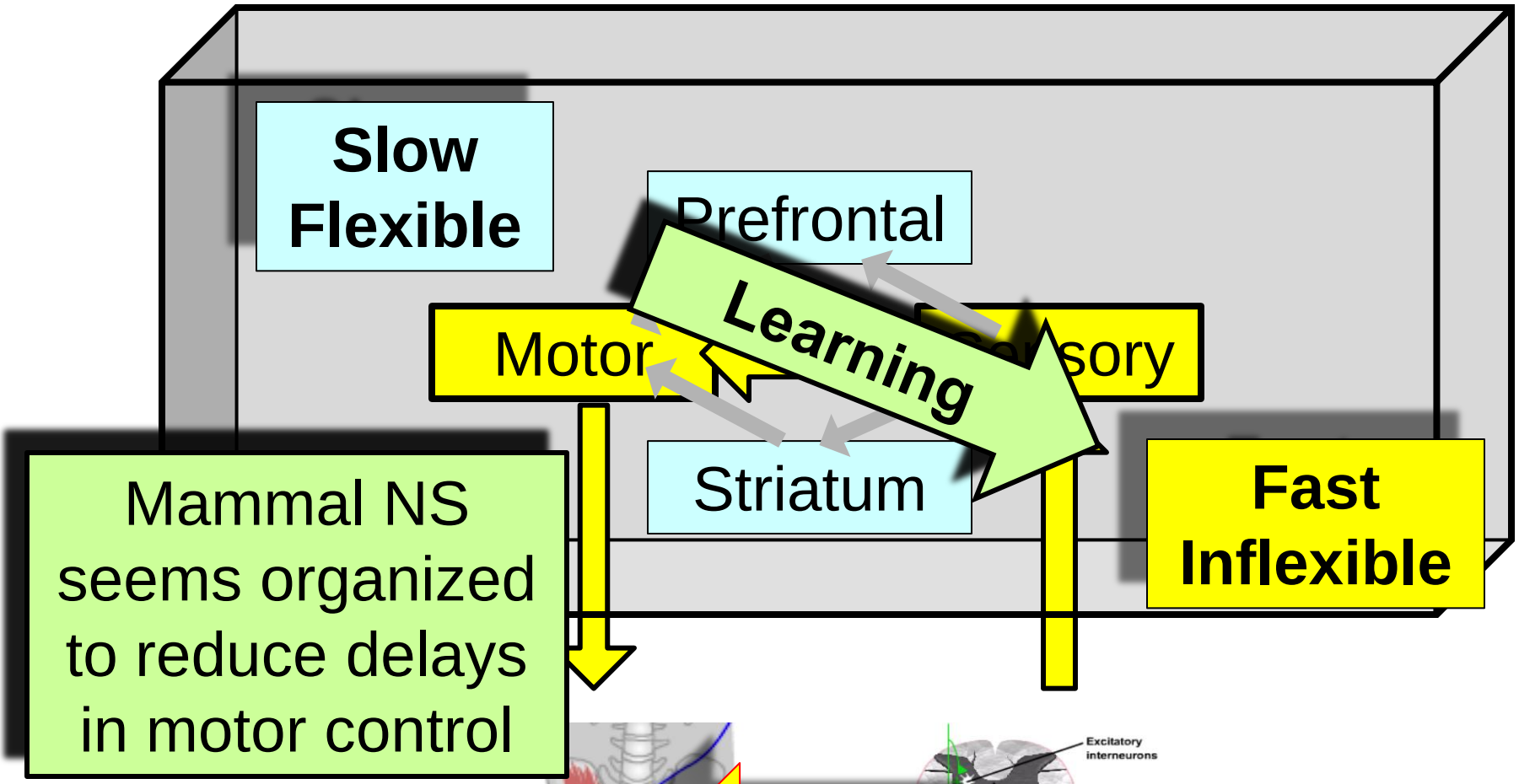
What I’m not going to talk about

- Connections between robustness and risk sensitivity
- Asymmetry between false positives and negatives
- Risk aversion and risk seeking
- Uncertainty is more in models than in probabilities
- Life is not like a casino

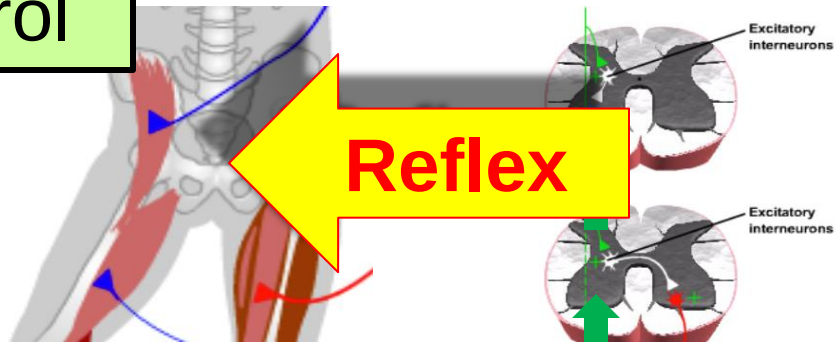
Going beyond black box: control is decentralized with internal delays.

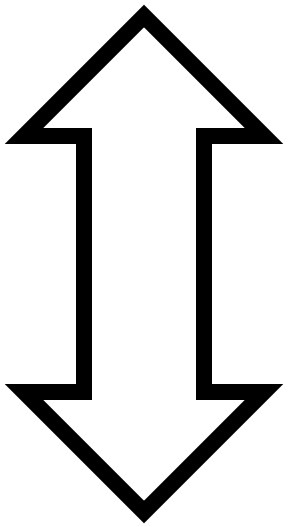


Going beyond black box: control is decentralized with internal delays.

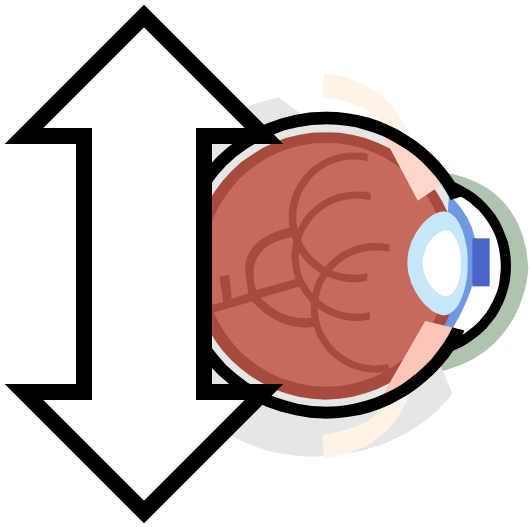


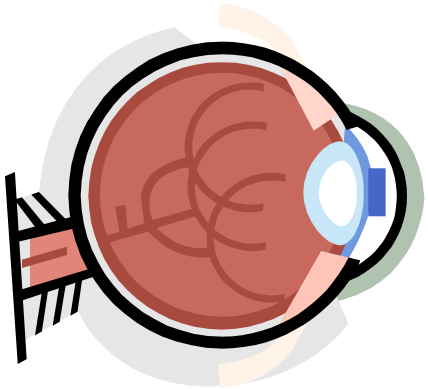
Mammal NS seems organized to reduce delays in motor control



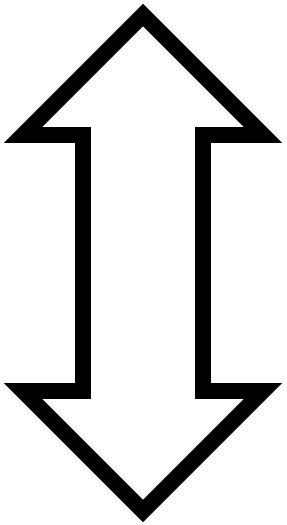


Move
head



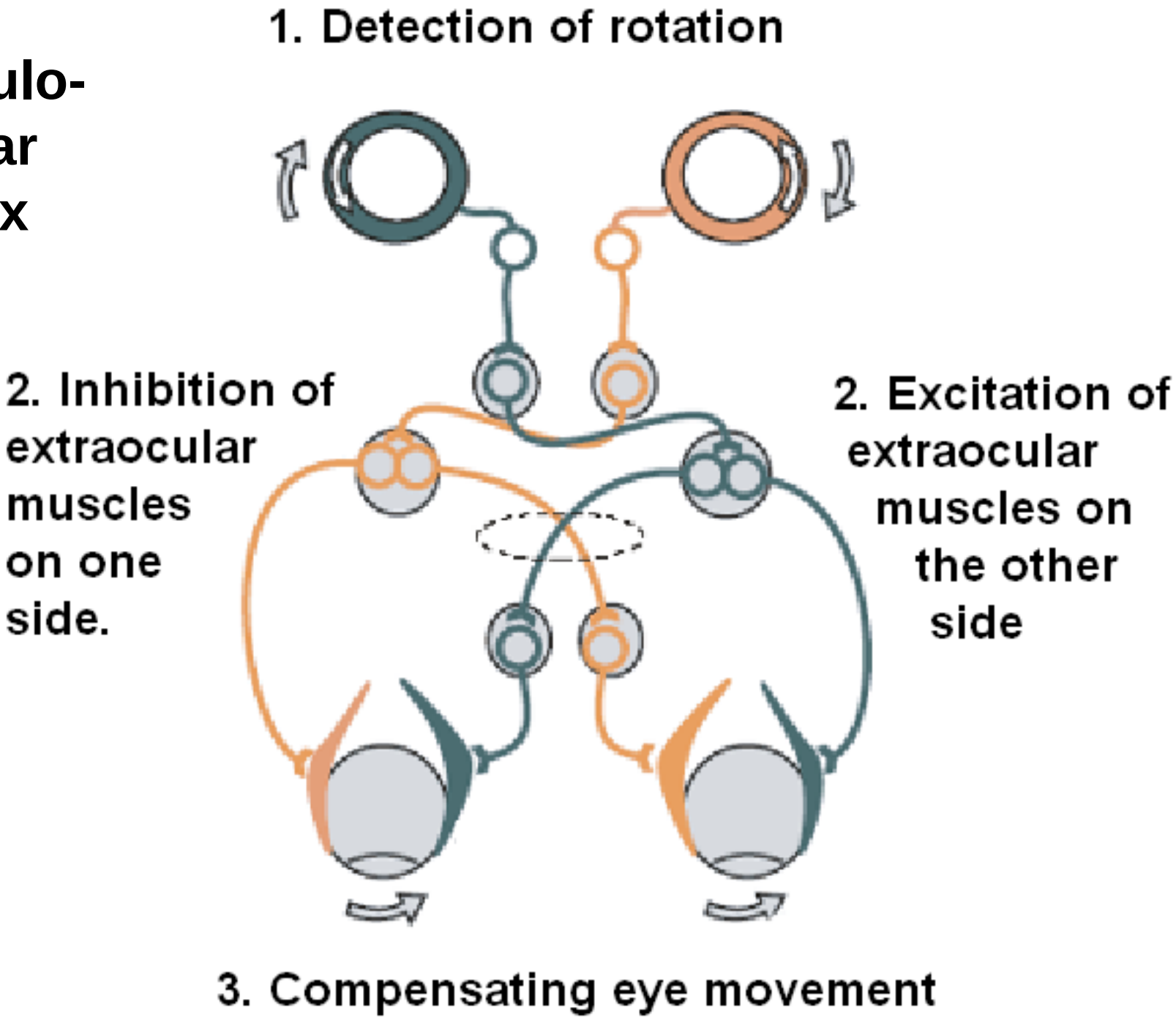


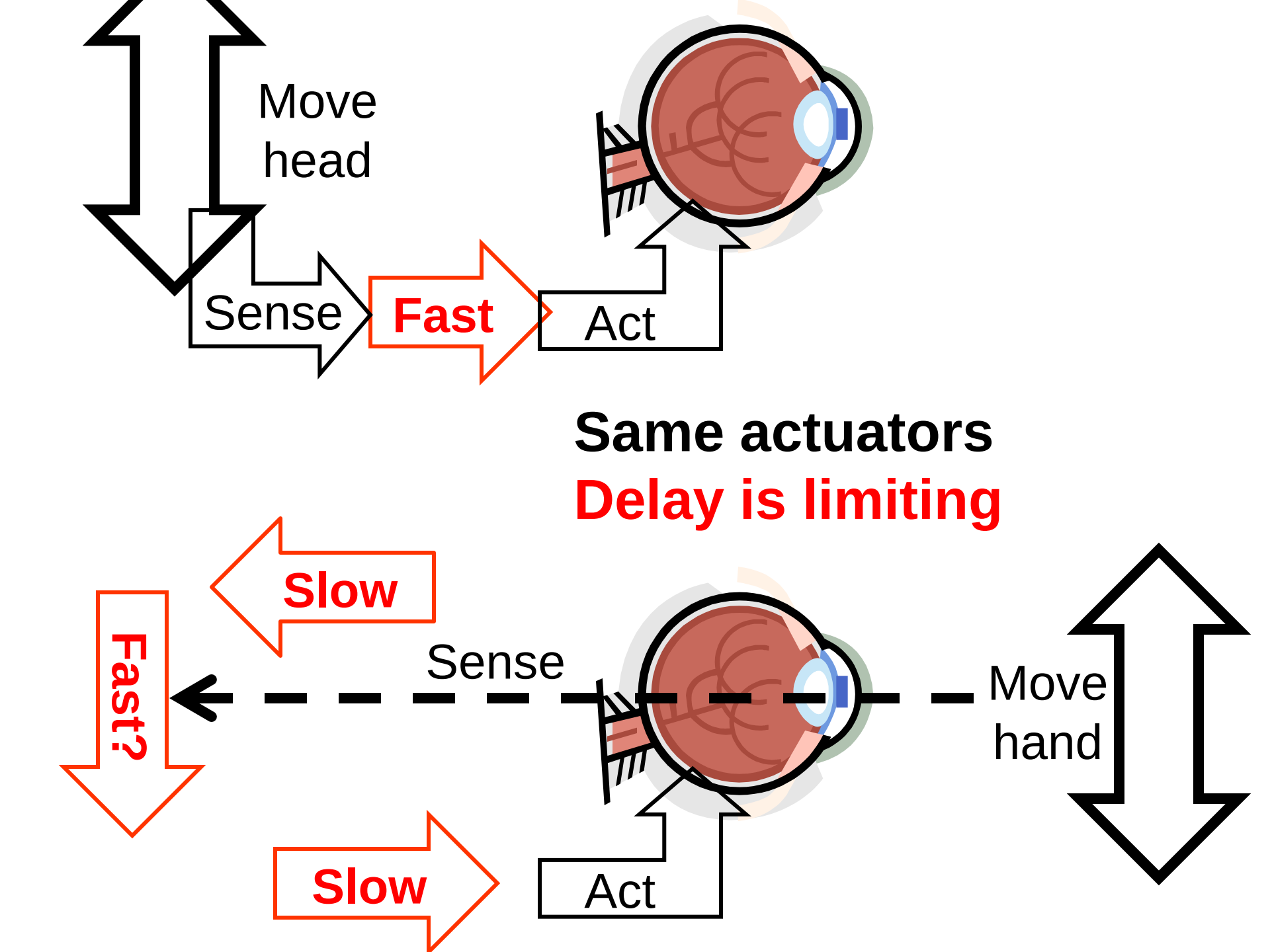
Move
hand



Bigger error

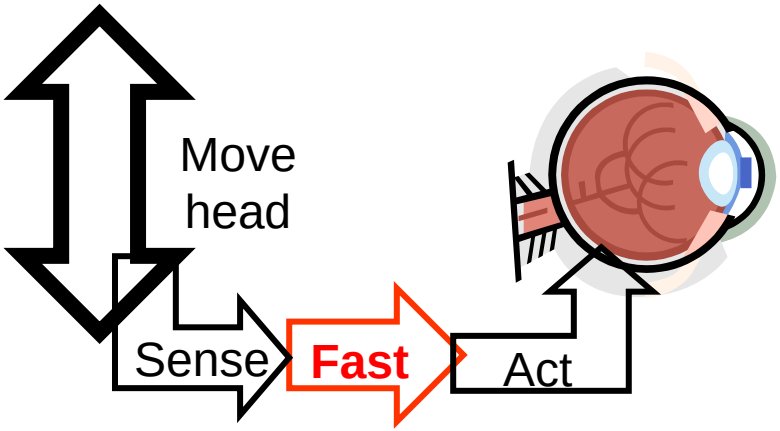
Vestibulo-ocular reflex




Move
head
Sense
Fast
Act
Same actuators
Delay is limiting
Slow
Fast?
Sense
Move
hand
Slow
Act

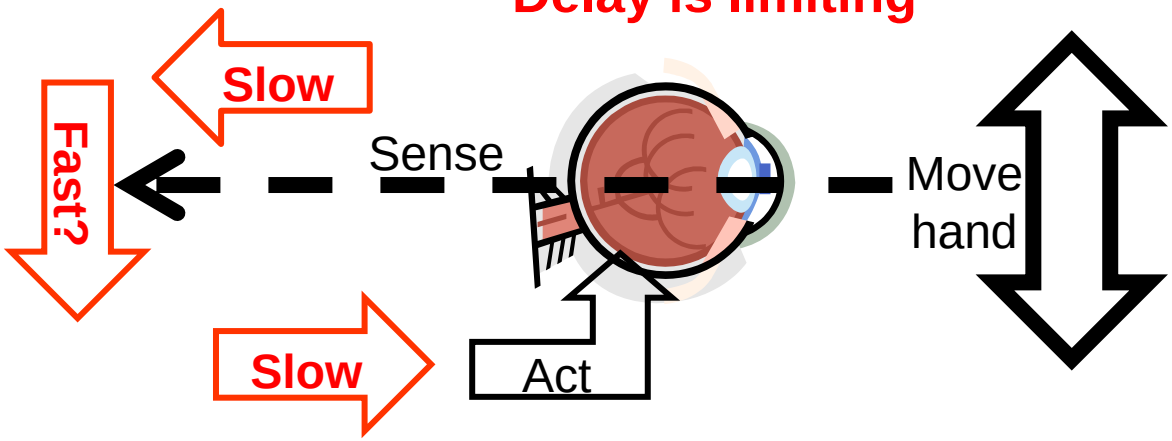
Versus standing on one leg

- Eyes open vs closed
- Contrast
  - young surfers
  - old football players



Same actuators

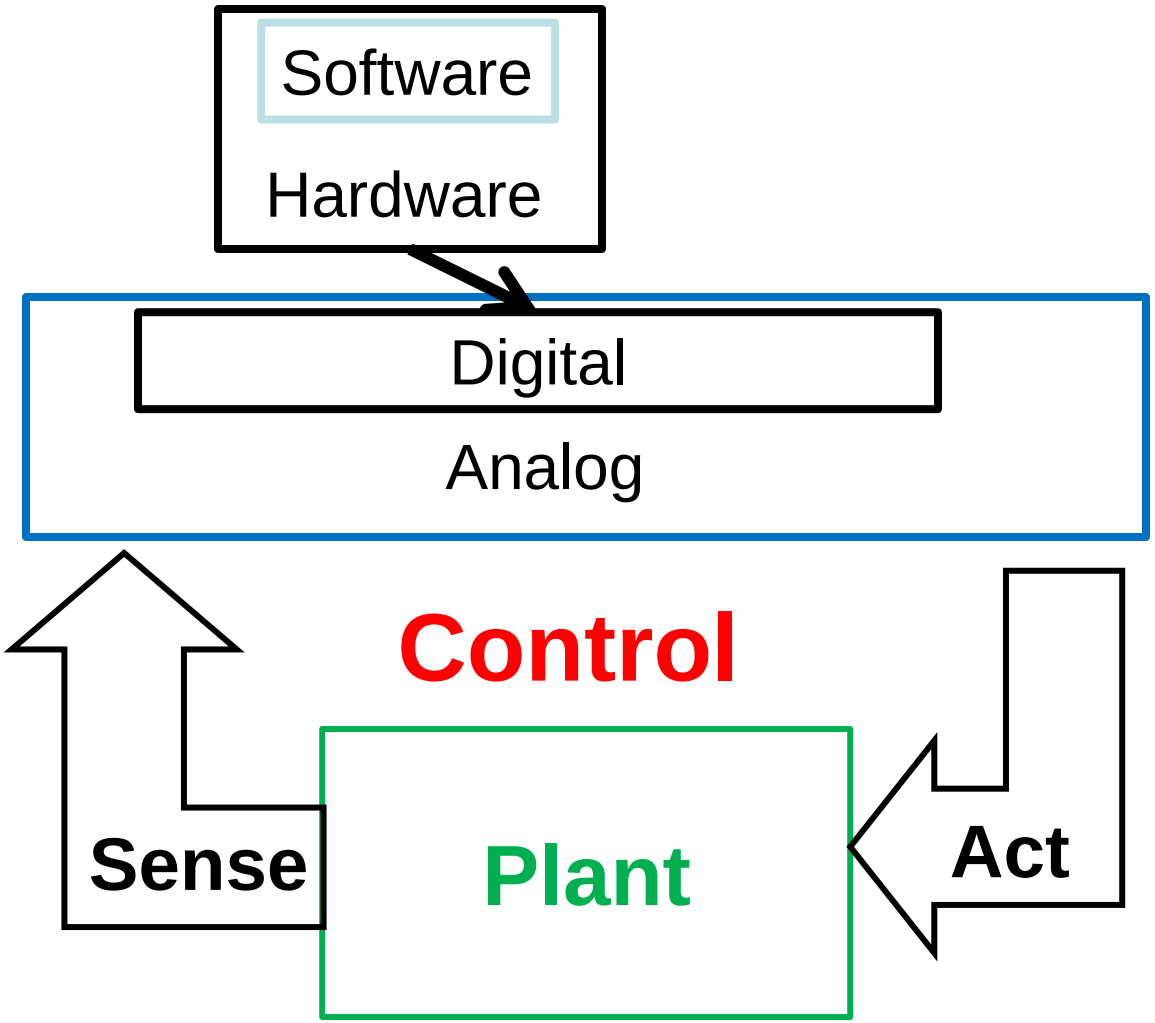
Delay is limiting



Compute

Computational complexity of
- ***Designing*** control algorithms
- ***Implementing*** control algorithms

Delay is *even more* important in control

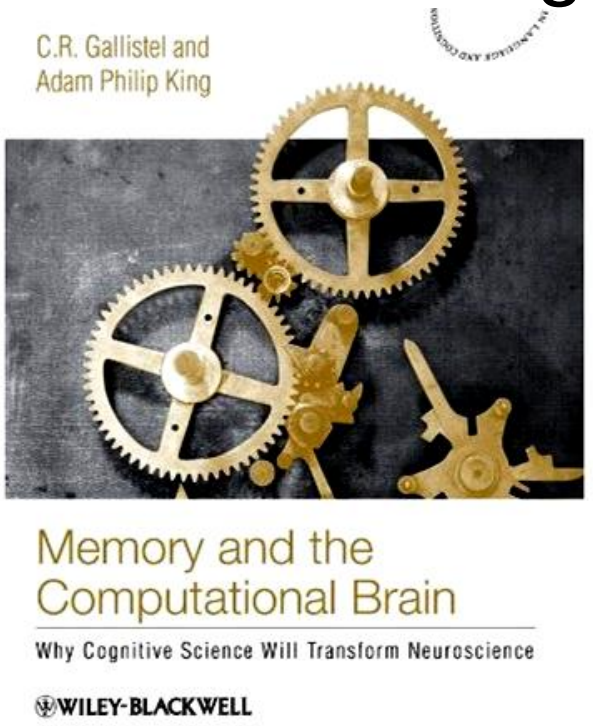


Control

Issues for neuroscience

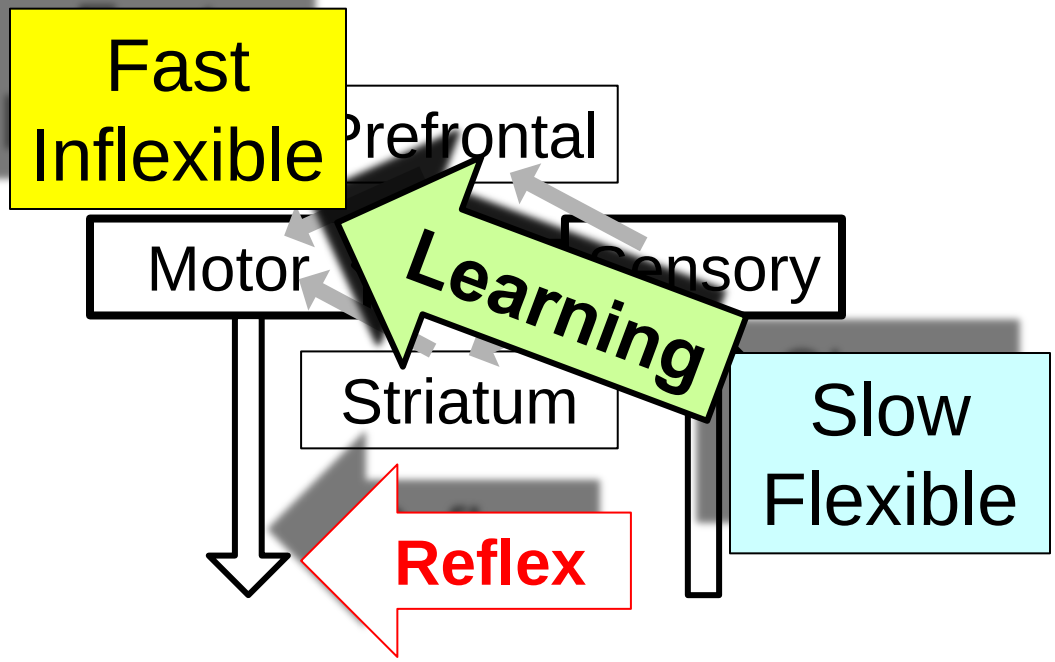
- Brains and UTMs?
  - Time is most critical resource?
  - Space (memory) almost free?
- Read/write random access memory hierarchies?
- Brain >> UTM?

Gallistel and King

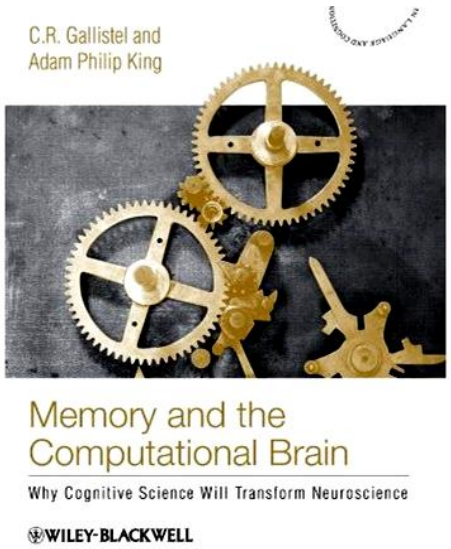


Conjecture

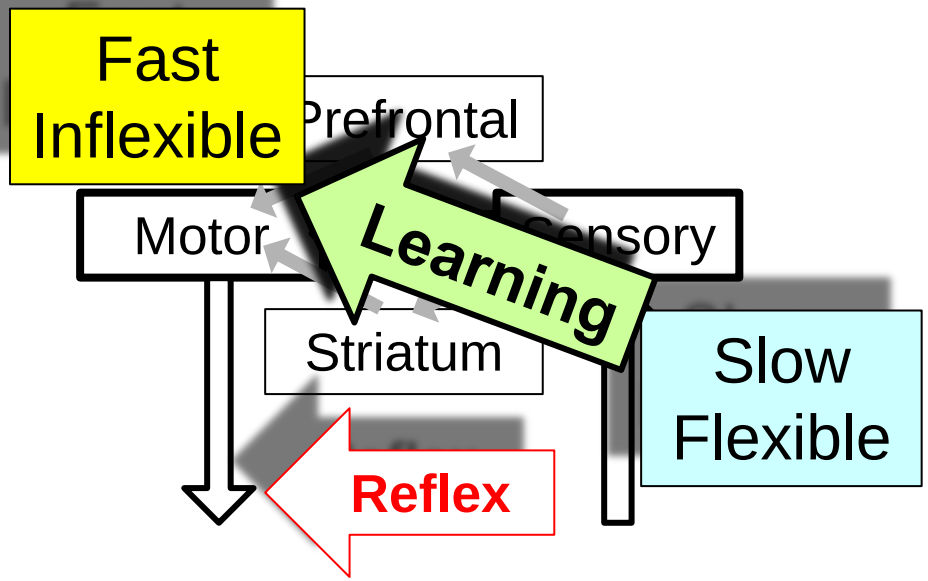
- Memory potential $\approx \infty$
- Examples
  - Insects
  - Scrub jays
  - Autistic Savants



Gallistel and King

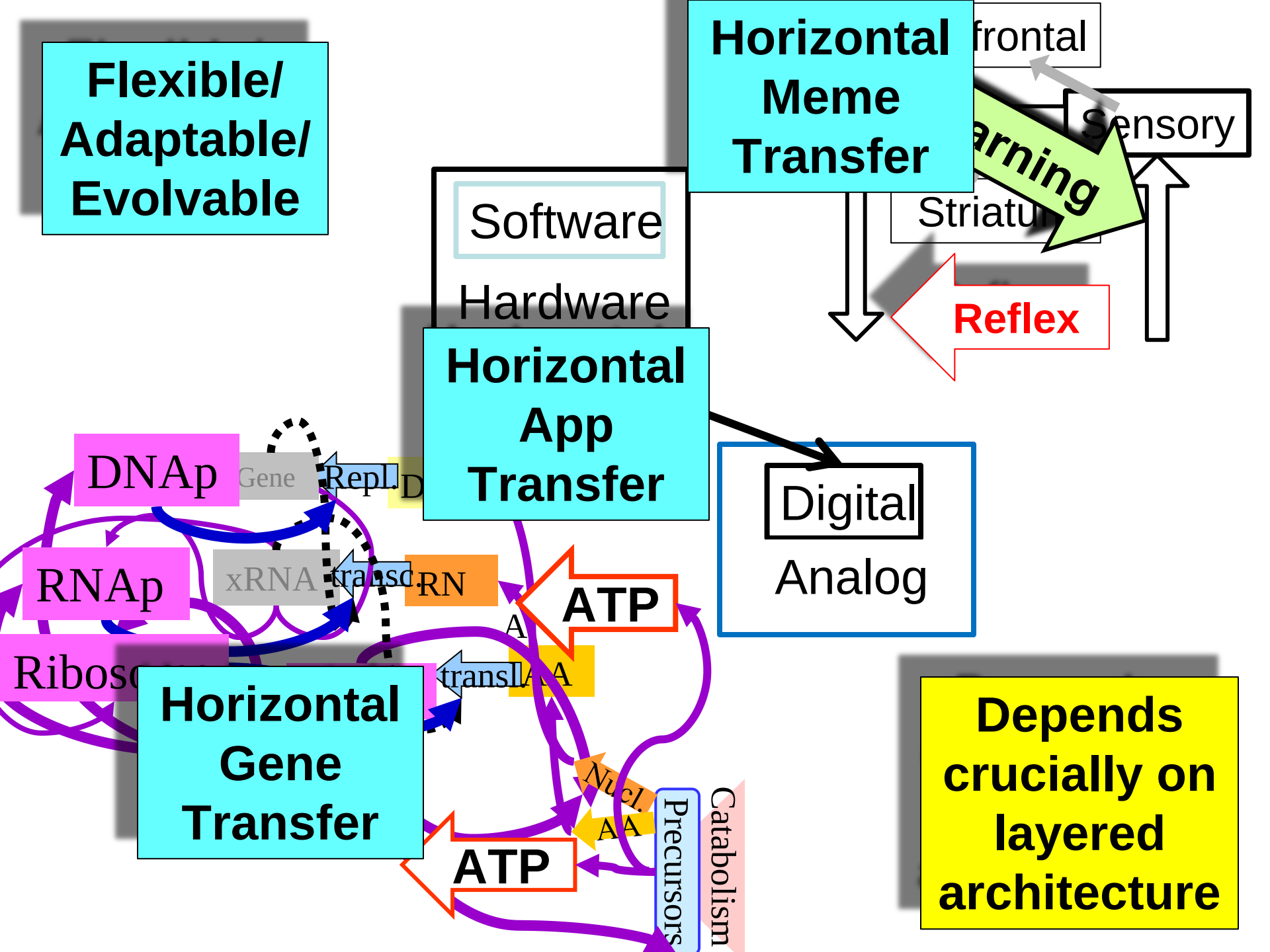


- Sensori-motor memory potential $\approx \infty$ (Ashby)
- Limits are on ***speed*** of
  - nerve propagation delays
  - learning
- But control is ***never*** centralized
- Is there a random access read/write memory?



The EvoPsycho question: why?

- Sensori-motor memory potential ≈ ∞ (Ashby)
- Limits are on ***speed*** of
  - nerve propagation delays (fish parts?)
  - learning ???
- I'm probably confused
- What about robust learning


Flexible/
Adaptable/
Evolvable
Horizontal
Meme
Transfer
frontal
Sensory
arning
Striatu
Software
Hardware
Reflex
Horizontal
App
Transfer
Digital
Analog
DNAp
Gene
Repl.
D
RNAp
xRNA
transc.
RN
ATP
A
Ribosc
transl.
A
A
Horizontal
Gene
Transfer
Nucl.
A
A
Precursors
Catabolism
ATP
Depends
crucially on
layered
architecture

What I’m not going to talk about

- It’s true that most “really smart scientists” think almost everything in this talk is nonsense
- Why they think this
- Why they are wrong

- Time (not space) is our problem, as usual
- Don’t have enough time for what is true, so have to limit discussion of what isn’t
- No one ever changes a made up mind (almost)

What I'm not going to talk about

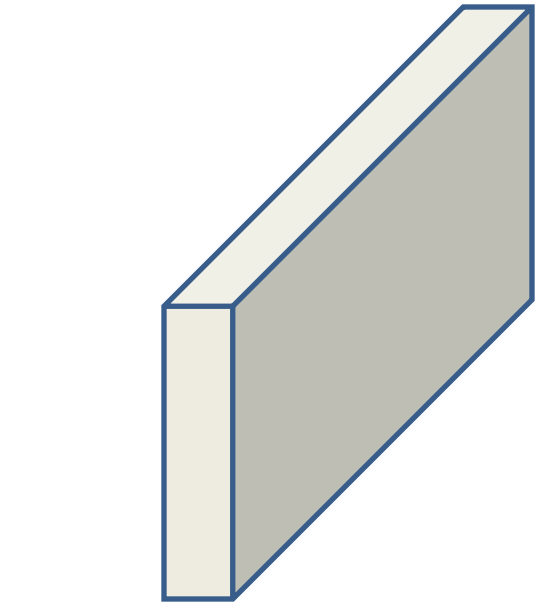
Compute

Turing

Delay is *most* important

Bode

Control, OR



Communicate

Shannon

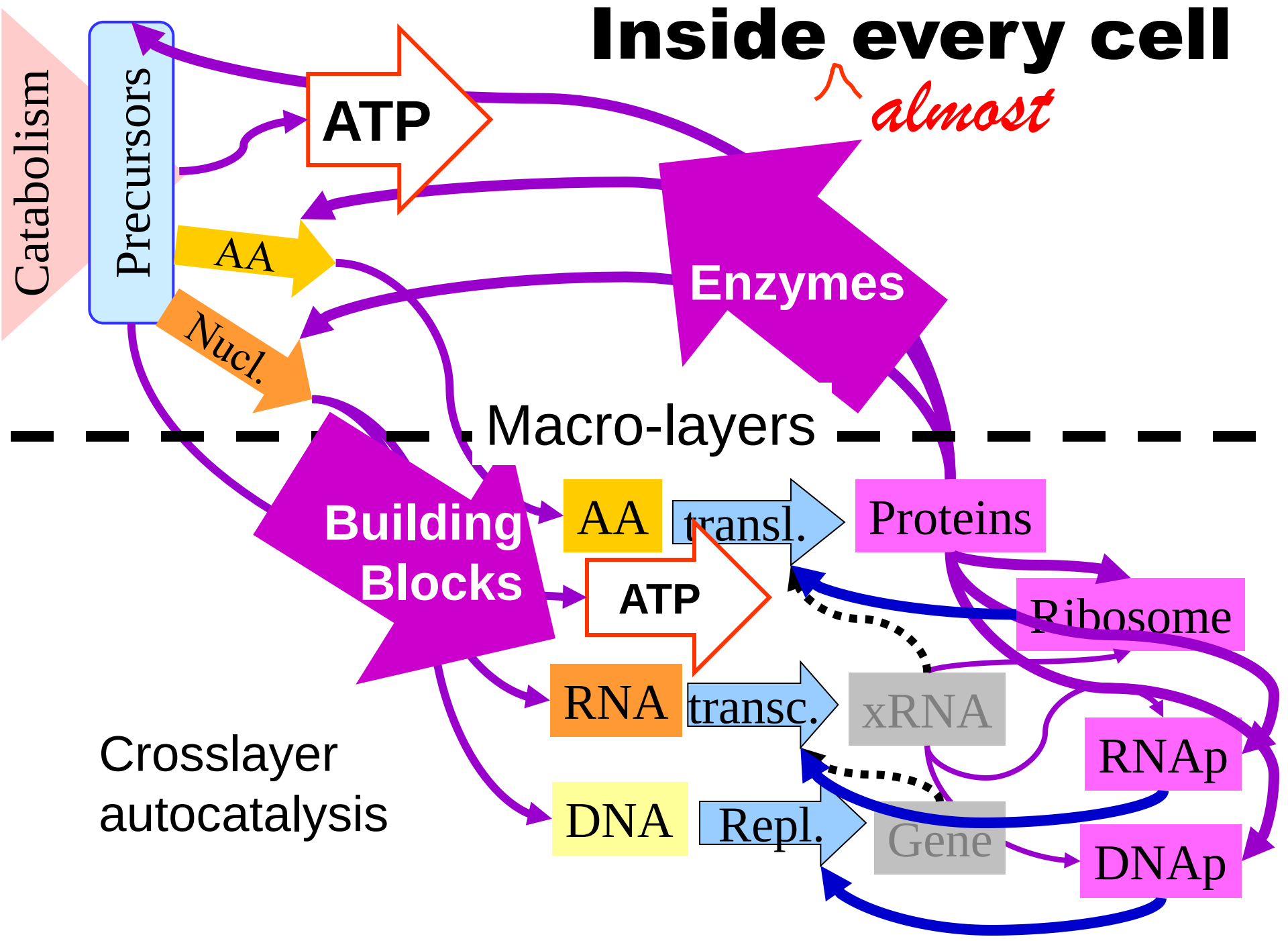
Delay is ~~*least*~~ important

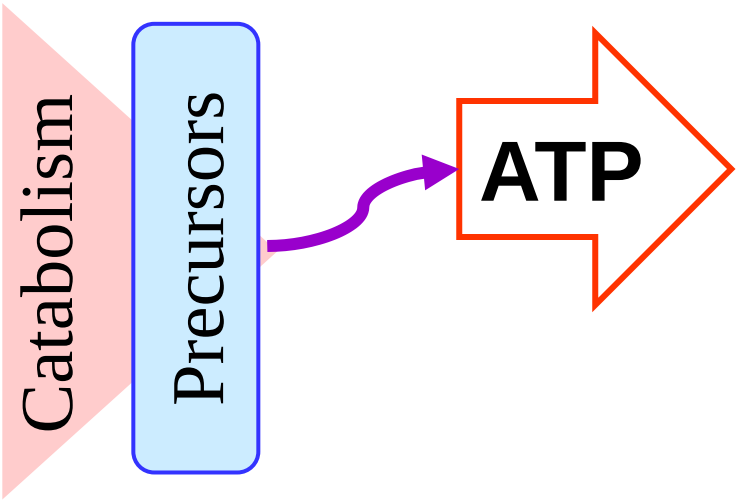
Carnot

Boltzmann

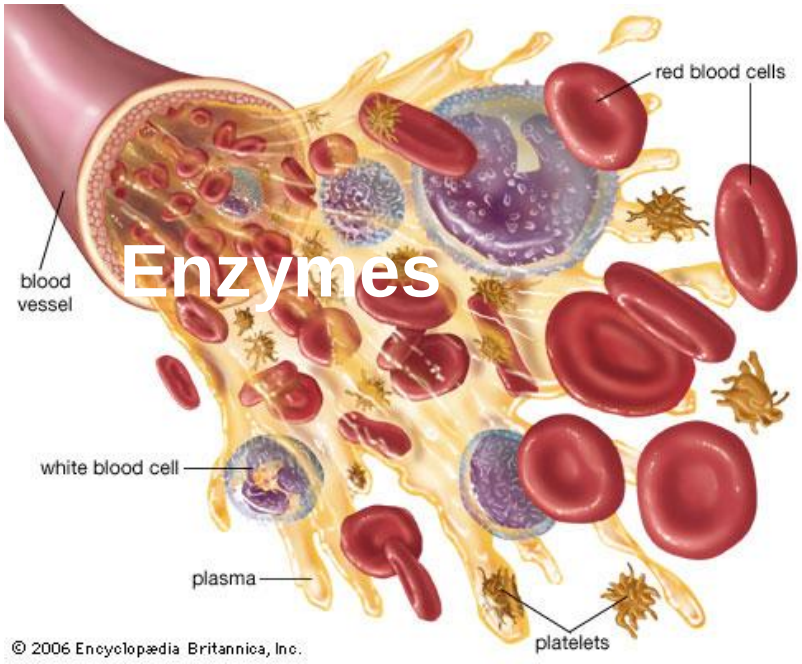
Heisenberg

Physics


Inside every cell
almost
Catabolism
Precursors
ATP
AA
Nucl.
Enzymes
Macro-layers
Building Blocks
AA
transl.
Proteins
ATP
Ribosome
RNA
transc.
xRNA
RNAp
DNA
Repl.
Gene
DNAp
Crosslayer autocatalysis

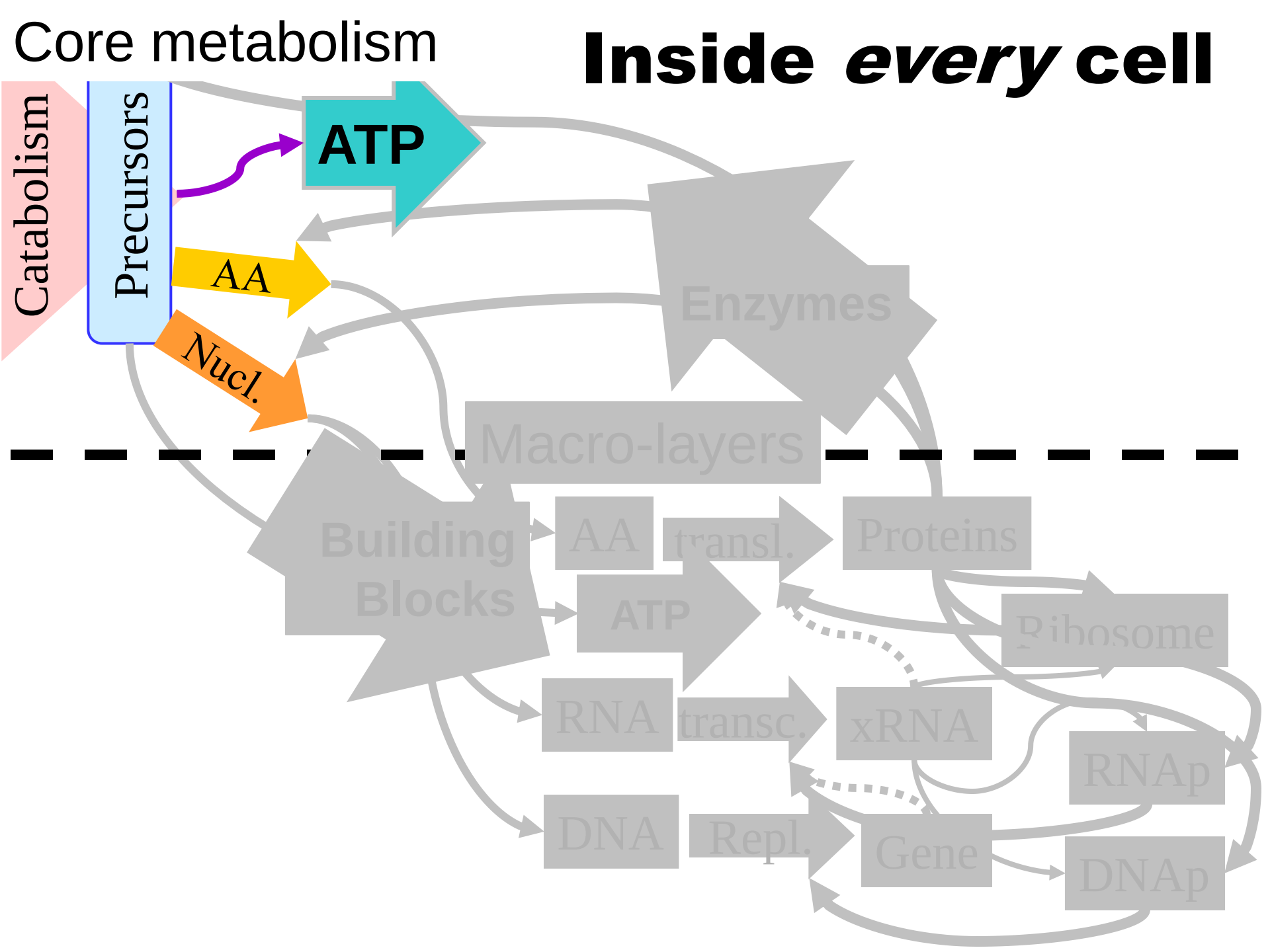


Inside every cell



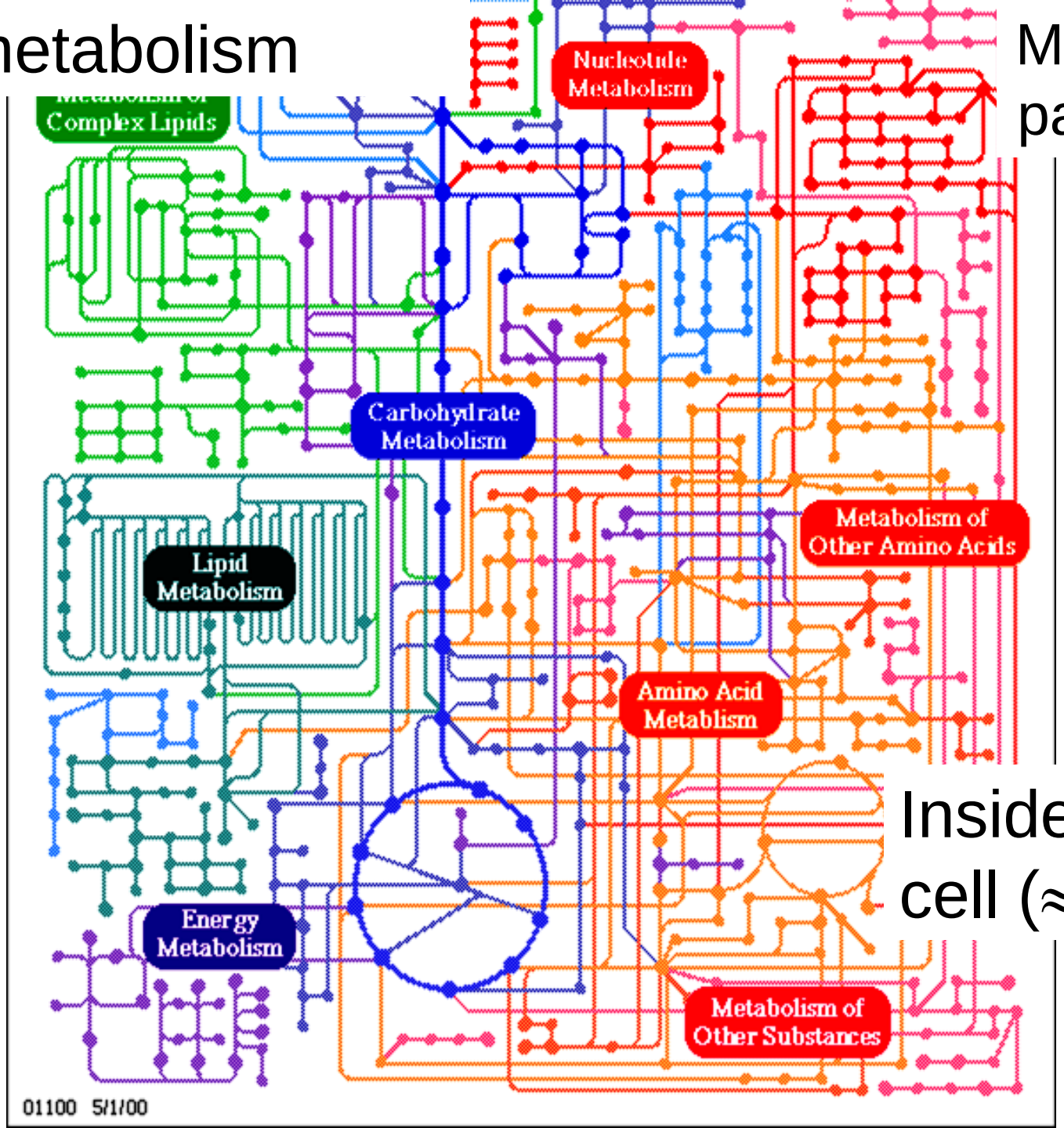
Mature red blood cells live 120 days

or “metabolism first” origins of life?


Core metabolism
Inside every cell
Catabolism
Precursors
ATP
AA
Nucl.
Enzymes
Macro-layers
Building Blocks
AA
transl.
Proteins
ATP
Ribosome
RNA
transc.
xRNA
RNAp
DNA
Repl.
Gene
DNAp

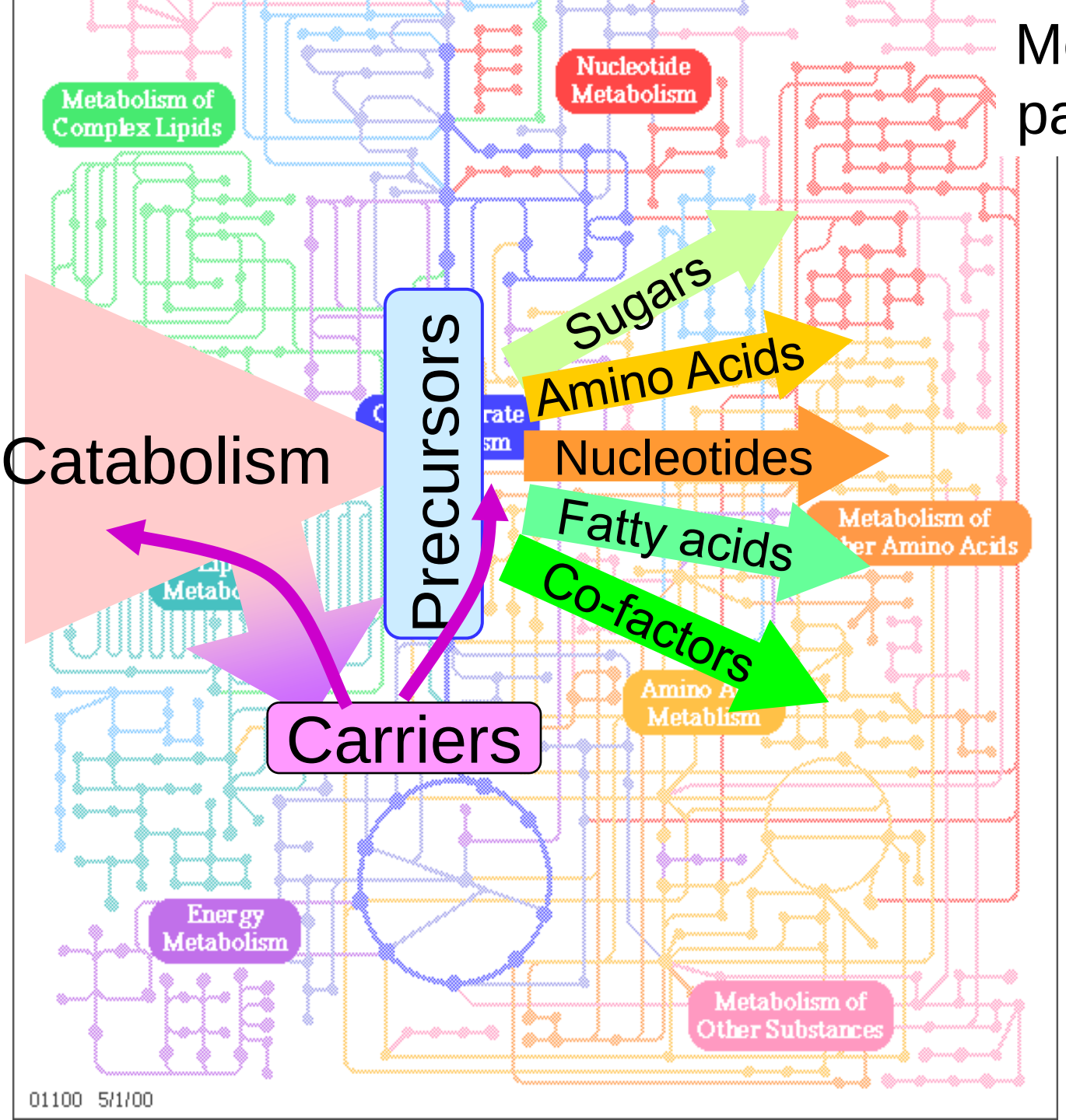
Core metabolism

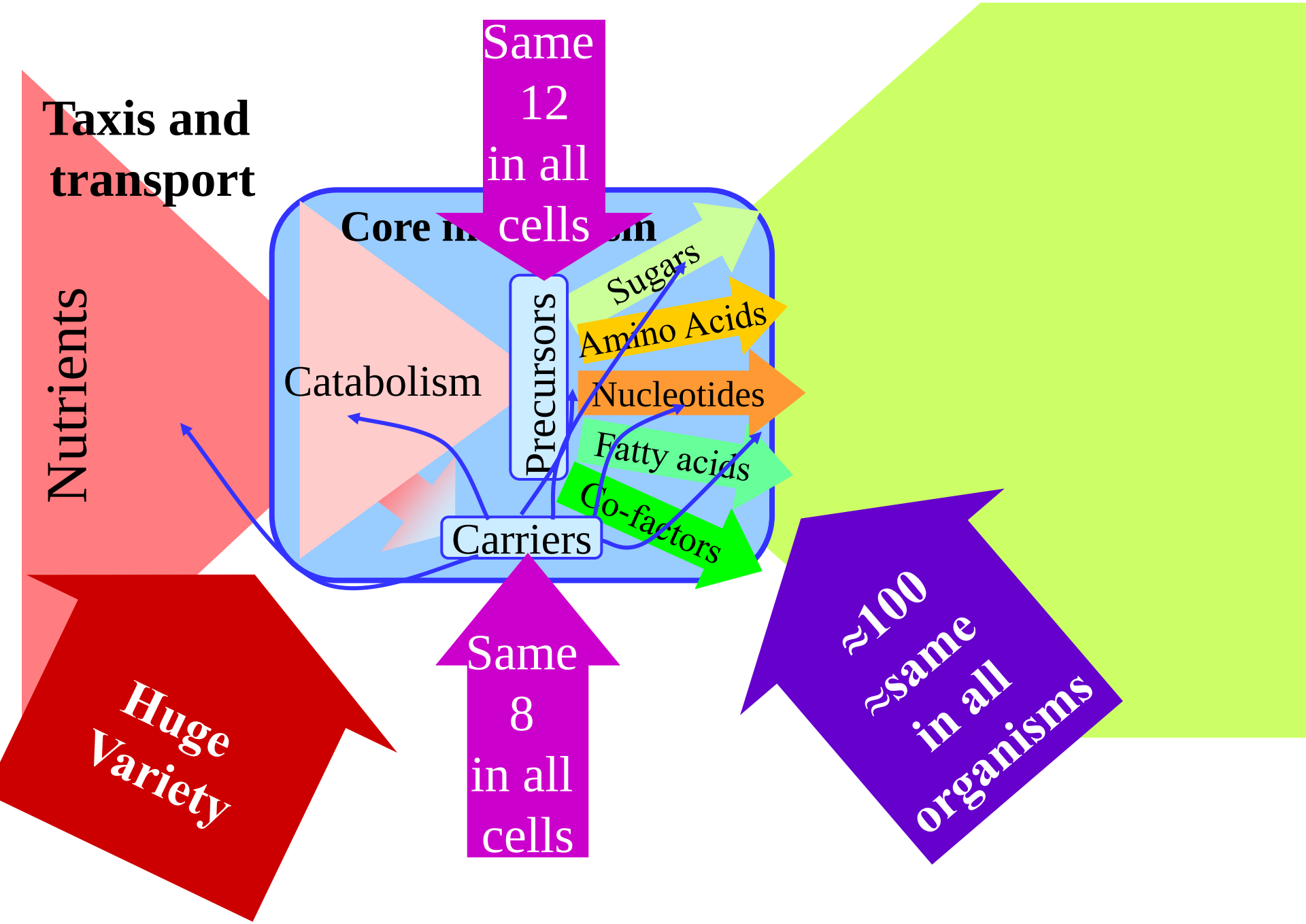
Metabolic pathways

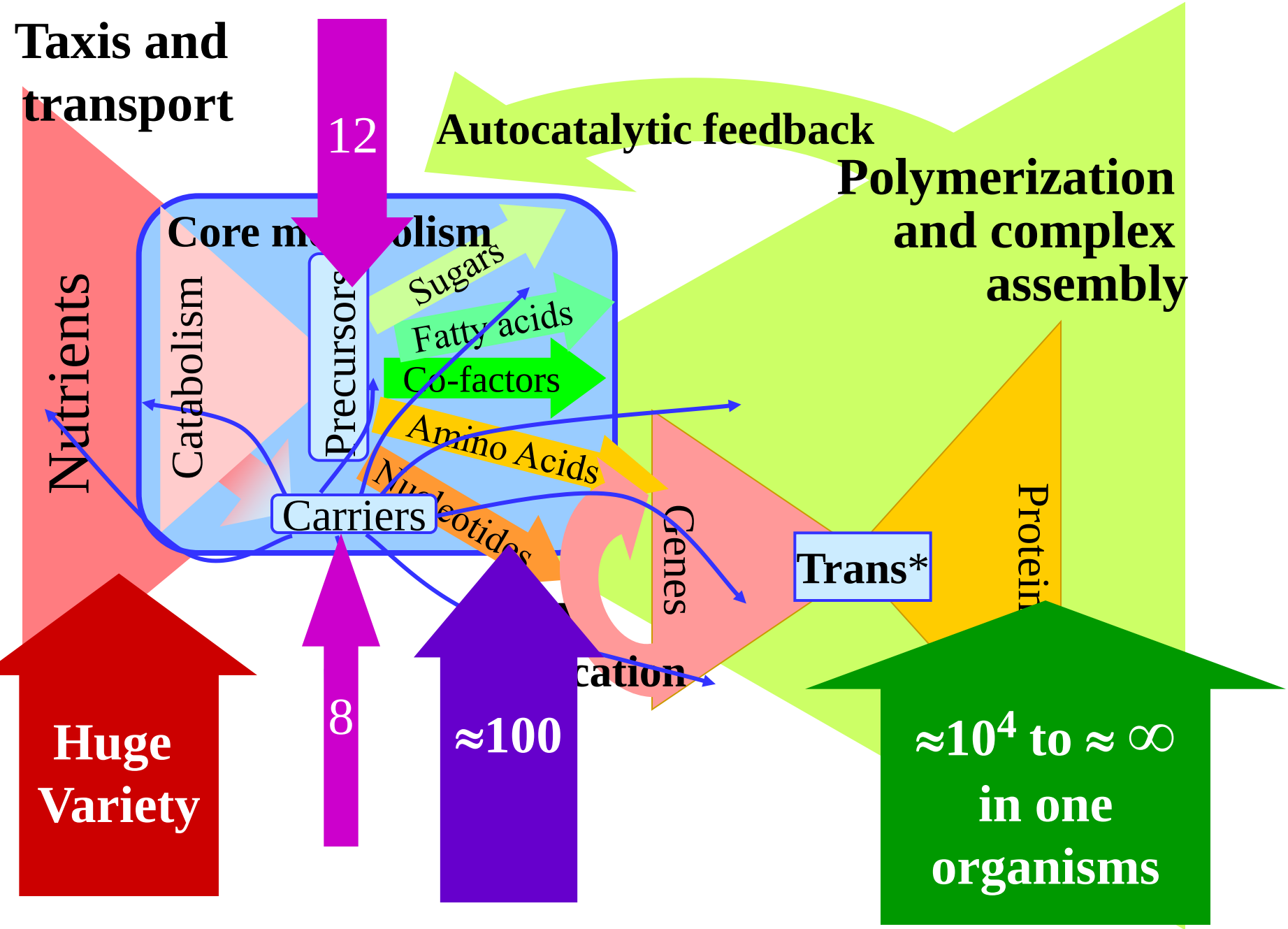


Inside every cell ($\approx 10^{30}$)

Metabolic pathways




Taxis and transport
Nutrients
Same 12 in all cells
Core
Catabolism
Precursors
Sugars
Amino Acids
Nucleotides
Fatty acids
Co-factors
Carriers
Same 8 in all cells
Huge Variety
≈100 ≈same in all organisms


Taxis and transport
12
Autocatalytic feedback
Polymerization and complex assembly
Core m olism
Nutrients
Catabolism
Precursors
Sugars
Fatty acids
Co-factors
Amino Acids
Carriers
Genes
Trans*
Protein
cation
Huge Variety
8
≈100
≈10^4 to ≈ ∞ in one organisms

sports
music
dance
crafts
art
toolmaking
sex
food

Universal reward systems

VTA dopamine

Reward
Drive
Control
Memory

Constraints that deconstrain

Blood

Glucose

Oxygen

Organs
Tissues
Cells
Molecules

Universal metabolic system

Modularity 2.0

Constraints

Blood

Glucose

Oxygen

Modularity 2.0

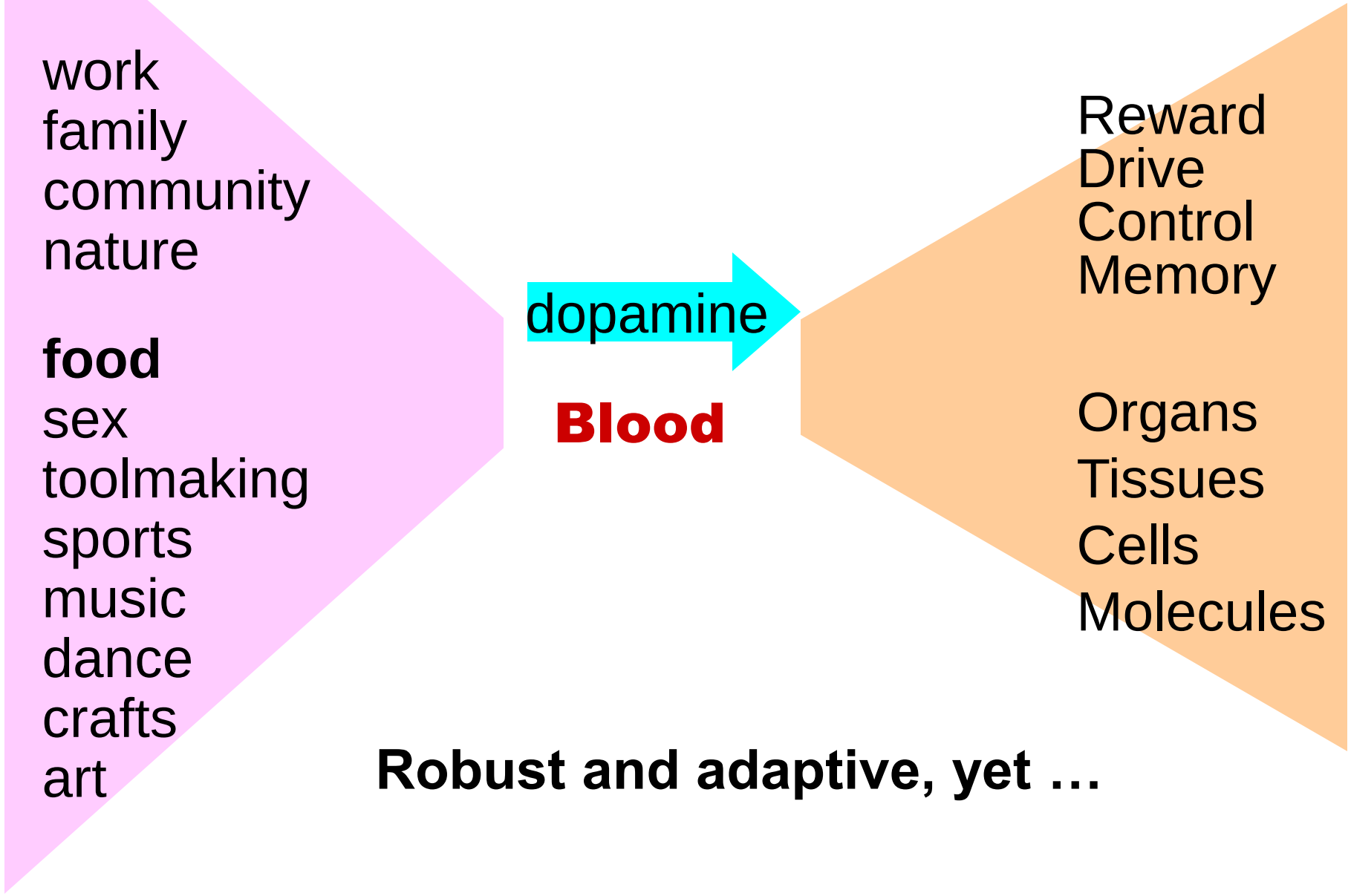
sports
music
dance
crafts
art
toolmaking
sex
food

that deconstrain

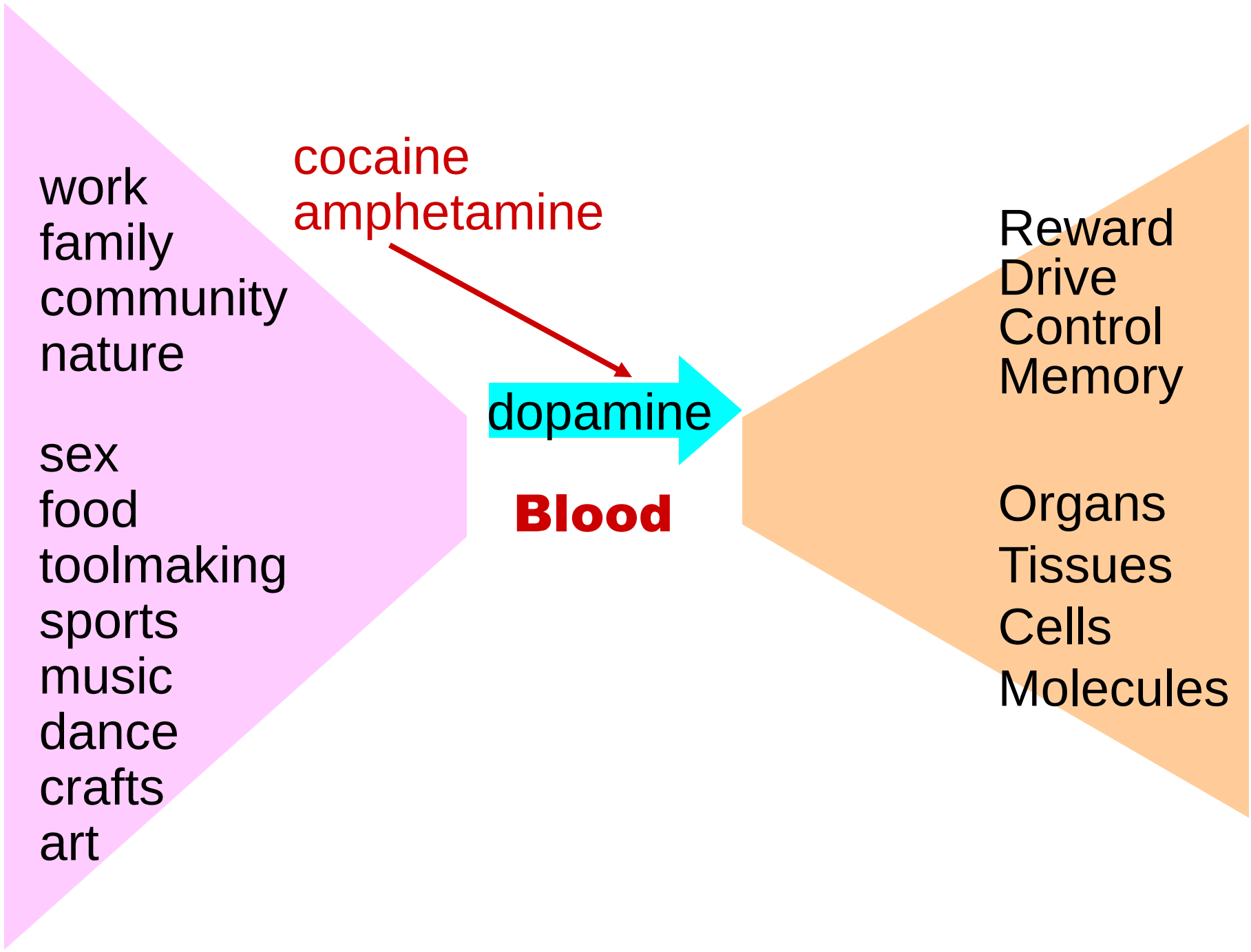
Reward
Drive
Control
Memory

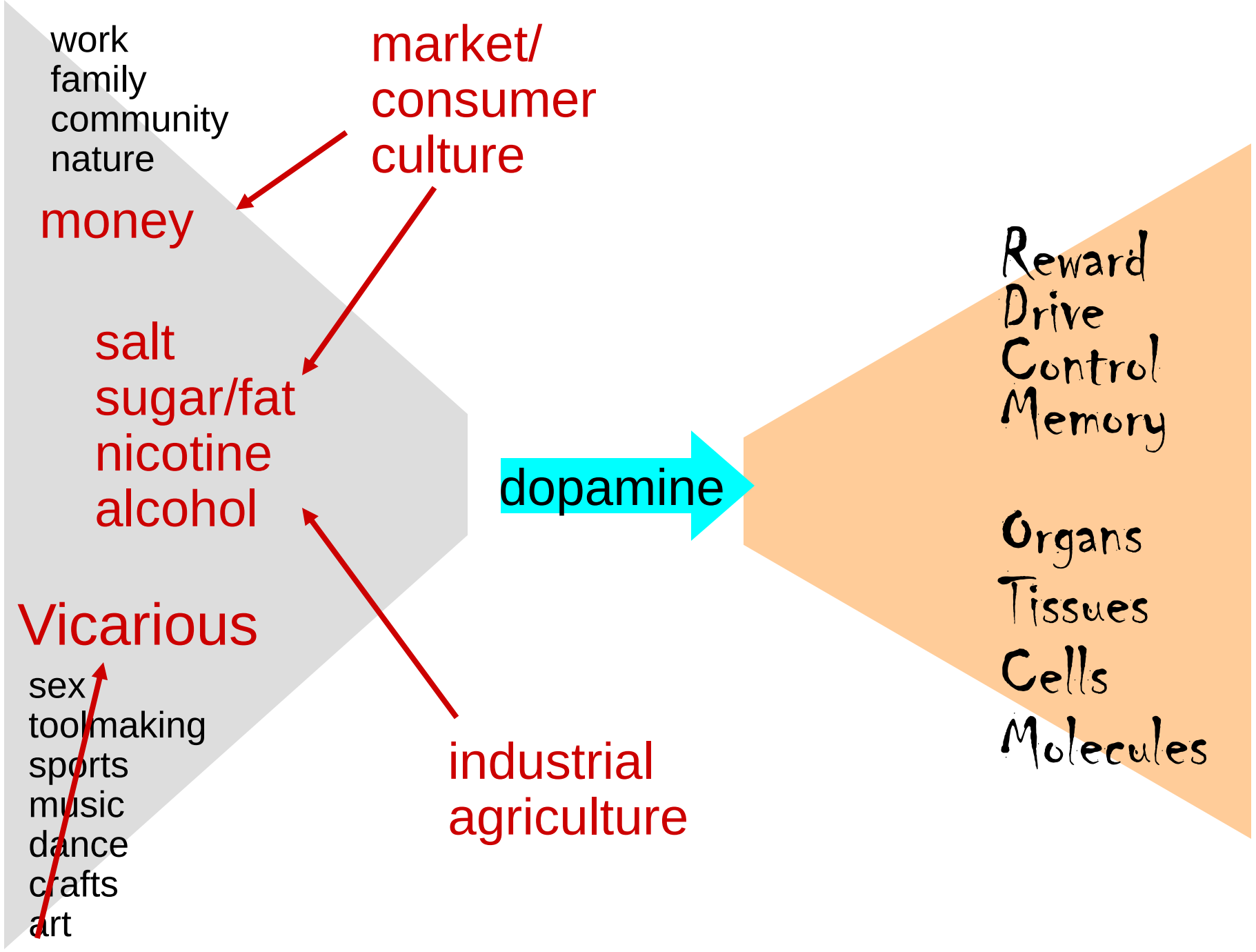
Organs
Tissues
Cells
Molecules

Universal reward/metabolic systems



Robust and adaptive, yet …

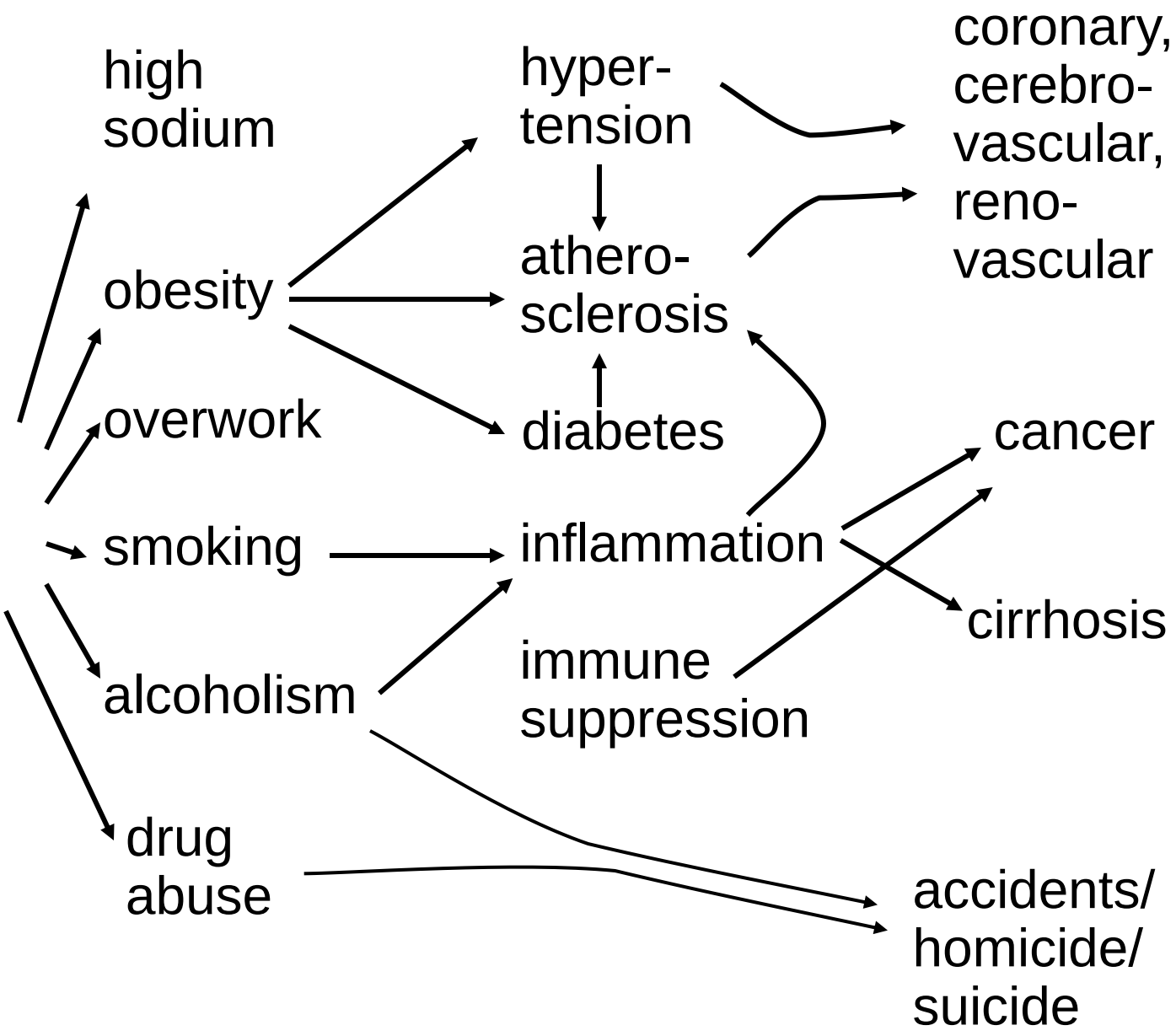

work
family
community
nature
sex
food
toolmaking
sports
music
dance
crafts
art
cocaine
amphetamine
dopamine
Blood
Reward
Drive
Control
Memory
Organs
Tissues
Cells
Molecules


work
family
community
nature
market/
consumer
culture
money
salt
sugar/fat
nicotine
alcohol
Vicarious
sex
toolmaking
sports
music
dance
crafts
art
industrial
agriculture
dopamine
Reward
Drive
Control
Memory
Organs
Tissues
Cells
Molecules

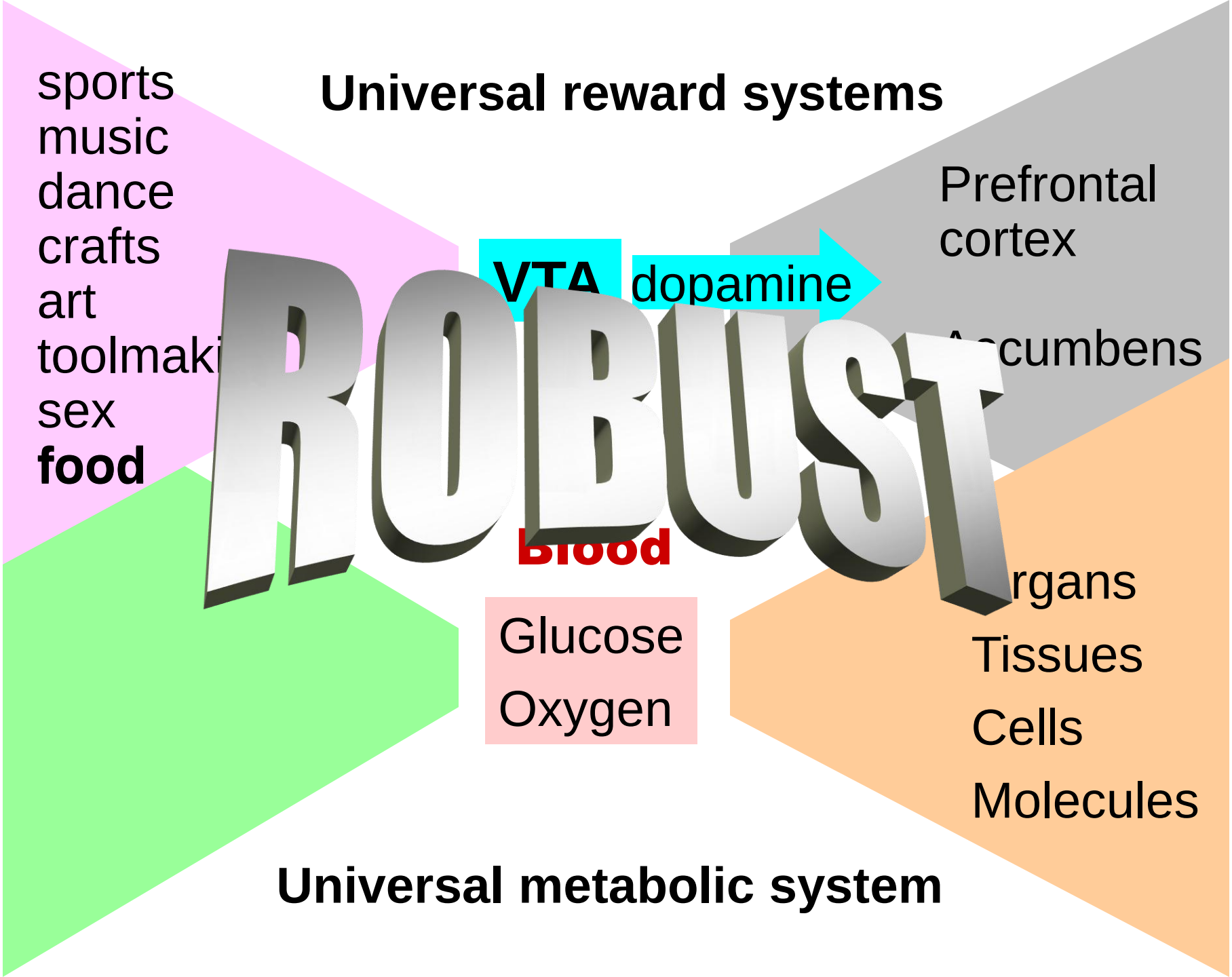
money

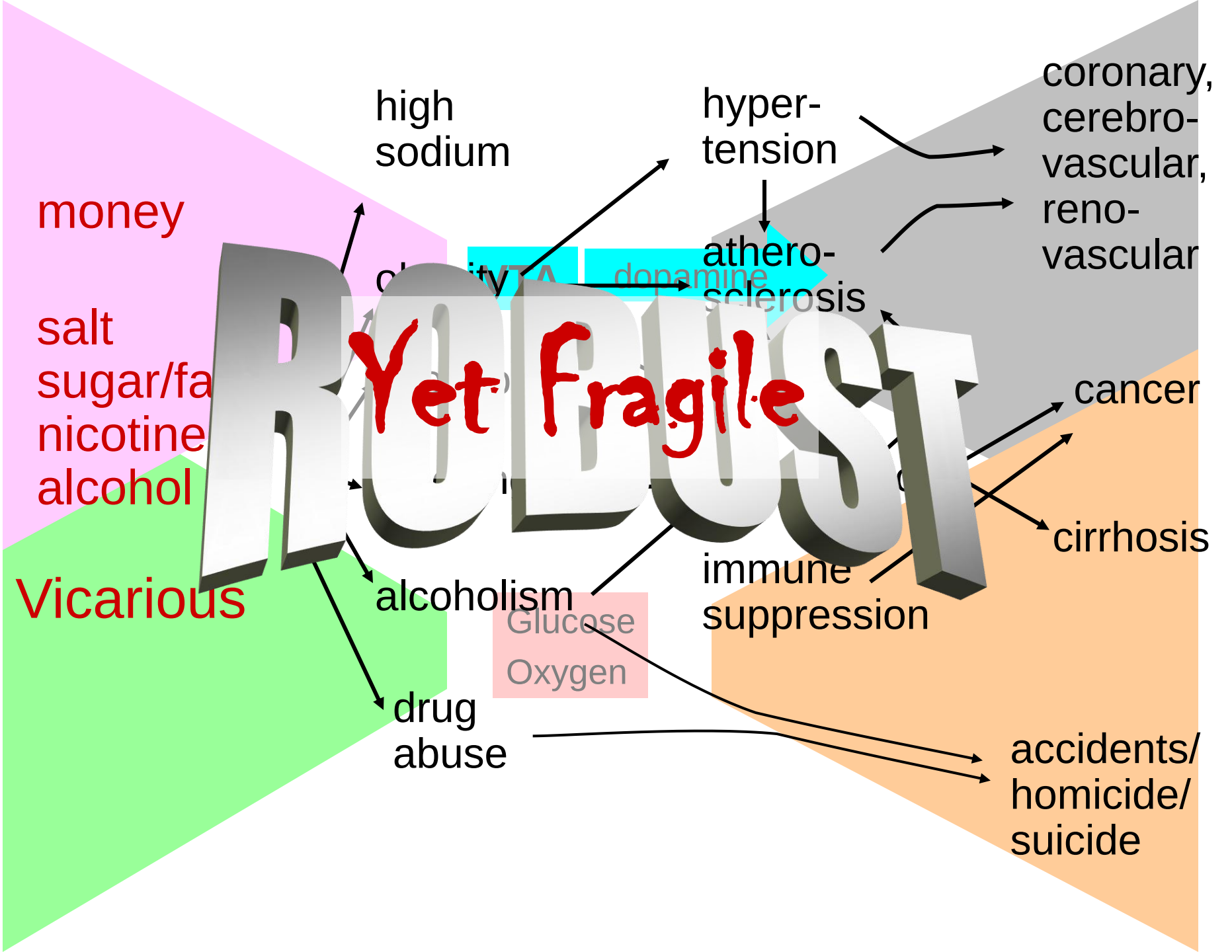
salt
sugar/fat
nicotine
alcohol

Vicarious

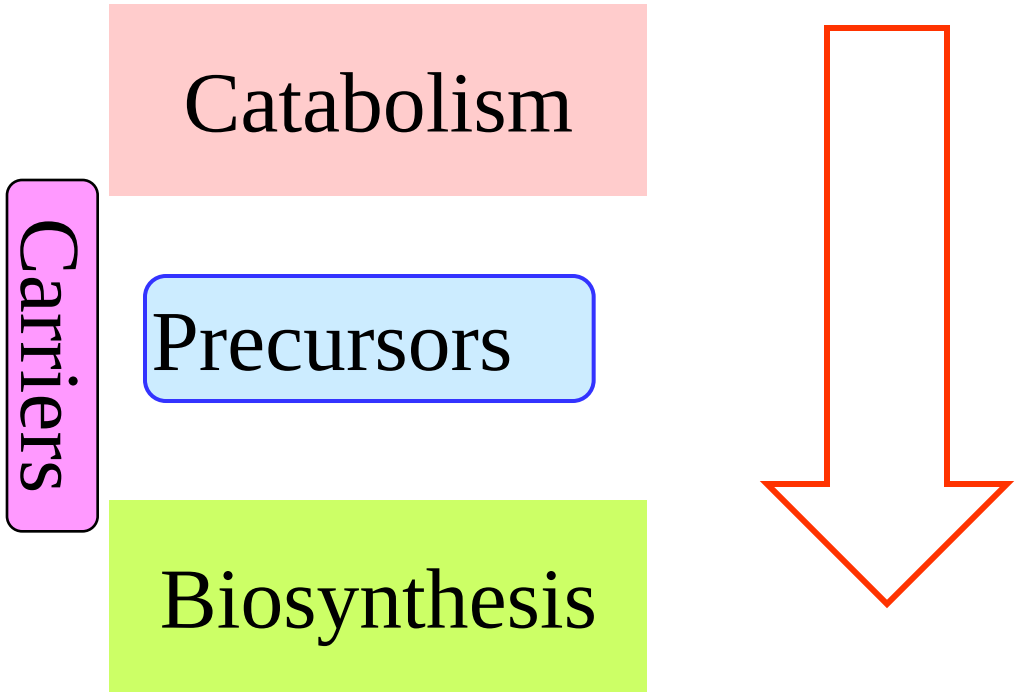


From Sterling


sports
music
dance
crafts
art
toolmaki
sex
food
Universal reward systems
VTA
dopamine
Prefrontal cortex
Accumbens
ROBUST
Blood
Glucose
Oxygen
rgans
Tissues
Cells
Molecules
Universal metabolic system

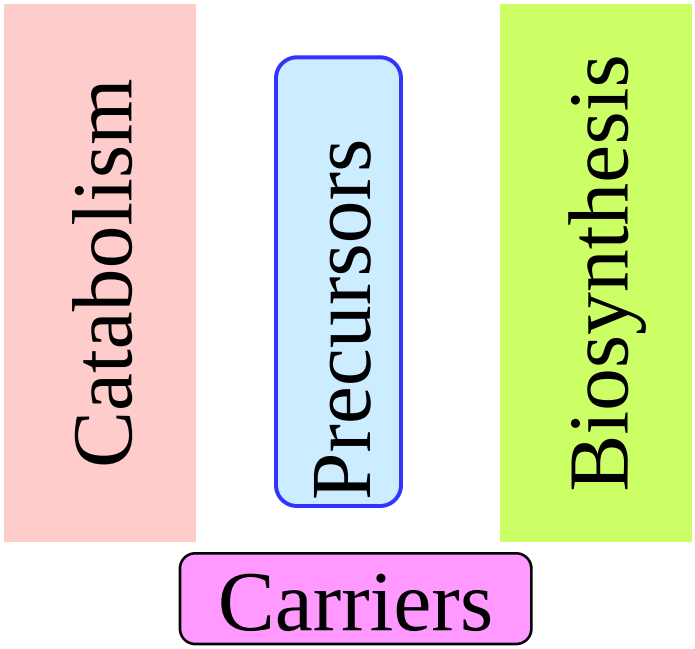

money
salt
sugar/fa
nicotine
alcohol
Vicarious
high
sodium
hyper-
tension
coronary,
cerebro-
vascular,
reno-
vascular
athero-
sclerosis
dopamine
ROBUST
Yet Fragile
cancer
cirrhosis
immune
suppression
alcoholism
Glucose
Oxygen
drug
abuse
accidents/
homicide/
suicide

Inside every cell

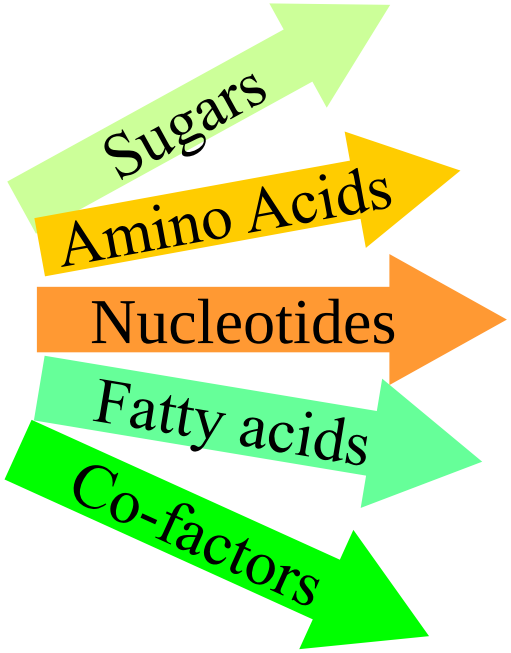


Layered architecture

Inside every cell

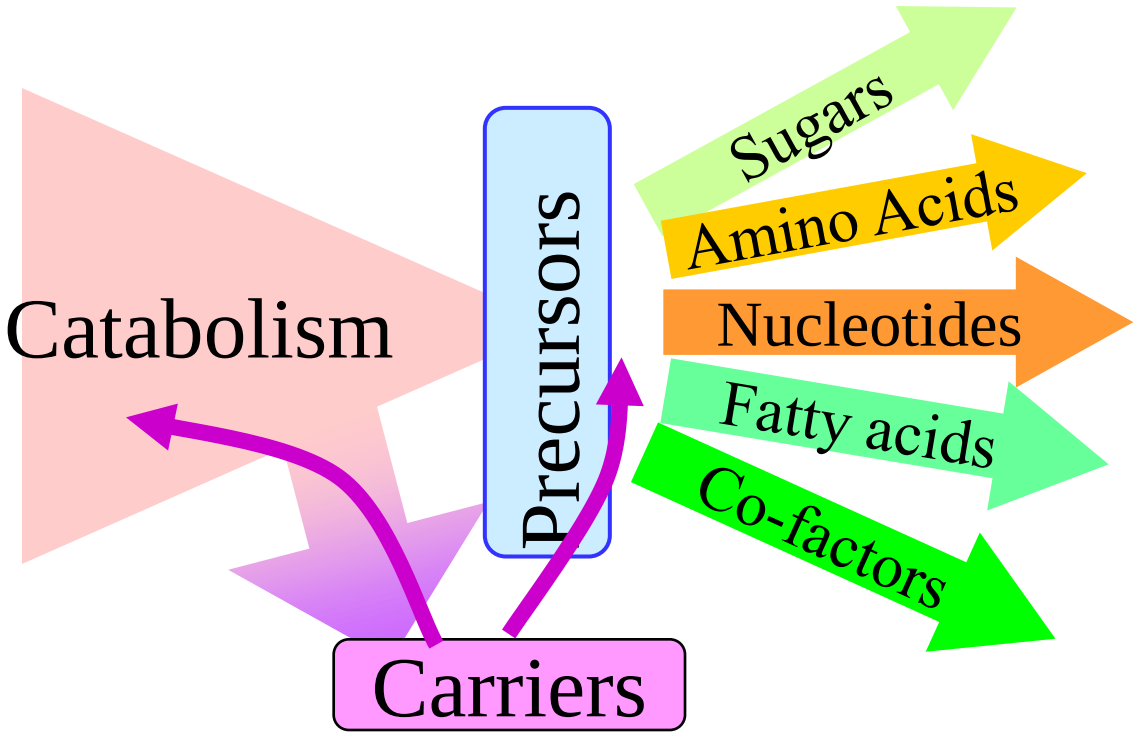


Layered architecture

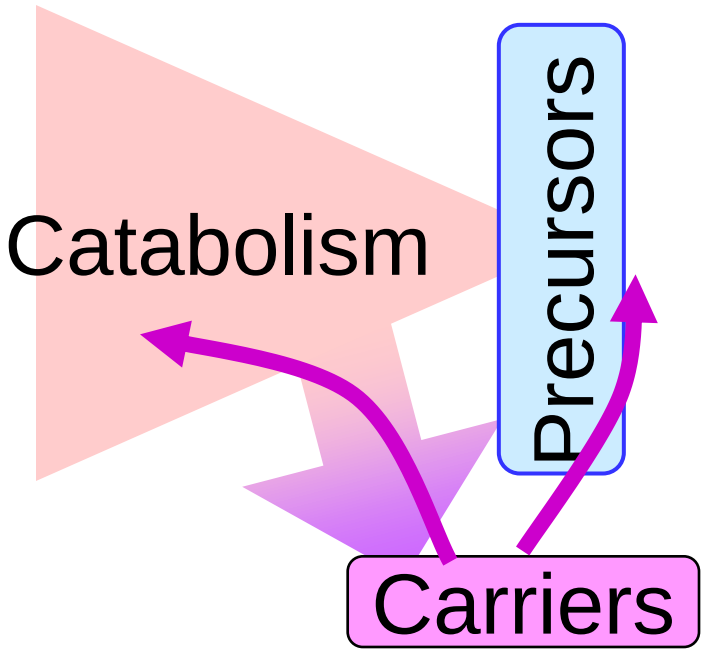


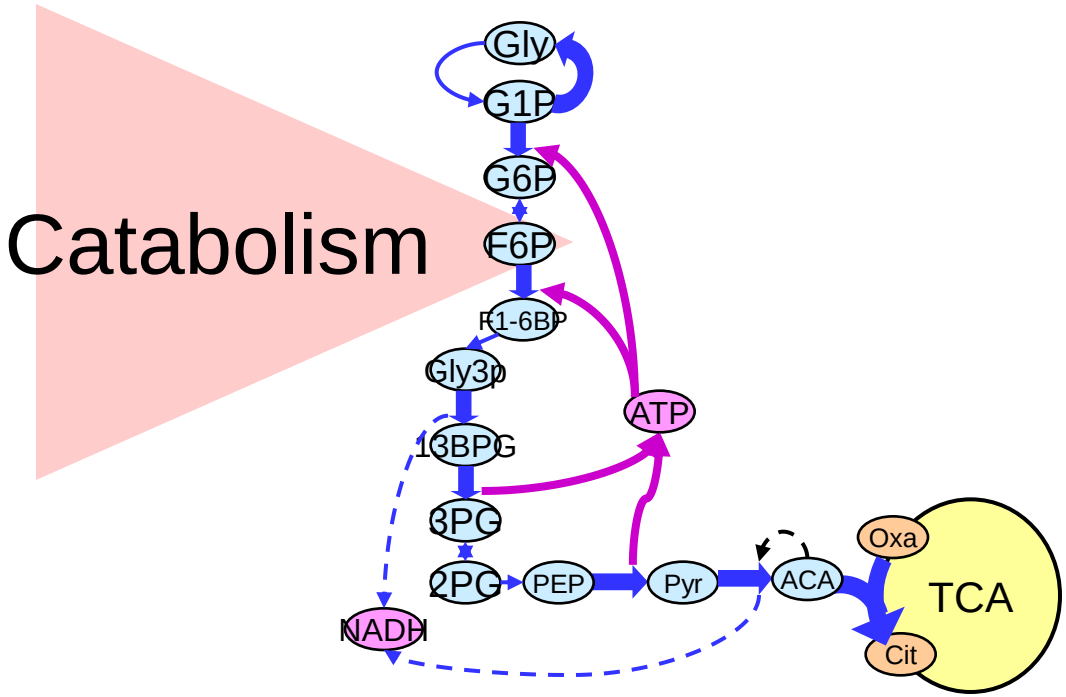
Biosynthetic Pathways

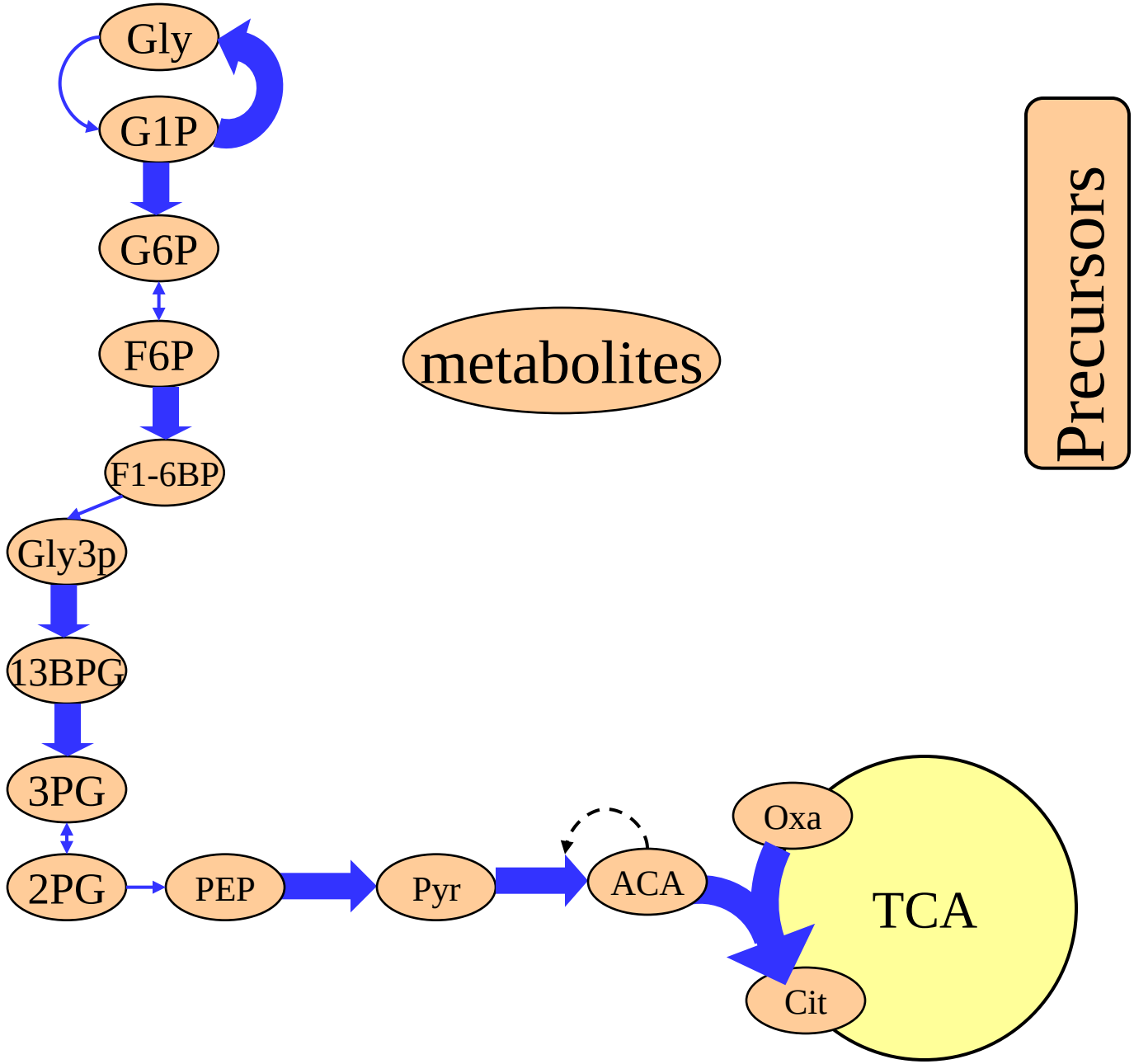
Inside every cell



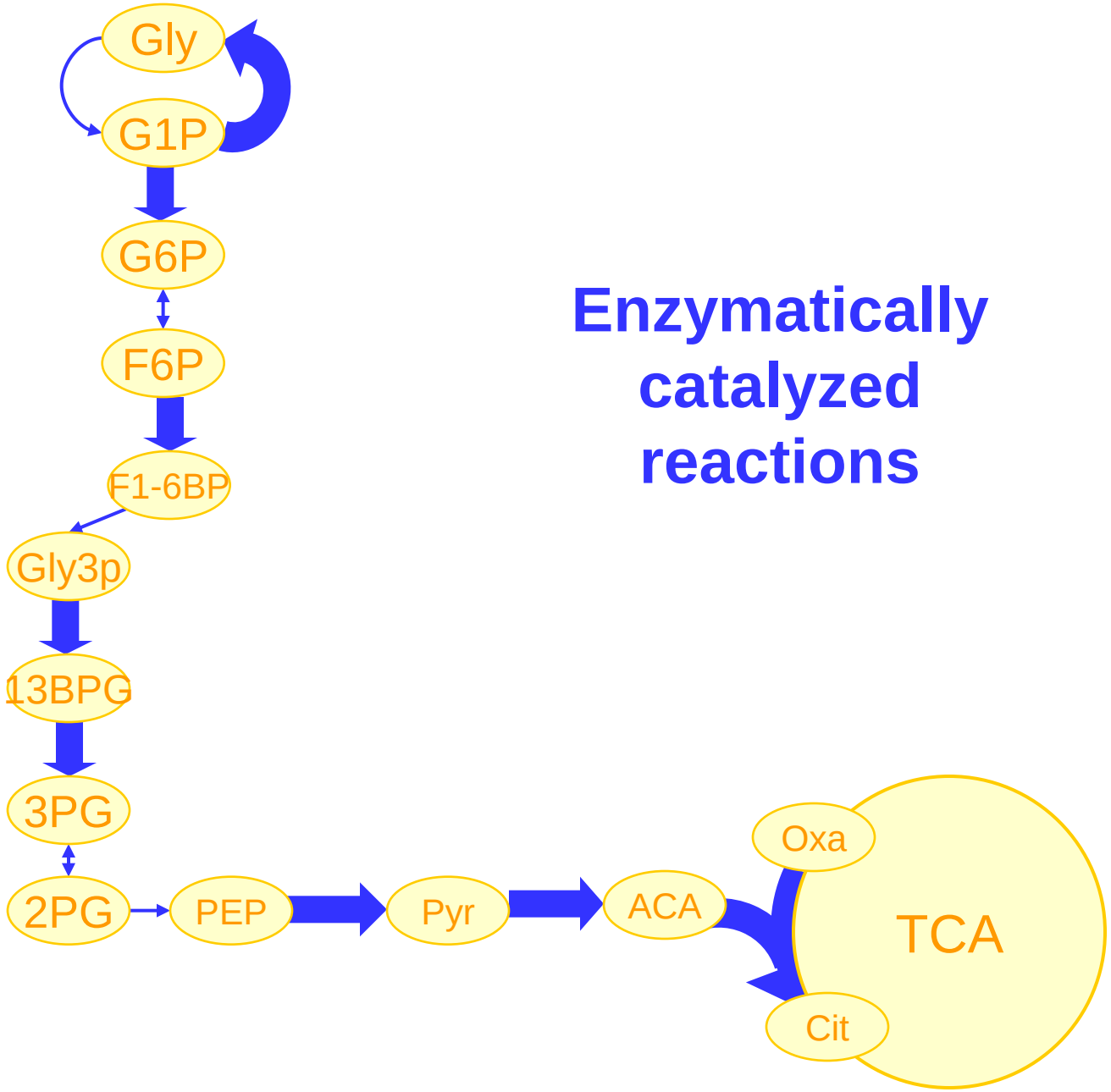
Core metabolic bowtie
Layered architecture

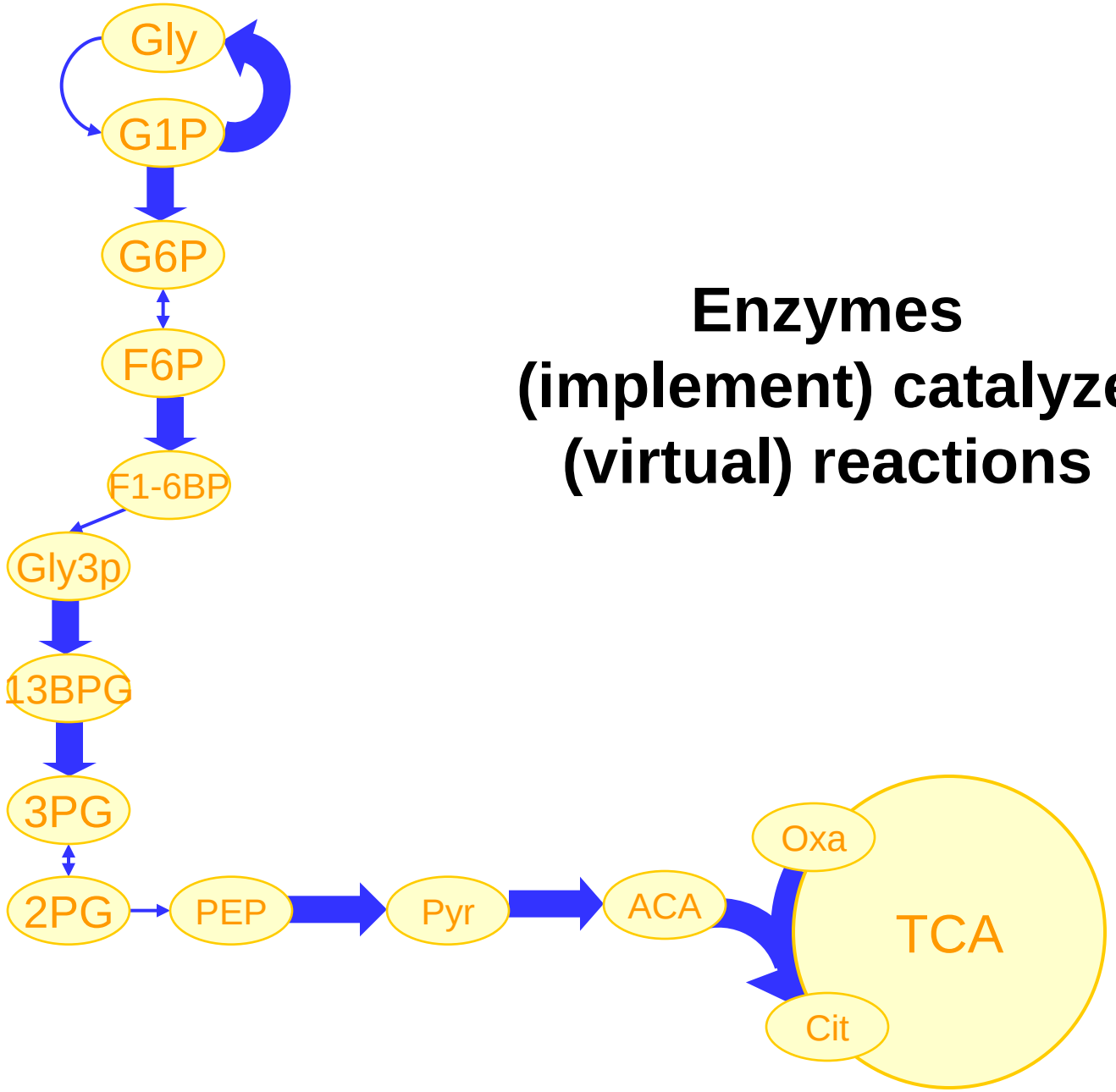

Catabolism
Precursors
Carriers


Catabolism
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit
ATP
NADH

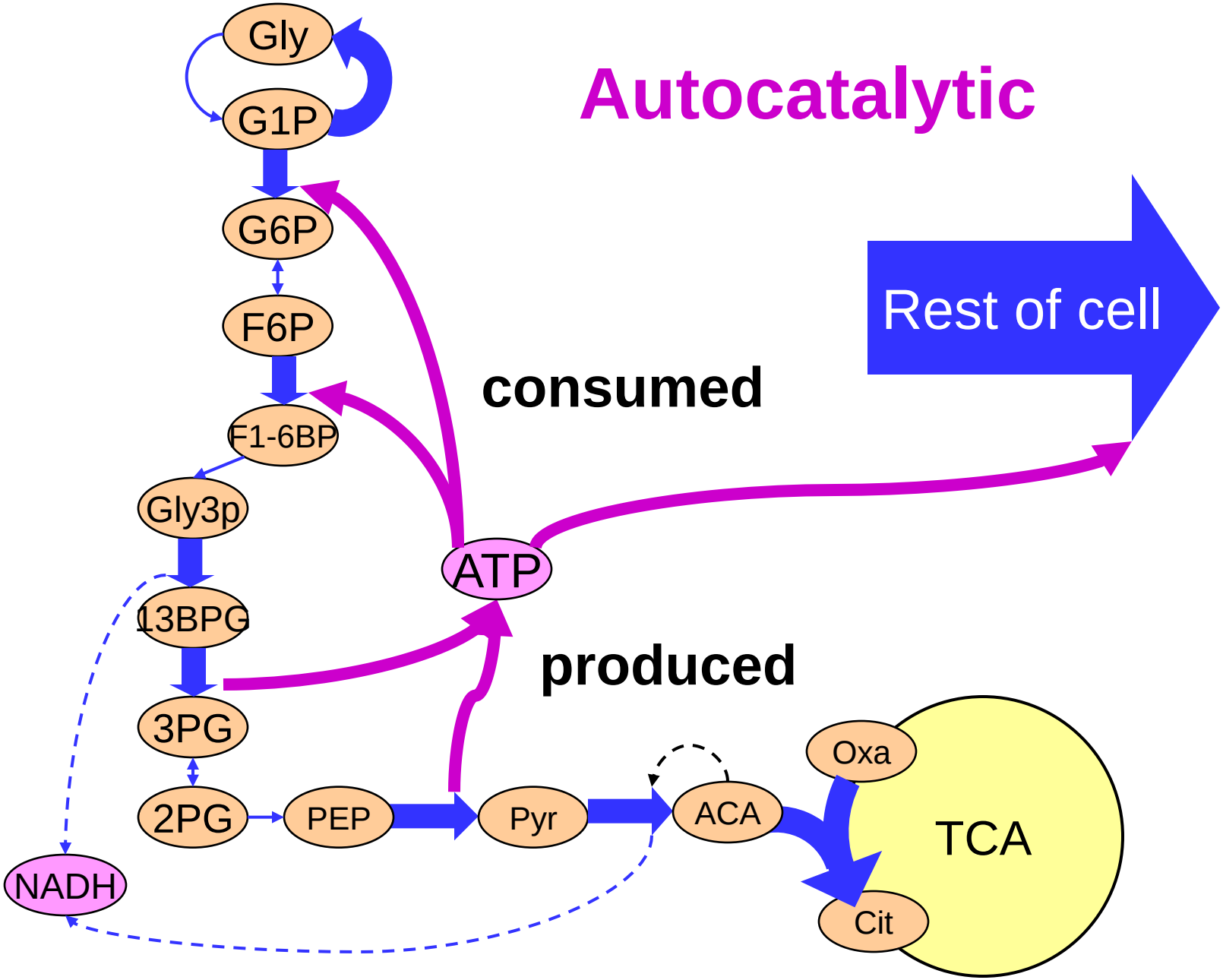

Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit
metabolites
Precursors

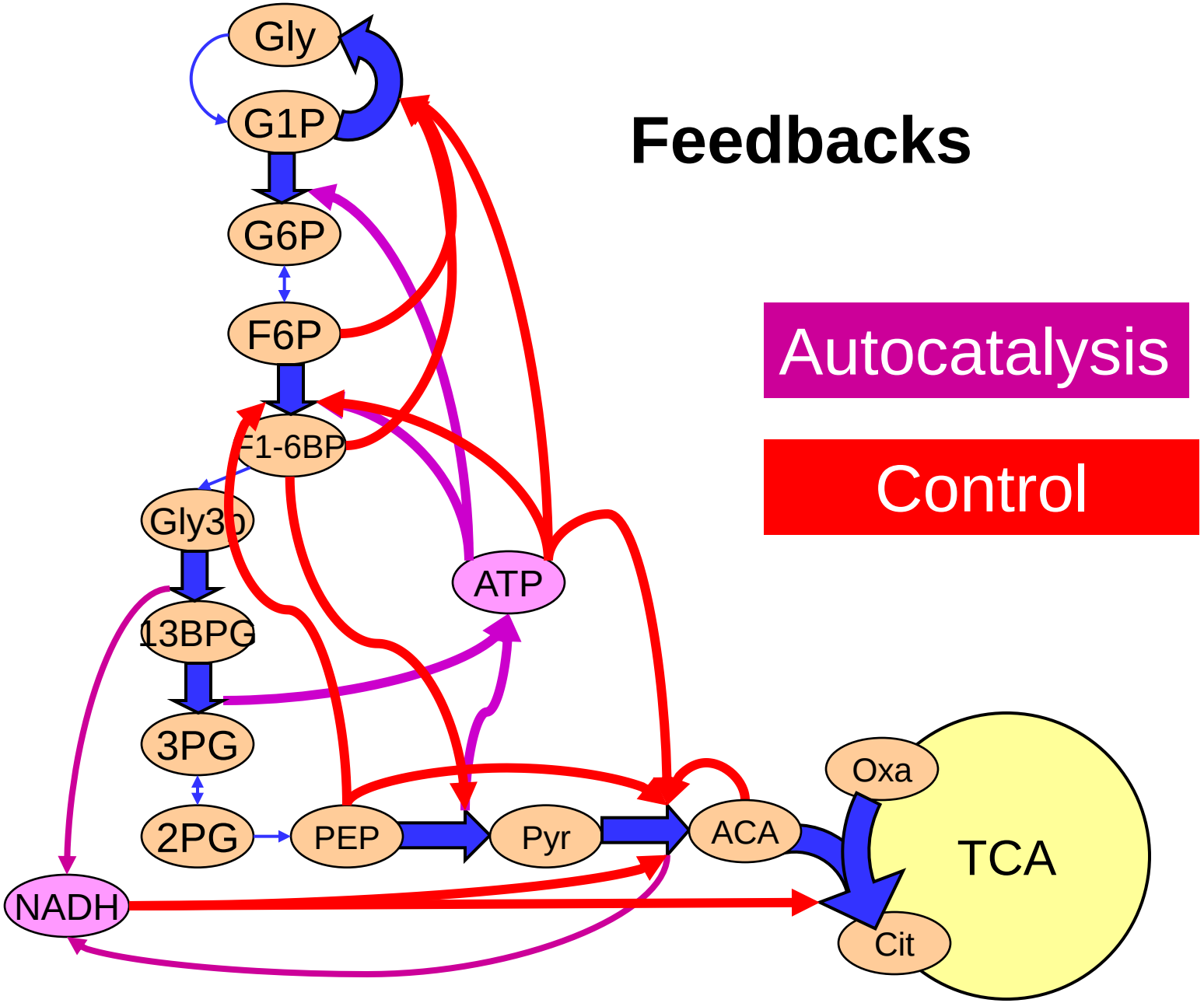
Enzymatically catalyzed reactions

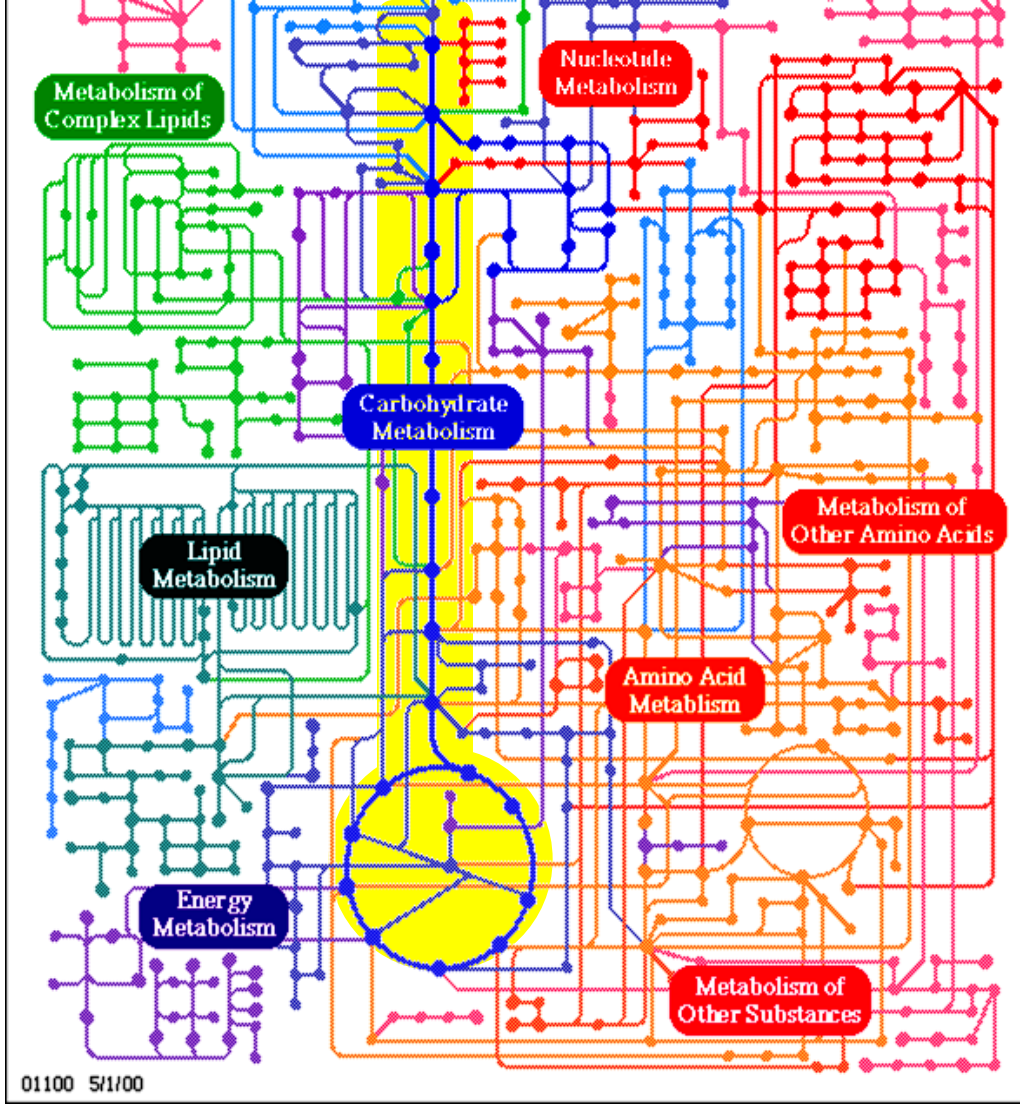


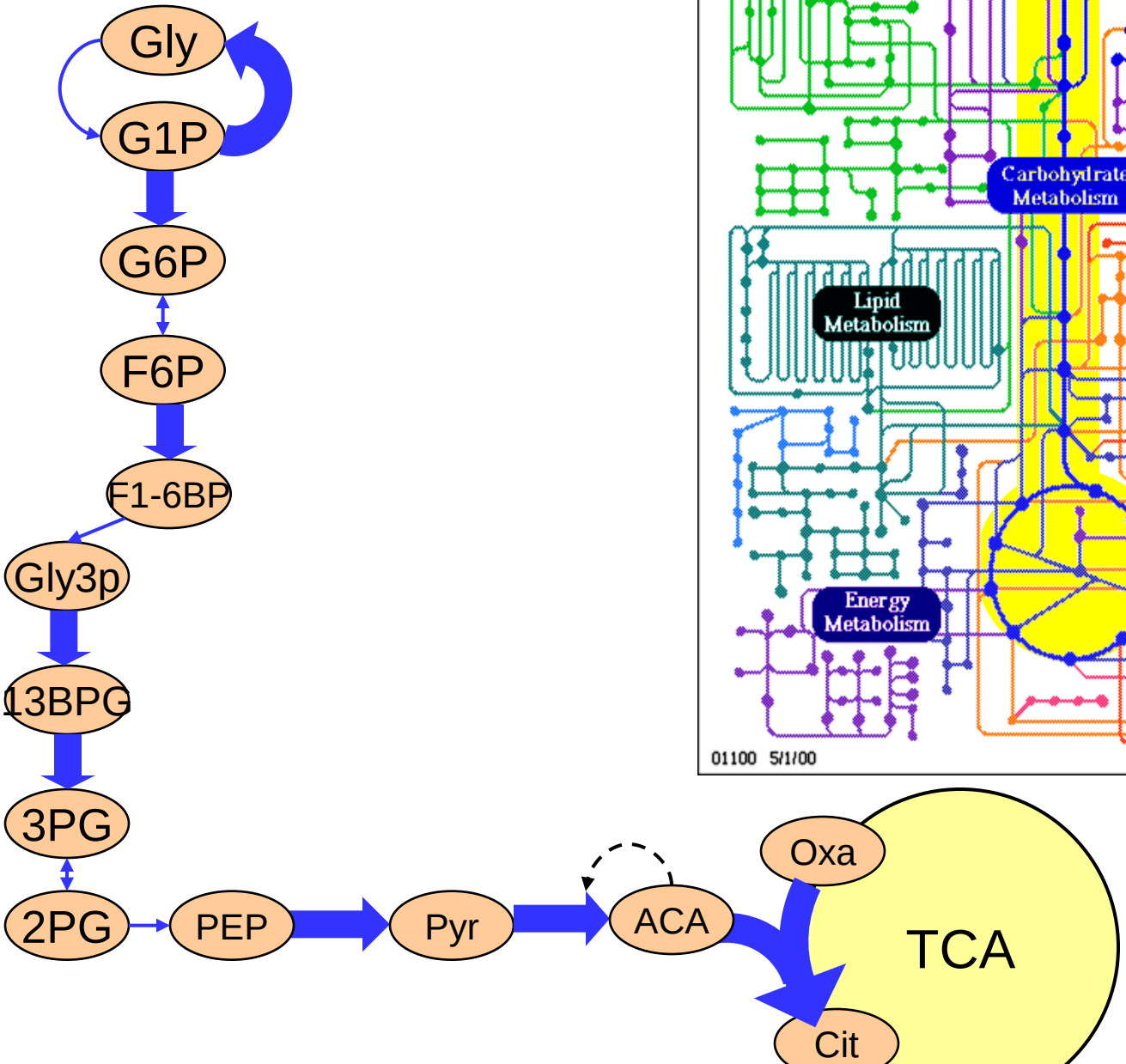


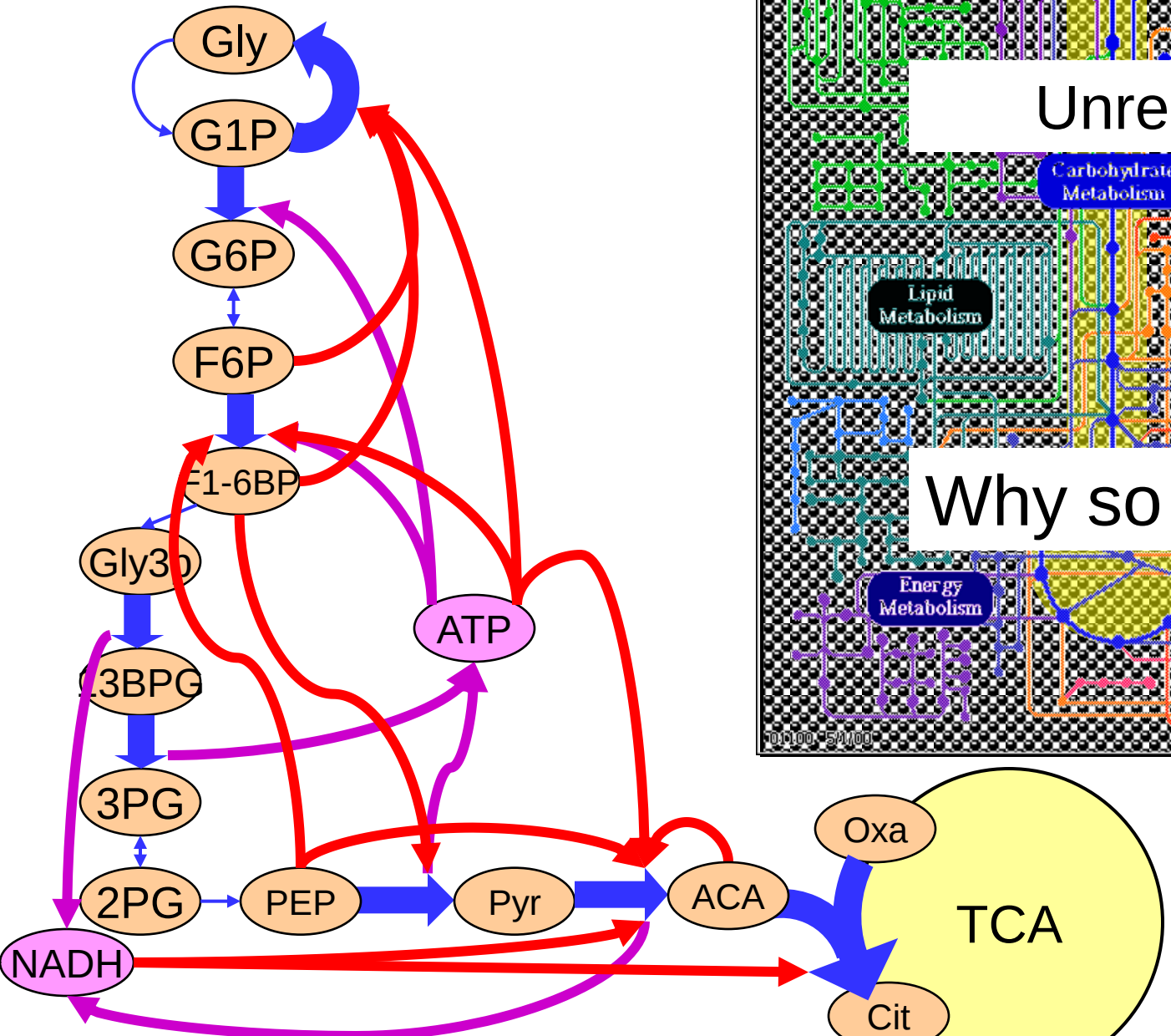
Enzymes (implement) catalyze (virtual) reactions

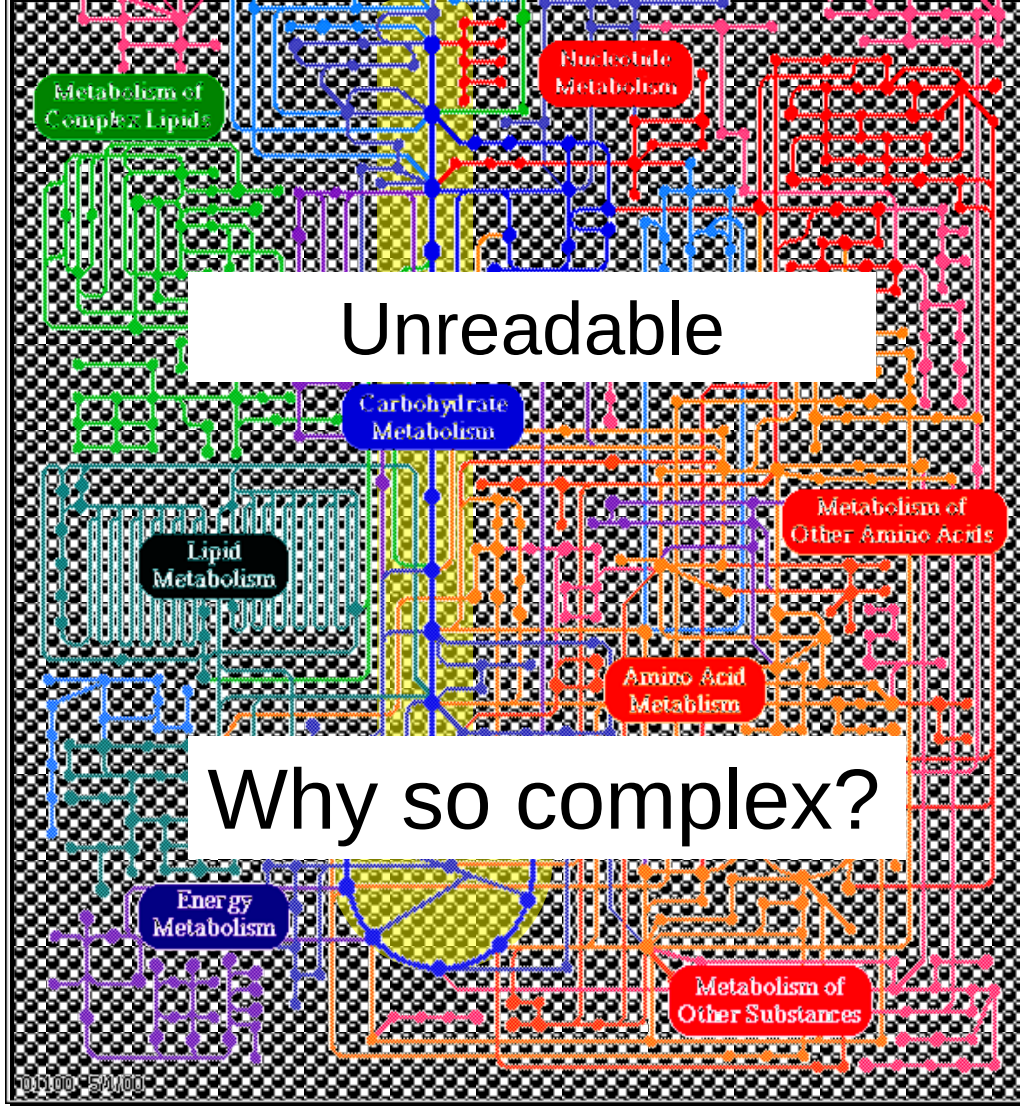

Autocatalytic
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit
NADH
ATP
consumed
produced
Rest of cell


Feedbacks
Autocatalysis
Control
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
TCA
Cit


Metabolism of Complex Lipids
Nucleotide Metabolism
Carbohydrate Metabolism
Lipid Metabolism
Metabolism of Other Amino Acids
Amino Acid Metablism
Energy Metabolism
Metabolism of Other Substances
01100 5/1/00


Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
Oxa
TCA
Cit

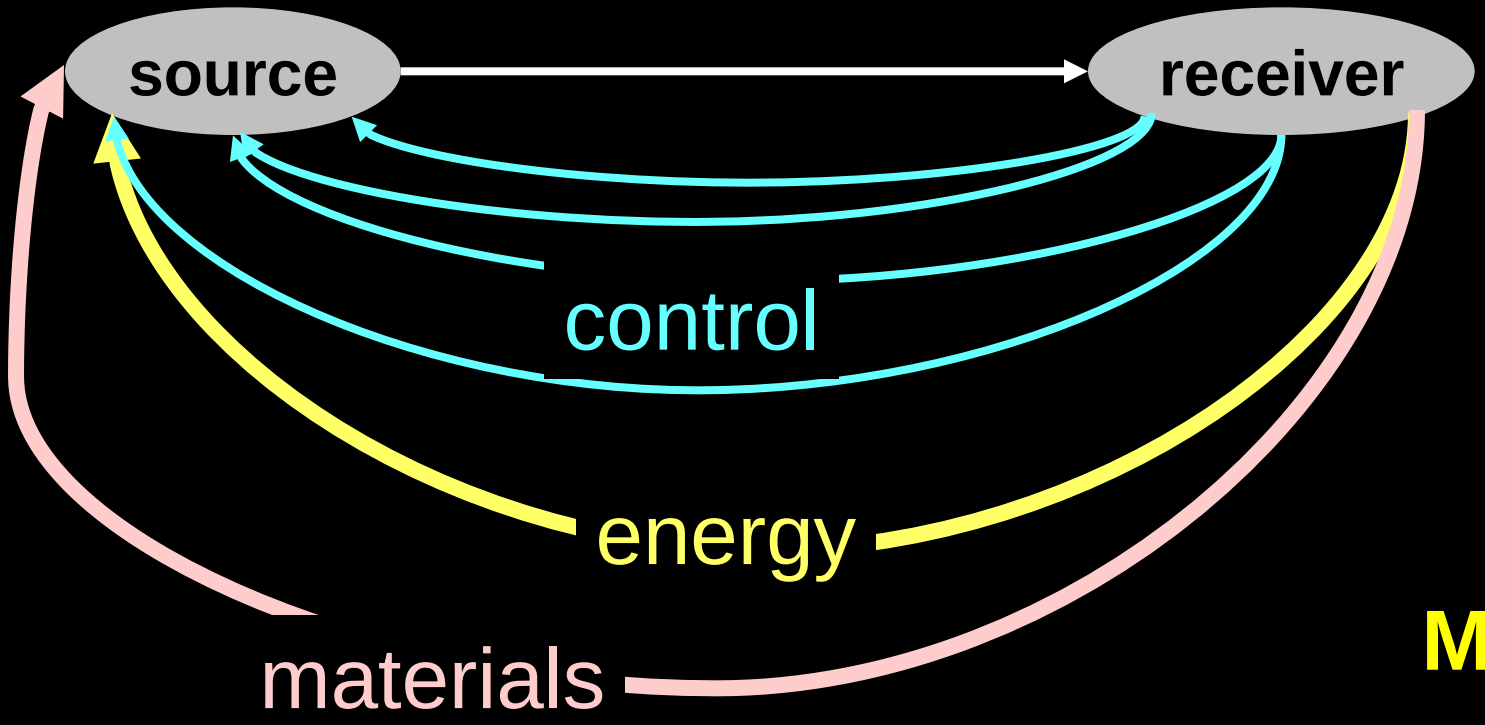

Gly
G1P
G6P
F6P
F1-6BP
Gly3
3BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
TCA
Cit


Metabolism of Complex Lipids
Nucleotide Metabolism
Unreadable
Carbohydrate Metabolism
Metabolism of Other Amino Acids
Lipid Metabolism
Amino Acid Metabolism
Why so complex?
Energy Metabolism
Metabolism of Other Substances

signaling
gene expression
metabolism
lineage

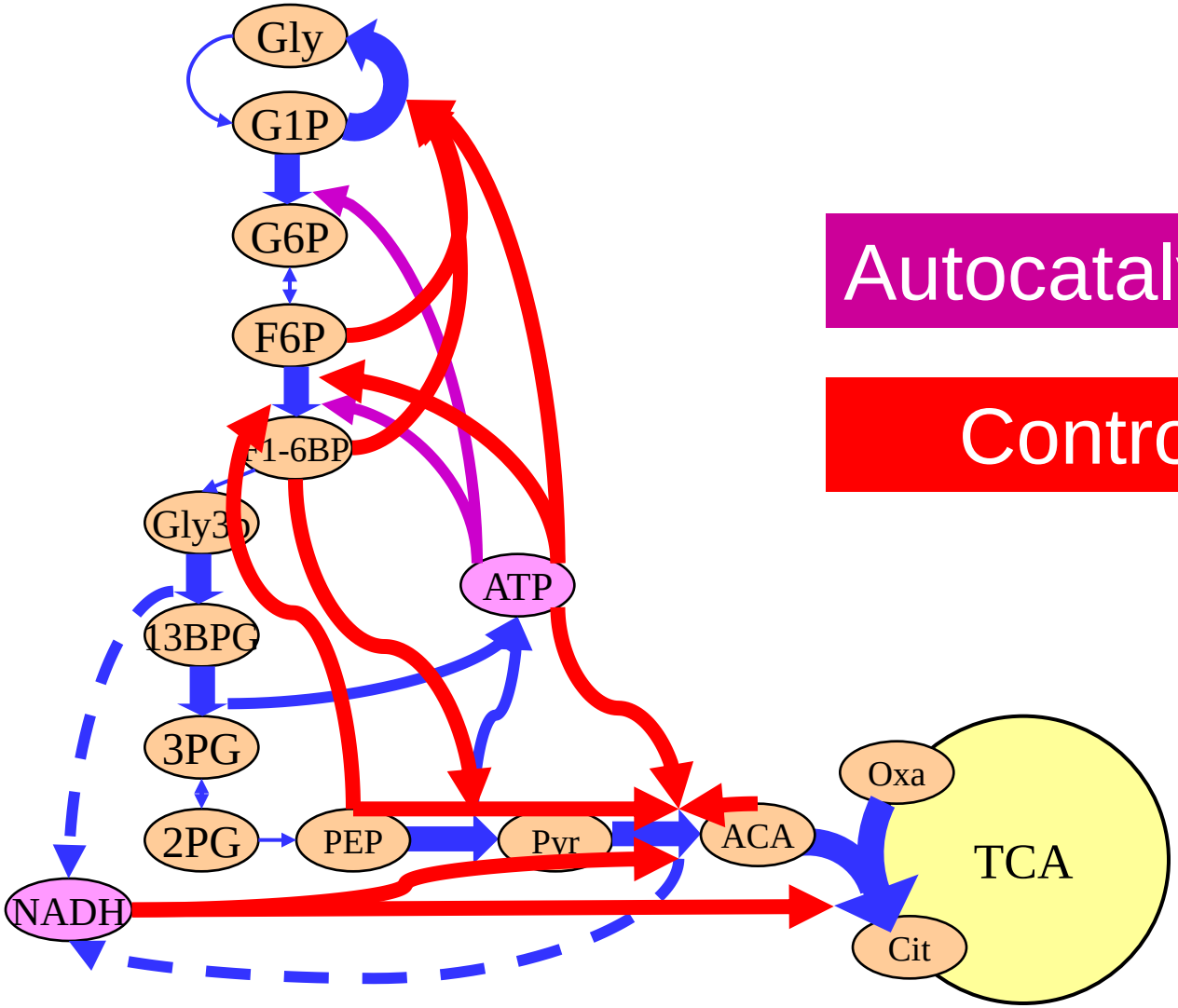
Biological pathways

signaling
gene expression
metabolism
lineage



More complex feedback

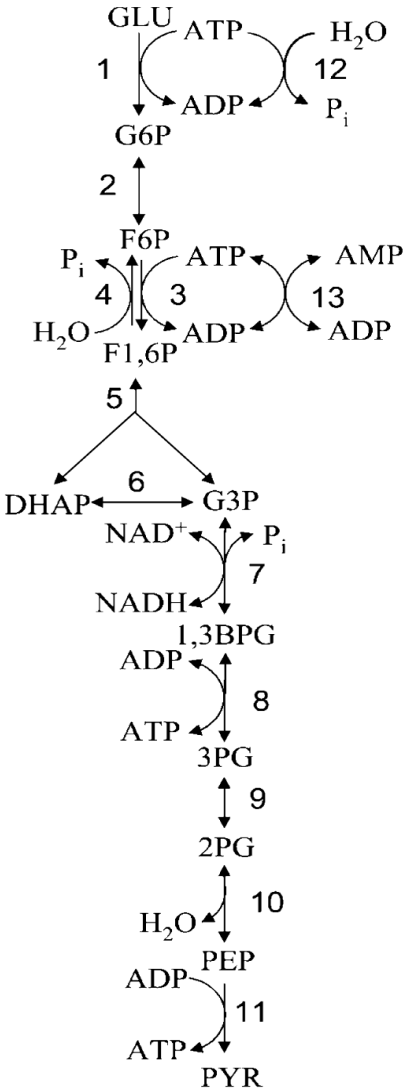
Feedbacks



Autocatalysis

Control

Nikolaev, …, Elucidation and Structural Analysis of **Conserved Pools** for Genome-Scale Metabolic Reconstructions, Biophysical Journal, Volume 88, Issue 1, January 2005, Pages 37-49



(P1) Total NAD moiety: $[NAD^+] + [NADH]$

(P2) Total adenylate moiety: $[ATP] + [ADP] + [AMP]$

(P3) Total carbon moiety: $2[GLU] + 2[G6P] + 2[F6P] + 2[F1,6P] + [DHAP] +$

(P4) Total phosphate moiety

(P5) Total oxygen moiety:

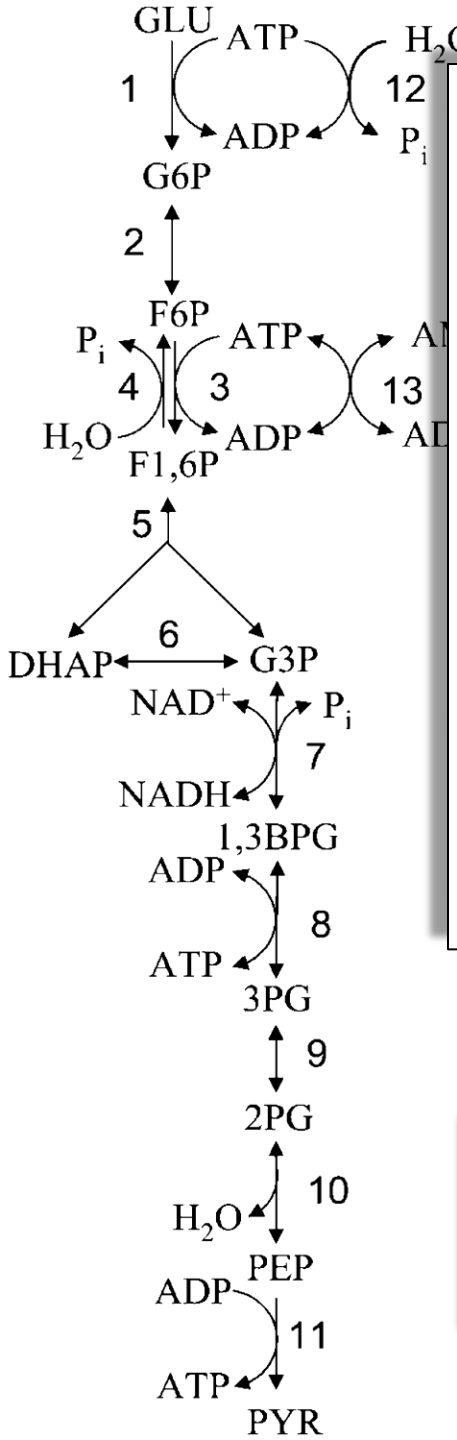
(P6) Oxidized state of meta

Constrained (conserved):

1. Total NAD moiety
2. Total Adenylate moiety
3. Total Carbon moiety
4. Total phosphate moiety
5. Total oxygen moiety
6. Oxidized state of metabolites
7. Reduced state of metabolites
8. High energy potential release

(P7) Reduced state of metabolites: $2[GLU] + 2[G6P] + 2[F6P] + 2[F1,6P] + + [DHAP] + [G3P] + [NADH]$

(P8) High energy potential release: $2[GLU] + [G6P] + [F6P] + [3PG] + [2PG] + + [PYR] + [ADP] + 2[AMP] + [H_2O]$



(P1) Total NAD moiety: $[NAD^+] + [NADH]$

Constrained ("conserved"):

Moieties

1. NAD
2. Adenylate
3. Carbon
4. phosphate
5. oxygen

6. Oxidized state of metabolites
7. Reduced state of metabolites
8. High energy potential release

2[F1,6P] + [DHAP] +

[2PG] + [PEP] + [PYR]

HAP] + [G3P] +

+ [PEP] +

DP] + [P_i]

P_i] + [H_2O]

] +

+ [PEP] + [PYR] + $[NAD^+]$

(P7) Reduced state of metabolites: 2[GLU] + 2[G6P] + 2[F6P] + 2[F1,6P] +

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|S(j\omega)\right| \left(\frac{z}{z^2+\omega^2}\right) d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

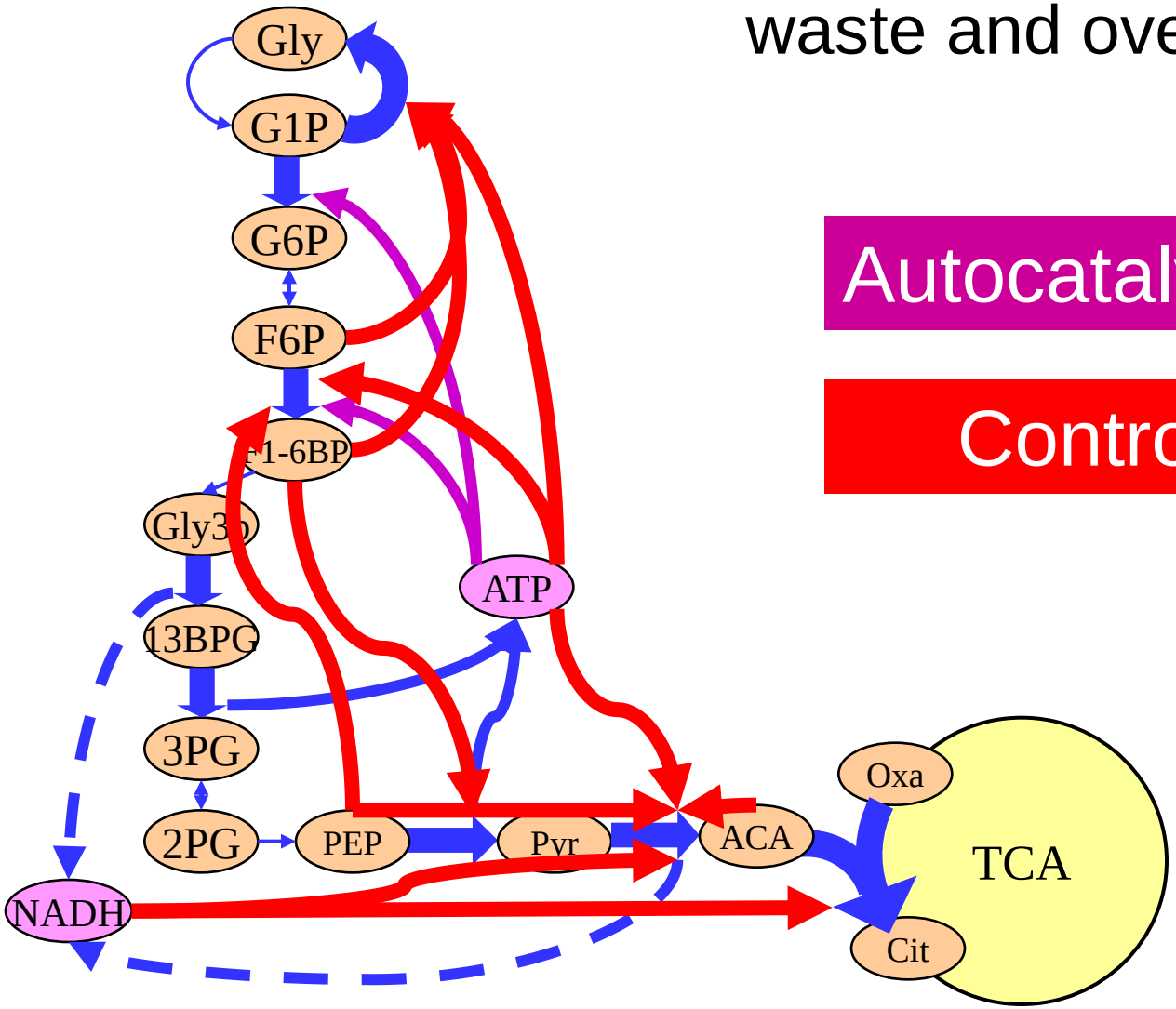
NADH]

[2PG] +

+ [PYR] + [ADP] + 2[AMP] + [H_2O]

Robust=maintain energy charge w/fluctuating cell demand

Efficient=minimize metabolic waste and overhead

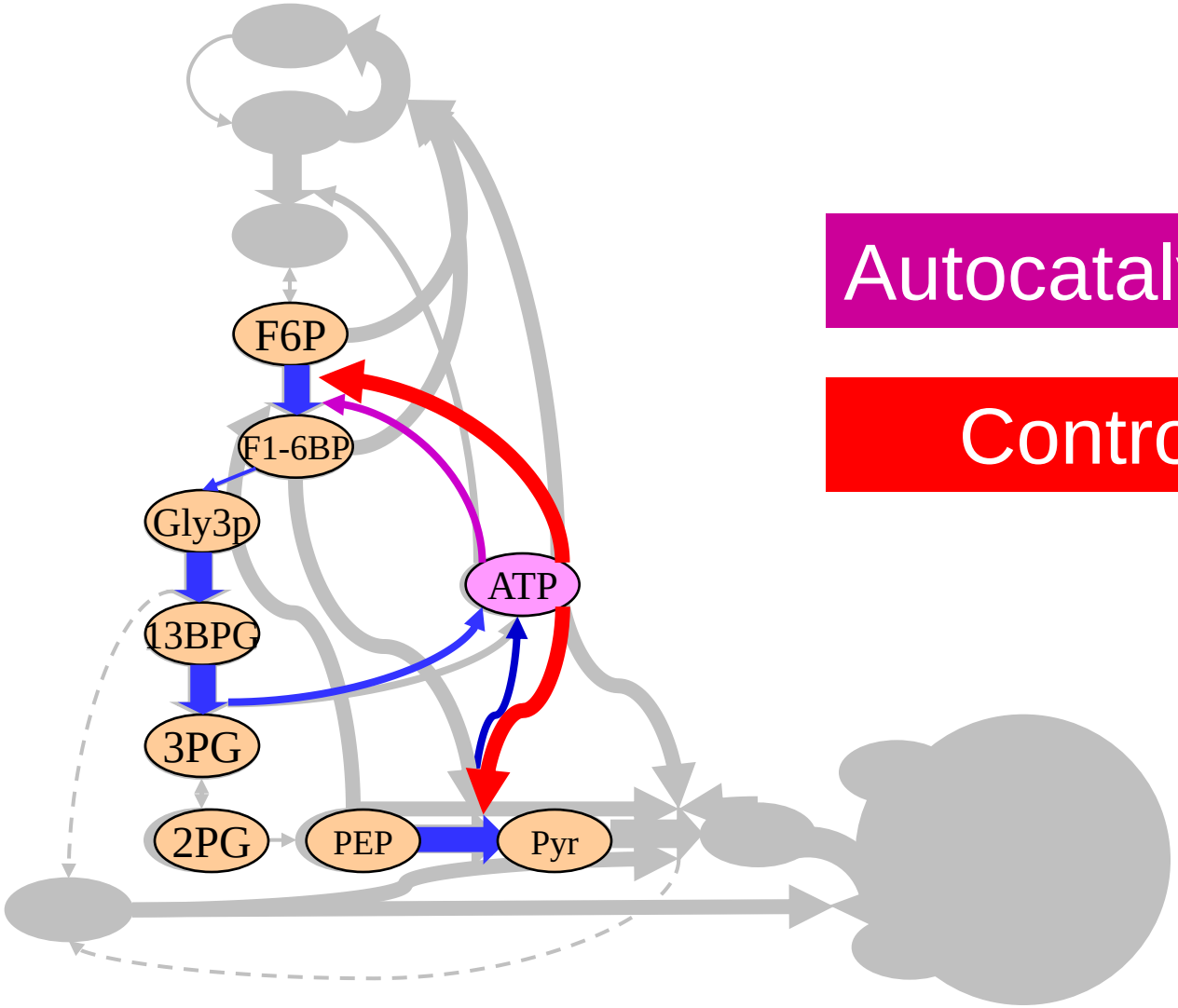


Autocatalysis

Control

Feedbacks

Minimal model?



Autocatalysis

Control

Minimal model

~1 equilibrium

2 metabolites

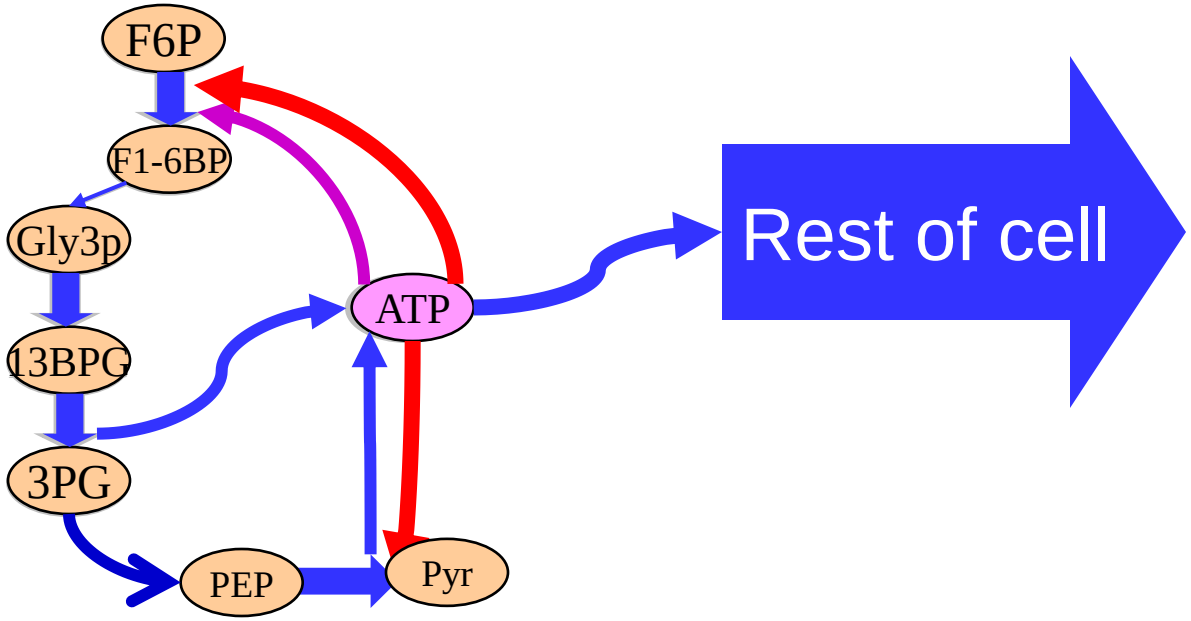
3 “reactions”

Control

Plus

Autocatalytic

Feedback

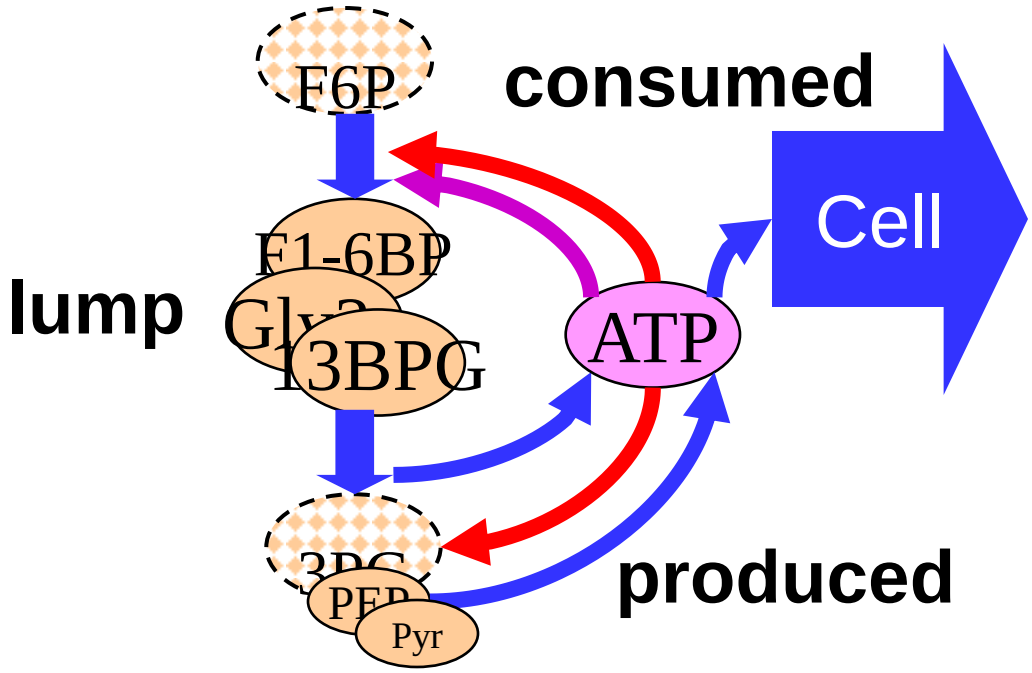


Minimal model

~1 equilibrium

2 metabolites

3 “reactions”



UG biochem, math, control theory

Glycolytic Oscillations and Limits on Robust Efficiency

Fiona A. Chandra,[1]* Gentian Buzi,[2] John C. Doyle[2]

Both engineering and evolution are constrained by trade-offs between efficiency and robustness, but theory that formalizes this fact is limited. For a simple two-state model of glycolysis, we explicitly derive analytic equations for hard trade-offs between robustness and efficiency with oscillations as an inevitable side effect. The model describes how the trade-offs arise from individual parameters, including the interplay of feedback control with autocatalysis of network products necessary to power and catalyze intermediate reactions. We then use control theory to prove that the essential features of these hard trade-off "laws" are universal and fundamental, in that they depend minimally on the details of this system and generalize to the robust efficiency of any autocatalytic network. The theory also suggests worst-case conditions that are consistent with initial experiments.

molecules are consumed upstream and four are produced downstream, which normalizes to $q = 1$ (each y molecule produces two downstream) with kinetic exponent $a = 1$. To highlight essential trade-offs with the simplest possible analysis, we normalize the concentration such that the unperturbed ($\delta = 0$) steady states are $\bar{y} = 1$ and $\bar{x} = 1/k$ [the system can have one additional steady state, which is unstable when $(1, 1/k)$ is stable]. [See the supporting online material (SOM) part I]. The basal rate of the PFK reaction and the consumption rate have been normalized to 1 (the 2 in the numerator and feedback coefficients of the reactions come from these normalizations). Our results hold for more general systems

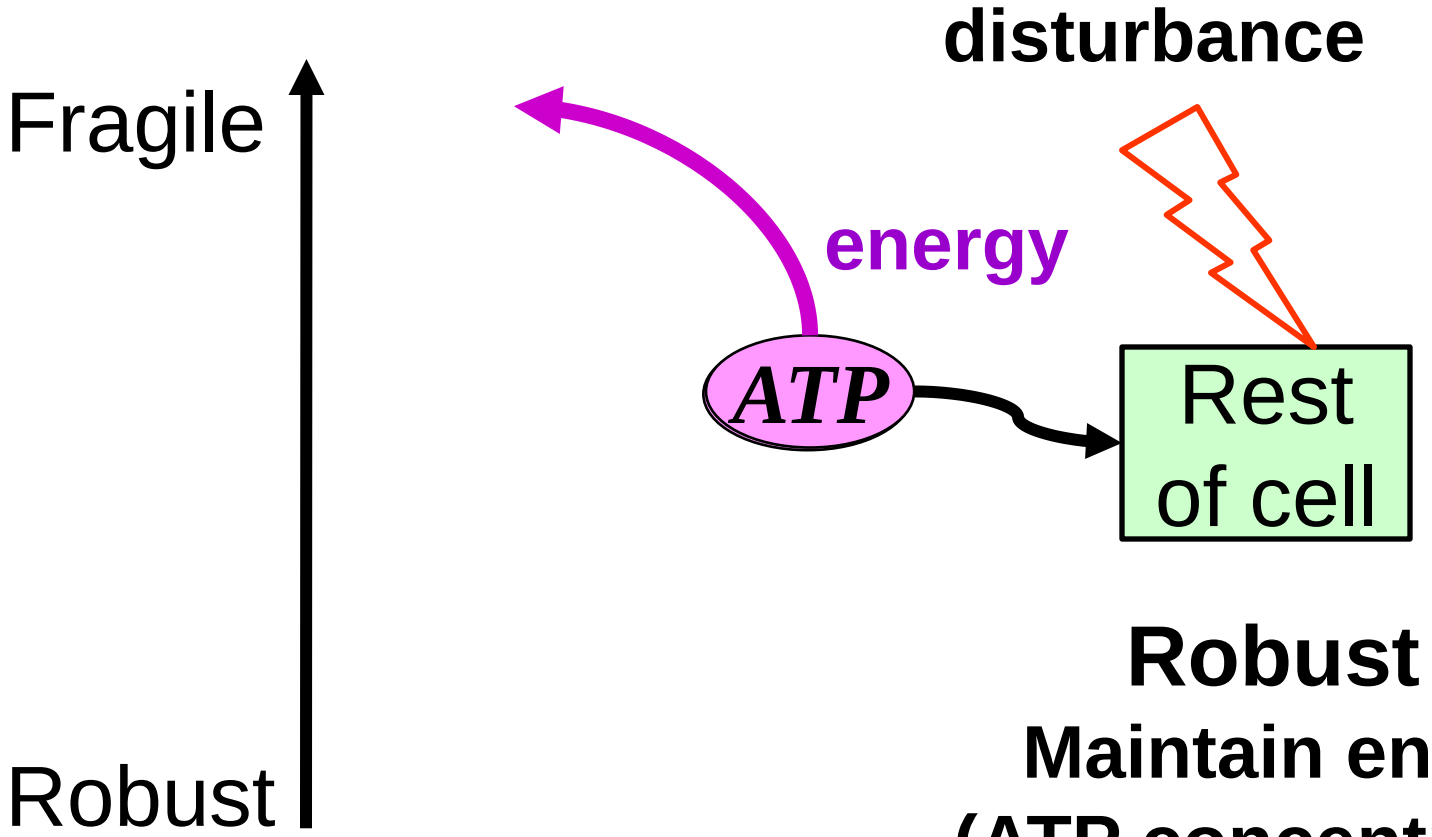
Chandra, Buzi, and Doyle

Science

AAAS

Most important paper so far.

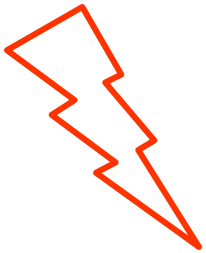
(May 21): Hard tradeoff in glycolysis



Robust =
Maintain energy
(ATP concentration)
despite demand fluctuation

disturbance

Accurate vs sloppy



Fragile

Robust

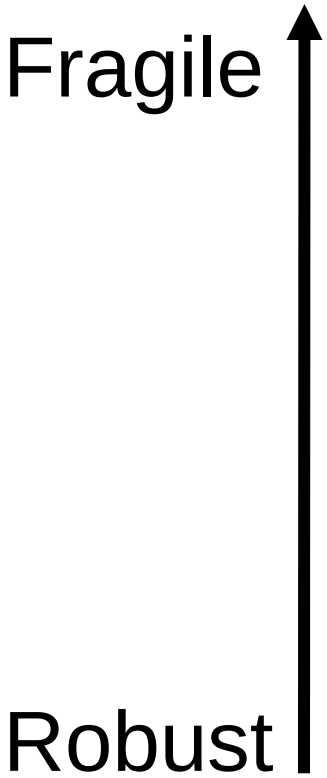
What makes this hard?

1. Instability (autocatalysis)
2. Delay (enzyme amount)

Robust

≈Disturbance rejection

≈ Accurate



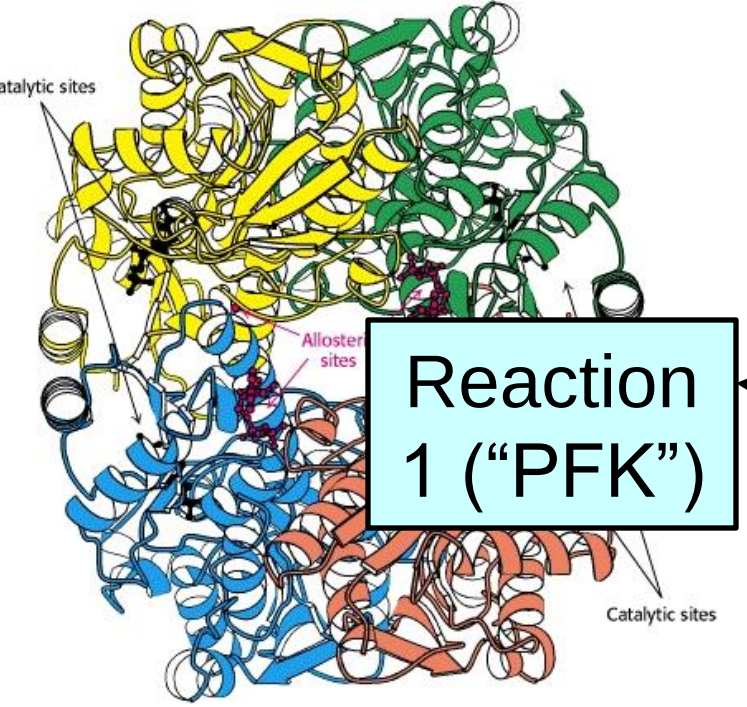
What makes this hard?

1. Instability
2. Delay

The CNS must cope with both

Today's important point

enzymes catalyze reactions



Reaction 1 ("PFK")

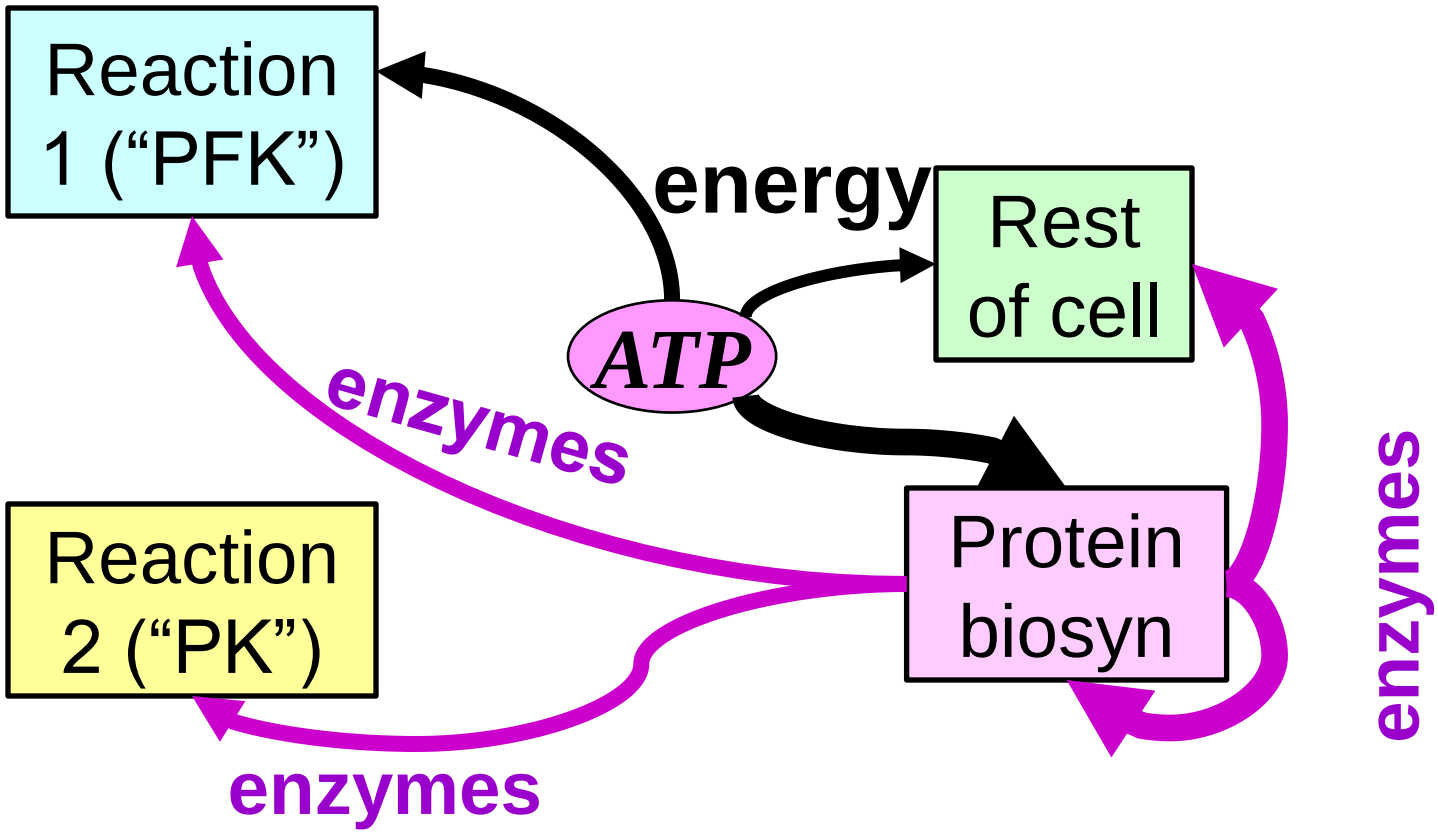
energy

ATP

Rest of cell

Reaction 2 ("PK")

enzymes catalyze reactions, another source of autocatalysis



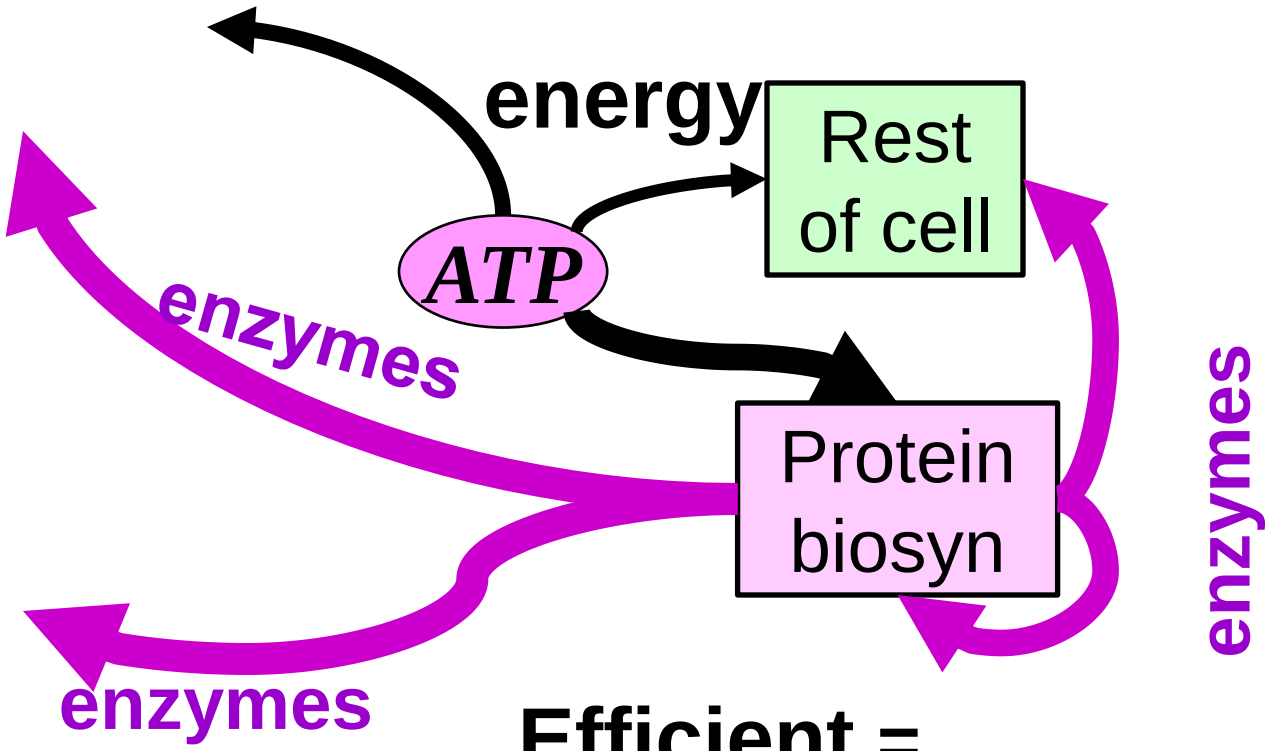
Efficient =
low metabolic overhead
≈ low enzyme amount

enzymes catalyze reactions, another source of autocatalysis

reaction rates

∝

enzyme amount



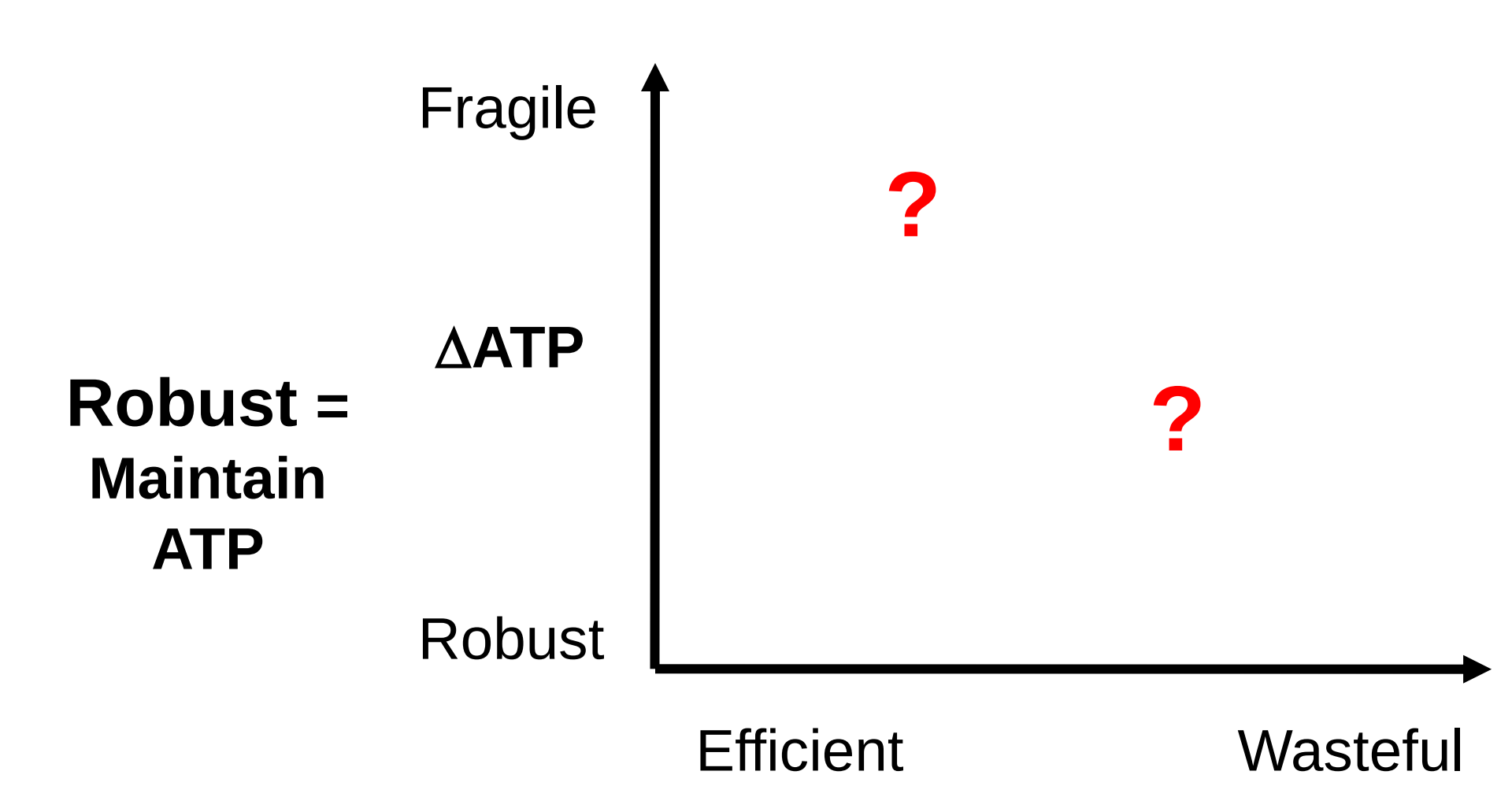
Can't make too many enzymes here, need to supply rest of the cell.

Efficient =

low metabolic overhead

≈ low enzyme amount

(⇒ slow reactions)

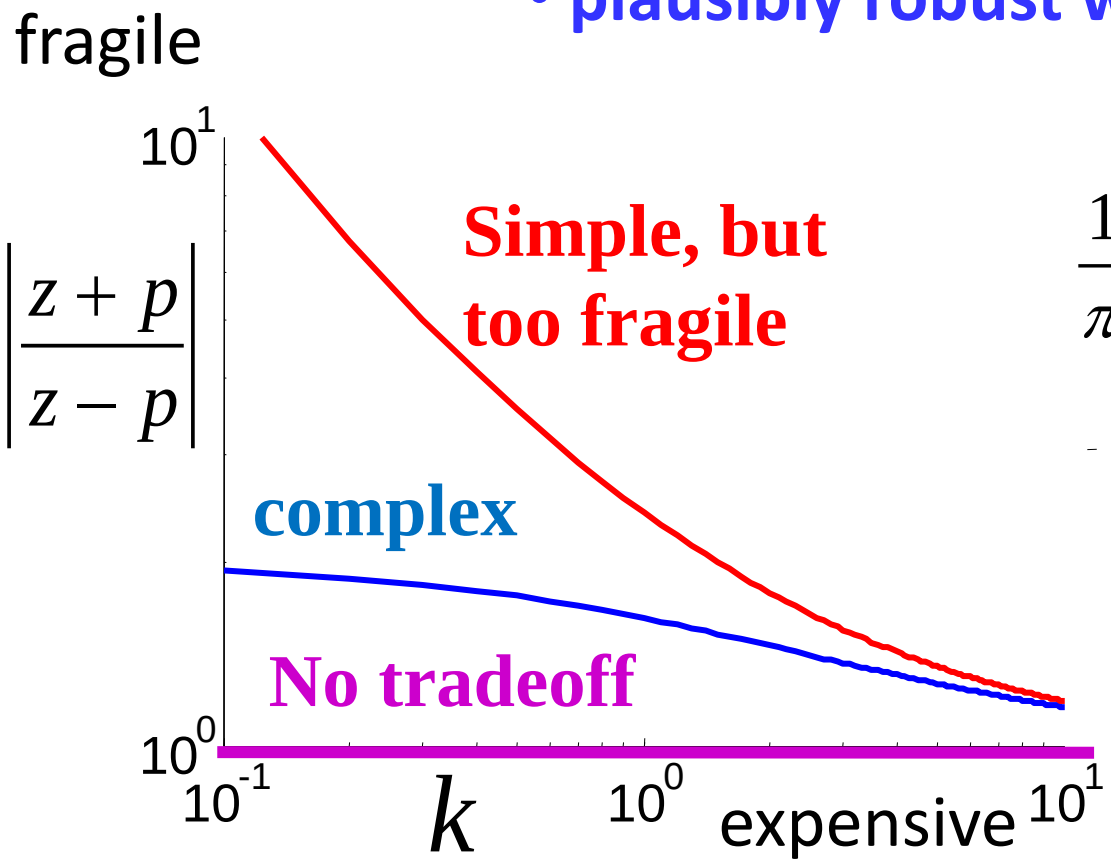


Robust =
Maintain ATP

Efficient =
low enzyme amount
(⇒ slow reactions)

(May 21): Hard tradeoff in glycolysis is

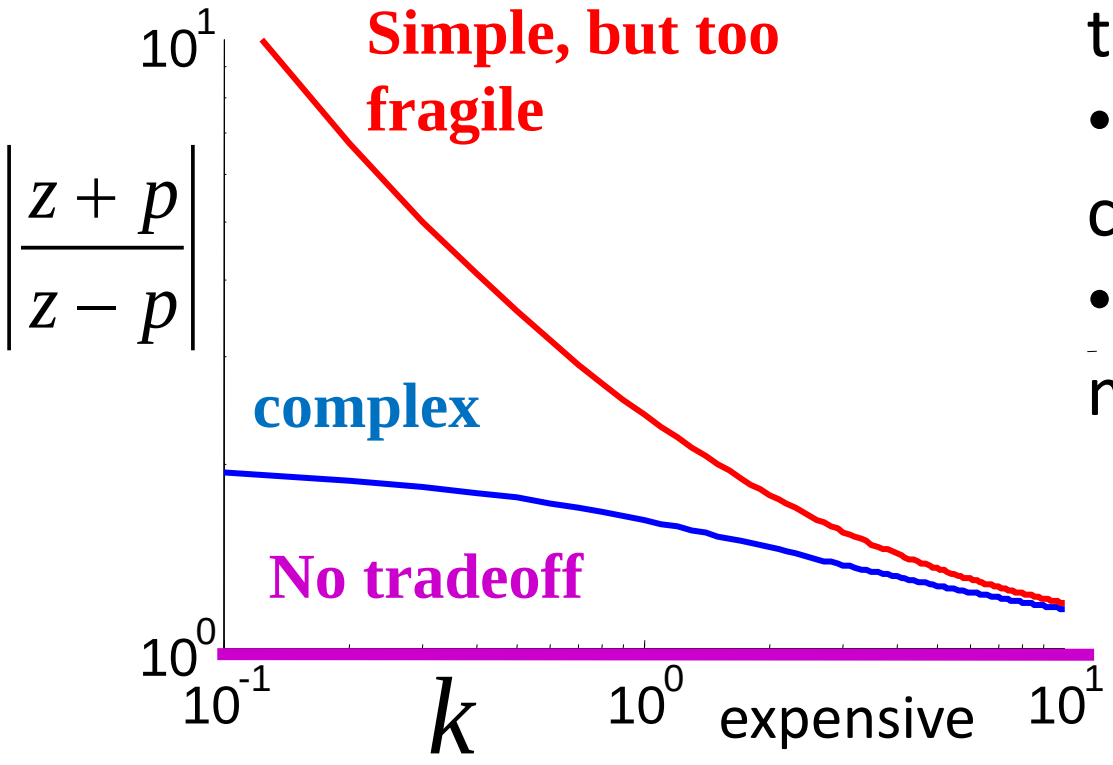
- **robustness vs efficiency**
- **absent without autocatalysis**
- **too fragile with simple control**
- **plausibly robust with complex control**



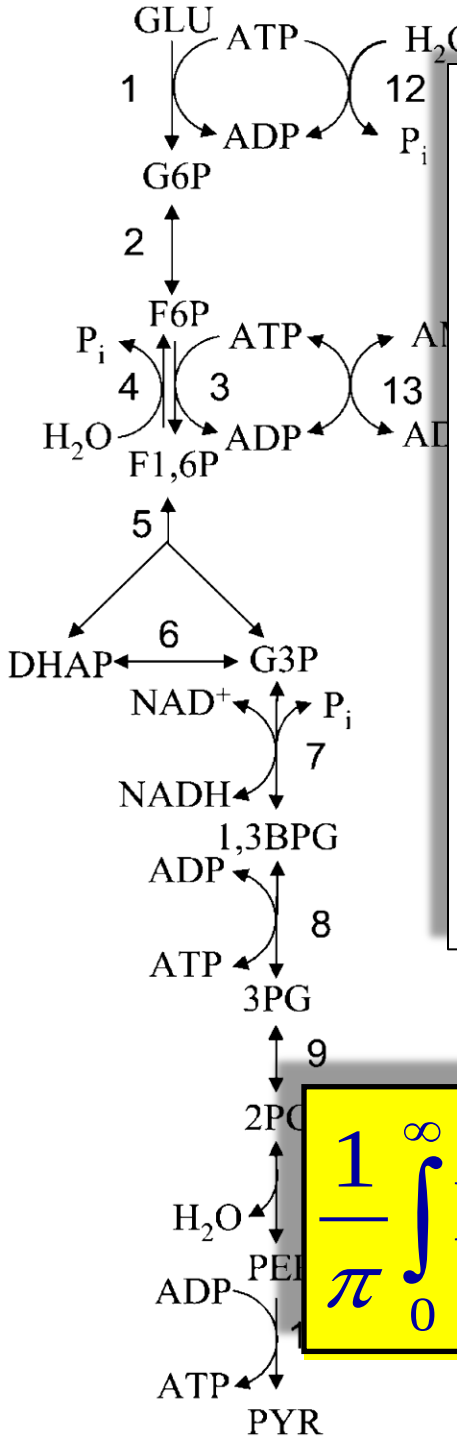
$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right|\left(\frac{z}{z^2+\omega^2}\right)d\omega$$

$$\geq \ln\left|\frac{z+p}{z-p}\right|$$

(May 21): Hard tradeoff in glycolysis is
- robustness vs efficiency
- absent without autocatalysis
- too fragile with simple control
- plausibly robust with complex control



- Evolution can
- increase complexity
- to improve robustness tradeoffs.
- But this complexity creates new fragilities
- so there is always more to this story.



(P1) Total NAD moiety: $[NAD^+] + [NADH]$

Constrained ("conserved"):

Moieties

1. NAD
2. Adenylate
3. Carbon
4. phosphate
5. oxygen

6. Oxidized state of metabolites
7. Reduced state of metabolites
8. High energy potential release

$2[F1,6P] + [DHAP] +$

$[2PG] + [PEP] + [PYR]$

$HAP] + [G3P] +$

$+ [PEP] +$

$DP] + [P_i]$

$P_i] + [H_2O]$

$] +$

$+ [PEP] + [PYR] + [NAD^+]$

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|S(j\omega)\right| \left(\frac{z}{z^2+\omega^2}\right) d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

$]$

$] +$

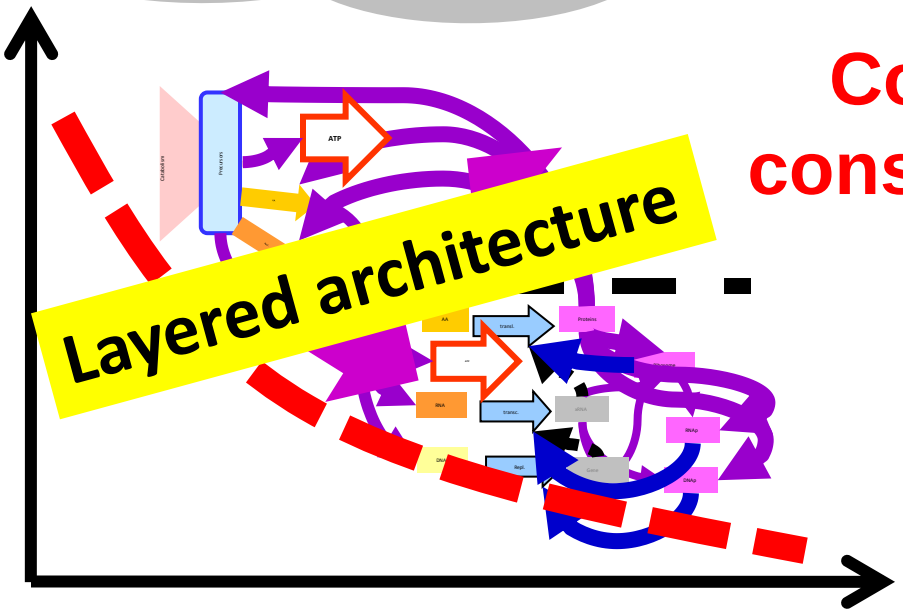
$+ [PYR] + [ADP] + 2[AMP] + [H_2O]$

What makes the bacterial biosphere so adaptable?

Deconstrained

Environment

Action



Core conserved constraints facilitate tradeoffs

+

Active control of the genome (facilitated variation)

Deconstrained

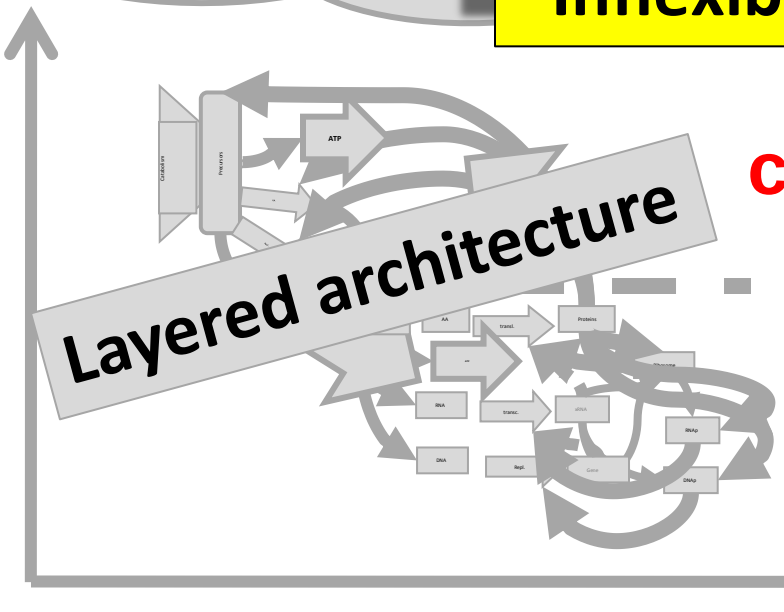
What makes the bacterial biosphere so adaptable?

Environment

Action

Deconstrained

Fast
Inflexible



Core conserved constraints facilitate tradeoffs

+

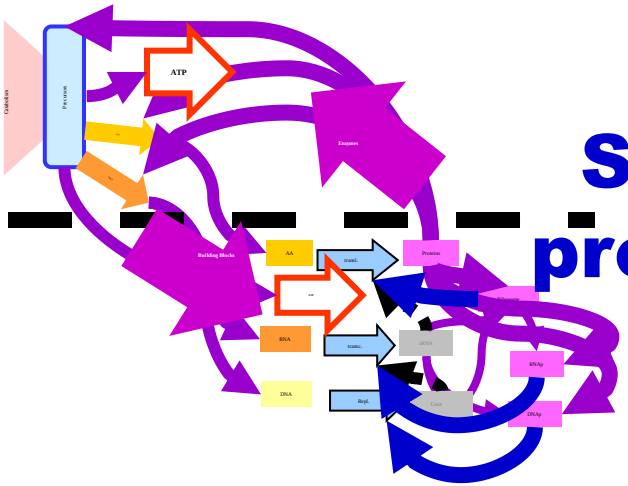
Active control of the genome (facilitated variation)

Deconstrained

Slow
Flexible

Bacterial biosphere

Deconstrained Environments



Shared protocols

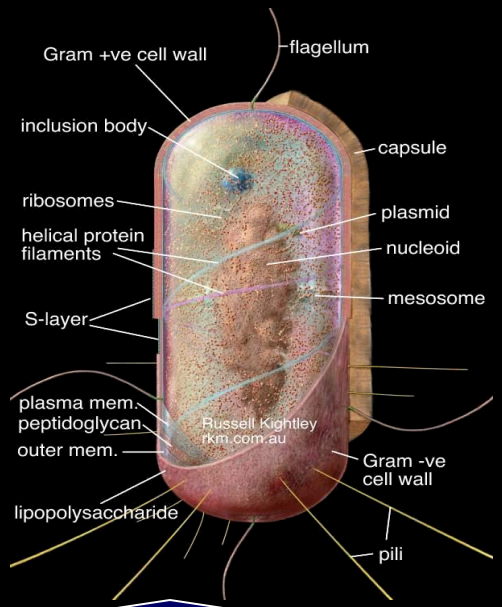
Architecture
=
Constraints
that
Deconstrain

Deconstrained Genomes

System

“Emergent”: “Nontrivial” consequences of other constraints

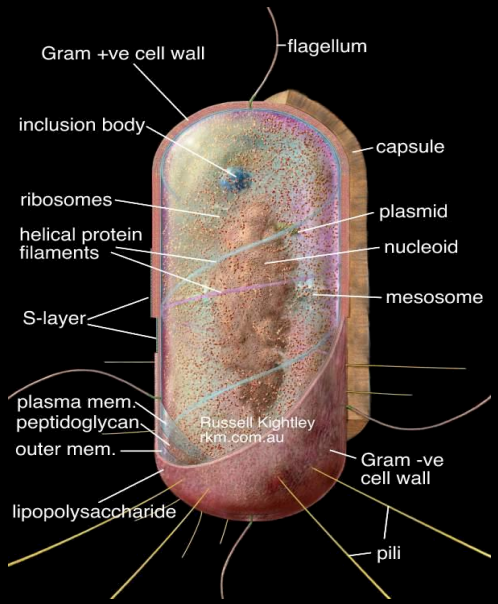
Architecture =Constraints



Protocols

Components

Systems requirements:
Survive in hostile environments



Constraints

Components and materials:
“Chemistry”

Constrained (“conserved”):

Moieties

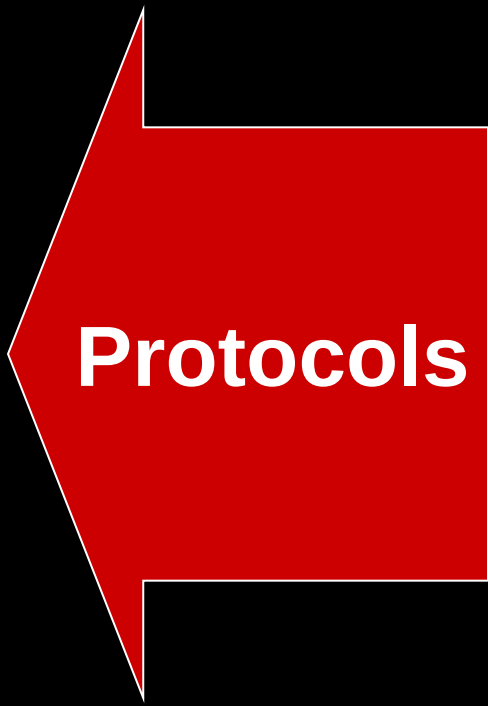
1. NAD
2. Adenylate
3. Carbon
4. phosphate
5. oxygen
6. Oxidized state of metabolites
7. Reduced state of metabolites
8. High energy potential release

Constraints

Components and materials:
“Chemistry”

Bacterial biosphere

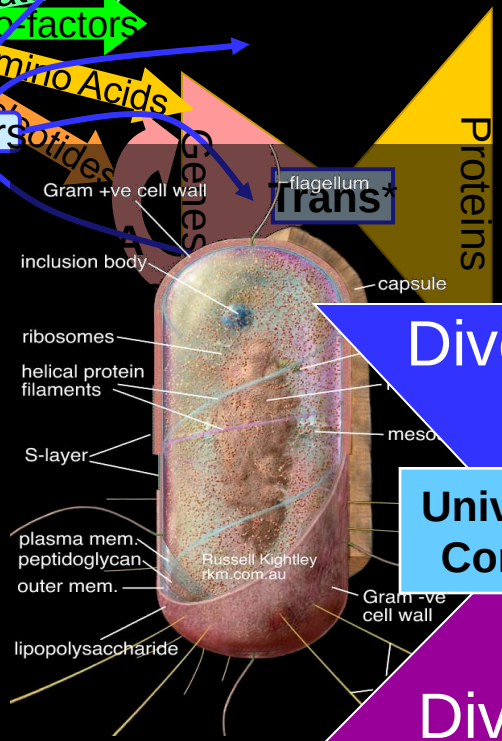
- carriers: ATP, NADH, etc
- Precursors, …
- Enzymes
- Translation
- Transcription
- Replication
- …



Architecture = protocols
= “constraints that deconstrain”

Systems requirements:
functional, efficient,
robust, evolvable

Hard constraints:
Thermo (Carnot)
Info (Shannon)
Control (Bode)
Compute (Turing)



Diverse

Universal Control

Diverse

Protocols

Constraints

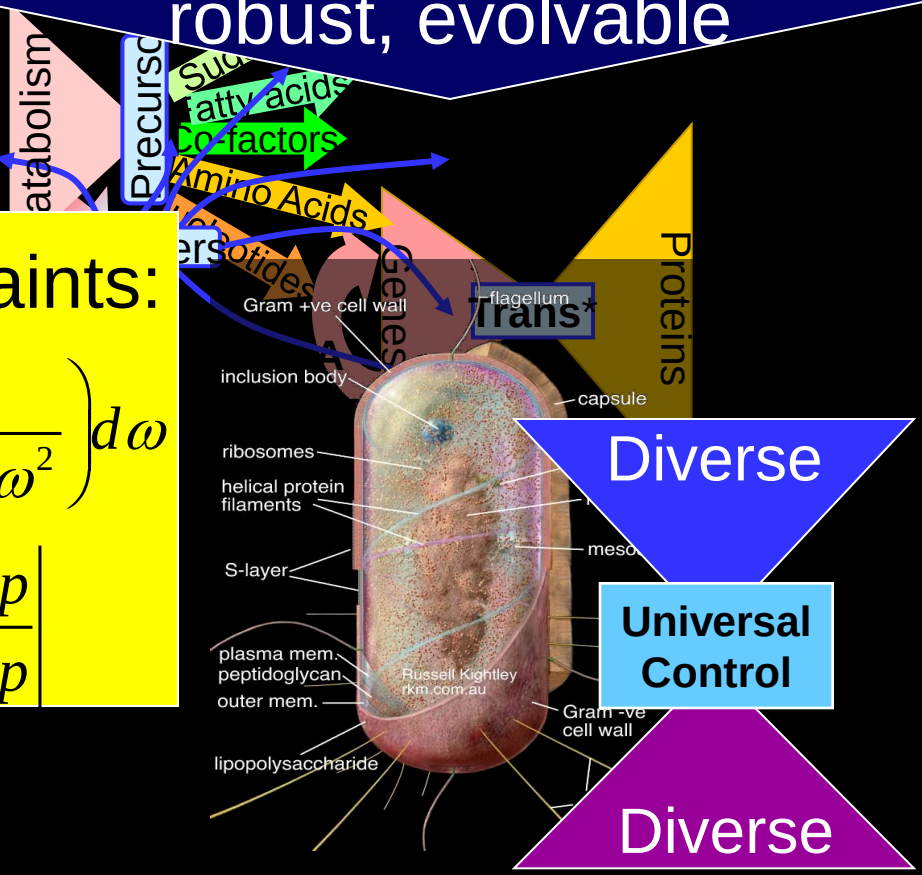
Components and materials:
Energy, moieties

Systems requirements:
functional, efficient,
robust, evolvable

Hard constraints:

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|S(j\omega)\right| \left(\frac{z}{z^2+\omega^2}\right) d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

Constraints



Protocols

Components and materials:
Energy, moieties

OPEN ACCESS Freely available online PLOS BIOLOGY

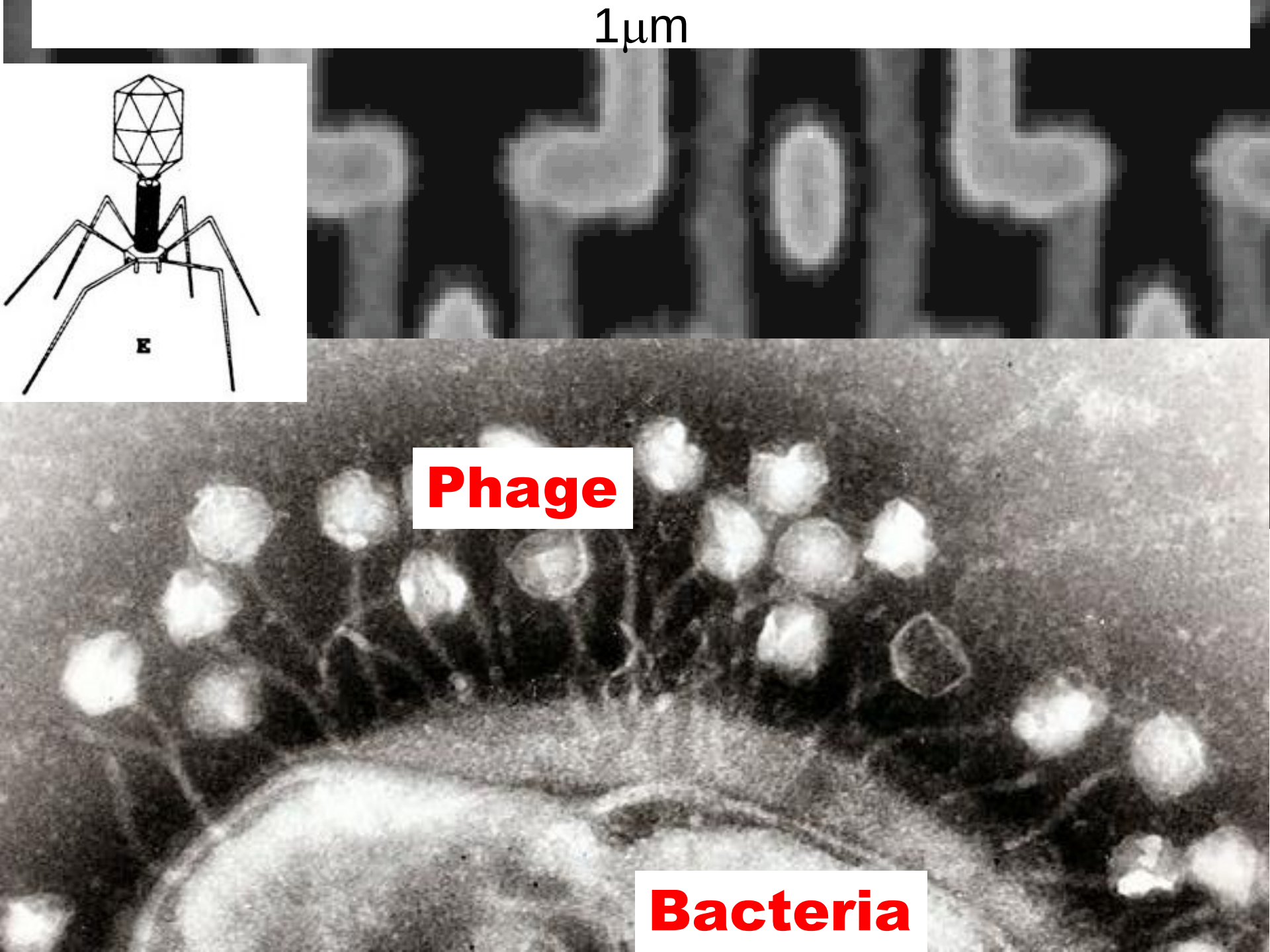
Viruses' Life History: Towards a Mechanistic Basis of a Trade-Off between Survival and Reproduction among Phages

Marianne De Paepe, François Taddei*

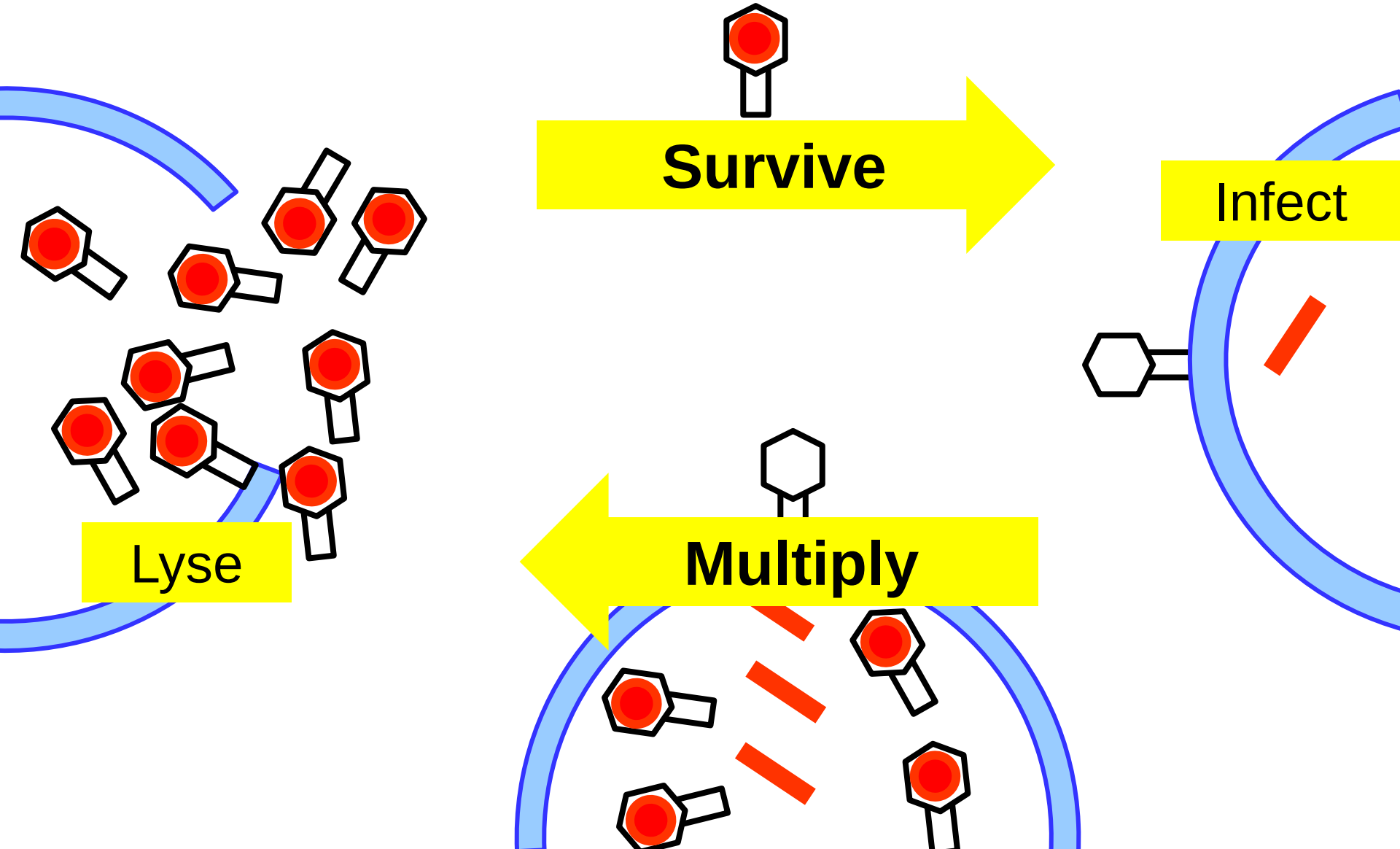
Laboratoire de Genetique Moleculaire, Evolutive et Medicale, University of Paris 5, INSERM, Paris, France

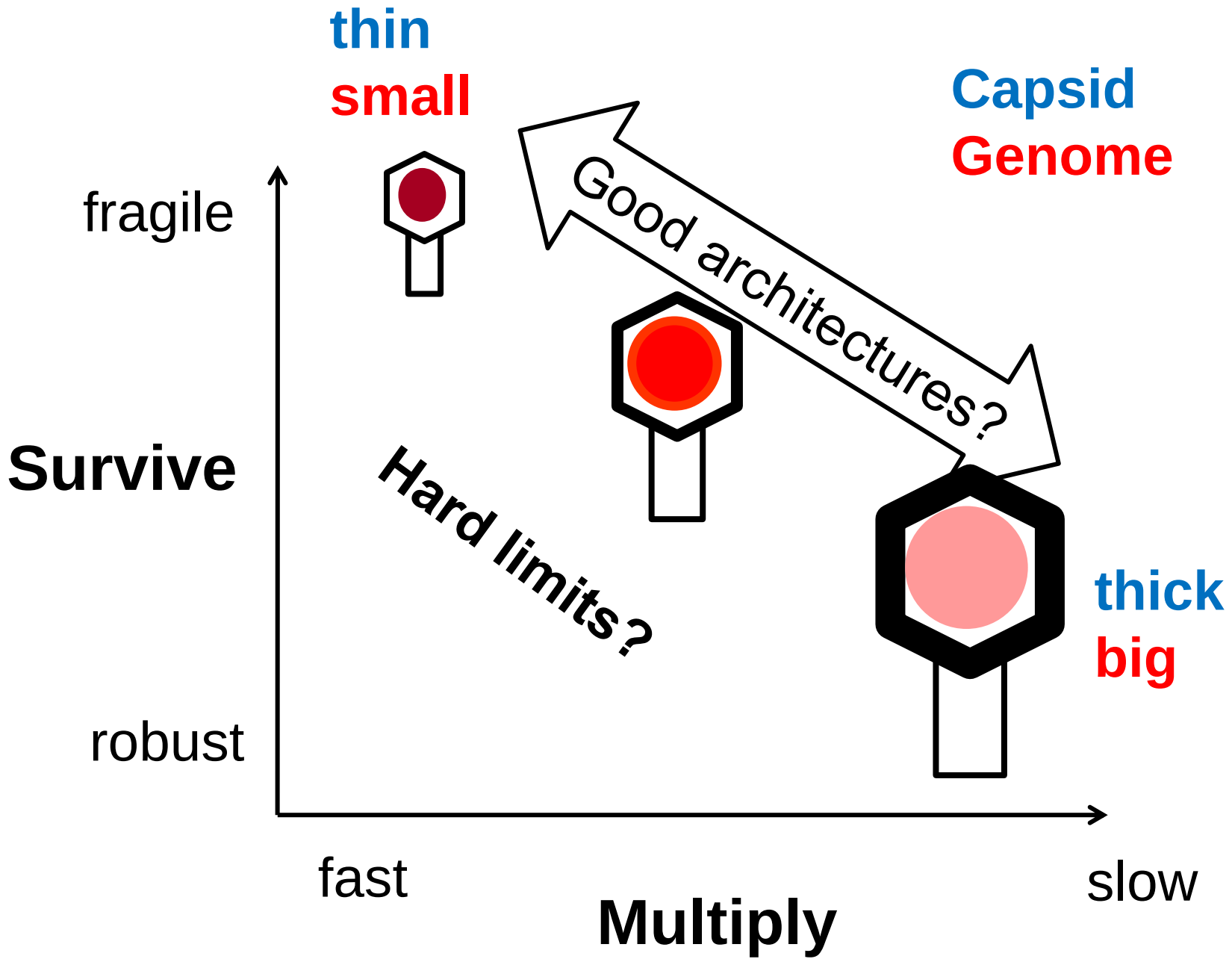
July 2006 | Volume 4 | Issue 7 | e193

I recently found this paper, a rare example of exploring an explicit tradeoff between robustness and efficiency. This seems like an important paper but it is rarely cited.


1μm
E
Phage
Bacteria

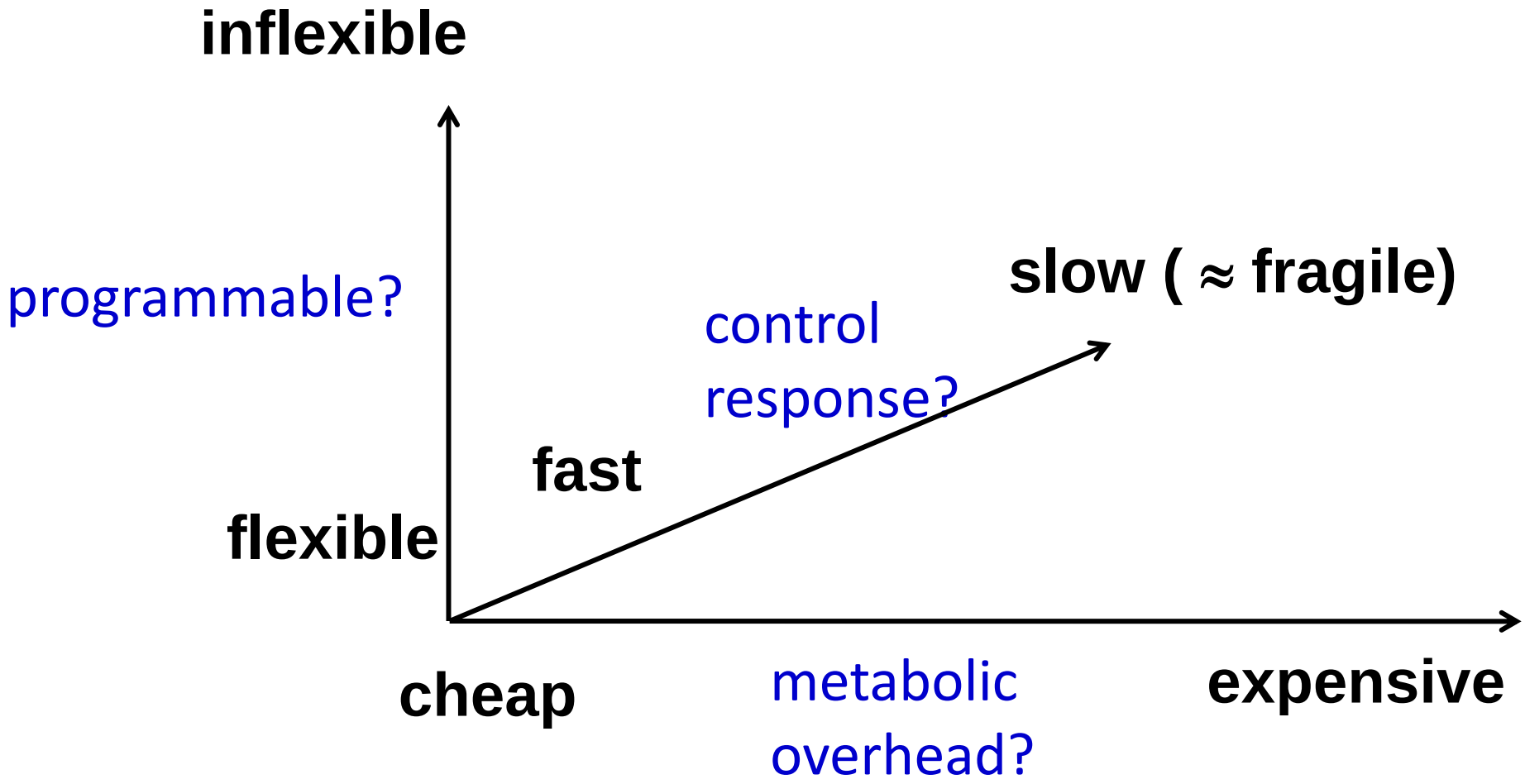
Phage lifecycle




thin
small
Capsid
Genome
fragile
Good architectures?
Survive
Hard limits?
thick
big
robust
fast
slow
Multiply

Tradeoffs?

Accurate vs sloppy is now an implicit dimension of robust/fragile



Conjecture: human brain tradeoffs dominated by fast vs flexible more than robust vs cheap

1. For hunter/gatherer metabolism is far above basal, and dominated by active muscle
2. Brain homeostasis is a much greater challenge than basal metabolic demands

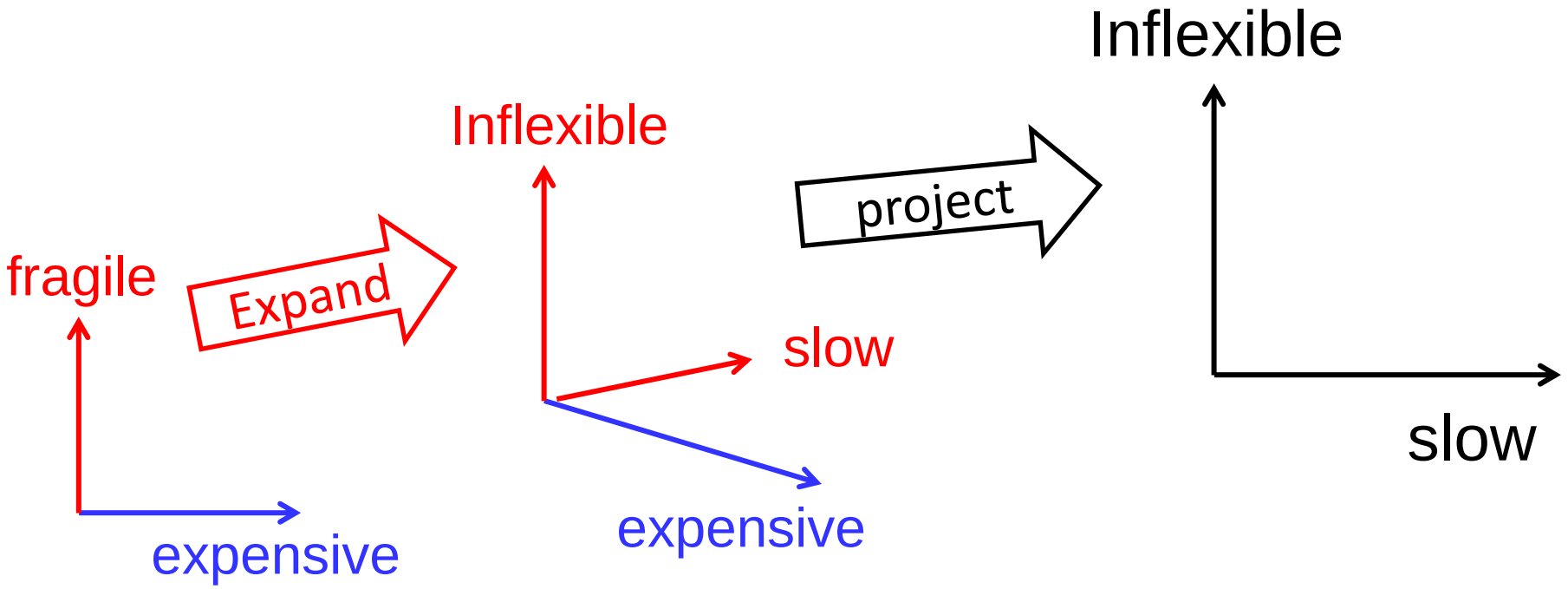
Creates new fragilities in modern lifestyle

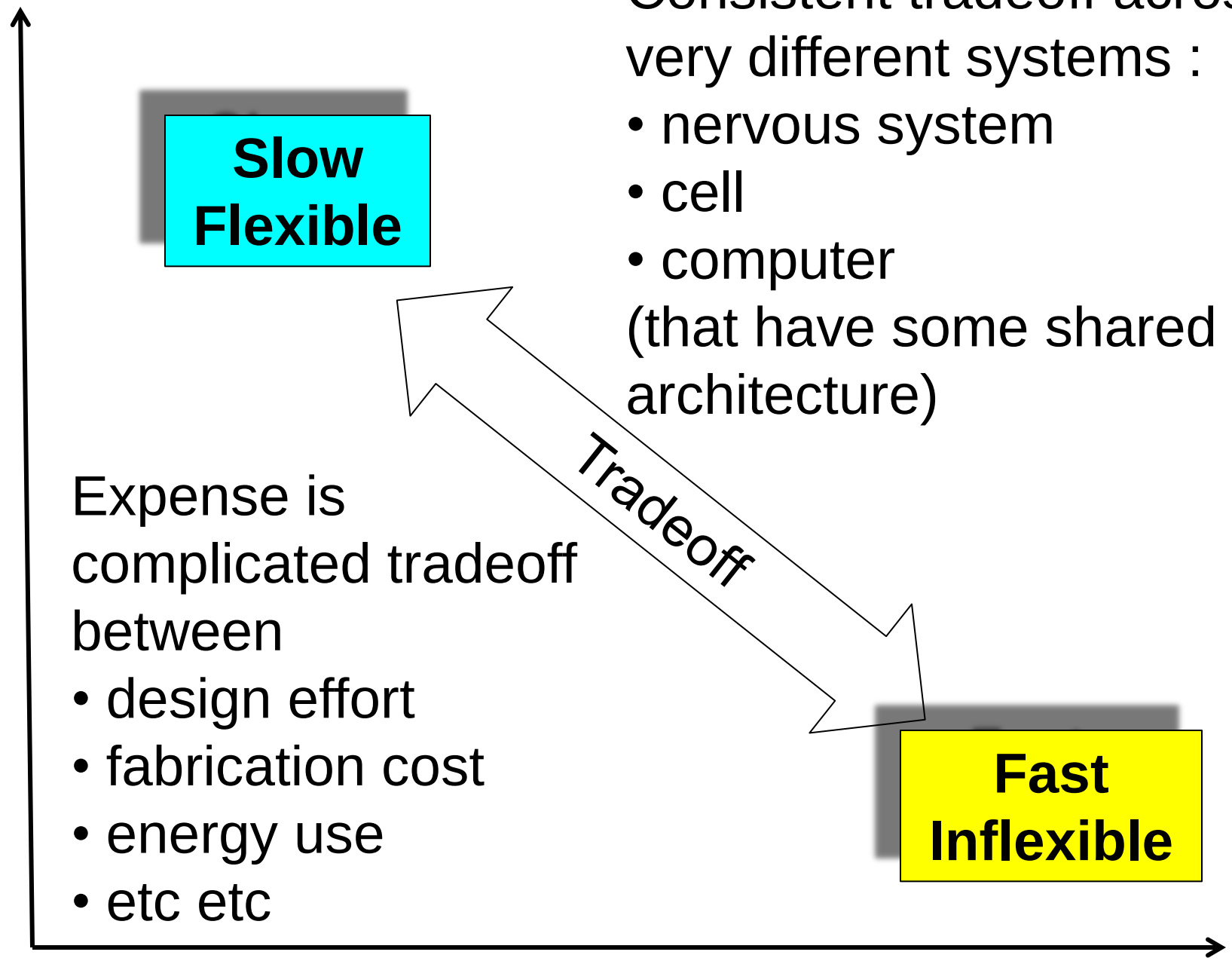
Not true for sedentary organisms with limited nutrient diets (e.g. Koala, Panda, …)

Conjecture: human brain tradeoffs dominated by fast vs flexible more than robust vs cheap

Fragility dimensions with most important tradeoffs:

1. latency/delay/speed of control vs.
2. flexibility/adaptability





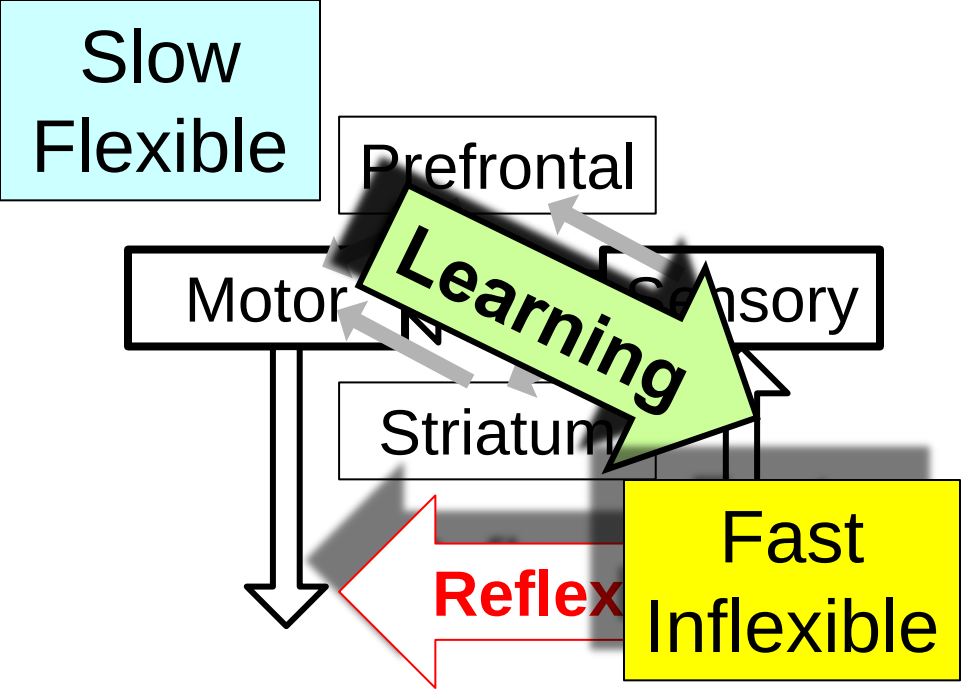
Consistent tradeoff across very different systems :

- nervous system
- cell
- computer

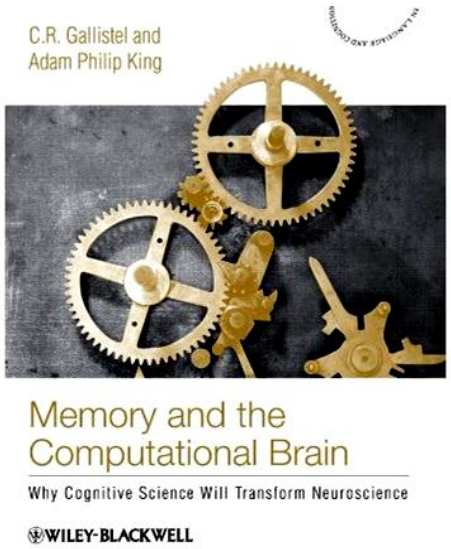
(that have some shared architecture)

Expense is complicated tradeoff between

- design effort
- fabrication cost
- energy use
- etc etc



Gallistel and King



- Sensori-motor memory potential $\approx \infty$ (Ashby)
- Limits are on ***speed*** of
  - nerve propagation delays
  - learning
- But control is ***never*** centralized
- Is there a random access read/write memory?

Horizontal Meme Transfer

Very Slow Process

Slow Flexible

"Vertical" App Migration

Prefrontal

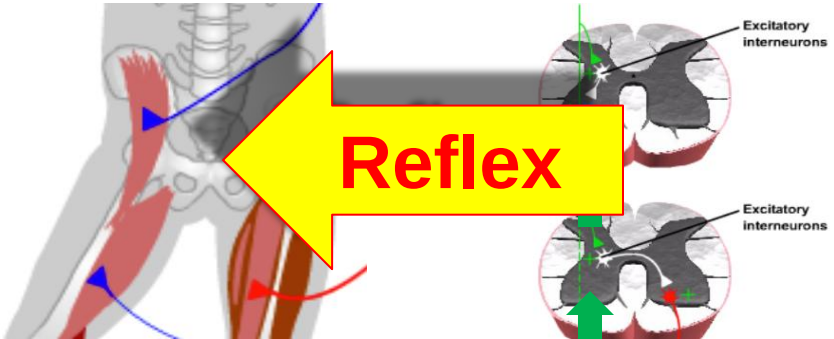
Motor

Sensory

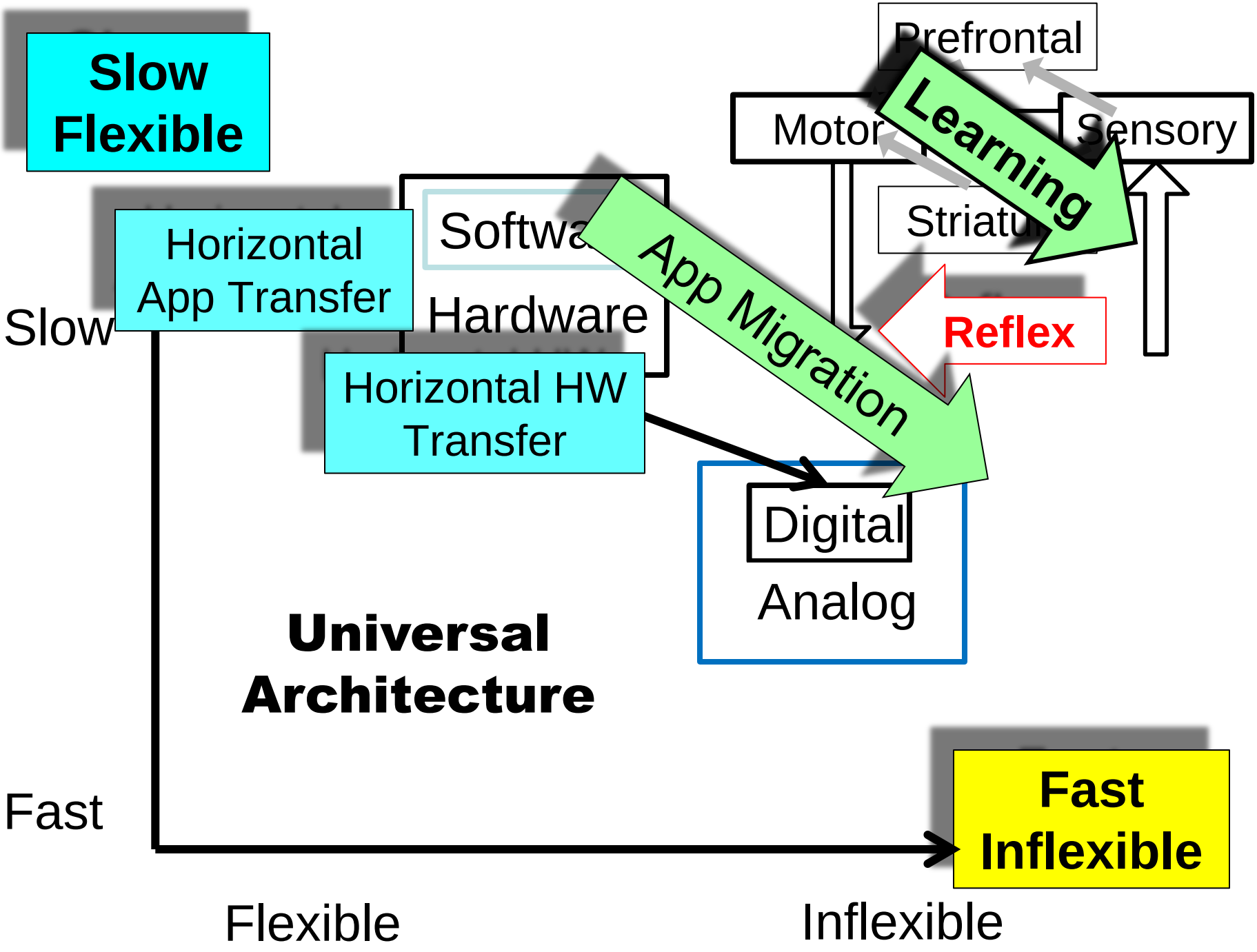
Striatum

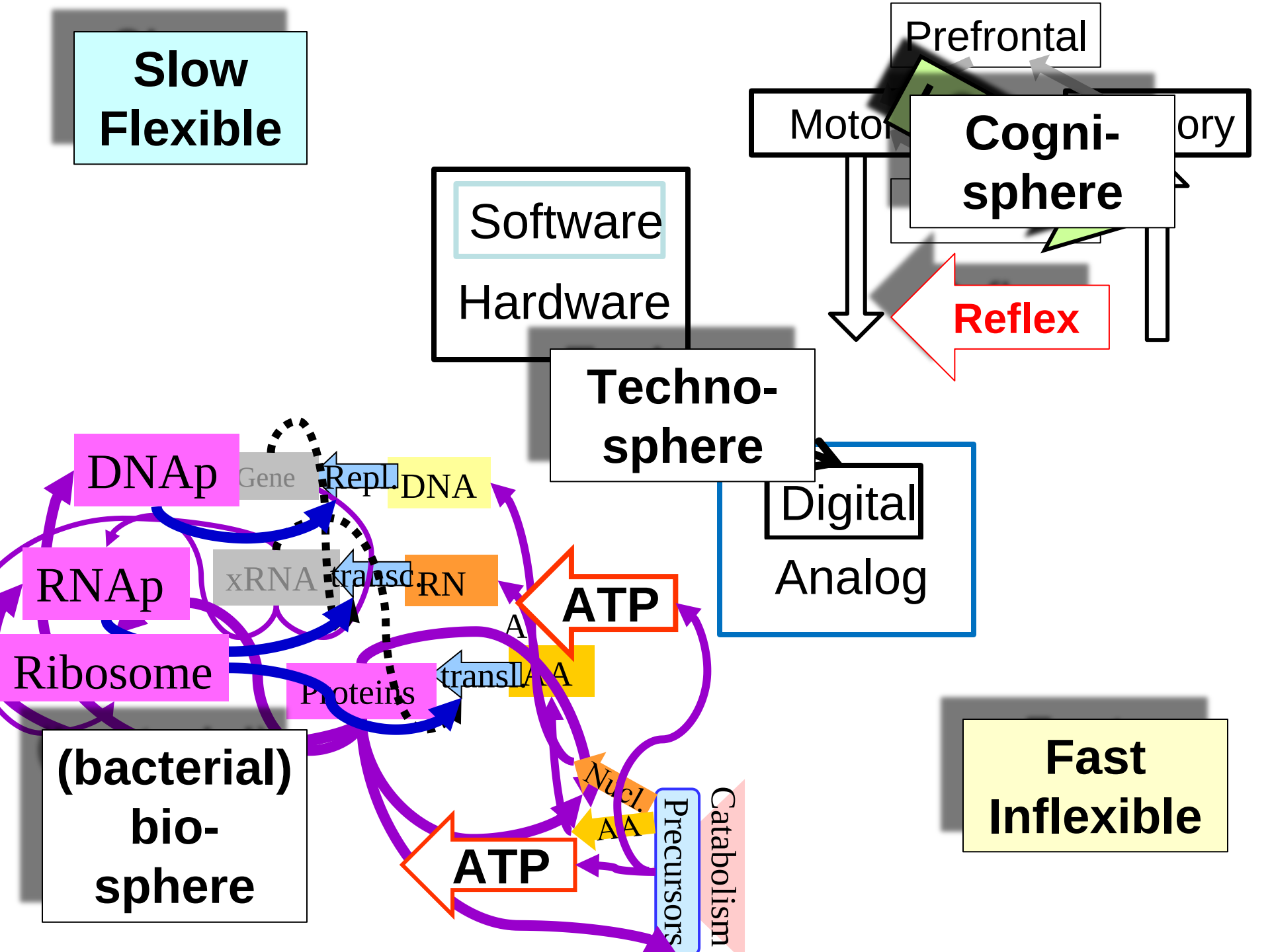
Fast Inflexible

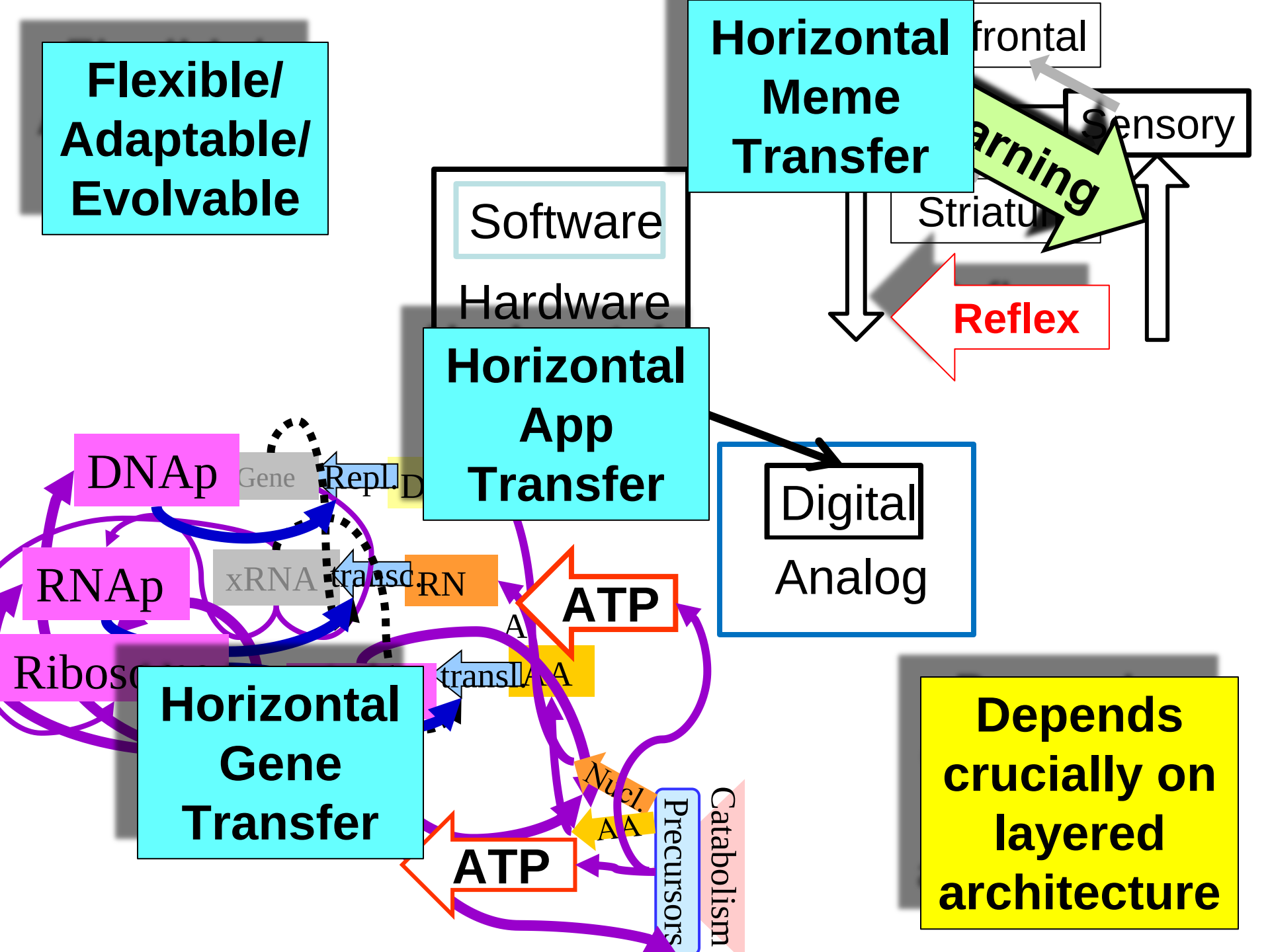
- **Acquire**
- **Translate/ integrate**
- **Automate**



Reflex


Slow
Flexible
Prefrontal
Motor
Sensory
Learning
Striatum
Reflex
Horizontal
App Transfer
Softwa
Hardware
App Migration
Horizontal HW
Transfer
Digital
Analog
Universal
Architecture
Slow
Fast
Fast
Inflexible
Flexible
Inflexible


Slow
Flexible
Prefrontal
Motor
ory
Cogni-
sphere
Software
Hardware
Techno-
sphere
Reflex
Digital
Analog
DNAp
Gene
Repl.
DNA
RNAp
xRNA
transc.
RN
ATP
A
Ribosome
Proteins
transl.
A
(bacterial)
bio-
sphere
Nucl.
A
A
ATP
Precursors
Catabolism
Fast
Inflexible


Flexible/
Adaptable/
Evolvable
Horizontal
Meme
Transfer
frontal
Sensory
arning
Striatu
Software
Hardware
Reflex
Horizontal
App
Transfer
Digital
Analog
DNAp
Gene
Repl.
D
RNAp
xRNA
transc.
RN
ATP
A
Ribosc
transl.
A
A
Horizontal
Gene
Transfer
Nucl.
A
A
Precursors
Catabolism
ATP
Depends
crucially on
layered
architecture

Horizontal Meme Transfer

Horizontal App Transfer

Horizontal Gene Transfer

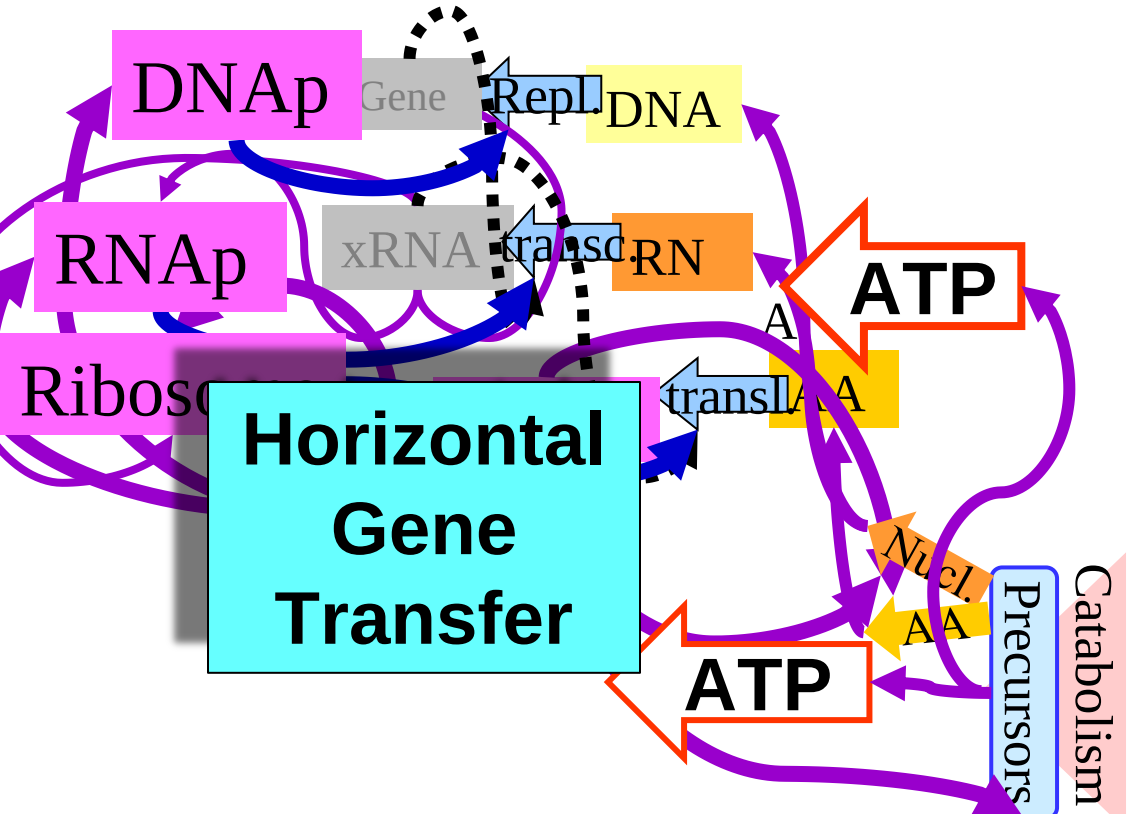
Most

- software and hardware
- new ideas (humans)
- new genes (bacteria)

is acquired by “horizontal” transfer,
though sometimes it is evolved locally

Sequence ~100 E Coli (*not* chosen randomly)

- ~ 4K genes per cell
- ~20K *different* genes in total
- ~ 1K universally shared genes



See slides on bacterial biosphere

Exploiting layered architecture

Horizontal **Bad Meme** Transfer

Virus

Horizontal **Bad App** Transfer

Fragility?

Horizontal **Bad Gene** Transfer

Virus

Parasites & Hijacking

Depends crucially on layered architecture

Build on Turing to show what is *necessary* to make this work.

Horizontal Meme Transfer

- Acquire
- Translate/ integrate
- Automate

Horizontal App Transfer

Horizontal Gene Transfer

Amazingly Flexible/ Adaptable

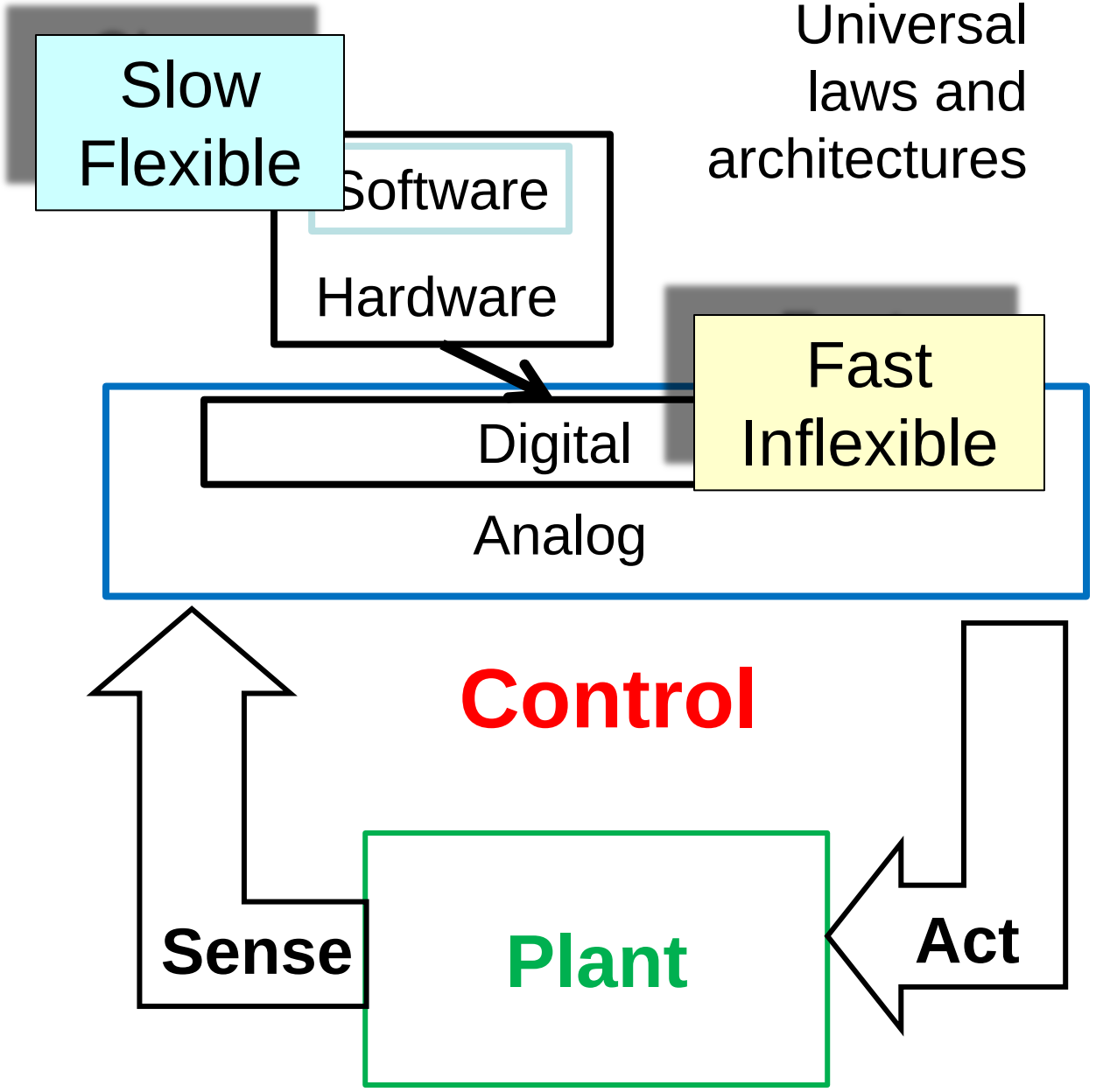
Compute

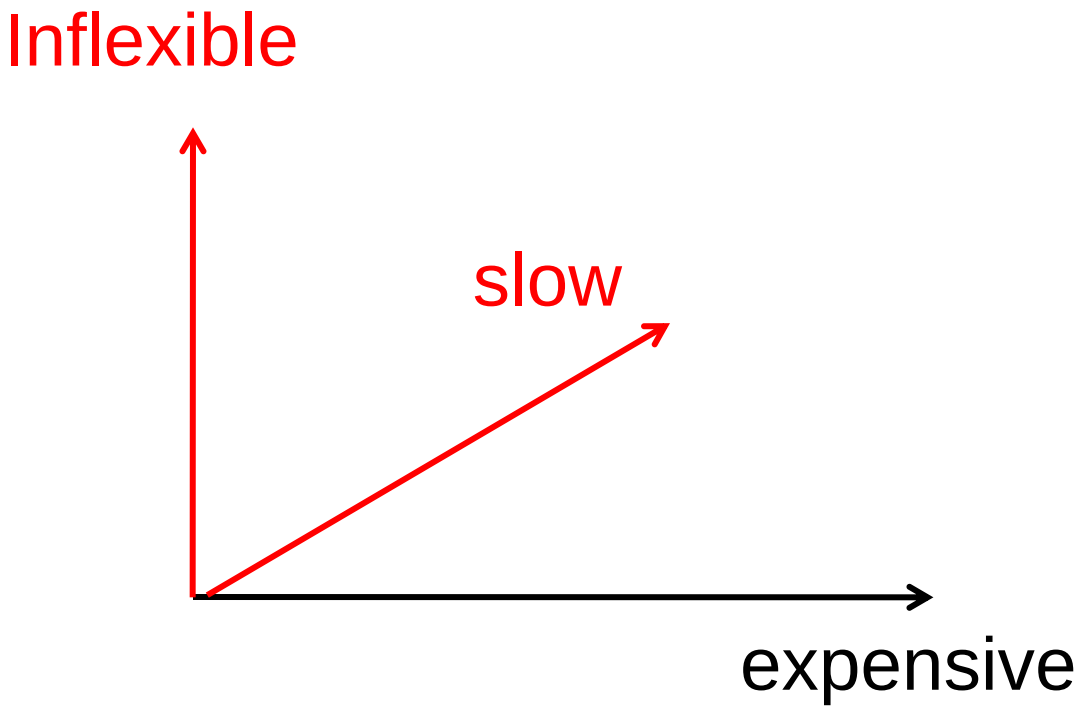
Turing

Delay is *even more* important

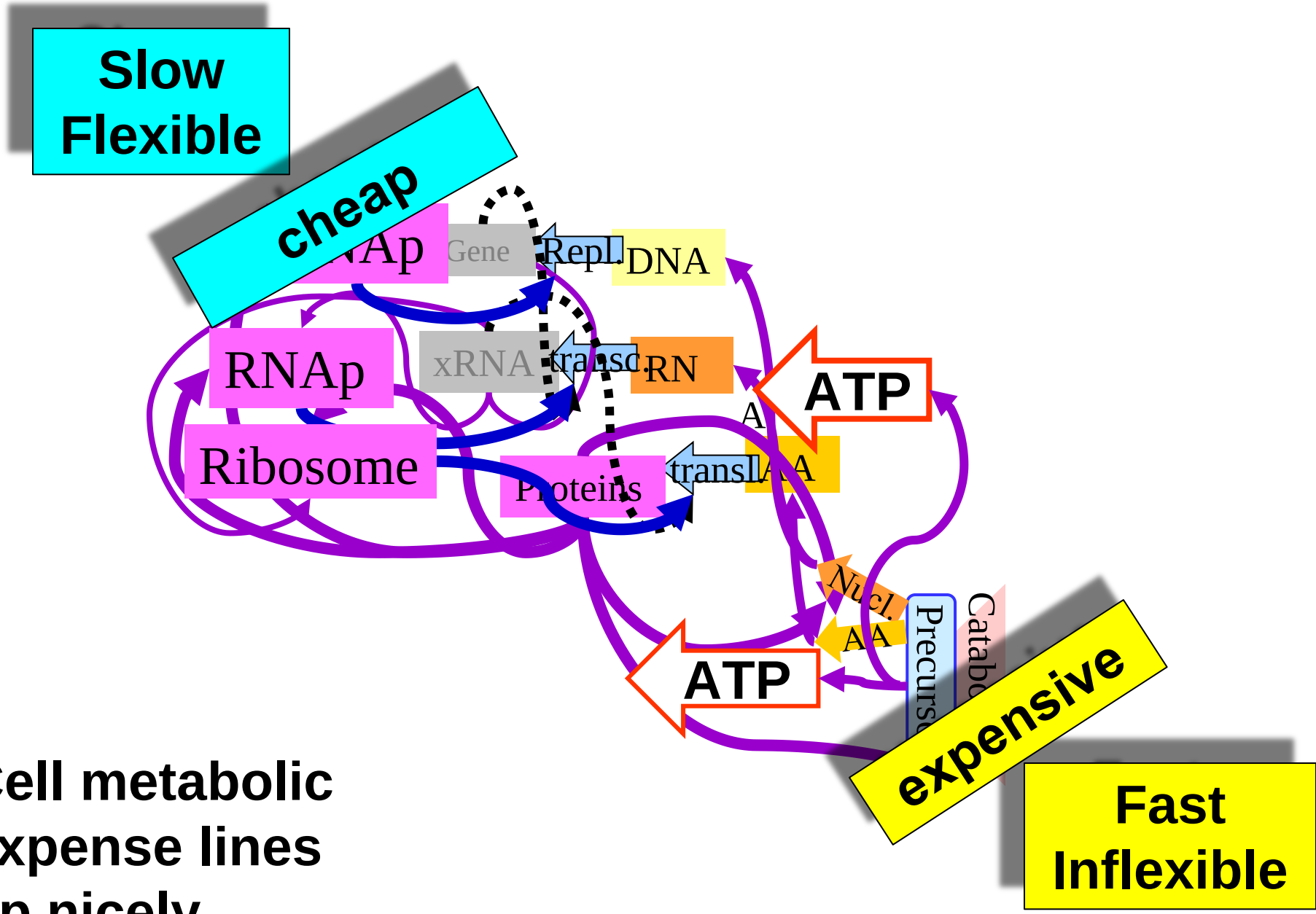
Bode

Control

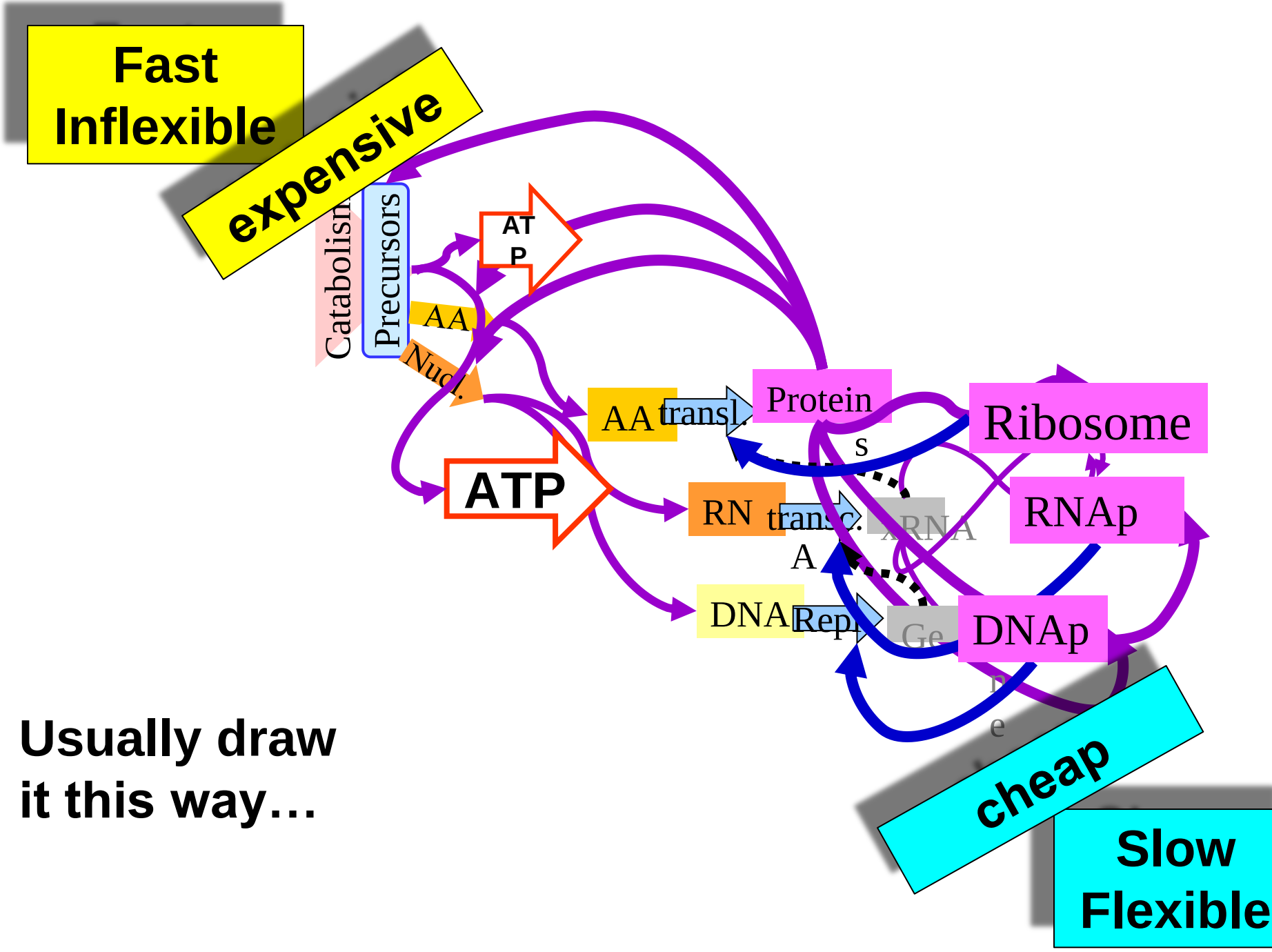




But efficiency tradeoffs are different.

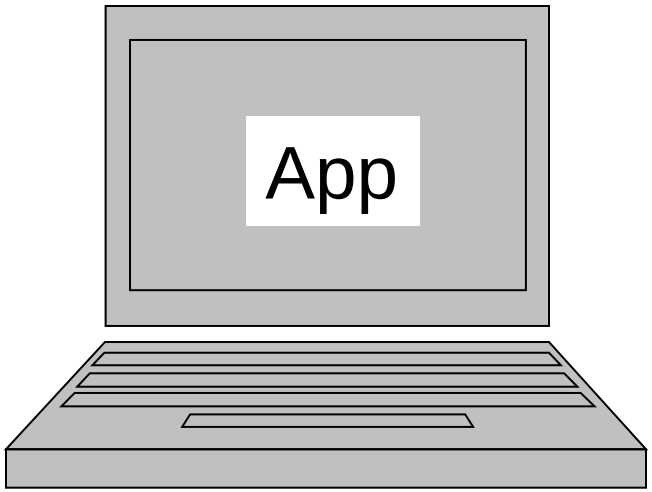


Cell metabolic expense lines up nicely

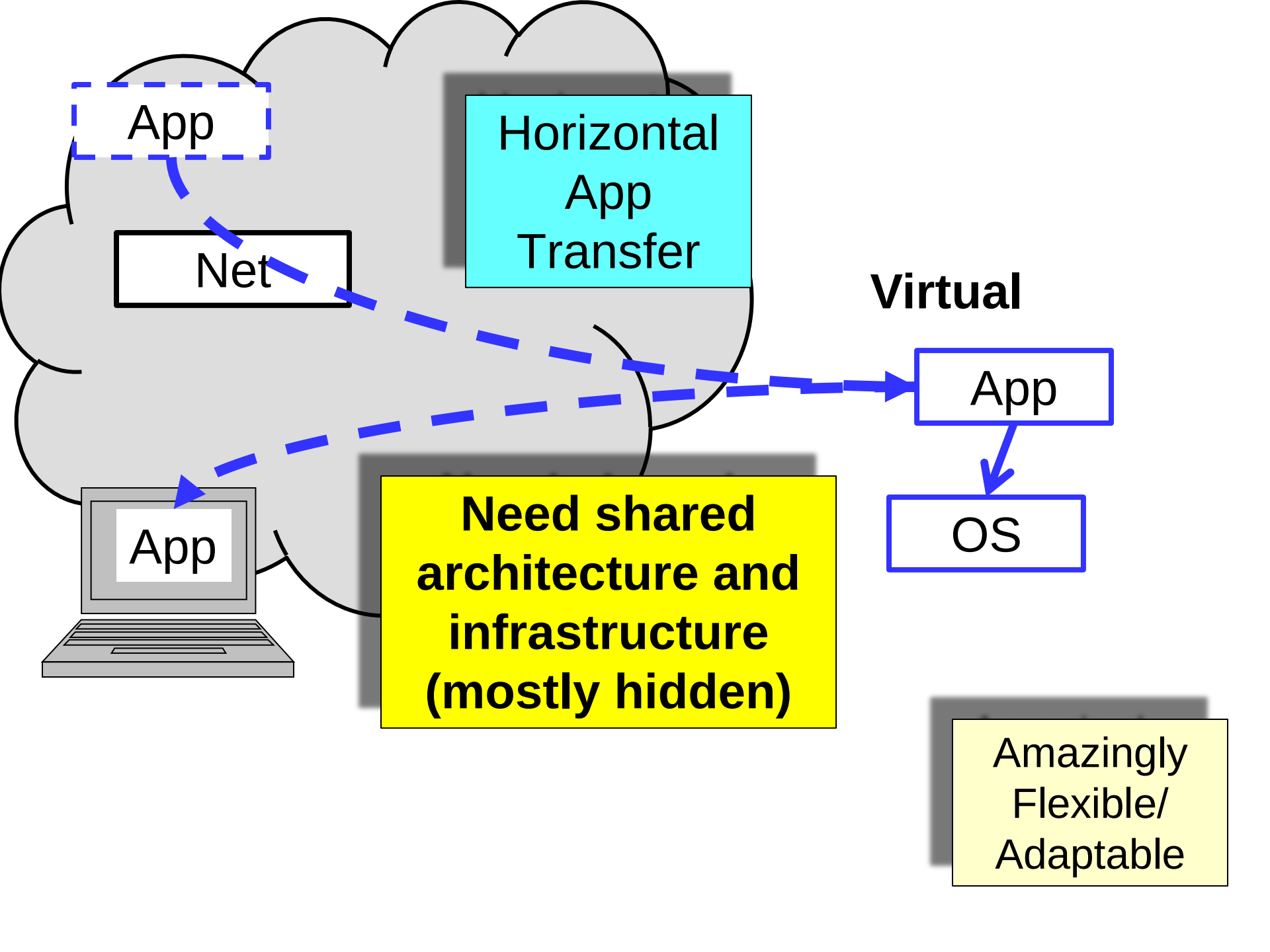


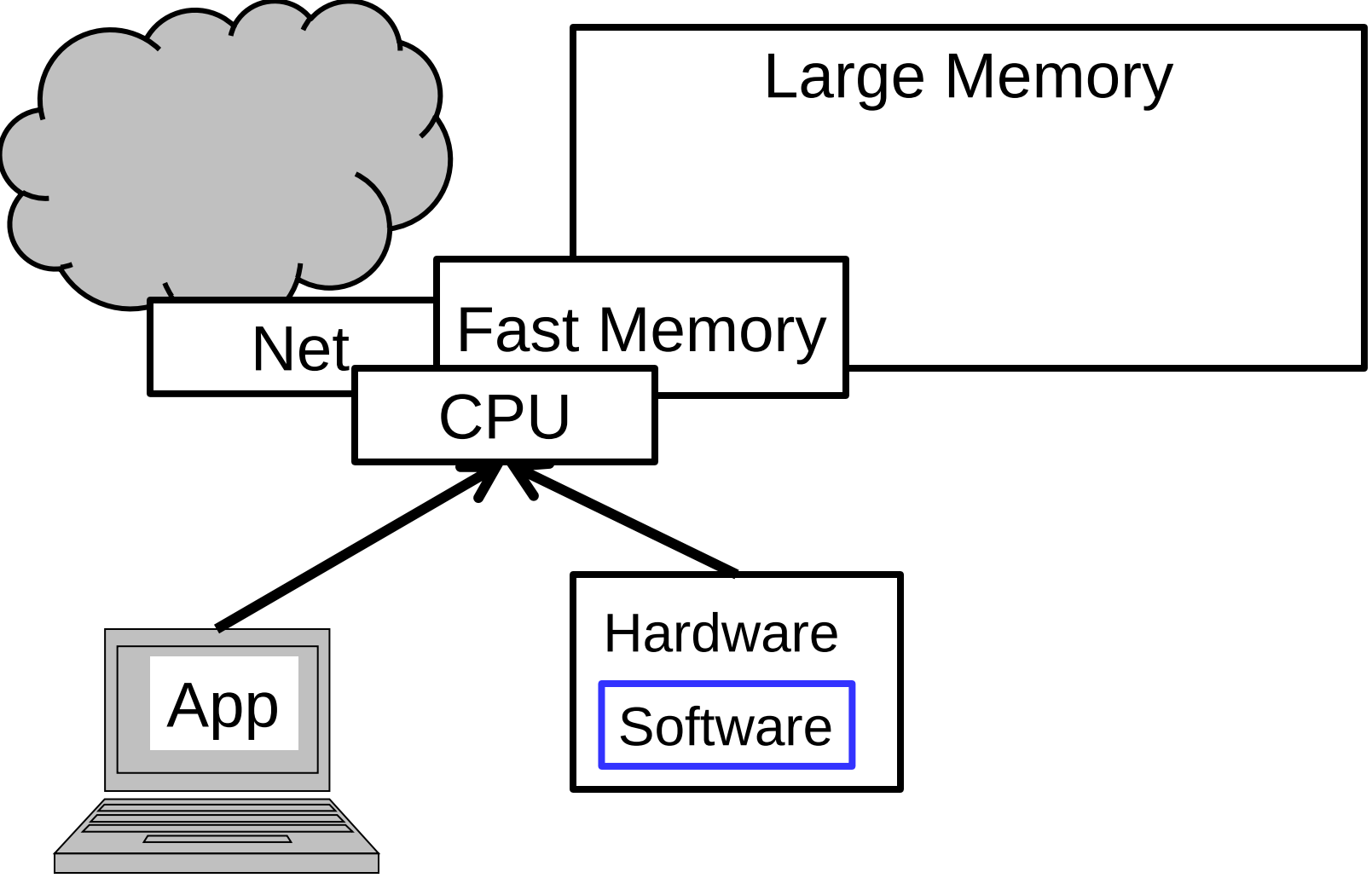
Usually draw it this way…

What you see: The hardware interface and the application function

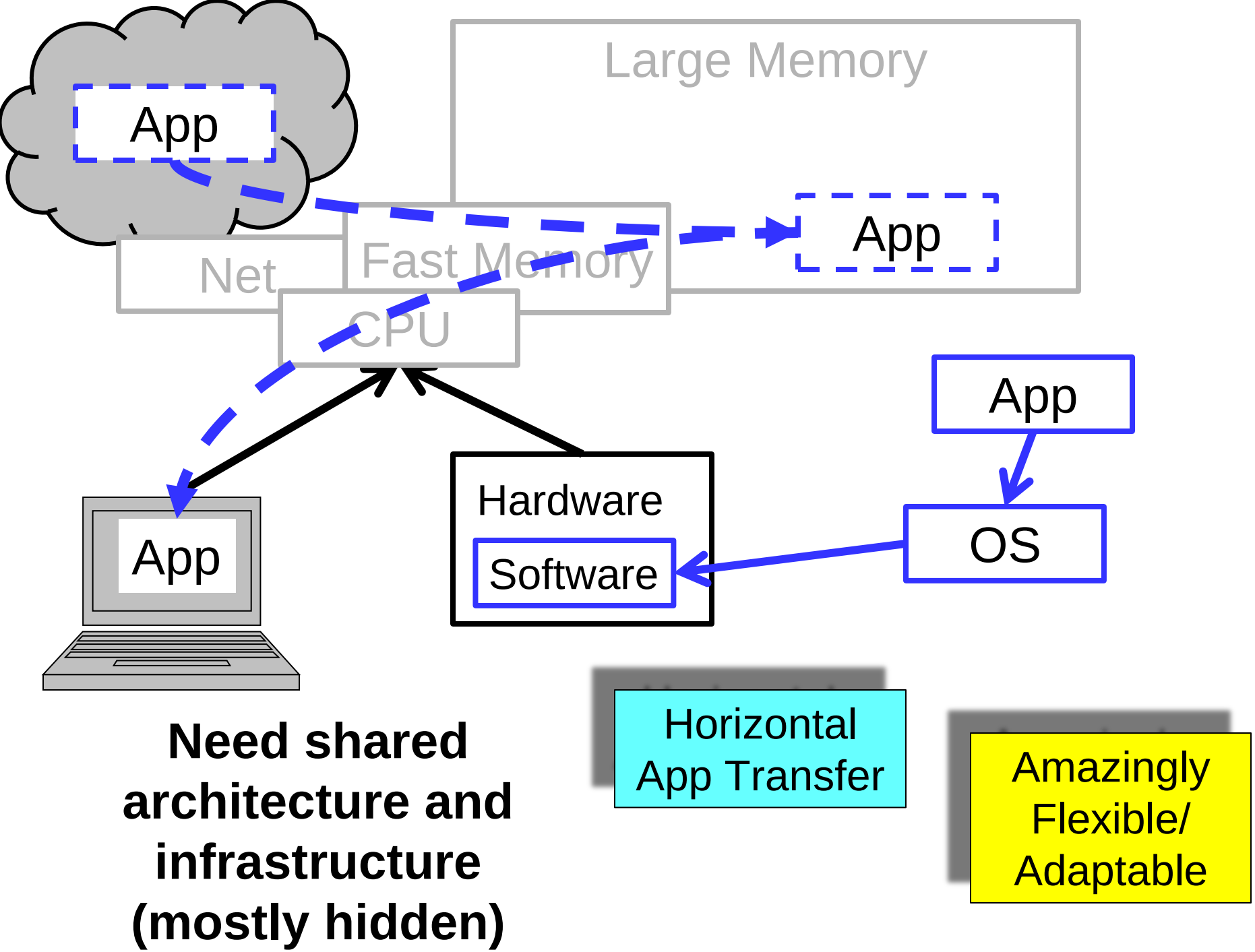


Need shared architecture and infrastructure (mostly hidden)


App
Net
Horizontal App Transfer
Virtual
App
OS
App
Need shared architecture and infrastructure (mostly hidden)
Amazingly Flexible/ Adaptable



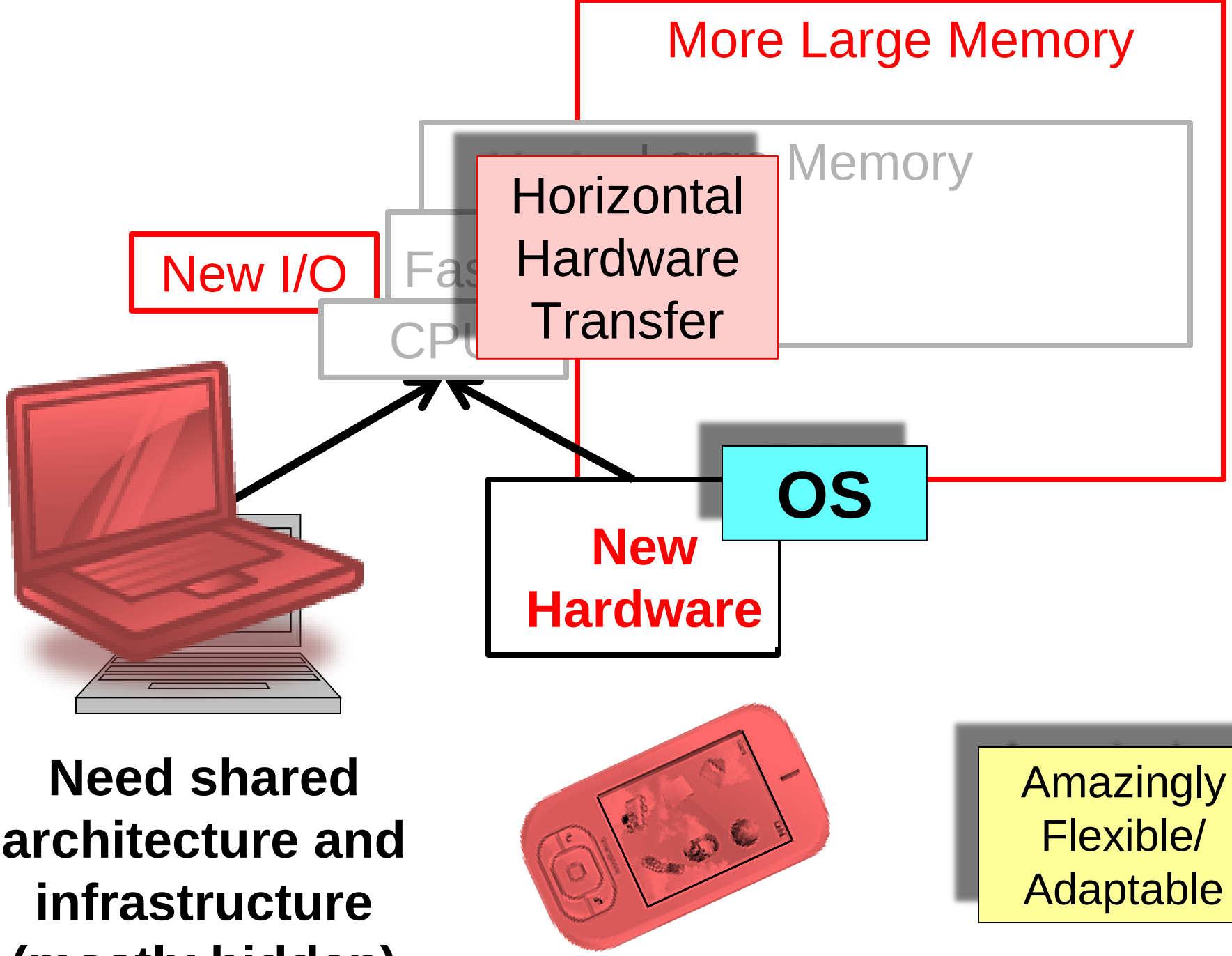
Need shared architecture and infrastructure (mostly hidden)



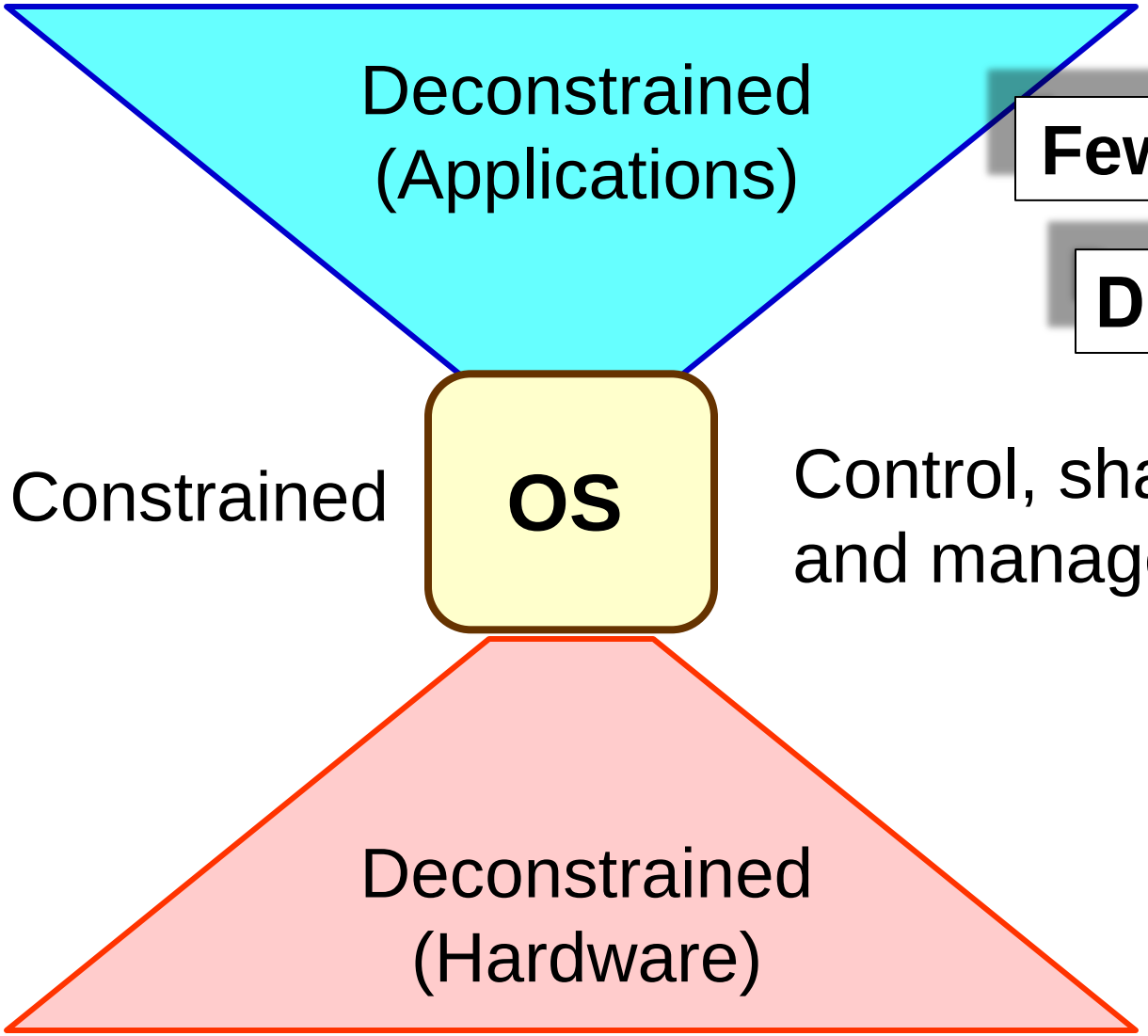
Need shared architecture and infrastructure (mostly hidden)

Horizontal App Transfer

Amazingly Flexible/ Adaptable


More Large Memory
Memory
Horizontal
Hardware
Transfer
New I/O
OS
New
Hardware
Need shared
architecture and
infrastructure
(mostly hidden)
Amazingly
Flexible/
Adaptable

Layered architectures



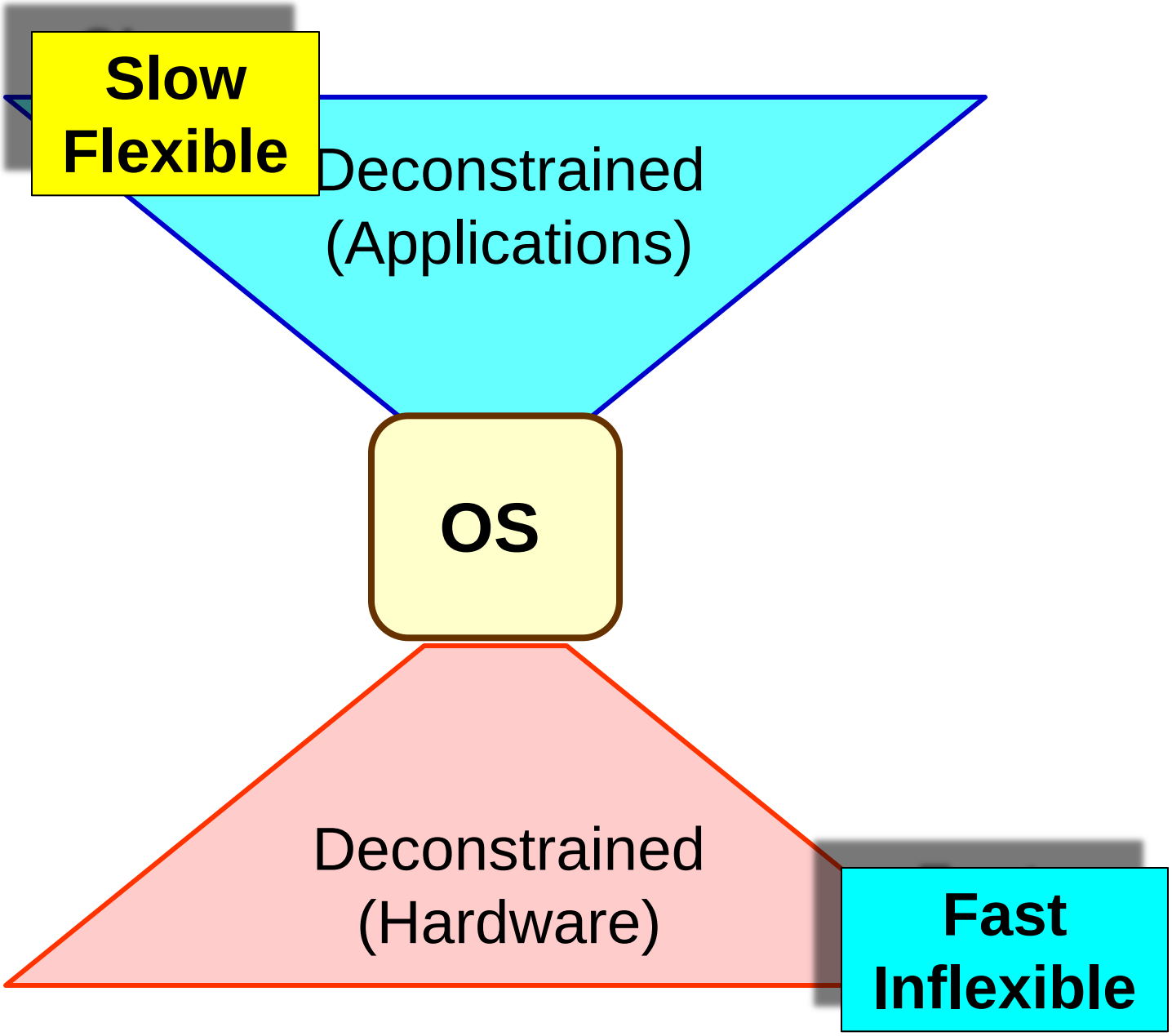
Essentials

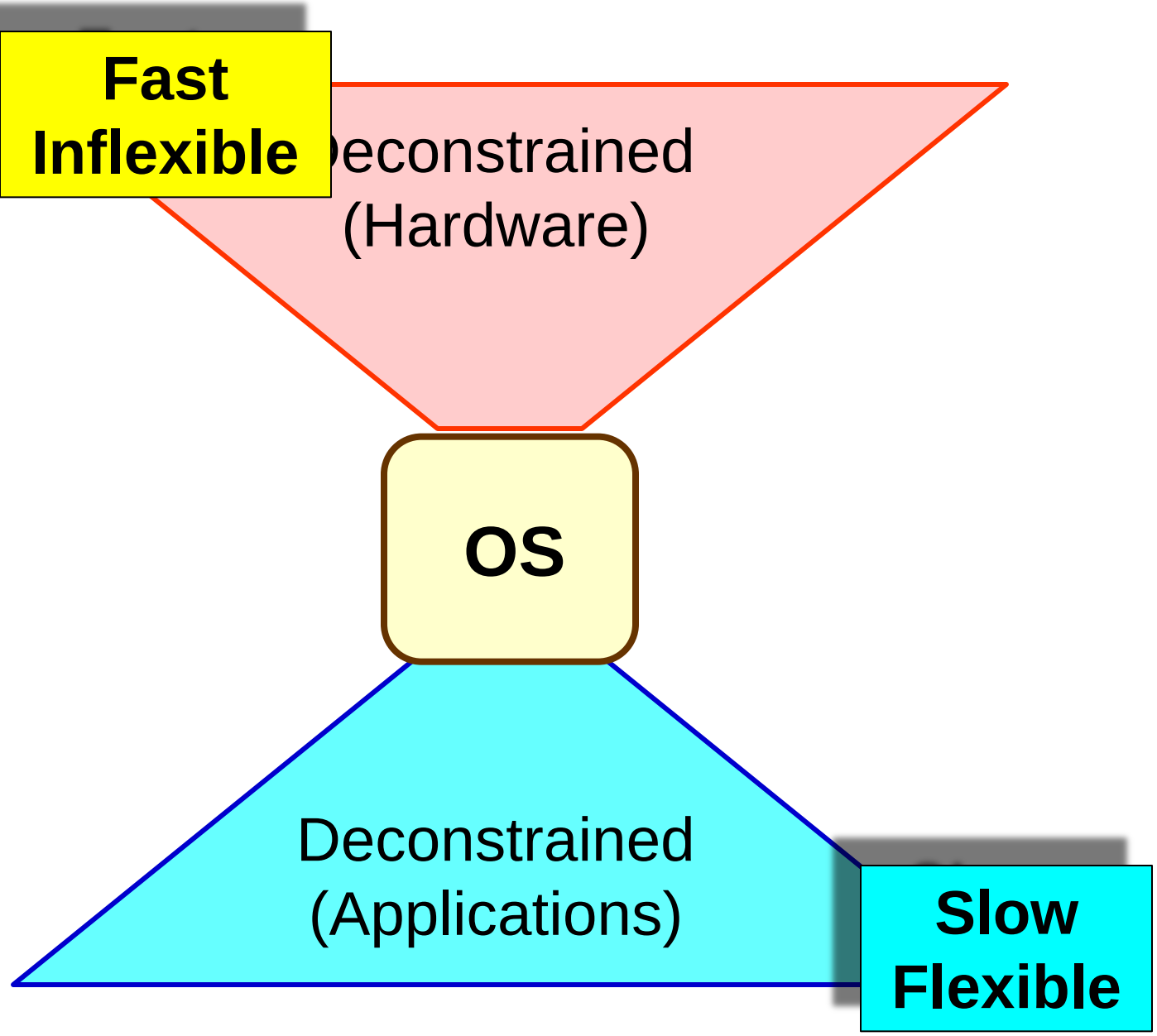
Few global variables

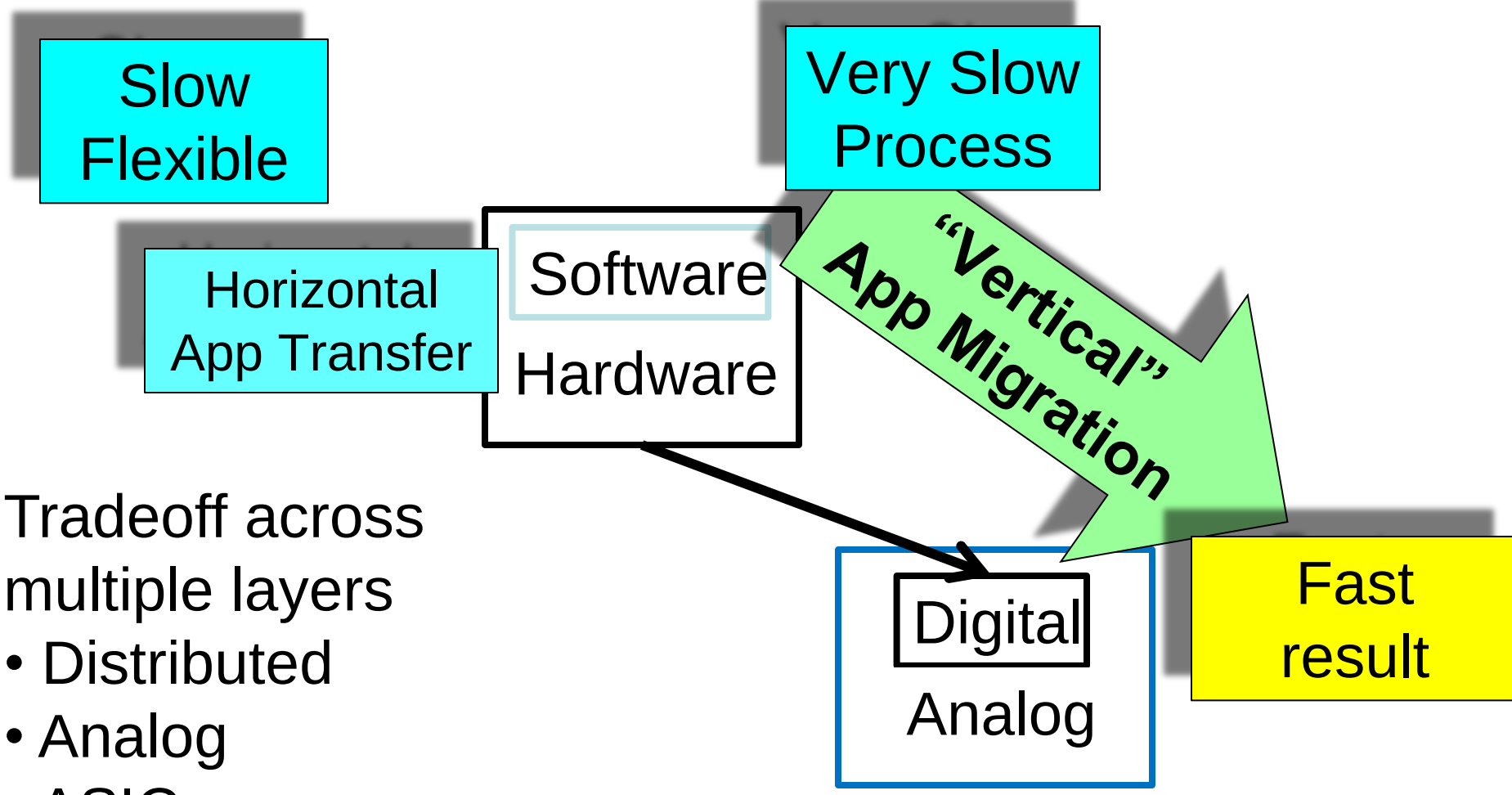
Don’t cross layers

Control, share, virtualize,
and manage resources

Processing
Memory
I/O

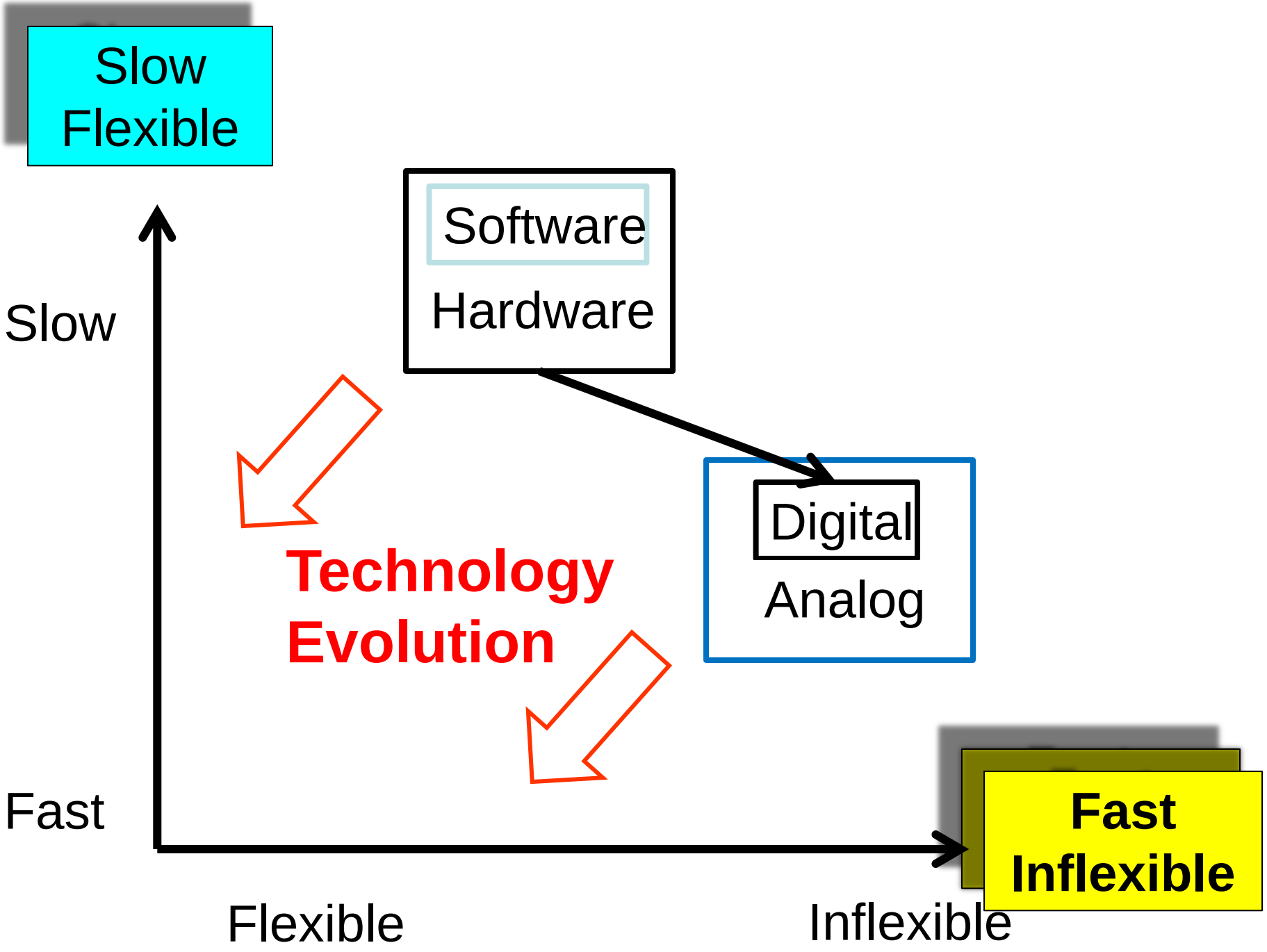

Slow
Flexible
Deconstrained
(Applications)
OS
Deconstrained
(Hardware)
Fast
Inflexible

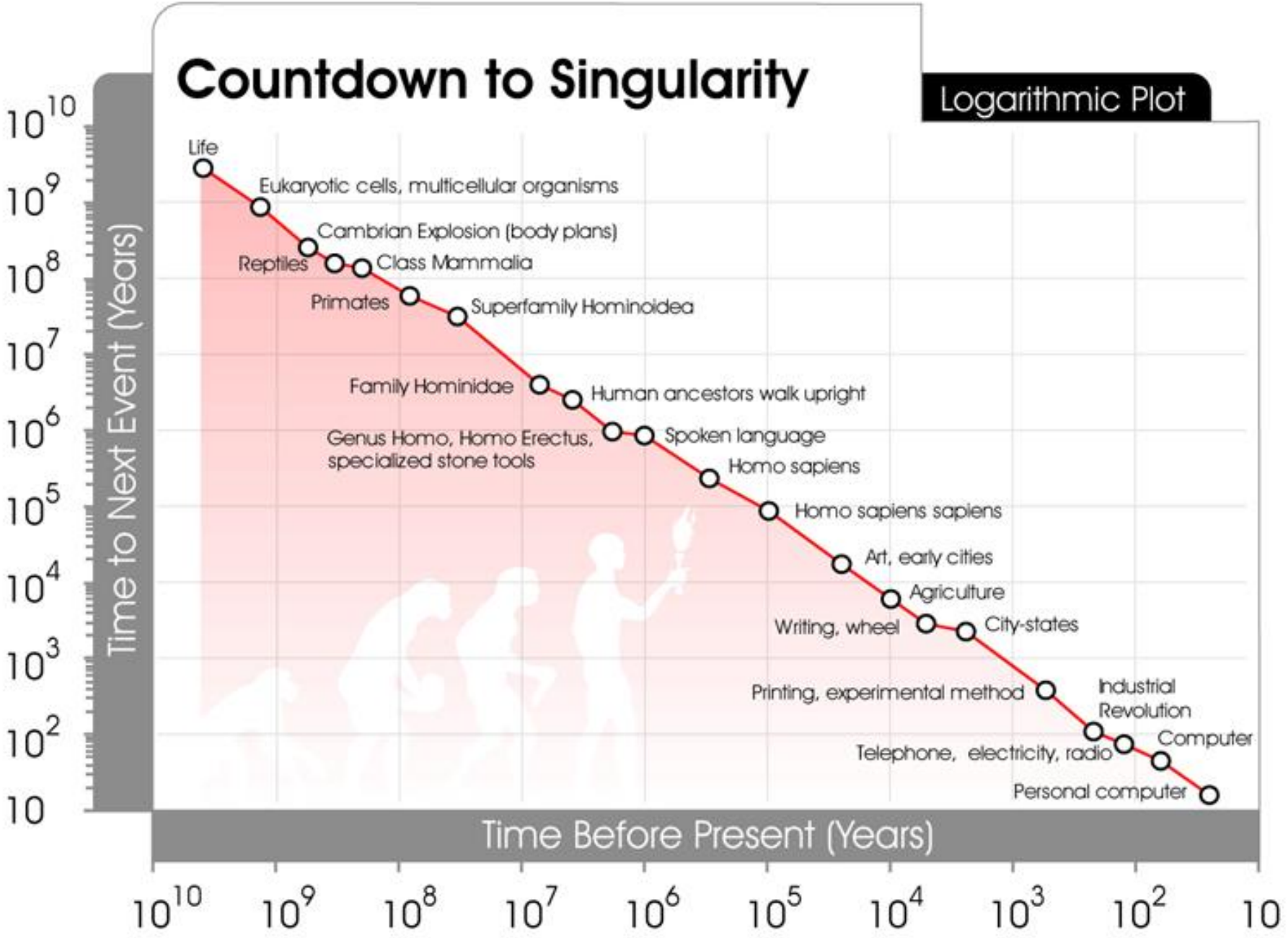

Fast
Inflexible
econstrained
(Hardware)
OS
Deconstrained
(Applications)
Slow
Flexible

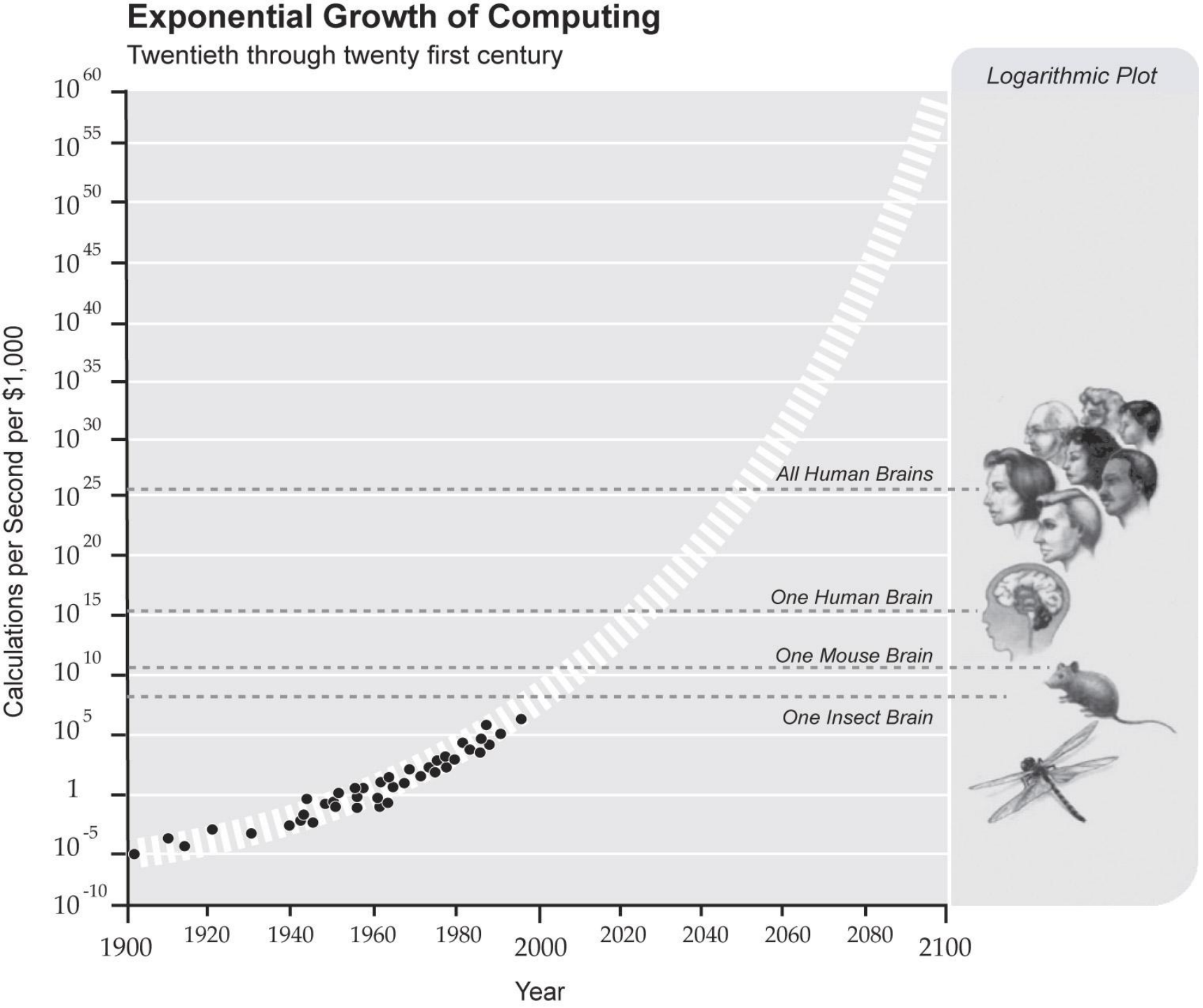


Tradeoff across multiple layers

- Distributed
- Analog
- ASICs
- FPGA
- …
- Compiled
- Interpreted


Slow
Flexible
Software
Hardware
Slow
Technology
Evolution
Digital
Analog
Fast
Fast
Inflexible
Flexible
Inflexible


Countdown to Singularity
Logarithmic Plot
Time to Next Event (Years)
Time Before Present (Years)
10^{10}
10^{9}
10^{8}
10^{7}
10^{6}
10^{5}
10^{4}
10^{3}
10^{2}
10
Life
Eukaryotic cells, multicellular organisms
Cambrian Explosion (body plans)
Reptiles
Class Mammalia
Primates
Superfamily Hominoidea
Family Hominidae
Human ancestors walk upright
Genus Homo, Homo Erectus, specialized stone tools
Spoken language
Homo sapiens
Homo sapiens sapiens
Art, early cities
Agriculture
Writing, wheel
City-states
Printing, experimental method
Industrial Revolution
Telephone, electricity, radio
Computer
Personal computer


Exponential Growth of Computing
Twentieth through twenty first century
Logarithmic Plot
Calculations per Second per $1,000
10^{60}
10^{55}
10^{50}
10^{45}
10^{40}
10^{35}
10^{30}
10^{25}
10^{20}
10^{15}
10^{10}
10^{5}
1
10^{-5}
10^{-10}
All Human Brains
One Human Brain
One Mouse Brain
One Insect Brain
1900
1920
1940
1960
1980
2000
2020
2040
2060
2080
2100
Year

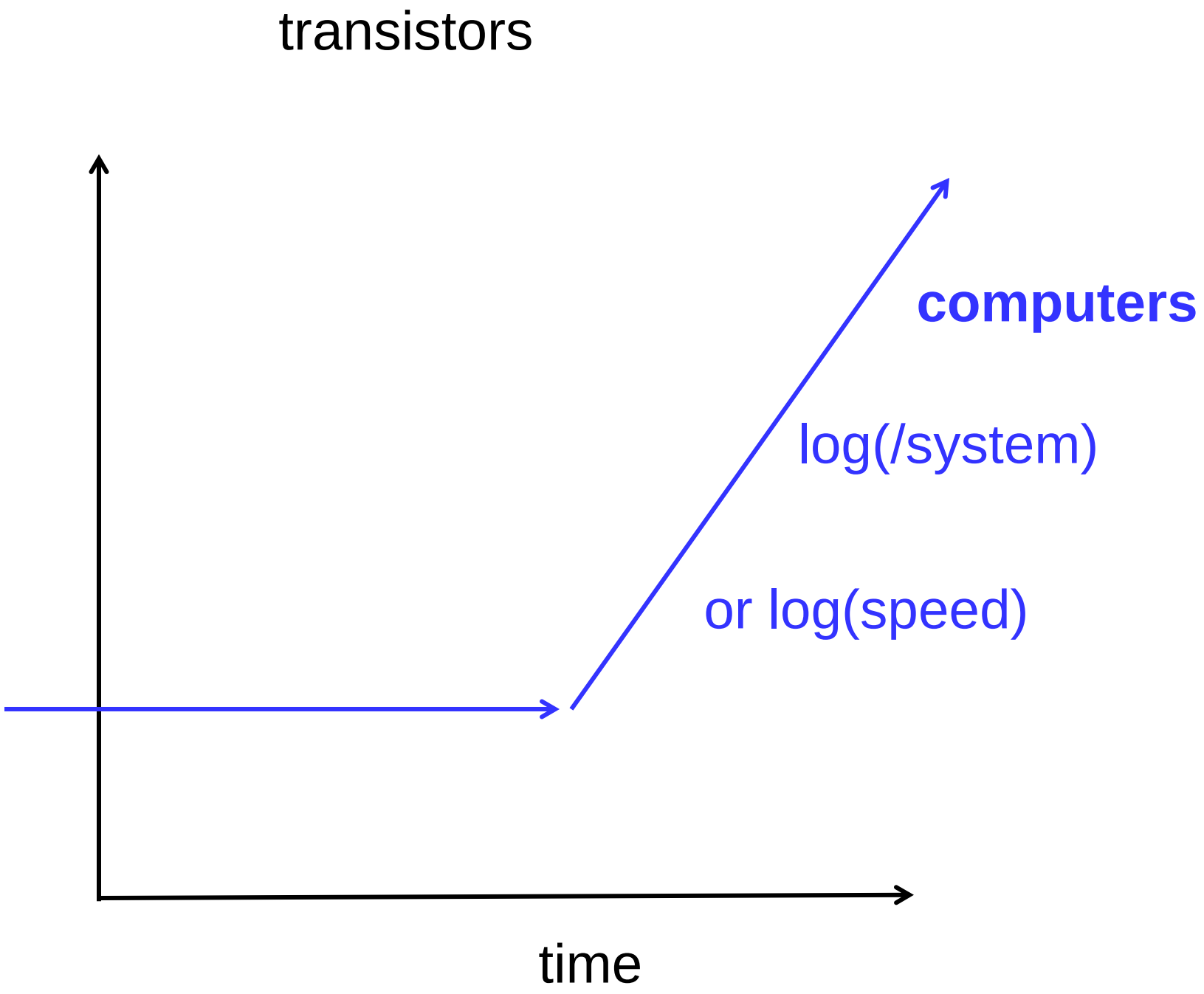
THE END OF THEORY

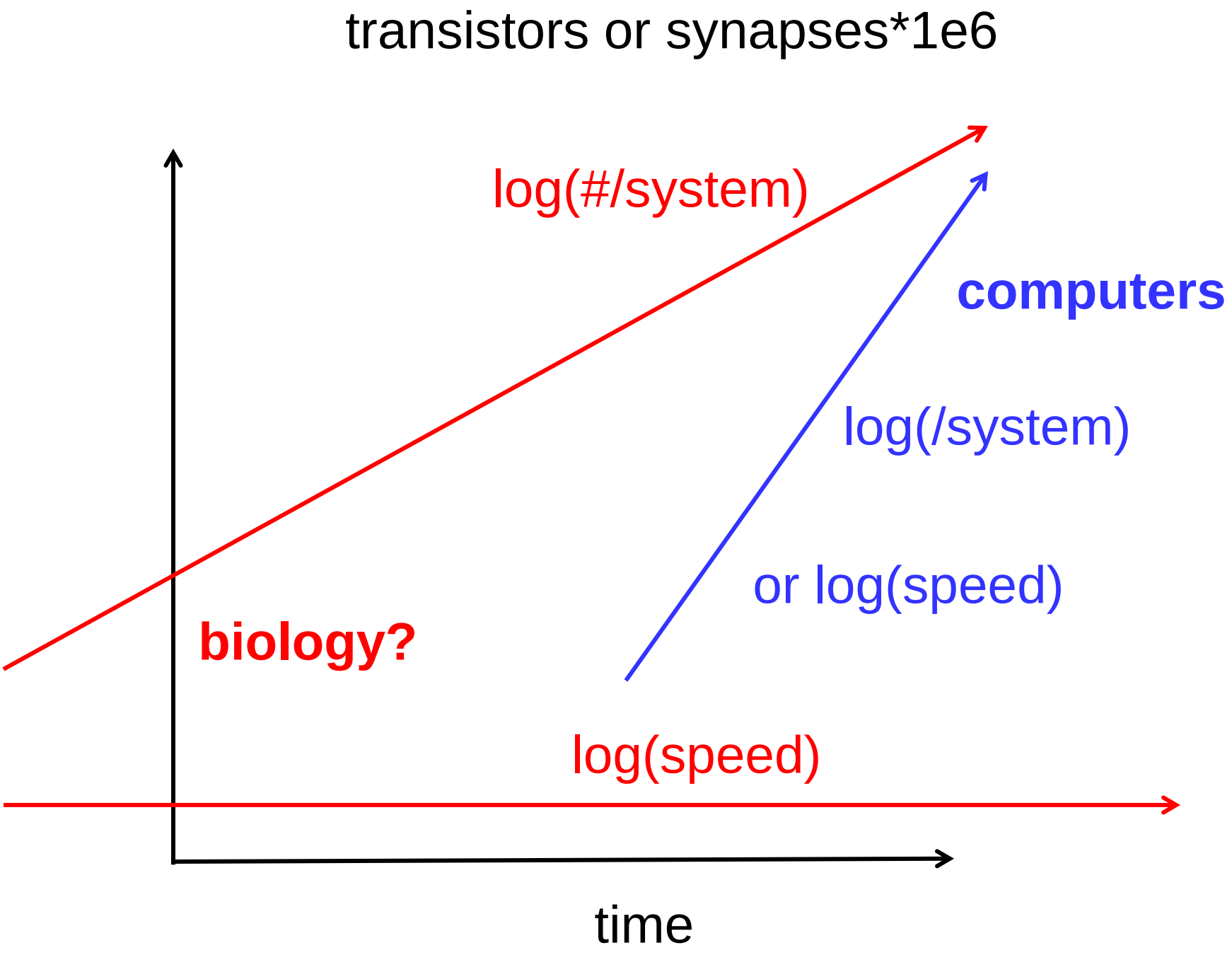
Scientists have always relied on hypothesis and experimentation. Now, in the era of massive data, there's a better way.

"All models are wrong, and increasingly you can succeed without them."

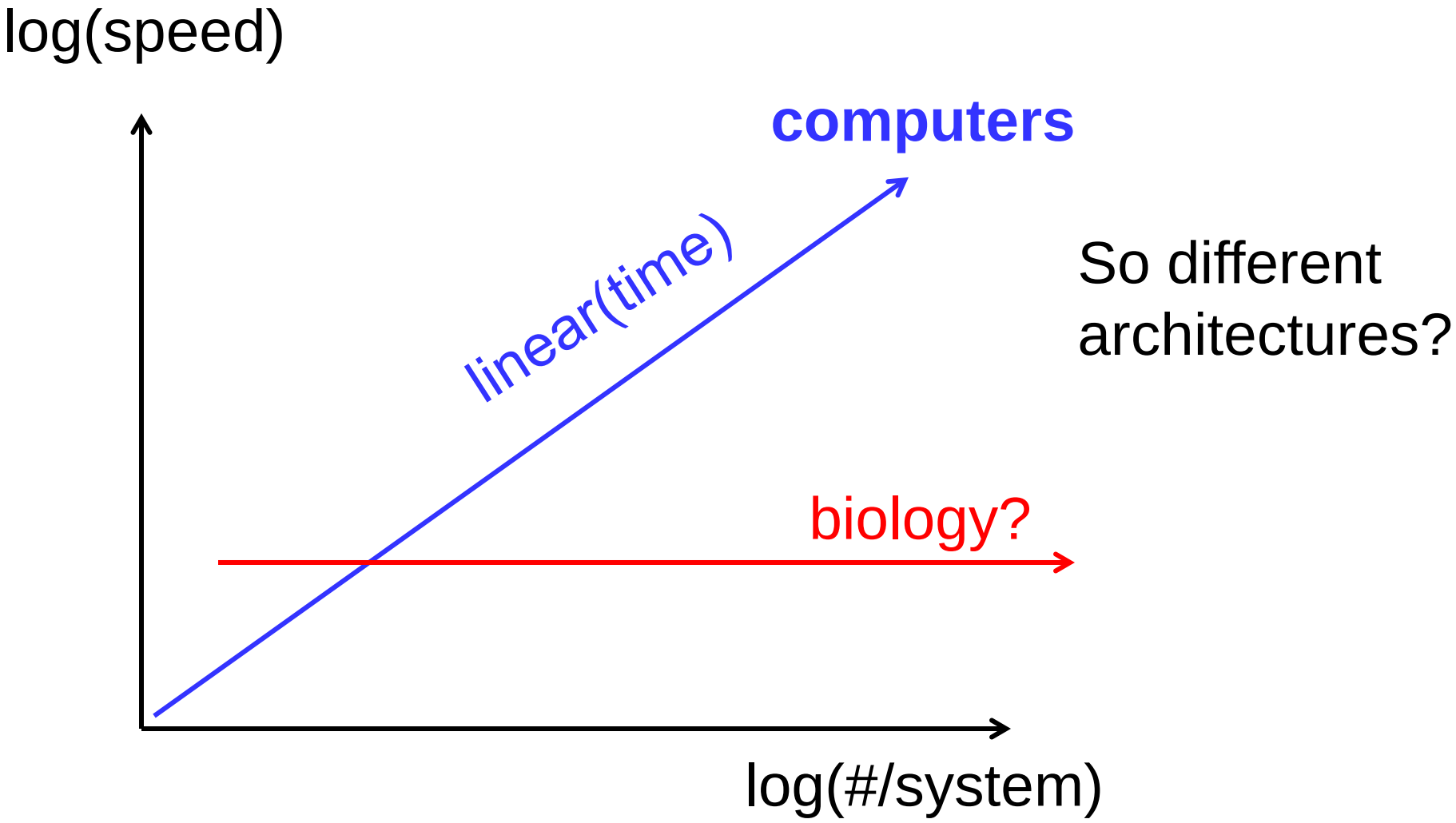
Save our children, stop

There is a treatment.


transistors
computers
log(/system)
or log(speed)
time

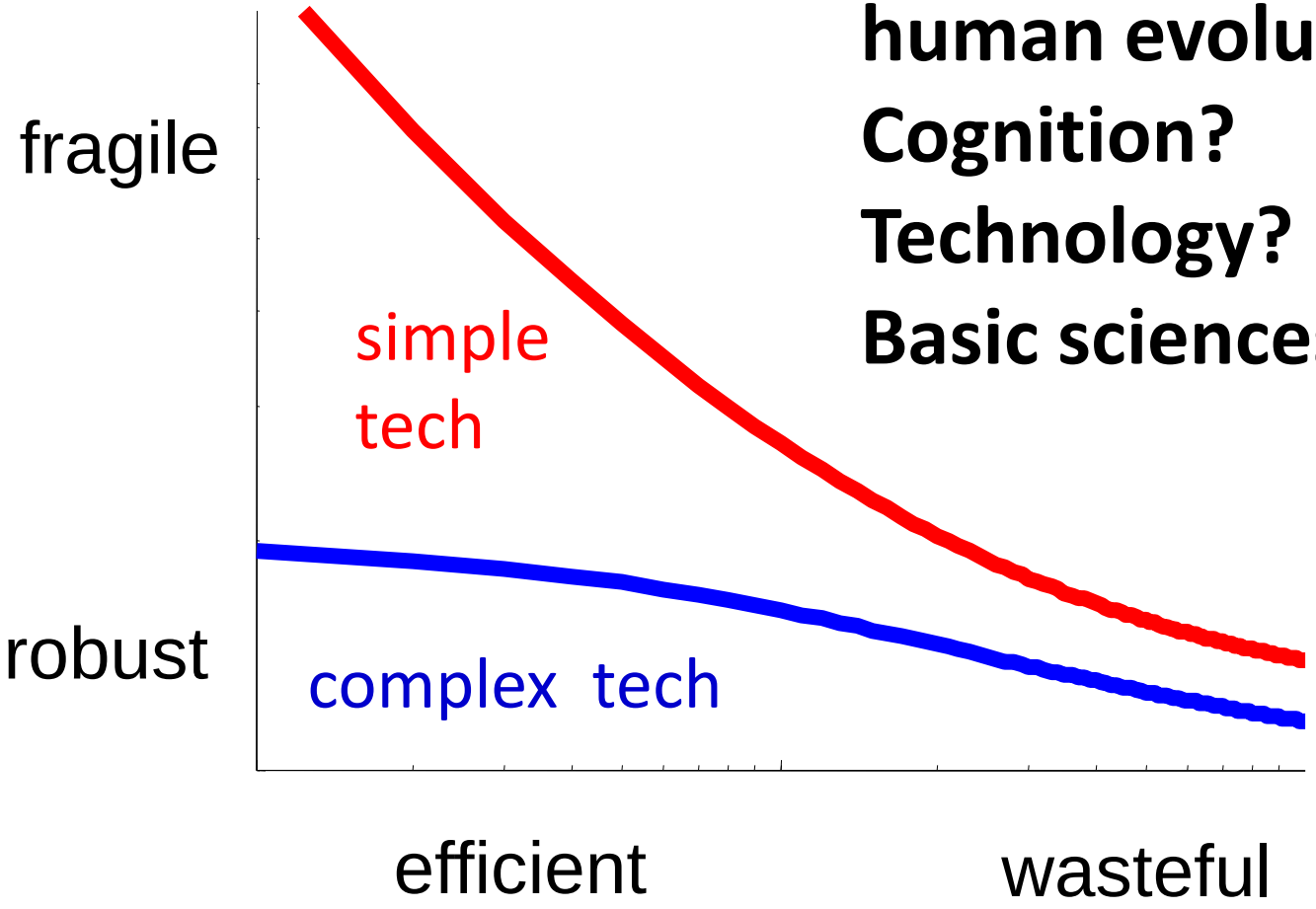

transistors or synapses*1e6
log(#/system)
computers
log(/system)
or log(speed)
biology?
log(speed)
time

transistors or synapses



So different architectures?

How general is this picture?



Implications for human evolution?
Cognition?
Technology?
Basic sciences?