CDS 212

2011 website:

https://www.cds.caltech.edu/wiki/index.php/CDS_212_Fall_2011

The two primary texts for the course (available via the online) are

[DFT] J. Doyle, B. Francis and A. Tannenbaum, *Feedback Control Theory*, Dover, 2009 (originally published by Macmillan, 1992). Available online at http://www.control.utoronto.ca/people/profs/francis/dft.html.

[DP] G. Dullerud and F. Paganini, *A Course in Robust Control Theory*, Springer, 2000.

The following additional texts may be useful for some students:

[FBS] K. J. Astrom and R. M. Murray, *Feedback Systems: An Introduction for Scientists and Engineers*, Princeton University Press, 2008. Available online at http://www.cds.caltech.edu/~murray/amwiki.

“Universal laws and architectures?”

- Universal “conservation laws” (constraints)
- Universal architectures (constraints that deconstrain)
- Start a dialog
- Mention recent papers*
- Focus on broader context not in papers
- Lots of case studies (motivate & illustrate)
- You can have all of the slides

*try to get you
to read them?

“Universal laws and architectures?”

- Universal “conservation laws” (constraints)
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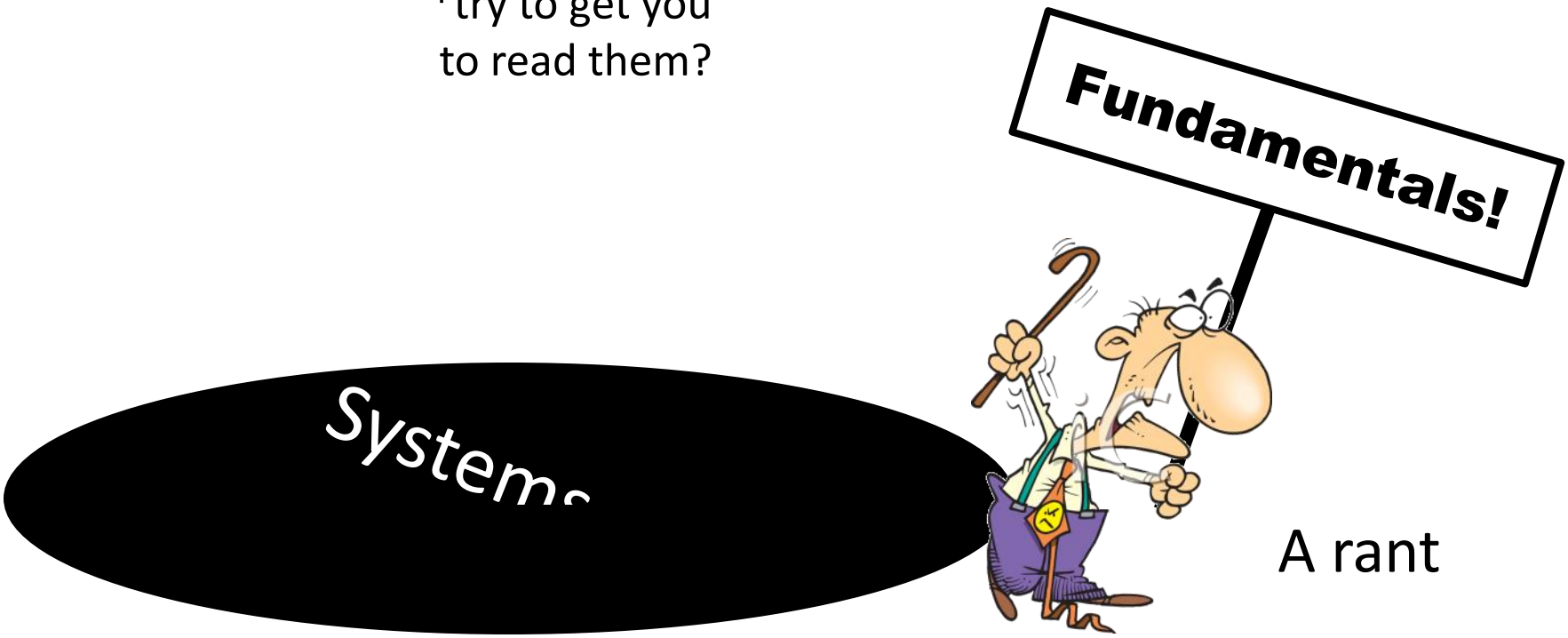
*try to get you
to read them?



A rant

This paper aims to bridge progress in **neuroscience** involving sophisticated quantitative analysis of behavior, including the use of **robust control**, with other relevant conceptual and theoretical frameworks from **systems engineering, systems biology, and mathematics.**

Most accessible
No math

Architecture, constraints, and behavior

John C. Doyle[a,1] and Marie Csete[b,1]

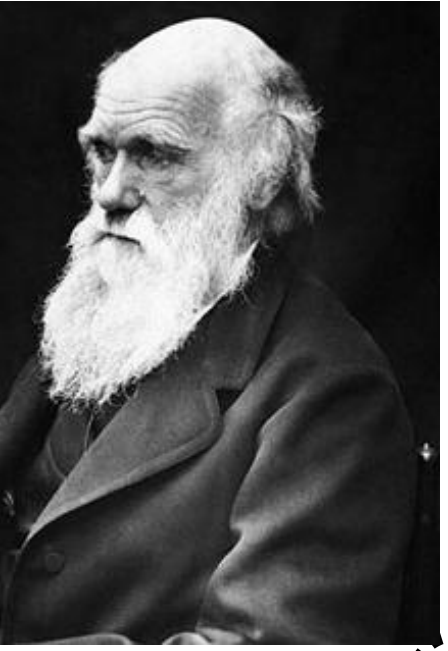
[a]Control and Dynamical Systems, California Institute of Technology, Pasadena, CA 91125; and [b]Department of Anesthesiology, University of California, San Diego, CA 92103

Edited by Donald W. Pfaff, The Rockefeller University, New York, NY, and approved June 10, 2011 (received for review March 3, 2011)

This paper aims to bridge progress in neuroscience involving sophisticated quantitative analysis of behavior, including the use of robust control, with other relevant conceptual and theoretical frameworks from systems engineering, systems biology, and mathematics. Familiar and accessible case studies are used to illustrate concepts of robustness, organization, and architecture (modularity and protocols) that are central to understanding complex networks. These essential organizational features are hidden during normal function of a system but are fundamental for understanding the nature, design, and function of complex biologic and technologic systems.

evolved for sensorimotor control and retain much of that evolved architecture, then the apparent distinctions between perceptual, cognitive, and motor processes may be another form of illusion (9), reinforcing the claim that robust control and adaptive feedback (7, 11) rather than more conventional serial signal processing might be more useful in interpreting neurophysiology data (9). This view also seems broadly consistent with the arguments from grounded cognition that modal simulations, bodily states, and situated action underlie not only motor control but cognition in general (12), including language (13). Furthermore, the myriad constraints involved in the evolution of circuit

Doyle, Csete, *Proc Nat Acad Sci USA*, JULY 25 2011



Horizontal Meme Transfer

Prefrontal

Learning

Sensory

Striatum

Software

Hardware

Horizontal App Transfer

Reflex

Digital

Analog

DNAp

Gene

RNAp

xRNA

transc.

RN

ATP

A

Ribosome

Proteins

transl.

A

Horizontal Gene Transfer

Nucl.

A

A

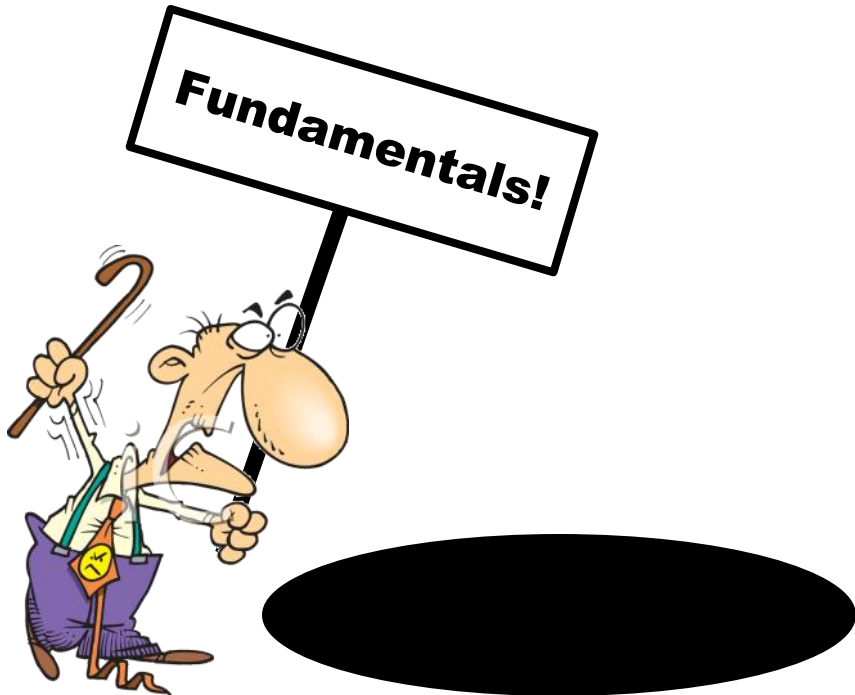
ATP

Precursors

Catabolism

- Cell biology
- Networking
- Neuroscience
- Medical physiology
- Smartgrid, cyber-phys
- Wildfire ecology
- Earthquakes
- Lots of aerospace
- Physics:
  - turbulence,
  - stat mech (QM?)
- “Toy”:
  - Lego,
  - clothing,
- Buildings, cities
- **Synesthesia**

case studies



Case studies (recent focus)

- Bacterial biosphere
- Internet, PC, smartphone, etc technology
- Human brain and mind
- Human physiology

- ***Amazing*** evolvability (sustainability?)
- Illustrate universal laws and architecture in (hopefully) accessible way

Case studies (purpose)

- Illustrate/motivate theory and universals
  - Laws (constraints, hard limits, tradeoffs)
  - Architectures (design, forward and reverse engineering, organization)
  - Otherwise publish in eng/systems/math journals
- Impact for domain experts
  - Frameworks to organize existing, isolated facts
  - Suggests new experiments
  - Publish in core domain journals (*Science, Cell, PNAS, ACM Sigcomm, Science Trans Med*, …)

Universal “laws” (constraints)

- Constraints “bottom up” from physics/chemistry
  - Gravity, speed of light
  - Energy, carbon, …
  - Small moieties (redox, …)… more later?

- ***But***, the most universal laws for bio&tech are largely ***independent*** of physics
- Most scientists and many engineers don’t understand and/or believe this is even possible
- So skepticism is warranted
- We’ll come back to this after we discuss universal architectures

When concepts fail, words arise

Faust, Goethe

Mephistopheles. …Enter the templed hall of Certainty.

Student. Yet in each word some concept there must be.

Mephistopheles. Quite true! But don't torment yourself too anxiously;
For at the point where concepts fail,
At the right time a word is thrust in there…

Requirements on systems and architectures

accessible
accountable
accurate
adaptable
administrable
affordable
auditable
autonomy
available
credible
process capable
compatible
composable
configurable
correctness
customizable
debugable
degradable
determinable
demonstrable
dependable
deployable
discoverable
distributable
durable
effective
efficient
evolvable
extensible
failure transparent
fault-tolerant
fidelity
flexible
inspectable
installable
Integrity
interchangeable
interoperable
learnable
maintainable
manageable
mobile
modifiable
modular
nomadic
operable
orthogonality
portable
precision
predictable
producible
provable
recoverable
relevant
reliable
repeatable
reproducible
resilient
responsive
reusable
robust
safety
scalable
seamless
self-sustainable
serviceable
supportable
securable
simplicity
stable
standards compliant
survivable
sustainable
tailorable
testable
timely
traceable
ubiquitous
understandable
upgradable
usable

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effective
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failure
transparent
fault-tolerant
fidelity
flexible
inspectable
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Integrity
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maintainable

manageable
mobile
modifiable
modular
nomadic
operable
orthogonality
portable
precision
predictable
reproducible
recoverable
relevant
reliable
repeatable
reproducible
resilient
responsive
reusable
robust

safety
scalable
seamless
self-sustainable
serviceable
supportable
securable
simplicity
stable
standards
compliant
survivable
sustainable
tailorable
testable
timely
traceable
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Long term

Lumping requirements into simple groups

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upgradable
usable

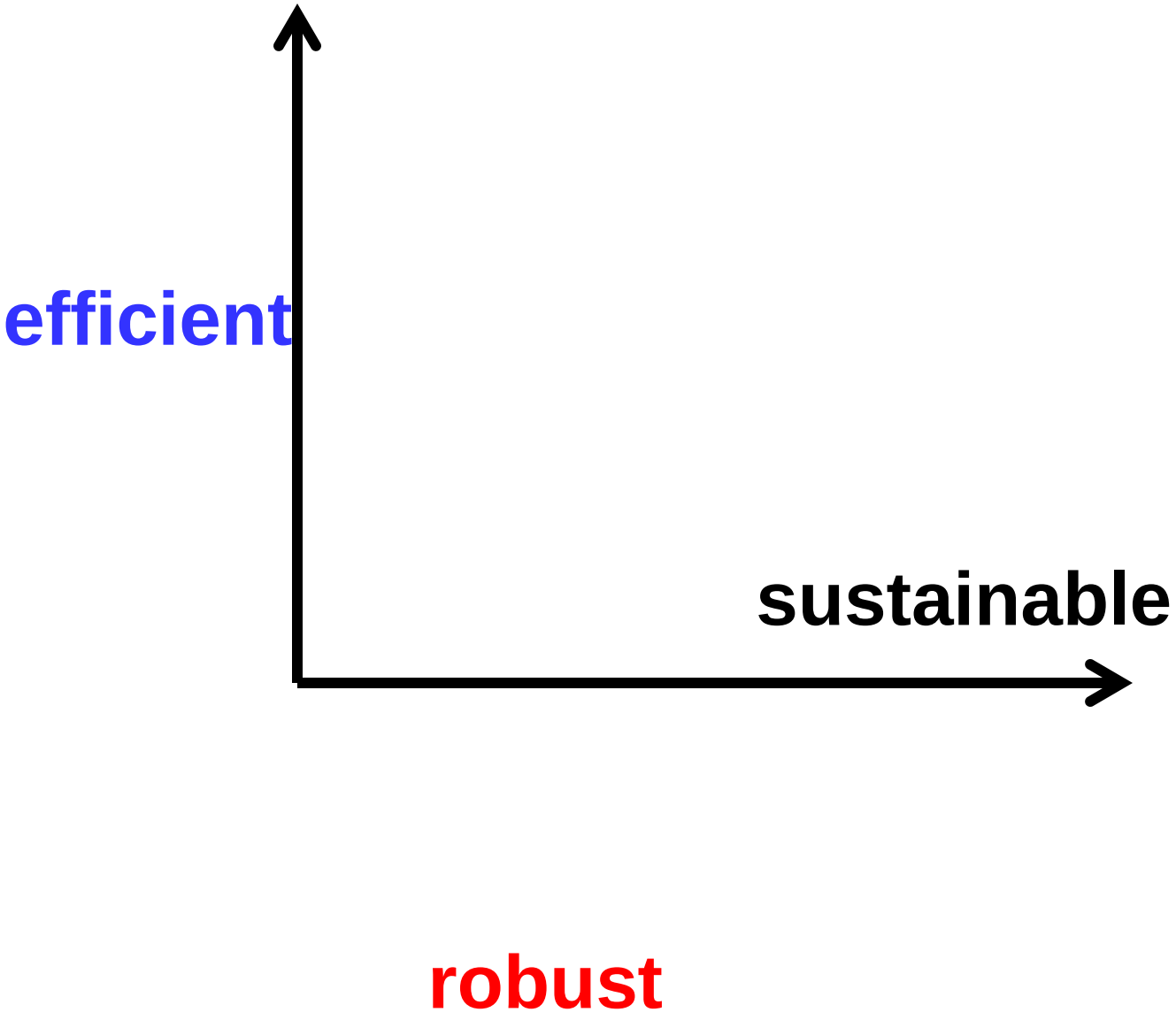
Requirements on systems and architectures

efficient

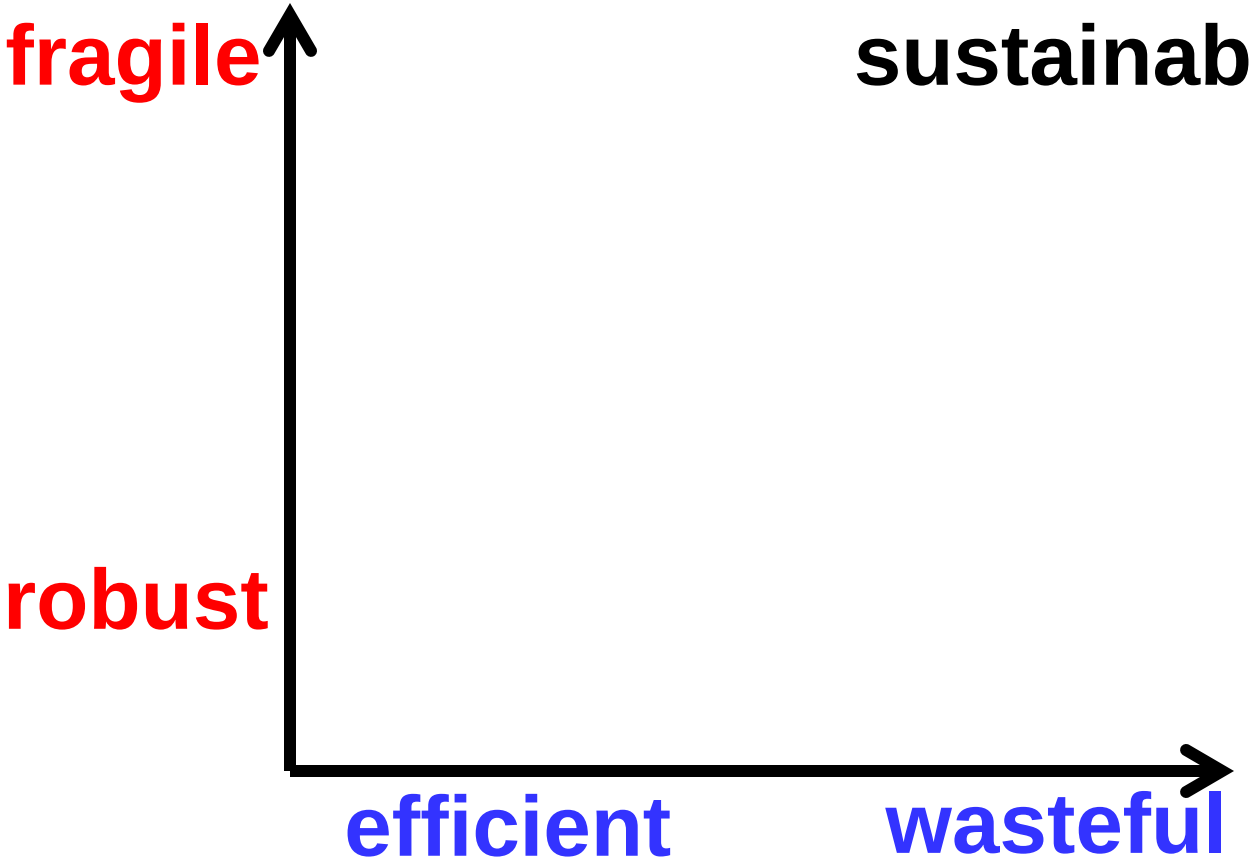
sustainable

robust

Requirements on systems and architectures

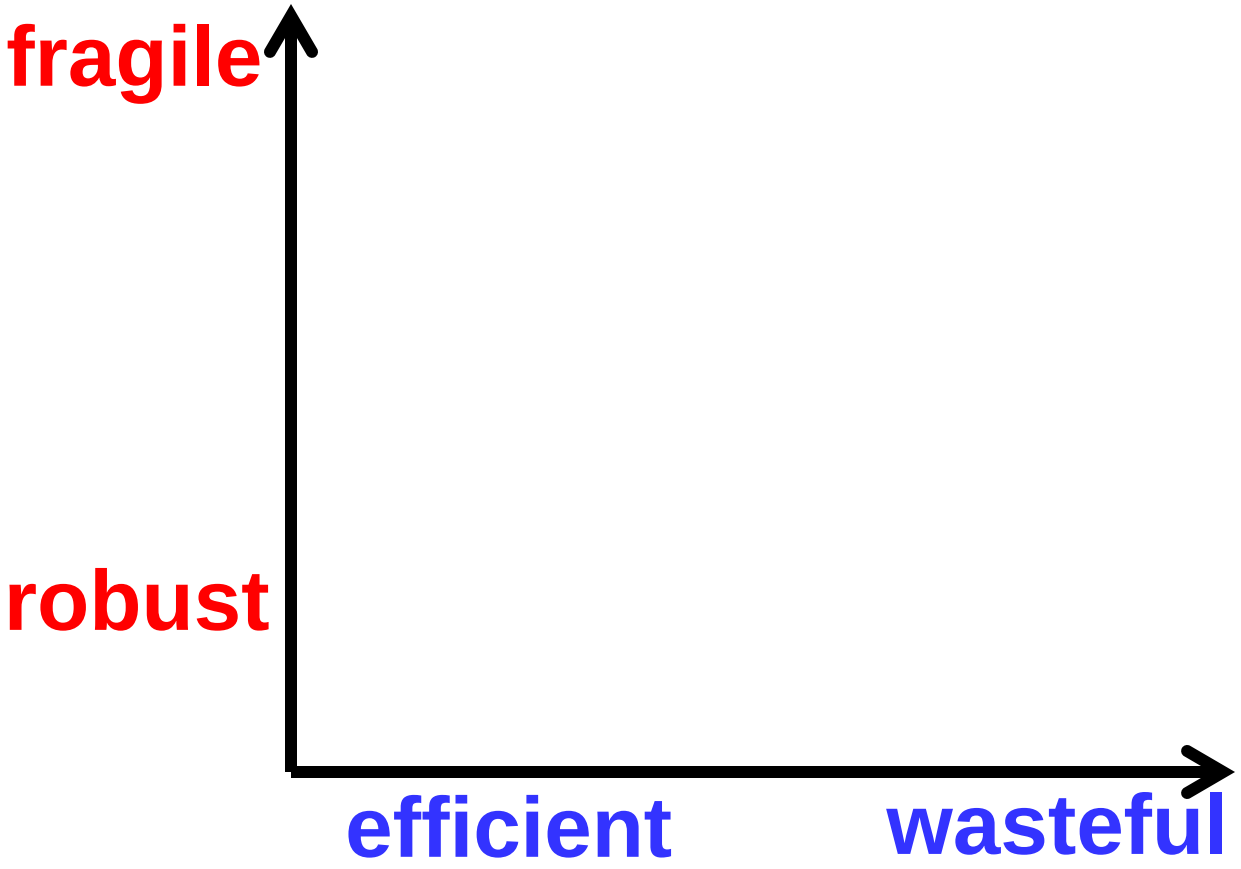


Requirements on systems and architectures



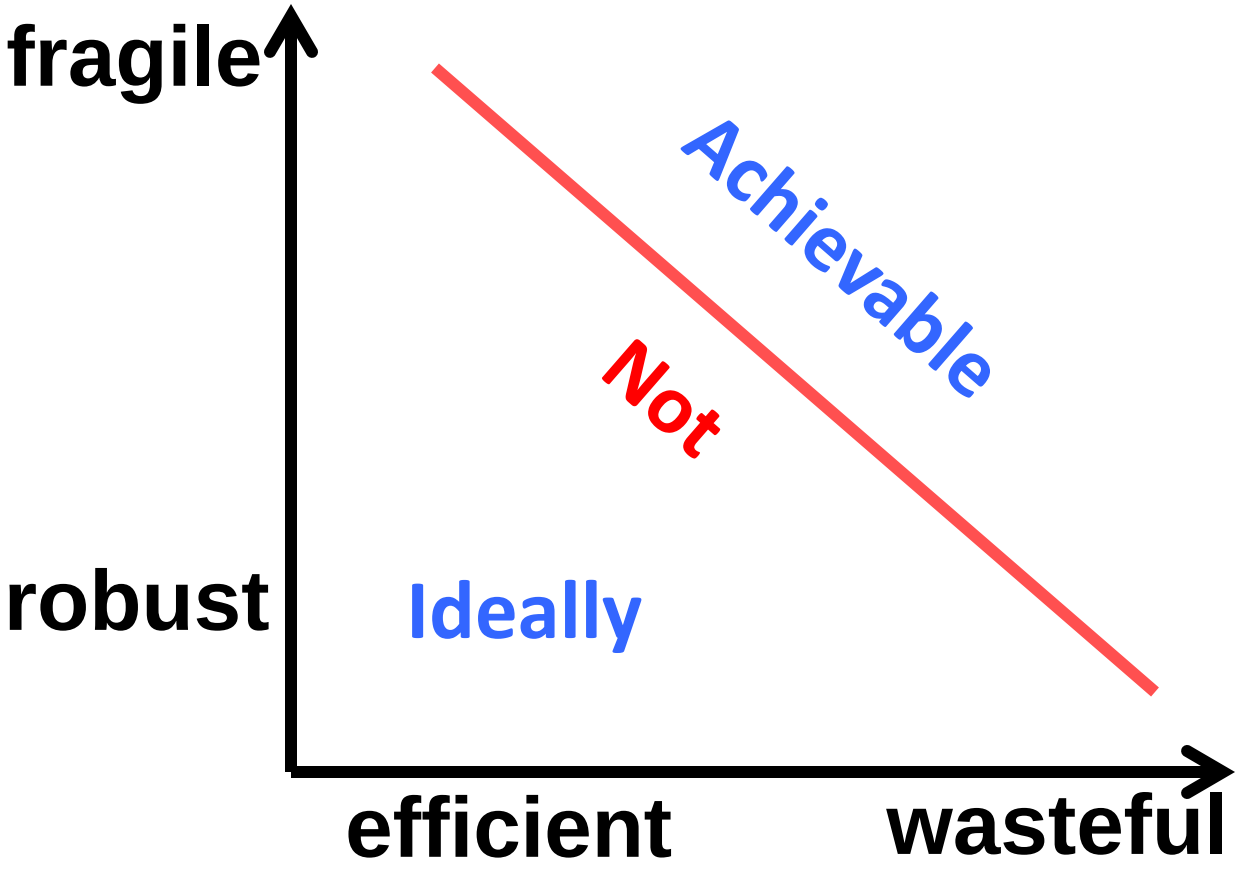
Requirements on systems and architectures

sustainable

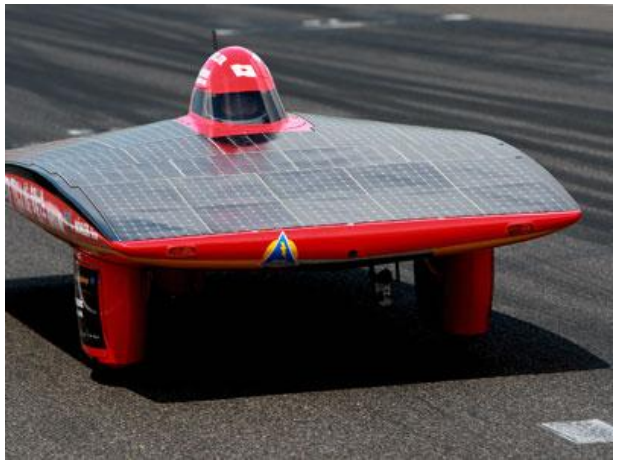


Requirements on systems and architectures

sustainable



Current Technology?



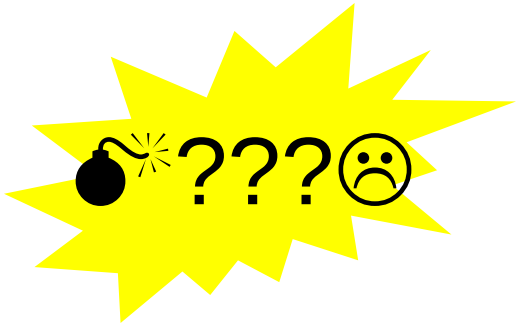
fragile

robust

efficient

wasteful

At best we get one



fragile

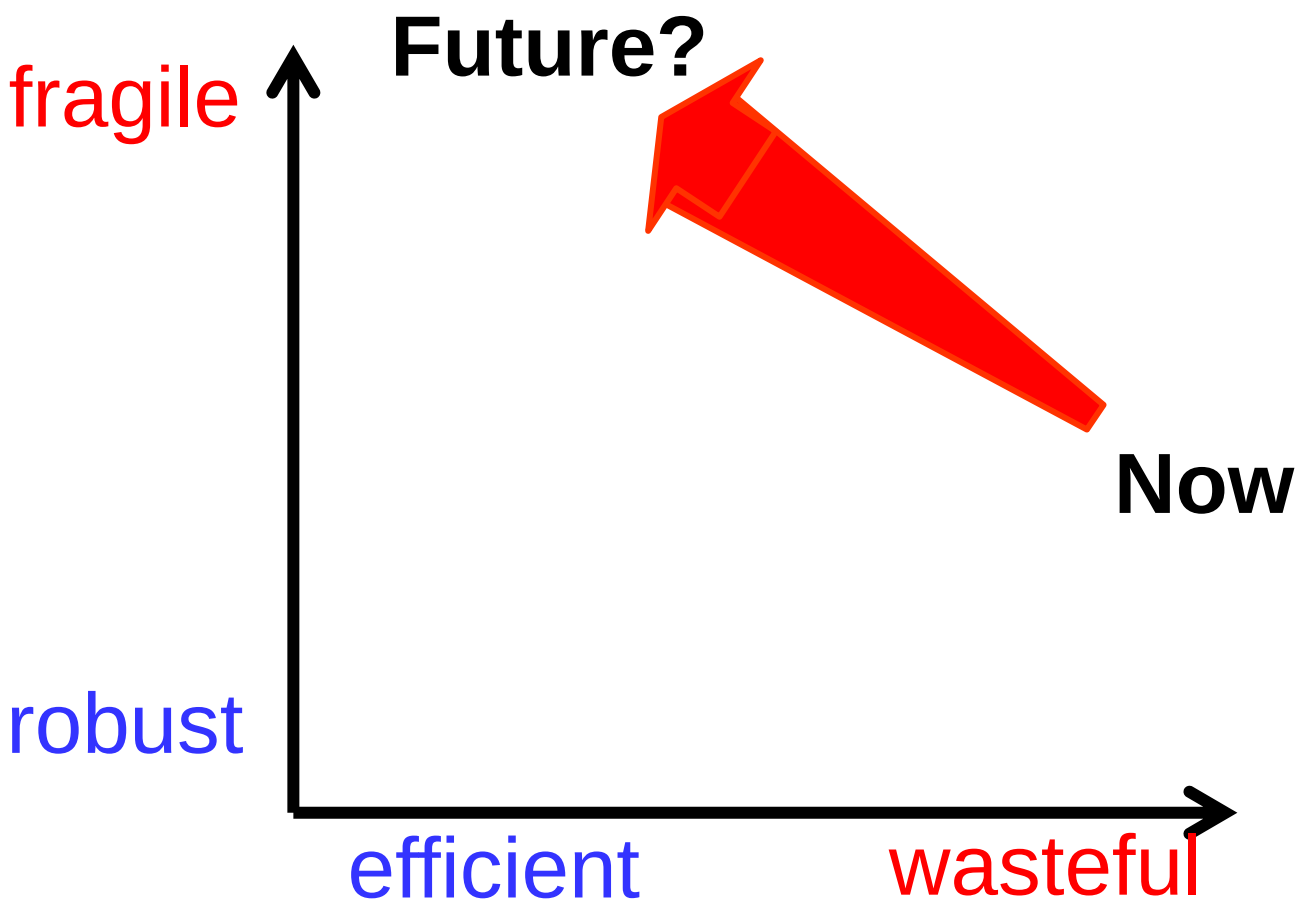
Often neither

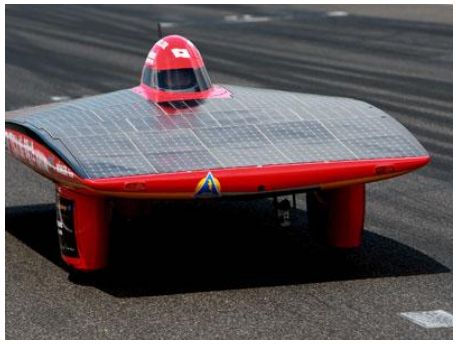
robust

efficient

wasteful

Future evolution of the “smart” grid?





Bad architectures?

fragile

?

gap?

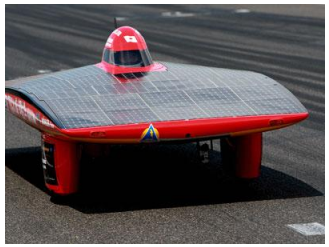
Bad theory?

?

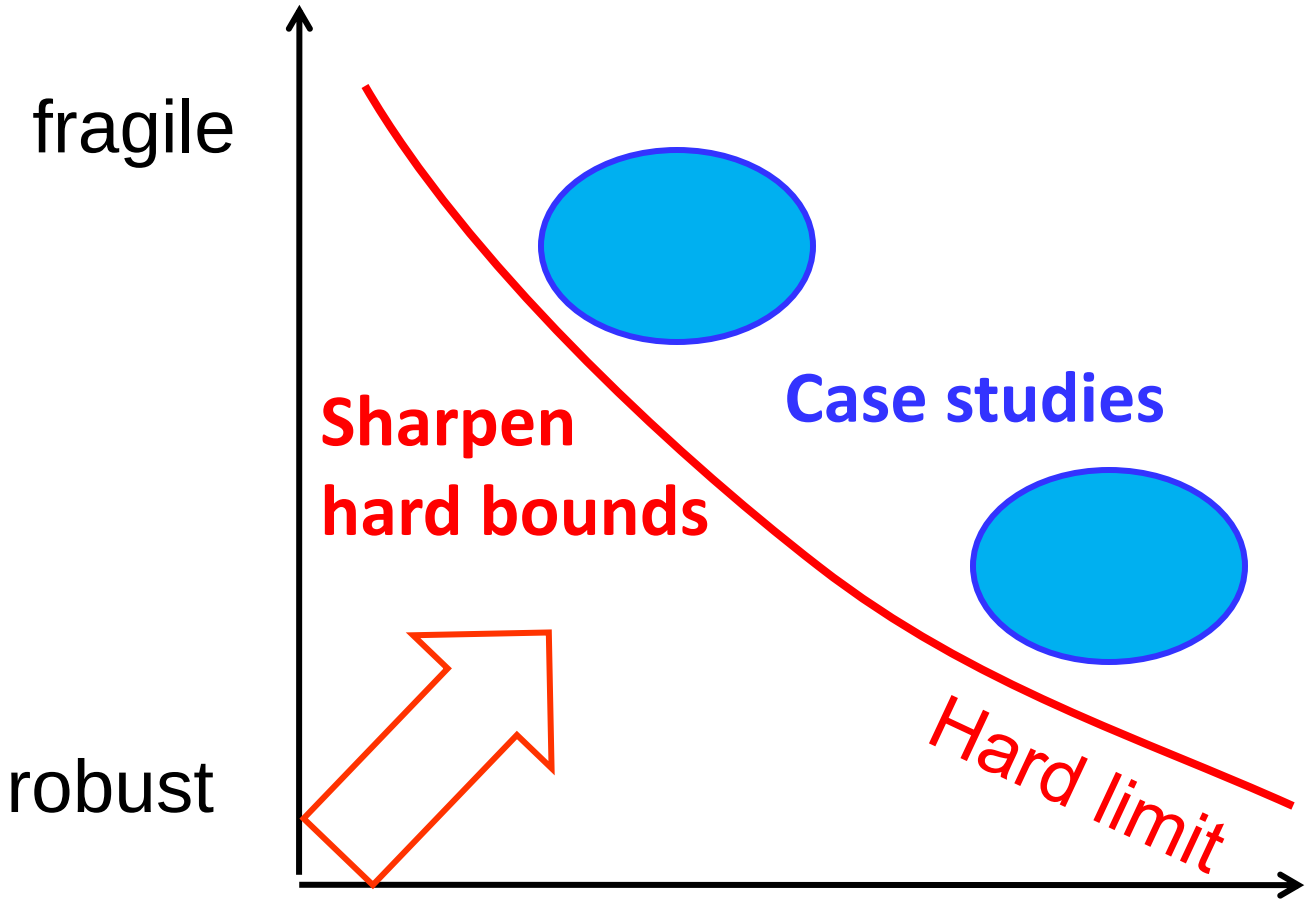
robust

efficient

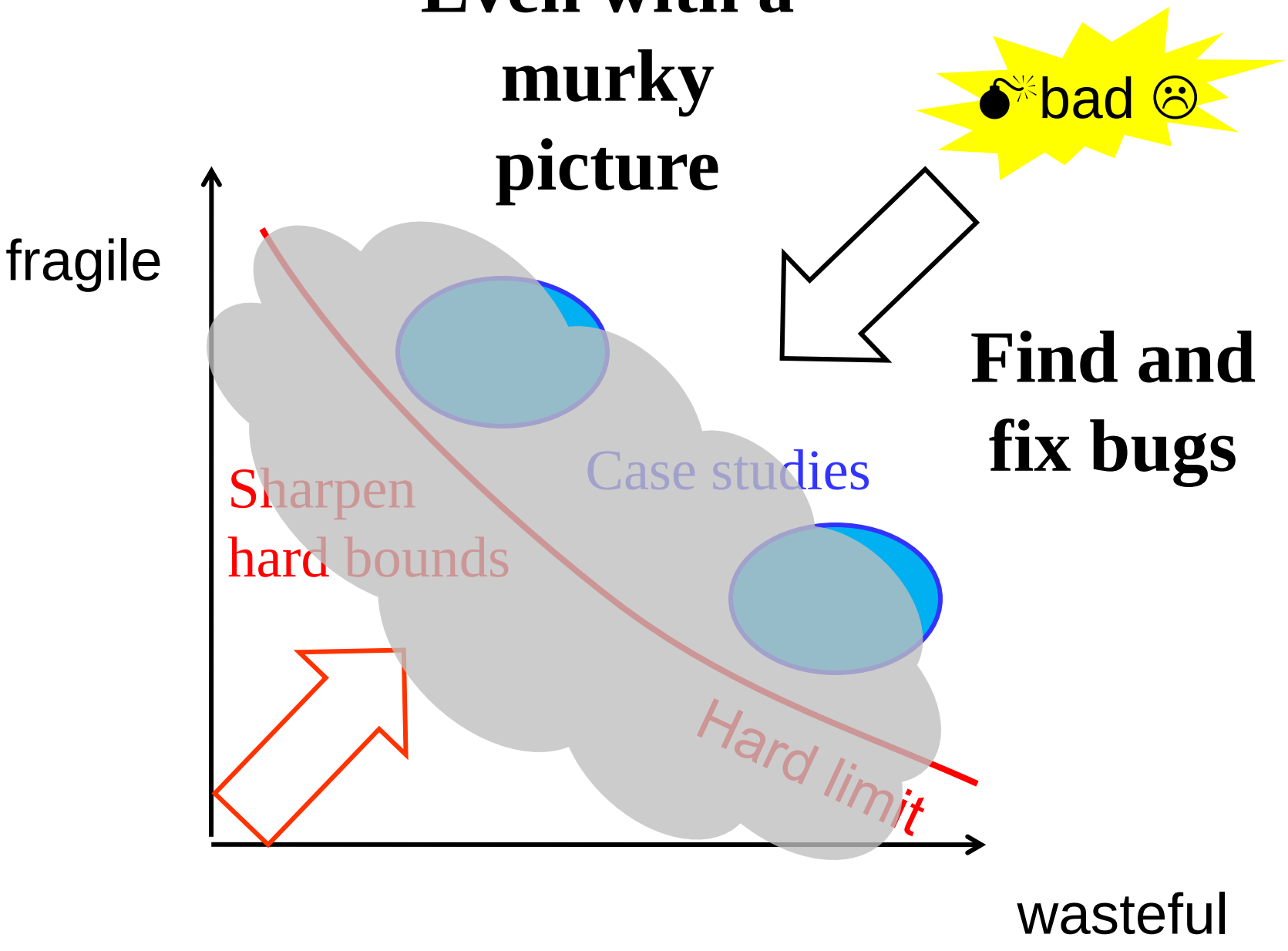
wasteful



laws and architectures?

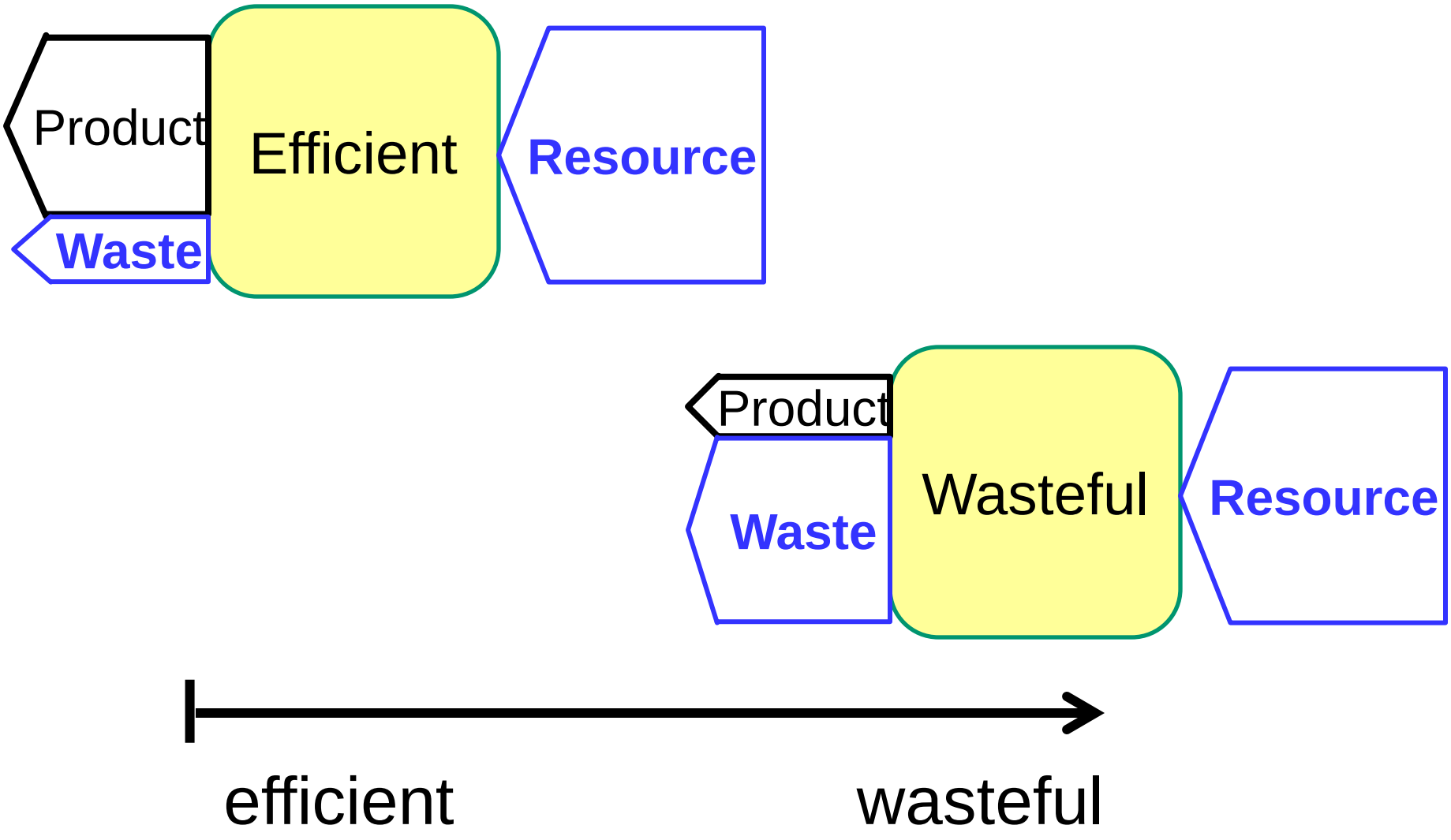


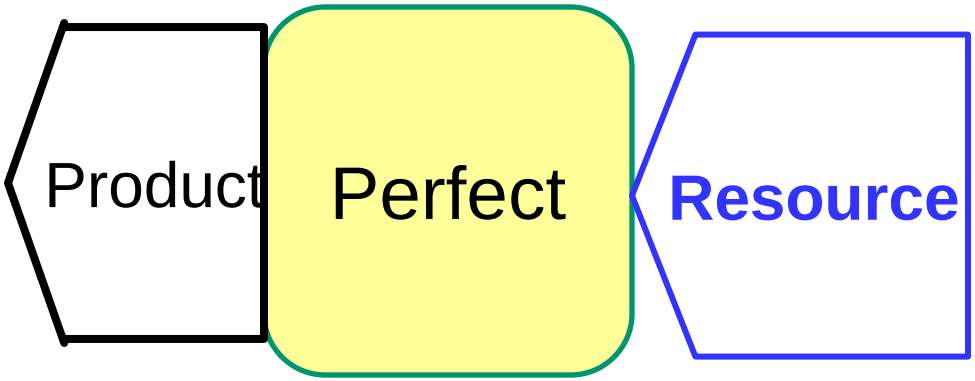
Even with a murky picture




efficient
wasteful

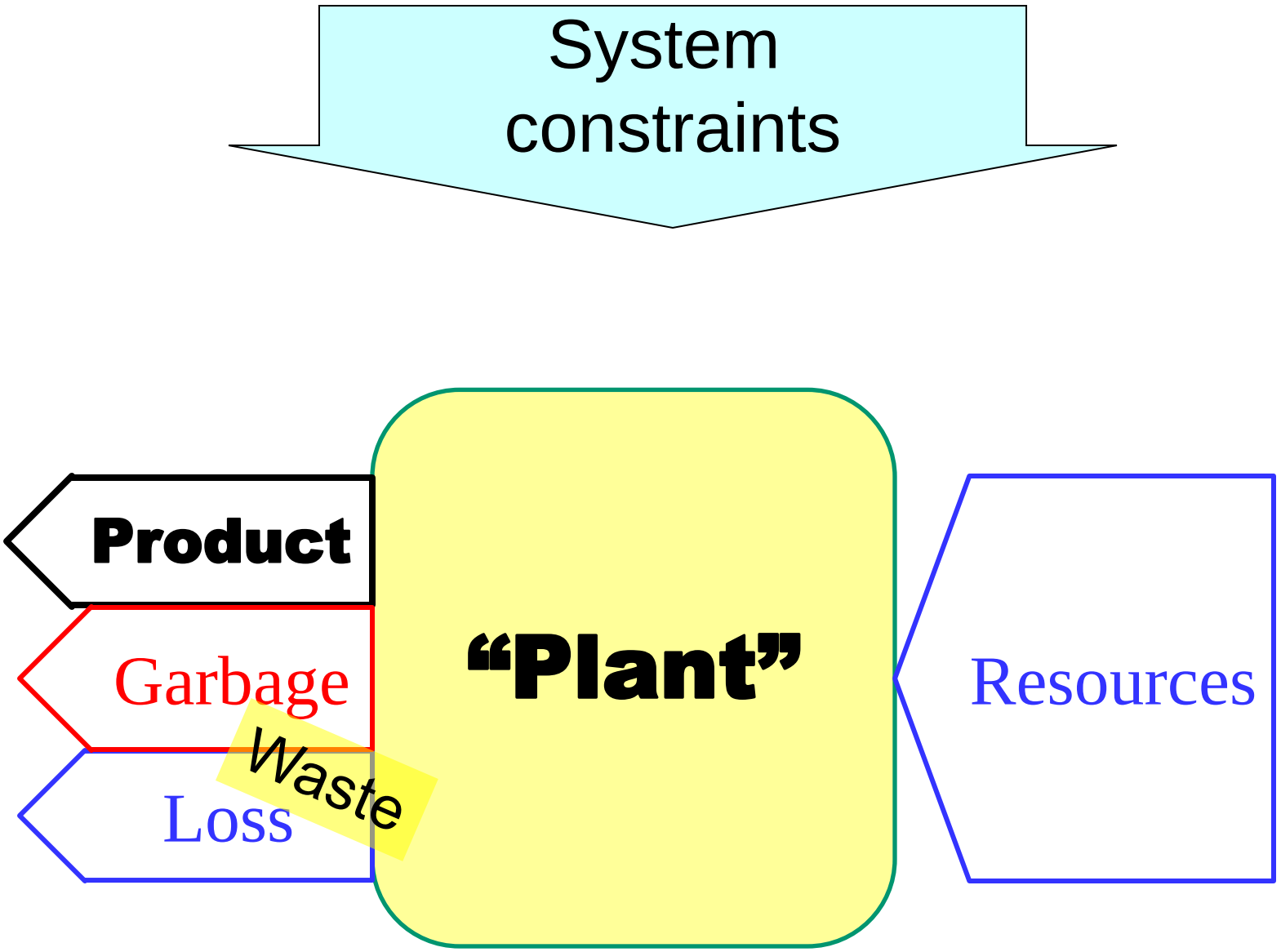
Flow of materials and energy

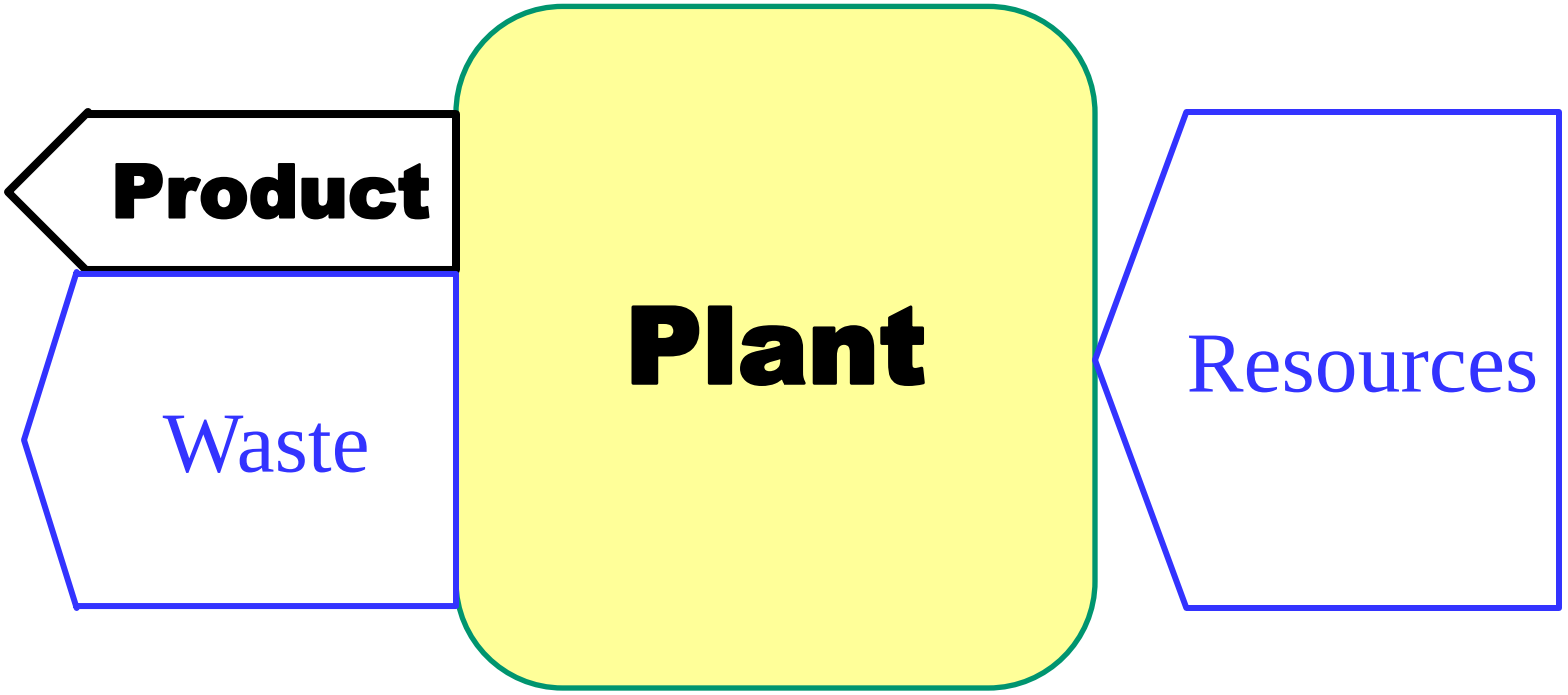


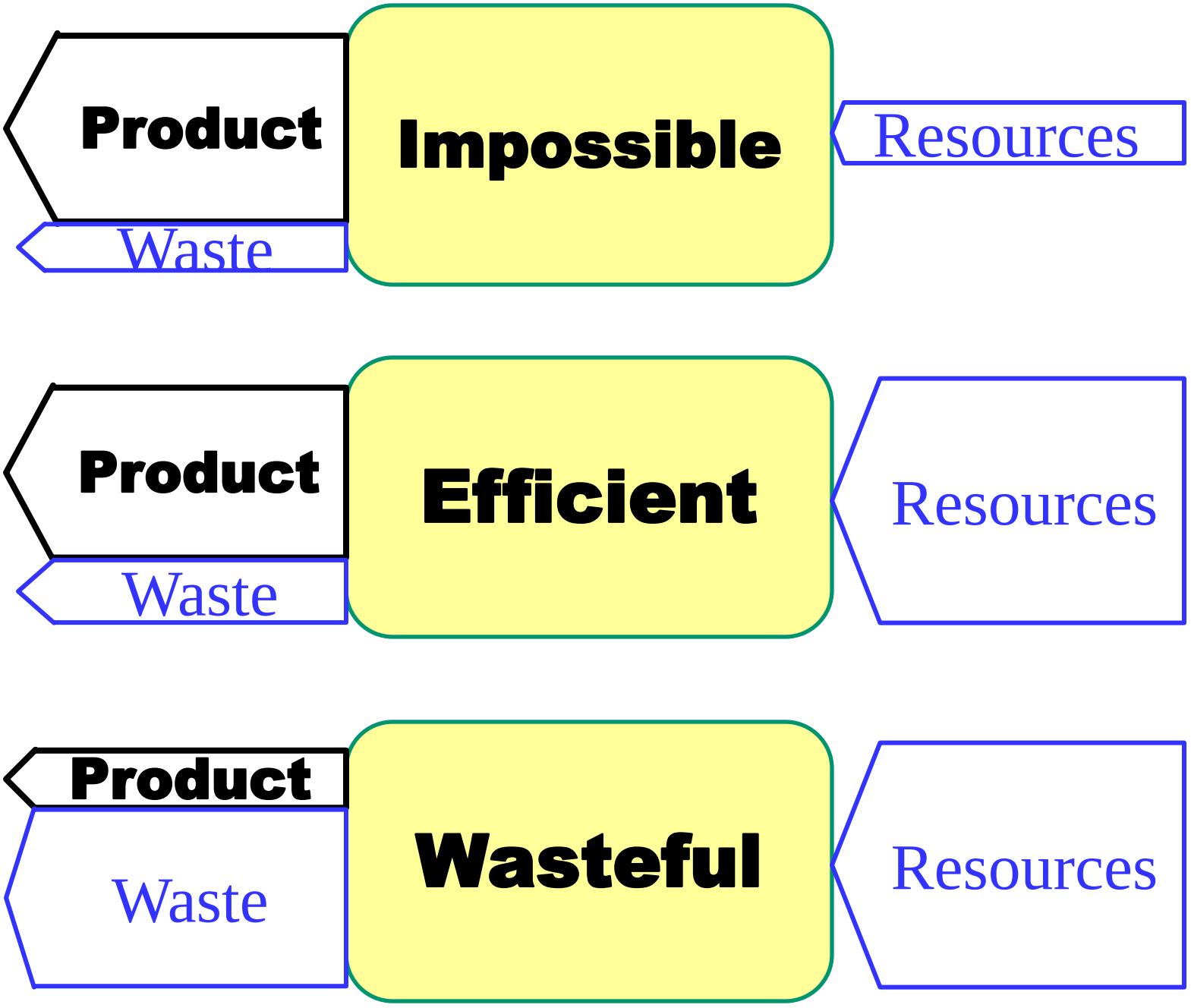


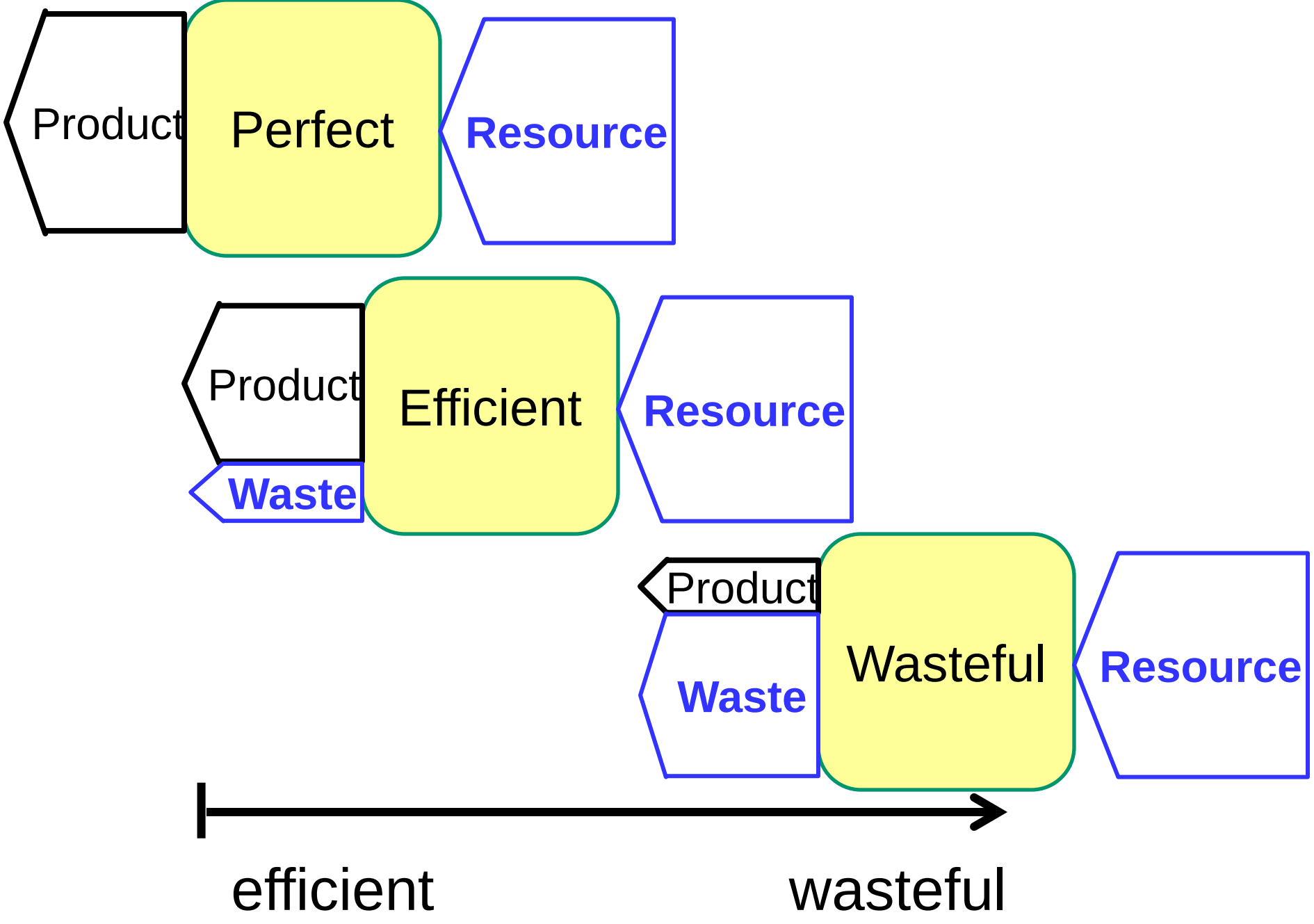
Perfect = all conserved resources are converted into product

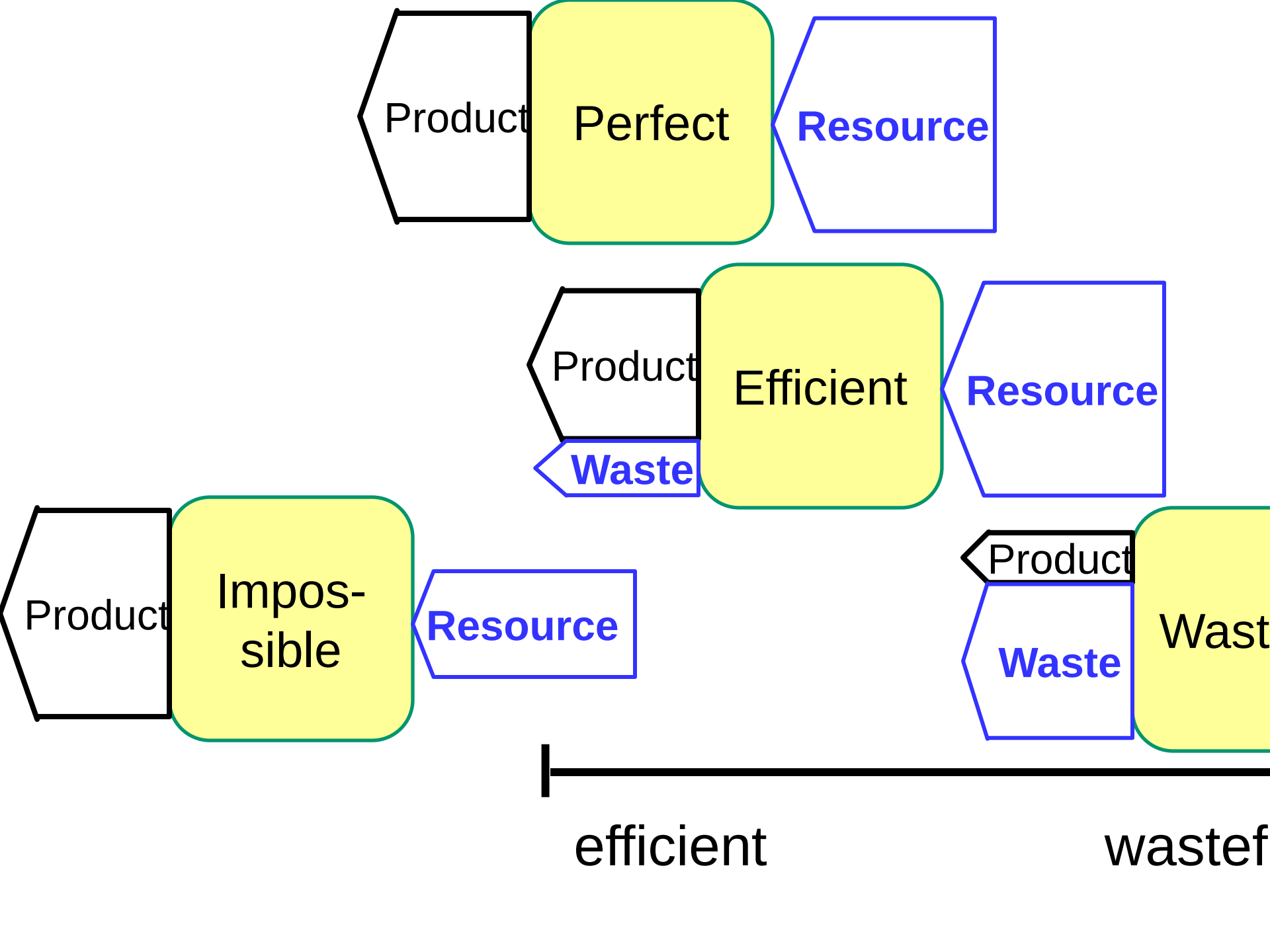
efficient wasteful


System constraints
Product
Garbage
Waste
Loss
“Plant”
Resources

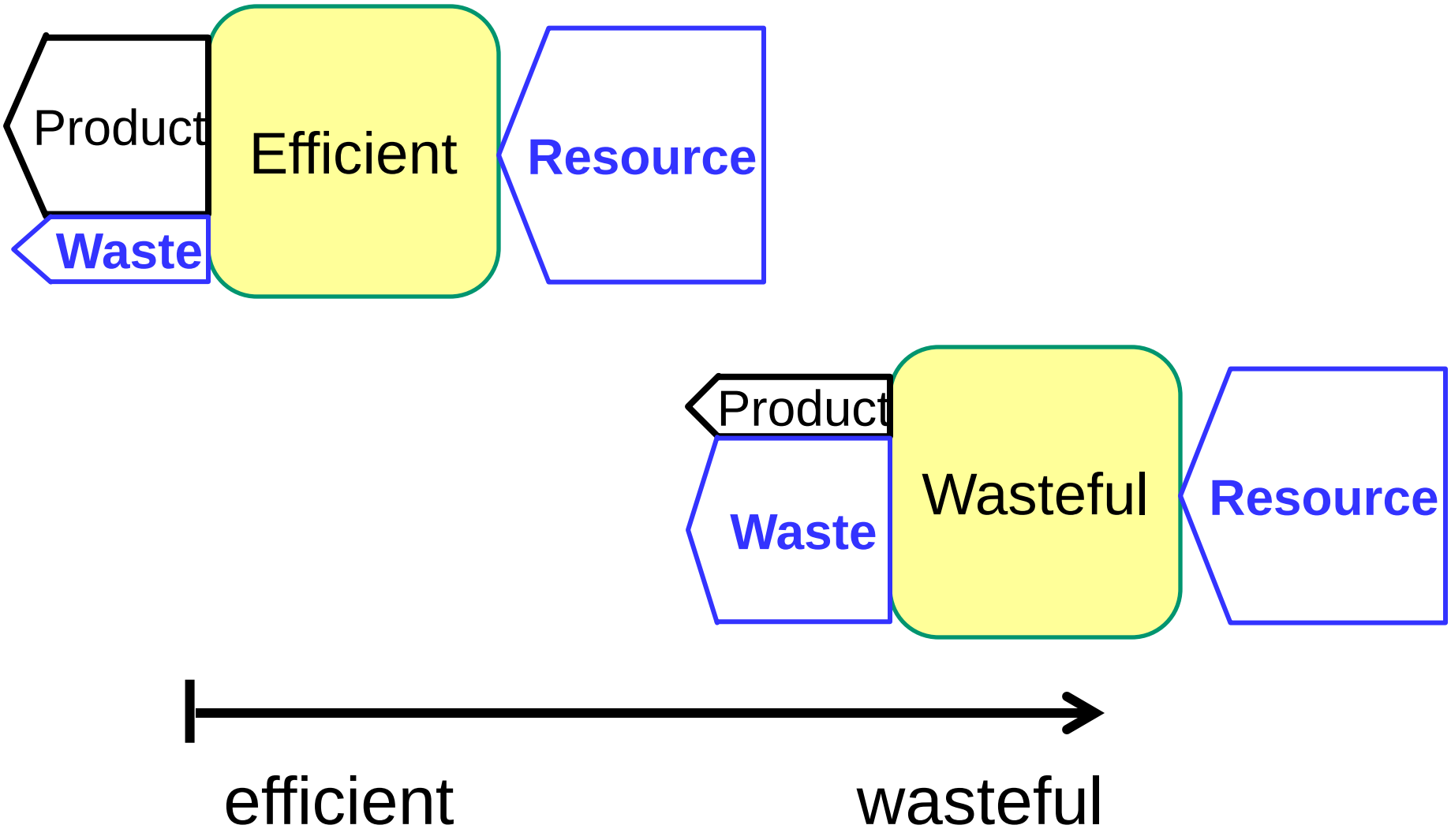

Product
Waste
Plant
Resources

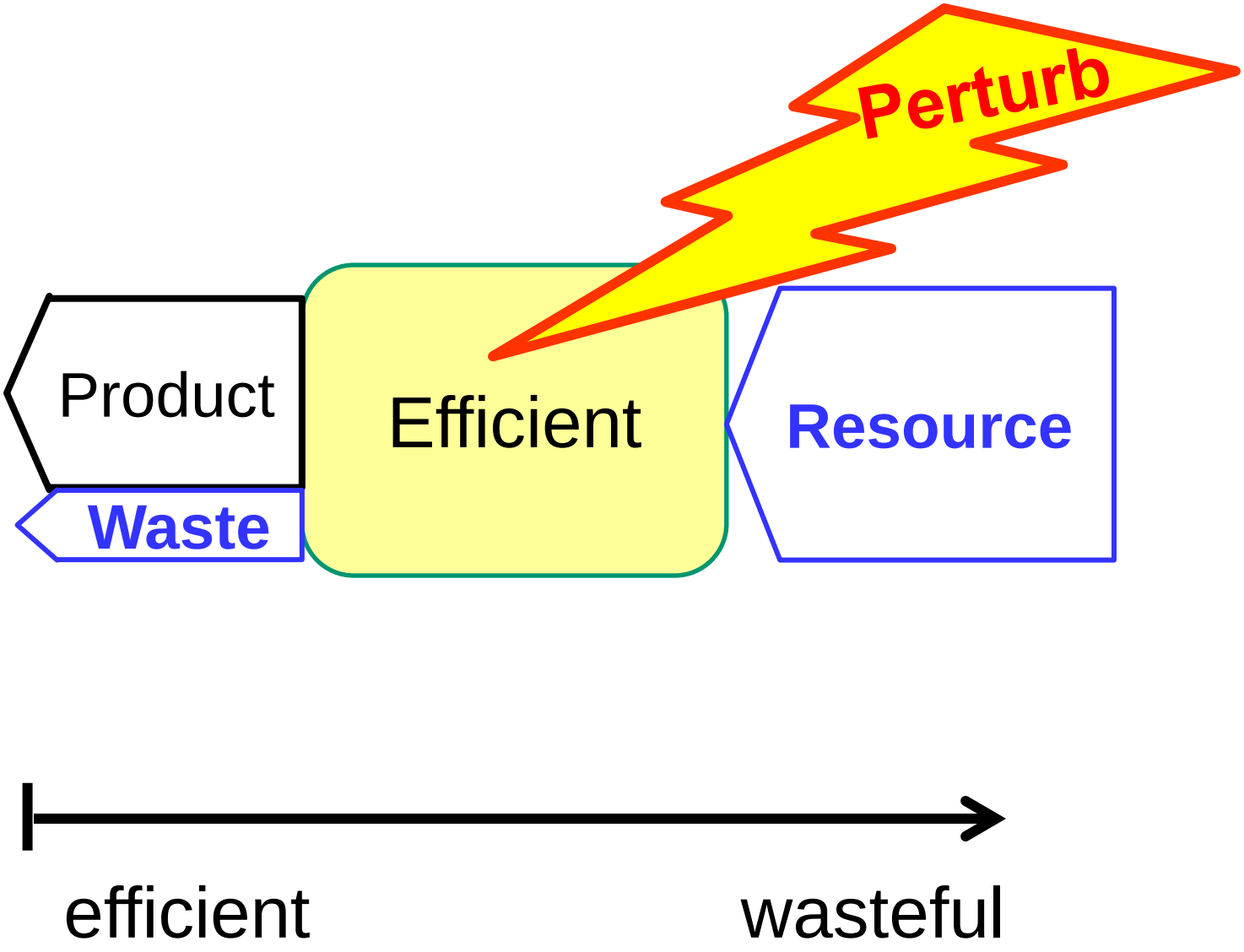

Product
Waste
Impossible
Resources
Product
Waste
Efficient
Resources
Product
Waste
Wasteful
Resources

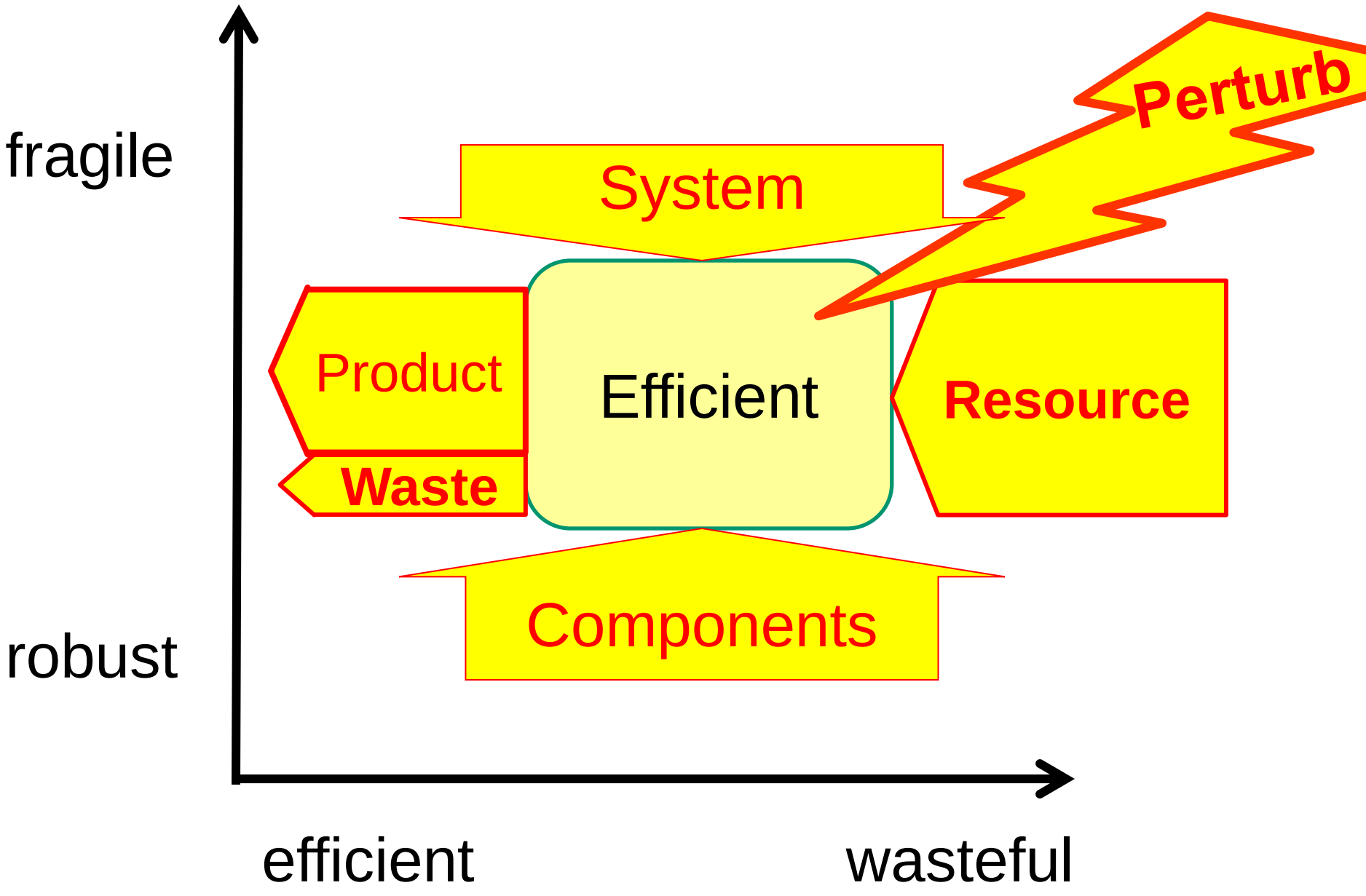

Product
Perfect
Resource
Product
Efficient
Resource
Waste
Product
Waste
Wasteful
Resource
efficient
wasteful

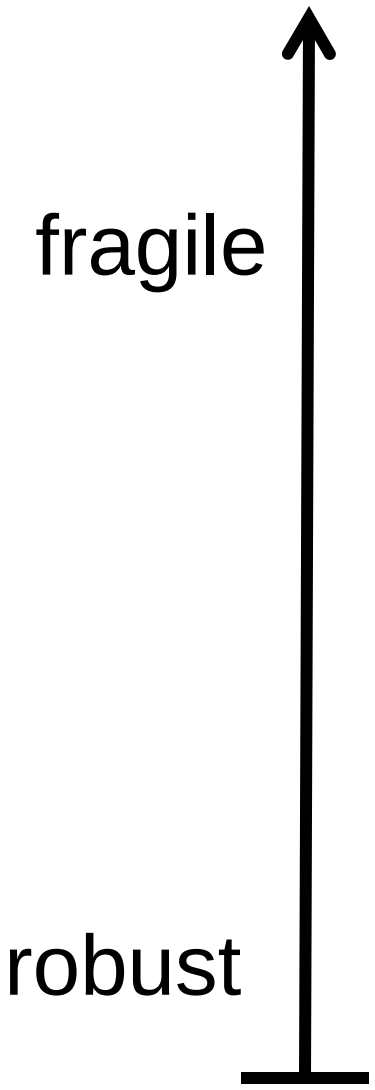

Product
Perfect
Resource
Product
Efficient
Resource
Waste
Product
Impos-
sible
Resource
Product
Waste
Wast
efficient
wastef

Flow of materials and energy

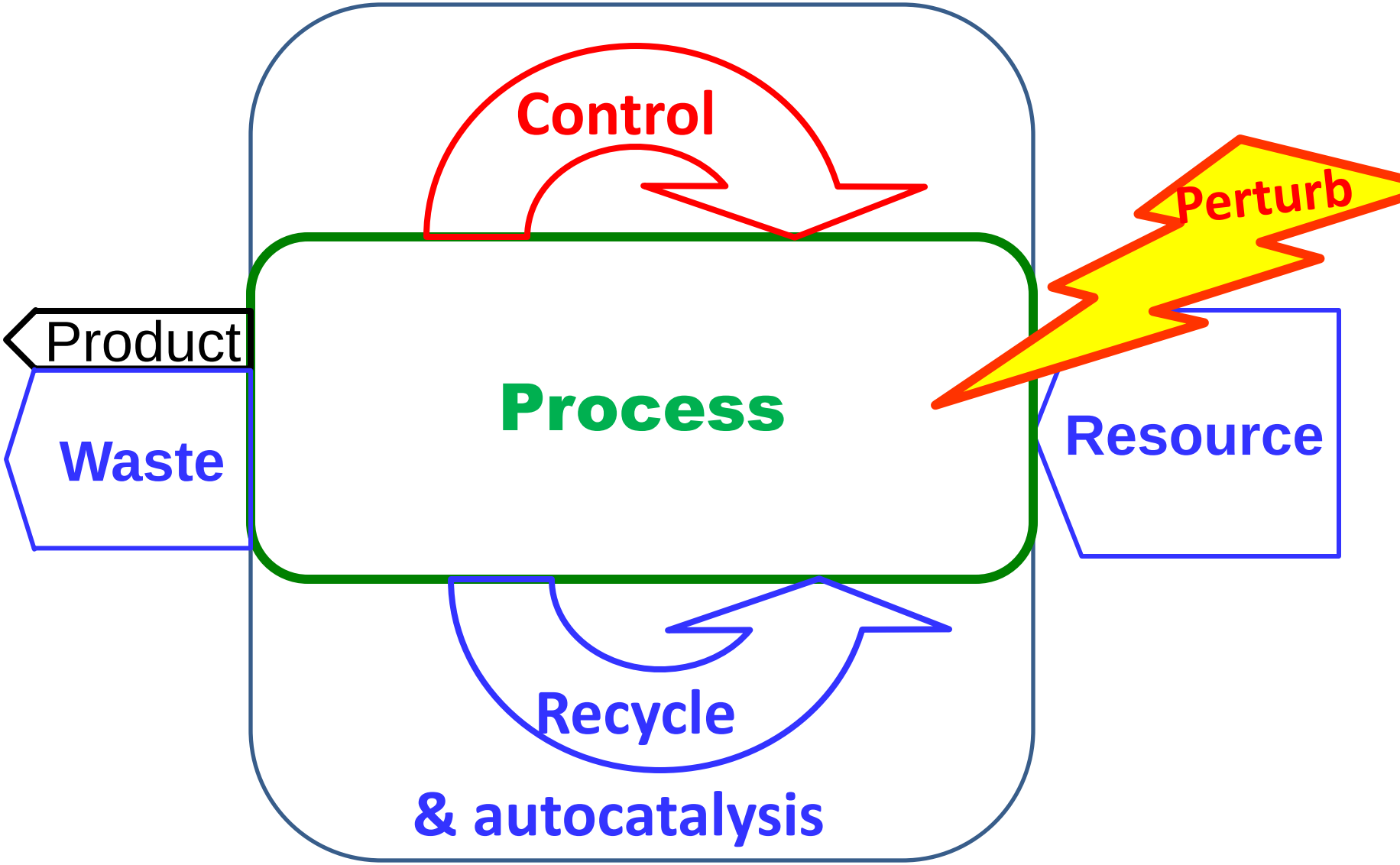



Perturb
Product
Efficient
Resource
Waste
efficient
wasteful


fragile
robust
efficient
wasteful
System
Perturb
Product
Efficient
Resource
Waste
Components


fragile
robust

Feedbacks for **robustness** and **efficiency**



Compute

Godel

Comms

Turing

Shannon

Von
Neumann

Theory?

Deep, but fragmented,
incoherent, incomplete

Nash

Bode

Carnot

Pontryagin

Boltzmann

Heisenberg

Kalman

Control, OR

Einstein

Physics

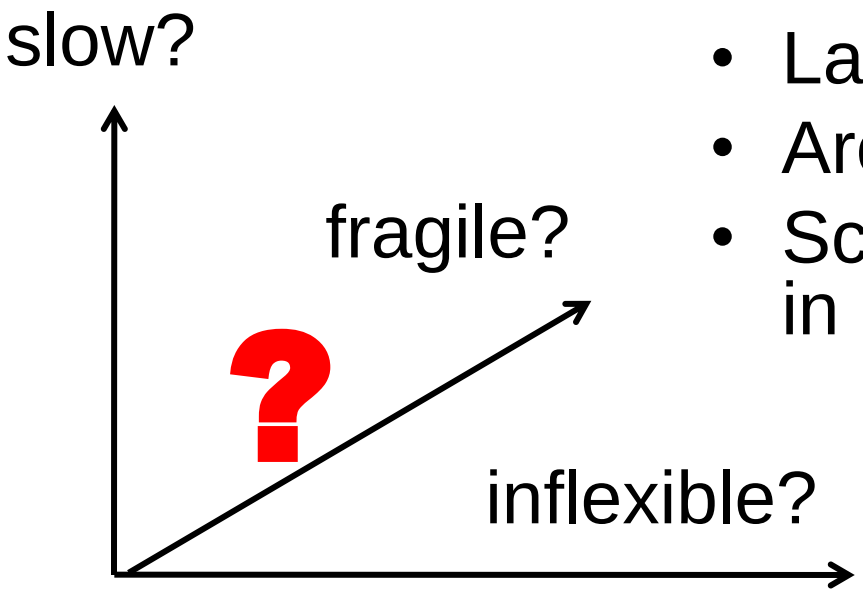
Compute

Godel

Turing

Comms

Shannon



- Each theory ≈ one dimension
- Laws=hard limits
- Architectures fixed
- Scalable algorithms for design in comp/comm/cont

Carnot

Boltzmann

Bode

Heisenberg

Control

Physics

Einstein

Compute

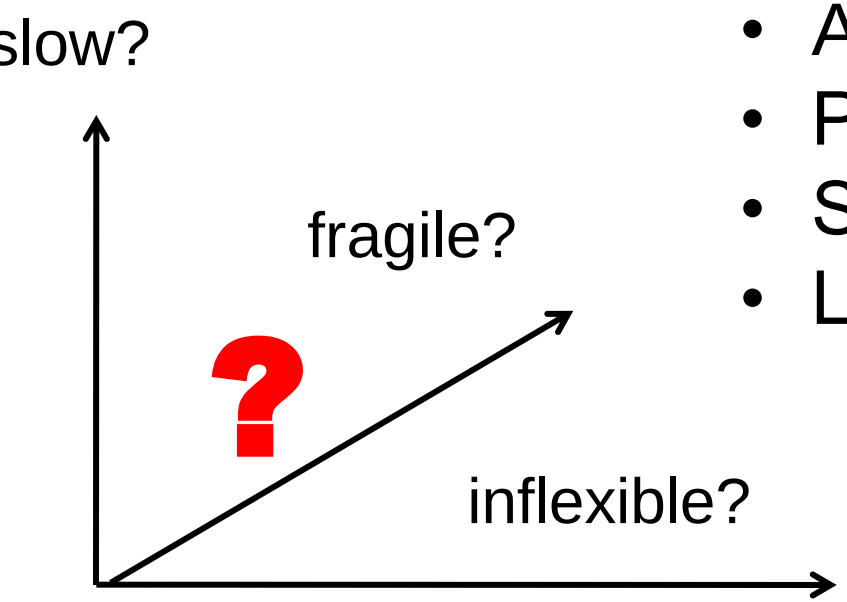
Godel

Turing

Comms

Shannon

- Each theory ≈ one dimension
- Tradeoffs ***across*** dimensions
- Assume architectures a priori
- Progress is encouraging, but…
- Stovepipes are an obstacle…
- Limited “universality”



Bode

Control

Carnot

Boltzmann

Heisenberg

Einstein

Physics

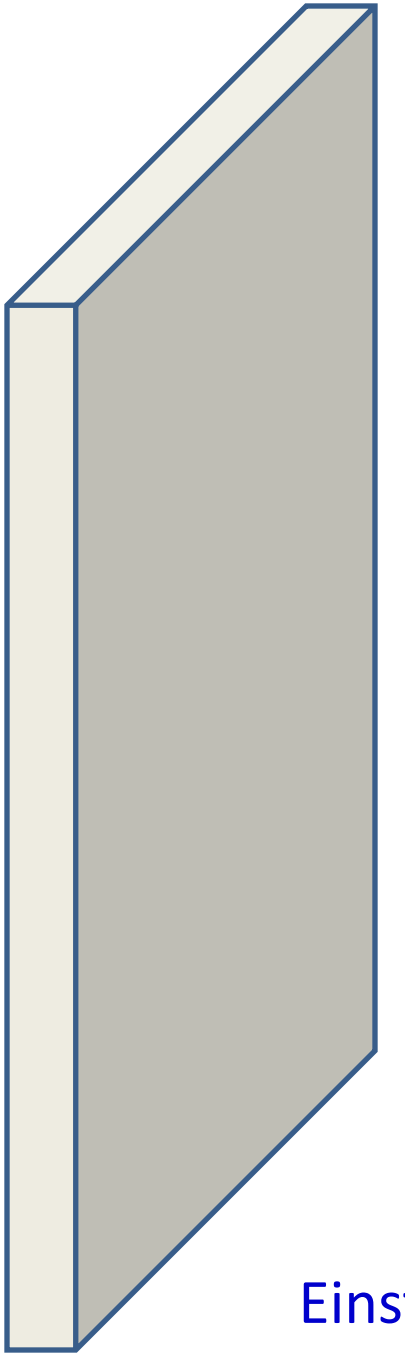
Compute

Turing

Delay is *most* important

Bode

Control, OR



Communicate

Shannon

Delay is *least* important

Carnot

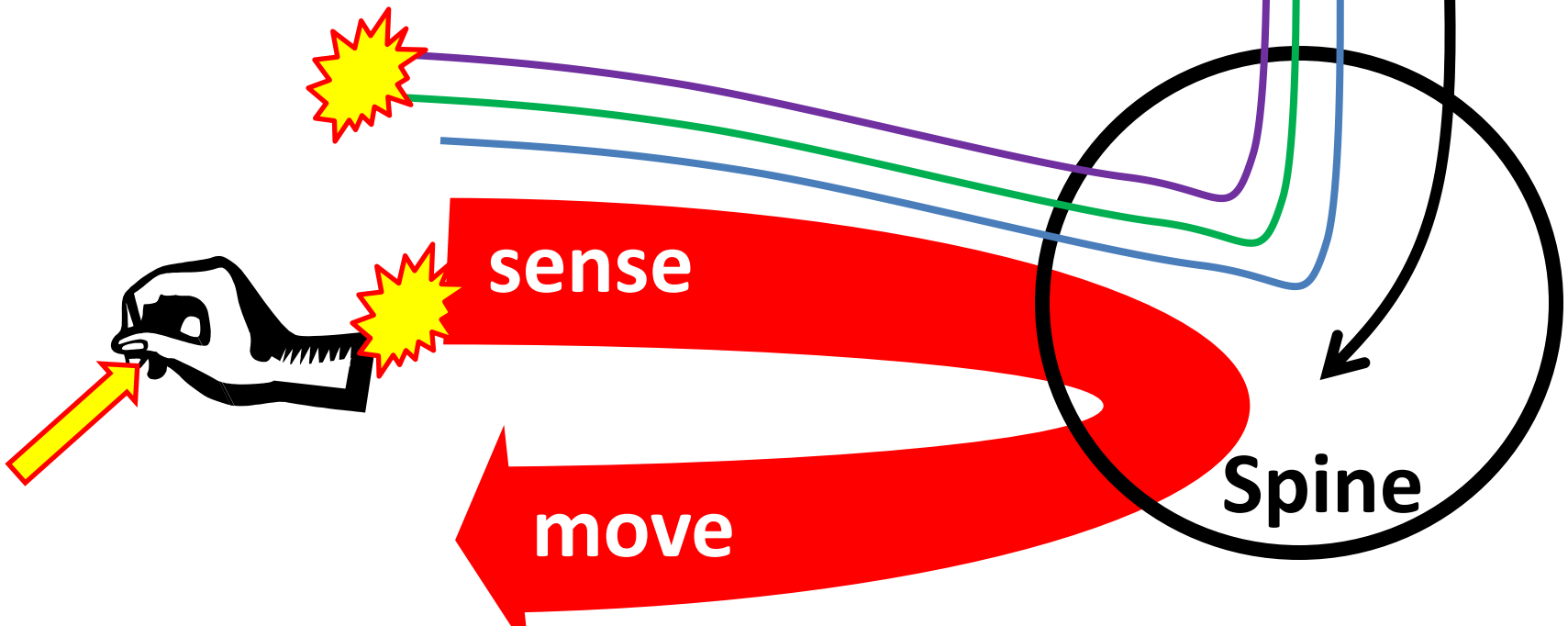
Boltzmann

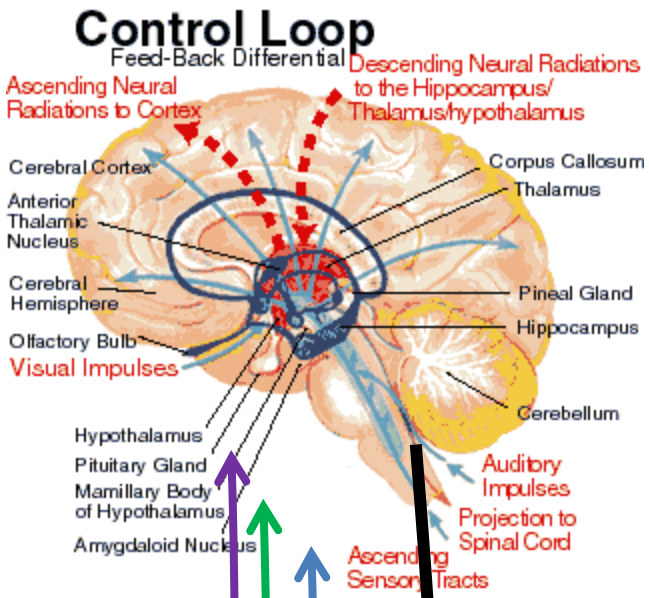
Heisenberg

Einstein

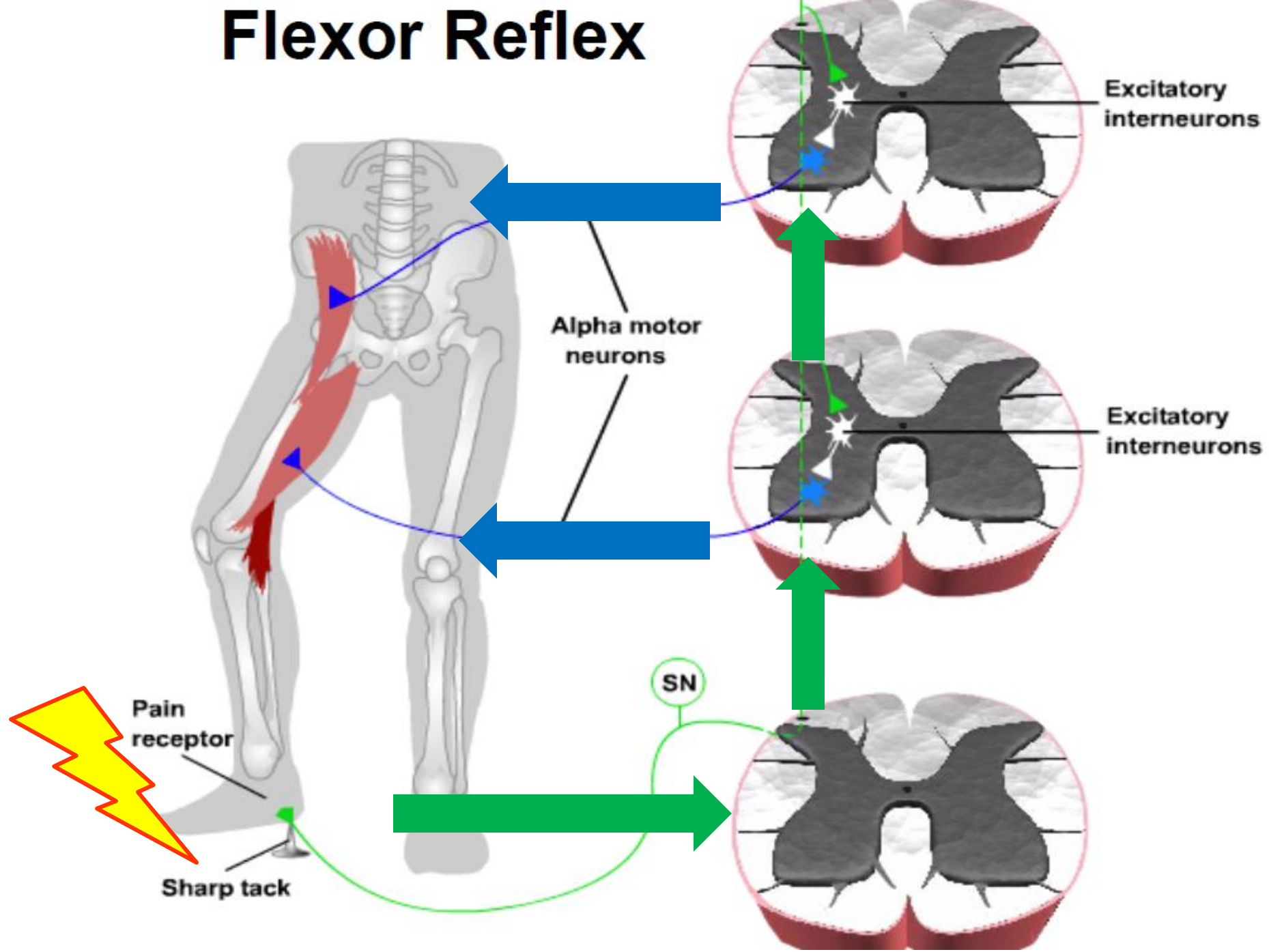
Physics

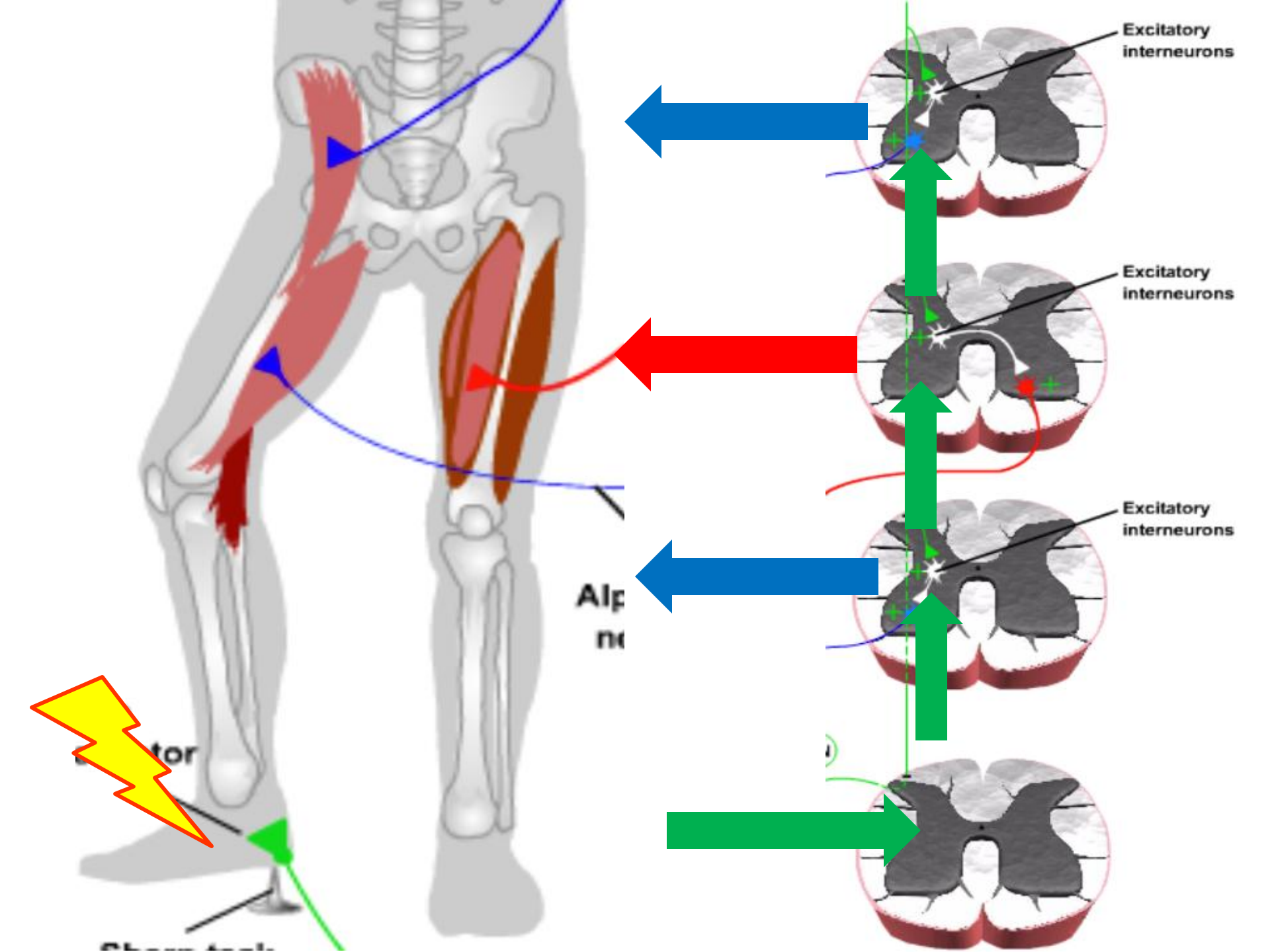
delay=death

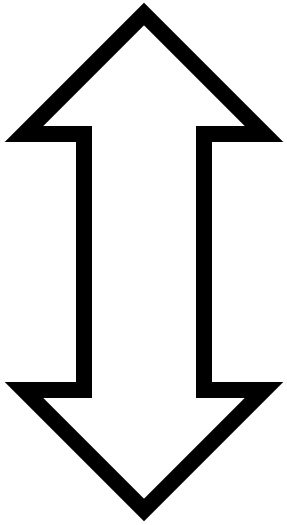

sense
move
Spine

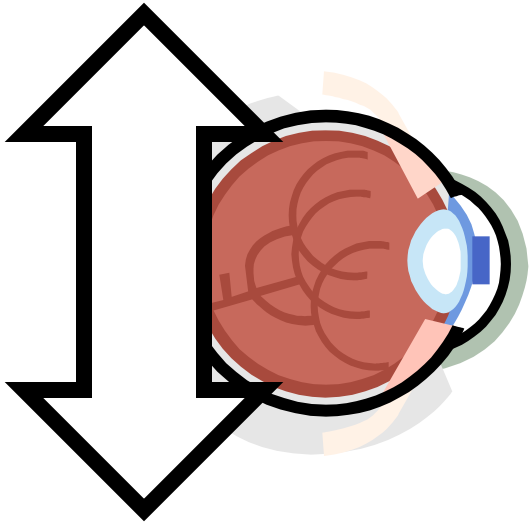

Control Loop
Feed-Back Differential
Ascending Neural Radiations to Cortex
Descending Neural Radiations to the Hippocampus/ Thalamus/hypothalamus
Cerebral Cortex
Corpus Callosum
Thalamus
Anterior Thalamic Nucleus
Cerebral Hemisphere
Pineal Gland
Hippocampus
Olfactory Bulb
Visual Impulses
Cerebellum
Hypothalamus
Pituitary Gland
Mamillary Body of Hypothalamus
Amygdaloid Nucleus
Auditory Impulses
Projection to Spinal Cord
Ascending Sensory Tracts

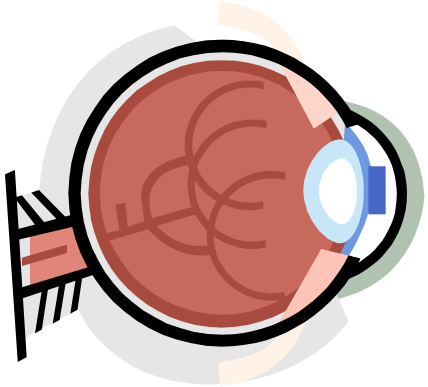
Flexor Reflex

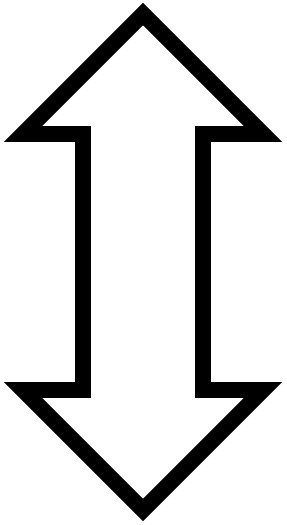


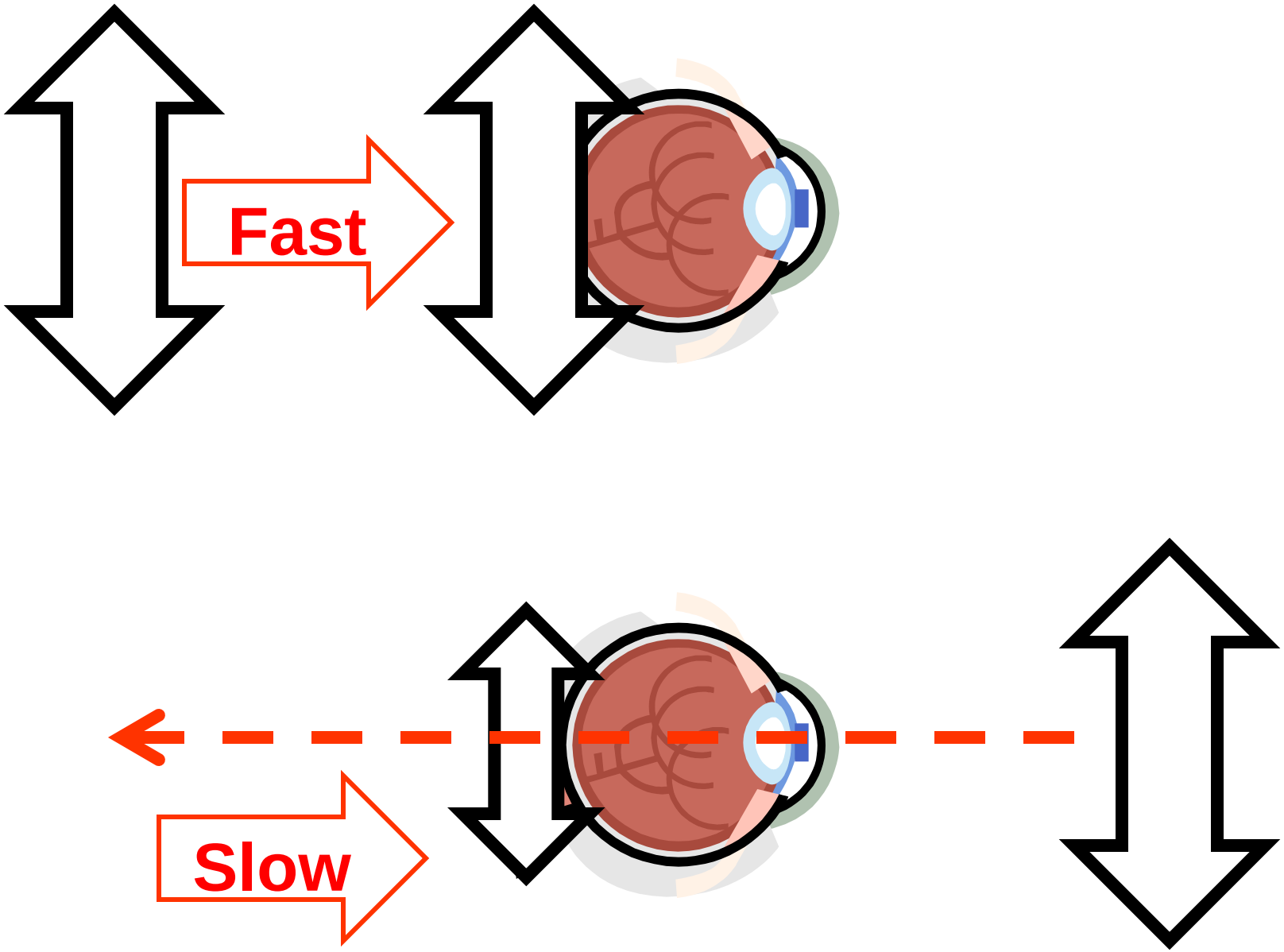

Excitatory interneurons
Excitatory interneurons
Excitatory interneurons



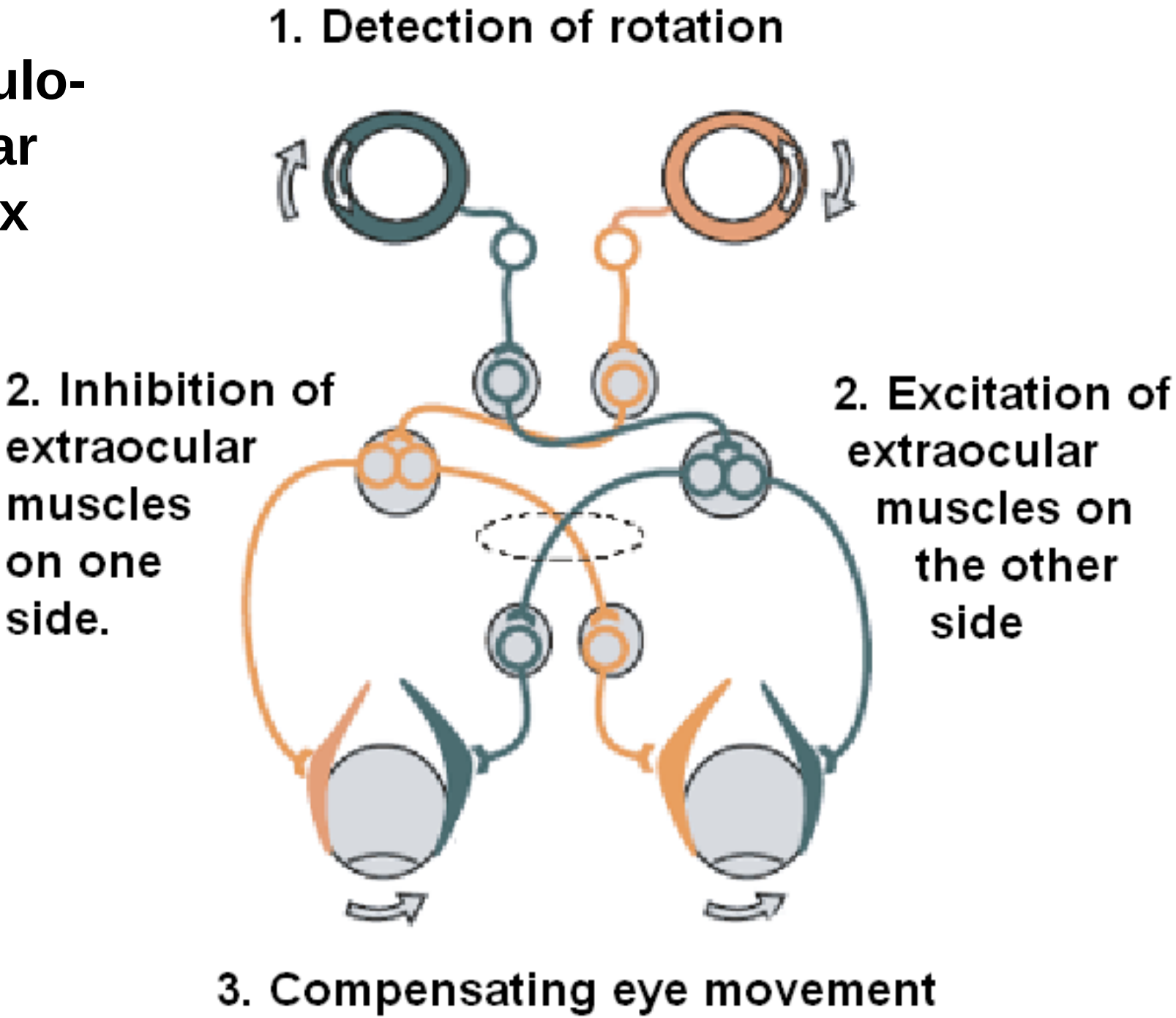


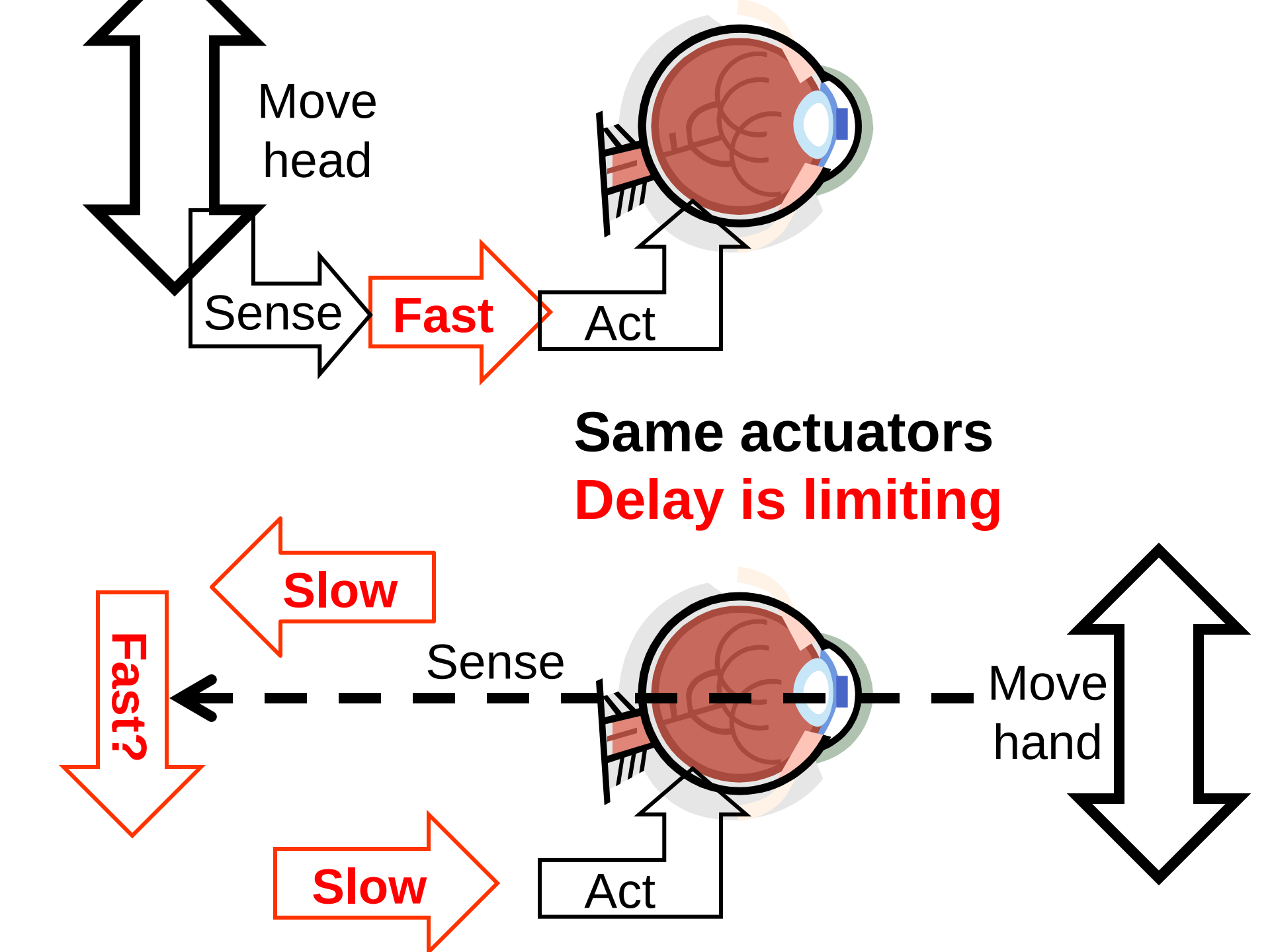


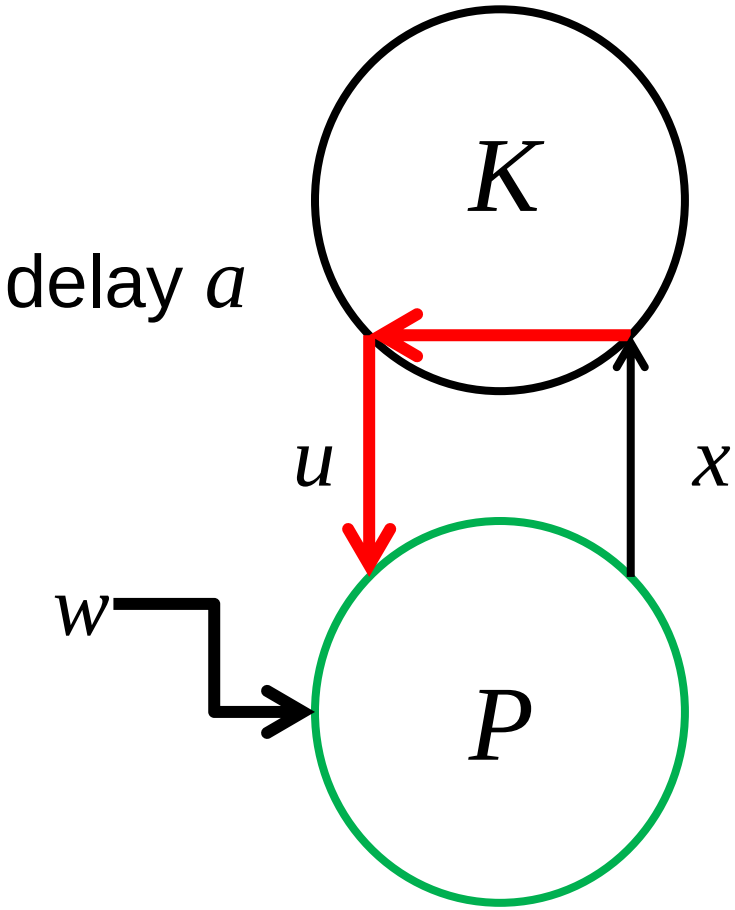



Fast
Slow

Vestibulo-ocular reflex



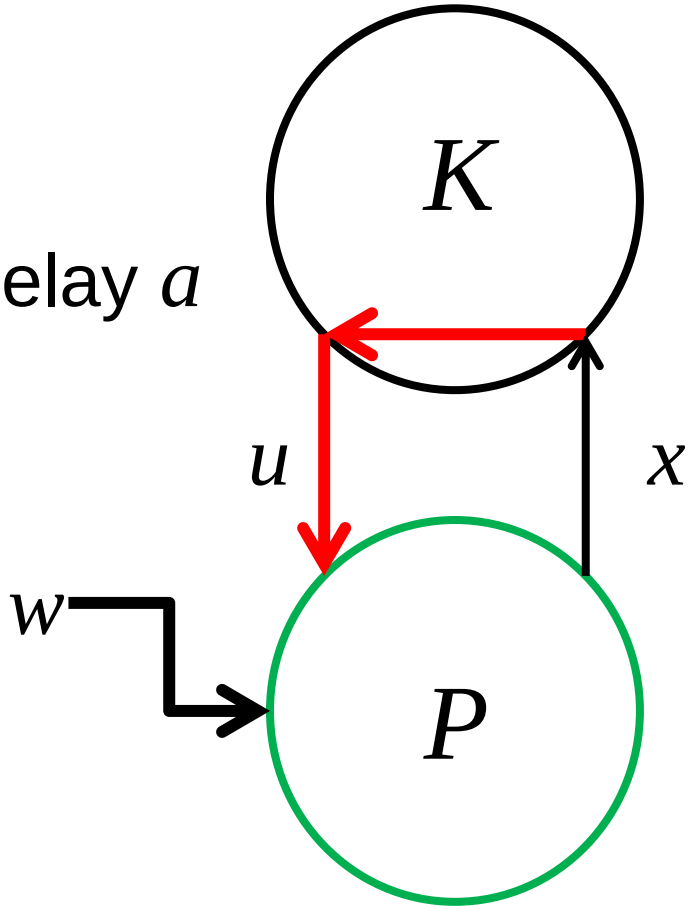

Move
head
Sense
Fast
Act
Same actuators
Delay is limiting
Slow
Fast?
Sense
Move
hand
Slow
Act



$$x_{t+1} = px_t + w_t + u_{t-a}$$

delay a

$$p > 1$$



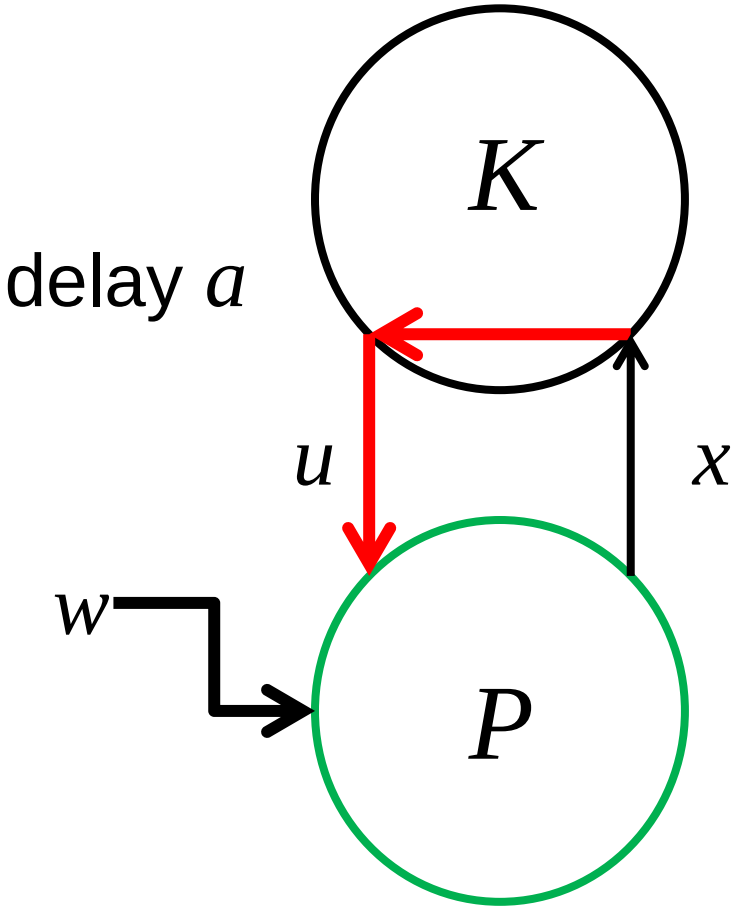
No delay or
no uncertainty

$$u_{t-a} = -\left(px_t + w_t \right)$$

$$\Rightarrow \|x\| \approx 0 \quad \|u\| \approx \|w\|$$

$$x_{t+1} = px_t + w_t + u_{t-a}$$

$$p > 1$$



No delay or
no uncertainty

$$u_{t-a} = -\left(p x_t + w_t \right)$$

$$\Rightarrow \|x\| \approx 0 \quad \|u\| \approx \|w\|$$

With delay ***and***
uncertainty

$$x_{t+1} = p x_t + w_t + u_{t-a}$$

$$p > 1$$

$$\Rightarrow \|x\| \approx \|u\| \approx p^a \|w\|$$

Compute

Communicate

Lowering the barrier

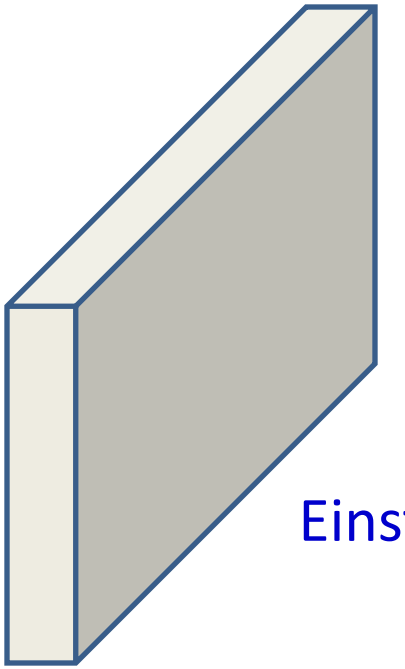
Turing

Shannon

Delay is *most* important

New progress!

Delay is ~~*least*~~ important



Carnot

Boltzmann

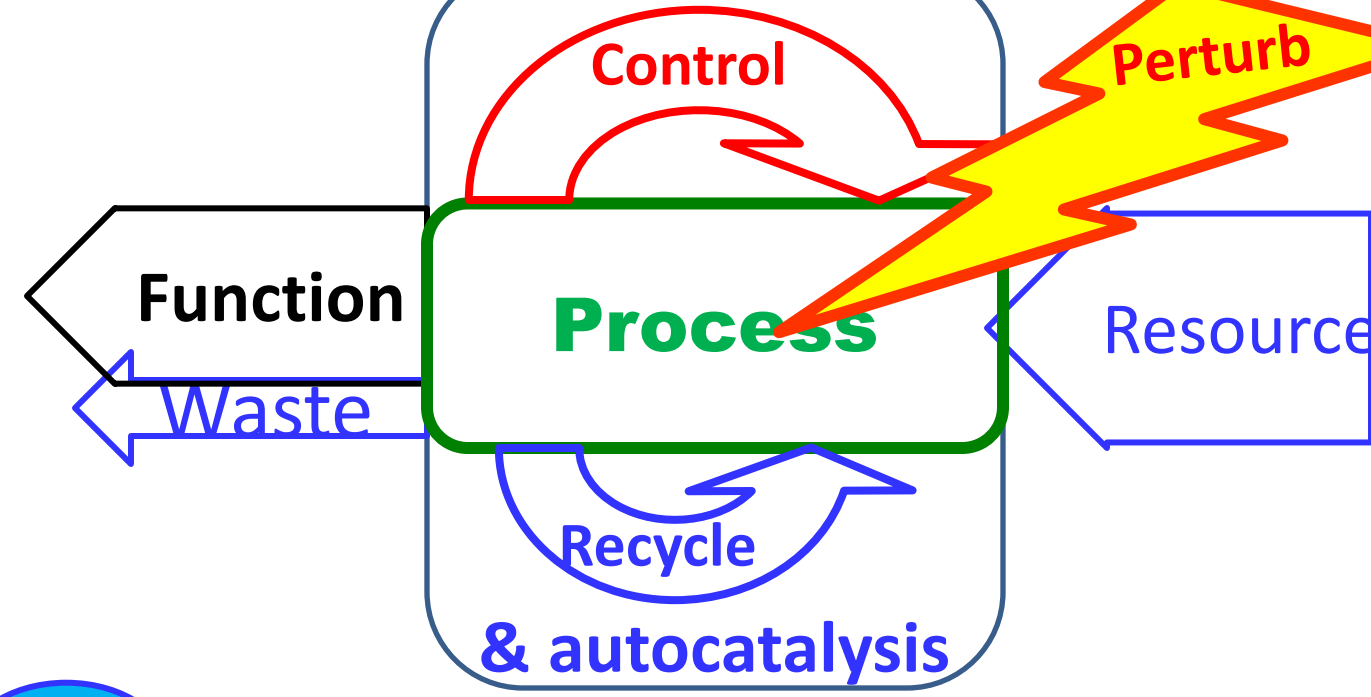
Bode

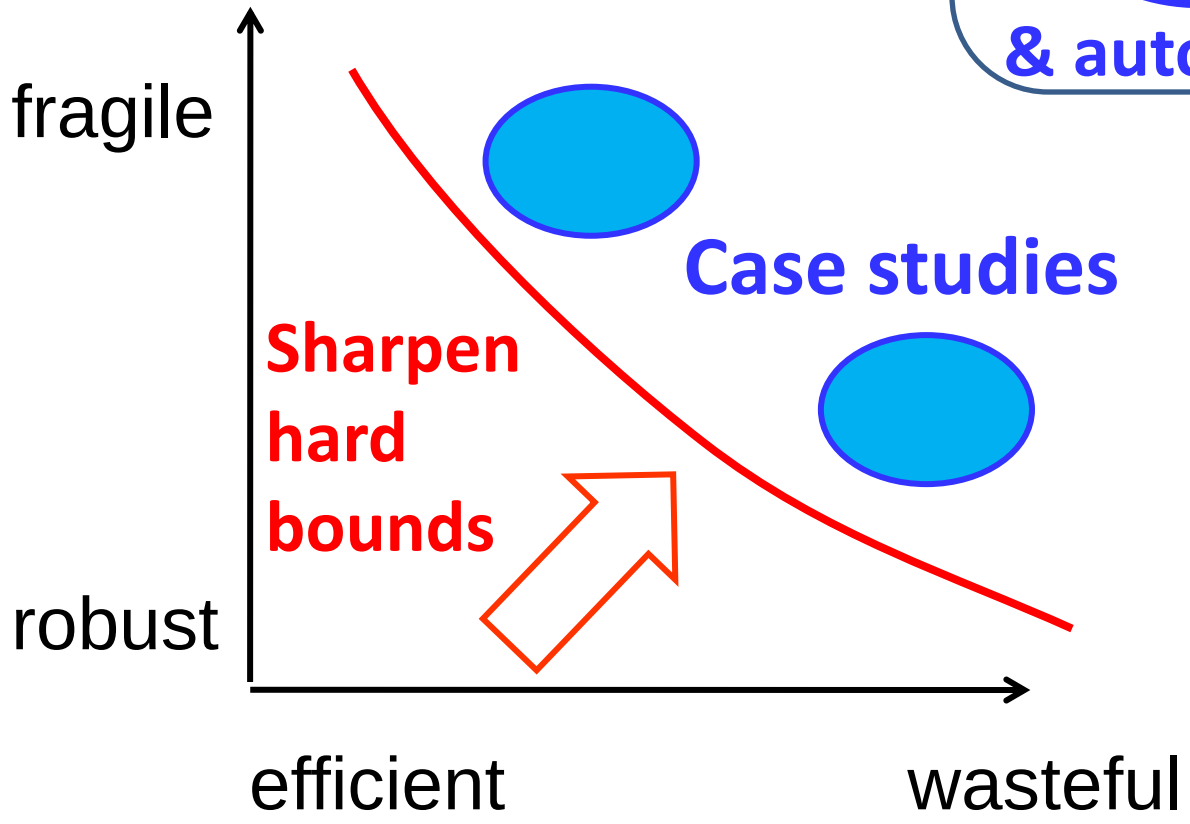
Heisenberg

Control, OR

Einstein

Physics

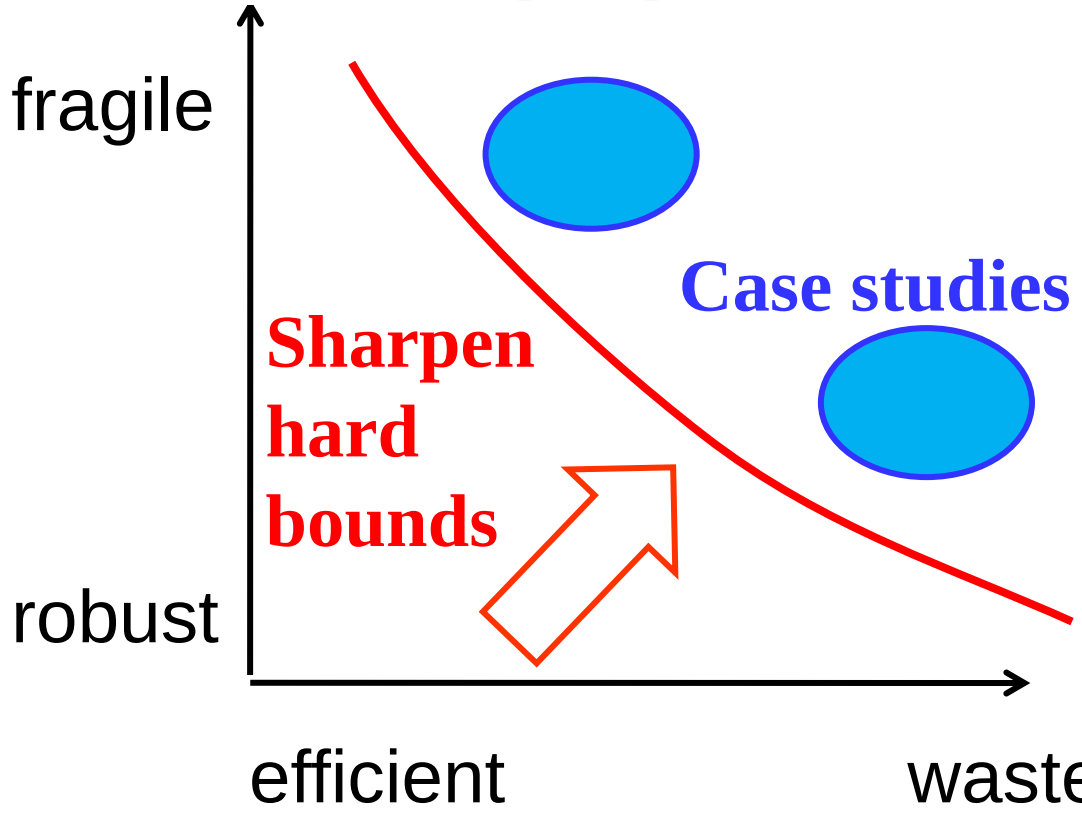

Control
Perturb
Function
Process
Resource
Waste
Recycle
& autocatalysis


fragile
robust
efficient
wasteful
Case studies
Sharpen
hard
bounds

Glycolytic Oscillations and Limits on Robust Efficiency

Fiona Chandra, Genti Buzi, and John Doyle

www.sciencemag.org SCIENCE VOL 333 8 JULY 2011



Most important paper so far.

Science
AAAS

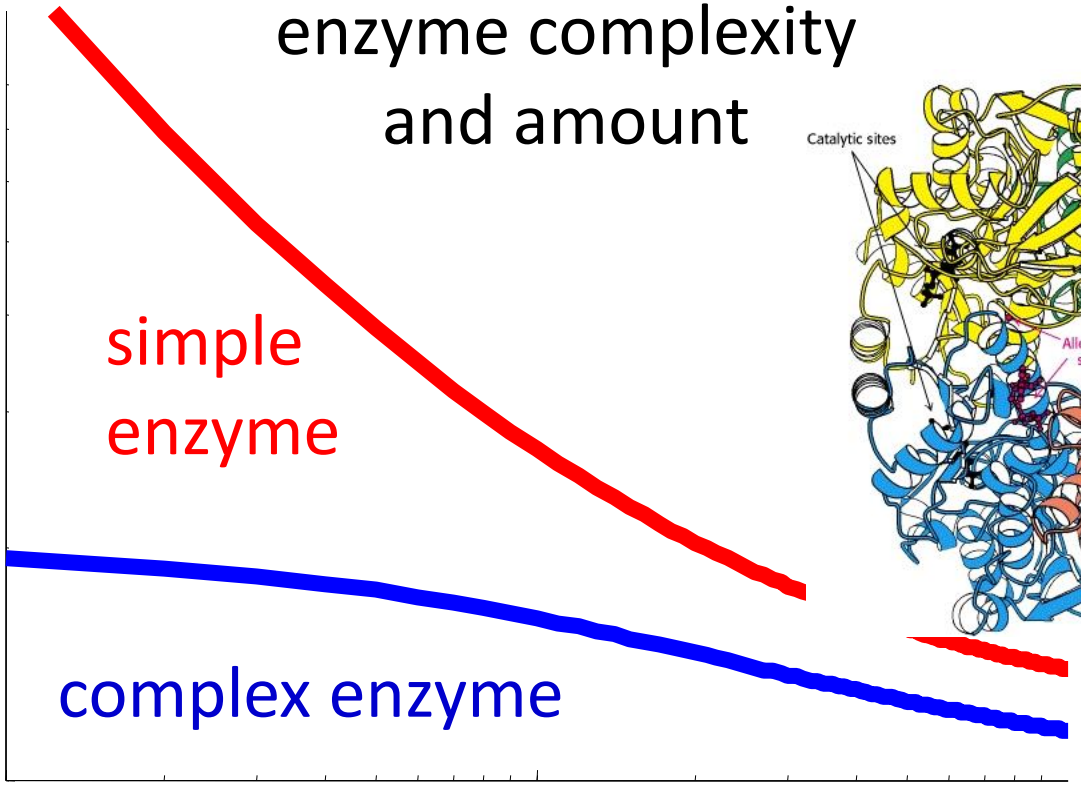
Theorem!

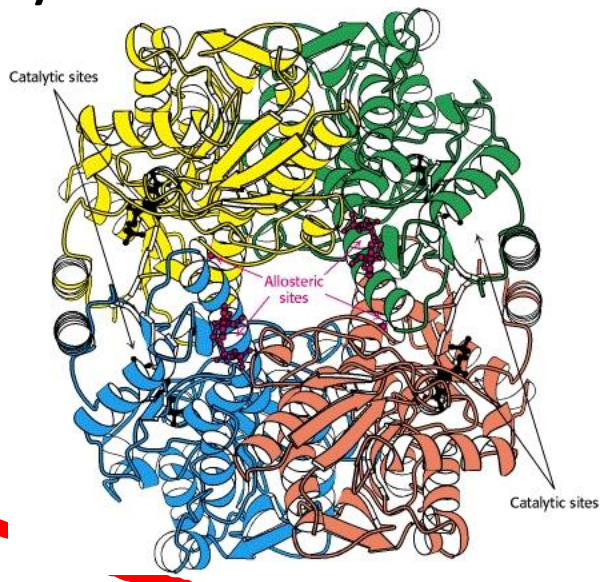
$$\frac{1}{\pi}\int_0^{\infty} \ln\left|S(j\omega)\right| \left(\frac{z}{z^2+\omega^2} \right) d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

Fragility

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

z and p functions of enzyme complexity and amount



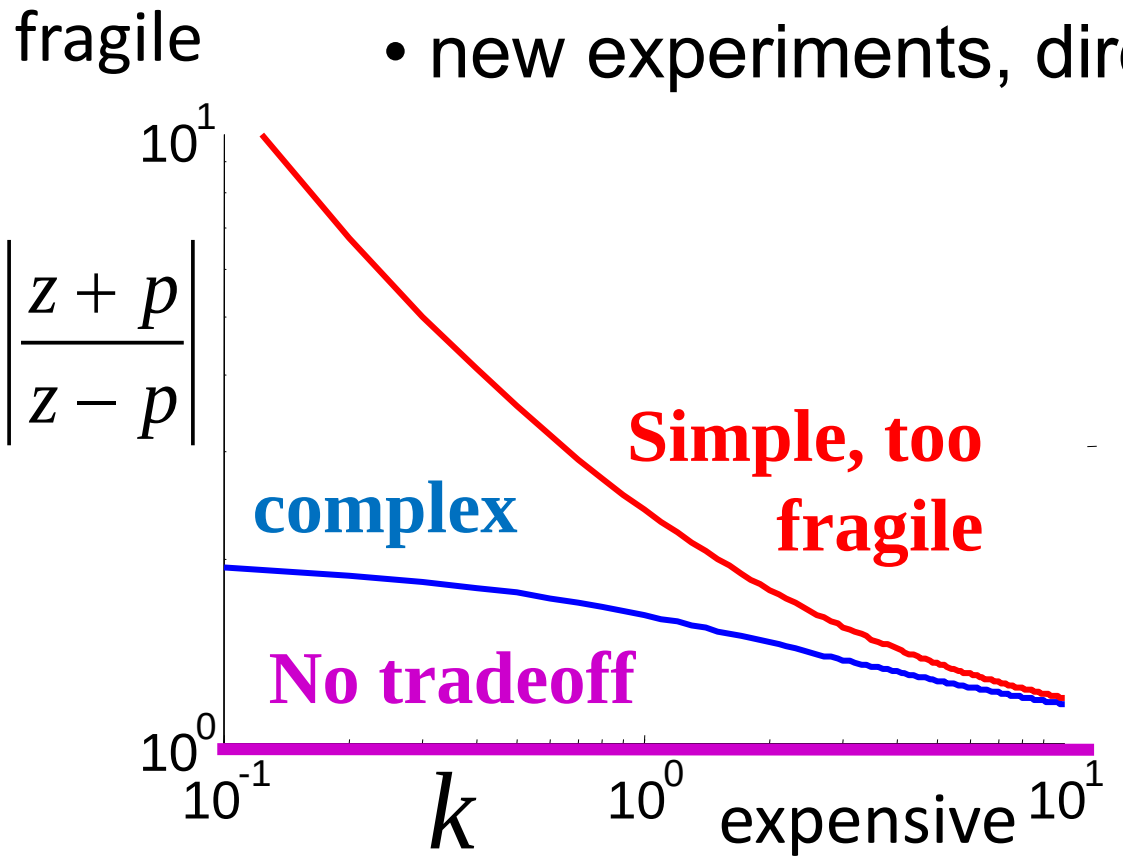


Enzyme amount

Savageaumics

Hard tradeoff/constraint in glycolysis

- resolves central, persistent mystery
- **robustness vs efficiency**
- **autocatalysis** has crucial role
- oscillations are side effects w/o “purpose”
- new experiments, directions, questions,…

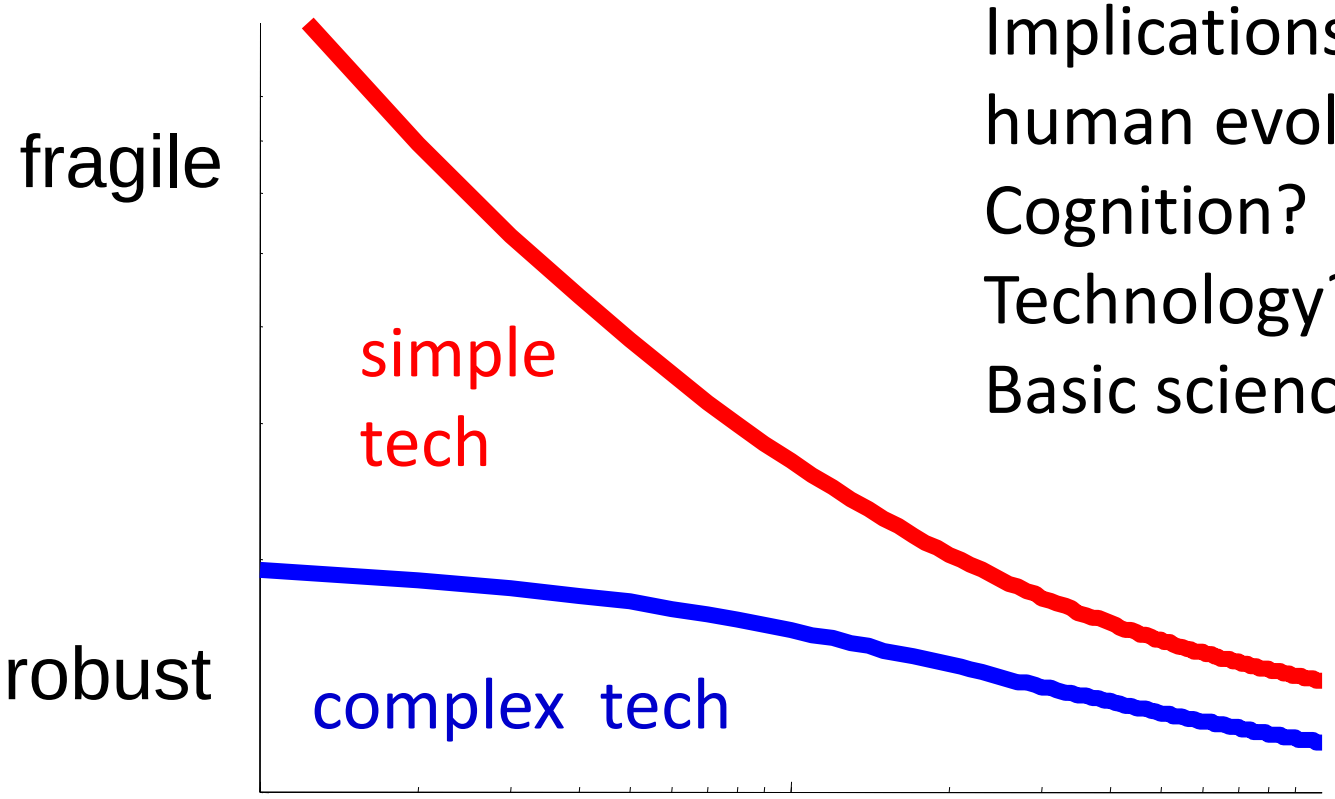


$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right|\left(\frac{z}{z^2+\omega^2}\right)d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

What (some) reviewers say

- "…to establish universality for all biological and physiological systems is **simply wrong**. It cannot be done…
- … a mathematical scheme **without any real connections to biological or medical**…
- …universality is well justified in physics… for biological and physiological systems …**a dream that will never be realized**, due to the vast diversity in such systems.
- …**does not seem to understand or appreciate** the vast diversity of biological and physiological systems…
- …a high degree of abstraction, which …make[s] **the model useless** …

This picture is very general



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

OPEN ACCESS Freely available online PLOS BIOLOGY

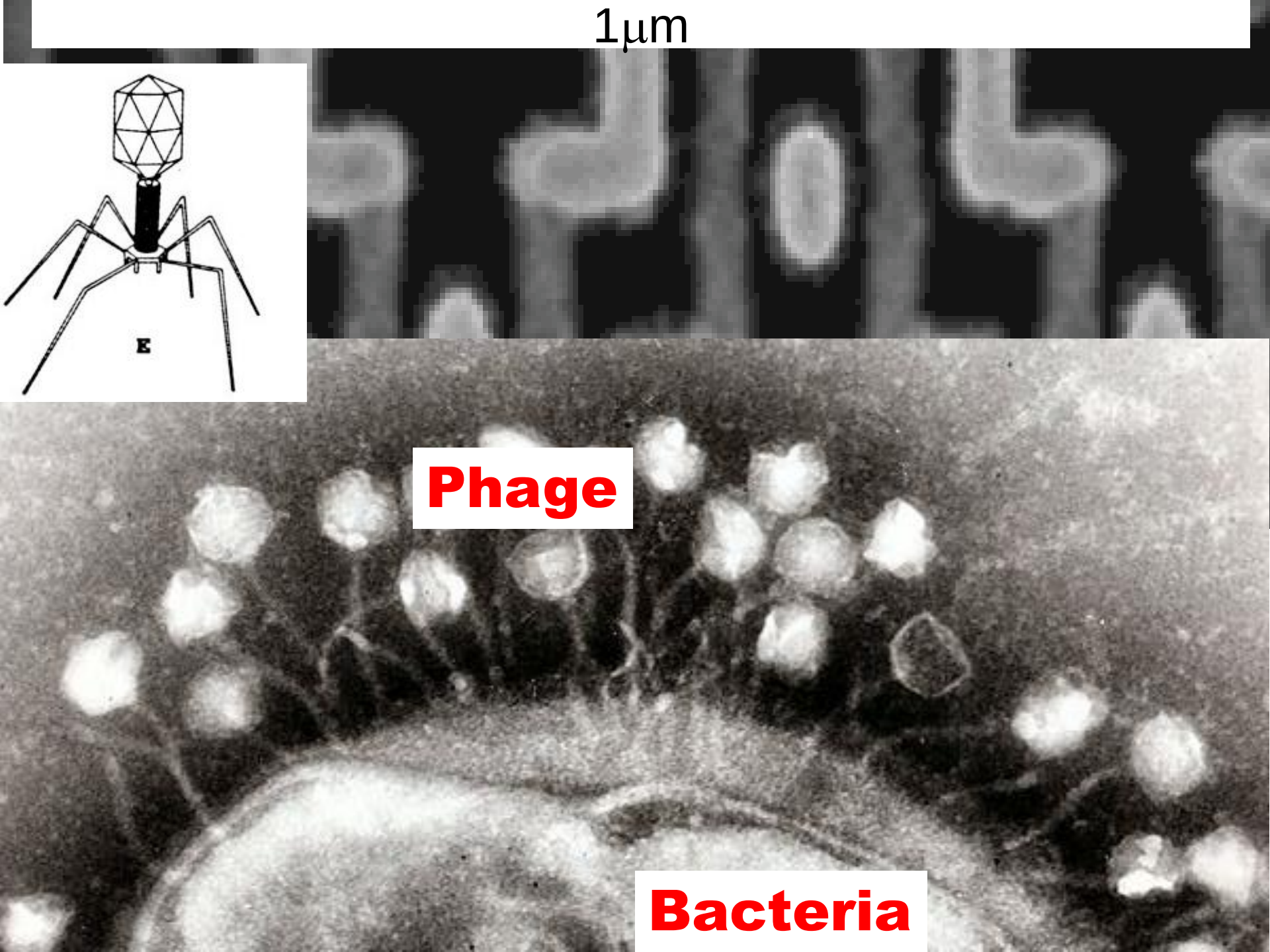
Viruses' Life History: Towards a Mechanistic Basis of a Trade-Off between Survival and Reproduction among Phages

Marianne De Paepe, François Taddei*

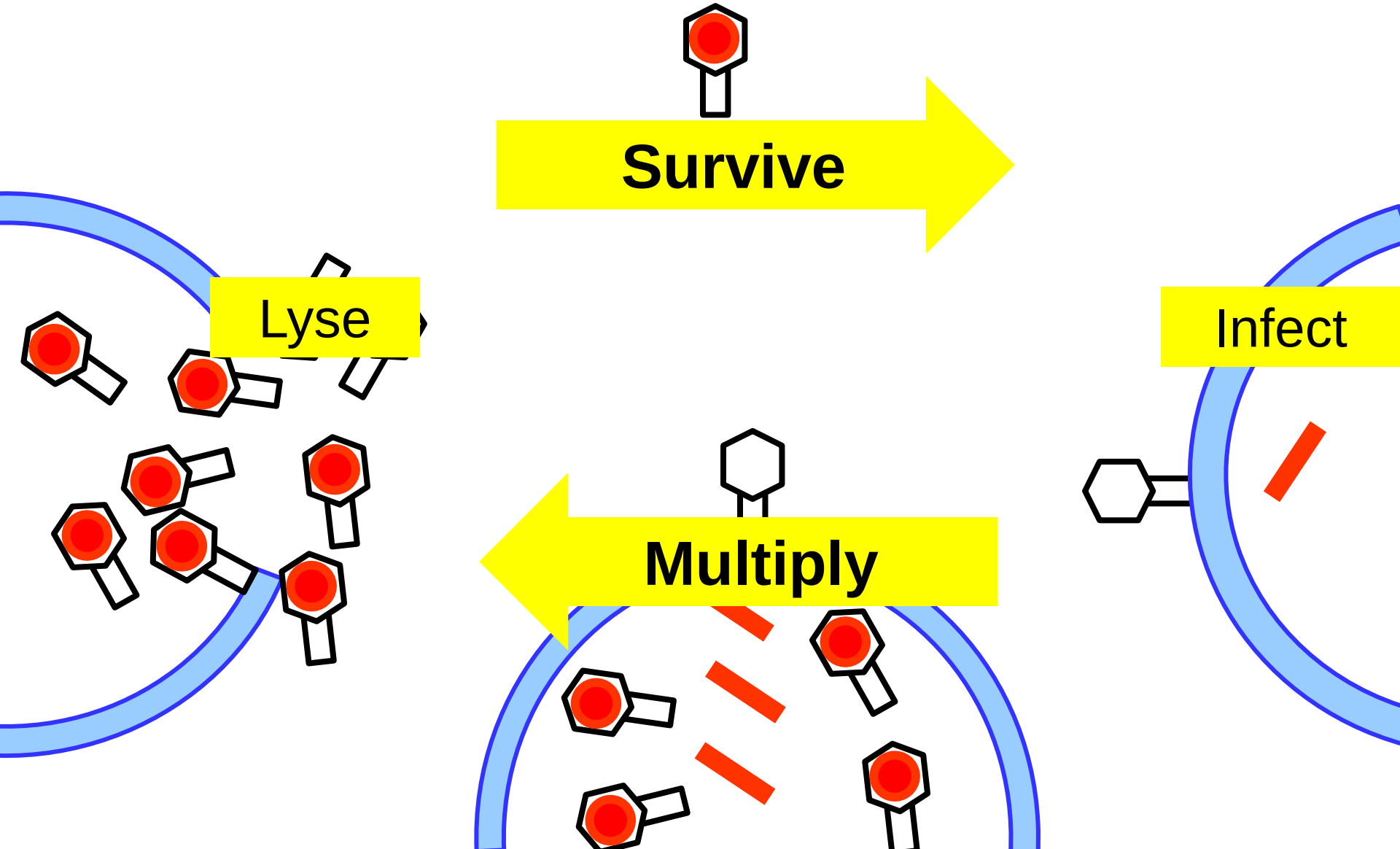
Laboratoire de Genetique Moleculaire, Evolutive et Medicale, University of Paris 5, INSERM, Paris, France

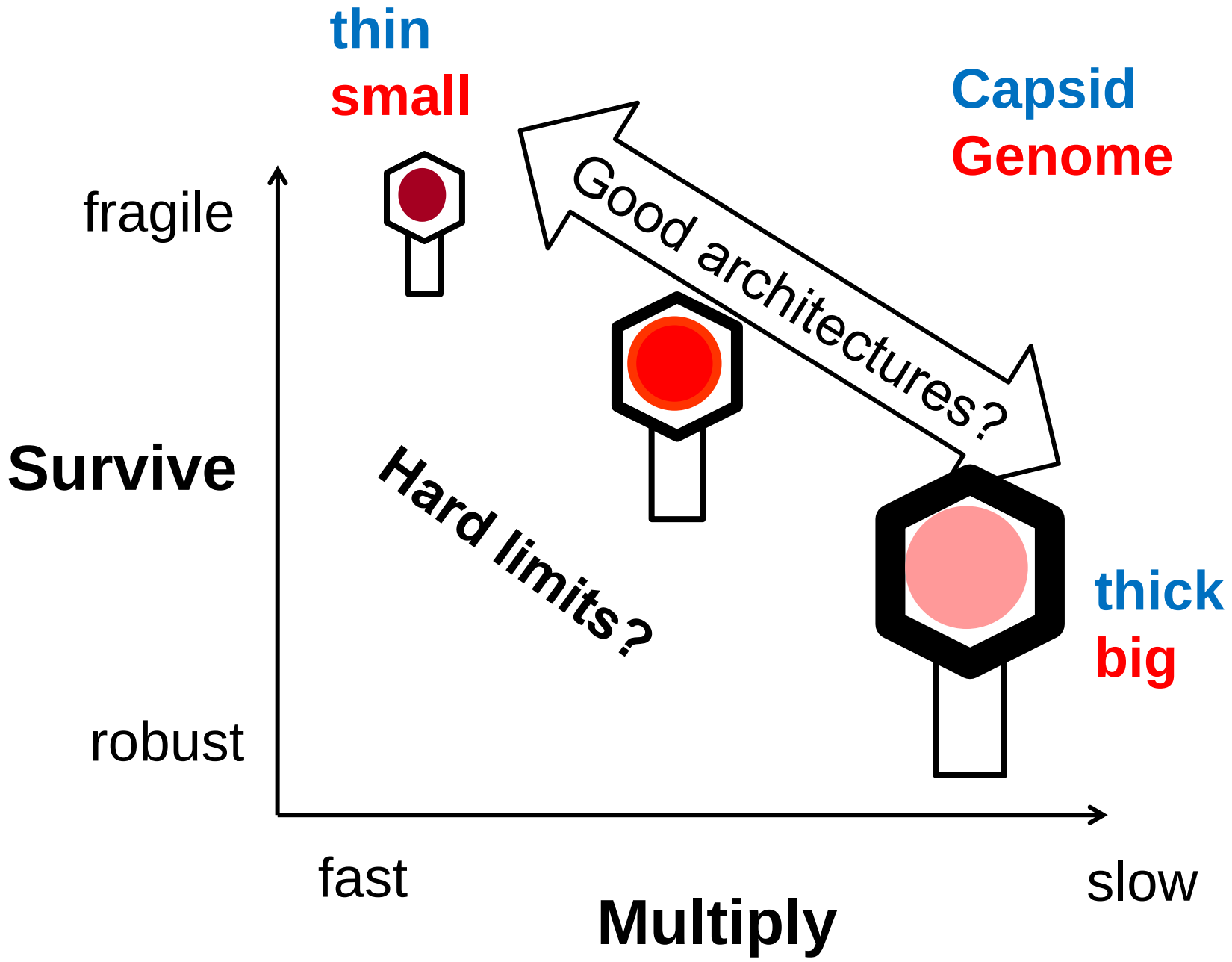
July 2006 | Volume 4 | Issue 7 | e193

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

Science
AAAS

Efficiency in Evolutionary Trade-Offs
Elad Noor and Ron Milo
Science **336**, 1114 (2012);

Evolutionary Trade-Offs, Pareto Optimality, and the Geometry of Phenotype Space
O. Shoval *et al.*
Science **336**, 1157 (2012);

Multidimensional Optimality of Microbial Metabolism

Robert Schuetz, Nicola Zamboni, Mattia Zampieri, Matthias Heinemann, Uwe Sauer*

Compute

Turing

Delay is *most* important

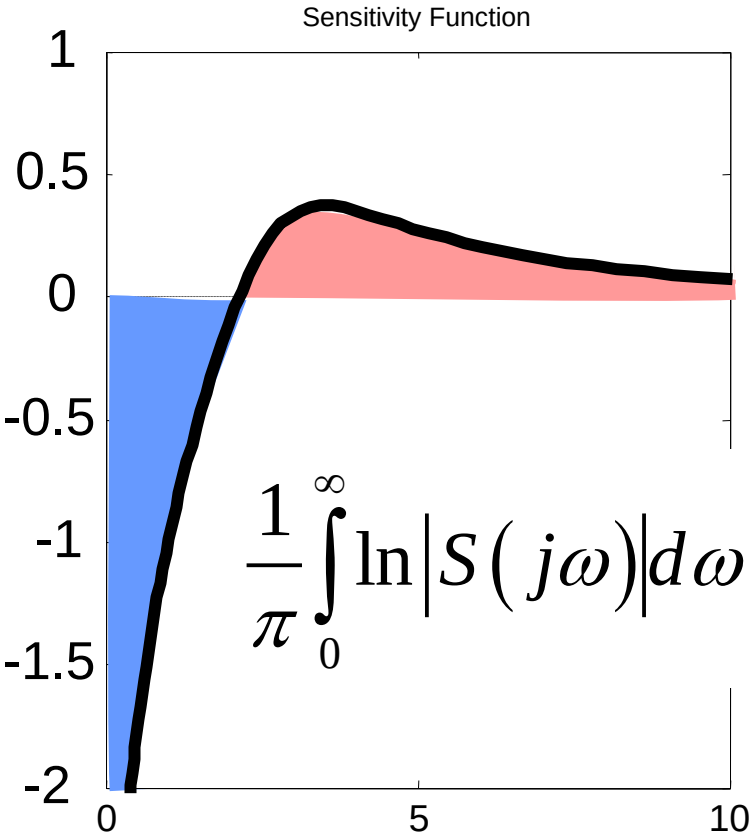
Why

Necessity

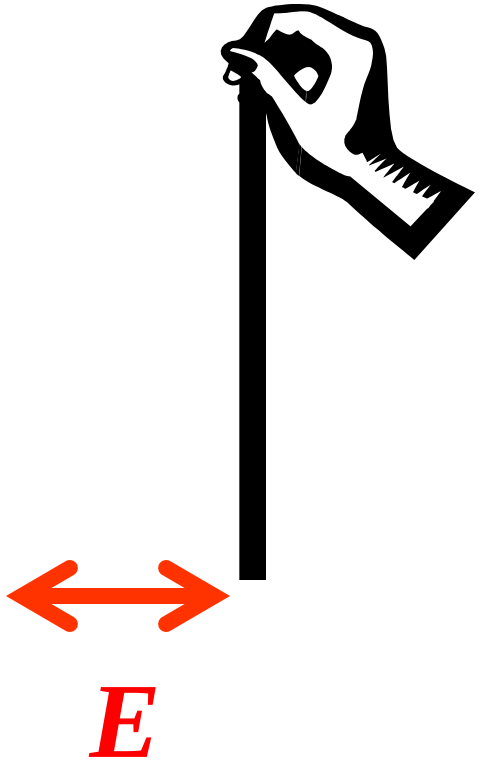
Bode

Control, OR

$$\ln\left|S(j\omega)\right|$$

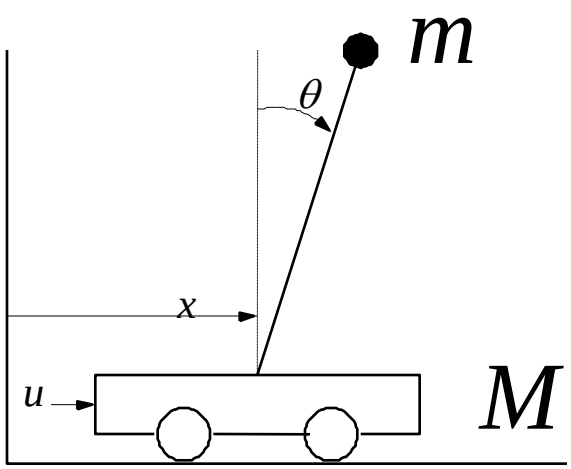


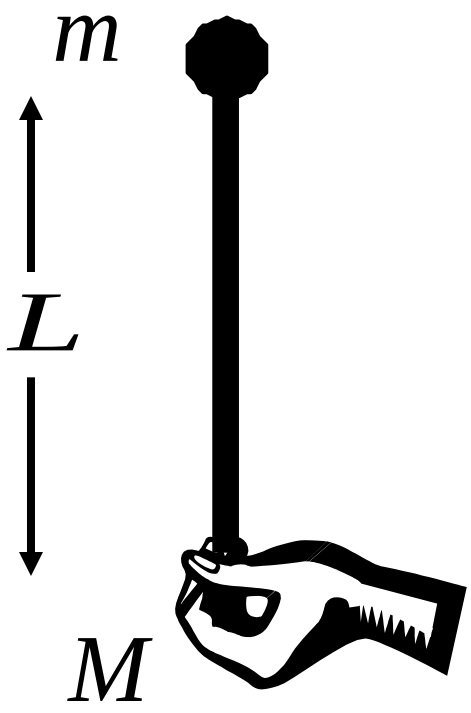
$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega = 0$$



$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega = \frac{1}{\pi}\int_0^\infty \left(\ln\left|E(j\omega)\right| - \ln\left|D(j\omega)\right|\right) d\omega 0$$

Linearized pendulum on a cart





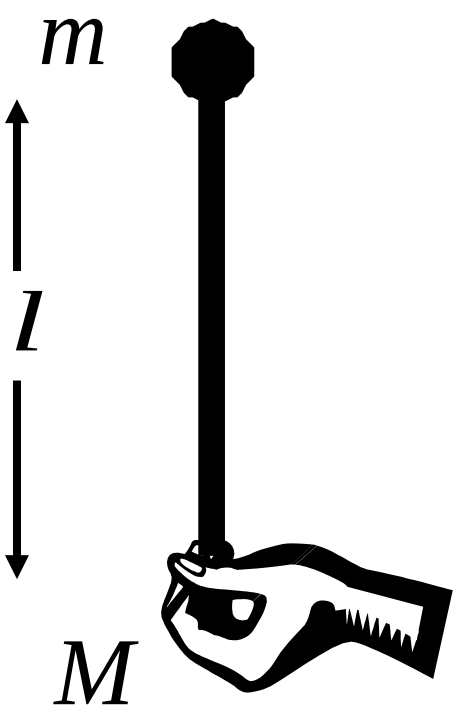
$$\frac{d}{dt}\begin{bmatrix} x \\ \theta \\ \dot{x} \\ \dot{\theta} \end{bmatrix} = \begin{bmatrix} 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & \frac{m^2 g l^2}{q} & \frac{-(J+ml^2)b}{q} & 0 \\ 0 & \frac{mgl(M+m)}{q} & \frac{-mlb}{q} & 0 \end{bmatrix} x + \begin{bmatrix} 0 \\ 0 \\ \frac{J+ml^2}{q} \\ \frac{ml}{q} \end{bmatrix} u$$

$$q = J(M+m) + Mml^2$$

$$\left(M+m\right)\ddot{x}+ml\left(\ddot{\theta}\cos\theta-\dot{\theta}^2\sin\theta\right)=u$$

$$\ddot{x}\cos\theta+l\ddot{\theta}+g\sin\theta=0$$

$$y=x+\alpha l\sin\theta$$



linearize

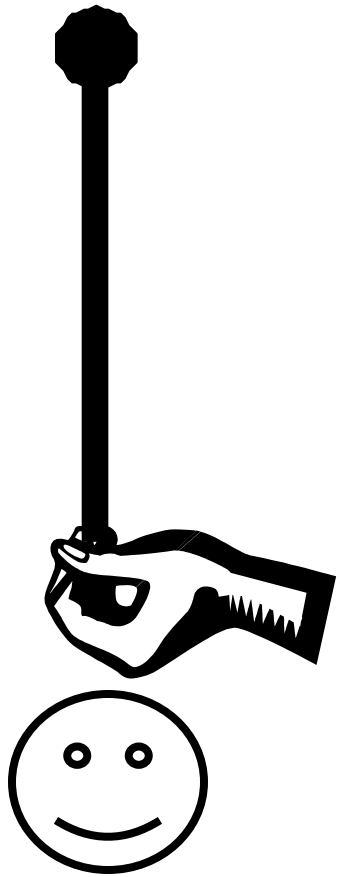
$$\left(M+m\right)\ddot{x}+ml\ddot{\theta}=u$$

$$\ddot{x}+l\ddot{\theta}\pm g\theta=0$$

$$y=x+\alpha l\theta$$

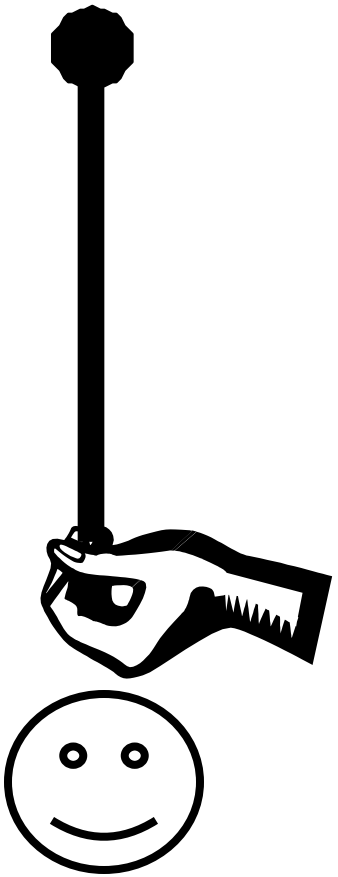
Robust

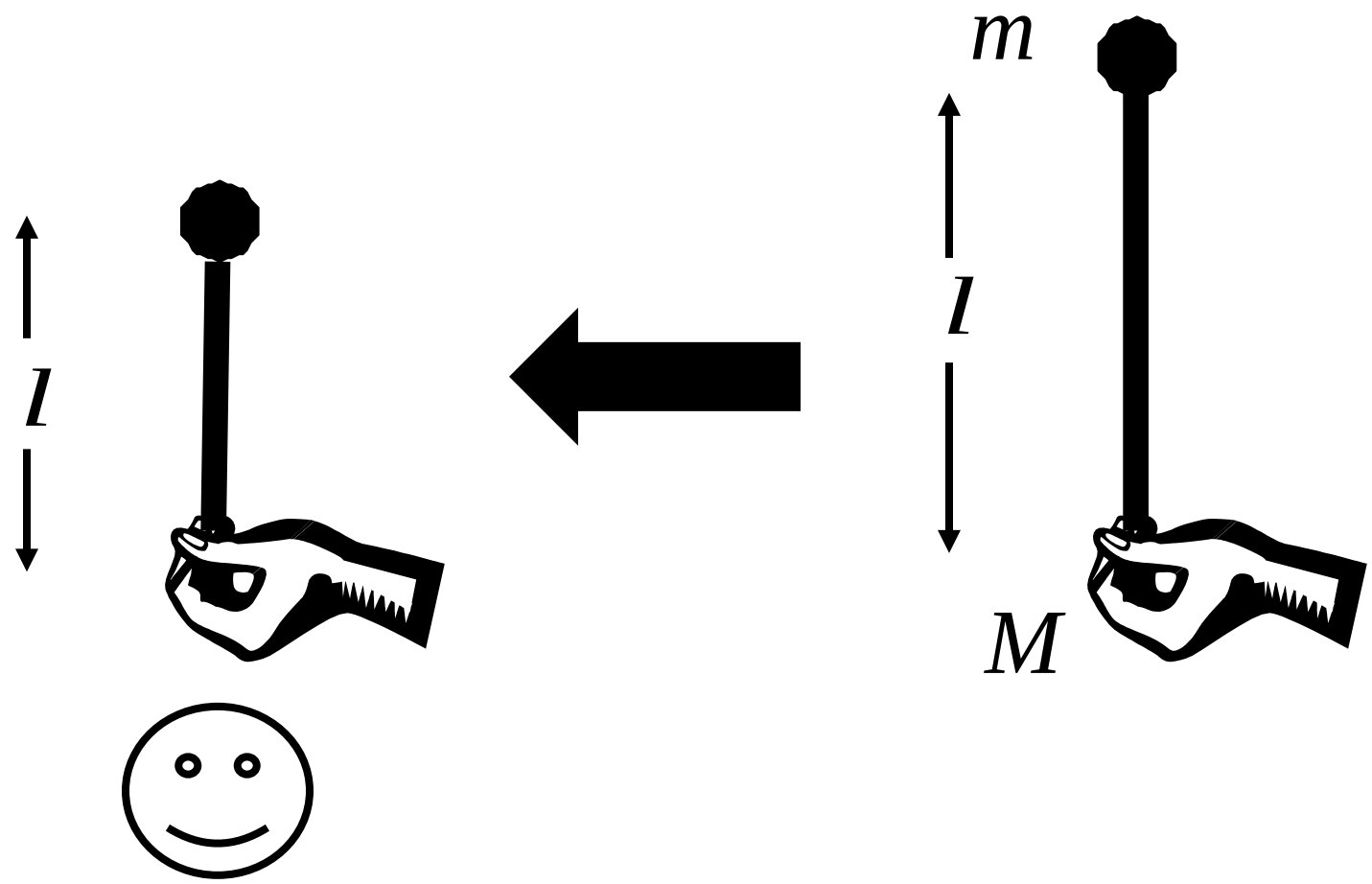
=agile and balancing



Robust

=agile and balancing





Efficient=length of pendulum (artificial)

$$\begin{bmatrix} x \\ \theta \end{bmatrix} = \frac{1}{D(s)} \begin{bmatrix} ls^2 \pm g \\ -s^2 \end{bmatrix} u \qquad D(s) = s^2\left(Mls^2 \pm (M+m)g\right)$$

$$y = x + \alpha l\theta = \frac{\varepsilon l s^2 \pm g}{D(s)} \qquad \varepsilon = 1 - \alpha$$

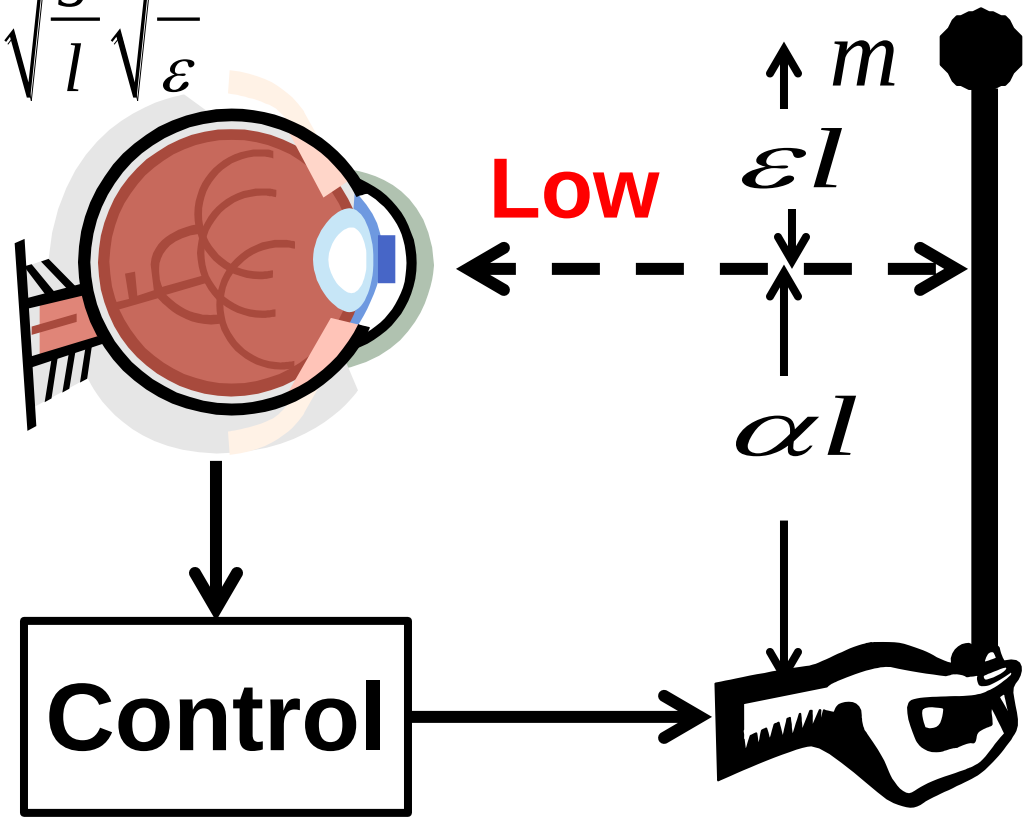
$$p = \sqrt{\frac{g}{l}}\sqrt{1+r} \qquad r = \frac{m}{M} \qquad z = \sqrt{\frac{g}{l}}\sqrt{\frac{1}{\varepsilon}}$$

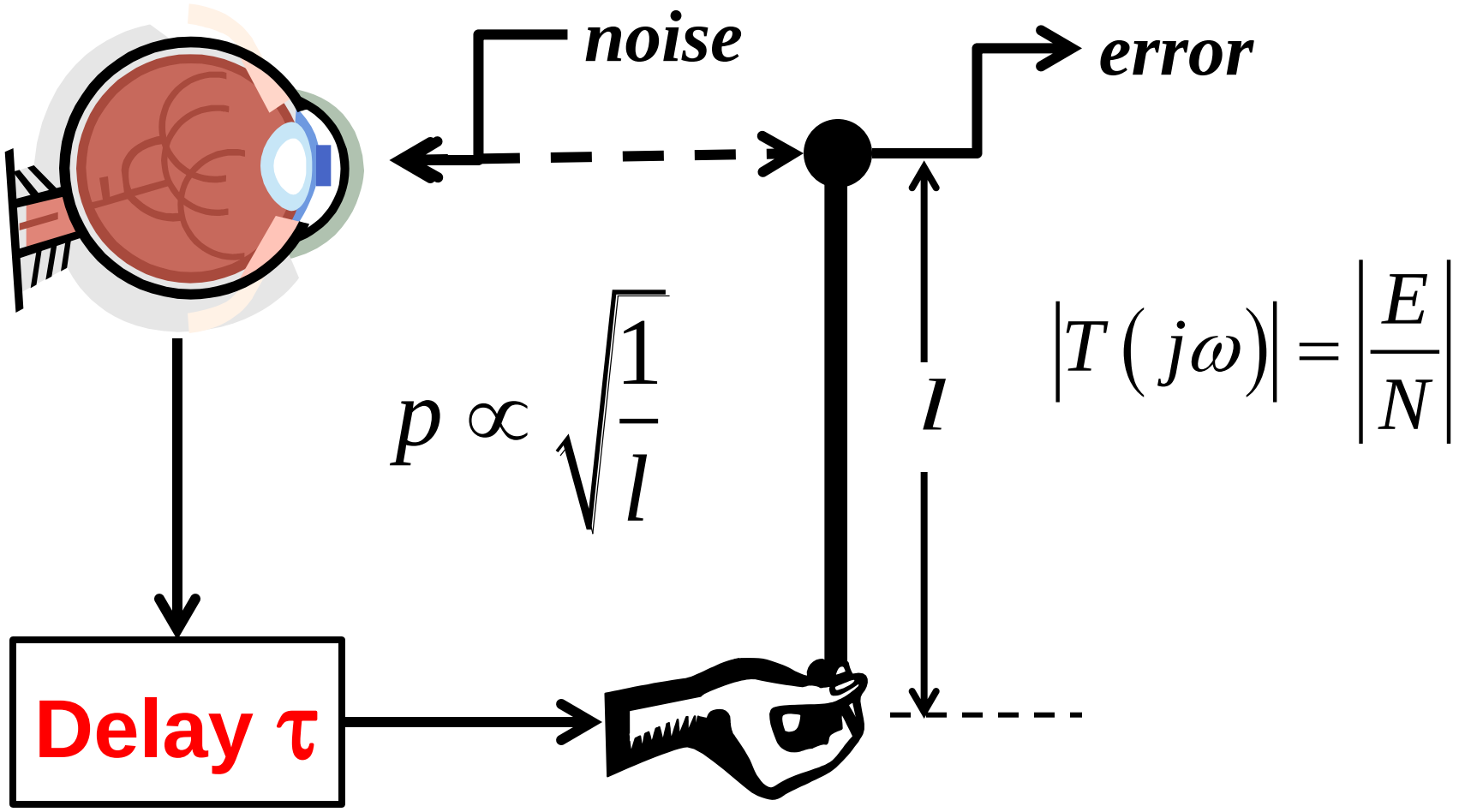
transform+
algebra

$$(M+m)\ddot{x} + ml\ddot{\theta} = u$$

$$\ddot{x} + l\ddot{\theta} \pm g\theta = 0$$

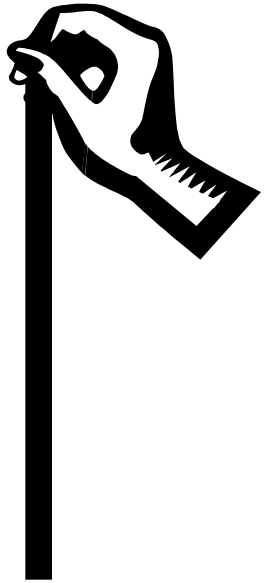
$$y = x + \alpha l\theta$$




noise
error
$p \propto \sqrt{\frac{1}{l}}$
l
$\left|T(j\omega)\right| = \left|\frac{E}{N}\right|$
Delay τ

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|T(j\omega)\right| d\omega \geq 0$$

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|S(j\omega)\right| d\omega \geq 0$$



Easy, even with eyes closed

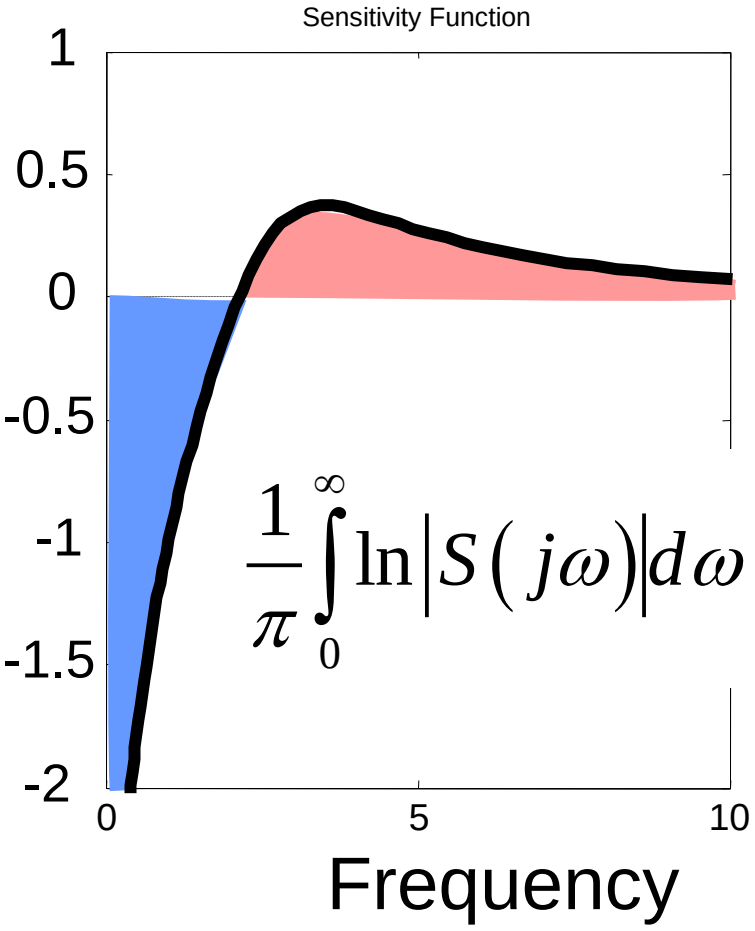
No matter what the length

Proof: Standard UG control theory:

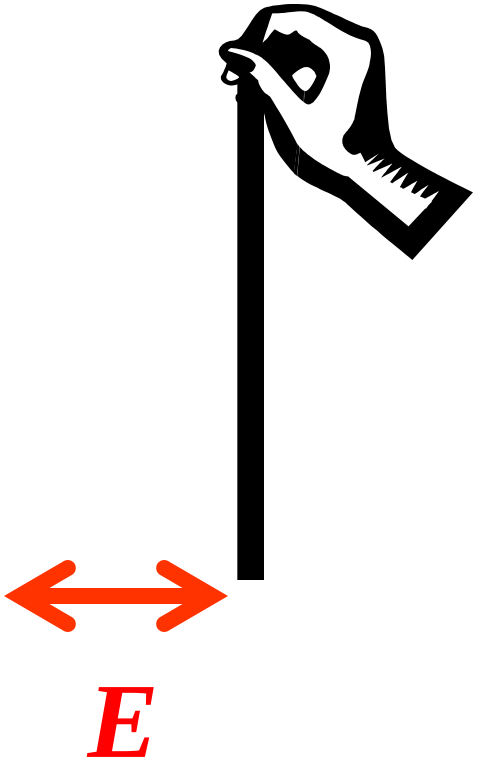
Easy calculus, easier contour integral,

easiest Poisson Integral formula

$$\ln\left|S(j\omega)\right|$$

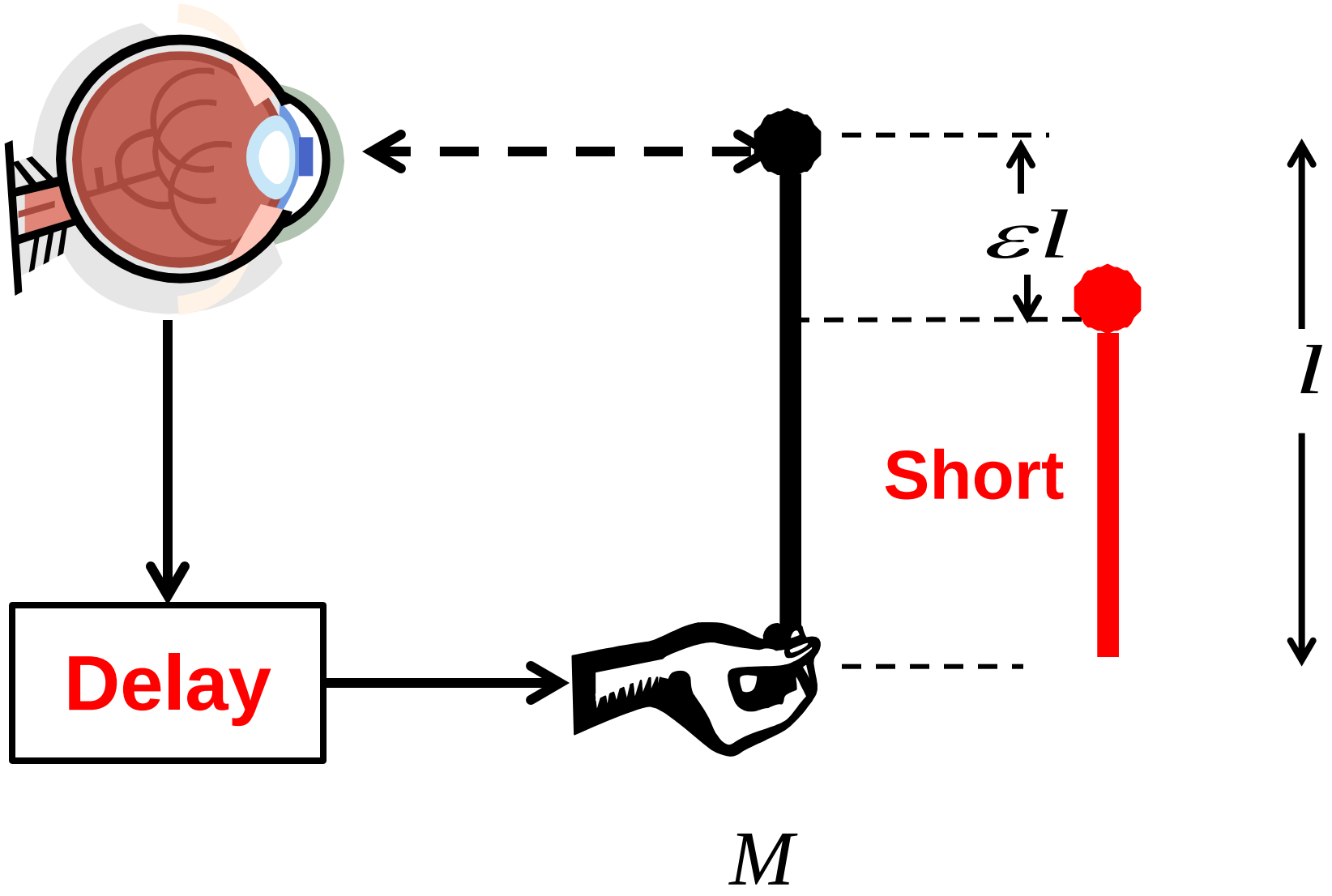


$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega = 0$$



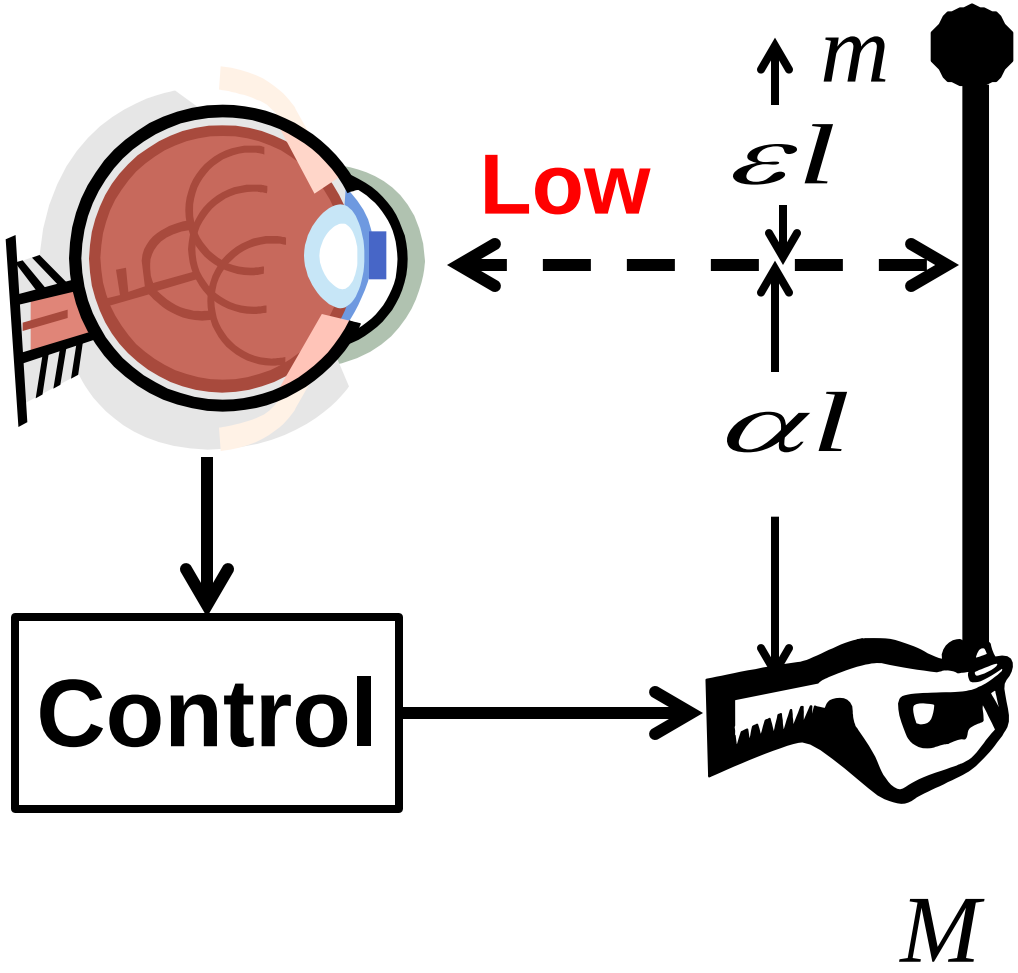
$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega = \frac{1}{\pi}\int_0^\infty \left(\ln\left|E(j\omega)\right| - \ln\left|D(j\omega)\right|\right) d\omega 0$$

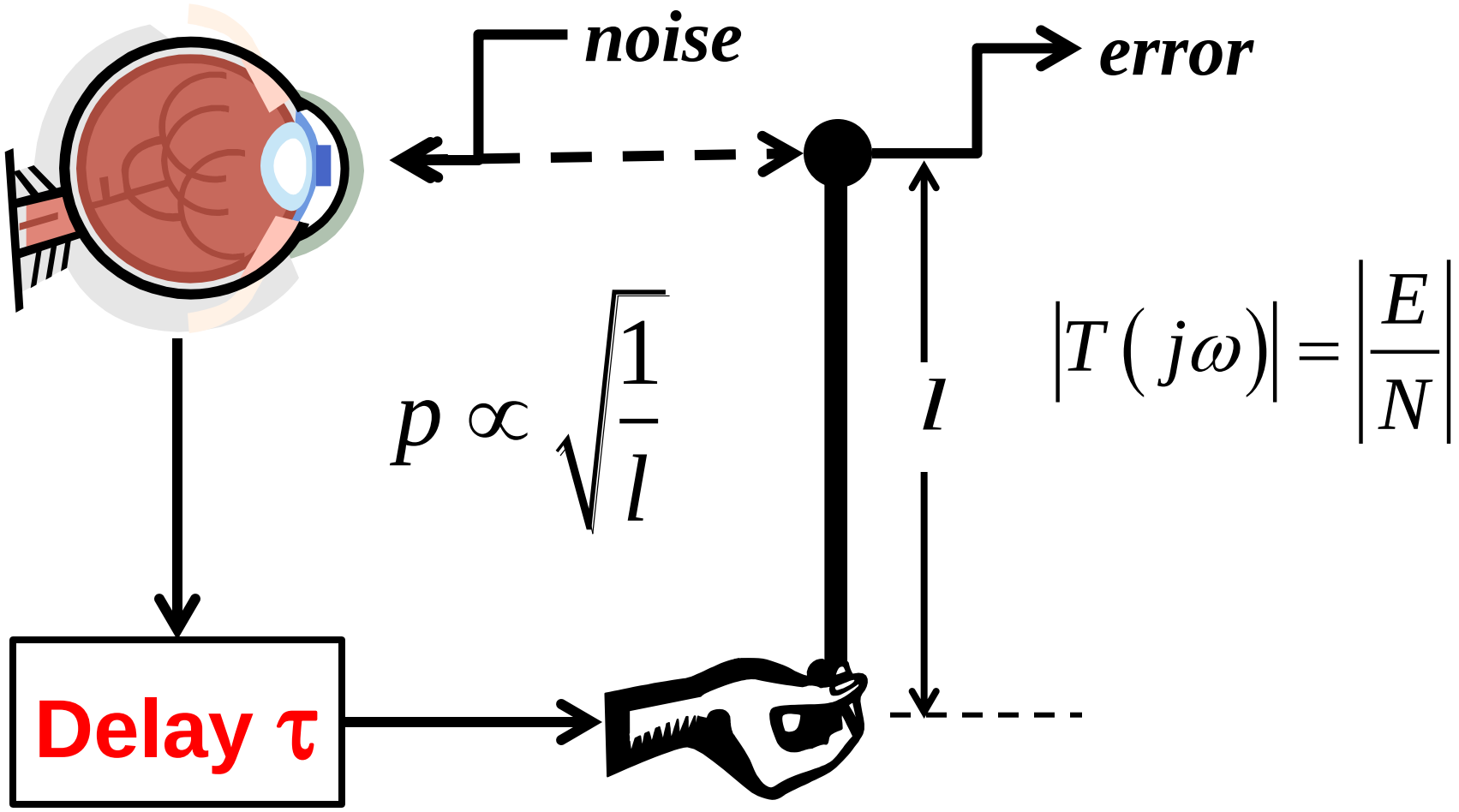
Harder if delayed or short

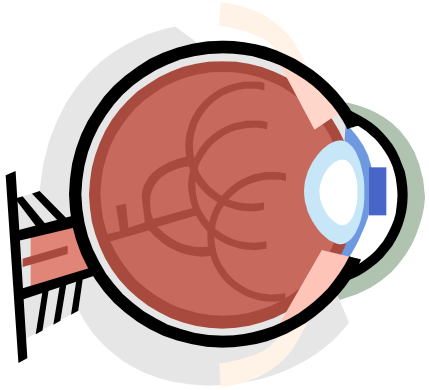


Also harder if sensed low (details later)

$$r = \frac{m}{M}$$




noise
error
$p \propto \sqrt{\frac{1}{l}}$
l
$\left|T(j\omega)\right| = \left|\frac{E}{N}\right|$
Delay τ



noise

error

$$p \propto \sqrt{\frac{1}{l}}$$

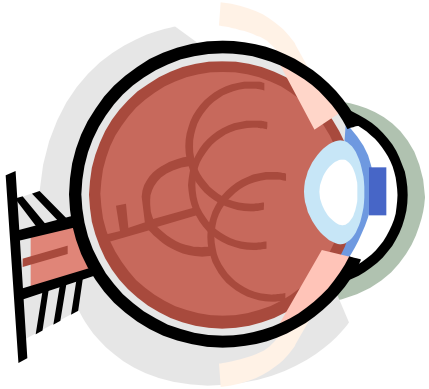
l

$$\left|T(j\omega)\right| = \left|\frac{E}{N}\right|$$

Delay τ

Delay is hard

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|T(j\omega)\right| \frac{2p}{p^2+\omega^2} d\omega \geq \ln\left|T_{mp}(p)\right| = p\tau \propto \tau\sqrt{\frac{1}{l}}$$



noise

error

This holds for ***any*** controller so is an intrinsic constraint on the difficulty of the problem.

$$\left|\frac{E}{N}\right|$$

Any **control**

Delay τ

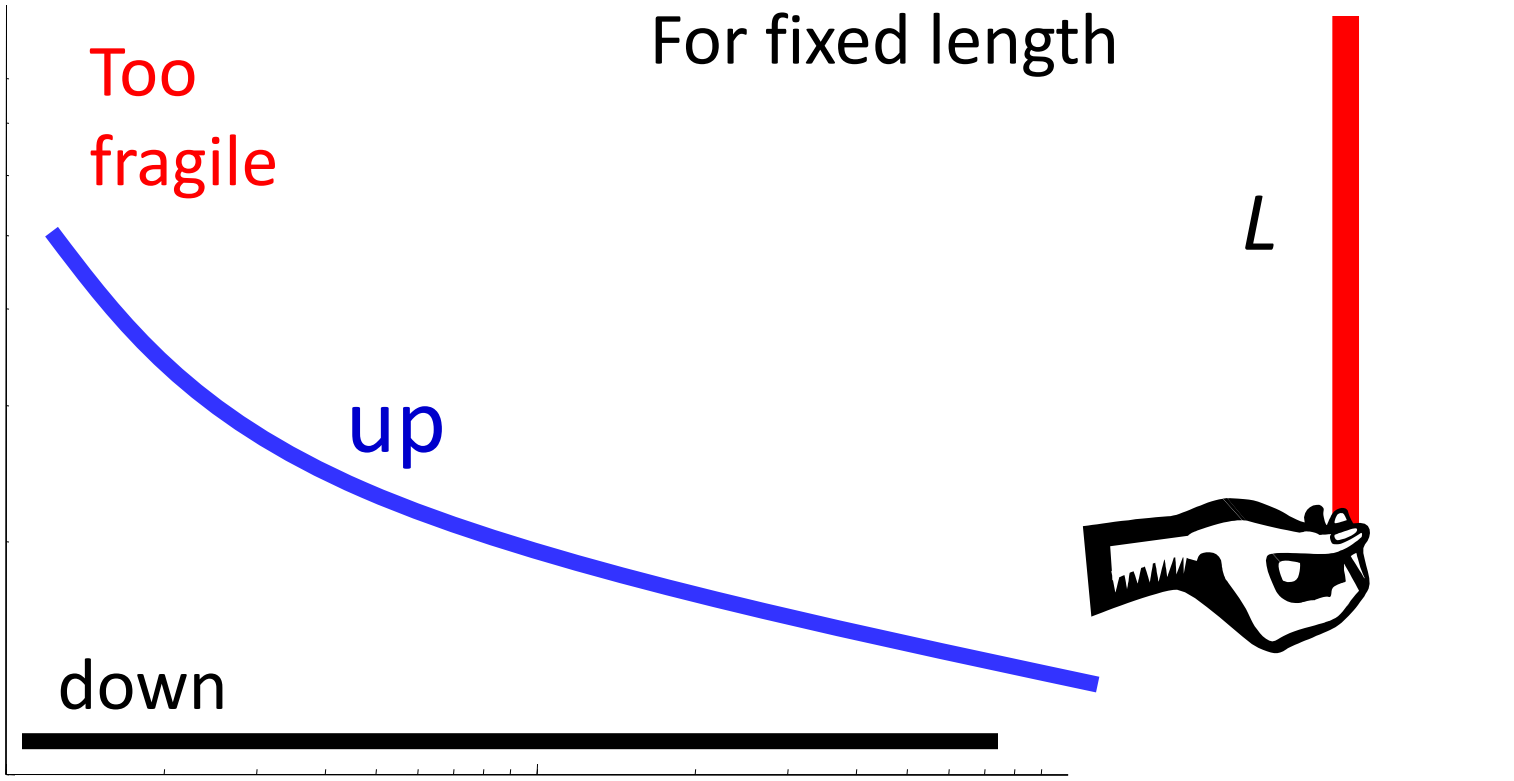
Delay is hard

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|T(j\omega)\right| \frac{2p}{p^2+\omega^2} d\omega \geq \ln\left|T_{mp}(p)\right| = p\tau \propto \tau\sqrt{\frac{1}{l}}$$

$$\frac{1}{\pi}\int_0^\infty \ln\left|T(j\omega)\right|\frac{2p}{p^2+\omega^2}d\omega \geq p\tau \propto \tau\sqrt{\frac{1}{l}}$$

Fragility

$$\tau\sqrt{\frac{1}{l}}$$



large τ
small $1/\tau$

small τ
large $1/\tau$

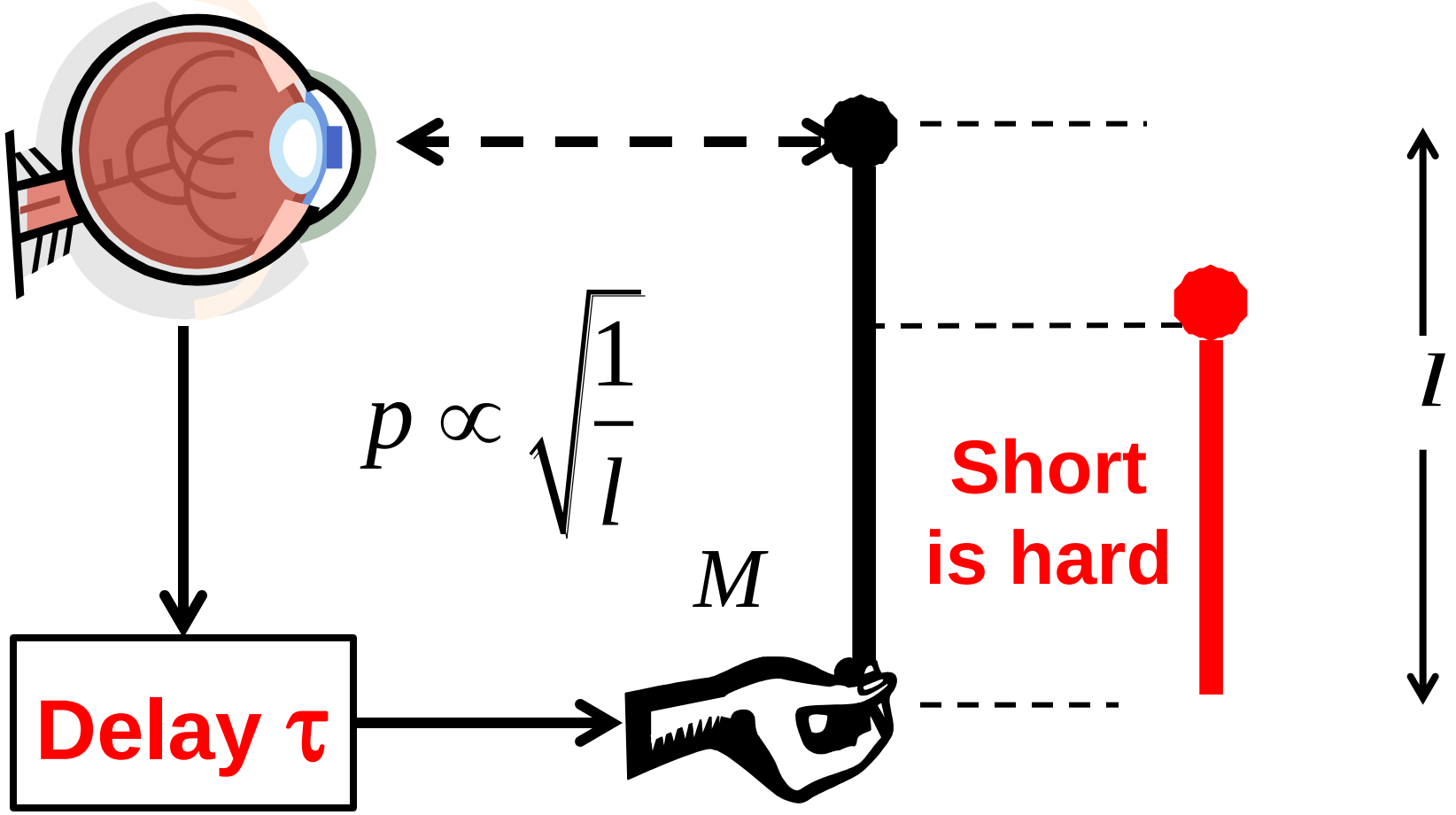
1/delay

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|T(j\omega)\right| \frac{2p}{p^2+\omega^2} d\omega \geq p\tau \propto \tau\sqrt{\frac{1}{l}}$$

We would like to tolerate large delays (and small lengths), but large delays severely constrain the achievable robustness.

large τ small τ

small $1/\tau$ large $1/\tau$



$$\frac{1}{\pi}\int_0^{\infty} \ln\left|T(j\omega)\right| \frac{2p}{p^2+\omega^2} d\omega \geq \ln\left|T_{mp}(p)\right| = p\tau \propto \tau\sqrt{\frac{1}{l}}$$

$$\frac{1}{\pi}\int_0^{\infty} \ln\left|T(j\omega)\right| \frac{2p}{p^2+\omega^2} d\omega \geq \ln\left|T_{mp}(p)\right| = p\tau \propto \tau\sqrt{\frac{1}{l}}$$

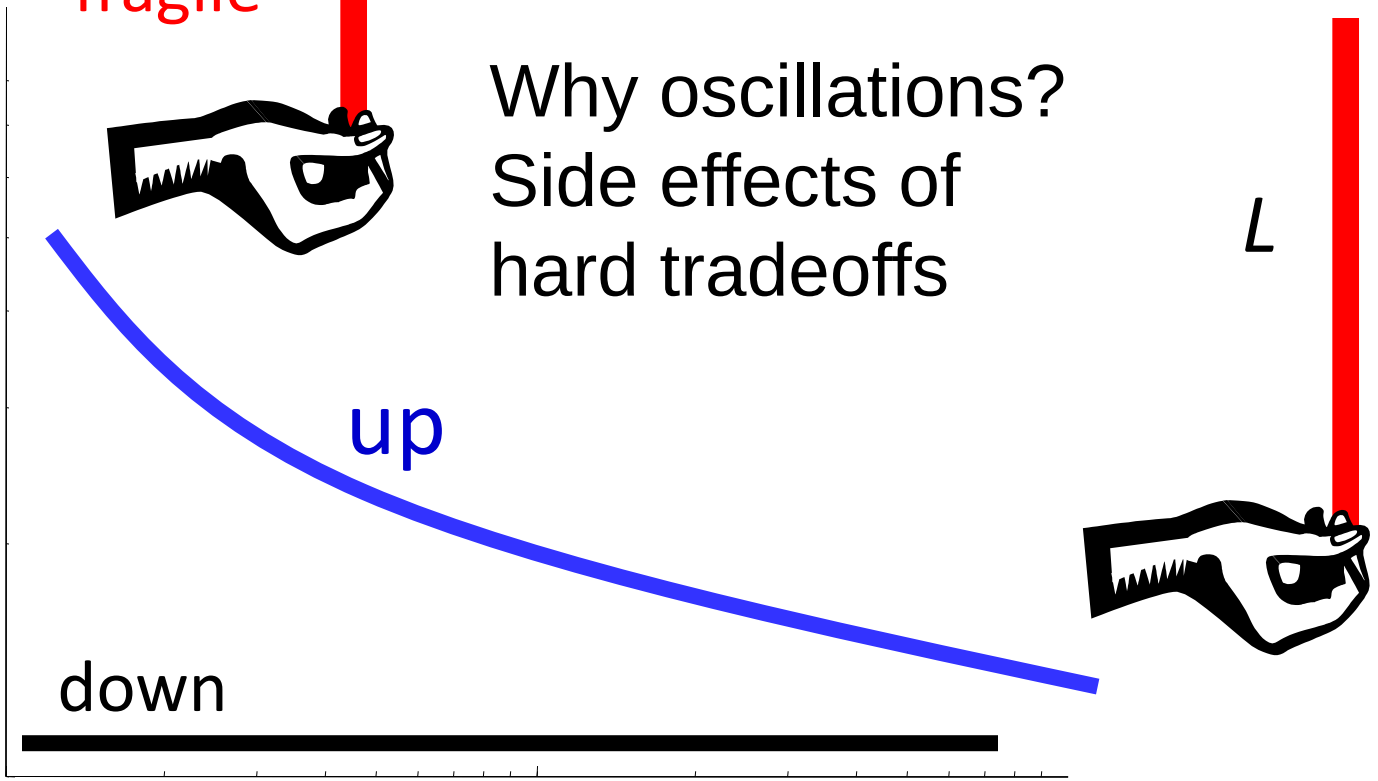
For fixed delay

Too fragile

Fragility

$$p \propto \sqrt{\frac{1}{l}}$$

Why oscillations?
Side effects of hard tradeoffs



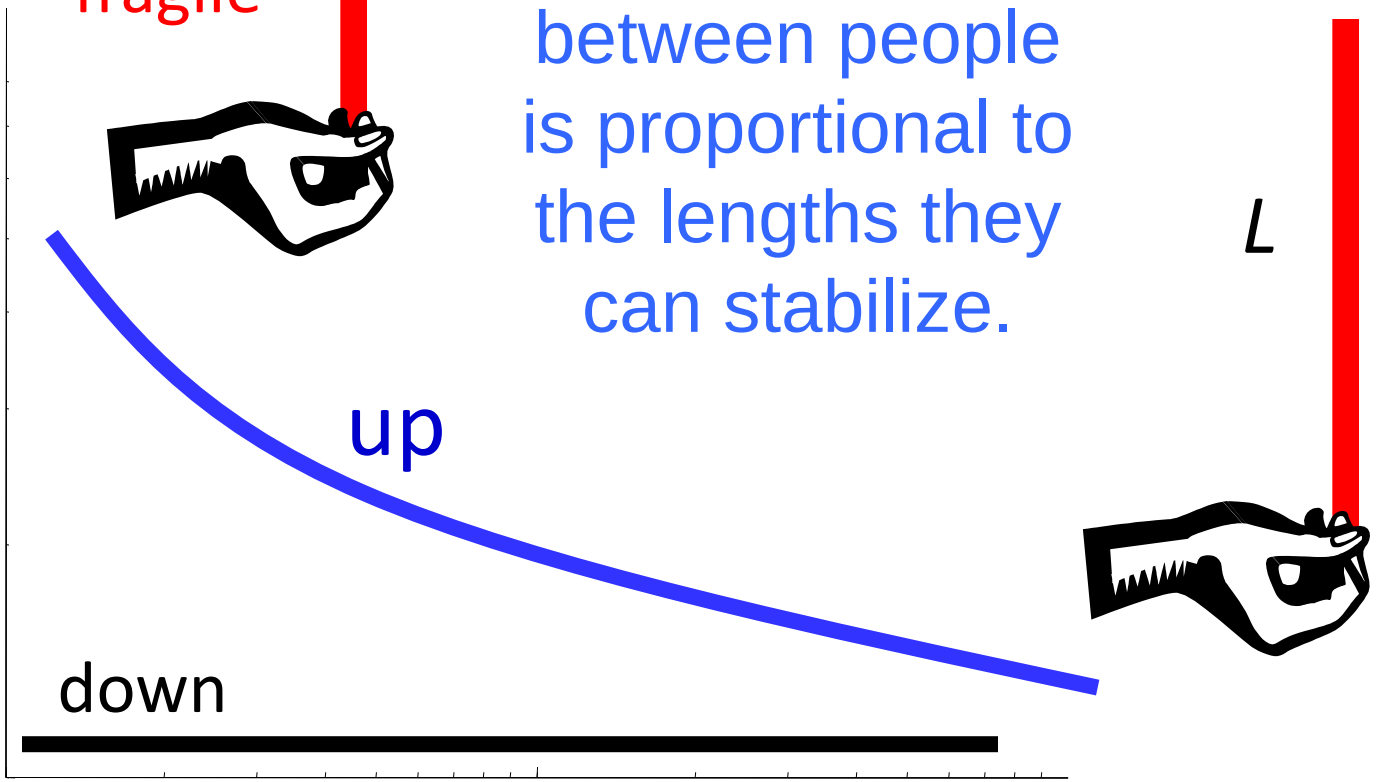
$$\frac{1}{\pi}\int_0^{\infty} \ln\left|T(j\omega)\right| \frac{2p}{p^2+\omega^2} d\omega \geq \ln\left|T_{mp}(p)\right| = p\tau \propto \tau\sqrt{\frac{1}{l}}$$

Too fragile

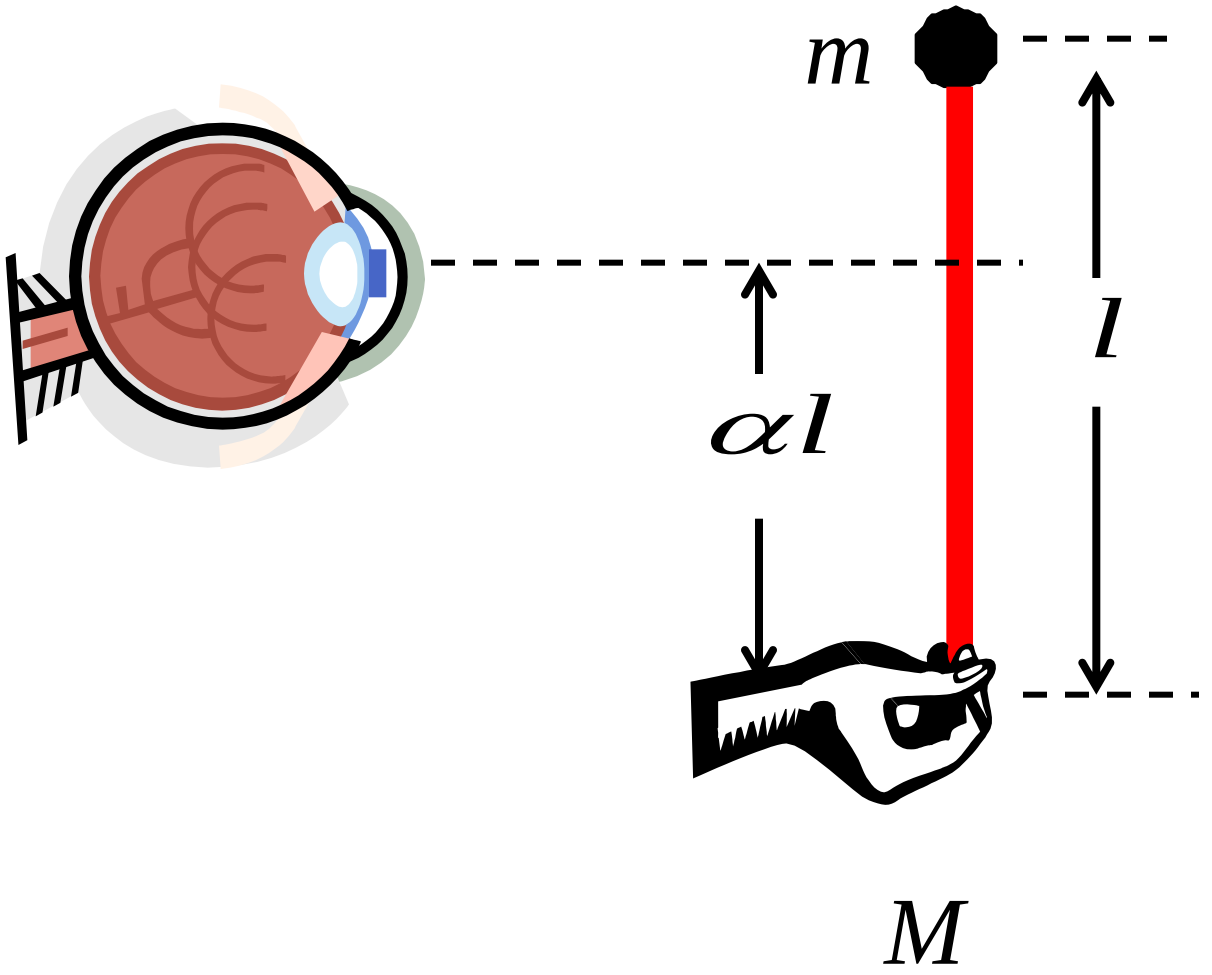
The ratio of delay between people is proportional to the lengths they can stabilize.

Fragility

$$p \propto \sqrt{\frac{1}{l}}$$

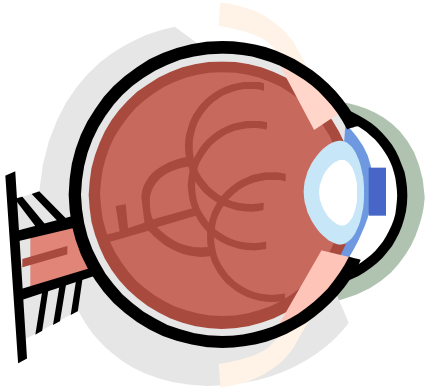


Eyes moved down is harder
(RHP zero)
Similar to delay

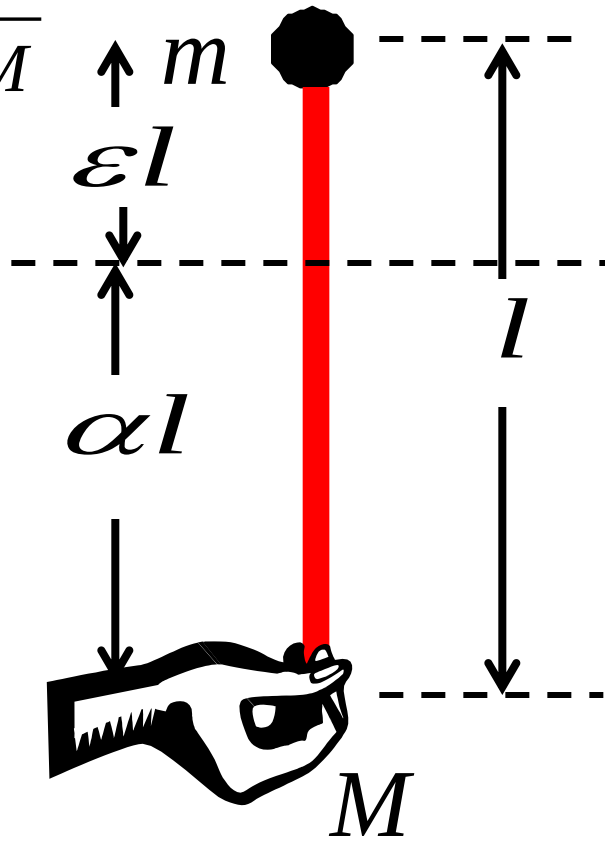


Suppose $r = \frac{m}{M} << 1$

Units $\Rightarrow M = g = 1$



$r = \frac{m}{M}$



$$y = x + \alpha l\theta = \frac{\varepsilon l s^2 \pm g}{s^2\left(l s^2 \pm g\right)} \qquad \varepsilon = 1 - \alpha$$

$$p \approx \sqrt{\frac{g}{l}} \qquad z = \sqrt{\frac{g}{l}}\sqrt{\frac{1}{\varepsilon}} \Rightarrow \frac{z+p}{z-p} = \frac{1+\sqrt{\varepsilon}}{1-\sqrt{\varepsilon}}$$

Compare

$$p = \sqrt{\frac{g}{l(1-\varepsilon)}}\sqrt{1+r} = p_0\sqrt{\frac{1}{(1-\varepsilon)}} \approx p_0\left(1+\frac{\varepsilon}{2}\right)$$

Move eyes

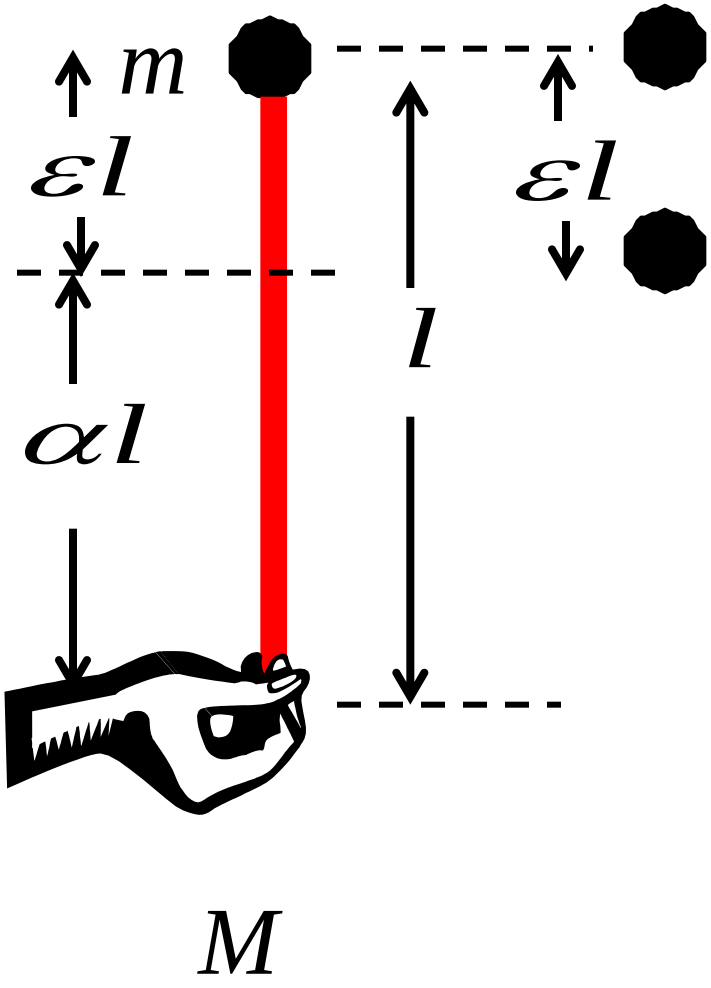
$$p = \sqrt{\frac{g}{l}}\sqrt{1+r} \quad r = \frac{m}{M} \quad z = \sqrt{\frac{g}{l}}\sqrt{\frac{1}{\varepsilon}}$$

$$p = z \Rightarrow 1+r = \frac{1}{\varepsilon} \Rightarrow \varepsilon = \frac{1}{1+r}$$

$$p\left(1+\frac{1}{3}\frac{p^2}{z^2}\right) = \sqrt{\frac{g}{l}}\sqrt{1+r}\left(1+\frac{1}{3}\varepsilon\right) = p\left(1+\frac{\varepsilon}{3}\right)$$

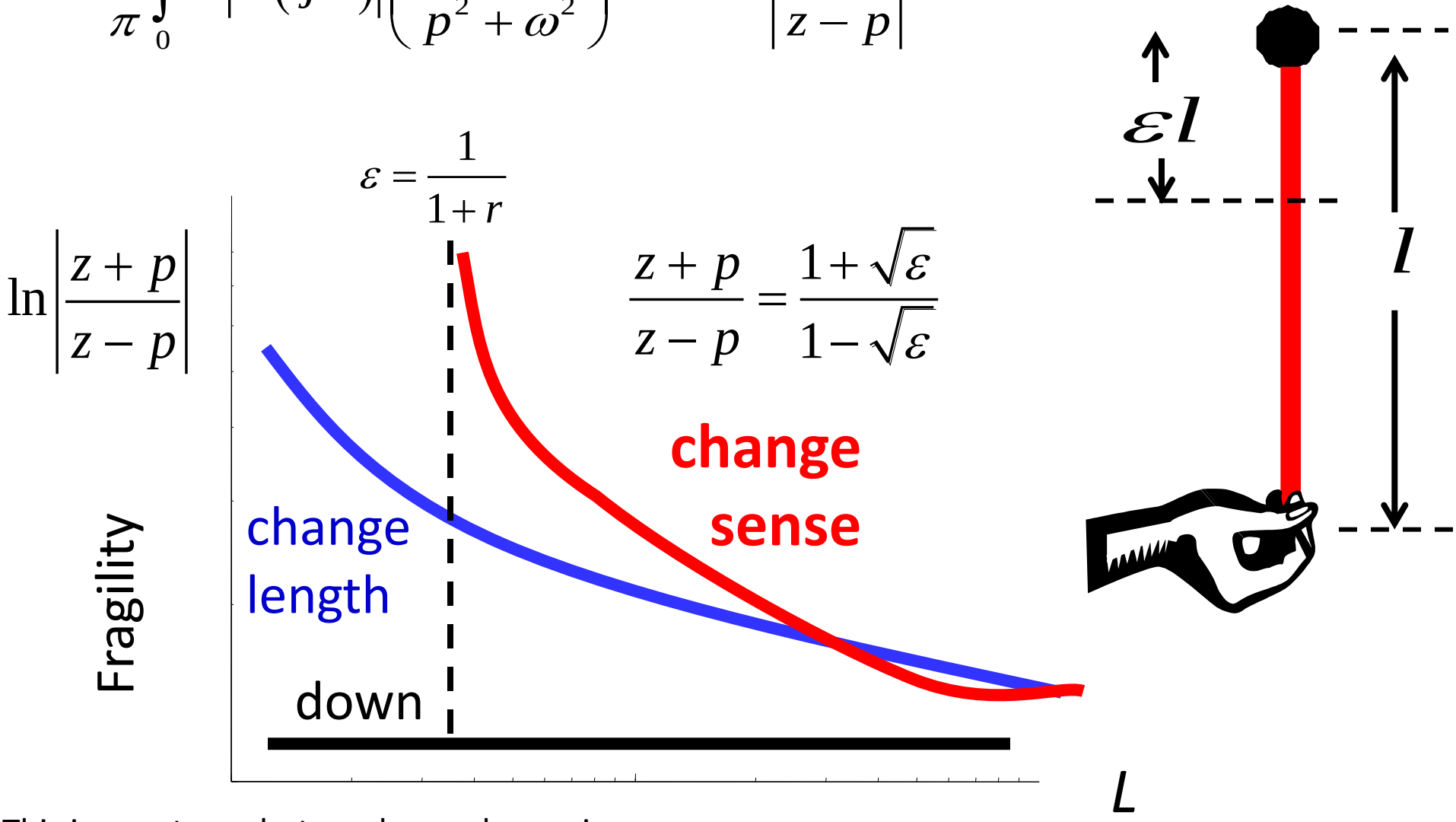
$$= p\left(1+\frac{1-\alpha}{3}\right)$$

$$r = \frac{m}{M}$$



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

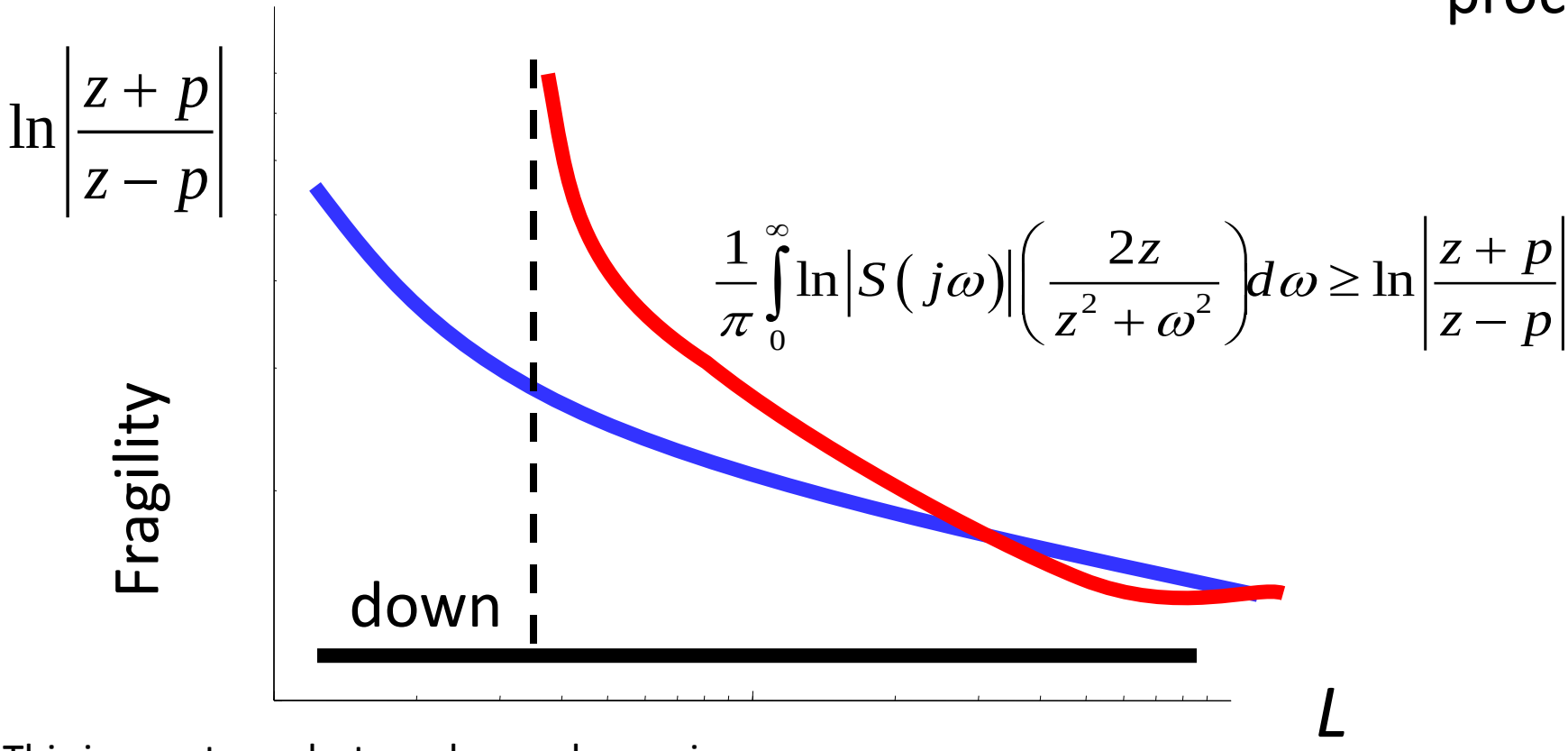
$$\frac{1}{\pi}\int_0^\infty \ln\left|T(j\omega)\right|\left(\frac{2p}{p^2+\omega^2}\right)d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$



This is a cartoon, but can be made precise.

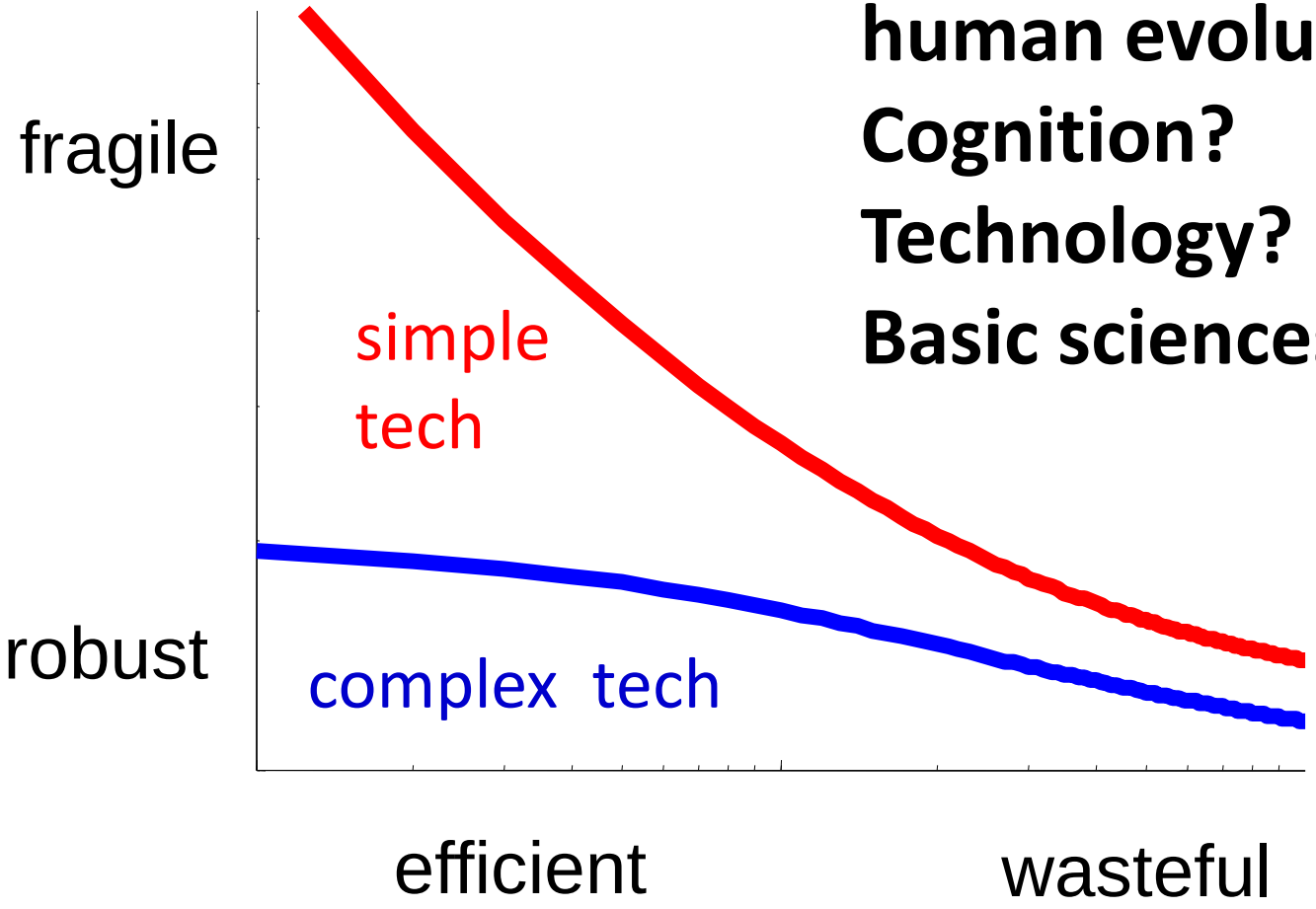
Hard limits on the ***intrinsic*** robustness of control ***problems***.

Must (and do) have algorithms that achieve the limits, and architectures that support this process.



This is a cartoon, but can be made precise.

How general is this picture?



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

OPEN ACCESS Freely available online PLOS BIOLOGY

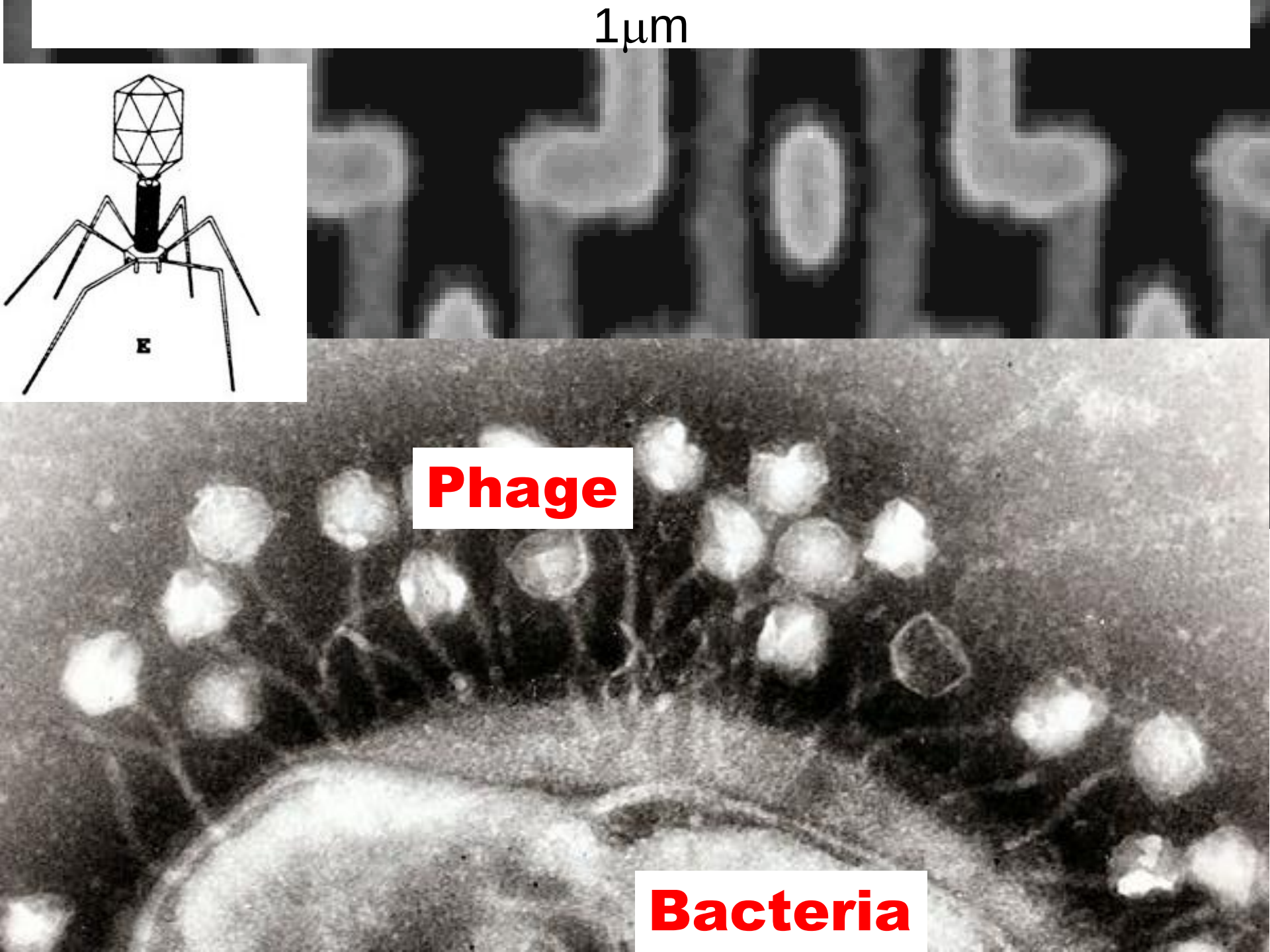
Viruses' Life History: Towards a Mechanistic Basis of a Trade-Off between Survival and Reproduction among Phages

Marianne De Paepe, François Taddei*

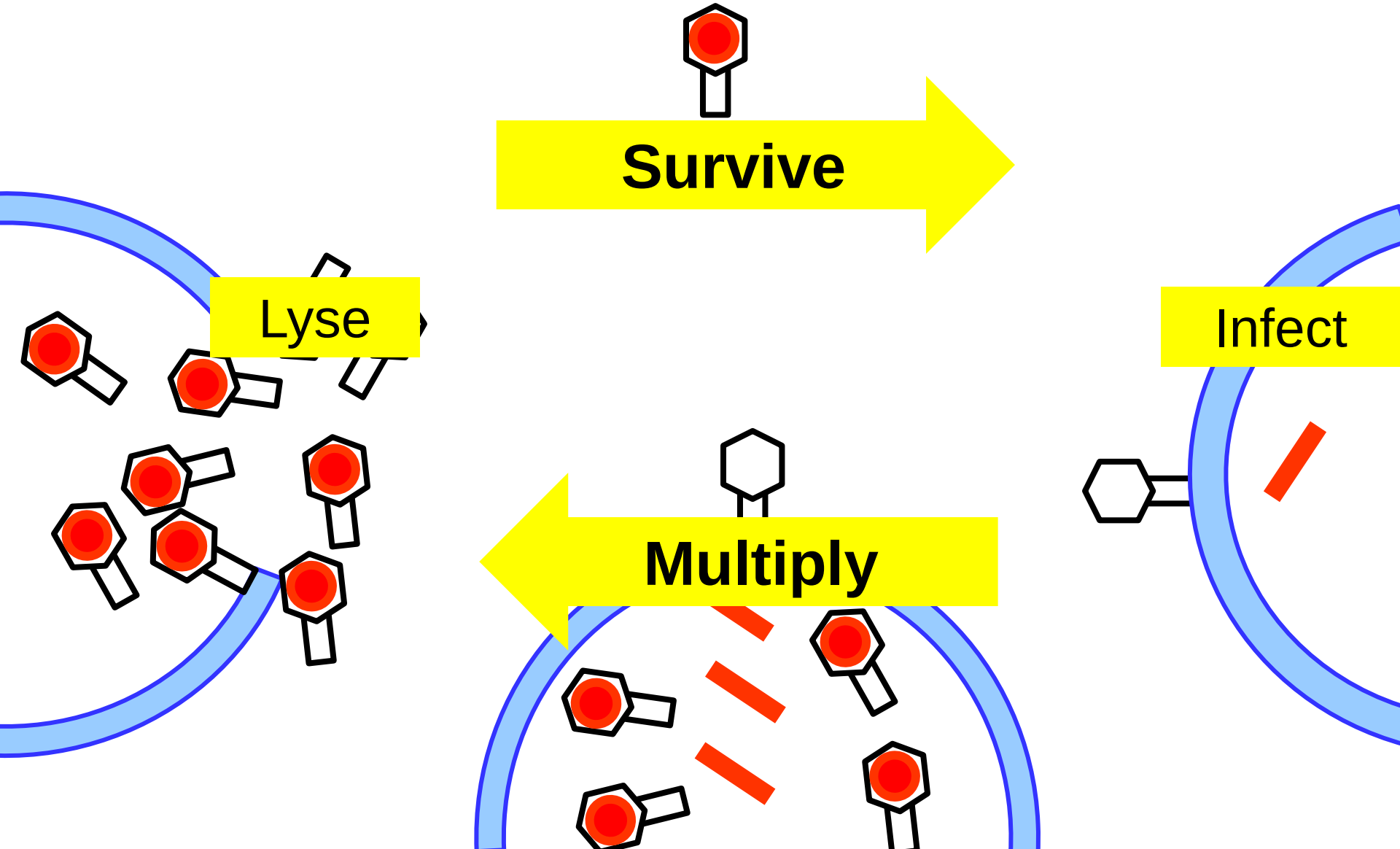
Laboratoire de Genetique Moleculaire, Evolutive et Medicale, University of Paris 5, INSERM, Paris, France

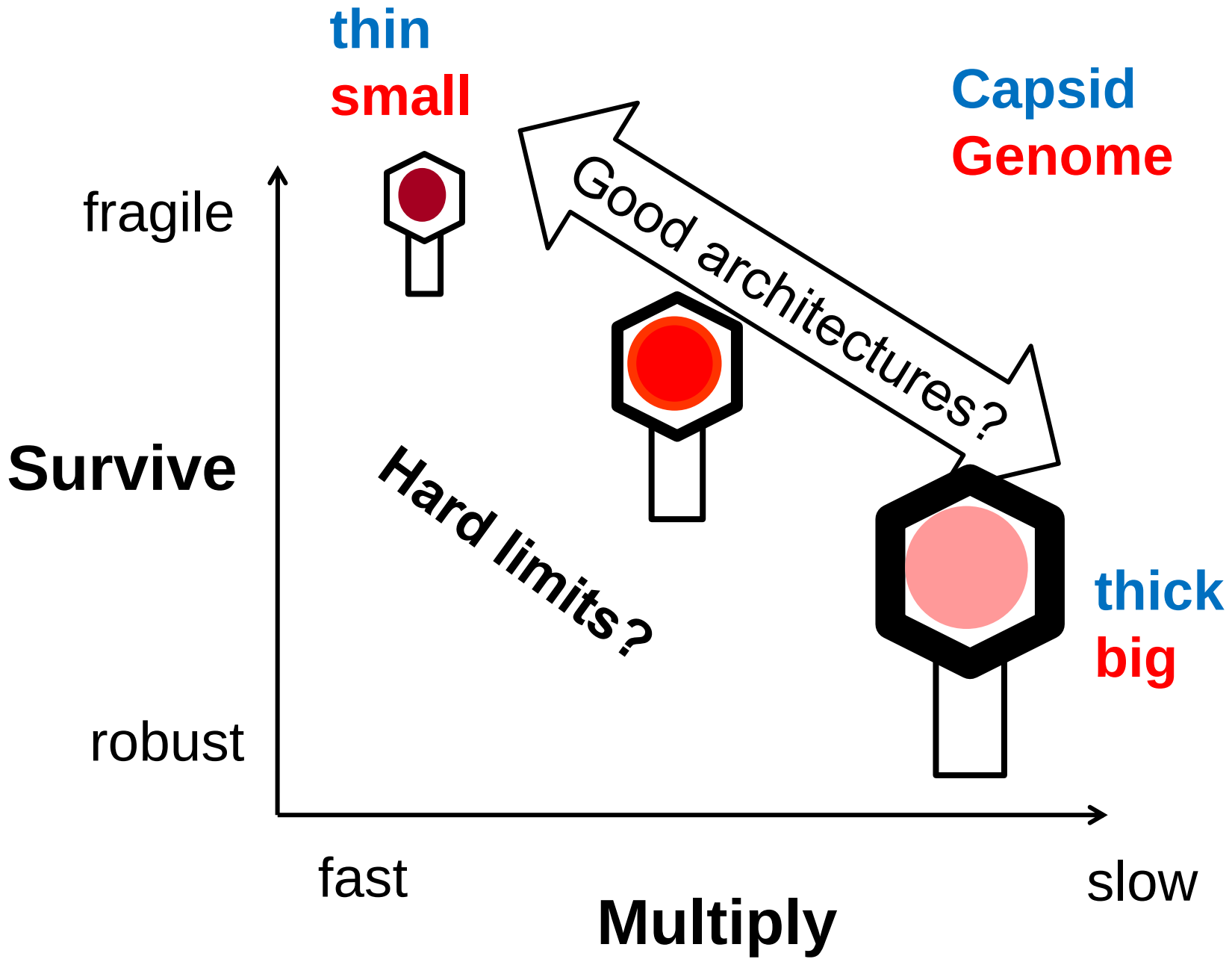
July 2006 | Volume 4 | Issue 7 | e193

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

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.

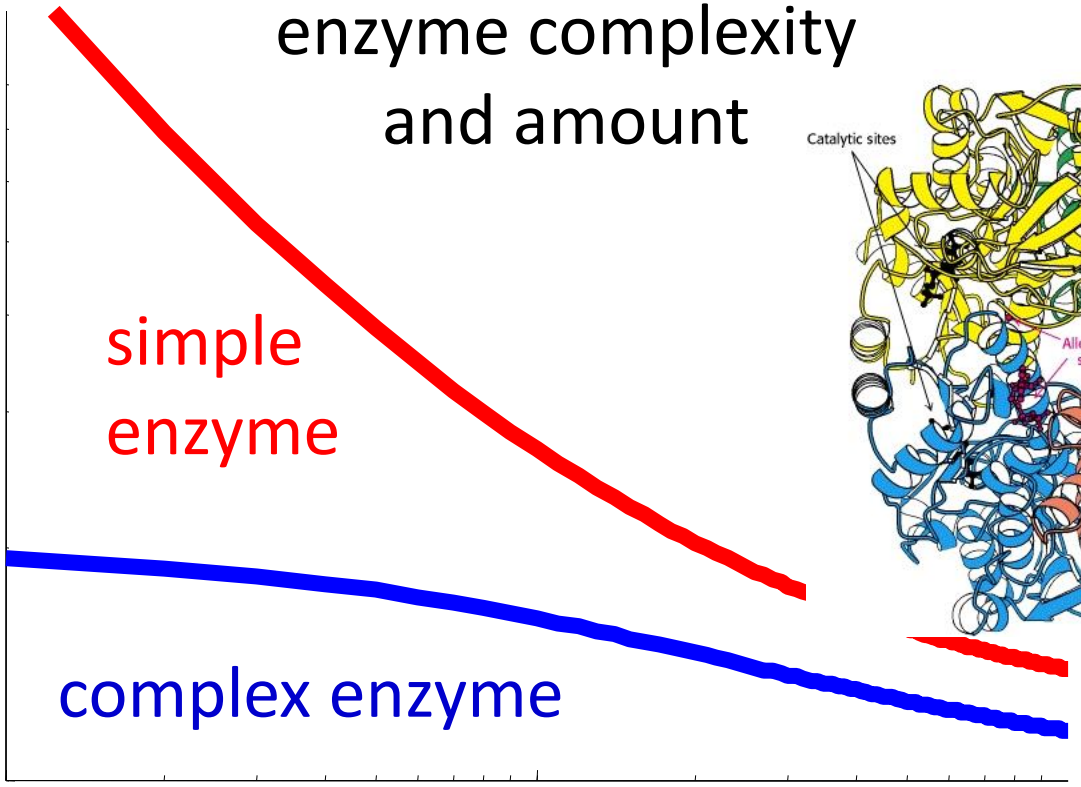
Theorem!

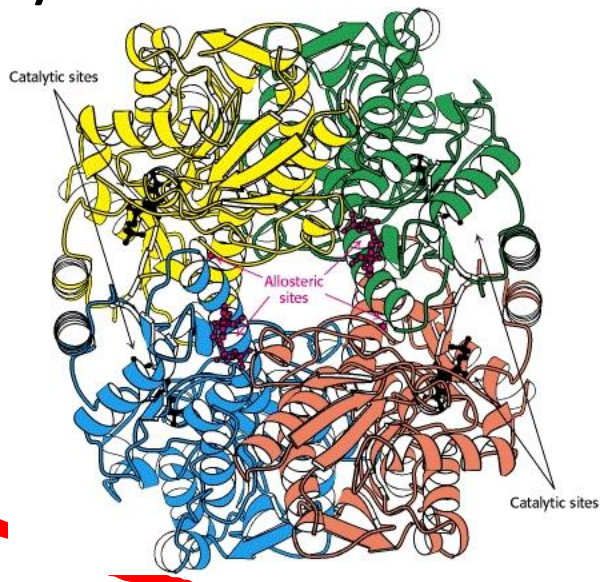
$$\frac{1}{\pi}\int_0^{\infty} \ln\left|S(j\omega)\right| \left(\frac{z}{z^2+\omega^2} \right) d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$

Fragility

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

z and p functions of enzyme complexity and amount



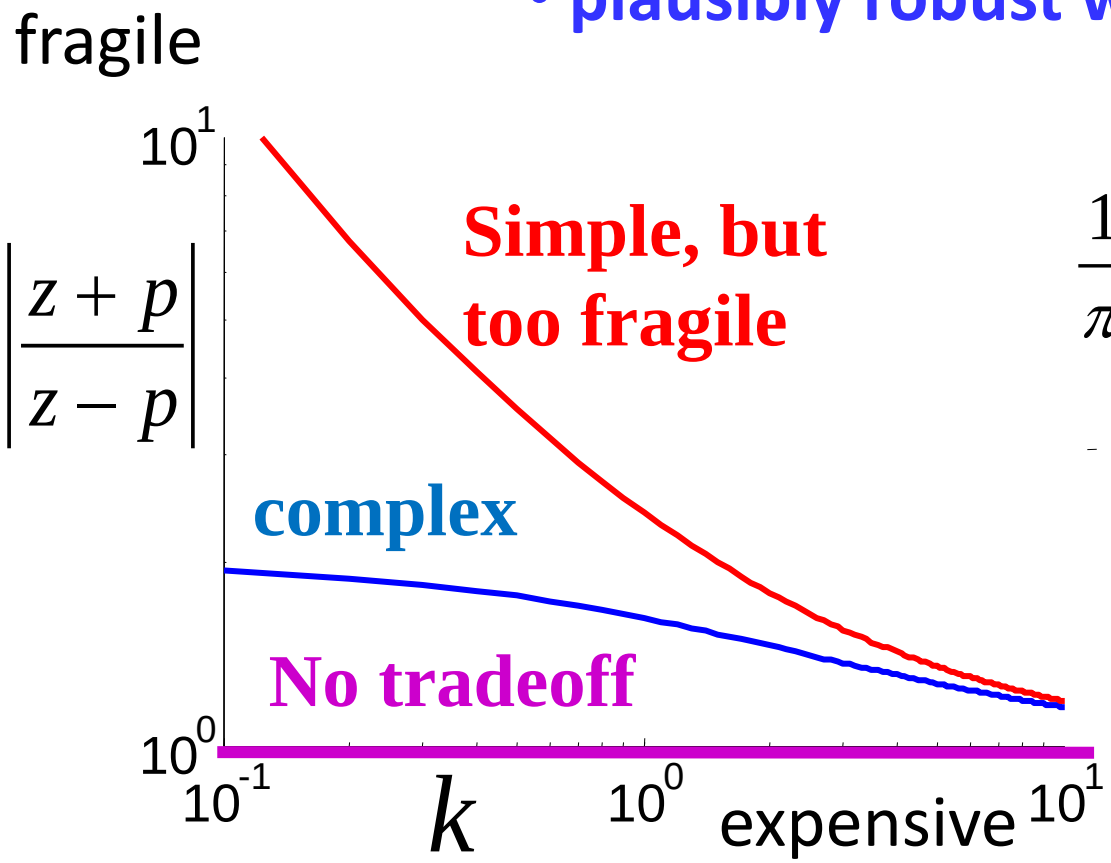


Enzyme amount

Savageaumics

Hard tradeoff in glycolysis is

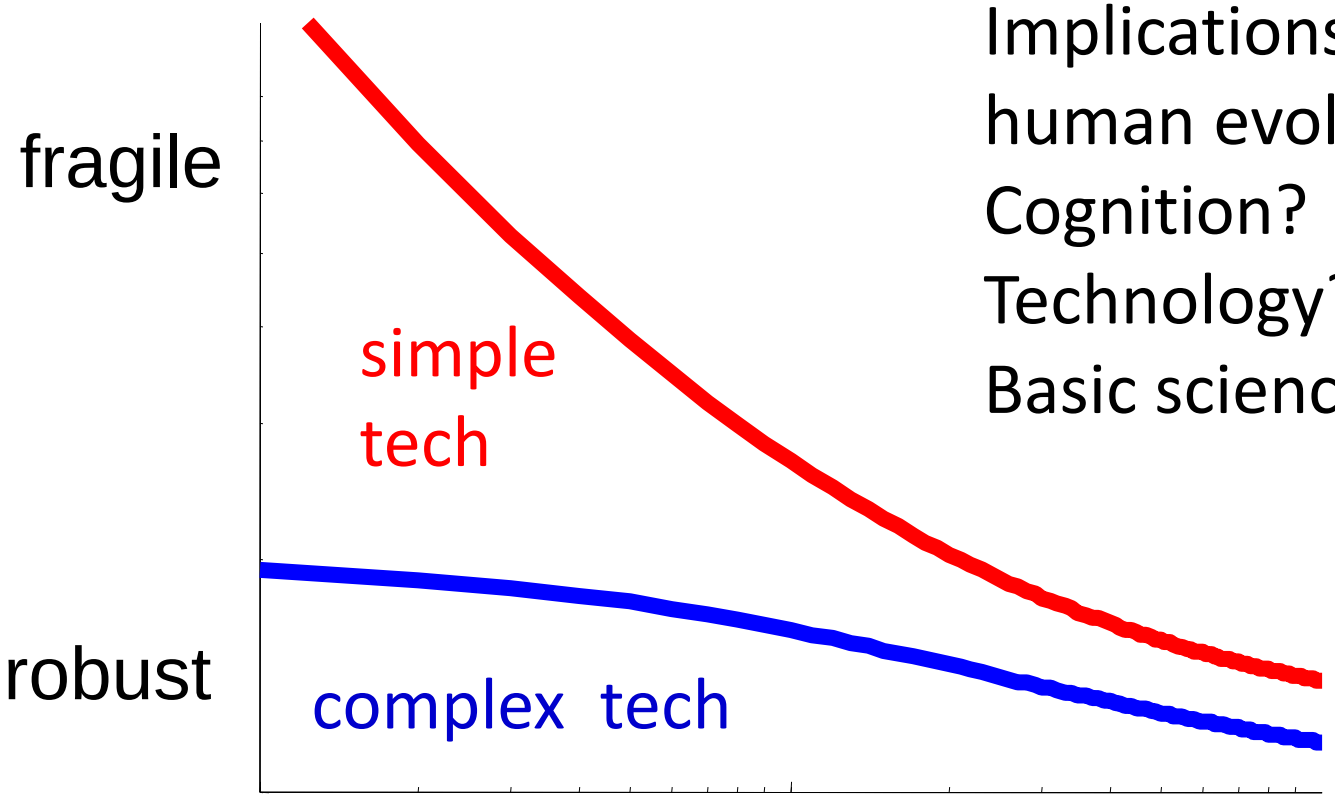
- **robustness vs efficiency**
- **absent without autocatalysis**
- **too fragile with simple control**
- **plausibly robust with complex control**



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

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

This picture is very general



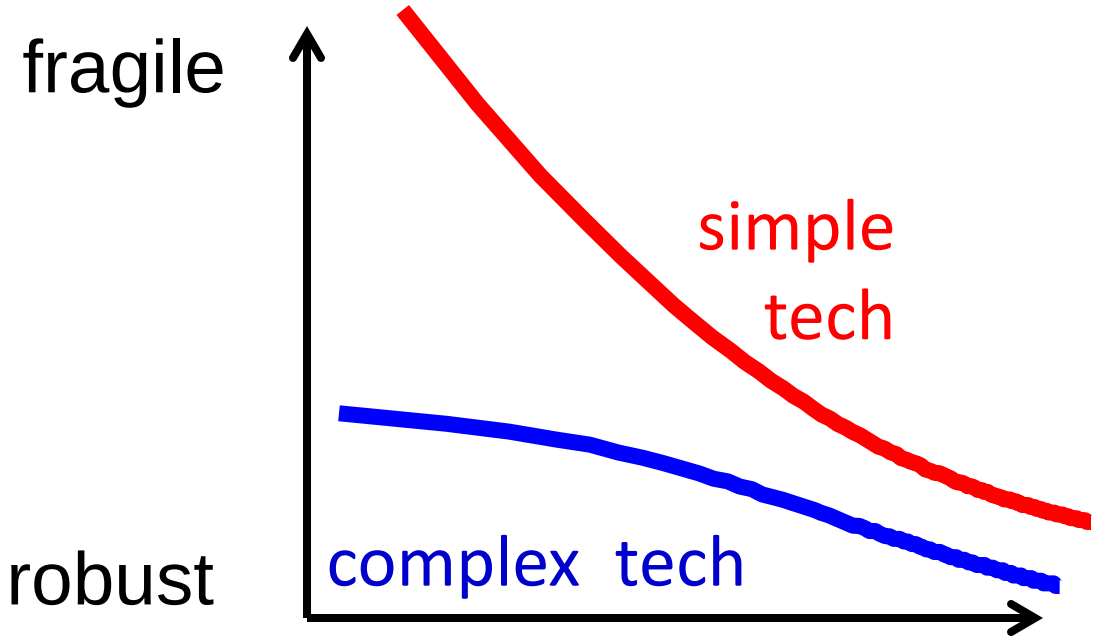
Implications for
human evolution?
Cognition?
Technology?
Basic sciences?

This picture is very general

Domain specific costs/tradeoffs

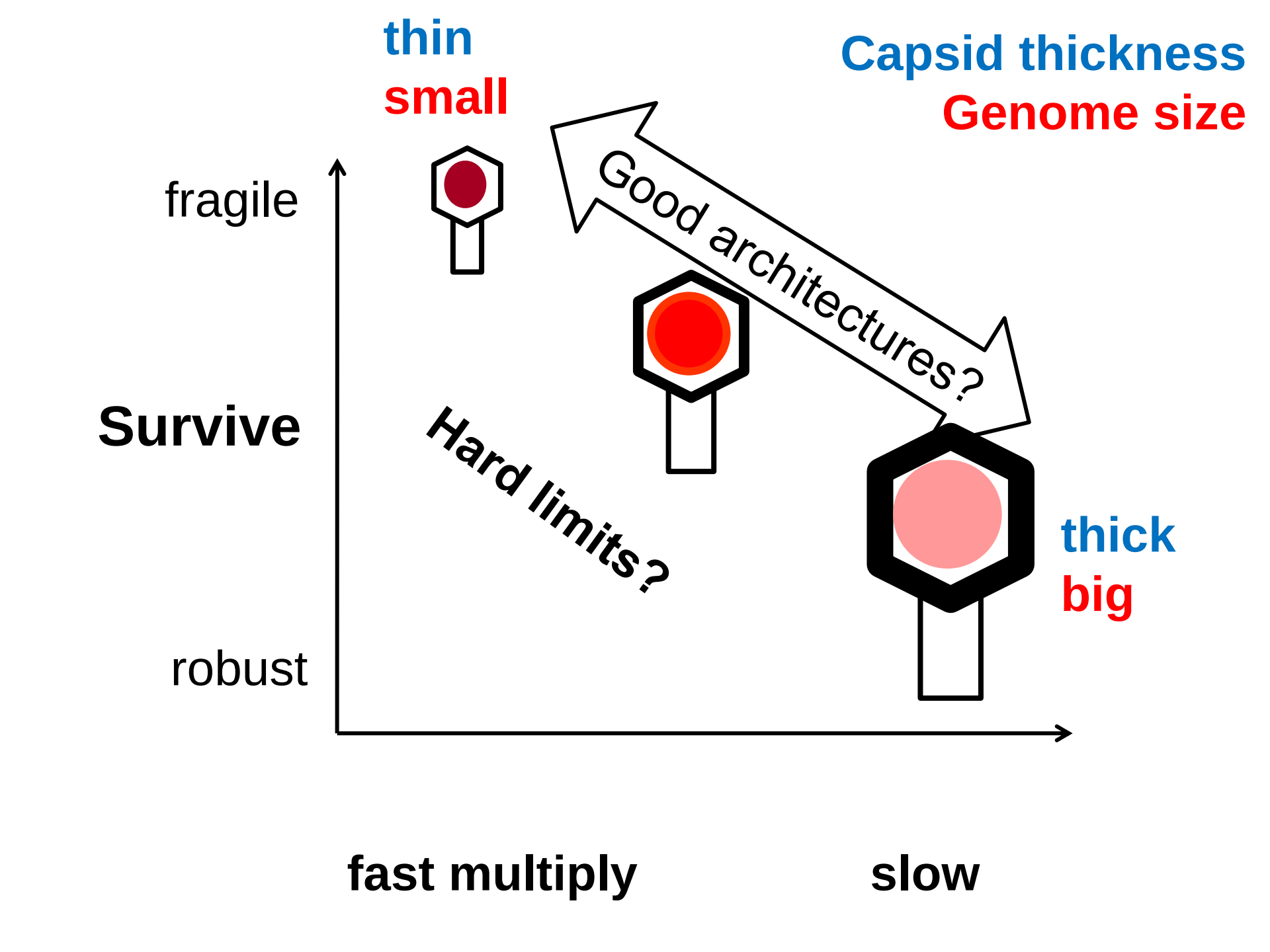
metabolic overhead	cheap ⟷	metabolic expensive
CNS reaction time τ (delay)	large τ ⟷	small τ
phage multiplication rate	fast multiply ⟷	slow

This picture is very general



metabolic cost	cheap	⟷	expensive
reaction time τ	large τ	⟷	small τ
phage x rate	fast	⟷	slow

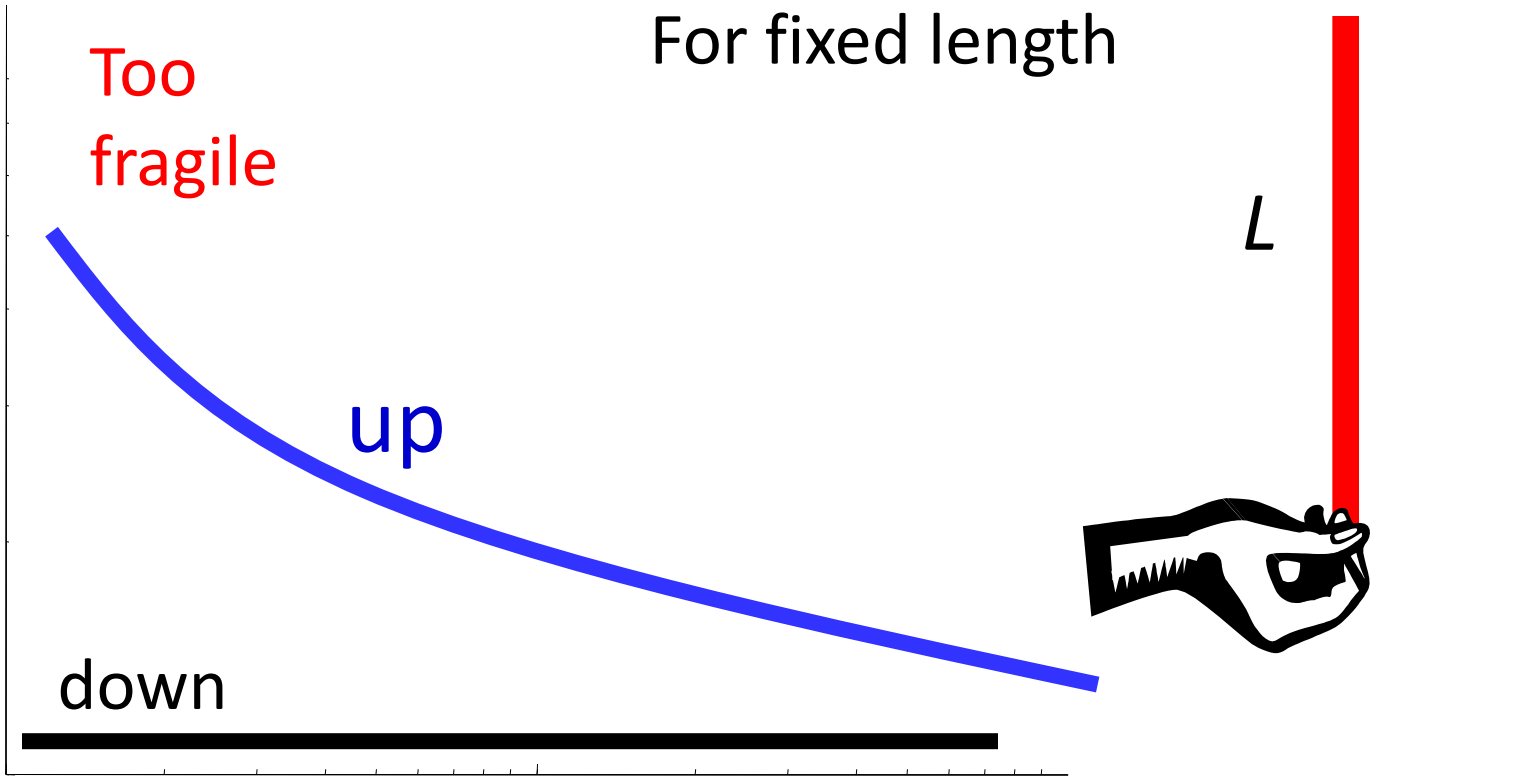
Domain specific costs/tradeoffs


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

$$\frac{1}{\pi}\int_0^\infty \ln\left|T(j\omega)\right|\frac{2p}{p^2+\omega^2}d\omega \geq p\tau \propto \tau\sqrt{\frac{1}{l}}$$

Fragility

$$\tau\sqrt{\frac{1}{l}}$$



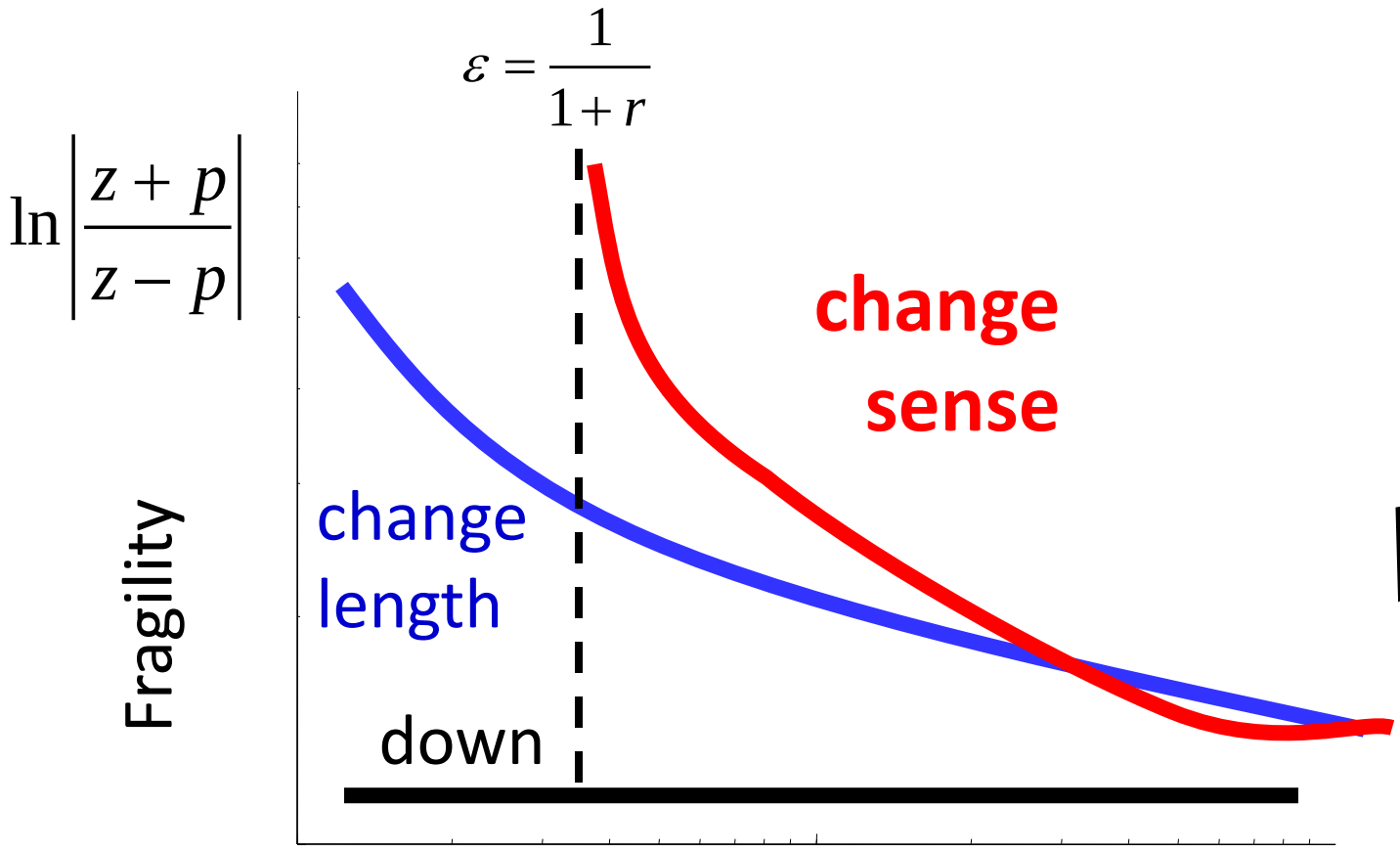
large τ
small $1/\tau$

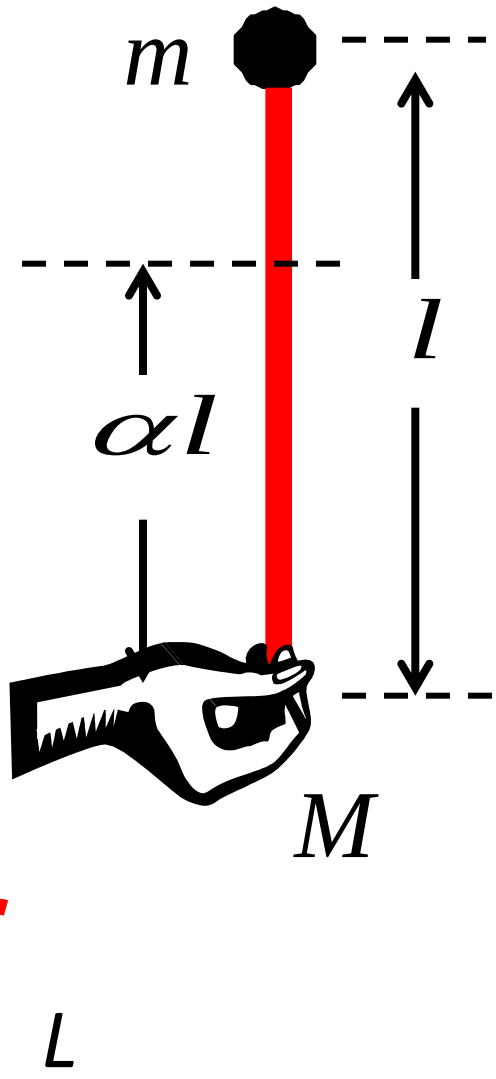
small τ
large $1/\tau$

1/delay

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

$$r = \frac{m}{M}$$

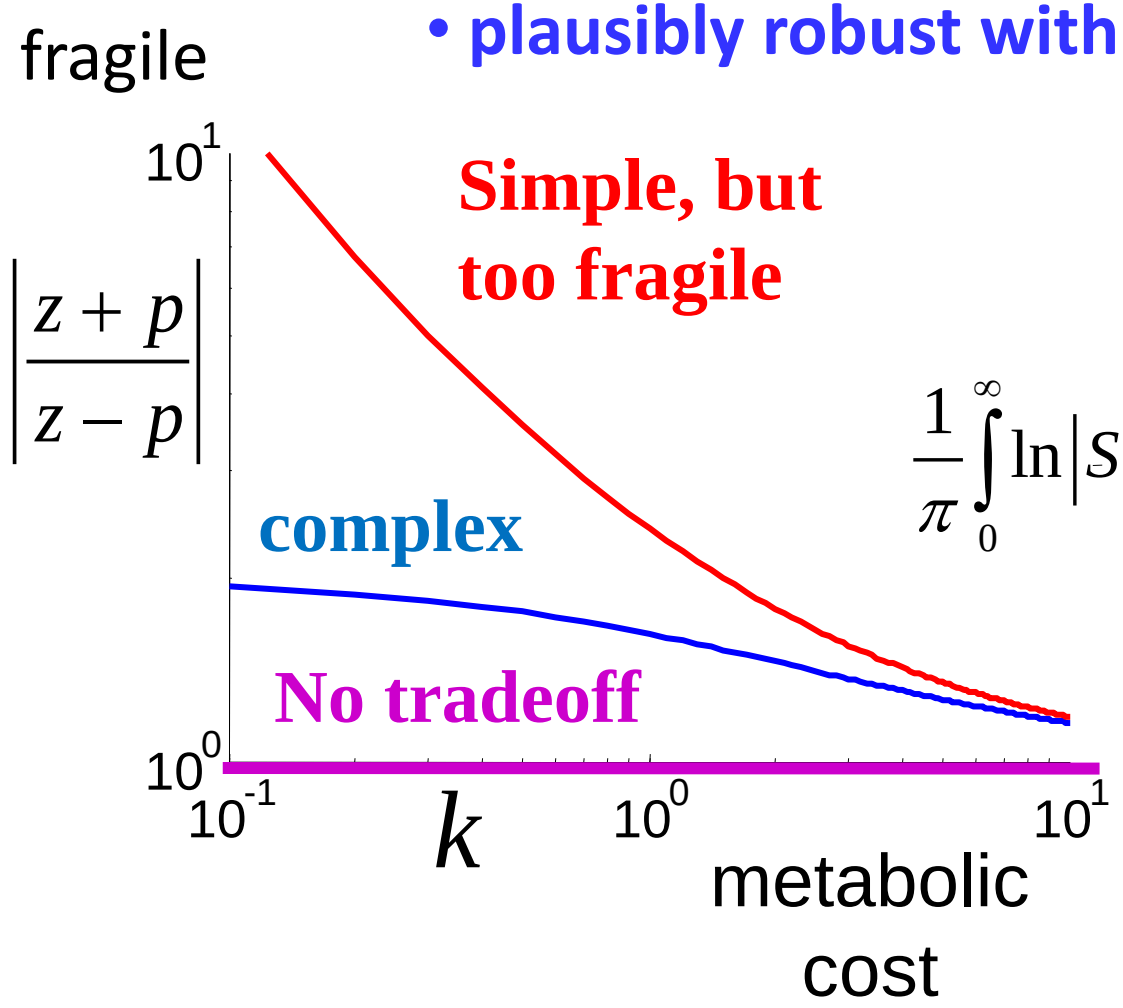




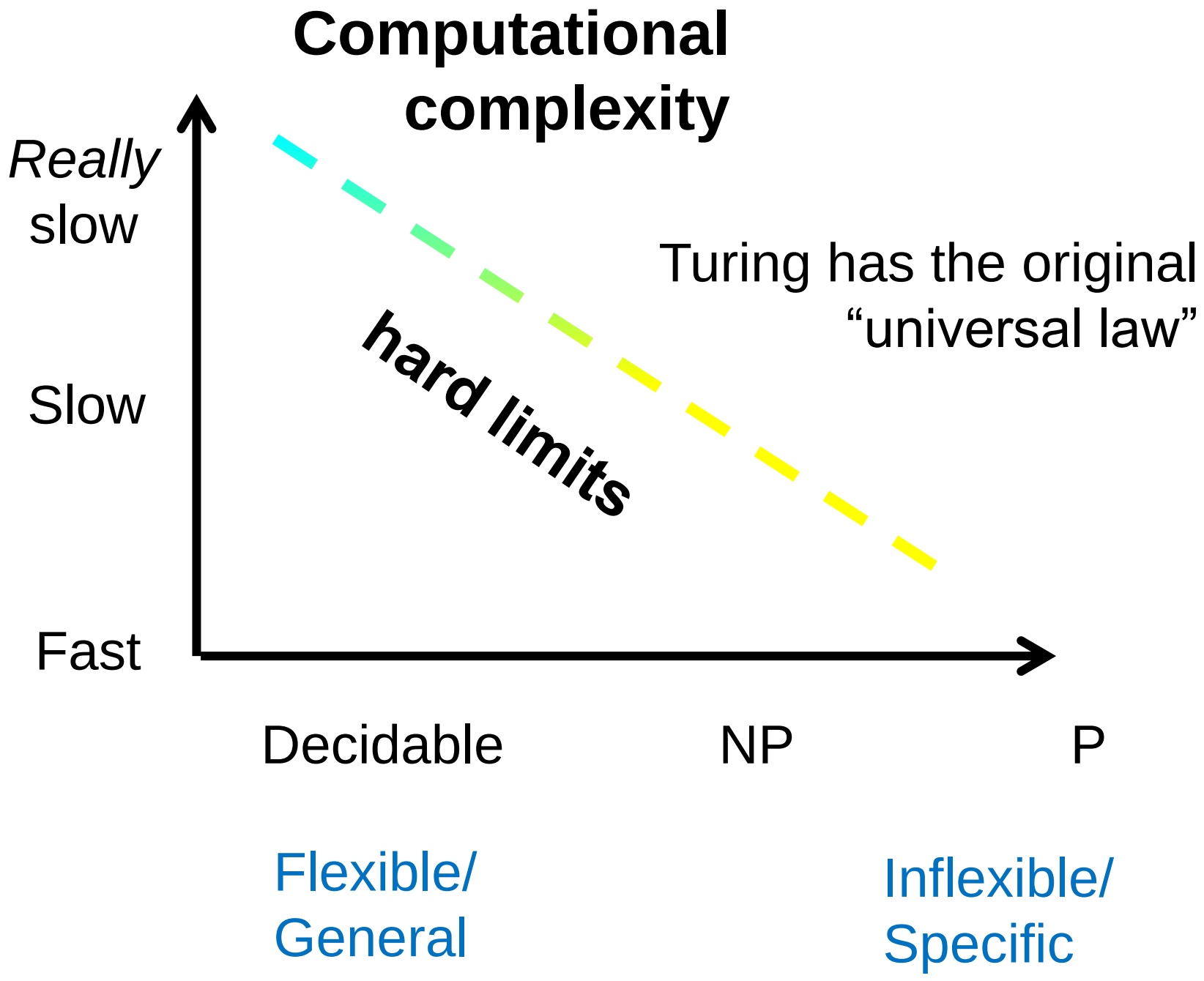
This is a cartoon, but can be made precise.

Hard tradeoff in glycolysis is

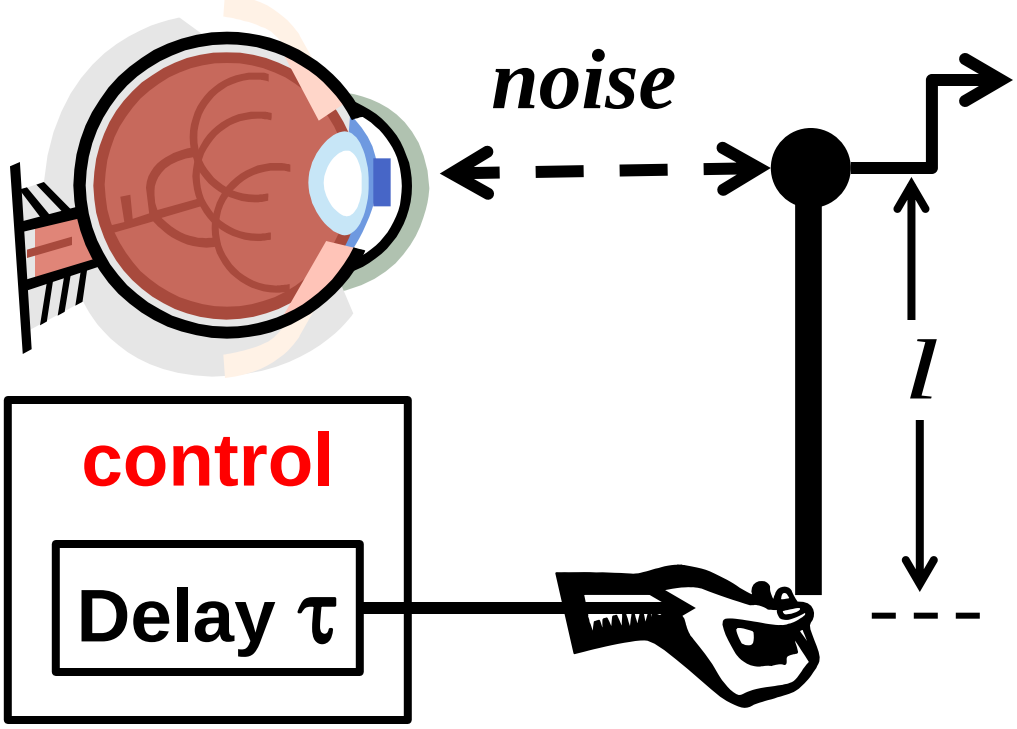
- **robustness vs efficiency**
- **absent without autocatalysis**
- **too fragile with simple control**
- **plausibly robust with complex control**



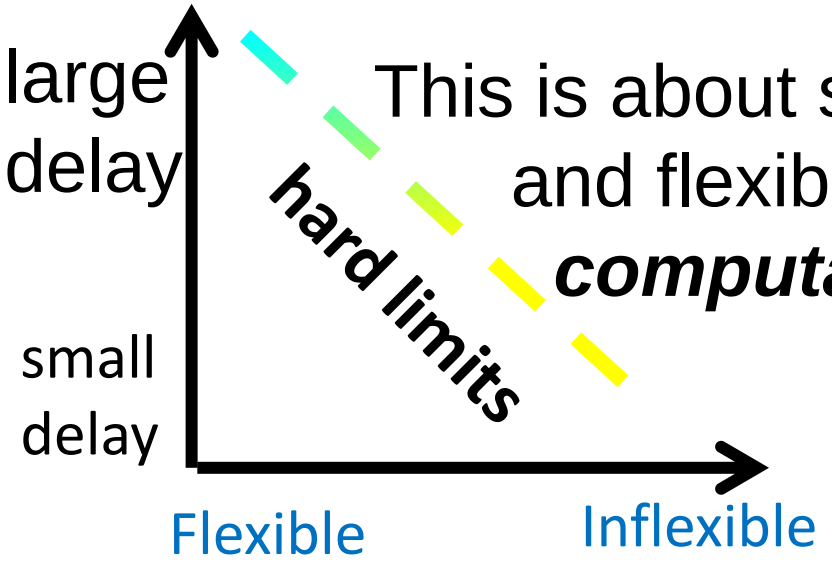
$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right|\left(\frac{z}{z^2+\omega^2}\right)d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$$


Computational complexity
Really slow
Slow
Fast
hard limits
Turing has the original "universal law"
Decidable
NP
P
Flexible/ General
Inflexible/ Specific

How do these two constraints (laws) relate?



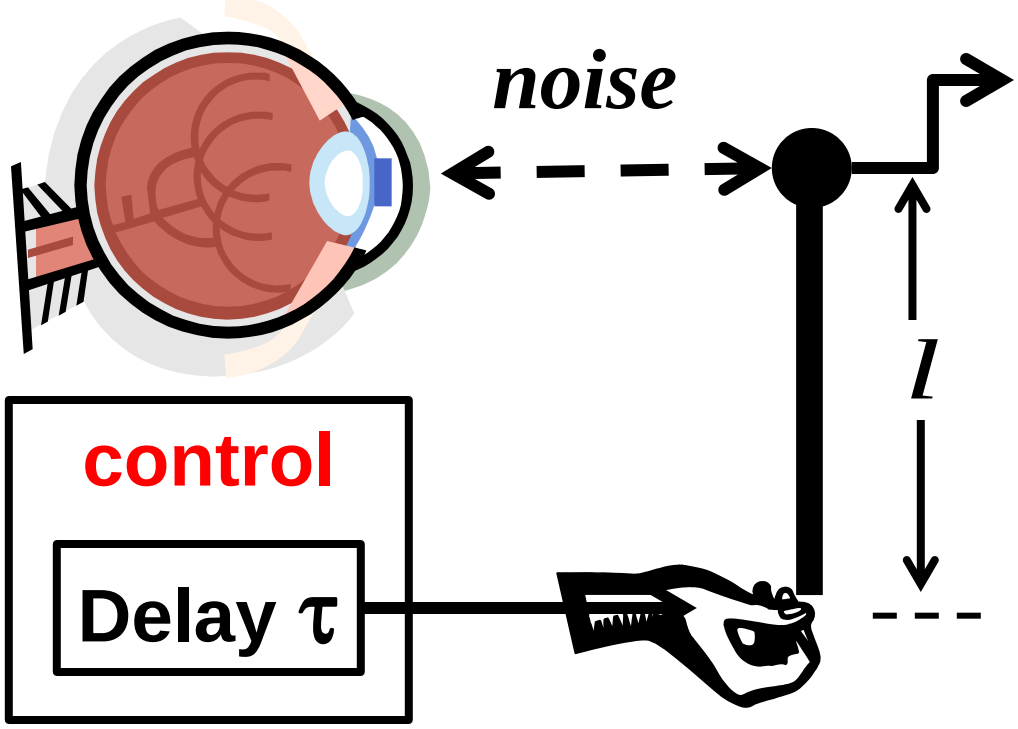
Computation delay adds to total delay.



This is about speed and flexibility of ***computation***.

Computation is a component in control.

Delay comes from sensing, communications, computing, and actuation.
Delay limits robust performance.



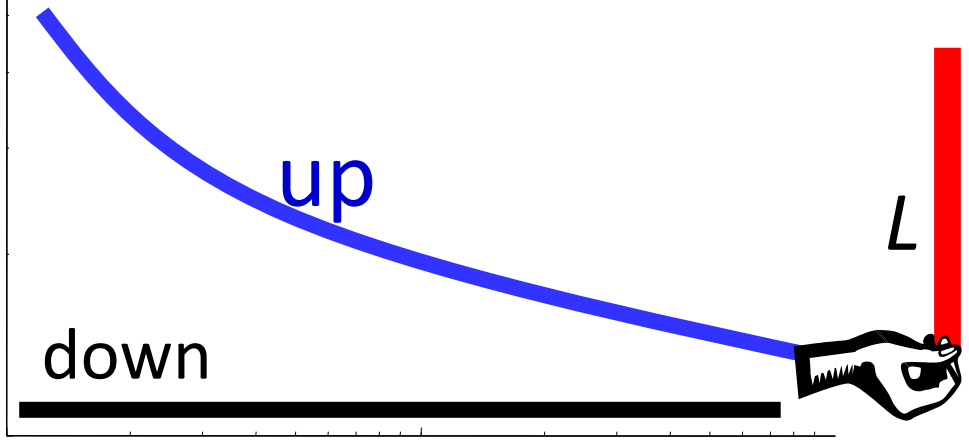
$$\frac{1}{\pi}\int_0^{\infty} \ln\left|T(j\omega)\right| \frac{2p}{p^2+\omega^2} d\omega \geq \ln\left|T_{mp}(p)\right| = p\tau \propto \tau\sqrt{\frac{1}{l}}$$

Fragility

$$\frac{1}{\pi}\int_0^\infty \ln\left|T(j\omega)\right|\frac{2p}{p^2+\omega^2}d\omega \geq p\tau \propto \tau\sqrt{\frac{1}{l}}$$

$\tau\sqrt{\frac{1}{l}}$

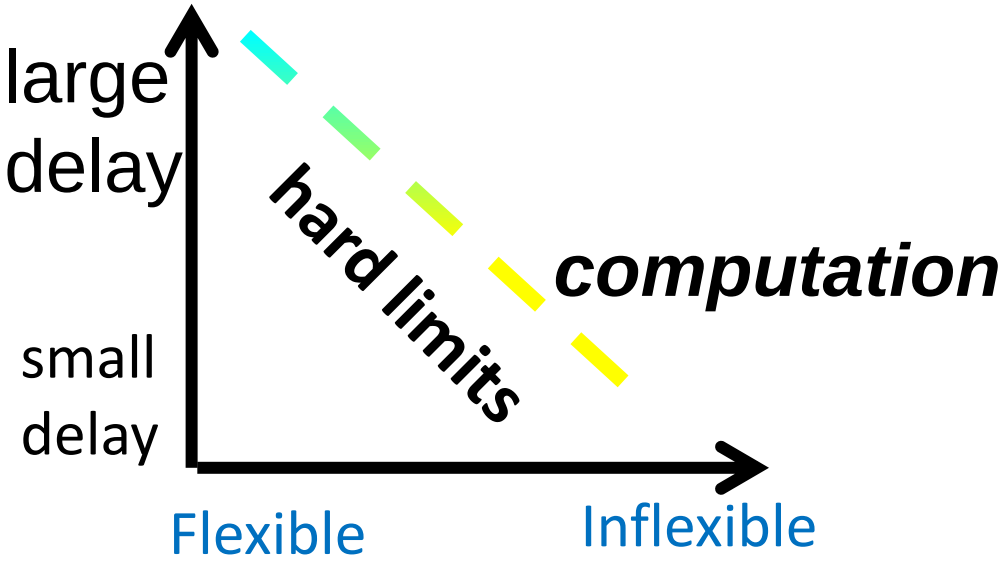
Delay makes control hard.



large τ

small τ

Computation delay adds to total delay.

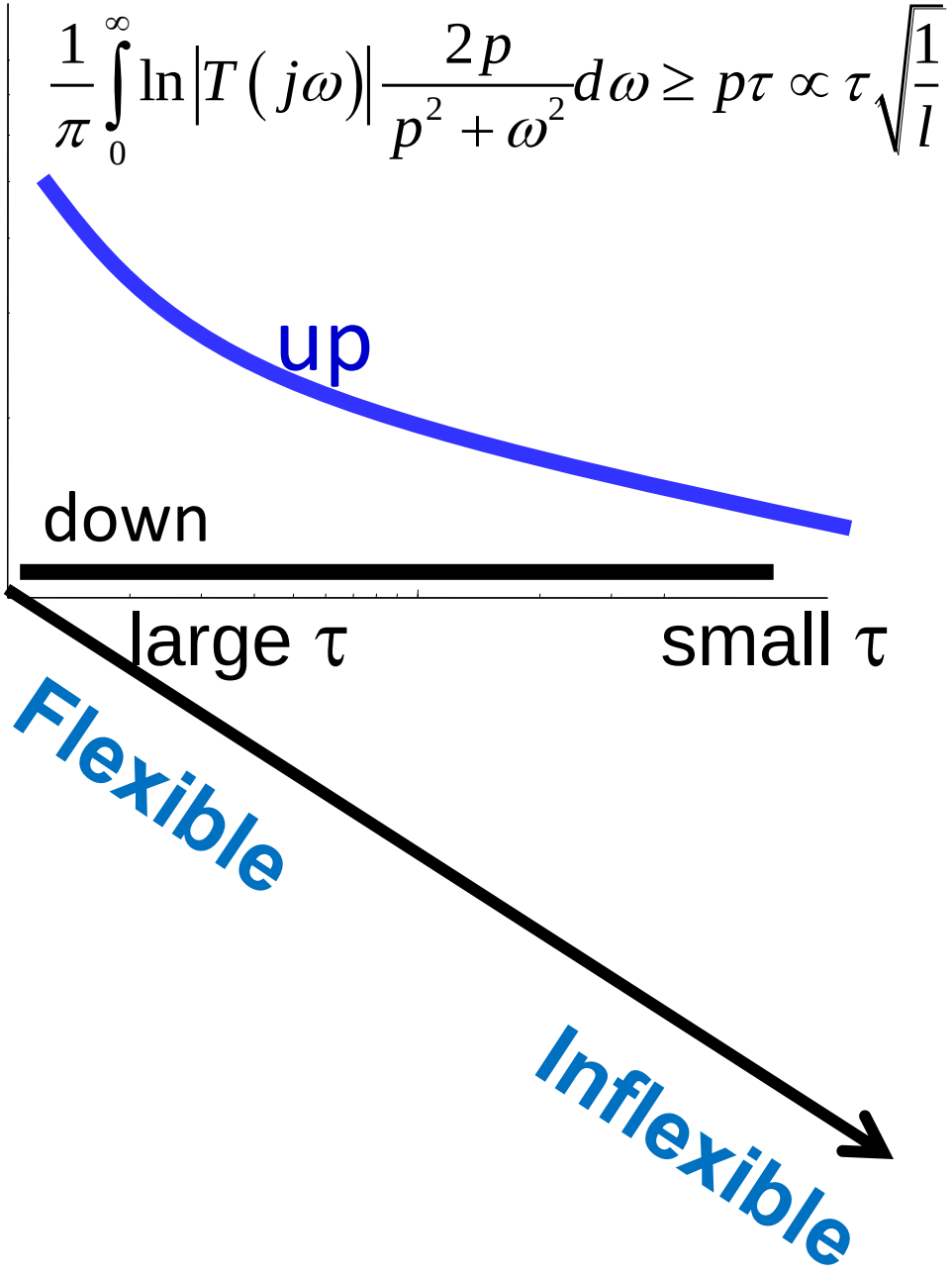


Computation is a component in control.

Fragility

$$\frac{1}{\pi}\int_0^\infty \ln\left|T(j\omega)\right|\frac{2p}{p^2+\omega^2}d\omega \geq p\tau \propto \tau\sqrt{\frac{1}{l}}$$

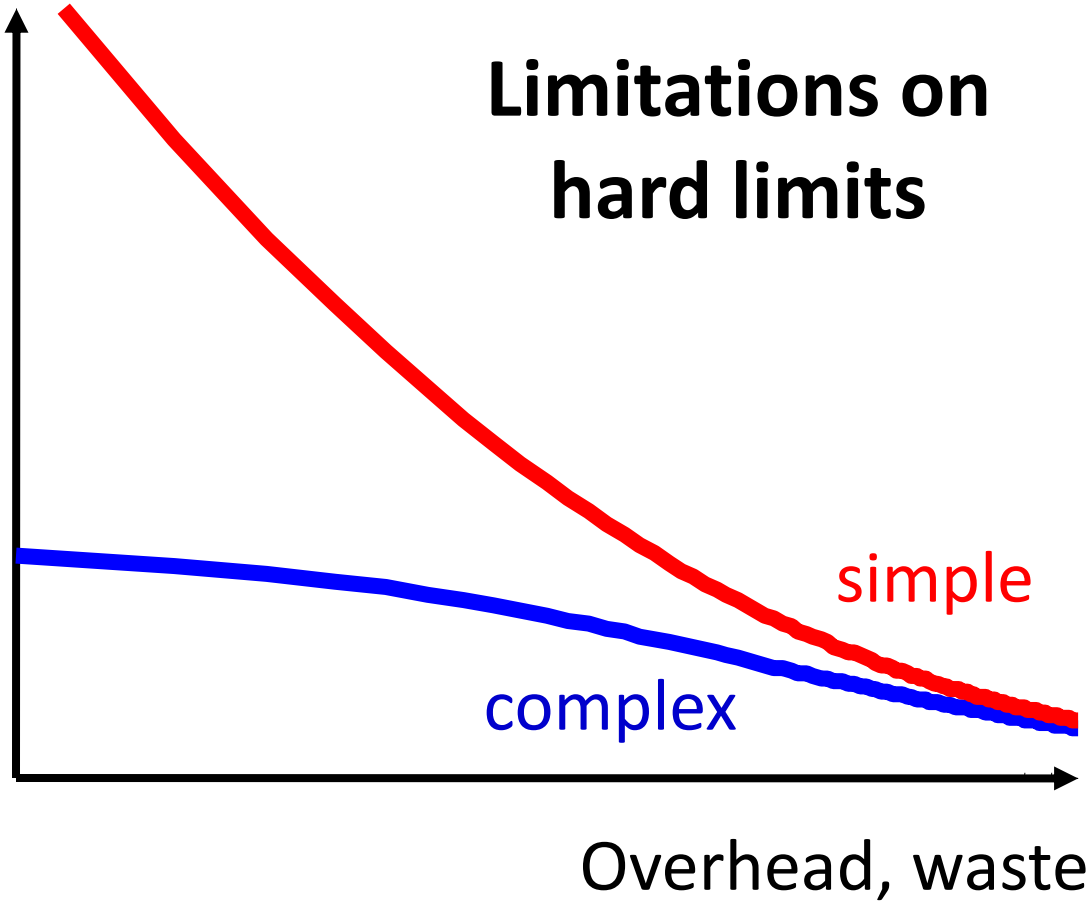
$$\tau\sqrt{\frac{1}{l}}$$



This needs formalization:

What ***flexibility*** makes control hard?

Large, structured uncertainty?



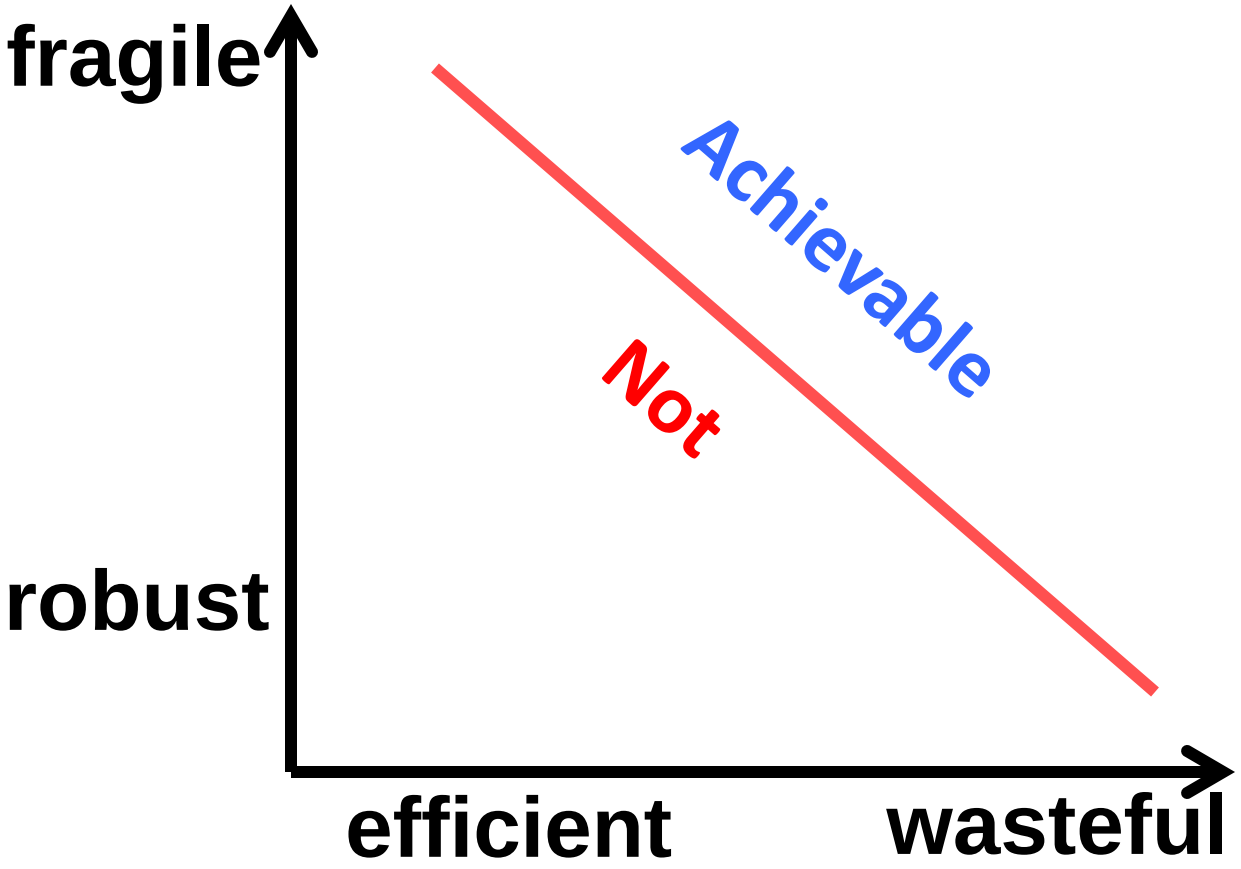
- General
- Rigorous
- First principle

?

Plugging in domain details

- Domain specific
- Ad hoc
- Phenomenological

Components of robustness



Components of robustness

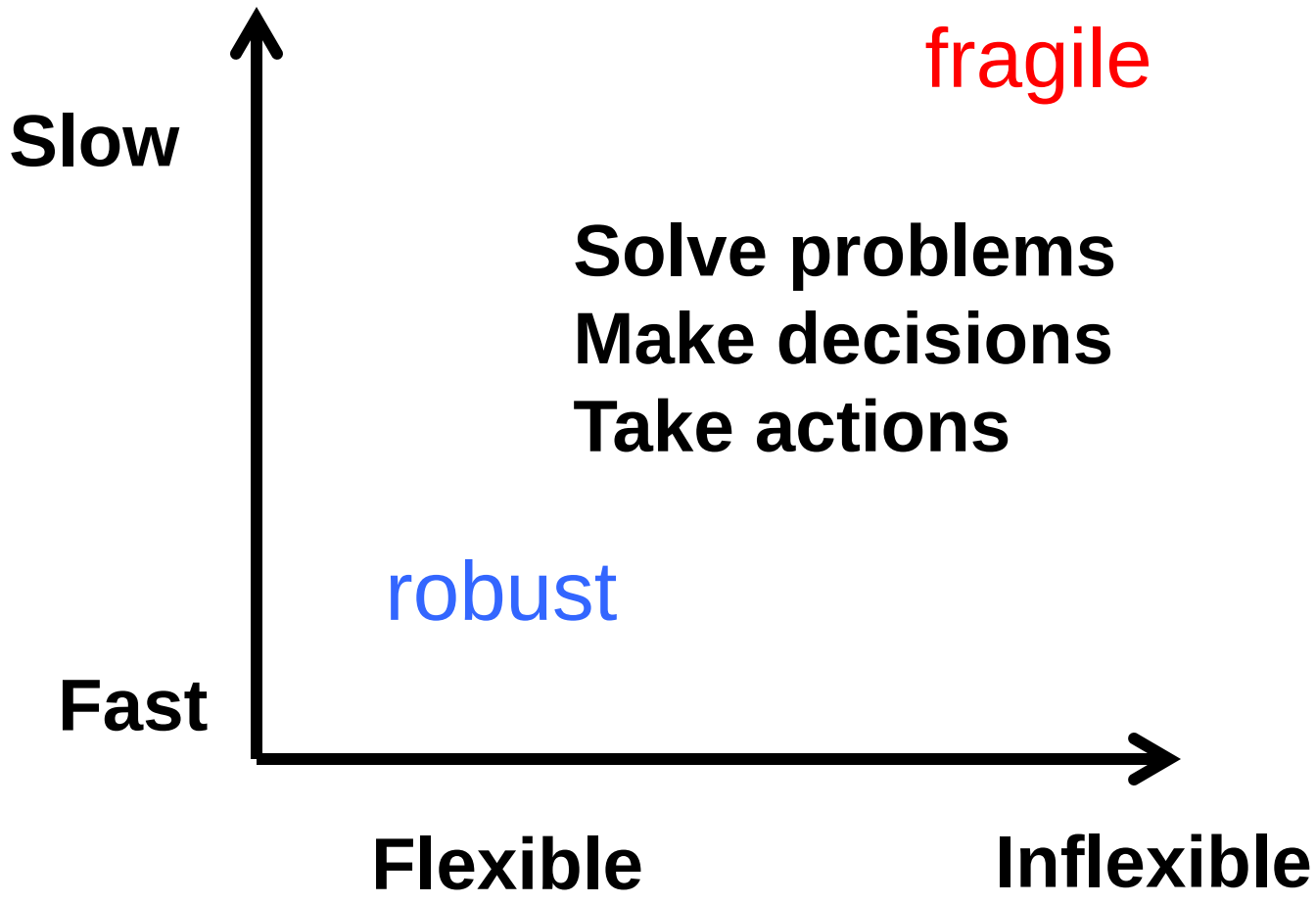
fragile

fragile

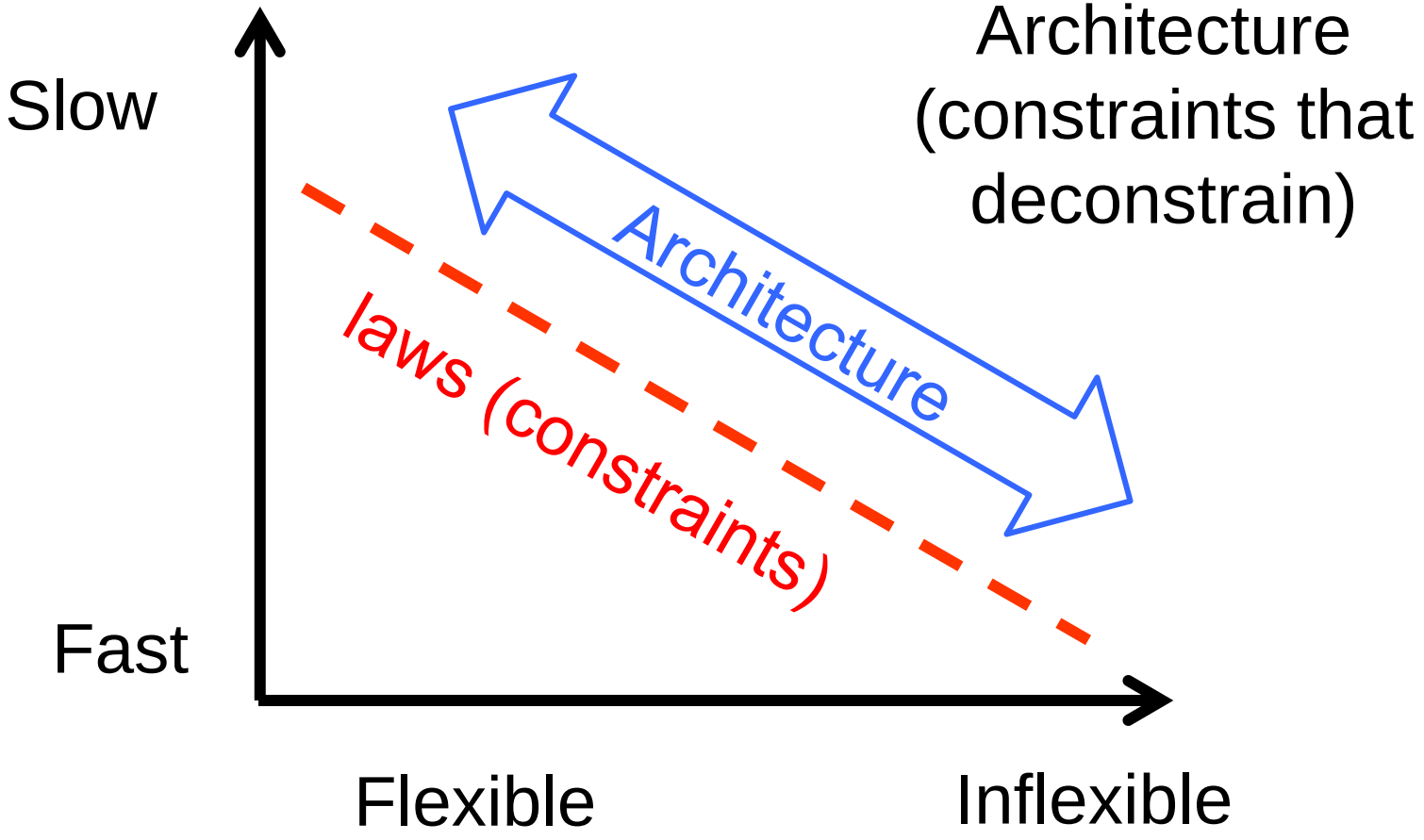
robust

robust

Speed and flexibility



Laws and architectures



Architecture case studies comparison

	Bacteria[+]	Internet[+]	Brain
Understood?	☺	☺☺	☹
By scientists?	☺	☹☹	☹
Live demos?!?	☹	☺	☺
Who cares?	☹*	☺	☺☺
Design quality?	☺☺	☺☹	☺☹
∃ Math?	☺	☺☺	☺☹

*Except for a few bacteriophiles (LC, SR, JD, ?)

[+]See also “Bacterial Internet” (LC)

“vertical” +“horizontal” evolution in Bacteria/Internet/Brain in Genes/Apps/Memes

- Vertical (lineages)
  - accumulation of small increments
  - de novo invention
  - Accelerated RosenCaporalian evolution
- Horizontal
  - Swap existing gene/app/meme
  - Source of most individual change?
- Both essential to large scale (r)evolution

“vertical” +“horizontal” evolution
in Bacteria/Internet/Brain
in Genes/Apps/Memes

- Evolution is ***not*** only (or even primarily) due to slow accumulation of random mutations
- Effective architectures facilitate ***all*** aspects of “evolvability”
- Lamarckian and Darwinian

“Evolvability”

- Robustness of lineages to large changes on long timescales
- Essentially an architectural question
  - What makes an architecture evolvable?
  - What does “architecture” mean here?
- What are the limits on evolvability?
- How does architecture, evolvability, robustness, and complexity relate?

- Key: tradeoffs, robustness, layering

"Nothing in *biology* makes sense except in the light of *evolution*."

T Dobzhansky

"Nothing in *evolution* makes sense except in the light of *biology*."

Tony Dean (U Minn) paraphrasing T Dobzhansky

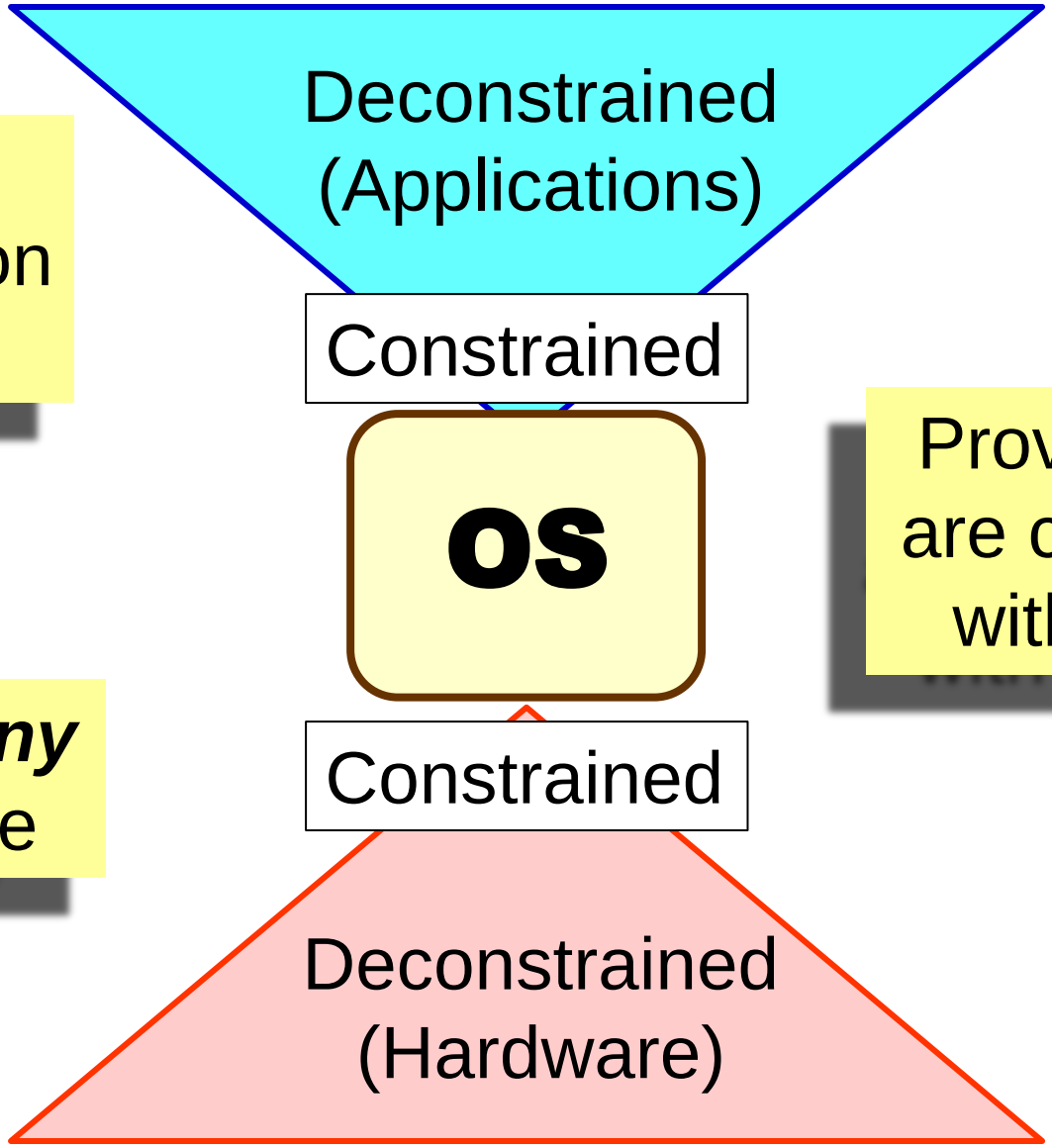
big picture from high level with a bit of Internet

	Bacteria	Internet	Brain
Understood?	☺	☺☺	☹
By scientists?	☺	☹☹	☹
Live demos?!?	☹	☺	☺
Who cares?	☹*	☺	☺☺
Design quality?	☺☺	☺☹	☺☹
∃ Math?	☺	☺☺	☺☹

Apps
OS
Hardware
Digital
Lumped
Distributed

Familiar layered architecture:
PC, smartphone, router, etc

“hourglass”



Any application can

Provided they are compatible with the OS

Run on ***any*** hardware

“hourglass”

Deconstrained
(Applications)

Many applications can

Constrained

OS

Run on ***this*** hardware

“hourglass”

almost

Any application can

Deconstrained (Applications)

Constrained

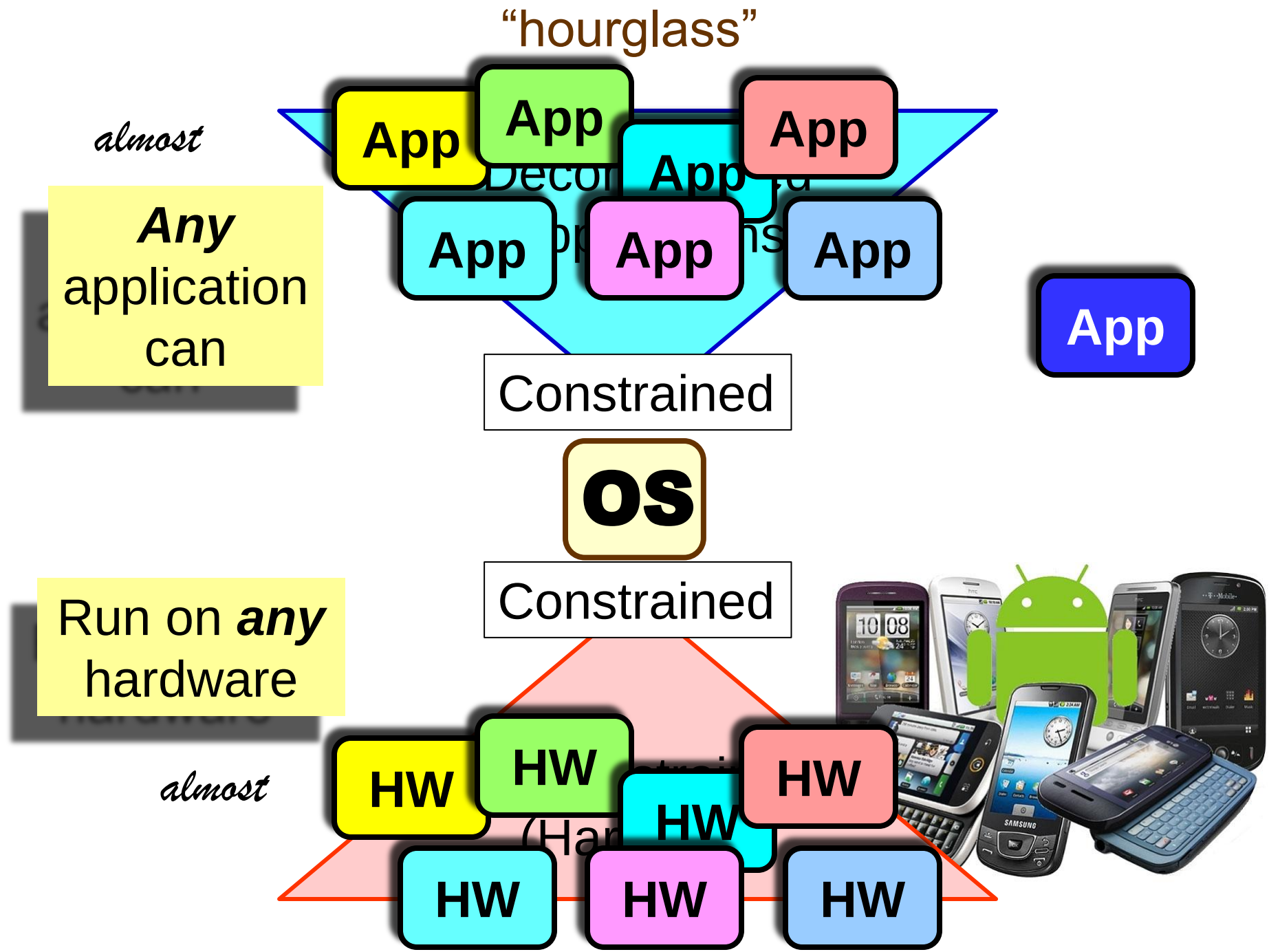
OS

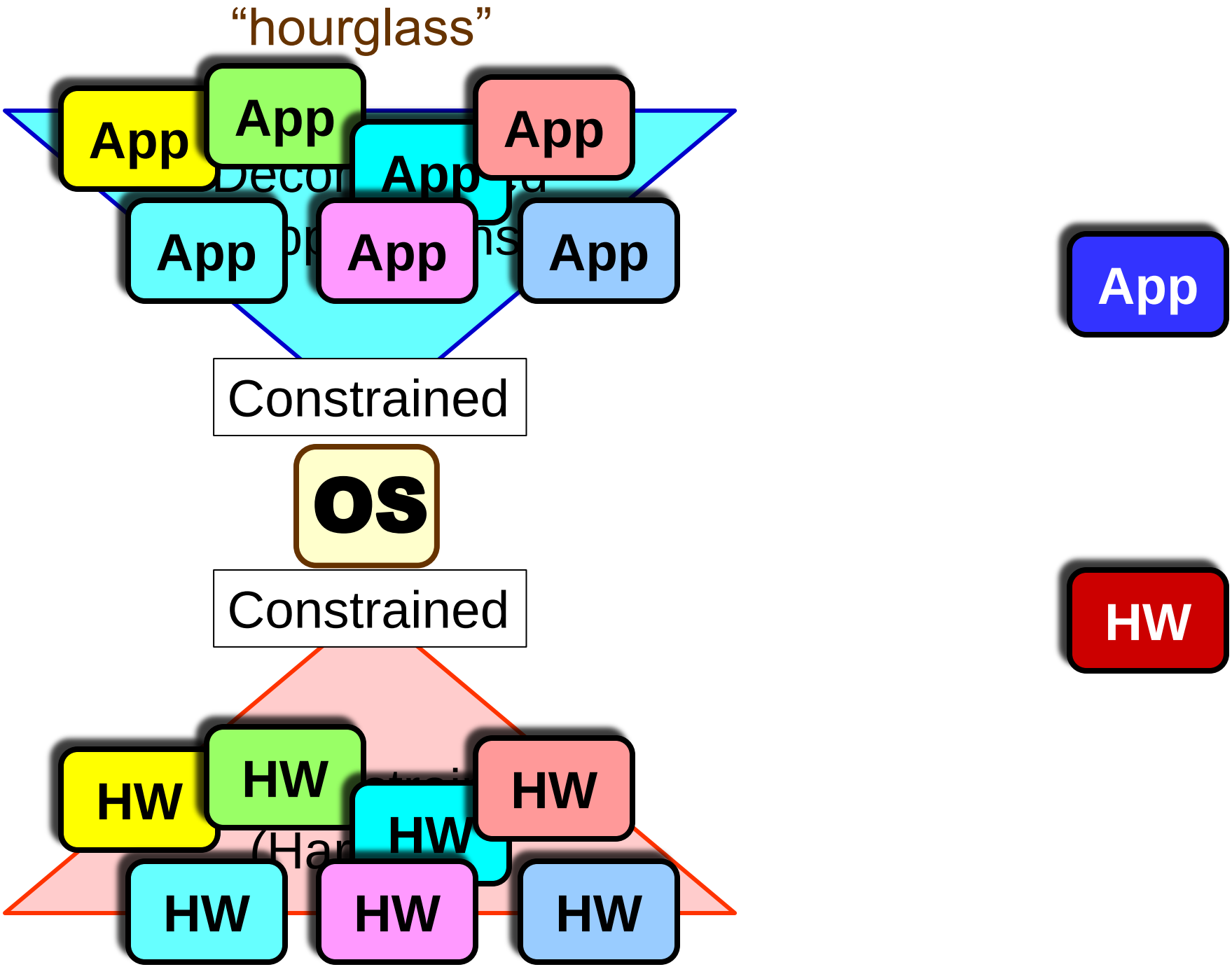
Run on ***any*** hardware

Constrained

Deconstrained (Hardware)

almost


"hourglass"
almost
Any application can
App
App
App
App
App
App
App
App
Constrained
OS
Constrained
Run on any hardware
almost
HW
HW
HW
HW
HW
HW
HW


“hourglass”
App
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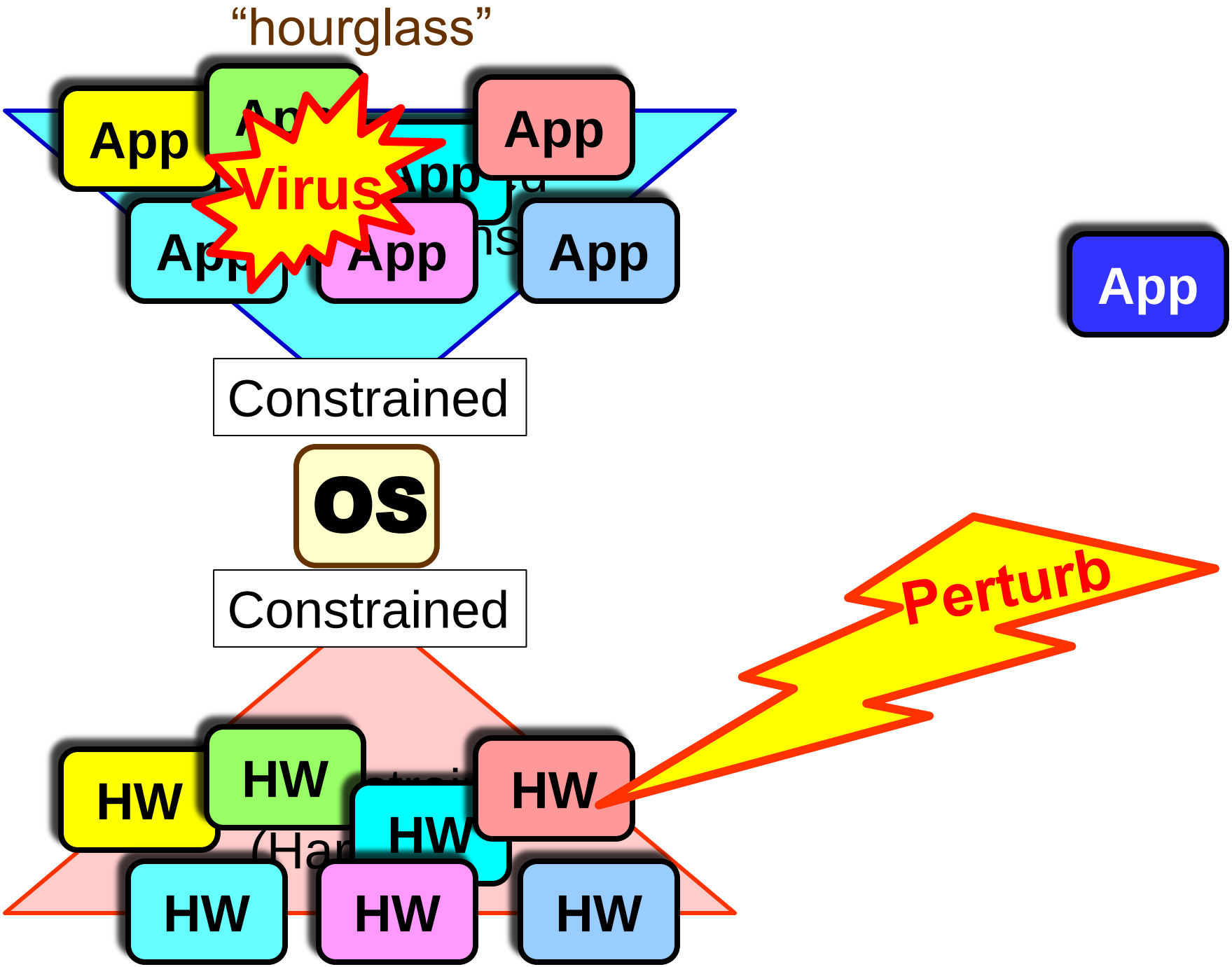
“hourglass”
App
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Constrained
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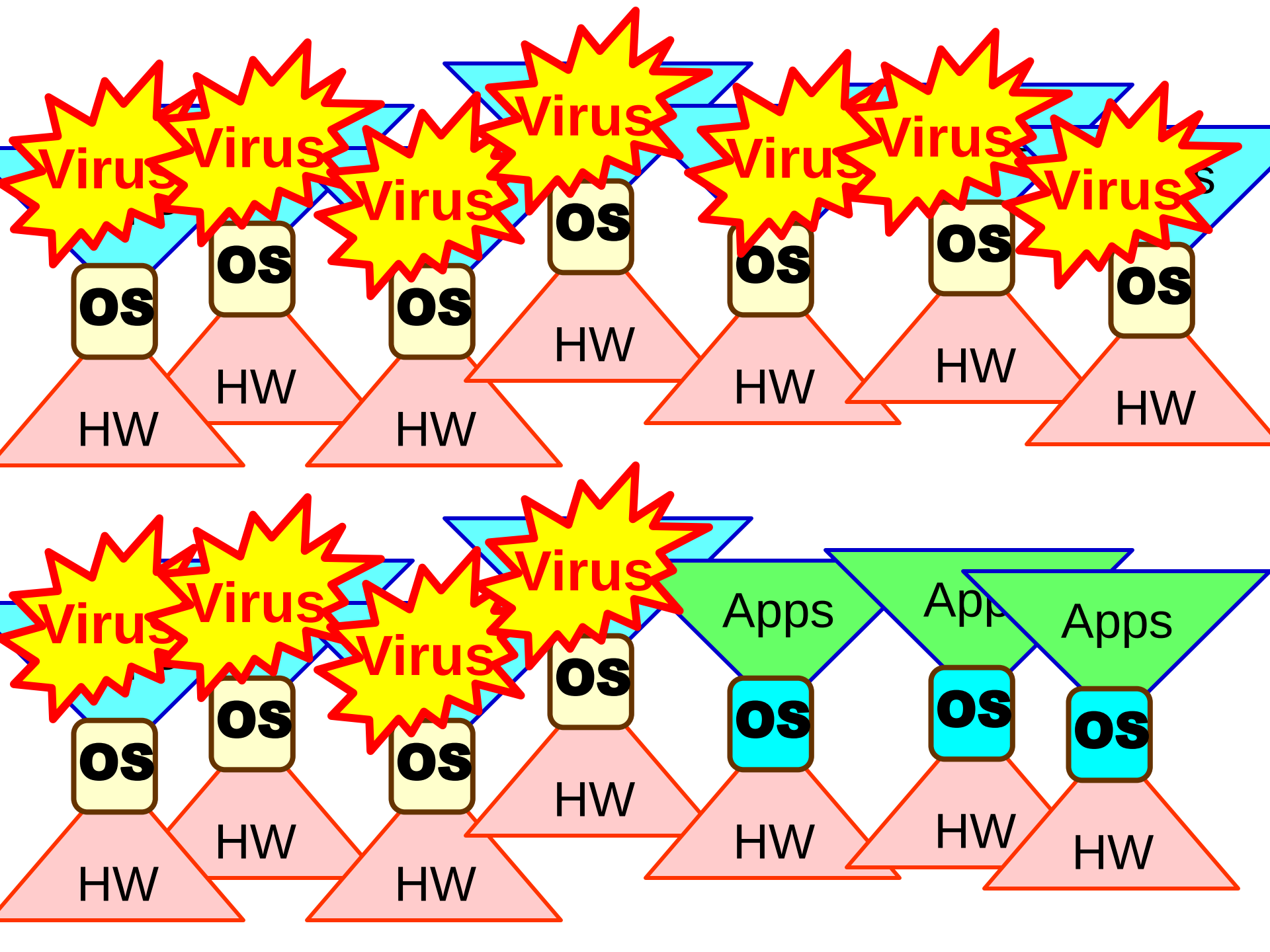
HW


Virus
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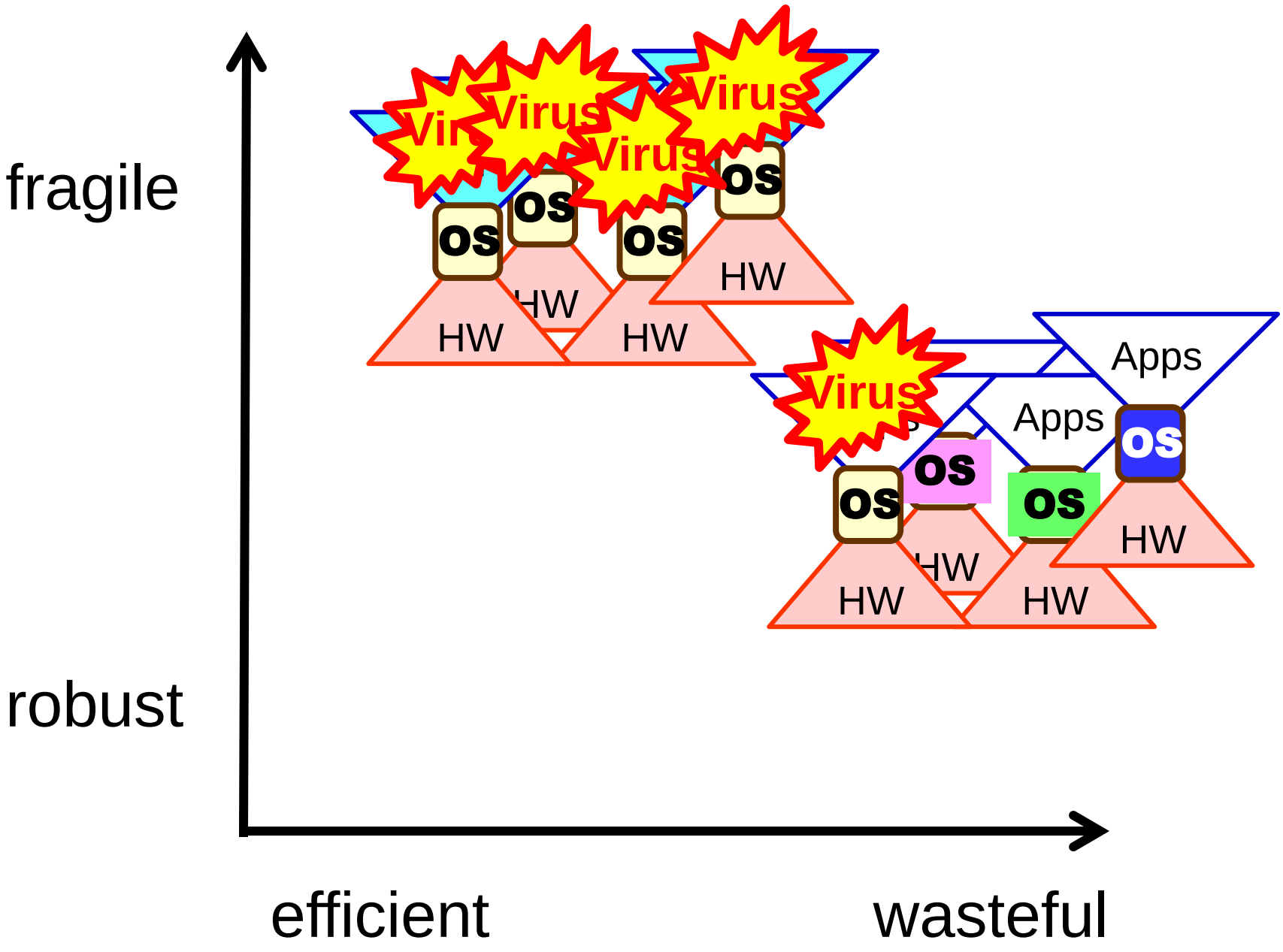
fragile
robust
efficient
wasteful
Virus
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Virus
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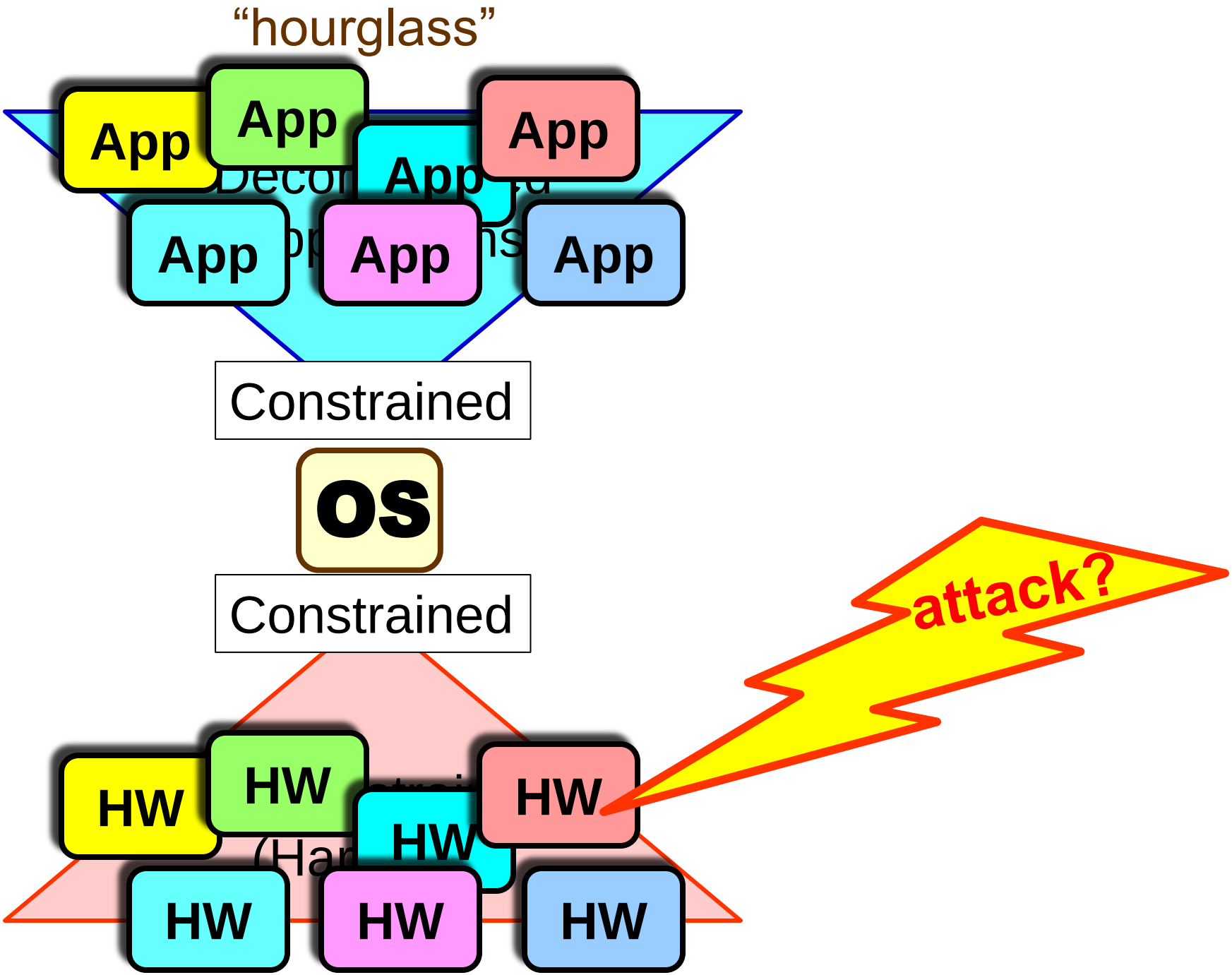
“hourglass”
App
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App
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App
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Constrained
OS
Constrained
attack?
HW
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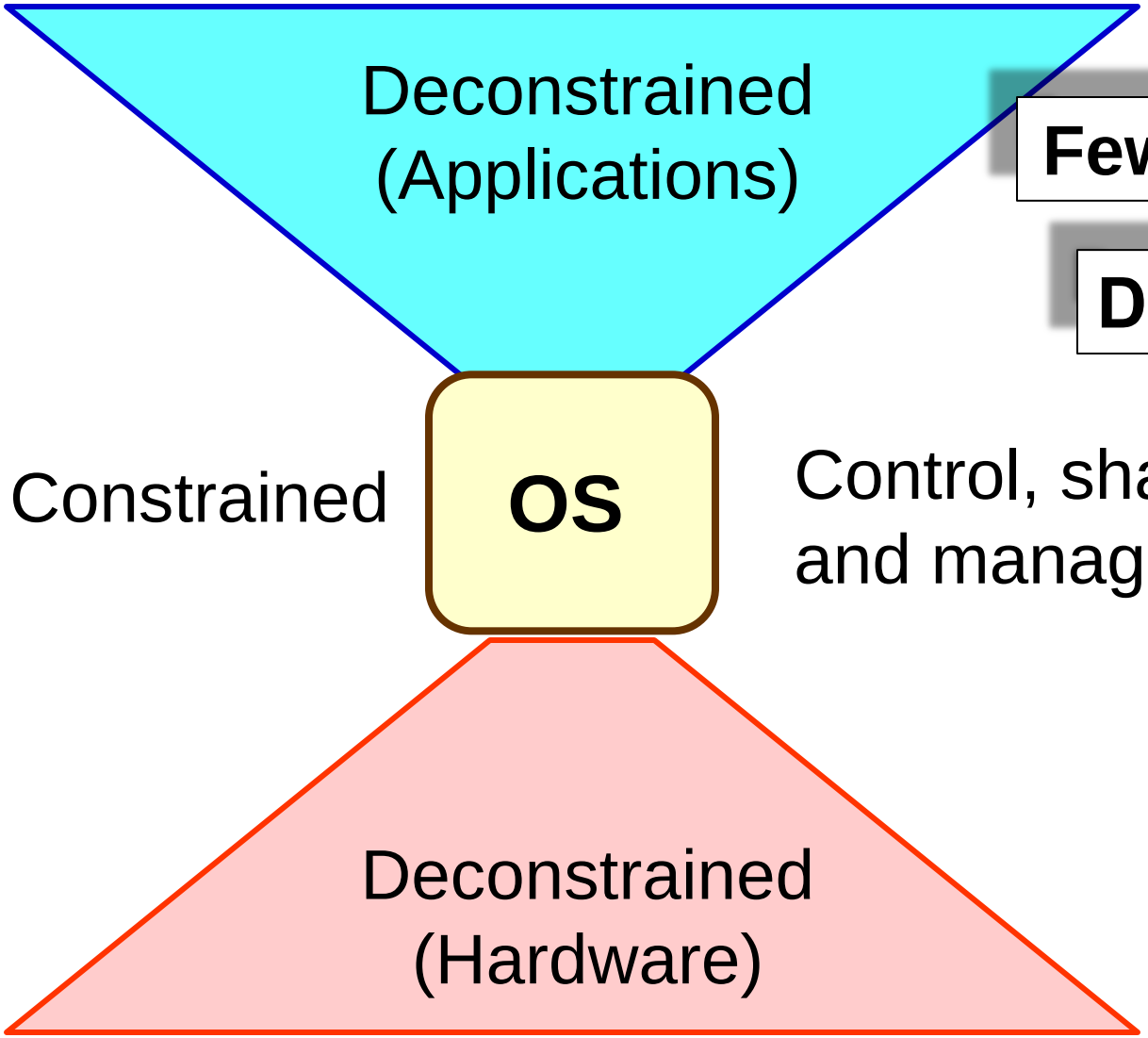
HW
HW
HW

Layered architectures

Essentials CS 101

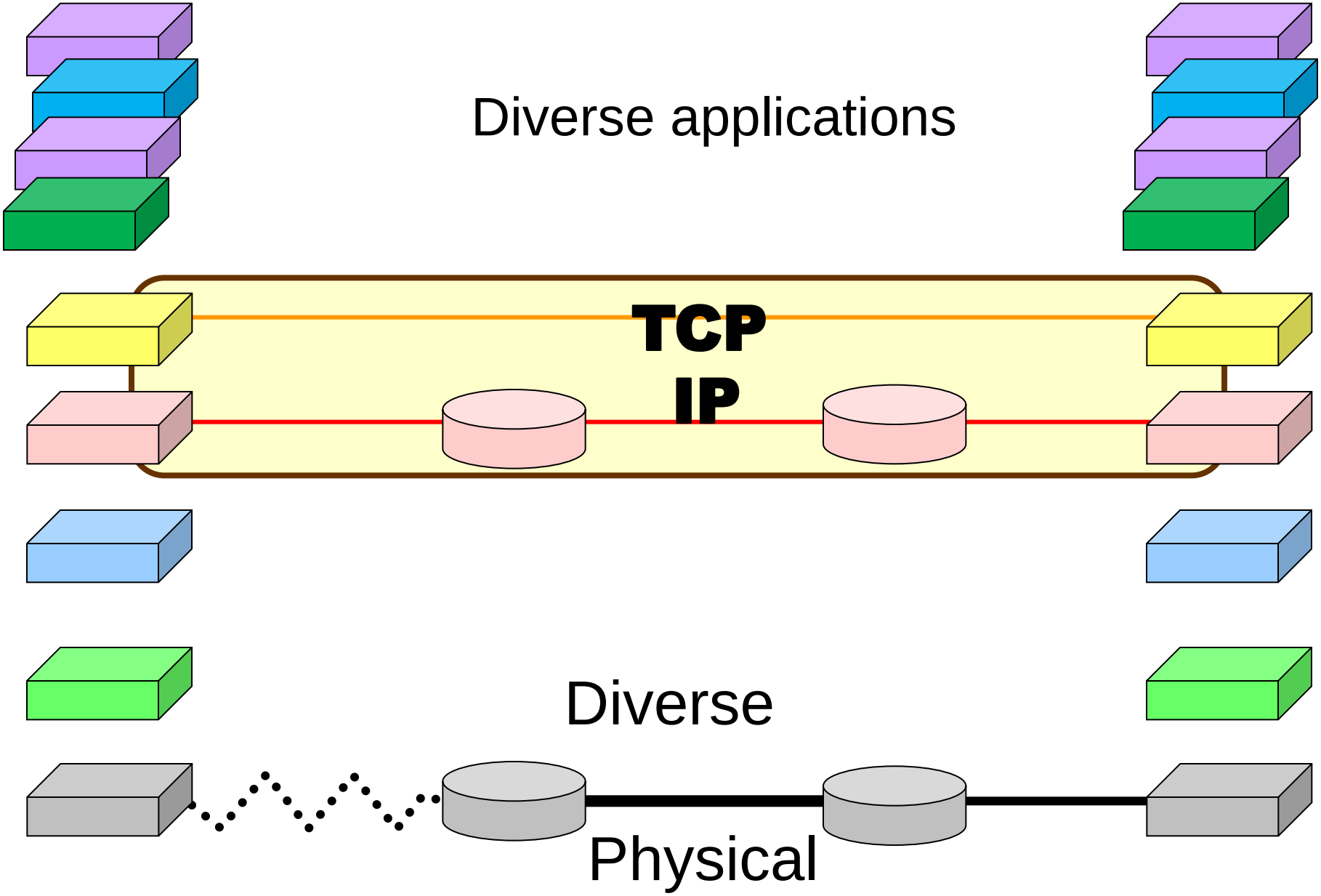


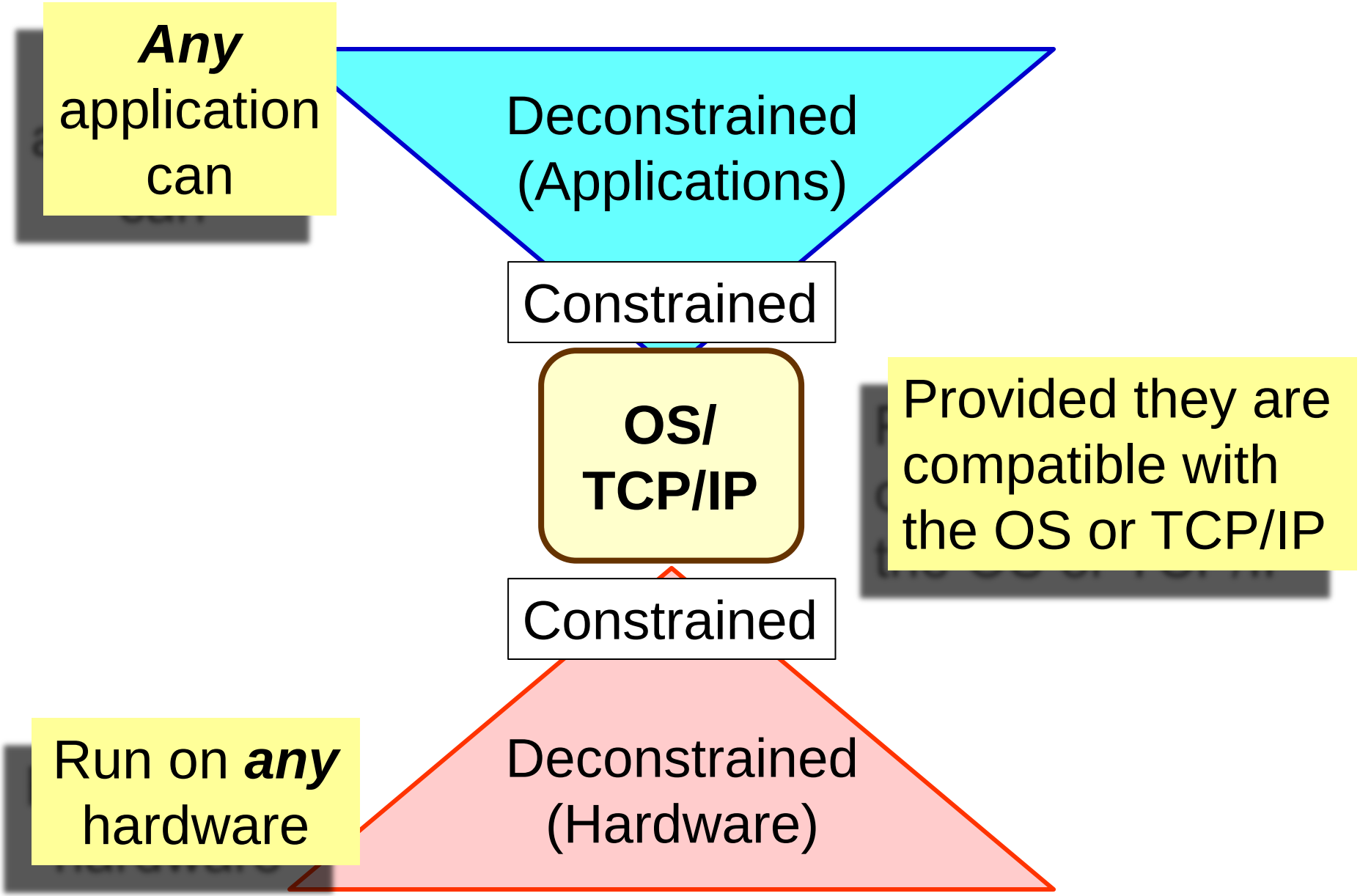
Few global variables

Don’t cross layers

Control, share, virtualize,
and manage resources

Processing
Memory
I/O


Diverse applications
TCP
IP
Diverse
Physical


Any application can
Deconstrained (Applications)
Constrained
OS/ TCP/IP
Provided they are compatible with the OS or TCP/IP
Constrained
Run on ***any*** hardware
Deconstrained (Hardware)

Tradeoffs:
PC, smartphone, router, etc

Apps

OS

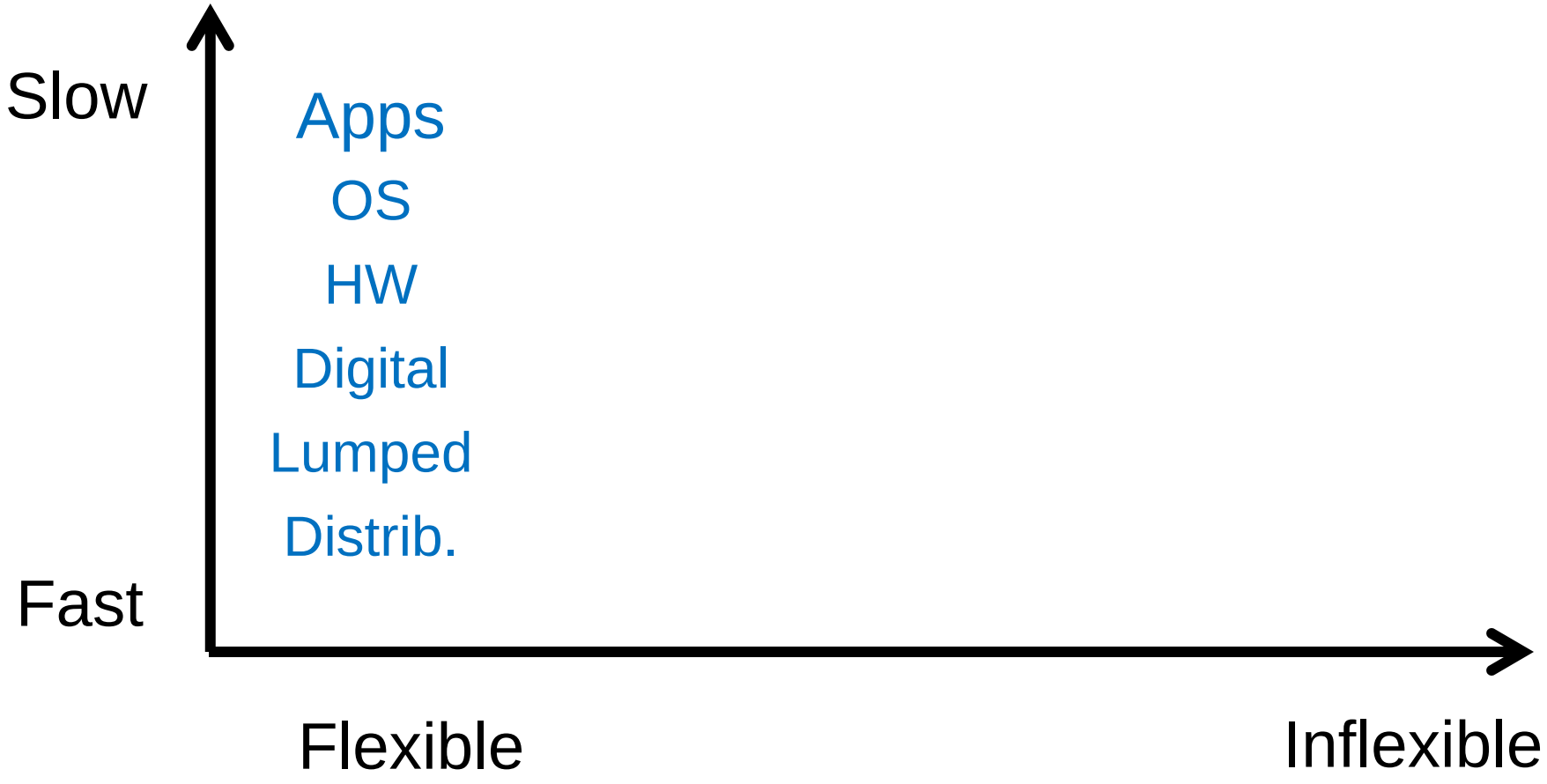
HW

Digital

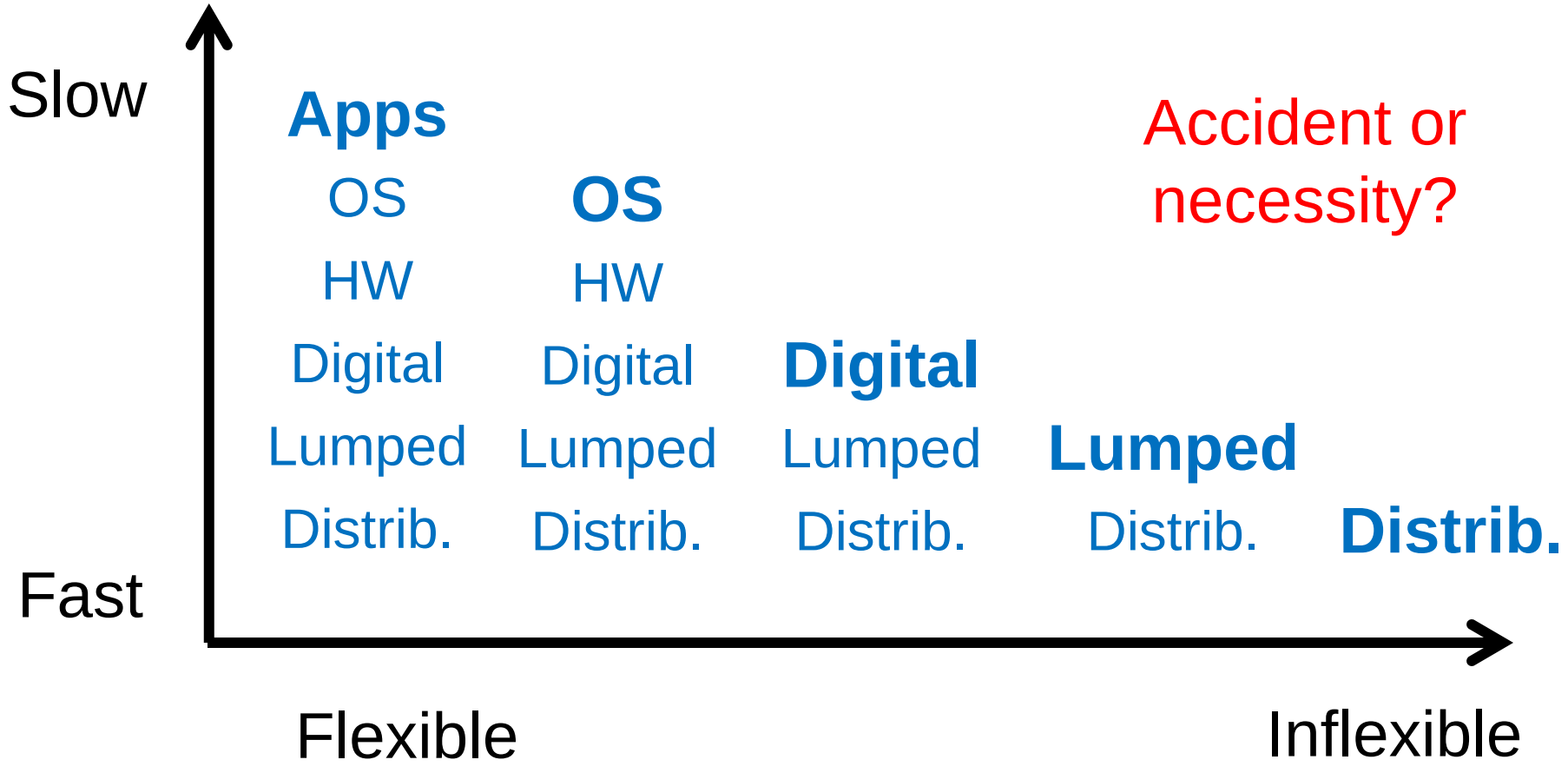
Lumped

Distrib.

Tradeoffs:
PC, smartphone, router, etc



Tradeoffs:
PC, smartphone, router, etc



Slow

Fast

Flexible

Inflexible

Apps

OS

HW

Digital

Lumped

Distrib.

OS

HW

Digital

Lumped

Distrib.

Digital

Lumped

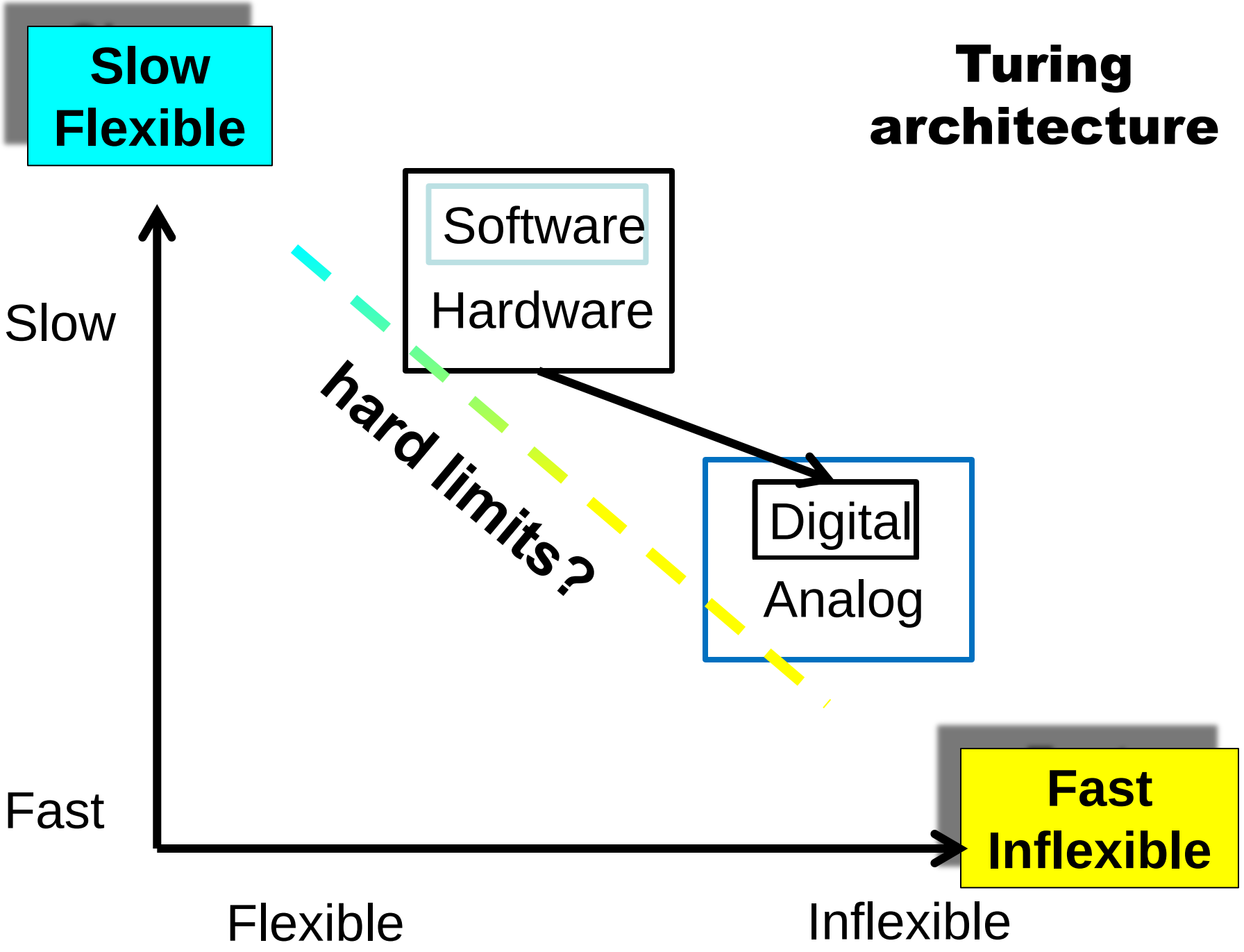
Distrib.

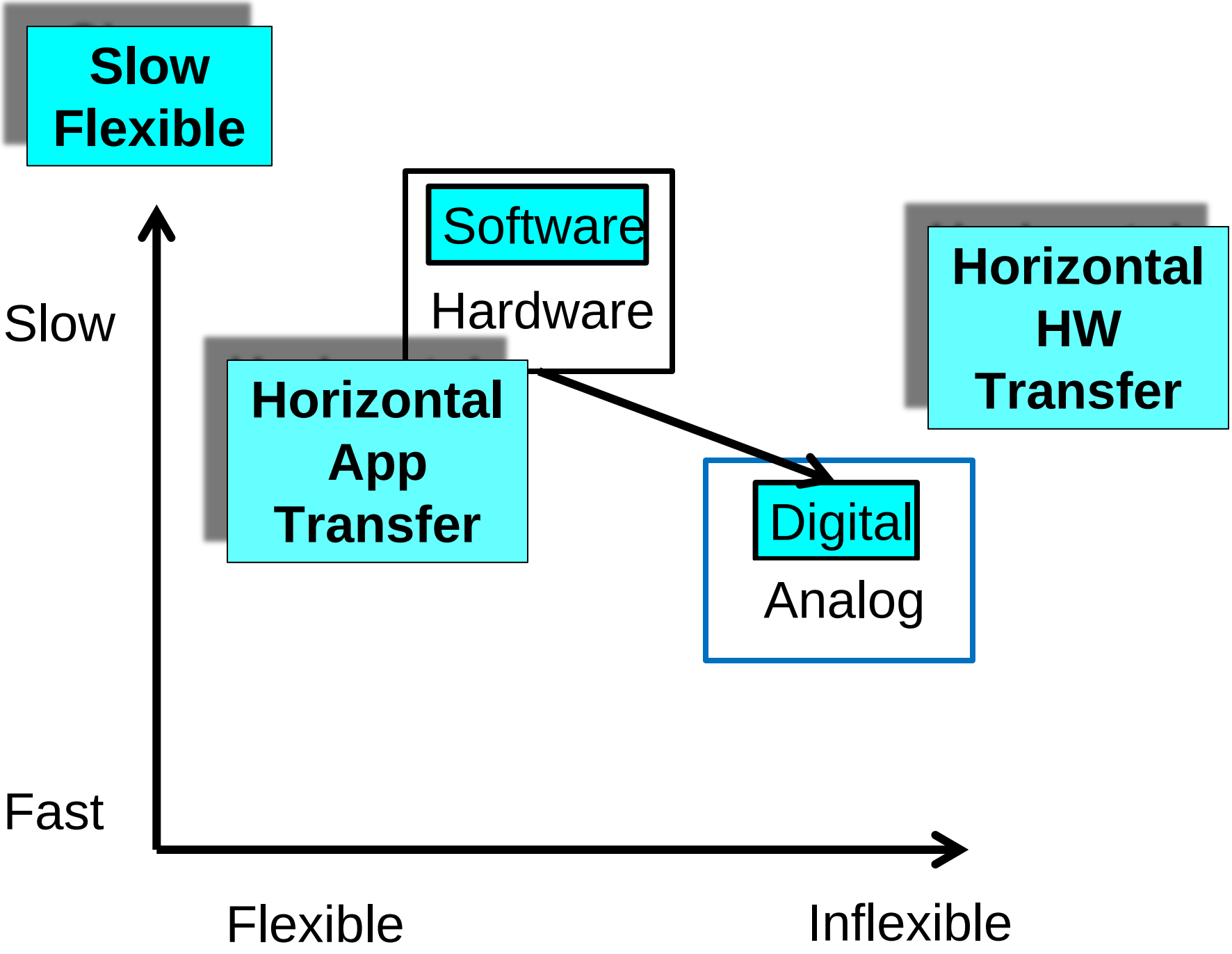
Lumped

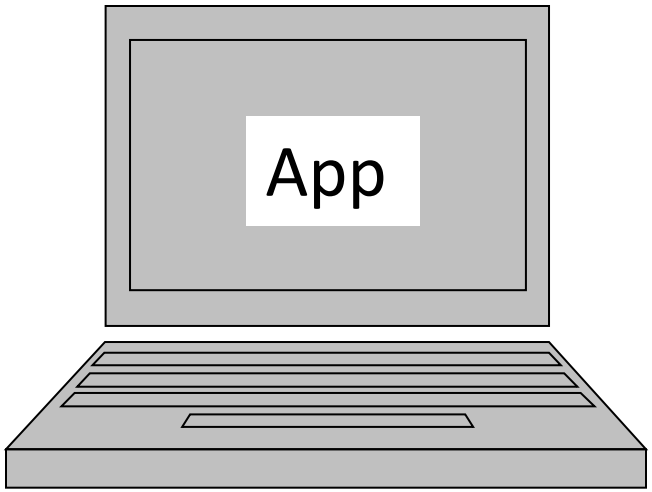
Distrib.

Distrib.

Architecture?

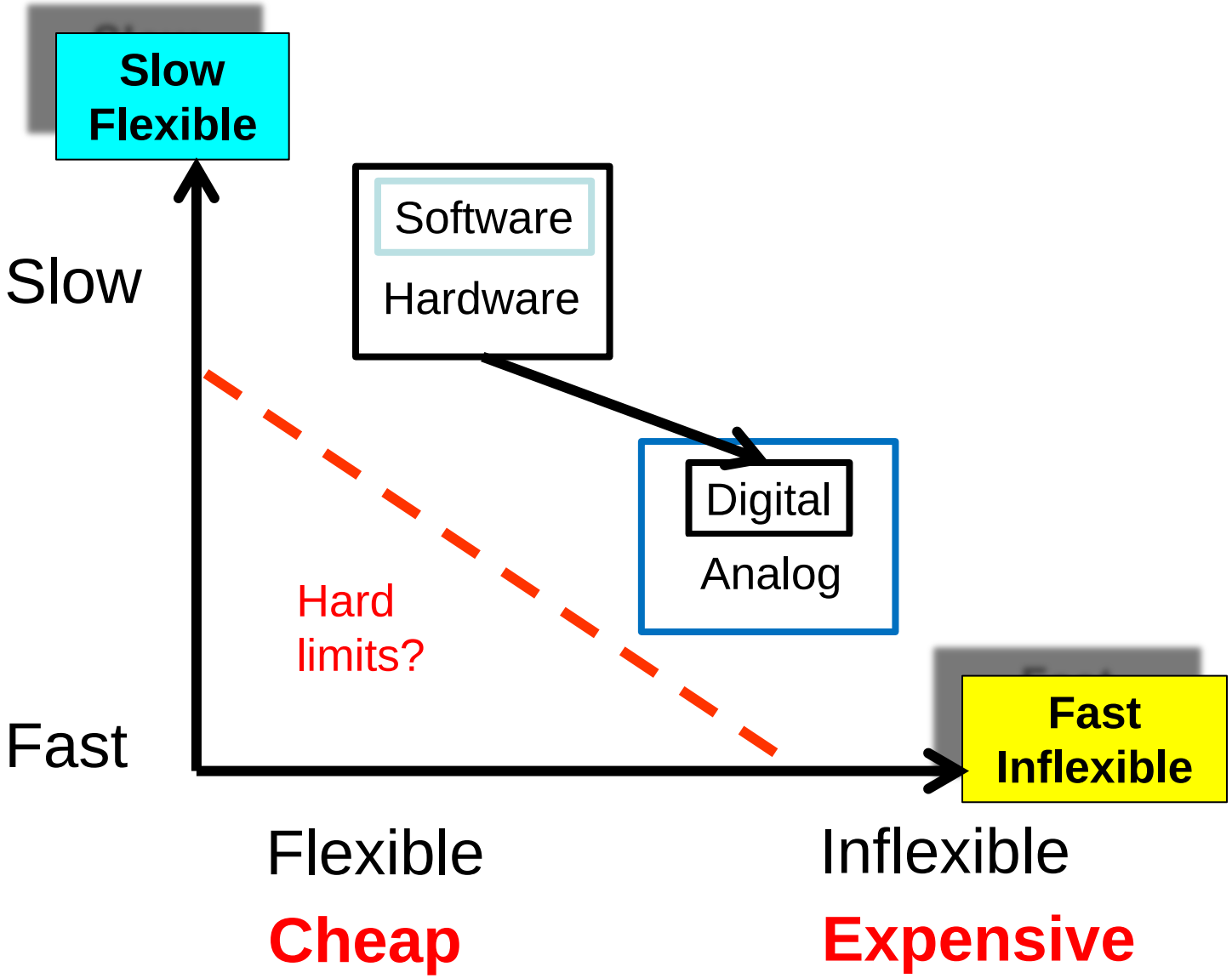

Slow
Flexible
Turing
architecture
Software
Hardware
hard limits?
Digital
Analog
Slow
Fast
Fast
Inflexible
Flexible
Inflexible


Slow
Flexible
Software
Hardware
Horizontal
HW
Transfer
Slow
Horizontal
App
Transfer
Digital
Analog
Fast
Flexible
Inflexible

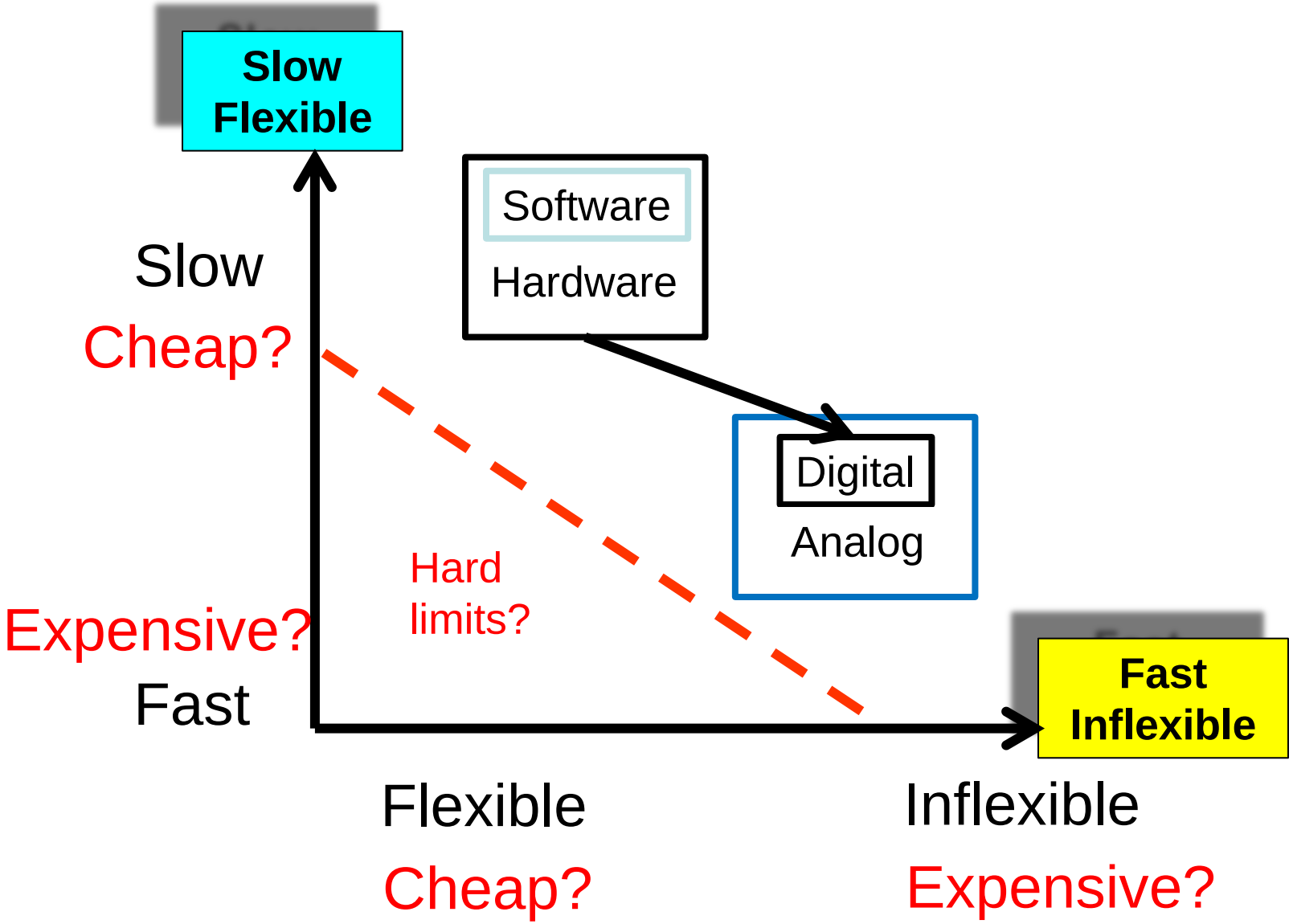


What you see:
The hardware interface and the application function

Shared architecture and infrastructure is and ***must be*** mostly hidden


Slow
Flexible
Software
Hardware
Slow
Digital
Analog
Hard
limits?
Fast
Fast
Inflexible
Flexible
Inflexible
Cheap
Expensive

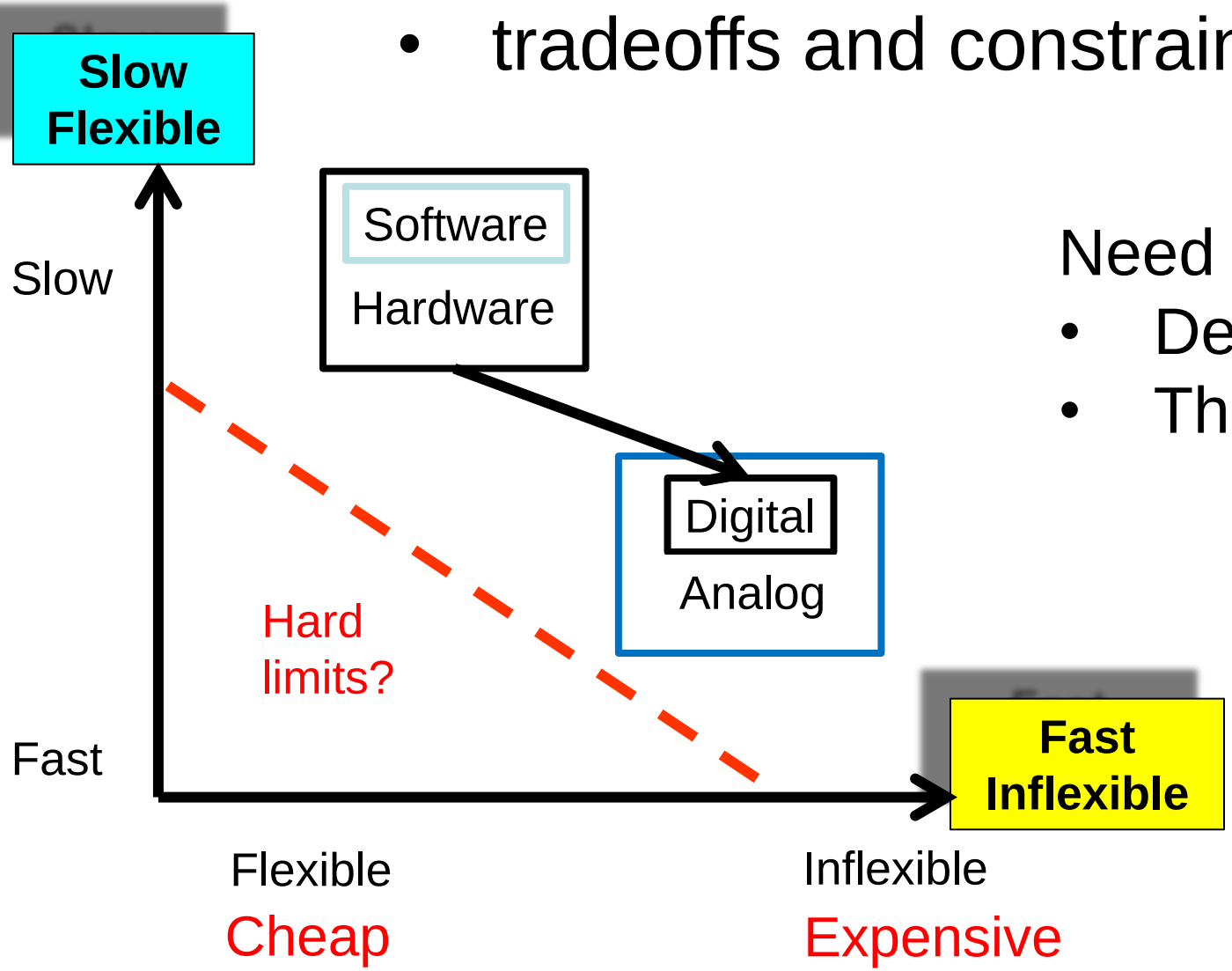
Efficiency?


Slow
Flexible
Software
Hardware
Digital
Analog
Fast
Inflexible
Slow
Cheap?
Expensive?
Fast
Hard
limits?
Flexible
Cheap?
Inflexible
Expensive?

Efficiency?

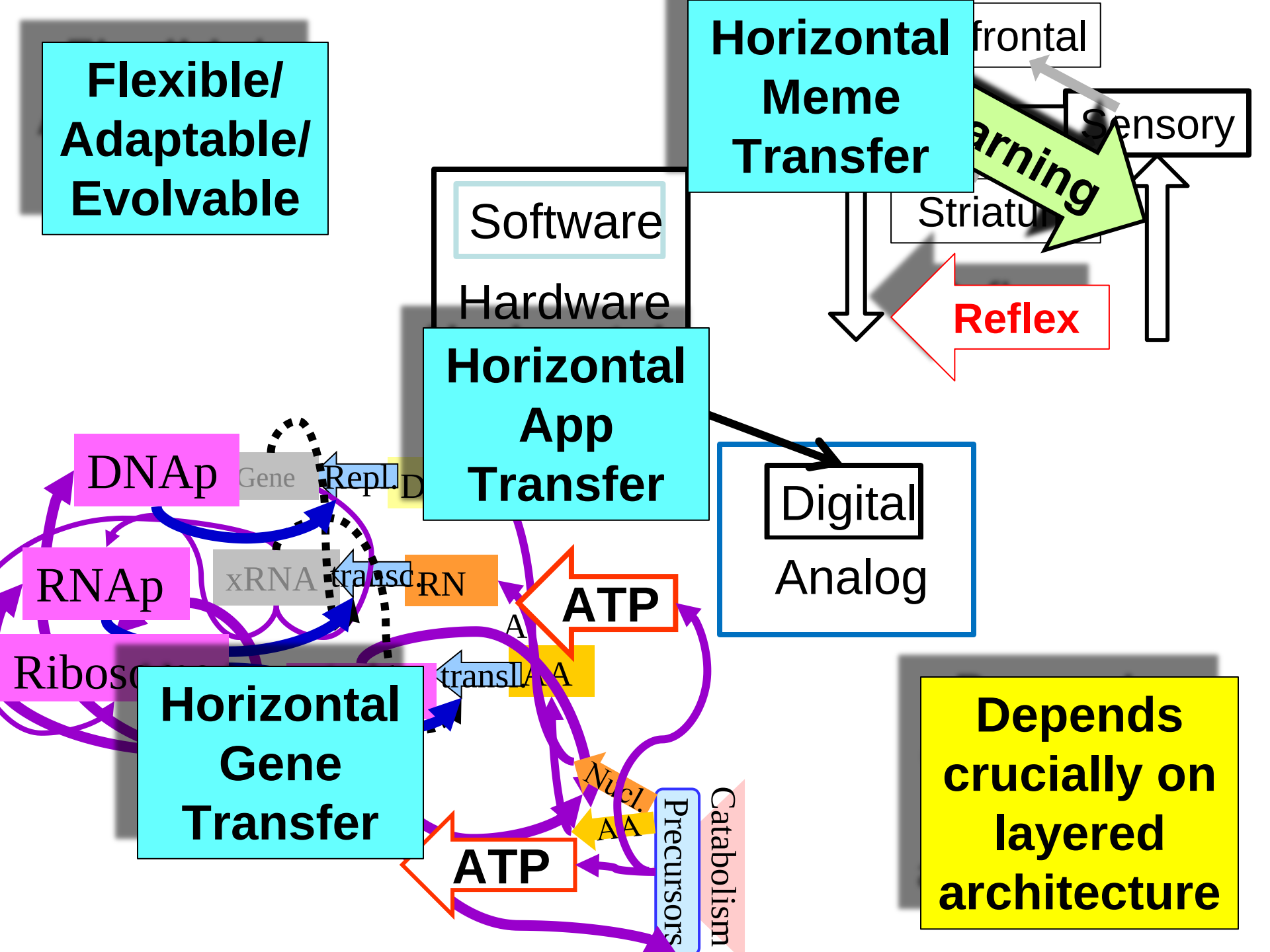
Bacteria and brains have similar:

- layered architectures
- tradeoffs and constraints



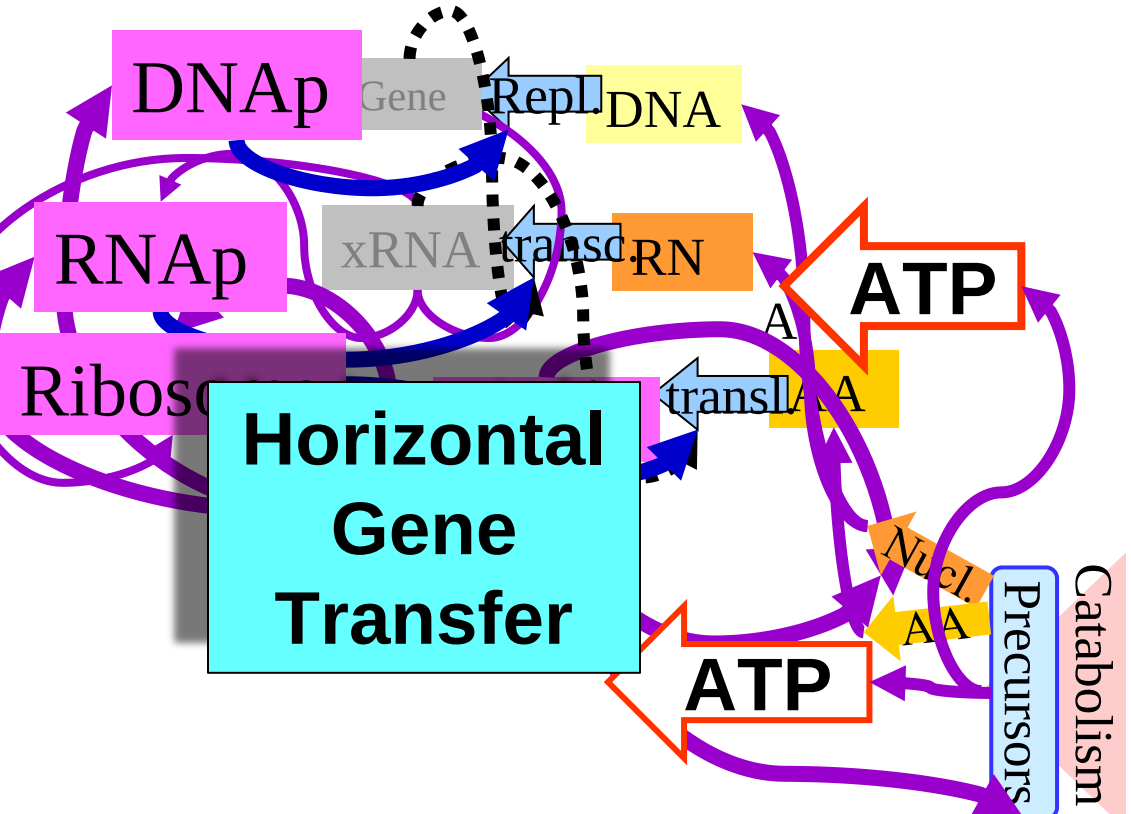
Need

- Details
- Theorems


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

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

- ~ 4K genes per cell
- ~20K *different* genes in total
- ~ 1K universally shared genes
- ~ 300 essential (minimal) genes



See slides on bacterial biosphere

Mechanisms in molecular biology

0. HGT (Horizontal Gene Transfer)
1. DNA replication
2. DNA repair
3. Mutation
4. Transcription
5. Translation
6. Metabolism
7. Signal transduction
8. …

Think of this as a “protocol stack”

Control 1.0

0. HGT
1. DNA replication
2. DNA repair
3. Mutation
4. Transcription
5. Translation
6. Metabolism
7. Signal transduction
8. …

Highly controlled

Think of this as a “protocol stack”

Control 2.0

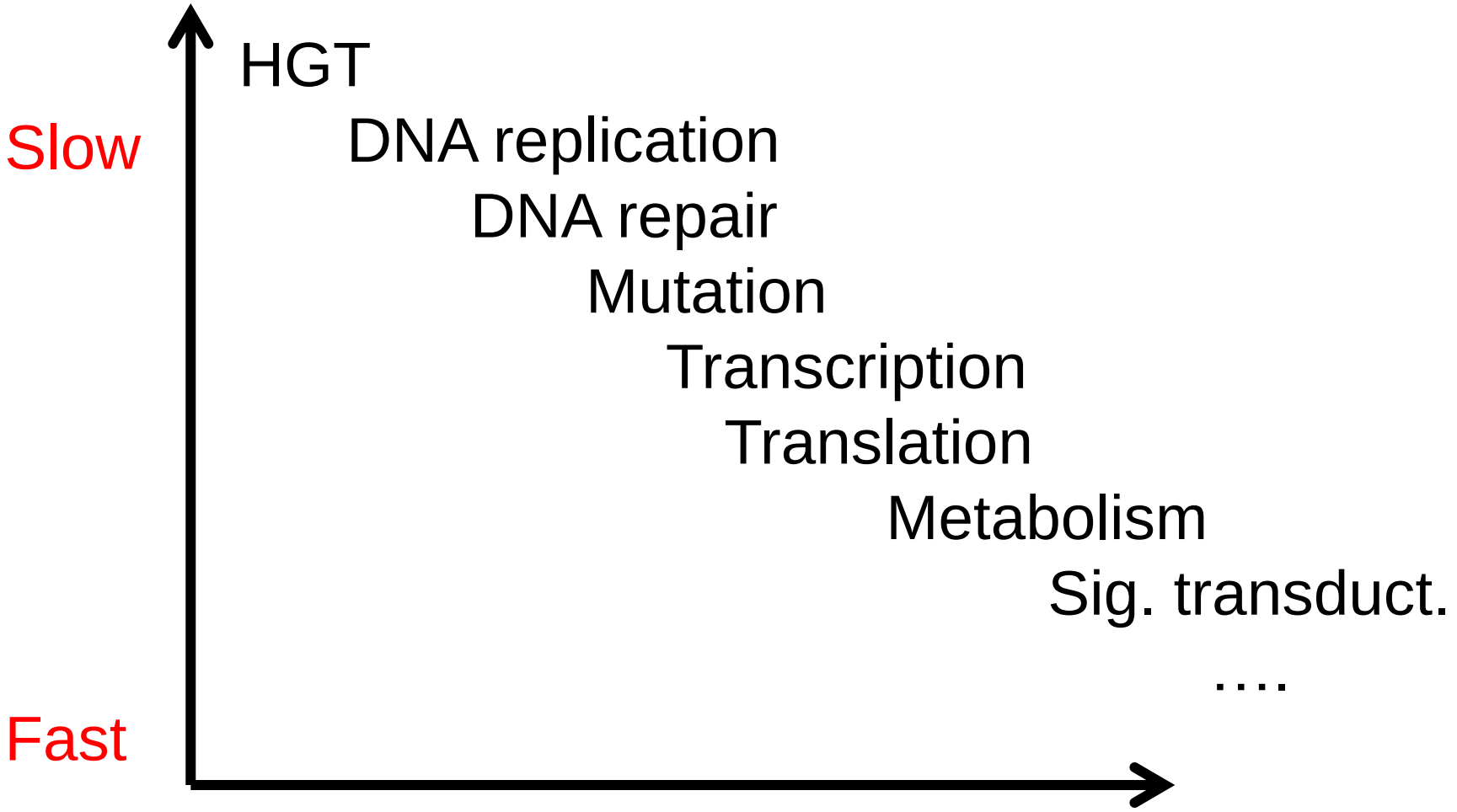
0. HGT
1. DNA replication
2. DNA repair
3. Mutation
4. Transcription
5. Translation
6. Metabolism
7. Signal transduction
8. …

Highly controlled ?!?

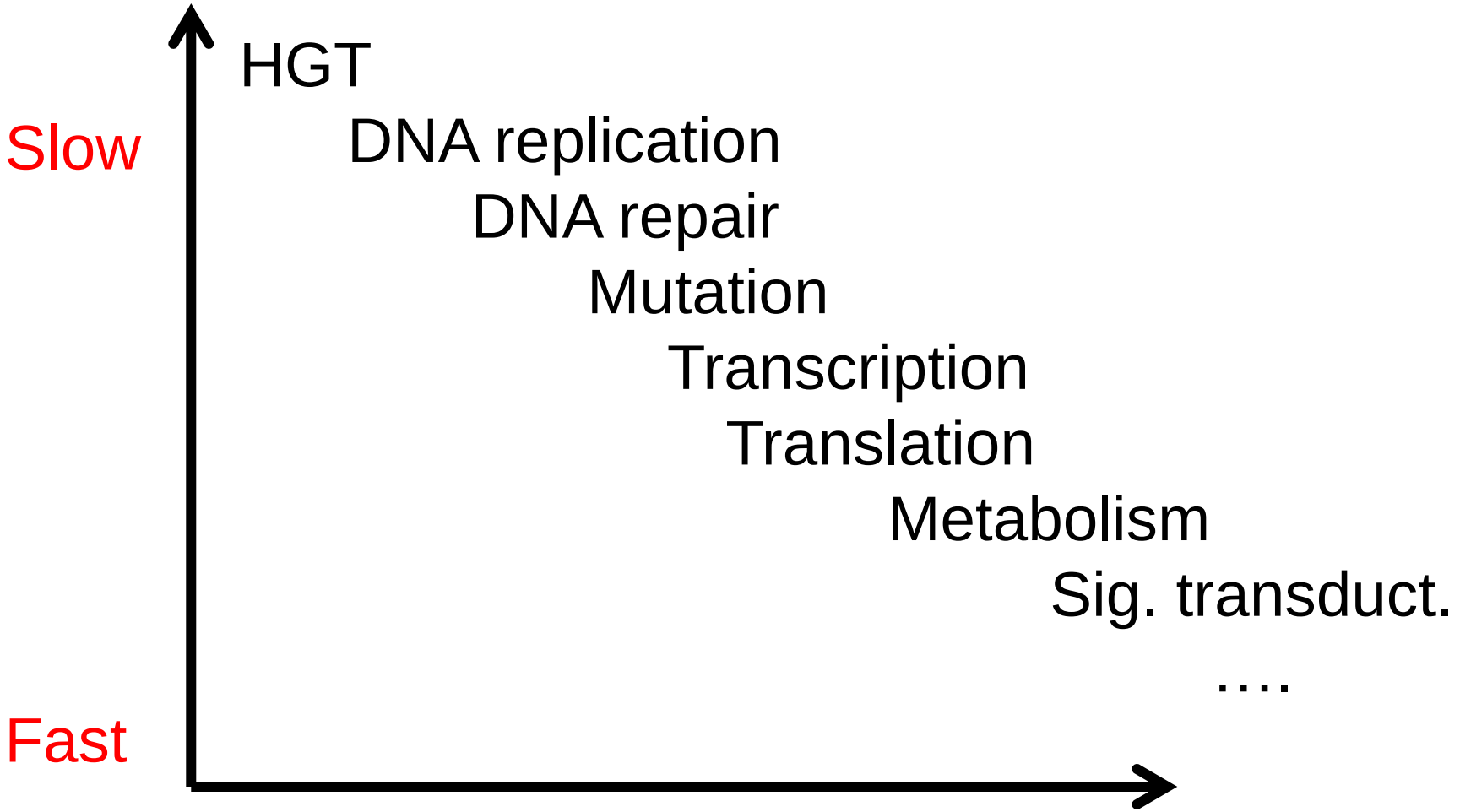
Highly controlled

Think of this as a “protocol stack”

Control 2.0


HGT
DNA replication
DNA repair
Mutation
Transcription
Translation
Metabolism
Sig. transduct.
….
Slow
Fast
Flexible
Cheap
Inflexible
Expensive

Control 2.0

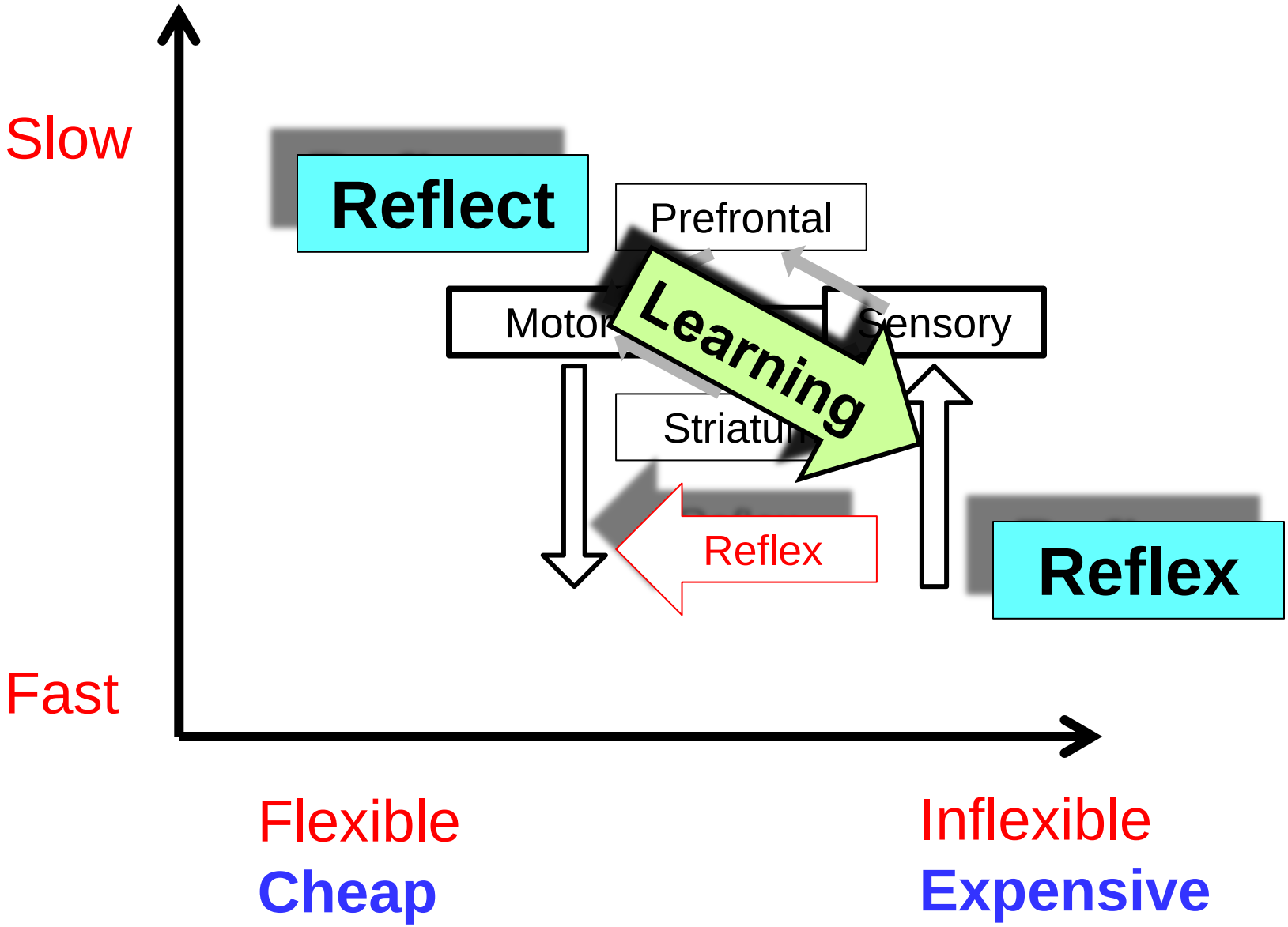

HGT
DNA replication
DNA repair
Mutation
Transcription
Translation
Metabolism
Sig. transduct.
….
Slow
Fast
Flexible
Cheap
Inflexible
Expensive

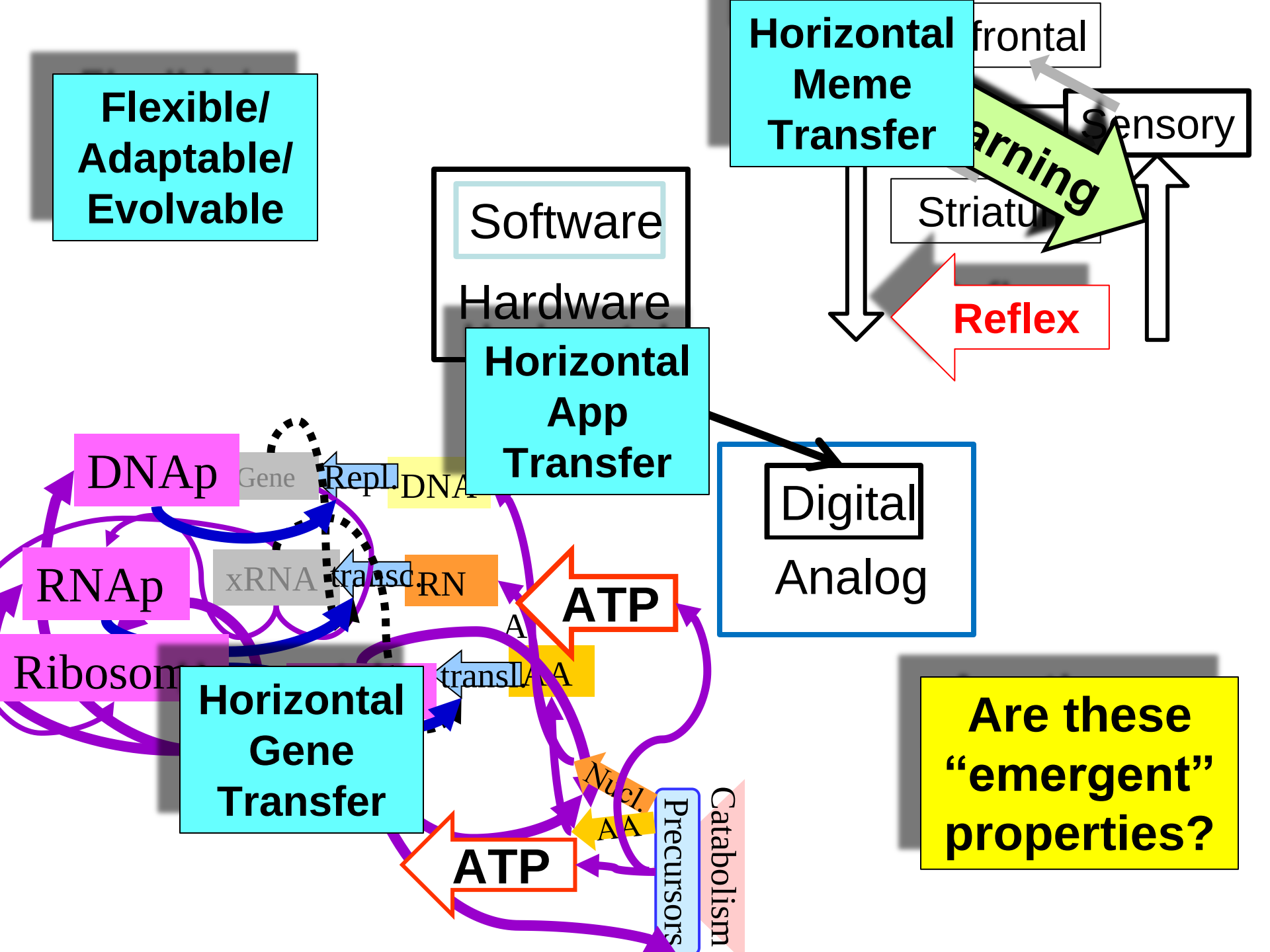
CNS “stack”

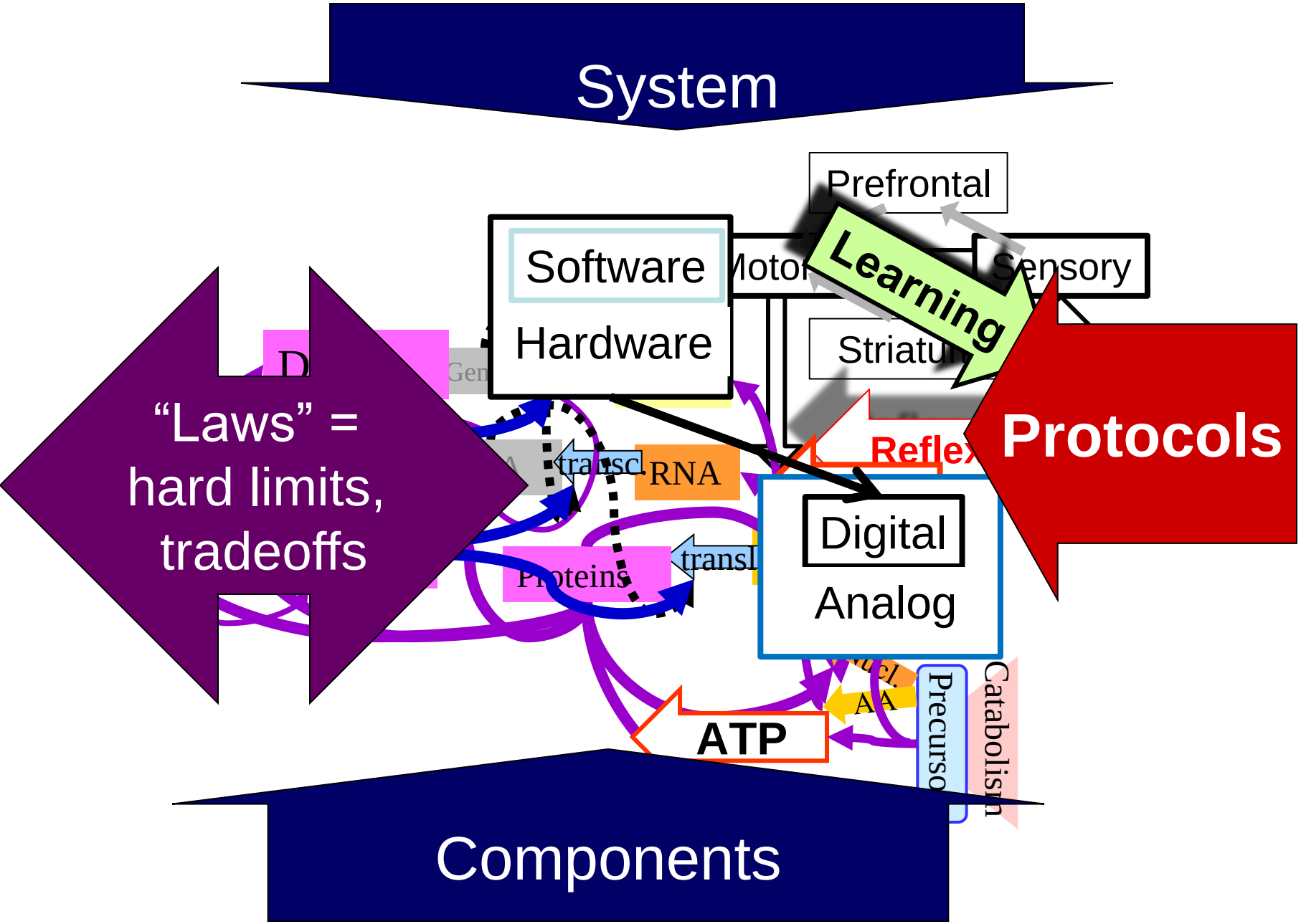
Central nervous system

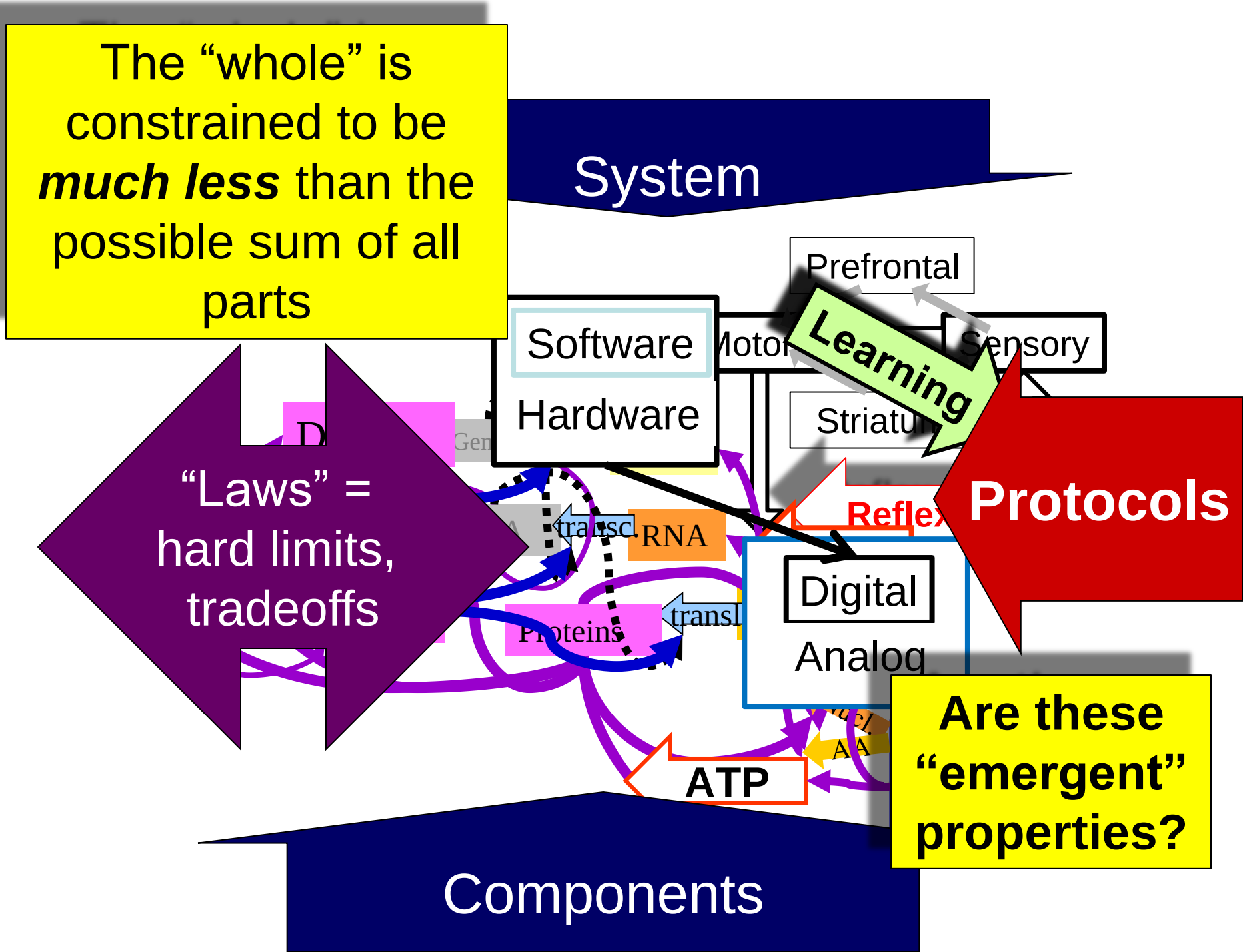
- Brain
  - Prosencephalon
    - Telencephalon: Rhinencephalon, Amygdala, Hippocampus, Neocortex, Basal ganglia, Lateral ventricles
    - Diencephalon: Epithalamus, Thalamus, Hypothalamus, Subthalamus, Pituitary gland, Pineal gland, Third ventricle
  - Brain stem
    - Mesencephalon: Tectum, Cerebral peduncle, Pretectum, Mesencephalic duct
    - Rhombencephalon
      - Metencephalon: Pons, Cerebellum
      - Myelencephalon: Medulla oblongata
- Spinal cord

CNS “stack”


Slow
Reflect
Prefrontal
Motor
Sensory
Learning
Striatum
Reflex
Reflex
Fast
Flexible
Cheap
Inflexible
Expensive


Flexible/
Adaptable/
Evolvable
Horizontal
Meme
Transfer
frontal
Sensory
arning
Striatu
Reflex
Software
Hardware
Horizontal
App
Transfer
Digital
Analog
DNAp
Gene
Repl.
DNA
RNAp
xRNA
transc.
RN
ATP
A
Ribosom
translA
A
Horizontal
Gene
Transfer
Nucl.
A
A
ATP
Precursors
Catabolism
Are these
“emergent”
properties?


System
Prefrontal
Learning
Sensory
Software
Hardware
Striatu
Reflex
Protocols
"Laws" =
hard limits,
tradeoffs
transc
RNA
Digital
Analog
Proteins
transl
ATP
AA
Precurso
Catabolism
Components


The “whole” is constrained to be ***much less*** than the possible sum of all parts
System
Prefrontal
Learning
Software
Hardware
Sensory
Striatu
Reflex
Protocols
“Laws” = hard limits, tradeoffs
RNA
Digital
Analog
Proteins
ATP
Are these “emergent” properties?
Components

Universal architectures

What can go wrong?

Exploiting layered architecture

Horizontal **Bad Meme** Transfer

Virus

Horizontal **Bad App** Transfer

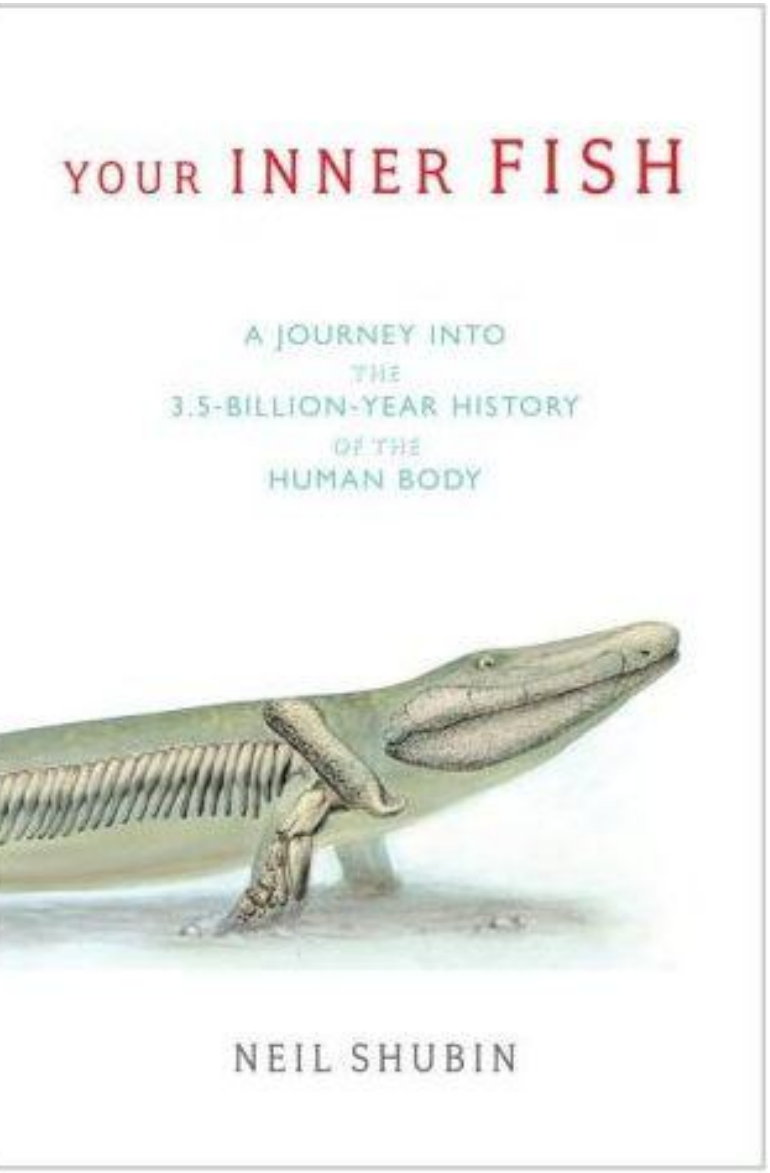
Fragility?

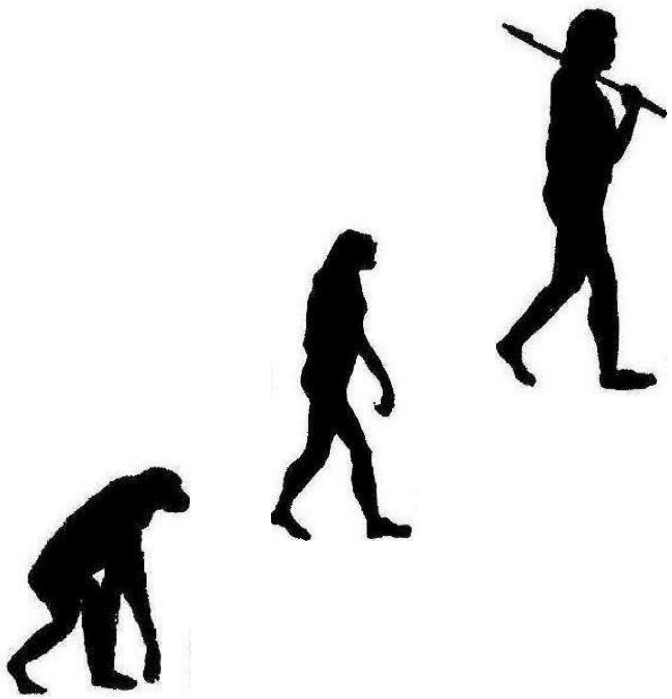
Horizontal **Bad Gene** Transfer

Virus

Parasites & Hijacking

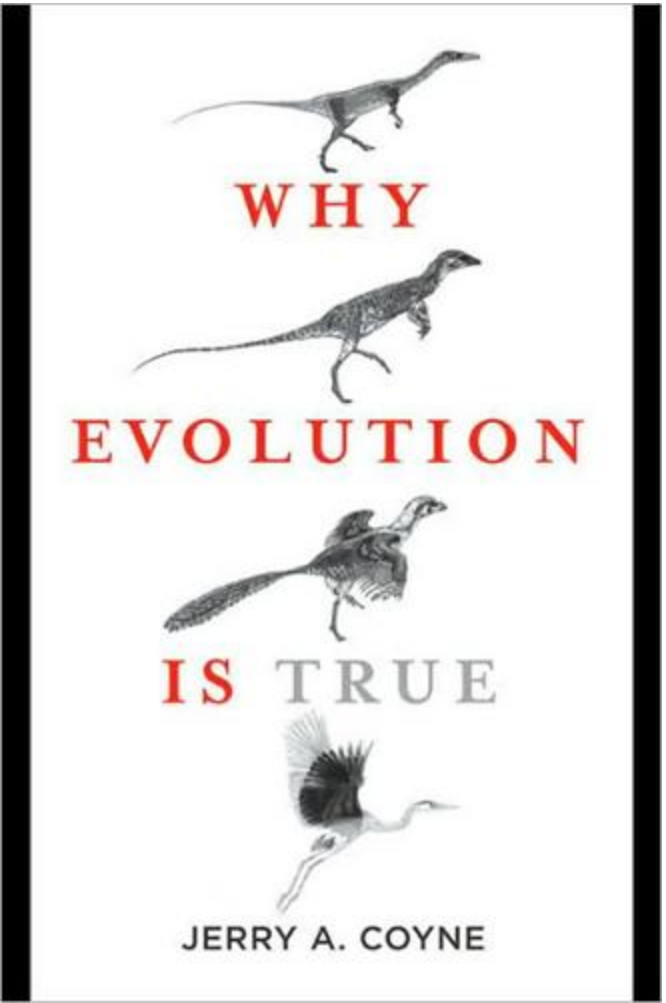
Unfortunately, not intelligent design

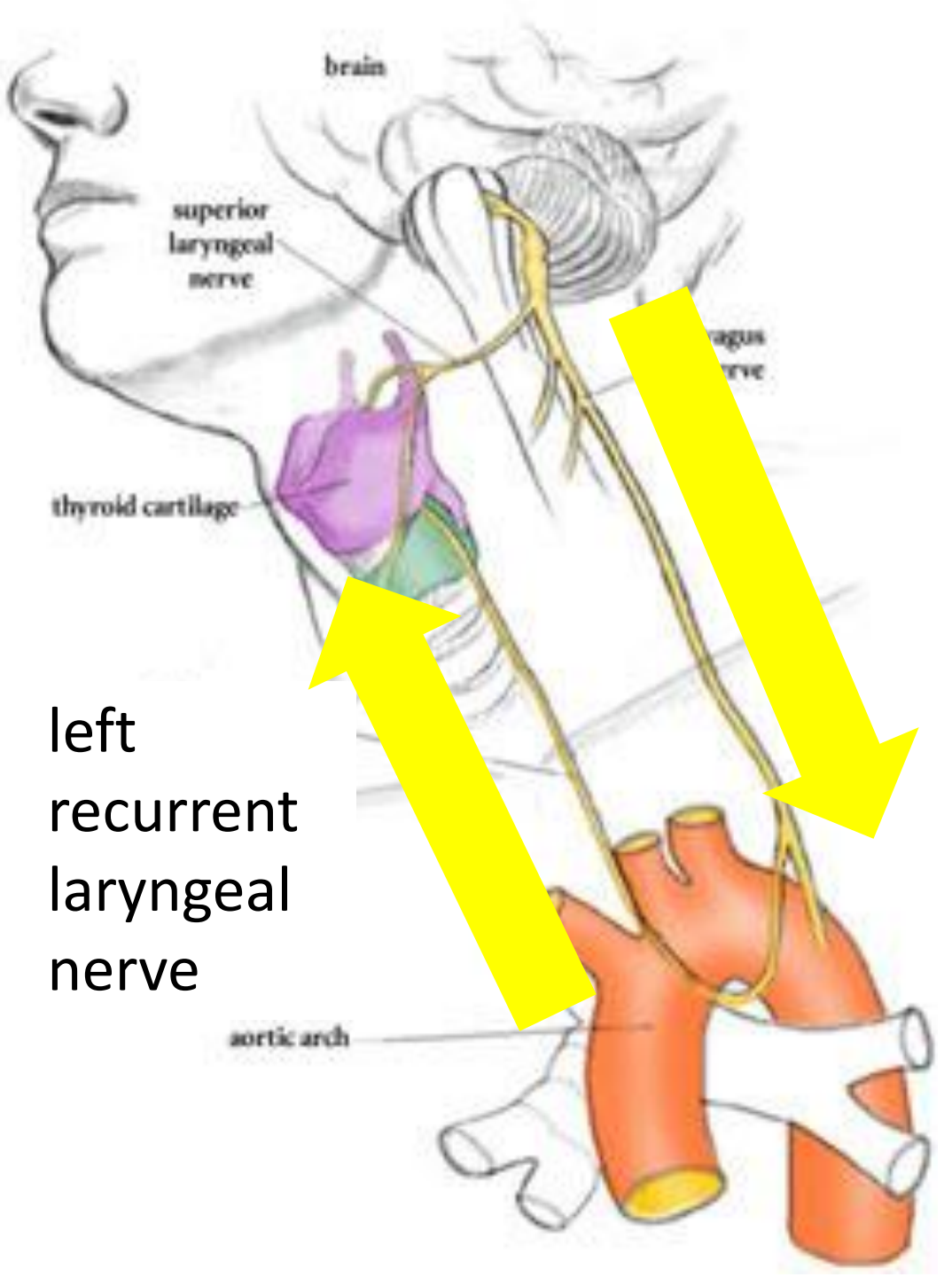




Ouch.

Why?





left recurrent laryngeal nerve

Why? Building humans from fish parts.

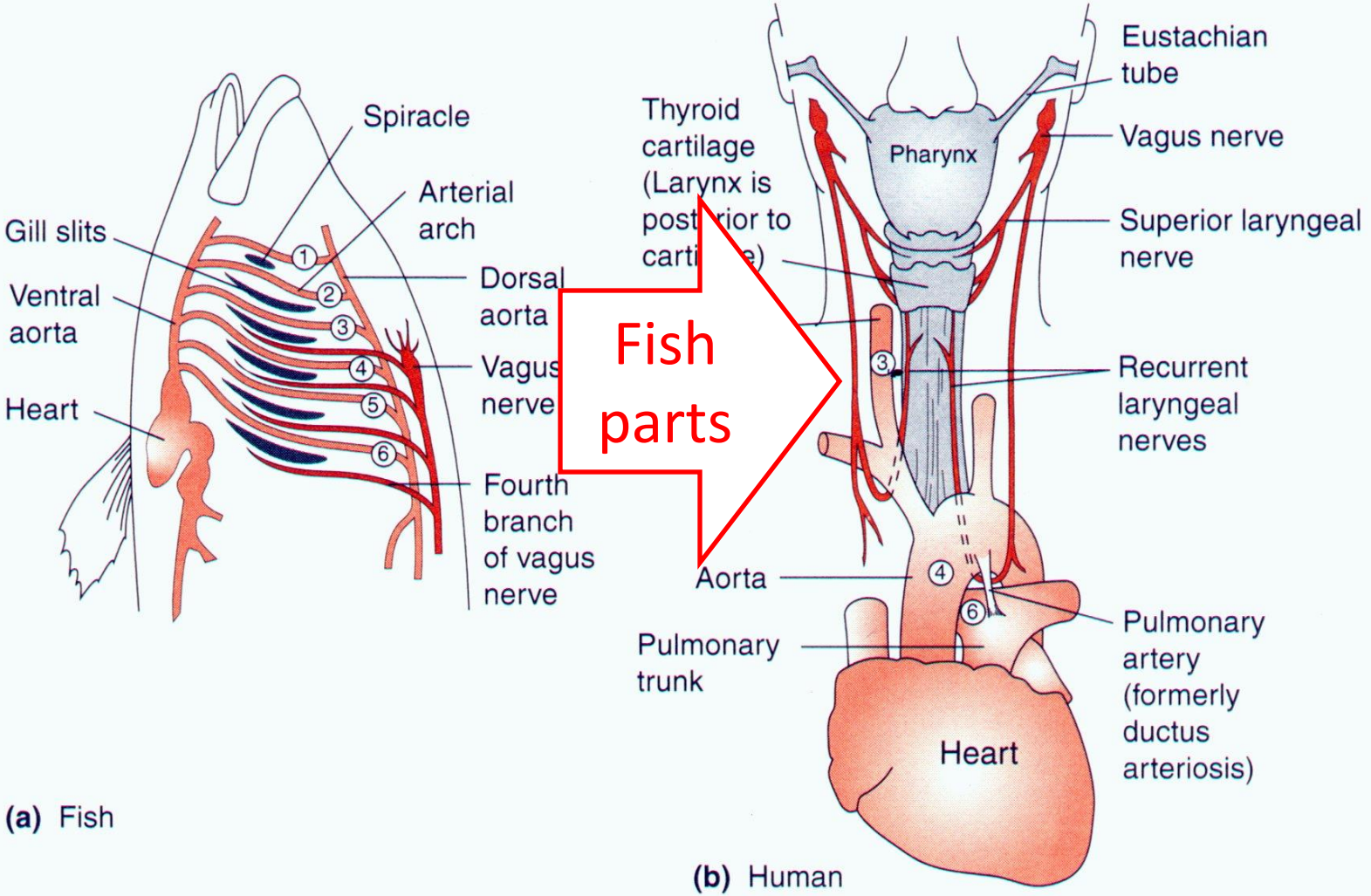
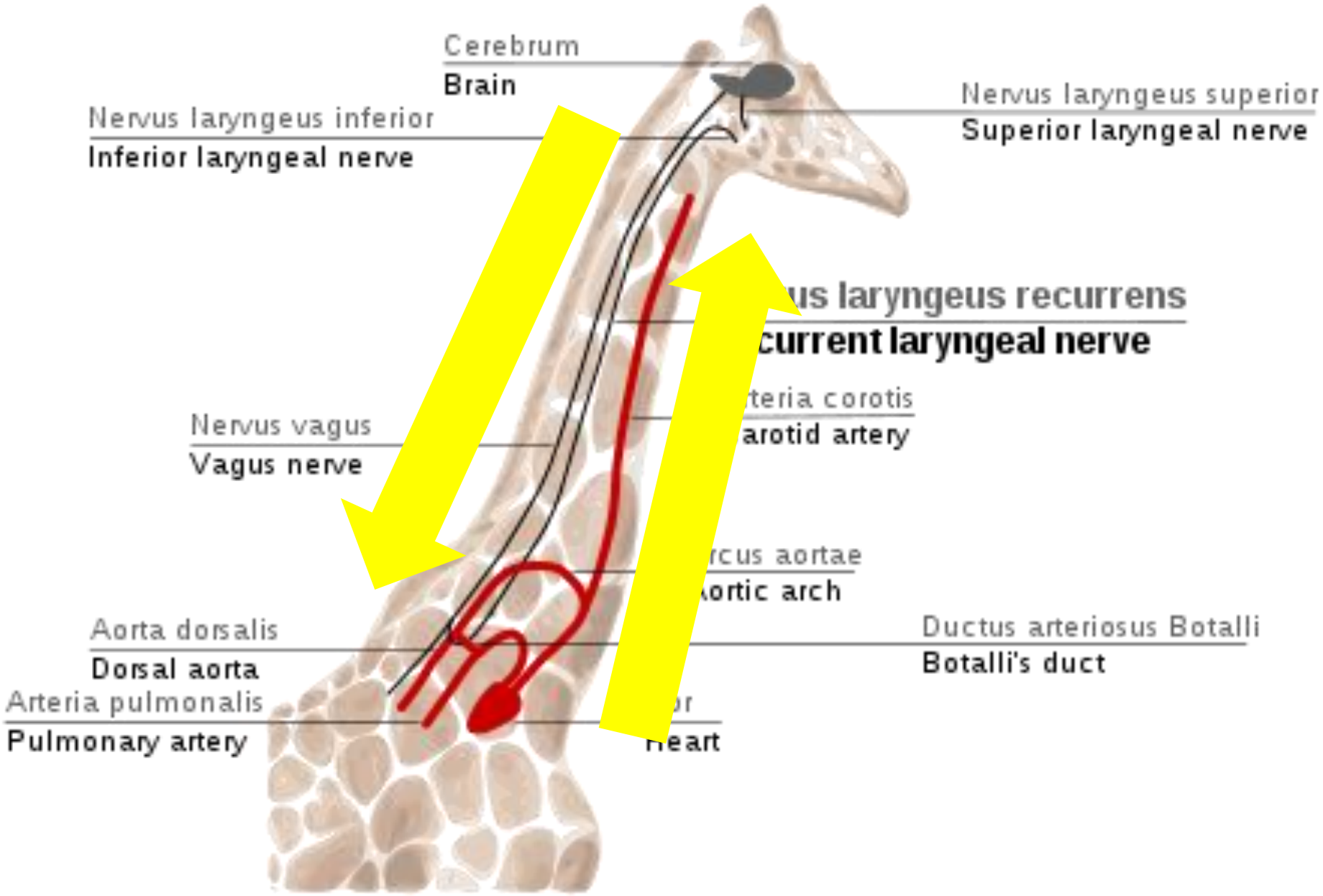
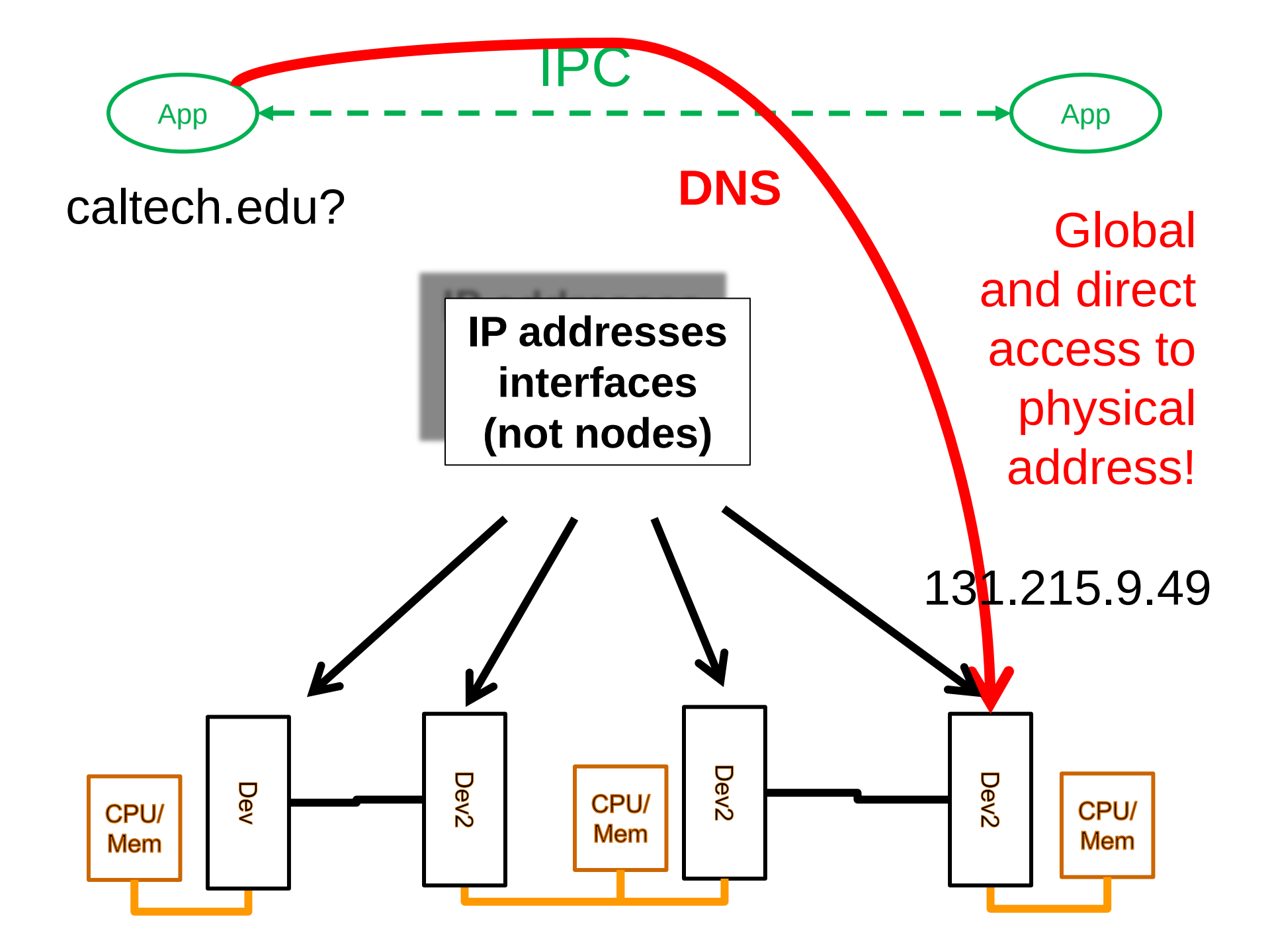
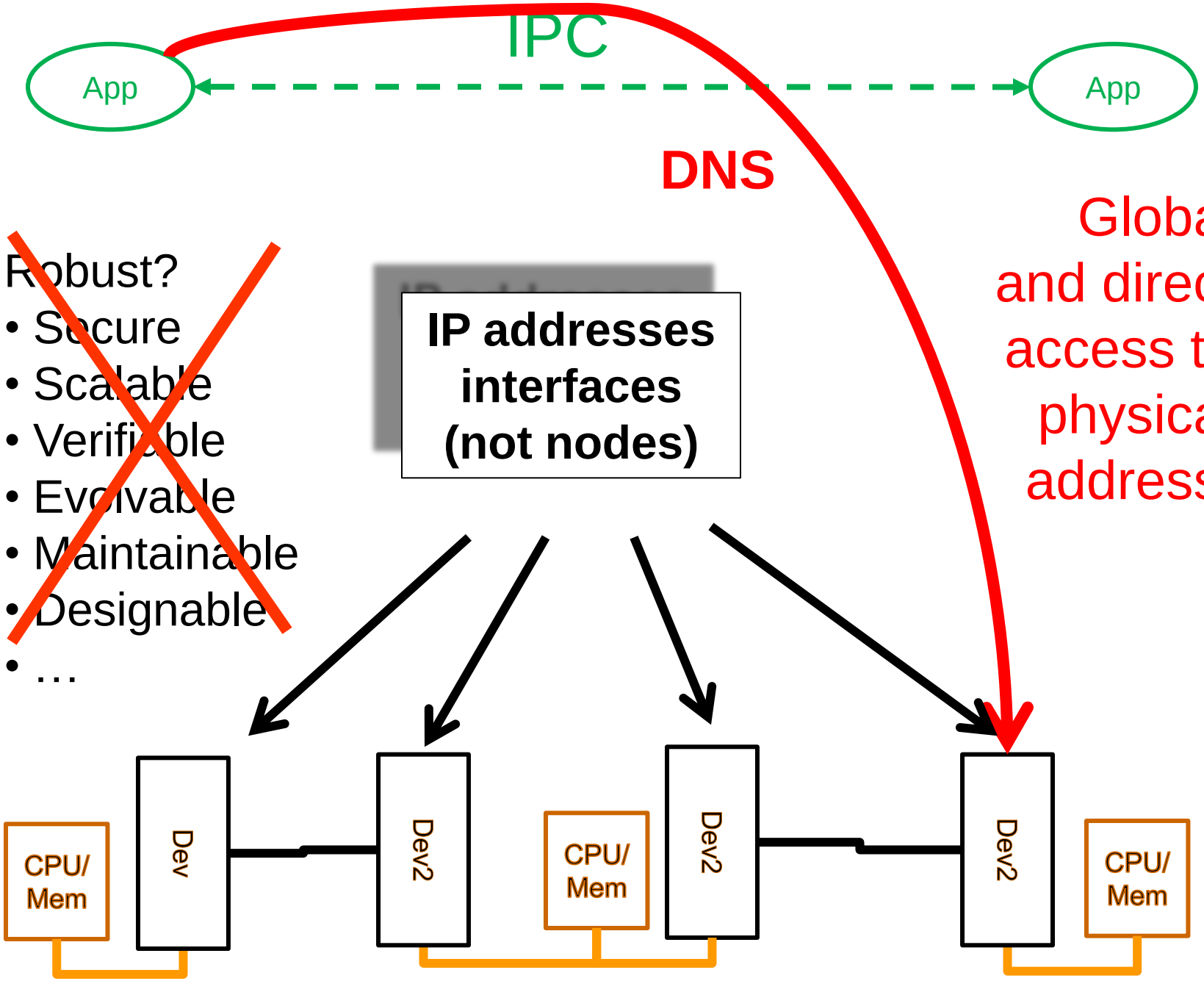


FIGURE 3–11 Schematic diagram showing the relationship between the vagus cranial nerve and the arterial arches in fish (*a*) and human (*b*). Only the third, fourth, and part of the sixth arterial arches remain in placental mammals, the sixth acting only during fetal development to carry blood to the placenta. The fourth vagal nerve in mammals (the recurrent laryngeal nerve) loops around the sixth arterial arch just as it did in the original fishlike ancestor, but must now travel a greater distance since the remnant of the sixth arch is in the thorax.

It could be worse.




IPC
App
App
DNS
caltech.edu?
Global and direct access to physical address!
IP addresses interfaces (not nodes)
131.215.9.49
CPU/ Mem
Dev
Dev2
CPU/ Mem
Dev2
Dev2
CPU/ Mem

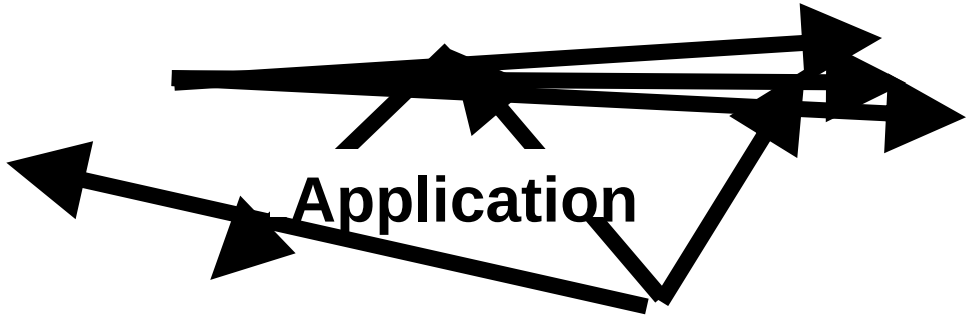

IPC
App
App
DNS
Global and direct access to physical address!
Robust?
• Secure
• Scalable
• Verifiable
• Evolvable
• Maintainable
• Designable
• …
IP addresses interfaces (not nodes)
CPU/ Mem
Dev
Dev2
CPU/ Mem
Dev2
Dev2
CPU/ Mem

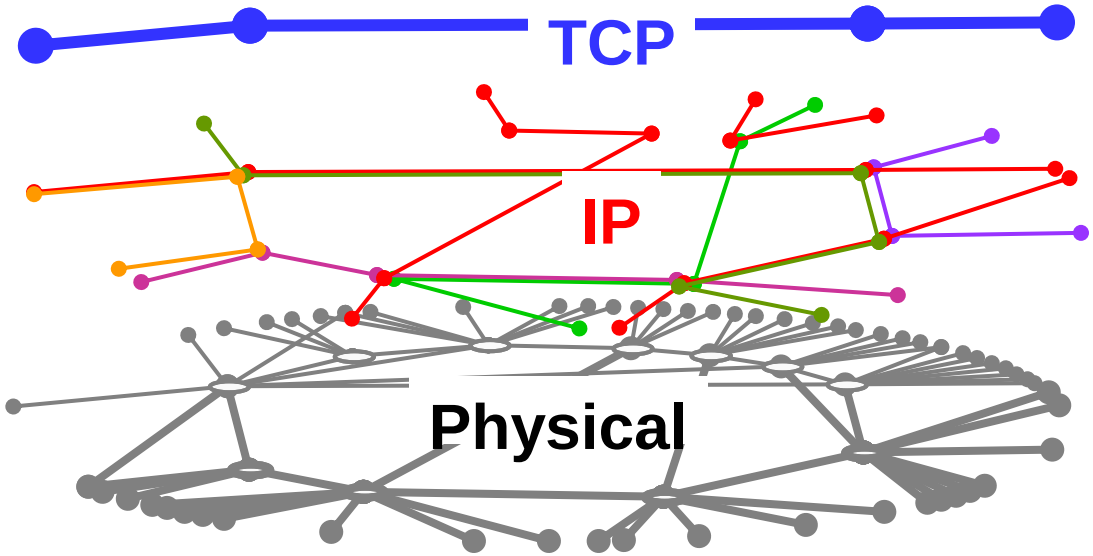
Naming and addressing need to have ***scope*** and

- resolved within layer
- translated between layers
- not exposed outside of layer

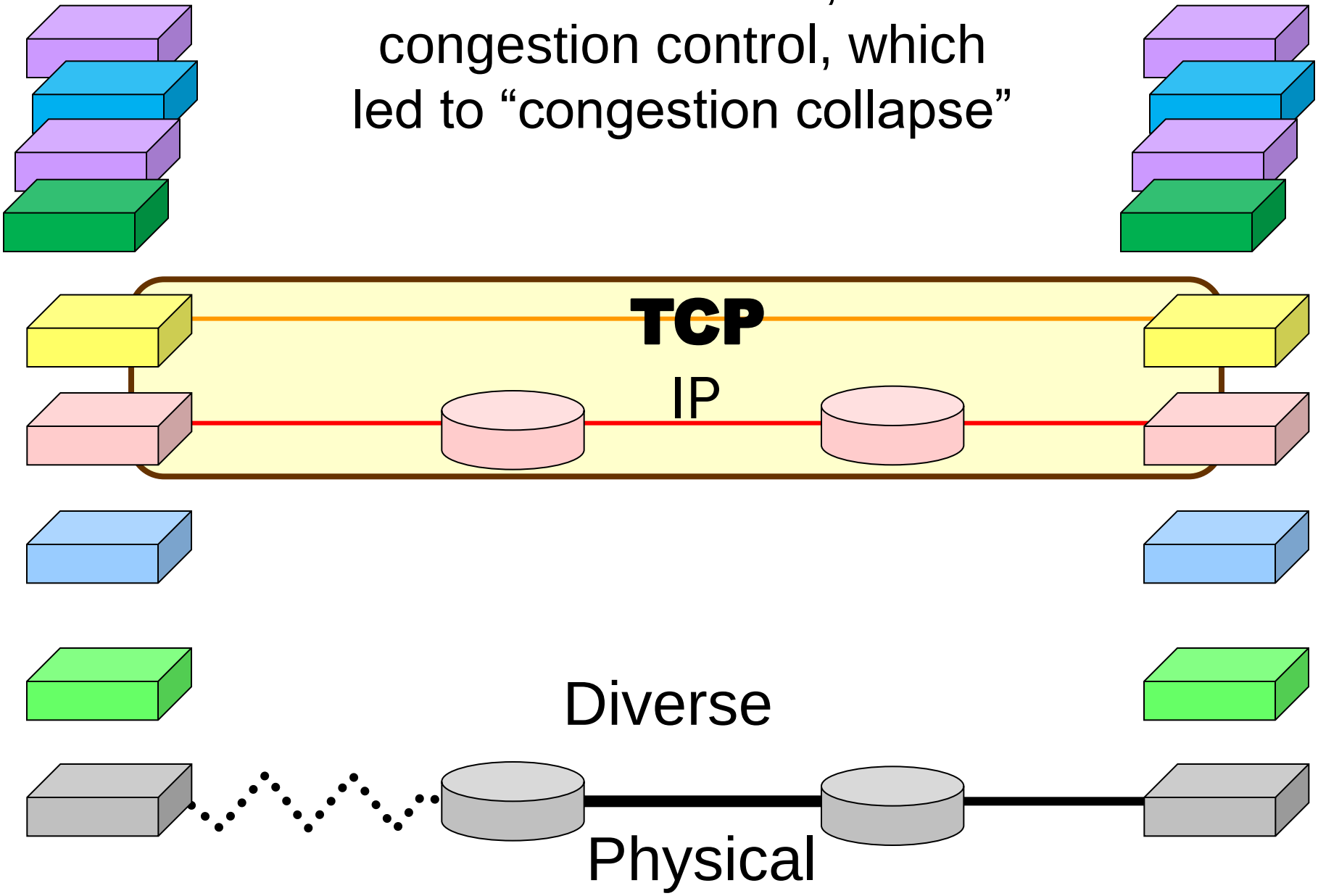
Related “issues”

- VPNs
- NATS
- Firewalls
- Multihoming
- Mobility
- Routing table size
- Overlays
- …

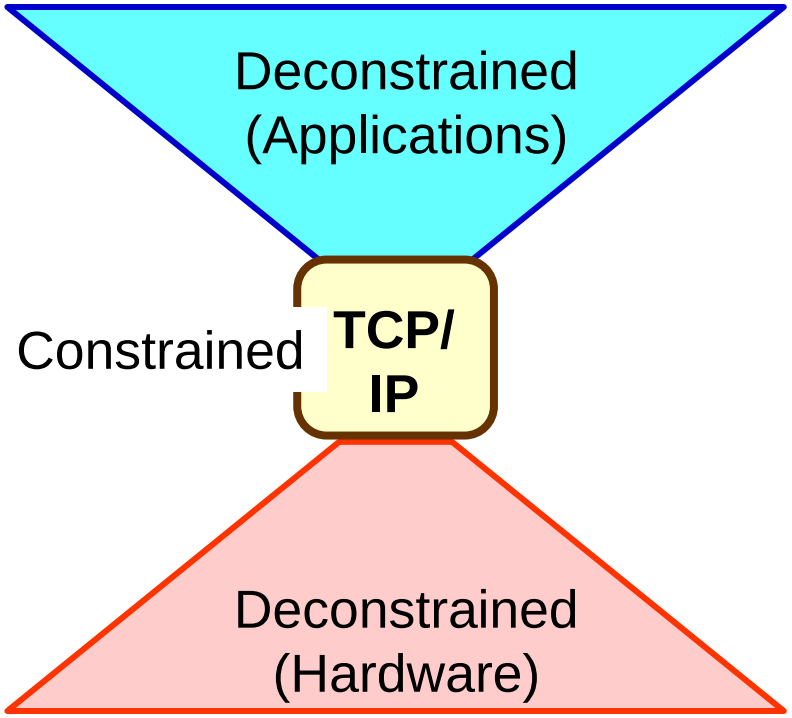




Until late 1980s, no congestion control, which led to “congestion collapse”



Original design challenge?



Networked OS

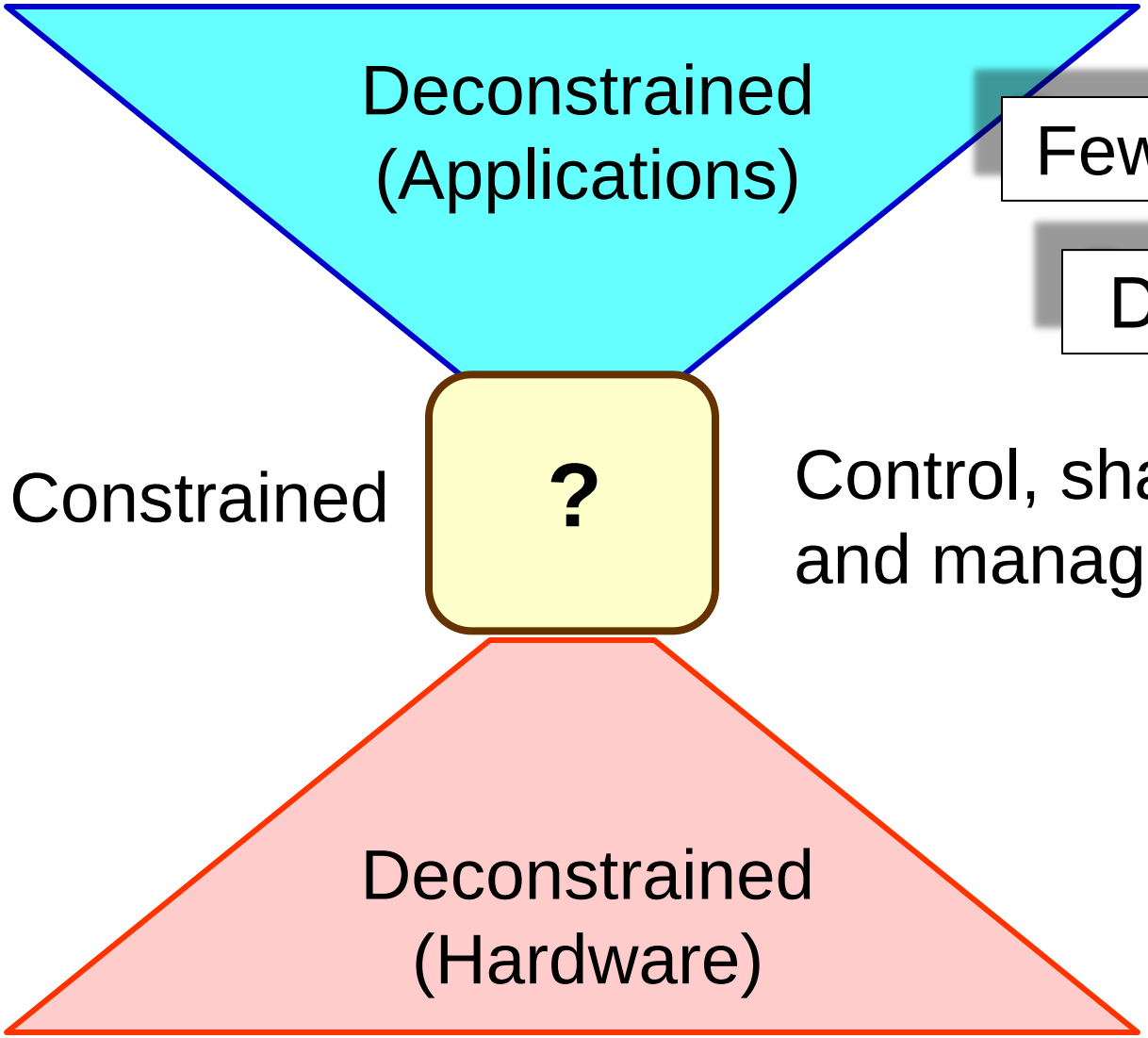
- ~~Expensive mainframes~~
- ~~Trusted end systems~~
- ~~Homogeneous~~
- ~~Sender centric~~
- Unreliable comms

Facilitated wild evolution

Created

- whole new ecosystem
- completely opposite

Next layered architectures



Few global variables

Don’t cross layers

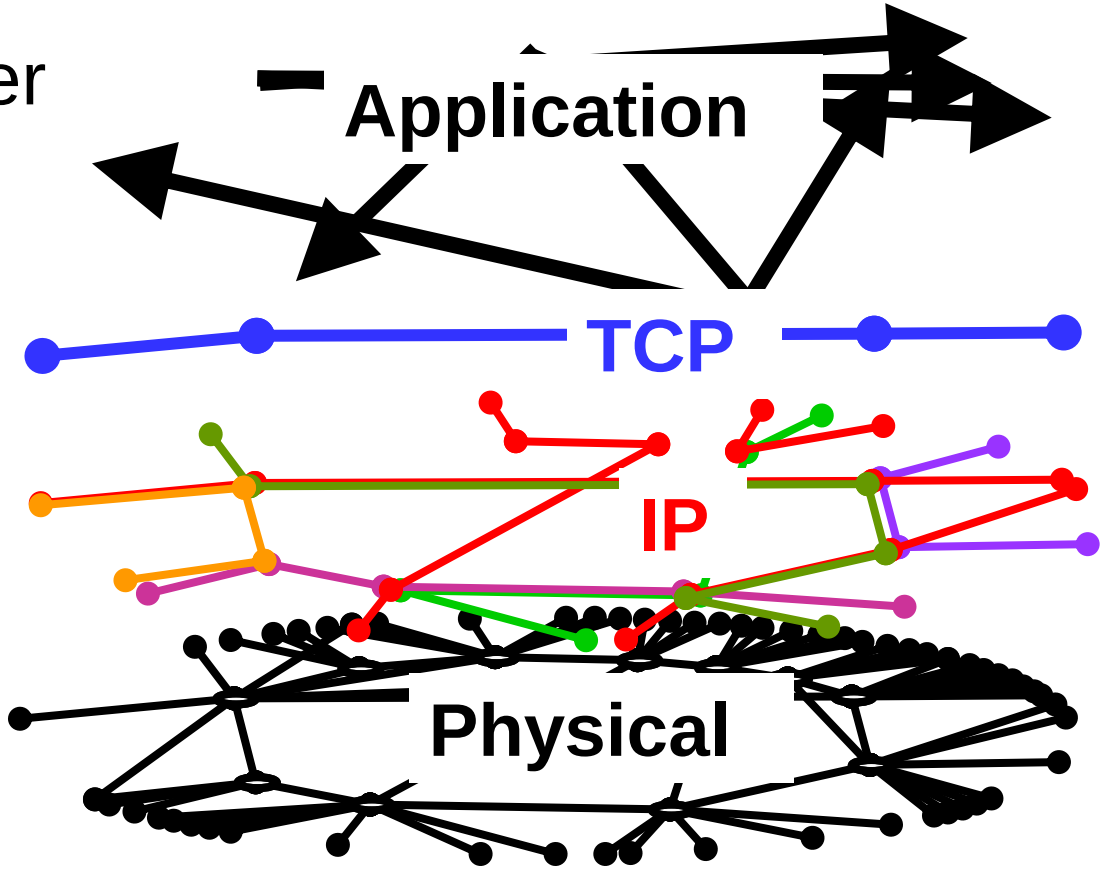
Control, share, virtualize,
and manage resources

Comms
Memory, storage
Latency
Processing
Cyber-physical

Persistent errors and confusion ("network science")

Architecture is ***least*** graph topology.

Every layer has different diverse graphs.



Architecture facilitates arbitrary graphs.

The "robust yet fragile" nature of the Internet

John C. Doyle*†, David L. Alderson*, Lun Li*, Steven Low*, Matthew Roughan‡, Stanislav Shalunov§, Reiko Tanaka¶, and Walter Willinger‖

*Engineering and Applied Sciences Division, California Institute of Technology, Pasadena, CA 91125; ‡Applied Mathematics, University of Adelaide, South Australia 5005, Australia; §Internet2, 3025 Boardwalk Drive, Suite 200, Ann Arbor, MI 48108; ¶Bio-Mimetic Control Research Center, Institute of Physical and Chemical Research, Nagoya 463-0003, Japan; and ‖AT&T Labs–Research, Florham Park, NJ 07932

Edited by Robert M. May, University of Oxford, Oxford, United Kingdom, and approved August 29, 2005 (received for review February 18, 2005)

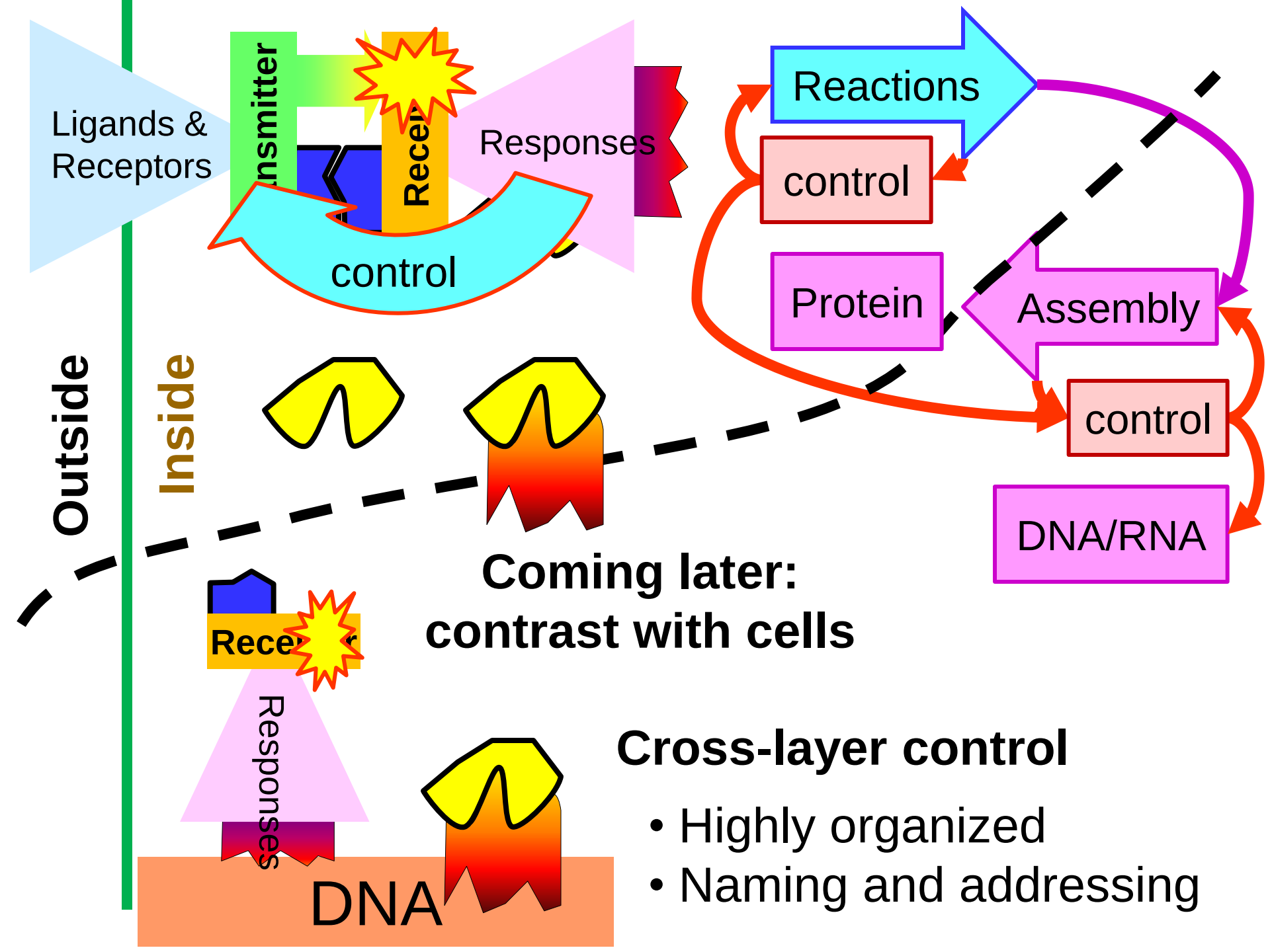
The search for unifying properties of complex networks is popular, challenging, and important. For modeling approaches that focus on

no self-loops or parallel edges) having the same graph degree
We will say that graphs $g \in G(D)$ have scaling-degree sequen

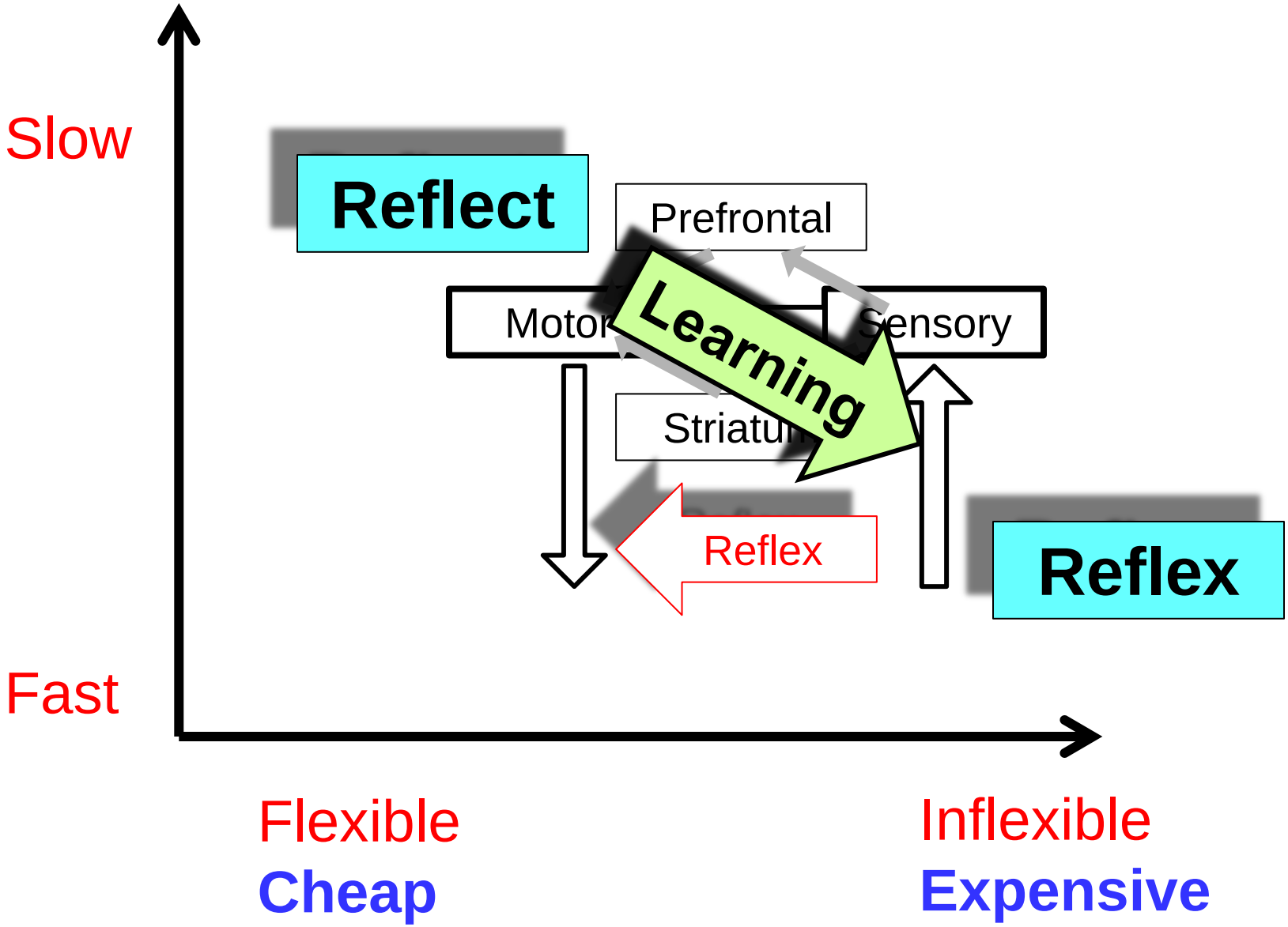
Notices of the AMS, 2009

Mathematics and the Internet: A Source of Enormous Confusion and Great Potential

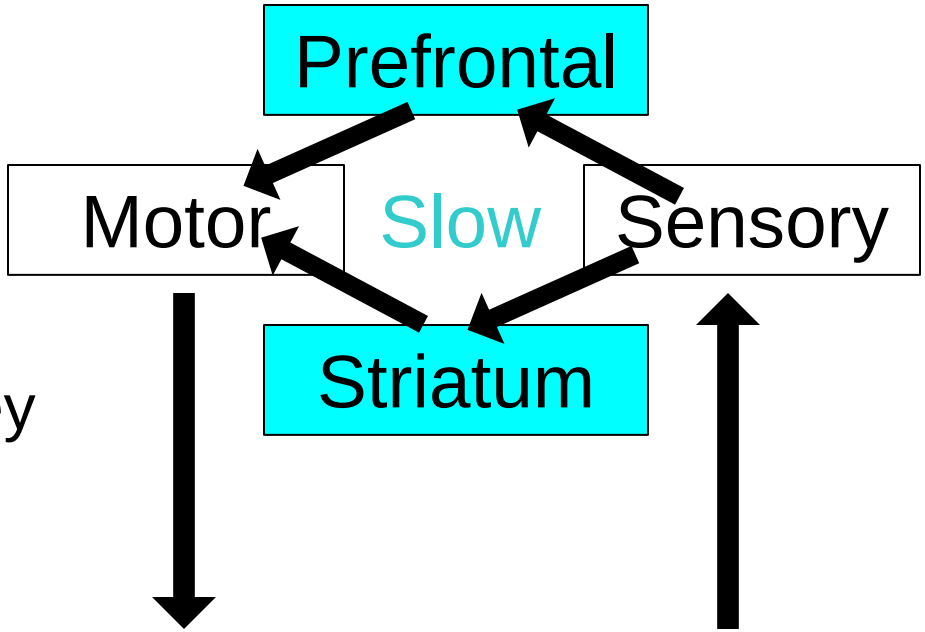
Walter Willinger, David Alderson, and John C. Doyle


Ligands &
Receptors
nsmitter
Recei
Responses
control
Reactions
control
Protein
Assembly
control
DNA/RNA
Outside
Inside
Recei
Responses
DNA
Coming later:
contrast with cells
Cross-layer control
• Highly organized
• Naming and addressing

CNS “stack”


Slow
Reflect
Prefrontal
Motor
Sensory
Learning
Striatum
Reflex
Reflex
Fast
Flexible
Cheap
Inflexible
Expensive

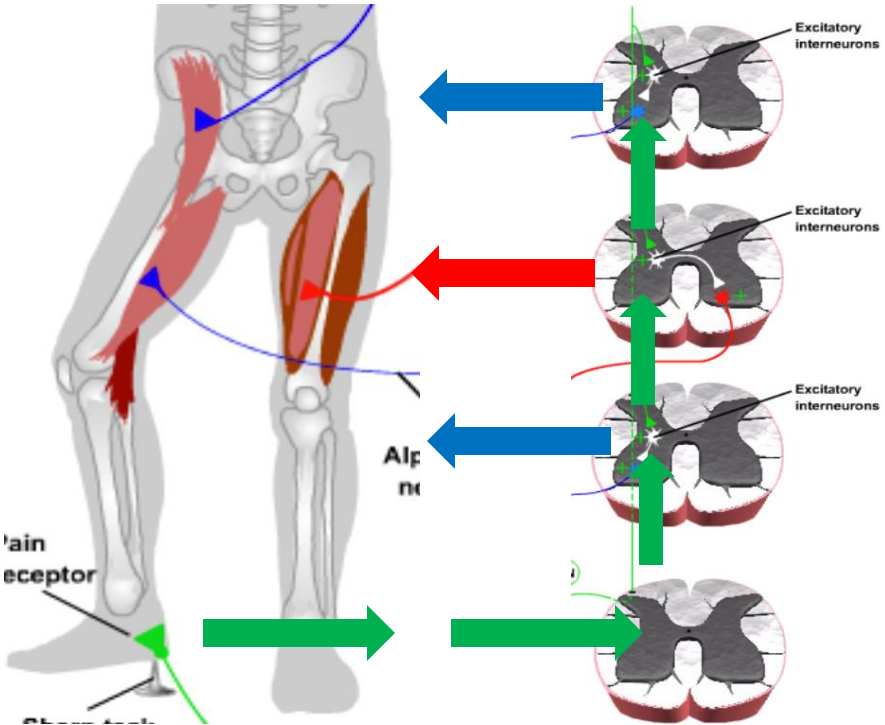
Slow Flexible



Learning

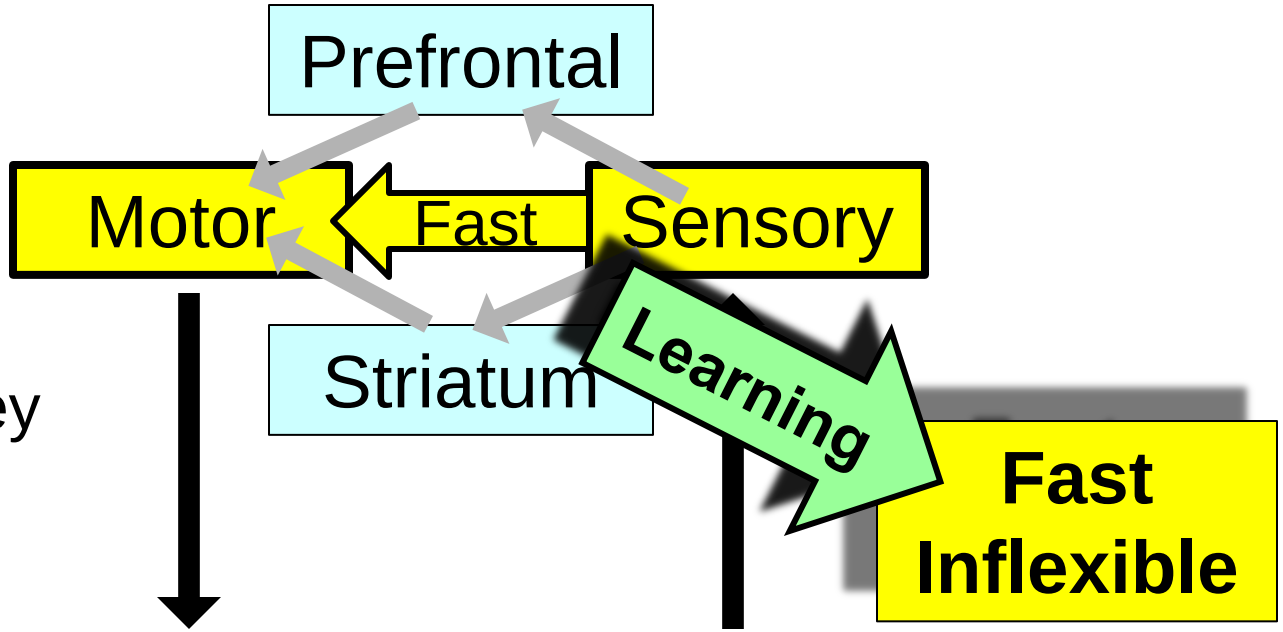
Ashby & Crossley

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



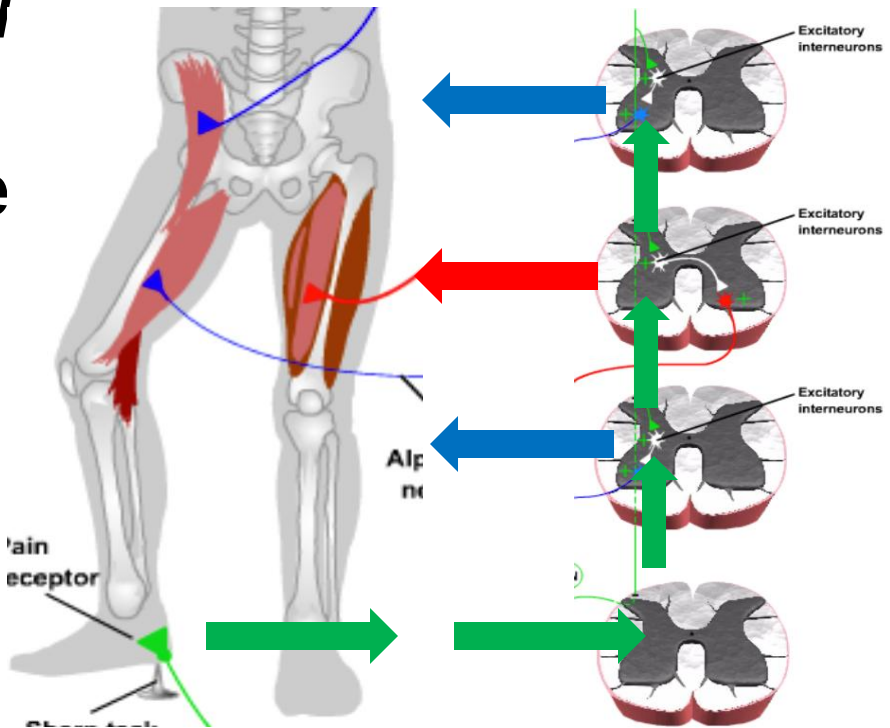
Thanks to Bassett & Grafton

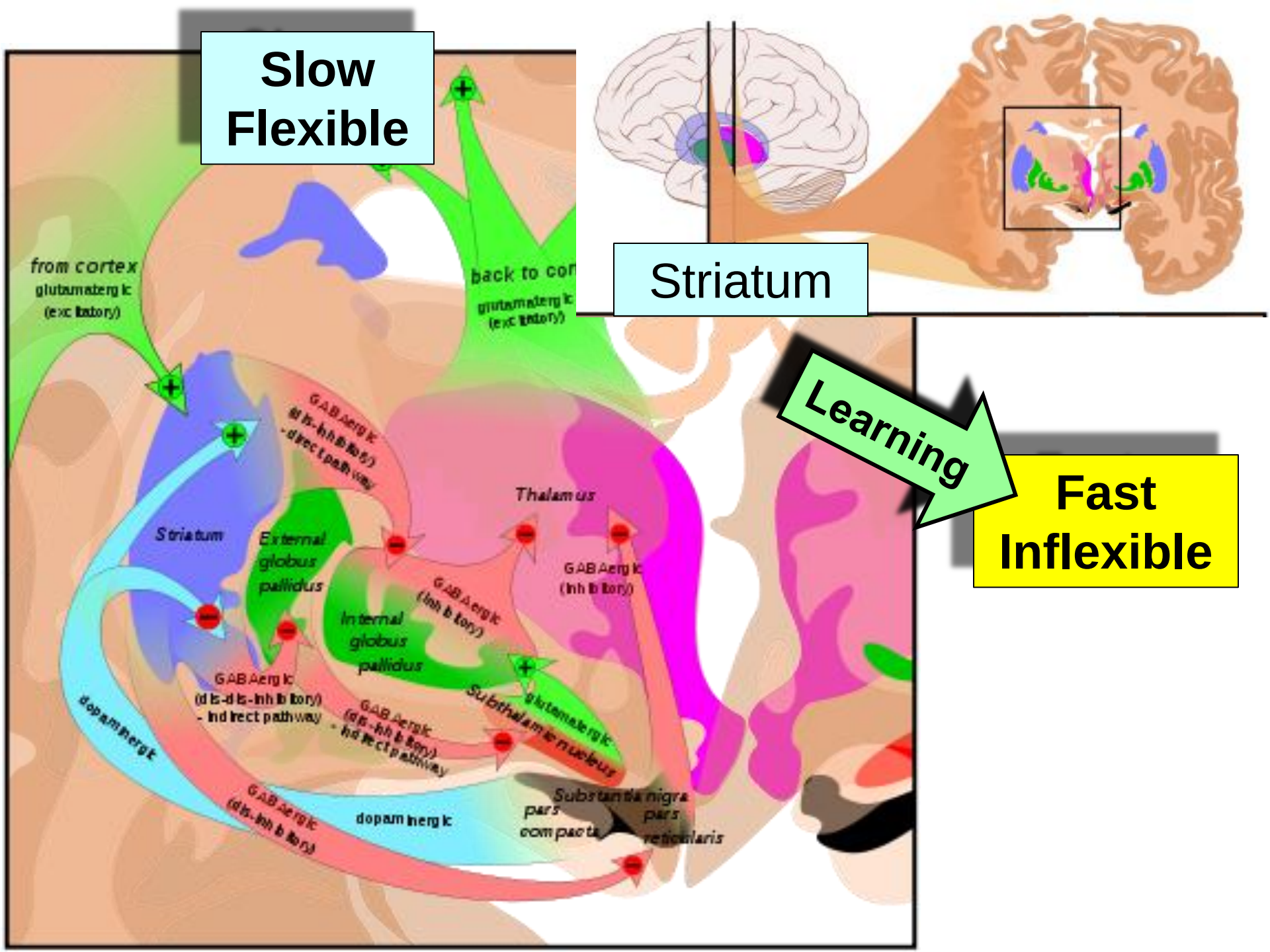
Slow Flexible



Ashby & Crossley

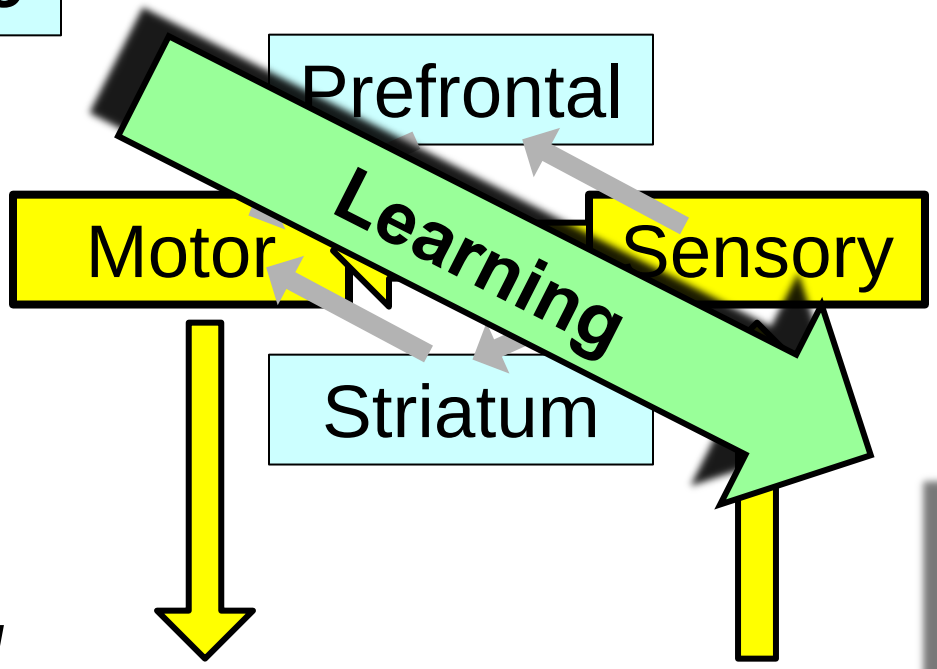
- Acquire
- **Translate/ integrate**
- **Automate**




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

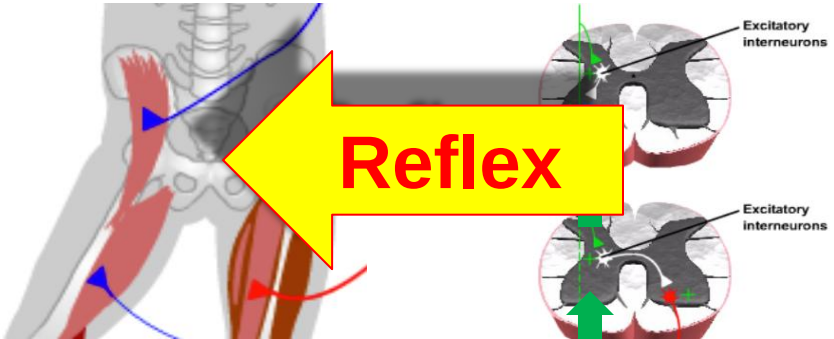
Build on Turing to show what is *necessary* to make this work.

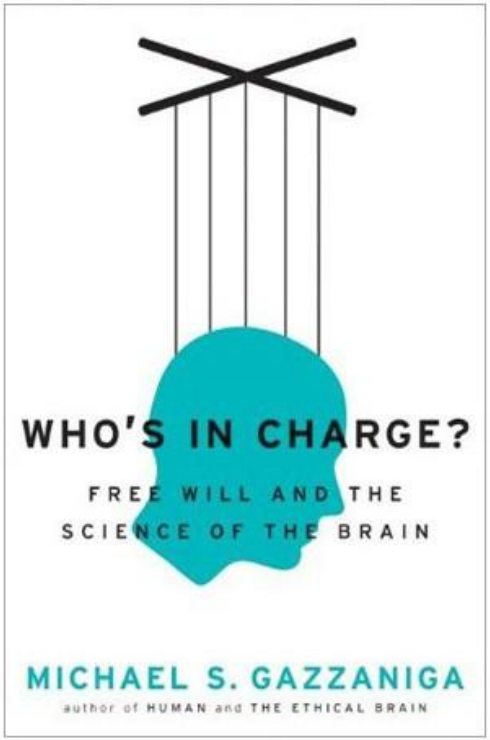
Slow Flexible

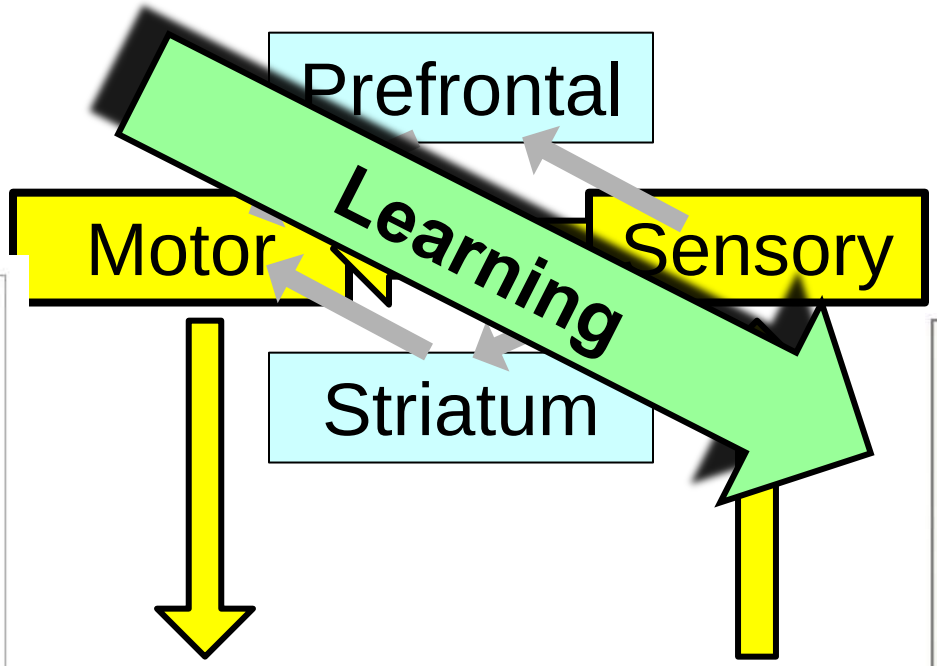


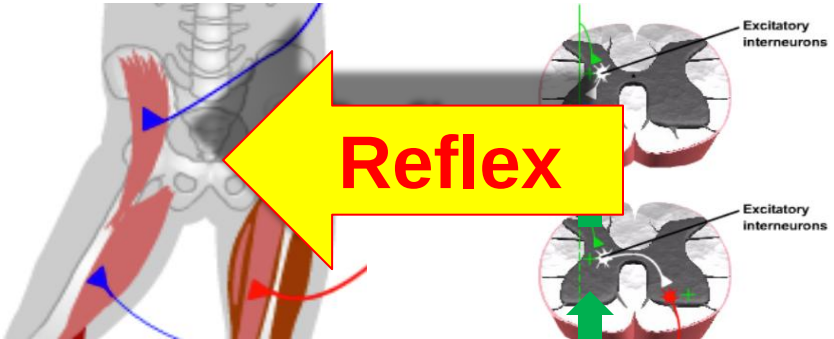
Fast Inflexible

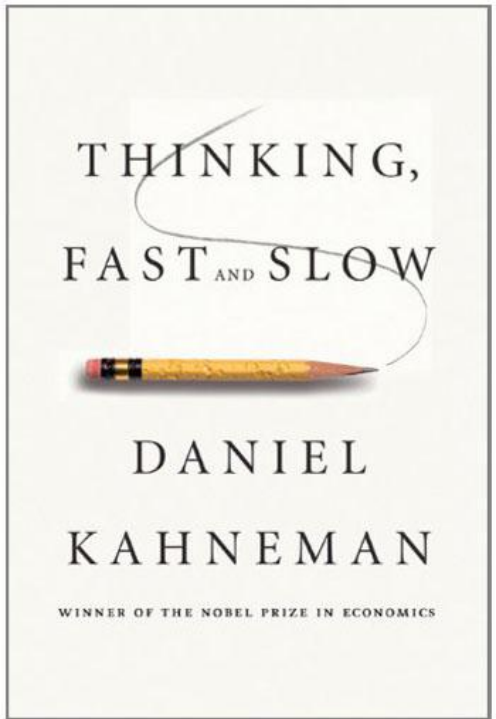
- **Acquire**
- **Translate/ integrate**
- **Automate**



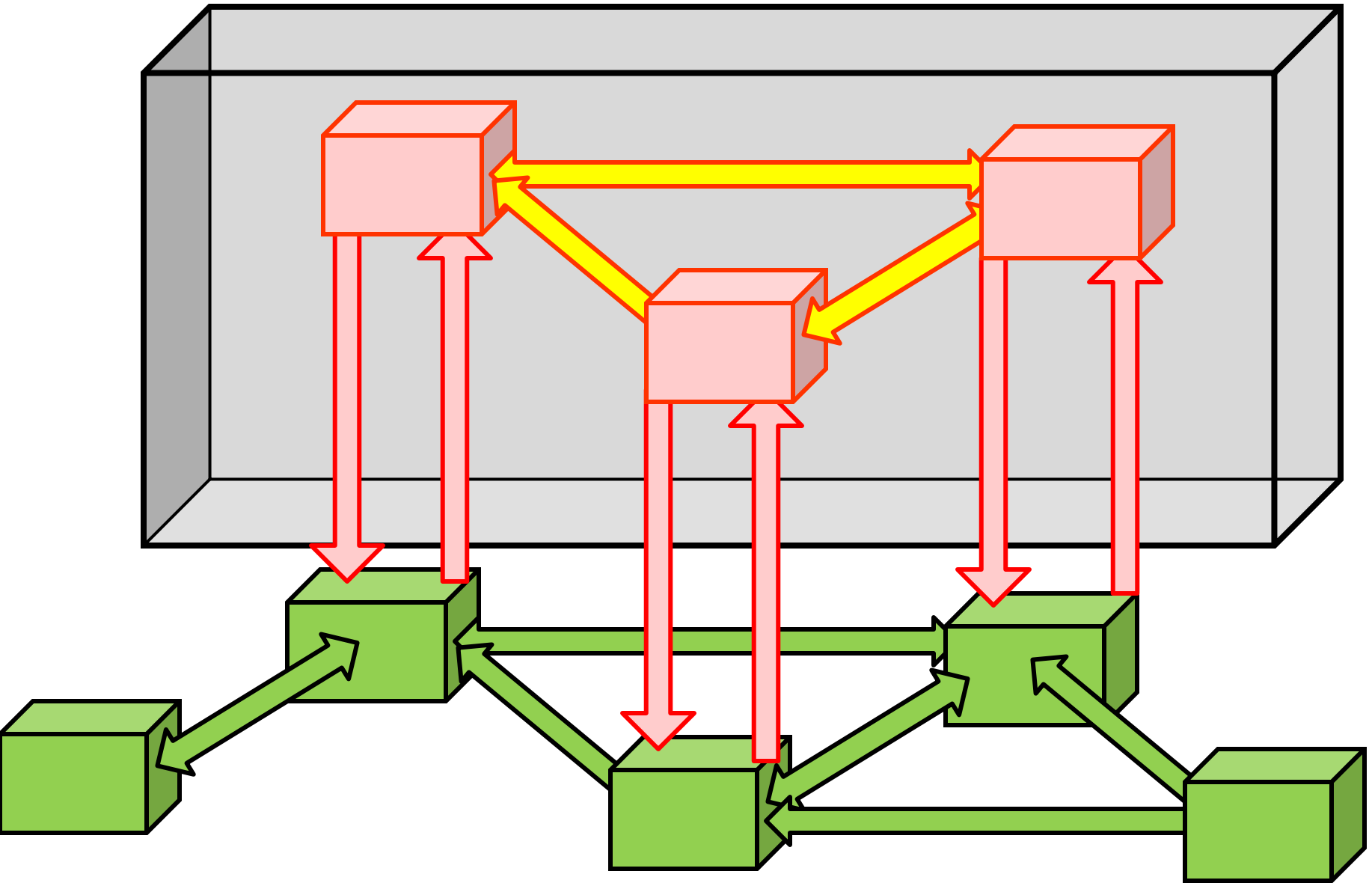

WHO'S IN CHARGE?
FREE WILL AND THE SCIENCE OF THE BRAIN
MICHAEL S. GAZZANIGA
author of HUMAN and THE ETHICAL BRAIN

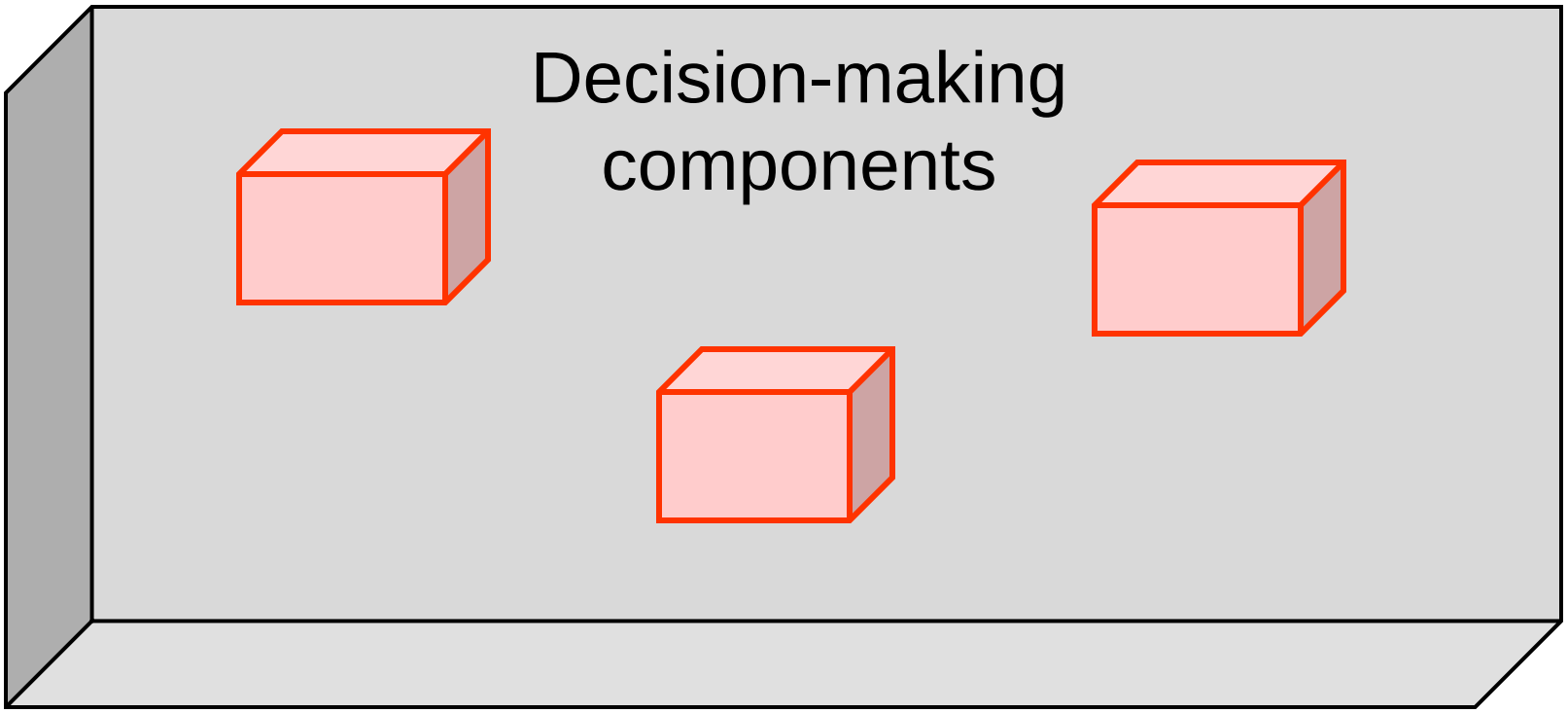

Prefrontal
Motor
Sensory
Striatum
Learning


Reflex
Excitatory interneurons
Excitatory interneurons

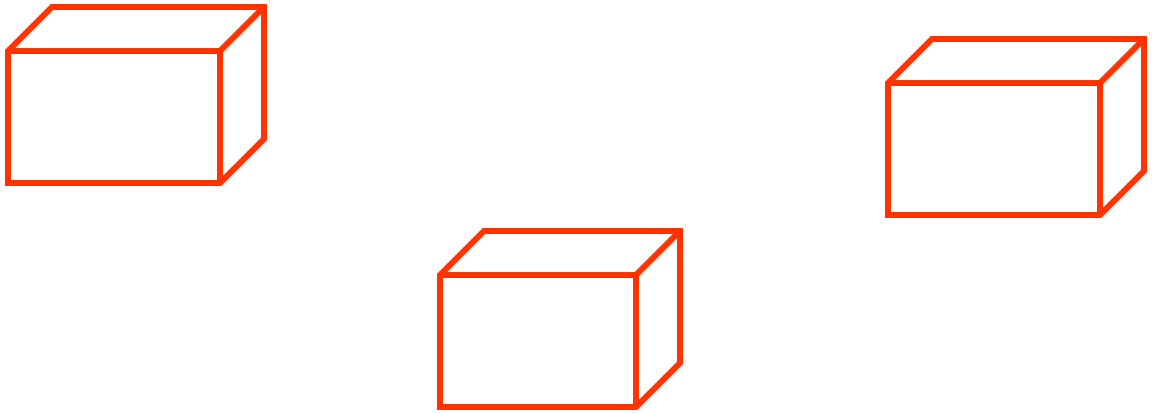

THINKING, FAST AND SLOW
DANIEL KAHNEMAN
WINNER OF THE NOBEL PRIZE IN ECONOMICS

Cyber-physical: decentralized control with internal delays.

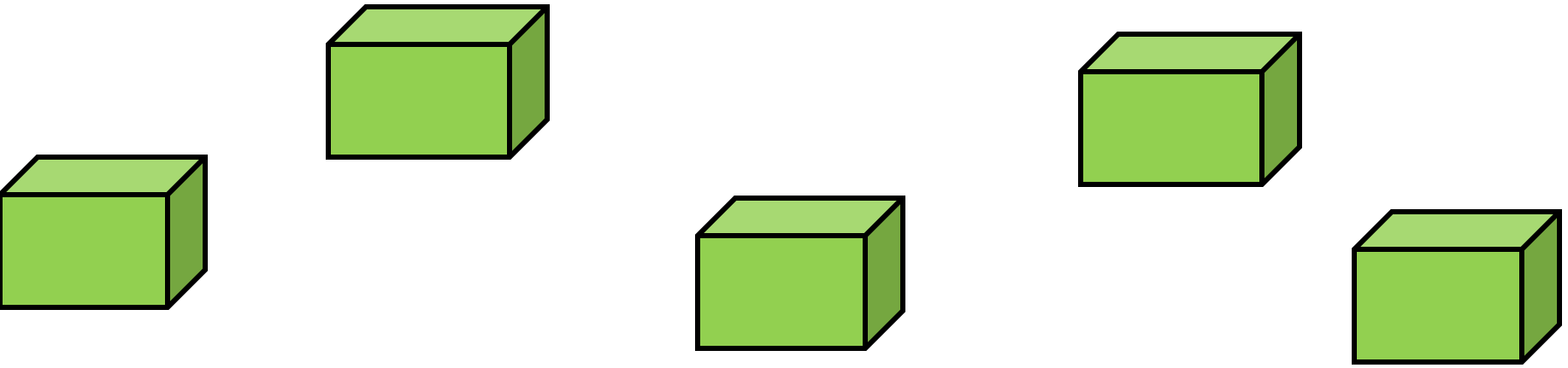




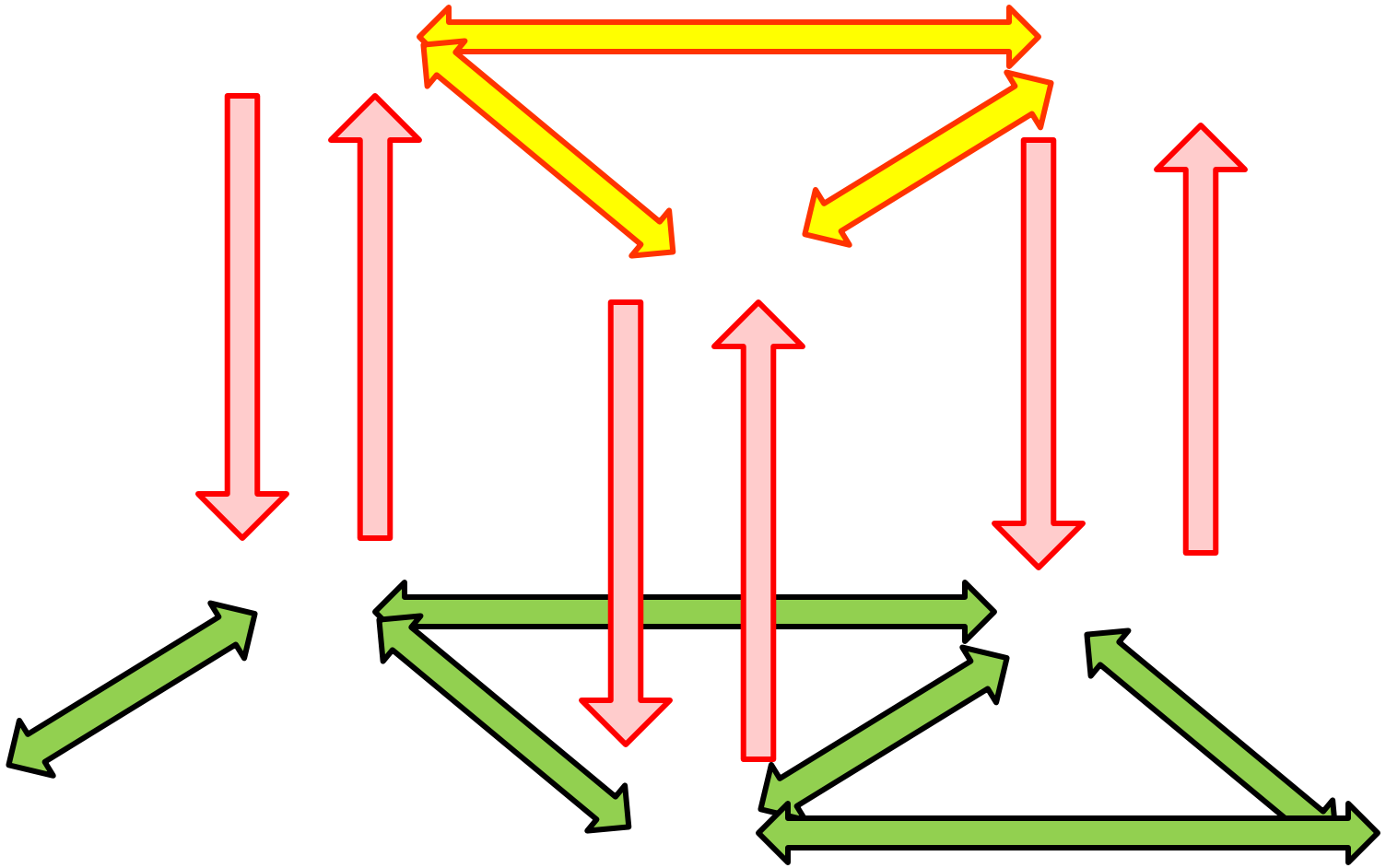
Decentralized, but initially assume computation is fast and memory is abundant.



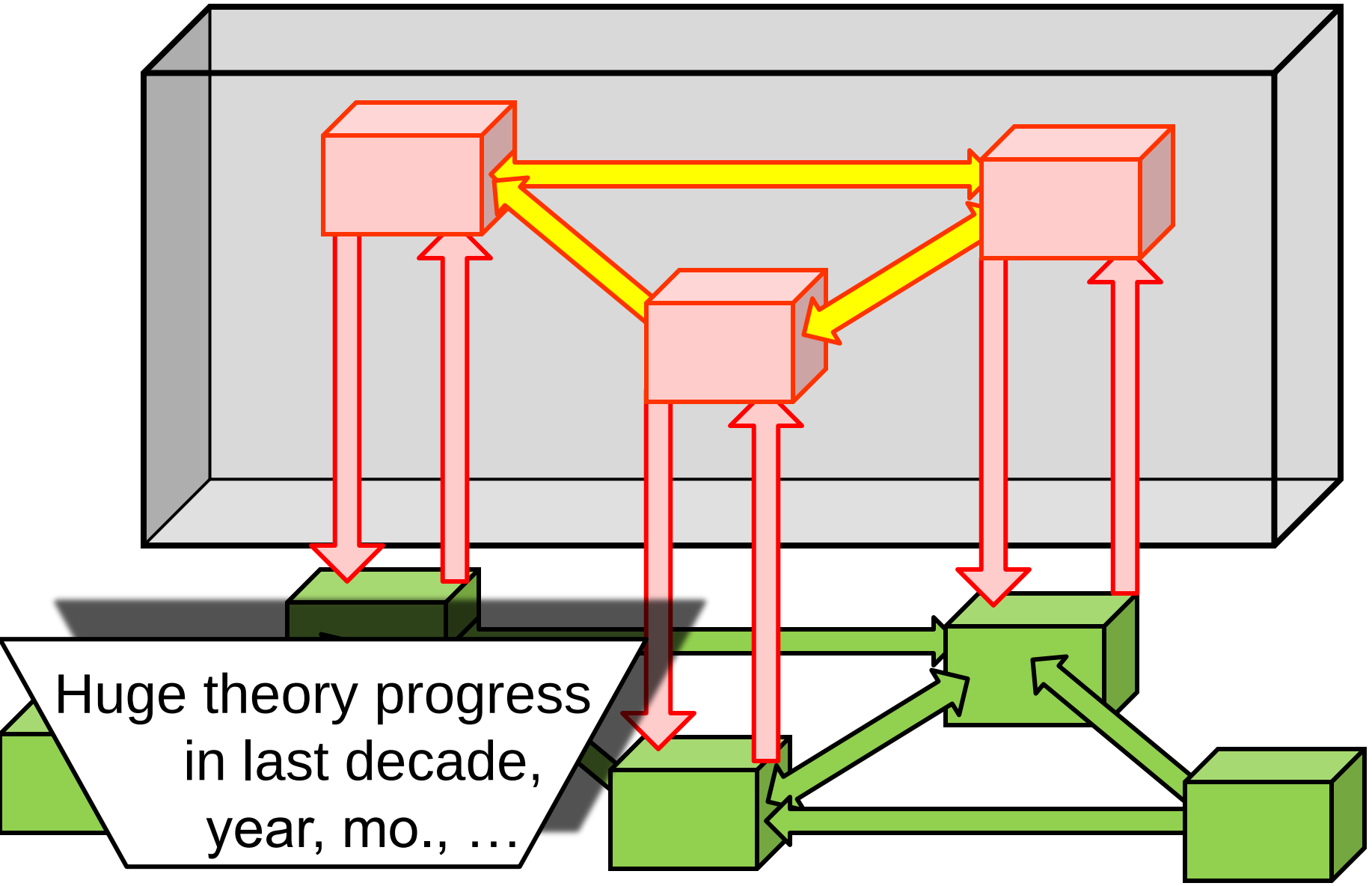
Plant is also distributed with its own component dynamics



Internal delays between components, and their sensor and actuators, and also externally between plant components



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

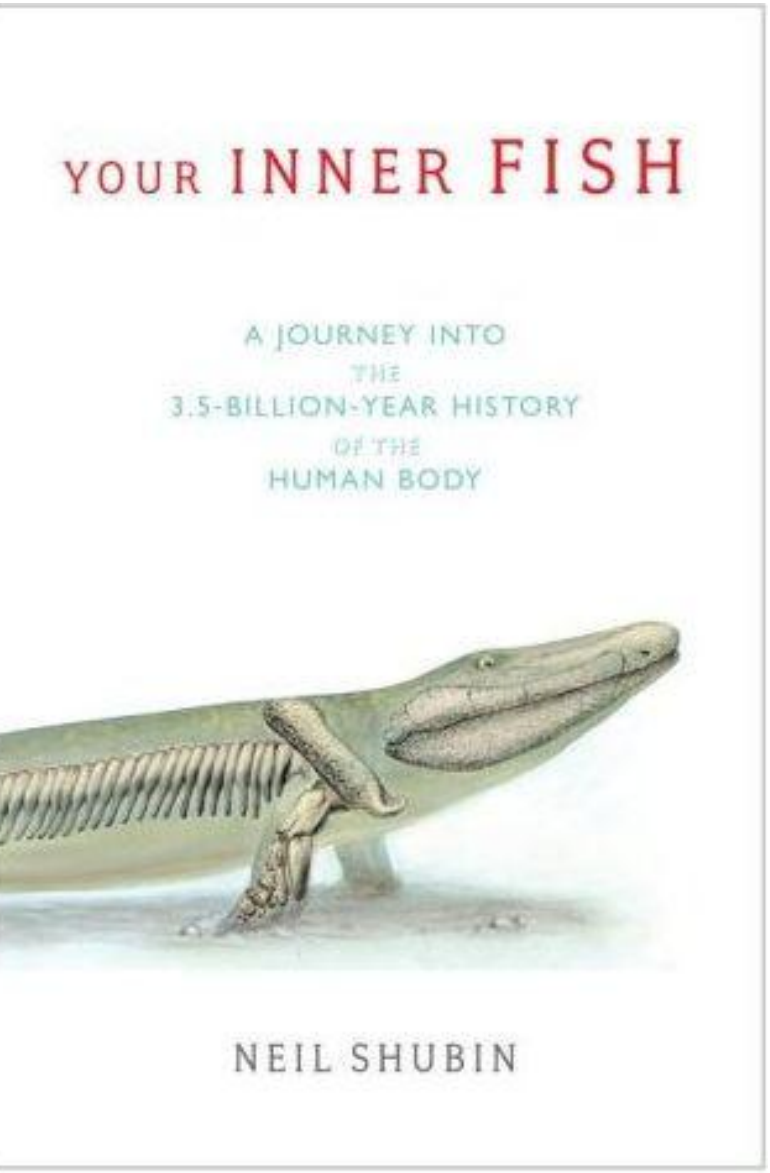


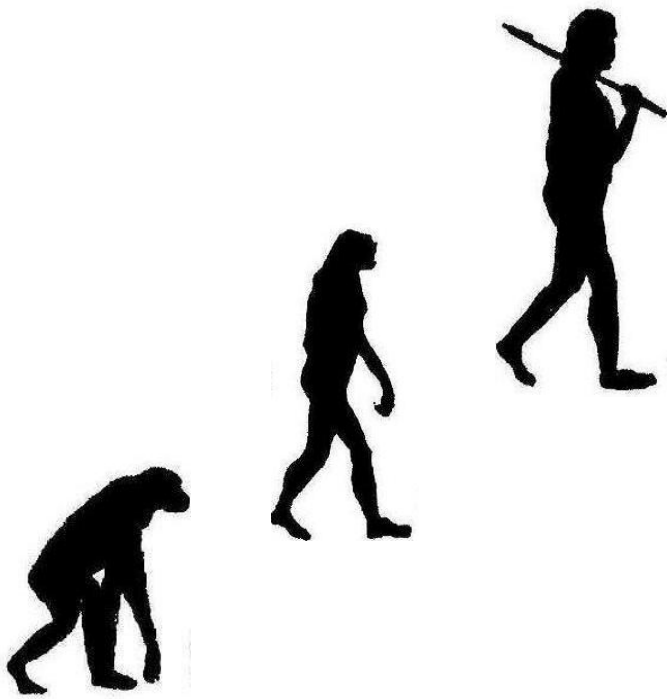
“Evolvability”

- **Robustness** of lineages to large changes on long timescales
- Essentially an ***architectural*** question
  - What makes an architecture evolvable?
  - What does “architecture” mean here?
- What are the limits on evolvability?
- How does architecture, evolvability, robustness, and complexity relate?

- Key: tradeoffs, robustness, layering

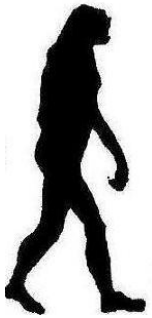
Unfortunately, not intelligent design





Ouch.

weak
fragile
slow



Human evolution

hands
feet
skeleton
muscle
skin
gut
long helpless childhood

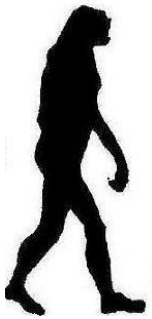
All very different.

Apes

strong
robust
fast

How is this progress?

Homo Erectus?



hands
feet
skeleton
muscle
skin
gut

Roughly modern

Very fragile

weak
fragile

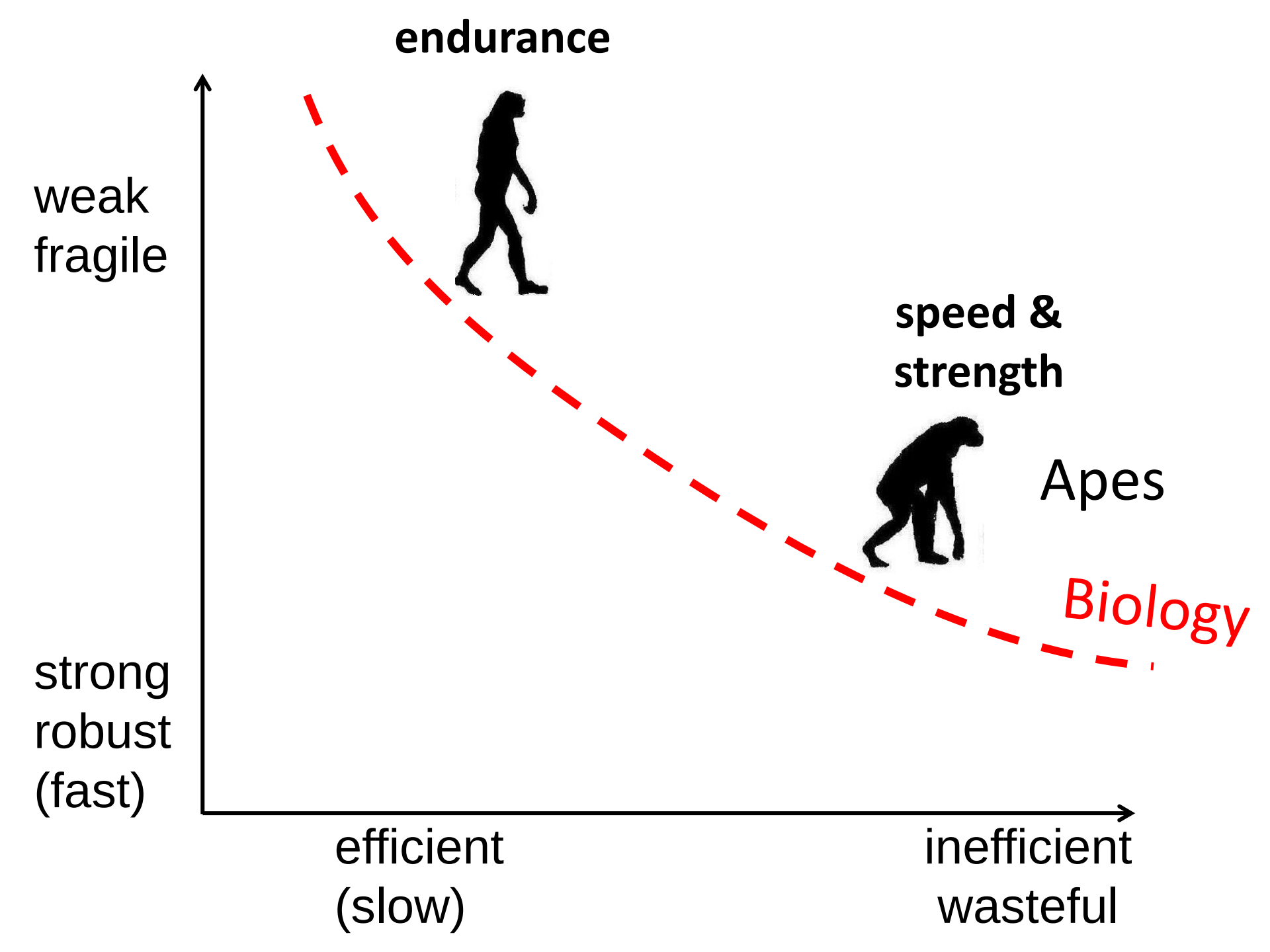
This much seems pretty consistent among experts regarding circa 1.5-2Mya

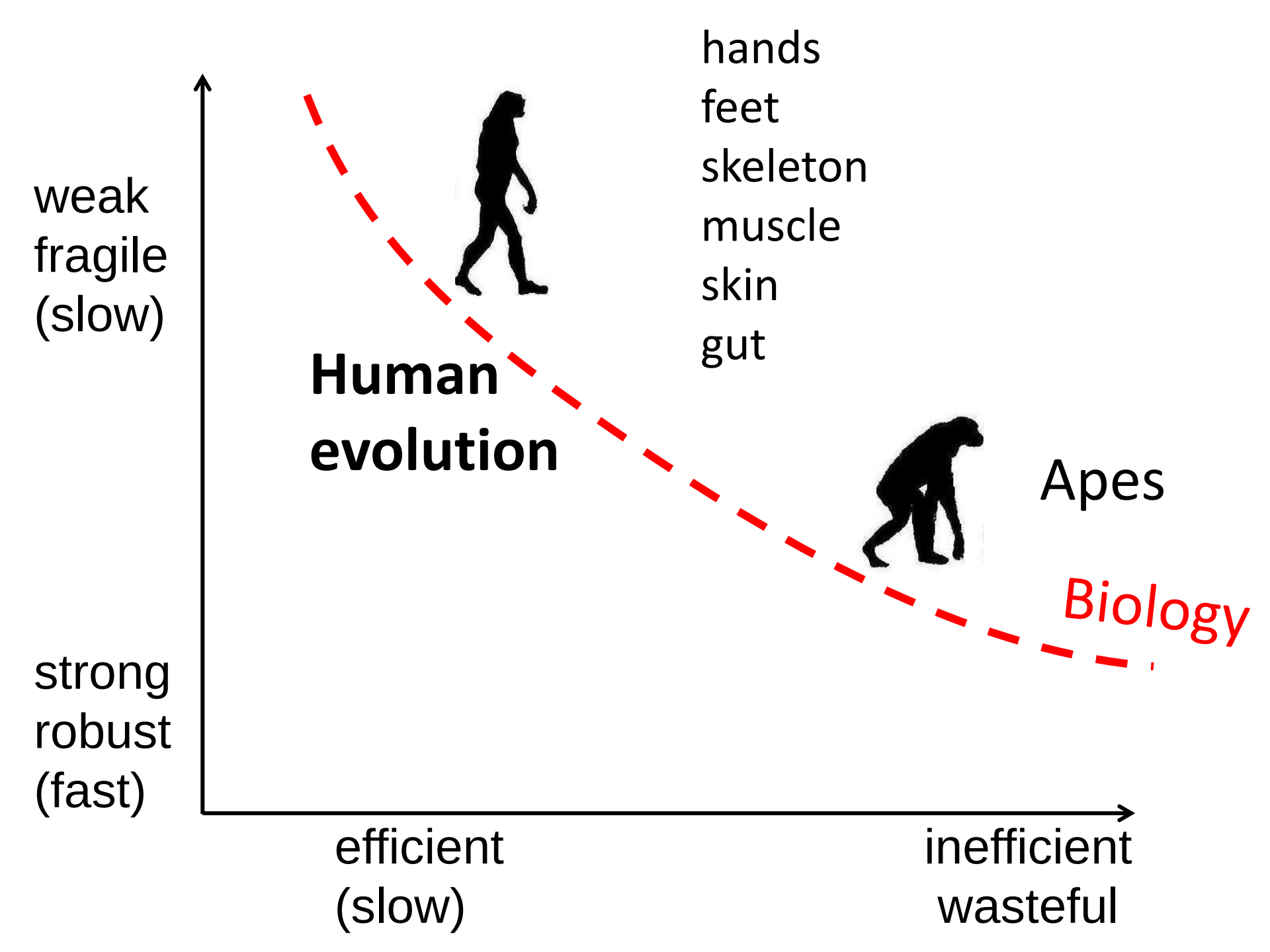
strong
robust

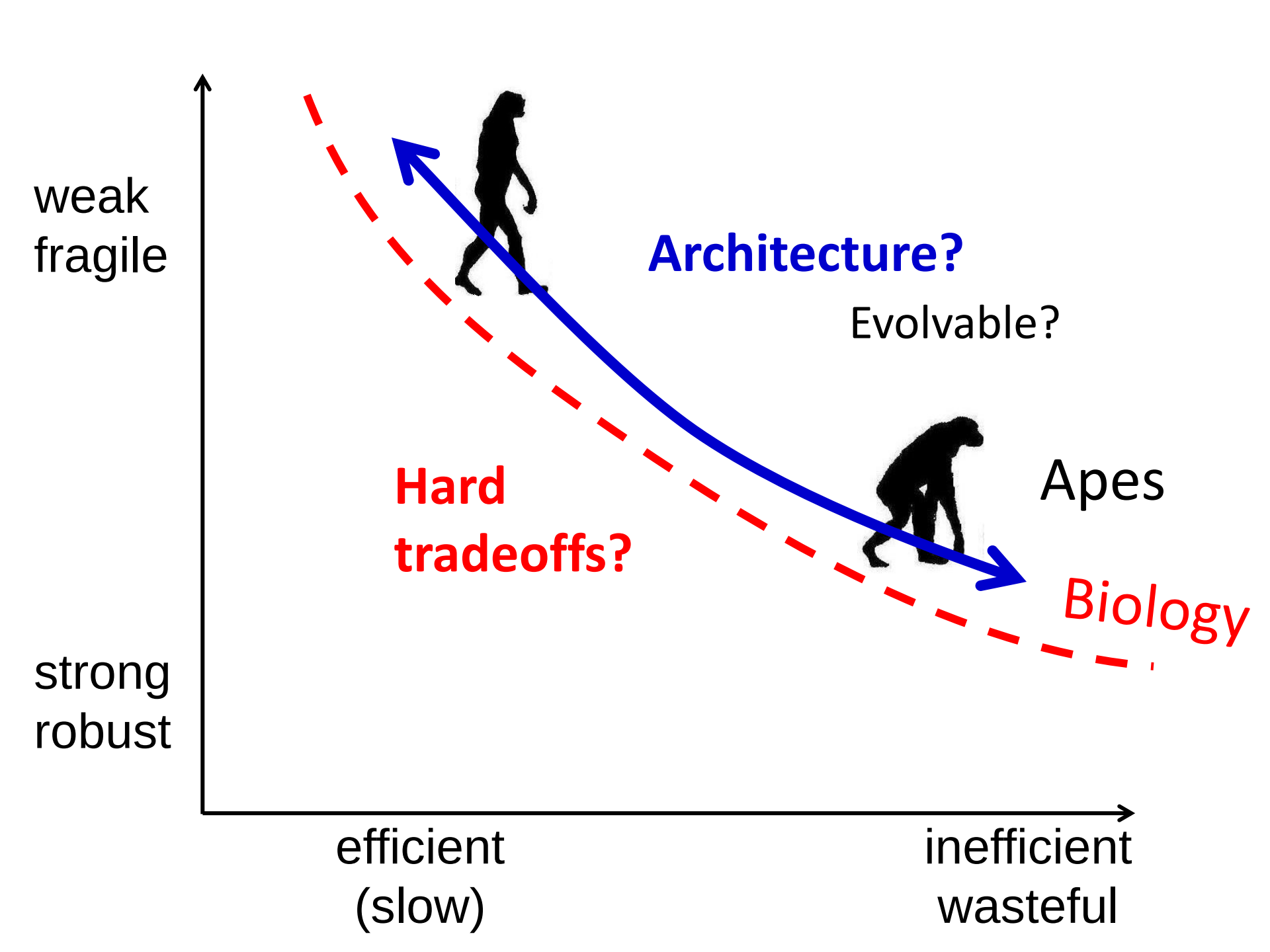
So how did H. Erectus survive and expand globally?

efficient
(slow)

inefficient
wasteful


endurance
weak
fragile
speed &
strength
Apes
Biology
strong
robust
(fast)
efficient
(slow)
inefficient
wasteful

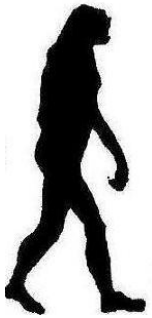

hands
feet
skeleton
muscle
skin
gut
weak
fragile
(slow)
Human
evolution
Apes
Biology
strong
robust
(fast)
efficient
(slow)
inefficient
wasteful


weak
fragile
strong
robust
efficient
(slow)
inefficient
wasteful
Architecture?
Evolvable?
Hard
tradeoffs?
Apes
Biology

endurance

weak
fragile

+
sticks
stones
fire
teams



From weak prey
to invincible
predator?

strong
robust

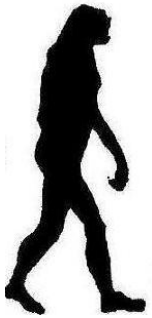
efficient
(slow)

Speculation? There is only evidence for crude stone tools. But sticks, fire, teams might not leave a record?

weak
fragile

strong
robust

efficient
(slow)



Speculation? With only evidence for crude stone tools. But sticks and fire might not leave a record?

+

sticks
stones
fire
teams

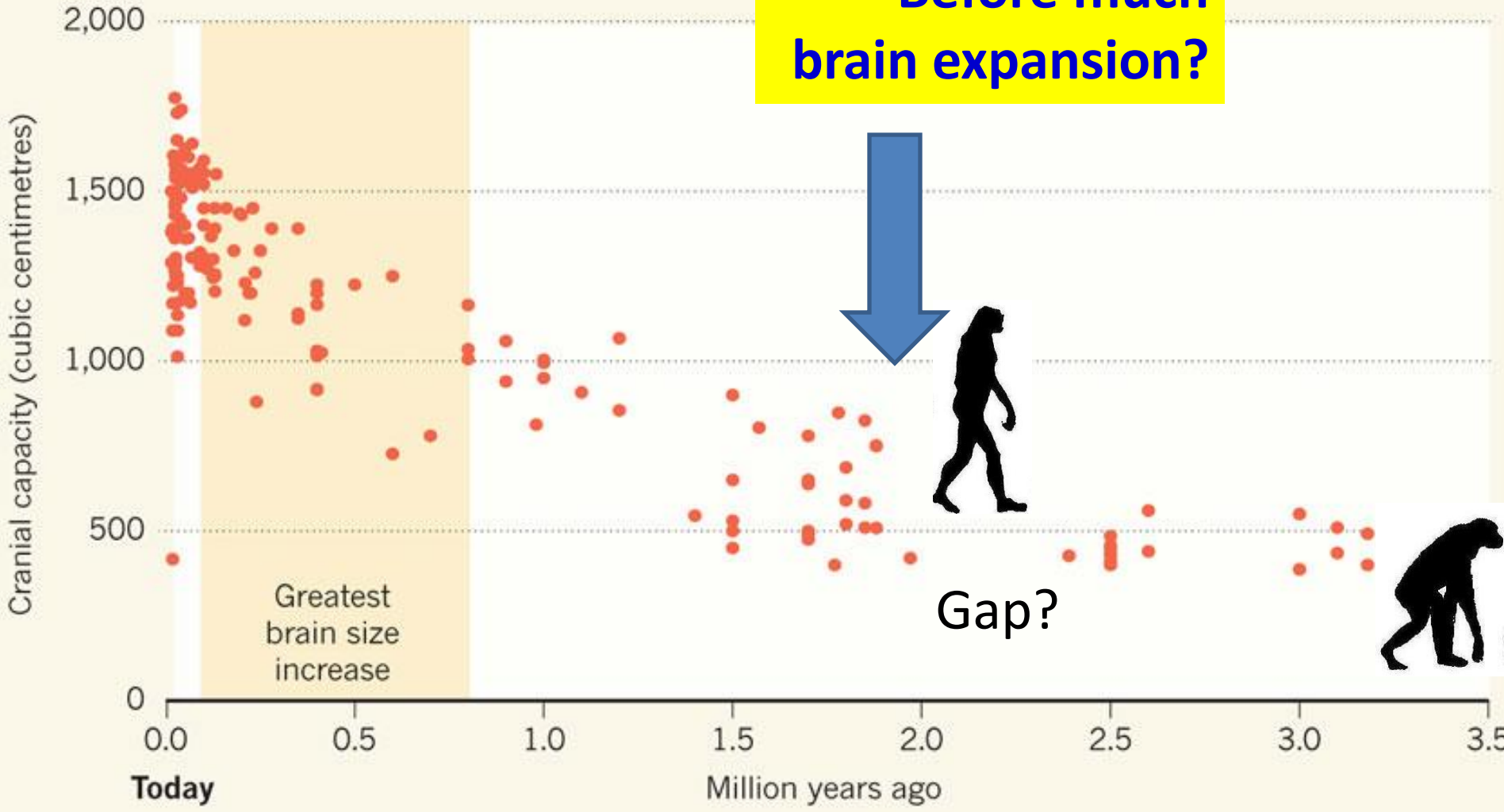
From weak prey to invincible predator

Before much brain expansion?

Plausible but speculation?

Cranial capacity

Before much brain expansion?

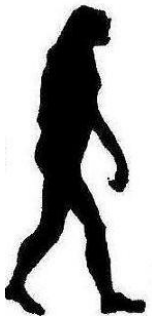


Today

2Mya

weak
fragile

strong
robust



hands
feet
skeleton
muscle
skin
gut

\+

sticks
stones
fire

From weak prey to invincible predator

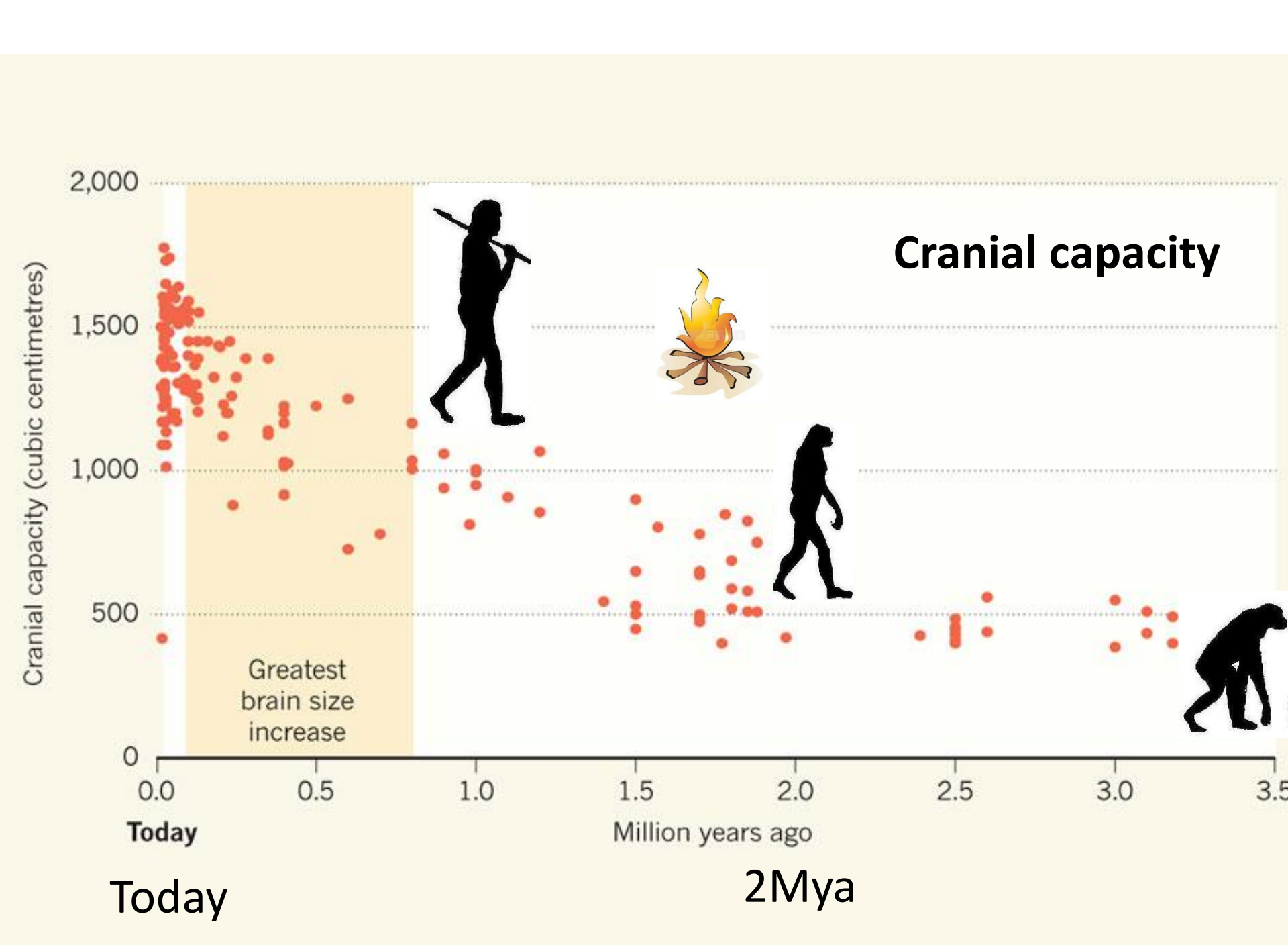
Before much brain expansion?

efficient (slow)

Key point:
Our physiology, technology, and brains have co-evolved

Probably true no matter what

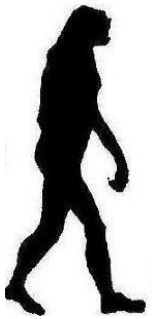
Huge implications.


Cranial capacity
2,000
1,500
1,000
500
0
Cranial capacity (cubic centimetres)
Greatest brain size increase
0.0
0.5
1.0
1.5
2.0
2.5
3.0
3.5
Today
Million years ago

Today

2Mya

weak
fragile



hands
feet
skeleton
muscle
skin
gut

Key point needing more discussion:
The evolutionary challenge of big brains is ***homeostasis***, not basal metabolic load.

\+

sticks
stones
fire

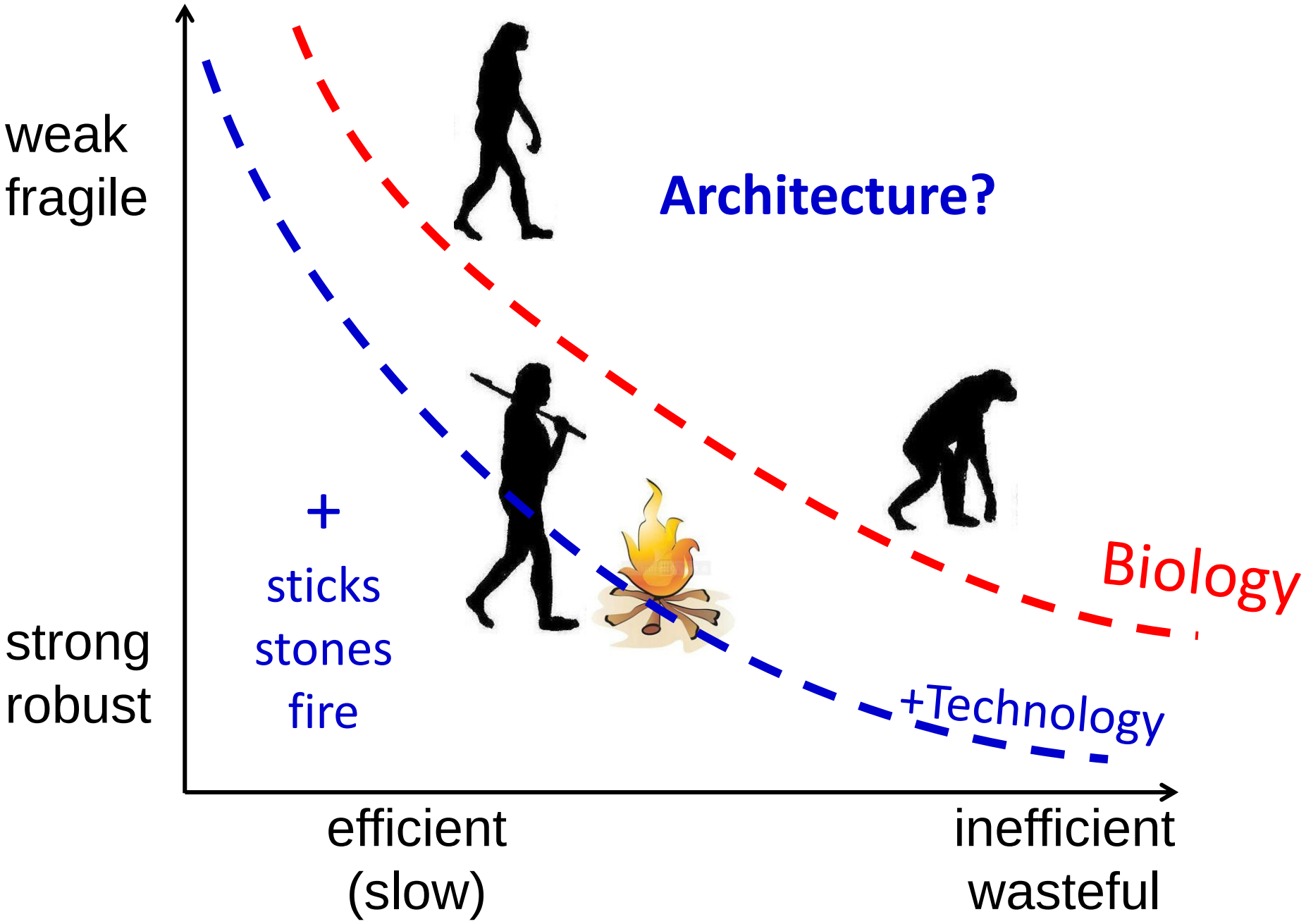
From weak prey to invincible predator

strong
robust

efficient
(slow)

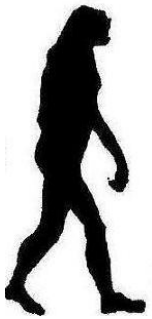
Before much brain expansion?

Huge implications.


weak
fragile
strong
robust
Architecture?
+
sticks
stones
fire
Biology
+Technology
efficient
(slow)
inefficient
wasteful

weak
fragile

strong
robust



hands
feet
skeleton
muscle
skin
gut

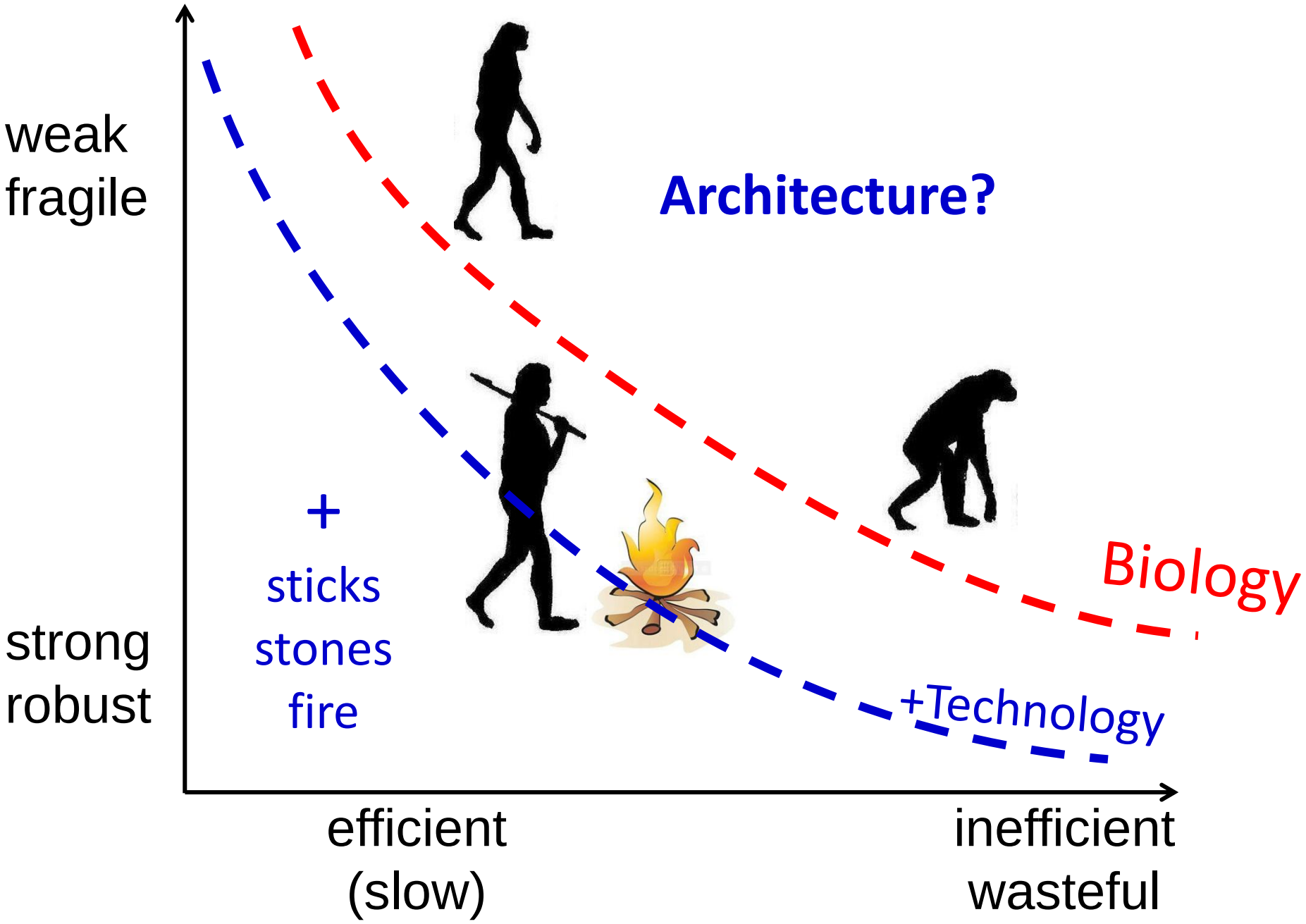
\+

sticks
stones
fire

From weak prey
to invincible
predator

efficient
(slow)

Before much
brain expansion?


weak
fragile
strong
robust
Architecture?
+
sticks
stones
fire
Biology
+Technology
efficient
(slow)
inefficient
wasteful

Human complexity?

Consequences of our evolutionary history?

fragile

robust

efficient

wasteful

sticks
stones
fire

Biology

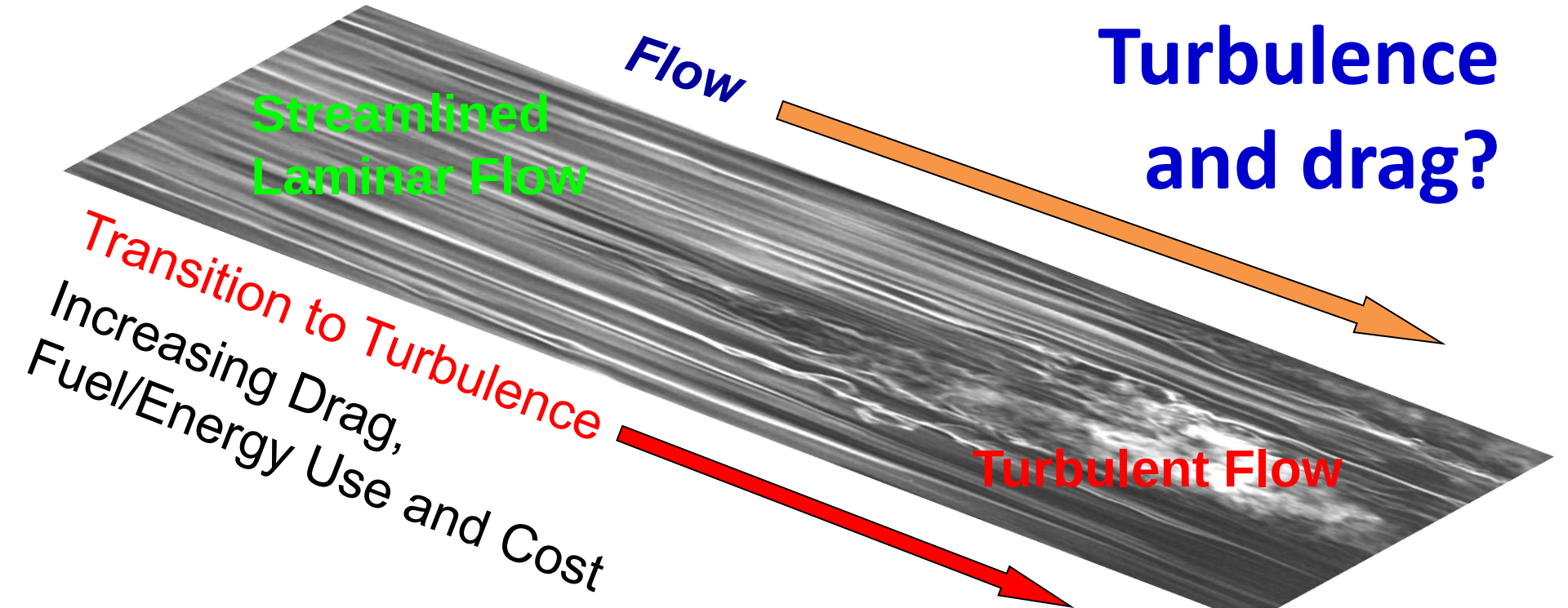
±Technology

J. Fluid Mech. (2010), vol. 665, pp. 99–119. © Cambridge University Press 2010
doi:10.1017/S0022112010003861

J. Fluid Mech (2010)

A streamwise constant model of turbulence in plane Couette flow

D. F. GAYME[1]†, B. J. McKEON[1], A. PAPACHRISTODOULOU[2], B. BAMIEH[3] AND J. C. DOYLE[1]

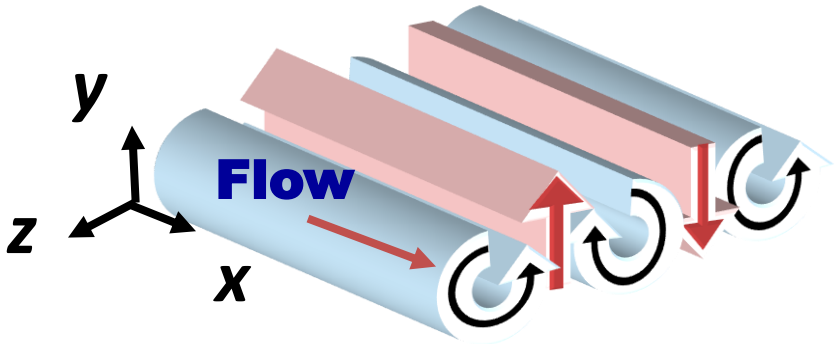


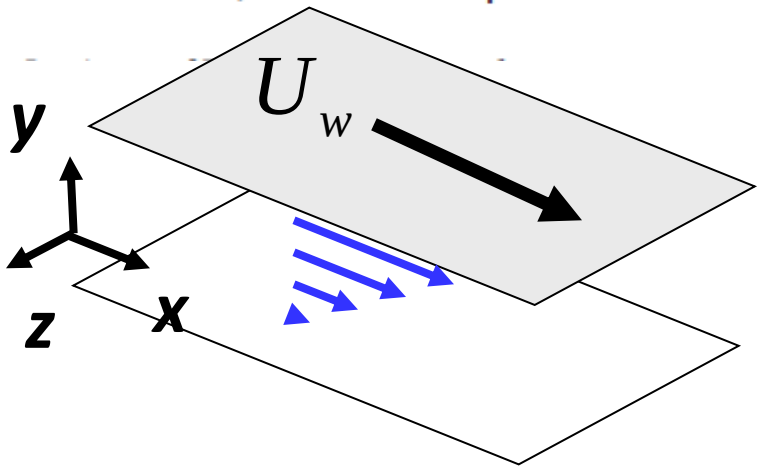
Physics of Fluids (2011)

PHYSICS OF FLUIDS **23**, 065108 (2011)

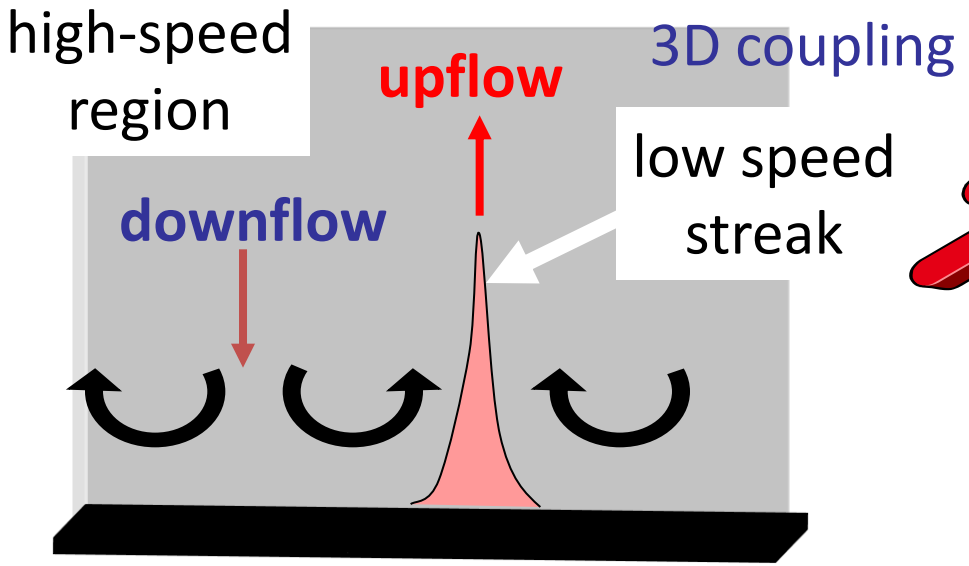
Amplification and nonlinear mechanisms in plane Couette flow

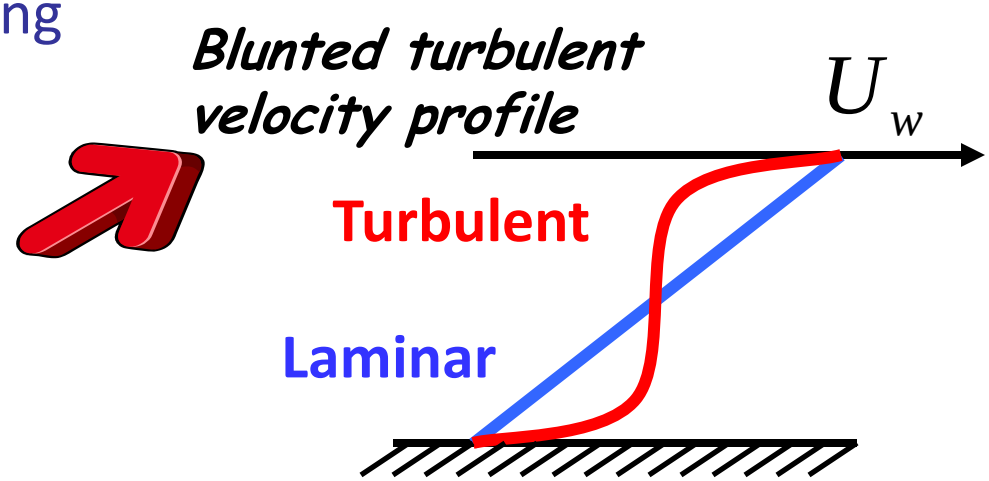
Dennice F. Gayme,[1] Beverley J. McKeon,[1] Bassam Bamieh,[2] Antonis Papachristodoulou,[3] and John C. Doyle[3]

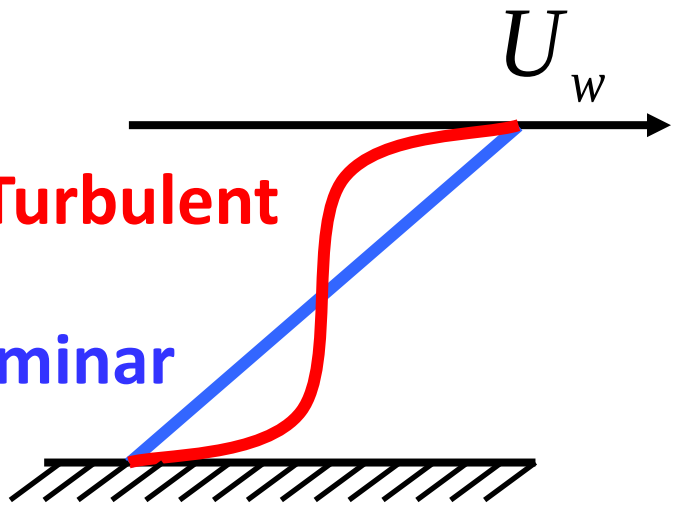




Coherent structures and turbulent drag







fragile

robust

Laminar

Control?

?

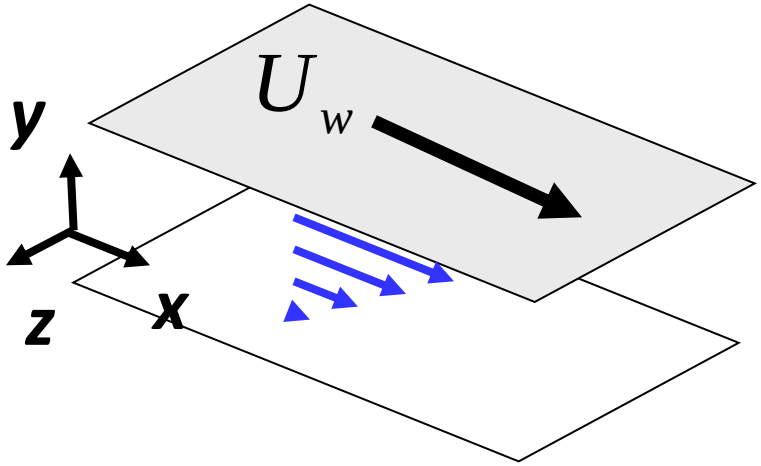
Turbulent

efficient

wasteful

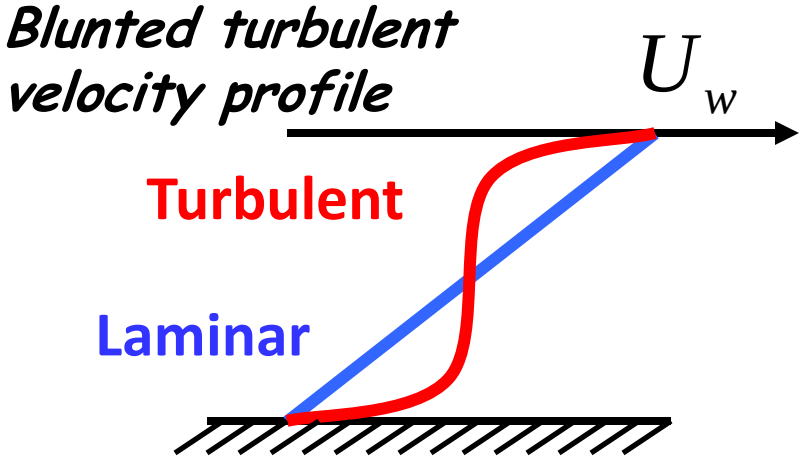
$$\frac{\partial \underline{u}}{\partial t} + \underline{u} \bullet \nabla \underline{u} = -\nabla p + \frac{1}{R} \Delta \underline{u}$$

$$\nabla \bullet \underline{u} = 0$$



"turbulence is a highly nonlinear phenomena"

Really?



$$\frac{\partial \underline{u}}{\partial t} + \underline{u} \bullet \nabla \underline{u} = -\nabla p + \frac{1}{R} \Delta \underline{u}$$

Complexity?

$$\nabla \bullet \underline{u} = 0$$

←Model→

	Small	Large
Robust	**Simple** 2d, linear	**Organized Computer**
Fragile	chaocritical **3d, nonlinear**	Irreducibile?

mildly nonlinear

highly nonlinear

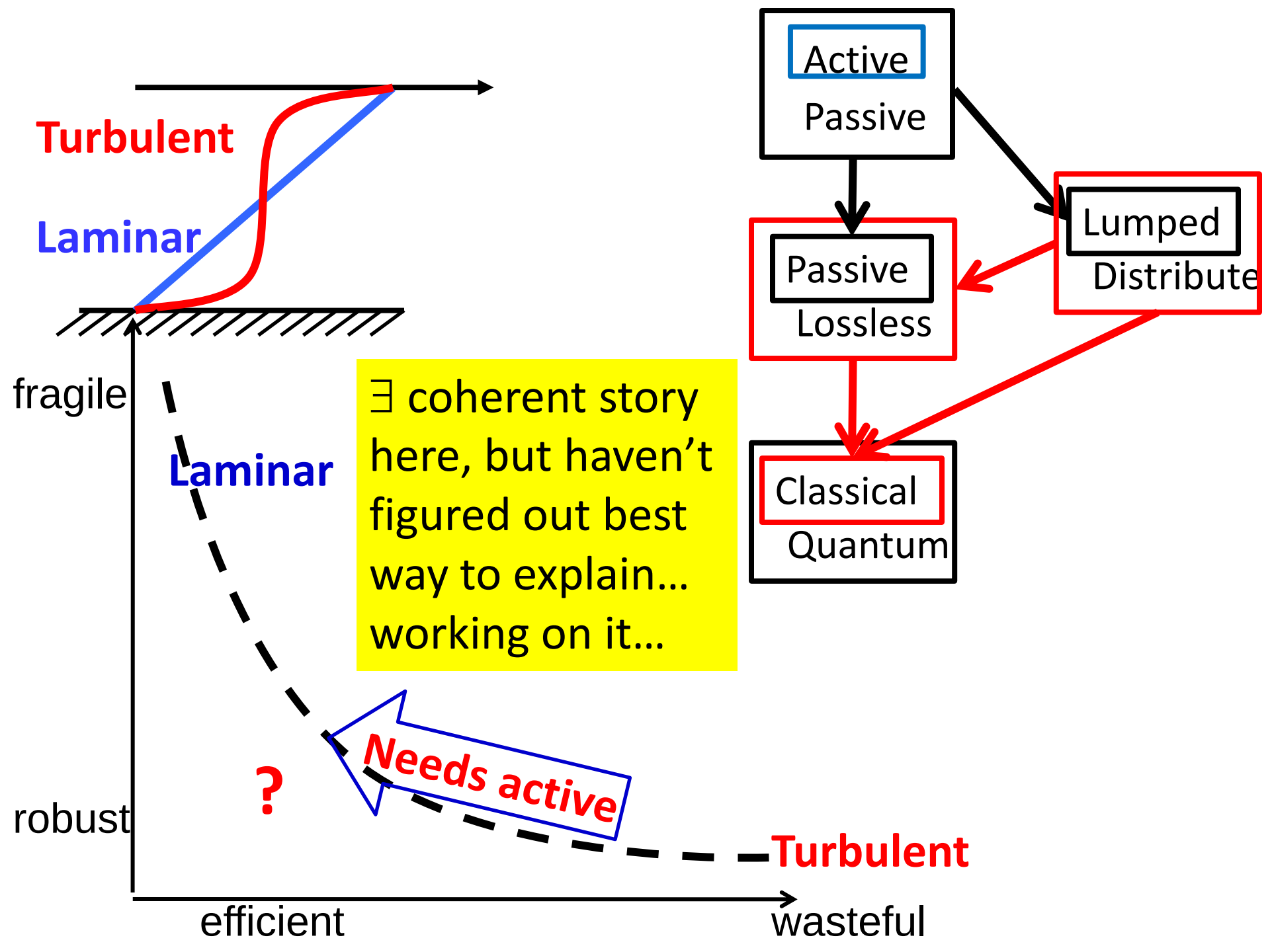
$$\frac{\partial \underline{u}}{\partial t} + \underline{u} \bullet \nabla \underline{u} = -\nabla p + \frac{1}{R} \Delta \underline{u}$$

$$\nabla \bullet \underline{u} = 0$$

Complexity?

- Numerical simulations can be ***highly predictive*** of real phenomena, yet still leave gaps in ***understanding***
- Our research is all about this deeper understanding
- The "highly organized" computer on which the simulations are run are truly "highly nonlinear"
- The PDEs that are simulated are mildly nonlinear

	Small ← Model → Large	
Robust	**Simple** 2d, linear	Organized Computer highly nonlinear
Fragile	chaotical 3d, nonlinear mildly nonlinear	Irreducibile?


Turbulent
Laminar
Active
Passive
Lumped
Distribute
Passive
Lossless
Classical
Quantum
fragile
Laminar
∃ coherent story here, but haven't figured out best way to explain… working on it…
?
Needs active
Turbulent
robust
efficient
wasteful

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

Other
nutrients

food

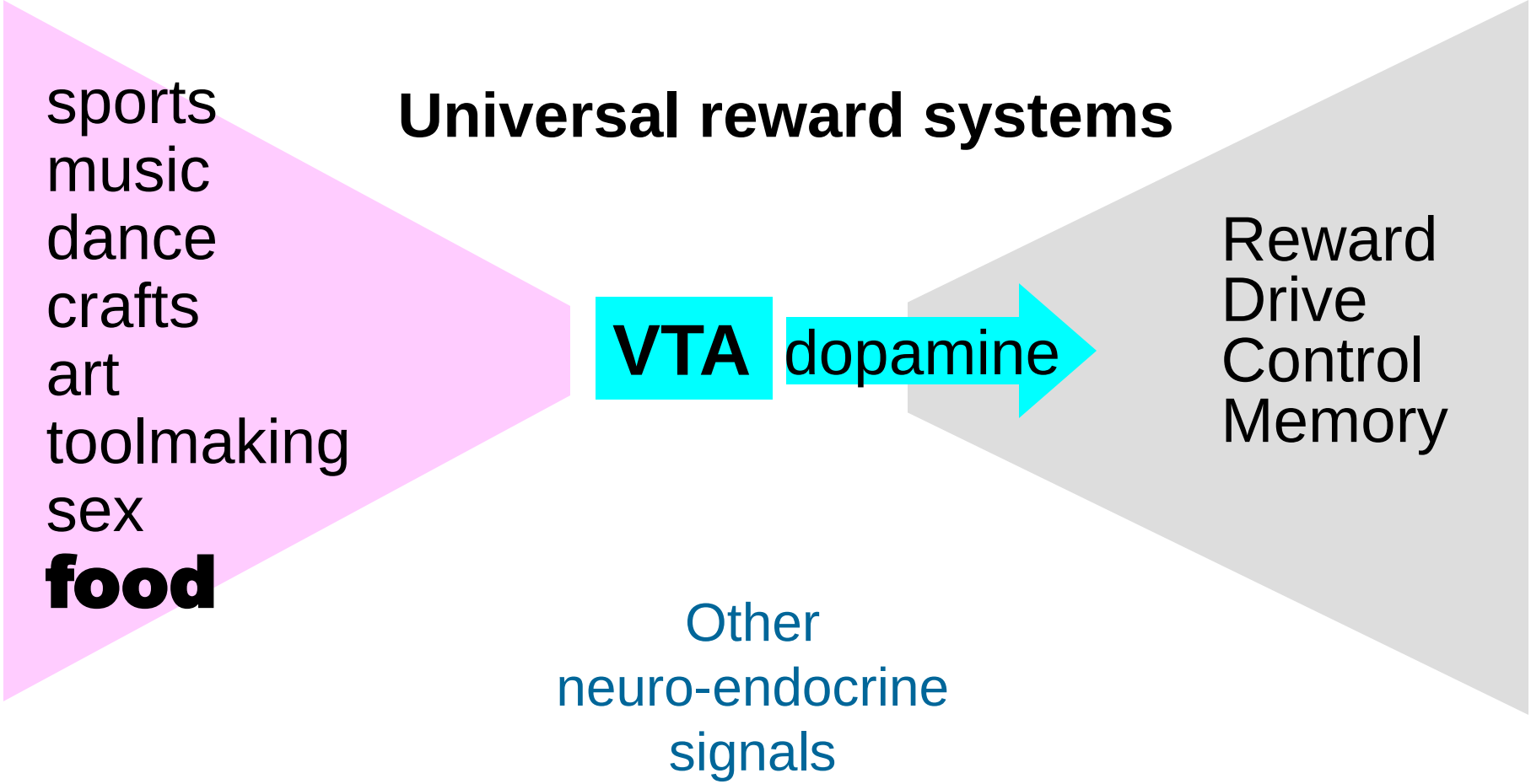
Blood

Glucose

Oxygen

Organs
Tissues
Cells
Molecules

Universal metabolic system


sports
music
dance
crafts
art
toolmaking
sex
food
Universal reward systems
VTA
dopamine
Reward
Drive
Control
Memory
Other
neuro-endocrine
signals

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 Architecture

Constraints

dopamine

Blood

Glucose

Oxygen

Fossil fuels

Electricity

Water

Modularity 2.0 Architecture

sports
music
dance
crafts
art
toolmaking
sex
food

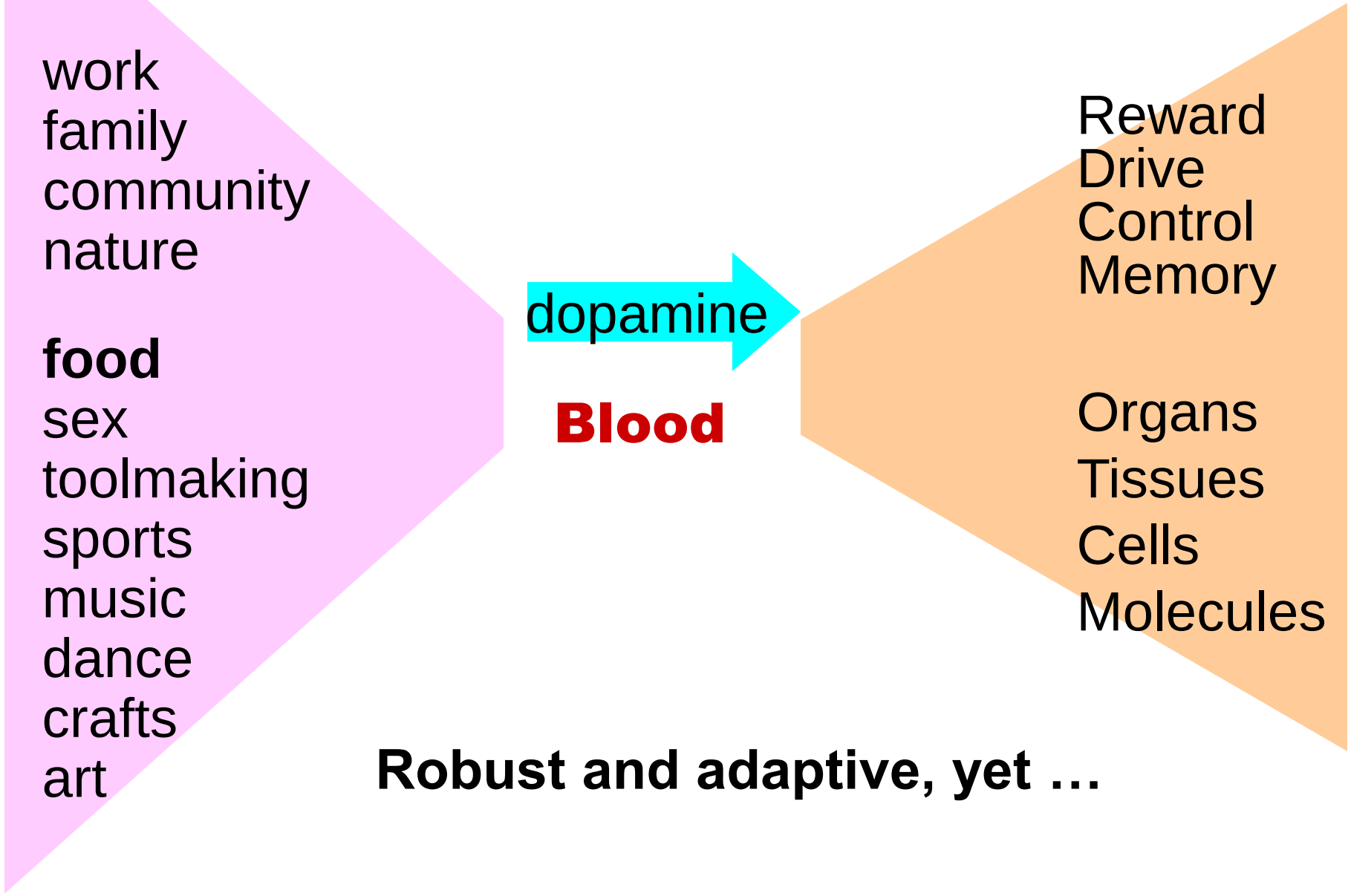
Reward
Drive
Control
Memory

that deconstrain

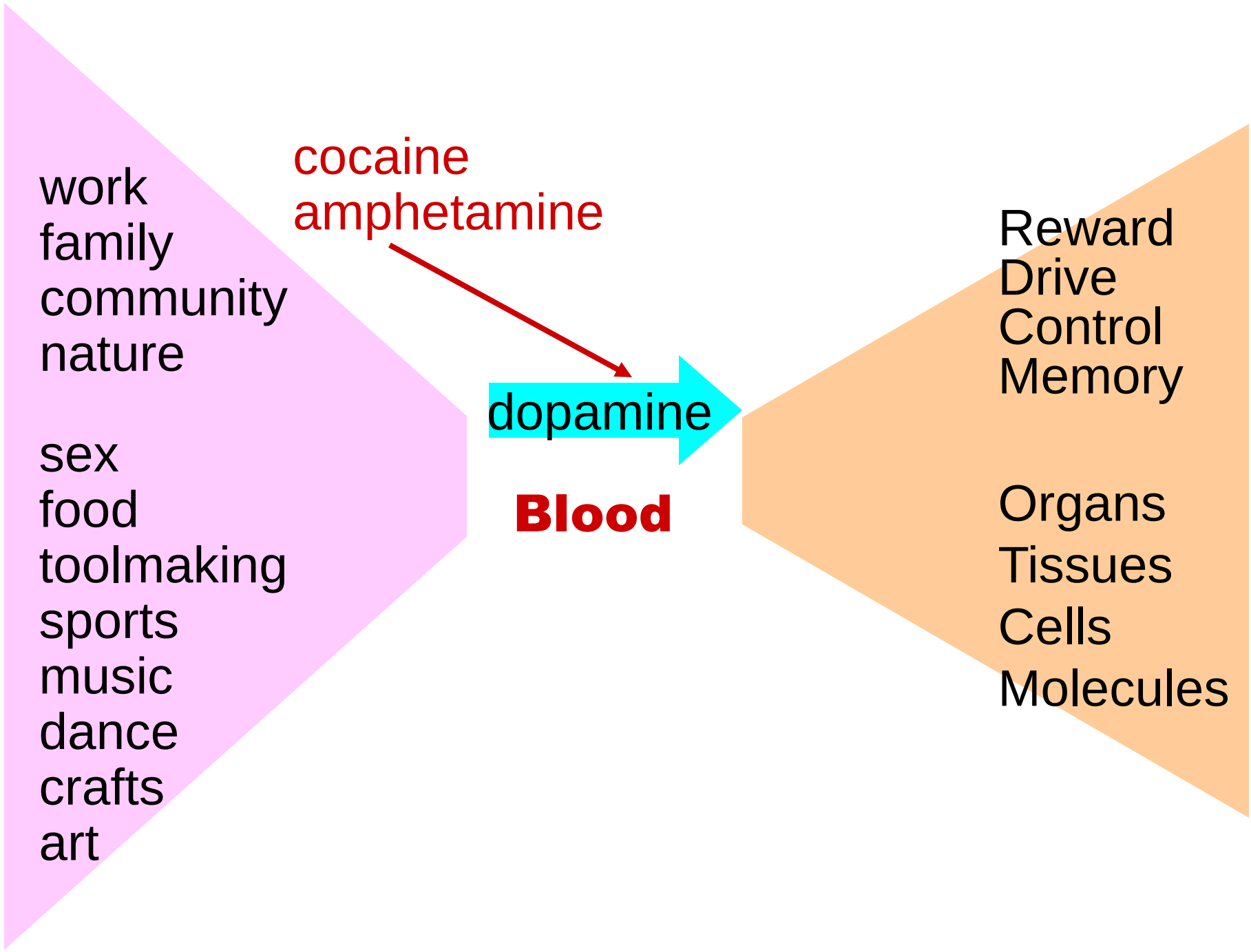
Organs
Tissues
Cells
Molecules

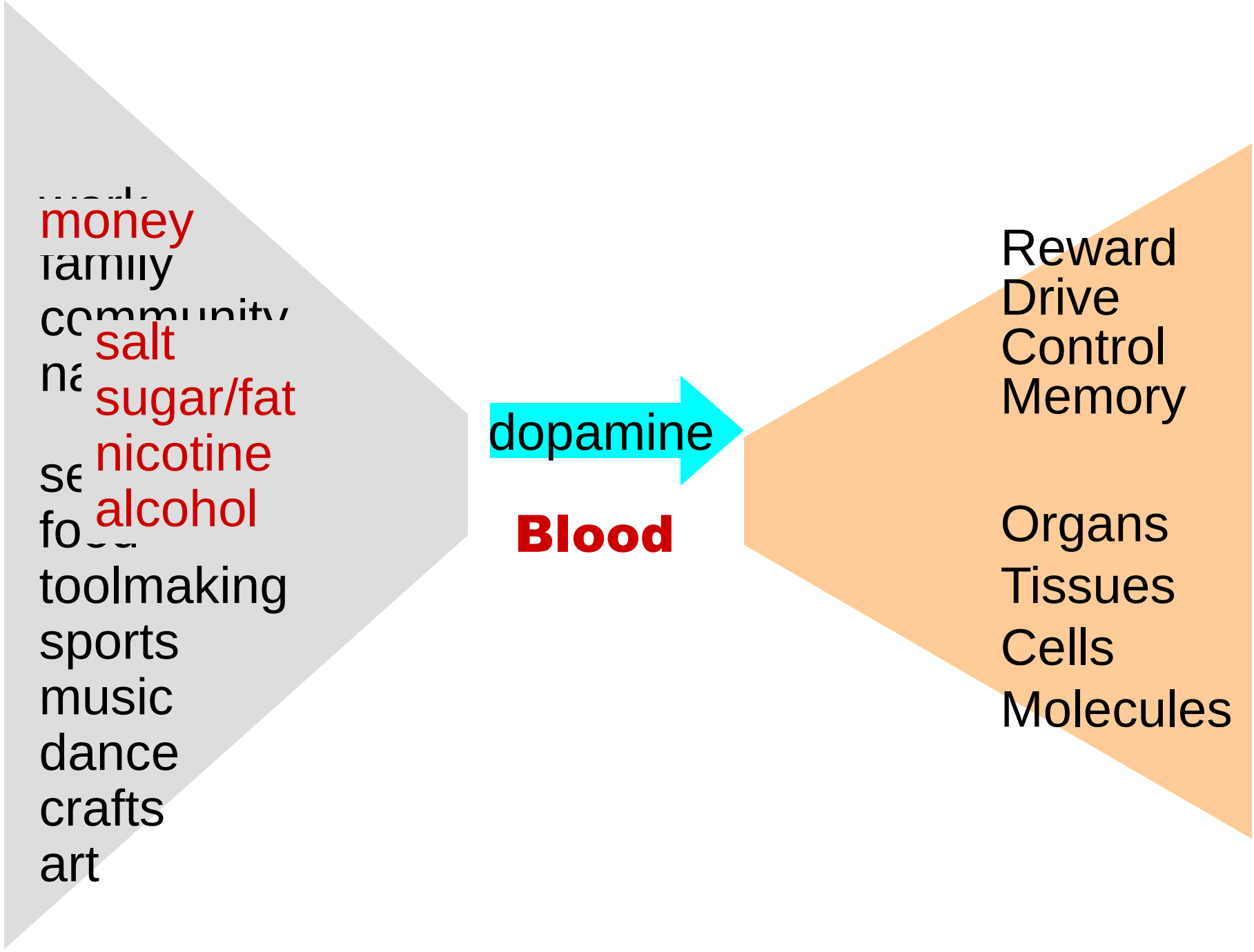
Extreme evolvability

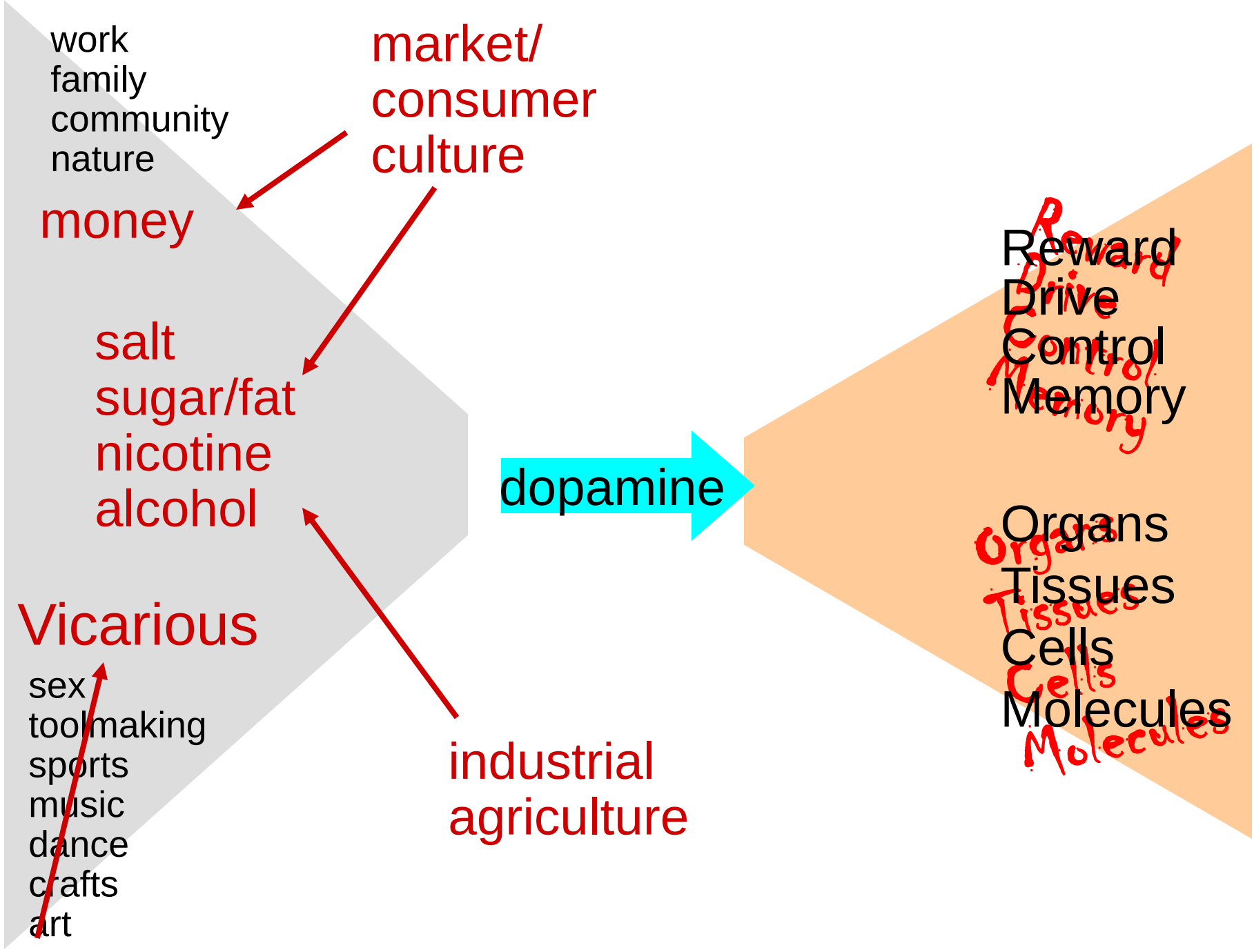
Universal reward/metabolic systems



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

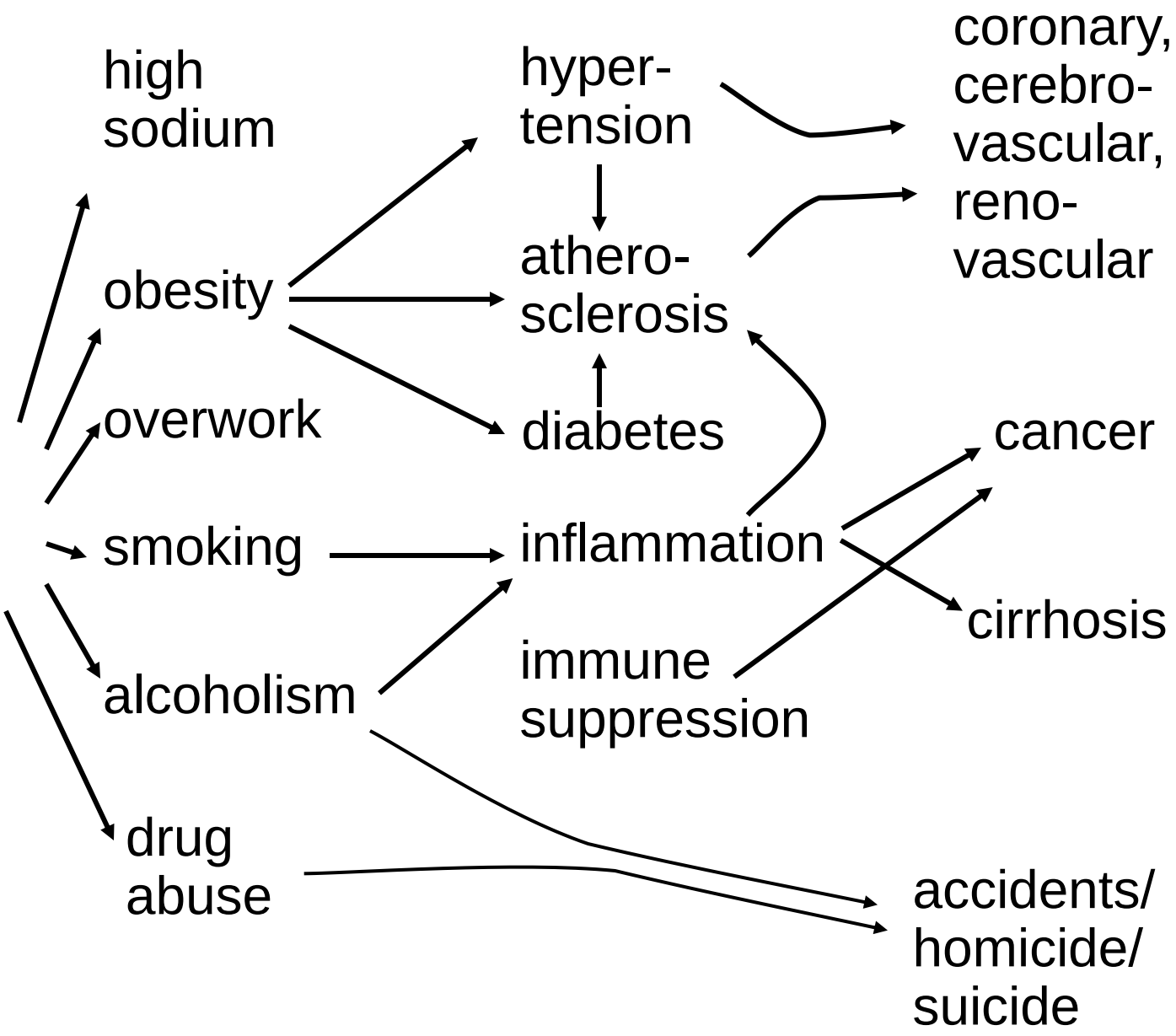

money
family
community
salt
sugar/fat
nicotine
alcohol
toolmaking
sports
music
dance
crafts
art
dopamine
Blood
Reward
Drive
Control
Memory
Organs
Tissues
Cells
Molecules


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

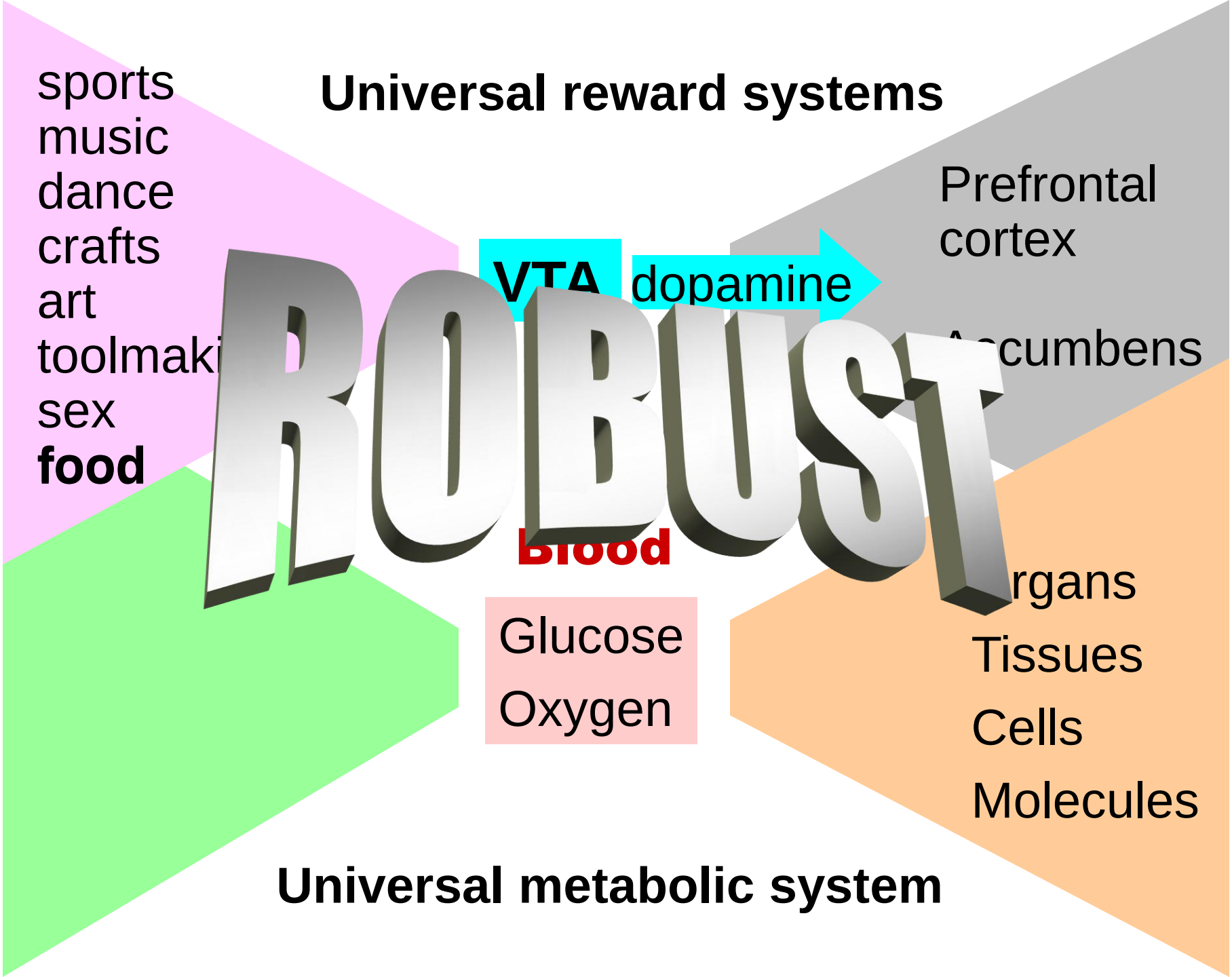
money

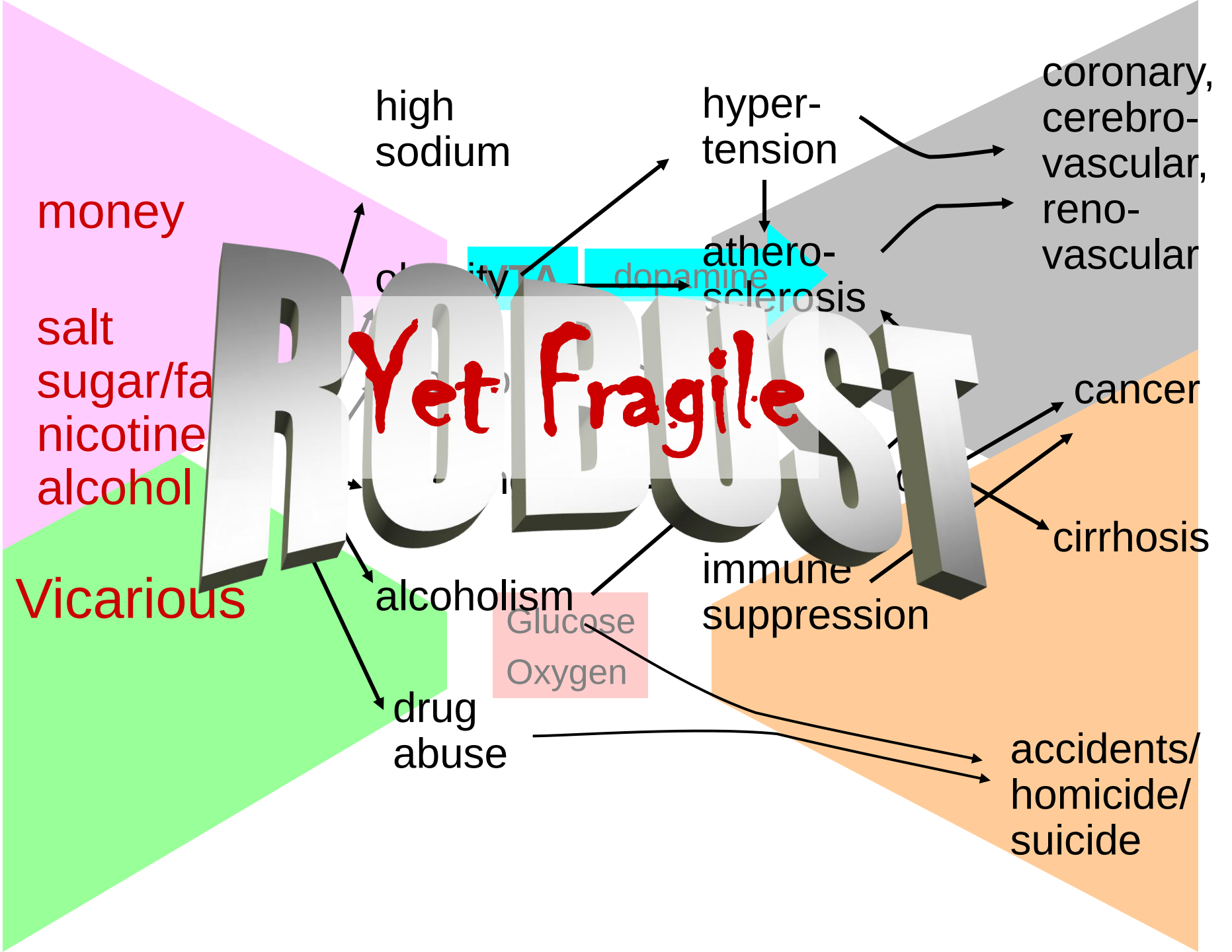
salt
sugar/fat
nicotine
alcohol

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

System

Architecture
=Constraints
(that deconstrain)

"Laws" =
hard limits,
tradeoffs

data

TM

UTM

Protocols

Four types of constraints

Components

System

sports
music
dance
crafts
aking

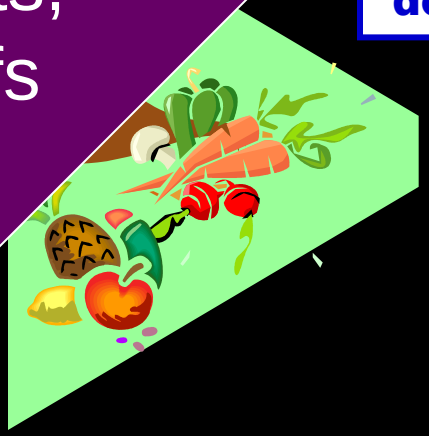
VTA dopamine

Reward
Drive
Control
Memory

"Laws" = hard limits, tradeoffs

Constraints that deconstrain

Blood
Glucose
Oxygen



Organs
Tissues
Cells
Molecules

Protocols

Components

Human complexity

Robust	Fragile
☺ Metabolism	☹ Obesity, diabetes
☺ Regeneration & repair	☹ Cancer
☺ Healing wound /infect	☹ AutoImmune/Inflame
	☹ Infectious diseases

Start with physiology

Lots of triage

Benefits

Robust

- ☺ Metabolism
- ☺ Regeneration & repair
- ☺ Healing wound /infect

- ☺ Efficient
- ☺ Mobility
- ☺ Survive uncertain food supply
- ☺ Recover from moderate trauma and infection

Mechanism?

Robust

- ☺ Metabolism
- ☺ Regeneration & repair
- ☺ Healing wound /infect
  - ☹ Fat accumulation
  - ☹ Insulin resistance
  - ☹ Proliferation
  - ☹ Inflammation

Fragile

- ☹ Obesity, diabetes
- ☹ Cancer
- ☹ AutoImmune/Inflame
  - ☹ Fat accumulation
  - ☹ Insulin resistance
  - ☹ Proliferation
  - ☹ Inflammation

What's the difference?

Robust

- ☺ Metabolism
- ☺ Regeneration & repair
- ☺ Healing wound /infect

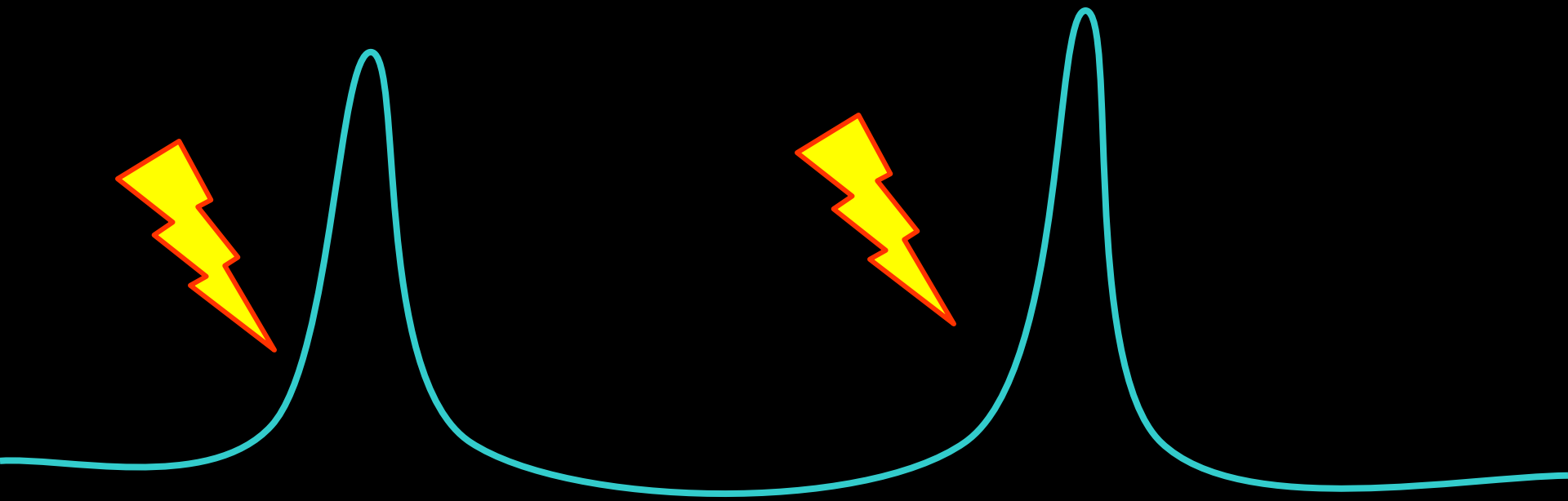
Fragile

- ☹ Obesity, diabetes
- ☹ Cancer
- ☹ AutoImmune/Inflame

- ☹ Fat accumulation
- ☹ Insulin resistance
- ☹ Proliferation
- ☹ Inflammation

Controlled
Dynamic

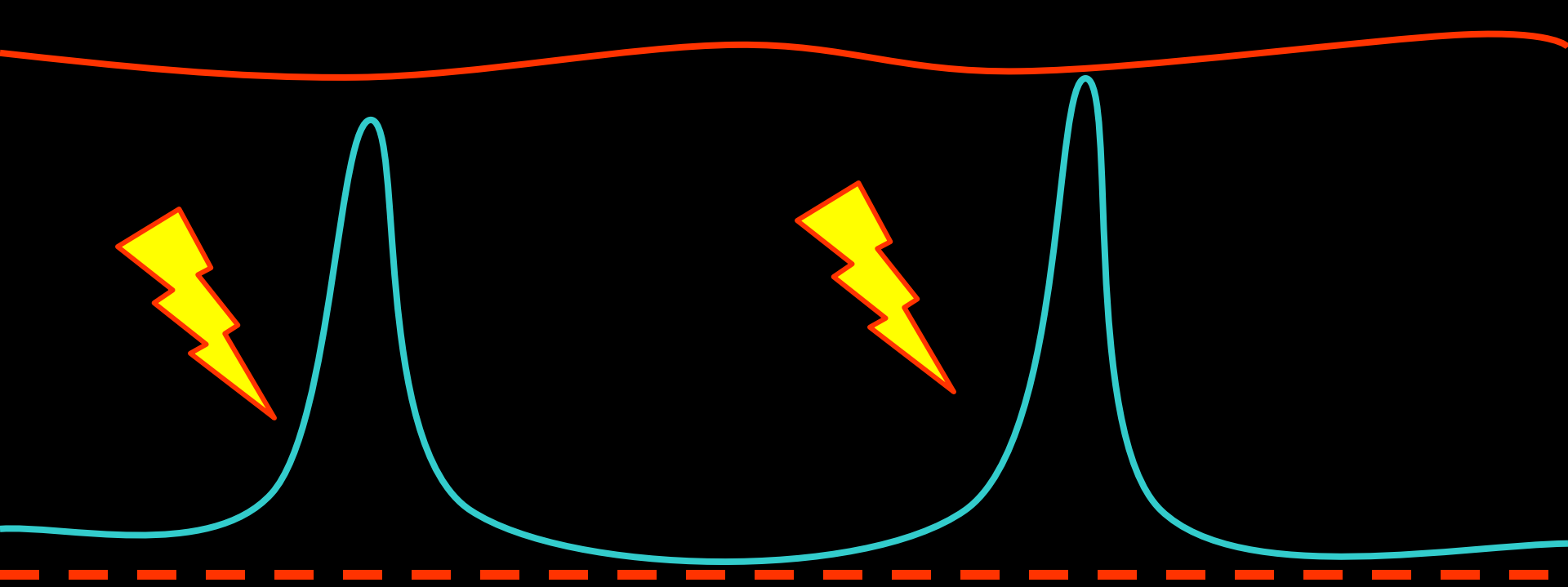
Uncontrolled
Chronic



- ☹ Fat accumulation
- ☹ Insulin resistance
- ☹ Proliferation
- ☹ Inflammation

Controlled
Dynamic

Low mean
High variability



Death

☹ Fat accumulation
☹ Insulin resistance
☹ Proliferation
☹ Inflammation

Controlled
Dynamic

Low mean
High variability

Uncontrolled
Chronic

High mean
Low variability

Mechanism?

Robust	Fragile
☺ Metabolism	☹ Obesity, diabetes
☺ Regeneration & repair	☹ Cancer
☺ Healing wound /infect	☹ AutoImmune/Inflame

Mainstream view is health

- = good genes (reductionist)
- = emergent, edge of chaos, fractals,…

- ***no*** physiology, homeostasis, tradeoffs, constraints, architecture, etc etc
- change is hopefully coming

Restoring robustness?

Robust

- ☺ Metabolism
- ☺ Regeneration & repair
- ☺ Healing wound /infect

- ☹ Fat accumulation
- ☹ Insulin resistance
- ☹ Proliferation
- ☹ Inflammation

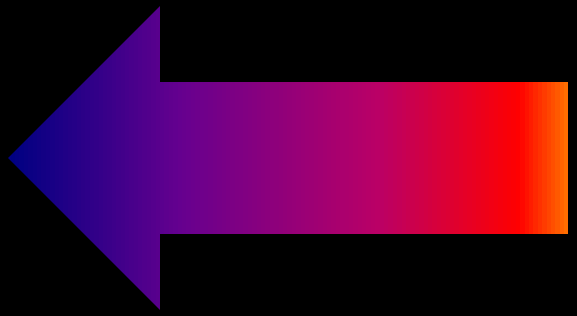
Fragile

- ☹ Obesity, diabetes
- ☹ Cancer
- ☹ AutoImmune/Inflame

- ☹ Fat accumulation
- ☹ Insulin resistance
- ☹ Proliferation
- ☹ Inflammation

Controlled
Dynamic

Low mean
High variability



Uncontrolled
Chronic

High mean
Low variability

Human complexity

Robust

- ☺ Metabolism
- ☺ Regeneration & repair
- ☺ Immune/inflammation
- ☺ Microbe symbionts
- ☺ Neuro-endocrine
- Complex societies
- Advanced technologies
- Risk “management”

Yet Fragile

- ☹ Obesity, diabetes
- ☹ Cancer
- ☹ AutoImmune/Inflame
- ☹ Parasites, infection
- ☹ Addiction, psychosis,…
- ☠ Epidemics, war,…
- 💣 Disasters, global &!%$#
- 💣 Obfuscate, amplify,…

Accident or necessity?

Robust

☺ Metabolism
☺ Regenerati
☺ Healing wo

Fragile

☹ Obesity, diabetes

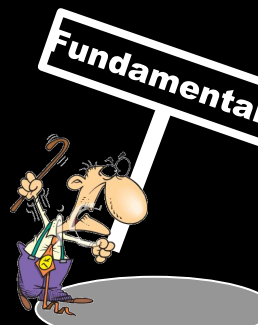
☹ Fat accumulation
☹ Insulin resistance
☹ Proliferation
☹ Inflammation

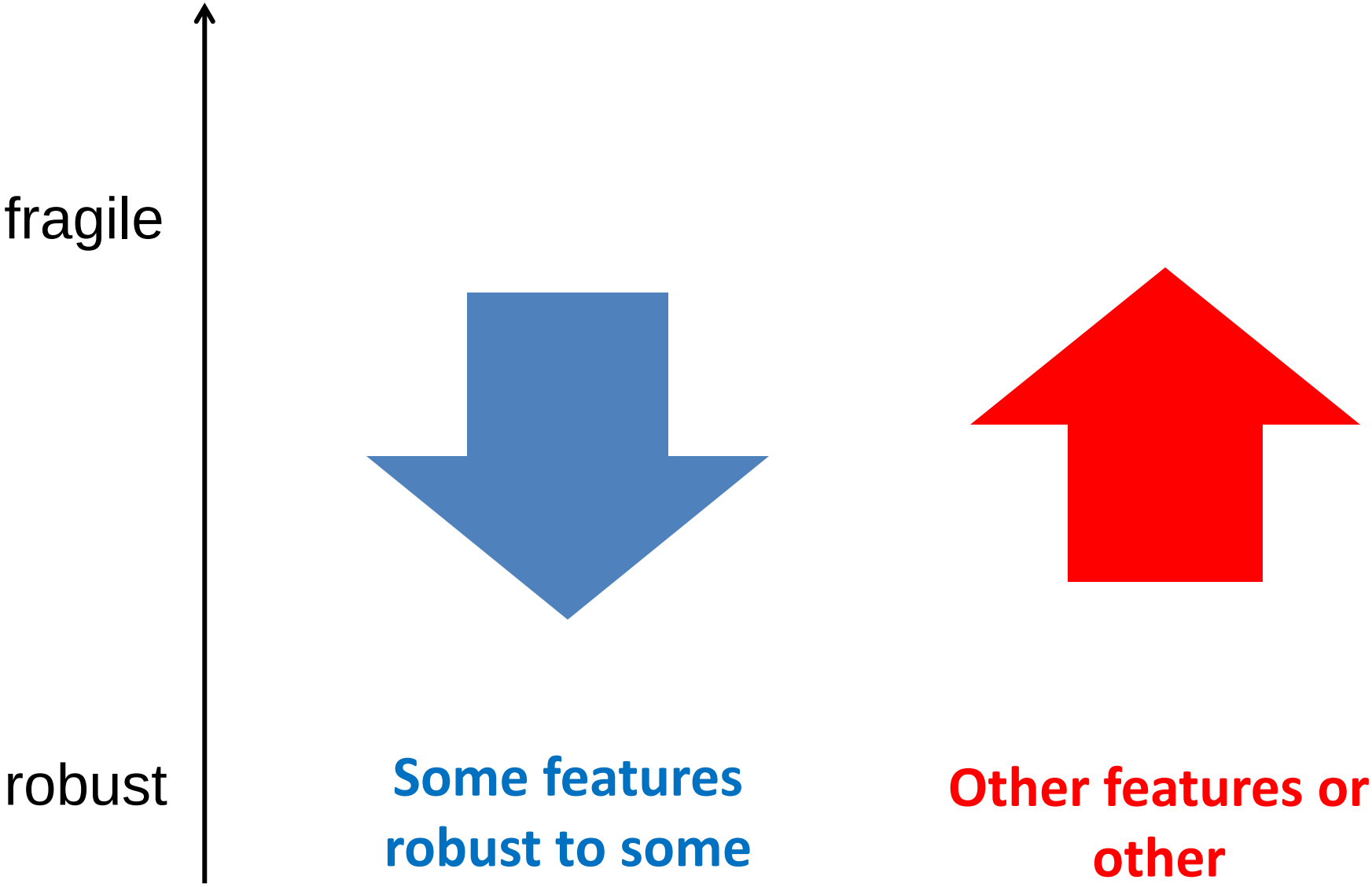
une/Inflame

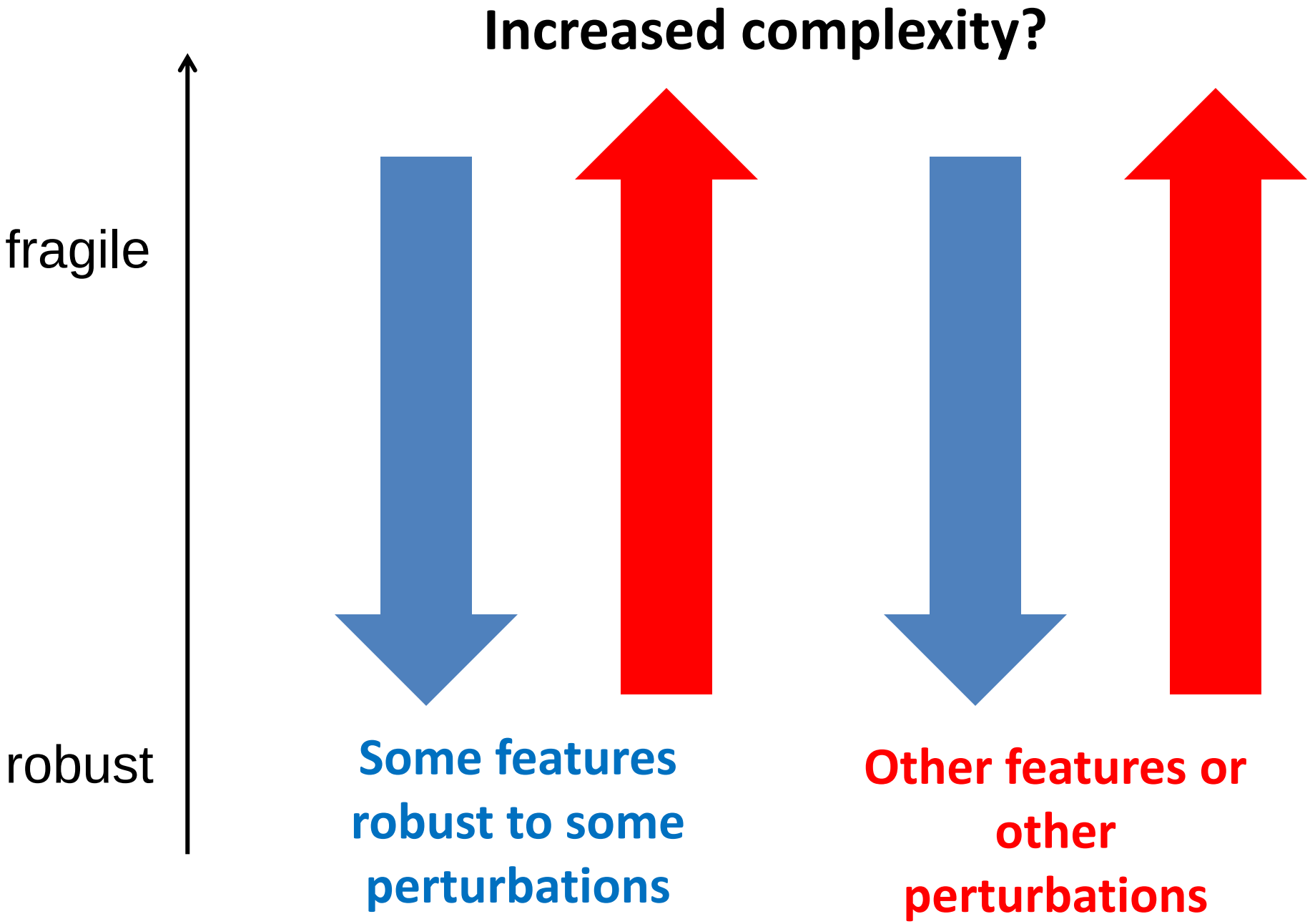
- Fragility ← Hijacking, side effects, unintended…
- Of mechanisms evolved for robustness
- Complexity ← control, robust/fragile tradeoffs
- Math: robust/fragile constraints (“conservation laws”)

Both

Accident or necessity?




fragile
robust
Some features robust to some perturbations
Other features or other perturbations


Increased complexity?
fragile
robust
Some features robust to some perturbations
Other features or other perturbations