John Doyle
John G Braun Professor
Control and Dynamical Systems, EE, BioE
Caltech

Architecture, constraints, and behavior

and zombies

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.

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

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

Understanding vision in wholly empirical terms

Dale Purves[a,1], William T. Wojtach[b], and R. Beau Lotto[c]

[a]Center for Cognitive Neuroscience, Department of Neurobiology, Duke University, Neuroscience and Behavioral Disorders Program, Duke–N
University of Singapore Graduate Medical School, Singapore 169857; [b]Center for Cognitive Neuroscience, Duke University, Levine Science Res
Durham, NC 27708; and [c]Institute of Ophthalmology, University College London, London EC1V 9EL, United Kingdom

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This article considers visual perception, the nature of the information on which perceptions seem to be based, and the implications of a wholly empirical concept of perception and sensory processing

numbers come up about equally, then a player shoul
if the dice are fair and bet accordingly; converse
numbers appear more frequently than others, then

Starting points

Variability, compensation, and modulation in neurons and circuits

Eve Marder[1]

Department of Biology and Volen Center, Brandeis University, Waltham, MA 02454

Edited by Donald W. Pfaff, The Rockefeller University, New York, NY, and approved December 14, 2010 (received for review Septe

I summarize recent computational and experimental work that addresses the inherent variability in the synaptic and intrinsic

Na^+ conductance and a high delayed rectif
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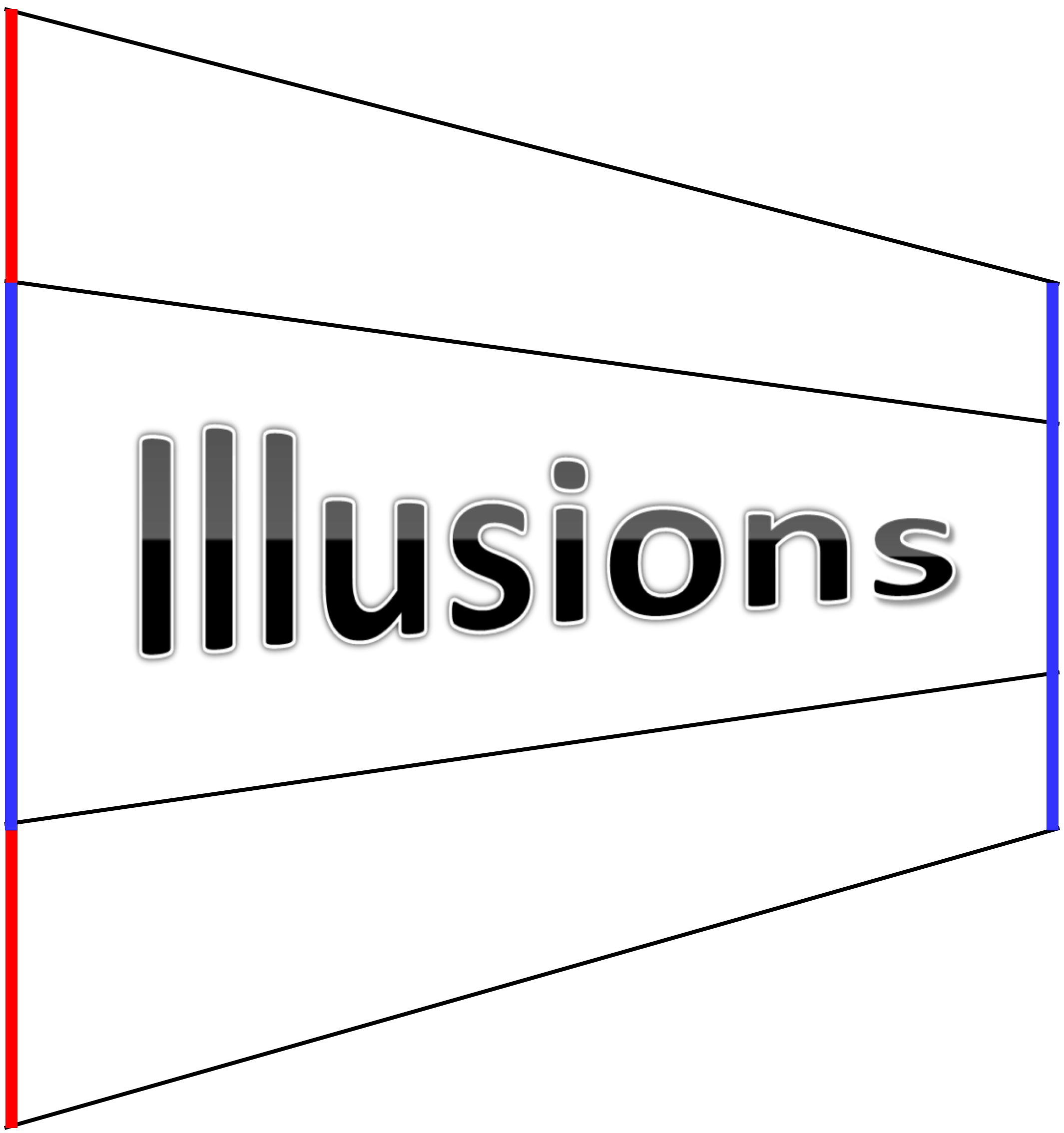


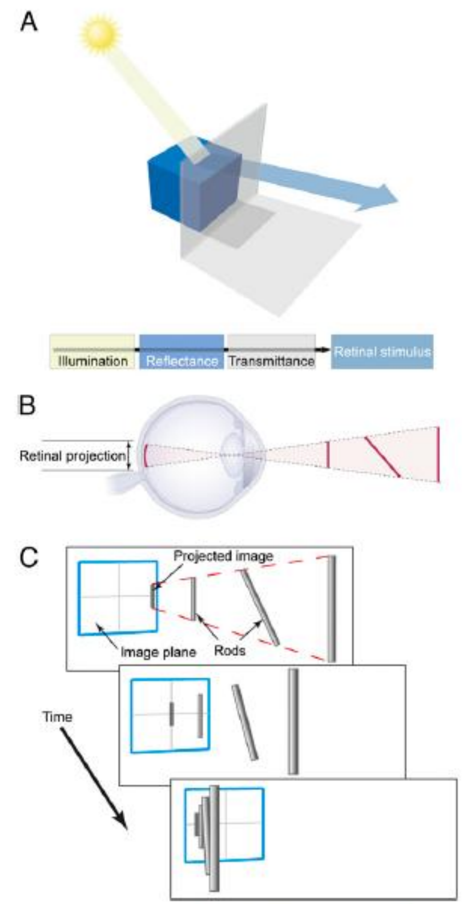
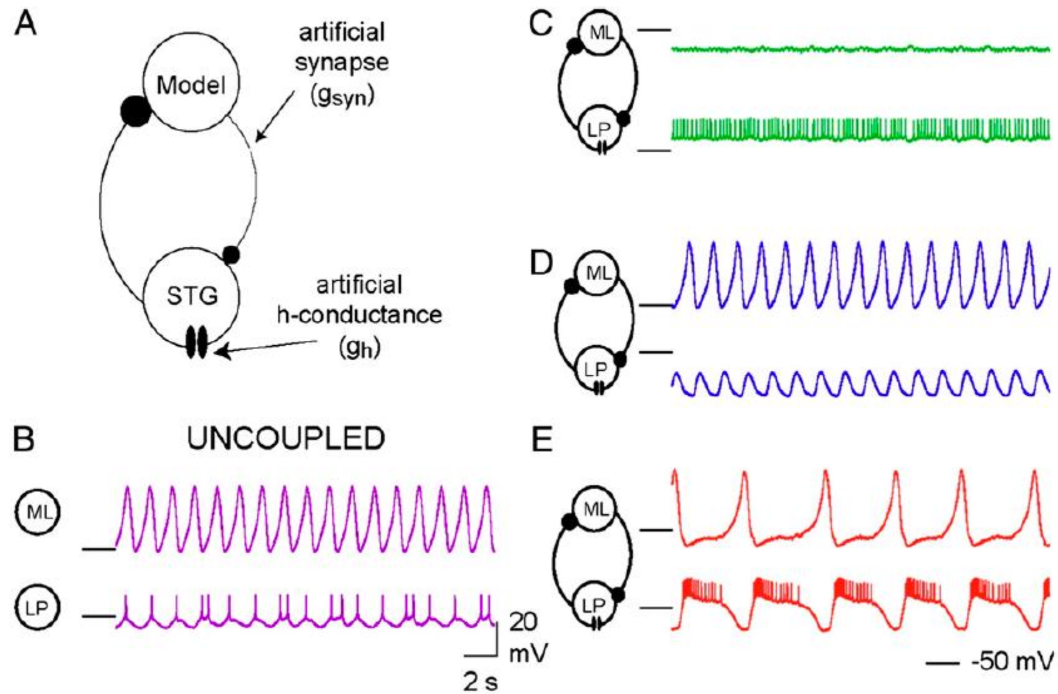


Fig. 1. The inverse optics problem. (*A*) The conflation of illumination, reflectance, and transmittance in retinal images. Many combinations of these physical characteristics of the world can generate the same retinal stimulus. (*B*) The conflation of physical geometry in images. The same image can be generated by objects of different sizes, at different distances from the observer, and in different orientations. (*C*) The conflation of speed and direction in images of moving objects. The same projected motion on the retina can be generated by different objects with various orientations moving in different directions and at different speeds in the physical world.

lobster somatogastric ganglia

large,
thin,
nonconvex



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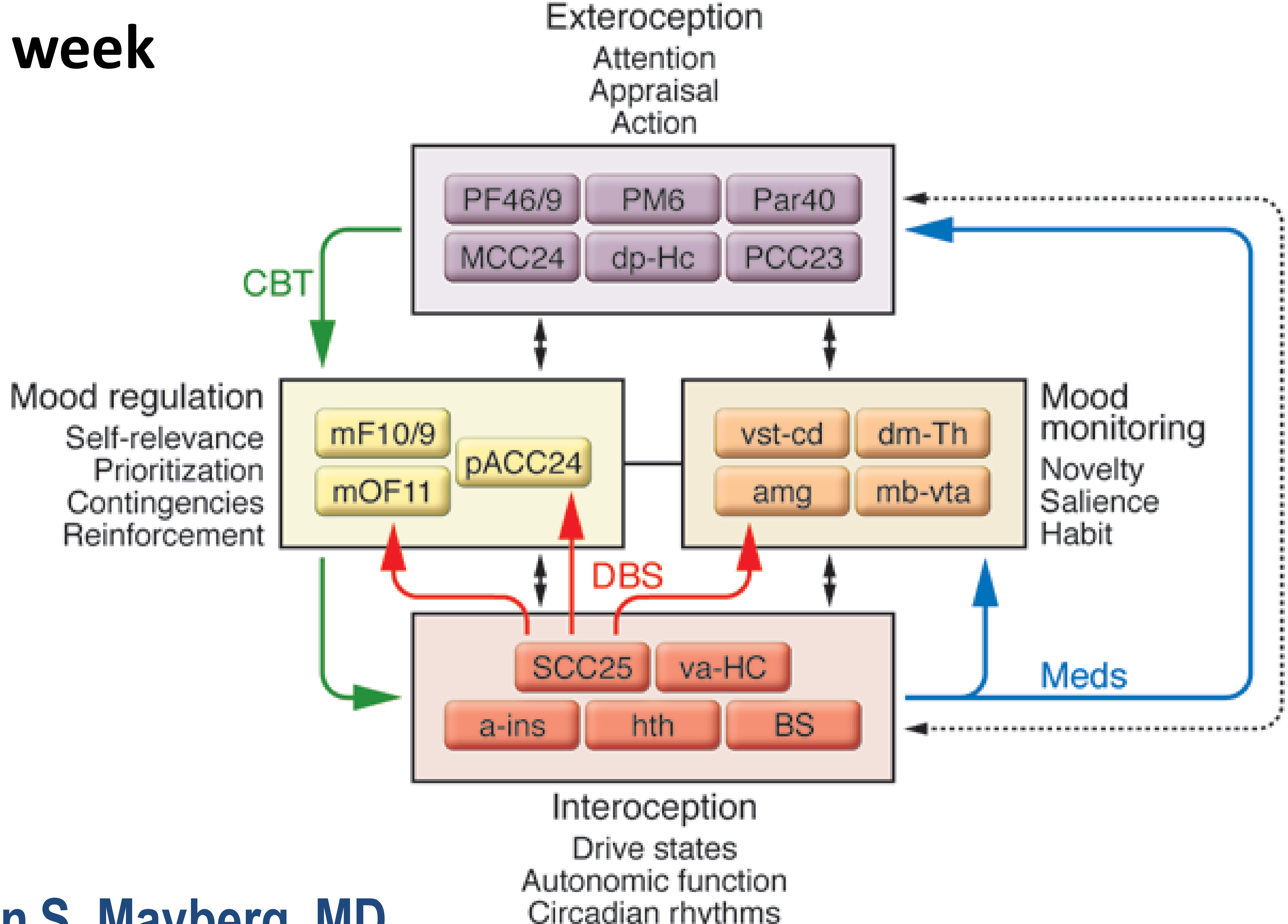
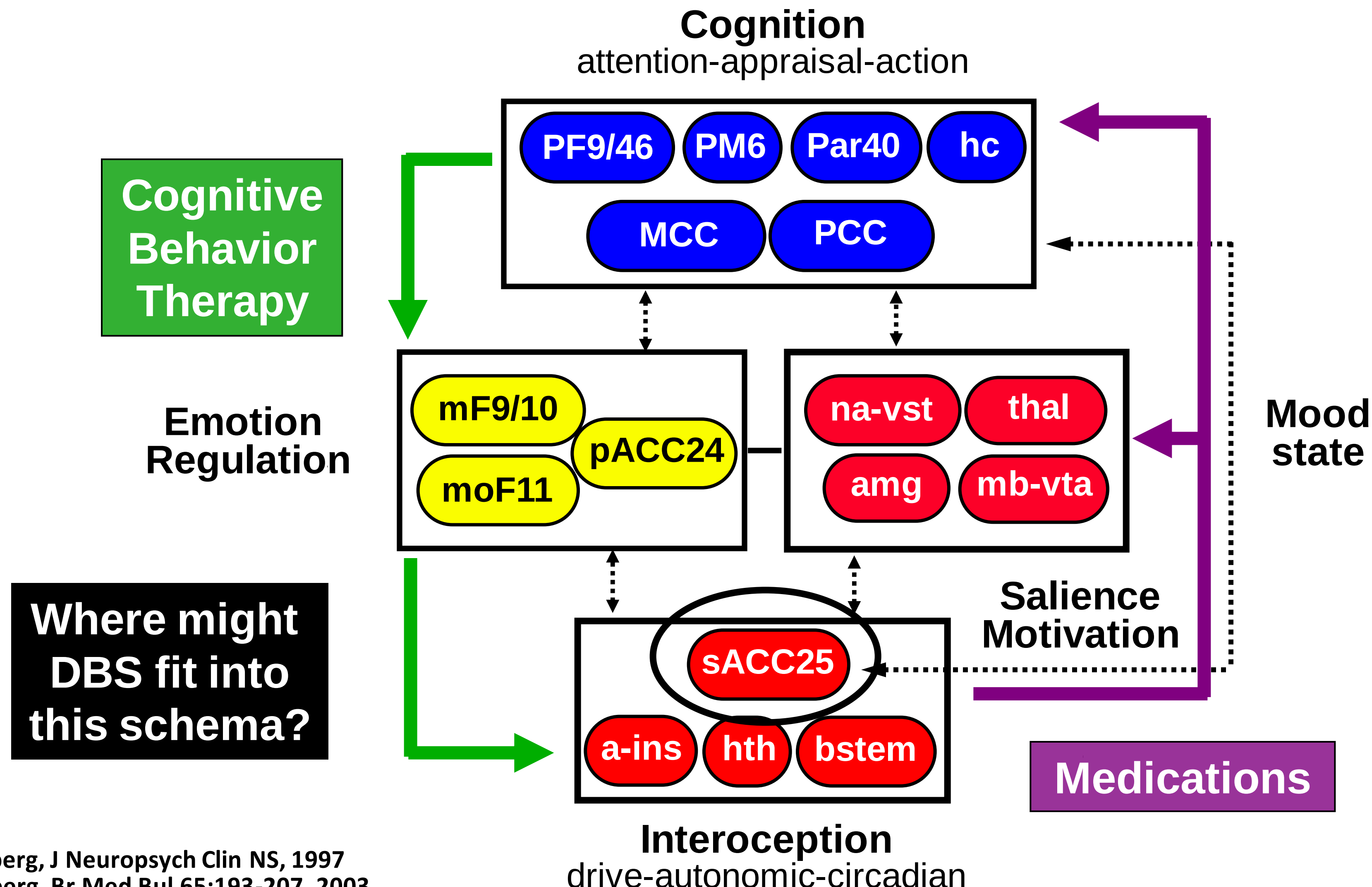
Last week



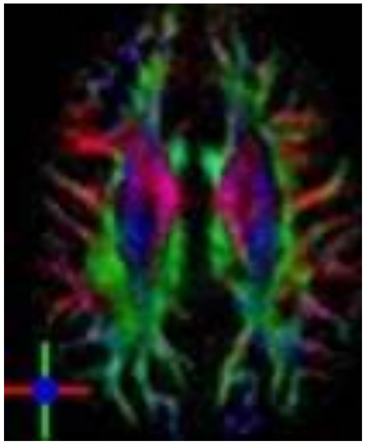
Helen S. Mayberg, MD
Professor, Psychiatry and Neurology
Dorothy C. Fuqua Chair in Psychiatric Neuroimaging and Therapeutics
Emory University School of Medicine

Putative "Depression" Network ~ 2001
defined using functional imaging

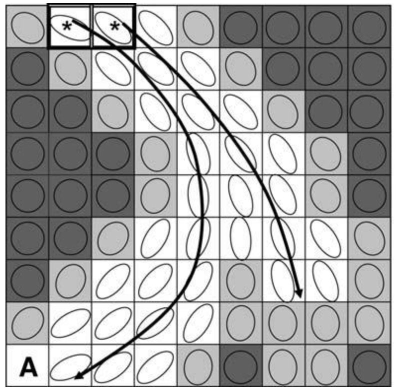


Mayberg, J Neuropsych Clin NS, 1997
Mayberg, Br Med Bul 65:193-207, 2003
Mayberg, J Clin Invest 119:717, 2009

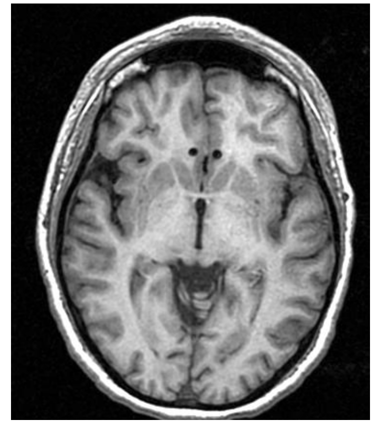
Rethinking Critical Pathways
Mapping Fibers of Passage thru SCC25



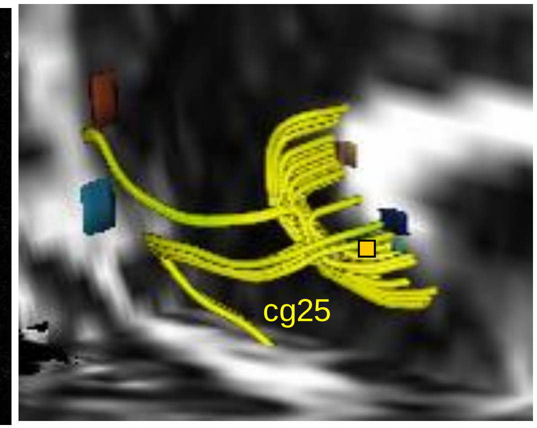
Diffusion Tensor Imaging



Fiber Assignment by Continuous Tracking along adjacent pixels

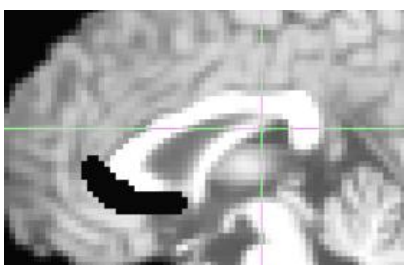


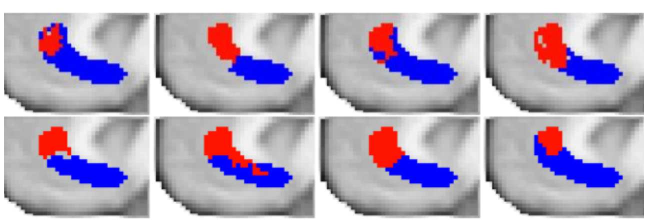
Cg25WM Target



Tracts thru Seed

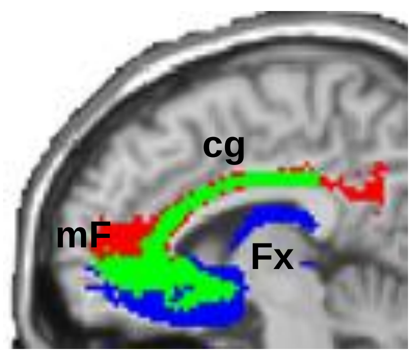
Cingulate ROI

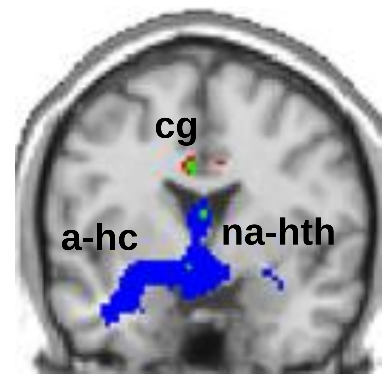




DTI: Blind ACC Parcellation →
SVD 2 clusters: sACC ≠ Pacc (n=18)

Probablistic Tractography



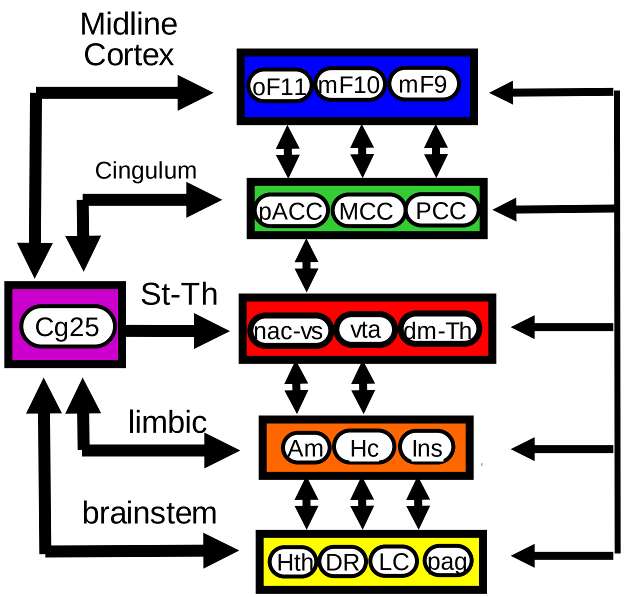


- Overlap
- Unique inferior ROI
- Unique superior ROI

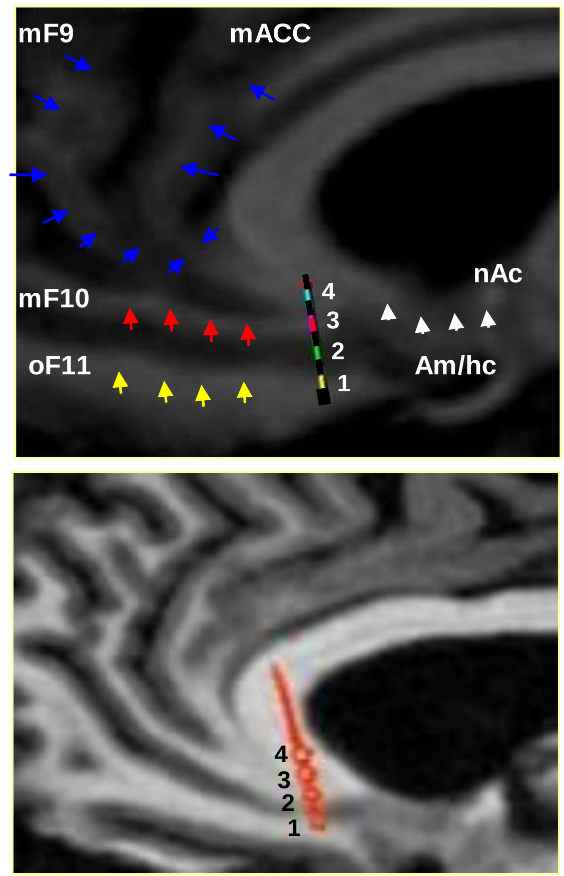
Johansen-Berg et al
Cerebral Cortex 2008

Rethinking Critical Pathways
Mapping Fibers of Passage thru SCC25

Model

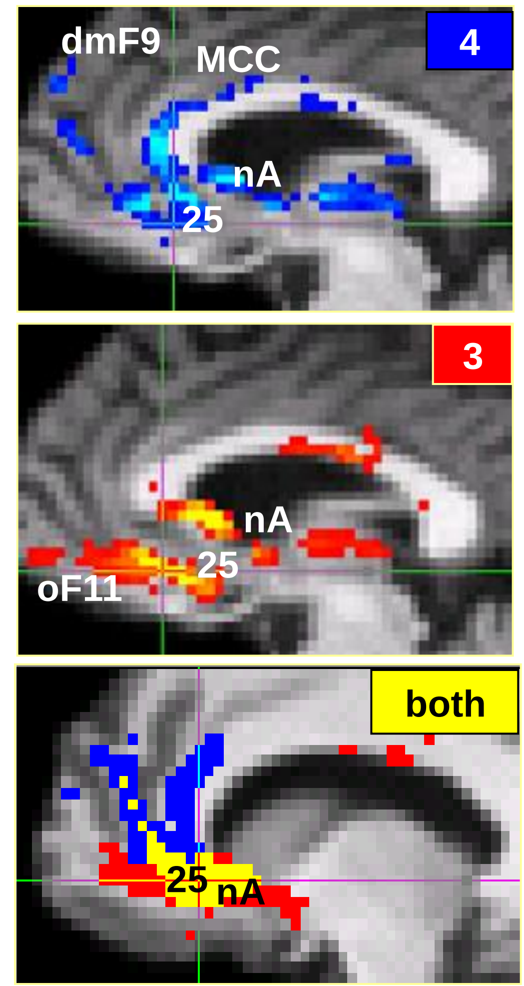


Define tracts affected by stimulation

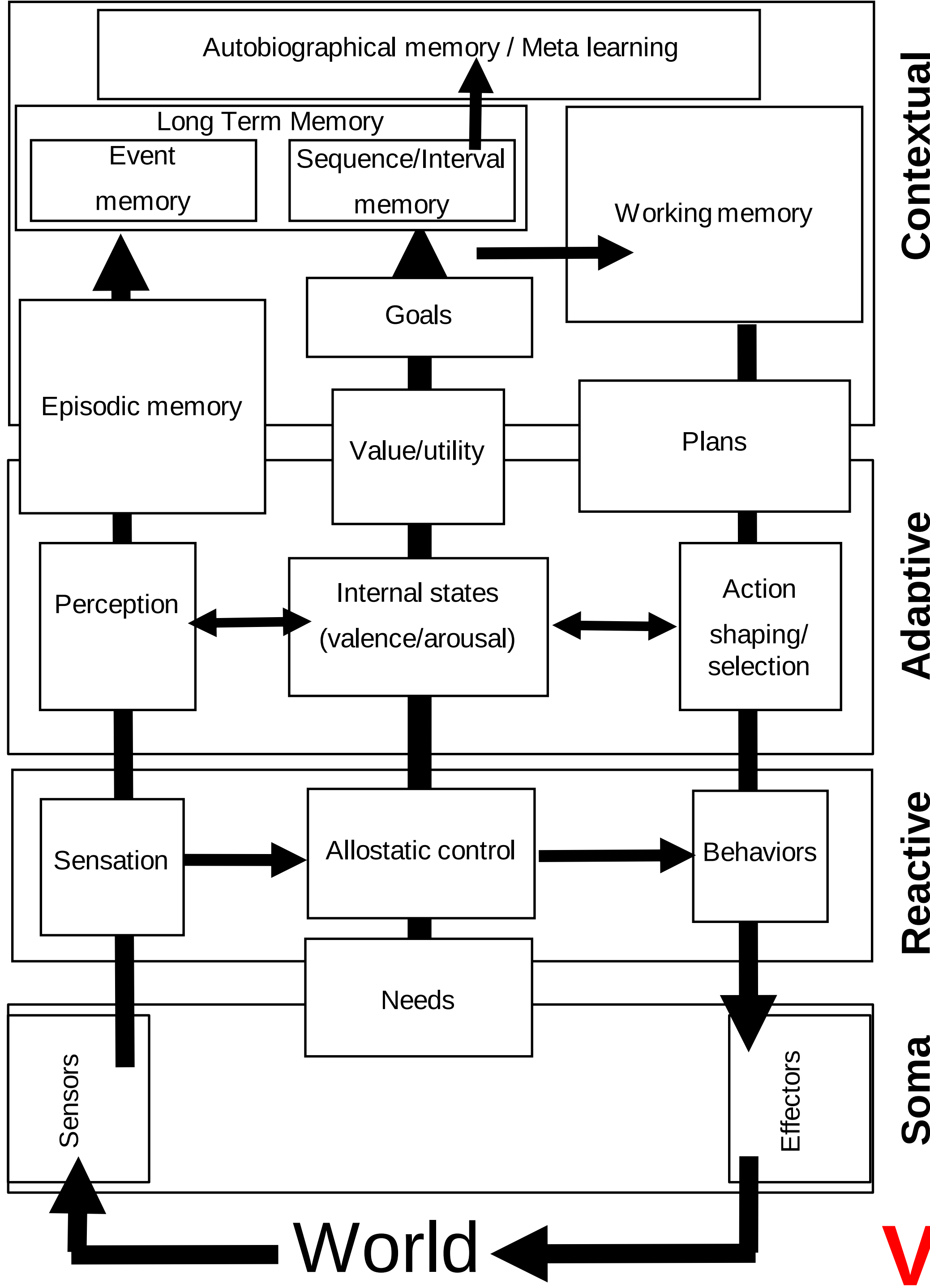


Post-op CT/MRI merge

Differences between Adjacent contacts



The Distributed Adaptive Control Architecture



Duff et al (2011) Br.Res.Bull.

Duff et al (2010) Neurocomputing

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Mathews et al (2009;2010) IROS09;IC

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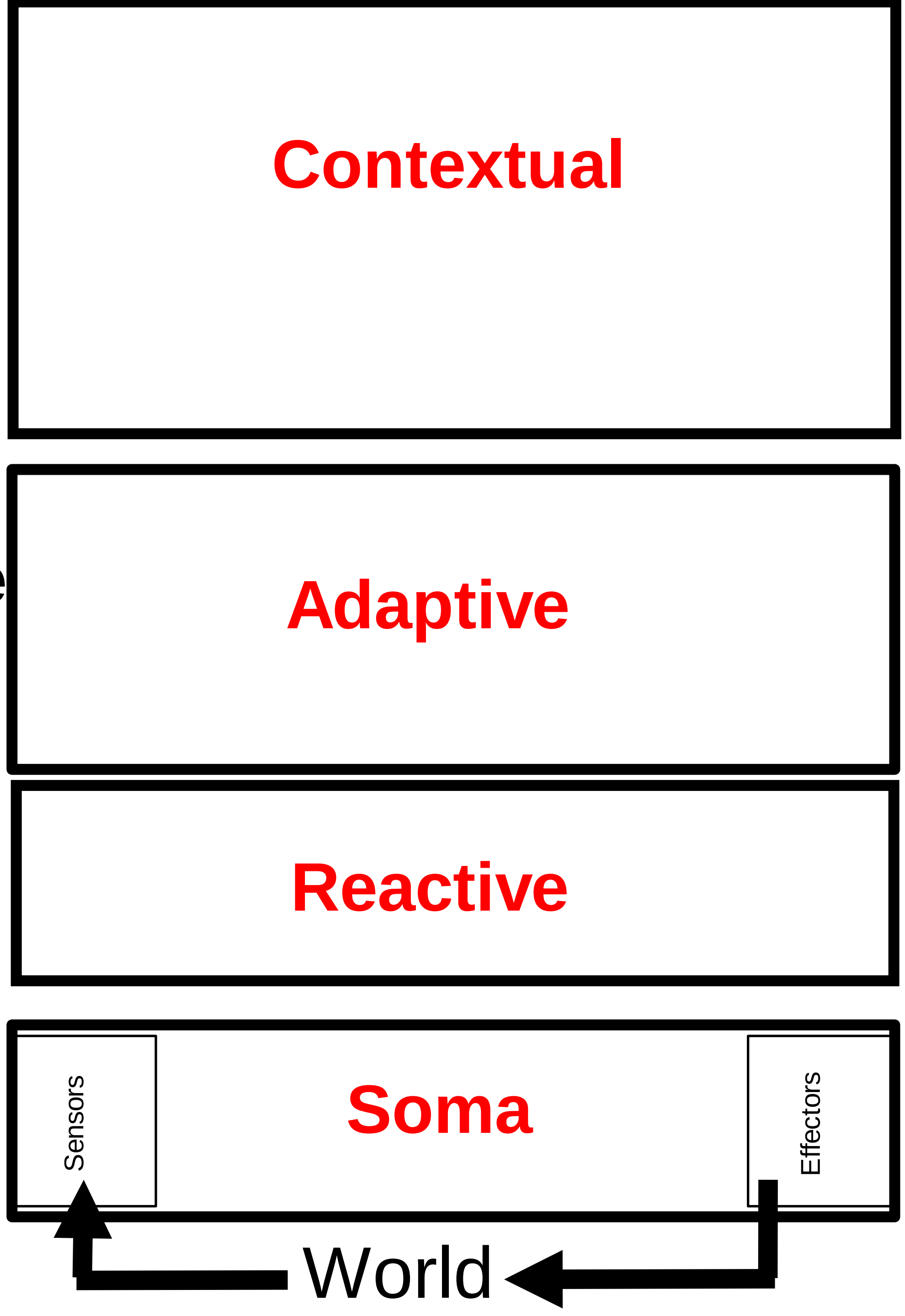
Verschure & Voegtlin (1998) Neural N

Verschure et al (1992) Rob. Aut. Sys.

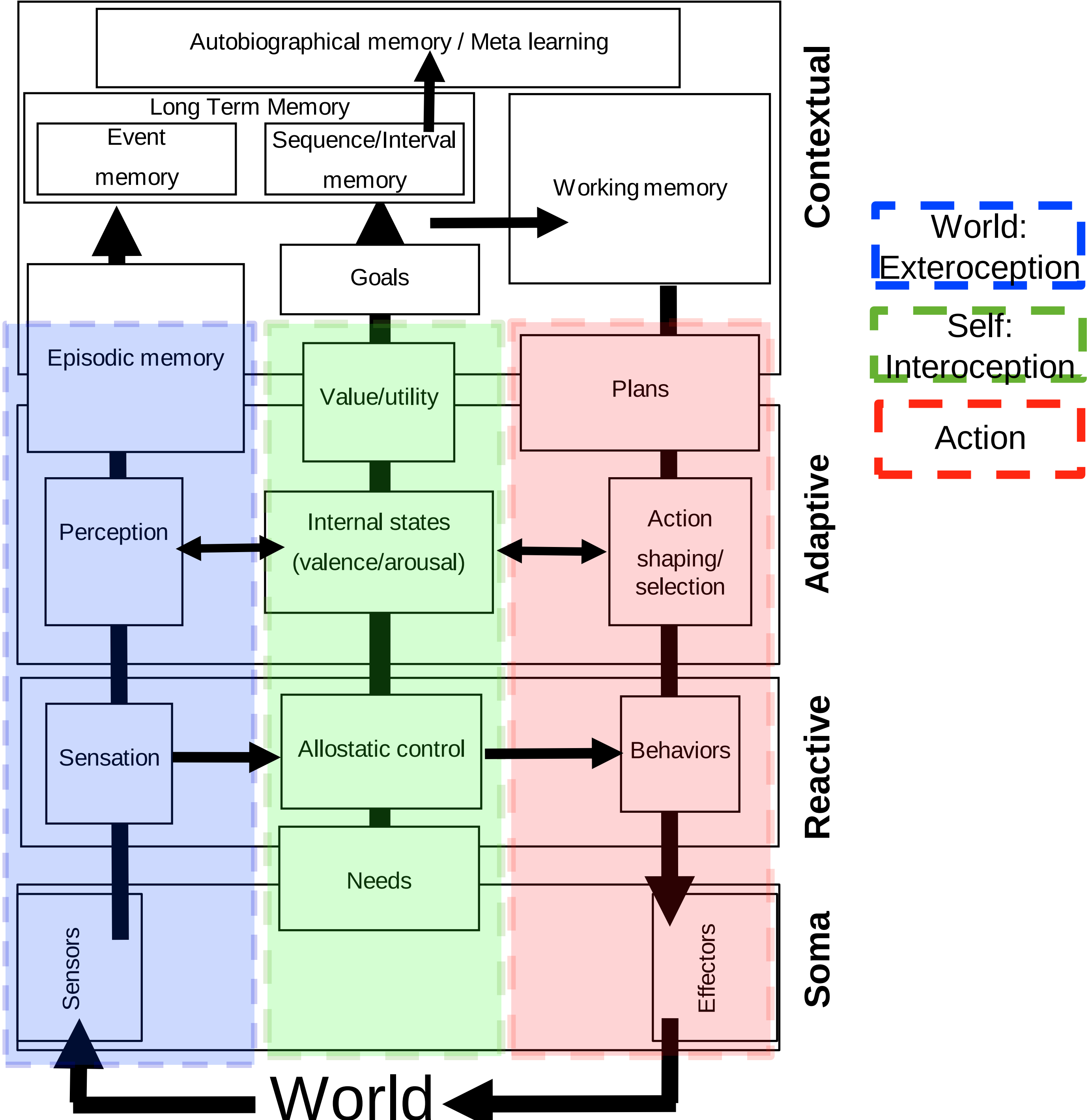
Verschure & Coolen (1991) Network

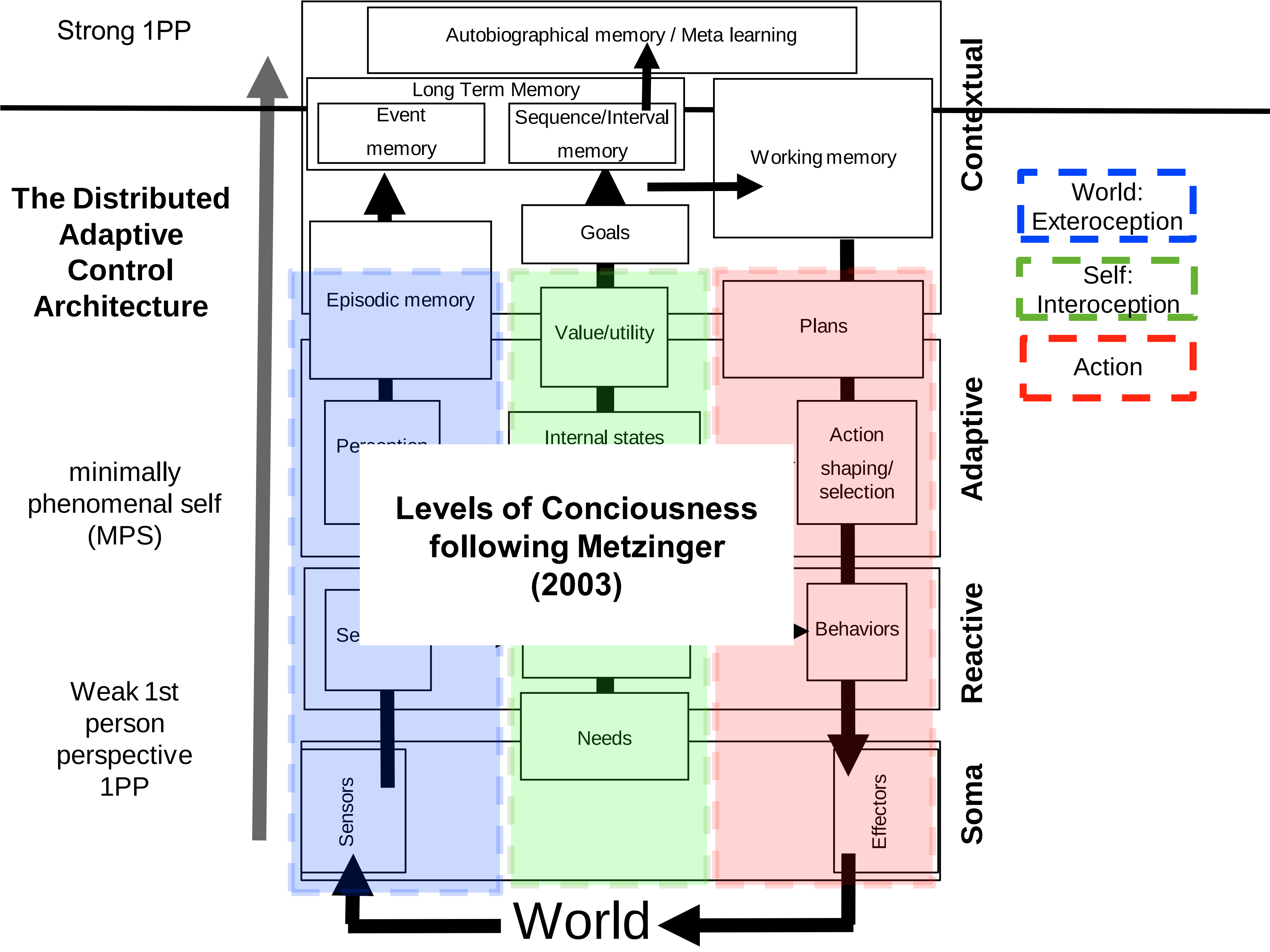
Paul Verschure

Layered Distributed Adaptive Control Architecture



The Distributed Adaptive Control Architecture




Strong 1PP
The Distributed Adaptive Control Architecture
minimally phenomenal self (MPS)
Weak 1st person perspective 1PP
Autobiographical memory / Meta learning
Long Term Memory
Event memory
Sequence/Interval memory
Working memory
Goals
Episodic memory
Value/utility
Plans
Internal states
Action shaping/ selection
Levels of Conciousness following Metzinger (2003)
Behaviors
Needs
Sensors
Effectors
World
Contextual
Adaptive
Reactive
Soma
World: Exteroception
Self: Interoception
Action

“Laws” and architectures

- Theory of hard limits, constraints,… (“laws”)
- Theory of “architecture”?
  - From platforms to
  - “systems of systems” to
  - Architecture
- Case studies: Internet, turbulence, smartgrid, cell biology, wildfire ecology, earthquakes, stat mech, brain architecture, UAVs, …

IEEE TRANS ON SYSTEMS, MAN, AND CYBERNETICS, JULY 2010, Alderson and Doyle

IEEE TRANSACTIONS ON SYSTEMS, MAN, AND CYBERNETICS—PART A: SYSTEMS AND HUMANS, VOL. 40, NO. 4, JULY 2010

Contrasting Views of Complexity and Their Implications For Network-Centric Infrastructures

David L. Alderson, *Member, IEEE*, and John C. Doyle

***Abstract*—There exists a widely recognized need to better understand and manage complex "systems of systems," ranging from biology, ecology, and medicine to network-centric technologies. This is motivating the search for universal laws of highly evolved systems and driving demand for new mathematics and methods that are consistent, integrative, and predictive. However, the theoretical frameworks available today are not merely fragmented but sometimes contradictory and incompatible. We argue that complexity arises in highly evolved biological and technological systems primarily to provide mechanisms to create robustness. However, this complexity itself can be a source of new fragility, leading to "robust yet fragile" tradeoffs in system design. We focus on the role of robustness and architecture in networked infrastructures, and we highlight recent advances in the theory of distributed control driven by network technologies. This view of complexity in highly organized technological and biological systems is fundamentally different from the dominant perspective in the mainstream sciences, which downplays function, constraints, and tradeoffs, and tends to minimize the role of organization and design.**

***Index Terms*—Architecture, complexity theory, networks, optimal control, optimization methods, protocols.**

other complex engineering systems, but much of advanced technology has, if anything, made things worse. Computer-based simulation and rapid prototyping tools are now broadly available and powerful enough that it is relatively easy to demonstrate almost anything, provided that conditions are made sufficiently idealized. We are much better at designing, mass-producing, and deploying network-enabled devices than we are at being able to predict or control their collective behavior once deployed in the real world. The result is that, when things fail, they often do so cryptically and catastrophically.

The growing need to understand and manage complex systems of systems, ranging from biology to technology, is creating demand for new mathematics and methods that are consistent and integrative. Yet, there exist fundamental incompatibilities in available theories for addressing this challenge. Various "new sciences" of "complexity" and "networks" dominate the mainstream sciences [3] but are at best disconnected from medicine, mathematics, and engineering. Computing, communication, and control theories and technologies flourish but

Human complexity

Robust

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

Fragile

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

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

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

Fluctuating energy

Static energy

Accident or necessity?

What's the difference?

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

☹ Fat accumulation
☹ Insulin resistance
☹ Proliferation
☹ Inflammation

Controlled	Uncontrolled
Dynamic	Chronic
Low mean	High mean
High variability	Low variability

Restoring robustness

Robust

Fragile

Controlled
Dynamic

Low mean
High variability

Uncontrolled
Chronic

High mean
Low variability

Mechanism?

Robust

☺ Metabolism

☺ Regeneration & repair

☺ Healing wound /infect

☹ Fat accumulation

☹ Insulin resistance

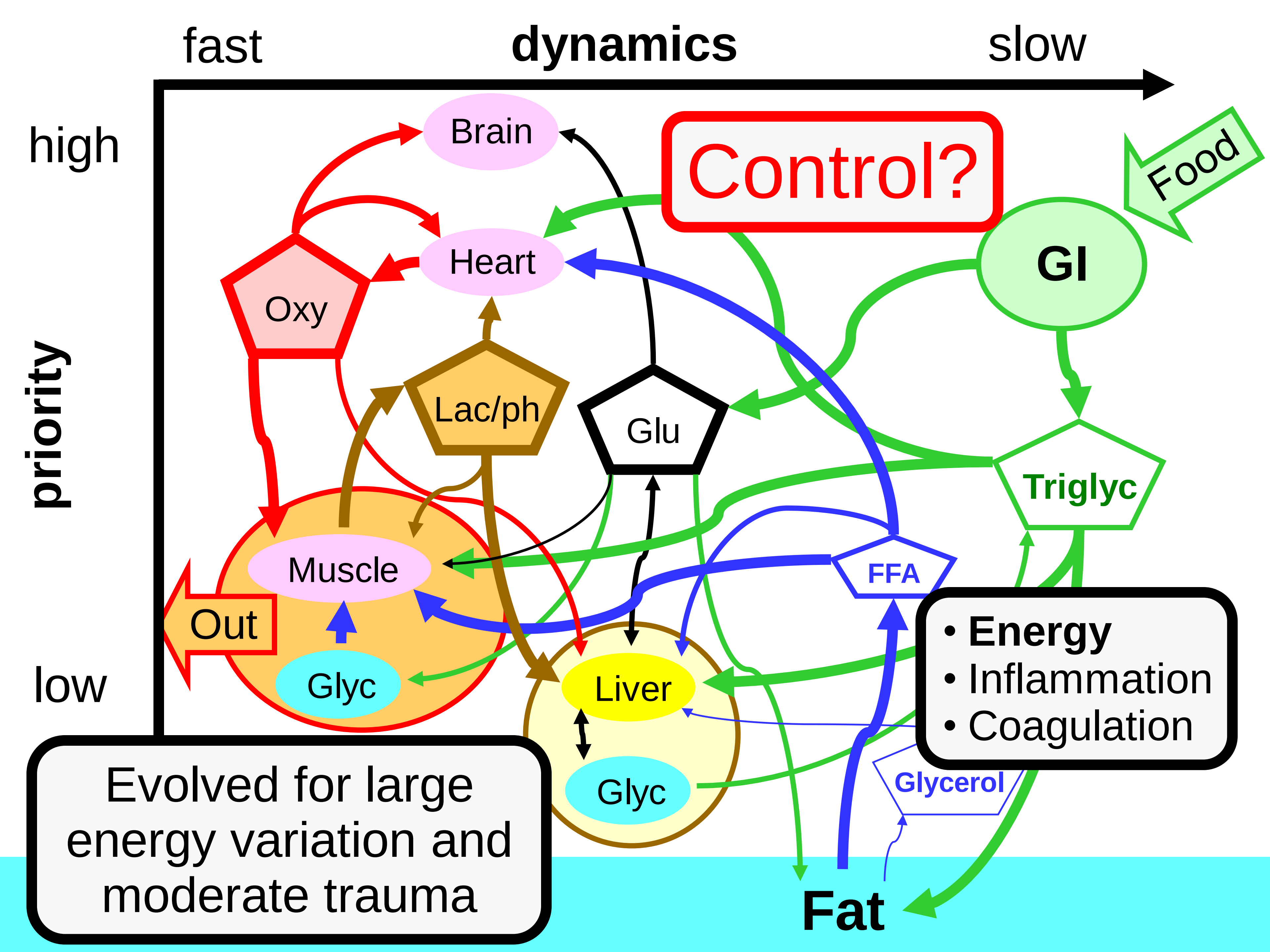
☹ Proliferation

☹ Inflammation

Controlled
Dynamic

Low mean
High variability

Fluctuating energy


fast
dynamics
slow
high
priority
low
Brain
Heart
Oxy
Lac/ph
Glu
Control?
Food
GI
Triglyc
Muscle
FFA
Out
Glyc
Liver
Glyc
Glycerol
• Energy
• Inflammation
• Coagulation
Evolved for large energy variation and moderate trauma
Fat

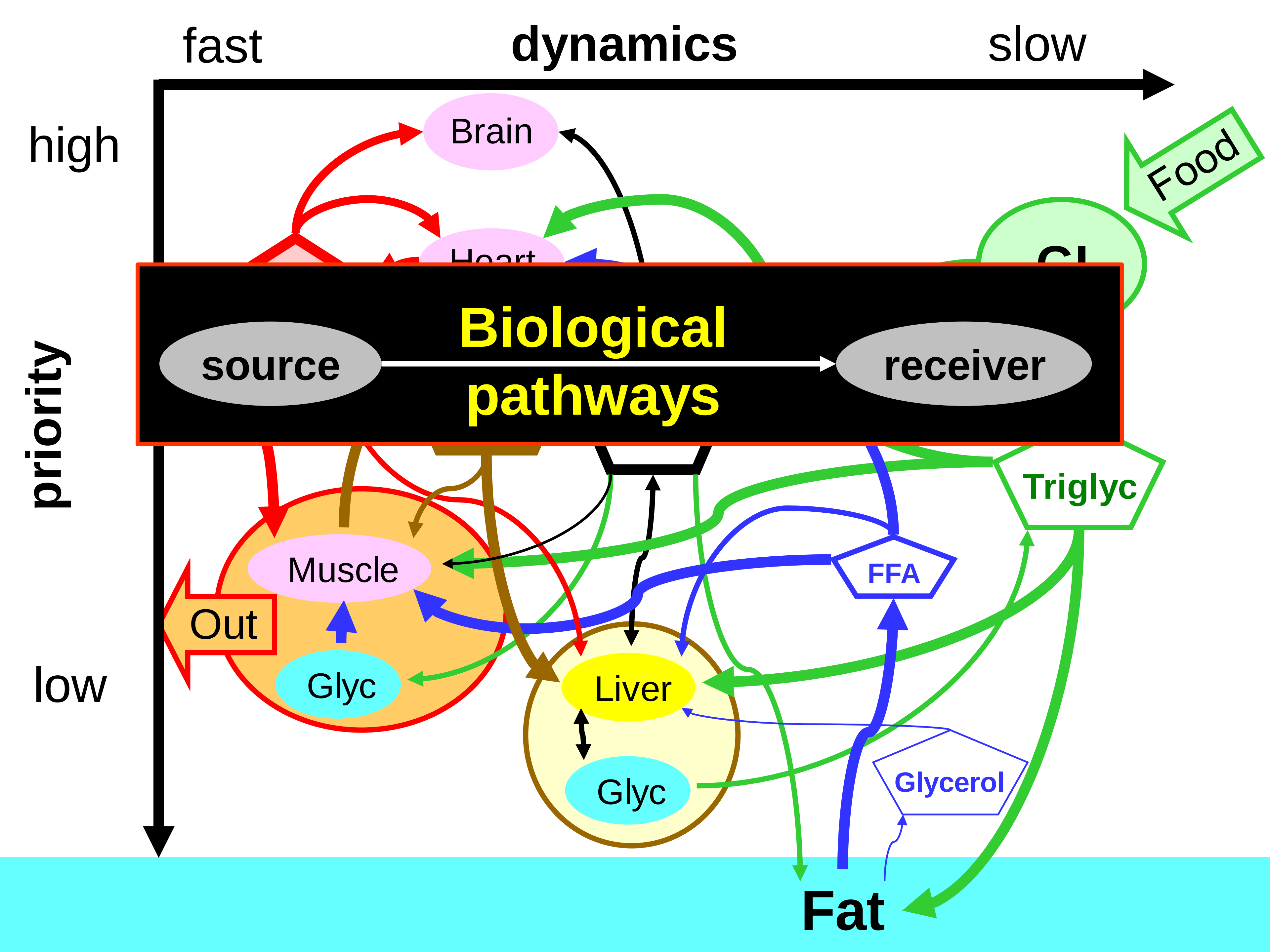
signaling

gene expression

metabolism

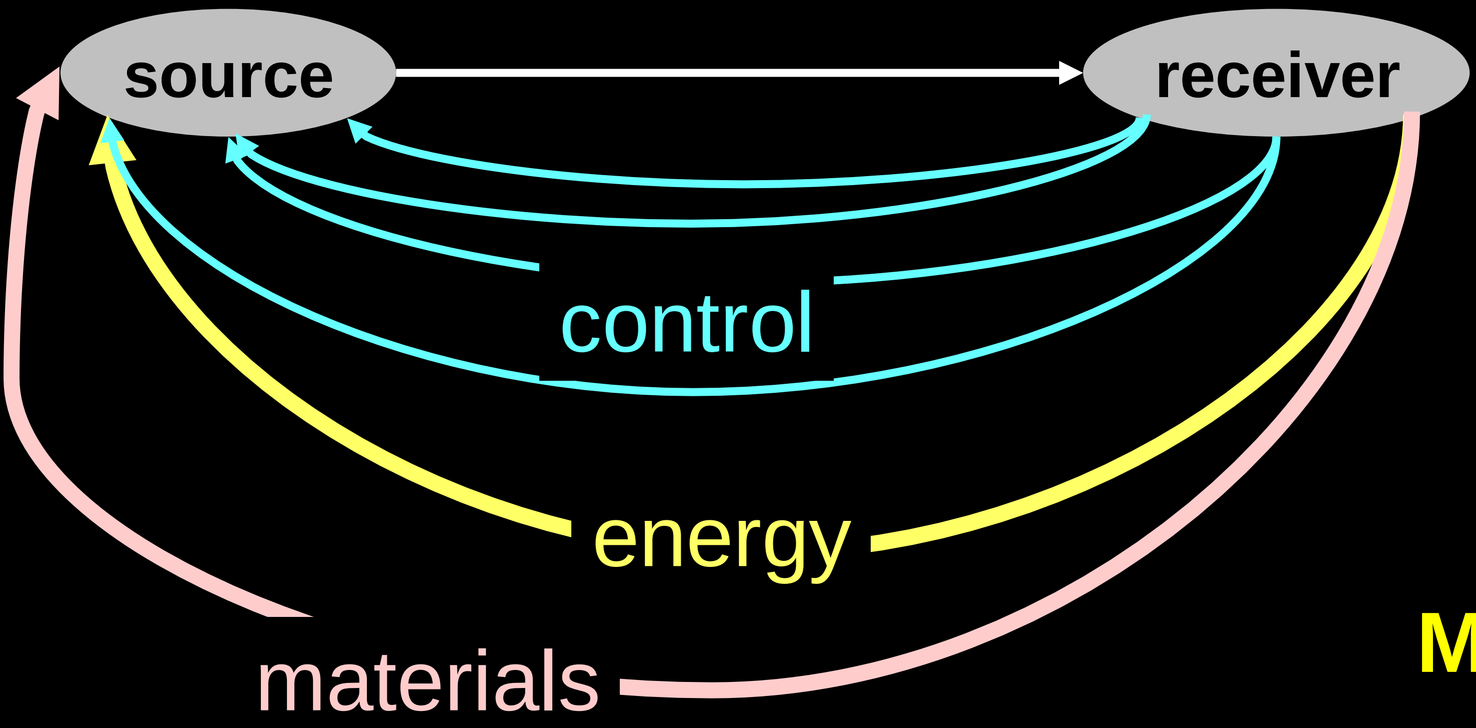
lineage

Biological pathways



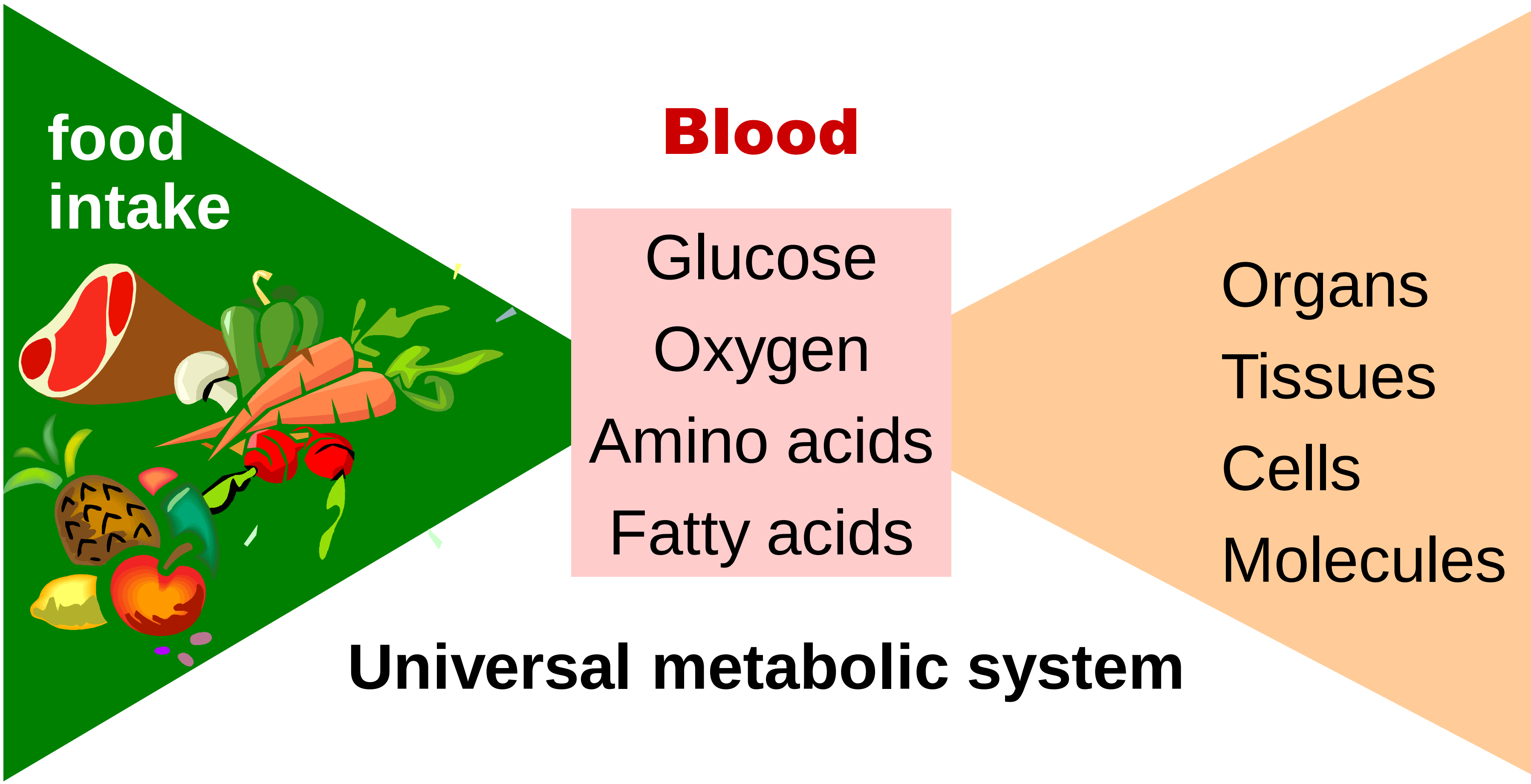
fast
dynamics
slow
high
priority
low
Brain
Food
Biological
pathways
source
receiver
Triglyc
Muscle
FFA
Out
Glyc
Liver
Glyc
Glycerol
Fat

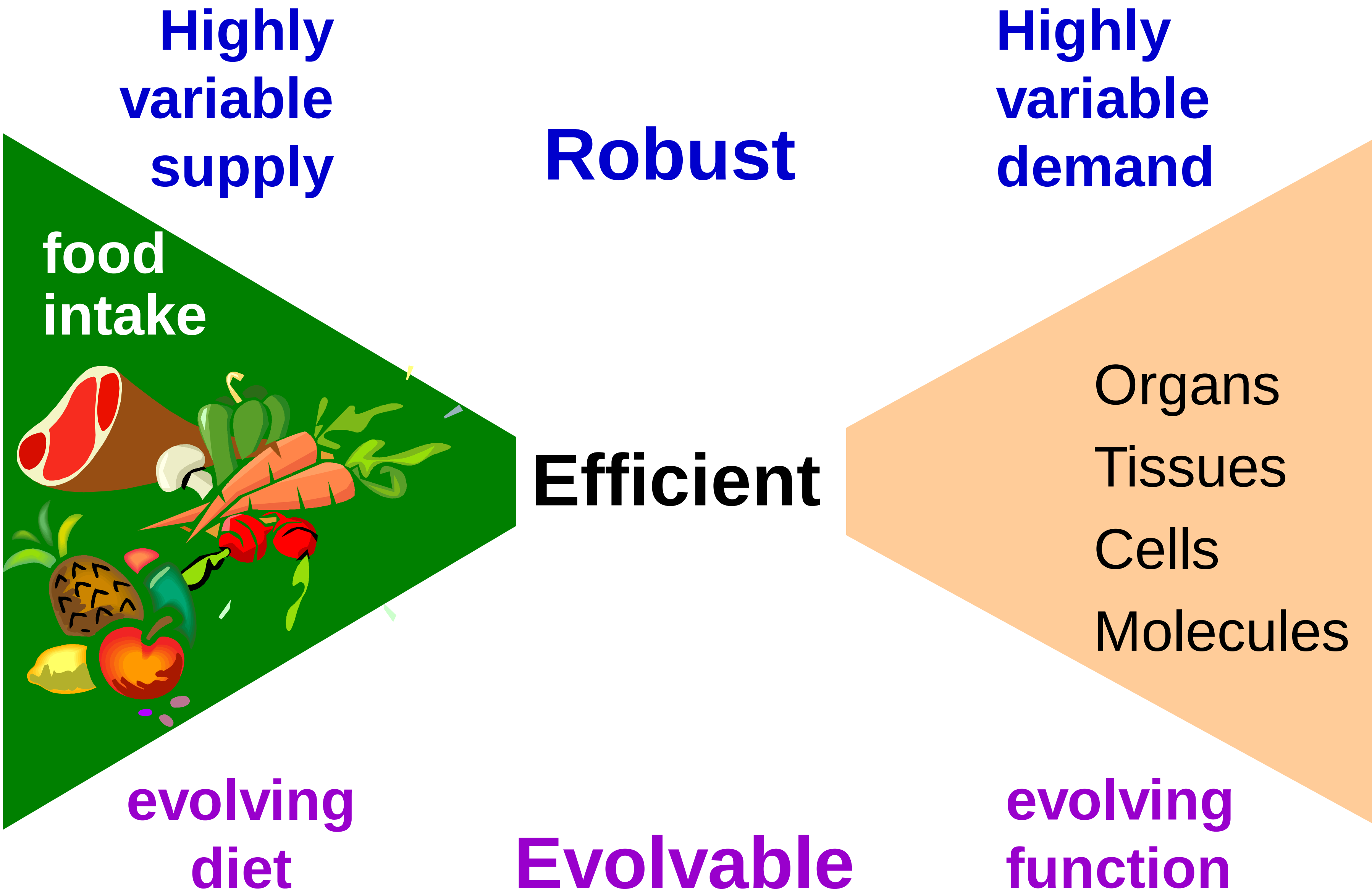
signaling
gene expression
metabolism
lineage



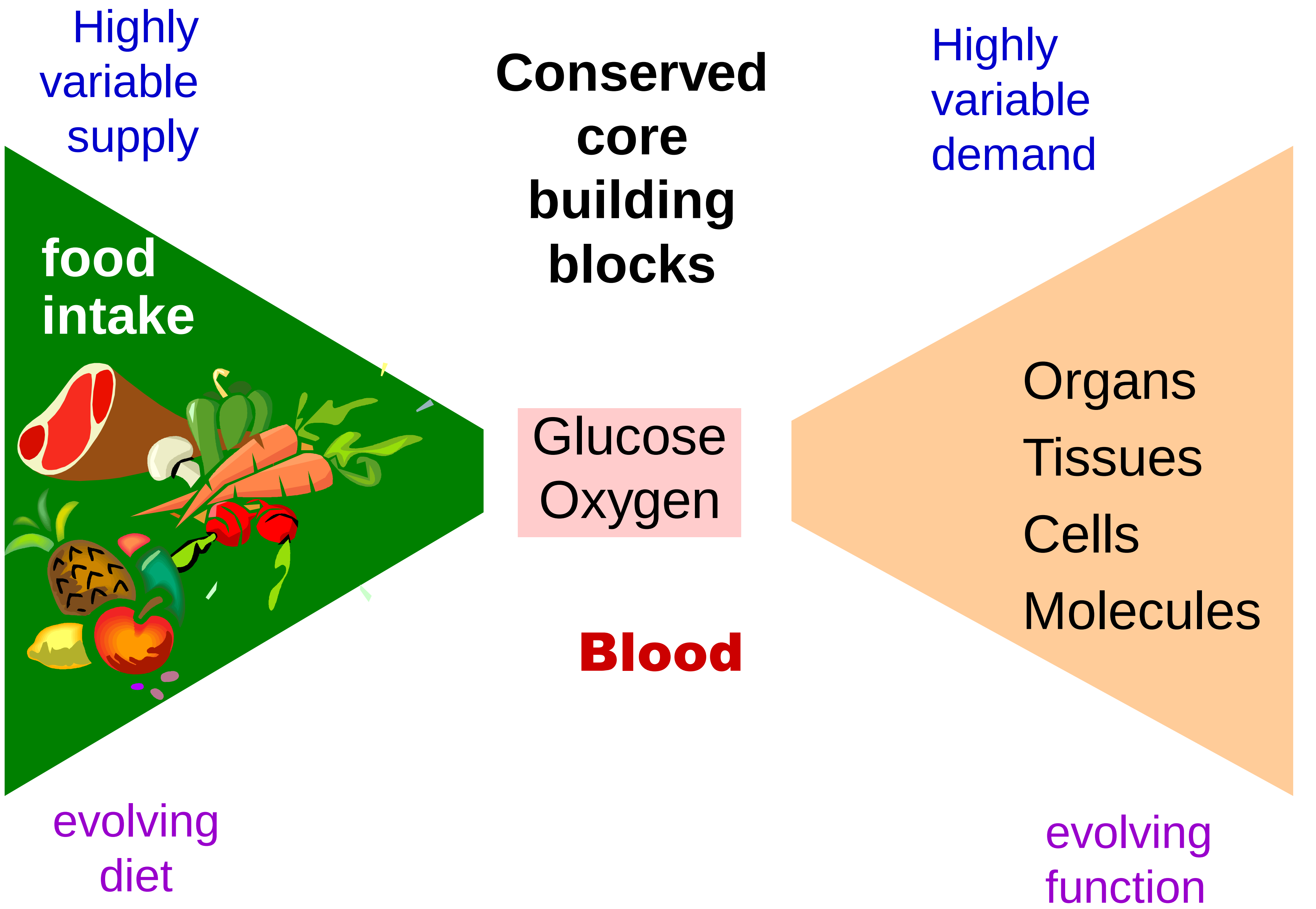
More complex feedback

Peter Sterling and Allostasis



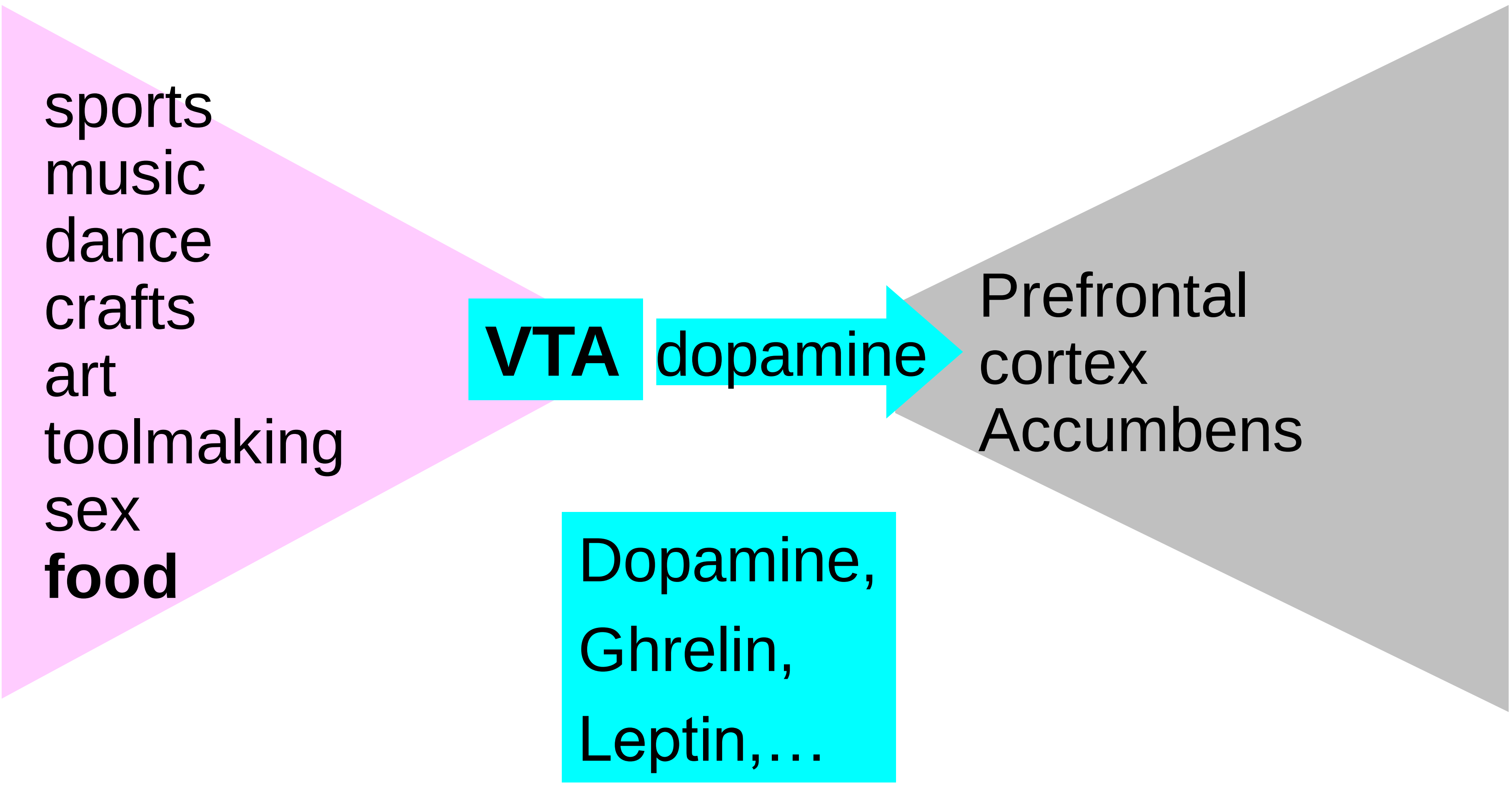


Highly
variable
supply
Robust
Highly
variable
demand
food
intake
Efficient
Organs
Tissues
Cells
Molecules
evolving
diet
Evolvable
evolving
function

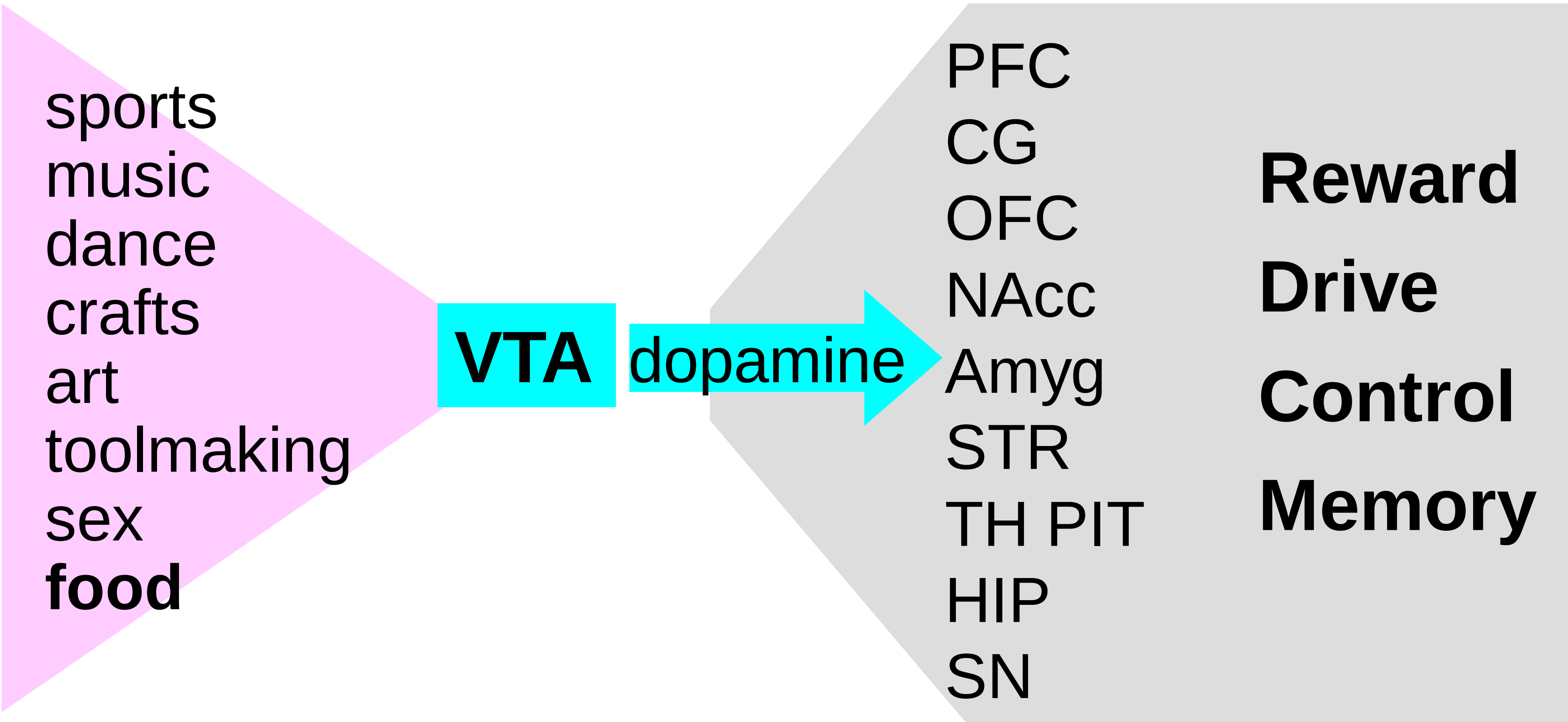


Highly variable supply
Conserved core building blocks
Highly variable demand
food intake
Glucose
Oxygen
Organs
Tissues
Cells
Molecules
Blood
evolving diet
evolving function

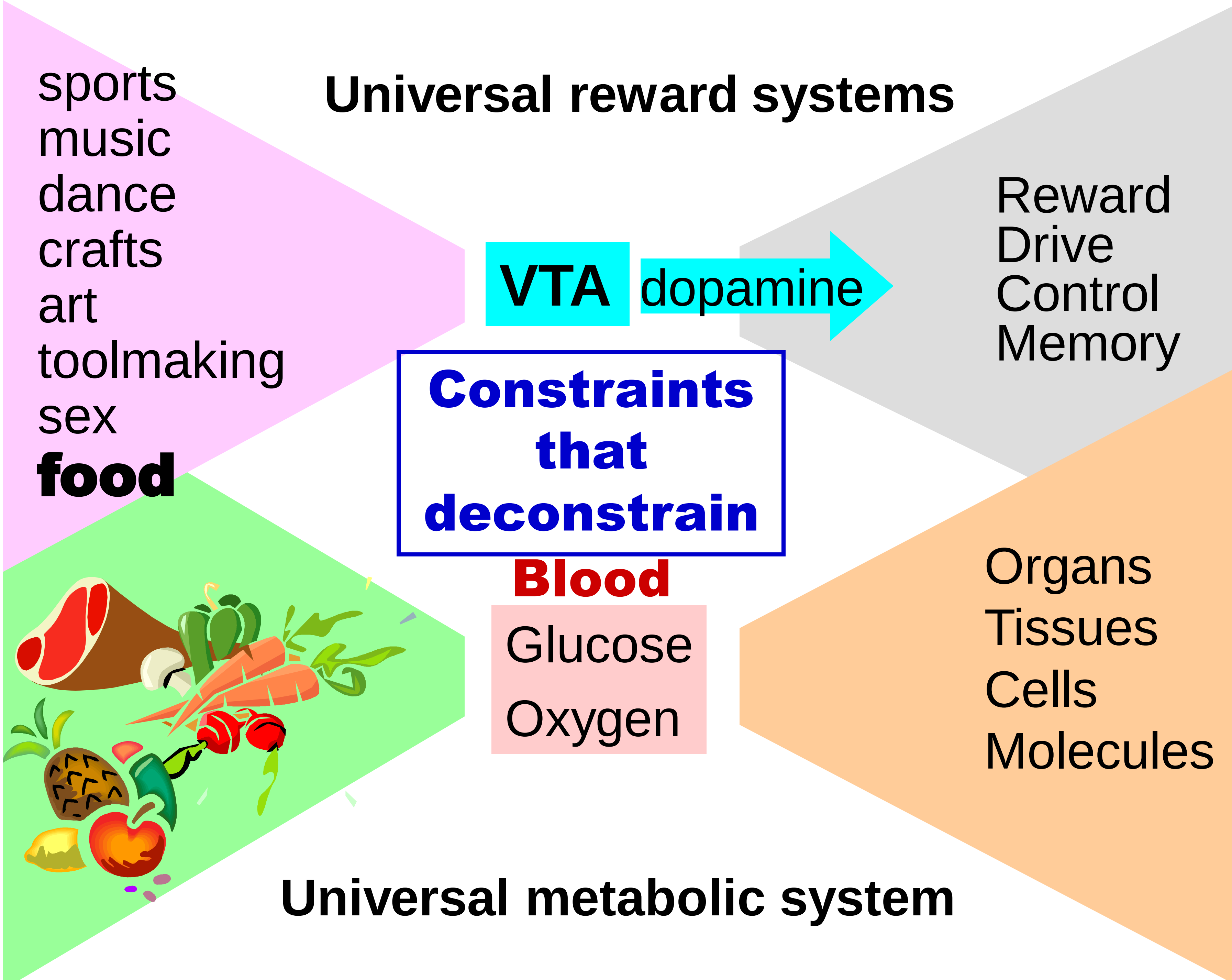
Universal reward systems



Universal reward systems



Robust and evolvable


Universal reward systems
sports
music
dance
crafts
art
toolmaking
sex
food
VTA
dopamine
Reward
Drive
Control
Memory
Constraints that deconstrain
Blood
Glucose
Oxygen
Organs
Tissues
Cells
Molecules
Universal metabolic system

Modularity 2.0

Constraints

dopamine

Blood

Glucose

Oxygen

Modularity 2.0

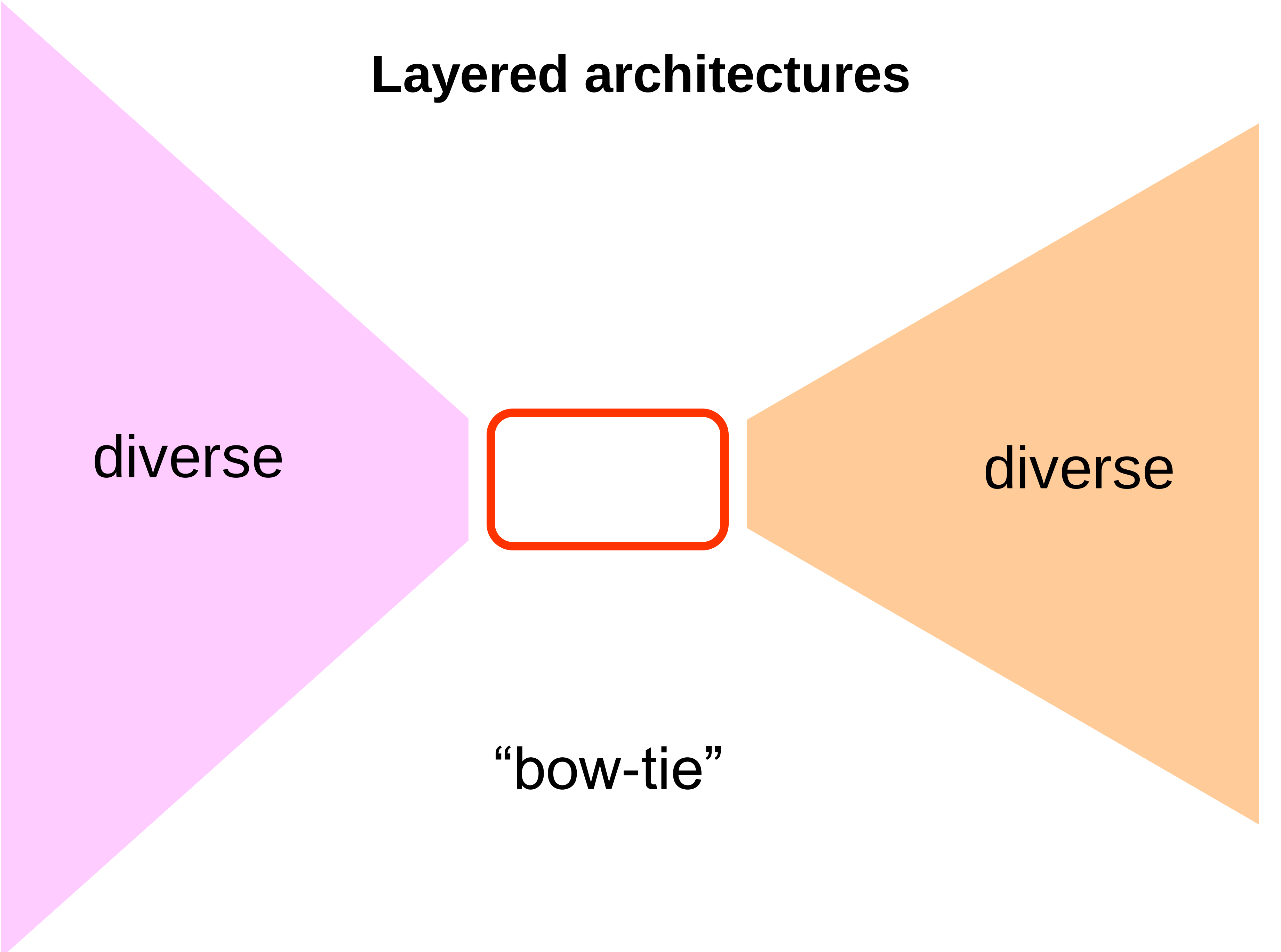
sports
music
dance
crafts
art
toolmaking
sex
food

that deconstrain

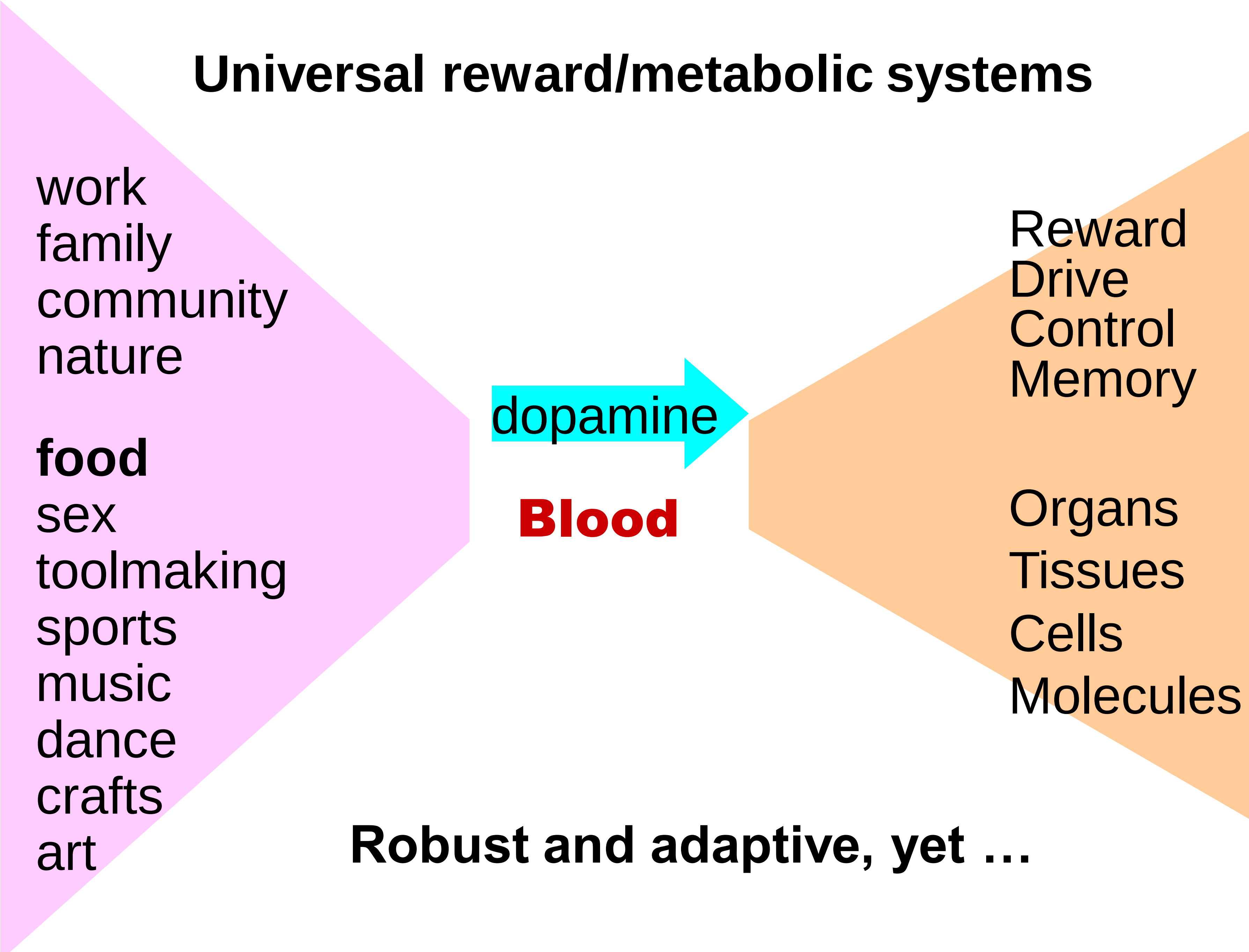
Reward
Drive
Control
Memory

Organs
Tissues
Cells
Molecules

Layered architectures



"bow-tie"



Universal reward/metabolic systems
work
family
community
nature
food
sex
toolmaking
sports
music
dance
crafts
art
dopamine
Blood
Reward
Drive
Control
Memory
Organs
Tissues
Cells
Molecules
Robust and adaptive, yet …

Modularity 1.0

work
family
community
nature

food
sex
toolmaking
sports
music
dance
crafts
art

Reward
Drive
Control
Memory

Organs
Tissues
Cells
Molecules

“Weak linkage”

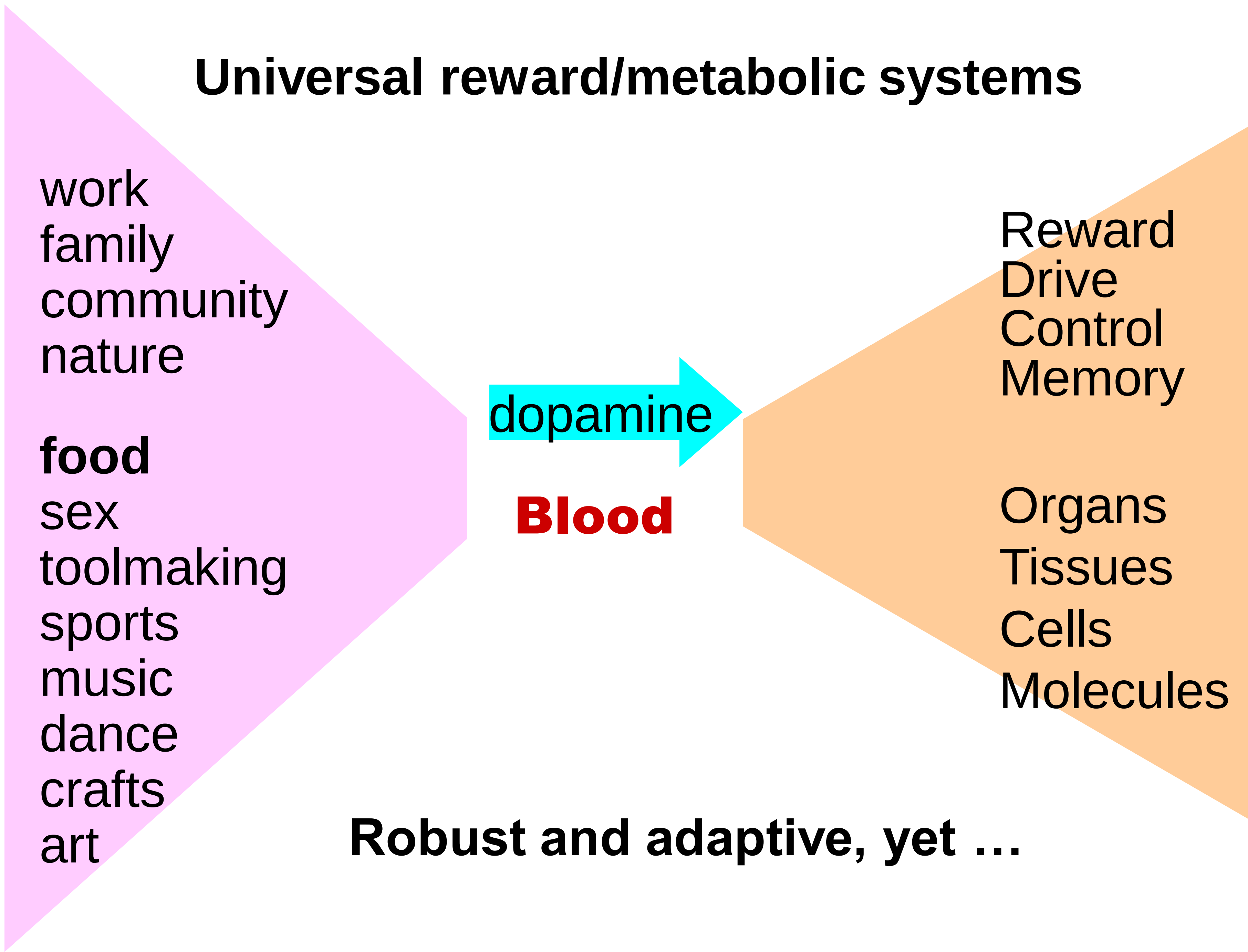
Modularity 2.0

Most important “modules”

dopamine

Blood

***Not* weakly connected to others,**
but *highly* connected


Universal reward/metabolic systems
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Blood
Reward
Drive
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Organs
Tissues
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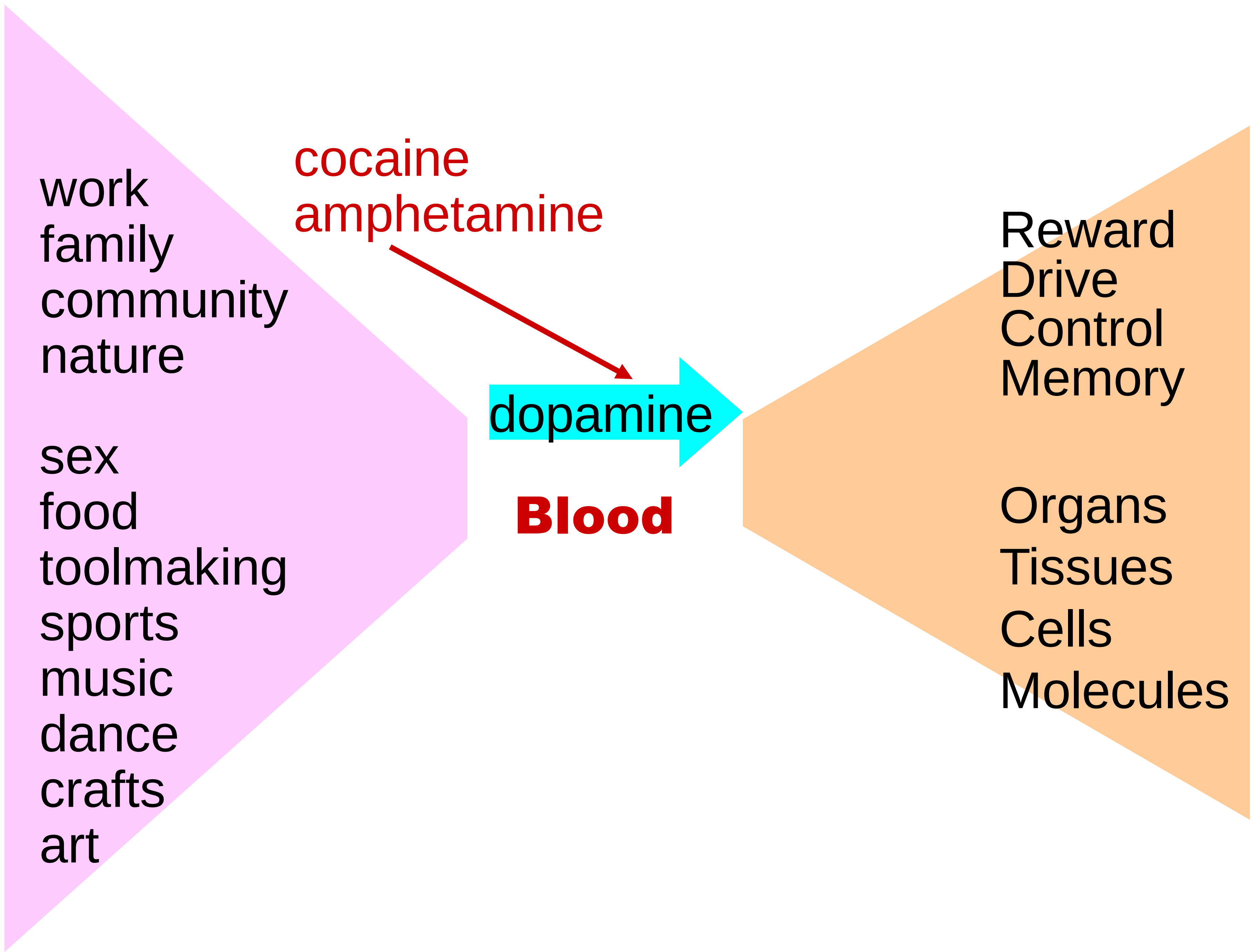
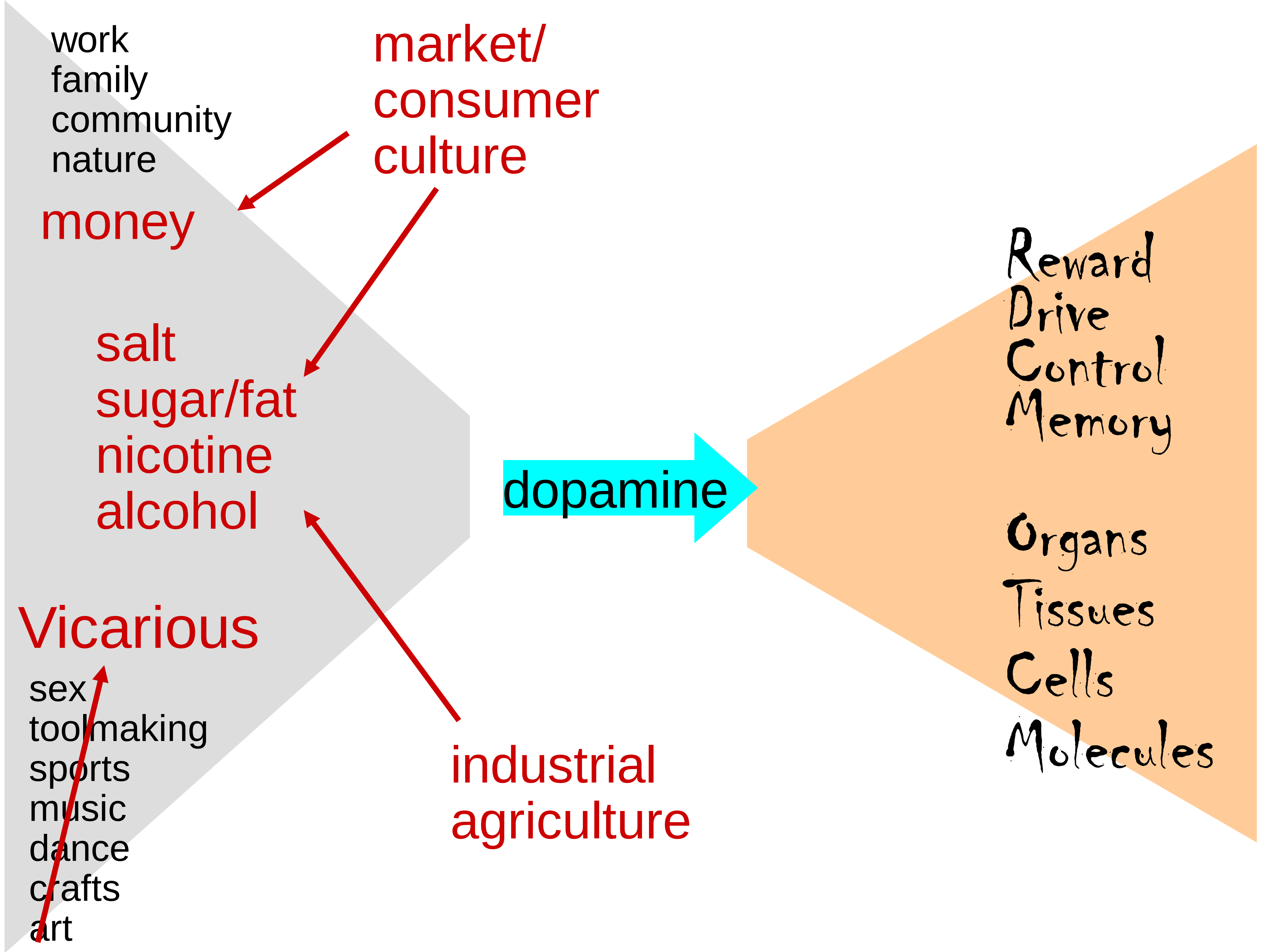
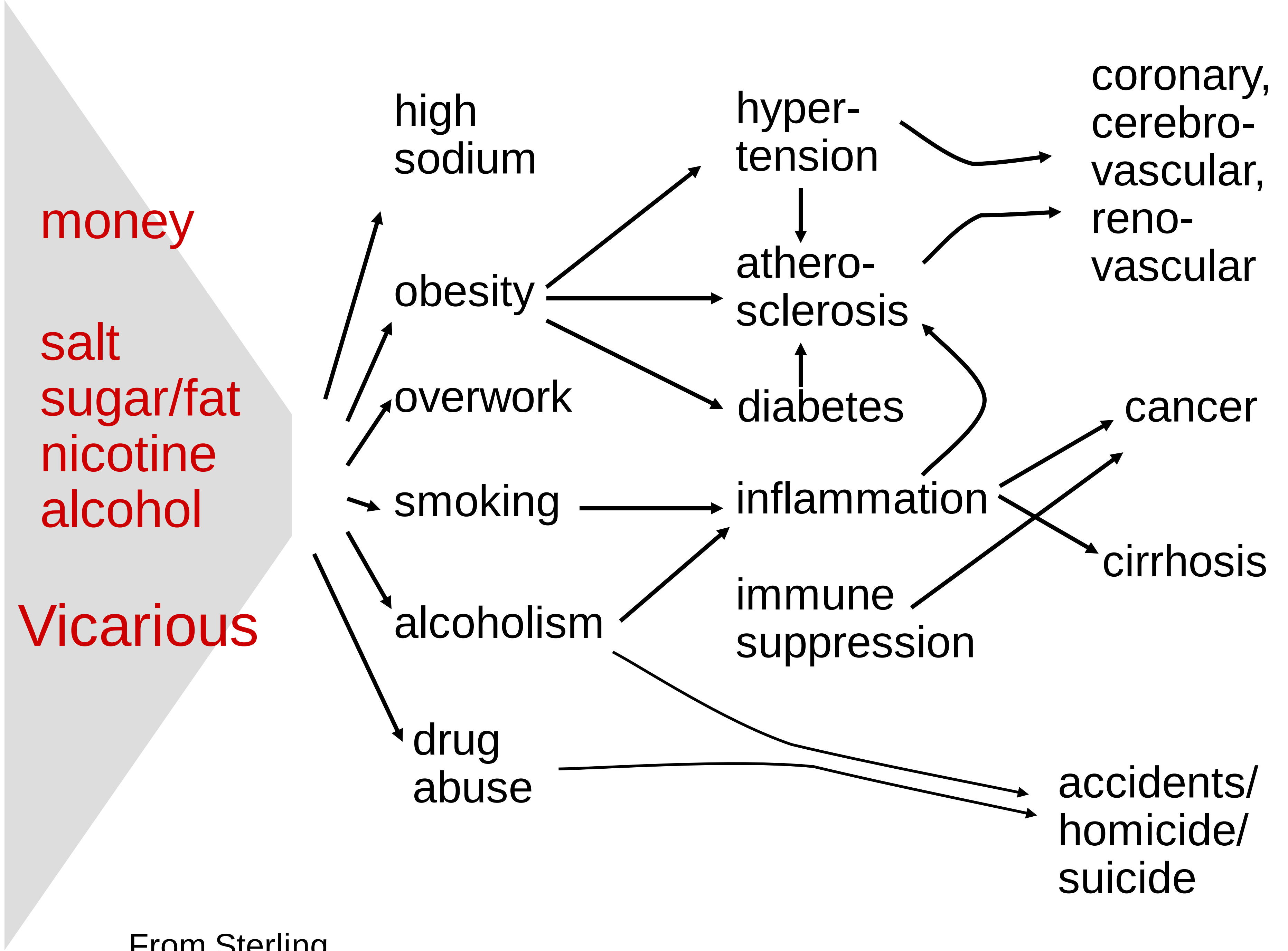
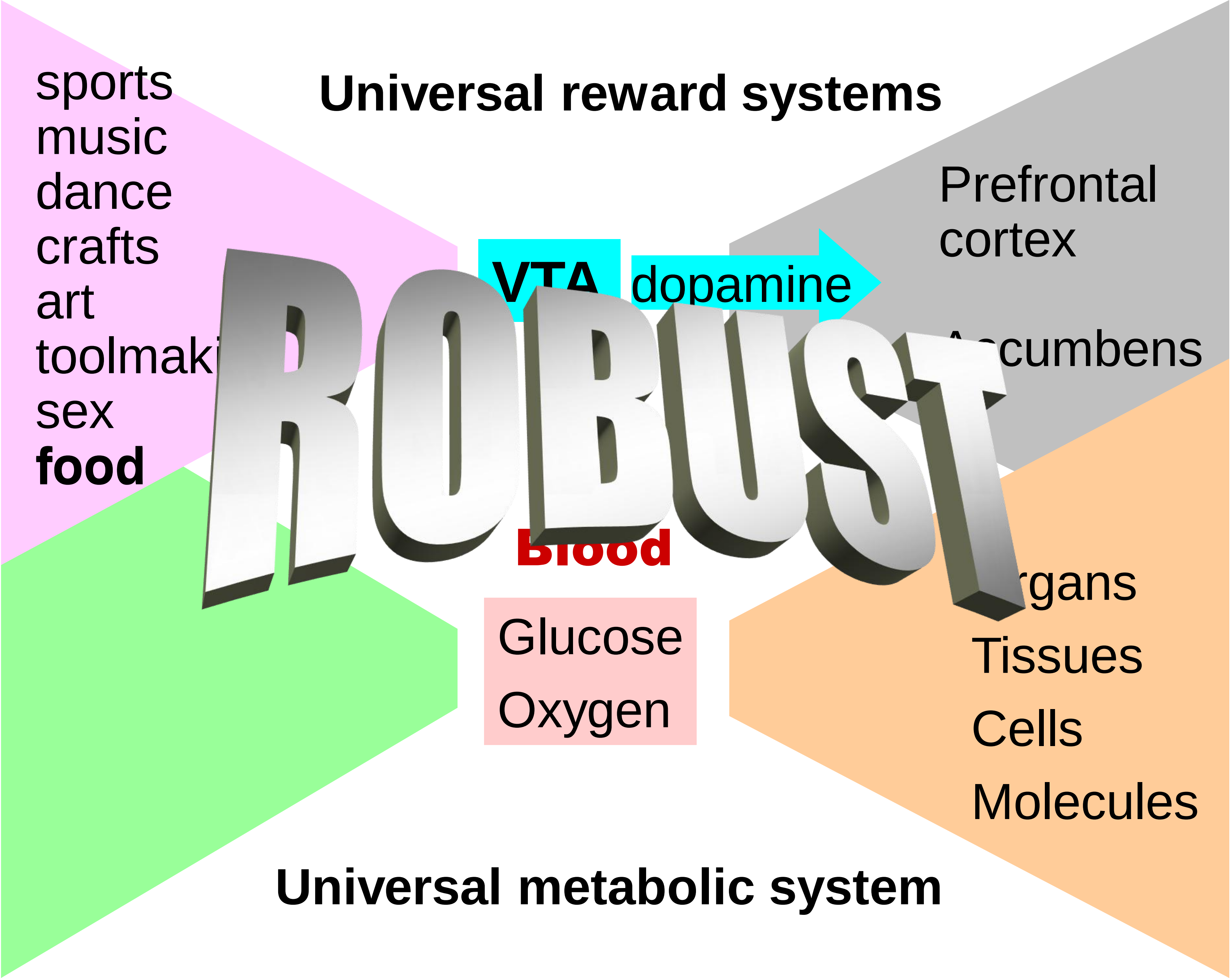
Robust and adaptive, yet …

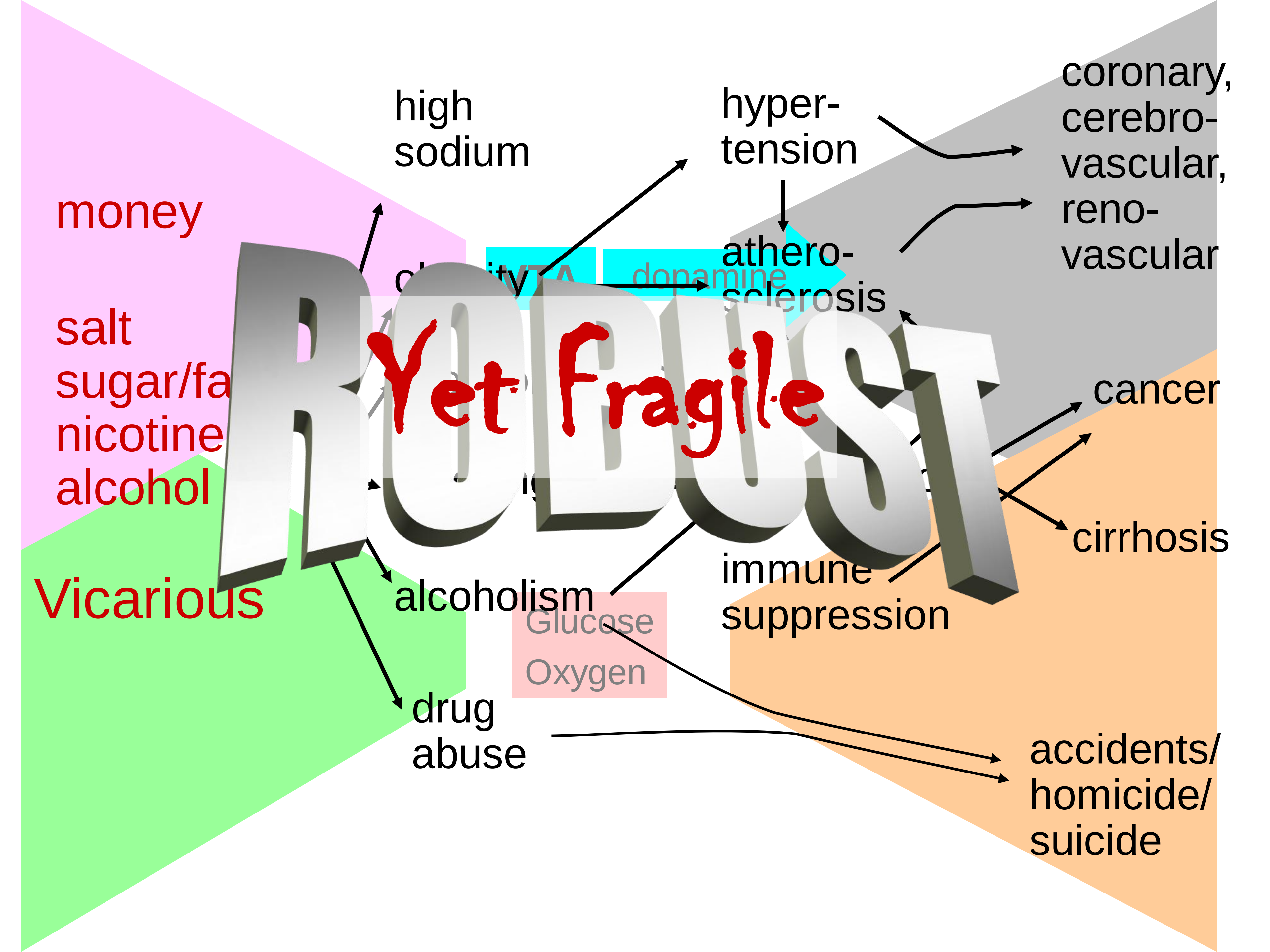

work
family
community
nature
sex
food
toolmaking
sports
music
dance
crafts
art
cocaine
amphetamine
dopamine
Blood
Reward
Drive
Control
Memory
Organs
Tissues
Cells
Molecules


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



From Sterling


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



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

Human complexity

Robust	Yet Fragile
☺ Metabolism	☹ Obesity, diabetes
☺ Regeneration & repair	☹ Cancer
☺ Microbe symbionts	☹ Parasites, infection
☺ Immune/inflammation	☹ AutoImmune/Inflame
☺ Neuro-endocrine	☹ Addiction, psychosis…
🗐 Complex societies	☠ Epidemics, war…
🗐 Advanced technologies	💣 Disasters, global &!%$#
🗐 Risk "management"	💣 Obfuscate, amplify,…

Accident or necessity?

Robust

☺ Metabolism

☺ Regenerati

☺ Healing wo

Fragile

☹ Obesity, diabetes

une/Inflame

☹ Fat accumulation

☹ Insulin resistance

☹ Proliferation

☹ Inflammation

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

Both

Accident or necessity?

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.

uvate kinase (PK) produces $q + 1$ molecules of y for a net (normalized) production of one unit, which is consumed in a final reaction modeling the cell's use of ATP. In glycolysis, two ATP 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 as discussed below and in SOM, but the analysis

Chandra, Buzi, and Doyle

Fix?

“Architecture”

Yet Fragile

- ☹ Obesity, diabetes
- ☹ Cancer
- ☹ Parasites, infection
- ☹ AutoImmune/Inflame
- ☹ Addiction, psychosis…
- ☠ Epidemics, war…
- 💣 Catastrophes
- 💣 Obfuscate, amplify,…

Don’t worry …

- “There’s an app for that.”
- “The rapture is near.”
- “There’s a gene…
- “The market will…”
- “The new sciences of …”
- “Order for free..”
- “Like, dude, like, chill…”

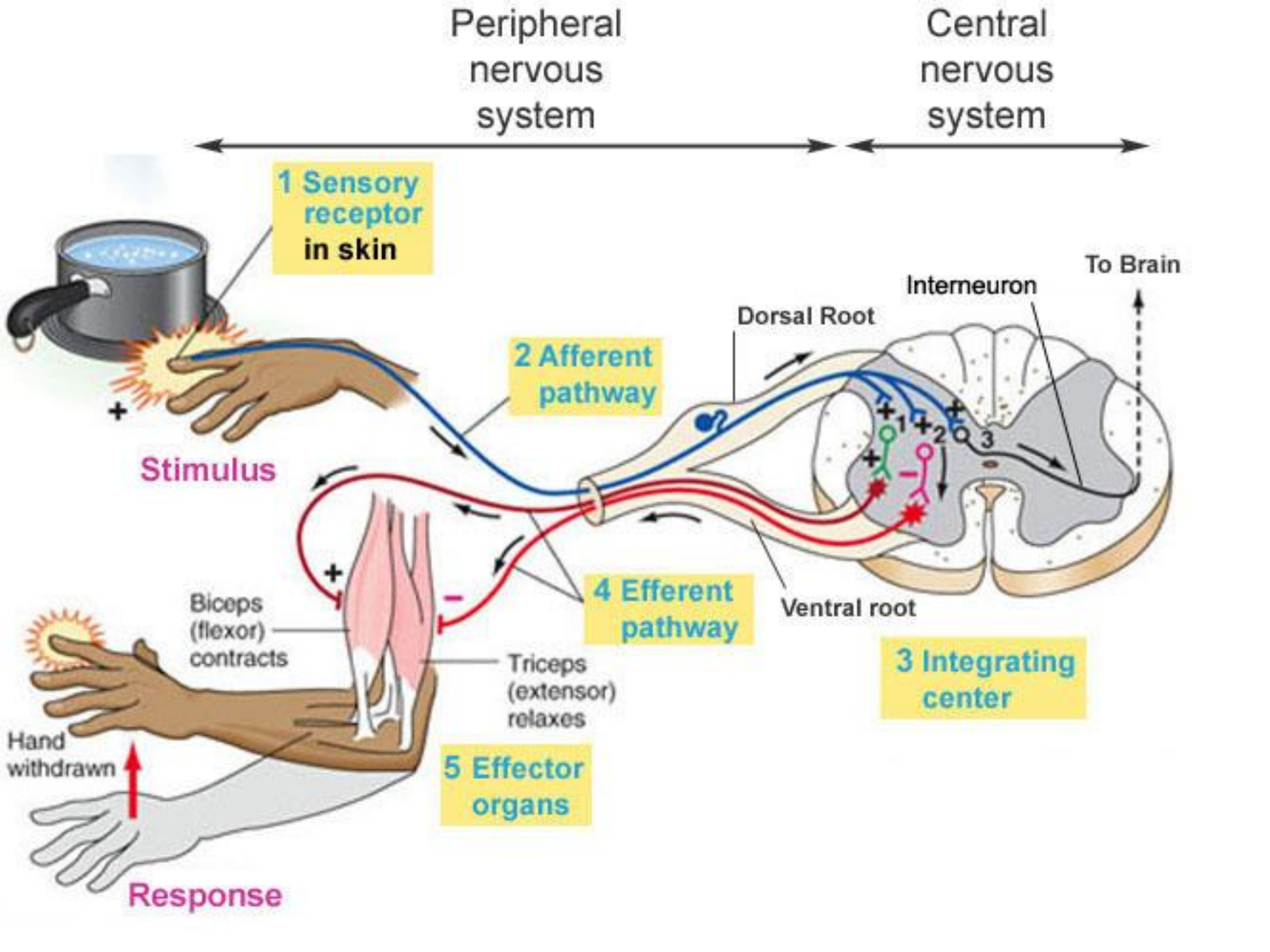
In the real (vs virtual) world

What matters:

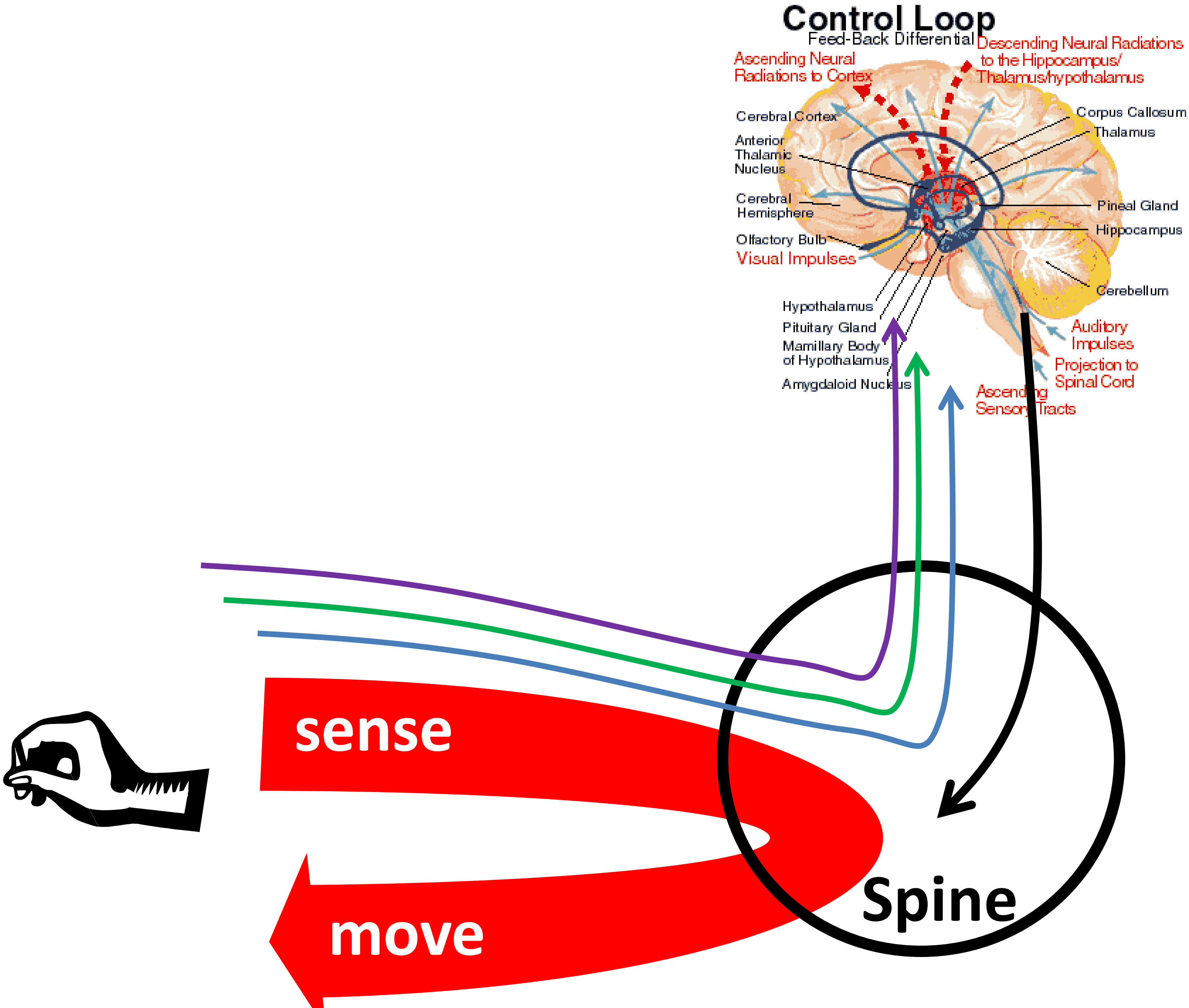
- Action

What doesn't:

- Data
- Information
- Computation
- Learning
- Decision
- …



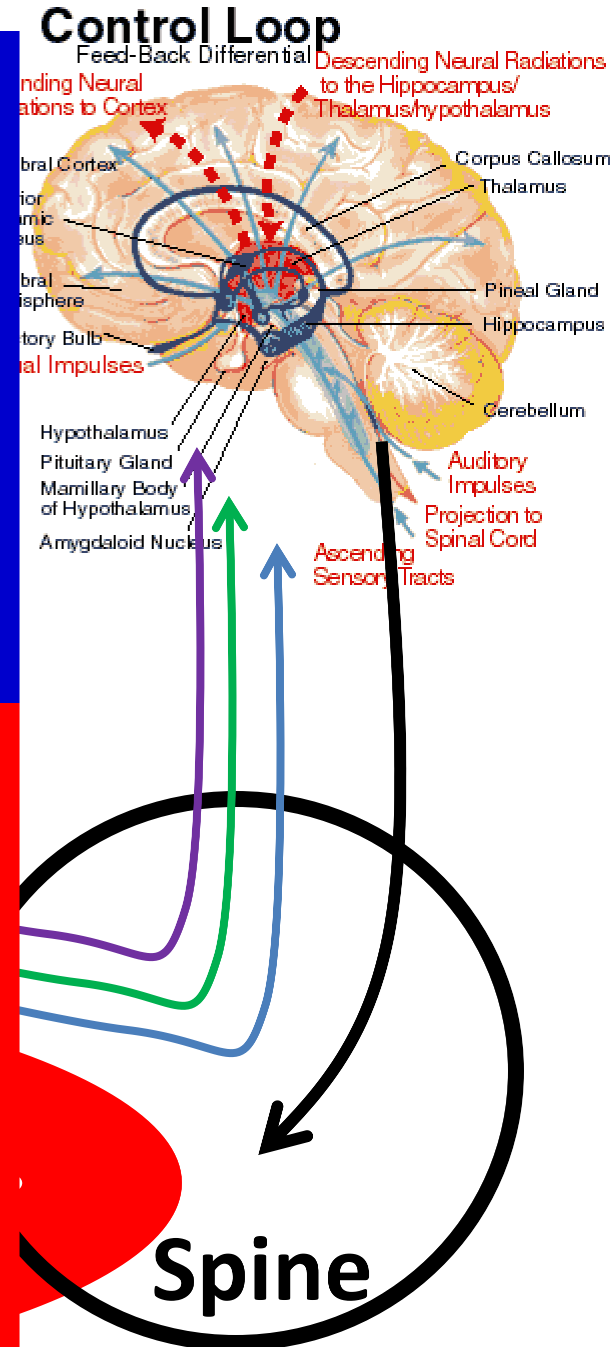
Peripheral nervous system
Central nervous system
1 Sensory receptor in skin
2 Afferent pathway
Dorsal Root
Interneuron
To Brain
Stimulus
Biceps (flexor) contracts
Triceps (extensor) relaxes
4 Efferent pathway
Ventral root
3 Integrating center
Hand withdrawn
5 Effector organs
Response



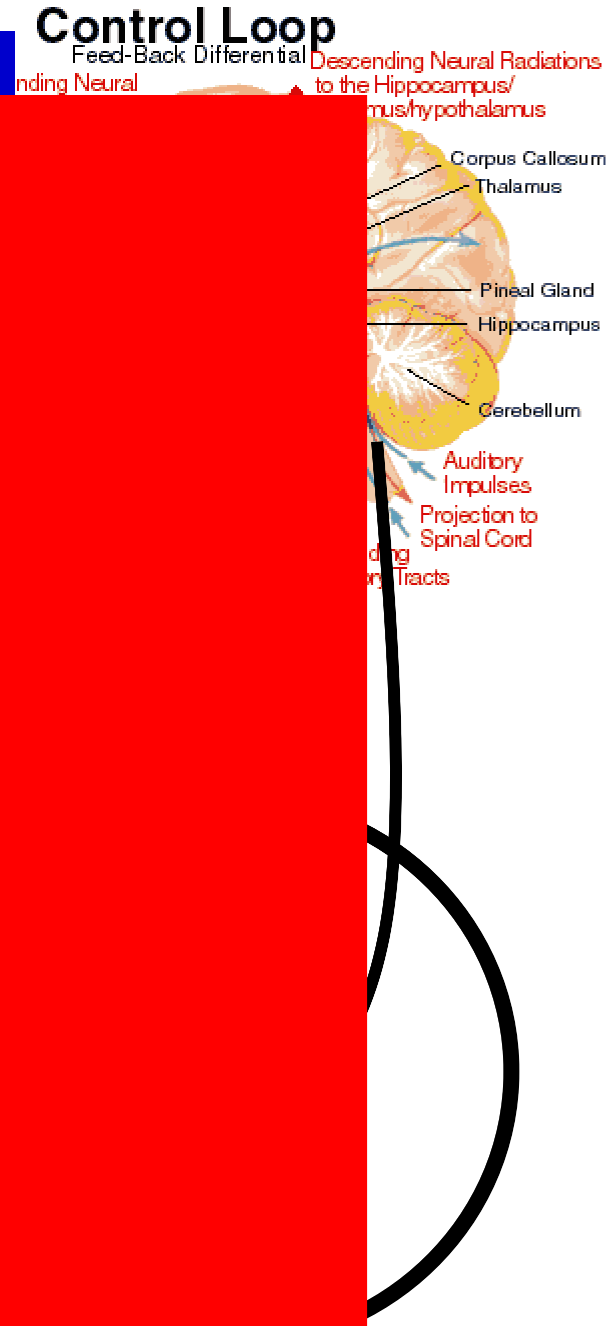
Control Loop
Feed-Back Differential
Ascending Neural Radiations to Cortex
Descending Neural Radiations to the Hippocampus/ Thalamus/hypothalamus
Cerebral Cortex
Anterior Thalamic Nucleus
Cerebral Hemisphere
Olfactory Bulb
Visual Impulses
Corpus Callosum
Thalamus
Pineal Gland
Hippocampus
Cerebellum
Hypothalamus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

Reflect

Reflex



Reflect



Reflex

Fix?

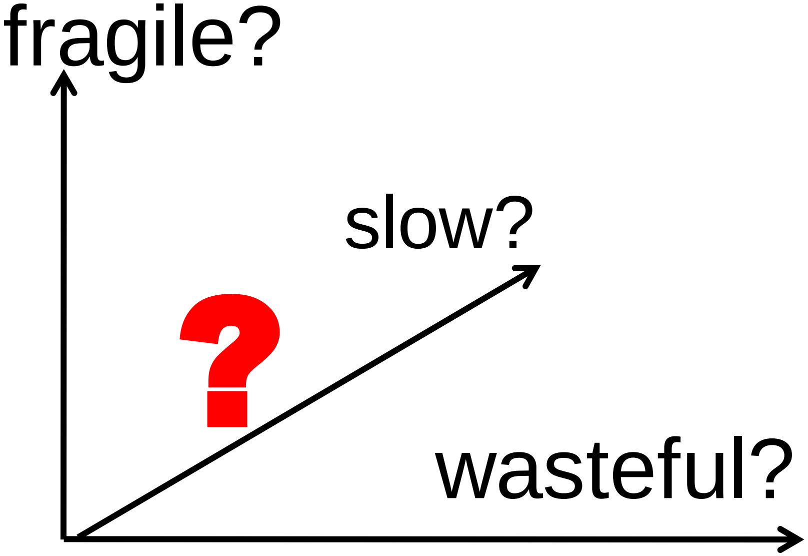
What matters:

- Action
- Automation
- Limits
- Tradeoffs

Yet Fragile

☹ Obesity, diabetes
☹ Cancer
☹ Parasites, infection
☹ AutoImmune/Inflame
☹ Addiction, psychosis…
☠ Epidemics, war…
💣 Catastrophes
💣 Obfuscate, amplify,…

Accident or necessity?



What we want to avoid.

IEEE TRANS ON SYSTEMS, MAN, AND CYBERNETICS, JULY 2010, Alderson and Doyle

IEEE TRANSACTIONS ON SYSTEMS, MAN, AND CYBERNETICS—PART A: SYSTEMS AND HUMANS, VOL. 40, NO. 4, JULY 2010

Contrasting Views of Complexity and Their Implications For Network-Centric Infrastructures

David L. Alderson, *Member, IEEE*, an… C. Doyle

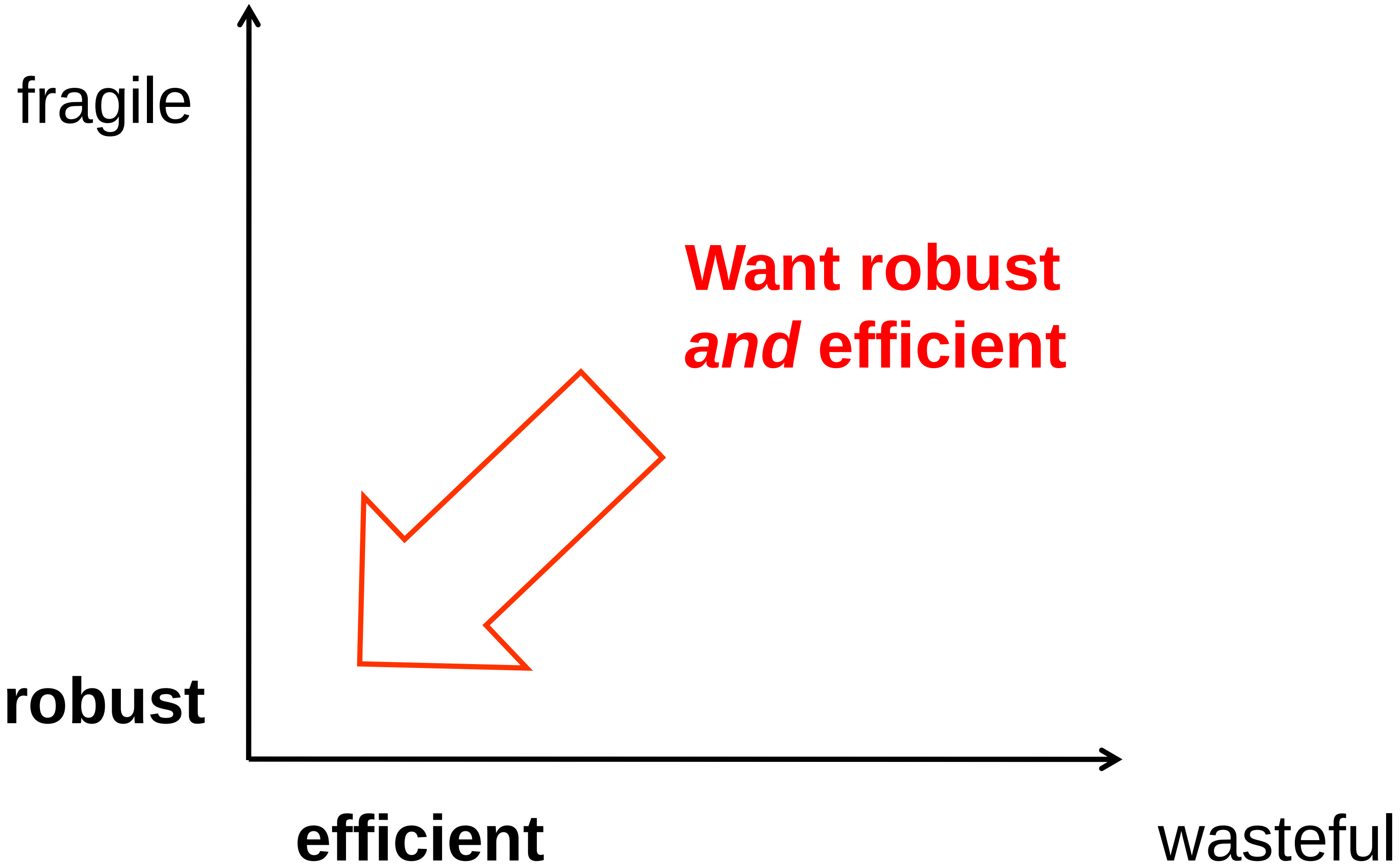
Fundamentals?

***Abstract*—There exists a widely recognized ne… derstand and manage complex "systems of … biology, ecology, and medicine to … This is motivating the search for …ved systems and driving demand for …d methods that are consistent, integrative, and … However, the theoretical frameworks available today … not merely fragmented but sometimes contradictory and incompatible. We argue that complexity arises in highly evolved biological and technological systems primarily to provide mechanisms to create robustness. However, this complexity itself can be a source of new fragility, leading to "robust yet fragile" tradeoffs in system design. We focus on the role of robustness and architecture in networked infrastructures, and we highlight recent advances in the theory of distributed control driven by network technologies. This view of complexity in highly organized technological and biological systems is fundamentally different from the dominant perspective in the mainstream sciences, which downplays function, constraints, and tradeoffs, and tends to minimize the role of organization and design.**

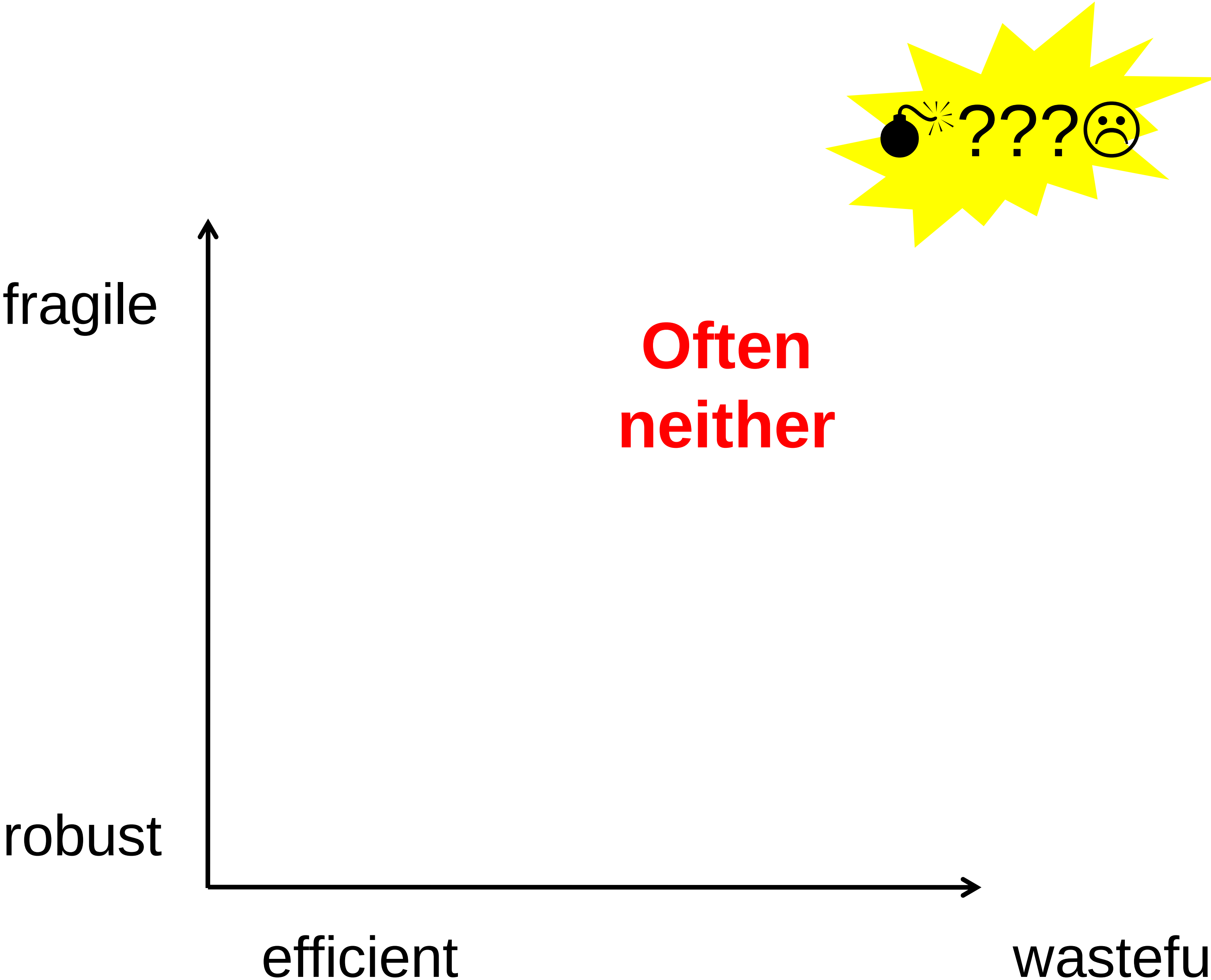
***Index Terms*—Architecture, complexity theory, networks, optimal control, optimization methods, protocols.**

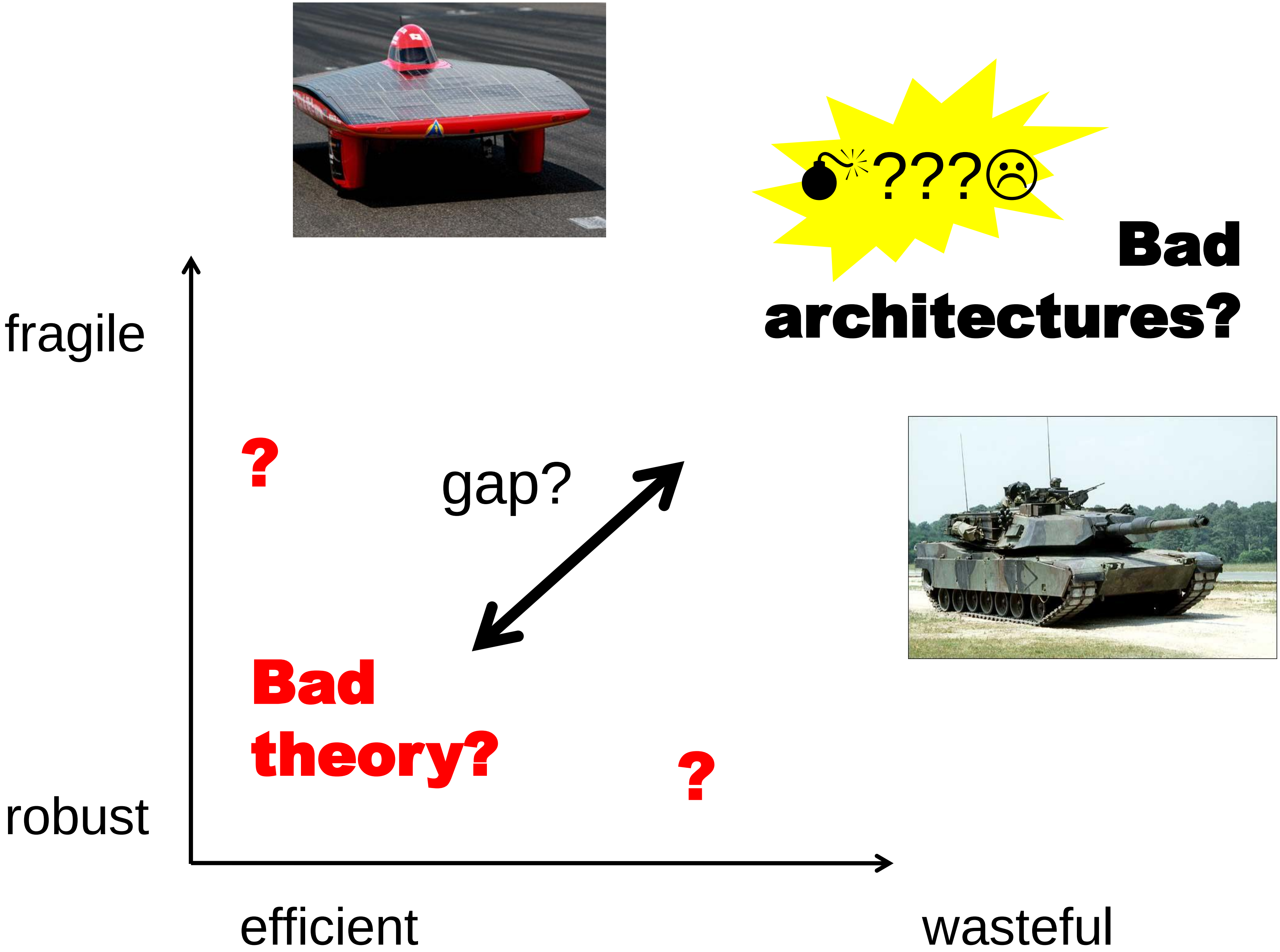
…ex engineering systems, but much of advanced …ology has, if anything, made things worse. Computer-based simulation and rapid prototyping tools are now broadly available and powerful enough that it is relatively easy to demonstrate almost anything, provided that conditions are made sufficiently idealized. We are much better at designing, mass-producing, and deploying network-enabled devices than we are at being able to predict or control their collective behavior once deployed in the real world. The result is that, when things fail, they often do so cryptically and catastrophically.

The growing need to understand and manage complex systems of systems, ranging from biology to technology, is creating demand for new mathematics and methods that are consistent and integrative. Yet, there exist fundamental incompatibilities in available theories for addressing this challenge. Various "new sciences" of "complexity" and "networks" dominate the mainstream sciences [3] but are at best disconnected from medicine, mathematics, and engineering. Computing, communication, and control theories and technologies flourish but


fragile
robust
Want robust
and efficient
efficient
wasteful


fragile
robust
efficient
wasteful
At best we get one


💣???☹
fragile
Often neither
robust
efficient
wasteful



???☹
Bad architectures?
fragile
robust
?
gap?
Bad theory?
?
efficient
wasteful

Control

Bode

Comms

Shannon

Theory?

Deep, but fragmented, incoherent, incomplete

Carnot

Boltzmann

Turing

Godel

Heisenberg

Compute

Physics

Einstein

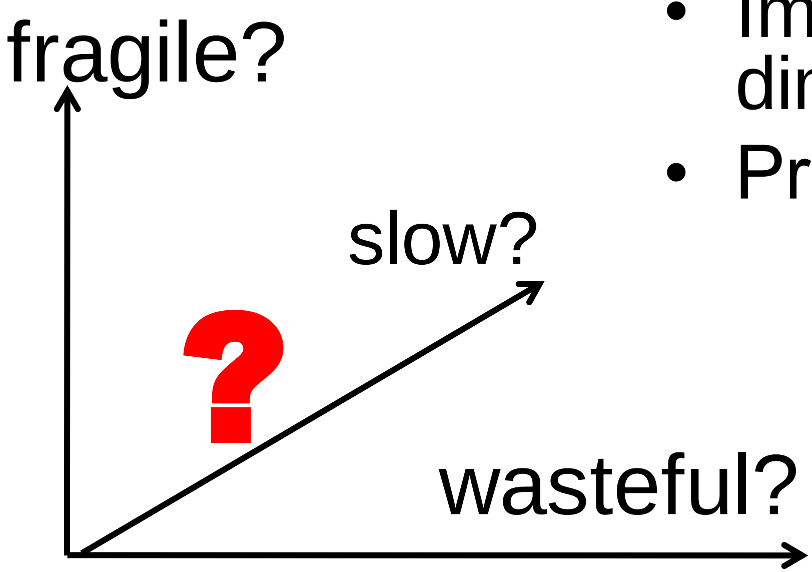
Control

Bode

Comms

Shannon

- Each theory ≈ one dimension
- Important tradeoffs ***across*** dimensions
- Progress is encouraging but…



Carnot

Turing

Boltzmann

Godel

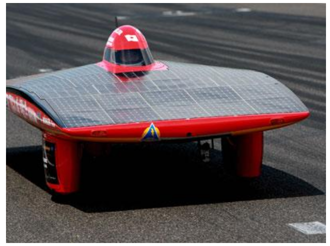
Heisenberg

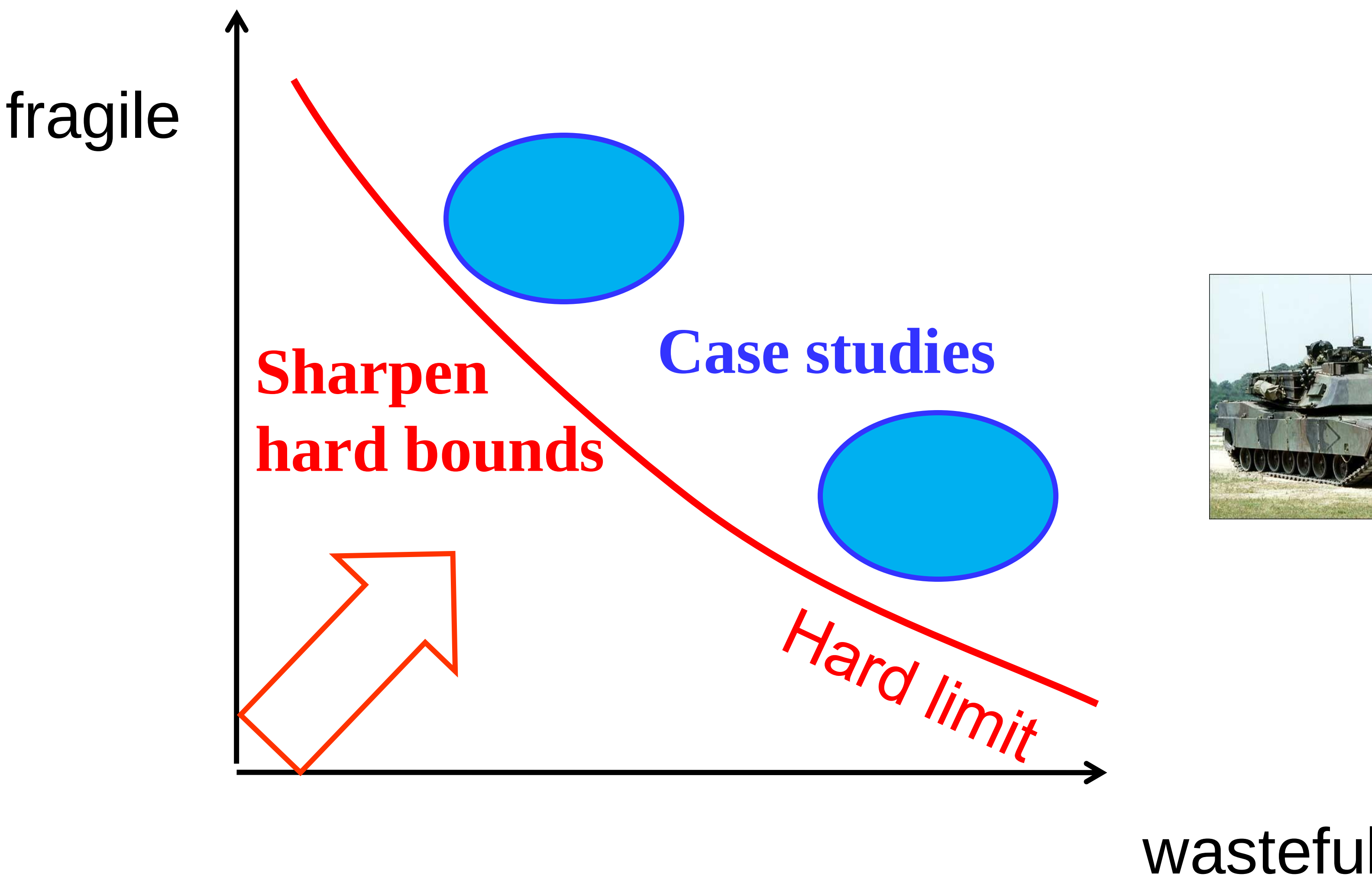
Compute

Physics

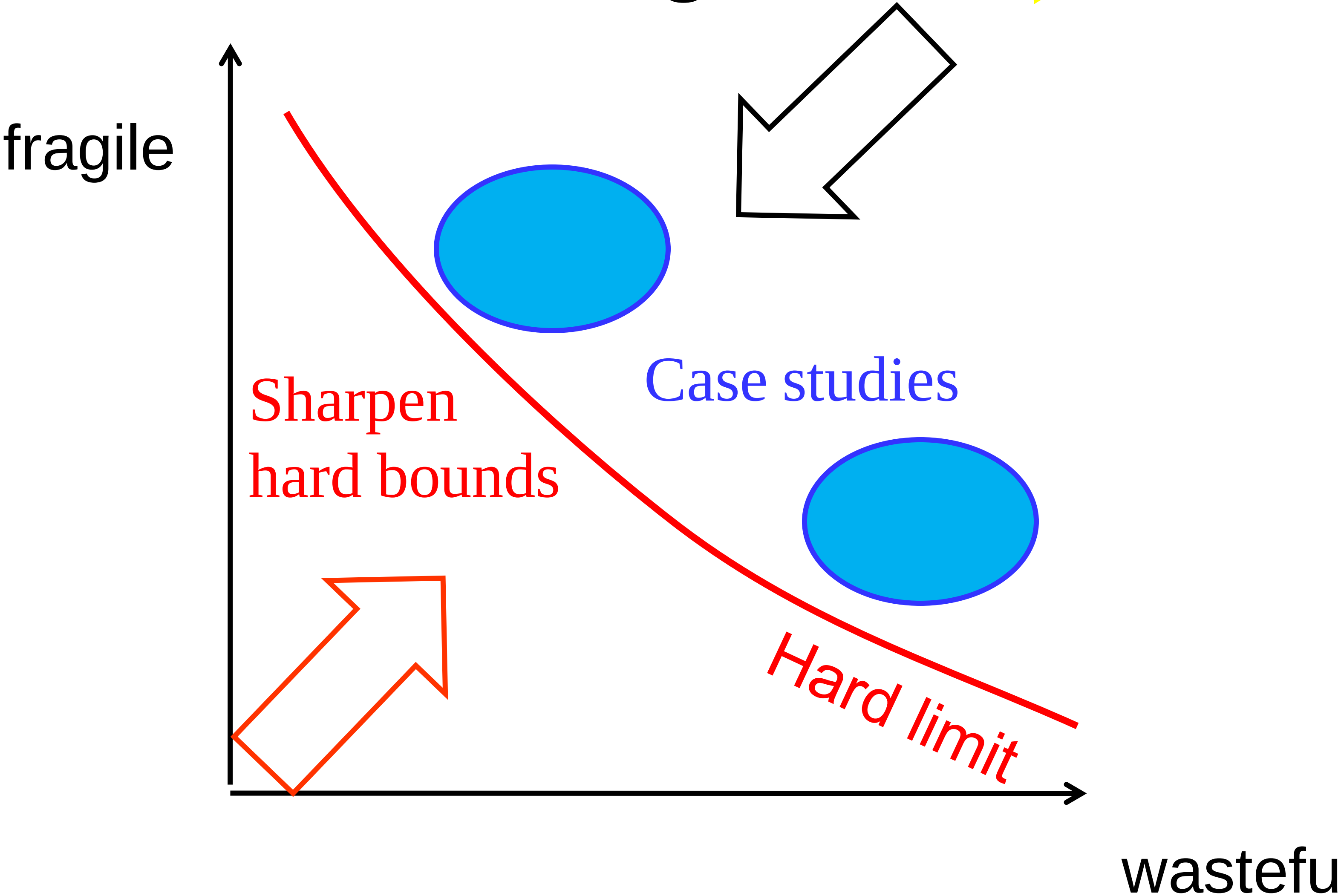
Einstein

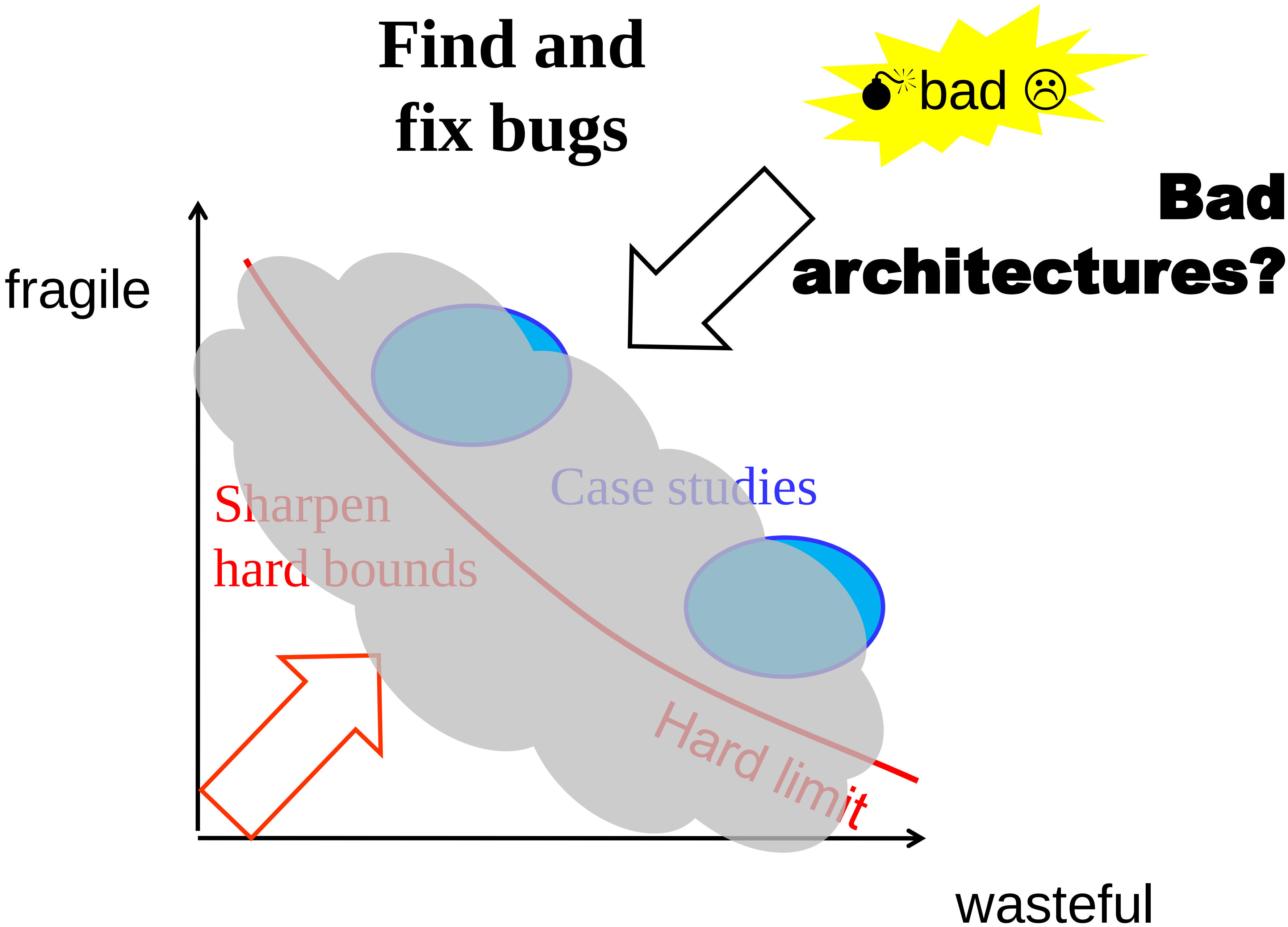
Conservation “laws”?





Find and fix bugs




Find and fix bugs
bad ☹
Bad architectures?
fragile
Sharpen hard bounds
Case studies
Hard limit
wasteful

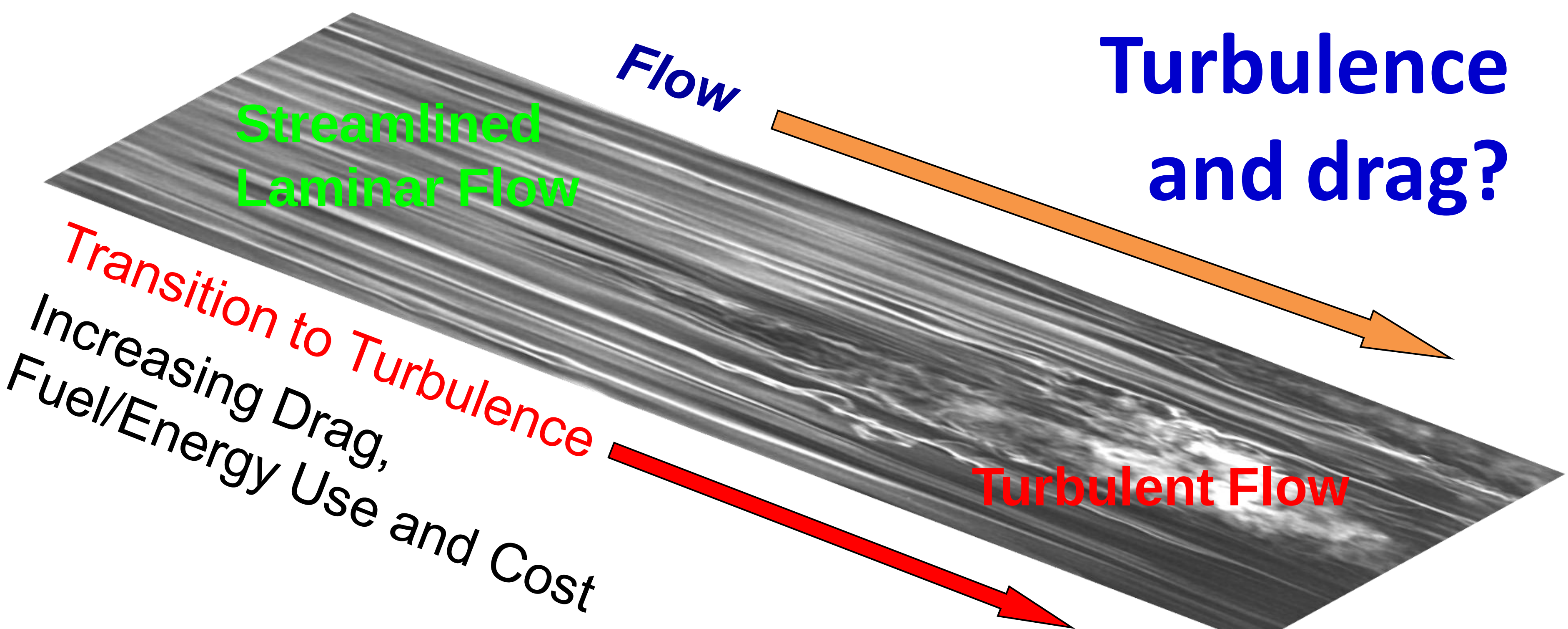
J. Fluid Mech. (2010), vol. 665, pp. 99–119.

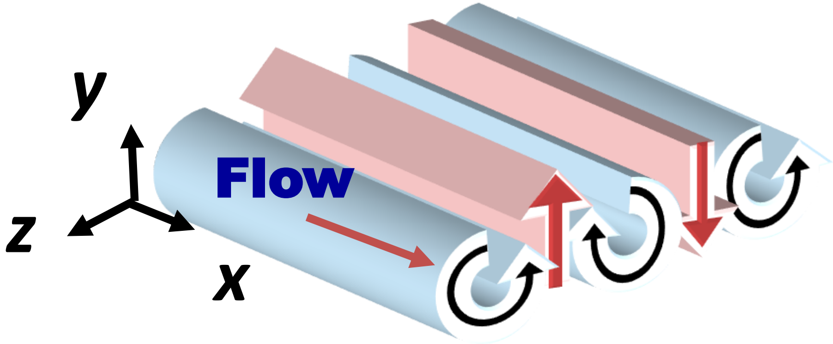
doi:10.1017/S0022112010003861

J. Fluid Mech (2010)

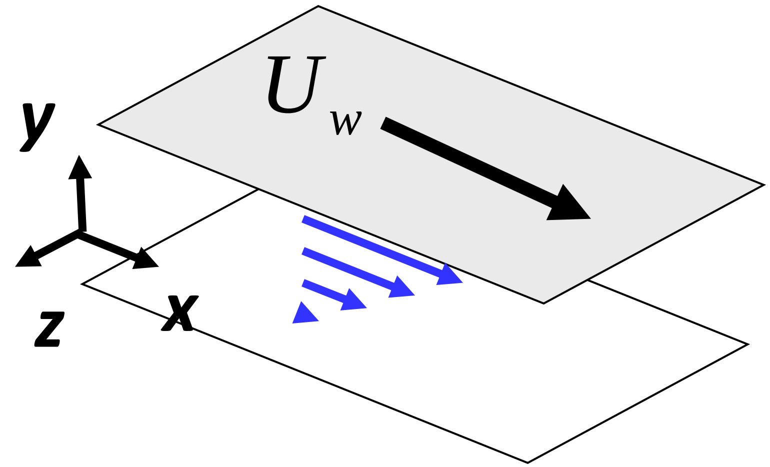
A streamwise constant model of turbulence in plane Couette flow

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

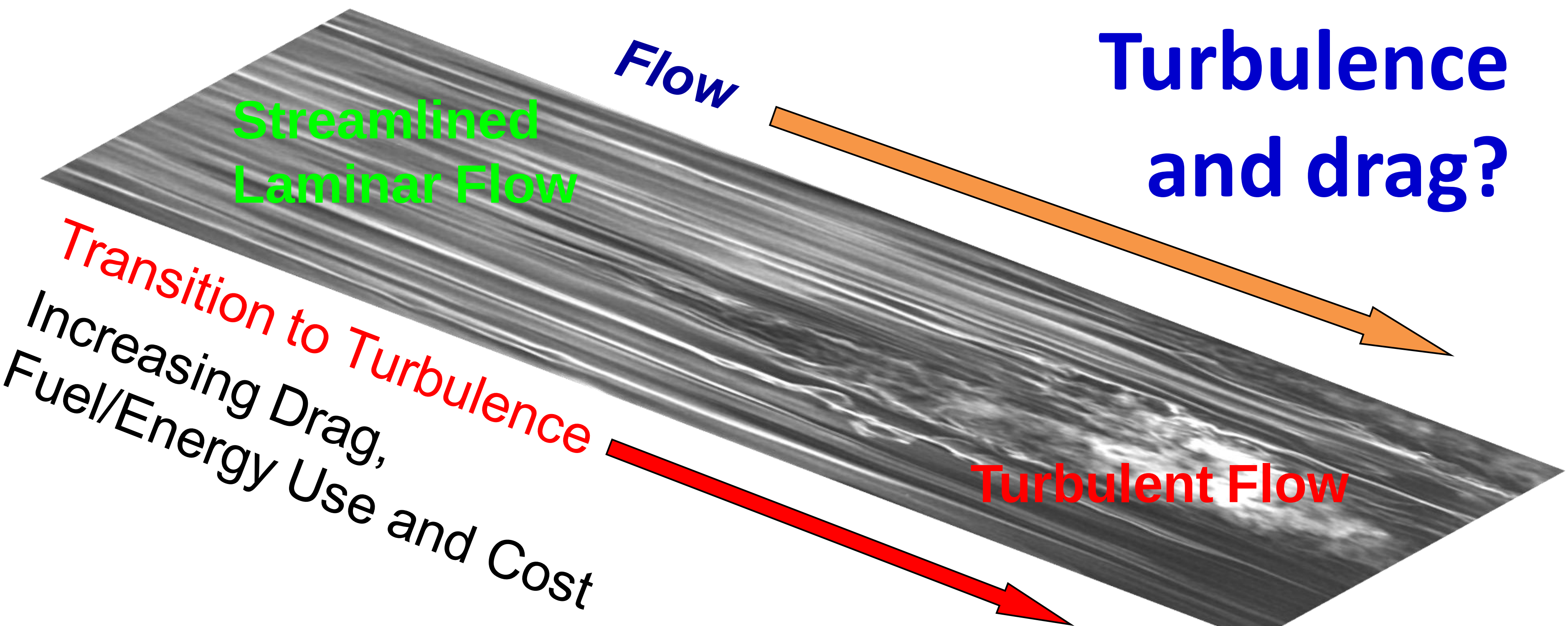




Coherent structures

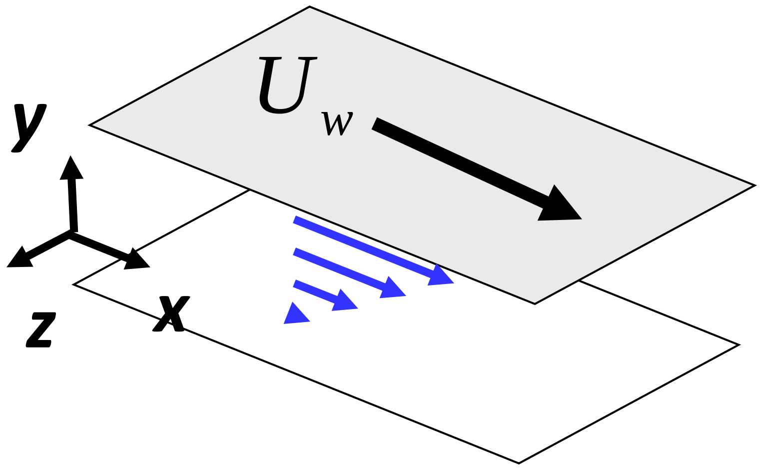


Turbulence and drag?

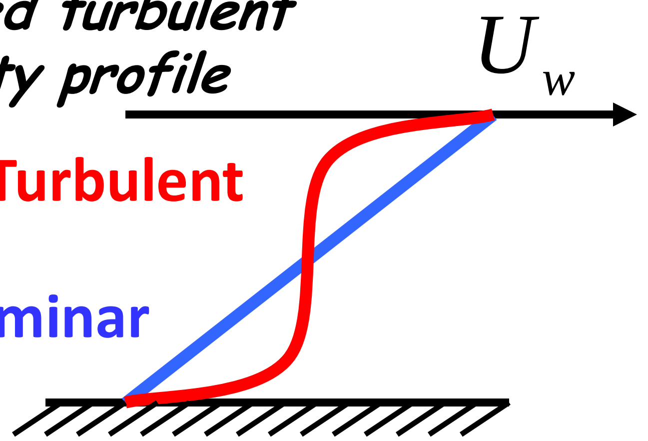


$$\frac{\partial \underline{u}}{\partial t} + \underline{u} \bullet \nabla \underline{u} = -\nabla p + \frac{1}{R} \Delta \underline{u}$$

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



"turbulence is a highly nonlinear phenomena"



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

Complexity?

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

	Small	Large
Robust	Simple	**Organized**
Fragile	chaocritical	Irreducibile

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

Complexity?

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

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

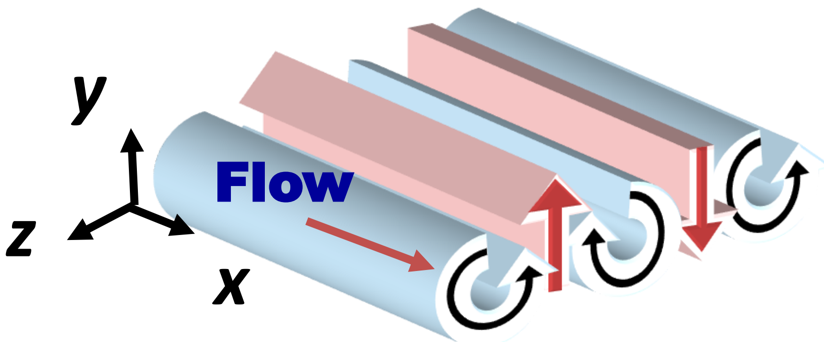
mildly nonlinear

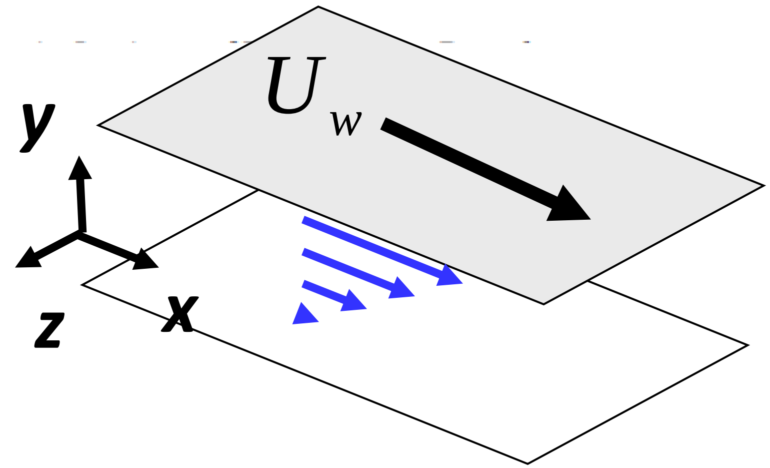
highly nonlinear

Physics of Fluids (2011)
PHYSICS OF FLUIDS 23, 065108 (2011)

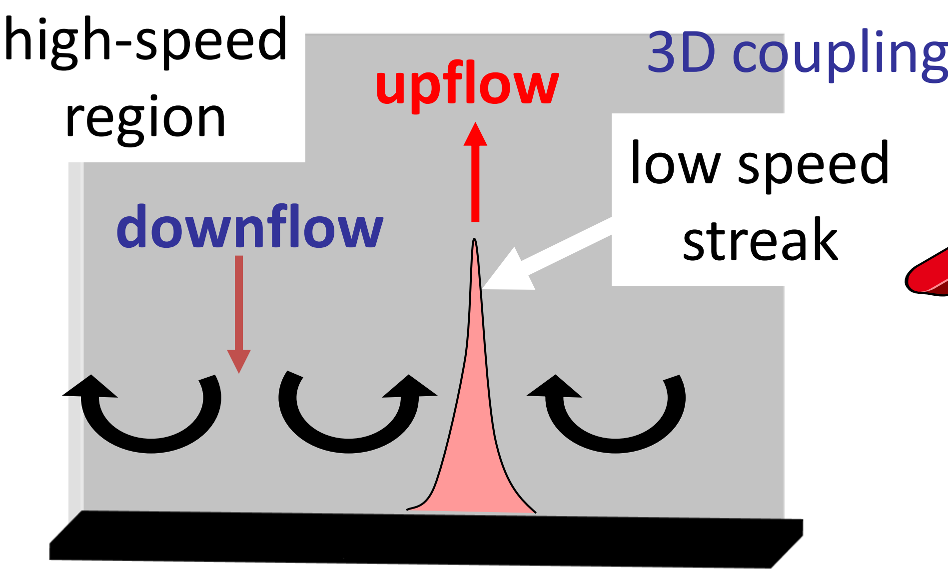
Amplification and nonlinear mechanisms in plane Couette flow

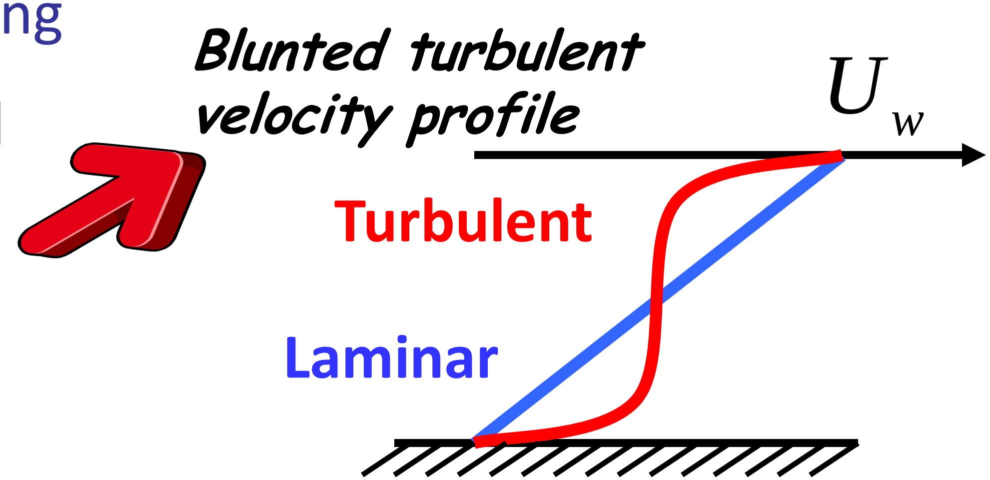
Dennice F. Gayme,[1] Beverley J. McKeon,[1] Bassam Bamieh,[2] Antonis Papachristodoulou,[3] and John C. Doyle[3]

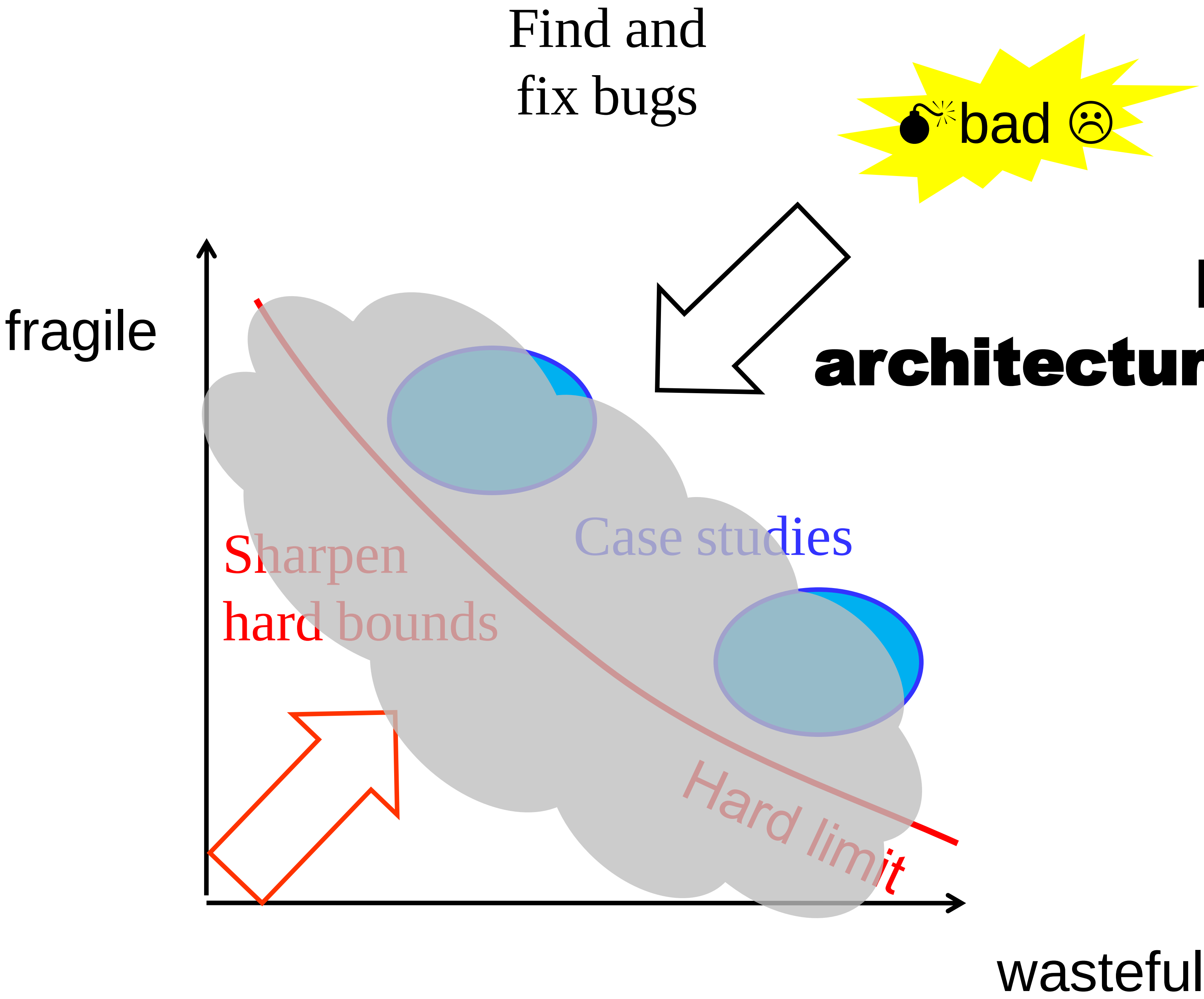




Coherent structures and turbulent drag

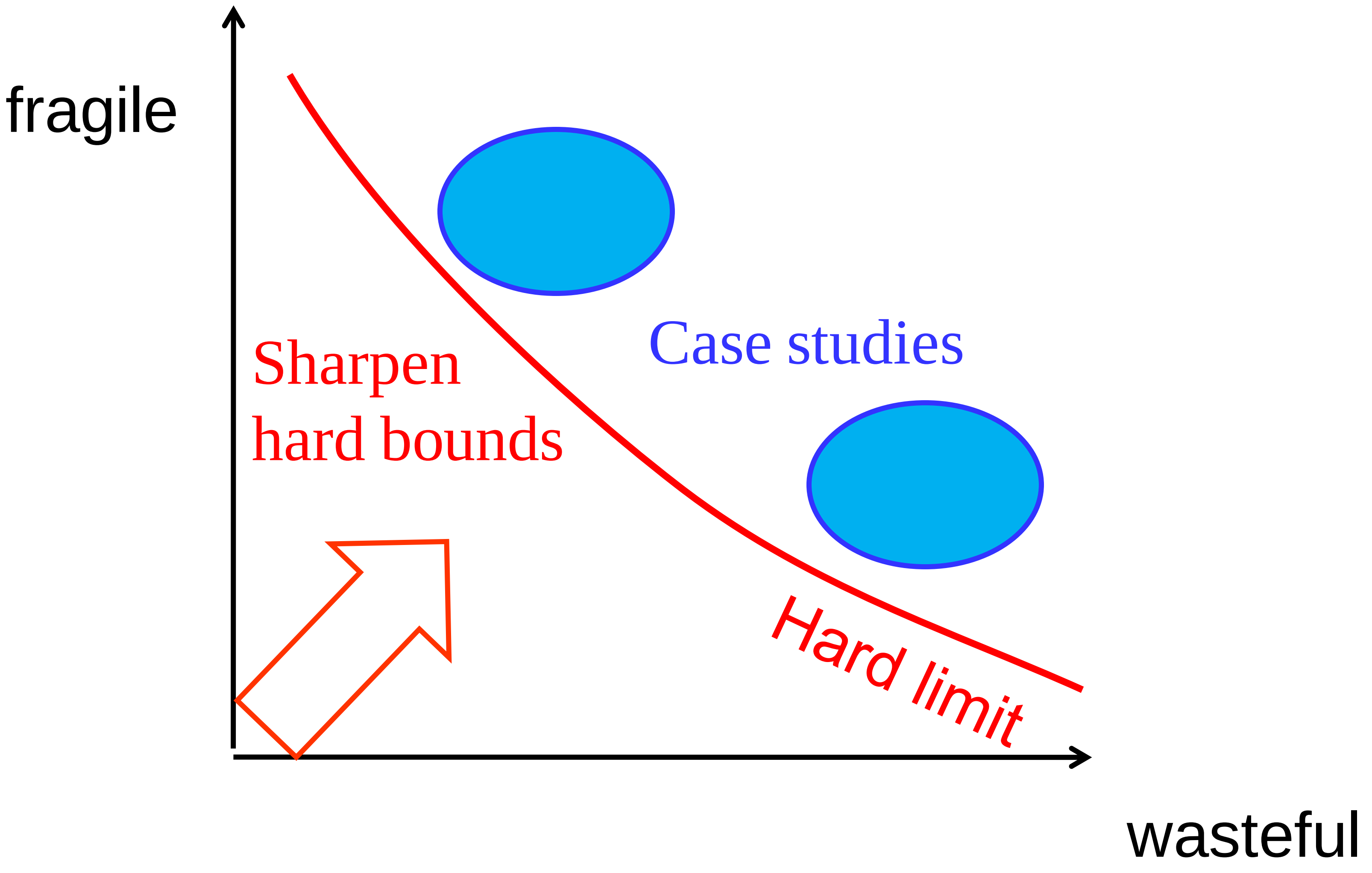






Find and
fix bugs
bad ☹
Bad
architectures?
fragile
Case studies
Sharpen
hard bounds
Hard limit
wasteful

Theory + biology case study



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.

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Chandra, Buzi, and Doyle

Theory + biology case study

- Universal issues
- Longstanding mystery (century? millennia?)
- Accessible, components “well-known”
- Evolution + physiology + “CDS/CME”
- Broadly relevant
- *Science* paper in press (w/ Fiona Chandra, Genti Buzi)
- Extreme responses typical

Glycolytic oscillations

Hard tradeoffs between

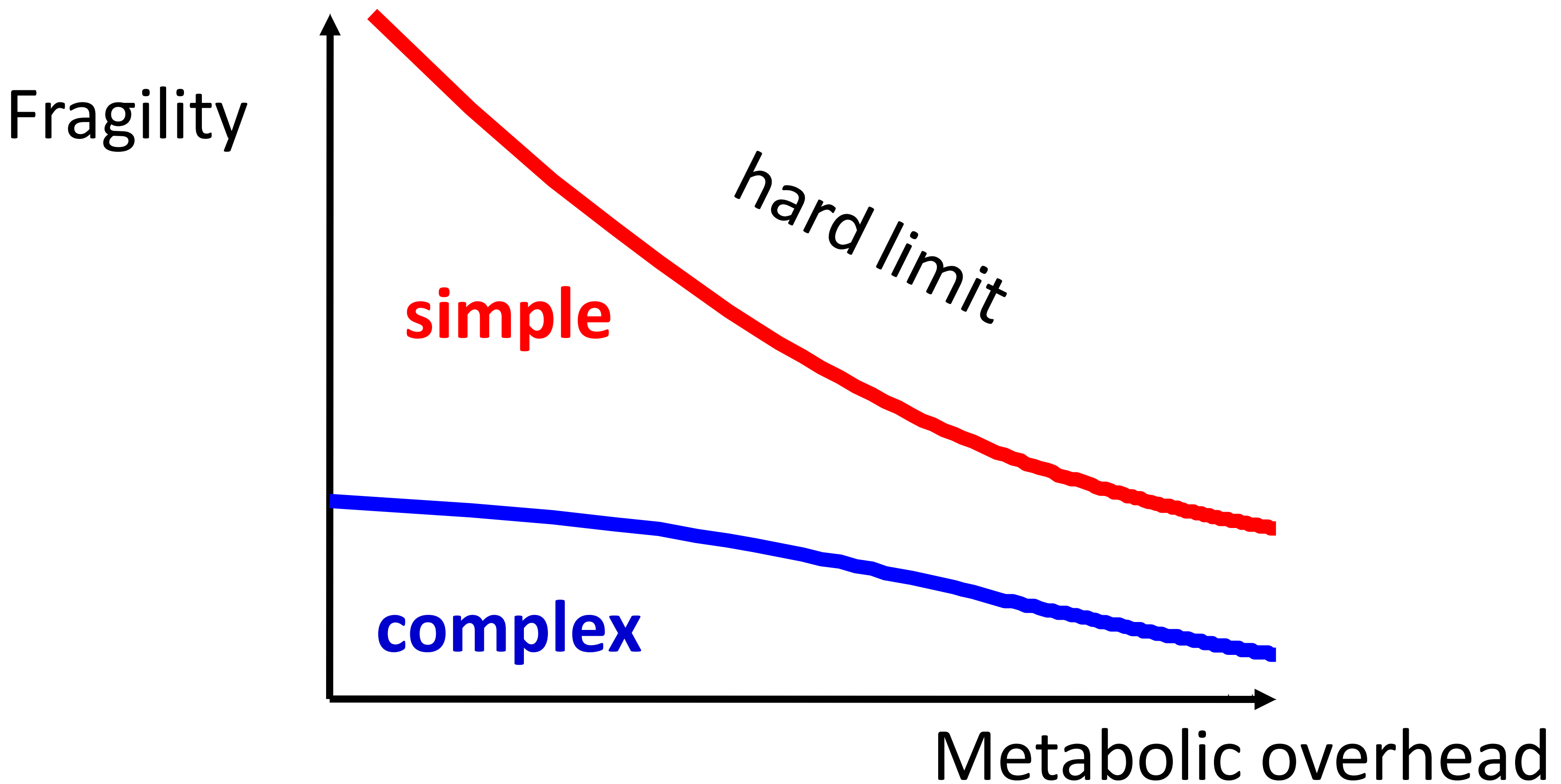
1. **Fragility** (disturbance rejection)
2. Amount (of enzymes)
3. Complexity (of enzymes)

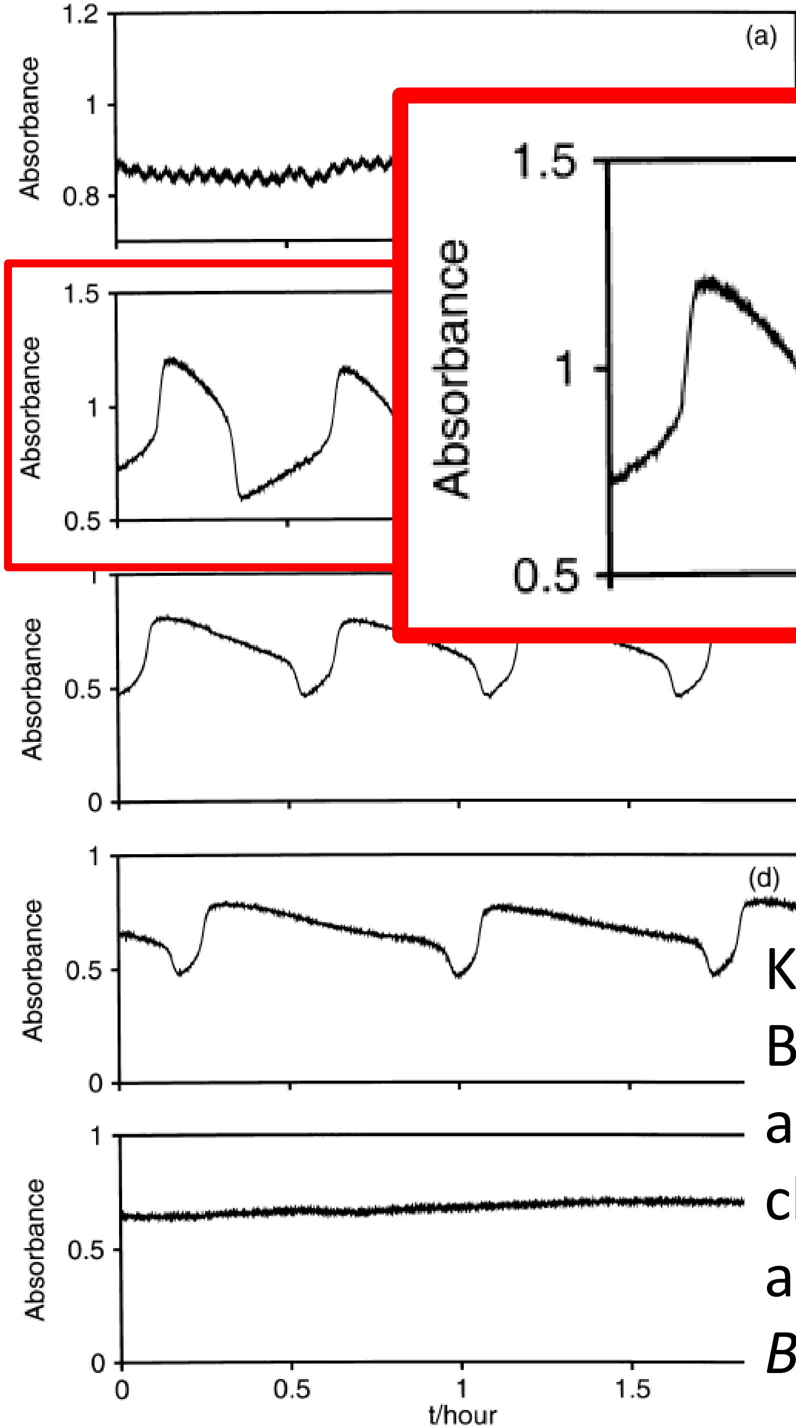
} **Metabolic overhead** (items 2–3)

- Most ubiquitous/studied "circuit" in science/engineering
- New insights and experiments

Hard tradeoffs between

1. Fragility (disturbance rejection)
2. Amount (of enzymes)
3. Complexity (of enzymes)





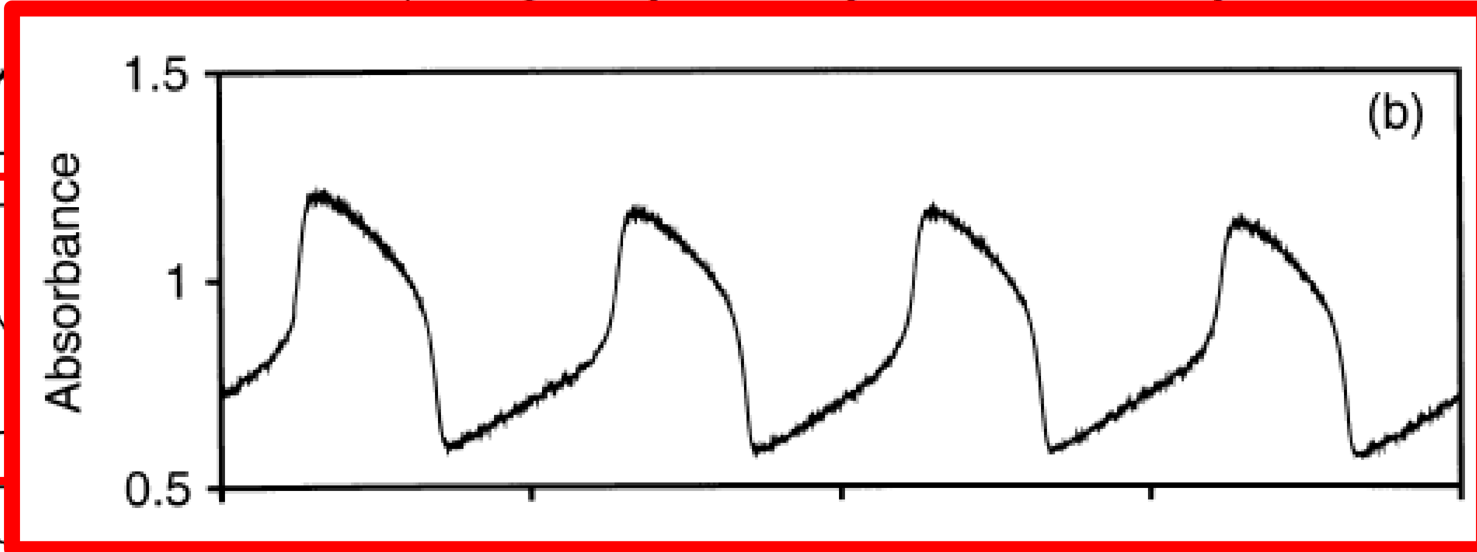


Fig. 2. Dependence of pattern on flow rate. Experimental time

tion becomes longer (b–d), and at the highest flow rate (e), the state is stationary.

Experiments

K Nielsen, PG Sorensen, F Hynne, H-G Busse. **Sustained oscillations in glycolysis**: an experimental and theoretical study of chaotic and complex periodic behavior and of quenching of simple oscillations. *Biophys Chem* 72:49-62 (1998).

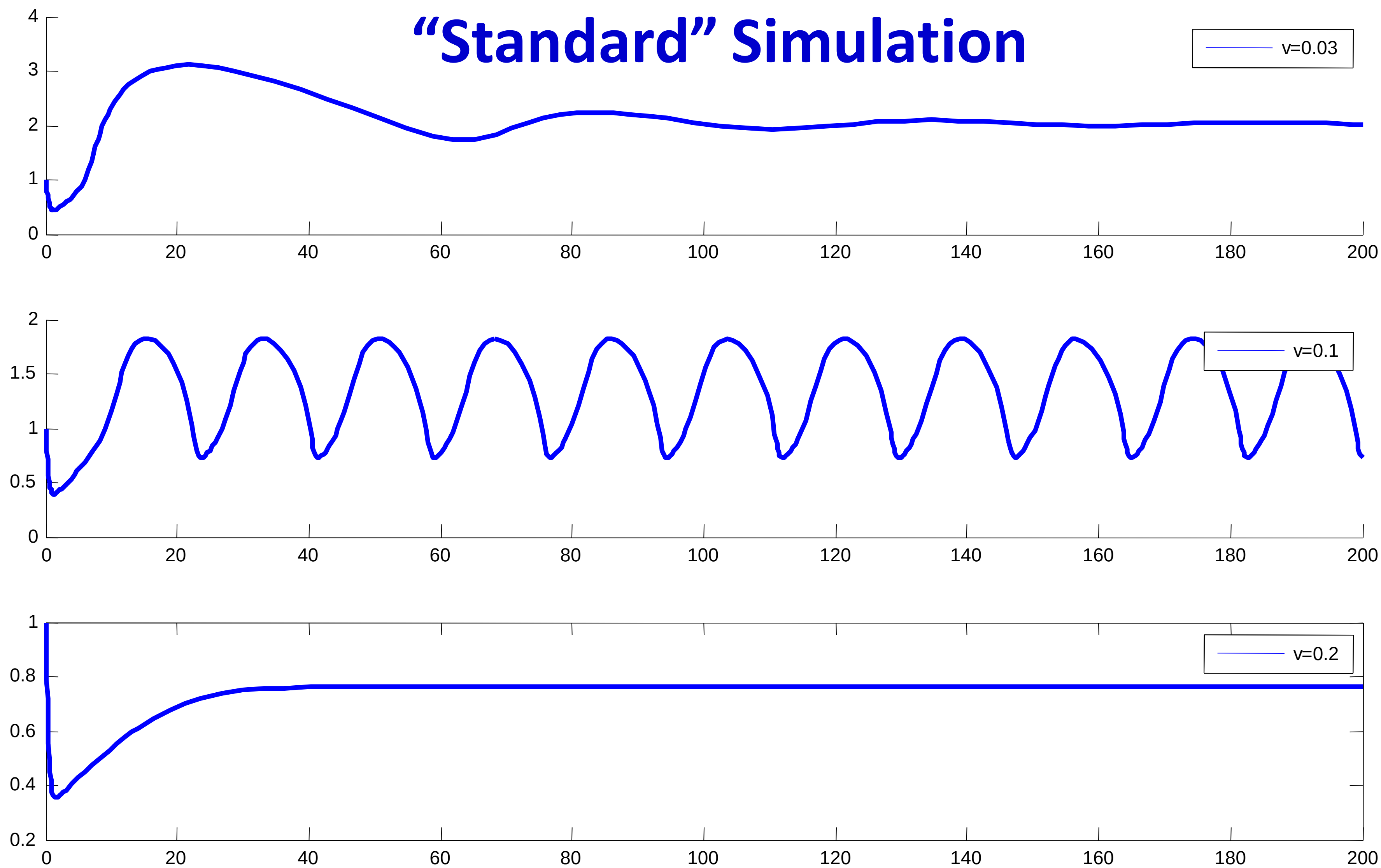
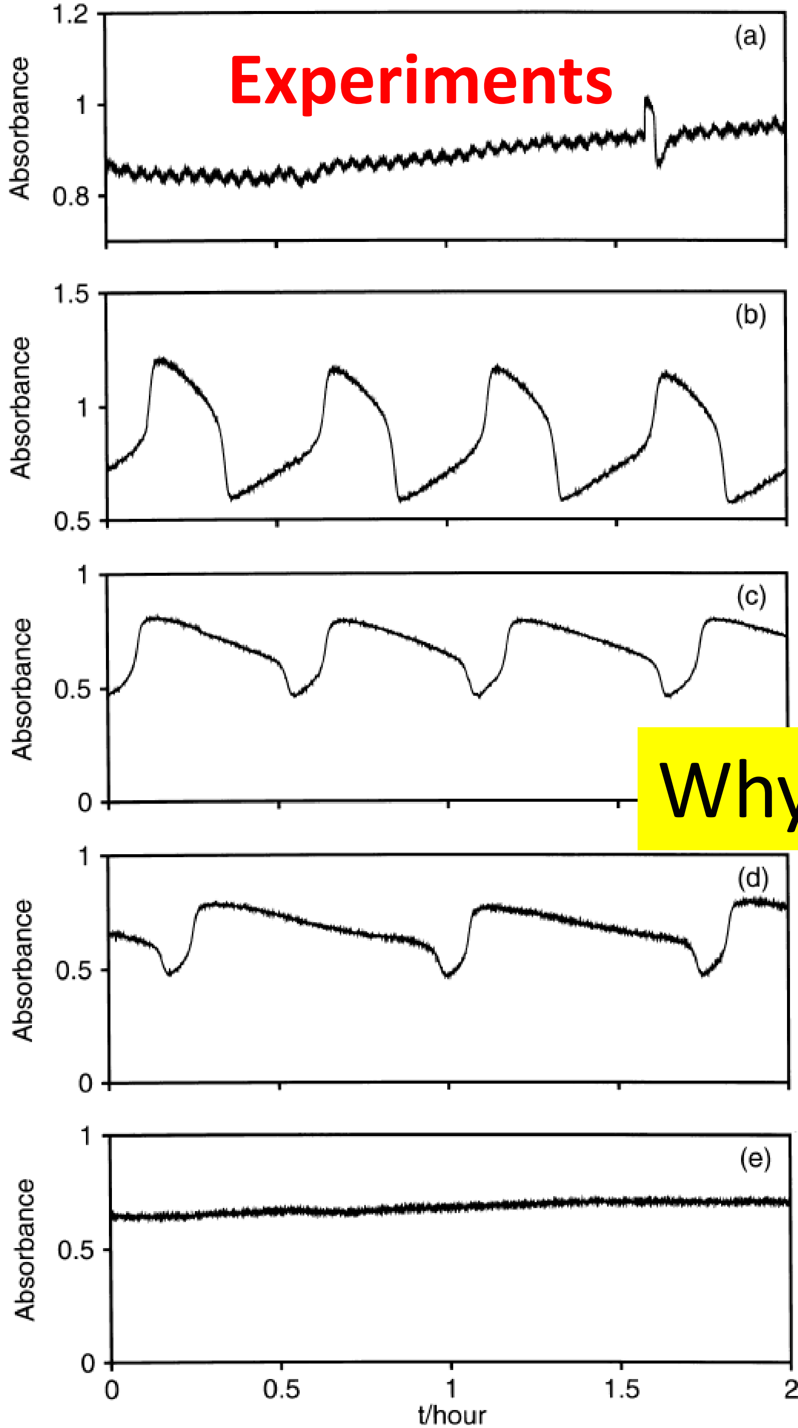
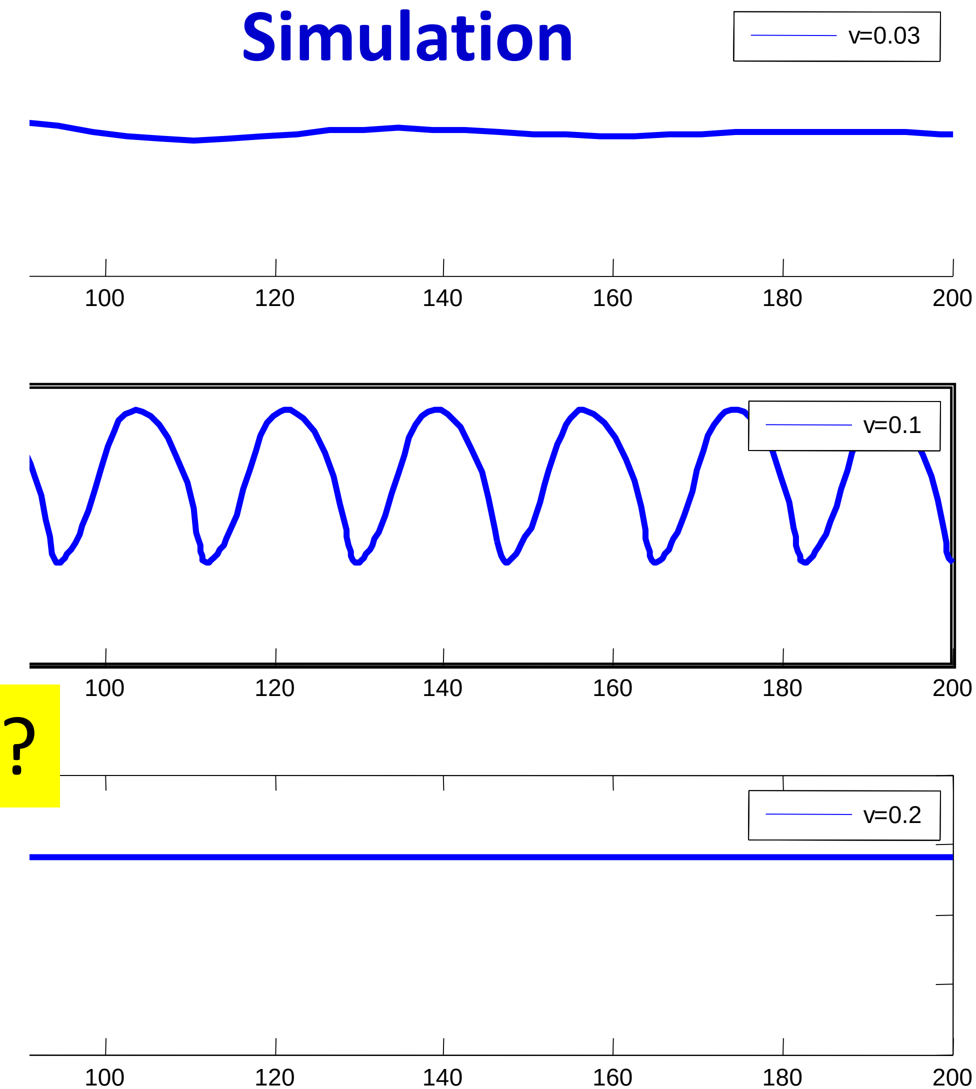


Figure S4. Simulation of two state model (S7.1) qualitatively recapitulates experimental observation from CSTR studies [5] and [12]. As the flow of material in/out of the system is increased, the system enters a limit cycle and then stabilizes again. For this simulation, we take *q=a=Vm=1, k=0.2, g=1, u=0.01, h=2.5.*





Why?

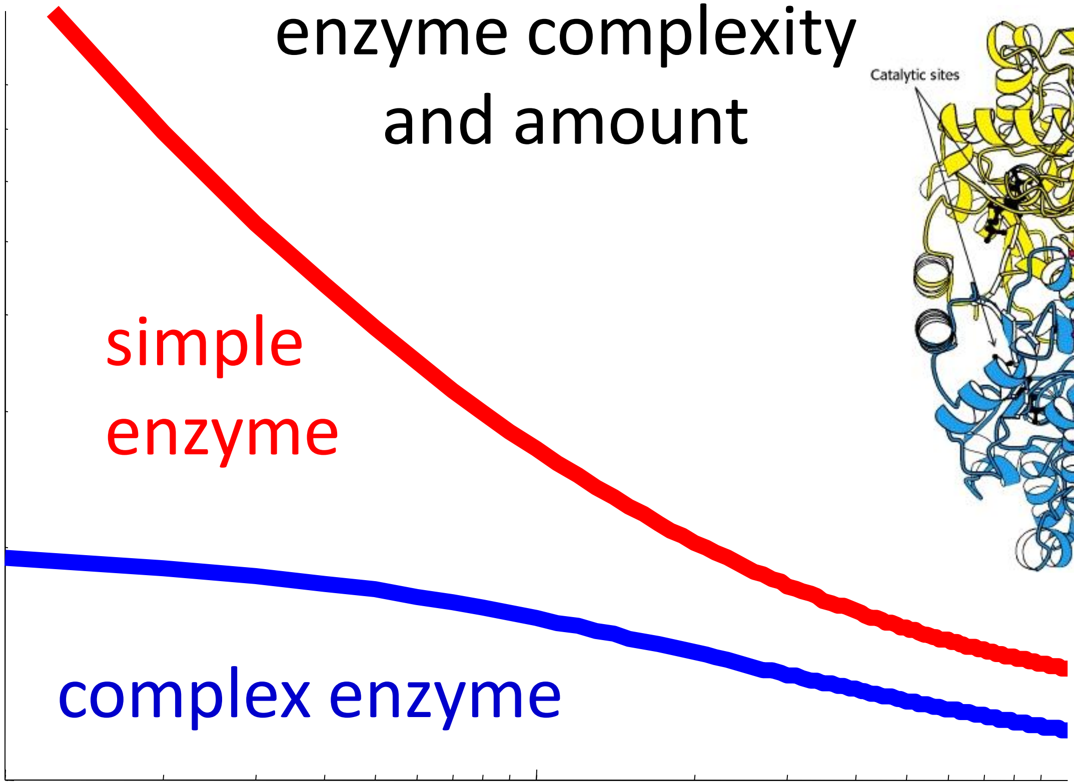
›del (S7.1) qualitatively recapitulates
studies [5] and [12]. As the flow of material
: system enters a limit cycle and then
ve take *q=a=Vm=1, k=0.2, g=1, u=0.01, h=2.5.*

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

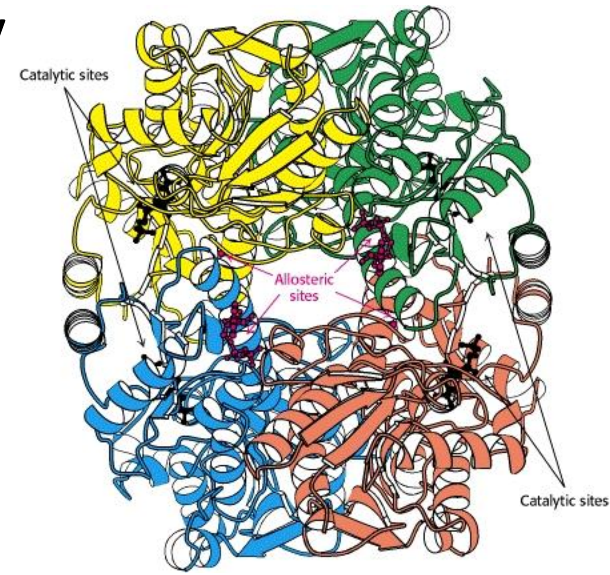
z and p functions of enzyme complexity and amount

Fragility

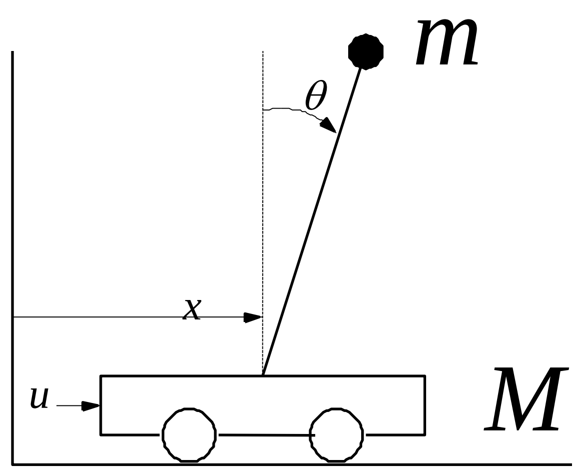
$$\ln\left|\frac{z+p}{z-p}\right|$$

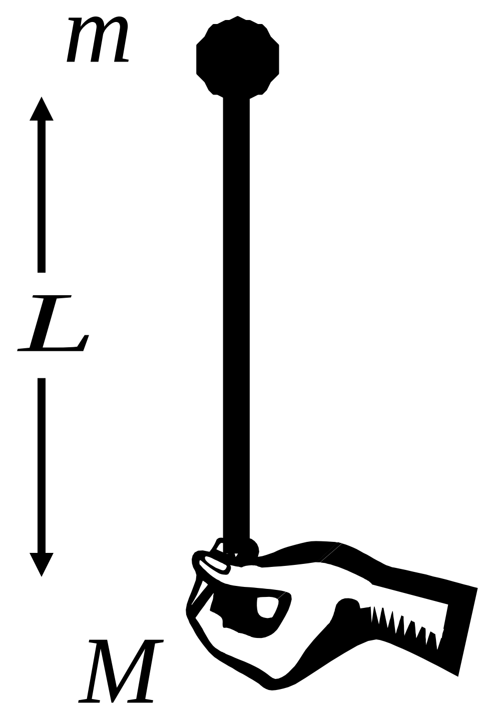


Enzyme amount



Linearized pendulum on a cart



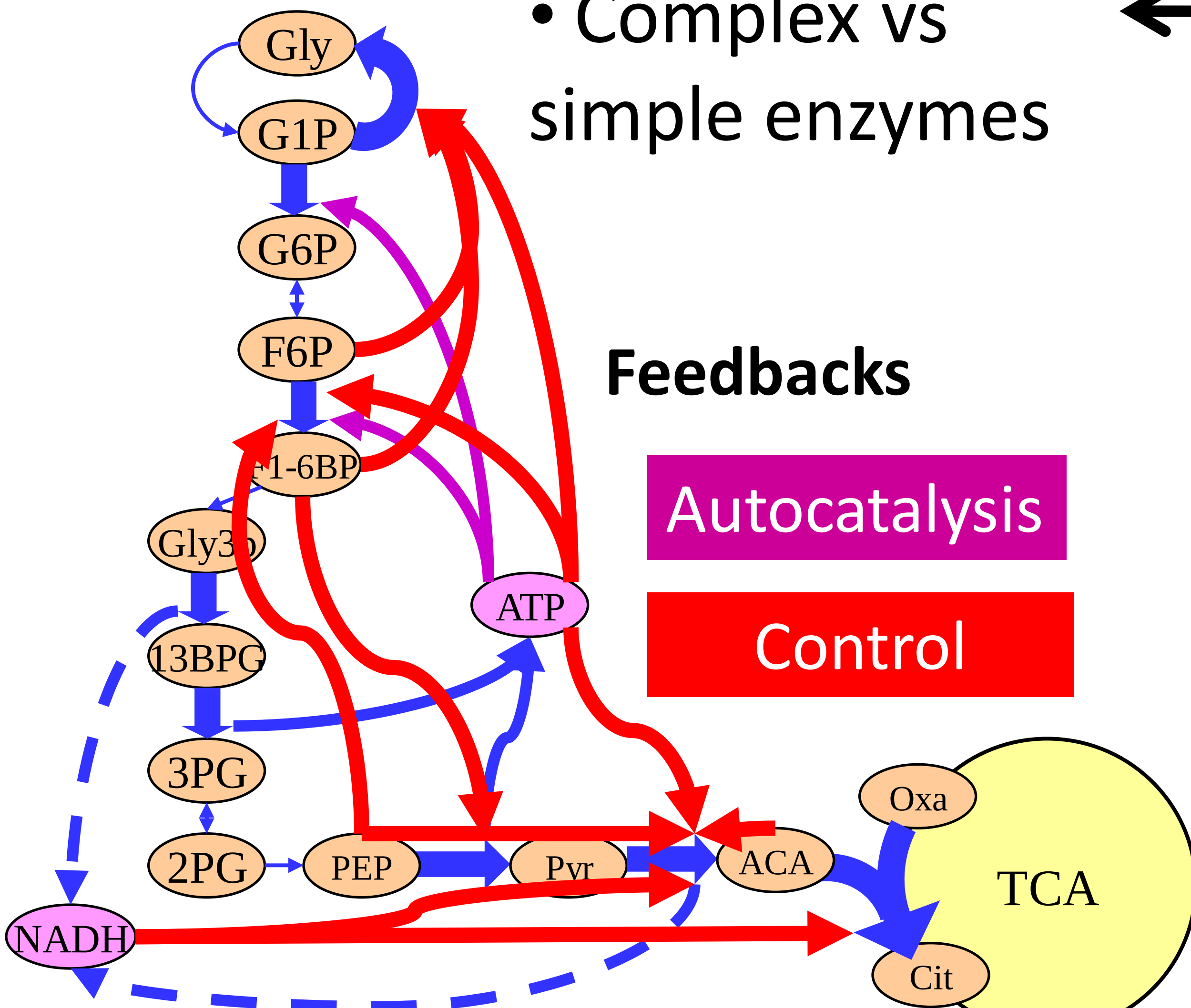


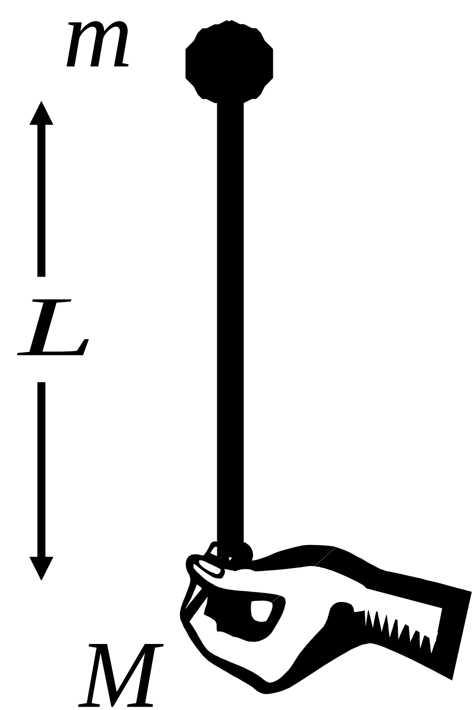
$$\frac{d}{dt}\begin{bmatrix} x \\ \theta \\ \dot{x} \\ \dot{\theta} \end{bmatrix} = \begin{bmatrix} 0 & 0 & 1 & 0 \\ 0 & 0 & 0 & 1 \\ 0 & \frac{m^2 g l^2}{q} & \frac{-(J+ml^2)b}{q} & 0 \\ 0 & \frac{mgl(M+m)}{q} & \frac{-mlb}{q} & 0 \end{bmatrix} x + \begin{bmatrix} 0 \\ 0 \\ \frac{J+ml^2}{q} \\ \frac{ml}{q}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

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

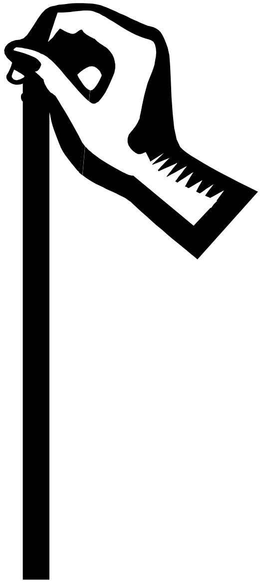
Translation

- Autocatalytic ⟷ • ≈ Up
- Complex vs simple enzymes ⟷ • ≈ eyes vs no eyes





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



Easy, even with eyes closed
No matter what the length

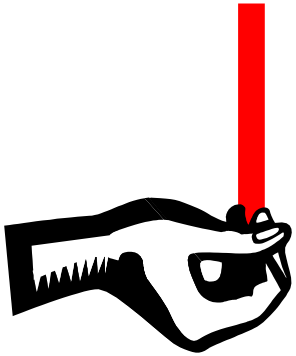
Gratuitous fragility
versus
fragile robustness

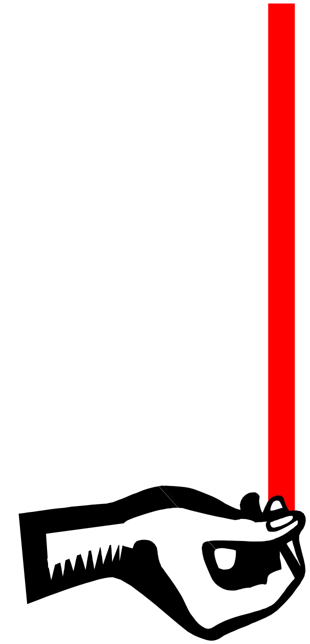
$$\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq 0$$

$\gg \quad \Rightarrow$ Gratuitous fragility

$= \quad \Rightarrow$ Fragile robustness

Up is hard for shorter lengths

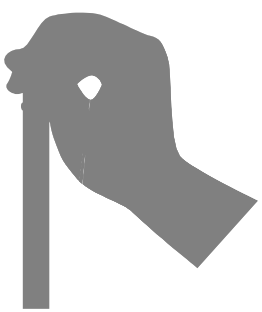


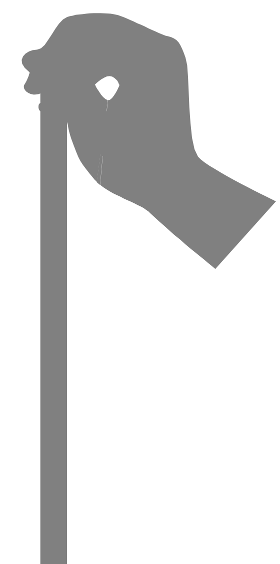


$$\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right| d\omega \geq |p|$$

$$p = z\sqrt{1+r} = \sqrt{\frac{g}{L}(1+r)}$$

$$p \text{ small} \Rightarrow L \text{ large}$$





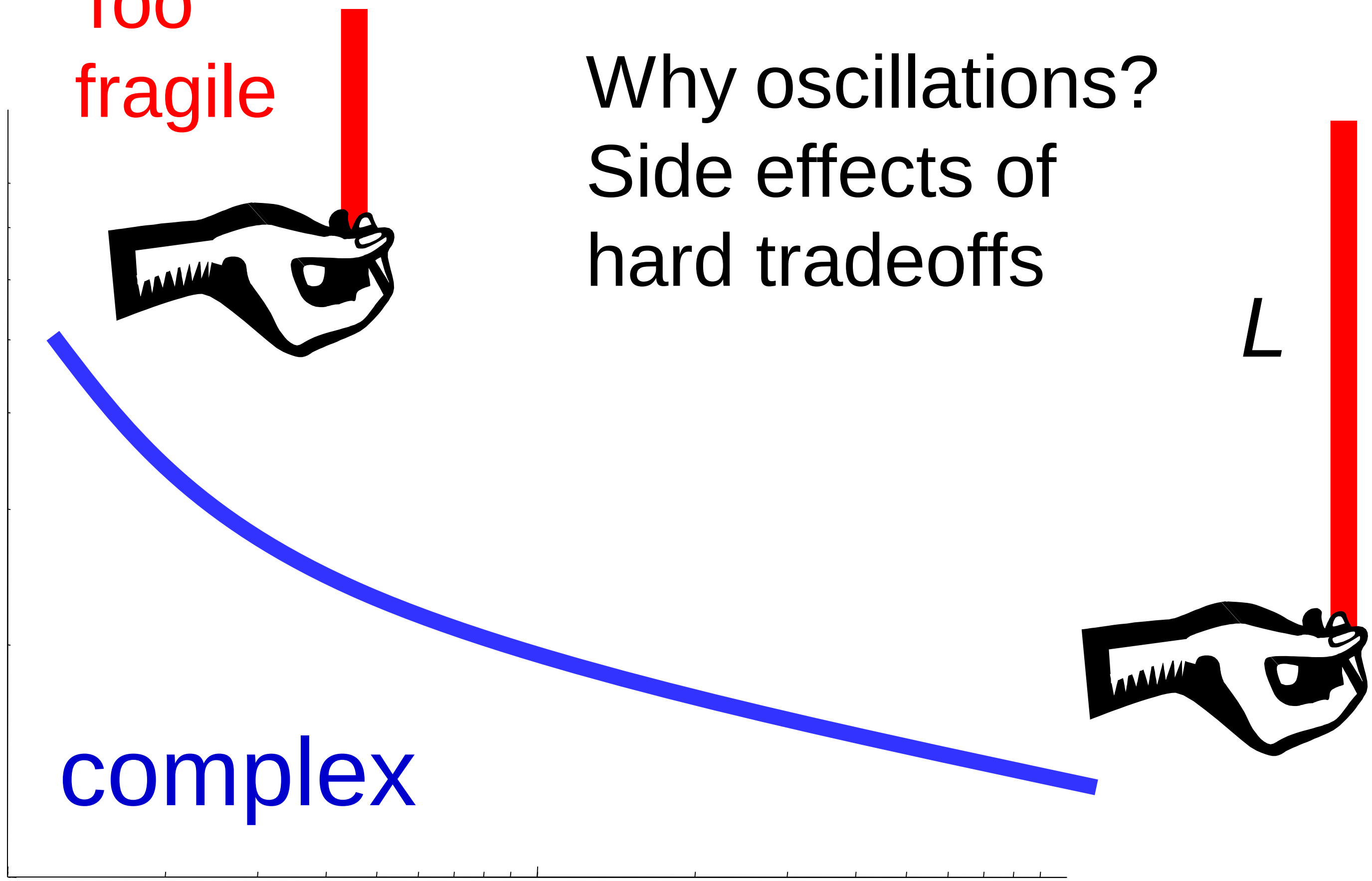
Down easy, even with

- eyes closed
- all lengths

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

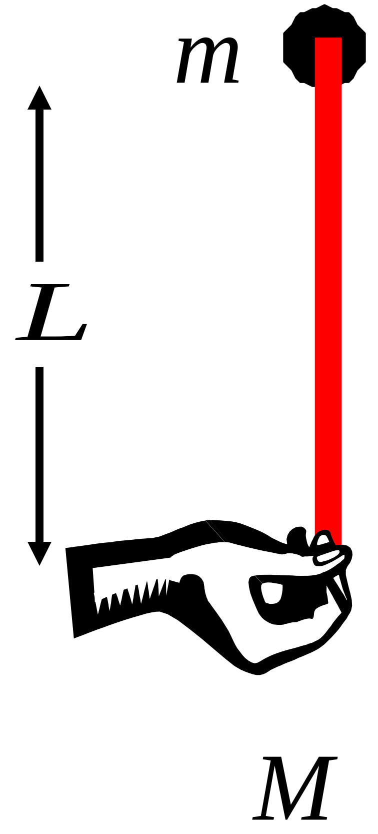
This is a cartoon, but can be made precise.

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



Why oscillations?
Side effects of hard tradeoffs

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



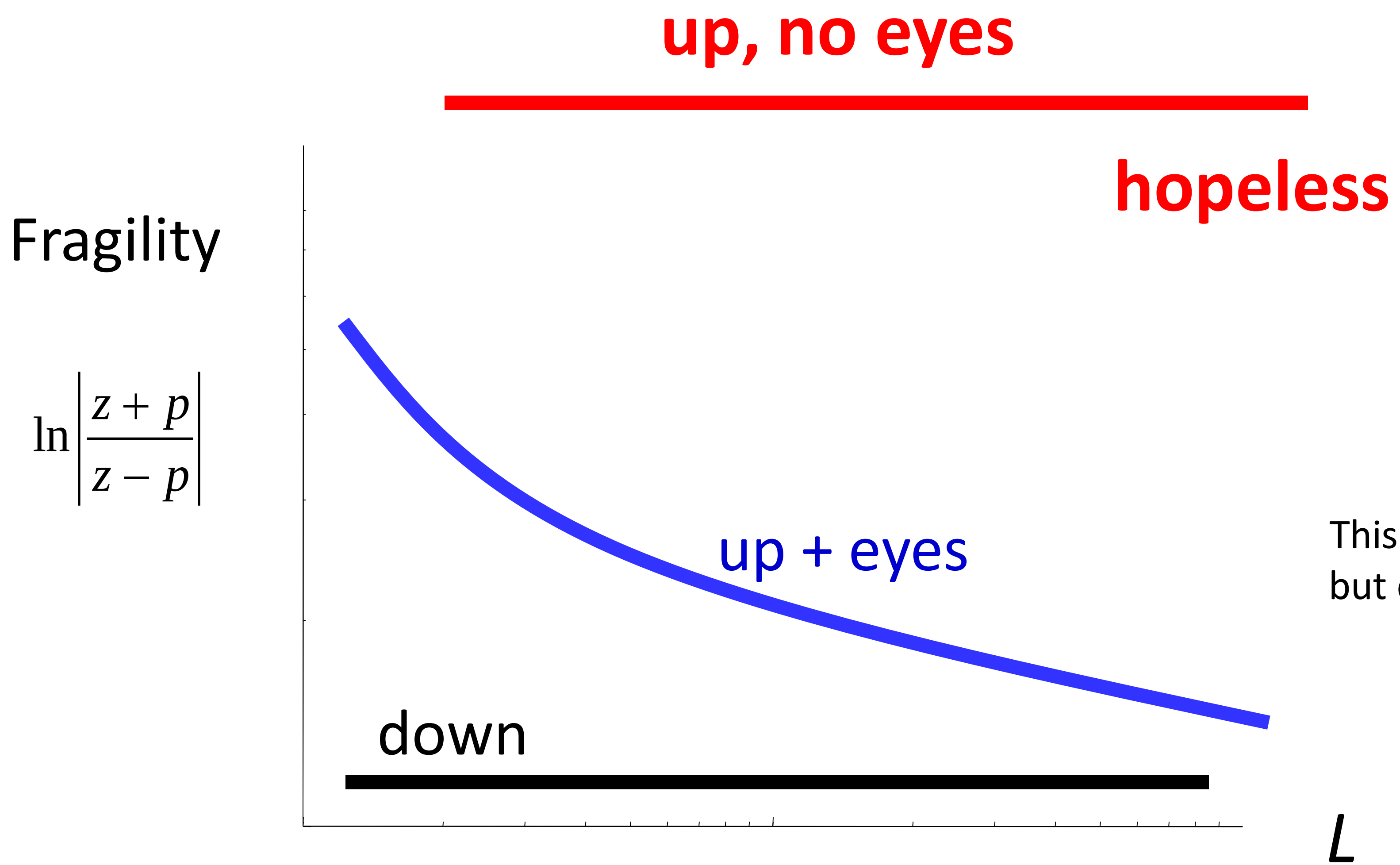
Eyes closed

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

$$\frac{p+z}{p-z}=\frac{\sqrt{1+r}+1}{\sqrt{1+r}-1}$$

Want r and z large (but p small).

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

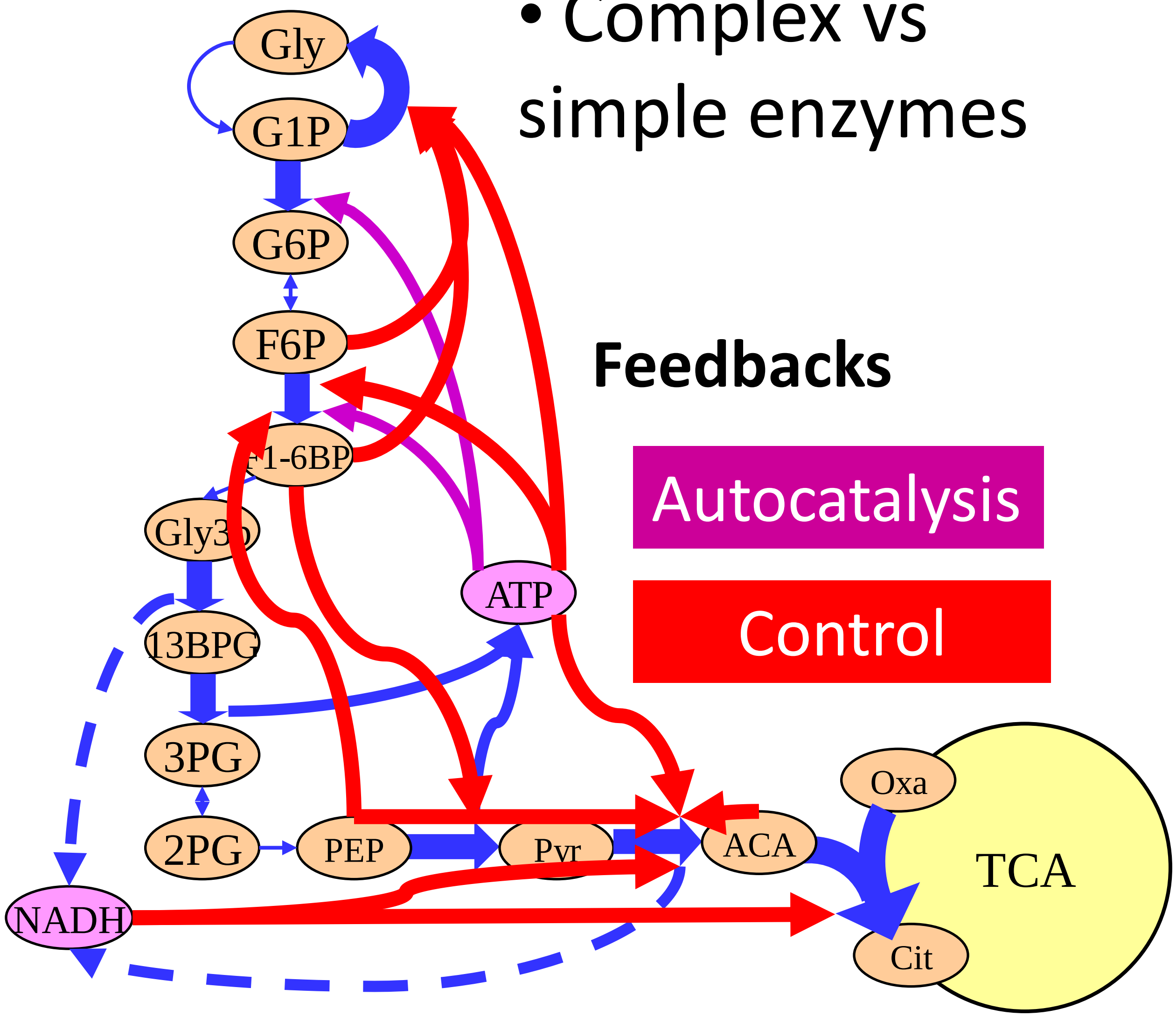


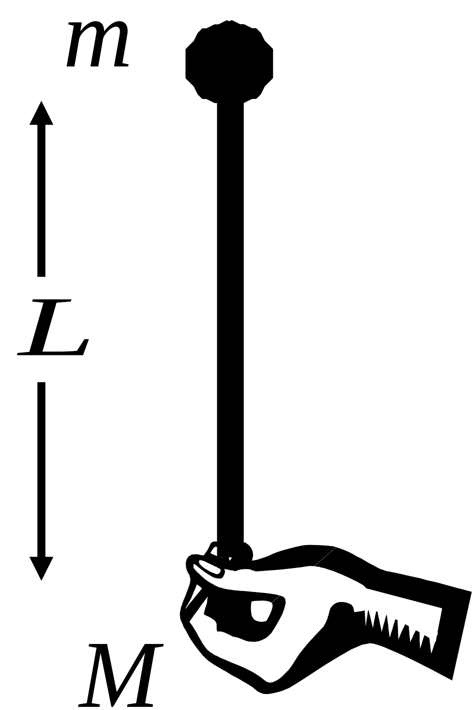
This is a cartoon, but can be made precise.

Translation

- Autocatalytic
- Complex vs simple enzymes

- ≈ Up
- ≈ eyes vs no eyes



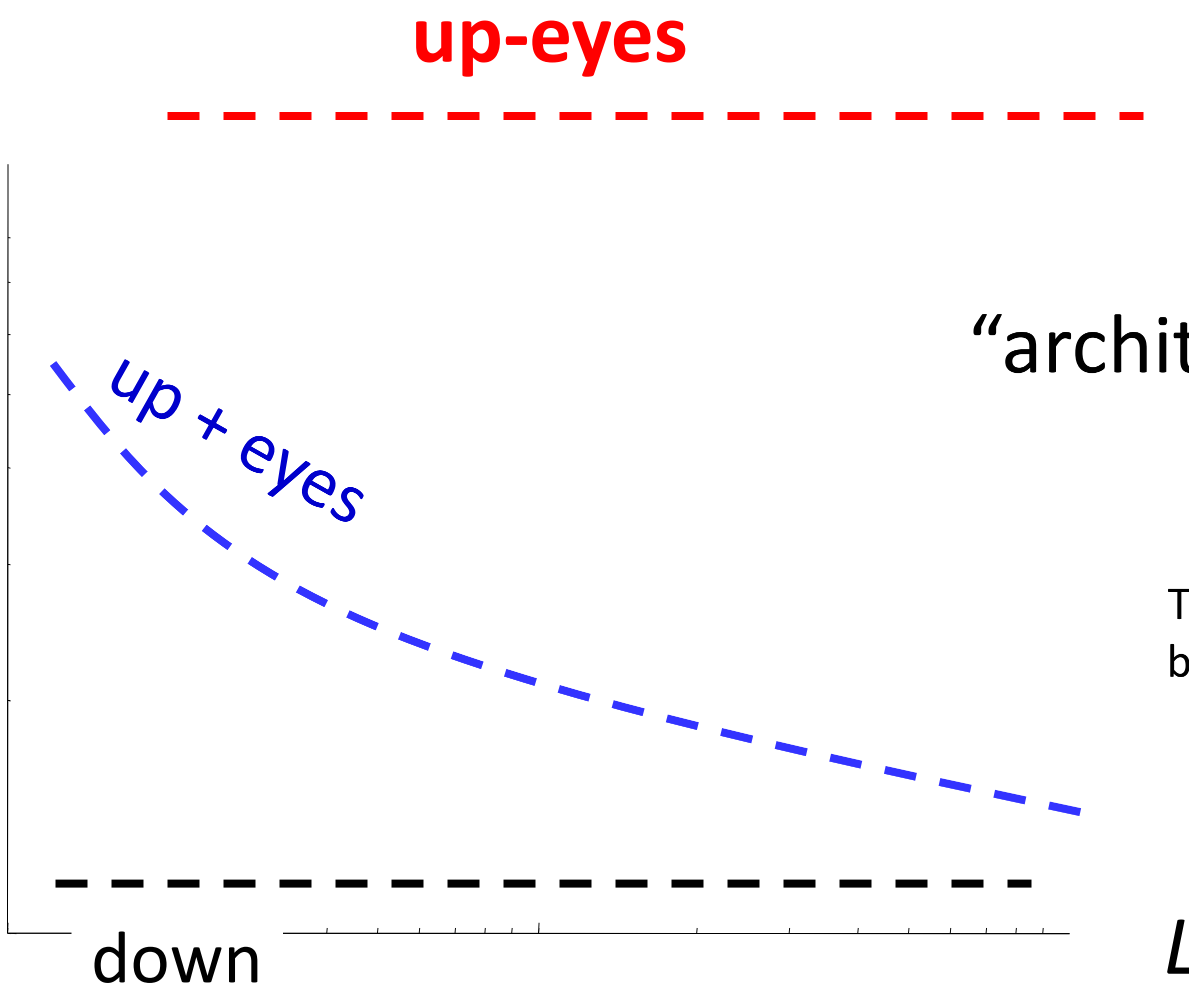


Theorem

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

Fragility

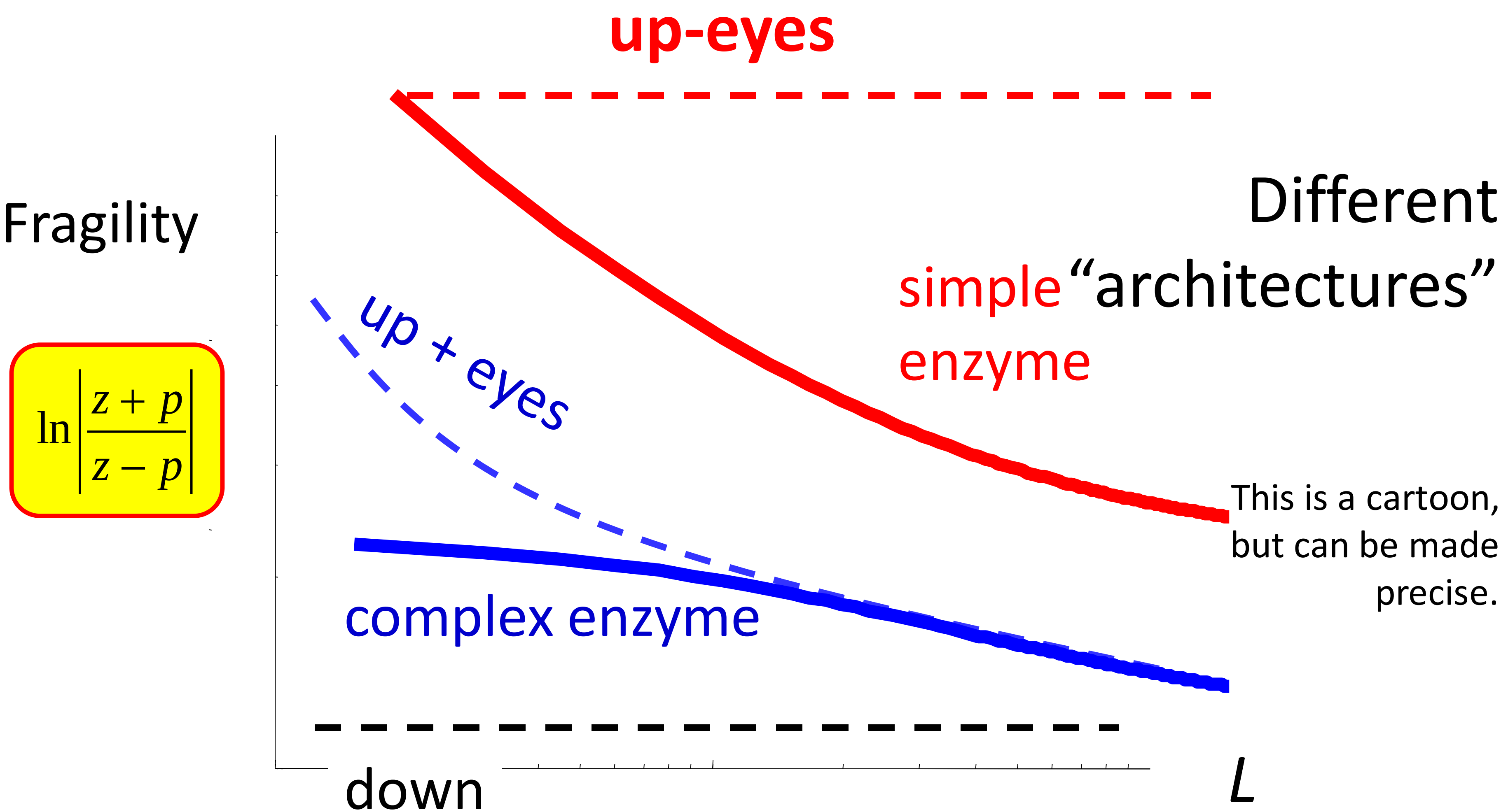
$$\ln\left|\frac{z+p}{z-p}\right|$$



Different "architectures"

This is a cartoon, but can be made precise.

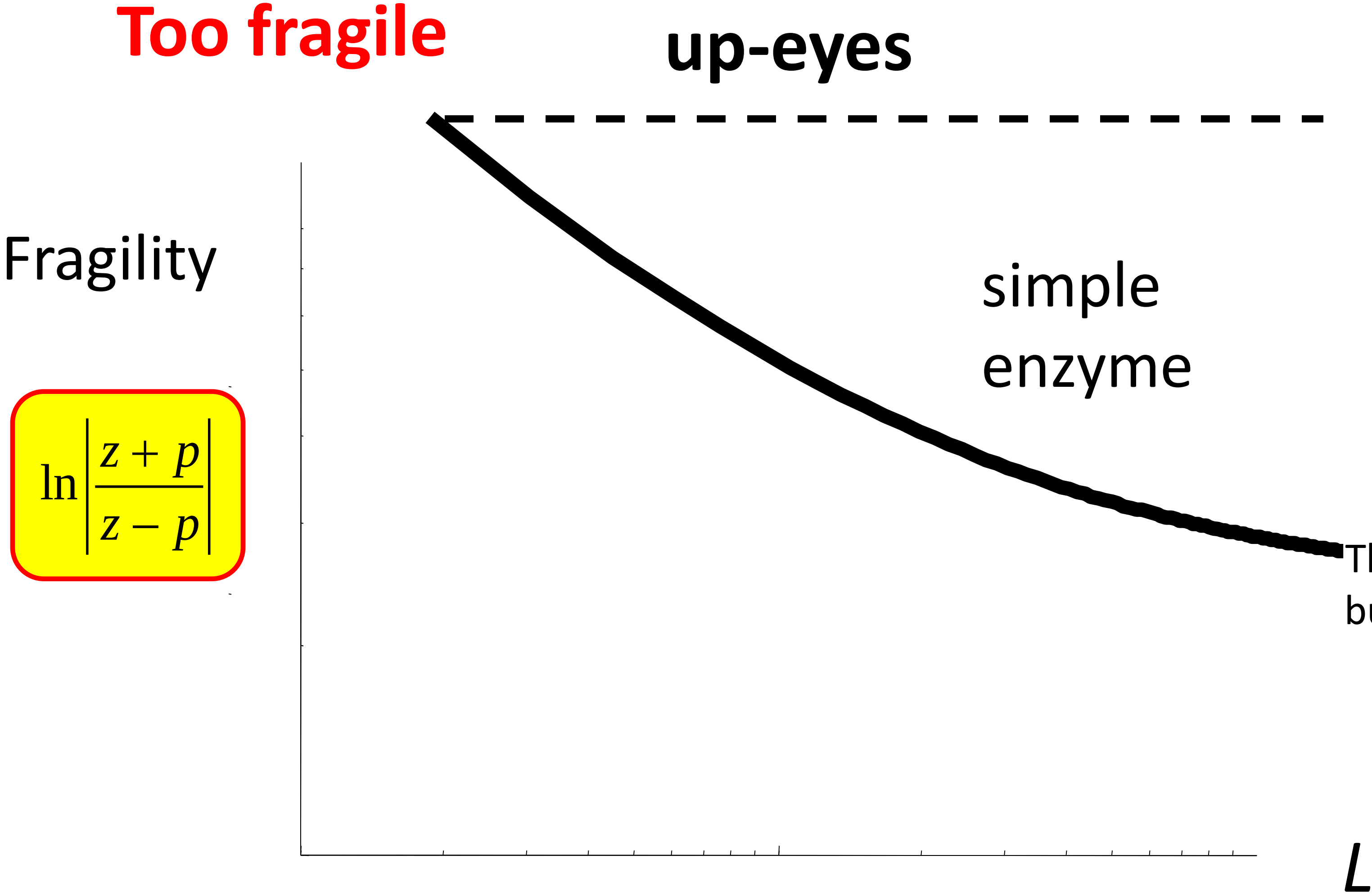
Theorem $\frac{1}{\pi}\int_0^\infty \ln\left|S(j\omega)\right|\left(\frac{z}{z^2+\omega^2}\right)d\omega \geq \ln\left|\frac{z+p}{z-p}\right|$



Theorem

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

Too fragile



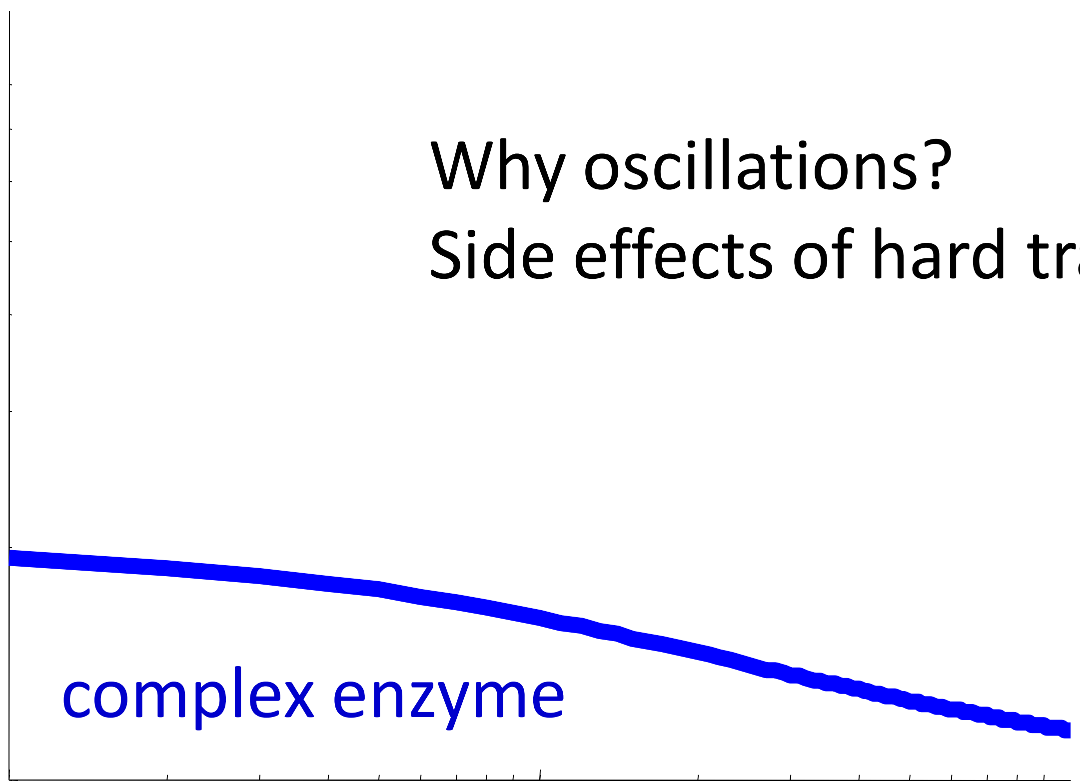
This is a cartoon, but can be made precise.

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

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

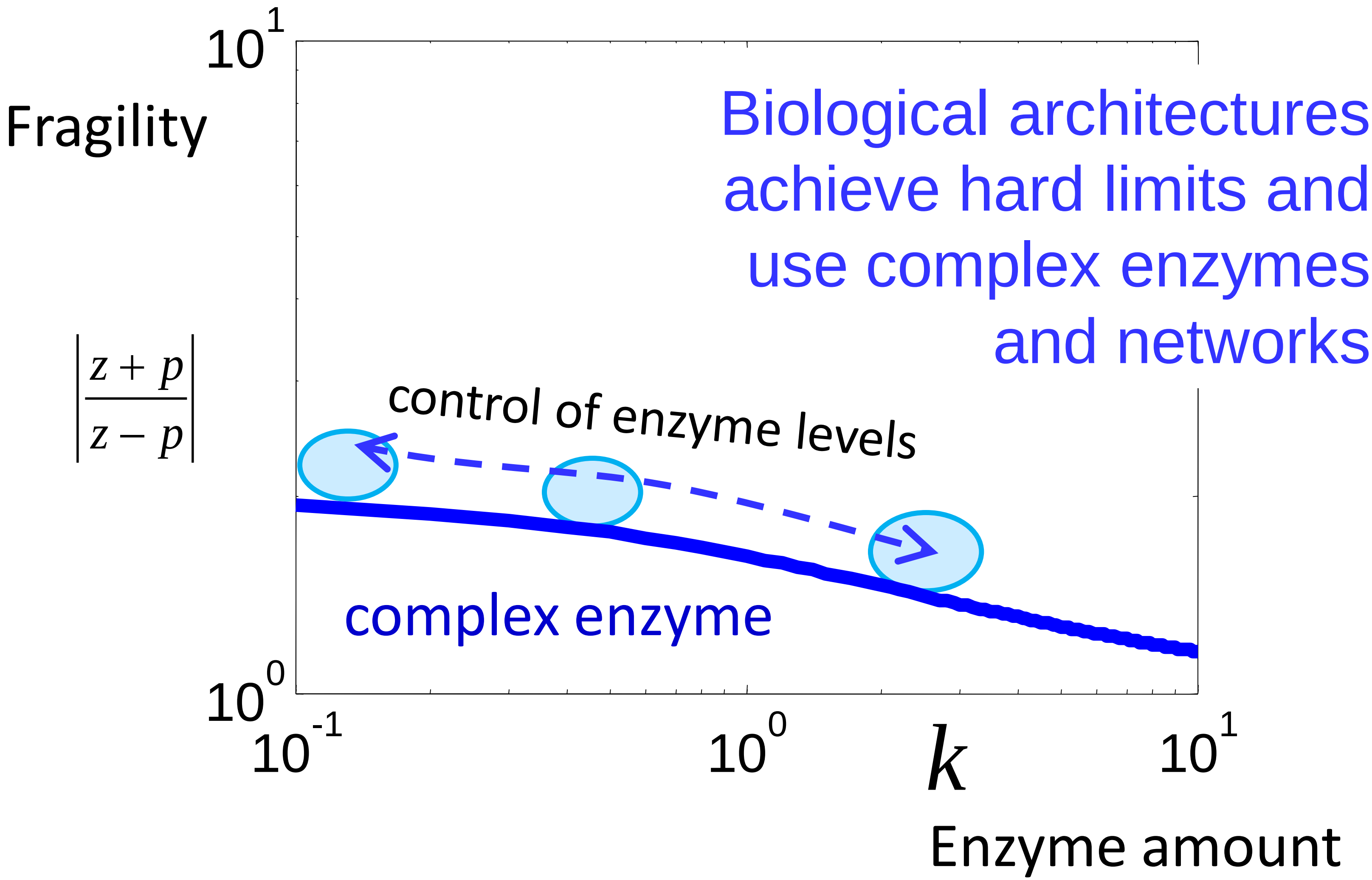


Why oscillations?

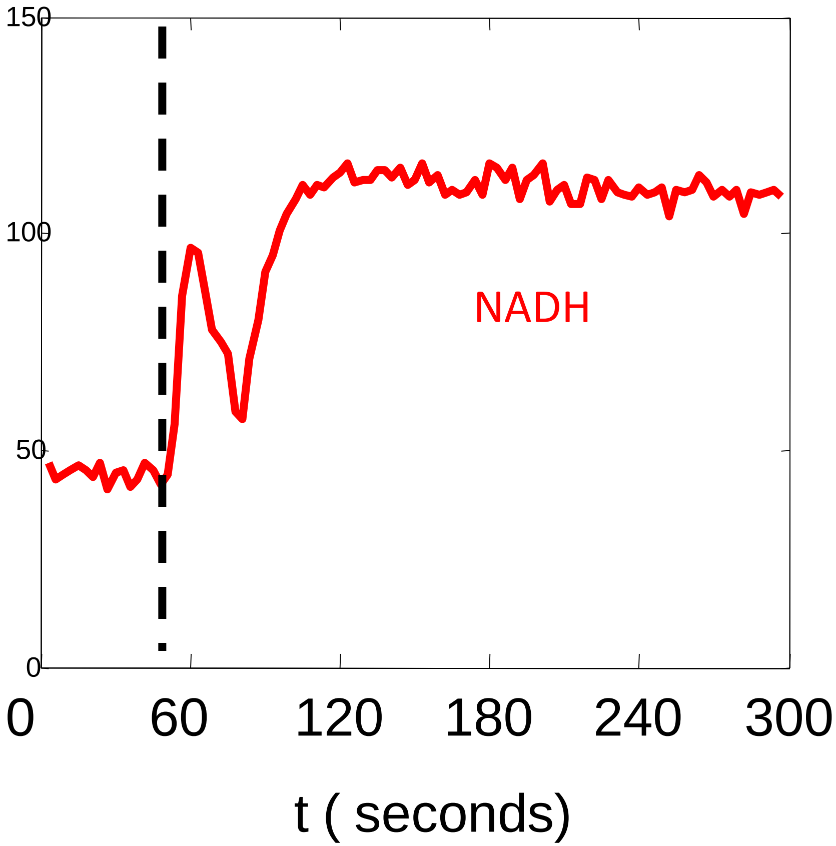
Side effects of hard tradeoffs

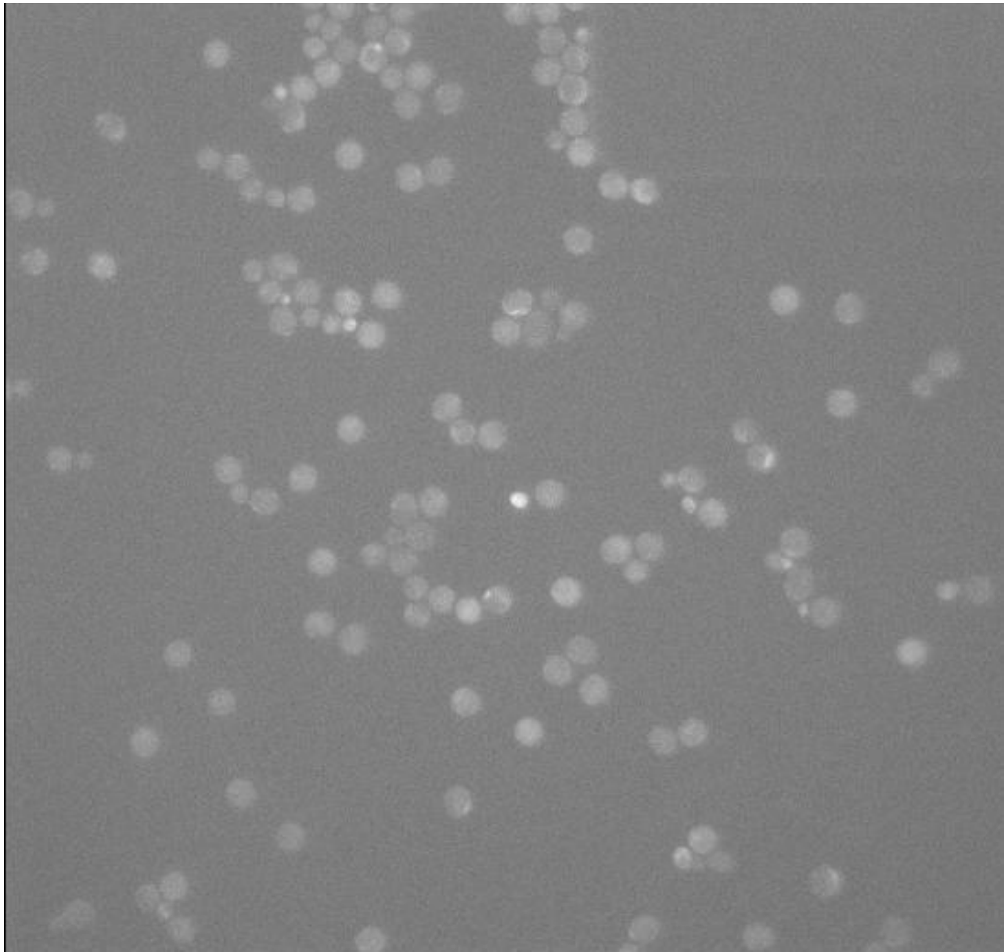
Enzyme amount

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



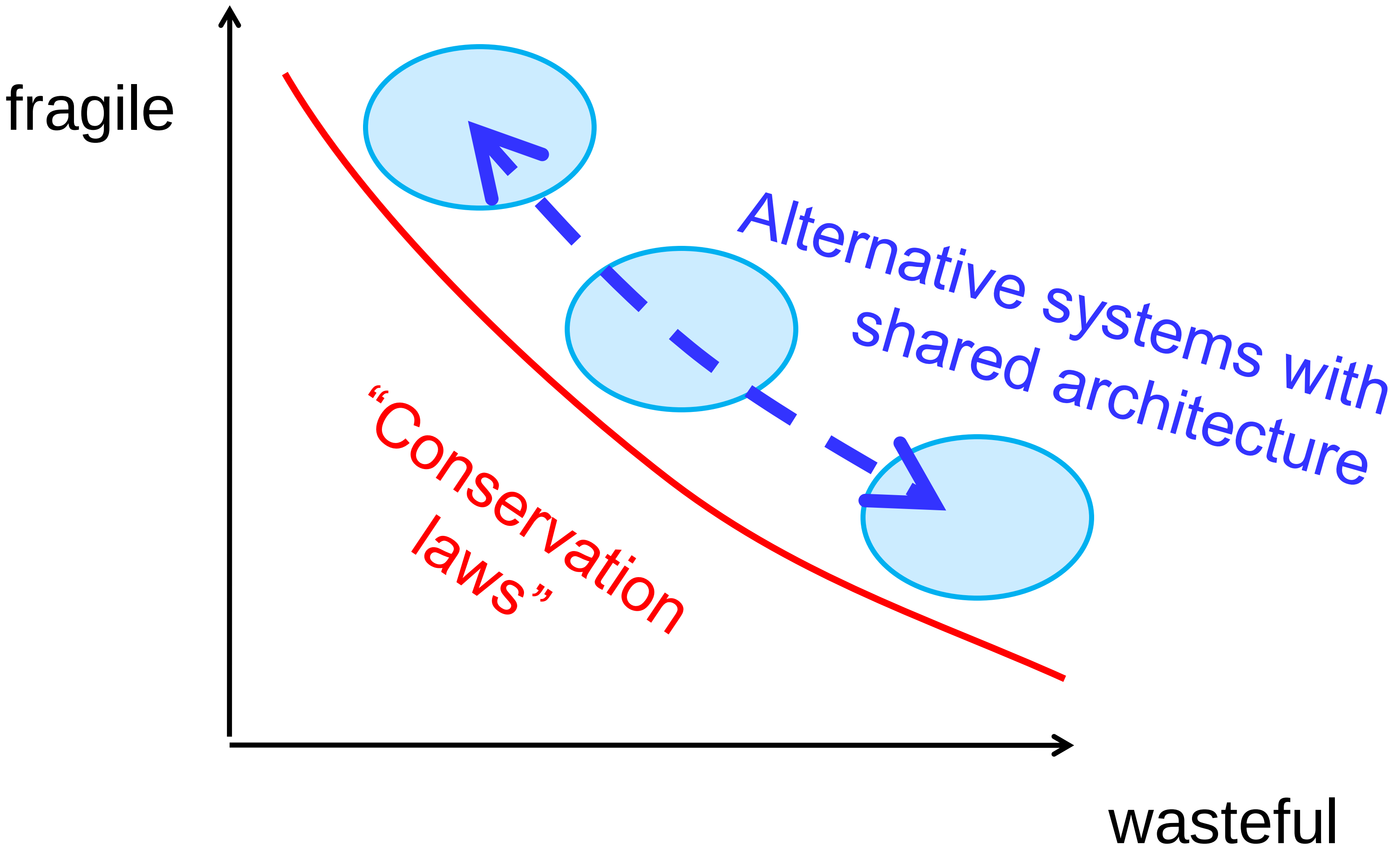
- Microfluidic experiments
- Yeast strain W303 grown in Ethanol
- Glucose and KCN added →anaerobic glycolysis
- NADH measured every 3 s





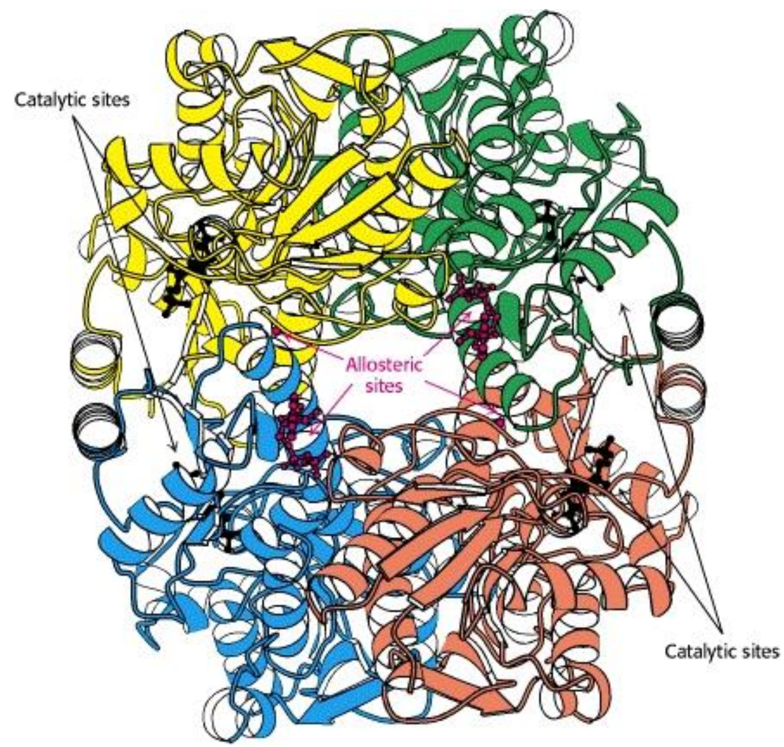
Architecture

Good architectures allow for effective tradeoffs



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

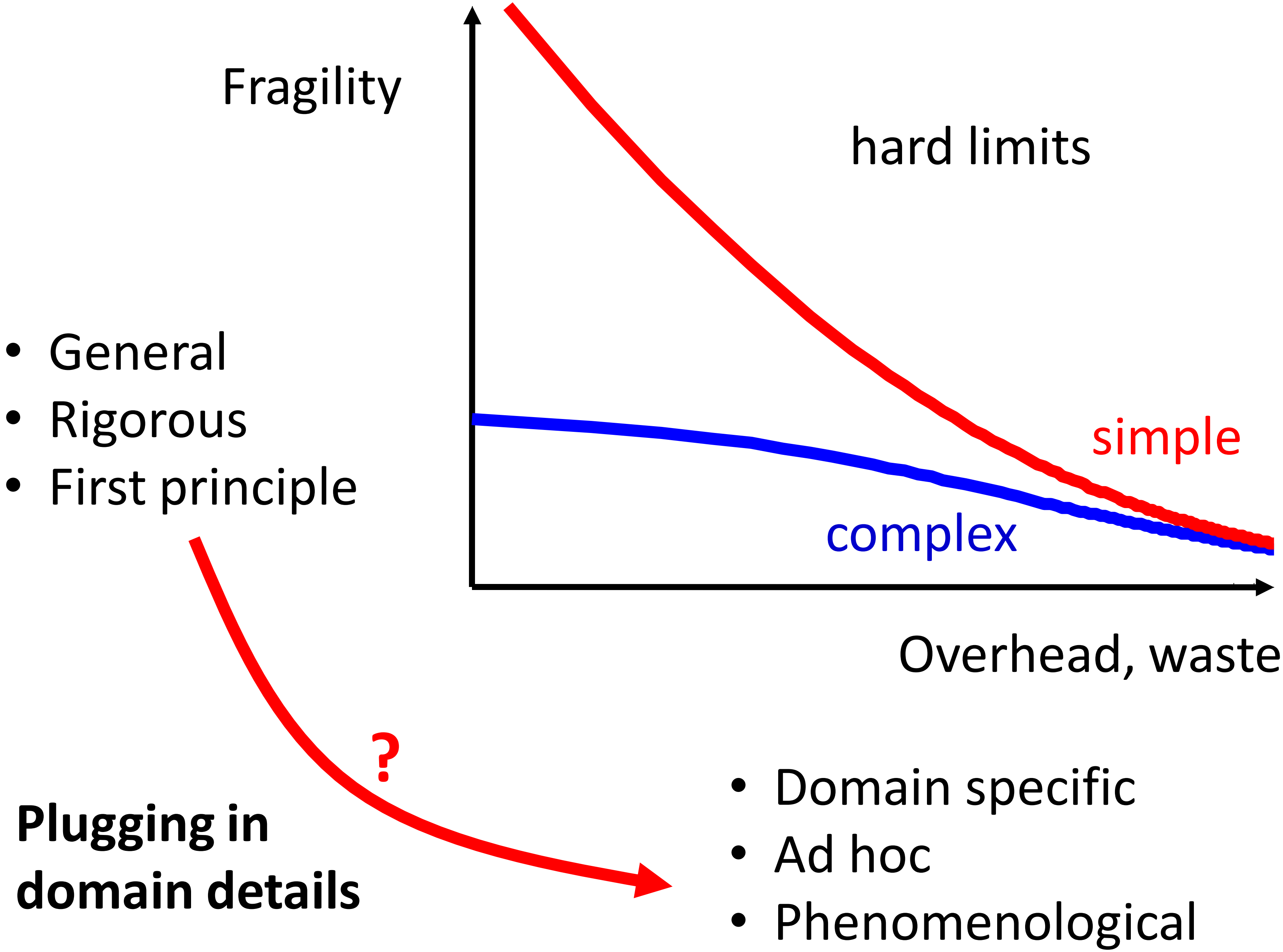
- z and p are functions of enzyme complexity and amount
- standard biochemistry models
- **phenomenological**



- **first principles?**

What reviewers say

- "If such oscillations are indeed optimal, why are they not universally present?"
- "The approach to establish universality for all biological and physiological systems is **simply wrong**. It cannot be done…"
- "While the notion of universality is well justified in physics, it is perhaps not so useful in biological sciences and medicine. To develop a set of universal principles for biological and physiological systems is mostly likely **a dream that will never be realized**, due to the vast diversity in such systems."
- "…**does not seem to have an understanding or appreciation** of the vast diversity of biological and physiological systems…"
- "…desire to develop rigorous framework is understandable, but usually this can be done only by imposing a high degree of abstraction, which would then **make the model useless** …"
- "… a mathematical scheme **without any real connections to biological or medical problems**…"


Fragility
hard limits
simple
complex
Overhead, waste
• General
• Rigorous
• First principle
?
Plugging in domain details
• Domain specific
• Ad hoc
• Phenomenological

Control

Wiener

Comms

Bode

robust control

Kalman

- General
- Rigorous
- First principle

- Fundamental multiscale physics
- Foundations, origins of
  - noise
  - dissipation
  - amplification

?

Carnot

Boltzmann

Heisenberg

Physics

IEEE TRANS ON AUTOMATIC CONTROL, FEBRUARY, 2011

Sandberg, Delvenne, and Doyle

http://arxiv.org/abs/1009.2830

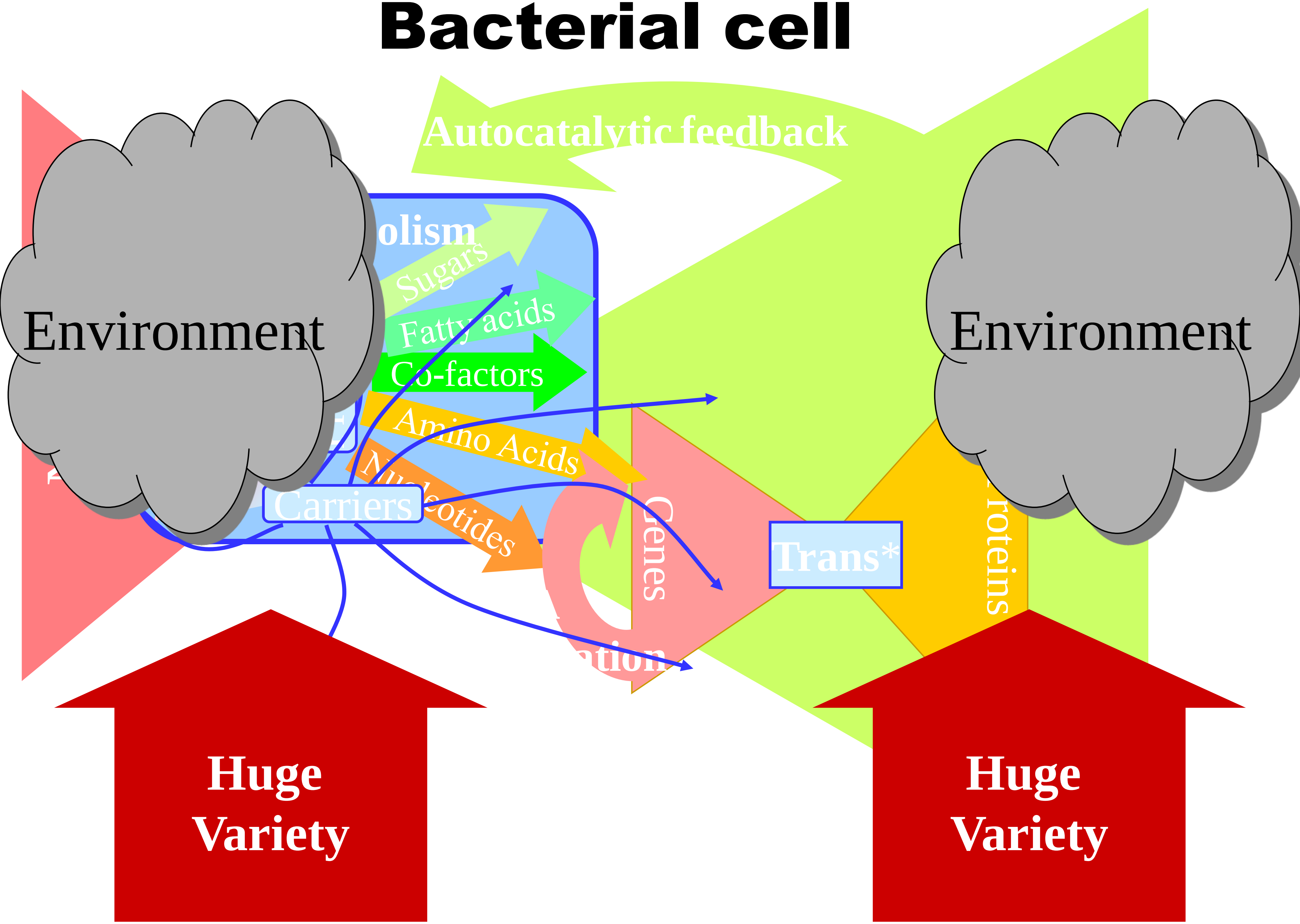
On Lossless Approximations, the Fluctuation-Dissipation Theorem, and Limitations of Measurements

Henrik Sandberg, Jean-Charles Delvenne, and John C. Doyle

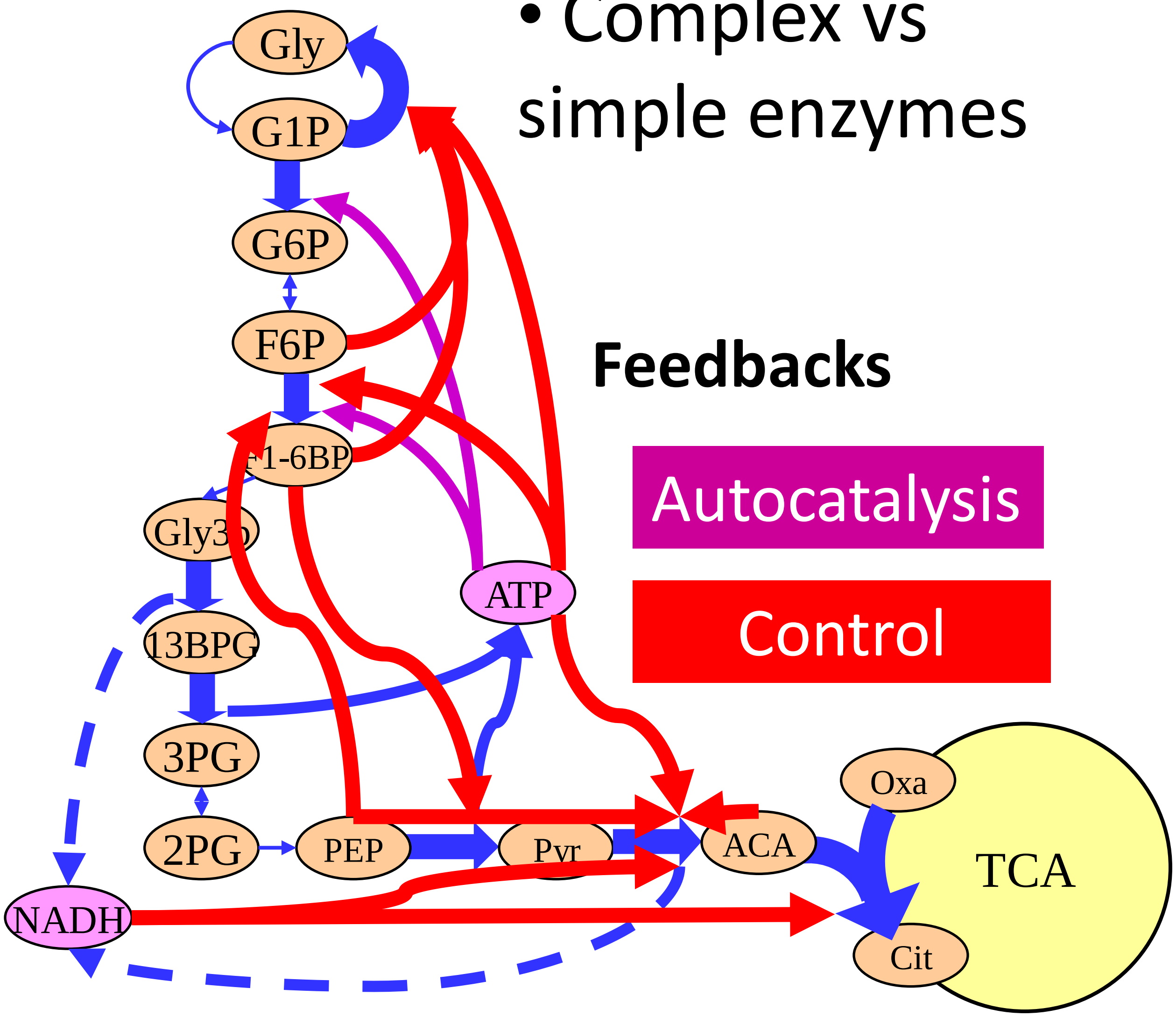
***Abstract*—In this paper, we take a control-theoretic approach to answering some standard questions in statistical mechanics, and use the results to derive limitations of classical measurements. A central problem is the relation between systems which appear macroscopically dissipative but are microscopically lossless. We show that a linear system is dissipative if, and only if, it can be approximated by a linear lossless system over arbitrarily long time intervals. Hence lossless systems are in this sense dense in dissipative systems. A linear active system can be approximated by a nonlinear lossless system that is charged with initial energy. As a by-product, we obtain mechanisms explaining the Onsager relations from time-reversible lossless approximations, and the fluctuation-dissipation theorem from uncertainty in the initial state of the lossless system. The results are applied to measurement devices and are used to quantify limits on the so-called observer effect, also called *back action*,**

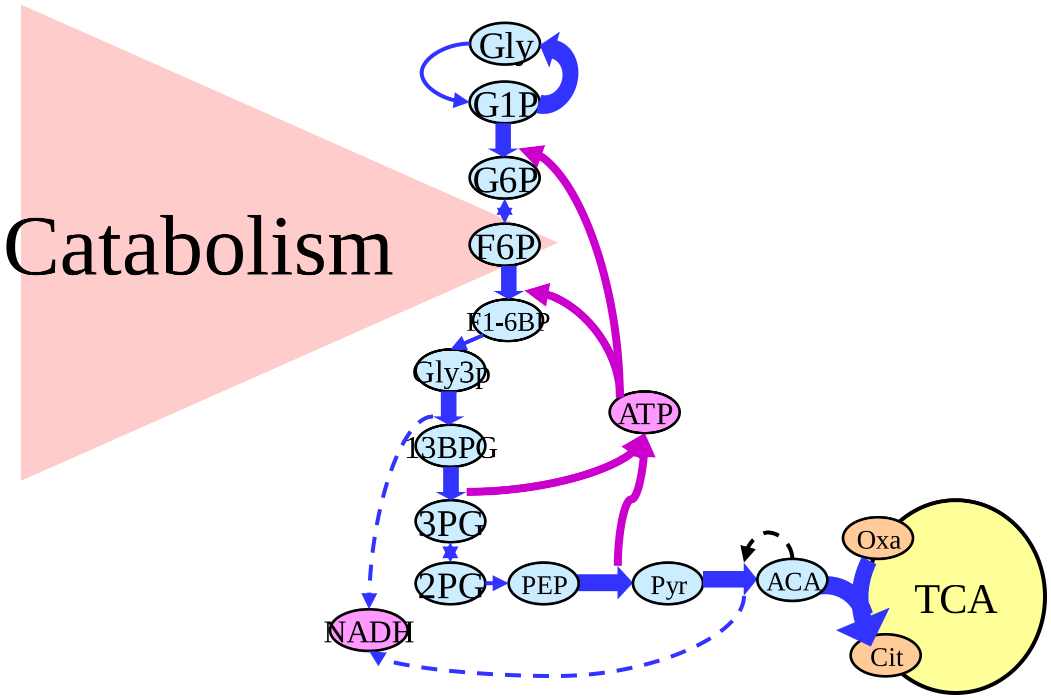
Derivation of limitations is also at the core of physics. Well-known examples are the laws of thermodynamics in classical physics and the uncertainty principle in quantum mechanics [6]–[8]. The exact implications of these physical limitations on the performance of control systems have received little attention, even though all components of a control system, such as actuators, sensors, and computers, are built from physical components which are constrained by physical laws. Control engineers discuss limitations in terms of location of unstable plant poles and zeros, saturation limits of actuators, and more recently channel capacity in feedback loops. But how does the amount of available energy limit the possible bandwidth of a control system? How does the ambient temperature affect the

Bacterial cell

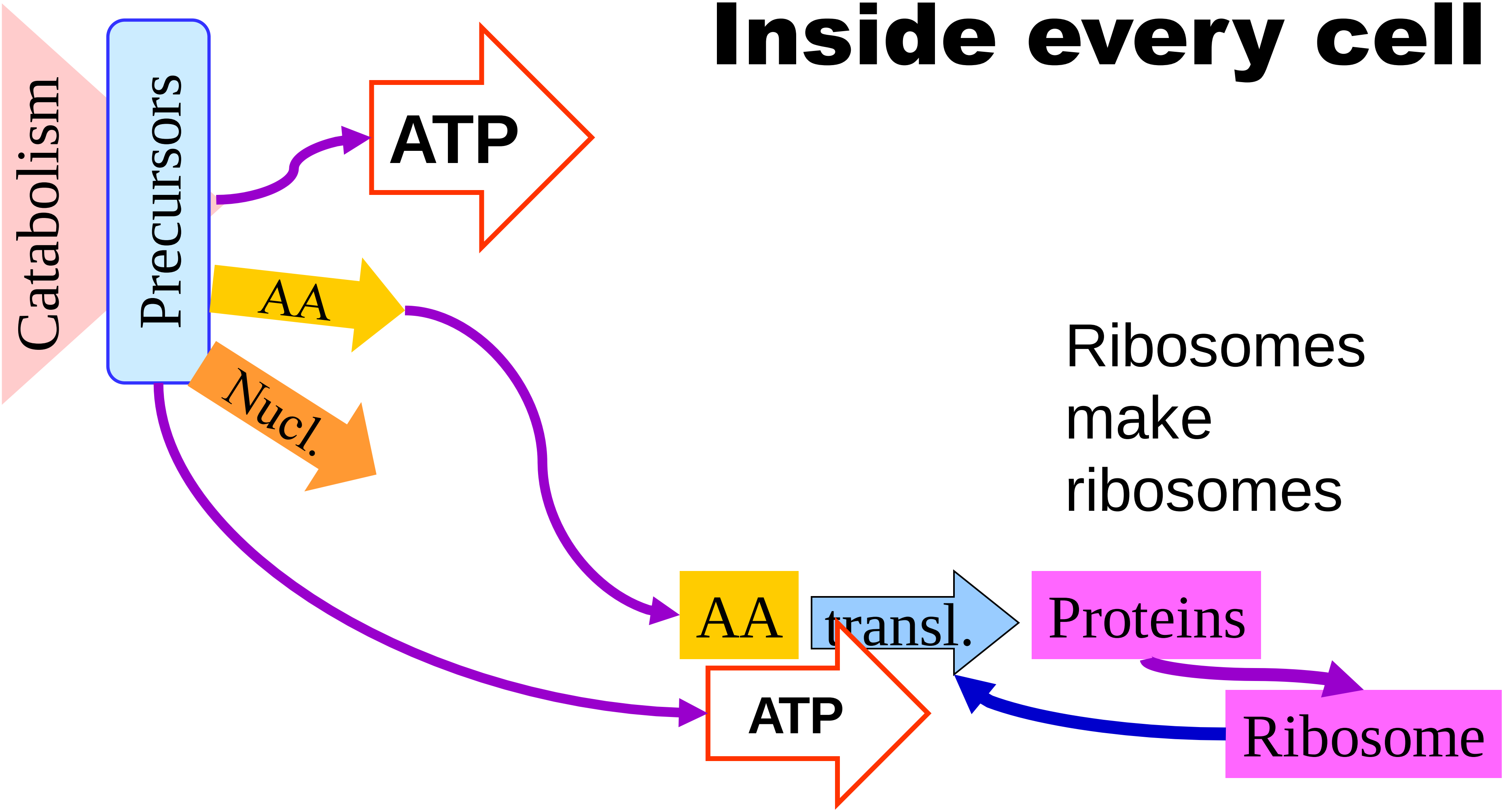


- Autocatalytic
- Complex vs simple enzymes



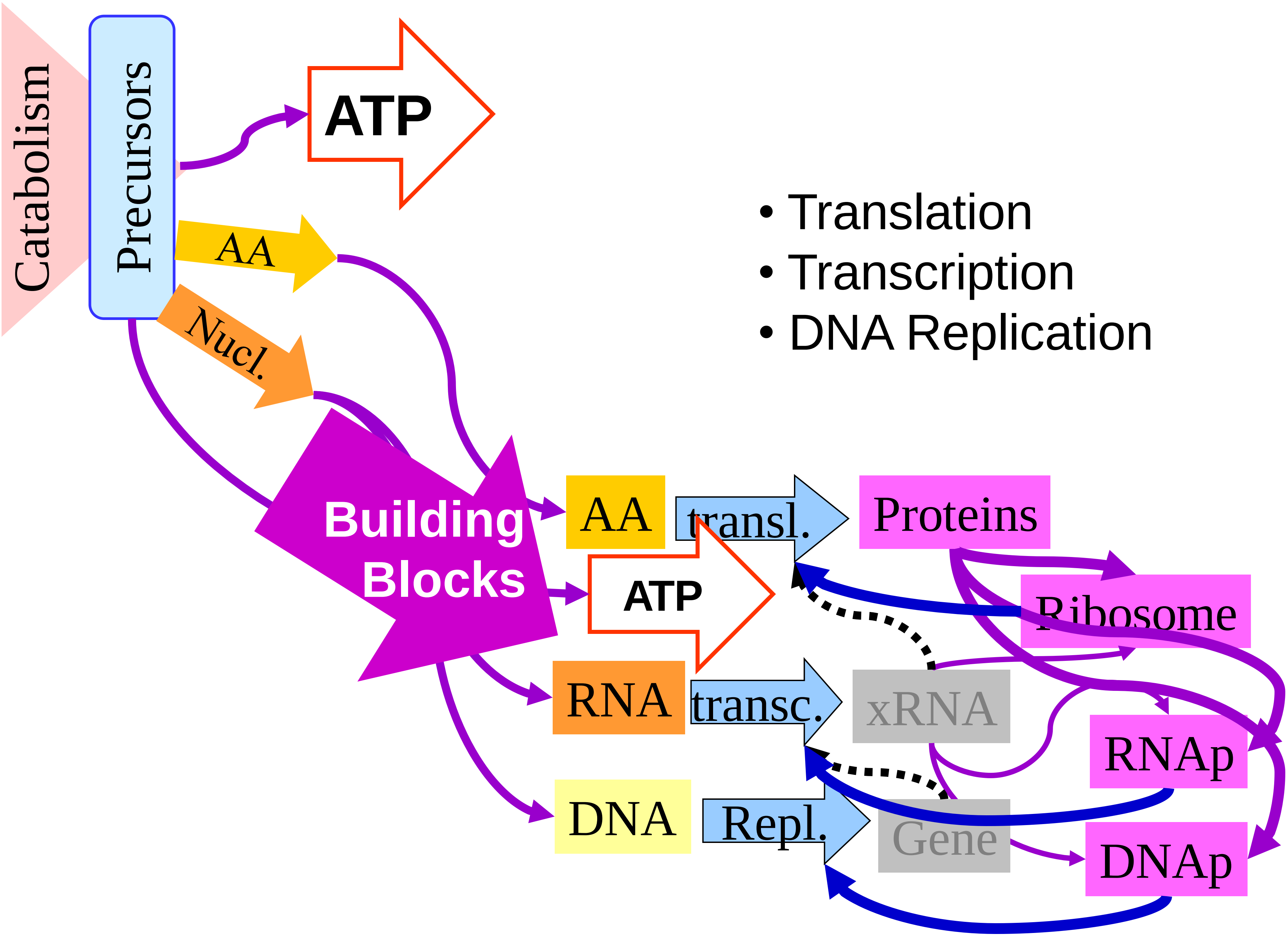

Catabolism
Gly
G1P
G6P
F6P
F1-6BP
Gly3p
13BPG
3PG
2PG
PEP
Pyr
ACA
ATP
NADH
Oxa
Cit
TCA

Inside every cell

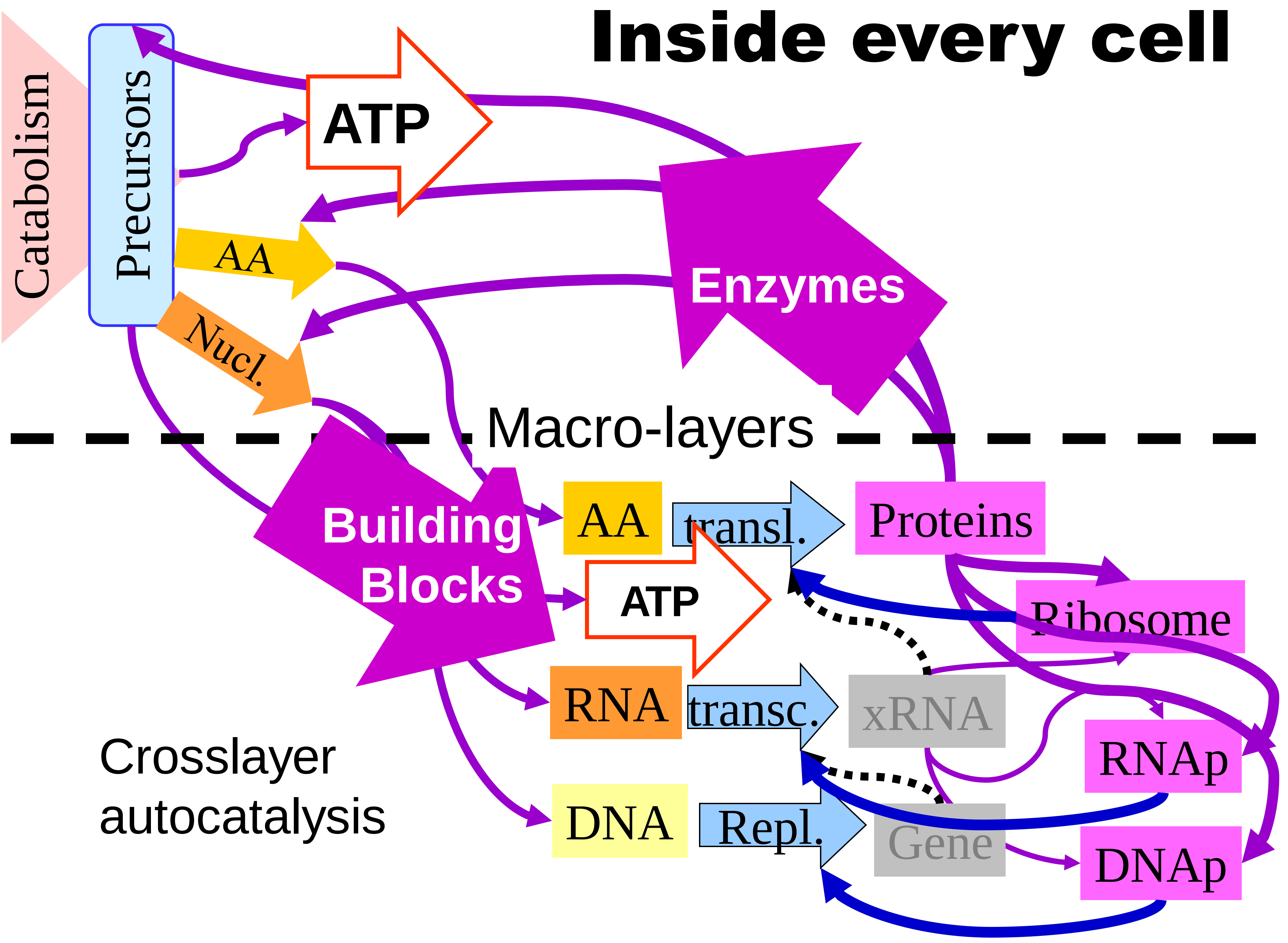


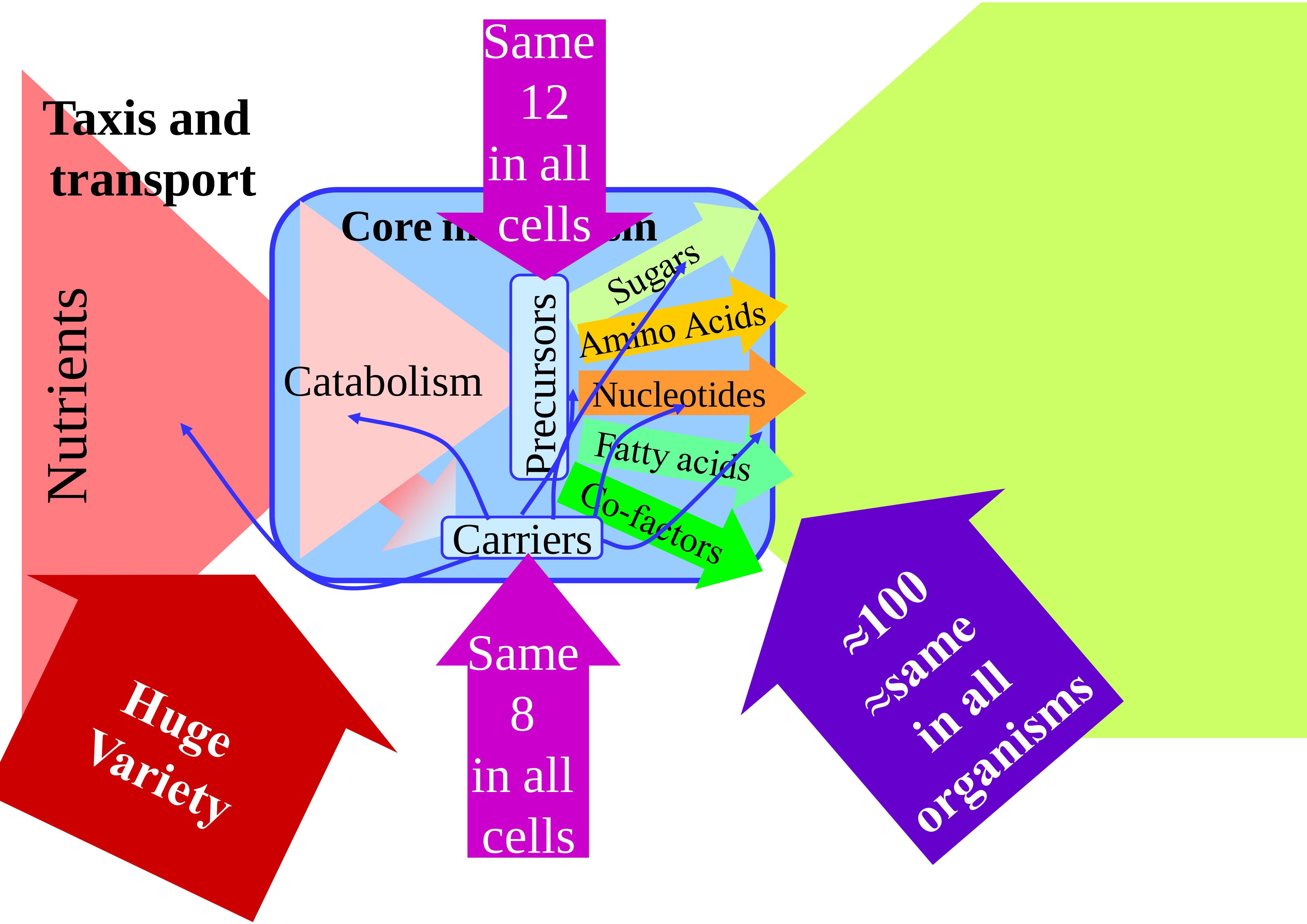
Ribosomes make ribosomes

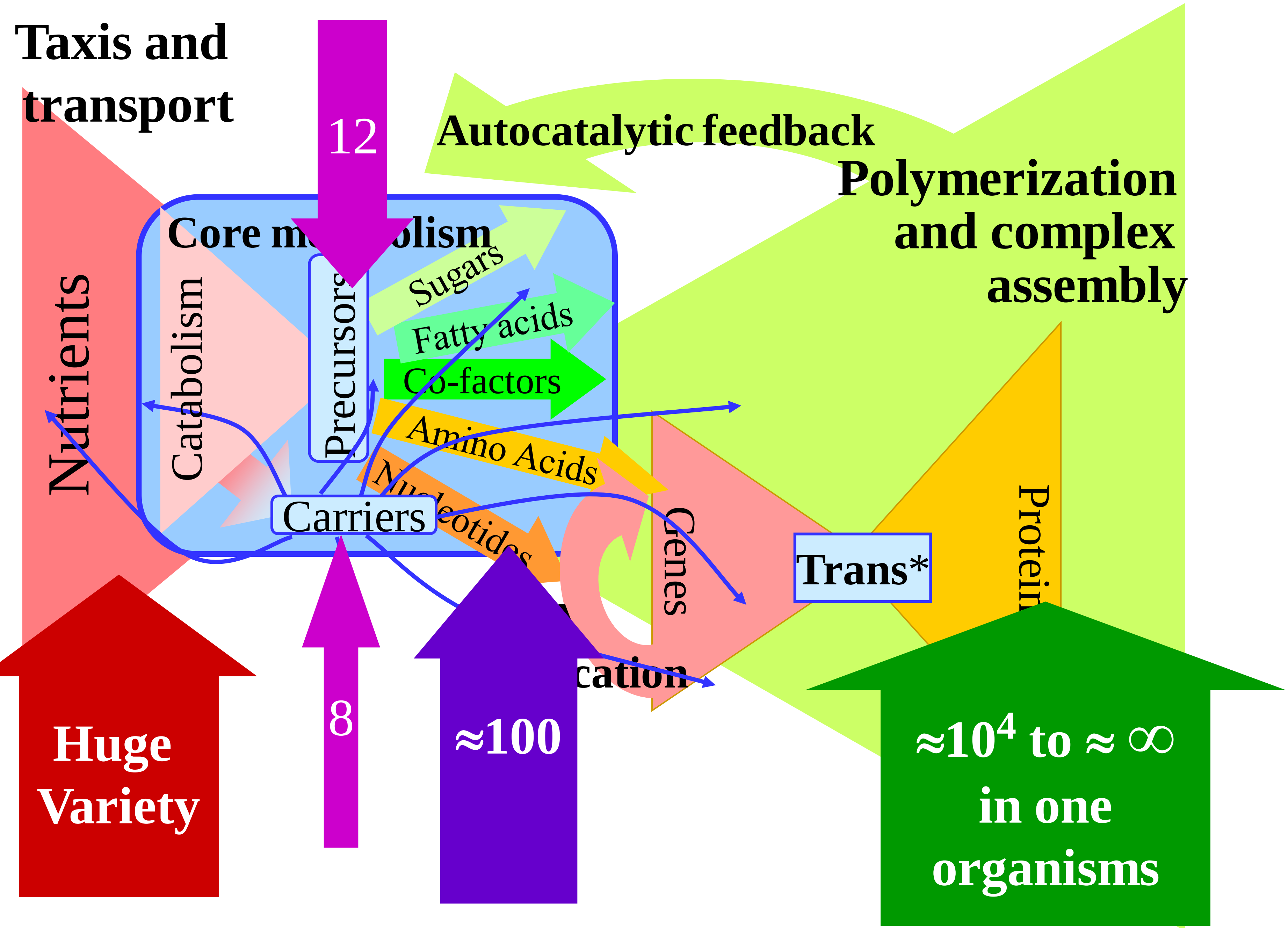
Translation: Amino acids polymerized into proteins



- Translation
- Transcription
- DNA Replication


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


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



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

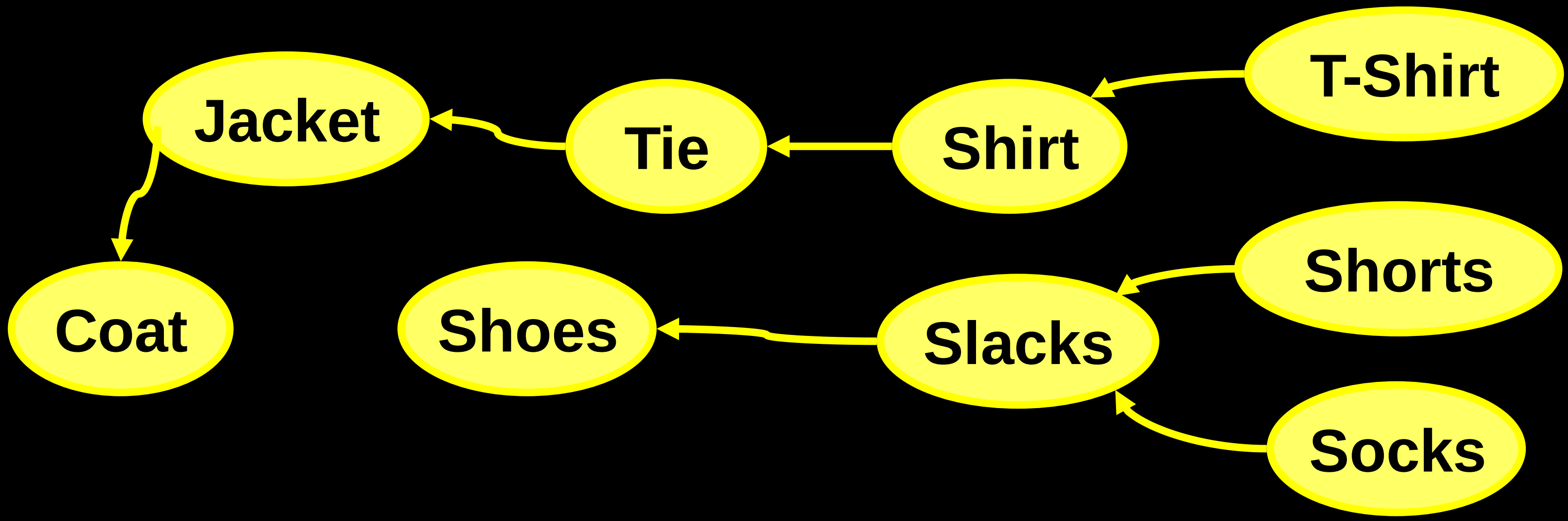
Other examples

Clothing

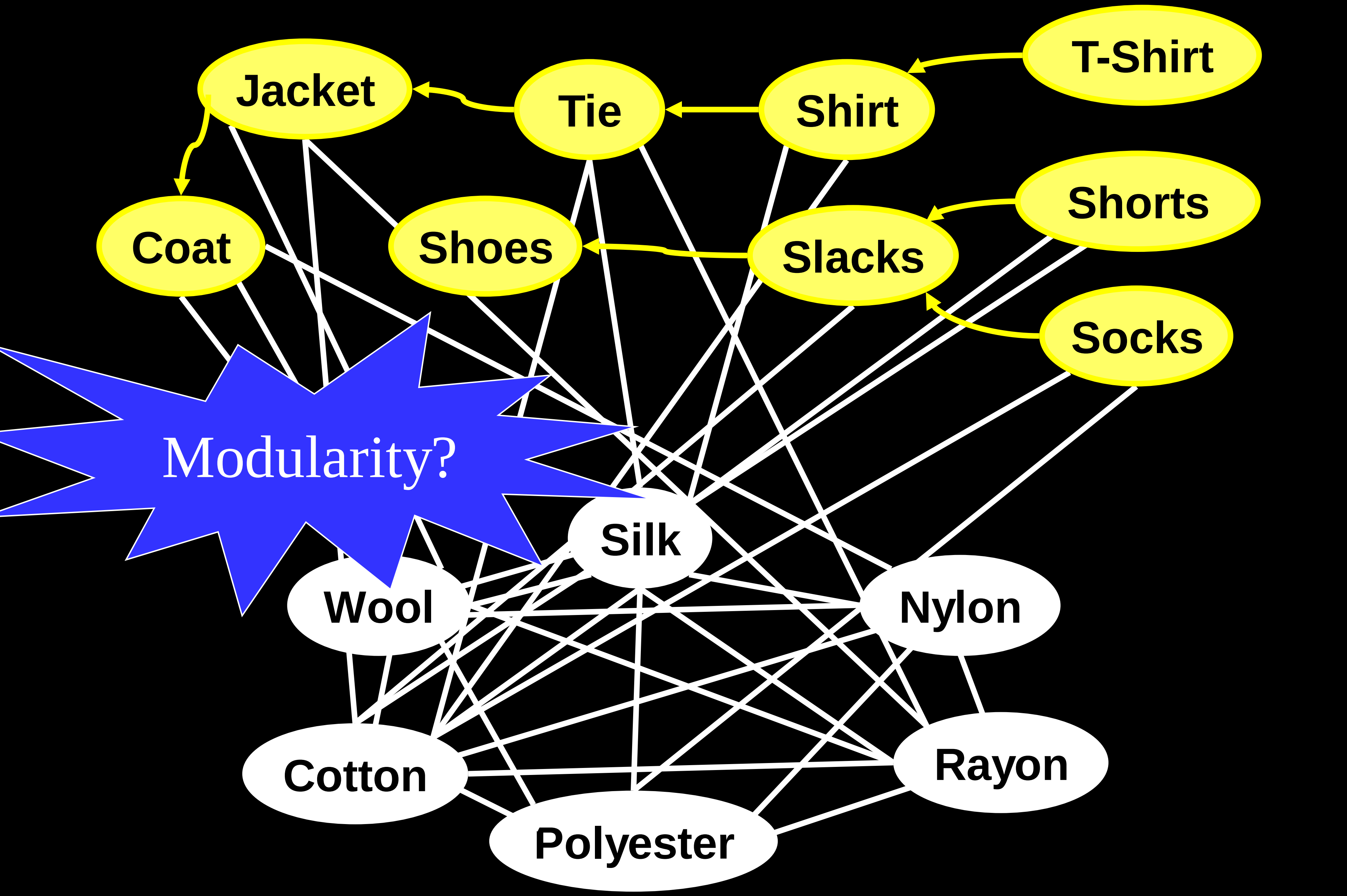
Lego

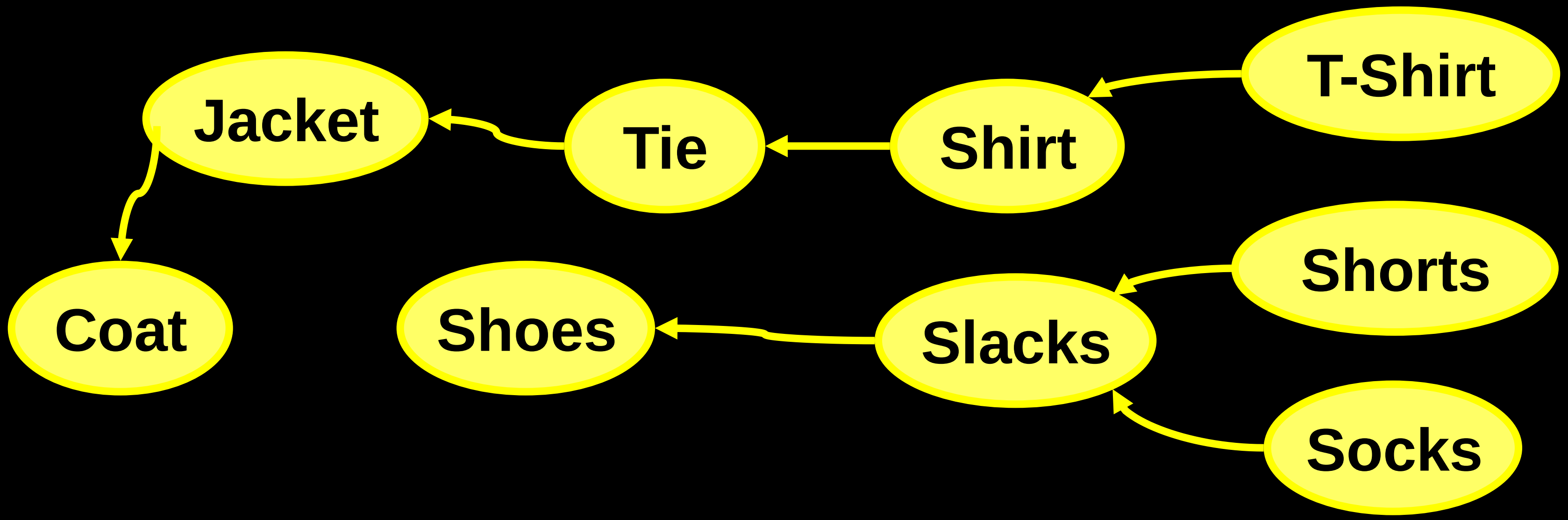
Money

Cell biology



Soft layering

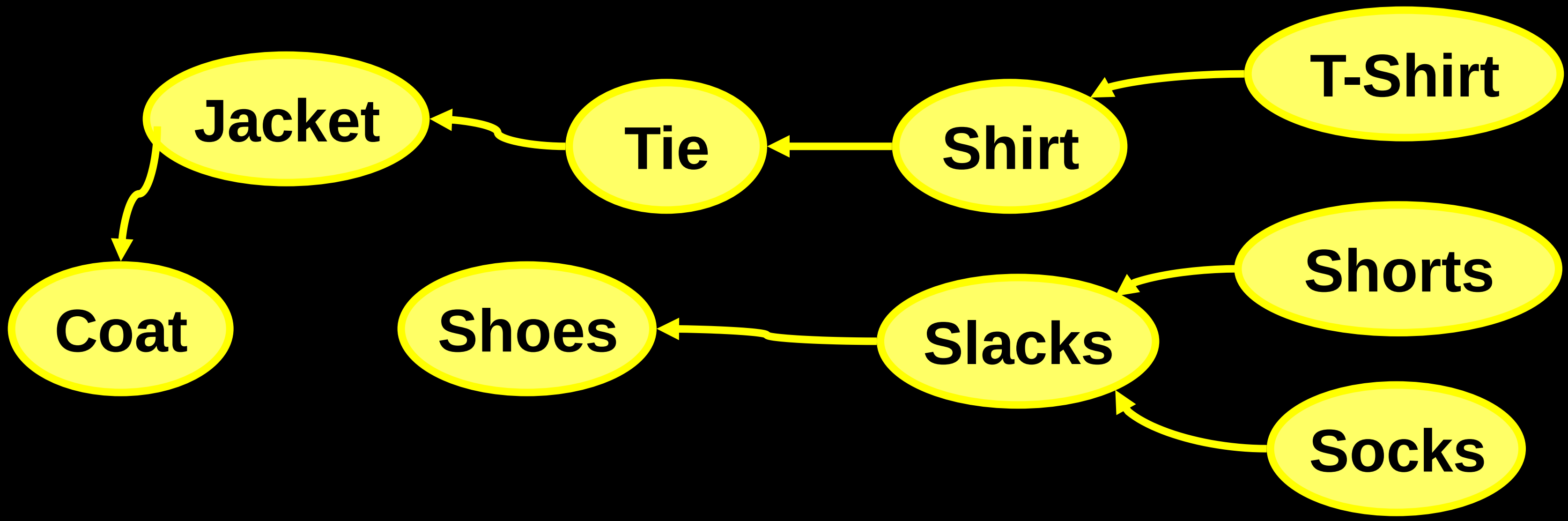

T-Shirt
Jacket
Tie
Shirt
Shorts
Coat
Shoes
Slacks
Socks
Modularity?
Silk
Wool
Nylon
Cotton
Rayon
Polyester



Given a wardrobe (set of garments)

1 << # outfits << # non-outfits

(random heaps are of garments are never outfits)



large **thin**

1 << # outfits << # non-outfits

(random heaps are of garments are never outfits)

large **thin**

1 << # toys << # non-toys

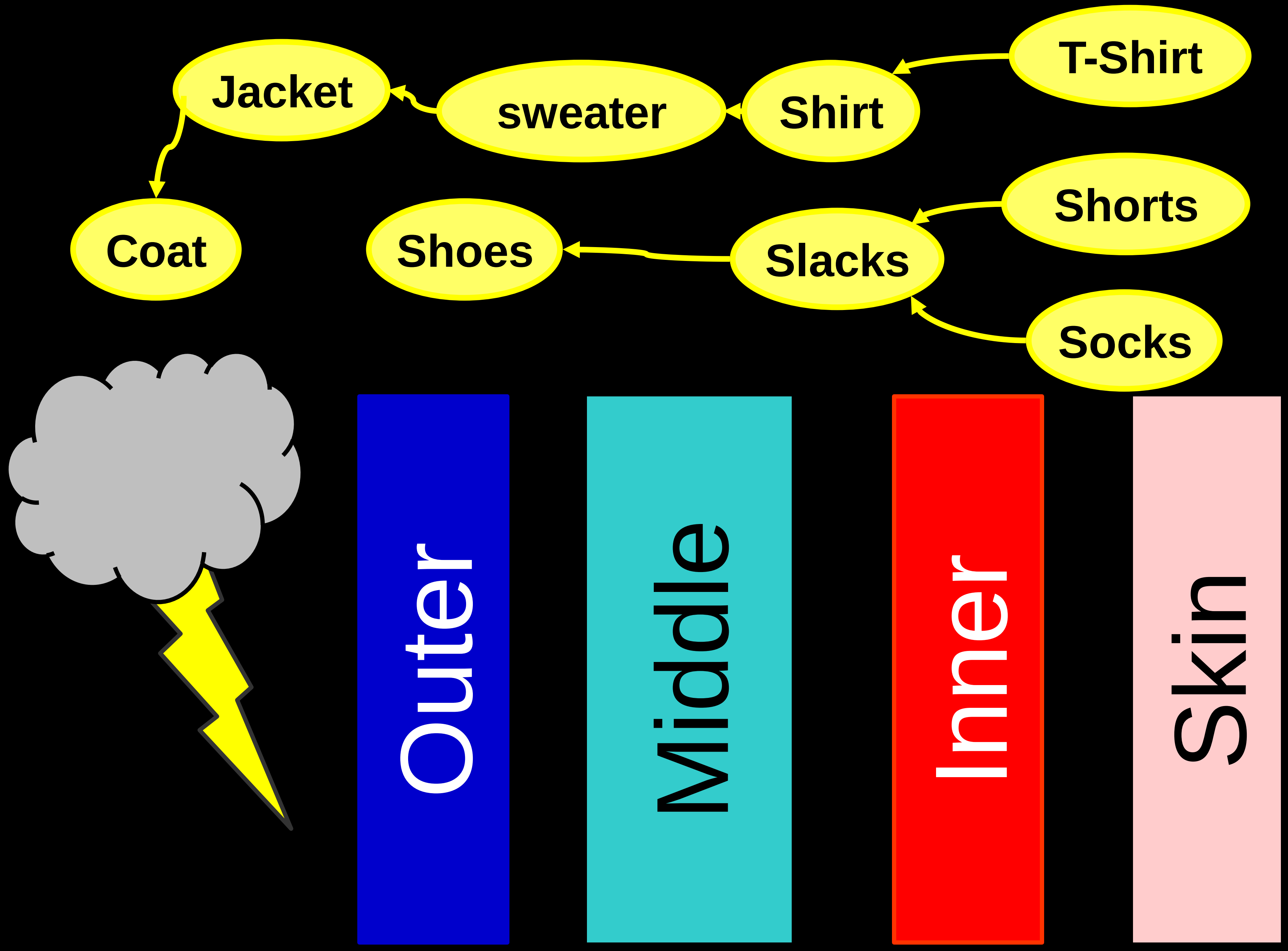
~~“order for free”~~

Letters and words

- 9 letters: adeginorz
- 9!= 362,880 sequences of 9 letters
- Only “organized” is a word

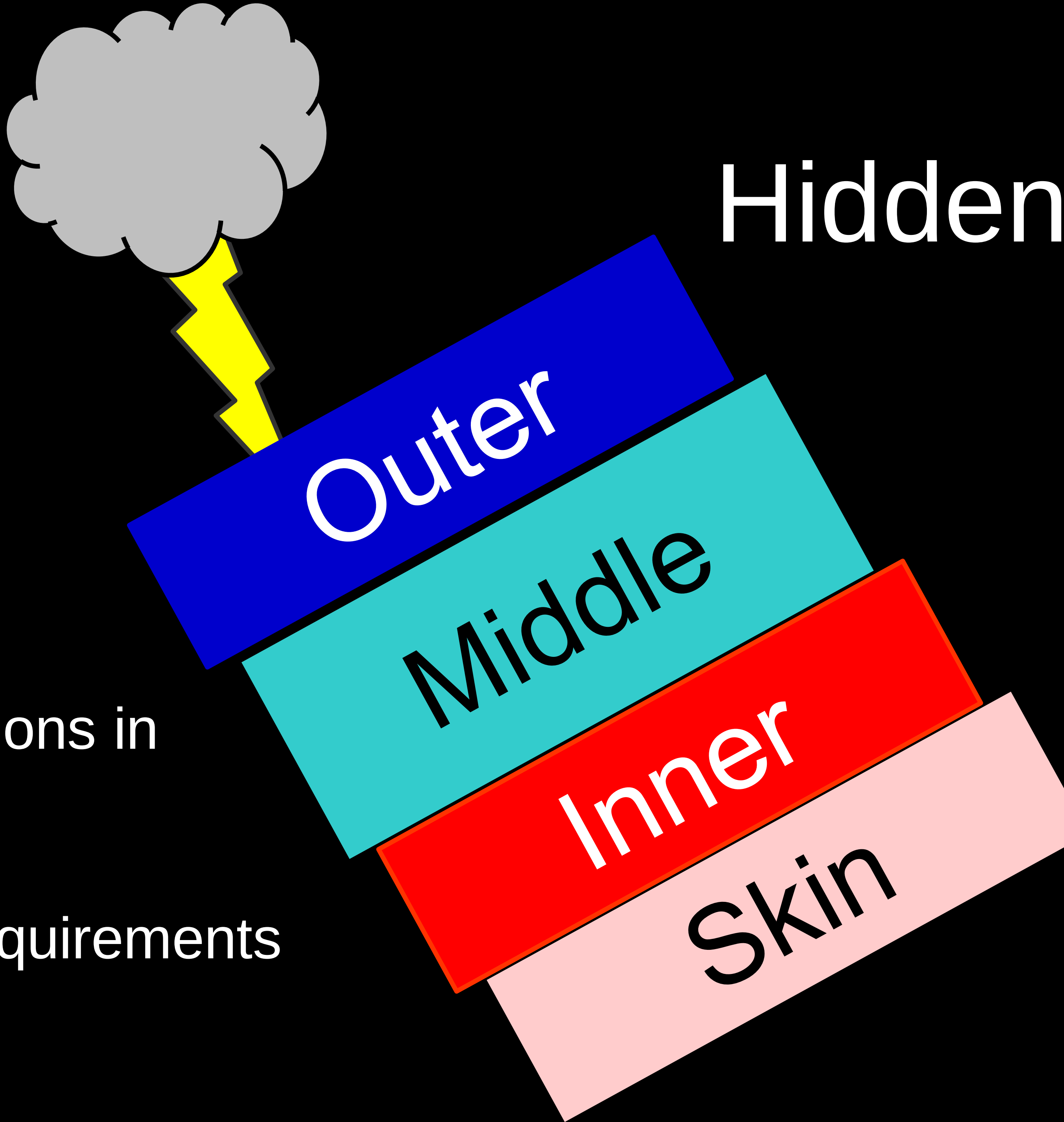
1 << (# words) << (# non-words)

large **thin**


T-Shirt
Jacket
sweater
Shirt
Shorts
Coat
Shoes
Slacks
Socks
Outer
Middle
Inner
Skin

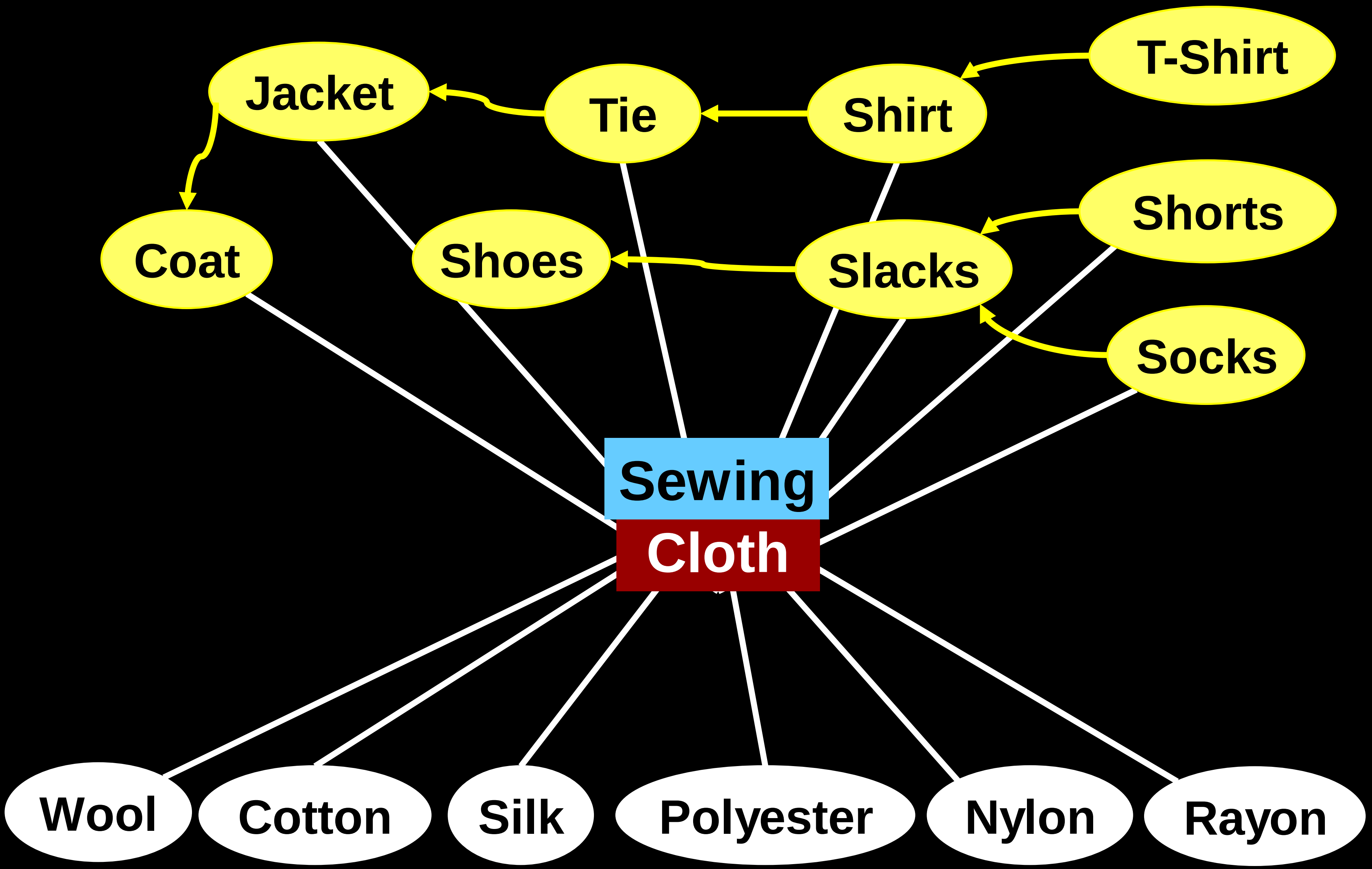
System constraints

Hidden

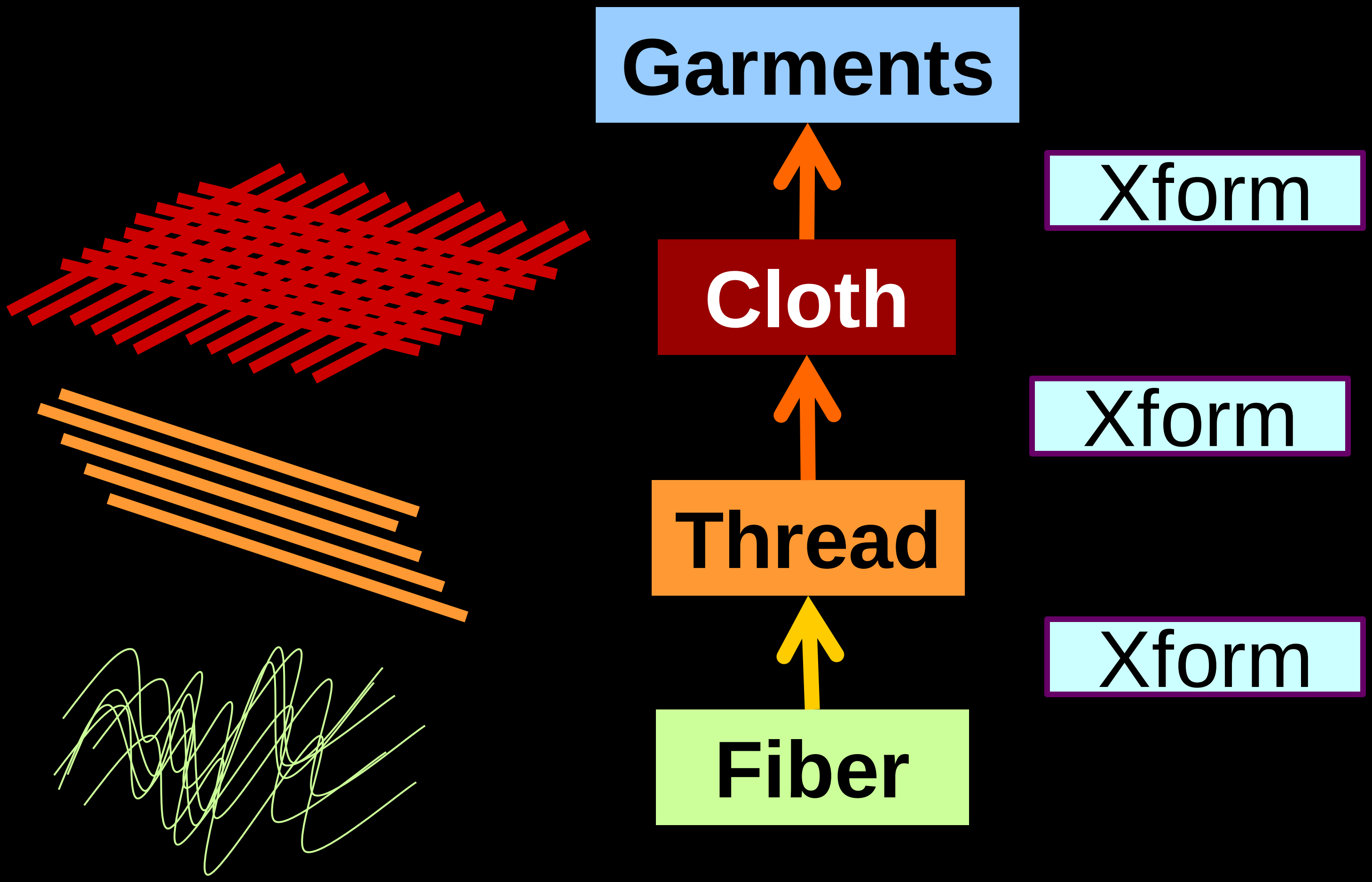


Robust to variations in

- weather
- activity
- appearance requirements
- wear and tear
- cleaning

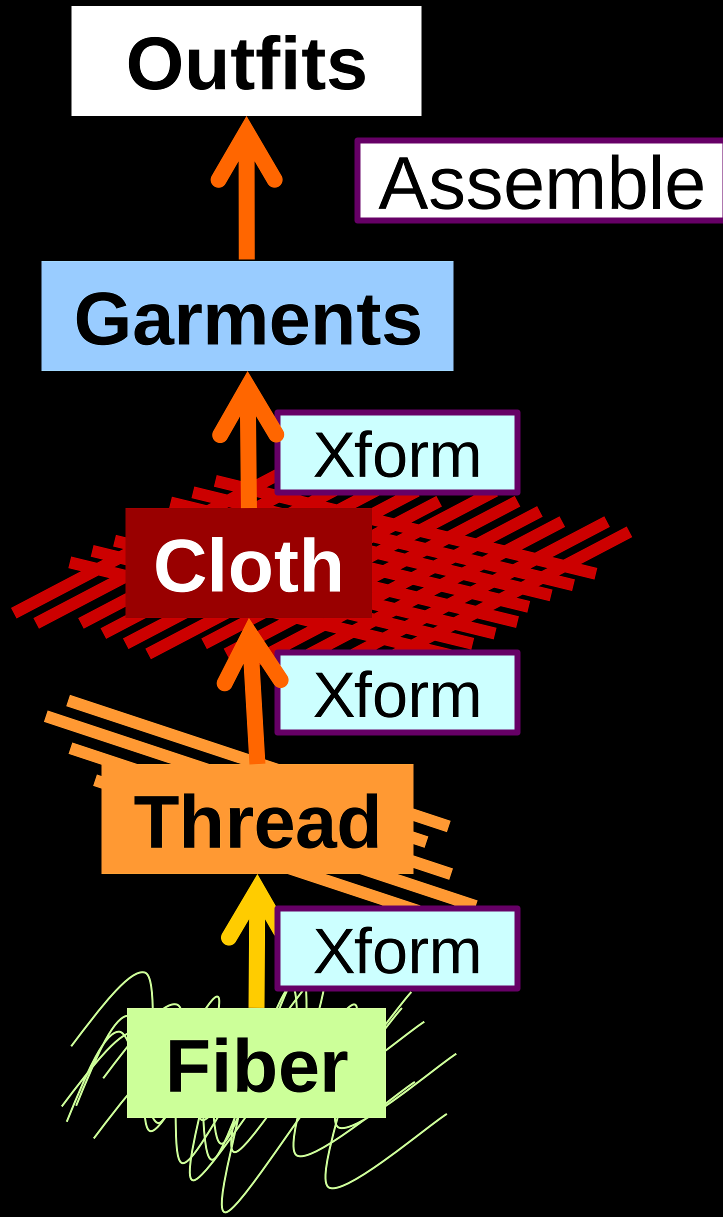

T-Shirt
Jacket
Tie
Shirt
Shorts
Coat
Shoes
Slacks
Socks
Sewing
Cloth
Wool
Cotton
Silk
Polyester
Nylon
Rayon

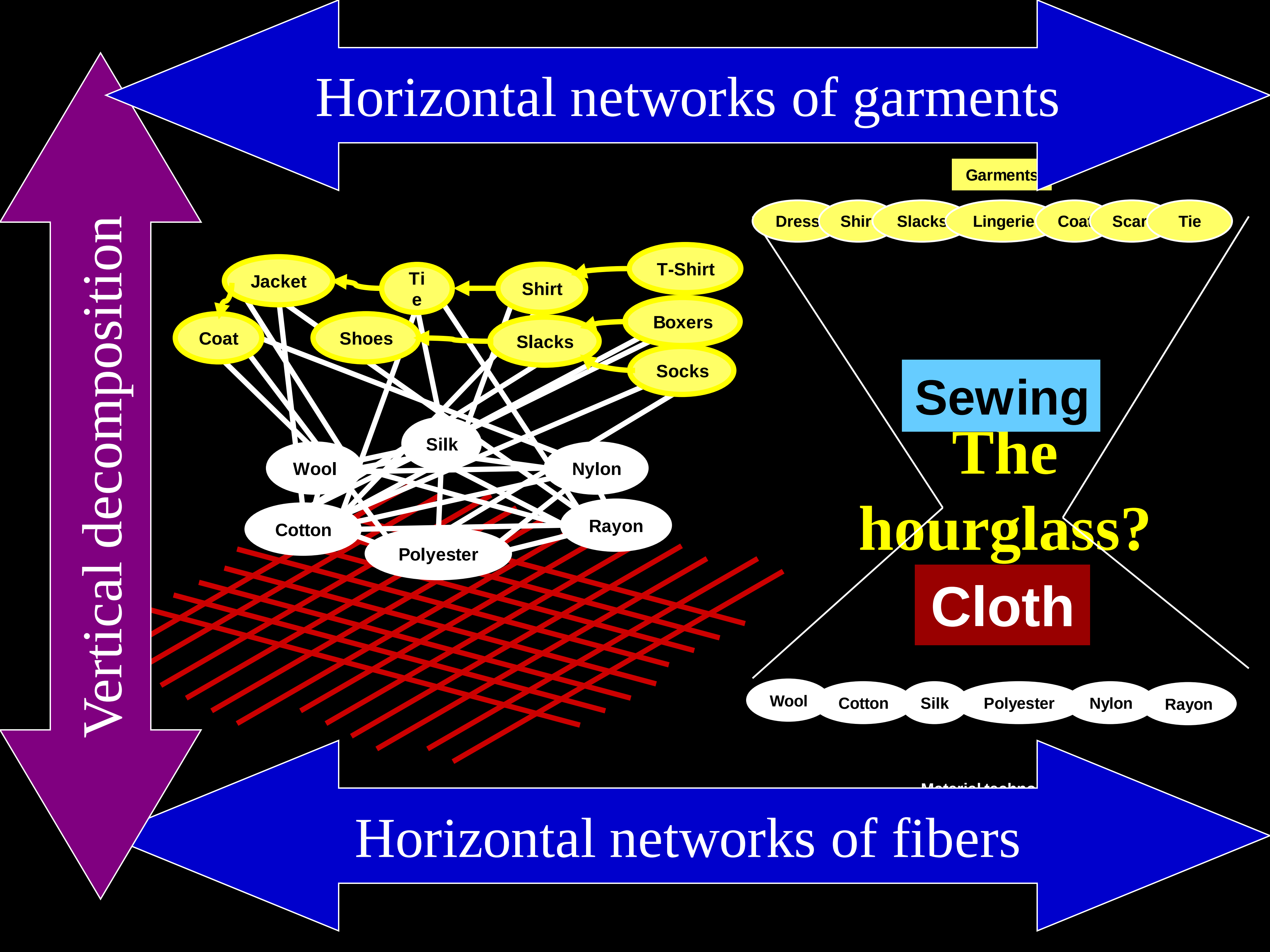
Modularity 2.0

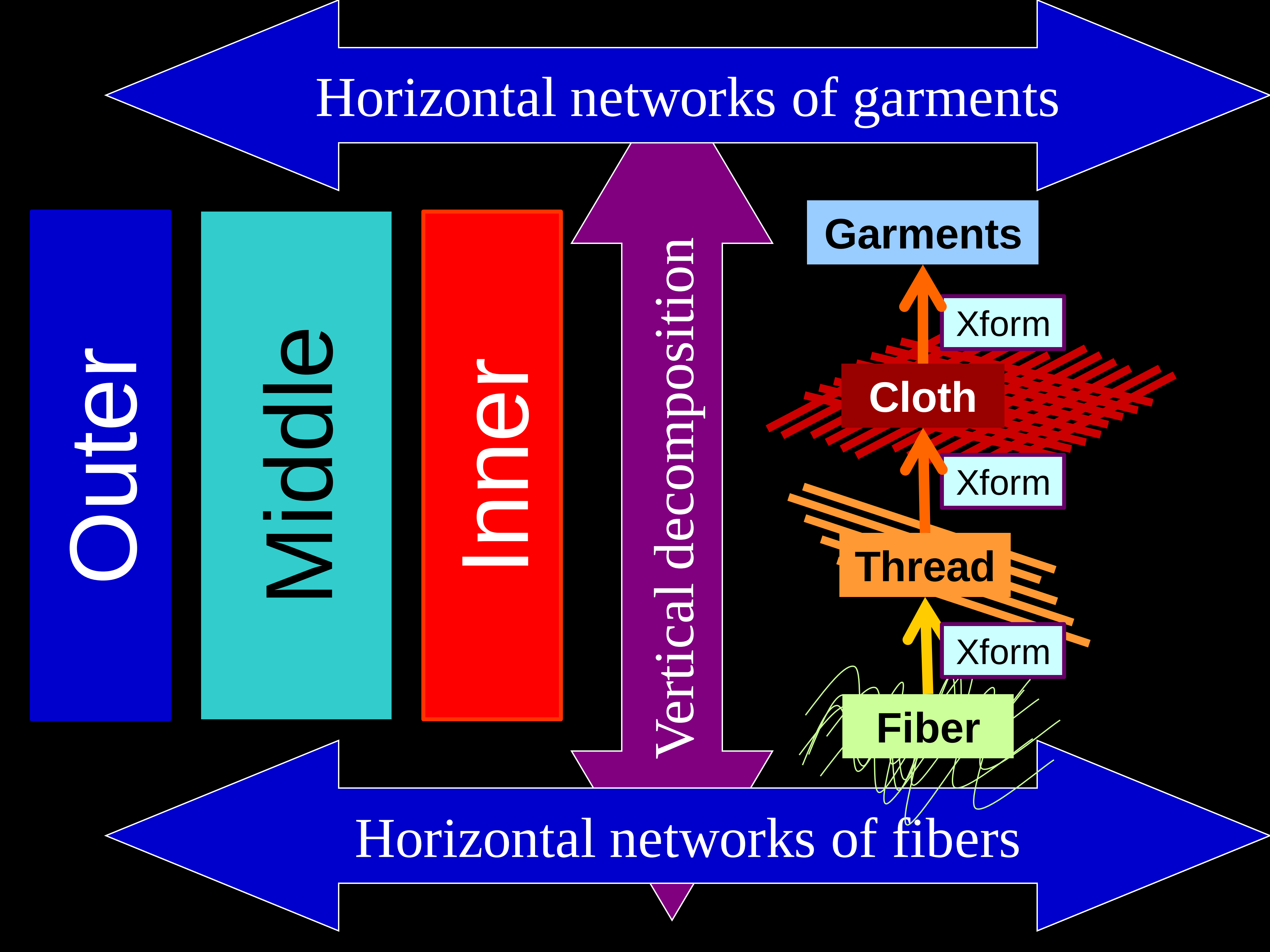


Prevents unraveling of lower layers

Hidden, large, thin, nonconvex



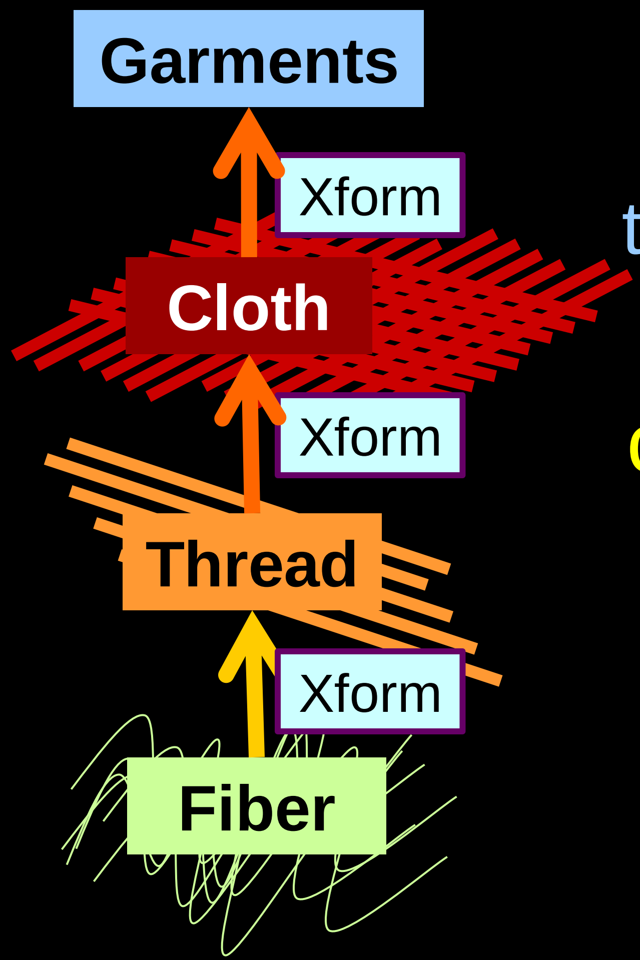

Horizontal networks of garments
Vertical decomposition
Garments
Dress
Shir
Slacks
Lingerie
Coat
Scar
Tie
Jacket
Ti
e
Shirt
T-Shirt
Coat
Shoes
Slacks
Boxers
Socks
Silk
Wool
Nylon
Cotton
Rayon
Polyester
Sewing
The
hourglass?
Cloth
Wool
Cotton
Silk
Polyester
Nylon
Rayon
Horizontal networks of fibers


Horizontal networks of garments
Outer
Middle
Inner
Vertical decomposition
Garments
Xform
Cloth
Xform
Thread
Xform
Fiber
Horizontal networks of fibers

Universal strategies?

Even though garments seem analog/continuous

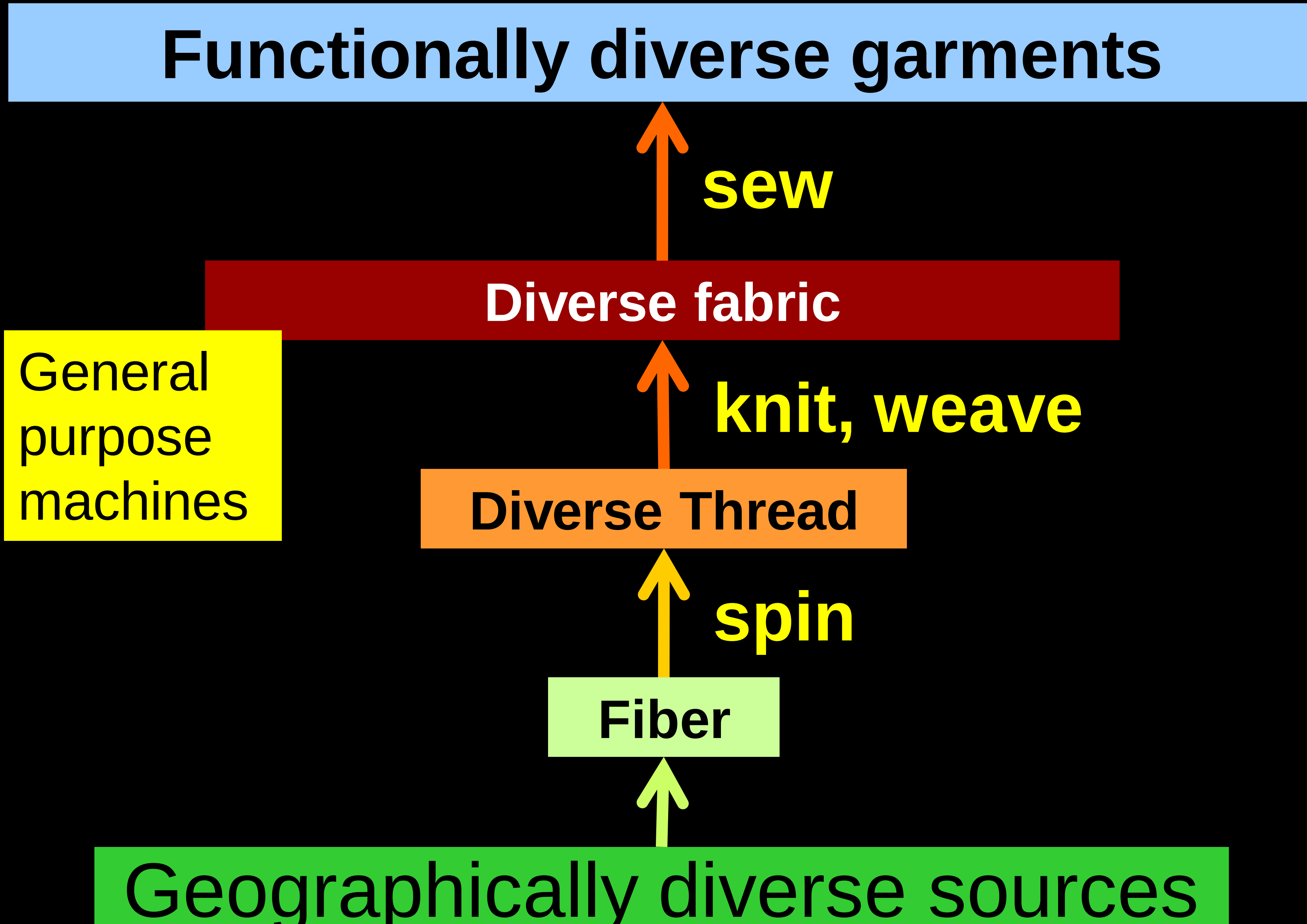
quantization for robustness



Garments have limited access to threads and fibers

constraints on cross-layer interactions

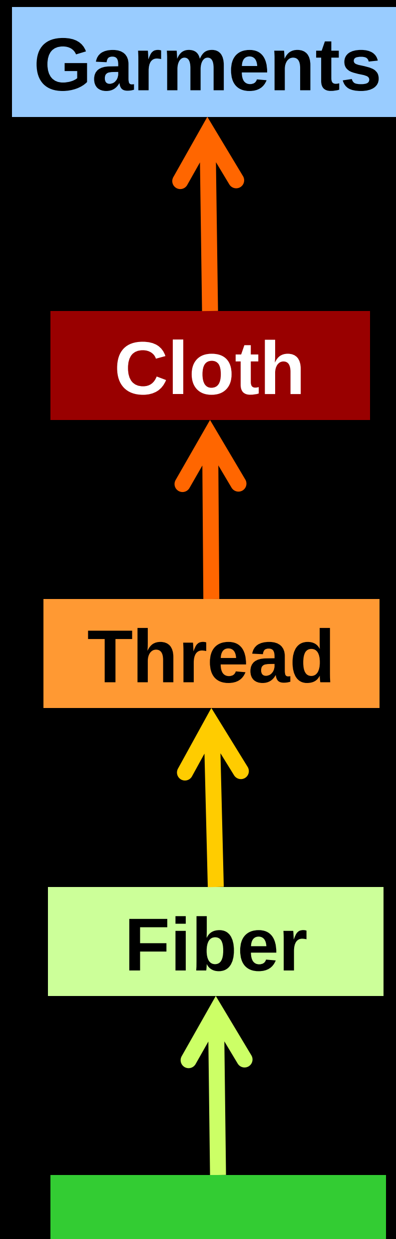
Prevents unraveling of lower layers



Functionally diverse garments
sew
Diverse fabric
General purpose machines
knit, weave
Diverse Thread
spin
Fiber
Geographically diverse sources

Functionally diverse garments

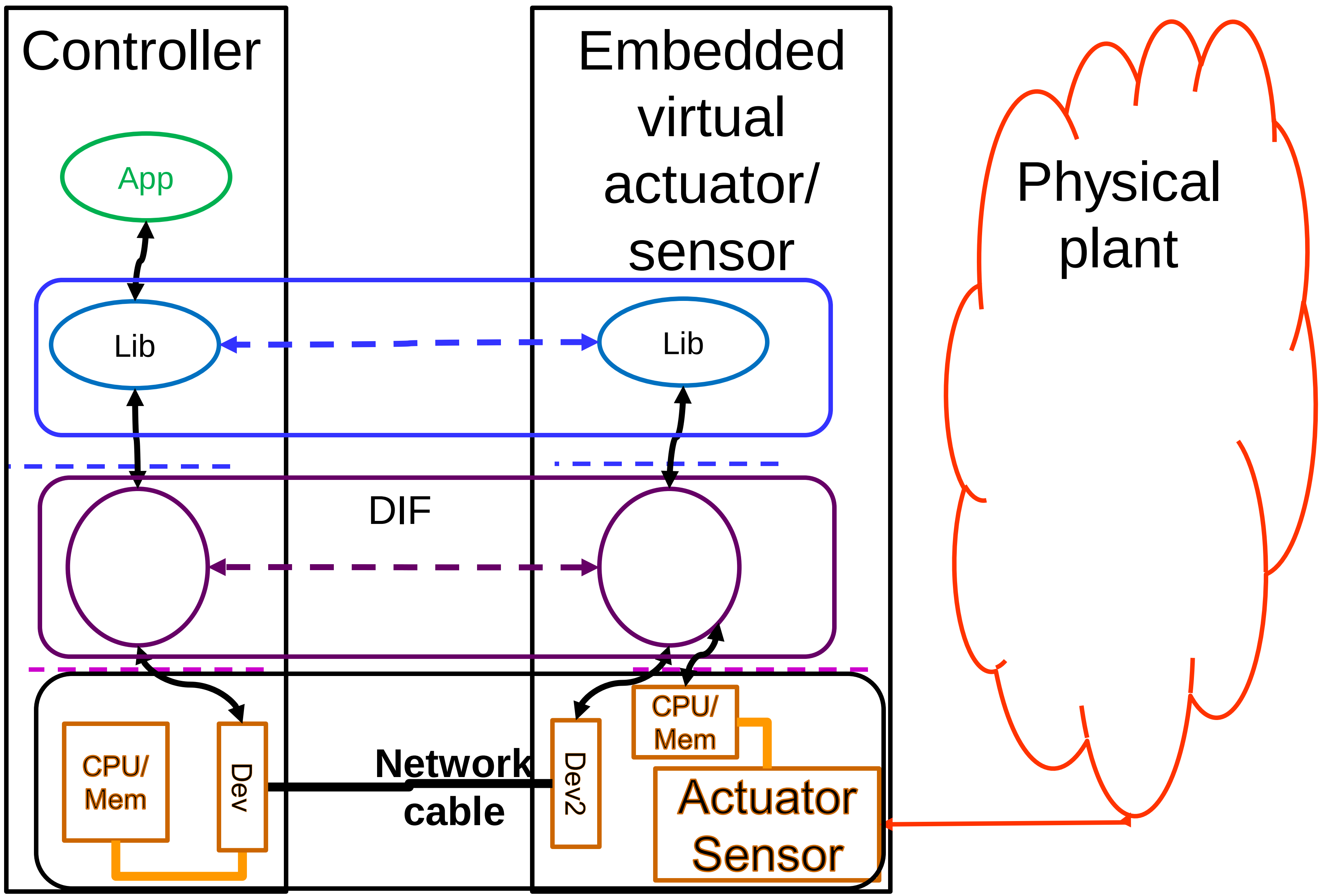

FASHION WARS
NEW YORK SPRING 2009
Garments
Fragilities?
Thread
Fiber



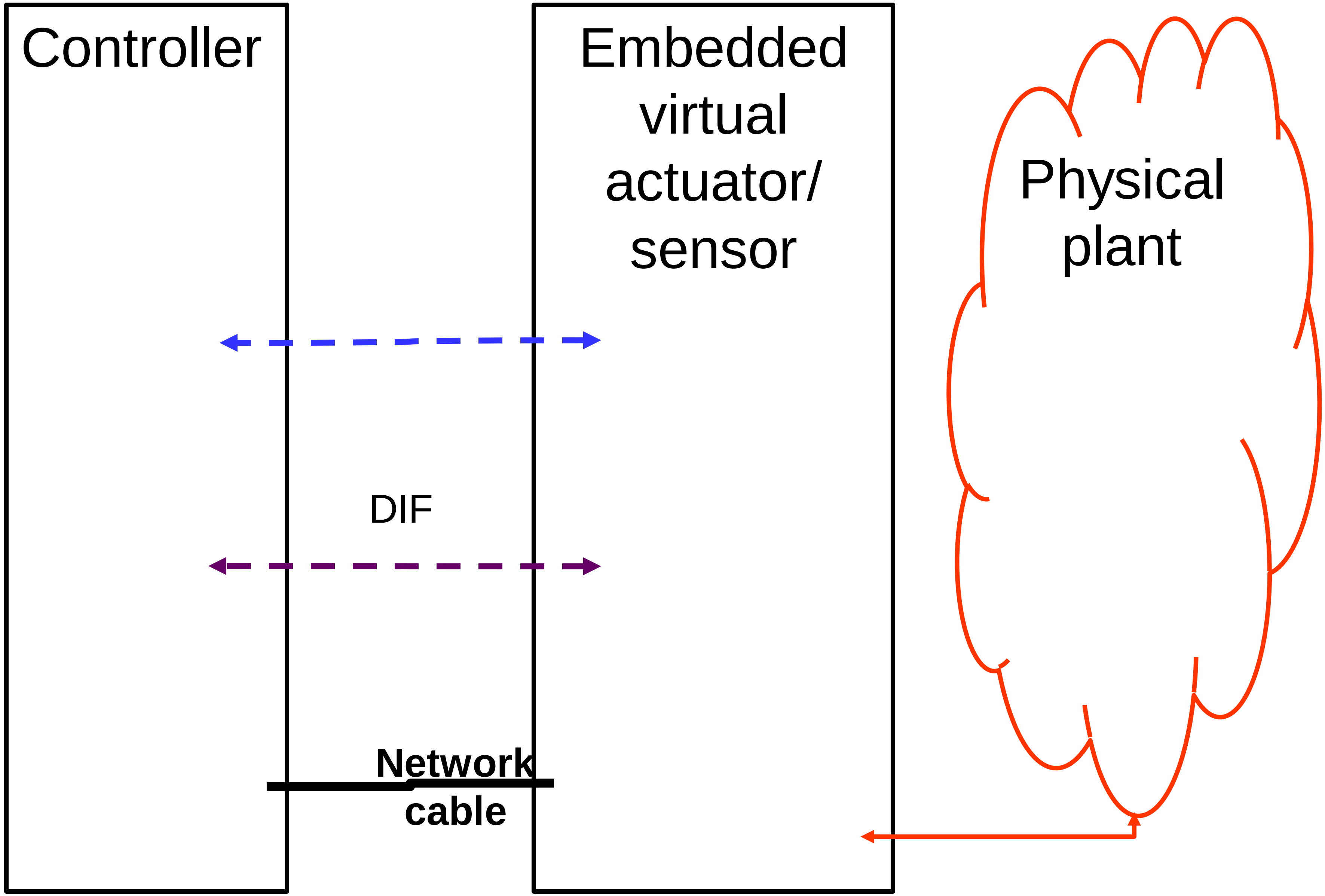
Scalable

Sustainable?

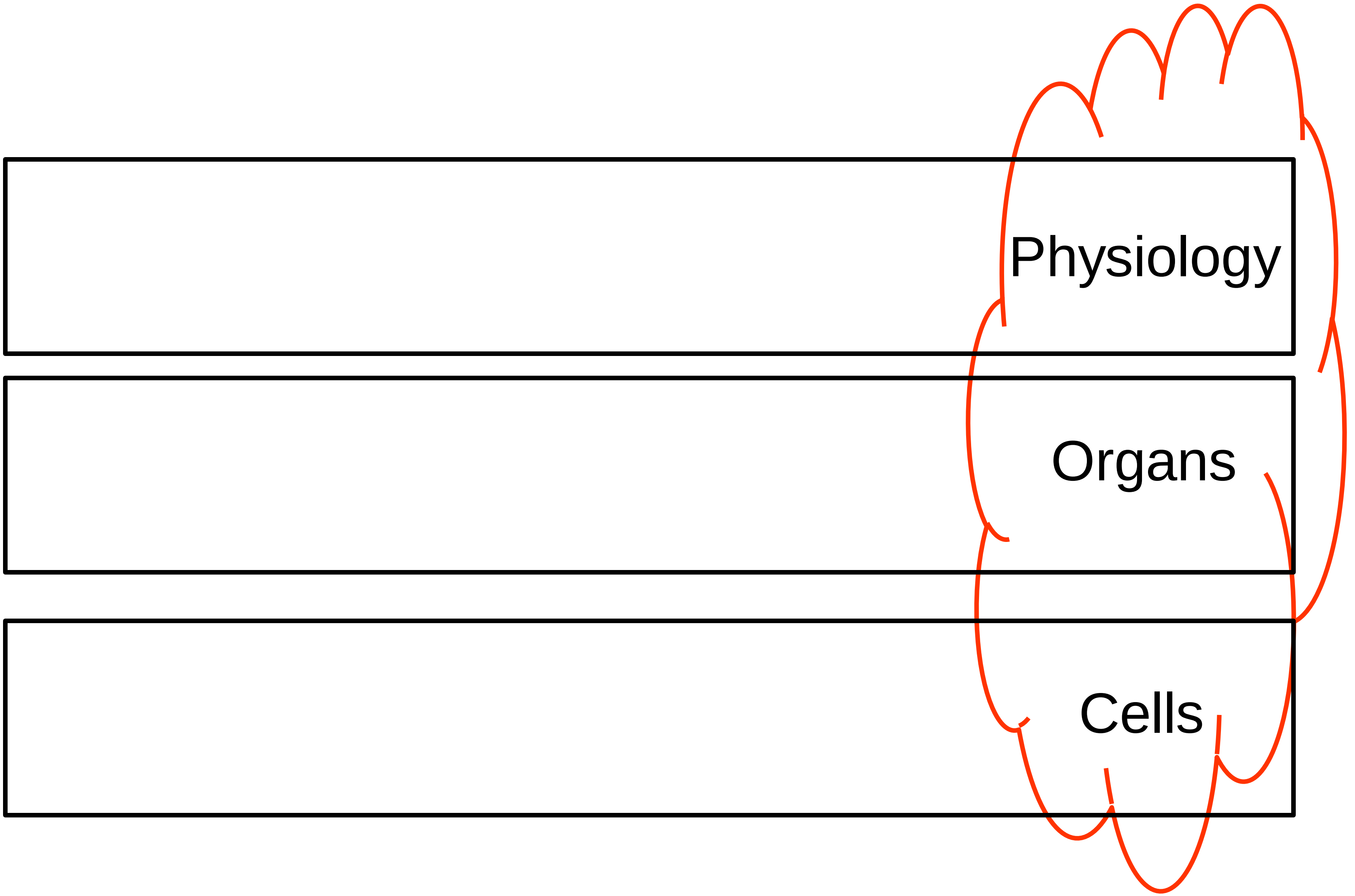
Networked/embedded/layered



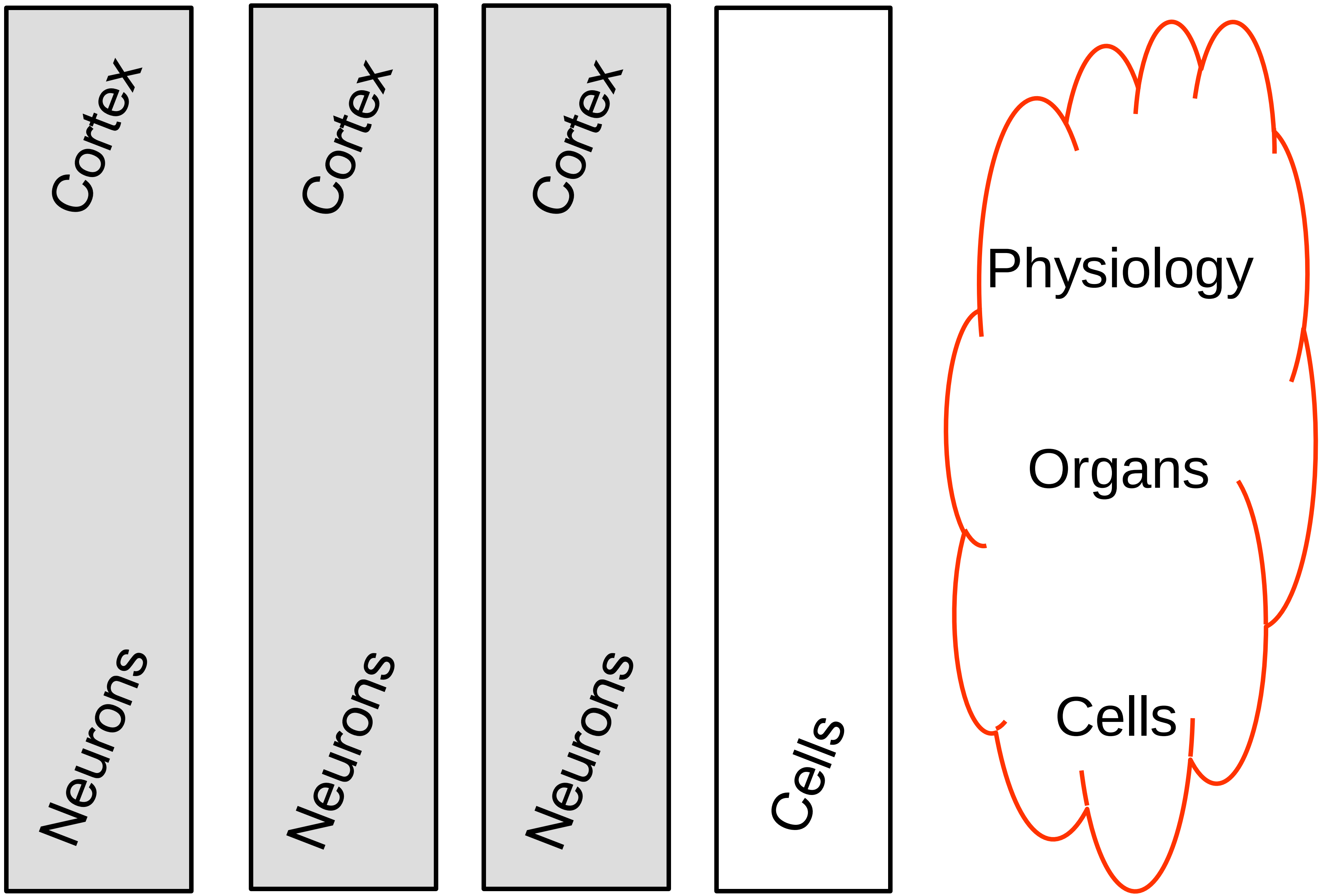
Meta-layering of cyber-phys control

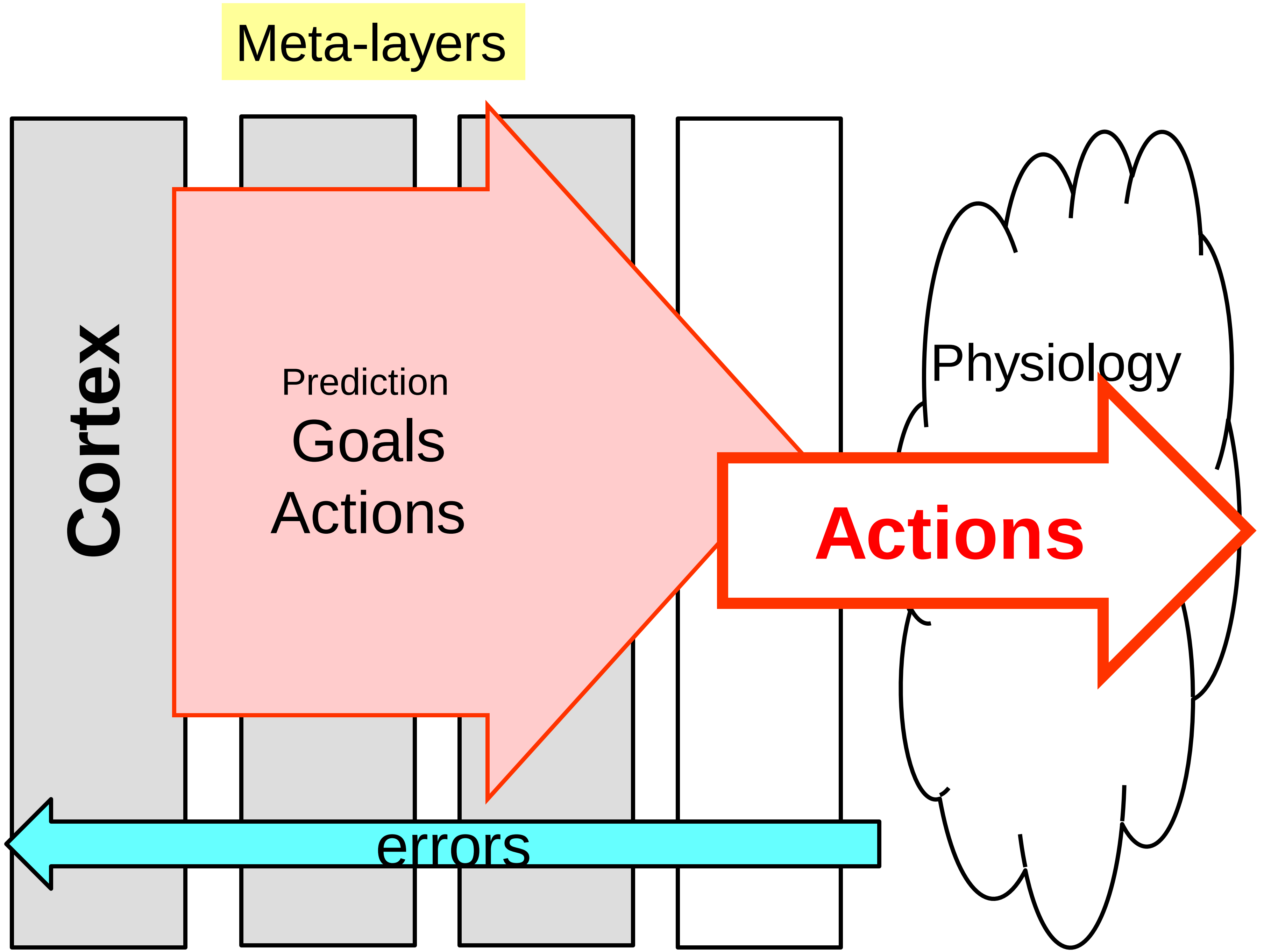


Layered architectures

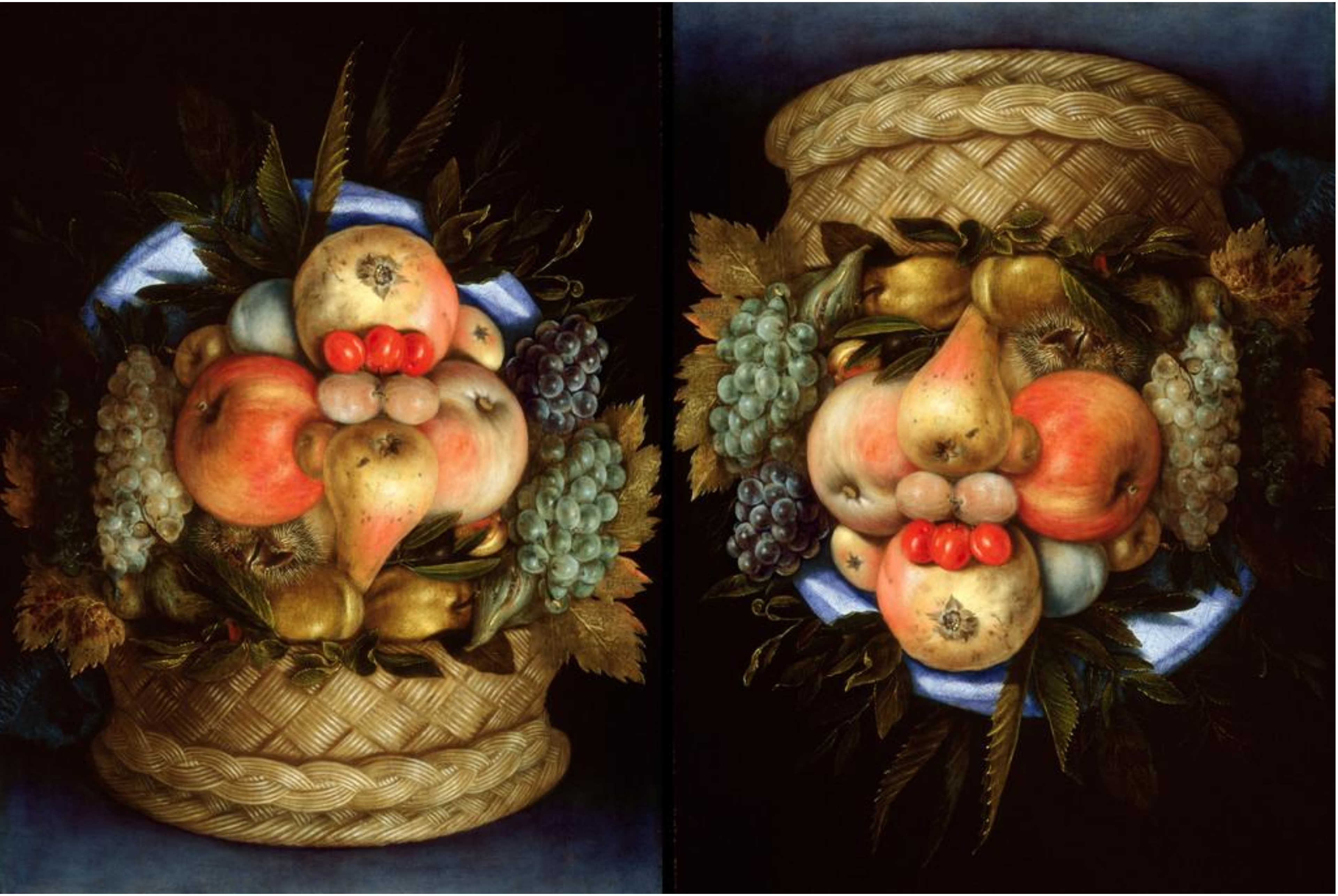


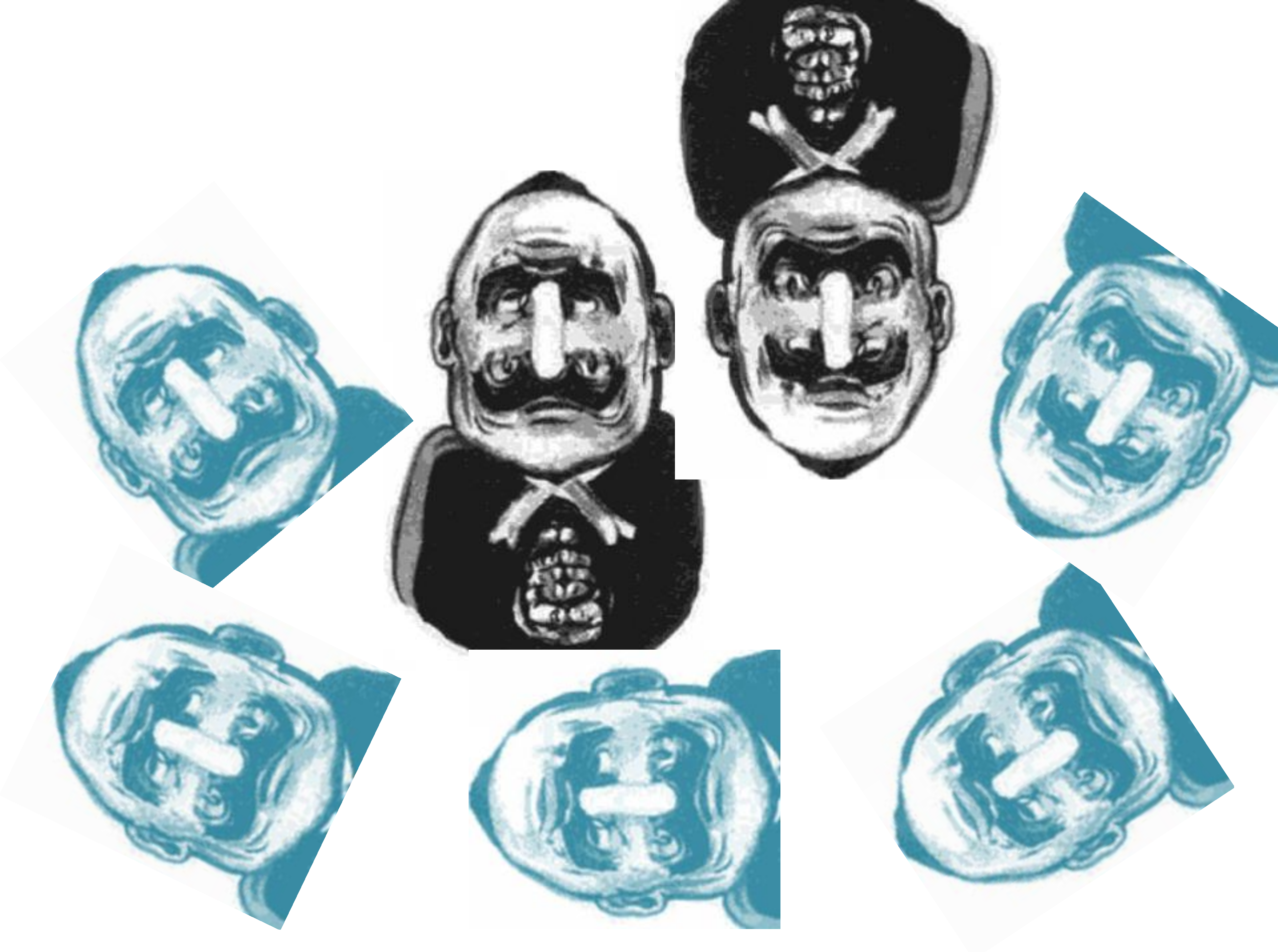
Layered architectures



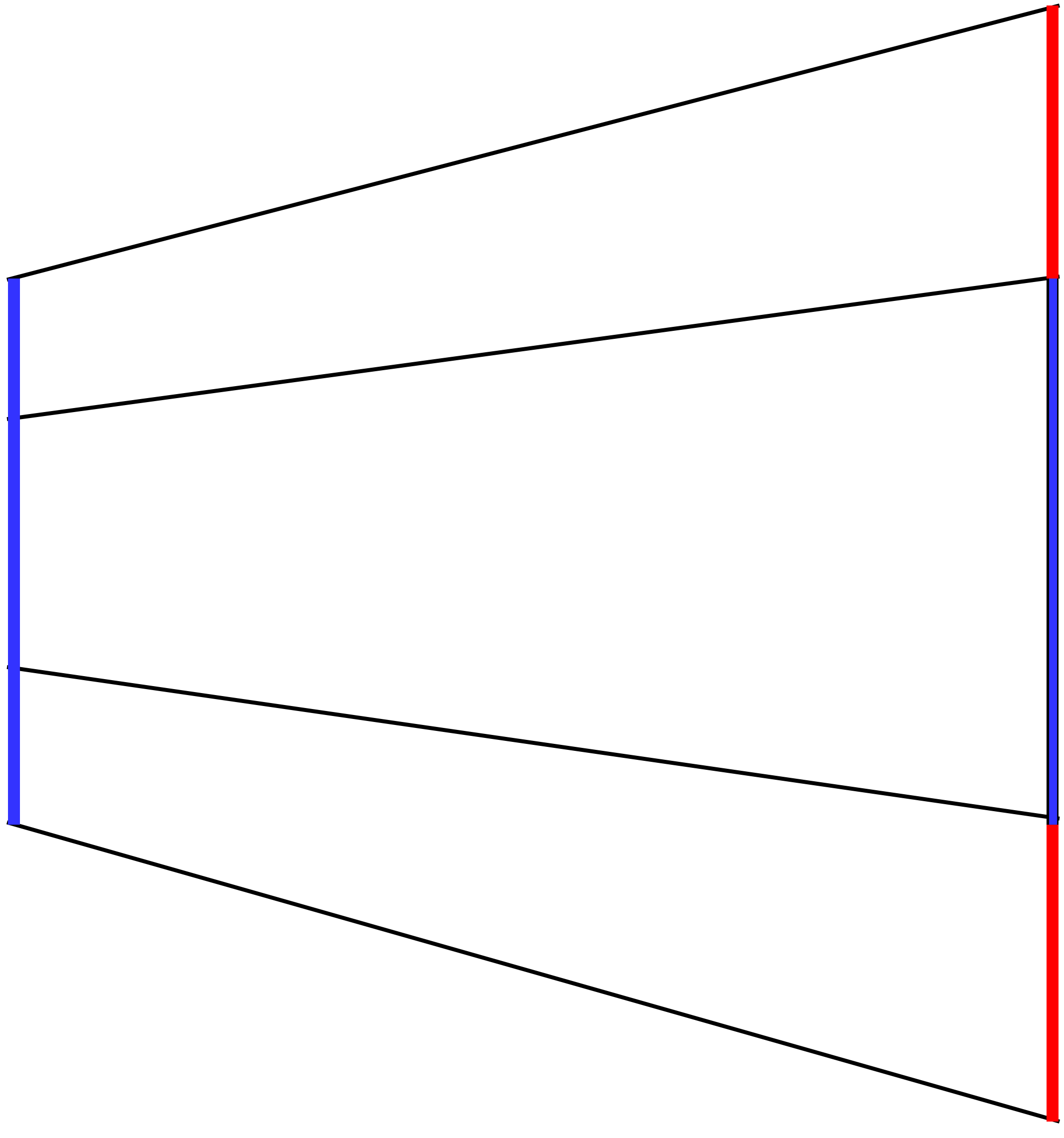


Meta-layers
Cortex
Prediction
Goals
Actions
Physiology
Actions
errors

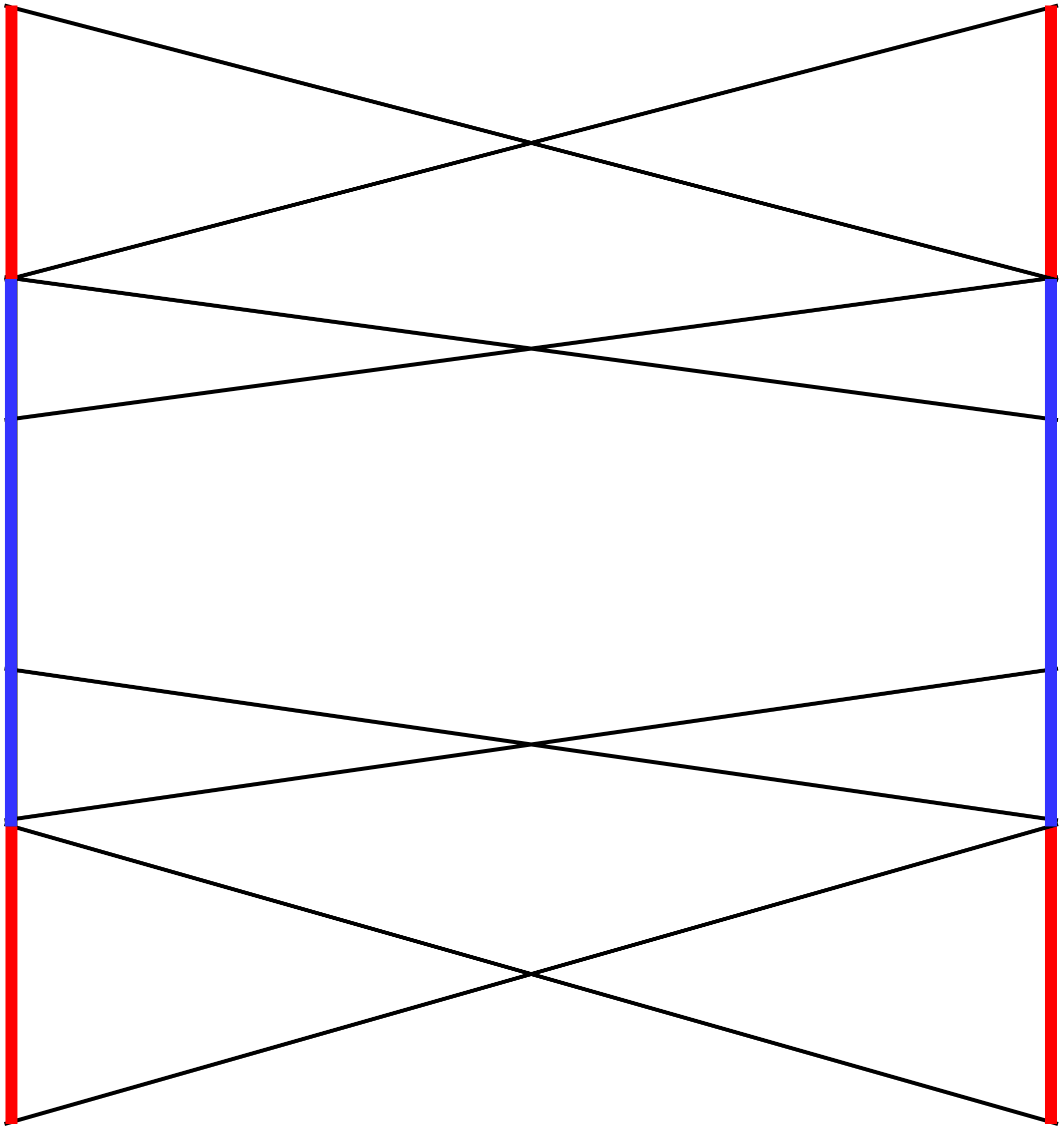




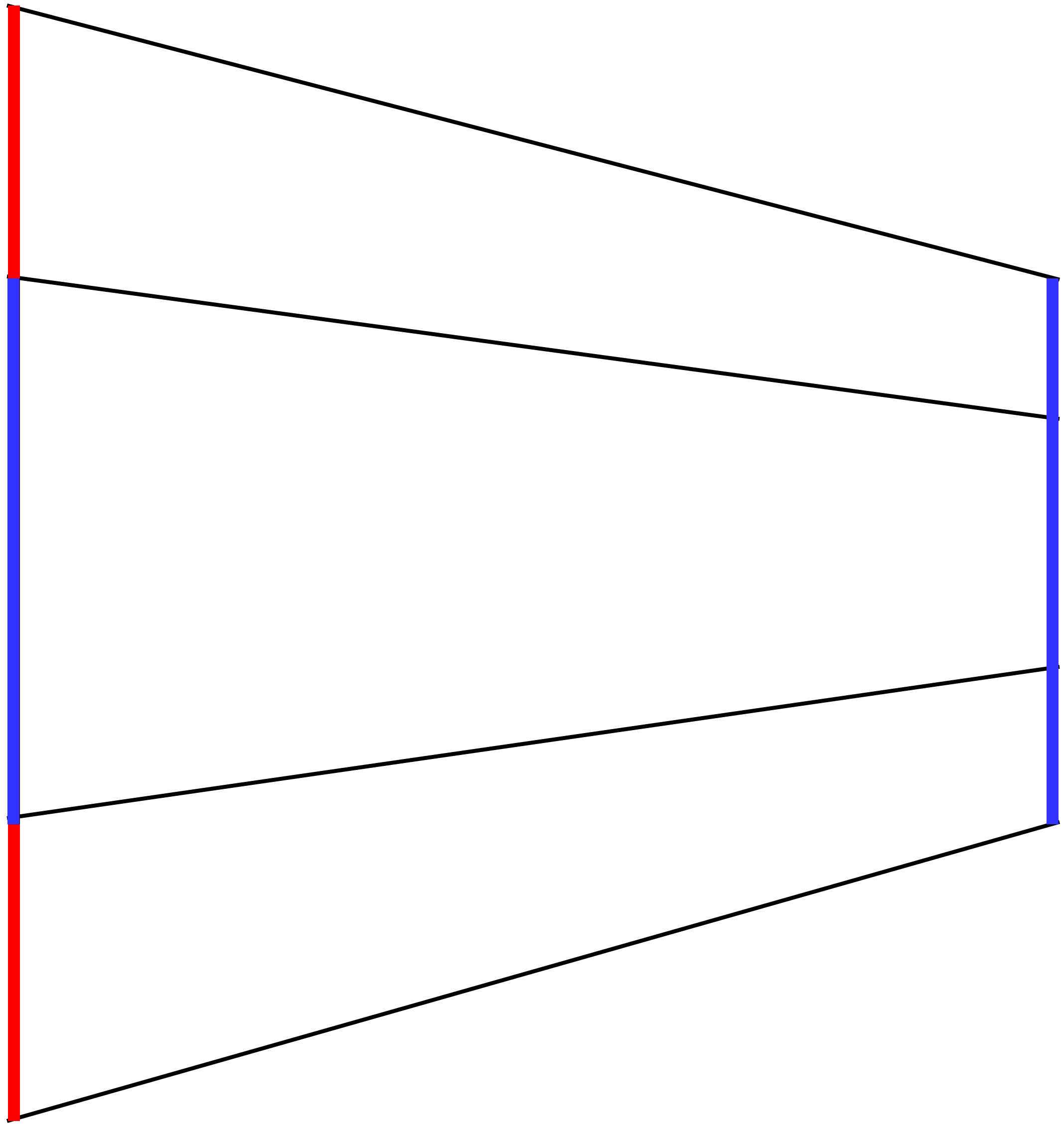
Which blue line is longer?



Which blue line is longer?

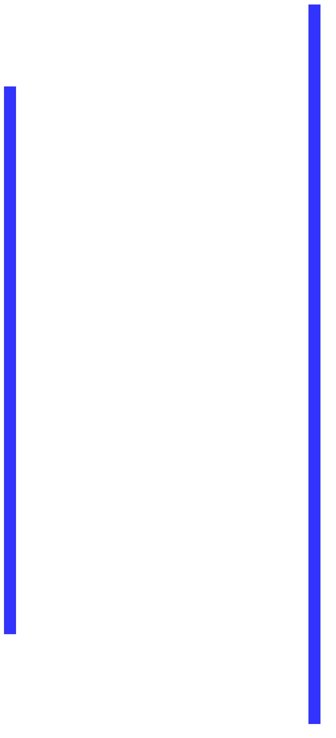


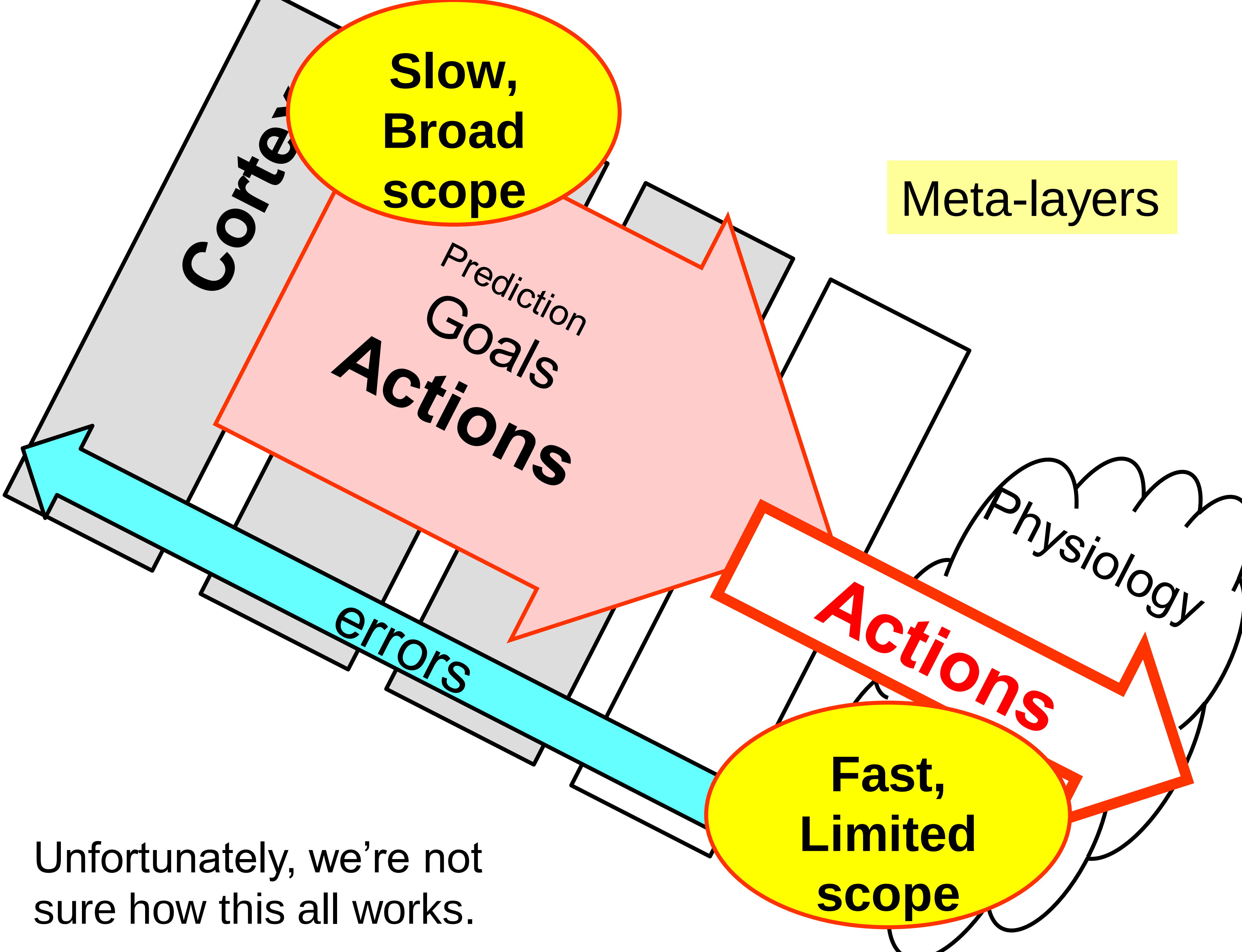
Which blue line is longer?



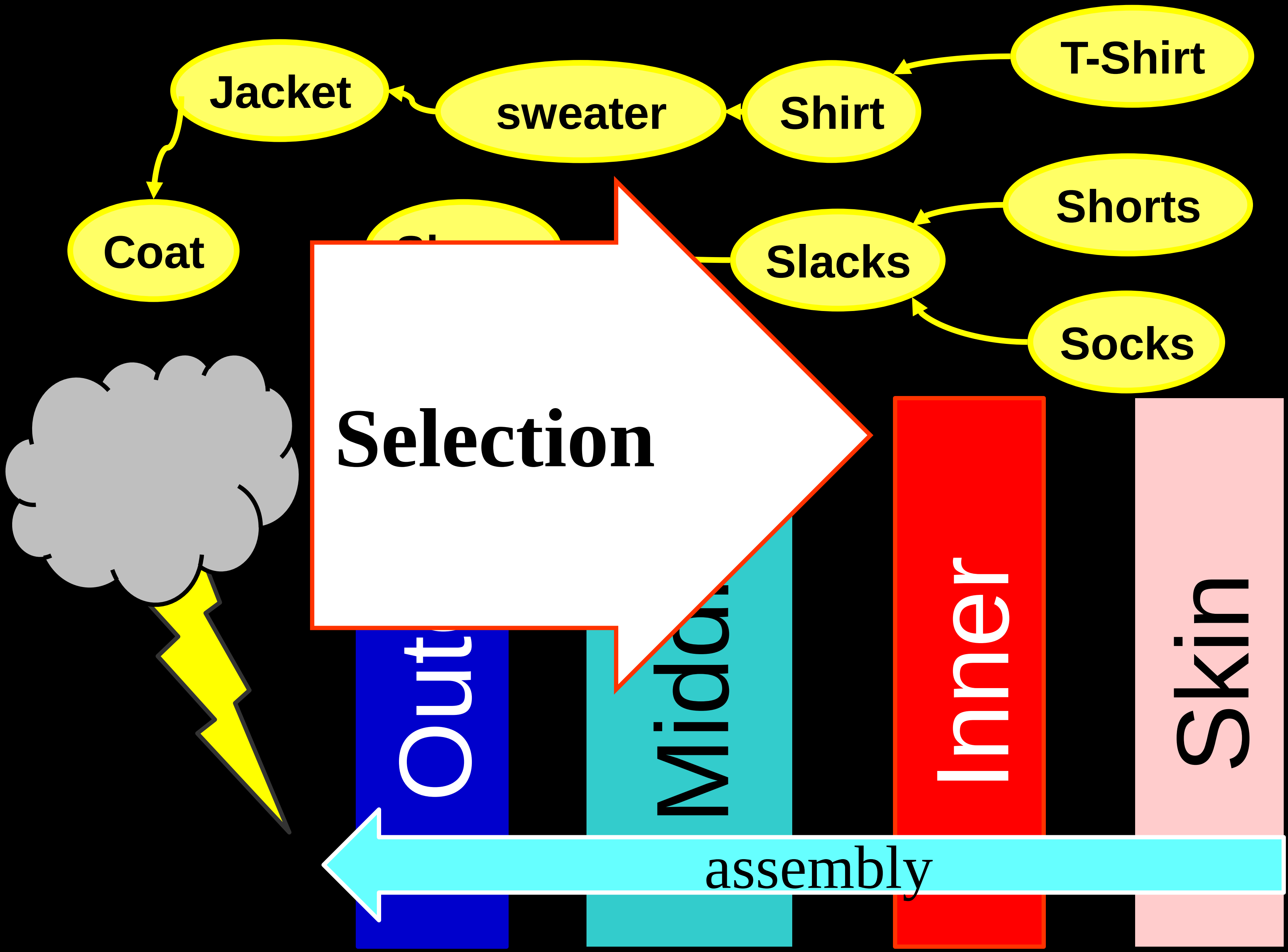
Which blue line is longer?

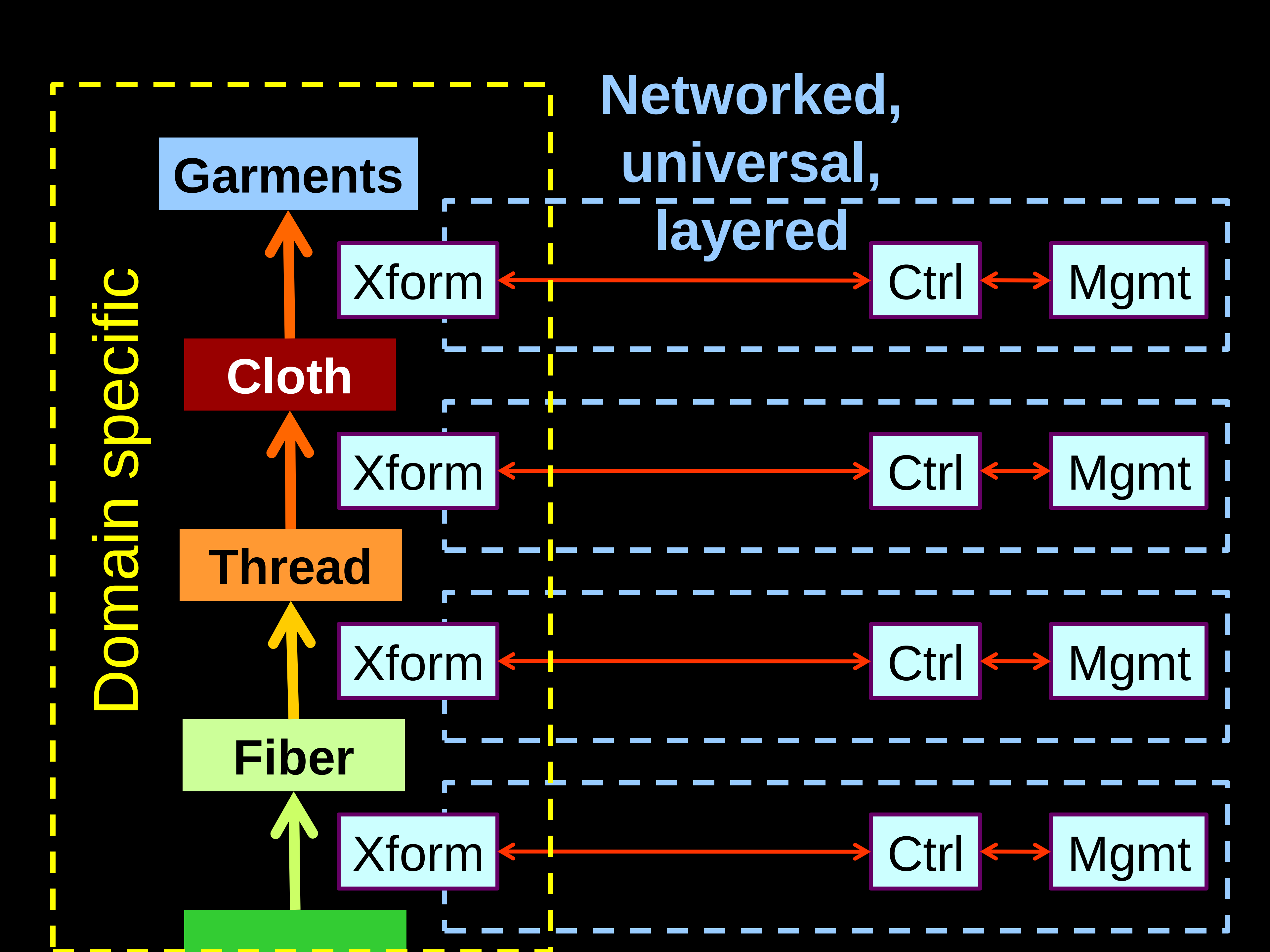
Which blue line is longer?



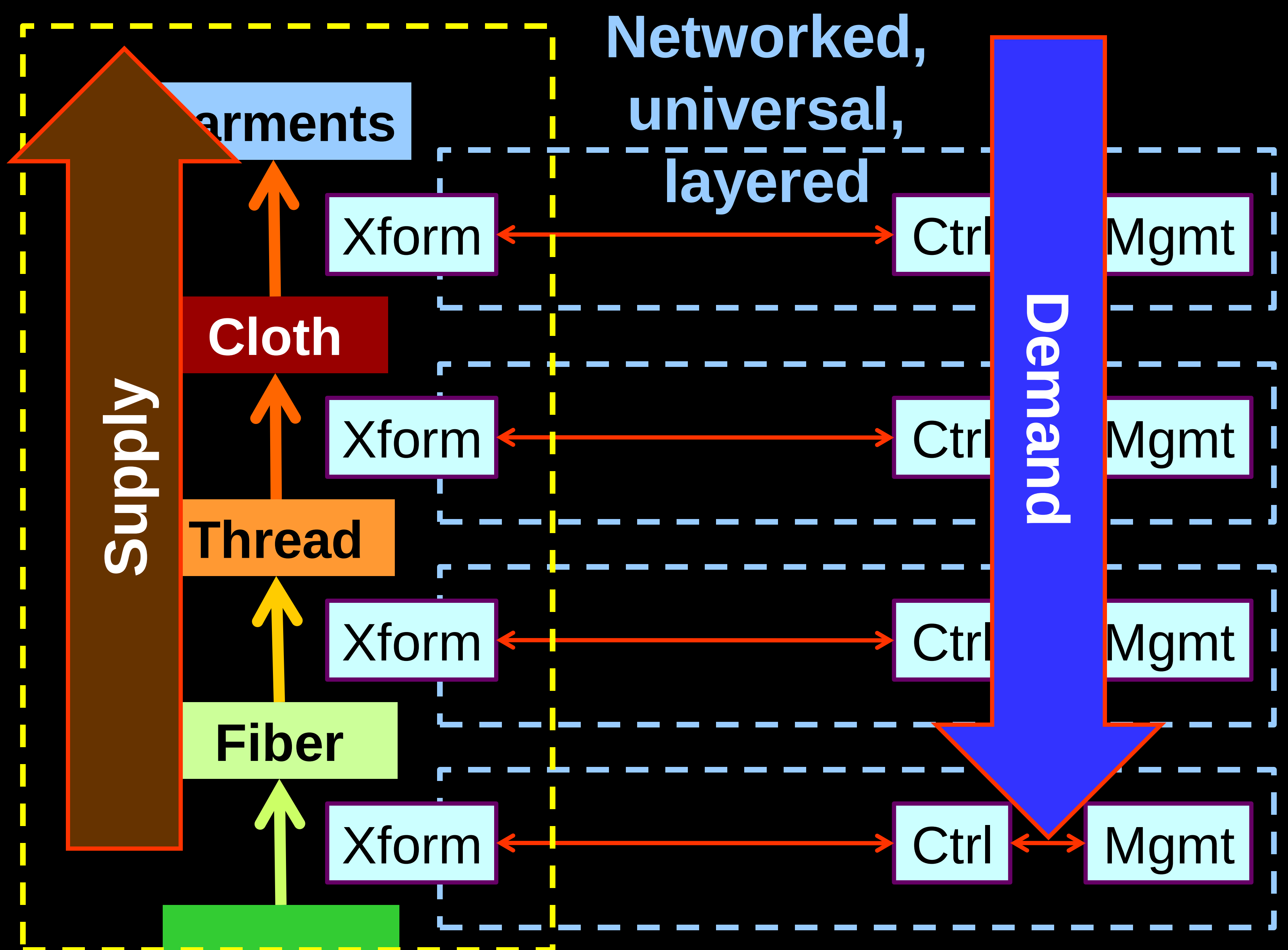


Unfortunately, we're not sure how this all works.

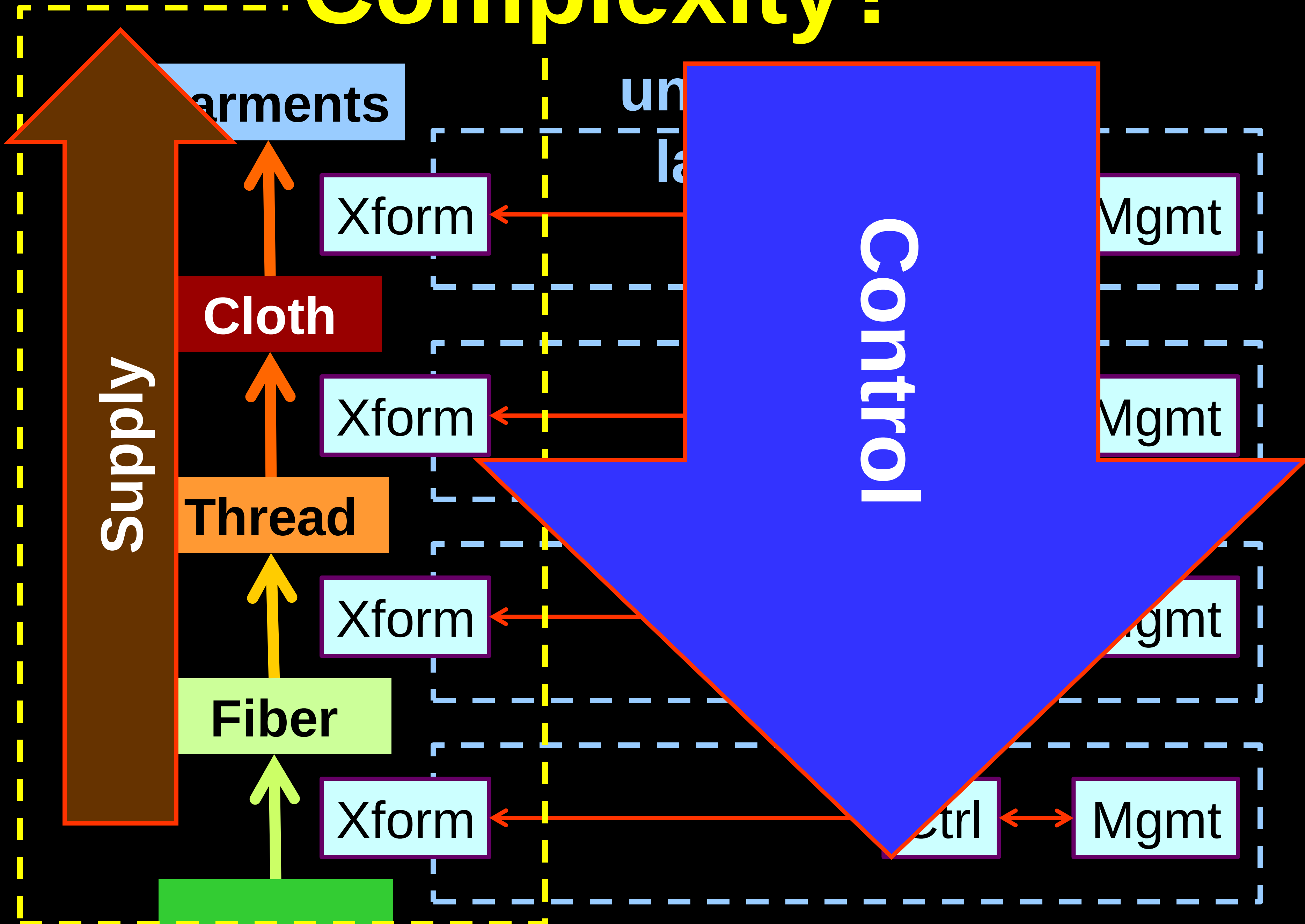

Jacket
sweater
Shirt
T-Shirt
Coat
Slacks
Shorts
Socks
Selection
Inner
Skin
assembly



Networked, universal, layered
Domain specific
Garments
Cloth
Thread
Fiber
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt


Networked, universal, layered
arments
Cloth
Thread
Fiber
Supply
Demand
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt
Xform
Ctrl
Mgmt

Complexity?



Supply
arments
Cloth
Thread
Fiber
Xform
Xform
Xform
Xform
un
la
Control
Mgmt
Mgmt
gmt
Ctrl
Mgmt

Fix?

What matters:

- Action
- Automation
- Limits
- Tradeoffs

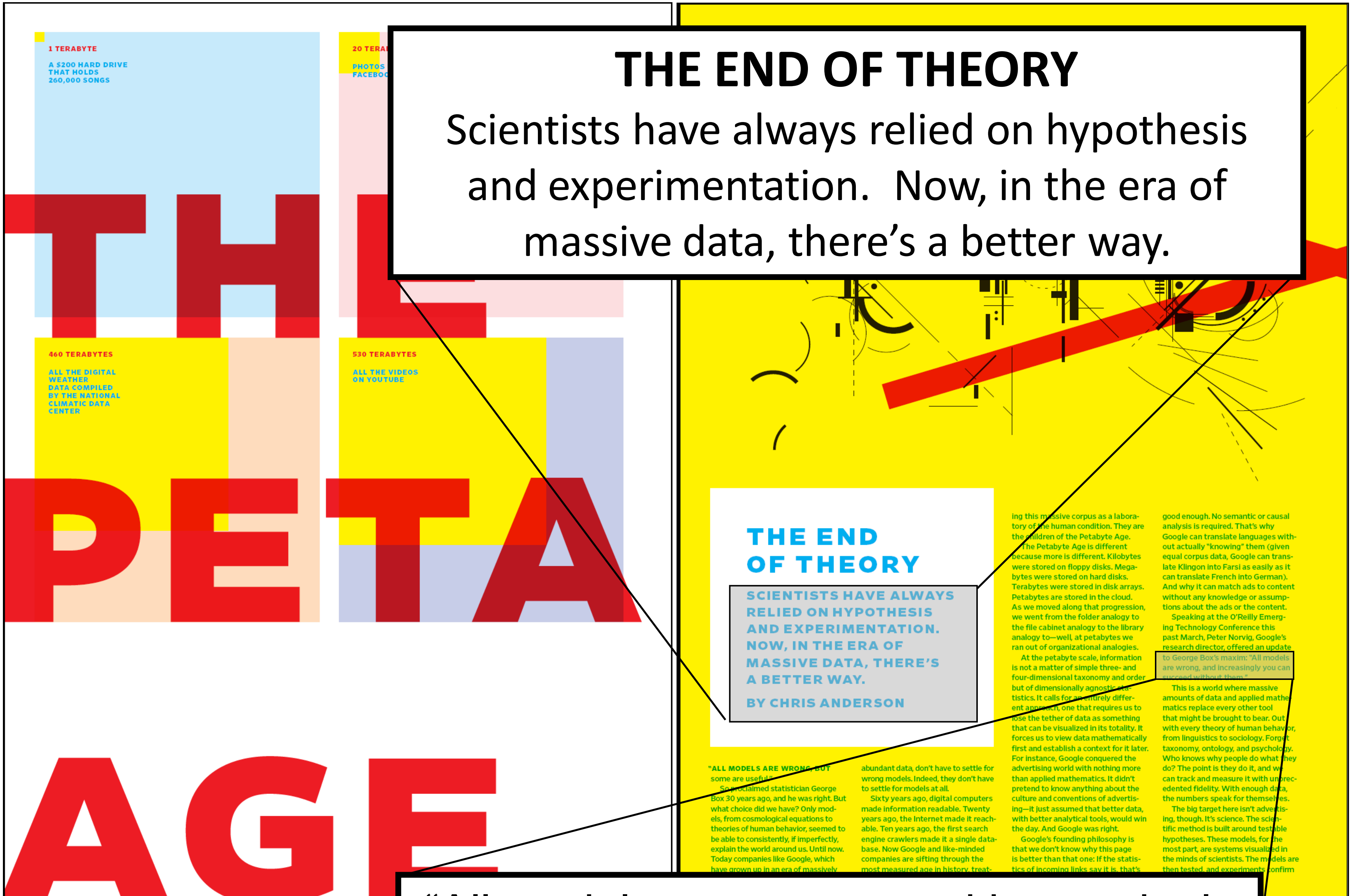
Yet Fragile

- ☹ Obesity, diabetes
- ☹ Cancer
- ☹ Parasites, infection
- ☹ AutoImmune/Inflame
- ☹ Addiction, psychosis…
- ☠ Epidemics, war…
- 💣 Catastrophes
- 💣 Obfuscate, amplify,…

Accident or necessity?

THE END OF THEORY

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



1 TERABYTE

A $200 HARD DRIVE THAT HOLDS 260,000 SONGS

20 TERA

PHOTOS FACEBOO

460 TERABYTES

ALL THE DIGITAL WEATHER DATA COMPILED BY THE NATIONAL CLIMATIC DATA CENTER

530 TERABYTES

ALL THE VIDEOS ON YOUTUBE

THE PETA AGE

THE END OF THEORY

SCIENTISTS HAVE ALWAYS RELIED ON HYPOTHESIS AND EXPERIMENTATION. NOW, IN THE ERA OF MASSIVE DATA, THERE'S A BETTER WAY.

BY CHRIS ANDERSON

"ALL MODELS ARE WRONG, BUT some are useful."

So proclaimed statistician George Box 30 years ago, and he was right. But what choice did we have? Only models, from cosmological equations to theories of human behavior, seemed to be able to consistently, if imperfectly, explain the world around us. Until now. Today companies like Google, which have grown up in an era of massively abundant data, don't have to settle for wrong models. Indeed, they don't have to settle for models at all.

Sixty years ago, digital computers made information readable. Twenty years ago, the Internet made it reachable. Ten years ago, the first search engine crawlers made it a single database. Now Google and like-minded companies are sifting through the most measured age in history, treating this massive corpus as a laboratory of the human condition. They are the children of the Petabyte Age.

The Petabyte Age is different because more is different. Kilobytes were stored on floppy disks. Megabytes were stored on hard disks. Terabytes were stored in disk arrays. Petabytes are stored in the cloud. As we moved along that progression, we went from the folder analogy to the file cabinet analogy to the library analogy to—well, at petabytes we ran out of organizational analogies.

At the petabyte scale, information is not a matter of simple three- and four-dimensional taxonomy and order but of dimensionally agnostic statistics. It calls for an entirely different approach, one that requires us to lose the tether of data as something that can be visualized in its totality. It forces us to view data mathematically first and establish a context for it later. For instance, Google conquered the advertising world with nothing more than applied mathematics. It didn't pretend to know anything about the culture and conventions of advertising—it just assumed that better data, with better analytical tools, would win the day. And Google was right.

Google's founding philosophy is that we don't know why this page is better than that one: If the statistics of incoming links say it is, that's good enough. No semantic or causal analysis is required. That's why Google can translate languages without actually "knowing" them (given equal corpus data, Google can translate Klingon into Farsi as easily as it can translate French into German). And why it can match ads to content without any knowledge or assumptions about the ads or the content.

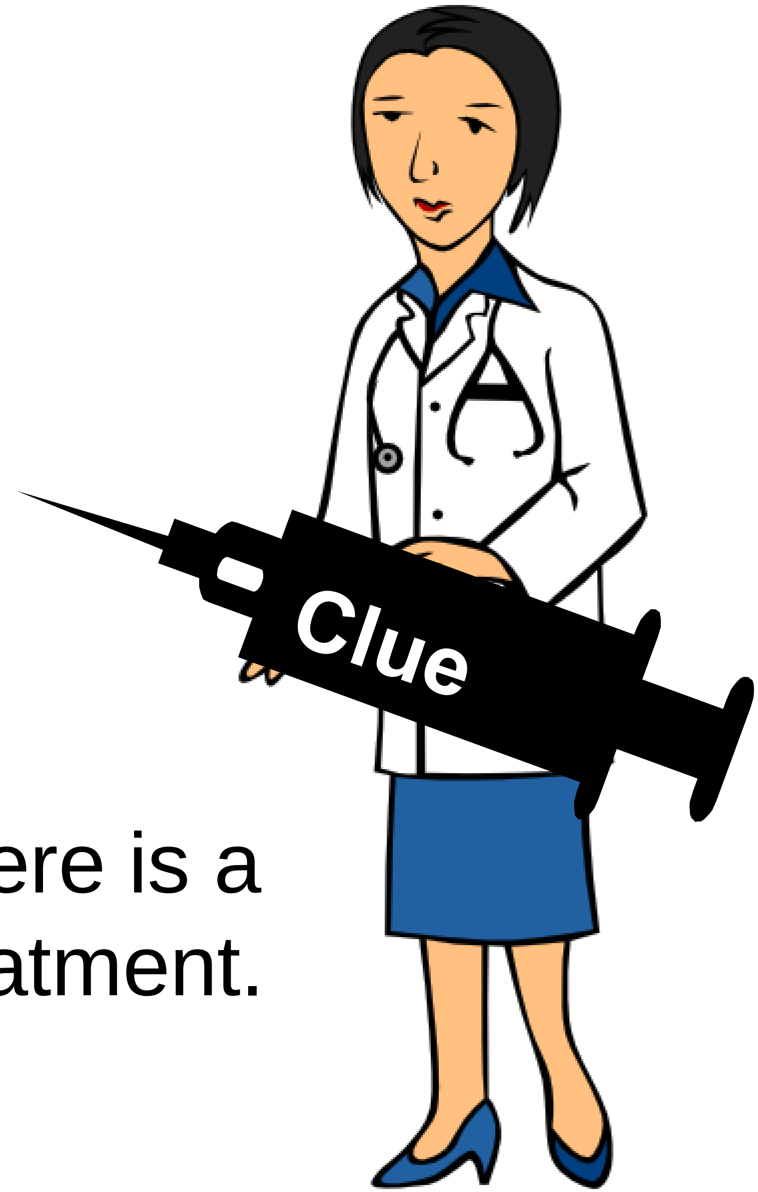
Speaking at the O'Reilly Emerging Technology Conference this past March, Peter Norvig, Google's research director, offered an update to George Box's maxim: "All models are wrong, and increasingly you can succeed without them."

This is a world where massive amounts of data and applied mathematics replace every other tool that might be brought to bear. Out with every theory of human behavior, from linguistics to sociology. Forget taxonomy, ontology, and psychology. Who knows why people do what they do? The point is they do it, and we can track and measure it with unprecedented fidelity. With enough data, the numbers speak for themselves.

The big target here isn't advertising, though. It's science. The scientific method is built around testable hypotheses. These models, for the most part, are systems visualized in the minds of scientists. The models are then tested, and experiments confirm

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

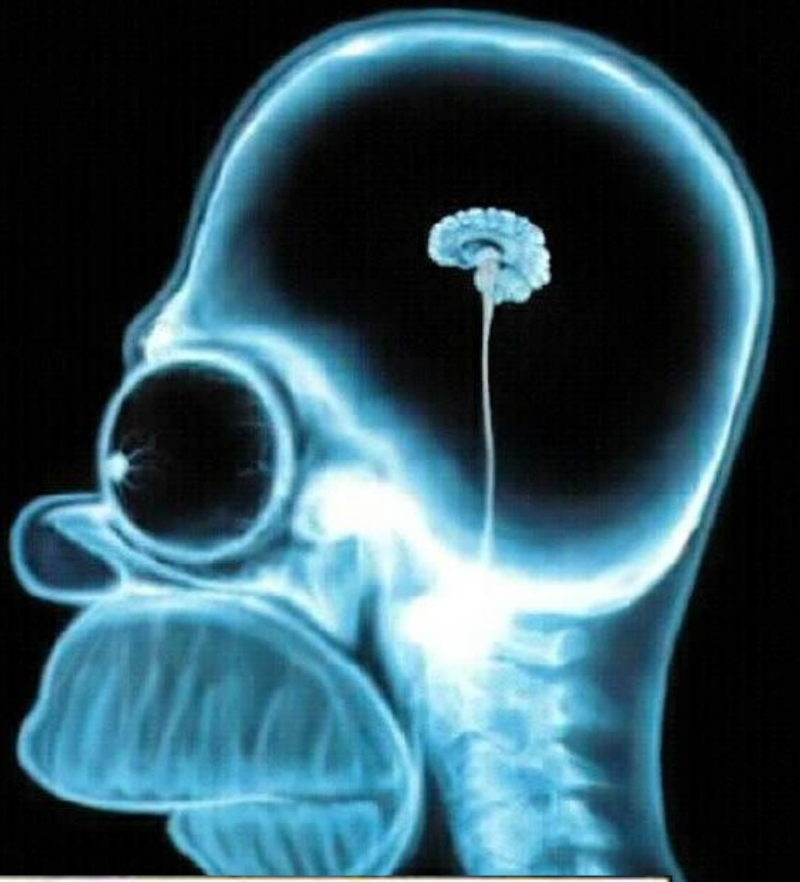
Save our children

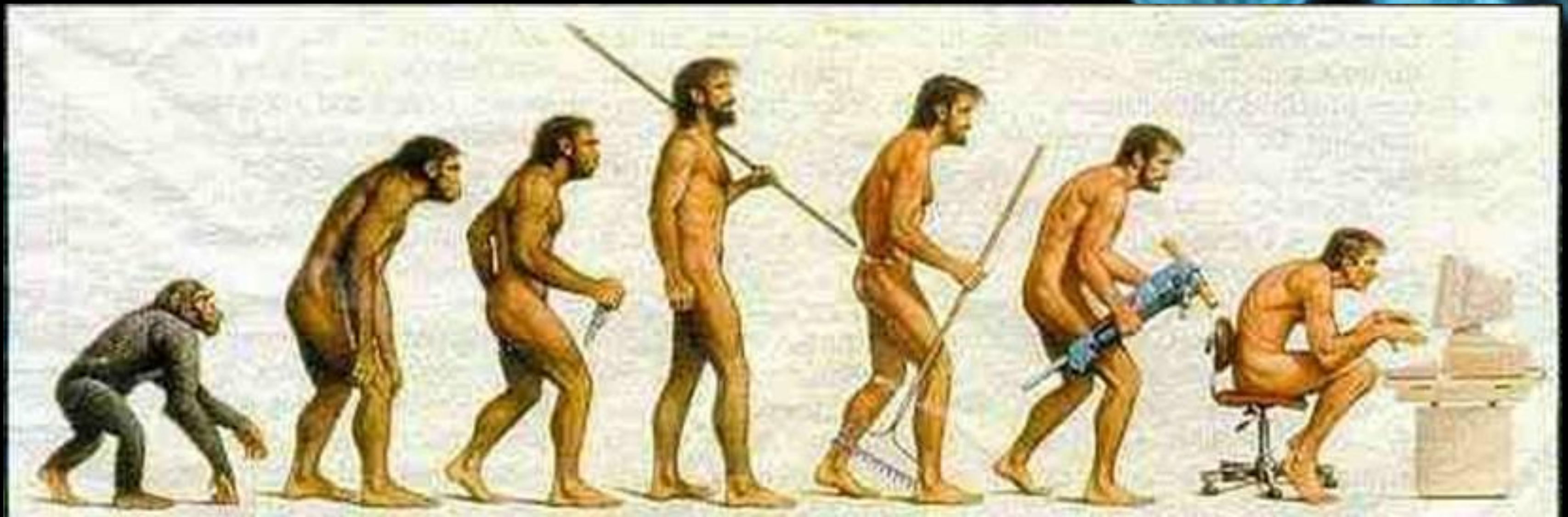


There is a treatment.

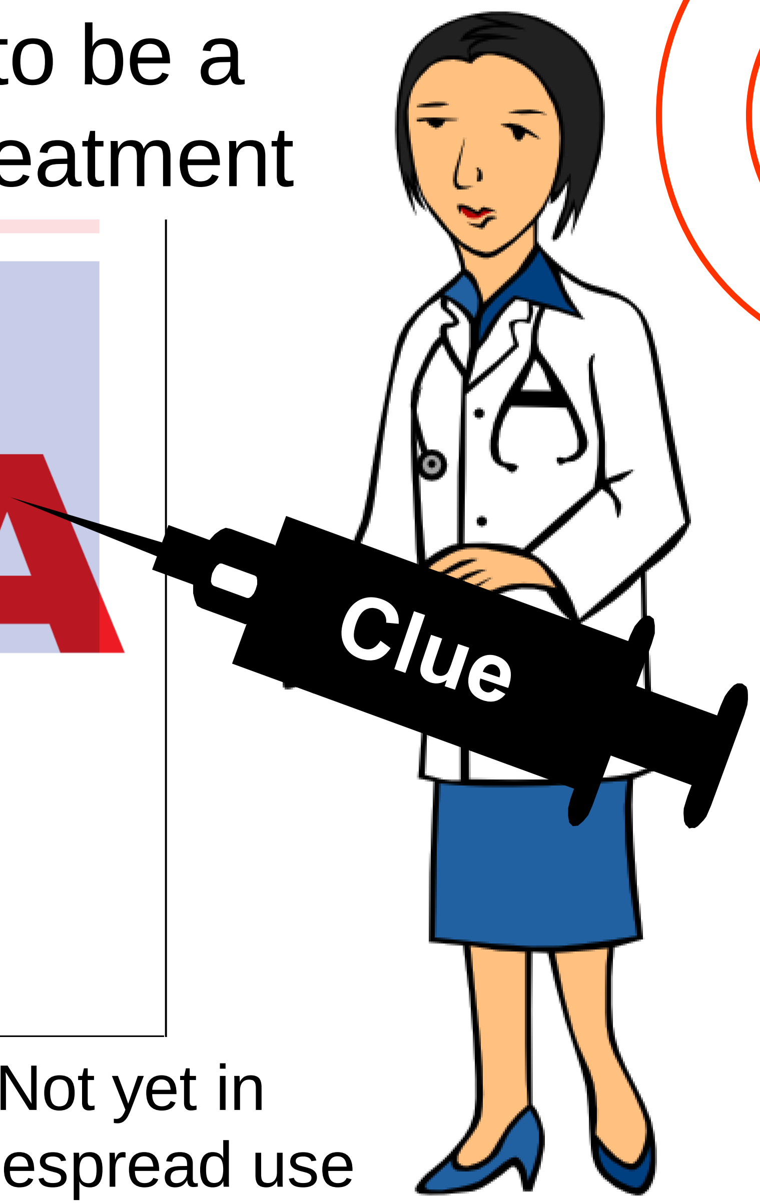
New words

- **Peta-philia**: Perverse love of data and computation
- **Peta-fop**: Someone who profits from peta-philia
- **Exa-duhs**: Loss of clue from excessive peta-philia

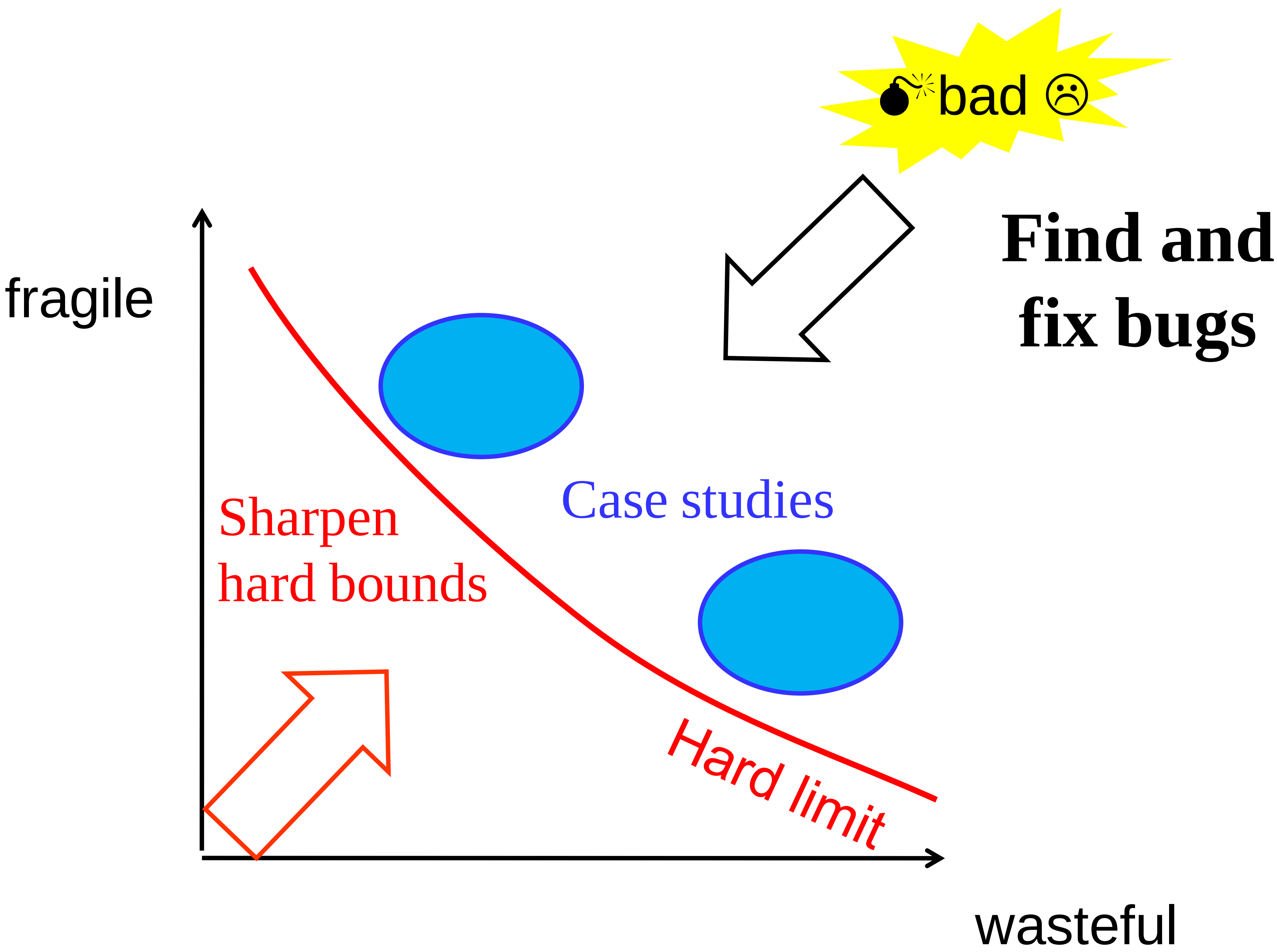




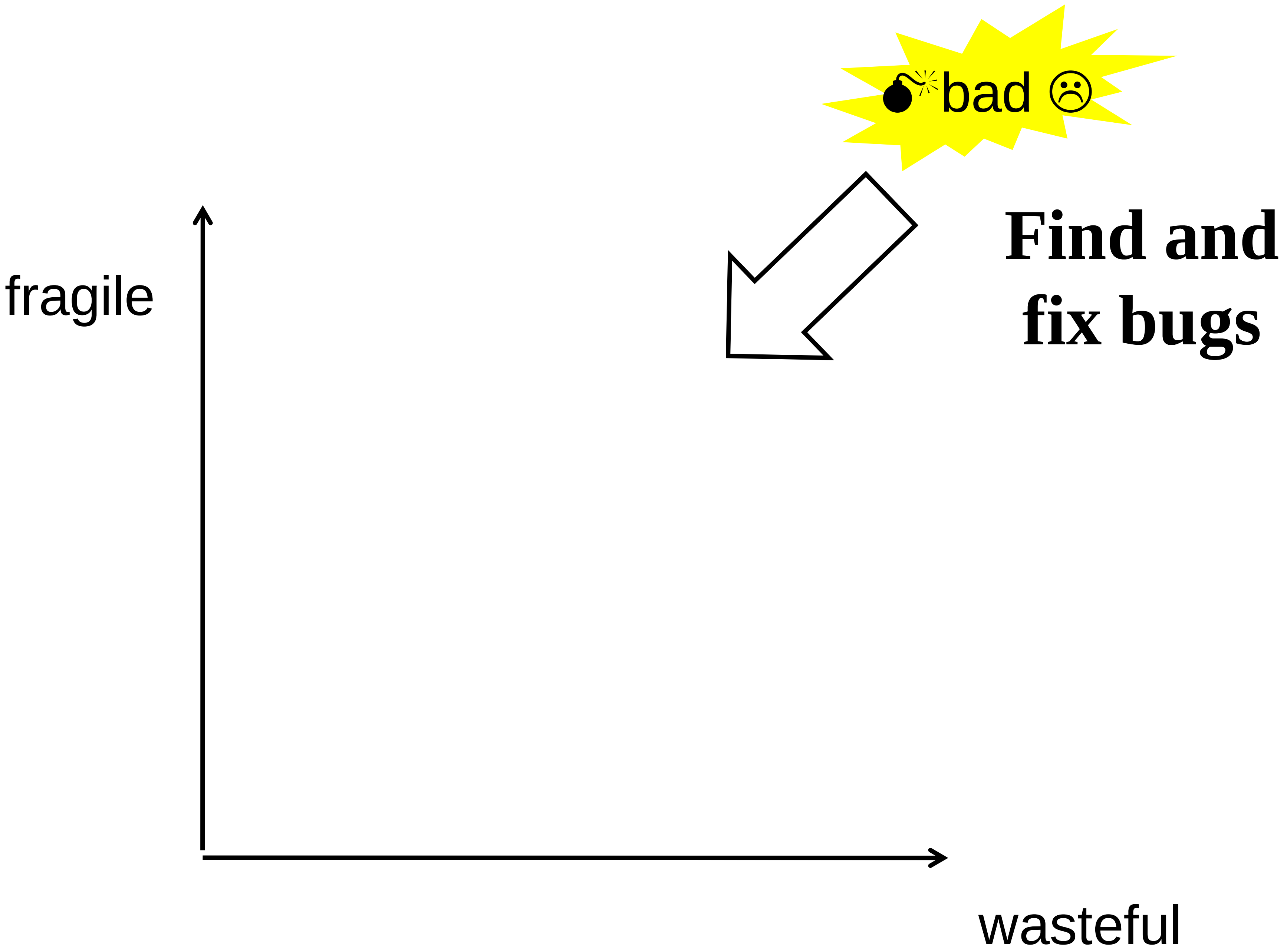
Fortunately there seems to be a treatment

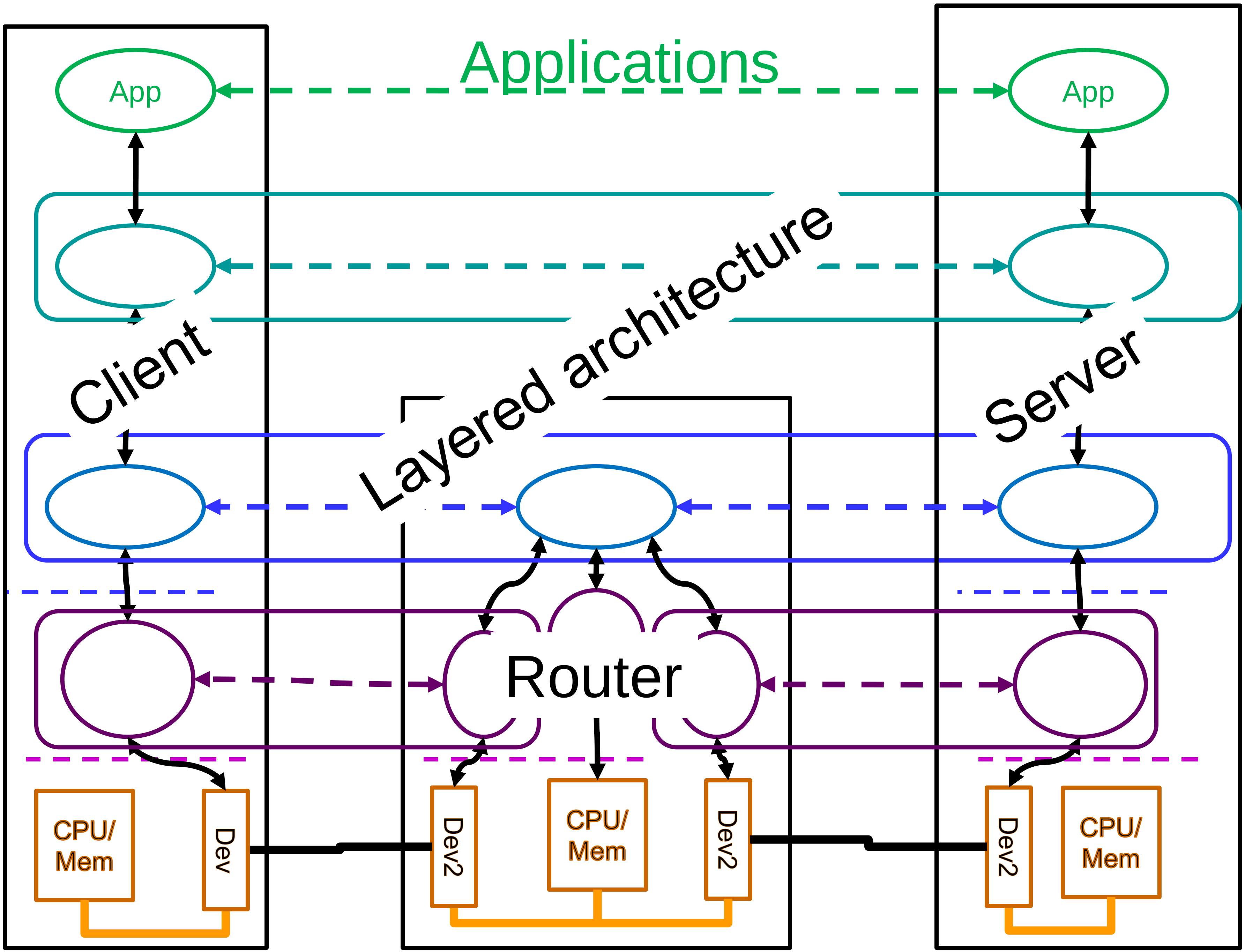


Not yet in widespread use



bad ☹
Find and fix bugs
fragile
Case studies
Sharpen hard bounds
Hard limit
wasteful


💣bad ☹
Find and fix bugs
fragile
wasteful



Applications
App
App
Layered architecture
Client
Server
Router
CPU/
Mem
Dev
Dev2
CPU/
Mem
Dev2
Dev2
CPU/
Mem

Layering as Optimization Decomposition: A Mathematical Theory of Network Architectures

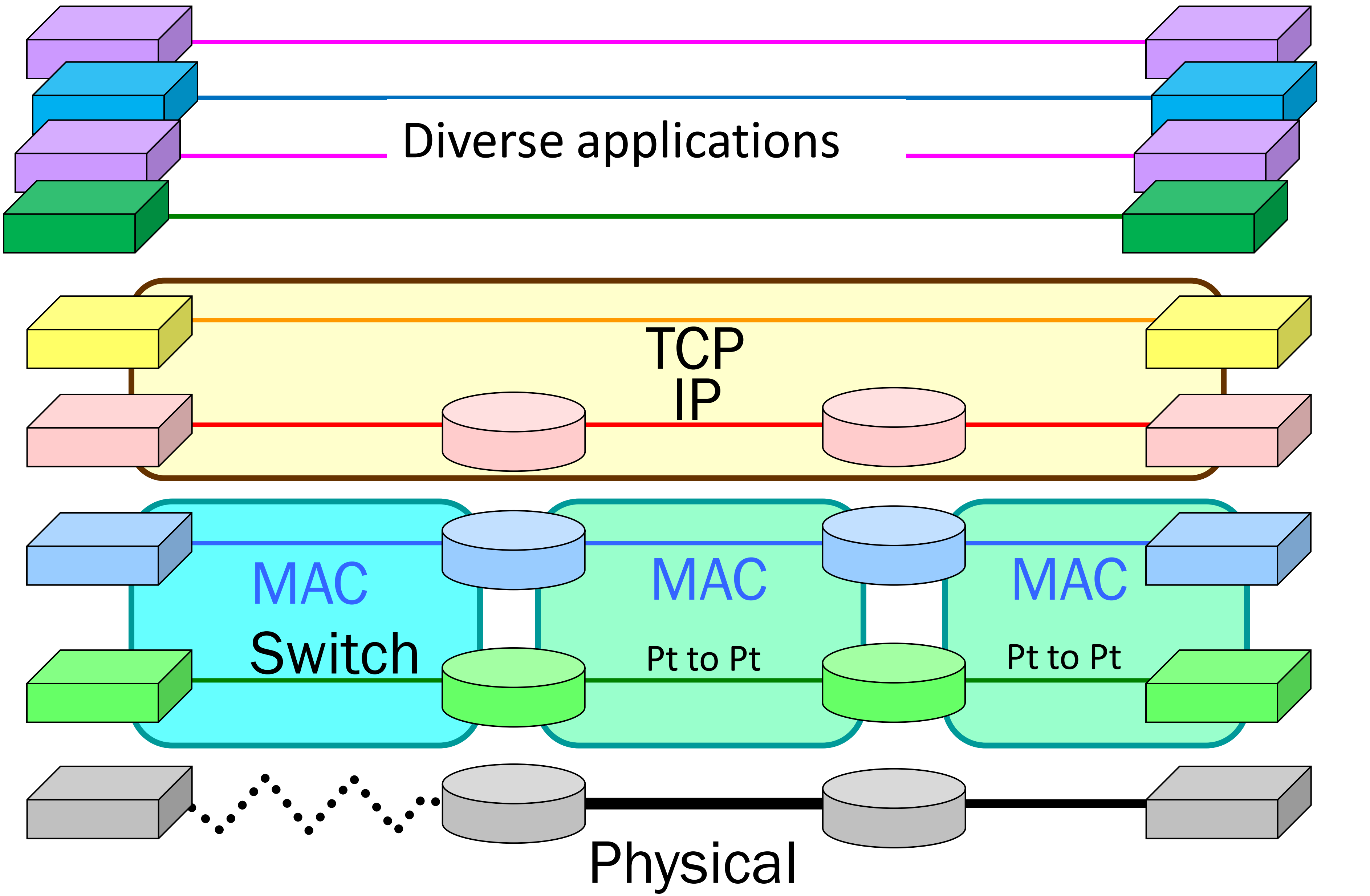
There are various ways that network functionalities can be allocated to different layers and to different network elements, some being more desirable than others. The intellectual goal of the research surveyed by this article is to provide a theoretical foundation for these architectural decisions in networking.

By Mung Chiang, *Member IEEE*, Steven H. Low, *Senior Member IEEE*,
A. Robert Calderbank, *Fellow IEEE*, and John C. Doyle

Chiang, Low, Calderbank, and Doyle

Vol. 95, No. 1, January 2007 | Proceedings of the IEEE

Layered architectures



Control

"Layering as optimization"

- 10+ years of progress & impact…

robust control

- Static optimization → dynamic control
- Wireless, scheduling, net coding, …

Internet

- But….
- Something is ***wrong architecturally***
- Better protocols/control won't fix it

optimization

- Design: from protocols to architectures

Compute

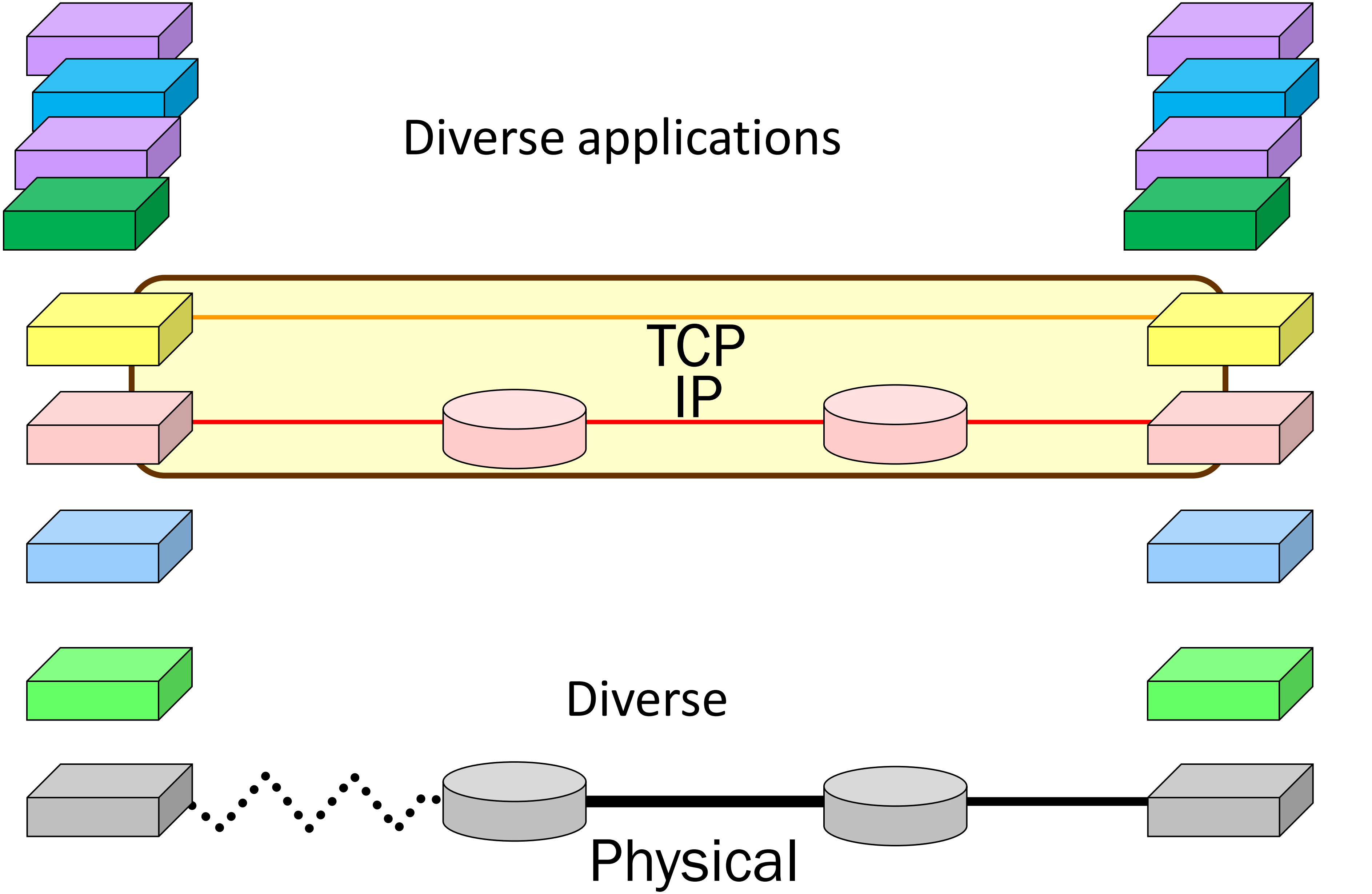
operating systems

Layered architectures everywhere

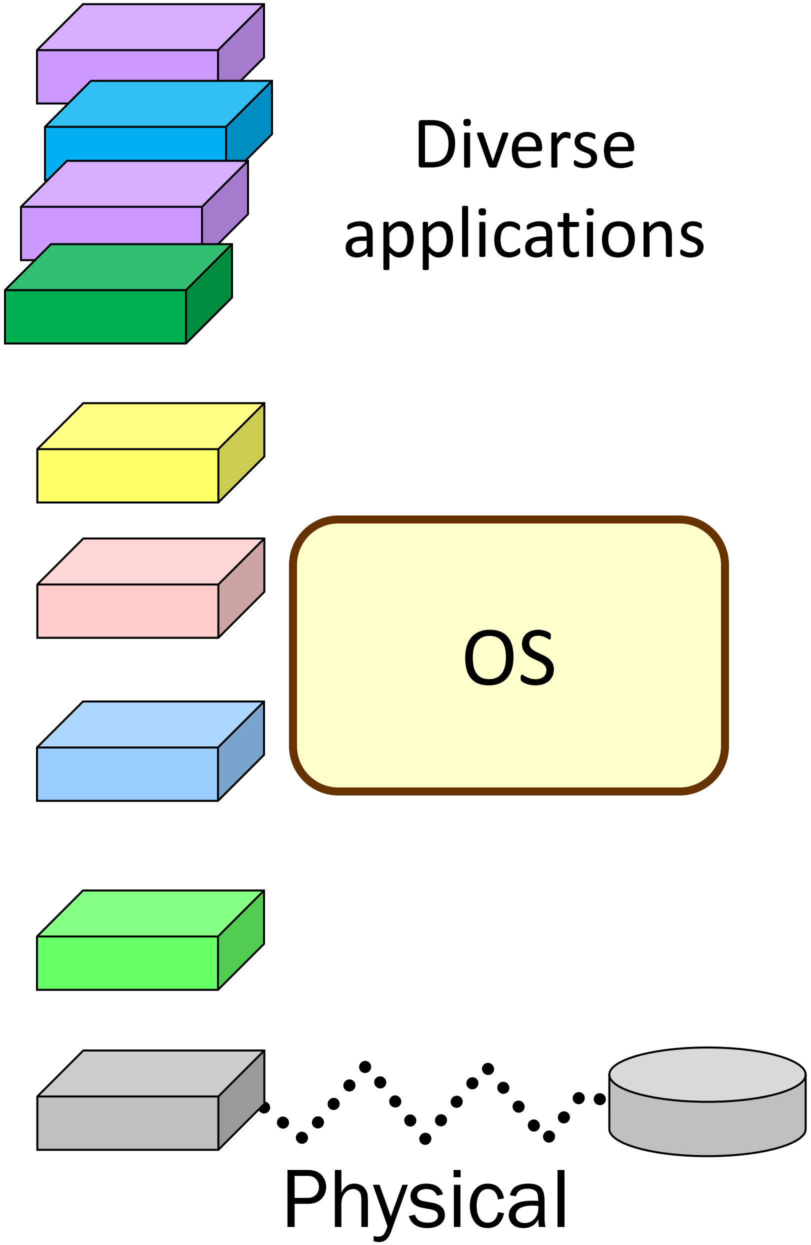
- Computers, Internet, software… cyber-physical?
- Bacterial biosphere
- Evo-devo
- Brain
- Lego, clothing, supply chain, …

- Useful “comparative physiology”

Layered architectures



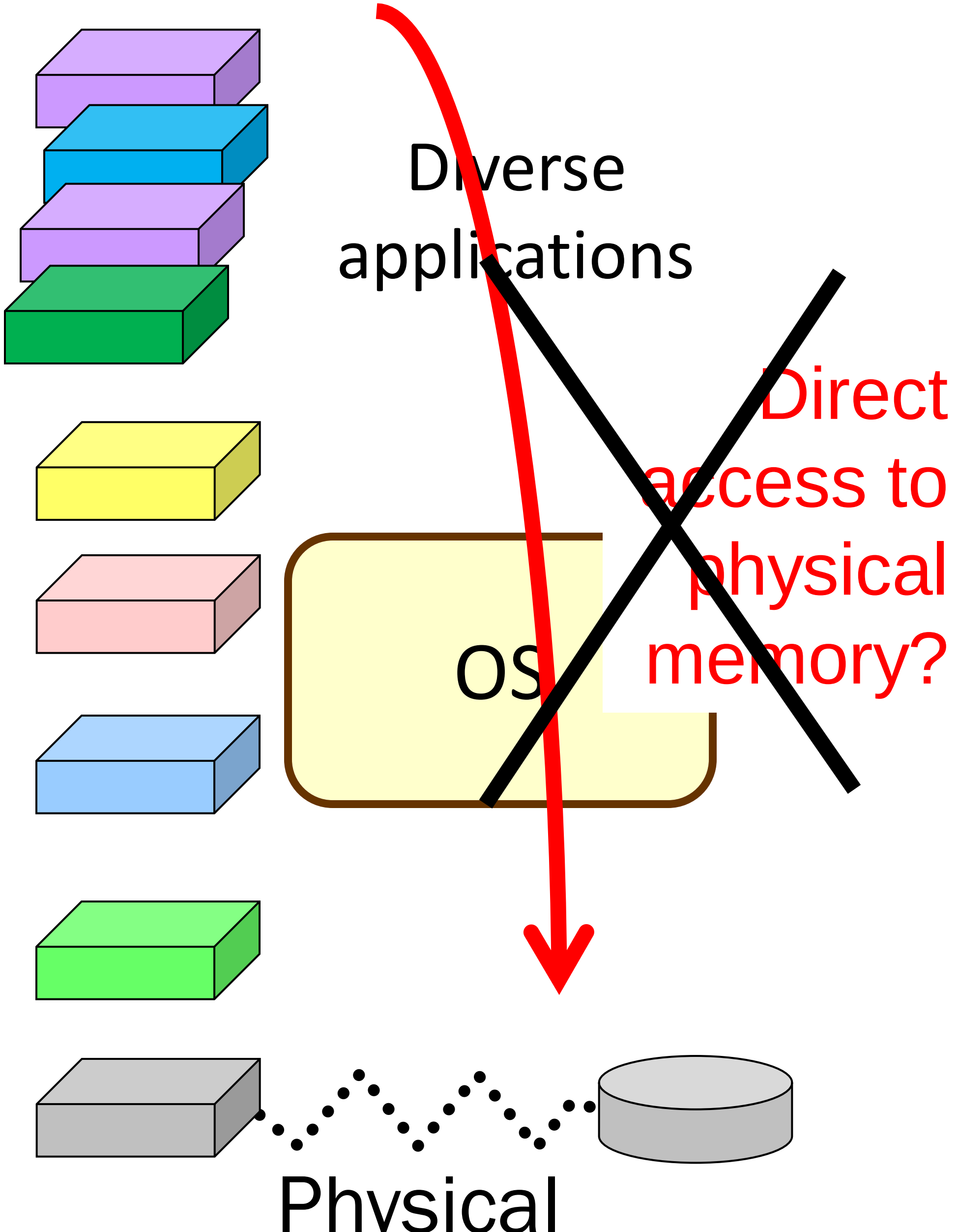
Layered architectures



- OS allocates/shares
  - diverse resources among
  - diverse applications
- “Strict layering” crucial, e.g. clearly separate
  - Application name space
  - Logical (virtual) name/address space
  - Physical (name/) address space

- Name resolution w/in appls
- Name/addr transl X layers

Layered architectures



In programming:
No global variables

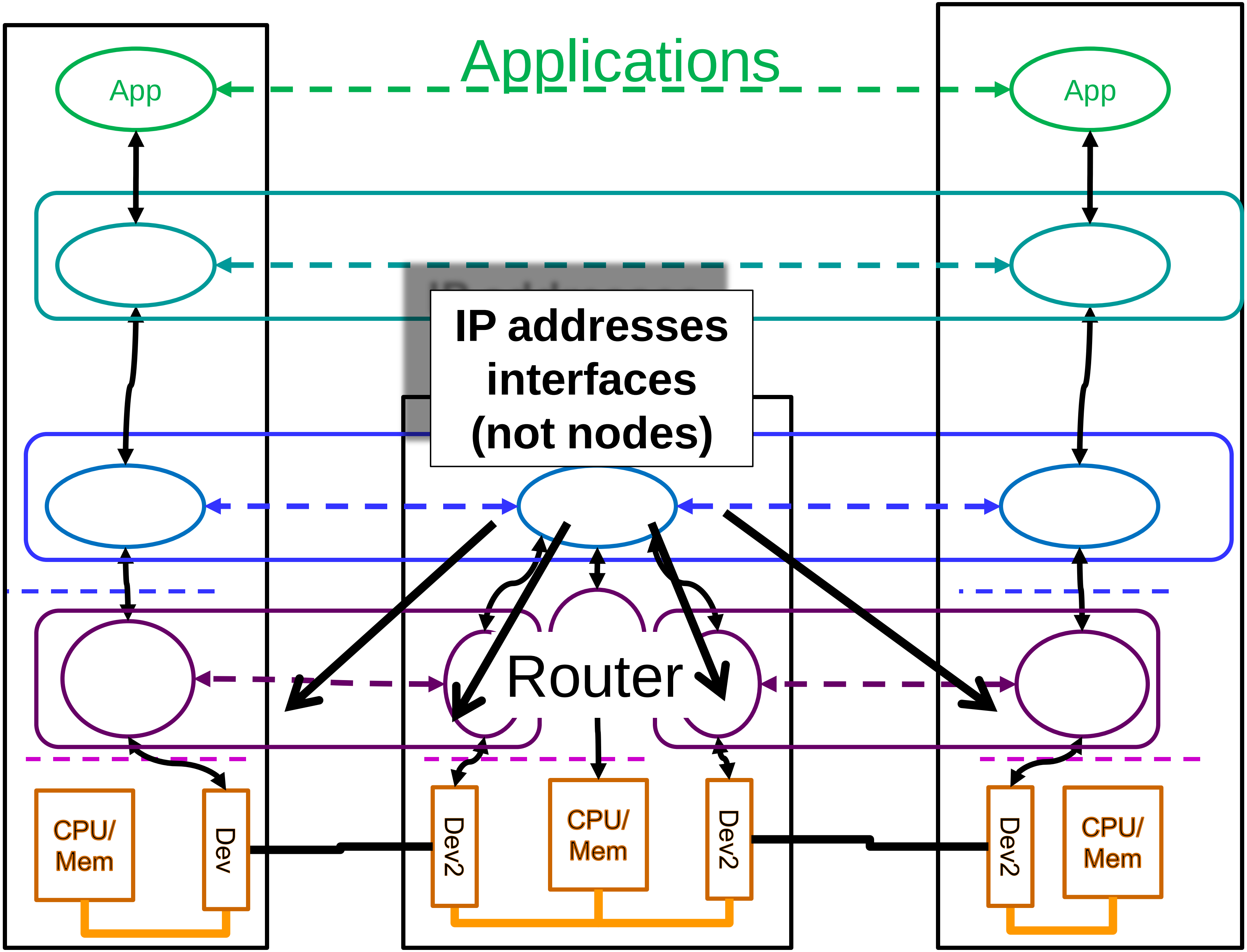
In operating systems:
Don't cross layers (rings)

Problems with *leaky* layering

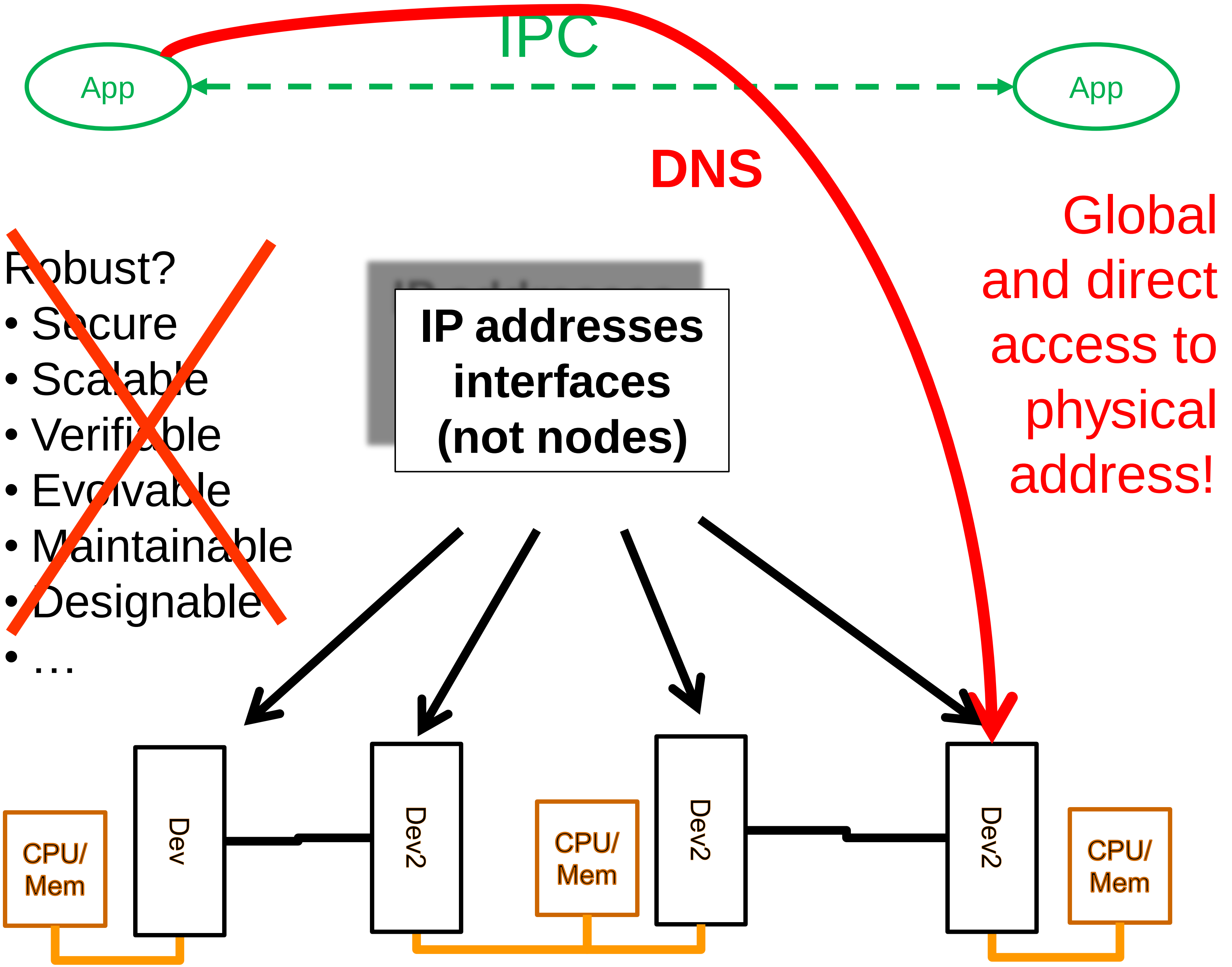
Modularity benefits are lost

- Global variables?   @$%*&!^%@&
- Poor portability of applications
- Insecurity of physical address space
- Fragile to application crashes
- No scalability of virtual/real addressing

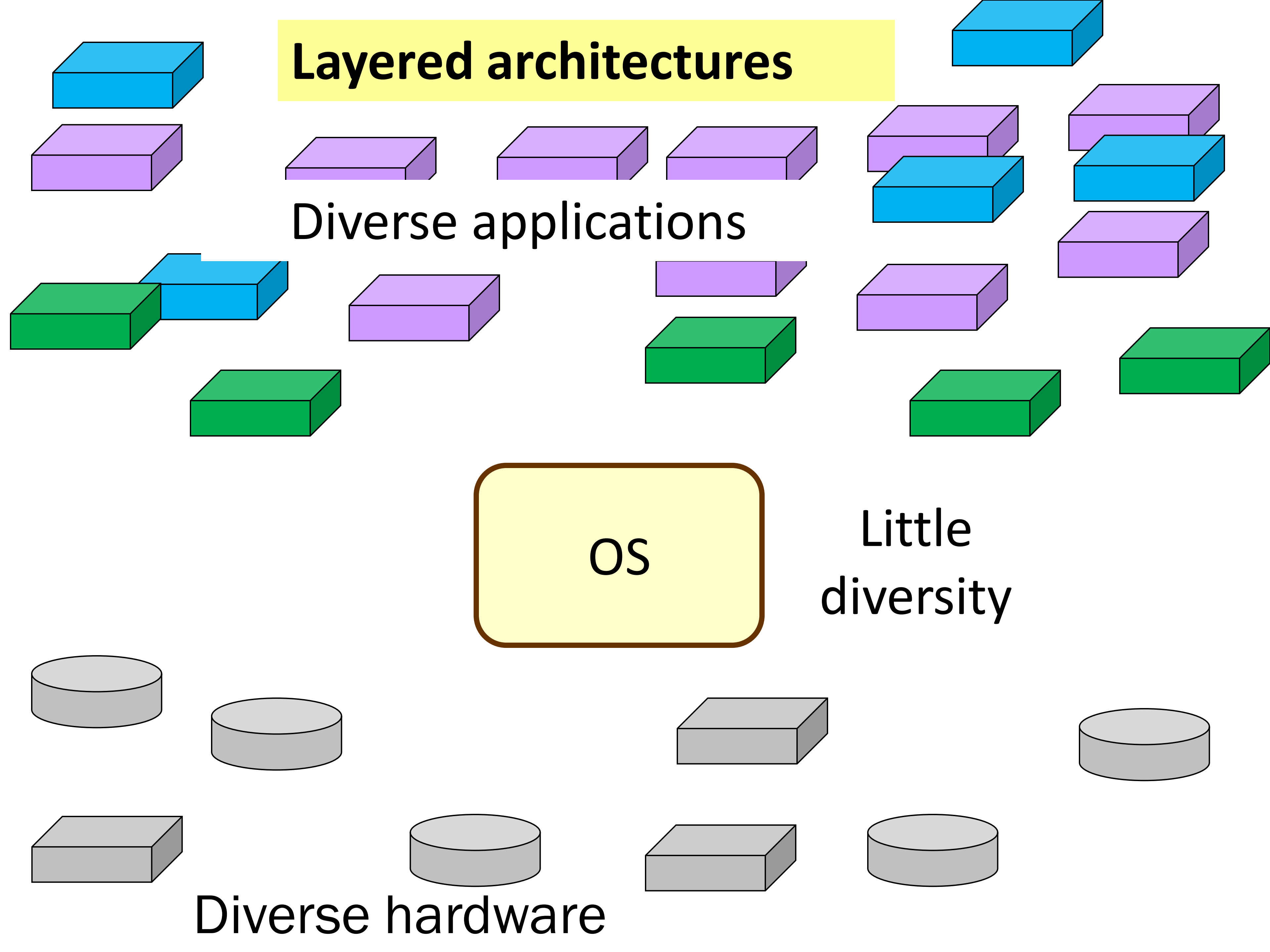
- Limits optimization/control by duality?



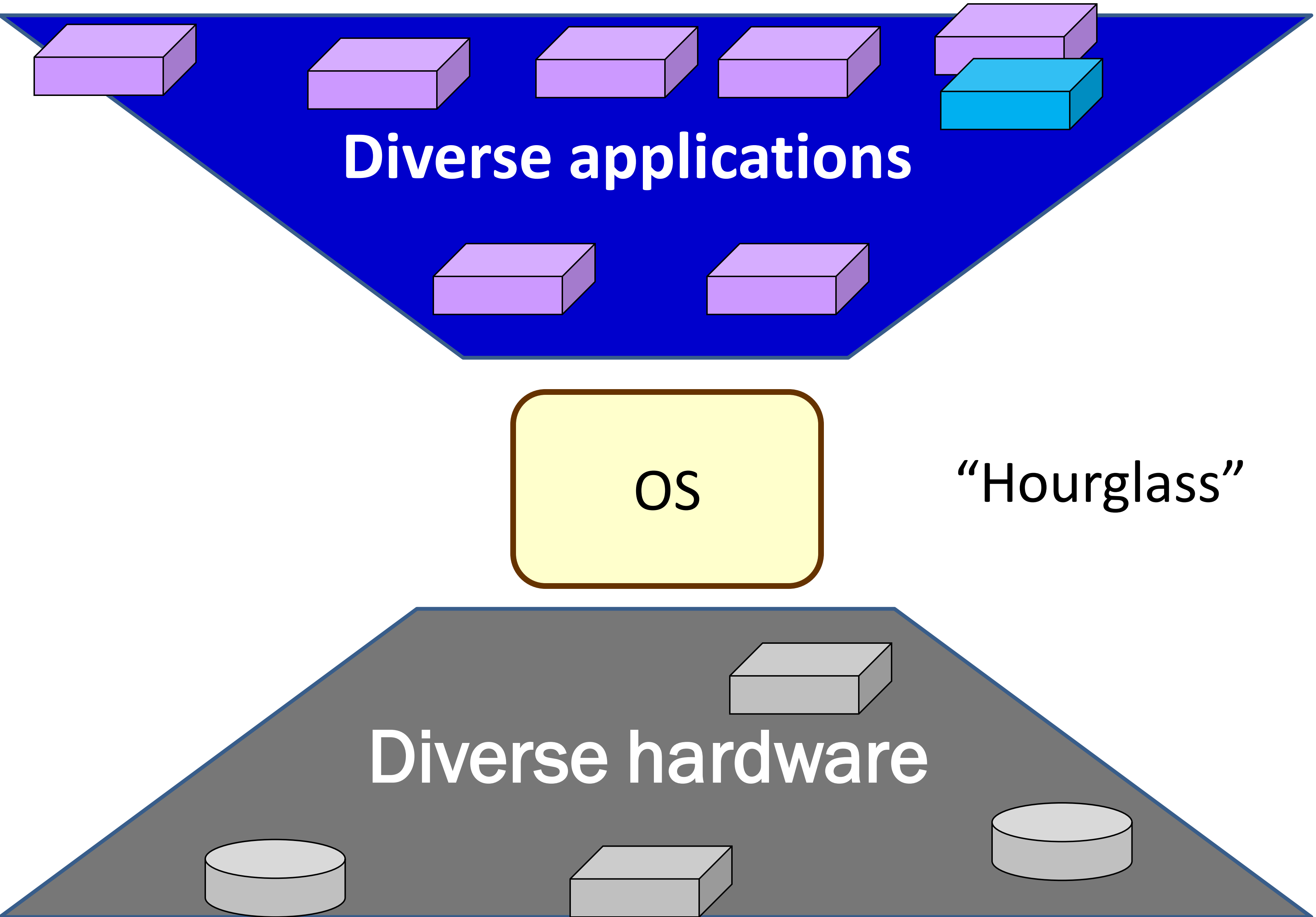
Applications
App
App
IP addresses
interfaces
(not nodes)
Router
CPU/
Mem
Dev
Dev2
CPU/
Mem
Dev2
Dev2
CPU/
Mem



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

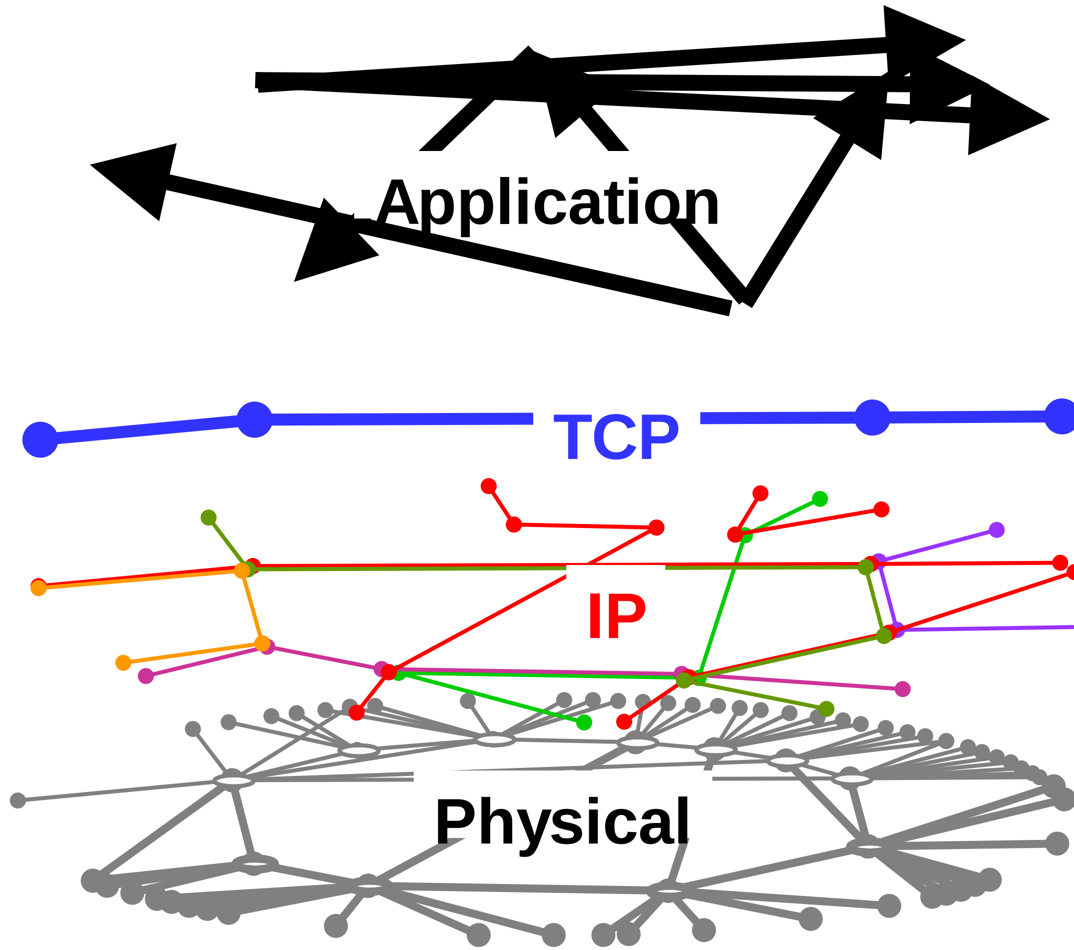

Layered architectures
Diverse applications
OS
Little
diversity
Diverse hardware

Layered architectures

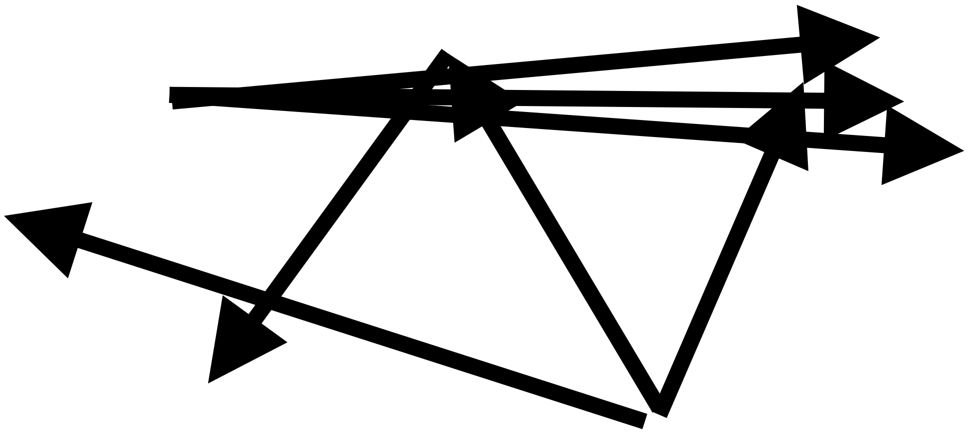


Naming and addressing need to be
- resolved within layer
- translated between layers
- not exposed outside of layer

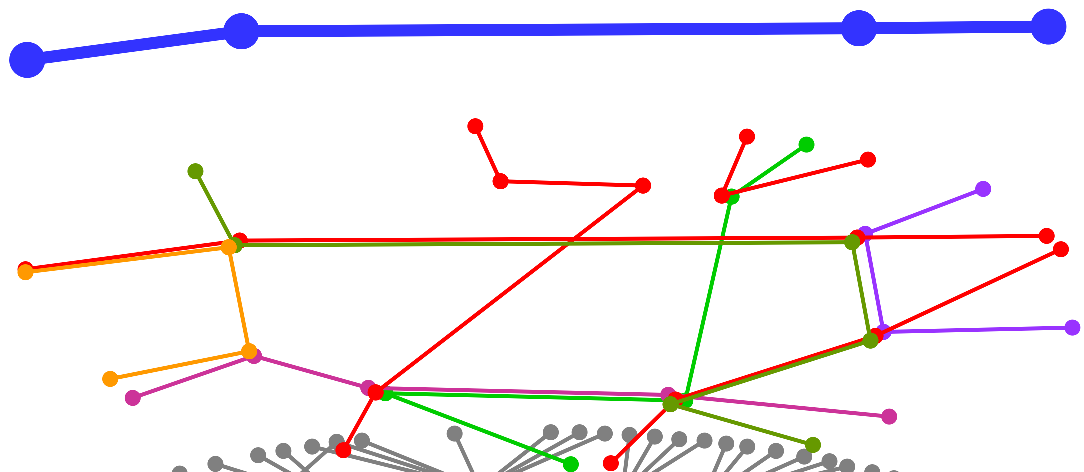
Related “issues”
- DNS
- NATS
- Firewalls
- Multihoming
- Mobility
- Routing table size
- Overlays
- ...



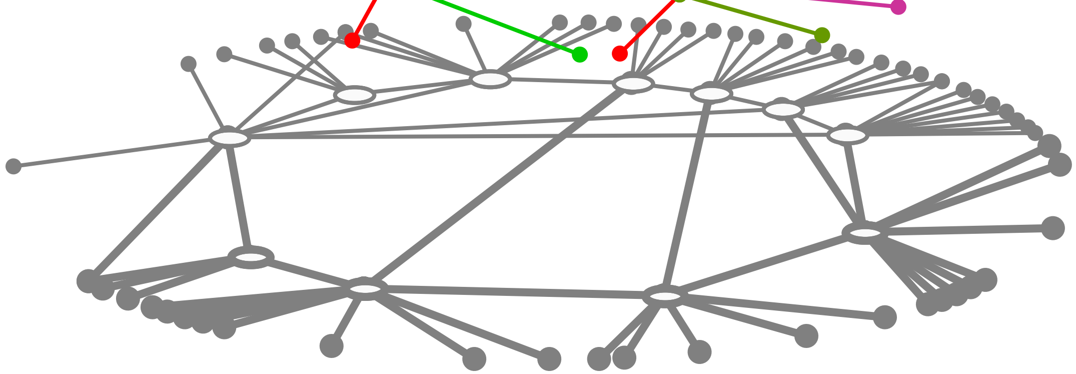
Persistent errors and confusion.



Architecture is ***not*** graph topology.



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

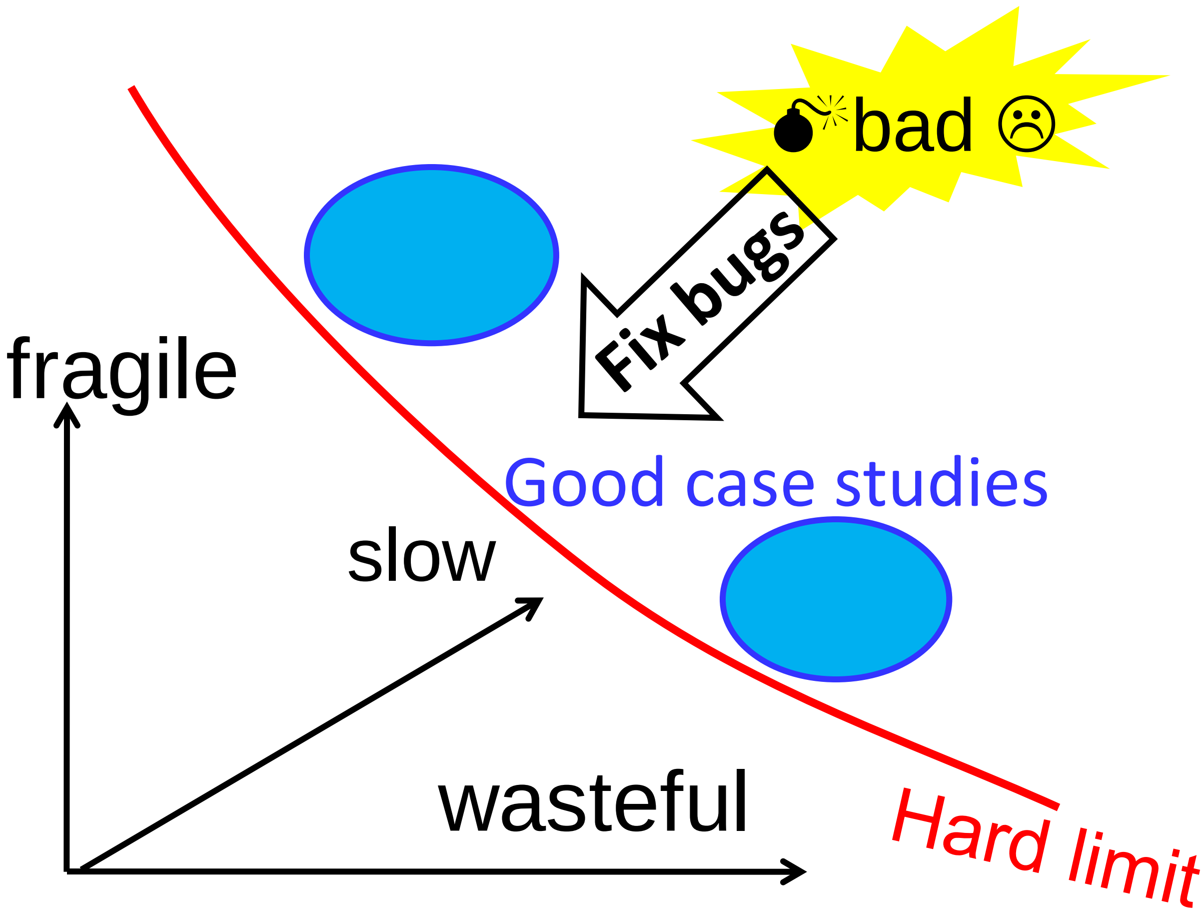
PNAS | October 11, 2005 | vol. 102 | no. 41 | 14497–14502

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

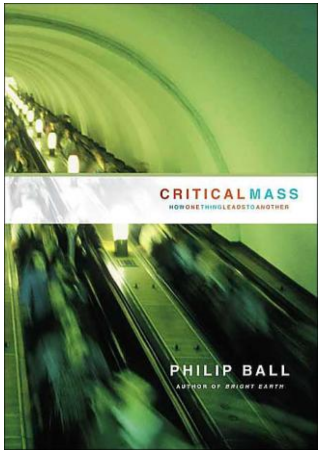
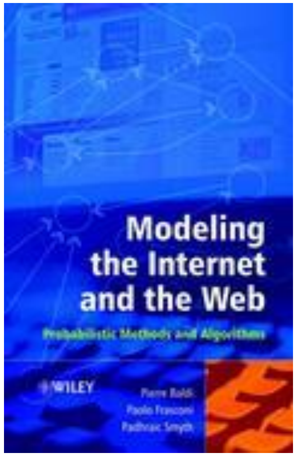
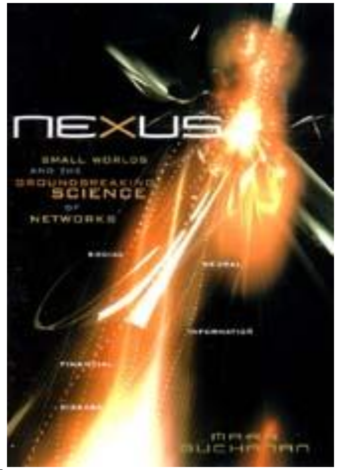
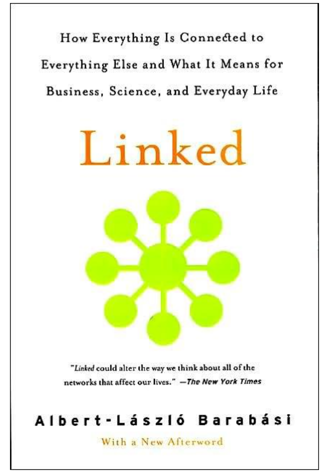
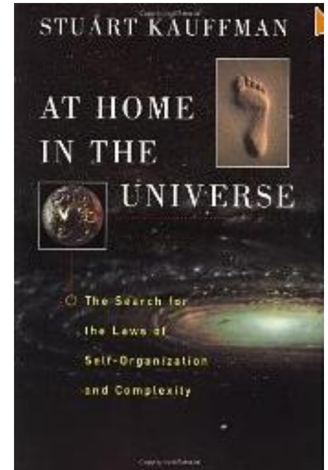
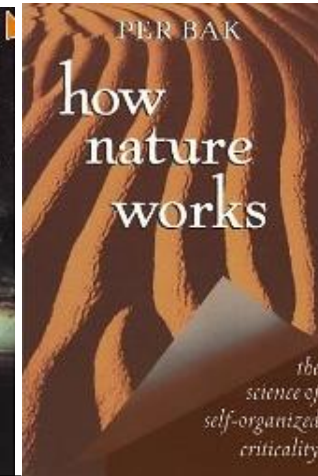
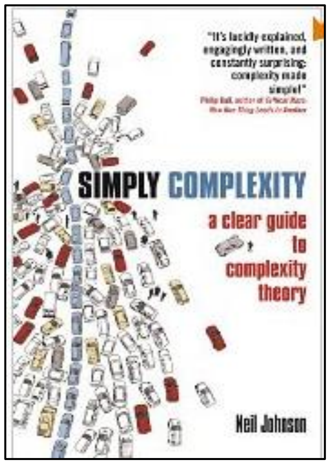
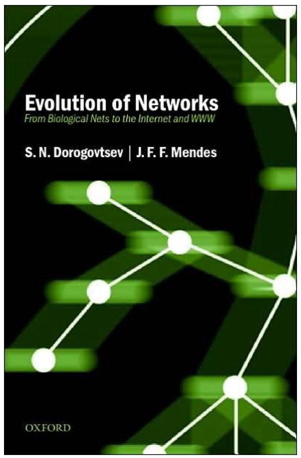
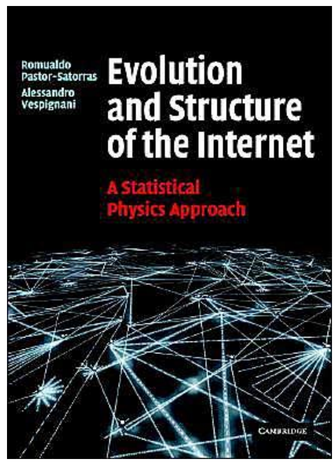
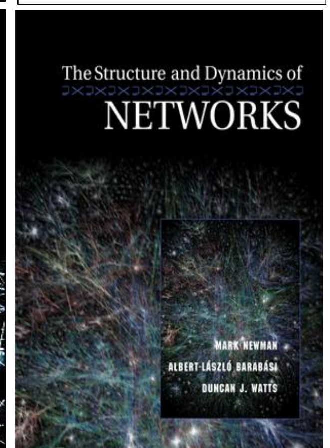
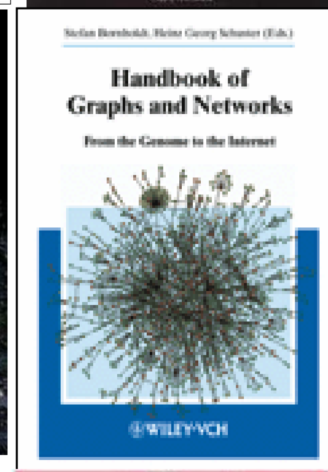
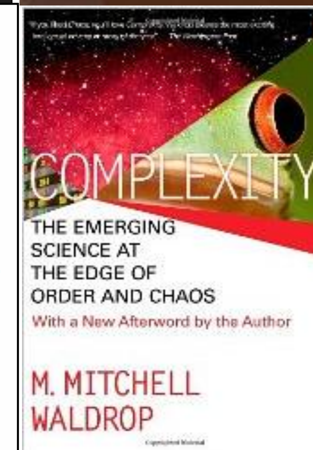
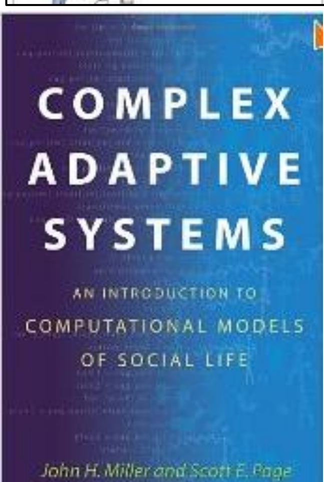
"New sciences" of "complexity" and "networks"?



"New sciences" of "complexity" and "networks"?

- Science as pure fashion
- Ideological
- Political
- Evangelical
- Nontech trumps tech

- Edge of chaos
- Self-organized criticality
- Scale-free "networks"
- Creation "science"
- Intelligent design
- Financial engineering
- Risk management
- "Merchants of doubt"
- …


CRITICAL MASS
HOW ONE THING LEADS TO ANOTHER
PHILIP BALL
AUTHOR OF BRIGHT EARTH

Modeling the Internet and the Web
Probabilistic Methods and Algorithms
WILEY
Pierre Baldi
Paolo Frasconi
Padhraic Smyth

NEXUS
SMALL WORLDS AND THE GROUNDBREAKING SCIENCE OF NETWORKS
MARK BUCHANAN

How Everything Is Connected to Everything Else and What It Means for Business, Science, and Everyday Life
Linked
"Linked could alter the way we think about all of the networks that affect our lives." —The New York Times
Albert-László Barabási
With a New Afterword

STUART KAUFFMAN
AT HOME IN THE UNIVERSE
The Search for the Laws of Self-Organization and Complexity

PER BAK
how nature works
the science of self-organized criticality

"It's lucidly explained, engagingly written, and constantly surprising: complexity made simple!"
SIMPLY COMPLEXITY
a clear guide to complexity theory
Neil Johnson

Evolution of Networks
From Biological Nets to the Internet and WWW
S. N. Dorogovtsev | J. F. F. Mendes
OXFORD

Romualdo Pastor-Satorras
Alessandro Vespignani
Evolution and Structure of the Internet
A Statistical Physics Approach
CAMBRIDGE

The Structure and Dynamics of
NETWORKS
MARK NEWMAN
ALBERT-LÁSZLÓ BARABÁSI
DUNCAN J. WATTS

Handbook of Graphs and Networks
From the Genome to the Internet
WILEY-VCH

COMPLEXITY
THE EMERGING SCIENCE AT THE EDGE OF ORDER AND CHAOS
With a New Afterword by the Author
M. MITCHELL WALDROP

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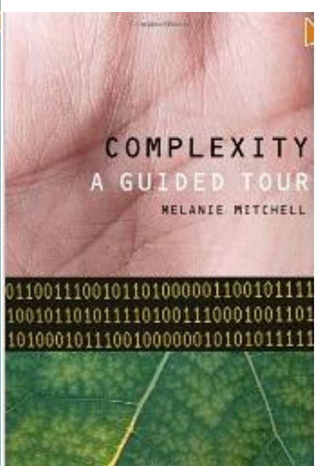
AN INTRODUCTION TO COMPUTATIONAL MODELS OF SOCIAL LIFE
John H. Miller and Scott E. Page

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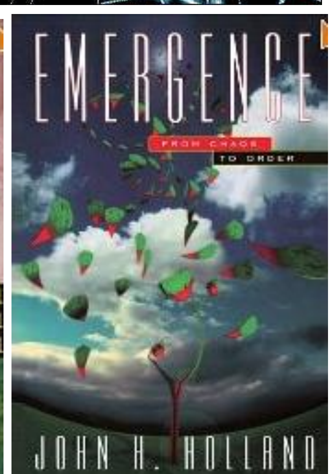
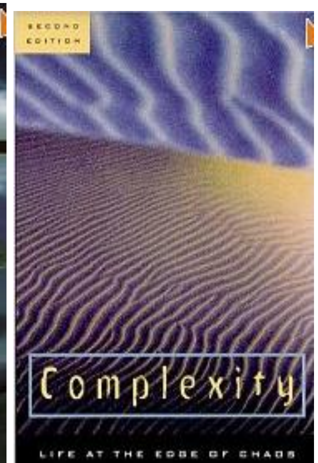
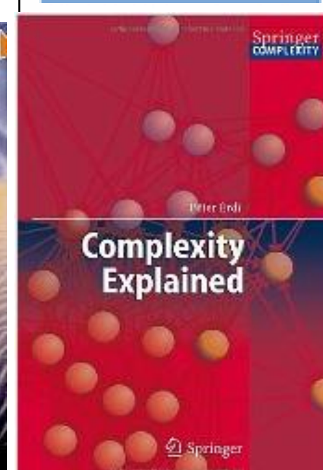
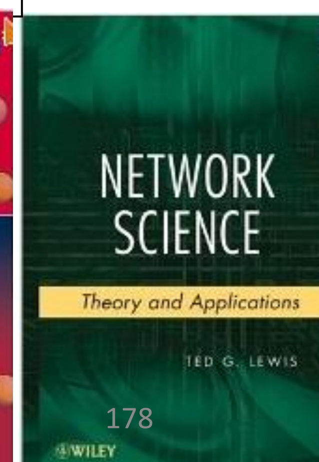
MELANIE MITCHELL

EMERGENCE
FROM CHAOS TO ORDER
JOHN H. HOLLAND

SECOND EDITION
Complexity
LIFE AT THE EDGE OF CHAOS

Springer COMPLEXITY
Péter Érdi
Complexity Explained
Springer

NETWORK SCIENCE
Theory and Applications
TED G. LEWIS
WILEY

Complexity = hard to understand, explain

- “Complexity science” = persistently in error
  - bionetworks: gene regulation, metabolism, PPI
  - wildfires, earthquakes
  - Internet, power grid
- Minimal impact on technology
- Diminishing impact on biology
- Of concern in medicine, neuroscience

Complex systems?

Even small amounts can create bewildering complexity

Fragile

- Scale
- Dynamics
- Nonlinearity
- Nonequlibrium
- Open
- Feedback
- Adaptation
- Intractability
- Emergence
- …

Complex systems?

Robust

- Scale
- Dynamics
- Nonlinearity
- Nonequlibrium
- Open
- Feedback
- Adaptation
- Intractability
- Emergence
- …

Fragile

- Scale
- Dynamics
- Nonlinearity
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Complex systems?

Robust complexity

- Scale
- Dynamics
- Nonlinearity
- Nonequlibrium
- Open
- Feedback
- Adaptation
- Intractability
- Emergence
- …

- Resources
- Controlled
- Organized
- Structured
- Extreme
- ***Architected***
- …

Architecture

Robust complexity

- Scale
- Dynamics
- Nonlinearity
- Nonequlibrium
- Open
- Feedback
- Adaptation
- Intractability
- Emergence
- …

- Resources
- Controlled
- Organized
- Structured
- Extreme
- Architected
- …

New words

Emergulent

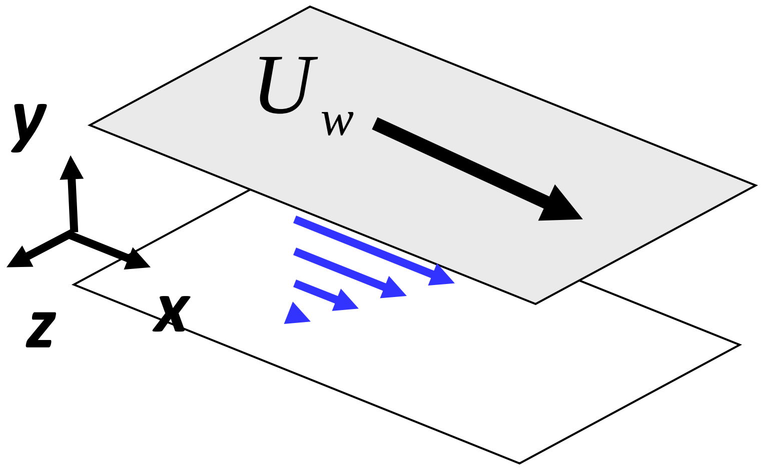
Emergulence at the edge of chaocritiplexity

Fragile complexity

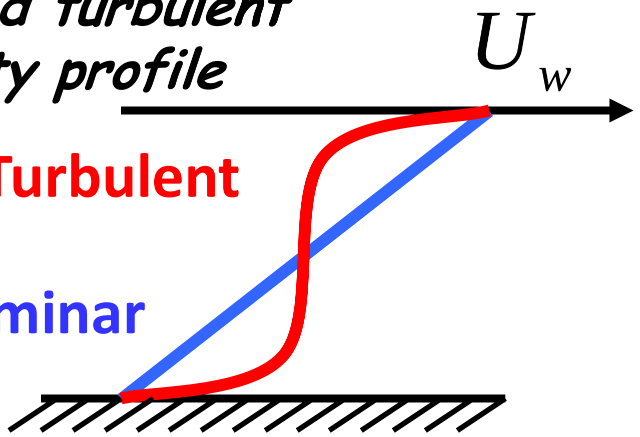
- Scale
- Dynamics
- Nonlinearity
- Nonequlibrium
- Open
- Feedback
- Adaptation
- Intractability
- Emergence
- …

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

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



"turbulence is a highly nonlinear phenomena"



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

Complexity?

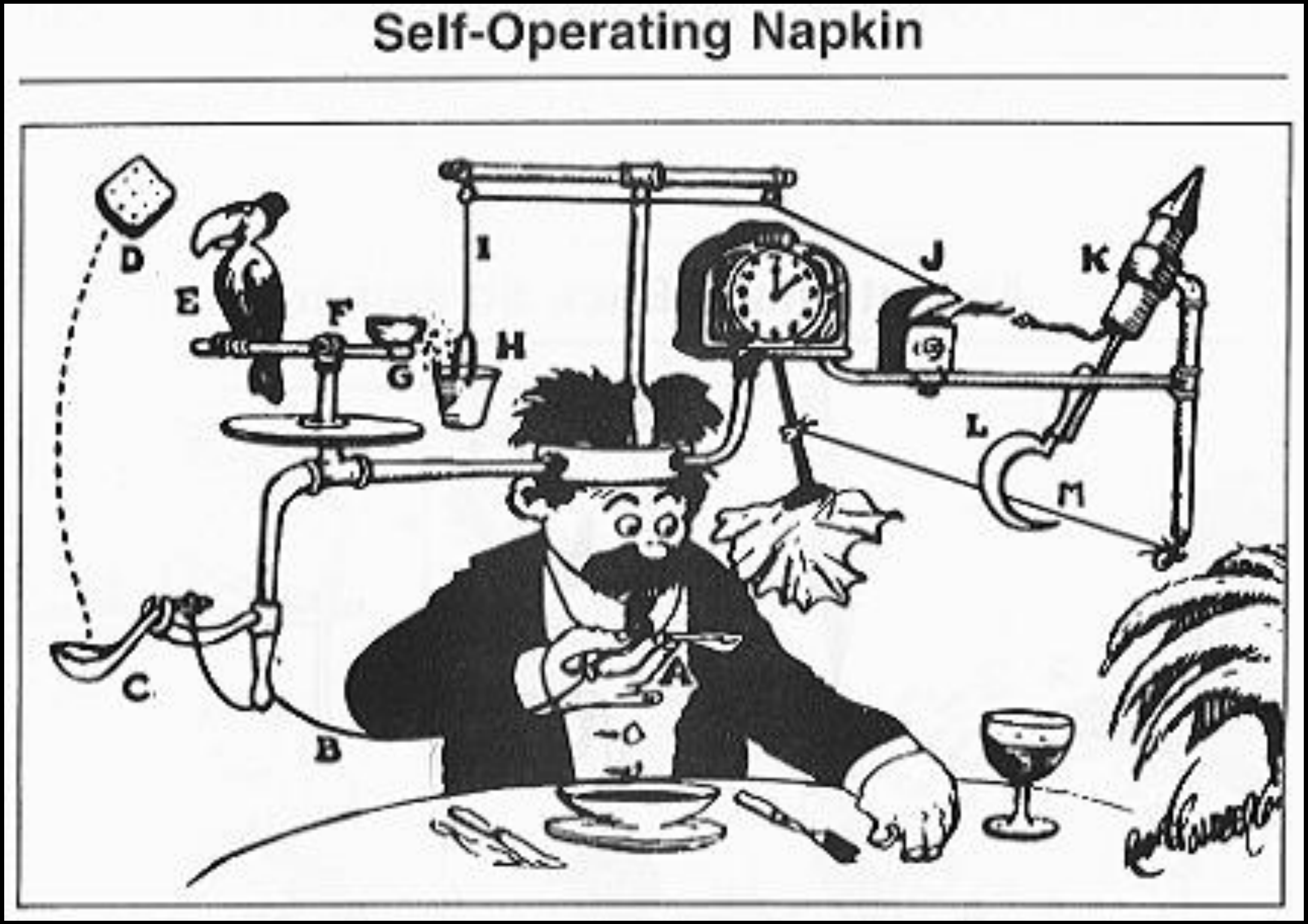
$$\nabla \bullet \underline{u} = 0$$

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

mildly nonlinear

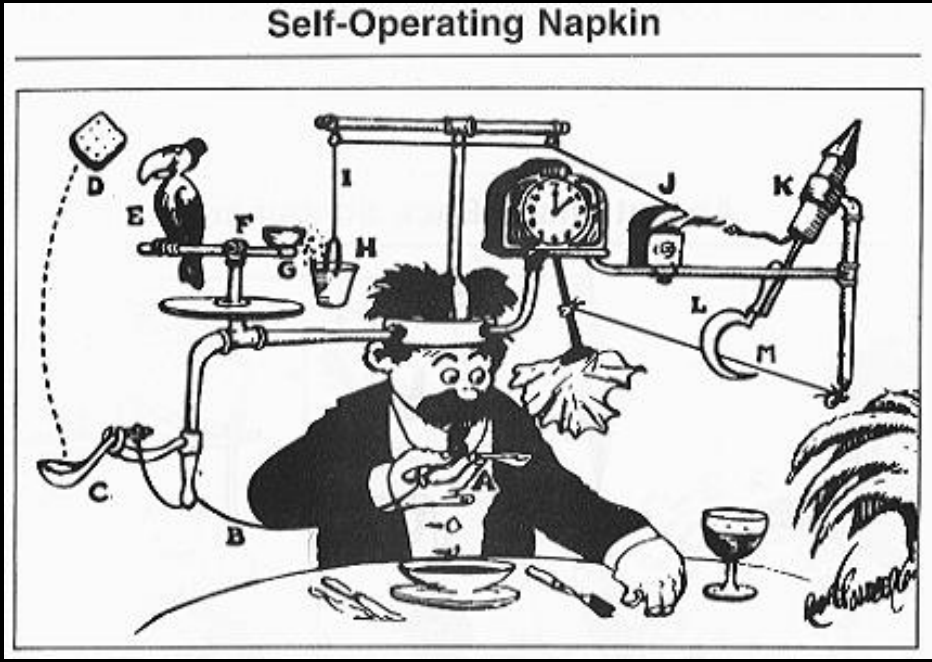
highly nonlinear

Irreducibility and "intelligent design"



Rube Goldberg

The essential ID argument

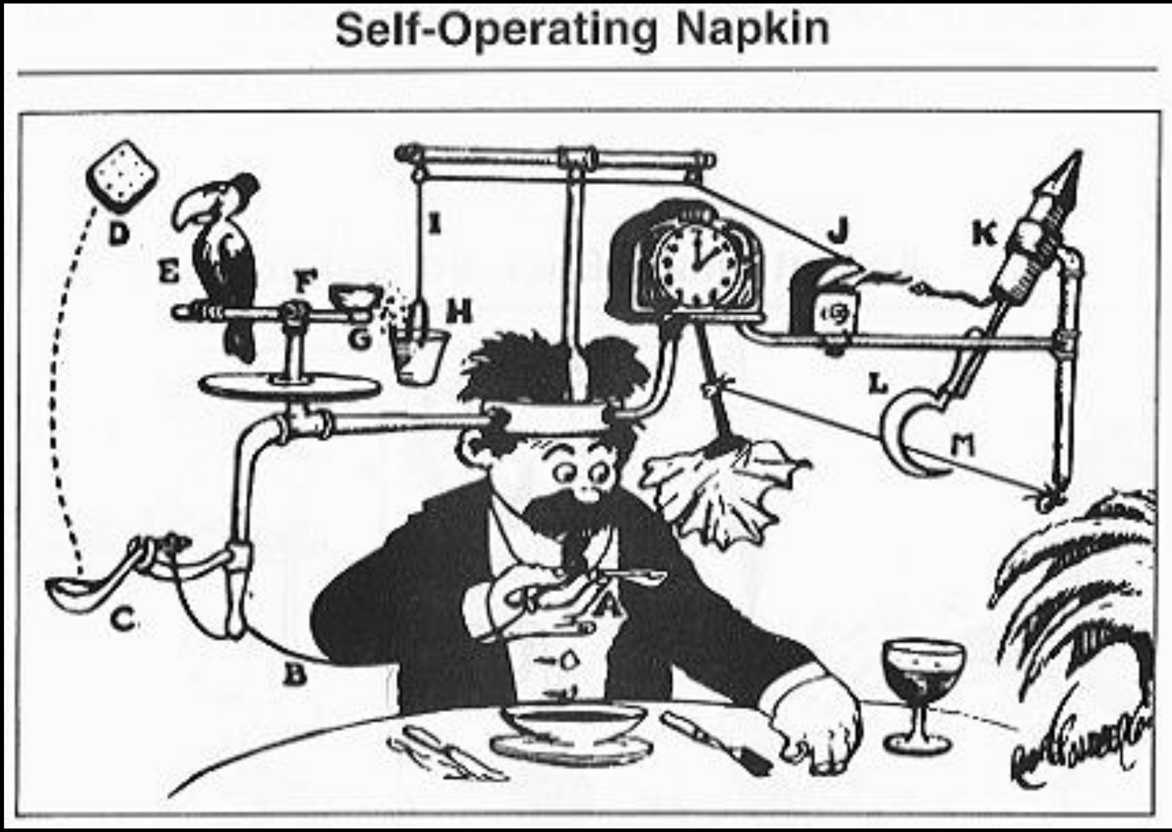


If biology is like this,
then it could not have evolved.

- This is actually ***true***, and in fact…
- ***If*** biology is like this,
- ***then*** it would be too fragile to persist,
- and would need the ***constant intervention*** of supernatural forces

The flaw

This is a cartoon.



- It is too fragile to actually build.
- Neither biology nor (most of) technology is ***anything*** like this.
- Who said otherwise? Lots of ***real*** scientists!
- Oops! (But we ***are*** too fragile and unsustainable.)