Universal laws and architecture:

Theoretical foundations for complex networks relevant to biology, medicine, and neuroscience?

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

Thanks again

Lectures

- 1) Concrete motivation
- 2-3) Universal laws and architectures*
- 4) A teensy bit of math

^{*}have you ever heard of anything more pretentious?

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**.

Architecture, constraints, and behavior

Very accessible

No math

John C. Doylea,1 and Marie Cseteb,1

^aControl and Dynamical Systems, California Institute of Technology, Pasadena, CA 91125; and ^bDepartment 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 and Csete, *Proc Nat Acad Sci USA*, JULY 25 2011

Lectures

- 1) Concrete motivation (recap)
- 2-3) Universal laws and architectures*
- 4) A teensy bit of math

^{*}have you ever heard of anything more pretentious?

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?

Human complexity



Accident or necessity?

Robust Fragile

Metabolism

Obesity, diabetes

- Regenerati
- Second Fat accumulation
- Healing wc
- 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?



Robust

Modular

Simple

Plastic

Evolvable

Fragile Dietribu

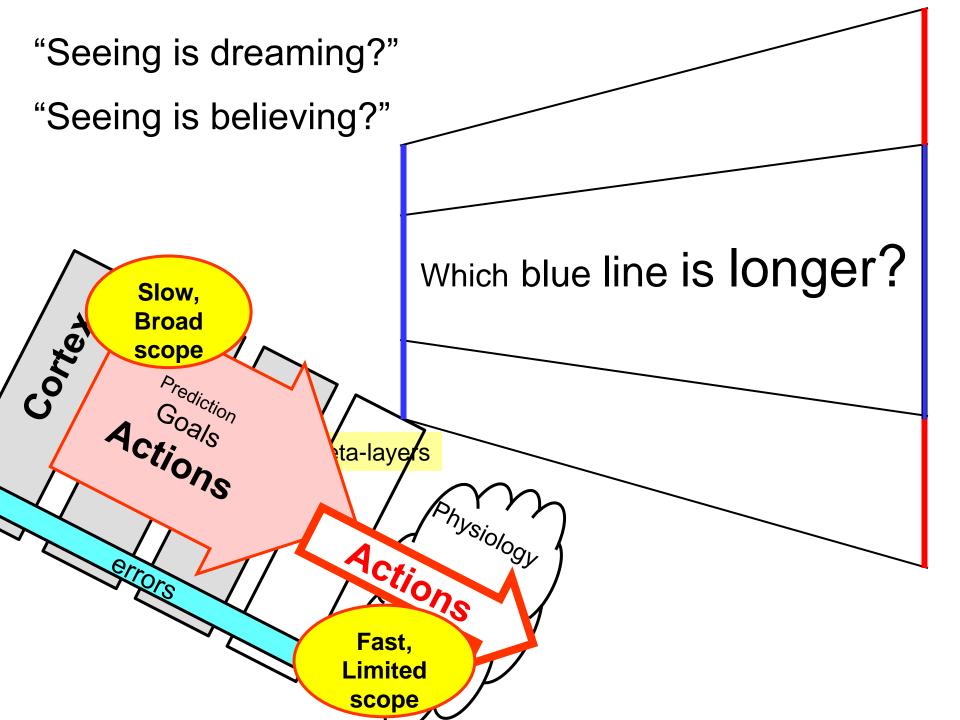
Distributed

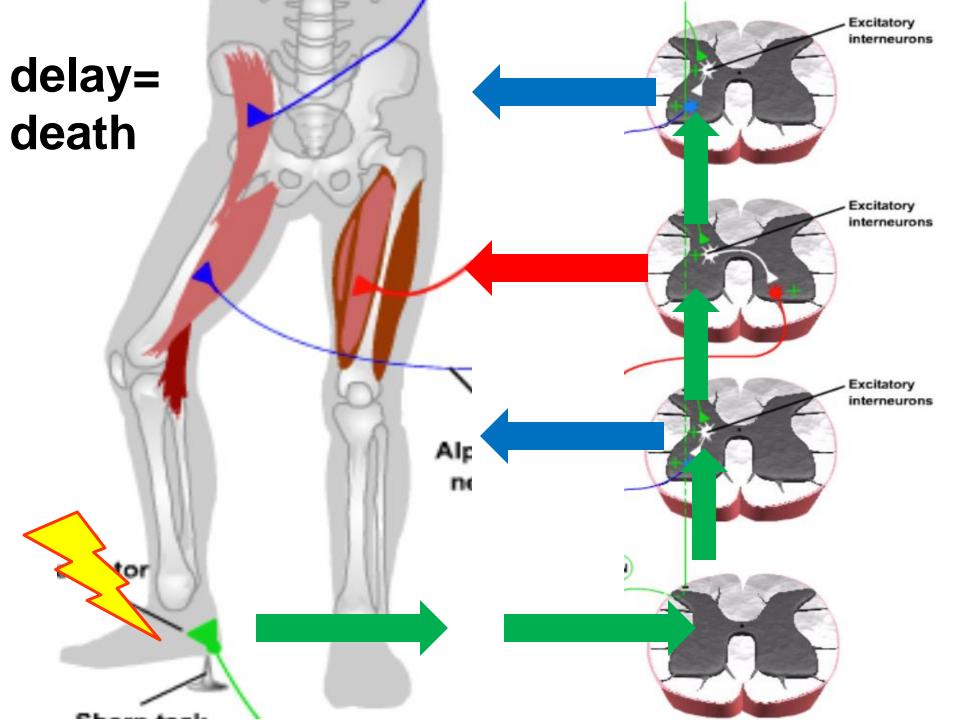
Complex

Frozen

Frozen

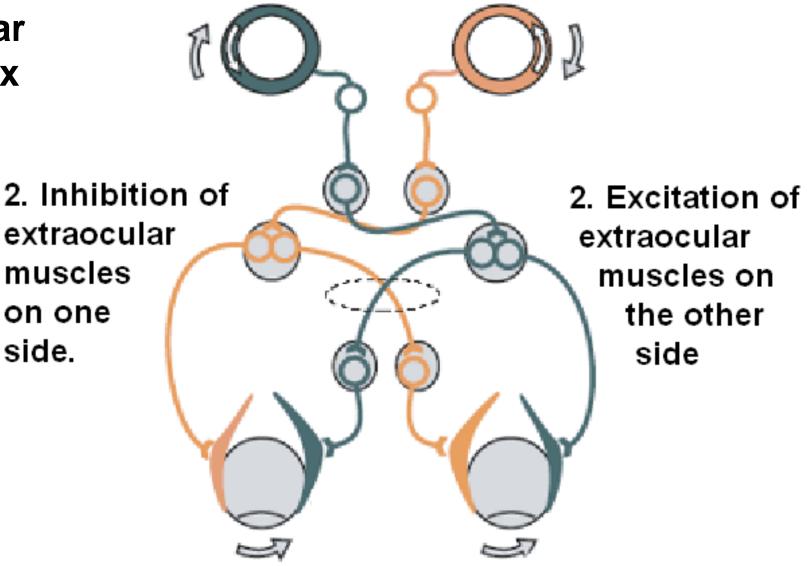






1. Detection of rotation

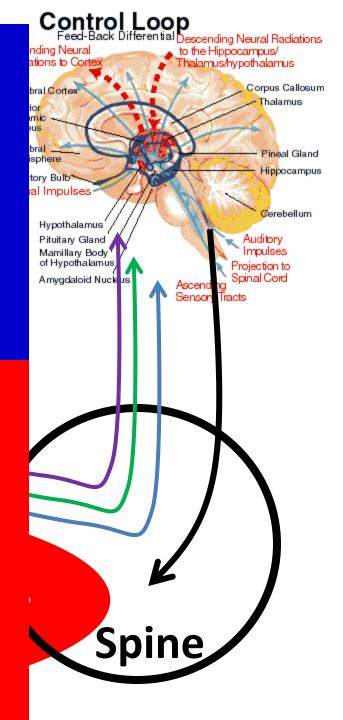




3. Compensating eye movement

Reflect

Reflex





Reflect

Control Loop
Feed-Back Differential Descending Neural Radiations nding Neural nus/hypothalamus

Corpus Callosum

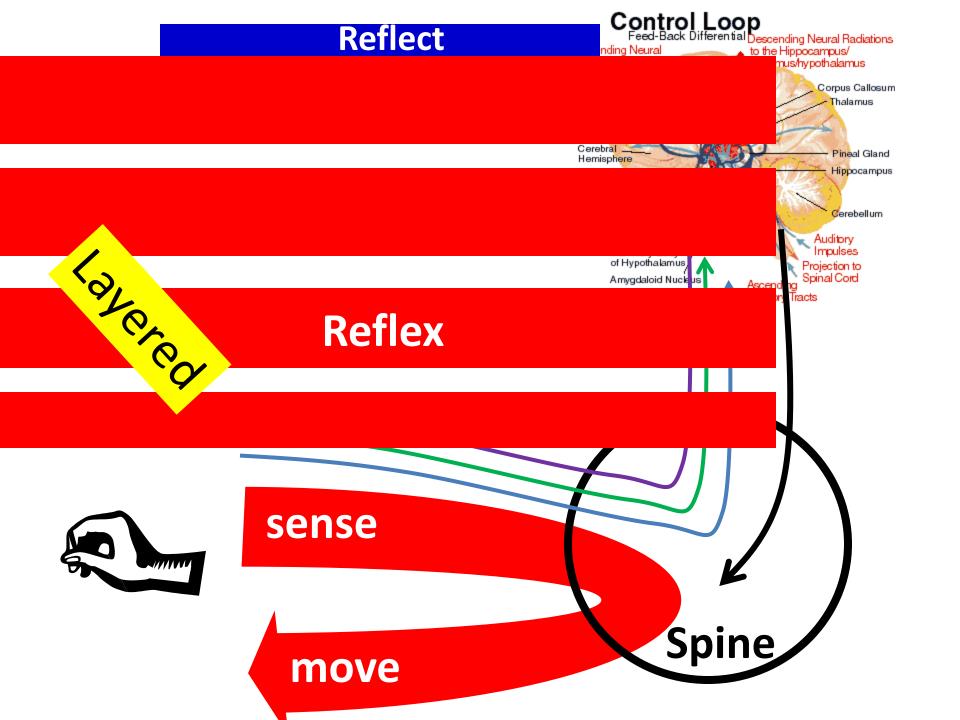
Pineal Gland Hippocampus

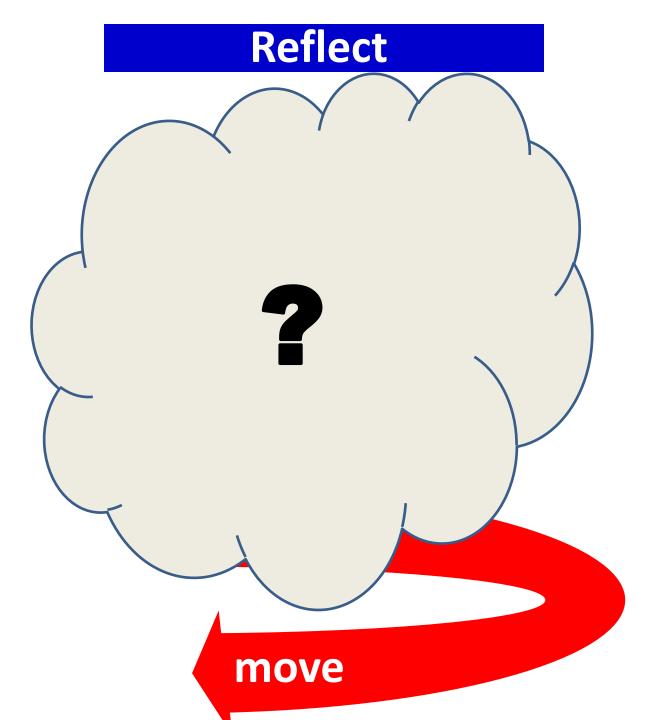
Cerebellum

Auditory Impulses

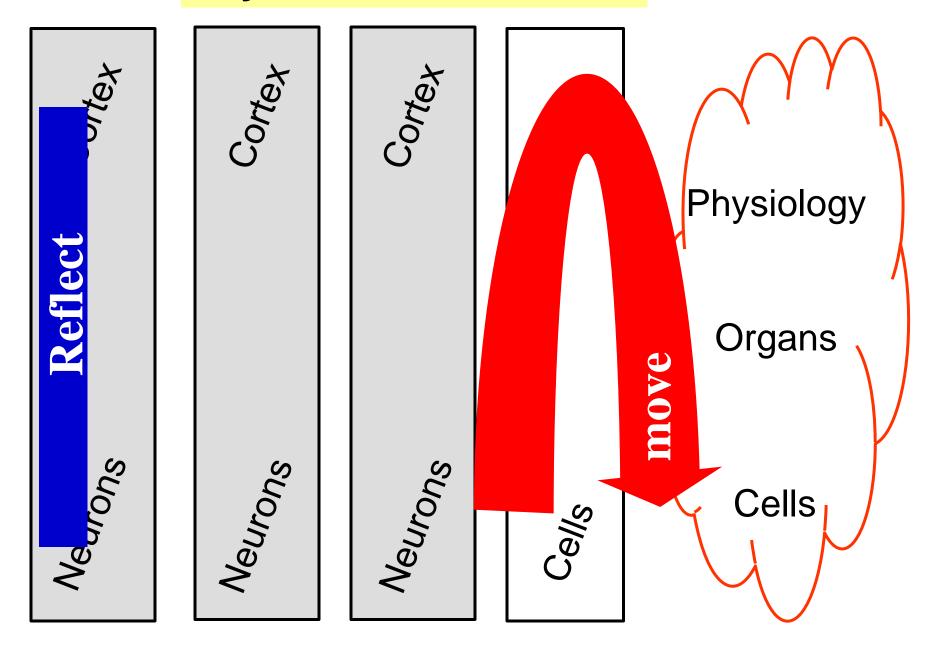
Projection to Spinal Cord

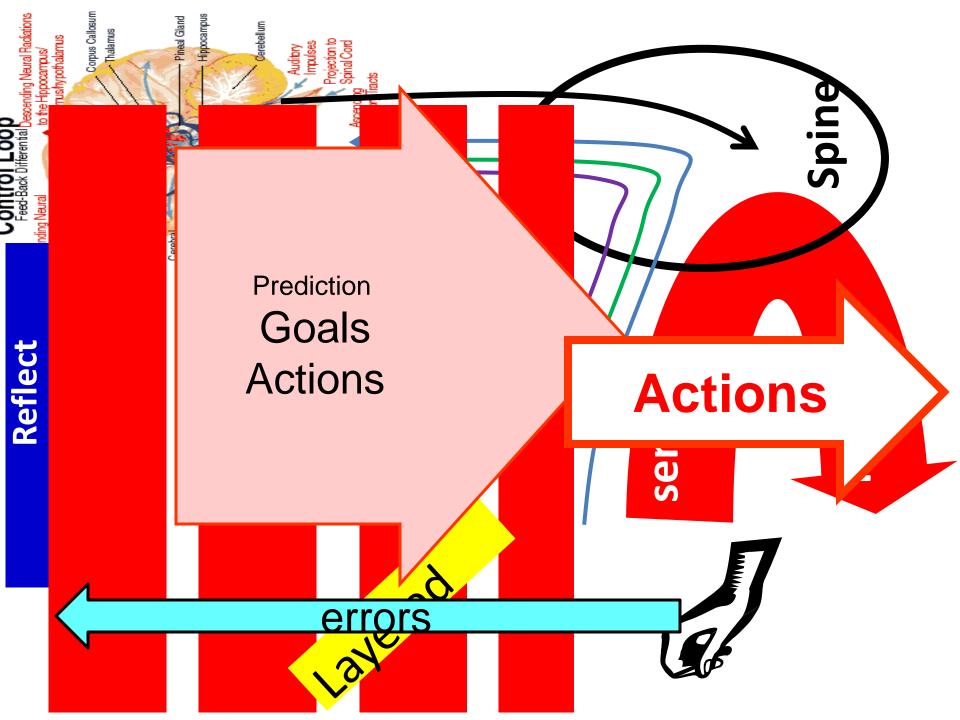
Reflex



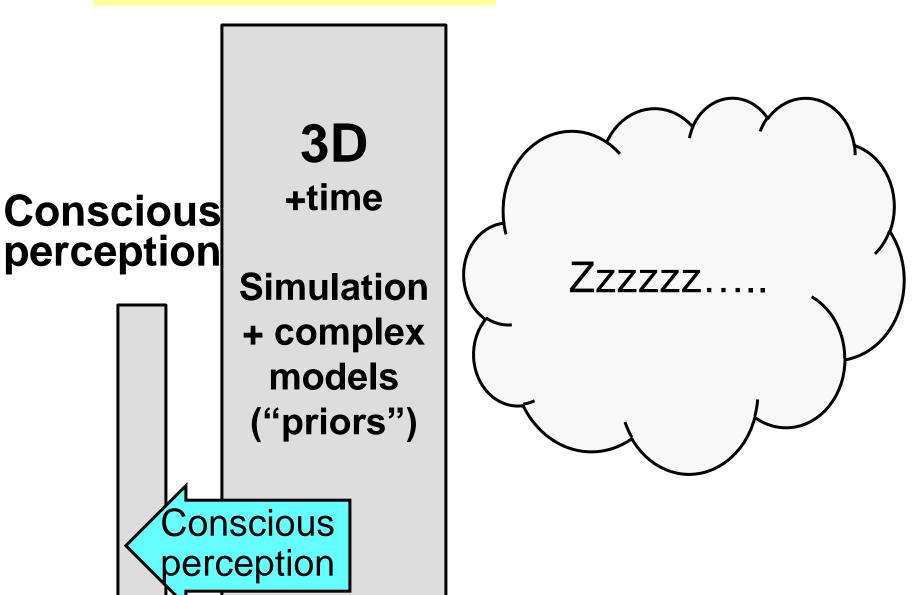


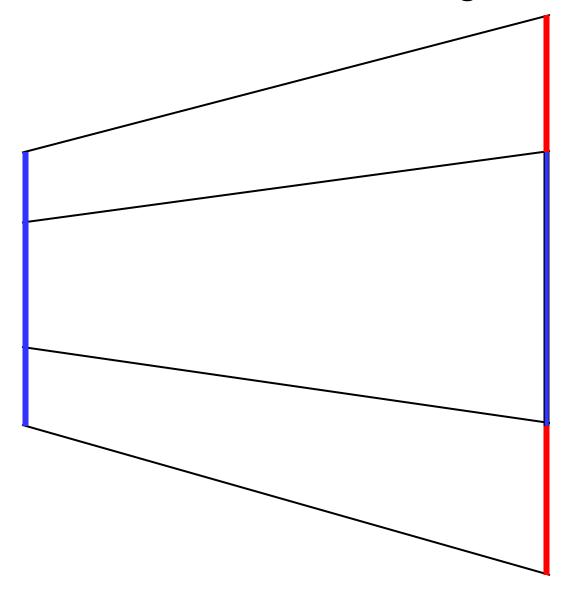
Layered architectures

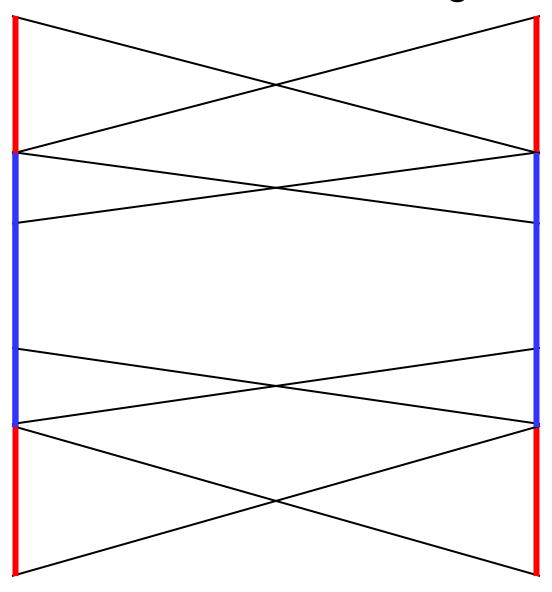


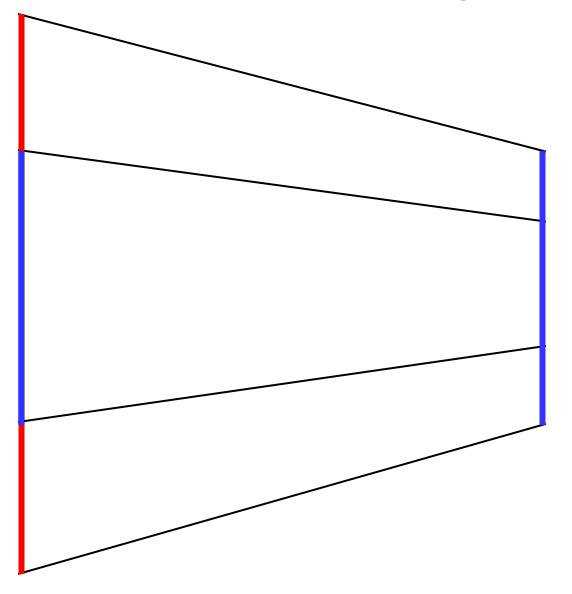


Seeing is *dreaming*







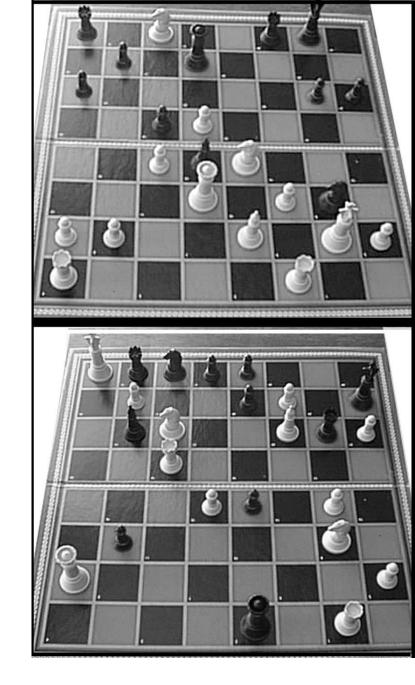


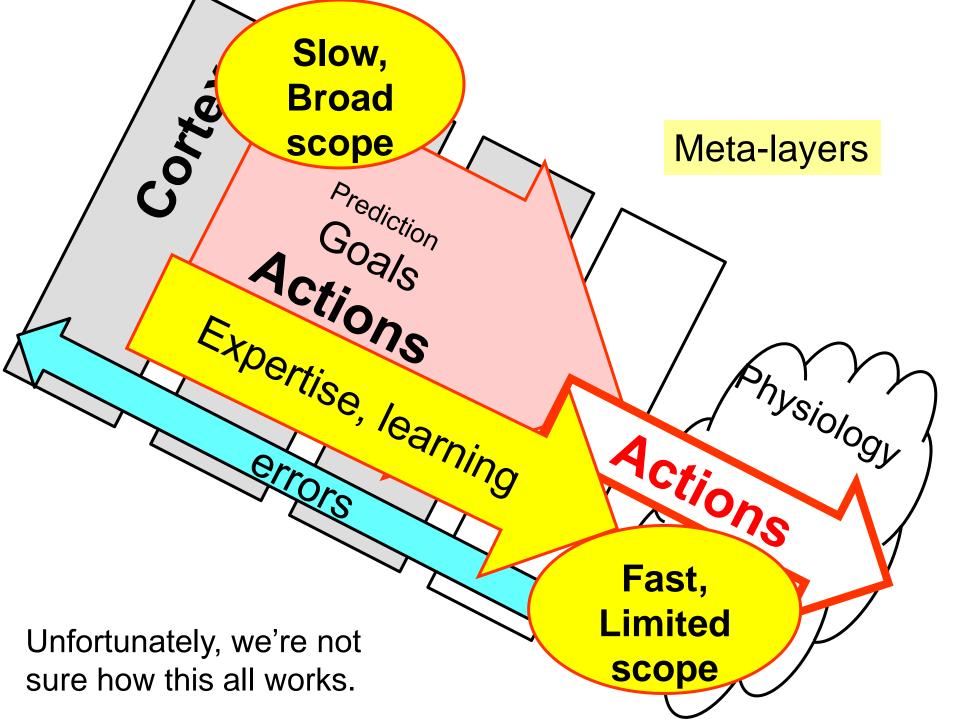


Chess experts

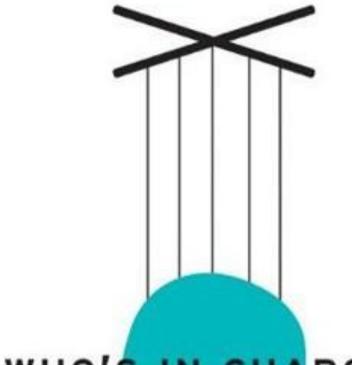
- can reconstruct entire chessboard with < ~ 5s inspection
- can recognize 1e5 distinct patterns
- can play multiple games
 blindfolded and simultaneous
- are no better on random boards

(Simon and Gilmartin, de Groot)





For more



WHO'S IN CHARGE?

FREE WILL AND THE SCIENCE OF THE BRAIN



author of HUMAN and THE ETHICAL BRAIN



INCOGNITO

THE SECRET LIVES
OF THE BRAIN

DAVID EAGLEMAN

AUTHOR OF SUM

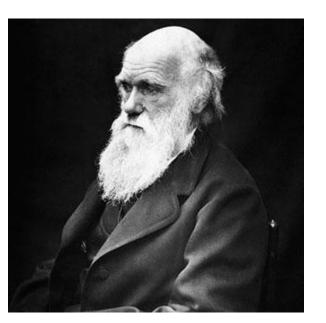
Evolution

Facilitated variation

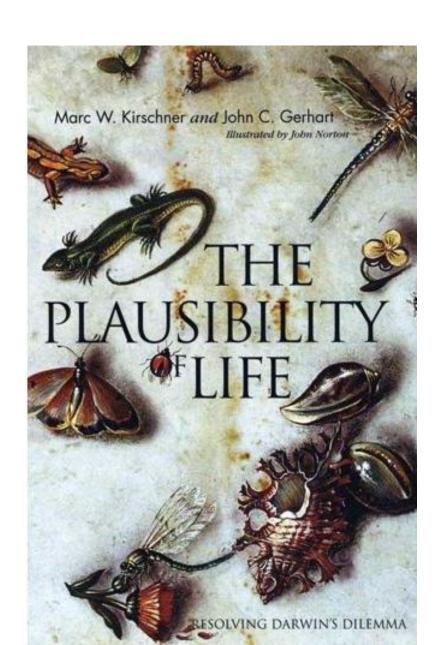
Architecture =

Constraints that deconstrain

- Weak linkage
- Exploratory mechanisms
- Compartmentalization



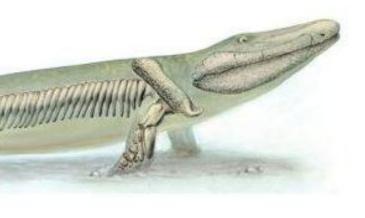
Kirschner and Gerhart



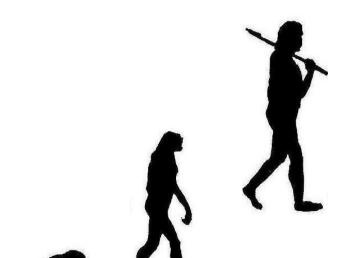
Unfortunately, not intelligent design

YOUR INNER FISH

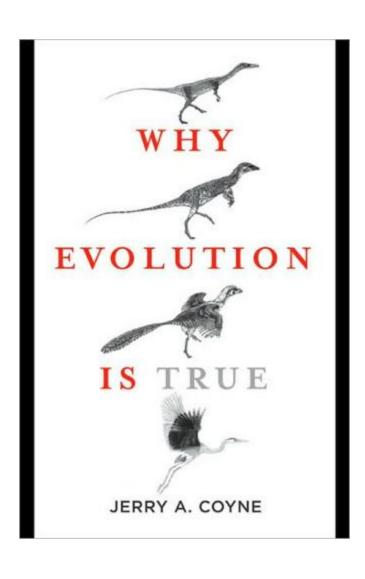
A JOURNEY INTO
THE
3.5-BILLION-YEAR HISTORY
OF THE
HUMAN BODY

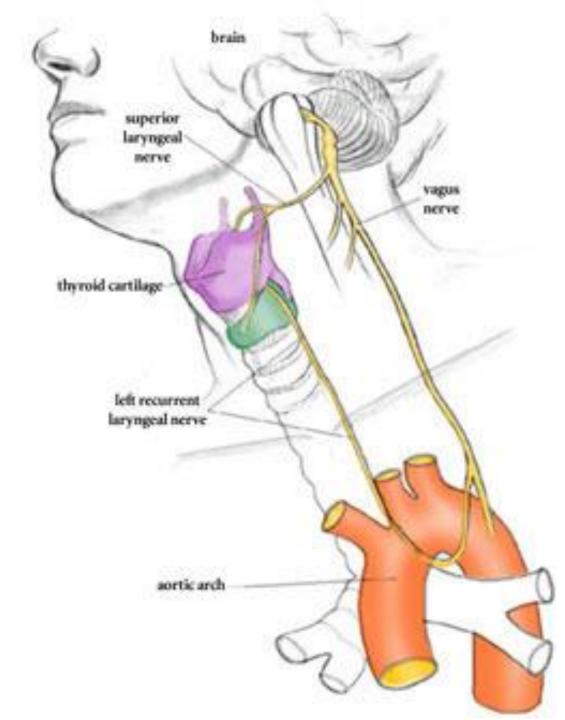


NEIL SHUBIN









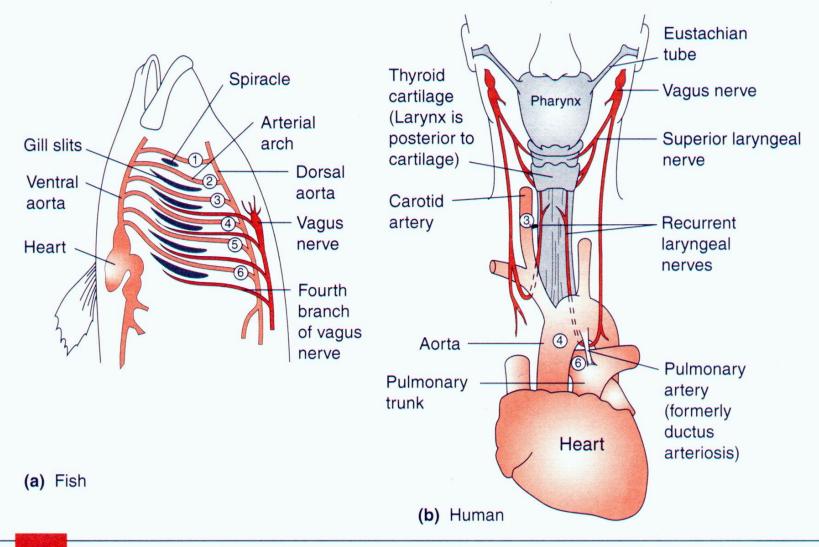
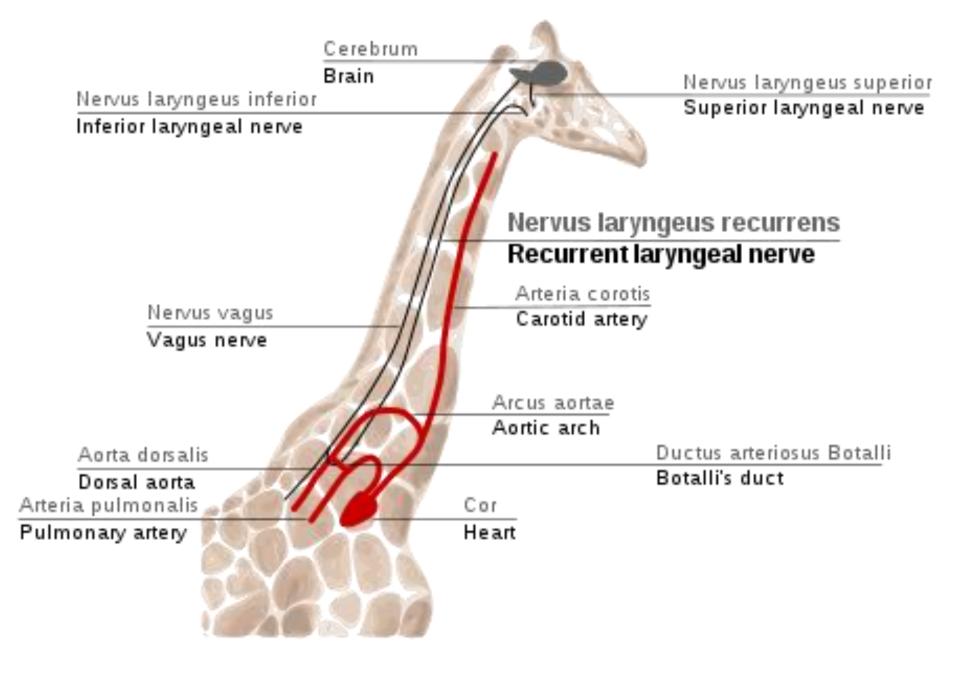
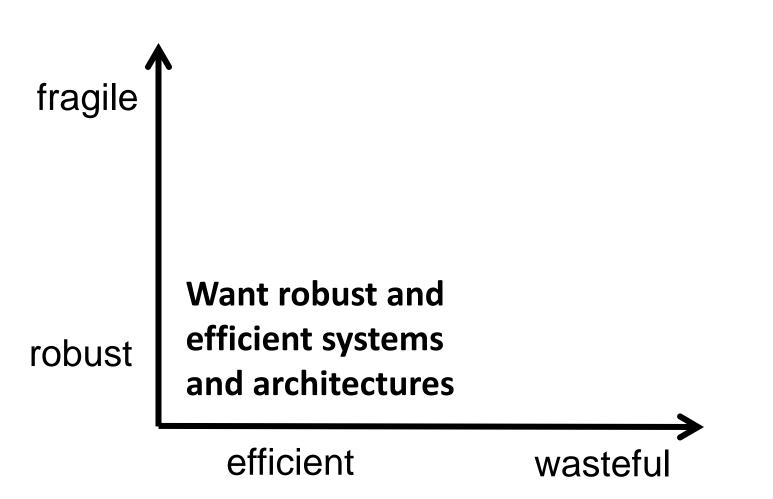


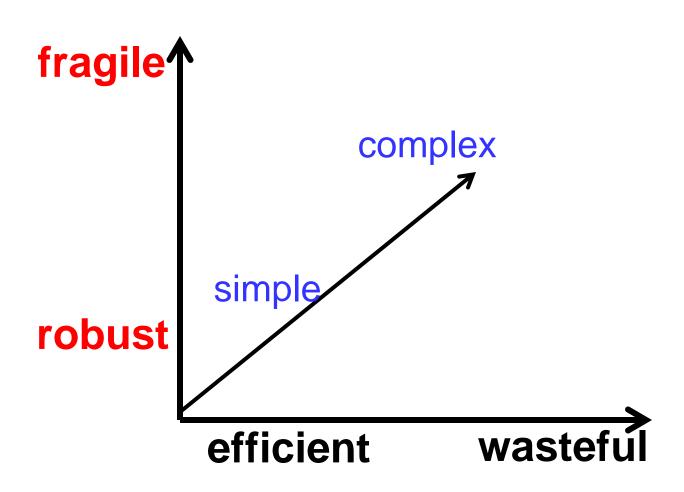
FIGURE 3–11 Schematic diagram showing the relationship between the vagus cranial nerve and the arterial arches in fish (a) and human (b). Only the third, fourth, and part of the sixth arterial arches remain in placental mammals, the sixth acting only during fetal development to carry blood to the placenta. 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.



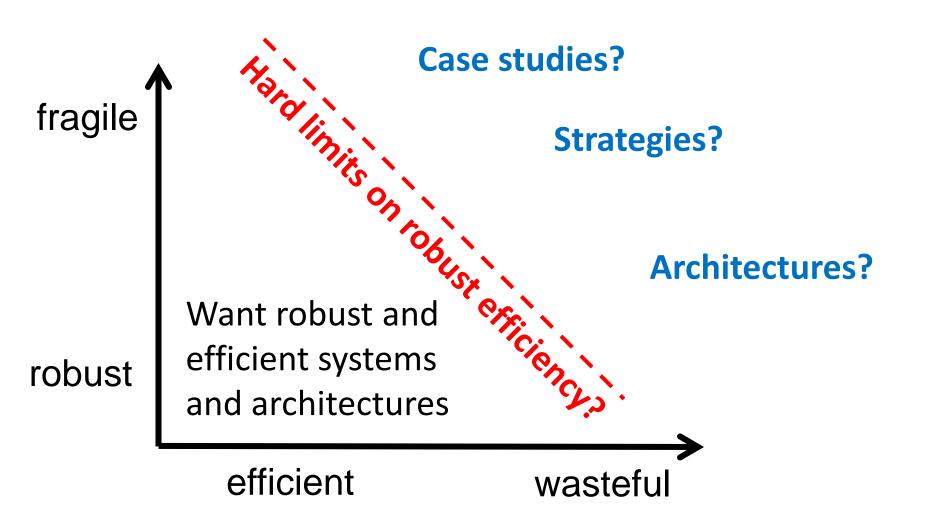
Want to understand the space of systems/architectures



Requirements on systems and architectures



Want to understand the space of systems/architectures



Control, OR

Kalman

Comms

Bode

Pontryagin

Shannon

Nash

Theory?

Von

Deep, but fragmented, incoherent, incomplete

Neumann

Carnot

Turing

Godel

Boltzmann

Heisenberg

Compute

Einstein

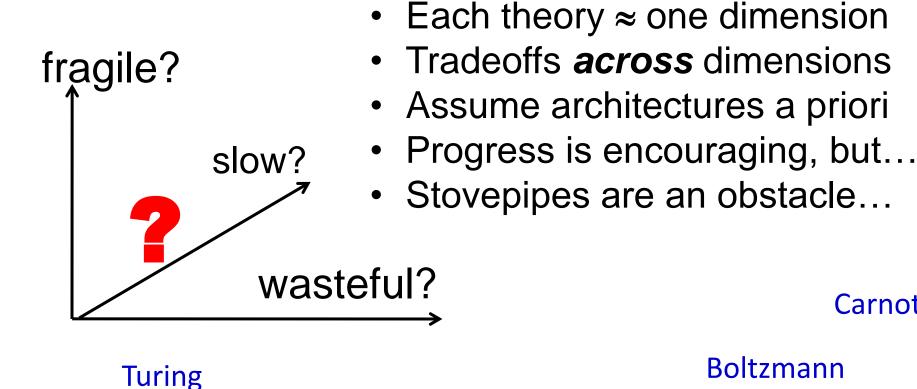
Physics

Control

Compute

Comms

Shannon Bode



Godel

Einstein

Heisenberg

Physics

Carnot

RESEARCH ARTICLES

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.

Chandra, Buzi, and Doyle

Most important paper so far.

UG biochem, math, control theory

the cen's use of ATT. III 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 $\overline{y} = 1$ 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 on discussed below and in SOM, but the analysis



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VOL 333

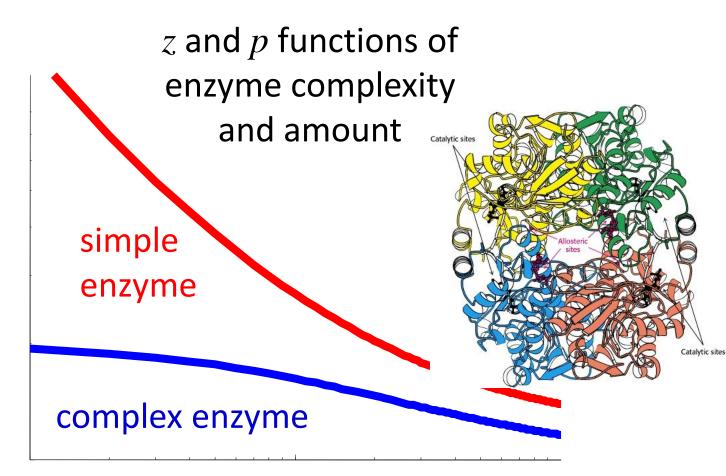
8 JULY 2011

Theorem!

$$\frac{1}{\pi} \int_{0}^{\infty} \ln |S(j\omega)| \left(\frac{z}{z^{2} + \omega^{2}}\right) d\omega \ge \ln \left|\frac{z + p}{z - p}\right|$$

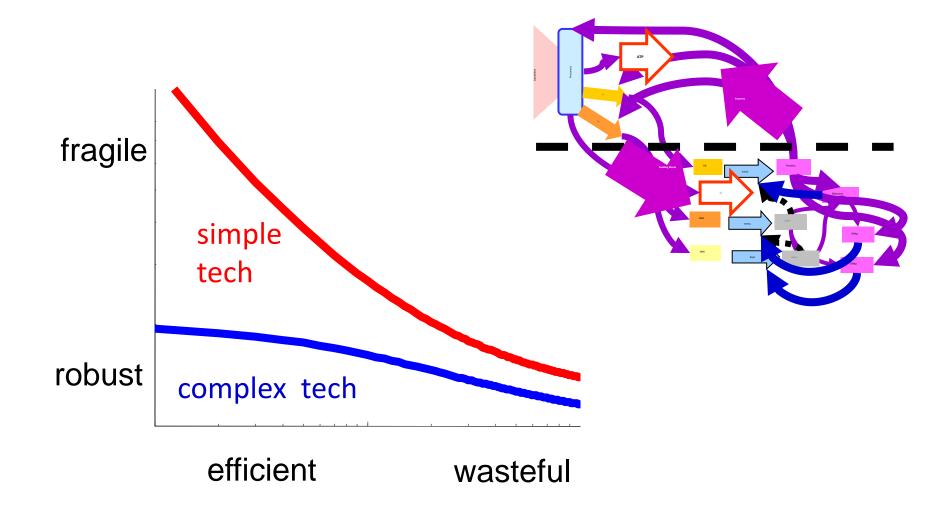


$$\ln \left| \frac{z+p}{z-p} \right|$$



Enzyme amount

How general is this picture?
Very! Constraints!
i.e. hard limits and architecture



Control, OR

Bode

Delay is most important

Turing

Compute

Communications

Shannon

Delay is least important

Carnot

Boltzmann

Heisenberg

Physics

Einstein

Control, OR

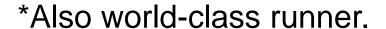
Communications

Bode Shannon **Delay** is **Delay** is most important important **Carnot Boltzmann Turing** Heisenberg Einstein **Physics** Compute

- Turing 100th birthday in 2012
- Turing
 - machine (math, CS)
 - test (AI, neuroscience)
 - pattern (biology)
- Arguably greatest*
 - all time math/engineering combination
 - WW2 hero
 - "invented" software

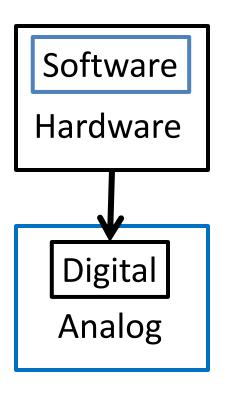
Turing (1912-1954)

Compute





Turing as "new" starting point?

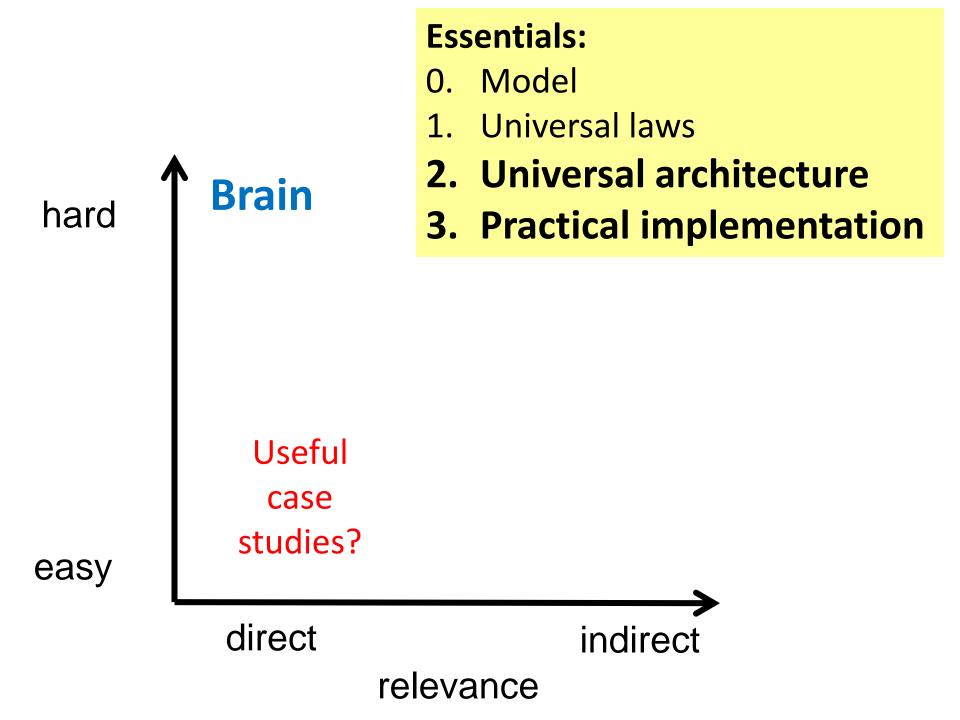


Essentials:

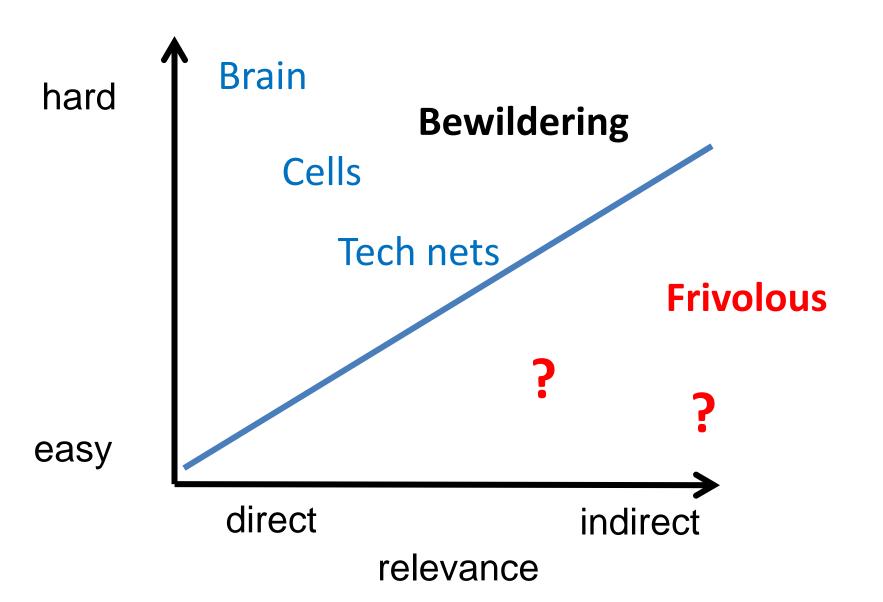
- 0. Model
- 1. Universal laws
- 2. Universal architecture
- 3. Practical implementation

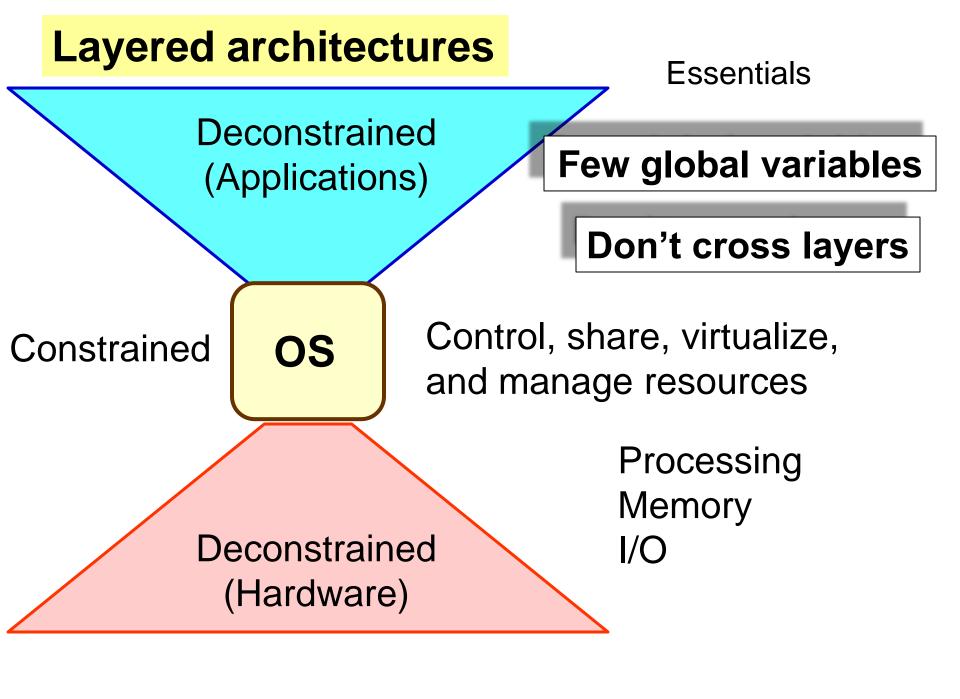
Turing's 3 step research:

- 0. Virtual (TM) machines
- hard limits, (un)decidability using standard model (TM)
- 2. Universal architecture achieving hard limits (UTM)
- 3. Practical implementation in digital electronics (biology?)



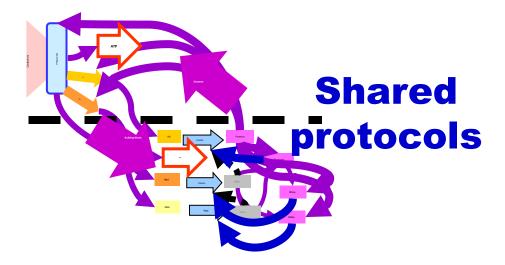
- 3. Universal architecture
- 4. Practical implementation





Layered architectures

Deconstrained (diverse) Environments



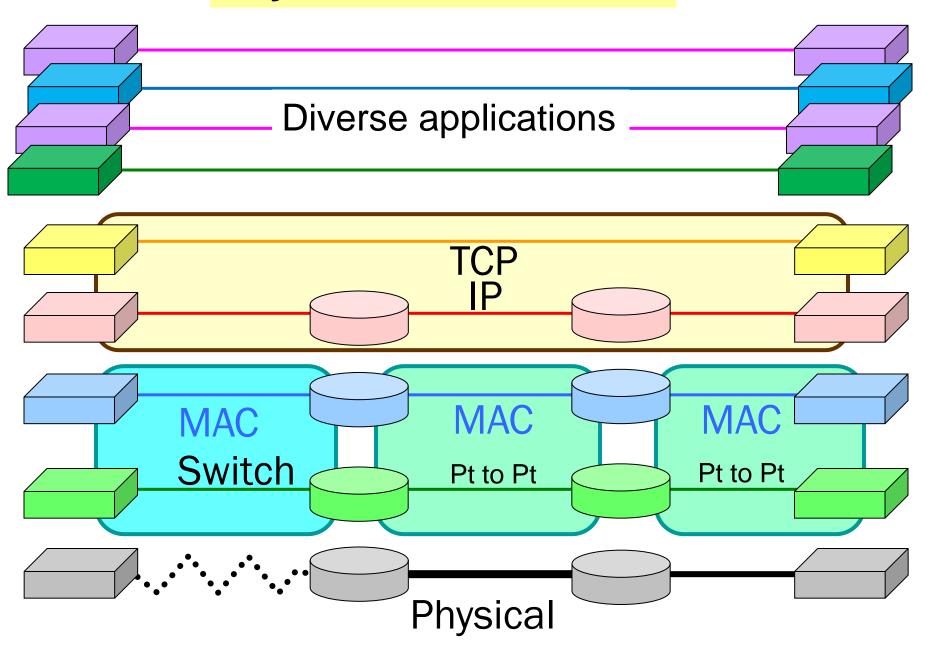
Deconstrained (diverse)
Genomes

Bacterial biosphere

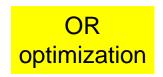
Architecture

Constraints that Deconstrain

Layered architectures



Proceedings of the IEEE, Jan 2007



Layering as Optimization Decomposition: A Mathematical Theory of Network Architectures

Fundamentals! There are various ways that network functionalities can be allocated to a layers and to different network elements, some being more desirable than others.

The intellectual goal of the research surveyed by this article is to provi

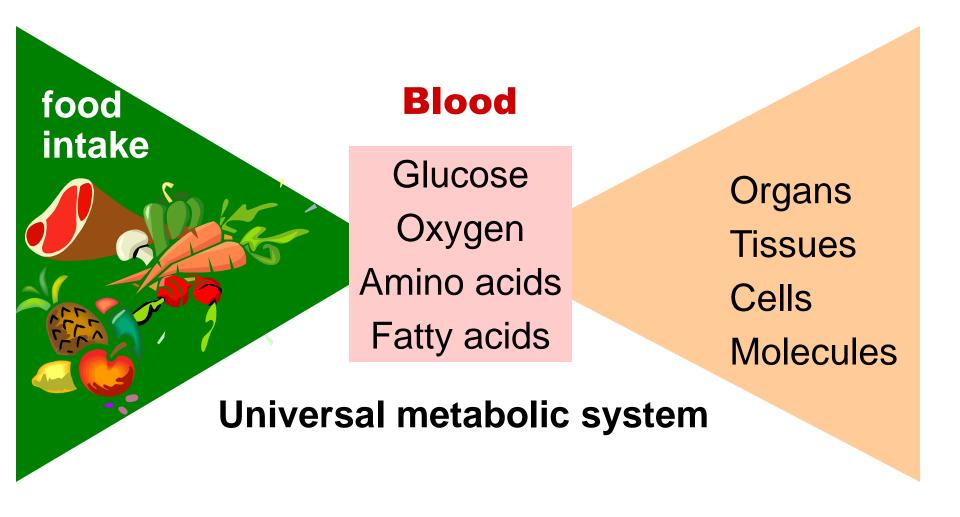
theoretical foundation for these architectural decisions in networking.

By M UNG CHIANG, Member IEEE, STEVEN H. LOW, Serior Member IEEE, A. Robert Calderbank, Fellow IEEE, and John C. Doyle

Chang, Low, Calderbank, Doyle



Peter Sterling and Allostasis



Blood

Glucose Oxygen Amino acids Fatty acids Organs
Tissues
Cells
Molecules



Organs **Tissues** Cells Molecules

Glucose Oxygen Amino acids Fatty acids



Highly variable supply

Robust

Highly variable demand

food intake

Efficient

Organs

Tissues

Cells

Molecules

evolving diet

Evolvable

evolving function

Highly variable supply

food intake



Conserved core building blocks

Glucose Oxygen

Blood

Highly variable demand

Organs

Tissues

Cells

Molecules

evolving diet

evolving function

Universal reward systems

sports music dance crafts art toolmaking sex food

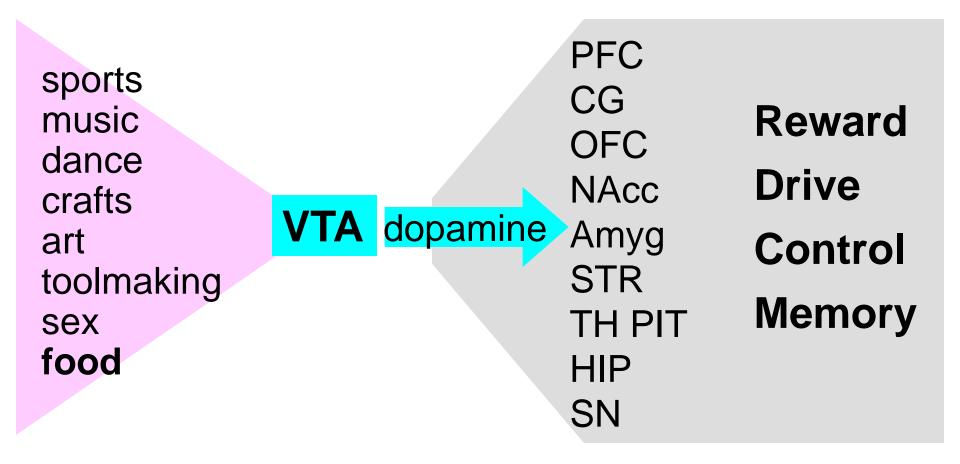
VTA dopamine

Prefrontal cortex Accumbens

Dopamine,
Ghrelin,
Leptin,...

Ridiculous oversimplification

Universal reward systems



Robust and evolvable

sports music dance crafts art toolmaking sex

Universal reward systems

VTA dopamine

Reward Drive Control Memory

food

Constraints that deconstrain

Blood

Glucose

Oxygen

Organs
Tissues
Cells
Molecules

Universal metabolic system

Modularity 2.0

Constraints

dopamine

Blood

Glucose

Oxygen

sports music dance crafts art toolmaking sex

food

Modularity 2.0

Reward Drive Control Memory

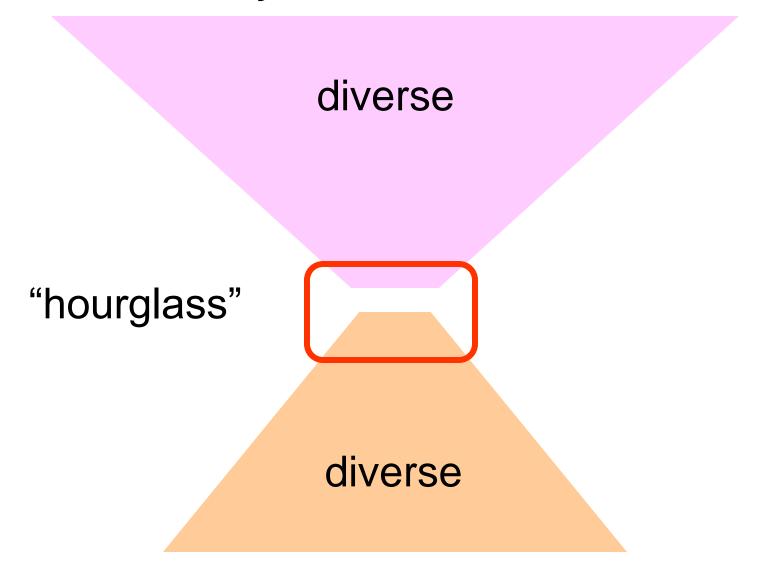
that deconstrain

Organs
Tissues
Cells
Molecules

Layered architectures

diverse diverse "bow-tie"

Layered architectures



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

art

sex toolmaking sports music dance crafts Reward Drive Control Memory

Organs
Tissues
Cells
Molecules

"Weak linkage"

Modularity 2.0

Most important "modules"



Not weakly connected to others, but highly connected

Universal reward/metabolic systems

work family community nature

food

sex toolmaking sports music

crafts

dance

art

dopamine

Blood

Reward Drive Control Memory

Organs

Tissues

Cells

Molecules

Robust and adaptive, yet ...

work family community nature

sex food toolmaking sports music dance crafts art

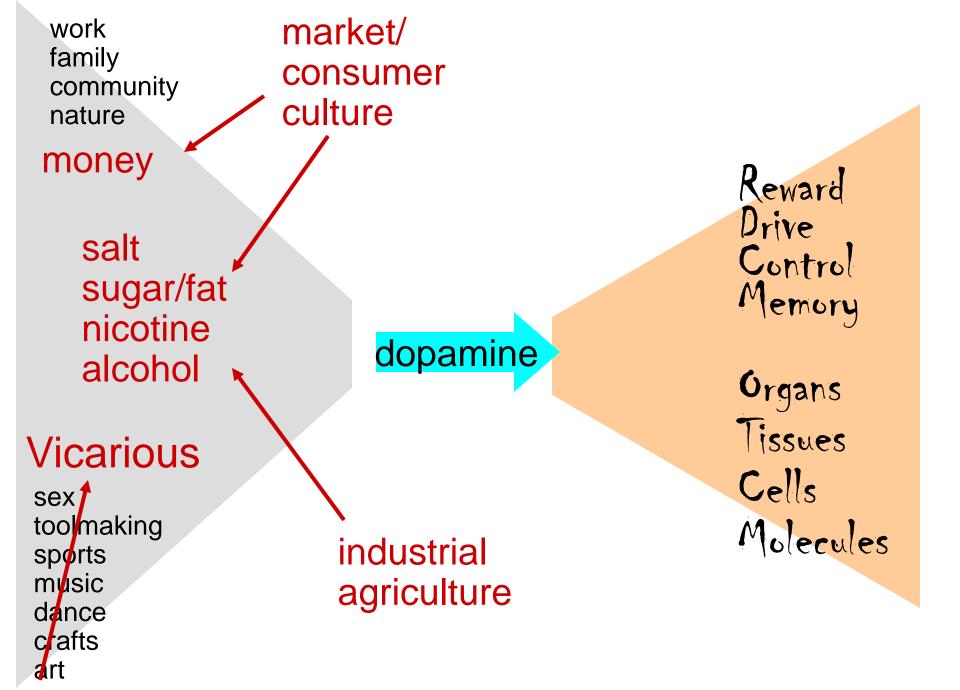
cocaine amphetamine

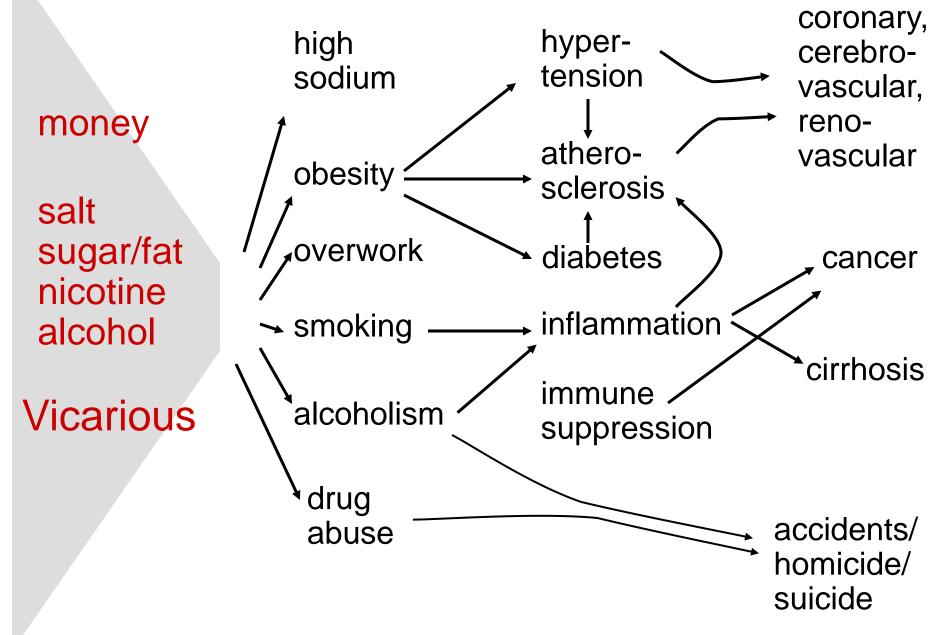
dopamine

Blood

Reward Drive Control Memory

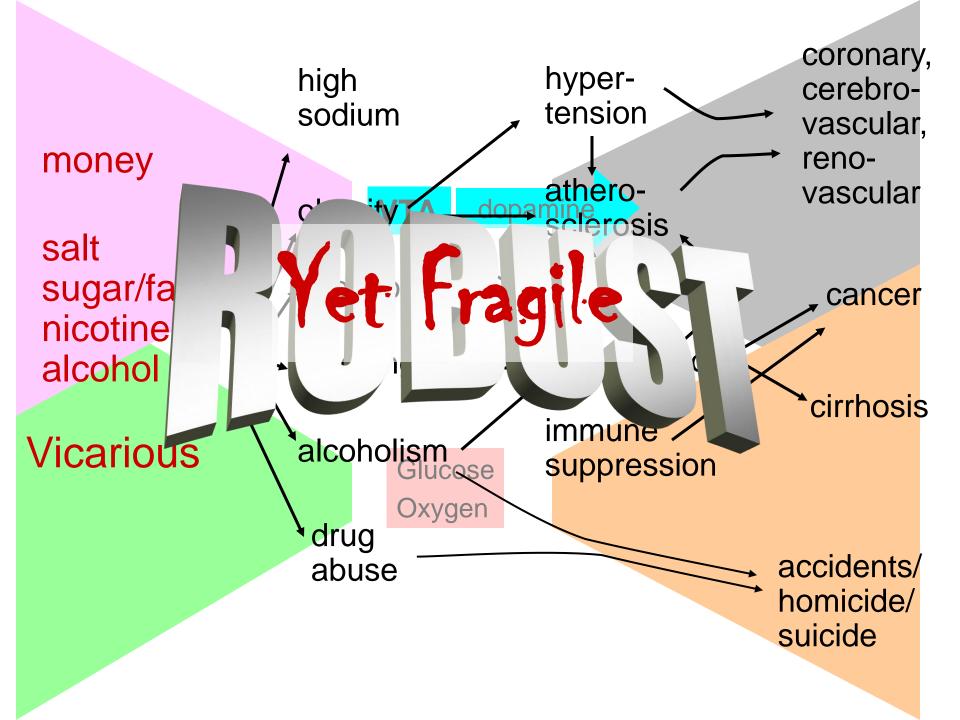
Organs
Tissues
Cells
Molecules



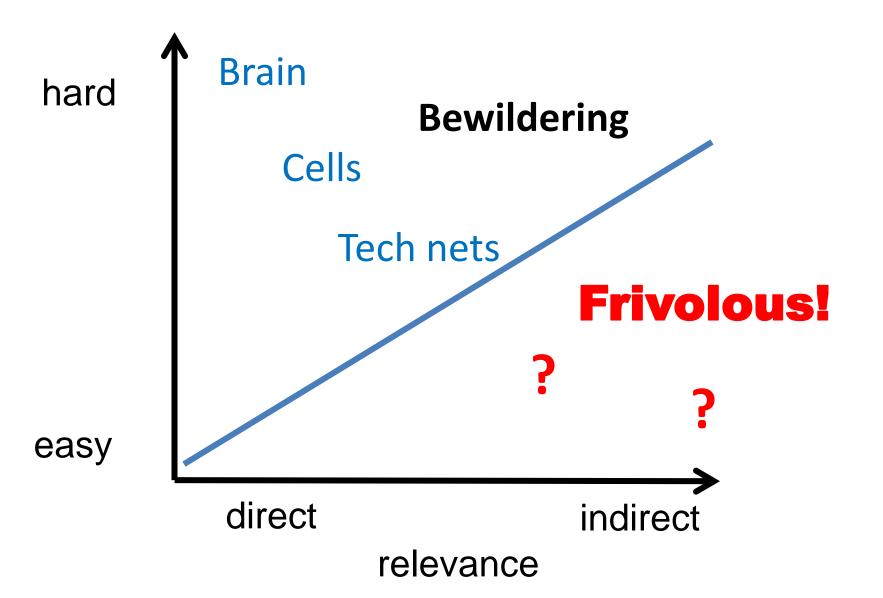


From Sterling

sports Universal reward systems music **Prefrontal** dance cortex crafts dopamine art cumbens toolmaki sex food Plood rgans Glucose **Tissues** Oxygen Cells Molecules Universal metabolic system



- 3. Universal architecture
- 4. Practical implementation





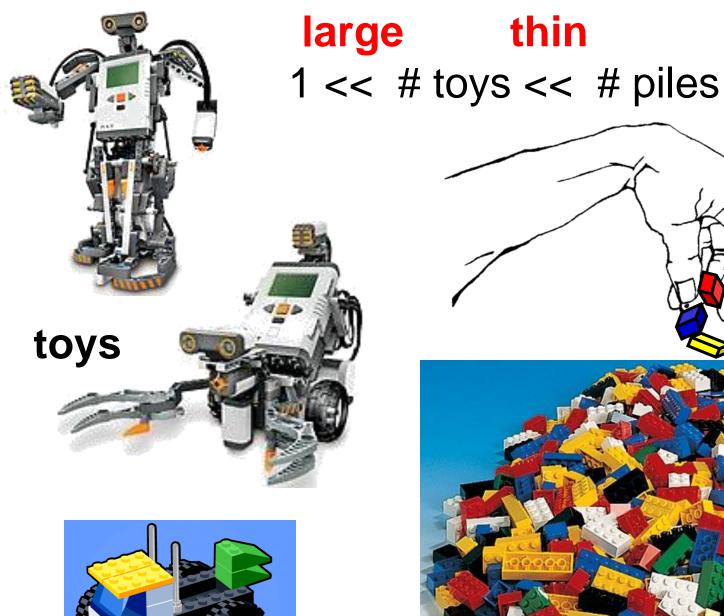
Other examples

Words Lego Clothing Cell biology Internet **Cyberphysical** Money

Letters and words

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

```
1 << (# words) << (# non-words)
large thin</pre>
```







edge of chaos self-organized criticality scale-free ???

statistical physics random ensembles minimally tuned phase transitions bifurcations



Reverse Engineering of Biological Complexity

Marie E. Csete¹ and John C. Doyle^{2*}

Advanced technologies and biology have extremely different physical implementations, but they are far more alike in systems-level organization than is widely appreciated. Convergent evolution in both domains produces modular architectures that are composed of elaborate hierarchies of protocols and layers of feedback regulation, are driven by demand for robustness to uncertain environments, and use often imprecise components. This complexity may be largely hidden in idealized laboratory settings and in normal operation, becoming conspicuous only when contributing to rare cascading failures. These puzzling and paradoxical features are neither accidental nor artificial, but derive from a deep and necessary interplay between complexity and robustness, modularity, feedback, and fragility. This review describes insights from engineering theory and practice that can shed some light on biological complexity.

Csete and Doyle

ty in components or the Biologists and biophysing complex networks ofte a biological network's (15). They find that "per homeostatic regulation are networks (16, 17), despite anisms" that can seem g (18–20). Some even conclusions and their resulting in engineering (20, 21). H is in the nature of their robi ity that biology and advantage of their robins.



wardrobe



large thin

1 << # outfits << # heaps





Cool

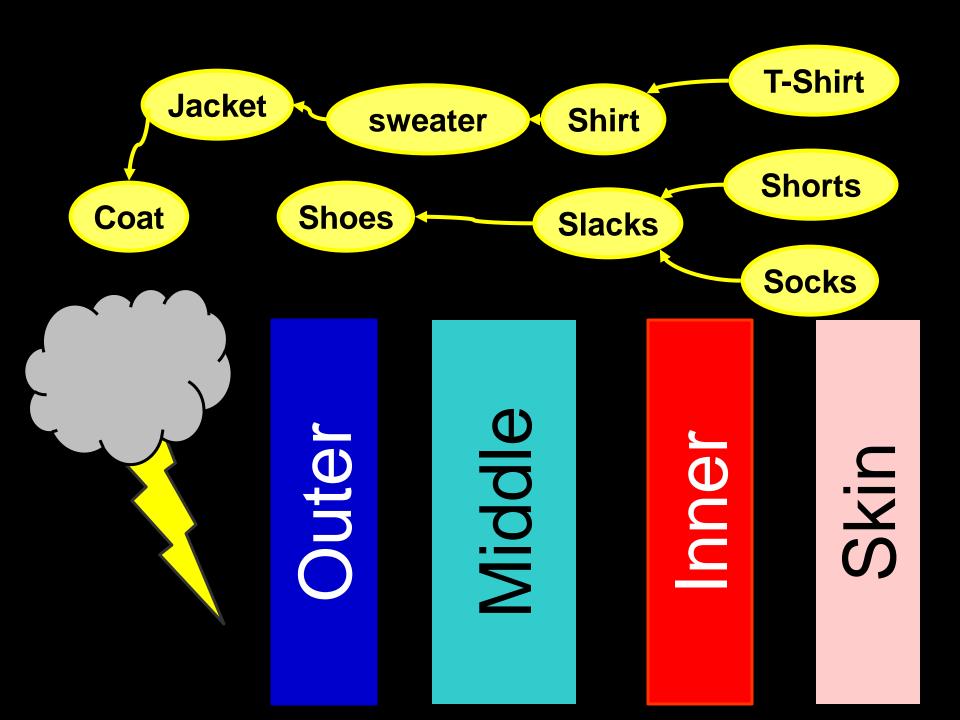


Hycreek Layering Guide

This guide is meant as a "suggested" guide only. The amount and type of layers that will keep you warm in any given condition may vary, so you can feel free to adapt it as necessary.



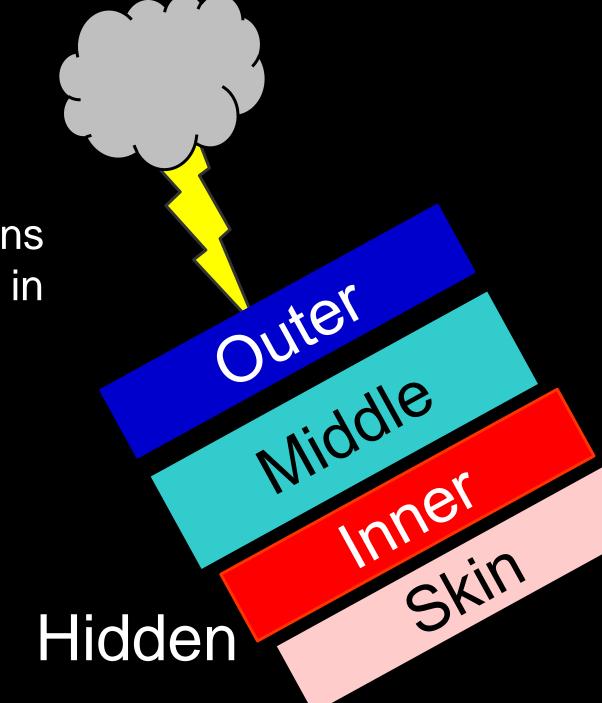


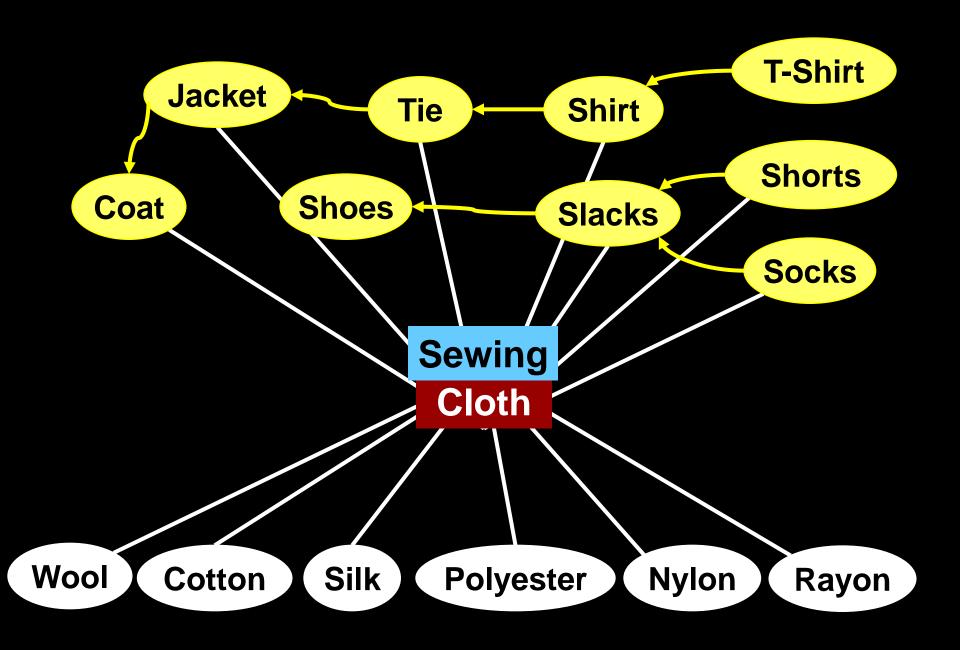


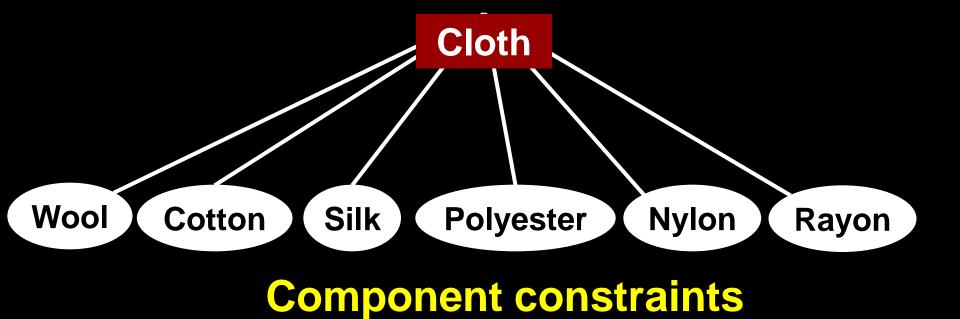
System constraints

Robust to variations and requirements in

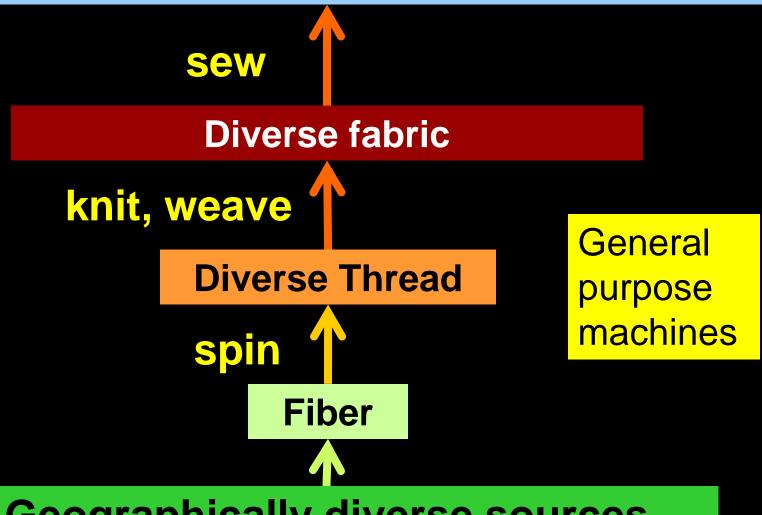
- weather
- activity
- appearance
- wear and tear
- washing





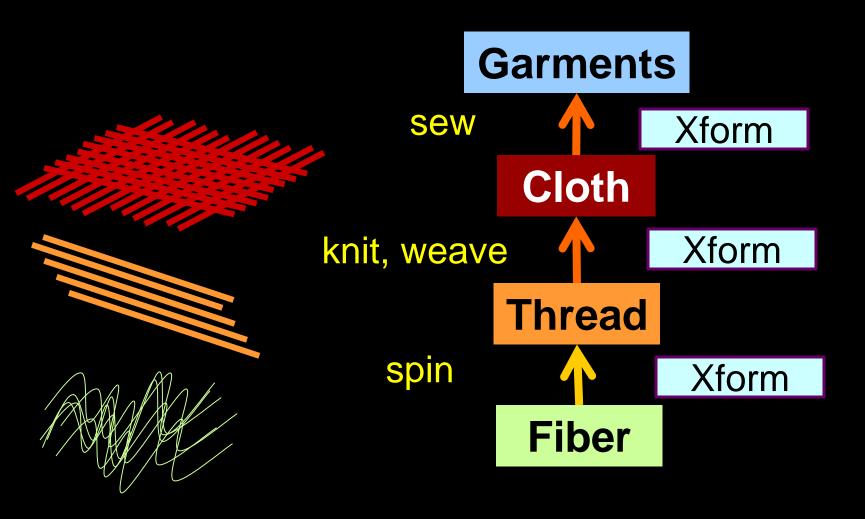


Functionally diverse garments

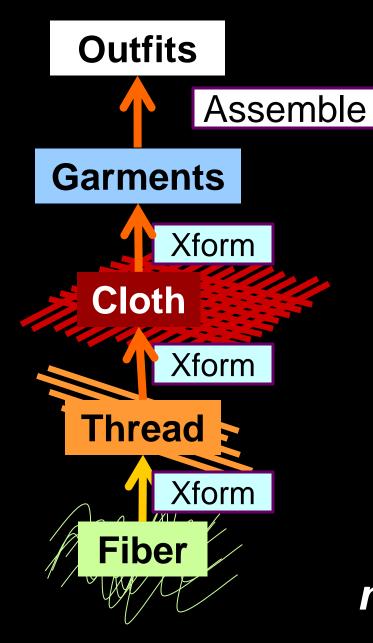


Geographically diverse sources

Architecture and Modularity 2.0



Prevents unraveling of lower layers

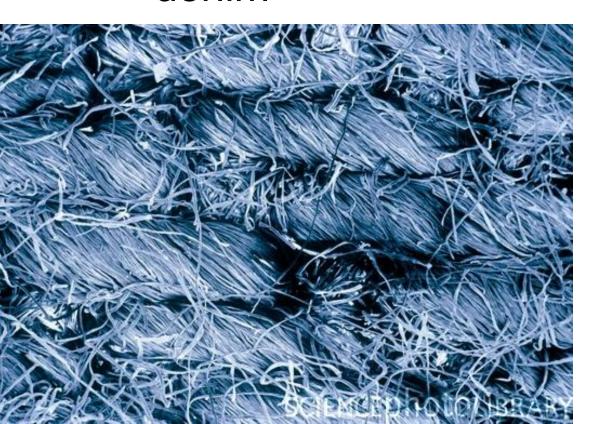


Hidden, large, thin, nonconvex

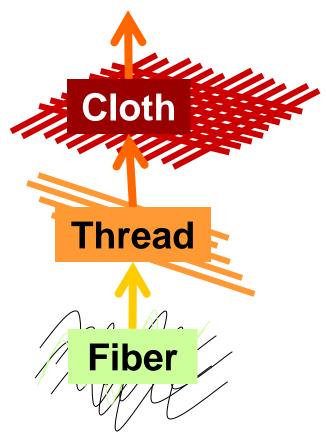
> are necessary

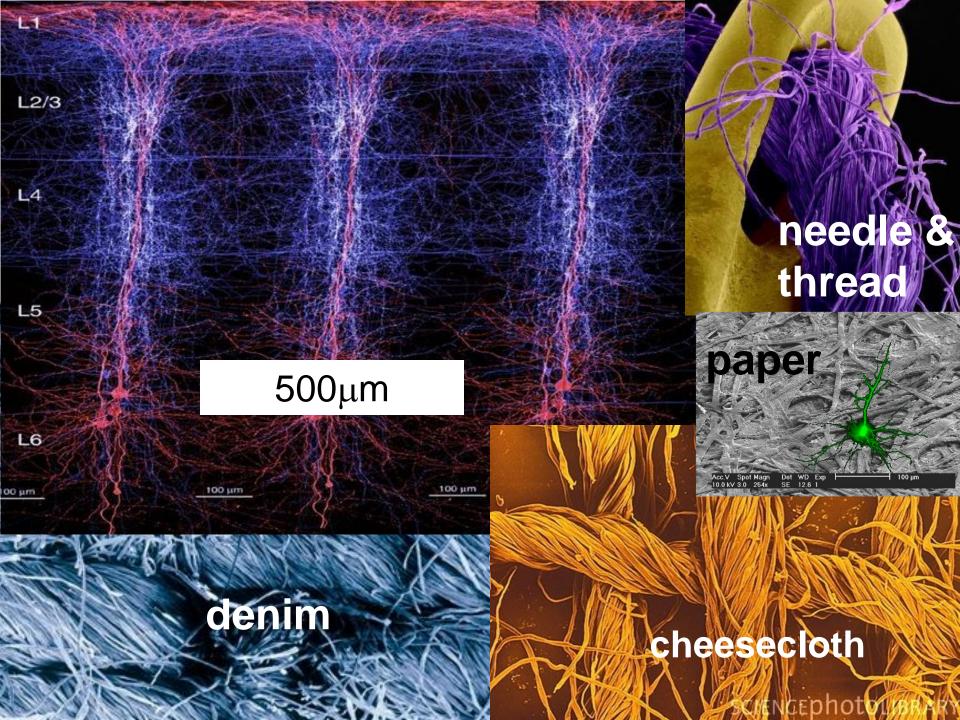
.5mm

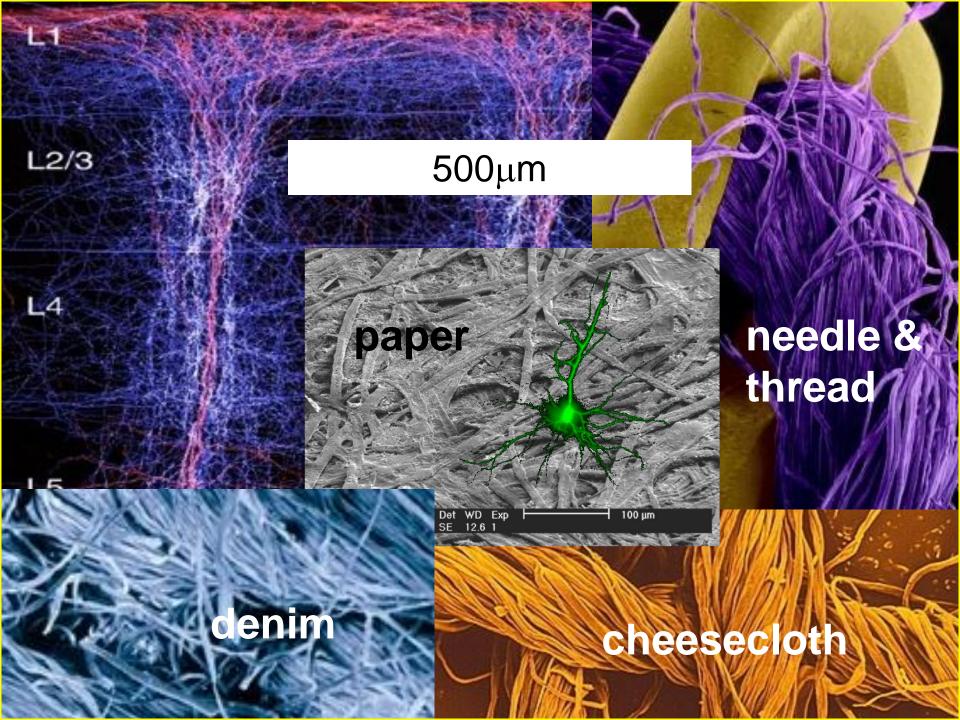






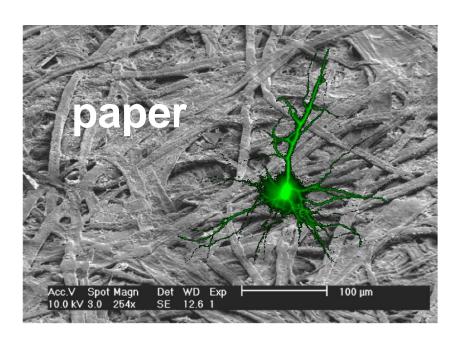


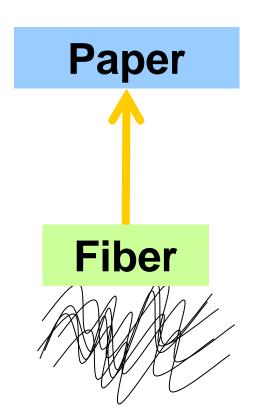


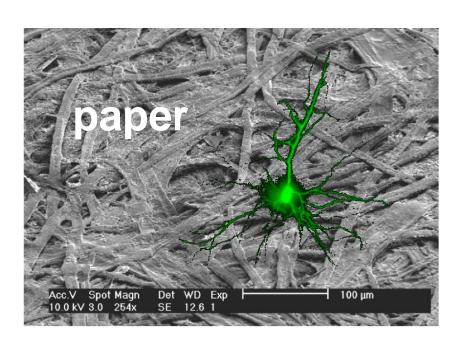


.5mm x .35 mm cotton paper

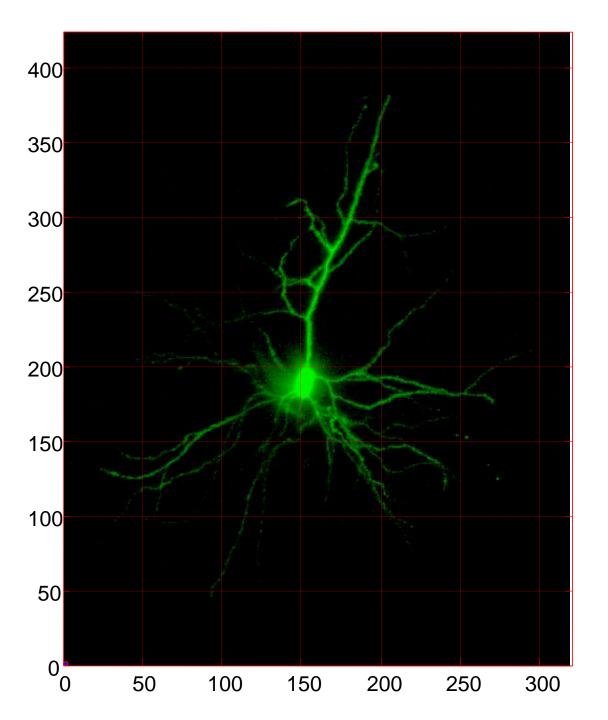
$500 \mu m$





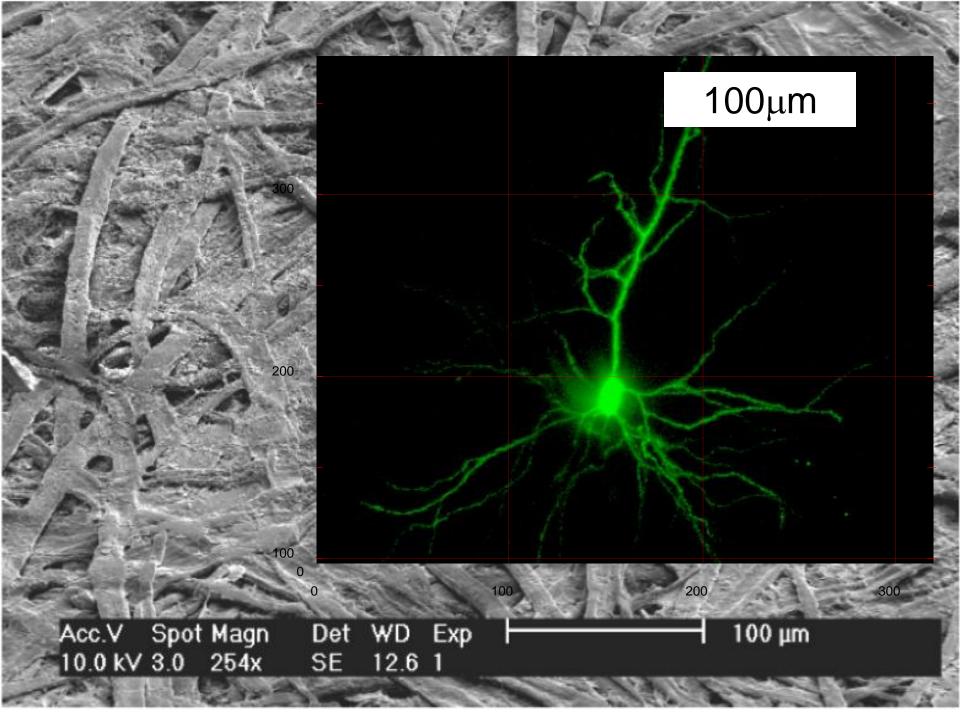


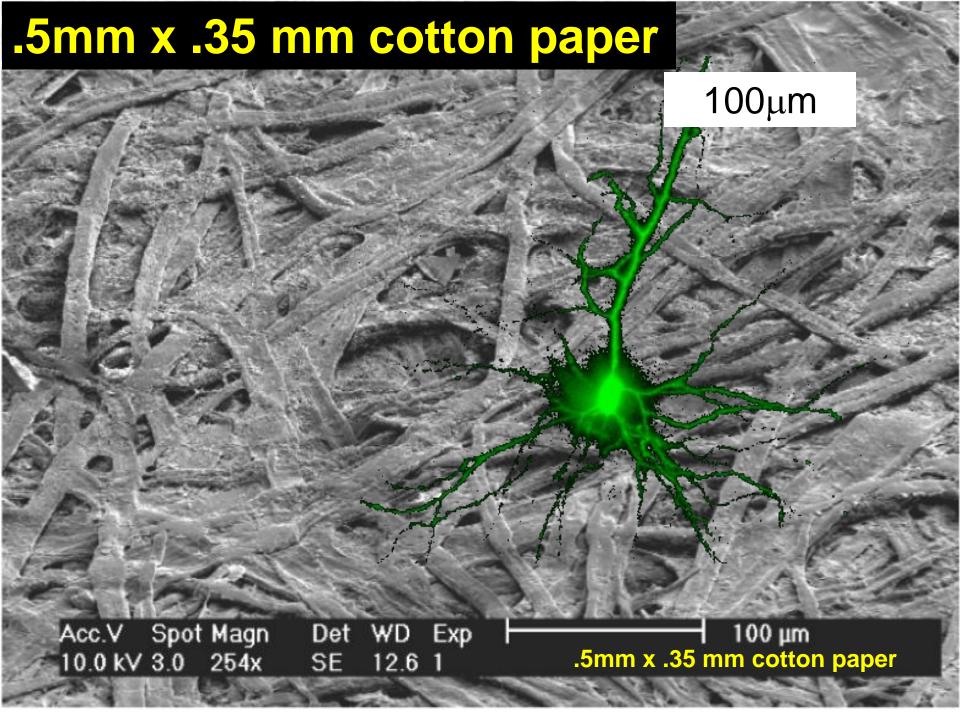
Minimal architecture

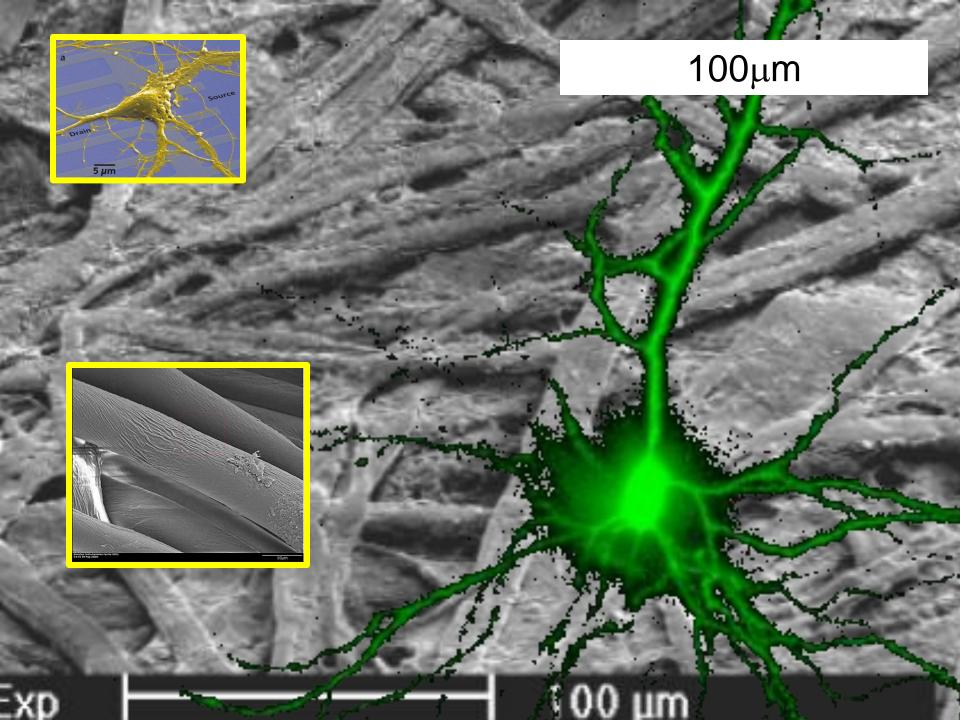


A neonatal rat pyramidal neuron

filled with Lucifer Yellow imaged on the BioRad MRC600 confocal microscope using a 20X oil objective, NA=0.8. Image size is 320 x 425 x 120 µm.



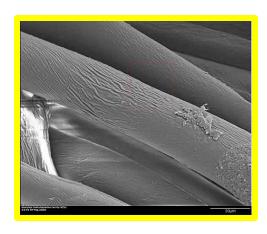




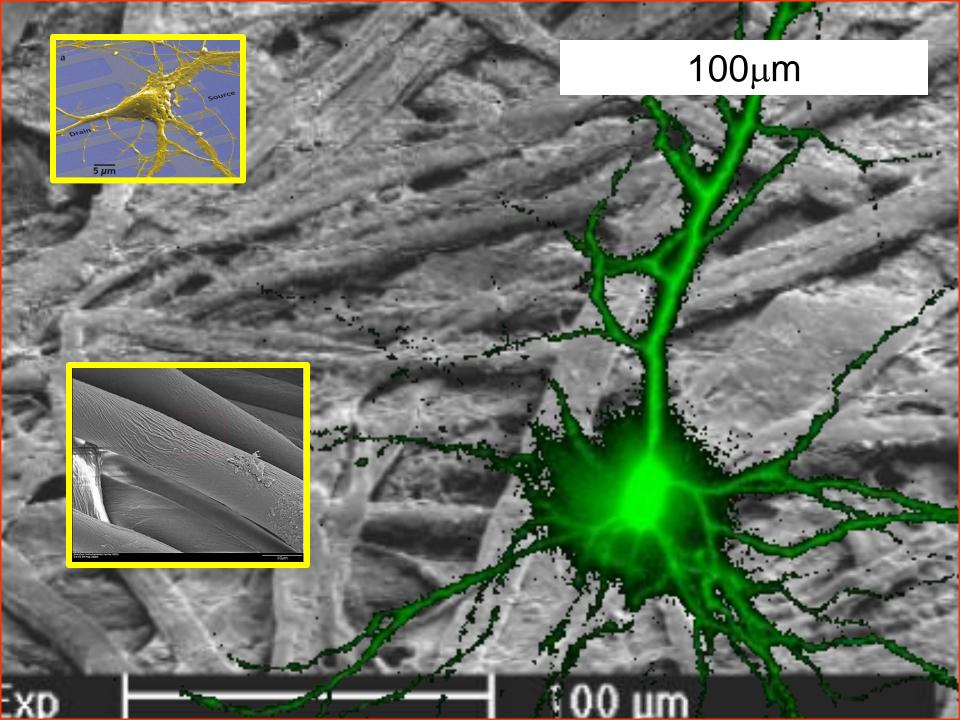
47x35 micron

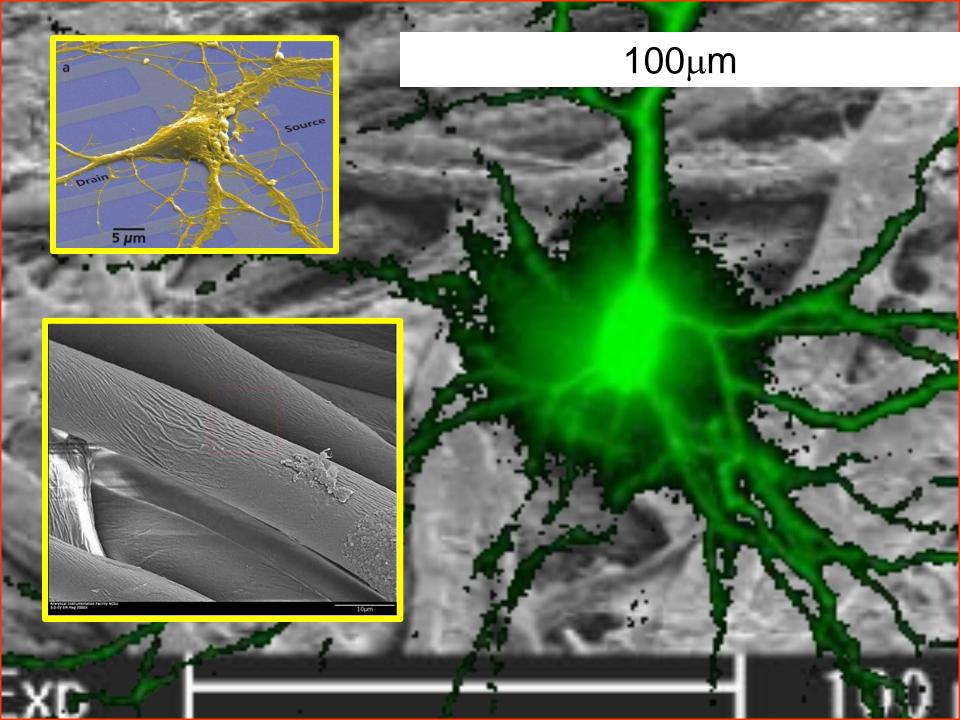
$100\mu m$

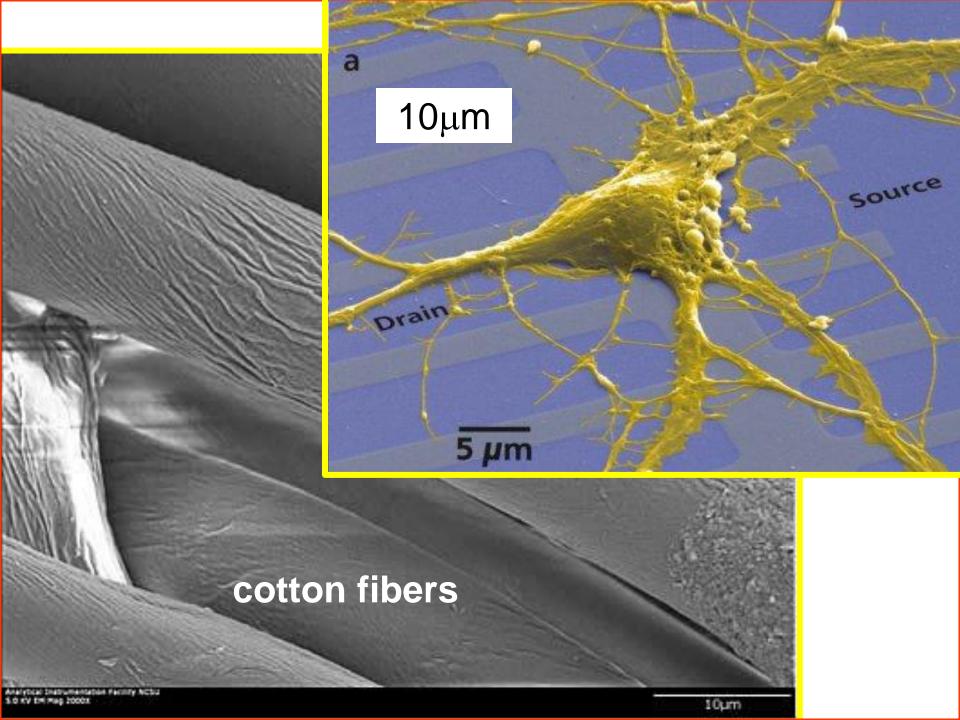
cotton fibers

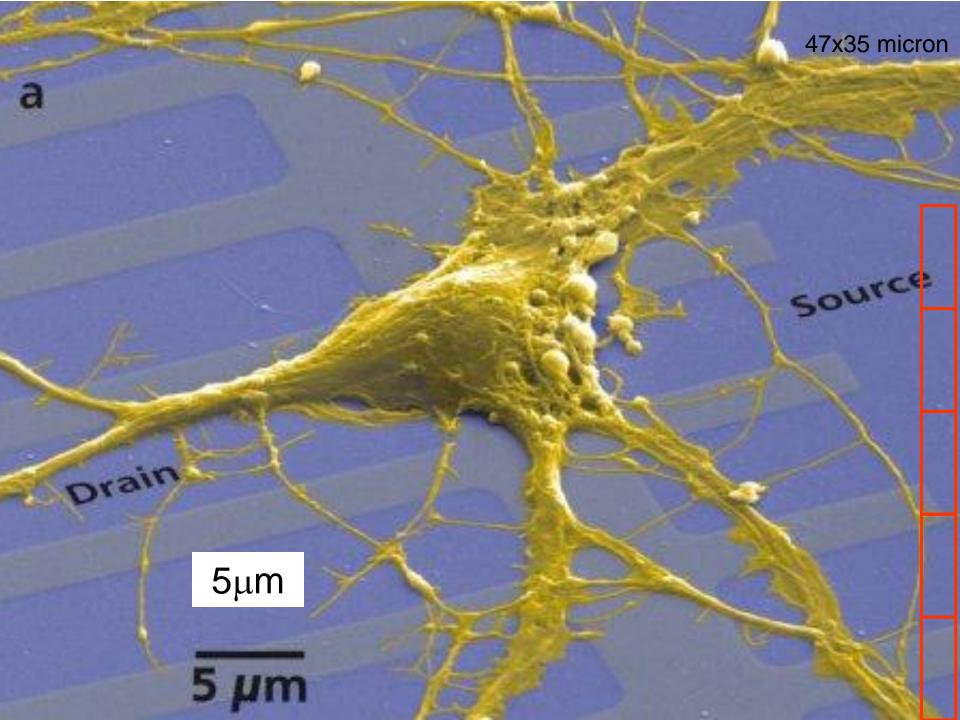


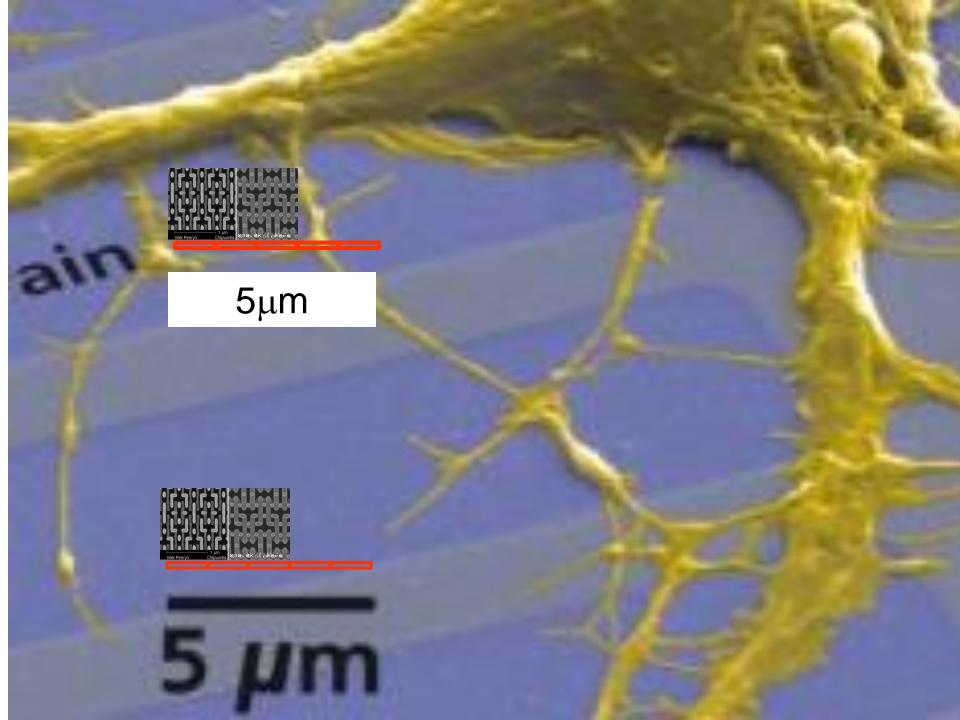
60x50 microns

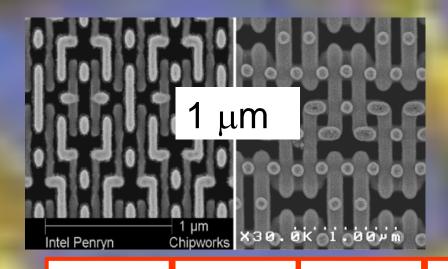




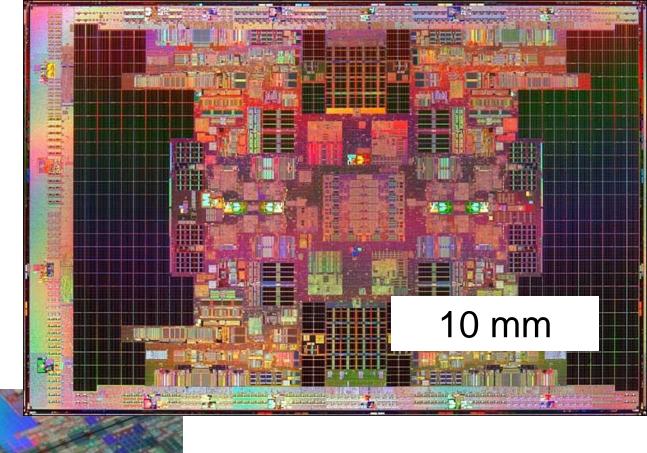


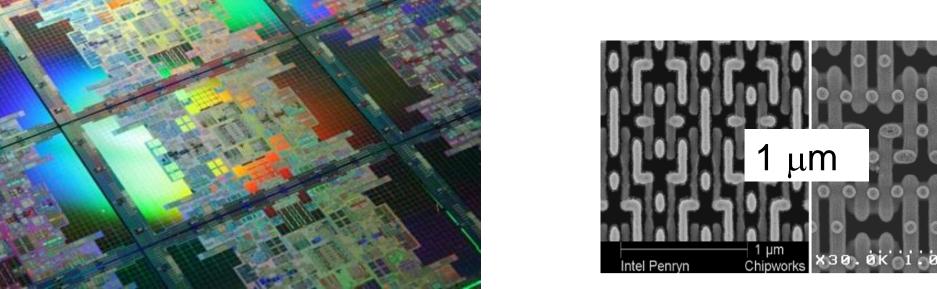


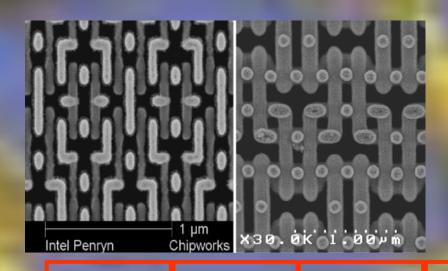


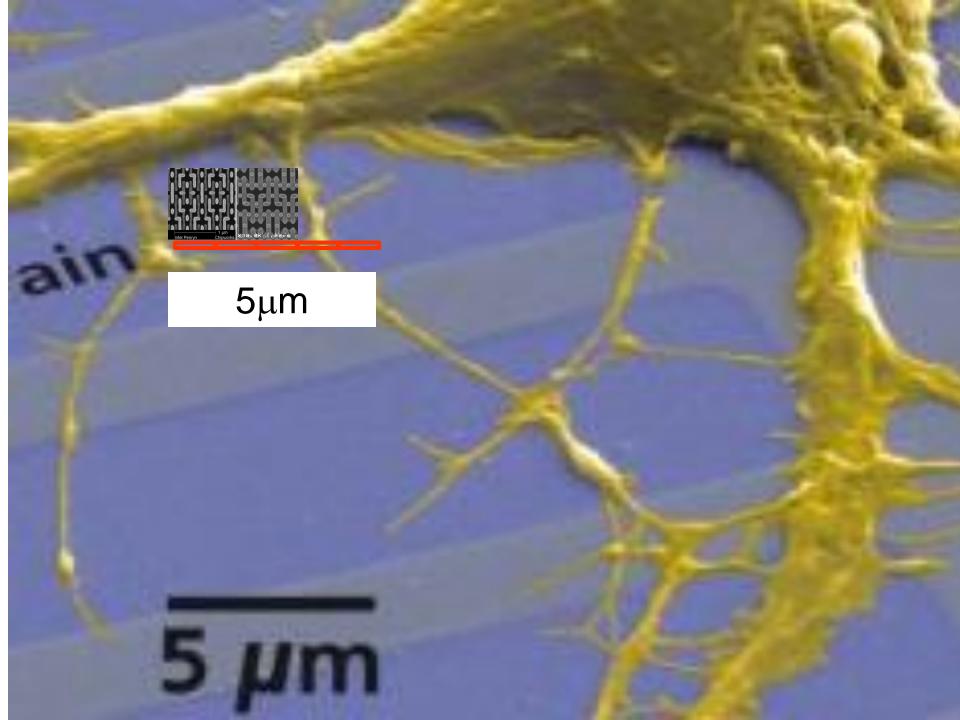


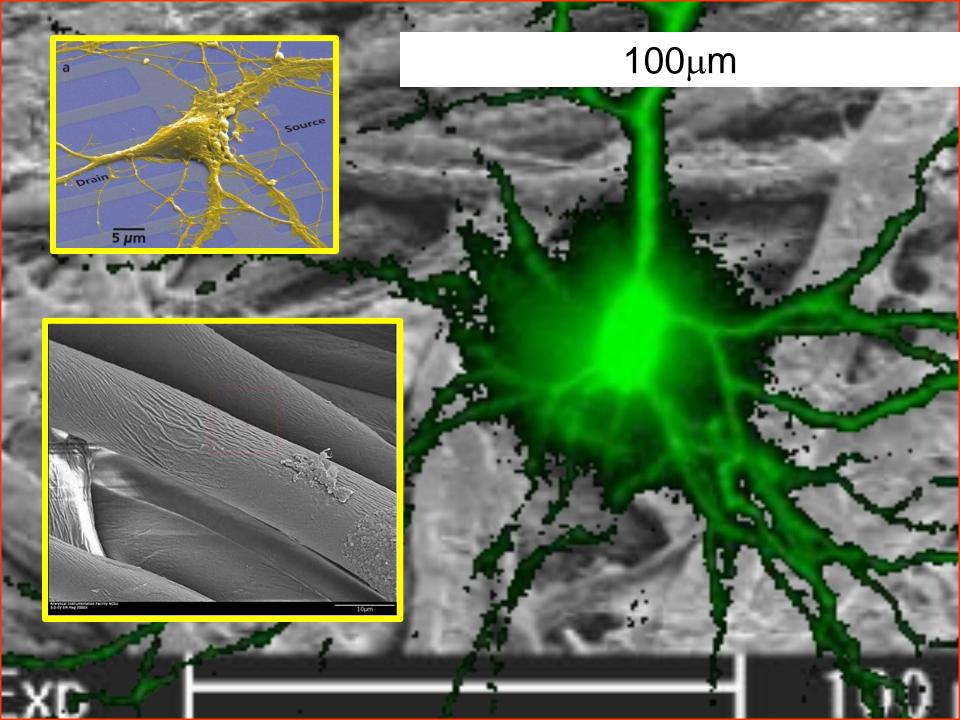
Intel Tukwila quad core chip with more than 2 billion transistors

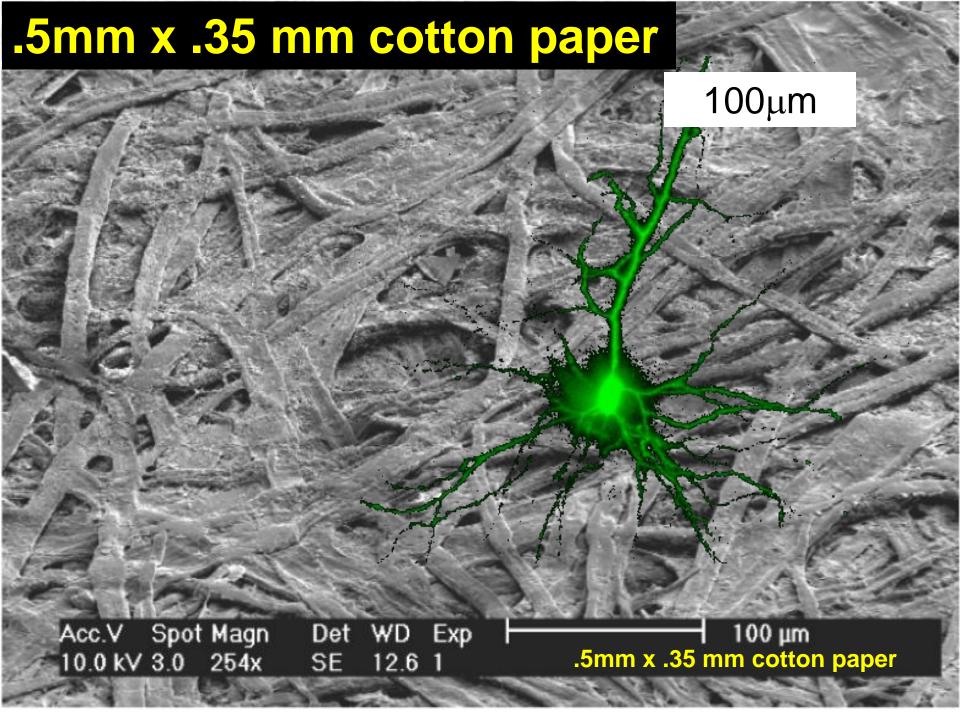






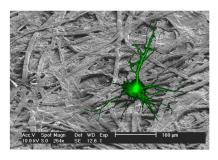






500μm

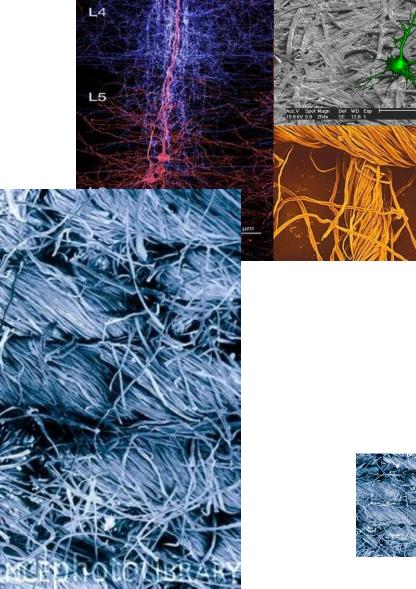
.5mm



500μm

.5mm

denim



cheesecloth

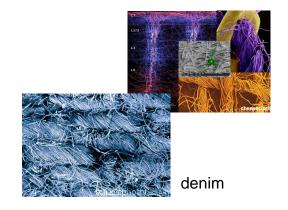
denim

L2/3

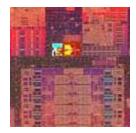


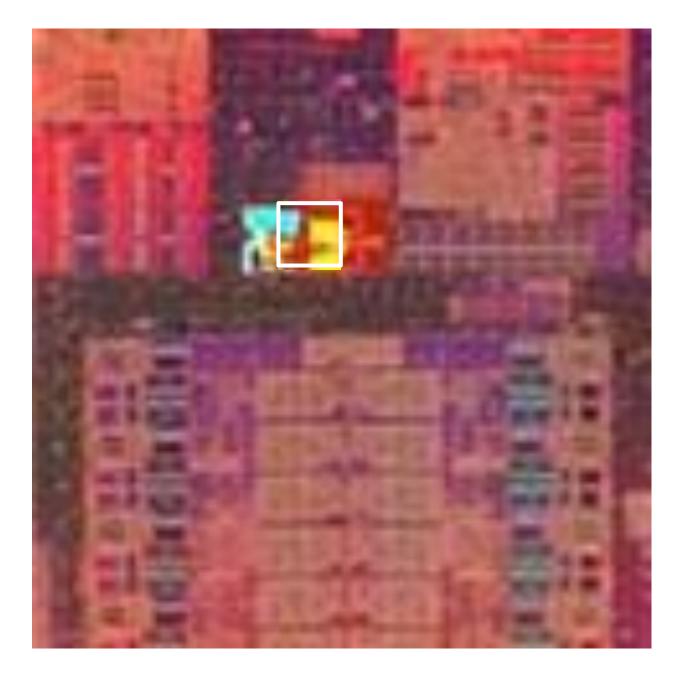
 $500 \times 500 \mu m$

.5×.5mm

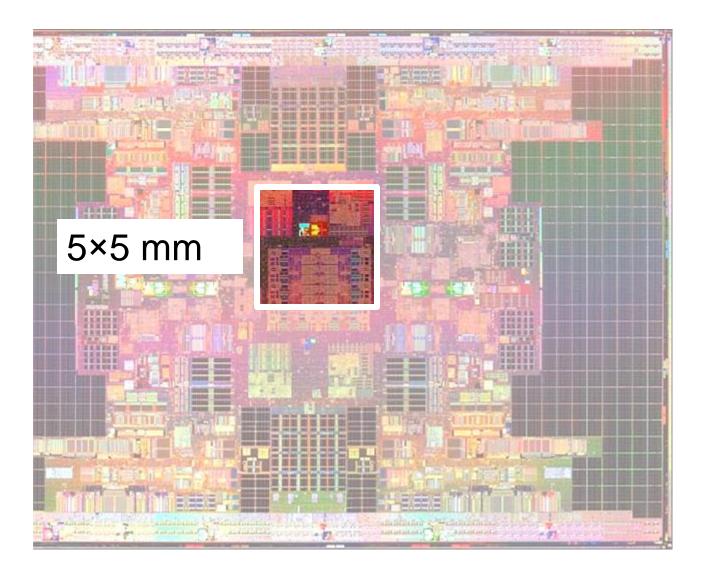


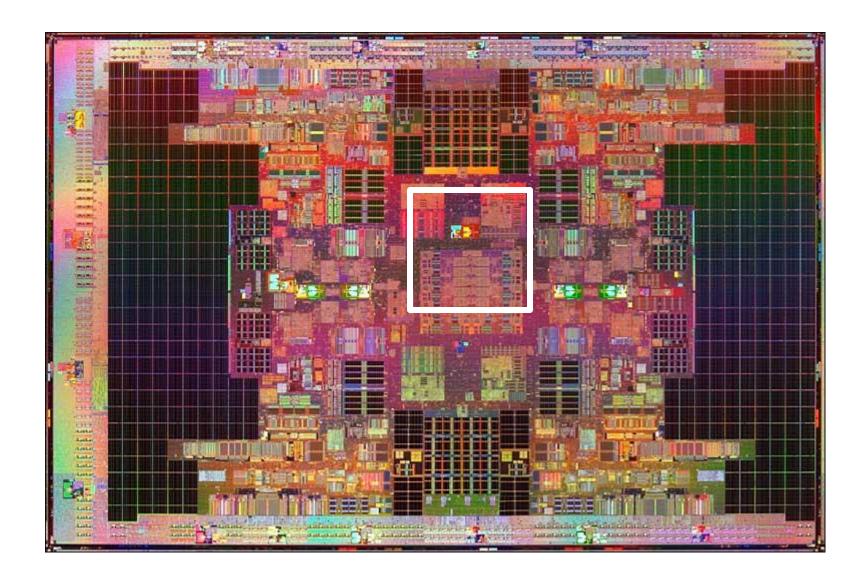


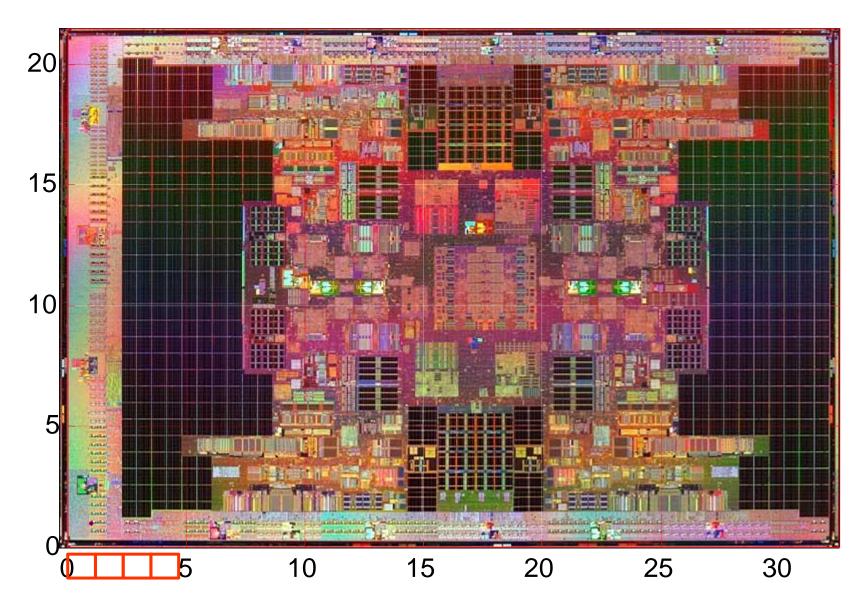




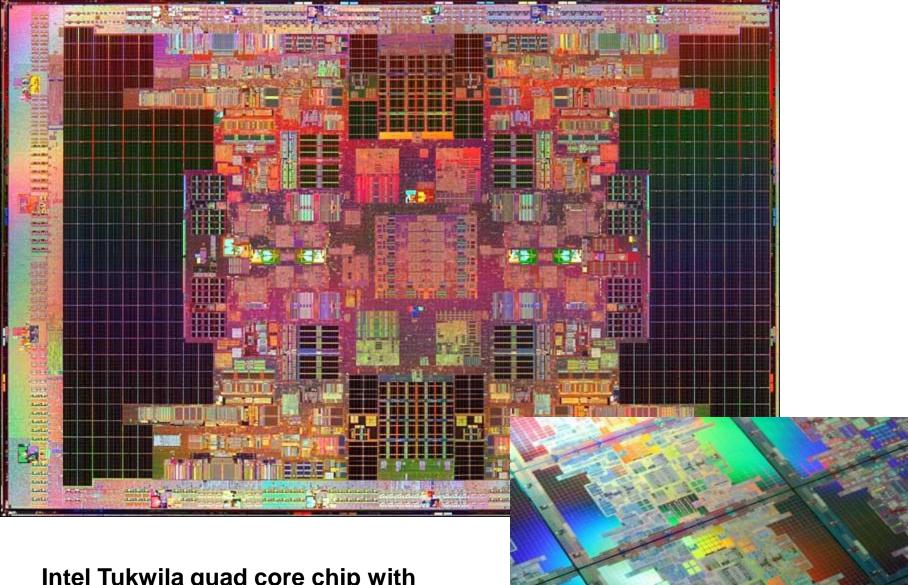






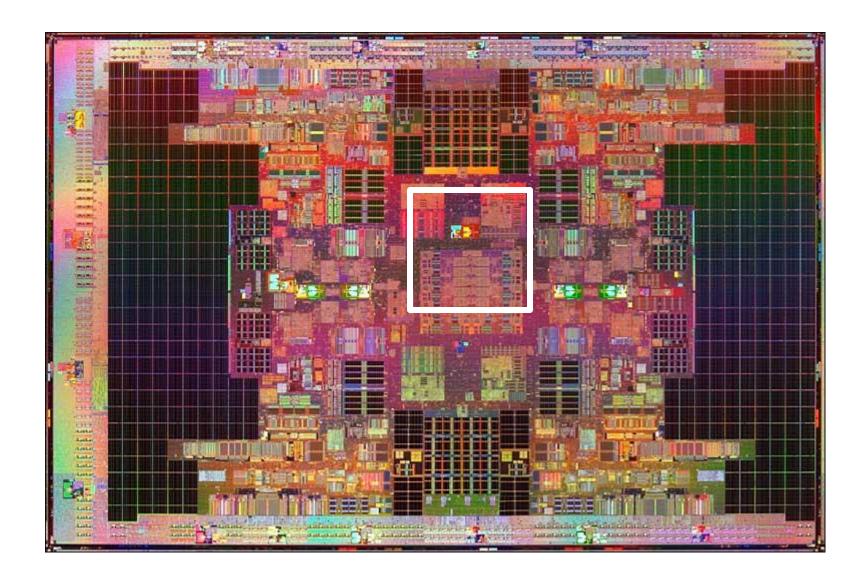


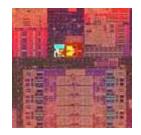
21.5×32.5 mm

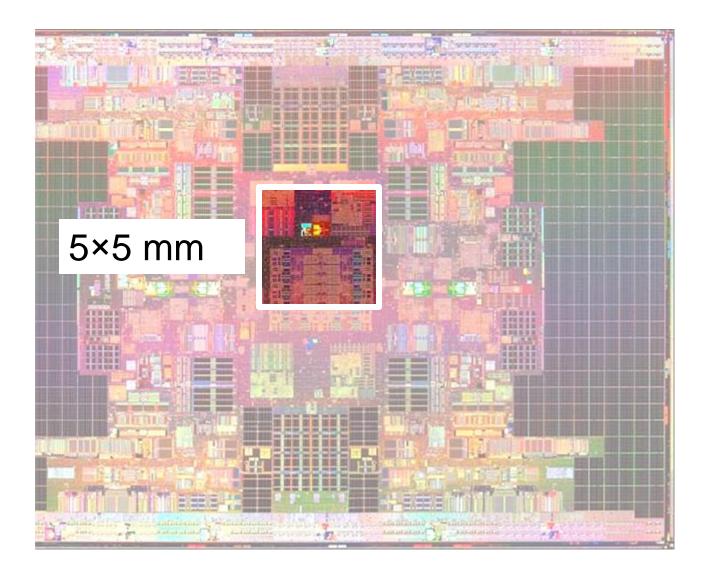


Intel Tukwila quad core chip with more than 2 billion transistors

21.5×32.5 mm



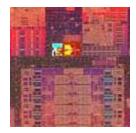


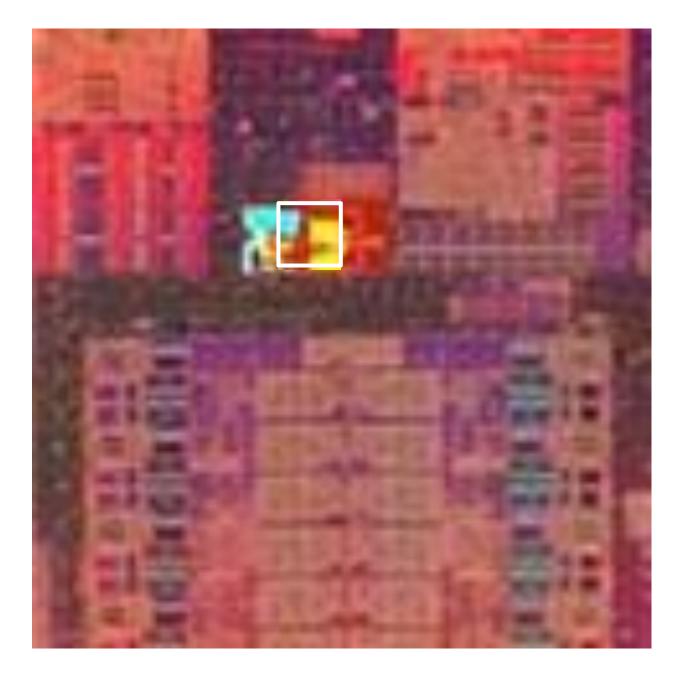










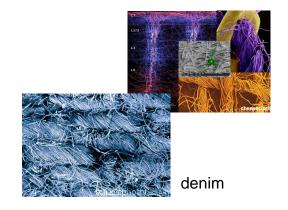






 $500 \times 500 \mu m$

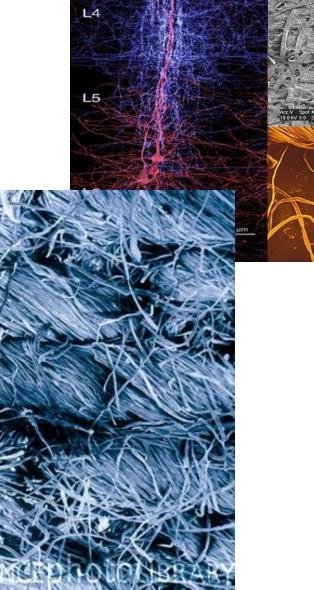
.5×.5mm



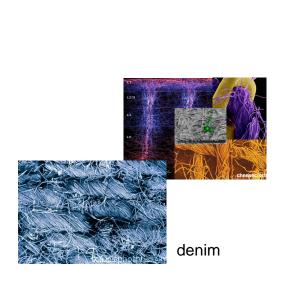
 $500 \mu m$

.5mm

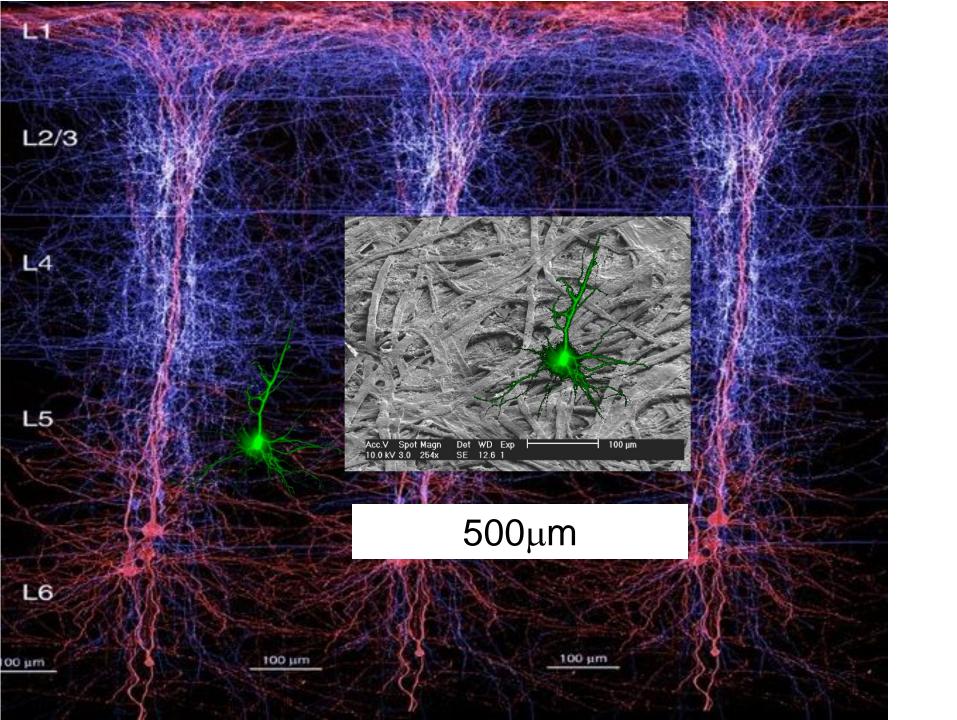
denim

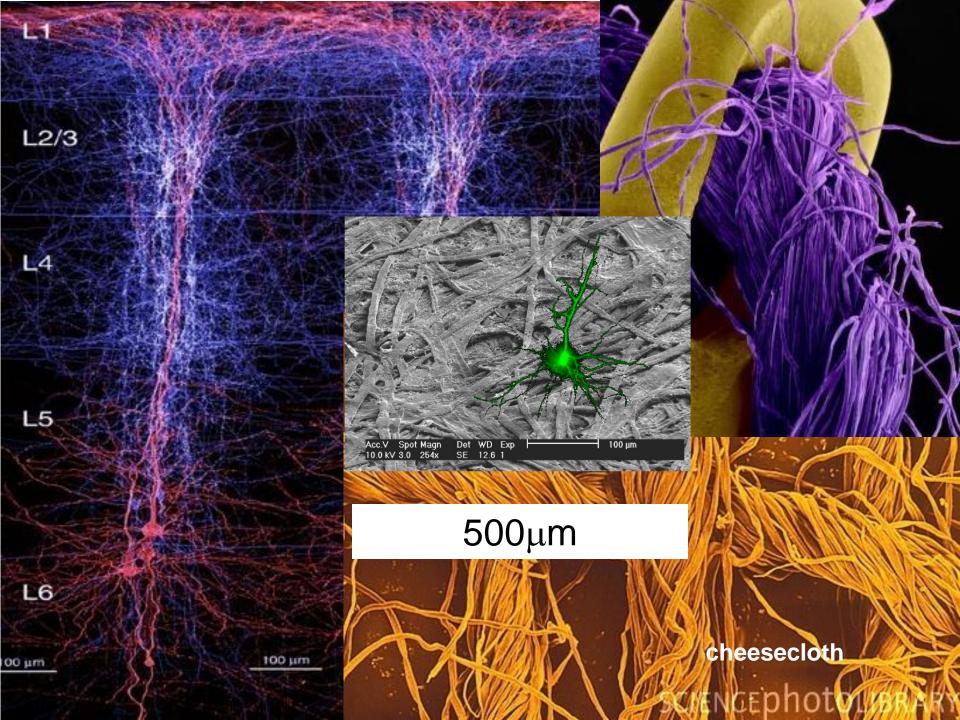


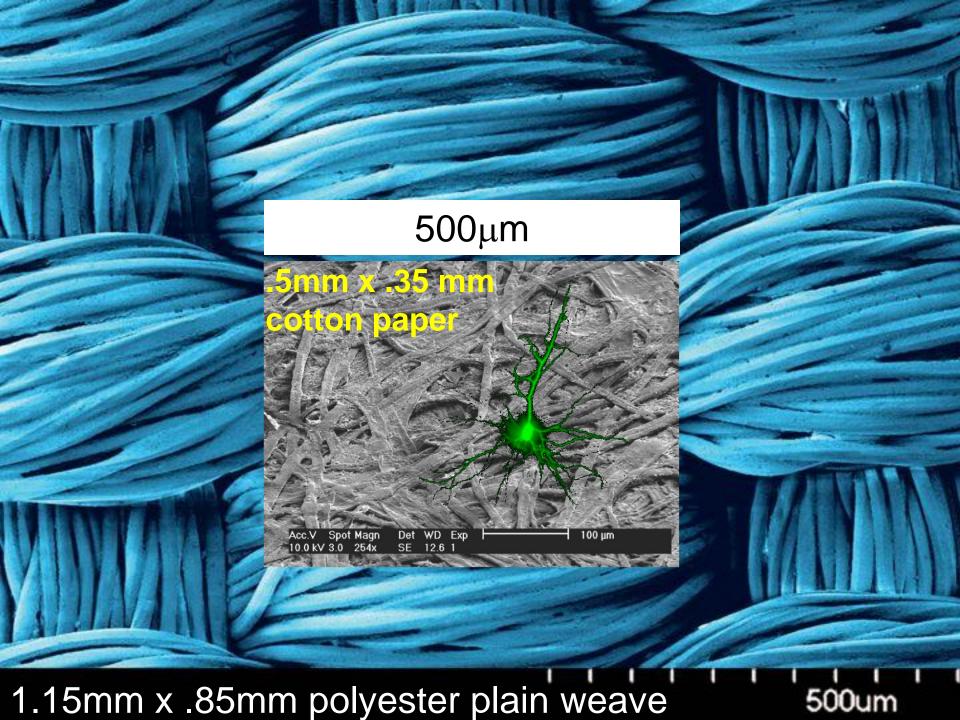
L2/3

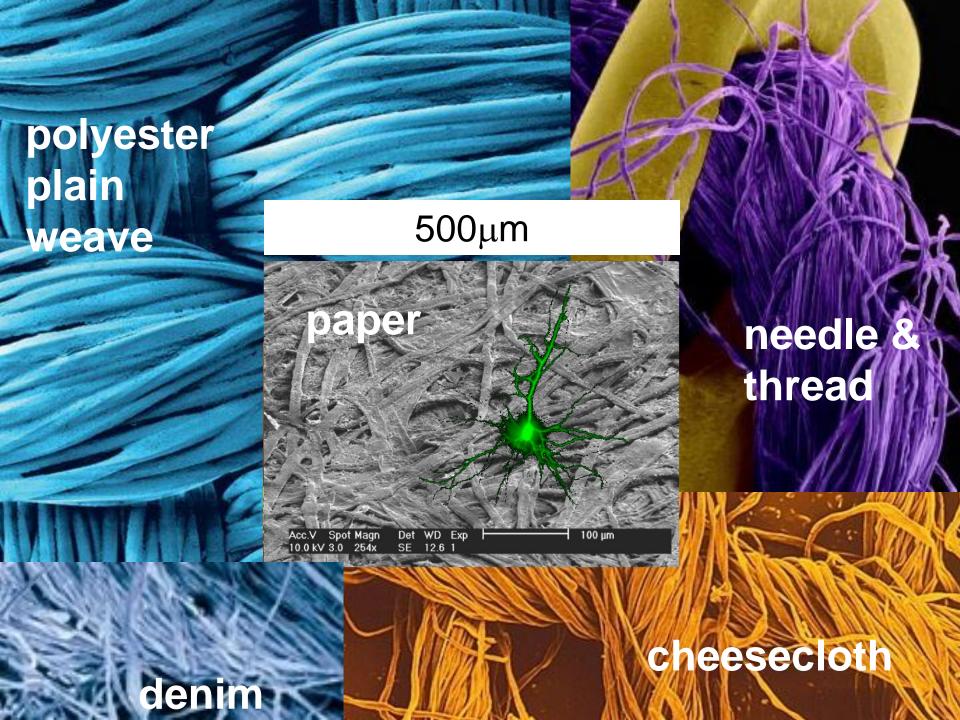


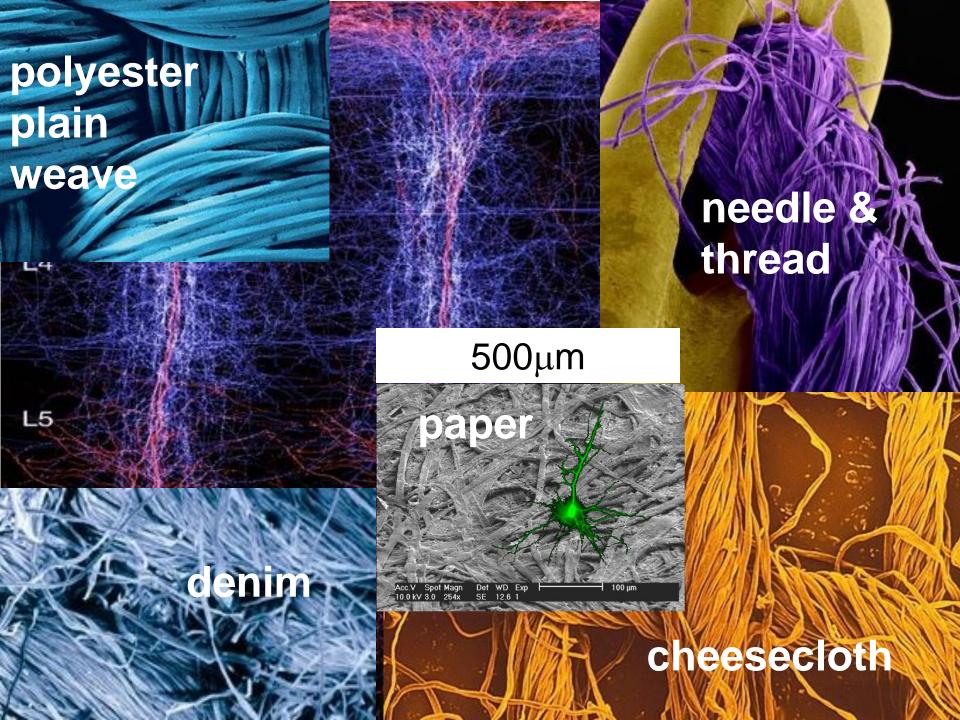
cheesecloth





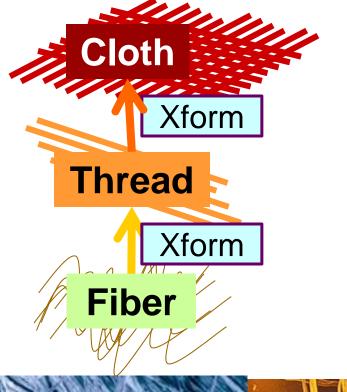


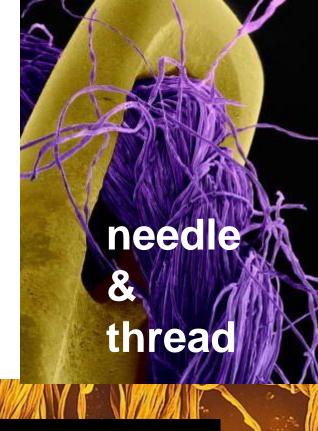




Hidden, large, thin, nonconvex

are necessary

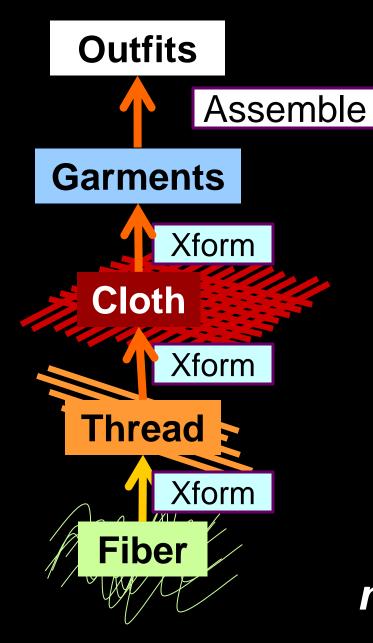






500μm

cheesecloth



Hidden, large, thin, nonconvex

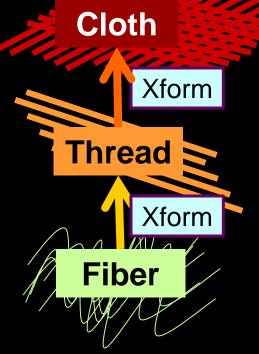
> are necessary

Universal strategies?

Even though garments seem analog/continuous

Garments Garments have limited access to threads and fibers

quantization for robustness



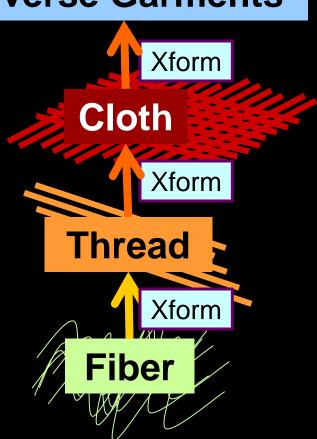
constraints on cross-layer interactions

Prevents unraveling of lower layers

Diverse outfits

Diverse Garments

Constraints that deconstrain

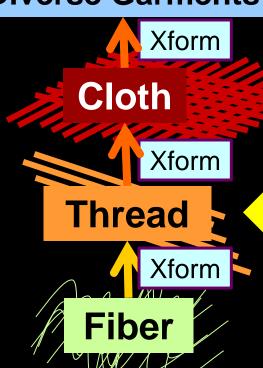


Geographically diverse sources

System constraints

Diverse Outfits Diverse Garments

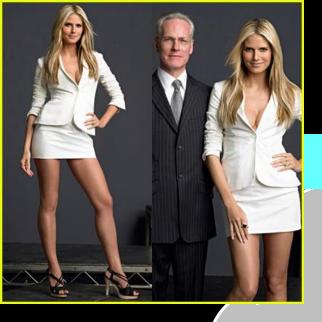
Constraints that deconstrain



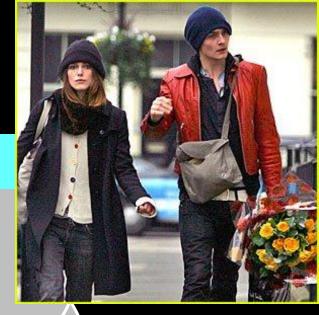
Protocol constraints

Component constraints

Diverse outfits Garments Xform Constraints Cloth **Protocol** Xform that **Thread** deconstrain Xform Fiber **Diverse sources**



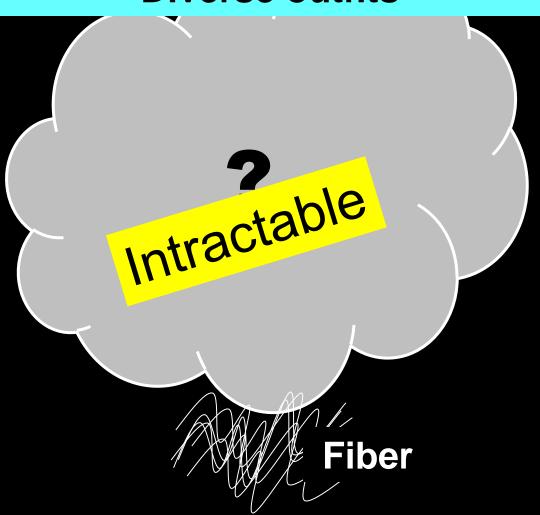
Diverse outfits



?

Fiber

Diverse outfits







SOC/EOC?



Self-Organized Clothing

Edge of Couture

Scale-Free Fashion



Standard error



Diverse outfits Small gap No architecture







Self-Organized Clothing

Edge of Couture

Scale-Free Fashion



Standard error

Diverse outfits



Huge gap
No architecture
Supernatural





Mysteries in the gaps No architecture

Diverse outfits









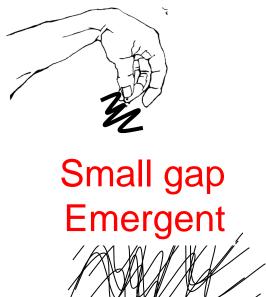


Small gap **Emergence** Self-organized Phase transition Edge-of Scale-free

Diverse outfits



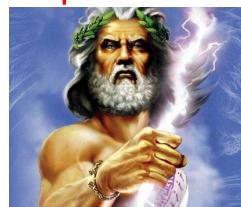


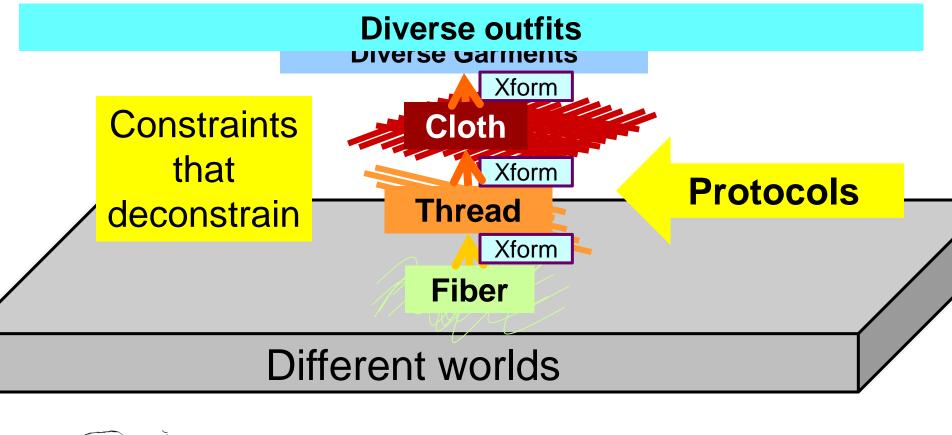


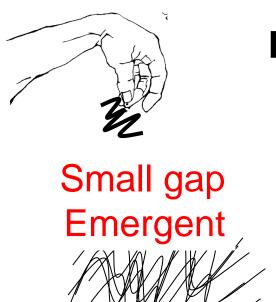
Mysteries in the gaps No architecture

Mainstream

Huge gap Supernatural



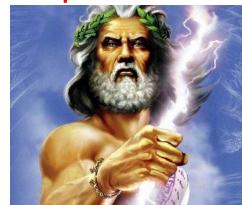


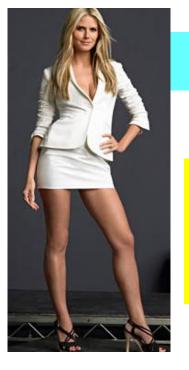


Mysteries in the gaps No architecture

Mainstream

Huge gap Supernatural





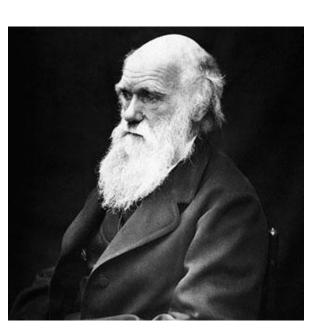
Diverse outfits

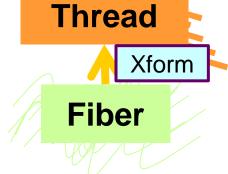
Diverse Garments

Constraints that deconstrain



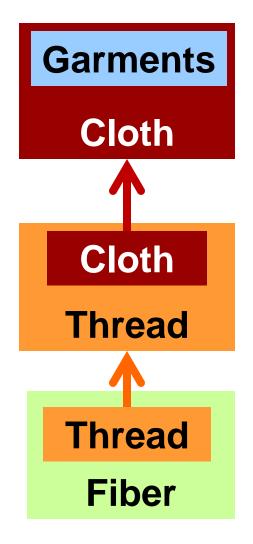
Protocols



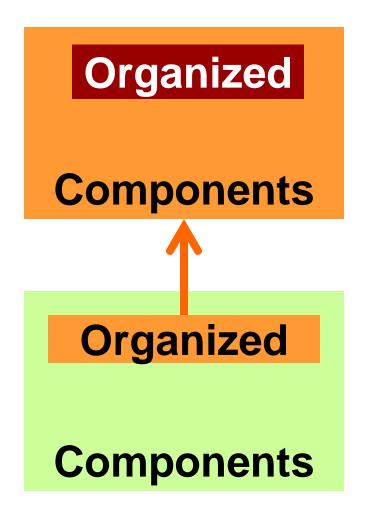


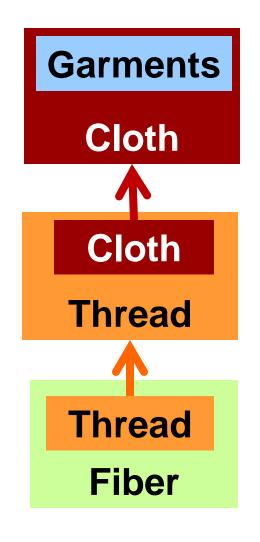






Layered, large, thin

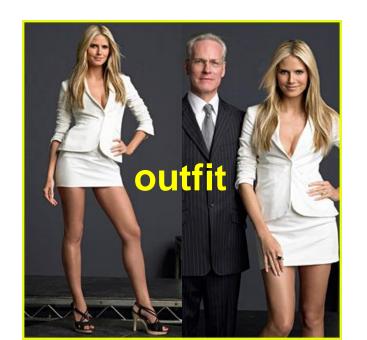




large thin
1 << # outfits << # heaps</pre>

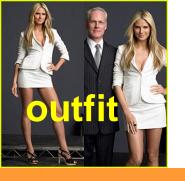
Organized

Components



Components





large thin

1 << # outfits << # heaps

Organized

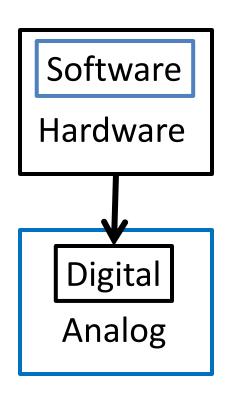


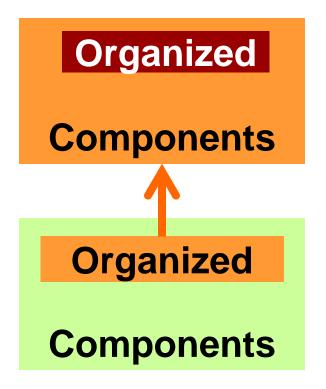
Components

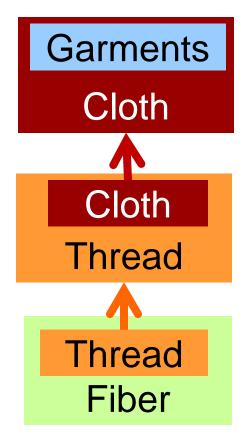


Architecture

What is the "true functional unit?"







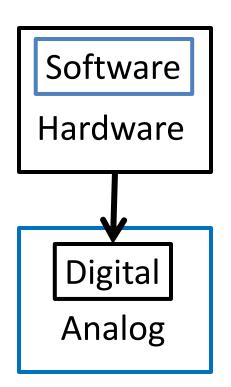
Virtual machines

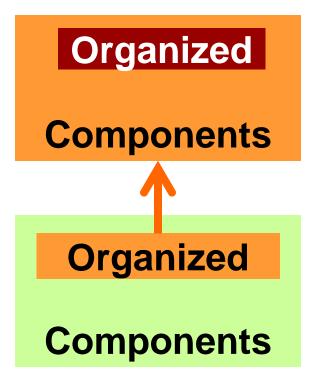
Software

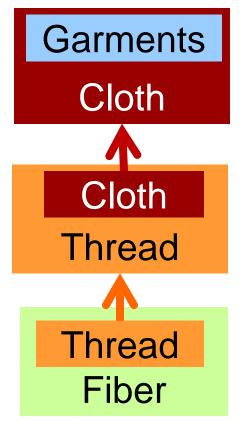
Organized

Garments

Implementations







Software

Organized

Garments

Virtual machines

Digital

Organized

Cloth

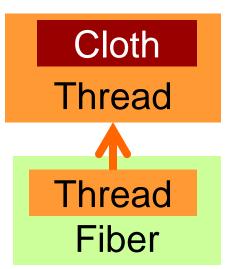
Implementations

Digital

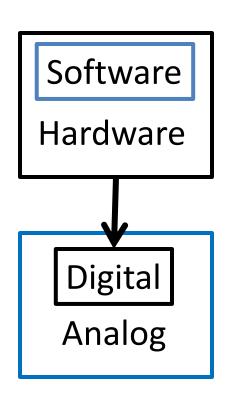
Analog

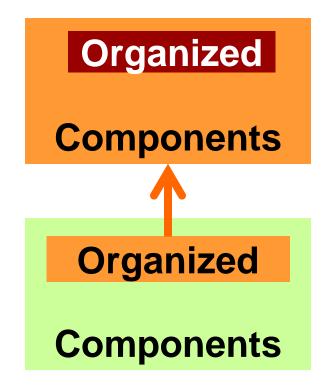
Organized

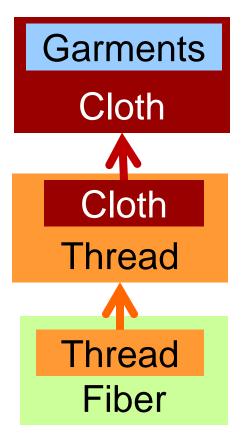
Components



Layered, large, thin Hidden Virtualized





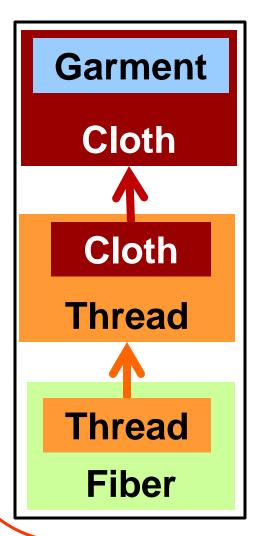


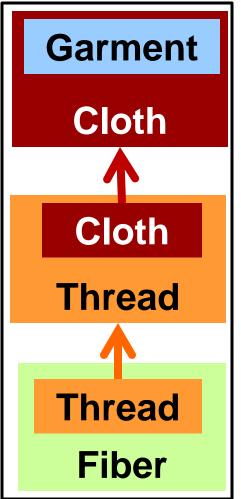
Outfit

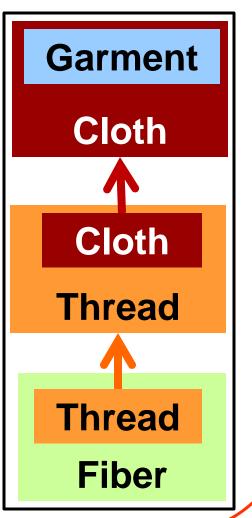
Garment Garment

Garment

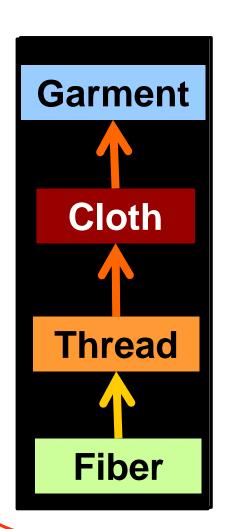
Outfit

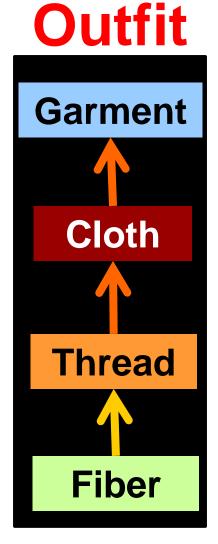




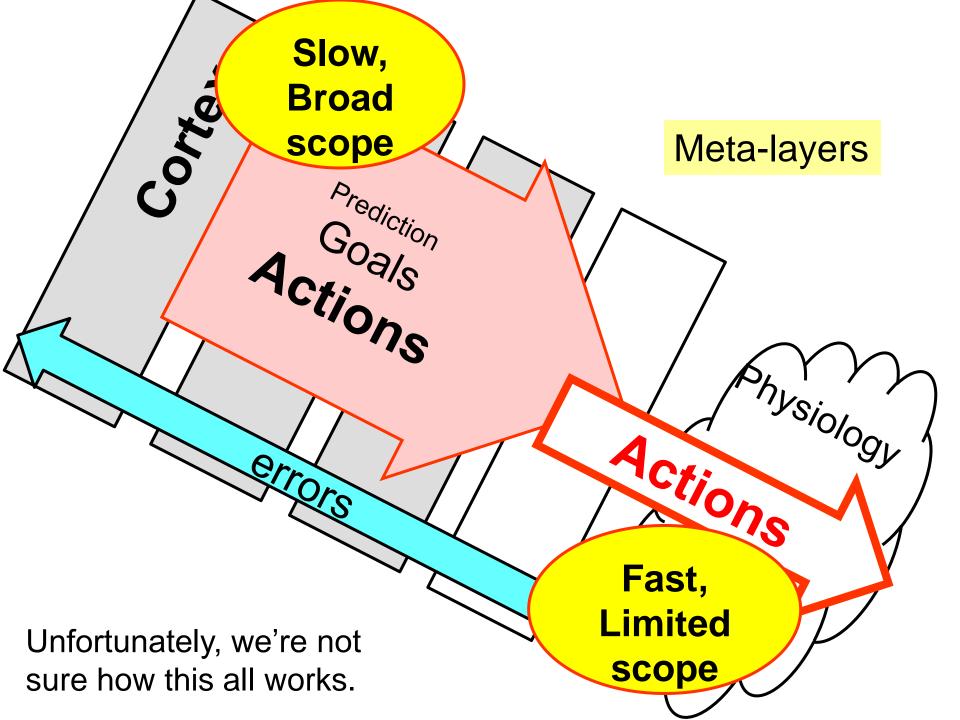


Layering within garments (textiles)



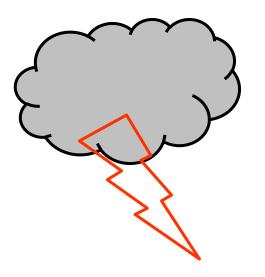








Environment



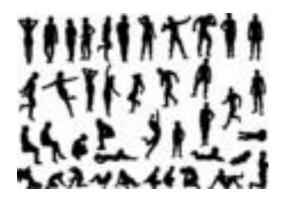
Outfit

Insulation

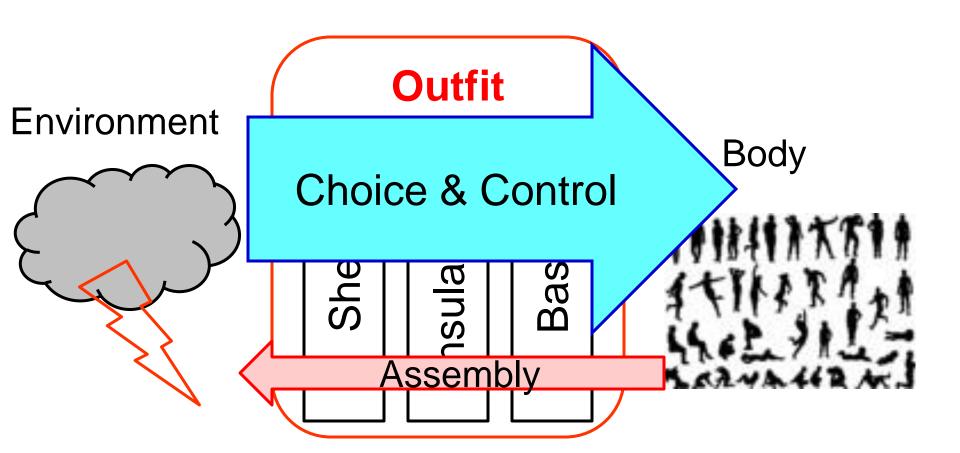
Shell

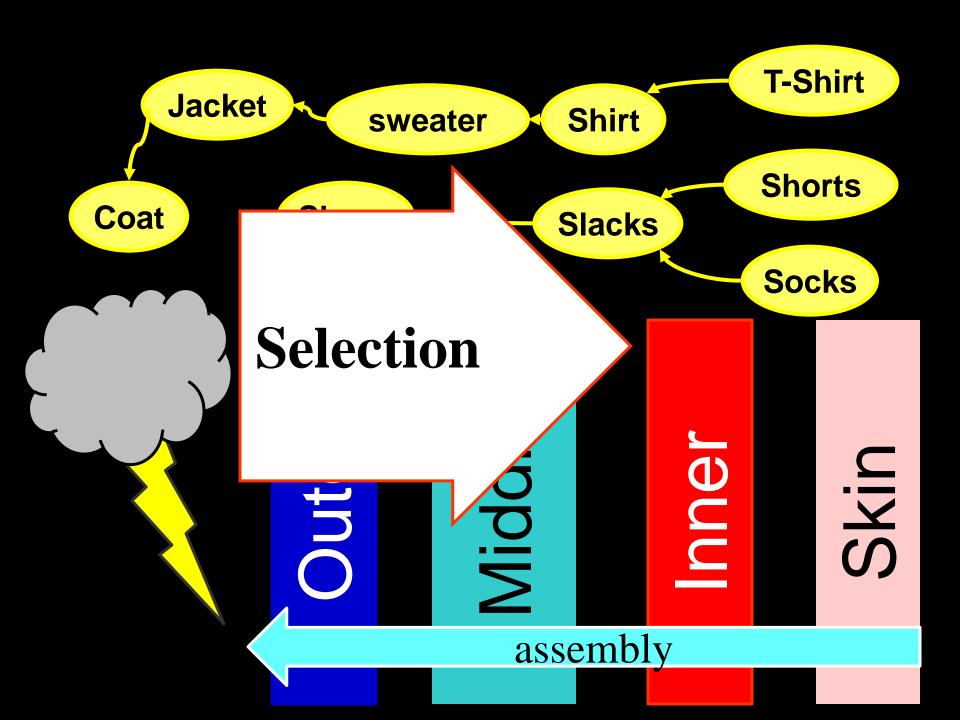
Base

Body

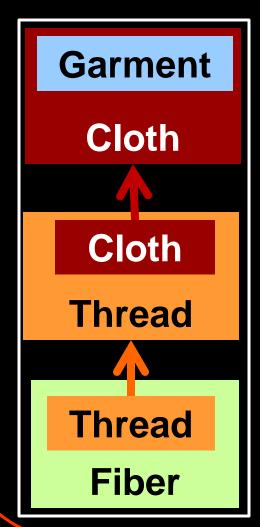


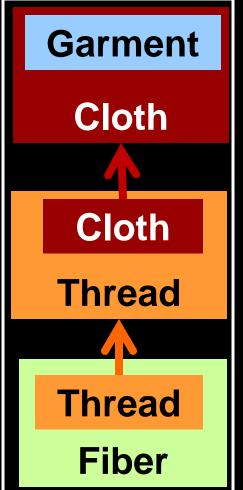
- Complexity ⇔ Robustness
- Layers must be hidden to be robust
- Choice (management and control) is more complex than assembly

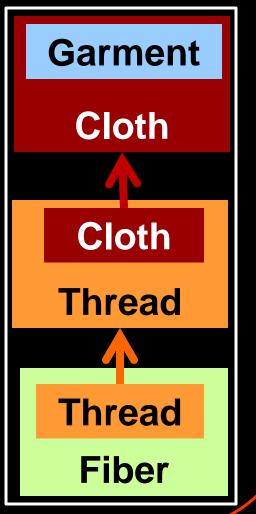




Outfit

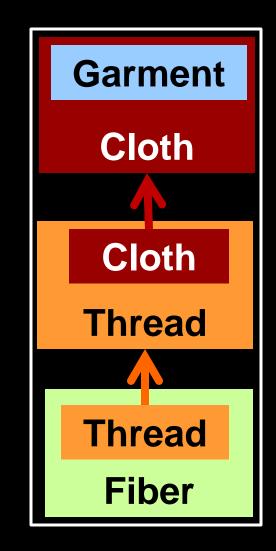






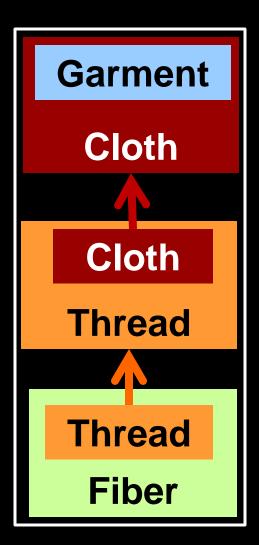
Outfit

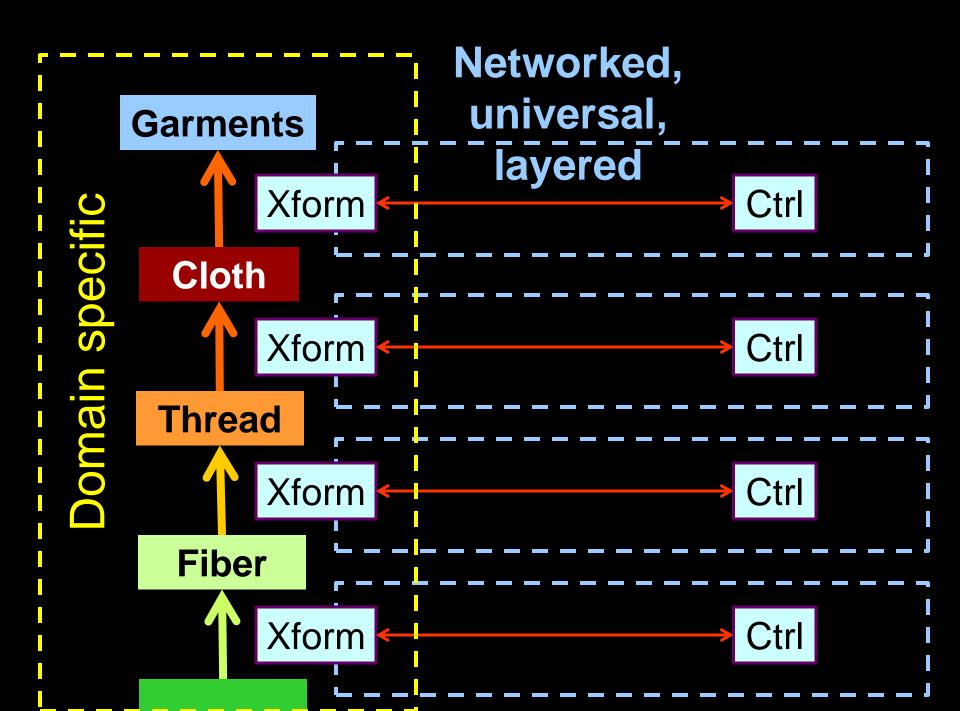
Assembly

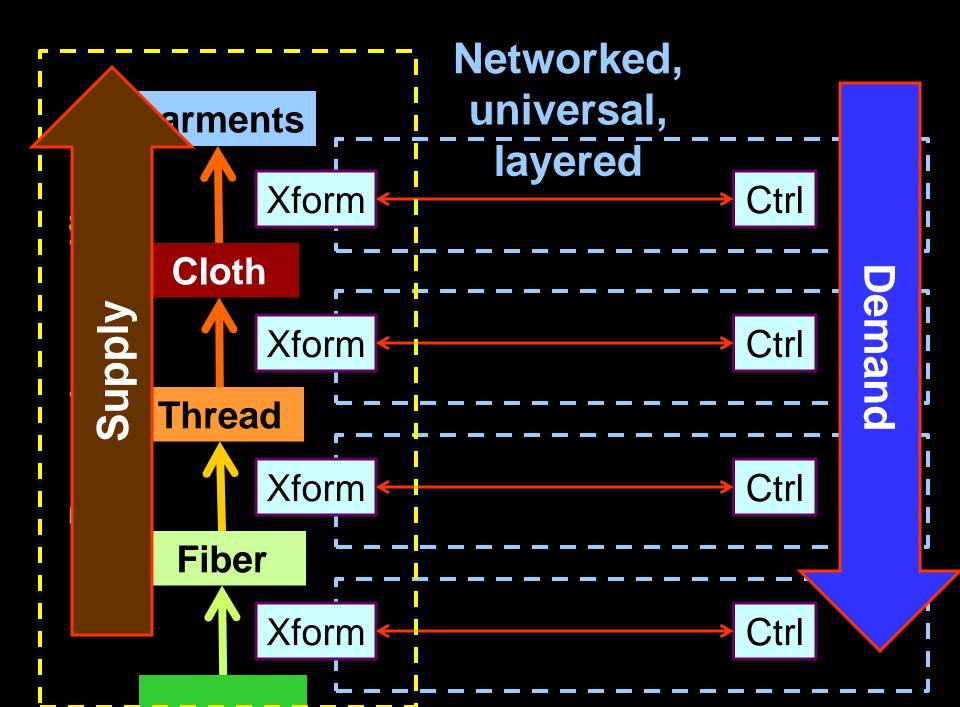


Garments Sew specific Cloth Weave Jomain **Thread** Spin **Fiber** Farm

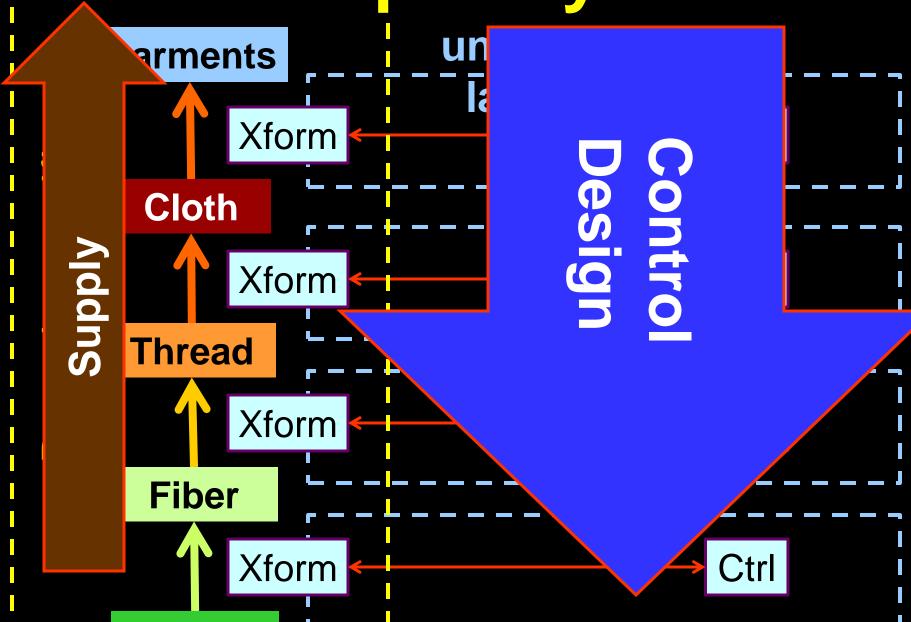
Assembly







Complexity?

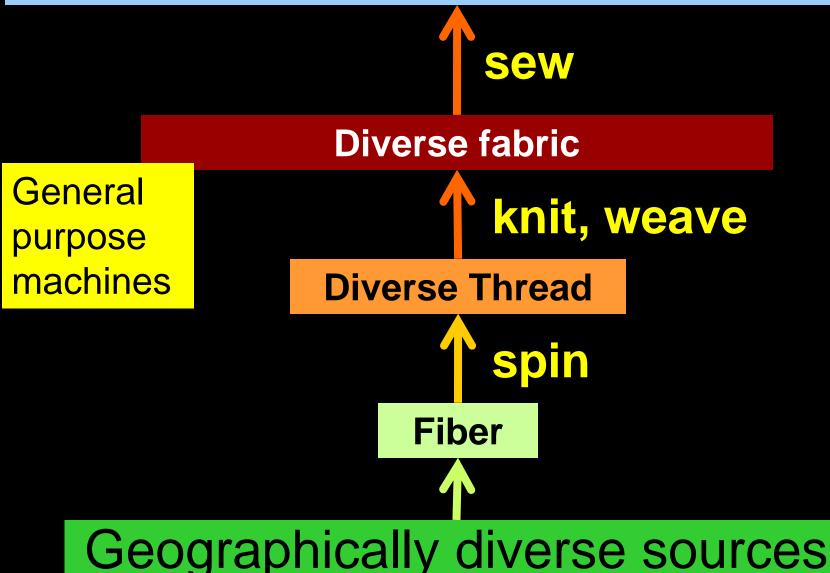


Assembly

constraints

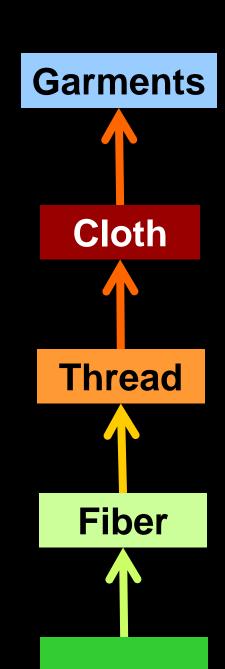
Assembly

Functionally diverse garments



Functionally diverse garments

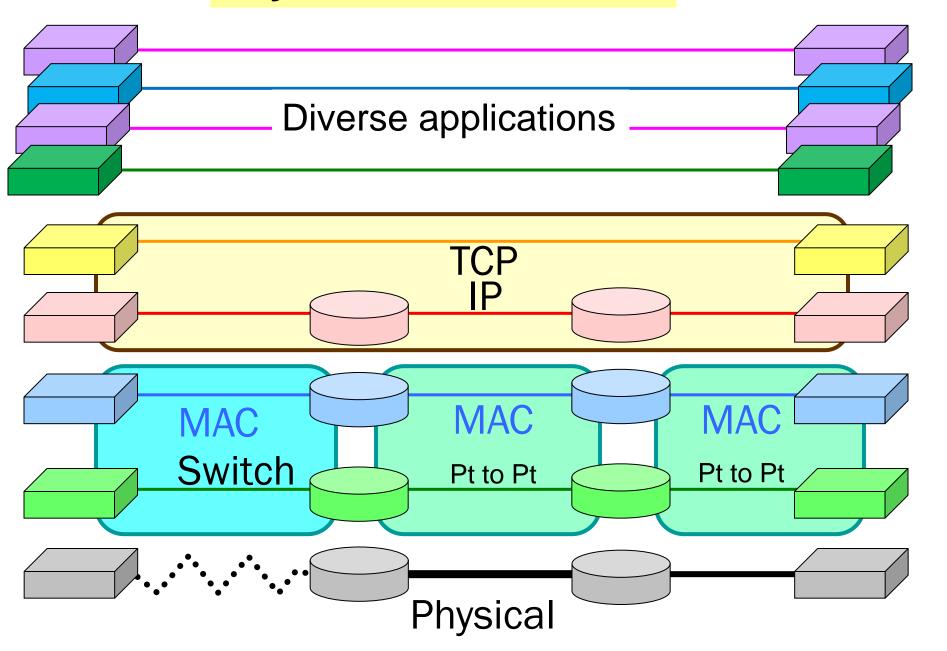




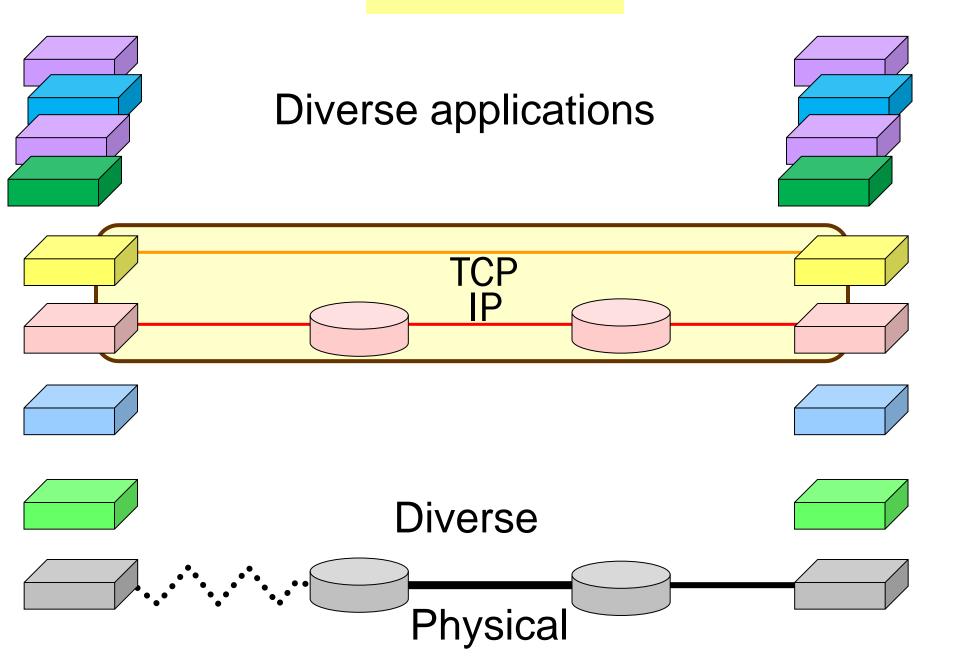
Scalable

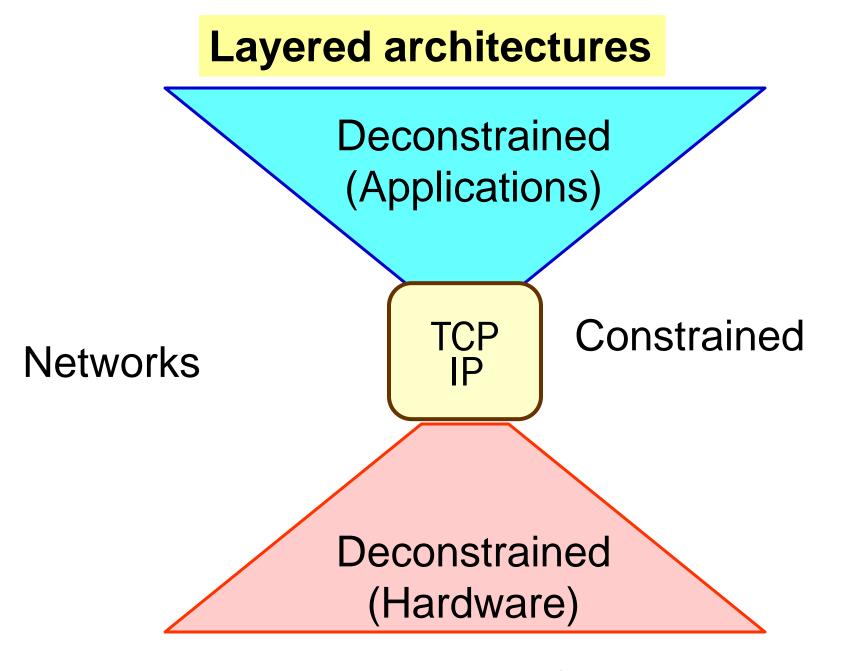
Sustainable?

Layered architectures



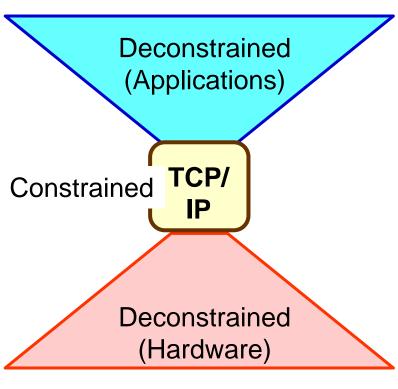
Too clever?





"constraints that deconstrain" (Gerhart and Kirschner)

Networked OS



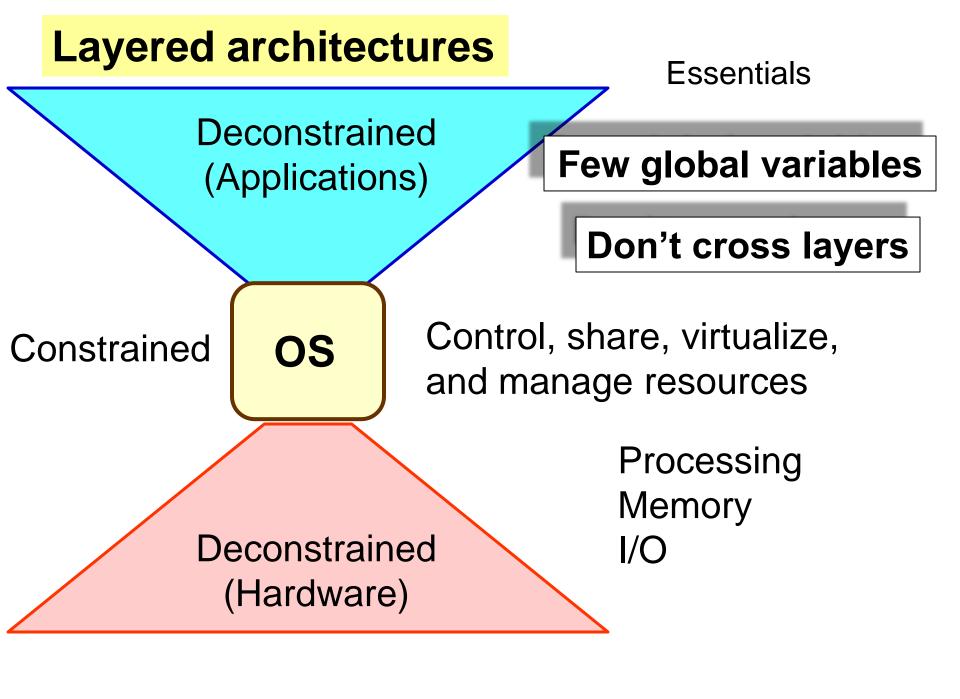
- OS better starting point than phone/comms systems
- Extreme robustness confers surprising evolvability
- Creative engineers
- Rode hardware evolution

Facilitated wild evolution Created

- whole new ecosystem
- completely opposite

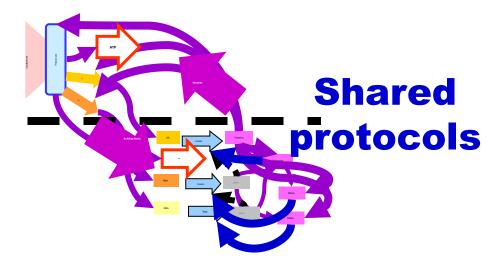
Why?

Architecture



Layered architectures

Deconstrained (diverse) Environments

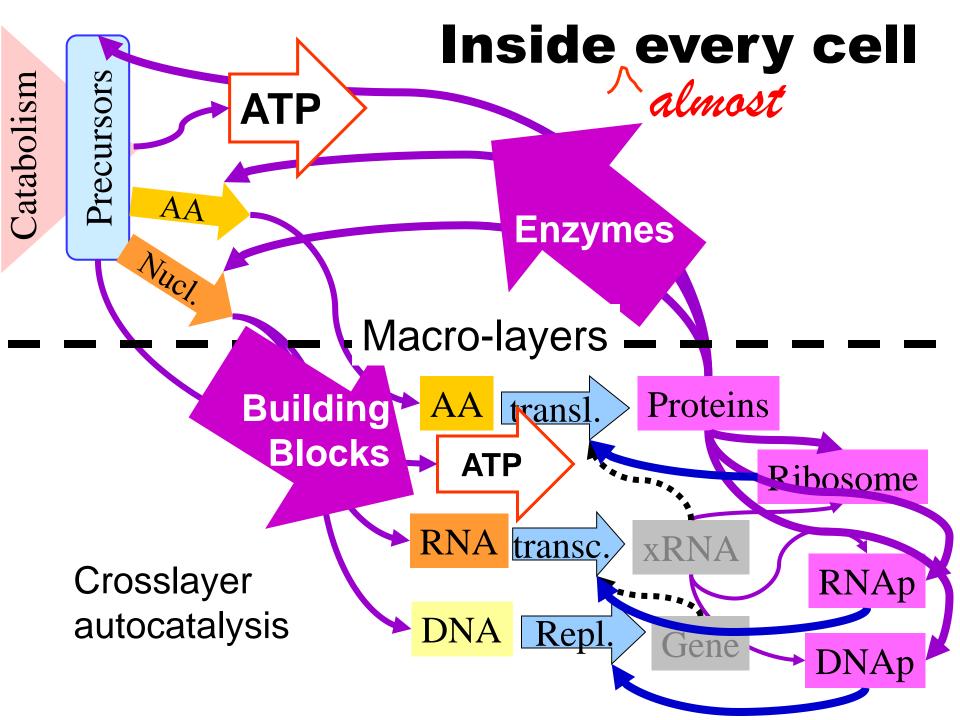


Deconstrained (diverse)
Genomes

Bacterial biosphere

Architecture

Constraints that Deconstrain

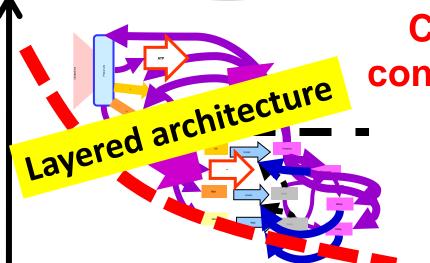


What makes the bacterial biosphere so adaptable?

Deconstrained phenotype

Environment

Action



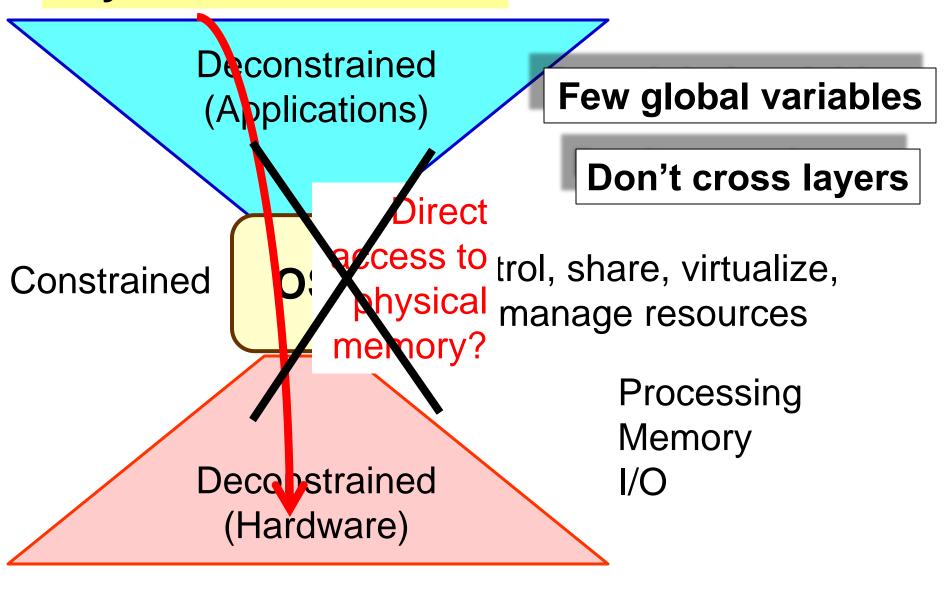
Core conserved constraints facilitate tradeoffs



Active control of the genome (facilitated variation)

Deconstrained genome

Layered architectures



Deconstrained (diverse) Environments

Bacterial biosphere

Few global variables

Ŀture

Shared protocols

Constraints

Don't cross layers

train

Deconstrumed (diverse)
Genomes

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?

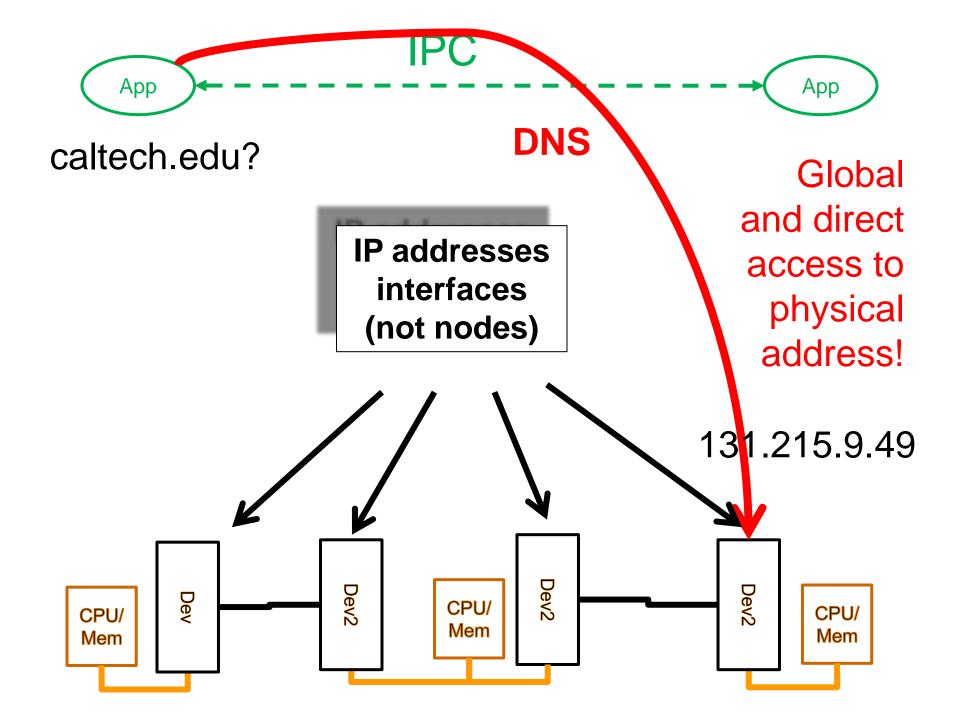
Fragilities of layering/virtualization

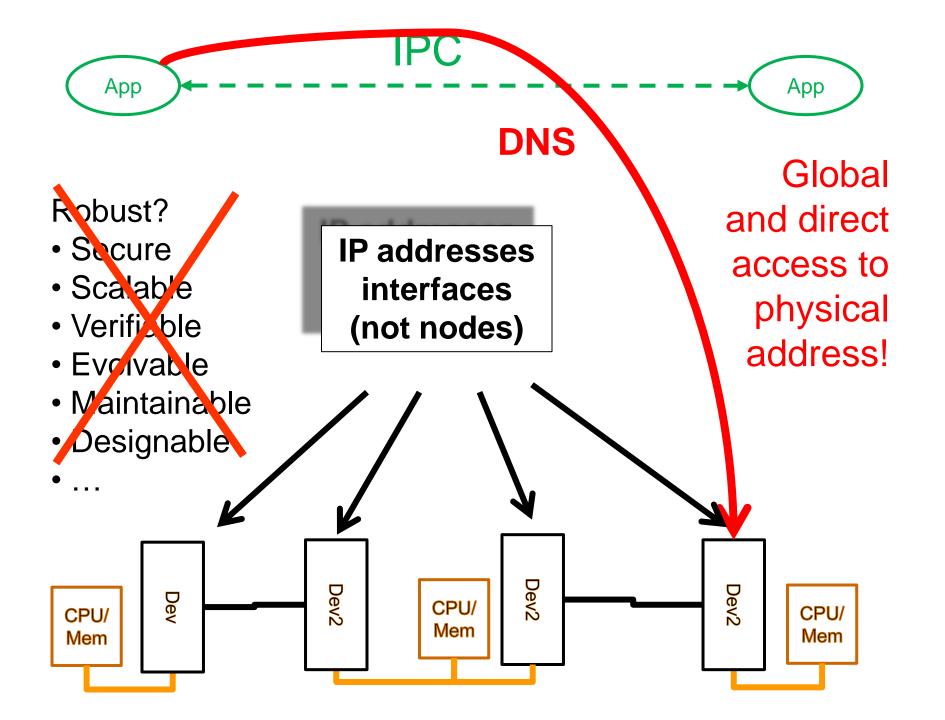
"Universal" fragilities that must be avoided

- Hijacking, parasitism, predation
 - Universals are vulnerable
 - Universals are valuable
- Cryptic, hidden
 - breakdowns/failures
 - unintended consequences
- Hyper-evolvable but with frozen core

Layered architectures

Deconstrained Few global variables? (Applications) Don't cross layers? TCP/ Control, share, virtualize, Constrained and manage resources I/O Comms Deconstrained Latency? (Hardware) Storage? Processing?





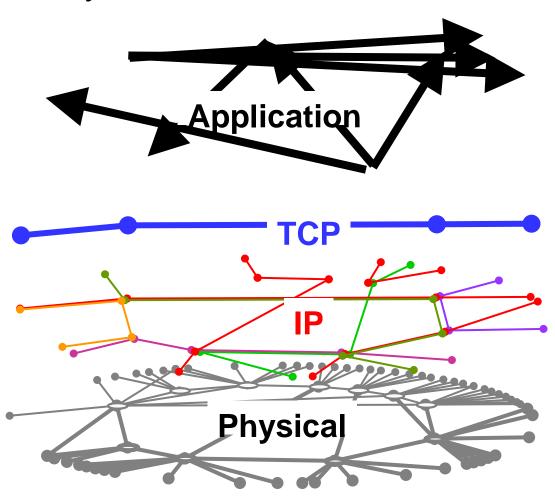
Naming and addressing need to be

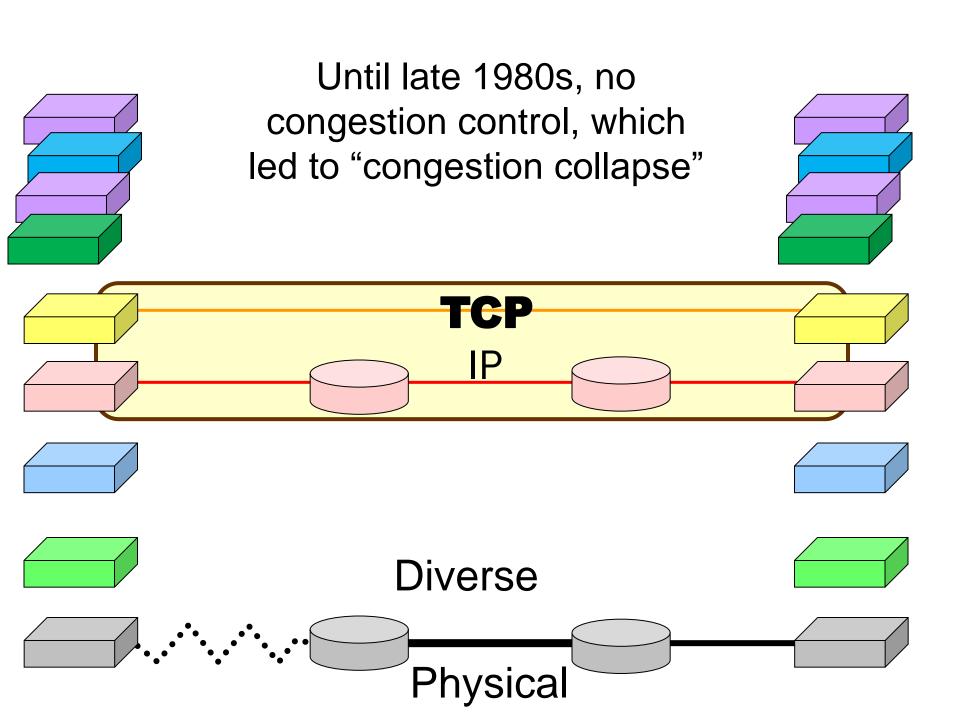
- resolved within layer
- translated between layers
- not exposed outside of layer

Related "issues"

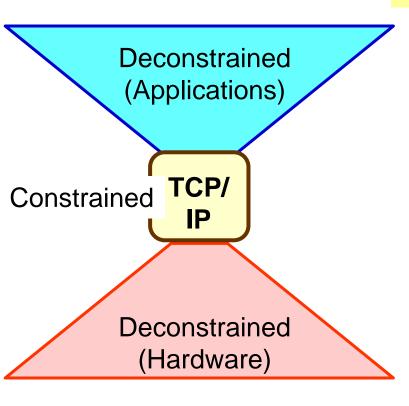
- VPNs
- NATS
- Firewalls
- Multihoming
- Mobility
- Routing table size
- Overlays

• . . .





Original design challenge?



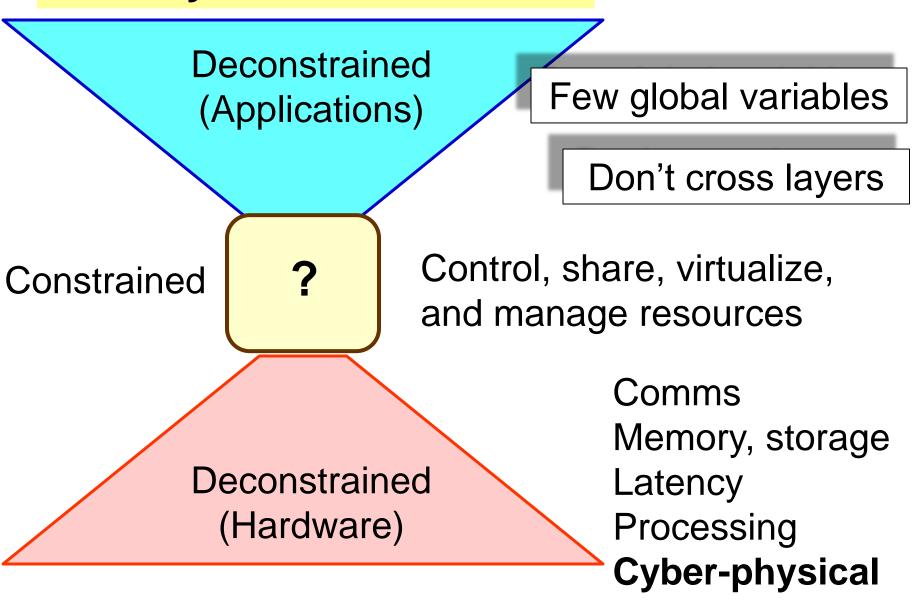
Networked OS

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

Facilitated wild evolution Created

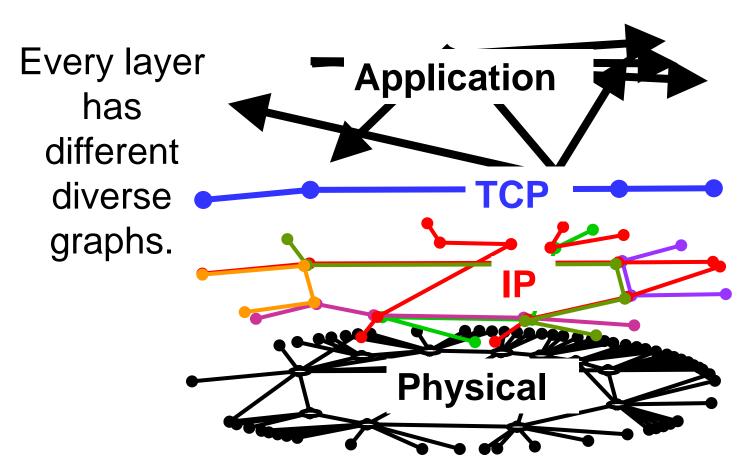
- whole new ecosystem
- completely opposite

Next layered architectures



Persistent errors and confusion ("network science")

Architecture is *least* graph topology.



Architecture facilitates arbitrary graphs.

PNAS

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

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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

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

Walter Willinger, David Alderson, and John C. Doyle

