Polymerization and complex Ligand Autocatalytic feedback assembly Receptor Proteins DP Fatty acids Ъ $G\alpha$ liα GTF Carriers Genes DNA nasn

John Doyle

John G Braun Professor Control and Dynamical Systems, BioEng, and ElecEng Caltech

www.cds.caltech.edu/~doyle



Core theory challenges

- Hard limits
- Short proofs
- Small models

• Architecture

Architecture?

- "The bacterial cell and the Internet have
 - architectures
 - that are robust and evolvable"
- What does "architecture" mean?
- What does it mean for an "architecture" to be robust and evolvable?
- Robust yet fragile?

Robust

- 1. Efficient, flexible metabolism
- 2. Complex development
- Immune systems 3.
- 4. Regeneration & renewal 4. Cancer
- 5. Complex societies

Yet Fragile

- Obesity and diabetes 1.
- 2. Rich parasite ecosystem
- 3. Auto-immune disease
- 5. Epidemics, war, genocide, ...

Human robustness and fragility



- Modern cars, planes, computers, etc have exploding internal complexity
- They are simpler to use and more robust.
- They tend to work perfectly or not at all.



exploding internal complexity

- They are simpler to use and more robust.
- They tend to work perfectly or not at all.

cresell Office PowerPoter

Microsoft Office PenerPoint has encountered a problem and needs to clean. We are easy for the inconvenience.

If you were in the middle of scinething, the information you were working on might be loot.

Finital House PowePoint

Please tell Microsoft about this problem.

Wa have created an error import that you can send to help us improve Microsoft Office. PassePoint, We reliated this report as contridential and anonymous

What data does the error report contain?

"House Must be toget 7 Monoral"

Robust yet Fragile

Send Eng Report | Dun't Send

Nightm

Biology: We might accumulate more complete parts lists but never "understand" how it all works.

Technology: We might build increasingly complex and incomprehensible systems which will eventually fail completely yet cryptically.

Nothing in the orthodox views of complexity says this won't happen (apparently).

HOPE?

Interesting systems are robust yet fragile.

Identify the fragility, evaluate and protect it.

The rest (robust) is "easy".

Nothing in the orthodox views of complexity says this can't happen (apparently).

To pursue the hope

- Hard limits
- Short proofs
- Small models
- Architecture
- Robustness

Hard limits and tradeoffs

On systems and their components

- Thermodynamics (Carnot)
- Communications (Shannon)
- Control (Bode)
- Computation (Turing/Gödel)

Assume *different* architectures a priori.

- Fragmented and incompatible
- We need a more integrated view and have the beginnings

The nature of simplicity

Simple questions:

- Simple models
- Elegant theorems
- Elegant experiments

Simple answers:

- Predictable results
- Short proofs
- Simple outcomes

Reductionist science: Reduce the *apparent complexity* of the world to an underlying simplicity.

Physics has for centuries epitomized the success of this approach.

1930s: The end of certainty

Simple questions:

- Simple models
- Elegant theorems
- Elegant experiments

Simple answers:

- Predictable results
- Short proofs
- Simple outcomes

- Godel: Incompleteness
- Turing: Undecidability
- Profoundly effected mathematics and computation.
- Little impact on science.

1960s-Present: "Emergent complexity"

Simple questions:

- Simple models
- Elegant theorems
- Elegant experiments

Dominates scientific thinking today

Complexity:

- Unpredictabity
- Chaos, fractals
- Critical phase transitions
- Self-similarity
- Universality
- Pattern formation
- Edge-of-chaos
- Order for free
- Self-organized criticality
- Scale-free networks

"Emergent" complexity

Simple question Undecidable

- No short proof
- Chaos
- Fractals



The "New Science of Complexity"

	Simple	
	question	
Predictable	Simplicity	
Unpredictable	"Emergence"	

Even simple systems with little uncertainty can yield completely unpredictable behavior.

1900s: The triumph (and horror) of organization



Simple answers:

- Predictable results
- Short proofs
- Simple outcomes
- Complex, uncertain, hostile environments
- Unreliable, uncertain, changing components
- Limited testing and experimentation
- Yet predictable, robust, reliable, adaptable, evolvable systems



Organized complexity

- Requires highly organized interactions, by design or evolution
- Completely different theory and technology from emergence

Simple answers:

- Predictable results
- Short proofs
- Simple outcomes

- Complex, uncertain, hostile environments
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Mathematics and technology

Question Answer	Simple	Complex
Predictable	Simplicity	Organization
Unpredictable	Emergenc e	

Emergence and organization are opposites, but can be viewed in a unified framework.

Irreducible complexity?

Question Answer	Simple	Complex
Predictable	Simplicity	Organization
Unpredictable	Emergence	?

Complexity and unpredictability are the key to successful cryptography and other security technologies.





The complete picture

Question	Simple	Complex
Simple	Simplicity	Organization
Complex	Emergenc	Irreduci
	e	bility

The challenge



How can we treat complex networks and systems with small models and short proofs?

The complete picture

Models Proofs	Small	Large
Short	Simplicity	Organization
Long	Emergenc	Irreduci
	e	bility

Breaking hard problems

- SOSTOOLS proof theory and software (Parrilo, Prajna, Papachristodoulou, ...)
- Nested family of (dual) proof algorithms
- Each family is polynomial time
- Recovers many "gold standard" algorithms as special cases, and immediately improves
- Nonlinear, hybrid, stochastic, ...
- No a priori polynomial bound on depth (otherwise P=NP=coNP)
- Conjecture: Complexity implies fragility

Architecture?

- - that are robust and evolvable (yet fragile) "
- What does "architecture" mean?
- What does it mean for an "architecture" to be robust and evolvable?
- Robust yet fragile?
- Rigorous and coherent theory?

A look back and forward

- The Internet architecture was designed without a "theory."
- Many academic theorists told the engineers it would never work.
- We now have a nascent theory that confirms that the engineers were right (Kelly, Low, Vinnicombe, Paganini, Papachristodoulou, ...)
- Parallel stories exist in "theoretical biology."
- For future networks, "systems of systems," and other new technologies, as well as *systems biology of the cell, organism and brain*, ...
- …let's hope we can avoid a repeat of this history. (Looks like we have a good start...)

Architecture?

- "The bacterial cell and the Internet have
 - architectures
 - that are robust and evolvable"
- For the Internet, we know how all the parts work, and we can ask the architects












Arbitrarily complex network

- Topology
- Number of routers and hosts
- Nonlinear
- Delays



Short proof

ters

- Global stability
- Equilibrium optimizes aggregate user utility

Papachristodoulou, Li

"FAST"

theory

TCP/A

Layering as optimization decomposition

- Each layer is abstracted as an optimization problem
- Operation of a layer is a distributed solution
- Results of one problem (layer) are parameters of others
- Operate at different timescales



Examples



Rate control/routing/scheduling: Eryilmax et al '05, Lin et al '05, Neely, et al '05, Stolyar '05, this paper

detailed survey in Proc. of IEEE, 2006

Architecture?

- "The bacterial cell and the Internet have
 - architectures
 - that are robust and evolvable"
- For the Internet, we know how all the parts work, and we can ask the architects
- For biology, we know how some parts work, and evolution is the "architect" (another source of confusion)

Bio: Huge variety of environments, metabolisms Internet: Huge variety of applications

Huge variety of components



Bio: Huge variety of environments, metabolisms Internet: Huge variety of applications

> Huge variety of genomes Huge variety of physical networks

Huge variety of components

Hourglass architectures

Bio: Huge variety of environments, metabolisms Internet: Huge variety of applications



Identical control architecture

Huge variety of genomes Huge variety of physical networks

Huge variety of components



Metabolism/biochem

5:Application/function: variable supply/demand



Feedback Control

4:Allosteric

3:Transcriptional

2:Potential physical network

1:Hardware components

Networked dynamical systems



of interconnection



"Emergent" complexity

Simulations and conjectures but no "proofs"

• Fractals



Networked dynamical systems



of interconnection





Statistical Physics and emergence of collective behavior



Spectacular progress



of interconnection

Open questions



Complexity of interconnection

Pursuing the hope

- Hard limits (Tues)
- Short proofs (Wed)
- Small models (Thu)

• Architecture

Pursuing the hope

- Hard limits (Tues)
- Short proofs (Wed)
- Small models (Thu)

• Architecture

Pursuing the hope

- Hard limits
- Short proofs
- Small models
- Architecture
- Robustness

Robustness = Invariance of a [property] of a [system] to a [set of perturbations]

Fragility =
Variability of a
[property] of a
[system] due to a
[set of perturbations]

- Both can be quantitative or qualitative
- Robustness and fragility coexist in the same system
- Are there conservation laws?

Robustness = Invariance of a [property] of a [system] to a [set of perturbations]

Fragility =
Variability of a
[property] of a
[system] due to a
[set of perturbations]

Qualitative

A [property] of a [system] can be *robust* to one [set of perturbations] *yet fragile* to another [set of perturbations] Robustness/fragility = (In)variance of a [property] of a [system] to a [set of perturbations]

Given a [system] and a [set of perturbations]: One [property] can be *robust while another* [property] *is fragile*.

Hard limits and tradeoffs

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Human robustness and fragility





Complex development Immune response Fragile

Robust

Autoimmune disease Parasites

Complex development Immune response Regeneration/renewal Autoimmune disease Parasites

Uncertainty



Fragile

Fragile

Robust

Cancer Autoimmune disease Parasites

Complex development Immune response Regeneration/renewal

Fragile

Robust

Cancer Autoimmune disease Parasites

Complex development Immune response Regeneration/renewal Complex society

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Robust




Complexity?

Fragile

Robust

Robust

There are new conservation laws for robustness/fragility. If exploited, net benefits are possible. If not, disasters loom.

> Yet fragile

Uncertainty



Thermodynamics and metabolism

$$\dot{x}_{k} = -V_{k}(x_{k}) + V_{k-1}(x_{k-1}) + \Delta \dot{x}_{k}$$
$$V(x(t)) \approx \frac{V_{\max}}{1 + \frac{K_{m}}{x(t)}}$$

It is well-known that many biological regulatory networks can oscillate, and presumably many more will be

- Are these tradeoffs an artifice of this model?
- Does it matter if the model is nonlinear, stochastic, distributed, PDEs, etc? Does it depend on the model at all?
- Are these tradeoffs due to a frozen accident of evolution and not an absolute necessity?
- The answer to all these questions is *no*.

Theorem

$$\int \log |\mathbf{F}(x_n)| d\omega = constant$$

This tradeoff is a *law*.

Transients, **Oscillations** $\log |S|$ ω Biological complexity is dominated by the evolution of mechanisms to more *finely tune* **Tighter** this robustness/fragility tradeoff. regulation

- benefits = attenuation of disturbance
- goal: make this as negative as possible

Constraint:
$$\int [\log |S|]_{-} d\omega \ge -\int [\log |S|]_{+} d\omega$$
benefitscosts

- What helps or hurts this tradeoff?
- Helps: remote sensing
- Hurts: instability, remote control

Control demo

 $\int_0^\infty \log |S(\omega)| d\omega \ge \pi / \sqrt{L}$ Note: assumes continuous time

- Unstable plants are intrinsically more difficult to control than stable ones, and are generally avoided unless the instability confers some great functional advantage, which it often does.
- A classic illustration of instability and control, the simple inverted pendulum experiment, illustrates the essential point.
- Here the pendulum is the plant, and the human is the controller. The experiment can be done with sticks of different lengths or with an extendable pointer, holding the proximal tip between thumb and forefinger so that it is free to rotate but not otherwise slip.

• With the controlling hand fixed, this system has two equilibria, down and up, which are stable and unstable, respectively. By watching the distal tip and controlling hand motion, the up case can be stabilized if the stick is long enough.

• For an external disturbance, imagine that someone is throwing objects at the stick and you are to move so that the stick remains roughly vertical and avoids the thrown object. Alternatively, imagine that the distal tip is to track some externally driven motion.

• You will soon find that it is much easier to control the distal tip down than up, even though the components in both cases are the same.

• Because the up configuration is unstable, certain hand motions are not allowed because they produce large, unstable tip movements. This presents an obstacle in the space of dynamic hand movements that must be avoided, making control more difficult.

• If you make the stick shorter, it gets more unstable in the up case, evident in the short time it takes the uncontrolled stick to fall over.

• Shorter pendulums get harder and ultimately impossible to control in the up case, while length has little such effect on the down case.

• Also, the up stick cannot be stabilized for any length if only the proximal tip is watched, so the specific sensor location is crucial as well.

• This exercise is a classical demonstration of the principle that the more unstable a system the harder it is to control robustly, and control theory has formally quantified this effect in several ways.

$$\int [\log |S|]_d \omega \ge -\int [\log |S|]_+ d\omega +\pi a$$

benefits costs stabilize

$$\int \left[\log |S| \right]_{d\omega} \ge -\int \left[\log |S| \right]_{+} d\omega +\pi a$$

benefits costs stabilize

$$X(z) = \sum_{k=0}^{N} x(k) z^{-k}$$

Then the discrete Fourier transform *D*, *U*, and *E* are polynomials in the transform variable *z*.

If we set $z = e^{i\omega}$, $\omega \in [0,\pi]$ then X(ω) measures the frequency content of *x* at frequency ω .

- Denote by $\{z_k\}$ the complex zeros for |z| > 1 of X(z)
- Jensen's theorem

$$\int_0^{\pi} \log |X(\omega)| d\omega = \sum \log |z_k| + \log |X(\infty)|$$

Proof: Contour integral

A useful measure of performance is in terms of the sensitivity function S(z) defined by Bode as

$$S(z) = \frac{E(z)}{D(z)} = \frac{D(z) - U(z)}{D(z)} = 1 - \frac{U(z)}{D(z)}$$

If we set $z = e^{i\omega}$, $\omega \in [0,\pi]$ then $|S(\omega)|$ measures how well *C* does at each frequency. (If *C* is linear then *S* is independent of *d*, but in general *S* depends on *d*.)

It is convenient to study $\log |S(\omega)|$

• Denote by $\{\varepsilon_k\}$ and $\{\xi_k\}$ the complex zeros for |z| > 1 of E(z) and D(z), respectively. Then

$$\int_0^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_k| - \sum \log |\xi_k| + \log |S(\infty)|$$

Proof: Follows directly from Jensen's formula.

If *d* is chosen so that D(z) has no zeros in |z| > 1 (this is an open set), then

$$\int_{0}^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_{k}| - \sum \log |\xi_{k}| + \log |S(\infty)|$$

$$S(\infty) = 1 - \frac{u(0)}{d(0)} = 1 \implies \log |S(\infty)| = 0$$

$$\int_0^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_k| + \log |S(\infty)|$$

$$\ge 0$$

$$e(k) = d(k) - u(k)$$

$$\int_0^{\pi} \log |S(\omega)| d\omega = \int_0^{\pi} \log |E(\omega)| d\omega - \int_0^{\pi} \log |D(\omega)| d\omega$$

$$\int_0^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_k| \ge 0$$

If the plant has (linear) instabilities, then e must have zeros at the plant poles.

$$\int_0^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_k| \ge 0$$

This is where plant instability hurts.

$$\int_0^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_k| - \sum \log |\xi_k| + \log |S(\infty)|$$

$$\int_0^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_k| - \sum \log |\xi_k| + \log |S(\infty)|$$

Usually this term is zero.

$$\int_0^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_k| - \sum \log |\xi_k| + \log |S(\infty)|$$

If the plant has (linear) instabilities

$$\int_0^{\pi} \log |S(\omega)| d\omega = \sum \log |\varepsilon_k| \ge 0$$

This is where plant instability hurts.


Recall

Shannon



Features of the theory:

1. Hard bounds

 Δr = total delay of encoding, decoding, and channel Δd =disturbance arrival delay from where it is remotely sensed

- 2. Achievable (⇐assumptions)
- 3. Solution decomposable (←assumptions)

* The interpretation of \approx depends on the details of the model.

Recall

Shannon



This is a nonstandard way of describing the results but will be convenient later. $\Delta r =$ total delay of encoding, decoding, and channel Δd =disturbance arrival delay from where it is remotely sensed

Shannon



- We can think of this as a simple "network" control problem with a disturbance that can be remotely sensed.
- A "controller" decodes a signal sent over a noisy channel and attempts to make the error small.
- The entropy reduction in the error is bounded by the channel capacity.



- 1. Hard bounds
- 2. Achievable (\Leftarrow assumptions)
- 3. Solution decomposable (⇐assumptions)

Incompatible assumptions (for 50+ years).



It's easy to *pose* a combined problem.

It's easy to *pose* a combined problem.

It's easy to *pose* a combined problem.

What is the benefit to control of remote sensing?

This looks too good to be true?

What is the benefit to control of remote sensing?

- 1. Hard bounds
- 2. Achievable (⇐assumptions)
- 3. Solution decomposable (⇐assumptions)

New unified comms, controls, and stat mech.?

Claim (or irresponsible speculation?):

- Biological complexity is dominated by the tradeoffs which are captured (simplistically) in this theorem.
- 2. Ditto for techno-networks.

What is likely (though not agreed upon) is Bode/Shannon is a much better point-topoint communication theory to serve as a foundation for networks than either Bode or Shannon alone.

Cost of remote control

What is the cost if the control action must be done remotely and communication to an actuator is over a channel with capacity C_C ?

Note: Actuator not shown.

$$\int [\log |S|]_d \omega - \log(a) \ge -C_C$$

benefits costs

(Note: needs directed information...)

 $\int \left[\log |S| \right]_{d\omega} - \log(a) \ge -C_{c}$

$$\int [\log |S|]_{d\omega} -\log(a) \ge -\int [\log |S|]_{+} d\omega -C$$

benefits costs

Bode/Shannon is likely a better p-to-p comms theory to serve as a foundation for networks than either Bode or Shannon alone.

http://www.glue.umd.edu/~nmartins/

Nuno C Martins and Munther A Dahleh, <u>Feedback Control in the Presence of Noisy Channels:</u> <u>"Bode-Like" Fundamental Limitations of Performance</u>.
(Submitted to the IEEE Transactions on Automatic Control) Abridged version in ACC 2005 <u>Fundamental Limitations of Disturbance Attenuation in the Presence of Side Information</u> Nuno C. Martins, Munther A. Dahleh and John C. Doyle
(Submitted to the IEEE Transactions on Automatic Control) Abridged version in CDC 2005