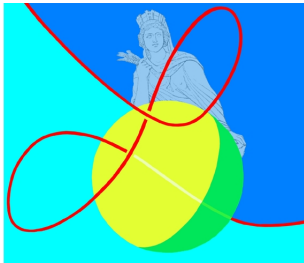
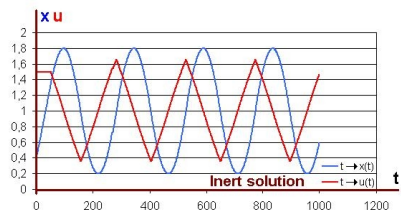


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'If people do not believe that mathematics is simple, it is only because they do not realize how complicated life is.

John von Neumann



LASTRE

*Laboratoire d'Applications
des Systèmes Tychastiques Régulés*

**What are the theoretical tools most useful
for understanding biological systems?**

**Ockham's razor:
Deriving cyclic evolutions from viability and
inertia constraints.**

Jean-Pierre Aubin

IHÉS

November 14, 2007



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What are the theoretical tools most useful for understanding biological systems?

I do not know how to answer this question, except by saying,

1. even if some of them exist, they have been mostly motivated by the observation of the inert (physical) systems,
2. analyze how the use of a method changes the formulation of the question (River Kwai bridge syndrome)
3. and not the other way around except when aware of the difficulties
4. let them **emerge** and being **selected by cognitive evolution**, with a ... Darwinian flavor, minimizing religion wars.

Mathematics?

Are biological systems sufficiently similar to systems currently studied in mathematics, physics, computer sciences or engineering?



1 *“If no one asks me, I know: if I wish to explain it to one that asketh, I know not: yet I say boldly that I know, ...”*

confessed Saint Augustine, in book XI (11.14.17) of his *Confessions*.

Mathematics : the production (end-results) or the process of production?

I just can bring a personal definitively *subjective negative* answer to the central question of this conference.



Mathematical Metaphors

Eugene Wigner's considerations on *the unreasonable effectiveness of mathematics in the natural sciences* are even more relevant in living sciences.

Many centuries and human minds used their potential “**mathematical capabilities**” to describe and share their “mathematical perceptions” of the world.

This mathematical *capability* of human brains is assumed to be analogous to the language *capability*.

Each child coming to this world uses this specific capability in social interaction with other people to reach (evolving) consensus on the perception of their world by learning their mother tongue (and few others before this capability fades away with age).

I suggest the same happens with mathematics. They play the “mathematical role” of *metaphors* that language uses for allowing us to understand a new phenomenon by metaphors comparing it with previously “understood phenomena”.



Before it exploded recently in a Babel skyscraper, this “mathematical father tongue” was quite consensual and perceived as universal.

This is this very universality which makes mathematics so fascinating, deriving mathematical theories or tools motivated by one field to apply them to several other ones.

However, *apparently*, because up to now, the mathematical “father tongue” was mainly shaped by “simple” physical problems of the inert part of the environment, letting aside, with few exceptions, the living world.

For good reasons.

Basic simple principles, such as the *Pierre de Fermat’s* “**variational principle**”, including *Isaac Newton’s* law thanks to *Maupertuis’s* **least action principle**, derived explanations of complex phenomena from simple principles, as *Ockham’s* razor prescribes:



Simplifying complexity

Ockham's razor prescribes a “**law of parsimony**” stating that an explanation of any phenomenon should make as few assumptions as possible, and to choose among competing theories the one that postulates the fewest concepts.

This is the result of an “**abstraction process**”, which is the (poor) capability of human brains that selects among the perceptions of the world the few ones from which they may derive logically or mathematically many other ones.

Simplifying complexity should be the purpose of an emerging science of complexity, if such a science will emerge beyond its present fashionable status.



Biology offers to our investigations myriads of biological clocks or oscillators, producing *periodic evolutions*, or, rather, *cyclic evolutions*.

This modification of the terminology is justified by the fact that nowadays, periodic evolutions are understood as produced by a system of differential equations.

The search of these equations is a very difficult undertaking, so that the question arises to look for other ways to produce periodic solutions, that we suggest to call *cyclic* to underlie the fact that *they are not periodic solutions of a given system of differential equations*.

As often in biology or in life sciences, we face the following dilemma:



Are the examples of **biological clocks** produced by complex systems of differential equations with complex coefficients or produced by very *simple dynamics*, confronted to a *complex maze of constraints*?

This may be how **Ockham's razor** can apply in this domain, because, in my subjective view, the right hand sides of these complex systems **are actually unknown or poorly known to us**.

Cyclic evolutions can alternatively be derived from non periodic control systems, subjected to **“viability constraints”** and **“inertia thresholds”**.



The universality of Mathematics is Partial.

Physics could be defined as the part of the cultural environment which is understandable by mathematical metaphors.

It has not yet, in my opinion, encapsulated the mathematical metaphors of living systems, from organic molecules to social systems, made of human brains controlling social activities.

The reason for me is that the adequate mathematical tongue does not yet exist.

And the challenge is that before creating it, the present one has to be **for-gotten, de-constructed, unlearn.**

This is quite impossible because mathematicians have been educated *in the same way* all over the world, depriving mathematics of the **Darwinian evolution** which has operated on languages.

This is the strength and the weakness of present day mathematics:

Its universality is partial.



The Search of Biomathematicians

The only possibility to perceive mathematically living systems will remain a dream:

To gather in secluded convents young children with good mathematical capability, but little training in the present mathematics, under the supervision or guidance of economists or biologists without mathematical training.

They possibly could come up with new mathematical languages unknown to us providing the long expected

unreasonable effectiveness of mathematics in the economic and biological sciences.



Qualitative versus Quantitative Properties

Even the concept of natural number is over simplifying, by putting in a same equivalence class so many different sets, **erasing their *qualitative* properties** or hiding them behind their *quantitative* ones.

Numbers, next measures, and then, statistics, how helpful they are for understanding and controlling the physical part of the environment, may be a drawback to address the qualitative aspects of our world, left to plain language for the quest of elucidation.

We may have to return to the origins and explore new **“qualitative”** routes, without overusing the mathematics that our ancestors accumulated so far and bequeathed to us.

Meanwhile, we are left with this paradox:

“simple” physical phenomena are explained by more and more sophisticated and abstract mathematics, whereas **“complex” phenomena of living systems** use, most of the time, relatively rudimentary mathematical tools.



1. economic evolution is *never* at equilibrium (stationary state),
2. thus, no need that it converges to it, in a stable or unstable way,
3. cognitive sciences doesn't accept that **rationality** of human brains can be reduced to **utility functions**, the existence of which was already questioned by *Henri Poincaré* in a letter to *Léon Walras* "*Satisfaction is thus a magnitude, but not a measurable magnitude*" (numbers again),
4. **that uncertainty** cannot be mathematically captured only by probabilities (numbers, again),



5. that **chaos**, a property of deterministic system, is not fit to represent a nondeterministic behavior of living systems which struggle to remain as stable (and thus, “non chaotic”) as possible,
6. that **intertemporal optimality**, a creation of the human brain to explain some physical phenomena, is not the only creation of Nature, (in the sense that “Nature” created it only through human brains!),
7. that those human brains should complement it by another and more recent principle, *adaptation of transient evolutions to environments*,
8. and so on



2 Finally, if everything in nature is linked to everything, if all motions are born from each other although they communicate secretly to each other unseen from us, we must hold for certain that there is no cause small enough or remote enough which sometimes does not bring about the largest and the closest effects on us. The first elements of a thunderstorm may gather in the arid plains of Lybia, then will come to us with the winds, make our weather heavier, alter the moods and the passions of a man of influence, deciding the fate of several nations.

Henri Thiry, baron d'Holbach (1694-1778)
Système de la nature (1750).



It resurrected under the name chaos, a polysemous and *reminescent, mimicking but not explaining* the fact that *some nonlinear differential equations produce chaotic* behavior, quite *sensitive* to initial conditions.

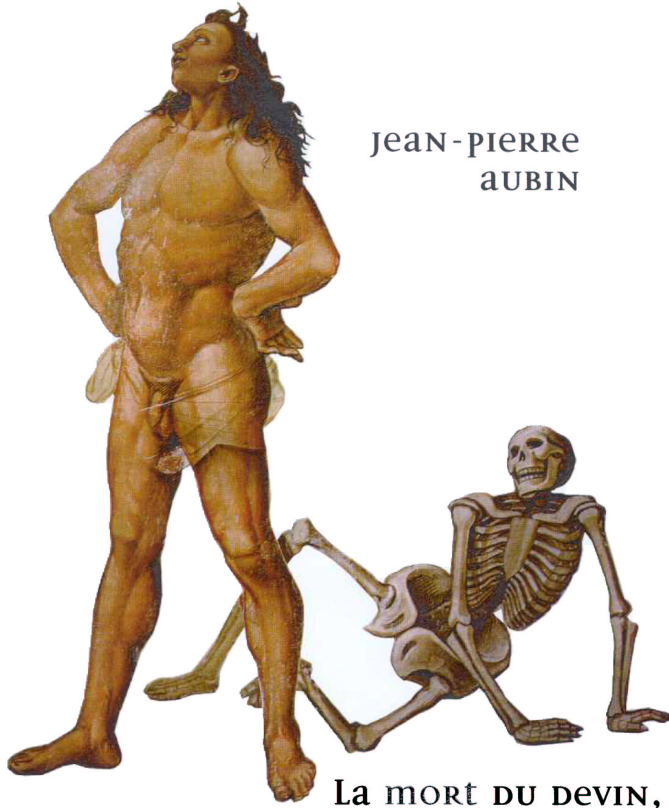
Was chance rooted in deterministic system? Is uncertainty observed in living systems living systems consistent with differential equations?

However, for many problems arising in biological, cognitive, social and economic sciences, I believe we face a completely *orthogonal situation*, governed by *differential inclusions*, but producing evolutions as *regular or stable* (in a very loose sense) as possible for the sake of adaptation and viability required for life.

Attractors: Why restrict evolution to stationarity and to asymptotic behavior? Living systems provide transient evolutions, dying long before infinity ...

In the long term, we are all dead said Keynes

Furthermore, evolutions starting outside never reach the attractor in finite time!



Jean-Pierre
Aubin

**La mort du devin,
L'émergence du démiurge**

*essai sur la contingence,
la viabilité et l'inertie des systèmes*

More developments
in the forthcoming book

“La mort du devin, l'émergence du
démiurge”

Éssai sur la contingence,
la viabilité et l'inertie
des systèmes

Éditions Beauchesne

,

It is by now a consensus that the evolution of many variables describing systems, organizations, networks arising in biology and human and social sciences do not evolve in a deterministic way, and in many instances, not even in a stochastic way as it is usually understood, but with a **Darwinian flavor**.

Viability theory started in 1976 by translating mathematically the title

<i>Chance</i>	<i>and</i>	<i>Necessity</i>
\Downarrow		\Downarrow
$x(t) \in \mathcal{S}(x)$	$\&$	$x(t) \in K$

of the famous 1973 book by *Jacques Monod* taken from an (apocryphical?) quotation of Democritus who held that

“the whole universe is but the fruit of two qualities, chance and necessity”.

□ - The mathematical translation of “chance” is a kind of evolutionary engine, called an *evolutionary system*, associating with any initial state x the subset $S(x)$ of evolutions starting at x .

The system is *deterministic* if for any initial state x , $S(x)$ is made of one and only one evolution, whereas “*contingent uncertainty*” happens when the subset $S(x)$ of evolutions contains more than one evolution for at least one initial state.

“Contingence is a non-necessity, it is a characteristic attribute of freedom”, wrote *Gottfried Leibniz*.

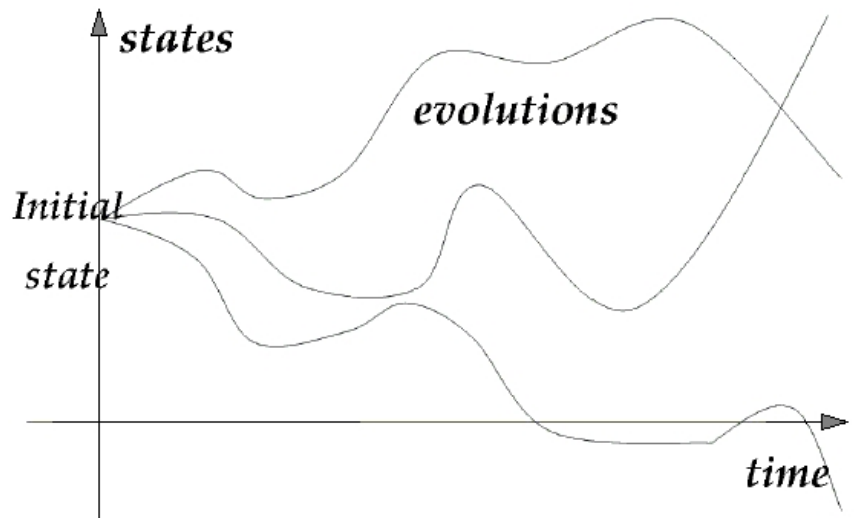


Figure 1:

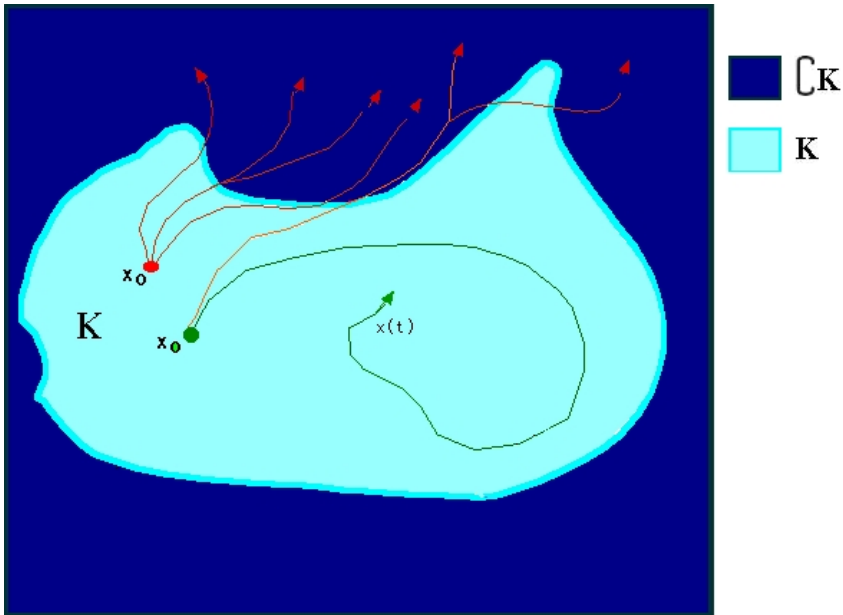


Figure 2:

which is not viable.

\square - The mathematical translation of “necessity” is the requirement that for all $t \geq 0$, $x(t) \in K$, meaning that at each instant, “viability constraints” are satisfied by the state of the system. The scheme represents the state spaces as the plane, and the environment defined a subset. It shows two initial states, one from which all evolutions violate the constraints in finite time, the other one from which starts one viable evolution and another one



Confrontation of Evolutionary Systems and Viability Constraints

In summary, *the environment is described by viability constraints* of various kinds, a word encompassing polysemous concepts as *stability, confinement, homeostasis, adaptation*, etc., expressing the idea that some variables must obey some constraints (representing physical, social, biological and economic constraints, etc.) that can never be violated.

So, viability theory started as *the confrontation of evolutionary systems governing evolutions and viability constraints* that such evolutions must obey.

Present evolves, too

**Initial conditions do evolve,
evolutionary systems should depend upon
a flow of past initial conditions
and on the (history of the) evolutions.**



It consists in studying properties of evolutions governed by an evolutionary system:

Gather the larger number of properties of evolutions starting from each initial state.

It may be an information both **costly and useless**, since our brains cannot handle simultaneously too many observations and concepts.

Moreover, it may happen that

1. evolutions starting from a given initial state satisfy properties which are lost by evolutions starting from another initial state, even close to it (**sensitivity analysis**),
2. or that, even if all evolutions share a given set of properties, they fade away for neighboring systems (**stability analysis**).



A set of prescribed properties of evolutions being given, study the (possibly empty) subsets of initial states from which

1. starts **AT LEAST** one evolution governed by the evolutionary system satisfying the prescribed properties,
2. **ALL** evolutions starting from it satisfy these prescribed properties.

These two subsets coincide whenever the evolutionary system is deterministic.



Stationarity, periodicity and asymptotic behavior

are examples of classical properties motivated by physical sciences. They are studied in terms of such parameters, as in **bifurcation theory, catastrophe theory, chaotic behavior, etc.**, as *Stephen Wiggins* observed in section 3.3 “*On the Interpretation and Application of Bifurcation Diagrams: A Word of Caution*” of his book *Introduction to nonlinear systems and chaos* by :

“At this point, we have seen enough examples so that it should be clear that the term bifurcation refers to the phenomenon of a system exhibiting qualitatively new dynamical behavior as parameters are varied. However, the phrase ”as parameters are varied” deserves careful consideration... In all of our analyses thus far the parameters have been constant. The point is that we cannot think of the parameter as varying in time, even though this is what happens in practice. Dynamical systems having parameters that change in time (no matter how slowly!) and that pass through bifurcation values often exhibit behavior that is very different from the analogous situation where the parameters are constant.”

□ - Let $\mathcal{U} := \mathbb{R}^c$ be a space of parameters. A regulated system is made of two “boxes”:

1 - The “*input-output box*” associating with any evolution $u(\cdot)$ of the parameter (*input*) the evolution governed by differential equation $x'(t) = f(x(t), u(t))$ starting from an initial state (*open loop*),

2 - The *non deterministic “output-input box”*, associating with any state a subset $U(x)$ of parameters (*output*).

The associated evolutionary system \mathcal{S} maps any initial state x to the set $\mathcal{S}(x)$ of evolutions $x(\cdot)$ starting from x ($x(0) = x$) and governed by

$$x'(t) = f(x(t), u(t)) \text{ where } u(t) \in U(x(t)) \quad (1)$$

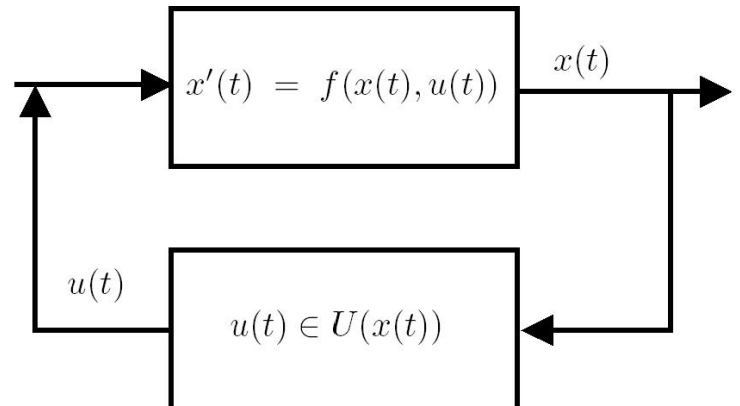


Figure 3:



The parameters range over a state-dependent *contingent map* $U : x \rightsquigarrow U(x)$, providing the system **opportunities to adapt at each state to viability constraints**.

The nature of the parameter differs according to the problems and to questions asked: They can be

1. **“controls”**, whenever a controller or a decision maker “pilots” the system by choosing the controls, as in engineering,
2. **“regulons”** or regulatory parameters in those living systems where no identified or consensual agent acts on parameters of the system,
3. **“tyches”** or disturbances, perturbations under which nobody has any control or influence.

If a subset $K \subset \mathbb{R}^d$ is regarded as an *environment* (defined by *viability constraints*), an evolution $x(\cdot)$ is said to be *viable in the environment* $K \subset \mathbb{R}^d$ if for every time $t \geq 0$, $x(t)$ belongs to K . The *viability kernel of K under the regulated system (1)*

$$x'(t) = f(x(t), u(t)) \text{ where } u(t) \in U(x(t))$$

is the set $\text{Viab}_{(1)}(K)$ of initial states $x \in K$ from which starts **AT LEAST** one evolution $x(\cdot)$ viable in K :

$$\text{Viab}_{(1)}(K) := \{x_0 \in K \mid \exists x(\cdot) \in \mathcal{S}(x_0) \text{ such that } \forall t \geq 0, x(t) \in K\}$$

Two extreme situations deserve to be singled out: The environment is said to be

1. *viable under (1)* if it is equal to its viability kernel: $\text{Viab}_{(1)}(K) = K$,
2. *a repeller under (1)* if it is empty: $\text{Viab}_{(1)}(K) = \emptyset$.

■ $\mathbb{C}K$

■ K

■ $Viab_F(K)$

3 From a point x_0 in the viability kernel starts of the environment K at least one evolution viable in K forever. All evolutions starting from $x_0 \in K$ outside the viability kernel leave K in finite time.

Hence, the viability kernel plays the role of a **viabilimeter**, the “size” of which measuring the degree of viability of an environment, so to speak.

The main results of viability theory characterize and study, under adequate assumptions, the mathematical and algorithmic properties of the viability kernel (as well as softwares computing it).

Above all, provides the *regulation map* $R : x \in K \rightsquigarrow u \in R(x)$ regulating the viable evolutions.

On the viability kernel, the regulation map associates a nonempty subset $R(x) \subset U(x)$ of regulons such that the new regulated systems

$$x'(t) = f(x(t), u(t)) \text{ where } u(t) \in R(x(t)) \tag{2}$$

governs viable evolutions.

This regulation map can be computed by the Viability Kernel Algorithm and used to pilot robots, portfolios, heavy evolutions, etc.

Intertemporal optimization demands

1. the **existence of an actor** (agent, decision-maker, controller, etc.),
2. an **optimality criterion**,
3. that **decisions are taken once and for all at the initial time**,
4. a **knowledge of the future** (or of its anticipation).

For systems involving living beings, there is not necessarily an actor governing the evolution of regulons according to the above prerequisites.

The choice of criteria is open to question even in static models, even when multicriteria or several decision makers are involved in the model.

Furthermore, the choice (even conditional) of the optimal controls is made *once and for all* at some initial time, and thus *cannot be changed at each instant so as to take into account possible modifications of the environment of the system*, thus forbidding **ADAPTATION to viability constraints** .



The intertemporal criterion involving the knowledge of the state at future times requires some *knowledge of the future*. Most living systems display a *myopic* behavior.

Instead of taking into account the future, their evolutions are certainly constrained by their *history*.

The knowledge of the future needs to assume some regularity (for instance, periodicity, cyclicity) of the phenomena (as in mechanics), or to make anticipations, or *demand experimentation*. Experimentation, by assuming that the evolution of the state of the system starting from a given initial state for a same period of time will be the same whatever the initial time, allows one to “translate” the time interval back and forth, and, thus, to “**know**” the future evolutions governed by the system.

But in life sciences as well as in economics, the systems are irreversible, *their dynamics may disappear and cannot be recreated*, forbidding any insight into the future.



Hence, we are left to forecast, predict or *anticipate* the future, i.e., extrapolate past evolutions and to constrain in the last analysis the evolution of the system as a *function of its history*. However, to quote *Paul Valéry*,

“Forecasting is a dream from which reality wakes us up”.

After all, in biological evolution, intertemporal optimization can be traced back to Sumerian mythology which is at the origin of Genesis:

1. one **Decision-Maker**,
2. deciding what is good and bad and choosing the best (fortunately, on an intertemporal basis with infinite horizon, thus wisely postponing to eternity the verification of optimality),
3. knowing the future,
4. and having taken the optimal decisions, well, during one week...



5 Punctuated Equilibria and the Inertia Principle

Darwin added the sixth edition of his celebrated book the sentence

“and lastly, although each species must have passed through numerous transitional stages, it is probable that the periods, during which each underwent modification, though many and long as measured by years, have been short in comparison with the periods during which each remained in an unchanged condition”

(personal communication by *Jim Murray*).

In the absence of an actor piloting the regulons, or by assuming that this actor is

myopic, lazy, opportunistic and conservative,

we **cannot** assume any longer that the regulons are chosen to **minimize an intertemporal criterion**.



We may assume instead that **regulons evolve as “slowly” as possible** because the **change of regulons** (or controls in engineering) is costly, even very costly.

Evolutions under constant coefficients, which do not evolve at all, may not satisfy required properties. Then the question arises to study

when, where and how

coefficients must cease to be constant and start to “evolve” in order to satisfy the required property, for instance.

In this case, their status of “coefficients” is modified, and they become controls or regulons, according to the context (engineering or life sciences where the problem is set).



Inertia Principle

Whenever the viability property is concerned, we shall give a name to this phenomenon which seems to be shared by so many systems dealing with living beings: In a loose way,

the *inertia principle* states that the “*regulons*” of the system are kept constant as long as possible and changed only when viability or inertia is at stake.

The inertia principle provides a mathematical explanation of the emergence of the concept of *punctuated equilibrium* introduced in paleontology by *Nils Eldredge* and *Stephen J. Gould* in 1972.

“**Heavy evolutions**” are evolutions **minimizing At Each Instant** (and not in an intertemporal way) **the velocity of their regulons**.

Heavy evolutions provide the simplest examples of evolutions satisfying the inertia principle.

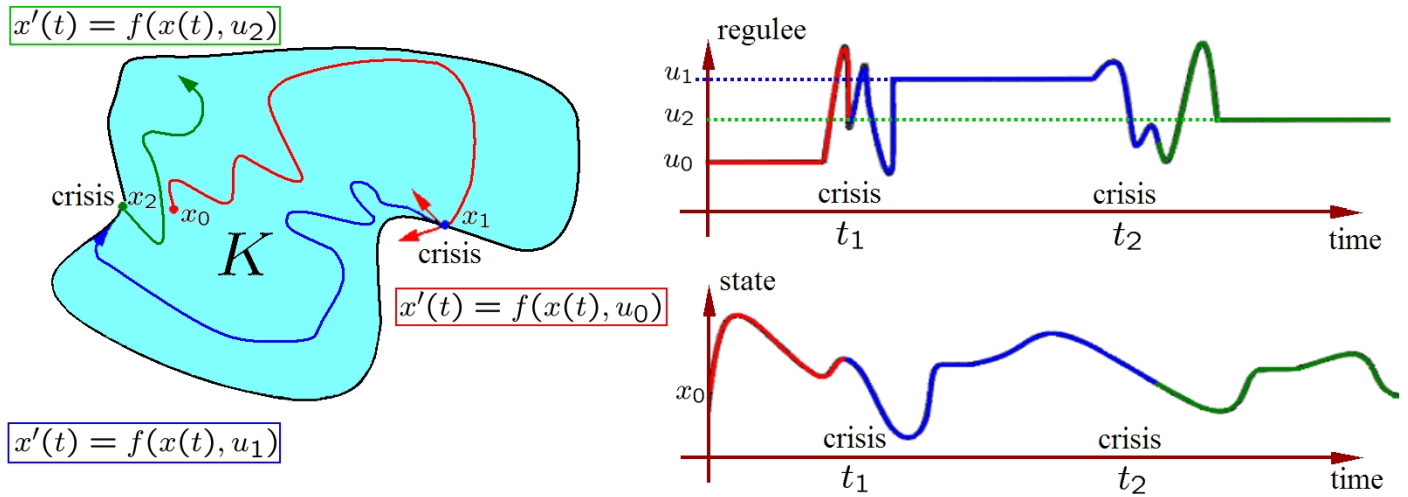


Figure 5.1 Punctuated Evolution. Starting from x_0 with the constant regulon u_0 , the solution evolves in K until warning time (kairos) t_1 , (first **punctuated equilibrium phase**) when the state $\bar{x}_1 := x(t_1)$ is about to leave the environment K and when the constant regulon u_0 **Must** start to evolve. Then a **critical phase** happens during which velocities also evolve (as slowly as possible) to maintain viability, until time \bar{t}_1 when the regulon $\bar{u}_1 := u(\bar{t}_1)$ can remain constant during a nonempty time interval: **second punctuated equilibrium phase, after which a second critical phase.**



Excavations at Lake Turkana

Excavations at Kenya's Lake Turkana have provided clear evidence of evolution from one species to another.

The rock strata there contain a series of fossils that show every small step of an evolution journey that seems to have proceeded in fits and starts.

Examination of more than 3,000 fossils by *Peter Williamson* showed how 13 species evolved. The record indicated that the **animals stayed much the same for immensely long stretches of time.**

But **twice**, about two million years ago and then, 700,000 years ago, the pool of life seemed to explode

set off, apparently, by **a drop in the lake's water level.**

Intermediate forms appeared very quickly, new species evolving in 5,000 to 50,000 years, after millions of years of constancy, leading paleontologists to challenge the accepted idea of continuous evolution.

A **viability niche** of a regulon u is the viability kernel of the system $x'(t) = f(x(t), u)$ regulated by the constant regulon u .

A regulon u is a **punctuated equilibrium** if and only if its viability niche is non empty.

We can prove the existence of **“heavy evolutions” locking in” the viability niche of a punctuated equilibrium** whenever the evolution of the regulon reaches such a punctuated equilibrium on its way, in the sense that it may remain viable in the viability niche forever.

The concept of “locking-in” had been introduced in the different field of economics (of innovation), and with other mathematical techniques, for explaining why, once adopted, some technologies, which may look non-optimal in regard of some criterion, are still adopted, whereas some better solutions are not adopted.

The same phenomenon appears in biological evolution, and may be explained mathematically by the inertia principle in the paradigm of adaptation to an environment.

Assume that we have to model a system, the dynamics of which are unknown to us. Hence, we describe our ignorance by an “open” right hand side

$$x'(t) = u(t) \text{ where } u(t) \in \mathbb{R} \quad (3)$$

where the right hand side can be regarded as a regulon or a control. It is tempting to try guessing right hand sides by selecting feedbacks $x \mapsto \tilde{u}(x)$ and solving

$$x'(t) := \tilde{u}(x(t))$$

For instance, the simple examples, besides constant right hands side $\tilde{u}(x) \equiv u$, are provided by *affine feedbacks* defined by $\tilde{u}(x) := r(b-x)$. The solution starting from $x \in [a, b]$ is equal to $x(t) = e^{-rt}x + b(1 - e^{-rt})$. It remains viable in the interval $[a, b]$, increases with time with negative acceleration with the norm smaller than or equal to $r^2(b-a)$ and converges to the equilibrium b when $t \mapsto +\infty$.

Instead, we can replace our ignorance of the dynamics by some more accessible knowledge, for instance,

$$\left\{ \begin{array}{l} (i) \quad \text{viability constraints: } x(t) \in K := [a, b], \quad 0 < a < b < +\infty \\ (ii) \quad \text{inertia threshold ; } c \in \mathbb{R}_+ : \|x''(t)\| \leq c \end{array} \right. \quad (4)$$

We denote by $\mathcal{P}(x, u)$ the set of solutions to differential equation (3)

$$x'(t) = u(t) \text{ where } u(t) \in \mathbb{R}$$

viable in the interval $[a, b]$ such that $x(0) = x$ and $u(0) = x'(0) = u$.

We introduce the notion of *inertia function* defined by

$$\alpha(x, u) := \inf_{x(\cdot) \in \mathcal{P}(x, u)} \sup_{t \geq 0} \|u'(t)\| = \inf_{x(\cdot) \in \mathcal{P}(x, u)} \sup_{t \geq 0} \|x''(t)\|$$

It happens that we can characterize it thanks to the concept of viability kernel. Let us introduce for that purpose the auxiliary system (5)

$$\left\{ \begin{array}{l} (i) \quad x'(t) = u(t) \\ (ii) \quad u'(t) = v(t) \\ (iii) \quad y'(t) = 0 \\ \text{where } \|v(t)\| \leq y(t) \end{array} \right. \quad (5)$$

One can prove that the inertia function is characterized by formula

$$\alpha(x, u) = \inf_{(x,u,y) \in \text{Viab}_{(5)}(K \times \mathbb{R} \times \mathbb{R}_+)} y$$

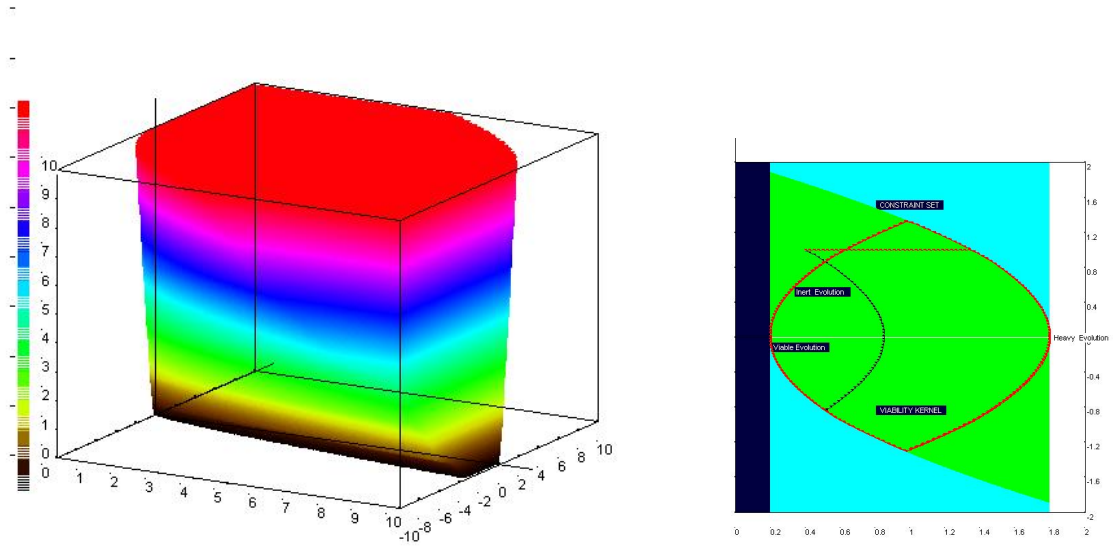


Figure 6.1 *Newtonian Inertia Function.* [Left.] *The Viability Kernel Algorithm computes the graph of the inertia function.* [Right.] *A lower level set of the inertia function: Its boundary is the critical zone.*

The inertia function α defined on $]a, b[\times \mathbb{R}$ is equal to:

$$\alpha(x, u) := \frac{u^2}{2(b-x)} \text{ if } u \geq 0 \text{ and } \frac{u^2}{2(x-a)} \text{ if } u \leq 0 \quad (6)$$

Its domain is $(\{a\} \times \mathbb{R}_+) \cup (]a, b[\times \mathbb{R}_+) \cup (\{b\} \times \mathbb{R}_-)$. Hence, from each state-regulon pair $(x, u) \in \text{Dom}(\alpha)$ starts at least one evolution with *bounded acceleration*, actually, bounded by $\alpha(x, u)$.

The inertia function is the (smallest positive lower semicontinuous) solution to the Hamilton-Jacobi partial differential equation

$$\forall (x, u) \in]a, b[\times \mathbb{R}, \quad \frac{\partial \alpha(x, u)}{\partial x} u - \alpha(x, u) \left| \frac{\partial \alpha(x, u)}{\partial u} \right| = 0$$

We associate with the inertia function the *inert regulation map* R_c defined by $R_c(x) := \{u \in \mathbb{R} \text{ such that } \alpha(x, u) = u\}$ and the *critical map* Ξ_c defined by $\Xi_c(u) := \{x \in [a, b] \text{ such that } \alpha(x, u) = u\}$. When $c > 0$, the subset $\Xi_c(u)$ is called the *critical zone* of the control u bounded by inertia threshold $c > 0$. When $c = 0$, the subset $\Xi_0(u)$ is called the *viability niche* of the control u . A regulon is a *punctuated equilibrium* (or, actually, *punctuated regulon*) if its viability niche $\Xi_0(u)$ is not empty.

We set

$$r^\sharp(x) := \sqrt{2(b-x)}, \quad r^b(x) := \sqrt{2(x-a)} \quad \text{and} \quad R(x) := \left[-r^b(x), +r^\sharp(x) \right] \quad (7)$$

The regulation map is equal to

$$R_c(x) := \sqrt{c} \left[-r^b(x), +r^\sharp(x) \right] = \sqrt{c} R(x)$$

The critical map Ξ_c ($c > 0$) is defined by

$$\Xi_c(u) = b - \frac{u^2}{2c} \quad \text{if } u > 0 \quad \text{and} \quad \Xi_c(-|u|) = a + \frac{u^2}{2c} \quad \text{if } u < 0$$

The viability niche $\Xi_0(u)$ of the regulon u is empty when $u \neq 0$ and equal to $\Xi_0(0) = [a, b]$ when $u = 0$.

The graph of the regulation map R_c associated to the inertia function is limited by the union $\sqrt{c} \left\{ -r^b(x), +r^\sharp(x) \right\}$ of the two graphs of $-\sqrt{c} r^b$ below and $\sqrt{c} r^\sharp$ above.

Heavy evolutions with an inertia threshold c are the ones which are viable, satisfy the inertia threshold and *which minimize AT EACH INSTANT the norm of the velocity of the regulon*. In our case, they minimize at each instant the norm of the acceleration.

We start with regulons with inertia $\alpha(x, u) < c$ strictly smaller than an imposed inertia threshold c . We can choose the heavy evolution which is governed by the regulon constant equal to u until it reaches the critical zone $\Xi_c(u)$ and, next, we shall have to switch the regulon to pilot an evolution until it reaches the equilibrium $(a, 0)$ or $(b, 0)$.

The *warning time* $\sigma_c(x, u) \in \mathbb{R} \cup \{+\infty\}$ is the first instant when evolutions $x_u(\cdot)$ starting from x when $x_u(\sigma_c(x, u)) \in \Xi_c(u)$ reaches the *critical zone* $\Xi_c(u)$ of the regulon u .



4 [Warning Time or “Kairos”.] *The concept of warning time is a mathematical translation of the anglo-saxon concept of **timing**, or the Italian concept of **tempismo**, modernizing the concept of **kairos** of classical Greece, meaning **propitious or opportune moment**.*

*The ancient Greeks used this **qualitative** concept of time by opposition to **chronos**, the **quantitative**... chronological time, which can be measured by clocks.*

*The search of kairos translates the search of decisions taken at the **right moment** (warning time) rather than static optimal decisions.*

Lysippos sculptured a wonderful concrete representation of this very abstract concept (in the museum of Torino).

Lemma ??, p.?? implies that solutions $x \pm |u|t$ regulated by constant regulons $\pm|u|$ reach the critical zone at *warning time* equal to

$$\sigma_c(x, u) := \frac{(b-x)}{|u|} - \frac{|u|}{2c} \text{ if } u > 0 \text{ and } \sigma_c(x, u) := \frac{(x-a)}{|u|} - \frac{|u|}{2c} \text{ if } u < 0 \quad (8)$$

because $x + u\sigma_c(x, u) = \Xi_c(u) = b - \frac{u^2}{2c}$ (when $u > 0$).

The inertia function α increases over the evolution under constant regulon u according

$$\forall t \in \left[0, \frac{(b-x)}{u} - \frac{|u|}{2c} \right], \quad \begin{cases} u_c(t) = u \\ x_c(t) := x + tu \\ \alpha(x_c(t), u) = \frac{u^2}{2((b-x)-ut)} \end{cases}$$

until *warning time* $\sigma_c(x, u)$ when the state reaches $\Xi_c(u)$ and the regulon $\alpha_c(\Xi_c(u), u) = c$.

This is the last moment when we have to change the regulon u because, otherwise, either it the regulon remains constant and leaves the environment $[a, b]$ in finite time $\frac{b-x}{|u|}$ ($u > 0$), or, in order to remain viable, it has to violate the inertia threshold strictly before reaching the part $\{b\} \times \mathbb{R}_+$ of the boundary $\{a, b\} \times \mathbb{R}$ of the environment $[a, b] \times \mathbb{R}$, when it has to leave *immediately* the environment $[a, b] \times \mathbb{R}$.

When it reaches the critical zone, then the regulon must change with a velocity smaller than or equal to c . A general theorem on the *semi-permeable barrier property* of the viability kernel implies that actually, *the norm of this velocity has to be equal to the inertia threshold until it reaches the boundary $\{a, b\} \times \mathbb{R}$ of the environment $[a, b] \times \mathbb{R}$.*



Critical Evolution

In our case, the state-regulon pair evolves according (when $u > 0$): $\forall t \in \left[\frac{(b-x)}{u} - \frac{|u|}{2c}, \frac{(b-x)}{u} + \frac{|u|}{2c} \right]$,

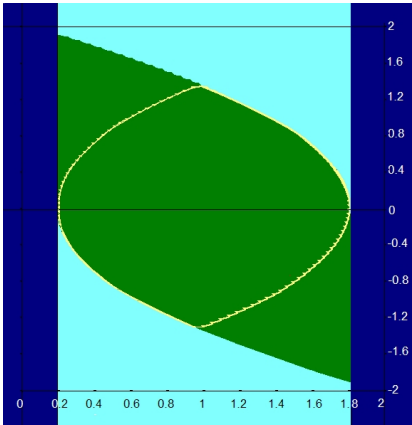
$$\begin{cases} u_c(t) = u - tc \\ x_c(t) := x + u \left(t - \frac{(b-x)}{u} + \frac{|u|}{2c} \right) - \frac{c}{2} \left(t - \frac{(b-x)}{u} + \frac{|u|}{2c} \right)^2 \\ \alpha(x_c(t), u) = c \end{cases}$$

until *warning time* $\frac{(b-x)}{u} + \frac{|u|}{2c}$ (when $u > 0$) .

James Ewin, a Scottish physicist discovered and coined the word *hysteresis* meaning *lagging behind* in classical Greek.

This polysemous word is used in many different fields, including in mathematics, where several mathematical translations have been observed (among which *Visintin*'one, related to subsets invariant with respect to affine time scaling).

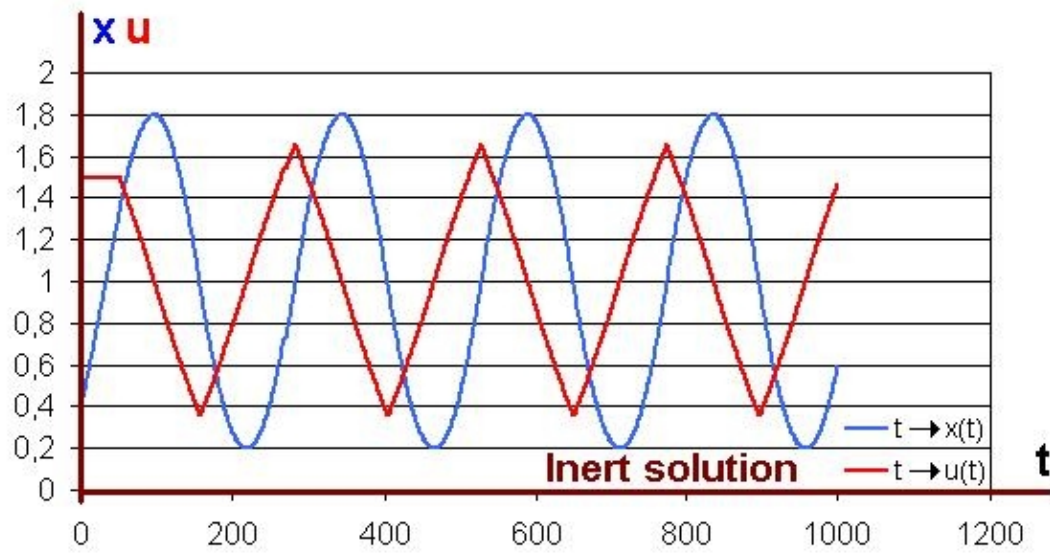
We use it here as an engine, called *hysteron*, producing *hysteresis loops* or *hysteresis cycles*: When the evolution of the state of a system with hysteresis is plotted on a graph against the applied force (in our case, the regulon), the resulting curve has the shape of a loop.



The Viability Kernel Algorithm computes the the graph of the regulation map R_c (which is a viability kernel) and the **inert hysteresis loop** when $u := \sqrt{c(b-a)}$, where the Inert Hysteresis Loop is governed by **two metacontrols $+c$ and $-c$** . The evolutions goes from a to b by one route and from b to a by another route.



Graph of the Inert Hysteresis Cycle Evolution



The Viability Kernel Algorithm computes both the graphs of the smooth inert evolution (in blue) and of its regulon (in red) are plotted. The *velocity* of the regulon oscillates from $+u^*$ to $-u^*$. The evolution is then **cyclic, alternatively increasing and decreasing from a to b .**

Let us choose an inertia threshold c and assume that $|u| \leq \sqrt{c}\sqrt{b-a}$ (the above example was obtained with $|u| = \sqrt{c}\sqrt{b-a}$).

Instead of choosing the heavy evolution which remains at one of the equilibria $(a, 0)$ or $(b, 0)$ forever by switching the acceleration (velocity of the regulon) to 0, we **continue the evolution by keeping the acceleration $-c$ or $+c$ as long as possible, and then, switch again to 0, again, as long as it is possible to obey viability and inertia constraints.** Recall that

$$\Xi_c(u) = b - \frac{u^2}{2c} \text{ if } u > 0 \text{ and } \Xi_c(-|u|) = a + \frac{u^2}{2c} \text{ if } u < 0$$

We set

$$x^* := \frac{b-a}{2} \text{ and } u^* := \sqrt{b-a}$$

We define the **heavy hysteresis cycle** $(x_h(\cdot), u_h(\cdot))$ of cycle 2 $\left(\frac{b-a}{|u|} + \frac{|u|}{c}\right)$ starting at $(\Xi_c(-|u|), u)$ with $u > 0$ where $\Xi_c(-|u|) := a + \frac{u^2}{2c}$ in the following way:

1. The state-regulon pair $(x_h(\cdot), u_h(\cdot))$ starts from $(\Xi_c(-|u|), u)$ by taking the **velocity of the regulon equal to 0**. It remains viable on the time interval $\left[0, \frac{b-a}{|u|} - \frac{|u|}{c}\right]$ until it reaches the state-regulon pair $(\Xi_c(u), u)$ where $\Xi_c(u) := b - \frac{u^2}{2c}$ because $\sigma_c\left(a + \frac{u^2}{2c}\right) = \frac{b-a}{|u|} - \frac{|u|}{c}$.

2. The state-regulon pair $(x_h(\cdot), u_h(\cdot))$ follows the **critical phase**, starting from $(\Xi_c(u), u)$ at time $\frac{b-a}{|u|} - \frac{|u|}{c}$ by taking the velocity of the regulon (acceleration) equal to $-c$.
- It ranges over the graph of $\sqrt{c} r^\sharp(x)$ on the time interval $\left[\frac{b-a}{|u|} - \frac{|u|}{c}, \frac{b-a}{|u|} \right]$ until it reaches the state-regulon pair $(b, 0)$.
 The heavy evolution would remain at this equilibrium forever with an acceleration equal to 0.
 - However, for defining the heavy hysteresis cycle, we assume that **we keep the acceleration equal to $-c$** . Hence the state-regulon pair $(x_h(\cdot), u_h(\cdot))$ ranges over the graph of $-\sqrt{c} r^\sharp(x)$ on the time interval $\left[\frac{b-a}{|u|}, \frac{b-a}{|u|} + \frac{|u|}{c} \right]$ until it reaches the state-regulon pair $(\Xi_c(u), -|u|)$.



3. The state-regulon pair $(x_h(\cdot), u_h(\cdot))$ starts from $(\Xi_c(u), -|u|)$ **at time** $\frac{b-a}{|u|} + \frac{|u|}{c}$ **by taking the velocity of the regulon equal to 0.** It remains viable on the time interval $\left[\frac{b-a}{|u|} + \frac{|u|}{c}, 2\frac{b-a}{|u|}\right]$ until it reaches the state-regulon pair $(\Xi_c(-|u|), -u)$.



4. The state-regulon pair $(x_h(\cdot), u_h(\cdot))$ starts from $(\Xi_c(-|u|), -u)$ at time $2\frac{b-a}{|u|}$ by taking the velocity of the regulon equal to $+c$.
- It ranges over the graph of $-\sqrt{c} r^b(x)$ on the time interval $\left[2\frac{b-a}{|u|}, 2\frac{b-a}{|u|} + \frac{|u|}{c}\right]$ until it reaches the state-regulon pair $(a, 0)$. The heavy evolution would remain at this equilibrium forever with an acceleration equal to 0.
 - However, for defining the heavy hysteresis cycle, we assume that we keep the acceleration equal to $+c$. Hence the state-regulon pair $(x_h(\cdot), u_h(\cdot))$ ranges over the graph of $+\sqrt{c} r^b(x)$ on the time interval $\left[2\frac{b-a}{|u|}c + \frac{|u|}{c}, 2\left(\frac{b-a}{|u|} + \frac{|u|}{c}\right)\right]$ until it reaches the state-regulon pair $(\Xi_c(-|u|), u)$.

This ends the heavy hysteresis cycle.

Heavy hysteresis cycles are governed by three velocities of regulons only, $-c$, 0 and c , which can be regarded as “meta-regulons”.

They provide an example of “**quantized**” **evolutions**, governed by a combination (called **amalgam**), of a finite number of (meta) regulons only. Quantization is a recent issue in control theory, where, instead of computing the complicated feedback regulating viable evolutions, the question arises to achieve the regulation of viable evolutions with a finite number of controls or feedbacks.

This number is reduced to two (meta) regulons in the limiting case $u := \sqrt{c} u^*$ and when $\Xi_c(\sqrt{c} u^*) = \Xi_c(-\sqrt{c} u^*) =: x^*$. In this case, heavy hysteresis cycles are called *inert hysteresis cycle* $x_h(\cdot)$ (of cycle $\frac{4u^*}{\sqrt{c}}$) in the following way:



- (a) The state-regulon pair $(x_h(\cdot), u_h(\cdot))$ starts from $(x^*, \sqrt{c} u^*)$ at time 0 by taking the velocity of the regulon equal to $-c$. It ranges over the graph of $\sqrt{c} r^\#$ on the time interval $[0, \frac{u^*}{\sqrt{c}}]$ until it reaches the equilibrium $(b, 0)$ and next, keeping the velocity of the regulon equal to $-c$, it ranges over the graph of $-\sqrt{c} r^\#$ on the time interval $[\frac{u^*}{\sqrt{c}}, \frac{2u^*}{\sqrt{c}}]$ until it reaches the state-regulon pair $(x^*, -\sqrt{c} u^*)$.
- (b) The state-regulon pair $(x_h(\cdot), u_h(\cdot))$ starts from $(x^*, -\sqrt{c} u^*)$ at time $\frac{2u^*}{\sqrt{c}}$ by taking the velocity of the regulon equal to $+c$. It ranges over the graph of $-\sqrt{c} r^b$ on the time interval $[\frac{2u^*}{\sqrt{c}}, \frac{3u^*}{\sqrt{c}}]$ until it reaches the equilibrium $(a, 0)$ and next, keeping the velocity of the regulon equal to $+c$, it ranges over the graph of $+\sqrt{c} r^b$ on the time interval $[\frac{3u^*}{\sqrt{c}}, \frac{4u^*}{\sqrt{c}}]$ until it reaches the state-regulon pair $(x^*, \sqrt{c} u^*)$.

Let us assume that $|u| \leq \sqrt{c}\sqrt{b-a}$. The *heavy hysteron* is the set-valued map Φ_{Heavy} defined by

$$\Phi(x) = \{-\min(u, \sqrt{c}r^b(x), \sqrt{c}r^\sharp(x)), \min(u, \sqrt{c}r^b(x), \sqrt{c}r^\sharp(x))\} \quad (9)$$

Its graph is the *heavy hysteresis loop* in the state-regulon space (actually, the phase space). Its cycle is equal to $2 \left(\frac{b-a}{|u|} + \frac{|u|}{c} \right)$.

When regulated by positive regulons, the state goes from a to b and the state-regulon pair ranges over the graph of $x \mapsto \min(u, \sqrt{c}r^b(x), \sqrt{c}r^\sharp(x))$ whereas, when regulated by negative regulons, the state goes from b to a , and the state-regulon pair ranges over the graph of $x \mapsto -\min(u, \sqrt{c}r^b(x), \sqrt{c}r^\sharp(x))$. The evolution $t \mapsto (x_h(t), u_h(t))$ is cyclic of cycle $2 \left(\frac{b-a}{|u|} + \frac{|u|}{c} \right)$.



Starting with any regulated system (and not only the simple system $x'(t) = u(t)$), viability constraints and inertia threshold, we can associate heavy viability cycles driven by the regulated system. Heavy evolutions lock-in the viability niche of a regulon in the sense that it enters this viability niche, it may remain in it forever. Viability theory deals not only with intertemporal optimality, but also with viability, implying that

decisions taken at warning time (kairos) instead of “optimal” ones.

This very simple mathematical metaphor implies that two excitatory/inhibitory simple mechanism of a DNA site with bounds on the quantities and their accelerations are sufficient to explain the production of an isolated protein increasing up to a given viability bound and then, decreasing to disappear and being produced again according to a clock, the cyclicity of which is concealed in this very simple viability oscillator, triggering a biological clock.

The results illustrated by this example are quite general, and apply to a large class of nonlinear regulated systems.



Merci pour votre attention
Thanks for your attention

