INtegral BIOmathics Support Action

INBIOSA Seminar : 8/6/2011, 11:00 to 13:00

Room: BU25 5/S1 (Aquarium)

Avenue de Beaulieu/Beaulieulaan 25, B-1160 Bruxelles, Belgium

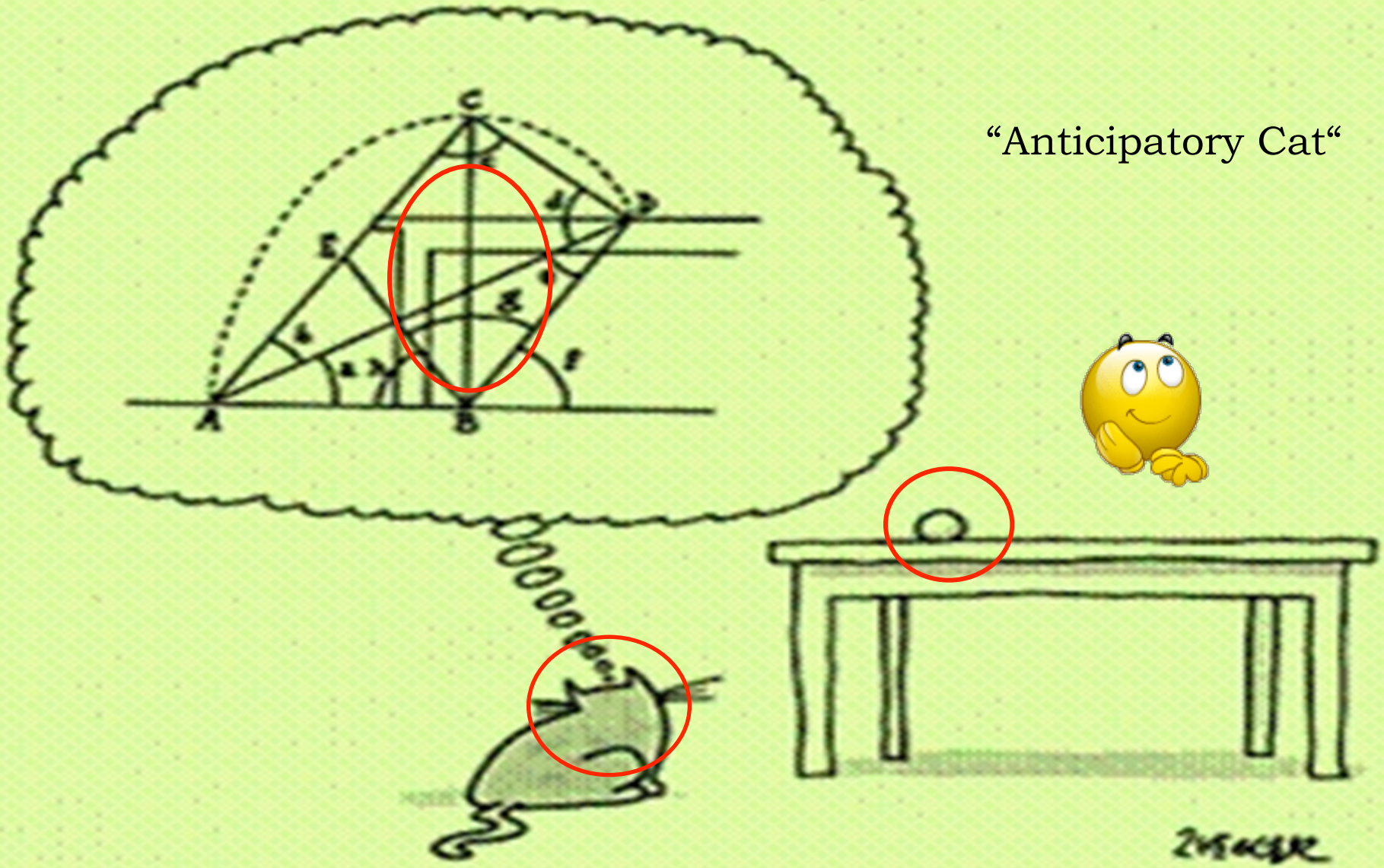
INBIOSA

What are we going to talk about?

Agenda

1. What does Integral Biomathics (IB) mean?
2. How the INBIOSA virtual collaborative process is working?
3. Some exciting scientific ideas coming forward
4. Questions and Answers
5: Post-session

What are we going to talk about?



Part I: What is Integral Biomathics?

Starting Point: The Challenges

1. the dearth of theory in biology

2. the lack of theoretical convergence

Science is only beginning to comprehend the scale of the conceptual and methodological challenges involved in the study of dynamic systems and in the complexity of living systems and their networks.

Yet, researchers *do not know really* how to approach the issue. The dilemma is not technical, but theoretical.

In the neurosciences, we are close to having the technical capacity to track every neuron and label every chemical transaction in the brain simultaneously.

Given such powerful investigative technology the problem is that researchers do not know what to ask of this technology.

The good news: biology can learn from the successes of other sciences (physics, chemistry, computer science) about how to formulate a better theoretical framework.

Yet, the law in biology is: *there is no law* (except for natural selection).

The Road Ahead

In the history of the physical sciences, *theory* was always far ahead of the empirical databases. It was the vital source of guidance in deciding what kind of evidence to seek.

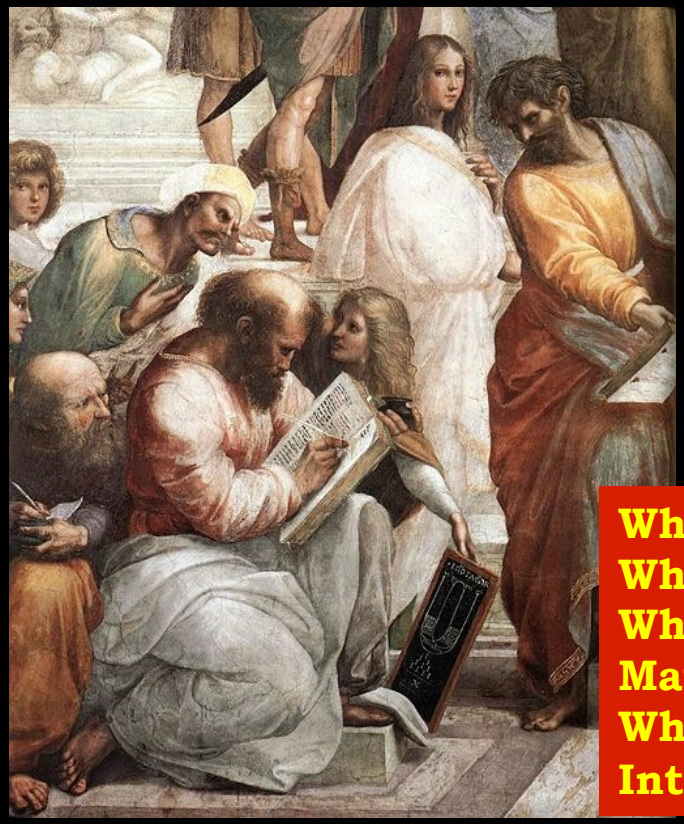
Theory leads the way, making its own breakthroughs, focussing investigation and enabling empirical researchers to ask the right questions.

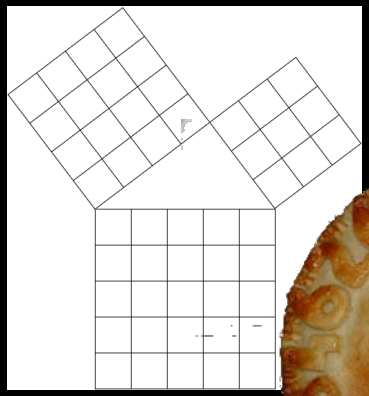
Biological theory needs a new strategy, an alternative to methodological empiricism, a strategic approach of its own, not one based on the metaphors of physics.

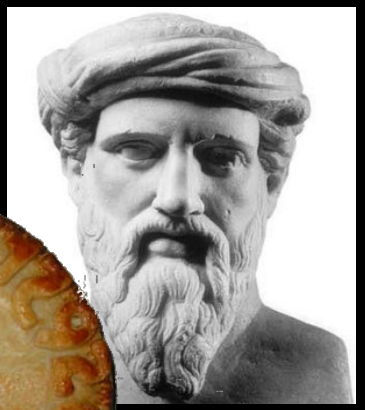
But what kind of new theory?

One with foundations in mathematics and computation, of course.

Why Mathematics?







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Why logic? Which logic?
What is Mathematical Biology?
What is Biological Mathematics?
Mathematics as it seems to be expressed in the living?
What about time? Which time? Sidereal time?
Internal clocks (metabolic rates)? ...

"If I were again beginning my studies, I would follow the advice of Plato and start with mathematics."

-- Galileo Galilei

Let's start: a view from 40.000 feet

Mathematical Biology

vs.

Biological Mathematics (Biomathics)

What is Mathematical Biology?

→„Mathematical Biology“
„Mathematical Biophysics“

Mathematical Biology is a derivative of the Mathematics of Physics.

„Relational Biology“ ←

Both good and bad with the Mathematics of Physics is the acceptance of the Equations of Motion in classical mechanics, i.e. equating the displacements of variables to the flow of time:

$$v = u + at$$
$$s = 0.5(u+v)t$$
$$s = ut + 0.5\,at^2$$
$$v^2 - u^2 = 2as$$

$$a = d^2s/dt^2$$

While some gains can be made from using the equations of Motion in Mathematical Physics, relating changes in variables to the flow of time, there are also major disadvantages in biology.

Who is equating ? Only the physicist!

What is Biological Mathematics?

… mathematics as it occurs in living systems.

Biological mathematics - encycloped...

http://en.citizendium.org/wiki/Biological_mathematics

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Main Article | Talk | Related A

*This is a **draft article**, unde*

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References

1. ↑ Kari L, Landweber LF. (2000) Computing with DNA. *Methods Mol.Biol.* 132:413-430.
2. ↑ Bray D. (2009) *Wetware: A Computer in Every Living Cell.* Yale University Press. ISBN 9780300141733. | Google Books preview.
3. ↑ Landweber LF, Kari L. (1999) The evolution of cellular computing: nature's solution to a computational problem. *Biosystems* 52:3-13.
4. ↑ Simeonov PL. (2010) Integral biomathics: A post-Newtonian view into the logos of bios. *Progress in Biophysics and Molecular Biology* Proof published online.

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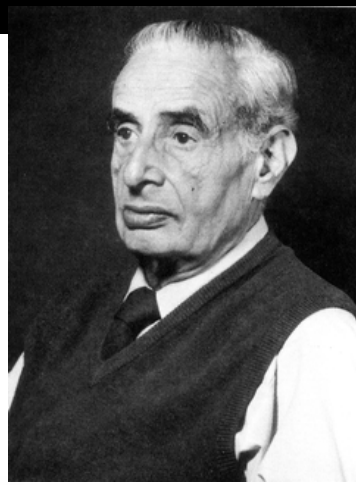
What is New in Biological Mathematics?

A Form of Logic Suited for Biology

Walter M. Elsasser
Department of Earth and Planetary Sciences
The Johns Hopkins University
Baltimore, Maryland
http://www.nap.edu/readingroom/books/biomems/welsasser.html



I. Introduction: Biology versus Physics

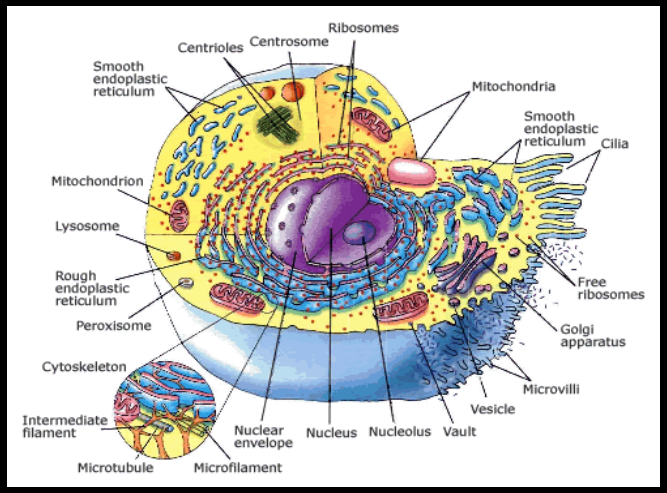
A comparison of two sciences might appear as a rather primitive exercise. It is introduced here only because there are still many who insist on the purely empirical character of biology, i.e., the absence of a meaningful "theory" of biological phenomena. If a person enters the subject matter of biology coming from physical science, as this writer did, he cannot help but be intensely aware of the difference in character of the two sciences. It soon becomes clear that what may be called the hierarchical structure of physics has little or no counterpart in biology. By hierarchical structure we mean the possibility, which normally exists in physics, of condensing a more or less extensive area of experience into one formal statement, usually a set of

Hierarchy is also central in biology, but it is of different nature; it allows for the existence of an interplay among different temporalities and logics at the root of the emergence of higher processes up to consciousness.

Hierarchy: The *Special* about Biology

Definition: A system in which the *specific* properties of the components can be ignored.

- **A cell is a hierarchical organization that has the ability to maintain itself *away from equilibrium*, which is something that none of its individual molecular components (organelles) *can do* (although we know well that the cell is composed of them).**



- **an organ is a collection of cells that take on functions (such as pumping blood or breathing air) that cannot be performed by the individual cells*.**

..a difference which makes a difference.

→„Natural Philosophy“

„Science of Logic“ ←

mathematical biology ⊢ (externalist, reductionistic)

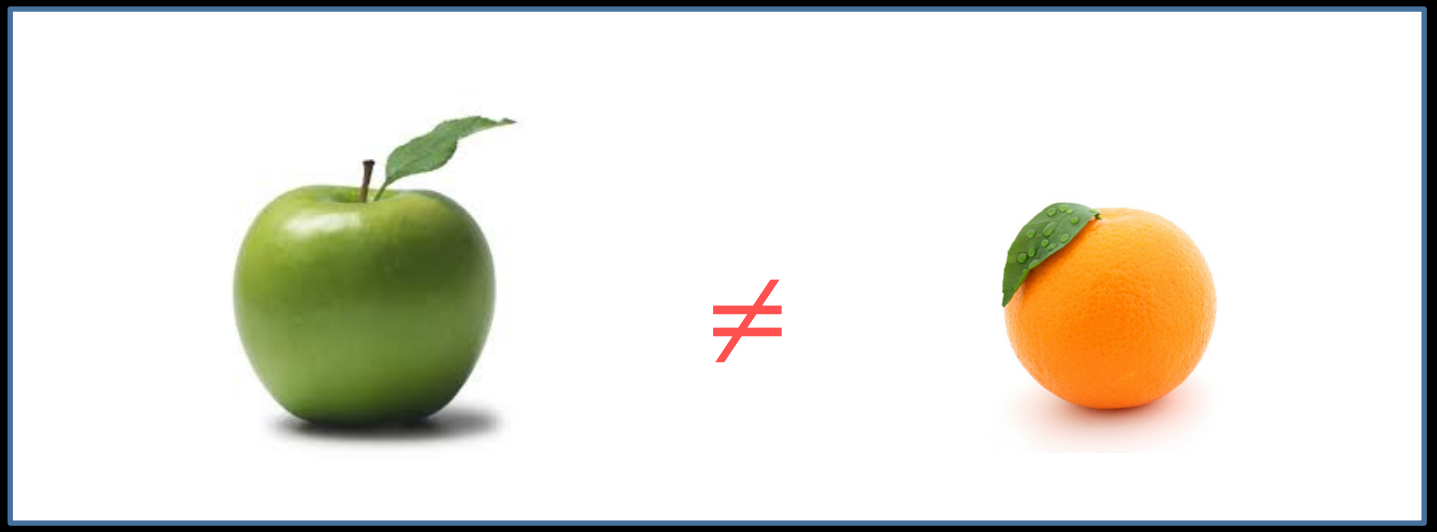
biological mathematics ⊢ (internalist, reductionistic)

integral biomathics ≡
mathematical biology ∪ biological mathematics

integral biomathics ⊢ (complementary, *integrative*)

both, internalist and externalist
both, reductionist and holistic

What is Integral Biomathics?



integral biomathics ≠ systems biology

Integrative* ***holistic***

***) implying *subsumptive hierarchy*: higher levels integrate the lower levels' properties and dynamics under their own rules; hence suitable for diachronic modeling of emergent forms as a process of the *acquisition of new informational constraints*.**

What is Integral Biomathics?

Why Integral Biomathics?

"…deducing models of function from the behaviour of a complex system is an *inverse problem*. …the programme of systems biology cannot be achieved because the inverse problem cannot be solved."

Sidney Brenner, 2010

"The way forward is to continue in the path of molecular biology, unveiling how the genome expresses its information through proteins and other molecules, how these build assemblages and how the functions of these are integrated in the cell.

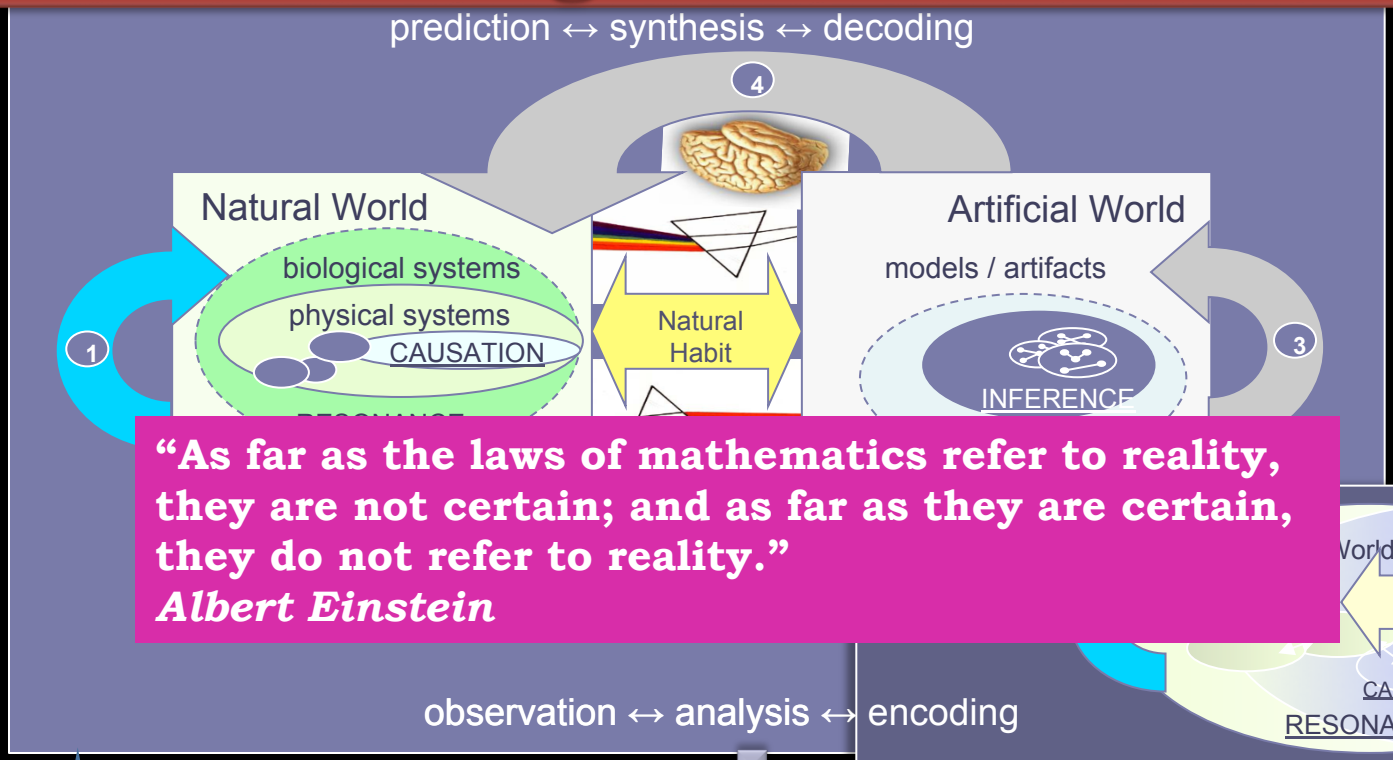
… We then solve the forward problem of *computing* the behaviour of the system from its components and their interactions."

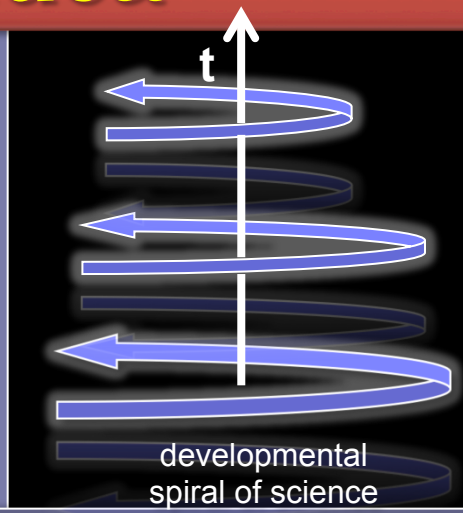
Sidney Brenner, 2010

… and *formalize the result* with a robust mathematical theory capable
i. to trace back the outcome, and
ii. to predict/project the next step of development.

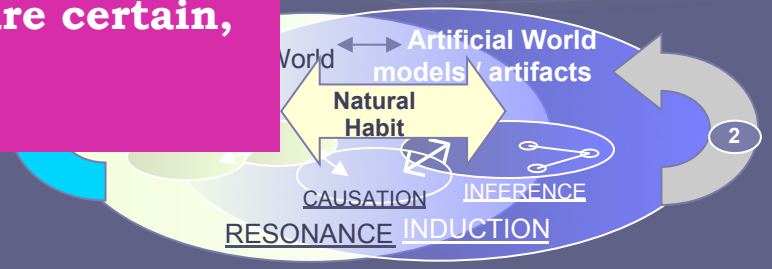
INBIOSA, 2011

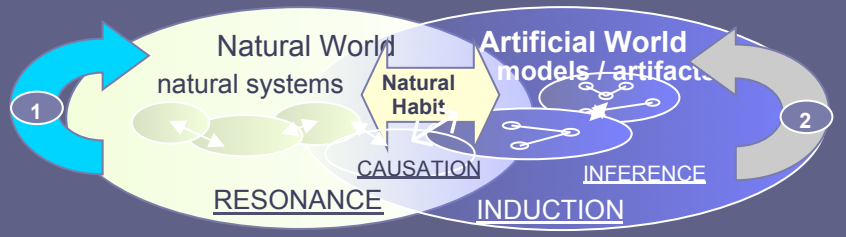
Integral Biomathics: Idea

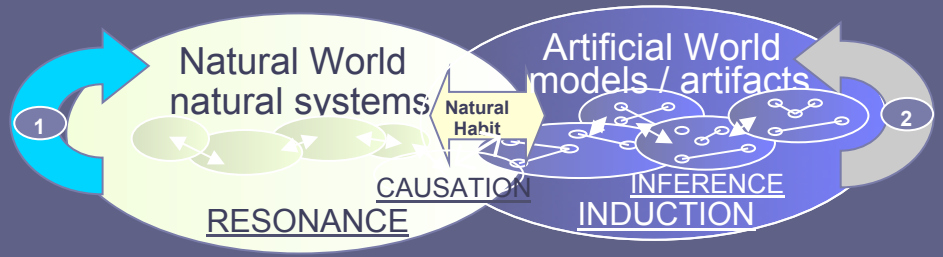




"As far as the laws of mathematics refer to reality, they are not certain; and as far as they are certain, they do not refer to reality."
Albert Einstein







to accelerate scientific development and evolution through balanced fusion of the Real and Artificial Worlds based on unifying classical mathematical biology with biomathics or biological mathematics on the way to genuine biological system engineering

FET INBIOSA Seminar, Brussels, 08.06.2011

Integral Biomathics: Ambition

Objective: a unifying approach to understanding Nature, aiming at *unraveling and explaining the gaps between machines and living organisms*

Challenges:

- to investigate the biological imperatives of computation in a profoundly new way based on understanding the fundamental characteristics of emergence, organization, development and evolution in biology
- to devise a new framework for research of complex biological phenomena
  - by integrating the multiple levels of organization and activity in living systems
  - by evolving the model autonomously, thus mimicking the system itself
  - by understanding intrinsic *bio*-logic based on different premises from the logic of today's engineered systems
- to inaugurate a *breakthrough paradigm change towards bio-logically driven mathematics and computation*
- to develop novel mathematical formalisms capable of addressing the multiple facets of an *integral model and a general theory for biocomputing* within an adequate engineering frame of relevance
- to design *novel biosynthetic systems which go beyond Turing's discrete computation* and von Neumann's self-replicating automata

Integral Biomathics: Premises

Living systems are characterized by the *complexity of biotonic phenomena*: *finiteness of classes* and *non-reducibility / individuality* (Elsasser); they are heterogeneous sets, the componets of which cannot be replaced by each other as physicalistic models do with homogeneous systems of molecules, atoms, etc.

- ***Different properties of (living) matter at different topological scales***
  - **We need treatment of finite heterogeneous classes which are common in biology, instead of infinite homogeneous physical world classes (Elsasser).**
  - **We need the kind of mathematics, *biomathematics*, able to describe these properties: at molecular scale, at cellular scale, at organic scale, etc.**
  - **We need *scalability of models*, but neither greedy reductionism, nor greedy holism.**
- ***Different kind of computational models***
  - **Internalist, implicit & integral models instead of *purely* explicit & externalist ones.**
  - **Relational, evolutionary & developmental models instead of absolute & static ones.**
  - **Models allowing an explicit representation of vagueness & uncertainty.**
- ***Different purpose (base) for computation in living systems***
  - **Present day biocomputation approaches, such as cellular, membrane, DNA computing, etc. *(mis)use biological systems* to perform calculations which are *not really natural* (e.g. Adleman's DNA solution of the NP-complete Hamiltonian Path problem in combinatorics).**
  - **We need a new concept for computation in biological context, a new eco-*bio-logic*.**
  - **We need to ask new questions about *living computation* and *computation for life*.**

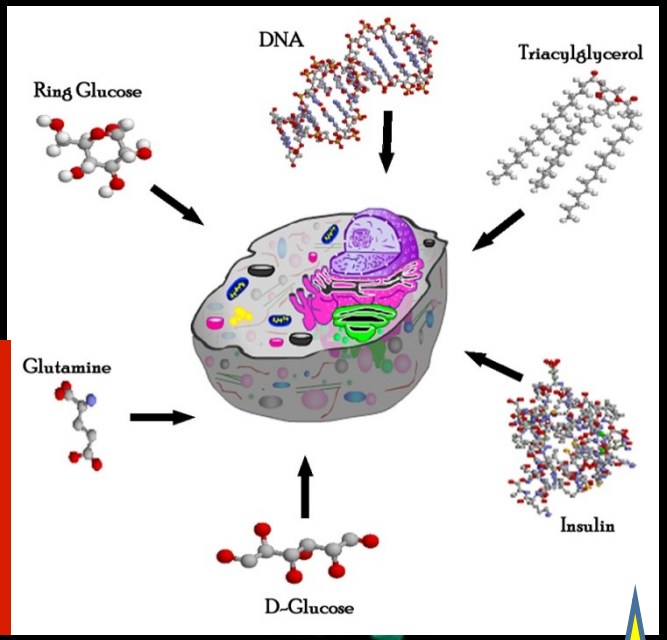
Integral Biomathics: Examples

Example 1: The Cell Description

a vague, indeterminate, holistic/reductionistic & relational non-static system: *the number of distinct types of molecules in a cell*

***Except for DNA itself*, every other molecular component varies in its absolute *numbers* (as molecules are synthesized, degraded, or endo- and exocytosed) and every molecular component turns over, each at a different rate, from the others.**

Πάντα ῥεῖ ("everything flows", Heraclitus): a cell at any given time point is not the same cell at any other time point.
... and yet it continues to function continuously as a *single entity*.



We need a mathematics that can describe such an ever-changing, indeterminate, yet persistent "thing" and *how it maintains its "identity"* within certain boundary conditions, yet ceases to function outside of those boundaries.

What about Fuzzy Logic/ Logic of Vagueness?

Integral Biomathics: Examples

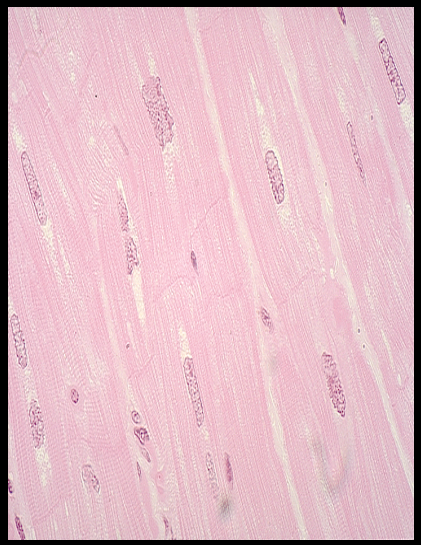
Example 2: The Processes Description

We need to integrate scalar and vector forms of mathematics: one of the key functions that living systems carry out is **to convert scalar processes** such as diffusion **into vectorial ones** such as active transport.

Examples: Inclusion and exclusion; the emergence of homochiral molecules from racemic mixtures; excretion; etc. These are all **vectorial processes that cannot be explained by simple physico-chemical properties, all of which are scalar.**

We need mathematics that does not just describe the physics of how the heart pumps.

Physics can describe the function of a pump or a heart once it exists, but tells us ***nothing about how a pump or a heart comes into being.***



We need also **a mathematics that explains how cells evolve and organize to become a heart** with the physical properties of a pump.

Developing such a novel mathematics would **not only describe how a heart comes into being, but also how we *think* about processes** by which pumps are invented.

Such an emergent, developmental and evolutionary, mathematics *does not exist.*

Integral Biomathics: R&D Agenda

Integral Biomathics aims at revising the conceptual framework of contemporary computing , information theory and systems biology to develop profoundly new theoretical foundations for biocomputation capable to answer such questions as:

- ***What is computation?*** **– within the biological context, because there is "no computer into which we could insert the DNA sequences to generate life, other than life itself" (Noble, 2010).**
- **How useful is computation? – for living systems, where "usefulness" is studied from the viewpoint of the computation performing entity.**
- **To what extent can a computation be carried out? – in an organism or an ecosystem, with the available resources (energy supply, time, number of 'computing' elements, etc.).**

Integral Biomathics: Questions

Do living systems compute at all?

Do we compute where a ball that has been thrown is going to land or do we use some other form of "calculation" to optimize our chances of catching it?

Most people don't think we compute.

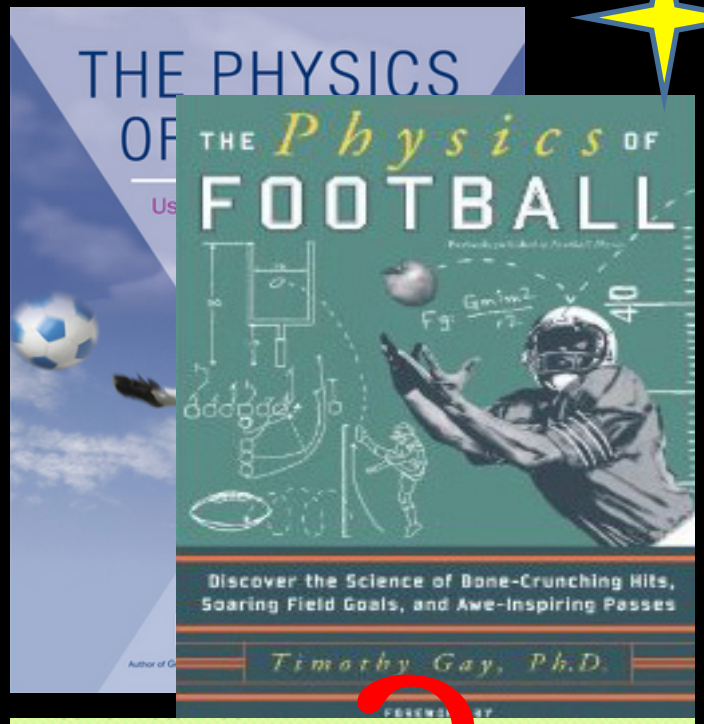
So what do we do?

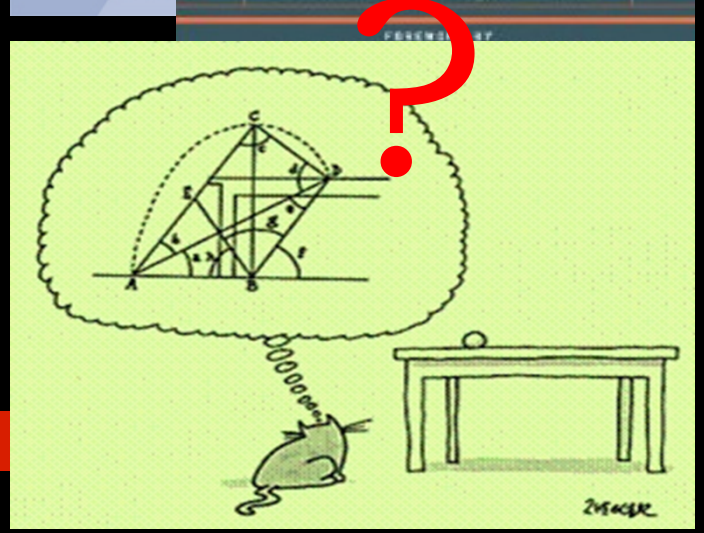
Do cells "compute" or do they merely optimize their functions by homeostasis in response to any given "input"?

Could we learn new ways of "calculating" by emulating what cells and people do instead of trying to brute force massive calculations?

Could we outperform IBM's Big Blue not by increasing computing power but by figuring out how cells perform optimizations without such electronic complexity?

Should we redefine computation in biological context?





Integral Biomathics: Focus

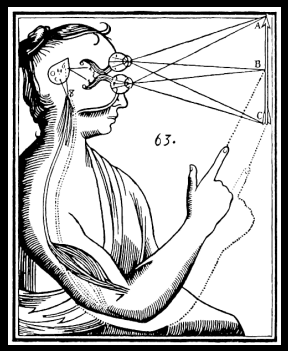
Integral Biomathics is about shifting the computation paradigm closer to the domains of quantum physics and biology with the ultimate objective of creating artificial life systems that evolve harmoniously with the natural ones.

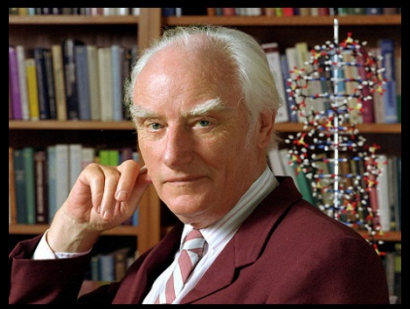
This new discipline is particularly interested in four essential *HOW* questions (implying also the Aristotelian *WHY*):

1. **How life and life-like properties and structures apparently emerge?**
2. **How abstract ontological categories and semantic entailments emerge?**
3. **How cognition and consciousness emerge and evolve in natural systems?**
4. **How life related information is transferred through space and time?**

"If I was a young researcher now, I would study *the mind-body problem.* This is the great challenge of the 21st century."

Ilya Prigogine





Integral Biomathics: Essence

1. IB is based on the mathematics that matters…

It is the mathematics of biological systems, namely the dynamics of closure to efficient causation (such as the system of interacting mappings of the f, β, Φ loops in Rosen's M-R theory) and its stabilization (according to Letelier) into a new hierachical system exhibiting organizational invariance.

2. IB is enabled by the computation that matters…

It is the computation inherent in biological systems, which we believe is the computation required to enable the dynamics of the *quantum-like attributes* of biological systems to be processed effectively (complementarity, simultaneity, superposition, entanglement, self-referentiality).

The potential for exploiting the similarities between the conceptual structure of quantum theory and the relational biology of *Rashevsky-Rosen-Louie* becomes possible through increasing capabilities in quantum logic and computing.

Integral Biomathics: Advantages

1. The promise of a new era in life sciences…

… the understanding of quantum-like traits at all levels of biological systems will revolutionize the modeling of all levels of life from the biomolecular to the neurocognitive; the understanding of emergence will enable new theories and preventive approaches to disease at the physiological and neurobiological levels).

2. The promise of a theoretical basis for engineering complex systems…

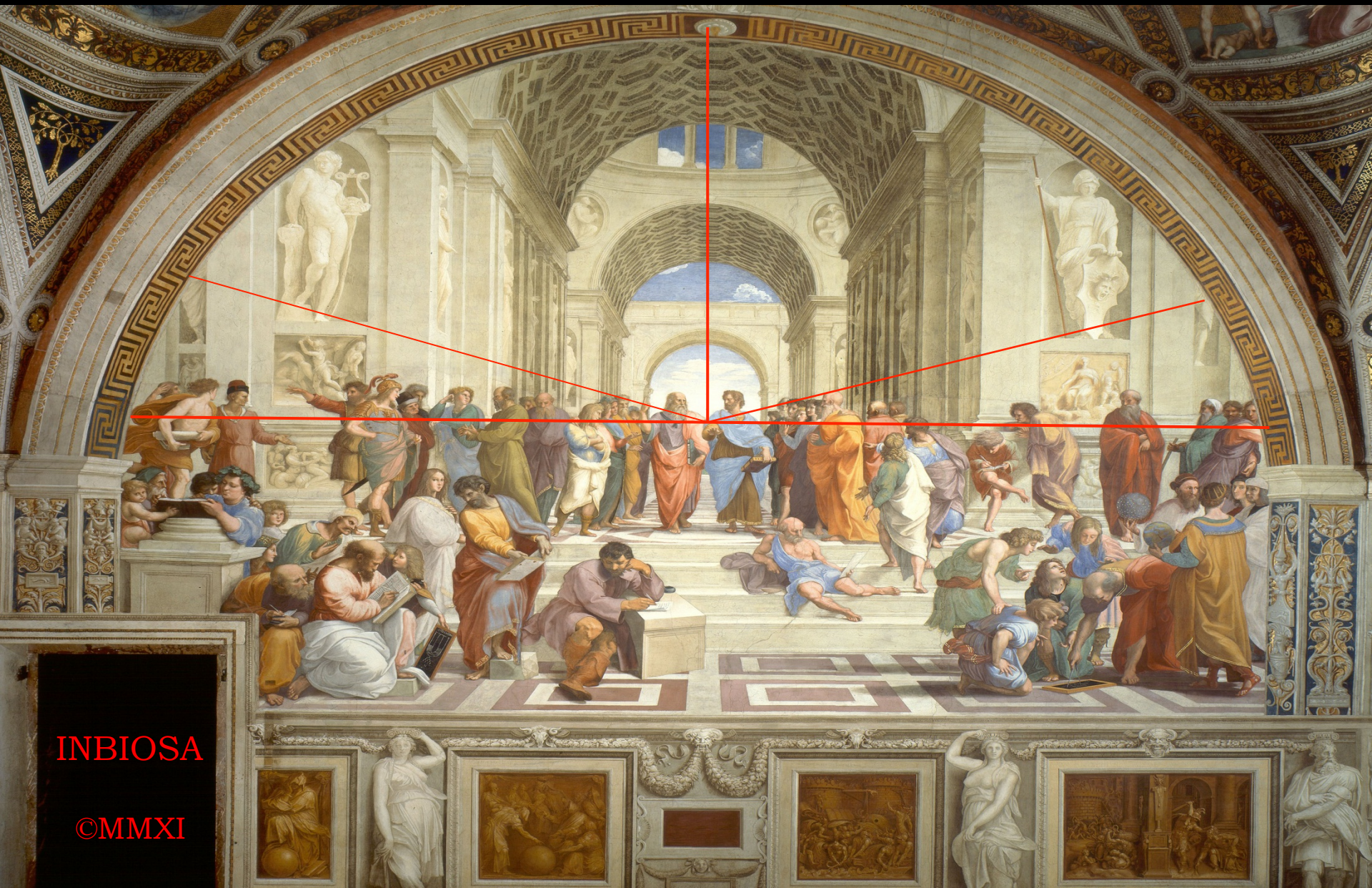
… the understanding of emergence will enable the anticipation of inappropriate, catastrophic interactions in complex interacting systems such as those that are the focus and main objectives of many current FET programs.

3. The understanding of the quantum-like traits in living systems will establish a new frontier in science…

… the potential homomorphism between living and quantum systems to enable across-the-board advance in science.

Part II: What are we doing in INBIOSA?

..discussing the perspective of science..



INBIOSA

INBIOSA: Motivation

The difference between living and non-living matter, understanding the human mind, understanding how living matter can be self-aware seems to be impossible within current scientific paradigms.

Vision: to investigate the imperatives of mathematics and computation in a cardinal new way by comprehending the fundamental principles of emergence, development and evolution in biology.

We believe in an intellectual community that challenges the current orthodoxy in science. INBIOSA's purpose is to enable and to support such a community of original thinkers in their pursuit of new horizons.

Mission: to bring together experienced scientists (mathematicians, computer scientists, physicists, biologists, ...), who believe that it is time for another scientific revolution.

INBIOSA: Organisation and Operation

- 2 members of the Project Management and Technical Board
  34 members of the Scientific Advisory Council – some of the best alternative thinkers (with ideas) in the world
  22 Scientific Collaboration Partners – future project partner candidates from a number of fields all over the world (mathematics, biology, computer science, chemistry, physics)

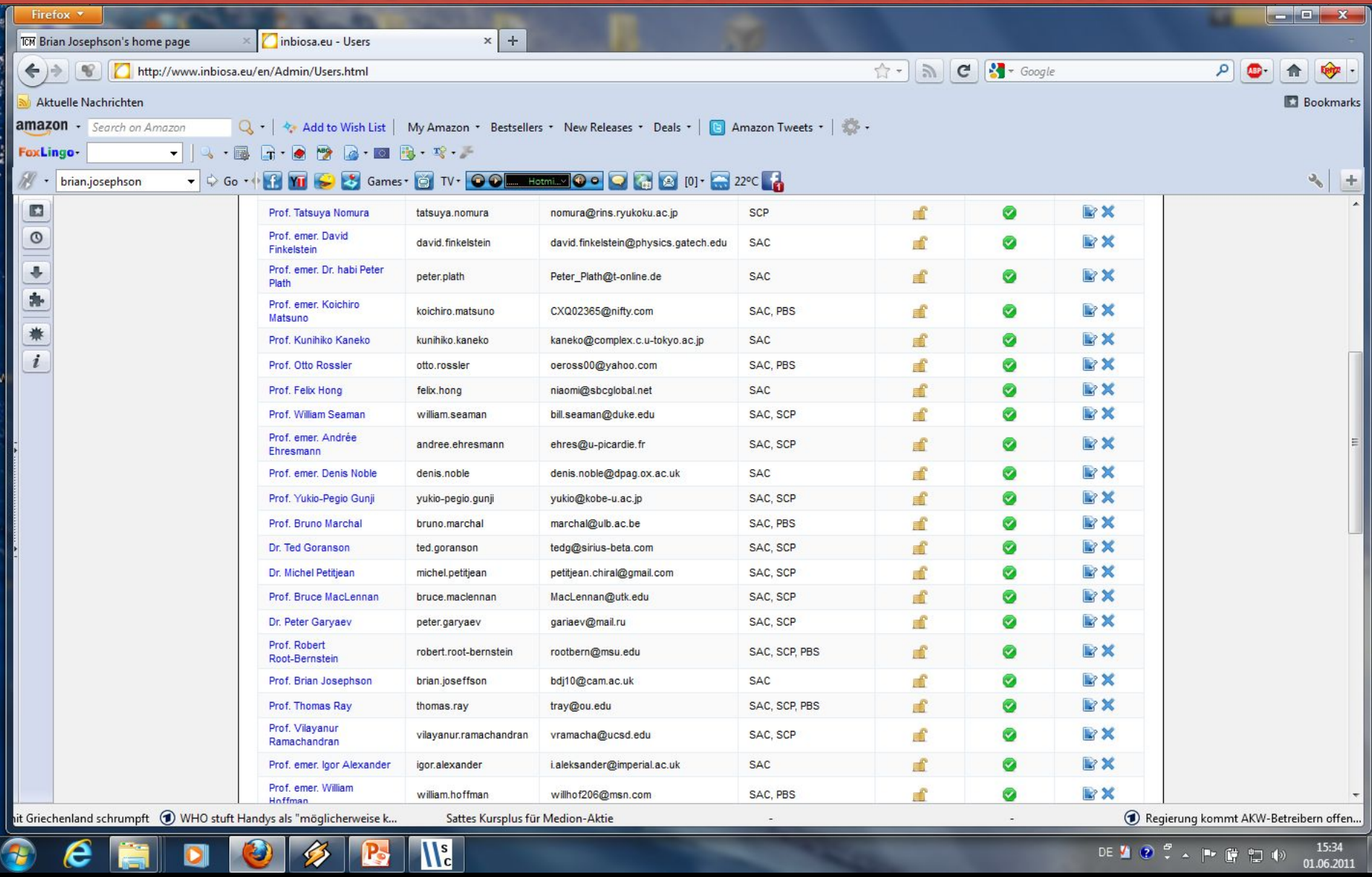
- Goal: White Paper for a novel FET research programme by 12/2011

- Advanced Online Scientific Community Service (AO-SCS): blogs, RSS feeds, newsletters, activity digests, group email announcements, virtual sessions, multimedia data repository, communication, project proposals

- press releases, calls for proposals, reflections, announcements

- Annual Conference on Integral Biomathics ACIB 11 in Stirling, UK
- iBioMath 2011workshops in Paris and San Jose (USA)
- Publication with Springer Verlag negotiated

INBIOSA: Virtual Collaboration



Some Exciting Scientific Ideas

… some ideas we are working on to ensure a continuing FET advance in biology, life sciences, computation and complex artificial systems engineering.

1. Biological Time

1. **Put the "*flow of time*" in a new category* at the same level as other parameters.**

2. **Put both *class* identity** and *individual* identities** on an equal footing.**

Merit: Facing Emergent Phenomena Head-On

*) **But what kind of "category" when time is vary*ing* with size, age, population, etc. ?**

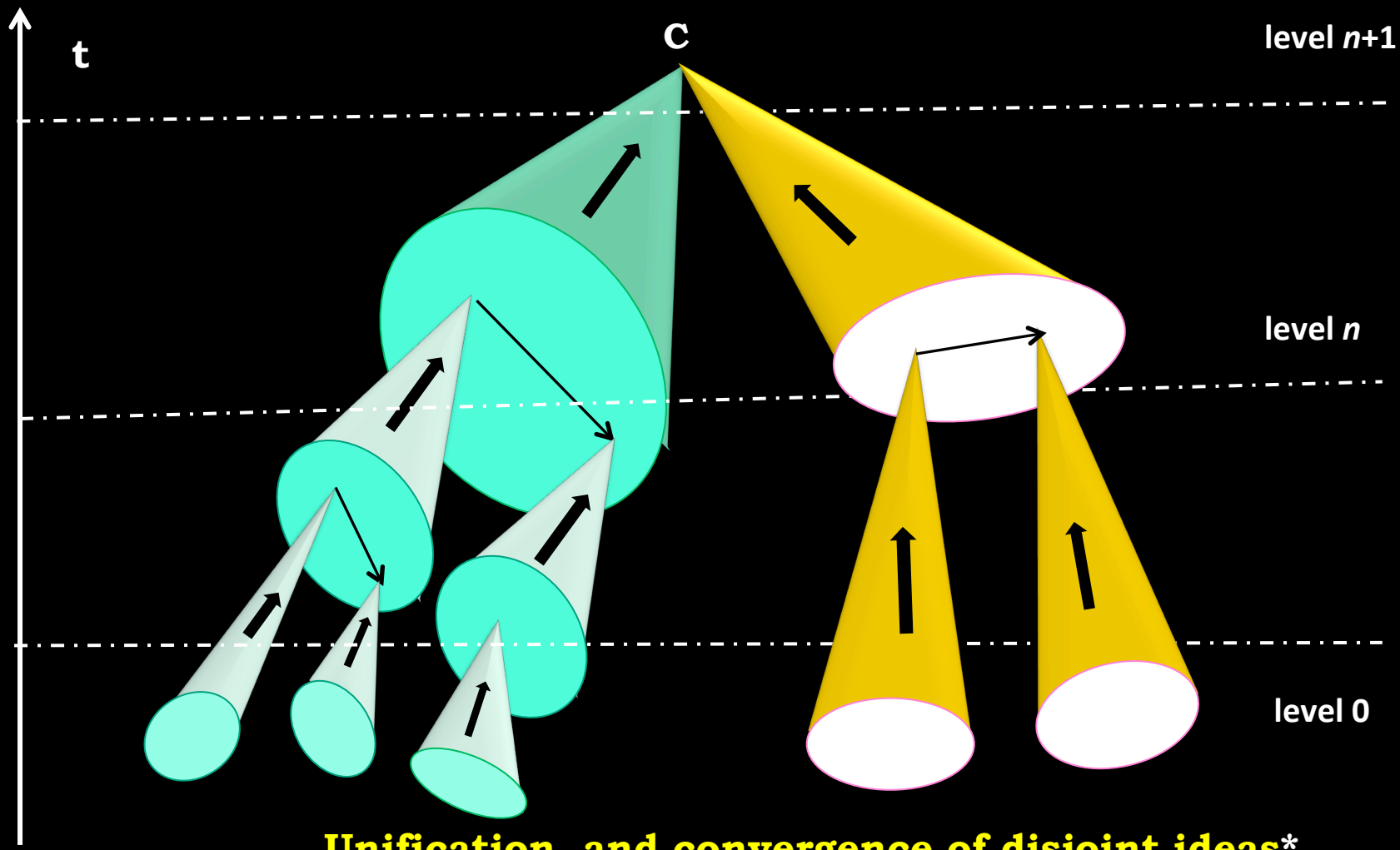
) **But what does "identity" mean when a living organism is constantly vary*ing* in its absolute constituents and turn*ing* them over at vary*ing* rates ?

More Exciting Scientific Ideas

2. Complementarity

- **Dissipative vs. Conservative Systems.** Life belongs to the class of natural phenomena which are not isolated and simplistic, but related and complex. Therefore, modelling computation and cognition in living systems is analogous to studying non-equilibrium / dissipative open systems capable of exchanging information in the context of noise, disturbances and fluctuations of their environment.
- **Resonance vs. Causation.** Whereas in causation multiple linear cause–implication chains about events in the domain of discourse can be clearly identified, we understand resonance usually as a non-linear, quantum-like (non-local) and semantically 'hidden' spatio-temporal relationship between entities in the broad sense.
- **Induction vs. Inference.**
- **Vaguesness vs. Crispness.**
- **Synchronicity and Choice vs. Determinism.**

INBIOSA's Idea Binding Approach



Unification and convergence of disjoint ideas*

Andrée Ehresmann

A dynamic model for emergence and self-organization in multi-scale systems

(Memory Evolutive Systems)

FET INBIOSA Seminar, Brussels, 08.06.2011

Ron Cottam

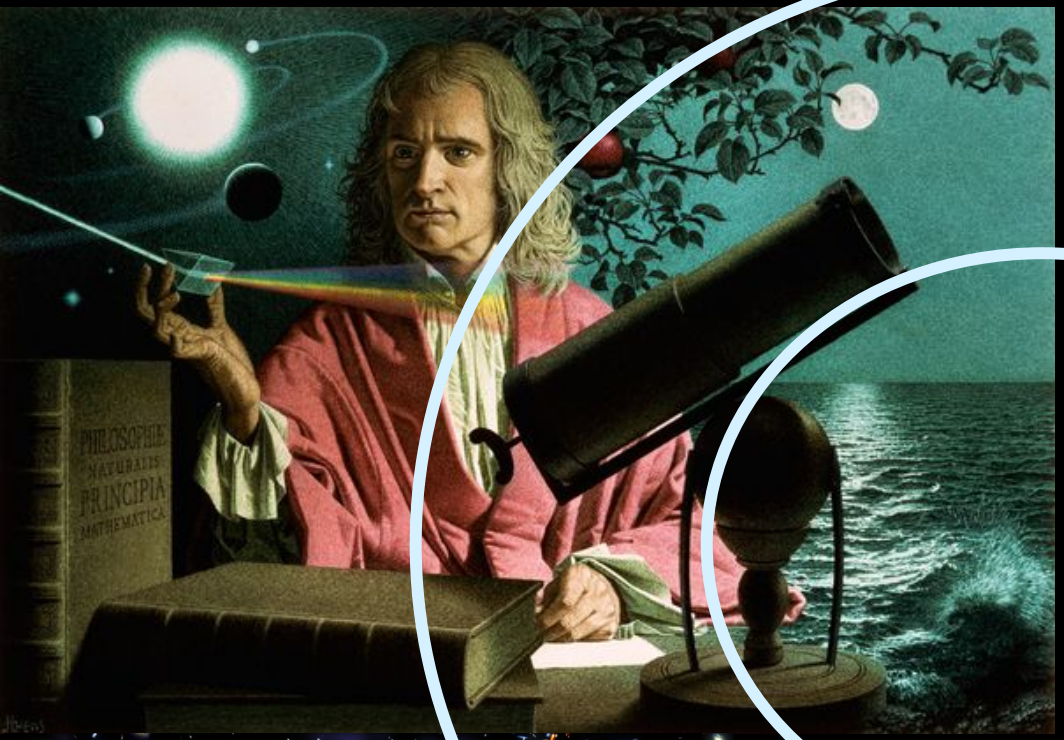
Creating Life from Logic

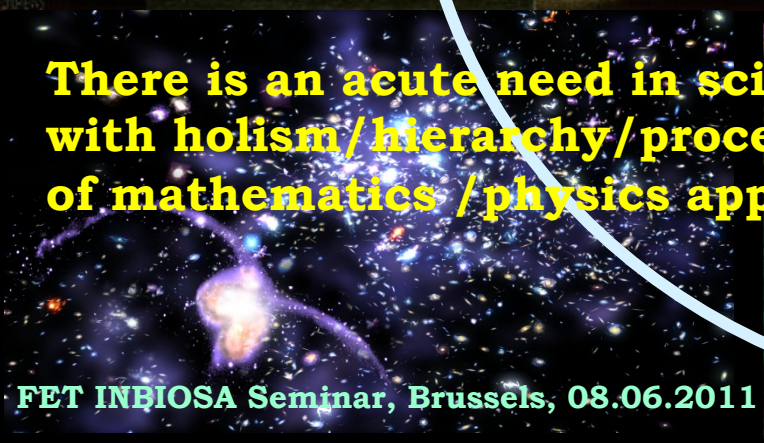
(Roll Back Driver)

Leslie Smith

Cells and Information

The Next Step: Knowledge Integration





There is an acute need in science to integrate reductionism/mechanism with holism/hierarchy/process thinking in order to make the methods of mathematics /physics applicable to biological systems. Let us do it!

Epilogue

The history of science teaches

how *extra-ordinary*
the quest for new ideas is.

The ideas being identified and developed by INBIOSA can be given the opportunity to prove themselves up to FET.

FET can let them die or can nurture them …

… under the *best possible circumstances*

that lead towards an optimal solution …

… in the hope that what is possible with the human mind can be achieved for the progress of science and mankind.

The INBIOSA team would be pleased to engage further with FET on the definition of those *circumstances* and their integration within our implementation concept.

Finis

"Following the light of the sun we left the Old World."

-- Christopher Columbus

Thank you!

Plamen L. Simeonov
Wilhelmstrasse 81
10117 Berlin
pls@ieee.org
www.simeio.org

Questions & Answers

Any Questions ?