

Mesdames et messieurs,

Je suis très heureux et honoré d'être présent aujourd'hui ici pour recevoir le titre de Doctor Honoris Causa de l'Université de la Méditerranée.

Malgré 6 ans d'apprentissage du français, il y a longtemps, il est préférable que je parle de mon travail en anglais;

J'ai un peu honte de le dire et je vous présente mes excuses.

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Experimental biology calls nowadays for extreme forms of specialisation.

This is because most research is in short projects, technical equipment is typically advanced and relevant literature is otherwise really extensive.

This specialisation increasingly hampers further progress.

My field, theoretical biology, is a specialisation in formal generalisation, linking biological specialisations and linking biology to physics, chemistry and geology.

It uses methodology, mathematics and computer science as tools, focussing on the links between the abstract and real worlds.

These links are complex enough to recognise theoretical biology as a field in itself, which can only flourish in tight interaction with experimental biology.

I think that modern research at an advanced level cannot longer be done by individuals working in isolation, but by groups of specialists of all relevant subdisciplines, coordinated by theoretical biologists.

The involved flow of knowledge requires sufficient overlap of knowledge;

its typical absence forms a practical obstacle, which should be removed.



Mathematical models in biology are typically used for description of data.

When it comes to description, nothing is more efficient than drawing curves by eye.

Sometimes models are used for scenario analysis, but rarely for understanding.

This is a pity, because this use of models can be a powerful tool, which should start from explicit assumptions.

It are the assumptions behind the model that give models their value.

The assumptions can subsequently be replaced to study alternatives.

Structuring the replacement process of assumptions is key to theoretical biology.



After identification of the problem, modern advanced research should start with the formulation of assumptions, from which models are derived and tested.

Enough is known from the literature to start research this way rather then from pattern-spotting experiments, which is still the more typical start of research.

Most models don't need to be tested against experimental data, because they don't pass the testing phase of the first part of the empirical cycle.

After having a model that passed all tests successfully, the next phase should start, which is still rare in biology:

model-inspired experimental research;

experiments that have been set up to answer very specific questions, that fit in a list of explicit consistent assumptions.

Then follows the closure of the cycle with statistics, which deals with the relationship between models and data.

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Over the years I asked myself the question:

Is it possible to `do' biology physical style, so on a formal basis, not accepting exceptions?

If you don't try, you can't know.

With field-biology as my hobby, and having visited remote habitats on all continents, I am aware of the huge biodiversity that exists.

Rather than emphasising the differences between organisms, I asked myself the question what they all have in common in a rather abstract perspective, choosing the organisation of metabolism as central theme.

It is much more than I thought 30 years ago, when I started focused research on this topic.



The resulting Dynamic Energy Budget (DEB) theory is a formal theory for the processes of uptake and use of substrates by organisms;

all organisms, i.e. micro-organisms, animals and plants.

DEB theory is not only biologically but also chemically implicit;

species and compounds only receive names in applications.

The theory consists of a list of coherent and consistent assumptions.

Practical applications require the derivation of specific mathematical models from these assumptions.

Originally I thought that these assumptions could easily be replaced by others in the process of testing the implications against experimental data.

Later it turned out difficult, if not impossible, to replace any of them without creating inconsistencies.

This points to the possible existence of a smaller set of deeper assumptions, from which these assumptions follow.

Many parts of the theory were originally more complex.

As is typical in science, simplicity does not come naturally, but must be acquired with hard work.

The core theory deals with the logic of quantitative aspects of metabolic organisation;

the setup has not been constrained by the necessity to test against experimental data.

It turned out that quantities that play key roles in DEB theory (maturity, reserve(s), structure(s)) cannot be measured directly, only indirectly.

This calls for elaborate auxiliary theory to relate DEB quantities to quantities that can be measured (lengths, weights, composition, performance in various situations).

This auxiliary theory relates sets of different types of measurements to sets of several DEB quantities.



Basic to DEB theory is the coherence between levels of organisation, using the life cycle of an individual as primary focus, from which suband supra-organismic levels are considered.

Space and time scales are tightly coupled methodologically.

Since many species are unicellular, the step to biochemical systems is not always big.

Populations are considered as sets of interacting individuals, ecosystems as sets of interacting populations.

While walking up- and down the time-space-scale, some processes loose their importance, others gain.

The primary motivation in my research on the theory is to answer the question:

how can we deal with the local coherence of levels of metabolic organisation, while avoiding the massive complexity of models with many variables and parameters;

I have never seen useful conclusions coming out of complex models.

Empirical special cases of DEB

year	author	model	year	author	model
1780	Lavoisier	multiple regression of heat against mineral fluxes	1950	Emerson	cube root growth of bacterial colonies
1825	DEB zth	eorv is axiomatic	1951	Huggett & Widdas	foetal growth
1889	Arrhenius Das	egy objime chanism	1951 S	Weibull	survival probability for aging
1891	Huxley <mark>not</mark>	meantotonglue em	pirrica	lemodels	diffusion limitation of uptake
1902	Henri	MichaelisMenten kinetics	1957	Smith	embryonic respiration
1905	BSHATCE	mäinv remointreat m	odels	Leudeking & Piret	microbial product formation
1910	Hill turn	Cooperative binding	1959	s ^{Hollin} DEB the	hyperbolic functional response
1920	Pütter	von Bertalanffy growth of	1962 moc	Marr & Pirt lels support	DEB theory
1927	Pearl	logistic population growth	1973	Droop	reserve (cell quota) dynamics
1928	Ficher & m	akes DEB theory	very v	well tested a	water loss in bird eggs
1932	Kleiber	respiration scales with body weight ^{3/4}	1975	Hungate	digestion
1932	Mayneord	cube root growth of tumours	1977	Beer & Anderson	development of salmonid embryos

Many existing empirical models turn out to be special cases of DEB models, or very good numerical approximations;

the list continued to grow over the years.

Many of them are quite old and together they concern very different aspects of life;

none of the original authors could be aware of the coherence of these empirical models.

This in itself is for me already a most rewarding side-result of DEB theory.

DEB theory reveals how they all follow from simple physical and chemical phenomena;

this helps to understand under what conditions these models will probably not work that well.

Each of these models was created because it described experimental data well.

Using all this evidence, and the results of some 200 man-year of research by the group working on DEB theory, I dare to state that, at present, DEB theory is the best tested quantitative theory in biology.



Defining life is still a challenge, but for me `a dynamic system that has metabolism' works in practice.

Since DEB theory deals with its organisation using physical and chemical principles in a quantitative way, it has many practical applications, ranging from biotechnology to climate change.

Some of them have been worked out in some detail, such a in ecotoxicology, others, such as in medicine, still have to be developed.



The interactions of my group with my esteemed colleage Jean-Christophe Poggiale go back more than a decennium, when we worked in collaboration with Pierre Auger on aggregation methods with support of a NSF-van Gogh grant.

These methods are used for simplification of models on the basis of time-scale separation;

a vital step in work with models in biology.

Two years ago JC invited me as professor to this university, where we gave a series of workshops and supervised two double doctorates;

we interacted in international summer-schools (Sequenza) and in the various DEB tele-courses.

We collaborate in the context of the AQUAdeb group, which receives support from Ifremer, and in the editorial board on a DEB-theme issue of the Transactions of the Royal Society, to be issued next year.

I like to thank him for proposing me for this honourable title of Doctor Honoris Causa at this university.

I look forward to a happy continuation of this productive collaboration.