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ECOCOM 664 No. of Pages 17

ARTICLE IN PRESS

Ecological Complexity xxx (2017) xxx–xxx

Contents lists available at ScienceDirect

Ecological Complexity

journal homepage: www.elsevier.com/locate/ecocom

Original Research Article

Models in stress research

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ARTICLE INFO

Article history:
Received 15 November 2016
Received in revised form 20 June 2017
Accepted 17 July 2017
Available online xxx

Keywords:
Empirical cycle
Dynamic systems
Model criteria
Statistics
Experimental design
Uptake and elimination routes
Compartment and film models
Chemical transformation
Dynamic energy budget theory

ABSTRACT

Mathematical models (should) play a central role in quantitative research, both in the design of experiments and in the analysis of their results. This also holds for research on stress on individual organisms, where stress is defined as an environmentally induced change in their (eco-physiological) behaviour, implying the necessity to know the behaviour in absence of stress in some detail. The individual can effectively be modelled in terms of a dynamical system, where stress shows up as a change in one or more parameters that control the behaviour of the system. After a more detailed presentation of the empirical cycle and an introduction to dynamic systems, I will discuss this approach in the context of generalised ecotoxicity, where presence (e.g. toxicants) or absence (e.g. dioxygen) of particular chemical compounds in the environment might affect a variety of endpoints (feeding, growth, reproduction, maintenance, survival). To this end I will discuss chemical transformation in the environment (speciation, ionisation, degradation, absorption), transport to and from the individual (various uptake and elimination routes, popular transport models), metabolic transformation, effects of nutritional status on kinetics and effects (lethal and sublethal).

1. Introduction

During my first exposure to ecotoxicity research in 1977 at the TNO laboratories in Delft, the Netherlands, I found myself between a group working on toxico-kinetics and one on effects, but they hardly interacted. With my background in theoretical biology, it was directly clear to me that molecules of any compound should first be in the neighbourhood of an individual before they could possibly have an effect. This coupling between toxico-kinetics and effects was the topic of my first paper in ecotoxicity (Kooijman, 1981). My next surprise during that first week of work in ecotoxicity was that people studied effects on the various endpoints (e.g. growth and reproduction) as if they are independent. I directly thought: if growth is reduced by eating less, how can it be that reproduction is not effected? There must be a coupling between effects on the various endpoints. To organise my thoughts on this took me a bit longer (Kooijman and Metz, 1984) and did send me deep down to the fundamentals of ecology and physiology, a life-filling enterprise that I later called the Dynamic Energy Budget (DEB) theory (Kooijman, 2010). It took long for DEB theory to became widely accepted. Apart of being more complex, involving the interaction of quite a few variables, I think that the main reason for this delay is the weak development of abstract thinking in biology. Many published models in biology suffer from dimension problems, illustrating the general lack of critical thinking about models. Even more frequently people seem to think that models are formulas that serve the task of describing data. I think, however, that a pencil does a better job than a model when it comes to describing data and that a formula itself is not really informative. The crucial information is in the assumptions behind a formula that generate it; different sets of assumptions can generate the same formula. I mentioned these two examples, linking toxicokinetics to effects and linking effects on different endpoints, to illustrate that some training in abstract thinking helps to see the broad picture. It affects the way you look at the world and the type of questions that jump into your mind.

A statement that is frequently heard from people with a distaste for models, is: 'a model is not more than you put into it'. If done in the proper way, this is absolutely right and it is the single most important aspect of the use of models. Put into other words: any mathematical statement is either wrong or follows from assumptions. Few people throw mathematics away for this reason. Many biologists think that mathematics is difficult and have problems to understand how you go from one equality sign to another. Yet I think that mathematics is the only discipline that you really can understand (if you start at the beginning) and most frequently used math is actually very simple. While very good math books exist to help dealing with its technicalities, both elementary and advanced, the issue is in abstract (formalised) thinking behind the symbols which needs frequent practising and cannot start too early in ontogeny, like many other skills in life.

http://dx.doi.org/10.1016/j.ecocom.2017.07.006
1476-945X/

Please cite this article in press as: S.A.L.M. Kooijman, Models in stress research, Ecol. Complex. (2017), http://dx.doi.org/10.1016/j.ecocom.2017.07.006

Knowing the chess rules do not make you a good chess player. Although training in abstract thinking is essential, it is not enough. The real challenge, as I see it, is not in mathematical derivations as such, but in stepping from the real world into the abstract one, and back again. These two crucial steps are not part of mathematics and require knowledge both on (parts of) the real as well as the abstract world. Linking abstract and real worlds is a discipline in itself. Happy enough, good books on this topic presently exist (van den Berg, 2011; Doucet and Sloep, 2011).

To make this point as explicit as possible, I first discuss the empirical cycle as I see it, and then the concept of dynamic systems as intro's to various aspects of understanding stress in individuals.

2. Empirical cycle

This paper discusses the empirical cycle in some detail, since experience learns that it is at the heart of a lot of misunderstandings, or at least disagreements, about the role of models in research and requirements that should be imposed on models to let them have this role: the empirical cycle is essentially about the interplay between the real and the abstract worlds to improve our understanding of the real world. Some empiricists do not seem to realise that measurements need interpretation before conclusions can be obtained from data, and, whether you like it or not, these interpretations involve models, even if not formalised. Given that the use of models in unavoidable, it is best to deal with them explicitly, to remain in control of the (otherwise implicit) assumptions. Few models in the literature are, however, derived from assumptions; they are simply posed, or even just coded. Such models are less suitable for application in the empirical cycle. The most important aspect of modeling, as I see it, is to make all assumptions explicit. If modeling procedures are followed in a sloppy way, by adapting models to fit data directly, it is likely that the conclusions from data will be sloppy too; one easily falls in the trap of curve-fitting in the sense of data description without helping understanding. If such a model fails one of the tests, nothing is left and one should start again from scratch. There cannot be a sequence of stepwise improvements in understanding and prediction. The fact that such a model fits data is of little use, perhaps only for interpolation purposes.

Models are idealizations and, therefore, always ‘false’ in the strict sense of the word. This limits the applicability of the principle of *falsification*. A model can fit data for the wrong reasons, which means that the principle of *verification* is even more limited in applicability. This points to the criterion usefulness to judge models, but *usefulness* is linked to a purpose. This is why a model should never be separated from its purpose. The purpose can contain elements such as increase in understanding, or in predictability. Increase in understanding can turn a useful model into a less useful one.

If a model passes all tests, including those against experimental data, there is no reason to change the assumptions, and work with them until new evidence forces reconsideration. It might seem counter intuitive, but models that fail the test against experimental data more directly serve their task in leading to greater insight, i.e. in guiding to the assumptions that require reconsideration. This obviously only works well if the steps of the formulation of assumptions have been adequate. Models are a mean in getting more insight, never an aim in themselves.

The next subsections highlight some steps in the two-segment empirical cycle, following the boxes in Fig. 1. Table 1 gives some practical hints.

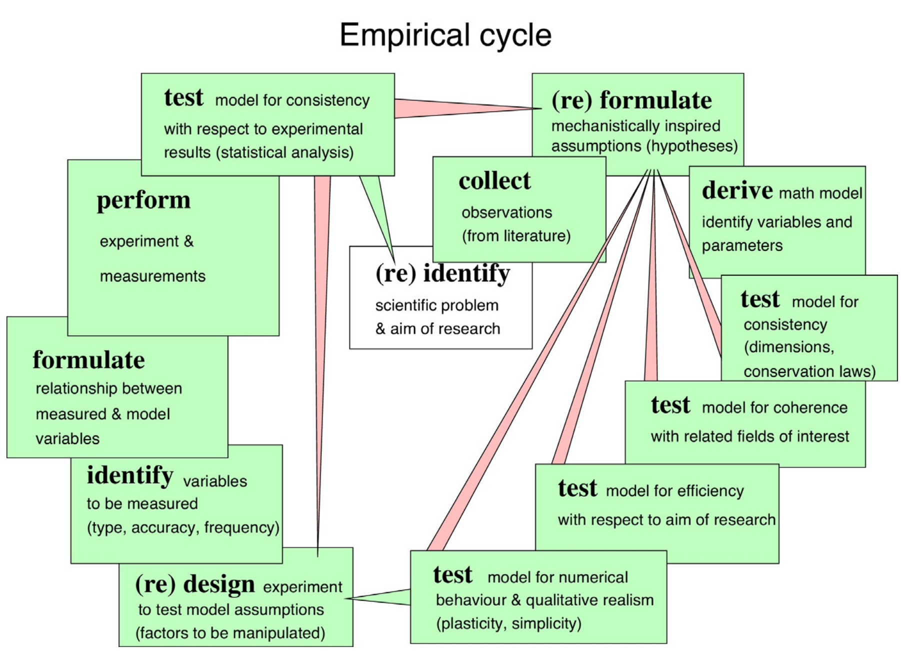

Fig. 1. The empirical cycle in the eyes of a theoretician starts with the formulation of the problem, using published work as source of inspiration for assembling a list of assumptions: the red arrows are followed in case of a bad result, the green ones otherwise. While experimentation is here only in one box, this does not mean that it is relatively little amount of work, but its significance fully rests on the rest of the cycle. The role of statistics is confined to the last step in the cycle. Many models don’t need to be tested against data, since they already should have failed earlier tests in the cycle. More than half of the models that are published in the biological literature suffer from dimension errors and are, therefore, useless; some 80% of the manuscripts that I reviewed that were submitted for publication by journals also suffer from this. Given that nonsense models can easily fit data very well if they are sufficiently flexible, fitting data well is not the most important criterion for useful models. If the step from assumptions to the specification of the model is sufficiently lucid, a bad fit should lead to the assumptions that need replacement. Since the assumptions reflect insight, this can be seen as a step-up and, perhaps, the most useful role of models that are derived from assumptions. Such models are rare, however. (For interpretation of the references to color in this figure legend, the reader is referred to the web version of the article.)

Please cite this article in press as: S.A.L.M. Kooijman, Models in stress research, Ecol. Complex. (2017), http://dx.doi.org/10.1016/j.ecocom.2017.07.006