Some philosophical remarks on the use of complex modelling in biology

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Introduction

The philosophy of modelling or does the philosophy of biology have *any* use?

Steven Hecht Orzack*

"To many scientists, the phrase 'the philosophy of modelling' generates a feeling akin to that experienced when anticipating a visit to the dentist. At best, it is boring. More likely, it is painful."

Outline

1. Historical remarks on the difficulties of mathematical modelling in biology
2. Choosing modelling strategies: desiderata and trade-off
3. Are simulations experiments?

1. Historical remarks

- For a long time and in many scientific domains, mathematical modelling has been used as a powerful way to gain knowledge about natural systems.
- It can lead to theoretical and general principles.
- However, this use of modelling has been resisted by many biologists until recently (and still now).

Historical remarks

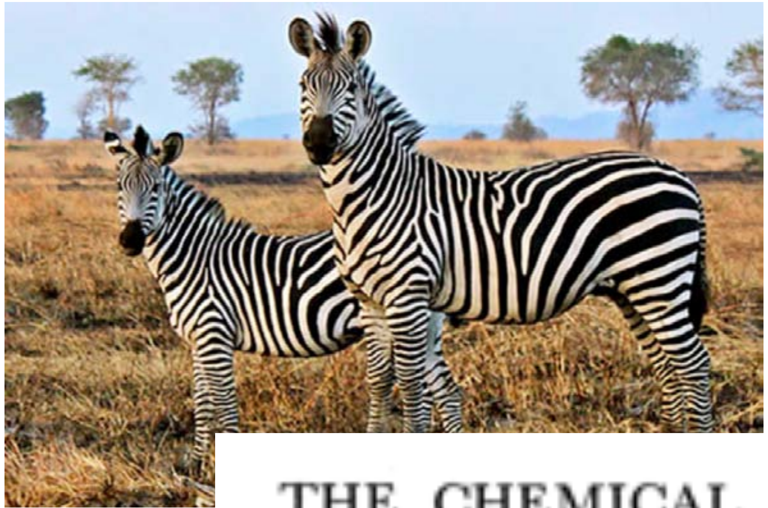
- Underlying question:

  when does a mathematical model provide a satisfactory explanation of a complex phenomenon? When can it be useful?

- Of course, no simple and general answer can be given. But it is interesting to reflect on the different views that are found in the scientific community.

- Why do we see so much scepticism in biology?

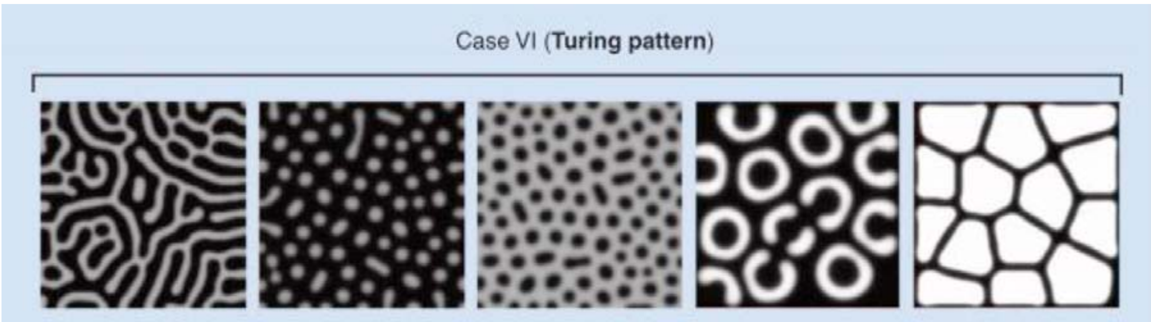
An historical example: Turing's model of morphogenesis



THE CHEMICAL BASIS OF MORPHOGENESIS

By A. M. TURING, F.R.S. *University of Manchester*

(*Received* 9 *November* 1951—*Revised* 15 *March* 1952)



Biologists' scepticism

- "Many theoreticians sought to explain how periodic patterns could be organized across entire large structures. While the math and models are beautiful, none of this theory has been borne out by the discoveries of the last twenty years. The mathematicians never envisioned that modular genetic switches held the key to pattern formation, or that the periodic patterns we see are actually the composition of numerous individual elements". (Sean B Carroll, *Endless Forms Most Beautiful*)
- For many biologists, such models are mathematically elegant but biologically irrelevant.

Several reasons behind this disinterest

- A difference in scientific culture between physicists and biologists.
  - They have different views about what counts as a good model or explanation, what are the more fruitful modelling strategies, etc.
  - Those biologists misunderstood the goal of models such as Turing's

In this section a mathematical model of the growing embryo will be described. This model will be a simplification and an idealization, and consequently a falsification. It is to be hoped that the features retained for discussion are those of greatest importance in the present state of knowledge.

This account of the problem omits many features, e.g. electrical properties and the internal structure of the cell. But even so it is a problem of formidable mathematical complexity. One cannot at present hope to make any progress with the understanding of such systems except in very simplified cases. The interdependence of the chemical and mechanical

Several reasons behind this disinterest

- Too much simplification:

  "Traditionally, most biologists have been hostile to the goals and methods of 'theoretical biology'. Skepticism seems to flow from the attention that theoreticians often give to models obviously and blatantly simplified to the point that nothing stands out about them other than their falsity and even absurdity." (Griesemer 2003, 185)

Several reasons behind this disinterest

- Lack of links with experimental biology
  - Not based on experimental knowledge
  - Not useful for experimentalists

”It is futile to conjure up in the imagination a system of differential equations for the purpose of accounting for facts which are not only very complex, but largely unknown. . . . It is said that if one asks the right question of Nature, she will always give you an answer, but if your question is not sufficiently specific, you can scarcely expect her to waste her time on you . . . what we require at the present time is **more measurement and less theory**." (Eric Ponder (Director of the Cold Spring Harbor Institute from 1936 to 1941), in his response to Nicolas Rashevsky (1934))

Question

- Theoretical models were more easily accepted in ecology and evolutionary biology.
- Why?

- Because experimental approaches are more difficult to develop?
- Because more generality is expected?

2. Choosing modelling strategies: desiderata and trade-offs

- Questions:
  - What are the explanatory virtues of different modelling strategies?
  - How do explanatory desiderata influence modelling choices?
  - What are the trade-offs between these desiderata?
  - What are the most fruitful ways to represent and analyze complex systems?
  - When is simplicity and generality to be preferred?

Choosing modelling strategies: desiderata and trade-off

We see sometimes in biology a tension between two tendencies:

1. Towards complex models

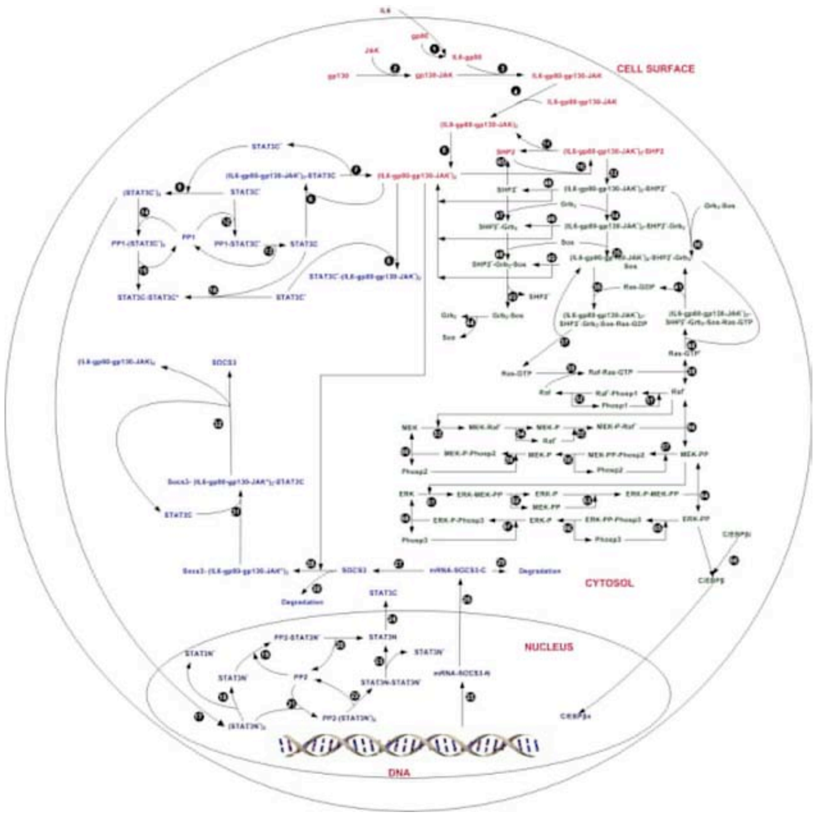
   Complex systems must be explained by complex models

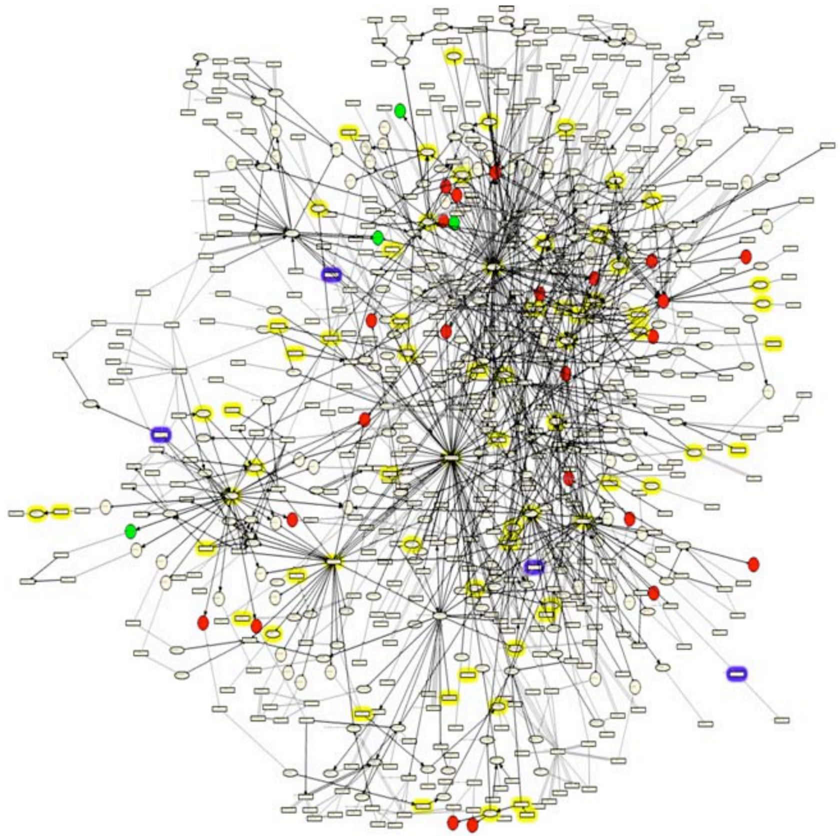
2. Search for simplicity

   Only simplicity can bring understanding and generality

The case of systems biology

- In the post-genomic age, molecular models are becoming increasingly complex.





The case of systems biology

- Some scientists aim for virtual cells, built in a B-U fashion based on biochemistry.
- But if models tend to become as complex as the systems what is the explanatory gain to be expected?

  "the objective of modeling is not to replace a complex cell with a marvelously complex model. Having reduced things to the molecular level, what does this tell us in terms useful to mere humans, about how cells work?" (Bhalla 2003, 52)

The case of systems biology

- General and abstract principles are needed. They provide understanding.
- But interestingly, many models identifying general principles of organization are partly based on detailed and data-driven modelling strategies.
- Very different from systems approaches from the 60s and 70s that rejected reductionism and that were not interested in mechanistic details.
- The belief of many systems biologists is that generality can be found through complex and detailed modelling.

What about ecology and evolution?

Example of the study of speciation:

- Gavrilets complained about the fact that a large number of modelling studies have not resulted in much theoretical progress. Others talk about “the ‘‘balkanization’’ of the theory of speciation and the absence of clear and general results”.
- “I believe the current situation stems primarily from the limitations of the methods used in theoretical speciation research. Most modeling papers on speciation use numerical simulations as the basic tool. The most general feature of simulation models is that their results are very specific. Interpretation of numerical simulations, the interpolation of their results for other parameter values, and making generalizations based on simulations are notoriously difficult.” (Gavrilets, 2003)

What about ecology and evolution?

“What is missing in the theoretical speciation research are general and transparent analytical results comparable to those in other areas of theoretical population genetics and ecology. It is simple mathematical models allowing for analytical investigation (rather than complex numerical models) that form the basis of most scientific theories, and there are no reasons why evolutionary biology, in general, and speciation research, in particular, should be an exception.” (Gavrilets, 2003)

What about ecology and evolution?

There seems to be a trade-off between the level of detail/the complexity of a model and its generality

What about ecology and evolution?

Do simple models lead to generality in ecology?

Matthew R. Evans[1*], Volker Grimm[2*], Karin Johst[2], Tarja Knuuttila[3], Rogier de Langhe[4], Catherine M. Lessells[5], Martina Merz[6], Maureen A. O'Malley[7*], Steve H. Orzack[8], Michael Weisberg[9*], Darren J. Wilkinson[10], Olaf Wolkenhauer[11], and Tim G. Benton[12*]

- This article discusses a maxim of ecological modelling: to achieve general insights ecologists should favour simple models.
- Distinction between strategic and tactical models (Holling; May).
- In this framework, “simple means general means good” and complex models have been interpreted as being of little use when attempting to obtain general insights.

Does simplicity necessary lead to generality? Maybe not!

Evans et al. argument:

- “In many cases, simple models require higher levels of idealisation than do complex models and, thus, are more likely to be biologically unrealistic. As a result, simple models may lead to theory that cannot apply to any real biological system”.
- “there is usually a trade-off between simplicity and generality, such that simpler models are, all other things being equal, less general than are complex models.”
- Simulations and computational analyzes (simulation experiments) must be used to identify general principles.

Questions

- How desirable is generality in scientific modelling?

  It is not clear that many general principles are to be found in biology. More idiosyncrasy than in physics.

- Does the increase in model complexity always hinder theoretical understanding?
- To what extent is intelligibility and understanding important?

3. Simulations as experiments?

- Computer simulations play several central roles in most scientific domains.
- One of these functions is to offer a substitute for experiment. They are often described as numerical or *in silico* experiments.
- Questions:
  - Is it legitimate to consider them as a kind of experiment?
  - In what sense can simulations be a substitute to experiments?
  - What are the differences with empirical experiments?

Simulations as experiments?

- Intuitively there is a clear difference:
  - Information produced by experiment is about the natural system
  - Information produced by simulation is about the model
- Hence experiment is epistemically superior. We can learn more about the system through experiment.
- But is it that simple?

Simulations as experiments?

One argument against this distinction

- Very often, in both cases the system that is manipulated is different from the target system (the system of interest).
- The experimental system or the model stand in for the target system.
- "the object being manipulated or observed speaks for more than itself, and it takes an argument that it can validly do so" (Winsberg 2009)
- Thus it is not obvious that there is a clear sense in which the experimentalist is studying nature directly whereas the simulationist is studying only a model.

Simulations as experiments?

- Simulation is not necessarily epistemically inferior to experiment. But scientists must have enough of a toolkit of trustworthy model building principles. These principles can be used to justify using the model to stand in for the target.

- However, such principles depend on a long history of observations and experiments. In that sense, experiments are epistemologically prior to simulations.

Philosophical conclusion

It's time to have a beer!