# Theory in Biology

# Theoretical embryology: a route to extinction?

# Peter Lawrence

Mathematics is the art of the perfect, physics the art of the optimal and biology the art of the satisfactory Sydney Brenner

Once upon a time, about thirty years ago, there were two species of developmental biologists. The first of these were the experimentalists. These had been around for more than a hundred years and had descended from predecessors such as Boveri, Morgan and Spemann. In attempting to understand the awesome complexity and reliability of development, they developed explanations verging on vitalism. They built concepts such as epigenesis (the hypothesis that development is essentially a process of elaboration from a simpler start), regulation (the notion that embryos are often able to correct damage done to them either by the environment or by the experimentalists) and fields (the idea that specific domains of embryos are to some extent self organising). These concepts were rather abstract and took little account of either cells or genes. Their experiments, which consisted mainly of transplanting or excising parts of embryos, were published in journals such as Journal of Experimental Zoology and Developmental Biology, and they built their careers as scientists always have. As ever, their fields of investigation evolved through a process of natural selection that was fuelled by fashion.

"Biologists... often have a plodding and somewhat cautious attitude"

But, around 30 years ago, there was also a growing number of theoretical embryologists, a more recently evolved species, and these usually came from a physics or mathematical background. Perversely, they denied themselves the pleasure of studying embryos and instead took a mix of equations and simulation and tried to model developmental processes. They published their results in special journals such as the Journal of Theoretical Biology. They needed the experimentalists largely to describe phenomena for analysis. But the experimentalists didn't need the theoreticians and usually ignored them, mostly because they could not understand their maths, or their language. The theoreticians were powered by the conviction that they were cleverer than the biologists (they were) and that thinking and argument and analysis alone can solve biological problems (they cannot).

## "Physicists are all too apt to concoct theoretical models that are too neat, too powerful and too clean. To produce a really good biological theory one must try to see through the clutter produced by evolution to the basic mechanisms lying beneath .... What seems to physicists to be a hopelessly complex process may have been what nature found simplest, because nature could only build on what was already there."

"Elegance and a deep simplicity, often expressed in an abstract mathematical form, are useful guides in physics, but in biology such intellectual tools can be very misleading. For this reason a theorist in biology has to receive much more guidance from the experimental evidence...."

In that period, in 1974, there was a meeting organised by Christopher Zeeman to bring the two species together in the UK. It was attended by the great French topologist, René Thom. The meeting was set up so that the two species could interact, something they usually failed to do; the biologists gave their talks with pictures, and the theoreticians Interest in quantitative and theoretical approaches to biology would seem to be on the increase, as evidenced for example by new institutes starting up that will focus on 'systems biology', and the increasing number of theoretical papers in high-profile biology journals.

#### In the light of these developments, we have invited authors likely to express a variety of views on these developments to write essays addressing the general issue of what theory can and cannot do for biology. This piece by Peter Lawrence is the first in what will be an occasional series. See also the editorial in our September 16 issue "Biophysics and the place of theory in biology" (Current Biology *13*, R719-R720).

Readers with any responses to these essays that they feel may be of general interest are welcome to send in a letter for possible publication in our correspondence section, in which case email the editor at: cbiol@current-biology.com

theirs with equations. I was there and I don't think we understood each other much. At the end of the meeting there was a question and answer session, and one of the few people who could speak both languages (Graeme Mitchison) mischievously asked Professor Thom how he valued experiments. There was a very long pause, and then he pronounced "Un experrimen eez a questionne, eef you ask a seely questionne you will get a seely answerrr!"

## "René Thom was a good mathematician.. but I suspected any biological idea he might have would probably be wrong."

The meeting then disbanded and it was followed by the gradual disappearance and nearextinction of those theoreticians who had attempted to model developmental processes. In relatively few years some of their journals died out and their impact on biology faded — they were killed off partly by the sheer unpredictability and illogicality of biological mechanism. And also because molecular biology as well as genetics gave the experimentalists new and powerful tools to solve problems. For example, one could spend years making mathematical models of how to form the stripes of a segmentation gene in the embryo of *Drosophila*, but one experimental result on the gene itself could destroy all of them.

### "The job of theorists, especially in biology, is to suggest new experiments."

Amongst the theoreticians there was a subspecies who interacted with experimentalists — these theorists tried to make sure that their ideas were testable and that someone tested them. Preeminent amongst these was Francis Crick who wrote all the quotes above shown in red italics (taken from Crick's autobiographical book *What Mad Pursuit: A Personal View of Scientific Discovery*; Basic Books, New York, 1990).

It is remarkable that almost an entire species of scientist can arise and die out in such a short period, but it has happened before - fashion influences young people too much when they choose their careers so that, at any time and in any one field, there are either too many, or too few scientists. Of course there are still theoreticians working in developmental biology, but they are few in number. So few that I think we need more, but only if they learn the lessons enumerated by Crick otherwise they will follow their predecessors into oblivion. Indeed just now there seems to be a new wave of theorists arriving, and most are recruits from physics, mathematics and computing. I hope they won't mind me warning them that they would be wise not to try to answer the problems of animal development with their heads alone. They must use their hands as well.

MRC Laboratory of Molecular Biology, Hills Road, Cambridge CB2 2QH, UK. E-mail: pal@mrc-Imb.cam.ac.uk

# **Arbour lights**

Alongside more traditional seasonal lights, the Wellcome Trust in London has sponsored a roadside installation in trees opposite its headquarters building. The feature, by Deborah Aschheim, has been instigated by the trust's curator of contemporary initiatives, Denna Jones. Aschheim is interested in how ideas from biology, our understanding of health and disease, have become cultural mythology for our rational, secular age.

The installation of lights and bright red cables represents a peripheral human nervous or arterial system, and it is hoped it will provide a festive and uplifting show. The local council are also backing the project. "We are delighted to be working with the Wellcome Trust to bring this stunning piece of public art to one of London's best connected roads," says Peter Bishop, director of the environmental department at the London Borough of Camden. And many thousands should see it: both drivers in the heavy traffic along the road and the many pedestrian commuters who pass each day from one of London's busiest rail termini close by.

The Wellcome Trust is committed to support selected artworks inspired by, or reflecting on, current science and medicine.

Also showing at the Trusts's gallery at 210 Euston Road, is the exhibition Pharmakon, a one-woman show by Beverly Fishman, of abstract paintings inspired by the cultural power of prescription pills and medicines.



Net effect: A seasonal installation in trees opposite the headquarters of the Wellcome Trust in London (right). Photograph: the Wellcome Trust.