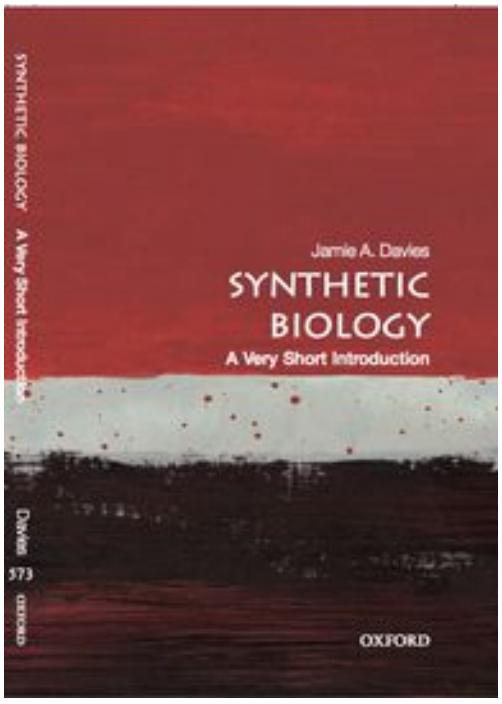
D'Arcy and the philosophers.

About a year ago, I was invited to speak at a conference, which has just taken place, organized by Alan Love of the Minnesota Center for Philosophy of Science. It was on the conceptual legacy of the book *On Growth and Form*, published 101 years ago by D'Arcy Thompson. This book polarizes people: to some, it is one of the most important scientific works to come out of these islands, part of a trinity with *Principia Mathematica* and *The Origin of Species*; to others it is a mildly diverting historical curio irrelevant to the progress of science. I read JT Bonner's abridged version of the work as an undergraduate, and I was fascinated by it: Thompson got much wrong, but I felt he got it wrong for very interesting reasons. I also felt, and still feel, that there was more to be learned from following the thoughts of someone who asked big questions and tackled them in original ways, even when he turned out to be wrong, than there was from following the plodding progress of the many researchers who asked only small questions and got correct, but dull, answers. I know that many of my colleagues would view that last sentence as a clear indication that I do not belong in science at all, but that kind of controversy is why the conference promised to be so interesting. Fortunately for me, attending did not involve a long flight because, as D'Arcy Thompson was based at St Andrews University, the conference took place there.

The delegates invited to the small conference were a varied bunch of people drawn mainly from from philosophy but with people from physics, biology and classics there too. About eight were invited to give talks while others were invited to join in the discussions, for which there was as much time reserved as for the talks themselves.

The energy of the exchanges of views was such that discussions carried on far beyond the time-tabled day, and serving staff at the evening dinners were looking variously confused or intrigued by the intense debates going on up and down the tables: the above image, captured by Alan, is typical and includes about four separate conversations, all on aspects of philosophy of science, taking place during, and apparently taking precedence over, dinner.

Most of the presentations were inspired by the aspect of Thomson's work that makes the book so famous: he was one of the first people to apply mathematical and physical reasoning to biological form. It was he, for example, who noticed the geometrical rules followed by growing spiral shells, or the way that bones follow 'mathematical engineering' rules for structural strength and stability. It was also he who showed that if one draws, say, a fish on graph paper and then applies a mathematical distortion to the paper, mimicking different growth, approximate shapes of other fish result (some time ago I wrote a simple java program, for use by undergraduates, to demonstrate this idea via a web browser – see links). Surrounded by people who knew far more about



these aspects than I, I was not going to try to talk about these themes. I wanted, instead, to explore a quite different aspect of D'Arcy Thompson's agenda, and his place in the history of synthetic biology. This was something I had not known about until relatively recently; I came across it while writing the historical introductory chapter of a book, to be published next month, *Synthetic Biology: A Very Short Introduction*. Synthetic biology is often represented as a 'new science' but it really is not. The existence of Stéphane Leduc's 1912 work *La Biologie Synthétique* is clear evidence of that. The book is cited several times in *On Growth and Form* and it is clear that, in some of his chapters, Thompson was following an important agenda set up by pioneers of synthetic biology half a century earlier. So what was that agenda, and what became of it?

To understand the rise of the first era of synthetic biology, it is necessary to consider one of the greatest controversies of nineteenth-century science, a controversy that remains unresolved but

seems to have been set aside by most practical scientists of our own era. The question was whether life emerged completely from the materials and laws of the non-living world, or whether some metaphysical 'vital spark', 'animating principle' or '*élan vitale*' was necessary. The position taken was (and still is) more a matter of faith than science: the vitalists could point to some strong evidence in support of their ideas, but nothing that would prove them. Examples of such evidence included subtle experiments, such as the then-recent work of Pasteur in showing that broth left alone would not spontaneously produce bacteria and fungi, but that if spores of these were added they would grow in it well. The point was, of course, that the broth contained all the non-living ingredients necessary for making living things, but that the appearance of life depended on life already being there. The evidence for vitalism also included commonplace observations: in a dead fly, the 'fly stuff' is all there, but it will not come to life again, arguing that something critical, a vital spark, was missing.

The materialists had less evidence, but strong hope. They had seen Wöhler make a 'biological' molecule, urea, from inorganic precursors, which showed that there was nothing special about the chemistry of life, and they already had a substantial body of analytical work on bodies that made them seem complicated, but still understandable in terms of physics and chemistry. They also knew that there was, in principle, a powerful way to prove the vitalists wrong: if someone could take non-living starting chemicals and make a living thing with them, then no vital spark was needed. Obviously, making a whole living cell would be a tall order, so the researchers began by creating chemical simulacra of aspects of living organisms (I don't want to use the word 'analogue' or 'homologue' because my choice between these would imply more knowledge than the researchers had at that time). Moritz Traube, in the 1860s, pioneered this with his Traube cells – hollow crystals that grew into tubes and allowed him to discover and study osmosis. Several researchers built on this work and, in 1912, Leduc summarized what they had done and added his own very intricate advances. Importantly, he set out an important justification for his science "*when a phenomenon has been observed in a living organism, and one believes that one understands its physical mechanism, one should be able to reproduce this phenomenon on its own, outside the living organism*".

D'Arcy Thompson cited this body of work (a body of work that was little known even amongst the company in that room), but did not add to it directly by inventing more physical biomimetic systems. Instead, he presented analogies between forms determined by purely physical means and

the forms of specific living organisms. One example, drawn from many in his book, is the similarity between the 'crown' splash shape made, fleetingly, when a drop of fluid falls into a container of more of the fluid, and the crown shapes of cnidarins (jelly-fish). This linked the idea of making synthetic versions of living phenomena, to problems of anatomy and embryology. There was a lot of discussion, throughout the meeting, about exactly what Thompson was claiming with his analogies. Was he just saying (as I came to the meeting assuming) "look, what seem to be very complex shapes in the physical world can have very simple origins, so what seem to be very complicated shapes in the biological world may also have simple underlying explanations: don't be scared to study them" or was he really proposing that the same processes were used to shape both the physical and biological entities? Two other biologist speakers, Celeste Nelson (Princeton) and Amy Shyer (Rockefeller), the work of both of whom I have followed with great interest for years, argued not only for the latter, but also argued that in some cases the same mechanisms really might be at work even though the time-scales are different. My brief presentation of the way that some work in current-era synthetic biology draws on Thompson provoked interesting suggestions for experiments from many people present (including the philosophers).

Beyond the specific 'Thompsonian' themes (and there were many more, including his views of evolution, and the links between his work as a zoologist and as a classicist), others came up that were grounded more on our own time. One was the difficulty faced in our own time by people trying to publish physical studies of embryonic development in an era when 'explanation' and 'genetic explanation' seem to some to be treated almost as synonyms., and work at any level other than molecular is undervalued. There were also themes about the role of analogy in biology, and how 'liberating' or how 'trapping' it can be of thought. There was also much discussion about the uses and value of modelling, inspired by a beautiful presentation of current-era work by Lisa Manning (Syracuse). Most particularly, there was much discussion about the relationship – tension even – between 'how could it work?' speculative research and 'how does it work?' analysis. None of these themes can be dealt with in a short blog, but there will probably be a joint work emerging from the conference, where they will be explored at greater length.

My own experience of the conference gave me one more surprise: usually, in scientific conferences, people may mention my data and experimental papers in the context of their talks, but never anything I write in books. Here, I was surprised to see sentences from my books quoted on other people's slides, those of philosophers especially. One graduate student, in particular, remembered

what I had written in far more detail than I did (which was a bit embarrassing!). I am really not used to wrods mattering, as scientists tend to express other people's ideas in our own words (with appropriate citation of the source of the idea, of course) rather than quoting the words themselves. It was gratifying, but a little odd, to realize that my may be more interesting to philosophers of science, whom I never had in mind when writing them, than they seem to be to dyed-in-the-wool experimentalists, for whom I thought I was writing.

Another interesting observation was that we scientists at the meeting had all read *On Growth and Form*, most of us in the formative years of our scientific careers, yet when Alan asked us to come he did not actually ask us whether we had read the book. He invited us on the basis of the science we do. Given that *On Growth and Form* is not widely read by biology students, and was read even less in the closing decades of the twentieth century than it is now thanks to the centenary, one is forced to wonder whether our early and atypical exposure to that book was one of the reasons that we take the approaches to science that we do. Thos of us at the meeting all do different things, to be sure, but one thing we have in common is that we view genetics as one of many interesting systems of life, not as some special, privileged level that is somehow 'above' the others. That may be due to our being influenced (/ corrupted!) by the largely gene-free Thompson.

As well as involving presentations and discussion, the conference included a visit to the University Archives, where an archivist had laid out collections of D'Arcy Thompson's notes and letters, so that we could see the evolution of the book over the years when most of the world was distracted by the first world war. It was a fascinating display, and quite apart from illustrating the specifics of this

work, it showed how some aspects of writing have not changed at all through the years, and others have been altered hugely by the IT revolution.

I am so grateful to Alan for organizing this conference and inviting me, and to his University and its donors for funding it. With its mix of people from many different fields, and its long and well chaired discussions, it really was one of the most stimulating meetings I have ever attended.

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Edinburgh

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Photo credits: Alan Love.

Links

On Growth and Form: https://www.amazon.co.uk/Growth-Form-Complete-Revised-Biology/dp/0486671356/ref=sr_1_2?ie=UTF8&qid=1529328484&sr=8-2&keywords=on+growth+and+form

(The 1917 edition is also available on the web, free).

The fish program - http://golgi.ana.ed.ac.uk/coursenotes/cto2/CTOWebPractical/darcyfish.html

(NB – this only works on a browser that will run Java. Many no longer do).

My own small book: https://global.oup.com/academic/product/synthetic-biology-a-very-short-introduction-9780198803492?q=synthetic%20biology&lang=en&cc=gb