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#### Competing interests statement

The author declares no competing financial interests.

#### DATABASES

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## SERIES ON HISTORICAL PROFILES — TIMELINE

# D'Arcy Thompson and the theory of transformations

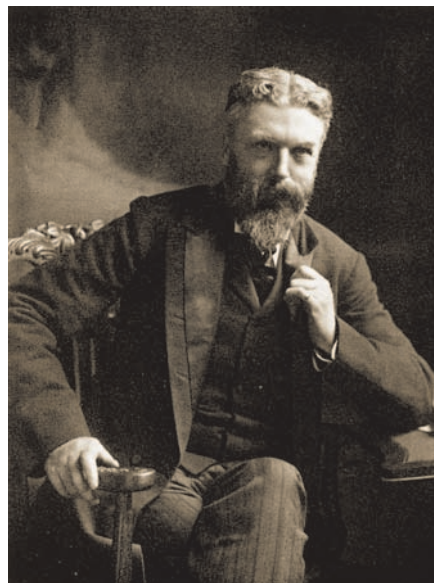
Wallace Arthur

**Abstract** | D'Arcy Thompson was a biologist, a mathematician and a classicist. His writing was great literature as well as great science. He is primarily known for a single book — *On Growth and Form* — and indeed for a single chapter within it, on his 'theory of transformations', which shows how the differences between the forms of related species can be represented geometrically. This theory cries out for causal explanation, which is something the great man eschewed. Perhaps the time is close when comparative developmental genetics will be able to provide such an explanation.

Evolutionary and developmental biology parted company from each other around 1900 and remained largely separate for about three-quarters of the twentieth century. They only began to reintegrate in the late 1970s and early 1980s, eventually producing the interdisciplinary endeavour that we now know as evolutionary developmental biology or 'evo-devo'<sup>1–6</sup>. The two main catalysts of reintegration were a series of books, most notably Stephen Jay Gould's *Ontogeny and Phylogeny* in 1977 (REF. 7), and the advances in developmental genetics that were made possible by the discovery of the homeobox in the early 1980s (REFS 8,9). In the period between 1900 and 1975, only a few lone voices had intermittently reminded biologists that the two great processes of biological creation — evolution and development — were deeply intertwined. D'Arcy Thompson (1860–1948) was one of them<sup>10</sup> (FIG. 1). Others included the neo-Darwinians Huxley<sup>11</sup> and de Beer<sup>12</sup>, the mutationist Goldschmid<sup>13</sup>, and the hard-to-classify Waddington<sup>14</sup>.

D'Arcy Thompson was unique; no one before him had attempted the kind of geometrical approach to development and evolution that he did. His entirely

novel theory of transformations has, for nearly a century, been an inspiration to biologists who are interested in how development and morphology evolve. The esteem in which D'Arcy Thompson is held by those who are interested in furthering the reintegration of theories of evolution



and development can be gauged from the dedication at the front of Gould's *Ontogeny and Phylogeny*: "To the philomorphs of Cambridge, the world, and beyond, where D'Arcy Thompson must lie in the bosom of Abraham."<sup>7</sup>

For those unfamiliar with the theory of transformations, here is a brief overview. You take either the outline of an entire animal or plant, or the outline of one of its component parts such as a bone or a leaf, and draw this against the background of a Cartesian grid (for example, ordinary graph paper). Then you submit the grid to some systematic mathematical transformation, such as stretching it in one dimension or distorting it so that its squares become rhombuses. You inspect the transformed outline of the animal that you drew faithfully on the original grid, and in many cases note that, far from being just a weird shape, the transformed outline corresponds closely to the shape of another related animal. Clearly, this intriguing finding is telling us something about how evolution works — but what? This is the key question.

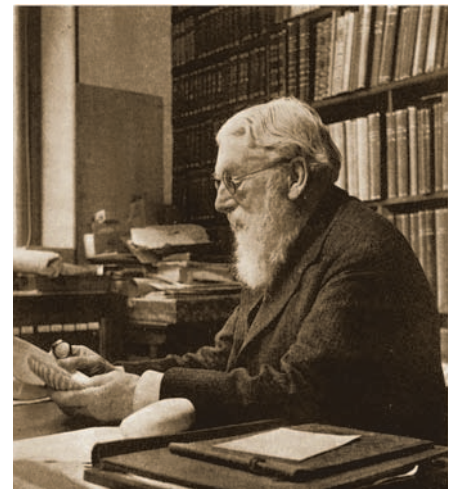
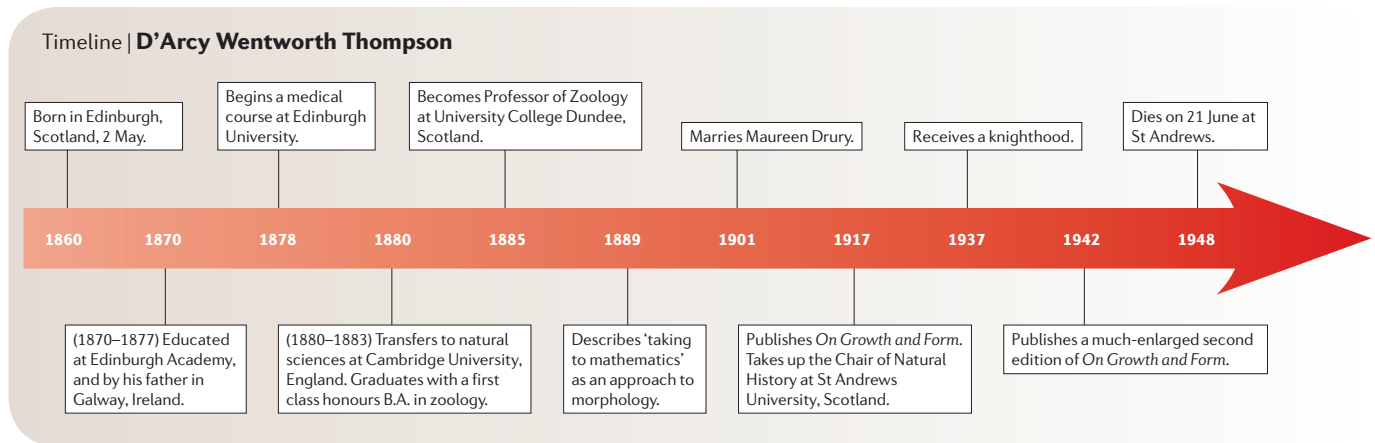


Figure 1 | D'Arcy Thompson in the early 1900s and in the 1940s. Reproduced with permission from REF. 15 © (1958) Oxford University Press.



The above account might give the impression that D'Arcy Thompson's approach was more 'blue sky' than it actually was. He did not try out countless transformations from the starting point of any particular animal and look at which of them produced the form of a related animal. Rather, he took two (or more) related forms, and tried to determine whether one could be produced from the other by some simple transformation. The forms he compared were typically from the same family or order; he did not believe that his approach was appropriate for higher-level taxonomic comparisons. His transformations suggest coordinated rather than piecemeal changes to development in the course of evolution, an issue which almost completely disappeared from view in the era of the 'modern synthesis' of evolutionary theory, but which is of central importance again in the era of evo-devo.

Here I take a brief look at D'Arcy Thompson's life, his general philosophy, and his approach to studying morphological evolution. I then examine the limitations and problems of his theory of transformations. This examination leads into an investigation of how modern comparative developmental genetics might be able to tackle the outstanding problem of the molecular causality of morphological transformations. I end with a short discussion of large-scale evolutionary changes to which the theory of transformations does not apply.

### A brief biography

This is a story of five places — three in Scotland, one in England and one in Ireland. D'Arcy Thompson was born in Edinburgh in 1860. His father was also called D'Arcy — indeed the names of both men were D'Arcy Wentworth Thompson. His mother, née Fanny Gamgee, died about a week after his birth. When D'Arcy junior was 3 years

old, his father was appointed to the Chair of Greek at Queen's College Galway, now the National University of Ireland, Galway. As a child, D'Arcy spent some of his time with his father in Galway (his first visit being in 1867), but most in the home of his grandfather, Joseph Gamgee, who practised as a veterinary surgeon in Edinburgh. He acquired a love of classics from the former, a love of science from the latter.

D'Arcy was educated at Edinburgh Academy, and subsequently began to study medicine at Edinburgh University. However, he later switched to reading science at Cambridge University, graduating with a B.A. in zoology in 1883, and spending a further year at Cambridge working as a demonstrator. In 1884, he was appointed to a professorship at University College Dundee, and in 1917 he took up the Chair of Natural History at the University of St Andrews. He produced some 300 publications, including his *magnum opus*, *On Growth and Form*<sup>10</sup>, first published in 1917, with a second edition in 1942, and with many abridged editions since. (His other publications were diverse; many of them derived from his long sea voyages as a member of various government commissions concerning fisheries.) D'Arcy Thompson died at St Andrews in 1948, at the age of 88. For further information on his life, see the **TIMELINE**; for a detailed biography, see the book written by his daughter Ruth<sup>15</sup>.

### D'Arcy Thompson's philosophy

The philosophy that pervades *On Growth and Form*, and indeed D'Arcy Thompson's publications in general, is the explanation of natural phenomena in terms of physical, and especially mathematical, laws. His mathematical approach was unusual among biologists then; and it is still a minority approach in the present day: compare, for example, the

relative frequency of papers that deal with the molecular details of developmental gene interactions and those that deal with their quantitative dynamics.

Most of *On Growth and Form* deals with the shapes of various parts of organisms: from cells and tissues to spicules, shells, horns, teeth and bones. In each case, D'Arcy Thompson attempts succinct mathematical descriptions, with their elegance and efficiency surpassing those of what he saw as 'mere words'. For example, in his chapter on spirals, he notes that the typical molluscan shell corresponds to the equiangular spiral, in which the breadth of a whorl increases as the spiral proceeds, as opposed to the spiral of Archimedes, in which it does not. This distinction connects with the broader one of isometric versus allometric (proportionate and disproportionate, respectively) growth<sup>11</sup>, which has had an important role in many subsequent studies of both evolution and development.

This mathematical philosophy was D'Arcy Thompson's major strength and weakness. His theory of transformations would have been impossible without it. But he allowed this philosophy to dominate his approach to the problems of evolution and development to the extent that he sometimes seemed to 'set little store' by genetic or biochemical approaches. In his introduction he makes the following point: "...in dealing with the facts of embryology or the phenomena of inheritance, the common language of the books seems to deal too much with the material elements concerned."<sup>10</sup> And he goes on to explain that in his view biologists should place less emphasis on matter (such as a piece of embryonic tissue) and more on the forces that shape it.

We have now reached a stage in the elaboration of biological knowledge at which we can try to knit the two approaches together. A gene is indeed a material thing. But its pattern of expression during development

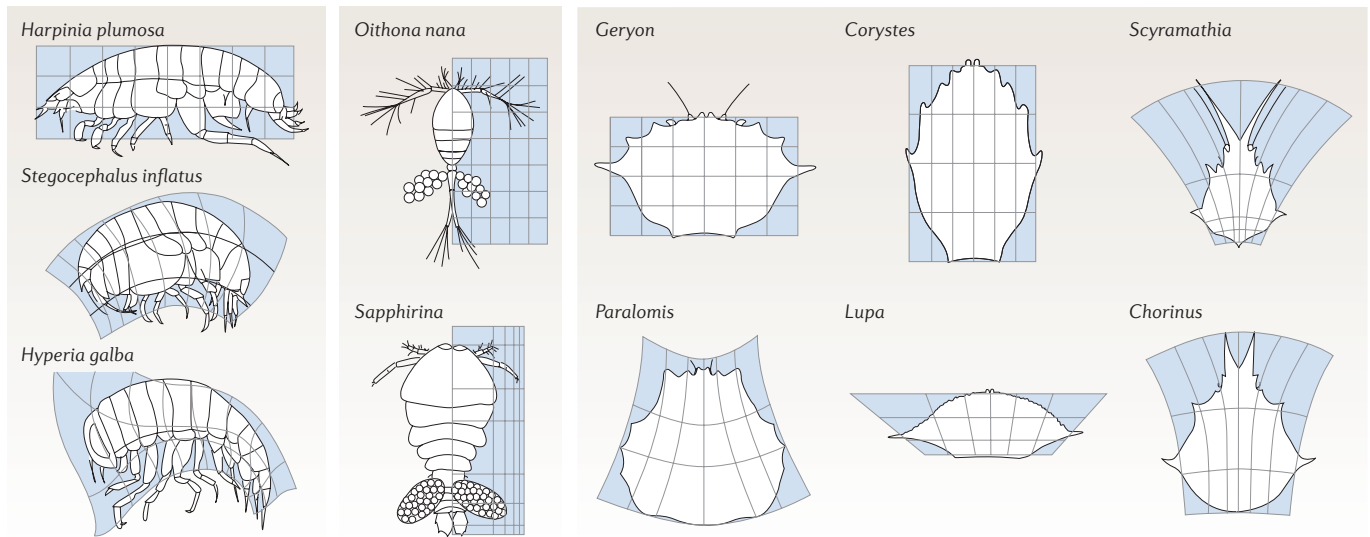


Figure 2 | Transformations that are used to relate different crustaceans to each other. Some of the transformations required are simple, as in the case of the copepods *Oithona* and *Sapphirina*; others are more complex, as in the case of the three amphipod genera *Harpinia*, *Stegocephalus* and *Hyperia*. Reproduced with permission from REF. 10 © (1917) Cambridge University Press.

is dynamic. And the forces that cause this dynamism include such things as transcription factors and morphogens, which are themselves material things. Old barriers are breaking down. There is no need to see biochemical and biomathematical approaches as antagonistic.

But the specific question of most interest is: can our modern developmental genetic approach to understanding how organisms grow and form themselves, and how evolution modifies this process, give us a significant causal insight into D'Arcy Thompson's transformations? This is the question to which we will turn, after first examining some problems in D'Arcy's theory, which help to point the way forward.

#### Limitations and problems of the theory

Some examples of particular transformations are given in FIGS 2,3. It can be seen that, in each case, a particular distortion of the initial Cartesian grid on which the outline of one body form was plotted leads to the appearance of another. Often, the different forms are related at about the level of the genus or family — give or take a taxonomic level. That is, the method works reasonably well for species, genera, families and orders. It works less well for intraspecific variation, which is typically rather minor. It also works less well for differences at very high taxonomic levels, such as those between classes and phyla, where there are often qualitative, as well as quantitative, differences in form. This in itself poses an interesting evolutionary question — one that I discuss in a later section.

**Phylogeny.** Working as he was in the early twentieth century, D'Arcy Thompson was well within the era of evolutionary trees (a generalized one of which is, famously, the only picture in the whole of Darwin's *Origin of Species*<sup>16</sup>). But he was working well before the rigorous treatment of such trees that began with the advent of phylogenetic systematics in the mid-twentieth century<sup>17</sup>. This limitation shows in the fact that he was usually content to note that the morphologies of a group of related genera could be derived from each other by appropriate transformations, and he was not terribly concerned with mapping the genera to a phylogeny so that it became apparent which way round the transformations had taken place (FIG. 4).

**Direct versus indirect development.** It is interesting that D'Arcy Thompson generally used, as examples, direct rather than indirect developers. He used many crustaceans as examples (FIG. 2), but no insects. Likewise, in the vertebrates, he used many fish (FIG. 3), but no amphibians. This is a limitation of the theory (so far anyway), but not a problem — indeed it was a wise strategy to limit his examples in this way. It is difficult enough to understand how a directly developing system evolves in quantitative terms, without adding the complexities of metamorphosis.

**Morphology of sub-adult stages.** The main deficiency of the theory of transformations, from a genetic or developmental point of view, is that no causal mechanism was proposed for their occurrence.

Of course, we cannot blame D'Arcy Thompson for a failure to incorporate ideas about transcription factors into his theory, as they were then unknown. Nor can we blame him, at least in the first edition of *On Growth and Form*, for omitting the embryological ideas of gradients, fields and morphogens, as these also awaited articulation<sup>18–20</sup>. But there is one thing that we can and perhaps should blame him for — a neglect of juvenile morphologies.

Notice that all the forms shown in FIGS 2–4 are those of adults. This is generally true of the other transformations pictured in the relevant chapter of *On Growth and Form*, which are not reproduced here. This concentration on adults is strange, given two facts. First, it must have been as obvious to D'Arcy Thompson as it is to biologists today that there is no way evolution can turn one sort of adult form into another except by modifying the course of development. Second, many of the chapters leading up to the one on transformations, such as the one on spirals mentioned above, did explicitly deal with both adult and juvenile morphology. It is as if the developmental and evolutionary parts of the book were disconnected from each other.

That is probably too harsh a criticism. In the pre-computer age, there was a limit to the dimensionality of a problem that could reasonably be dealt with. A series of growth stages of a species of gastropod constituted a tractable problem. So did the relationships between the adult forms of several kinds of fish. But putting together the

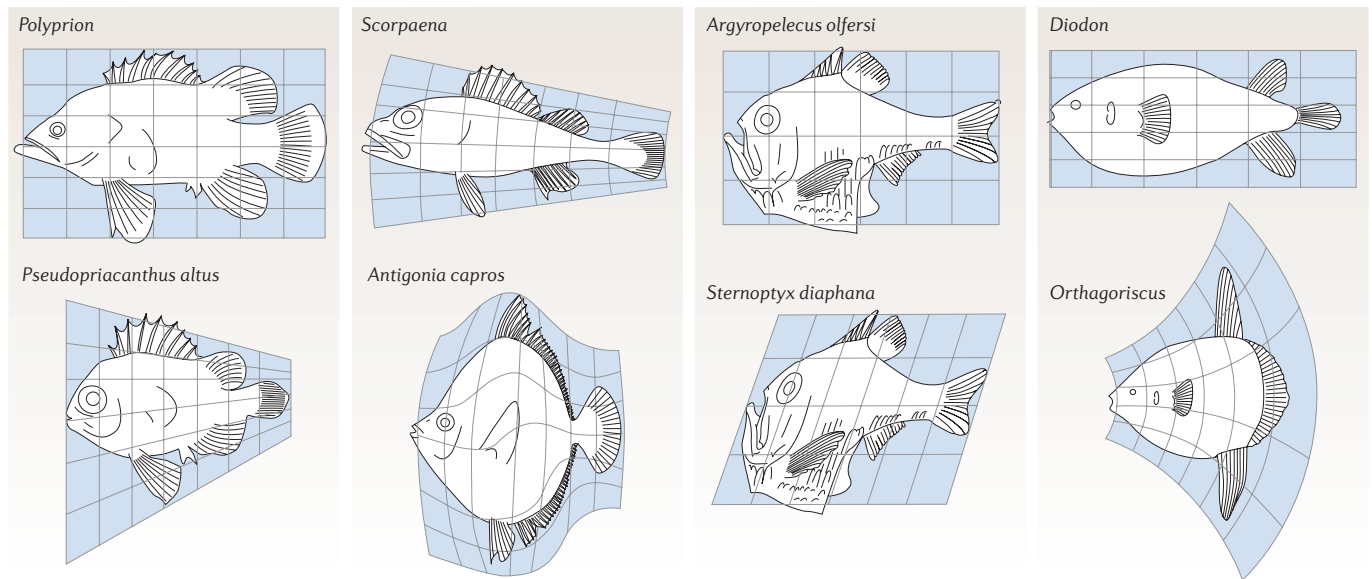


Figure 3 | **Transformations that are used to relate different fish to each other.** Again, some of the transformations are more complex than others. The simplest transformation is the ‘shear’ required to produce the form of *Sternoptyx diaphana* from that of *Argyropelecus olfersi*. Reproduced with permission from REF. 10 © (1917) Cambridge University Press.

evolutionary and developmental problems, especially in relation to the two-dimensional and three-dimensional morphologies that D’Arcy Thompson focused on (in contrast to univariate measures like body length), was, at the time, a step too far.

**Partial transformations.** One final difficulty with the theory of transformations deserves a brief mention. Not all intergenus morphological differences within a family are readily explicable in terms of a single, simple transformation. Often some part or other does not ‘fit’, unless, as well as the whole-body transformation, some other, more spatially limited transformation is applied — for example to the head. The need for such applications is reminiscent, perhaps, of attempts to save Ptolemy’s earth-centred solar-system model by introducing ‘epicycles’ into originally smooth orbits. Although the comparable conclusion — that the model was fundamentally flawed — would be inappropriate in relation to transformations, this line of thinking does lead to another interesting, and so-far unanswered, question: what proportion of interspecies comparisons (at the level of the genus, family or order) can be treated in terms of transformations, whether whole and/or partial, and what proportion cannot?

**Investigating causality**

Ideally, we would like to be able to understand, in molecular terms, the ways in which developmental processes are evolutionarily

modified to produce morphological transformations. However, achieving such an understanding is not straightforward — if it were, given the array of techniques now at our disposal, the relevant research would already have been carried out.

The main problem lies in the fact that an approach to analysing the mechanistic basis of transformations is a multi-step process, with the results of step 1 determining what should be done at step 2, and so on. The suggestions that follow must be considered in that light. At each step, I assume a particular outcome and proceed accordingly. This is a necessary restriction, for otherwise my account would have to deal with all of a large series of bifurcating possibilities and would therefore become far too long for a paper of this kind.

**Choosing a system.** The first task is to select an appropriate system, and, in doing so, to maximize the range of molecular techniques that could be used, while also putting the whole endeavour in the strongest possible phylogenetic context. These points argue for using two (or more) species in a well-established clade for which molecular and morphological phylogenies agree, and for which the species concerned preferably have well-characterized genomes. Already, these requirements severely limit our options. A genus or family level comparison where one of the species being compared is a ‘model organism’ (from a genetic perspective) would be best. Possibilities therefore include

humans, mice, chicks and zebrafish, but preferably not frogs or fruitflies (indirect developers), or nematodes (minimalist morphology).

There are already two problems. First, in most cases there is not a species that is clearly related to our starting-point species by a transformation and is equally well known genomically. A system that comes particularly close is the human–chimpanzee one (FIG. 4). However, ethical considerations preclude much of the desired work on embryos in this case. For this reason, and also because of the greater visibility of embryos, a system that is centred on the zebrafish would be a better choice. Second, the relevant molecular methods can only be used on living species (notwithstanding our ability to extract DNA from some fossil material), but transformations occur between ancestor and descendant, not between extant ‘cousins’. So we should use a system in which information on appropriate outgroups indicates that one of our two species has changed little since their lineages diverged, and the other much more so. In such cases, the comparison of the two extant forms might act as a surrogate for the comparison of ancestor with descendant that we would really like to make.

**When does development diverge?** Assuming that we can find an appropriate pair of species, the next step is to identify the stage in development during which a transformation can first be seen. This involves plotting

outline morphologies for a series of stages, not just the adult, as was D'Arcy Thompson's usual practice. Such a multiple-plot comparison identifies the point at or before which one or both ontogenies have been modified in a way that causes them to be relatable by a transformation. As well as simple graphical plots, it is now possible to look at shapes in terms of landmark features<sup>21</sup>, a method that has been profitably used in relation to the mouse mandible<sup>22</sup>. However, a drawback with this method for use in tracing transformations back in developmental time is that at early stages some landmarks will not yet have formed.

Again, we must assume an outcome in order to proceed to the next step. Looking at the transformations of FIGS 2–4, and all the others that D'Arcy Thompson revealed, it seems likely that the crucial evolutionary changes occur at a stage in development that is after the key early formative stages of gastrulation and neurulation, after the highly conserved phylotypic stage<sup>23</sup> (or phylotypic period<sup>24</sup>) and probably also after organogenesis, but early in the subsequent growth phase. If this is true, then in cellular terms transformations are probably caused by changes in the rates, durations and directions of cell proliferation, and not by changes in patterns of cell movement, or, for that matter, by changes in cell size or shape, although neither of these can be ruled out as contributory factors.

So, the developmental origins of transformations probably lie in the period in between the early stages that are typically studied by molecular developmental geneticists and the much later stages that are typically studied, with different methodologies, by quantitative geneticists. This in itself poses something of a challenge, but one that

we can rise to, in the knowledge that studies of these intermediate stages might ultimately help to unite these two currently rather disparate fields of genetics.

#### *Cells and genes: a four-way comparison.*

The best strategy now would be to make a four-way comparison. The four embryos/juveniles to be compared would be 'stage X' in each of our two species (pre-transformation) and 'stage Y' in each species (post-transformation). Confirmation of the causality residing in patterns of cell proliferation could be achieved using a standard technique for examining such patterns (for example, labelling with 5-bromo-uracil).

Assuming a positive result here, the next stage in our causal analysis of the transformation would be to investigate what causes the altered cell-proliferation patterns. One obvious candidate, given the spatial and temporal scale involved, is the interaction between hormones or growth factors and their receptors. Because these agents are relatively well known, in a wide range of species, they can be investigated with several established molecular techniques, both observational (for example, *in situ* hybridizations to look at the expression patterns of the genes involved, such as those that make receptors) and experimental (for example, alteration of hormone concentration patterns or signalling mechanisms). A particularly interesting example of the latter involved the manipulation of insulin signalling in the *Drosophila* wing, resulting in an enlarged anterior, but not posterior, compartment — in effect a transformation, although a rather abrupt one<sup>25</sup>.

Future studies of this and other kinds will hopefully reveal, in many systems, spatial patterns at the molecular level in

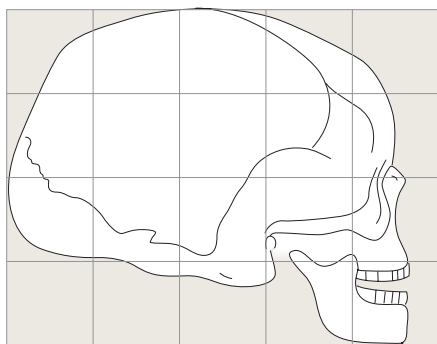
embryos that are the cause of the transformations D'Arcy Thompson observed at the morphological level in adults. But, as ever in development, there is the problem of potentially infinite regress (to the egg), in the sense that an altered spatial distribution of a hormone receptor at stage Y (for example) is itself caused by something else upstream of it. And so, our search would continue.

#### **The origin of new body plans**

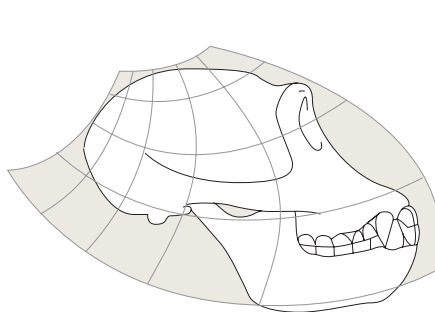
What of comparisons between distantly related taxa, such as chordates and echinoderms, where transformations do not 'work' at all? Here we come face to face with that age-old problem in evolutionary biology of whether those few phylogenetically deep lineage splits that resulted in radically different body plans were in some way different to most 'routine' evolutionary changes<sup>26</sup>. In other words: is mega-evolution<sup>27</sup> fundamentally different from microevolution? Or, conversely, is evolution really 'scale-independent'<sup>28</sup>?

D'Arcy Thompson seemed to take the former view — that there is a fundamental difference — when he said: "Our geometrical analogies weigh heavily against Darwin's conception of endless small continuous variations; they help to show that discontinuous variations are a natural thing, that 'mutations' — or sudden changes, greater or less — are bound to have taken place, and new 'types' to have arisen now and then."<sup>10</sup> I think he was right, although we should all admit that this is still an unresolved issue. But in any event, we should be careful to distinguish between D'Arcy Thompson's view, which put the discontinuity between the two types of evolutionary change at a high taxonomic level, and Richard

Human skull



Chimpanzee skull



Baboon skull

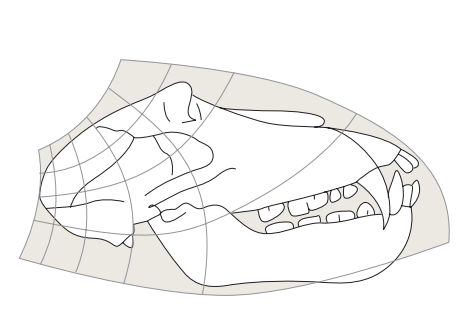


Figure 4 | **Transformations that are used to relate human, chimpanzee and baboon skulls.** Note that the starting point chosen, the modern human skull, does not represent the evolutionary starting point, which would be the last common ancestor of the three species. There

are two reasons for this non-correspondence: imperfect knowledge of the relevant ancestor; and D'Arcy Thompson's generally non-phylogenetic approach. Reproduced with permission from REF. 10 © (1917) Cambridge University Press.

Goldschmidt's view<sup>13</sup>, which put it at a much lower level — between intraspecific and interspecific evolutionary changes. Using Simpson's terminology of micro, macro and mega-evolution<sup>27</sup>, with brackets to denote similarity of mechanism, we can see that D'Arcy Thompson's view can be represented as (micro, macro) versus mega; whereas Goldschmidt's can be represented as micro versus (macro, mega).

**Prospect**

Despite the inspiration that D'Arcy Thompson's theory of transformations has provided, it has given rise to little in the way of experimentation to reveal the causal nature of the transformations. Why? Until recently, say the past 20 years, it could be argued that our knowledge of comparative developmental biology, and especially of comparative developmental genetics, was not sufficiently advanced to be up to the job. But that is hardly still the case now, some 20 years after the discovery of the homeobox, and with evo–devo being well established.

All the tools are now in place to examine the mechanistic basis of transformations. Not only do we have phylogenetic systematics and evo–devo, but, so obvious that it is easy to forget, we have computers, and especially, in this context, advanced computer graphics. (It seems almost incredible that D'Arcy Thompson achieved what he did without this modern aid to morphology, working in an era in which the forms of animals were all individually hand-drawn.)

We owe it to the great man to put these three things together to investigate the mechanisms that produce the morphological changes that he captured so elegantly with little more than sheets of graph paper and, of course, a brilliant mind.

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**Competing interests statement**

The author declares no competing financial interests.

**FURTHER INFORMATION**

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**ERRATUM**

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