

## REVIEW

# The old and new faces of morphology: the legacy of D’Arcy Thompson’s ‘theory of transformations’ and ‘laws of growth’

Arhat Abzhanov<sup>1,2,\*</sup>**ABSTRACT**

In 1917, the publication of *On Growth and Form* by D’Arcy Wentworth Thompson challenged both mathematicians and naturalists to think about biological shapes and diversity as more than a confusion of chaotic forms generated at random, but rather as geometric shapes that could be described by principles of physics and mathematics. Thompson’s work was based on the ideas of Galileo and Goethe on morphology and of Russell on functionalism, but he was first to postulate that physical forces and internal growth parameters regulate biological forms and could be revealed via geometric transformations in morphological space. Such precise mathematical structure suggested a unifying generative process, as reflected in the title of the book. To Thompson it was growth that could explain the generation of any particular biological form, and changes in ontogeny, rather than natural selection, could then explain the diversity of biological shapes. Whereas adaptationism, widely accepted in evolutionary biology, gives primacy to extrinsic factors in producing morphological variation, Thompson’s ‘laws of growth’ provide intrinsic directives and constraints for the generation of individual shapes, helping to explain the ‘profusion of forms, colours, and other modifications’ observed in the living world.

**KEY WORDS:** D’Arcy Thompson, Growth and form, Theory of transformations, Laws of growth, Evolution, Morphology, Morphometrics

## Before Thompson: Goethe’s science on natural forms ‘complete but never finished’

*‘The beautiful is a manifestation of secret laws of nature, which but for this phenomenon would have remained hidden from us for ever.’*

Johann von Goethe (Bielschowsky, 1905)

There is a bewildering diversity of life on our planet, as it comes in a huge variety of shapes and sizes ranging from bacteria to mollusks, sea urchins, insects and birds. Multicellular organisms, both animals and plants, have generated a remarkable panoply of biological forms featuring bodies with segments, legs, tentacles, wings and heads. Cataloguing, describing and explaining this vast multiplicity of species, both living and extinct, have been some of the main challenges for biological sciences in the past and remain so today. In particular, we still have an incomplete understanding of how particular biological forms are generated during development, and how they change over evolutionary time. These questions were a particular preoccupation of D’Arcy Wentworth Thompson (Fig. 1A) in his book *On Growth and Form* (Thompson, 1917a),

which celebrates its 100th anniversary this year. In this Review, I discuss some of the book’s key ideas in a historical perspective, in particular geometric transformations of biological shapes and the ‘laws of growth’ underpinning biological diversity, and consider the significance of these concepts to the modern developmental genetics and evolutionary biology fields.

The first attempts to describe the appearance of animals and plants, mostly for taxonomic reasons, started thousands of years ago. Works by Aristotle and colleagues in classical times laid the foundations of the science of morphology (morphé, meaning ‘form’, and lógos, meaning ‘study’). This field of biology is interested in overall appearance, both external (size, shape, colour and pattern) and internal (anatomical features of inner organs). The main formal principles for studying morphology were first formulated by Johann Wolfgang von Goethe (1749–1832), a German naturalist and prolific writer, renowned for both his scientific and literary works. The main themes for Goethe and his followers have been to qualitatively and quantitatively describe external and internal features of complex organisms in an attempt to exploit their taxonomic significance and to find their deeper biological meaning. Today, studies of morphology include, but are not limited to, exploring and understanding normal and abnormal variation, evolutionary origins, developmental transitions or biomechanical and other functions. As discussed below, a combination of Goethe’s structuralism and the functionalism of Bertrand Russell provided the true ideological and spiritual foundation for morphometric mathematical work by D’Arcy Thompson, infused by an interest in physical mechanics, as described in *On Growth and Form*.

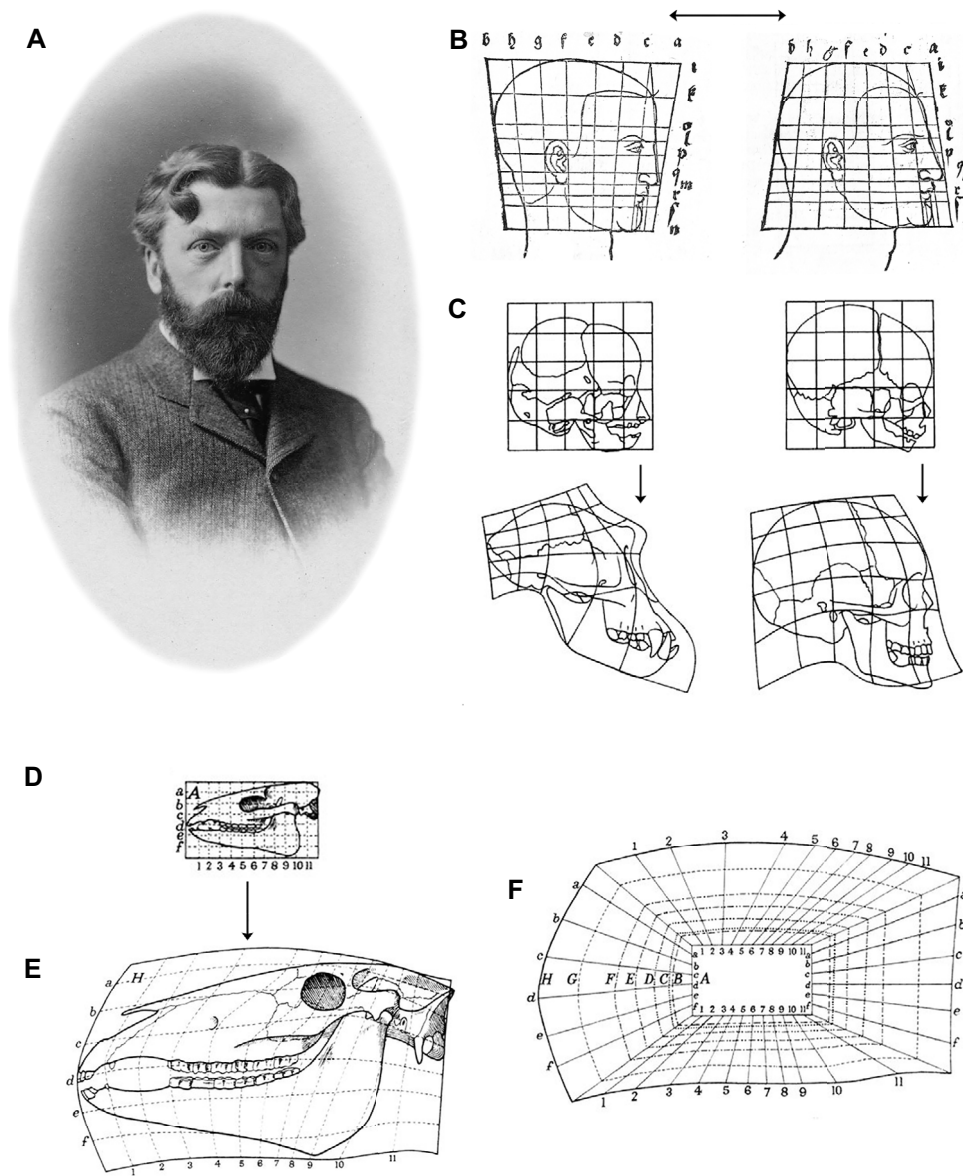
Goethe’s study of morphology was both a benefactor and a beneficiary of the growing interest in taxonomy. However, he also realized the limitations of the Linnaean classification system based on stereotypical assumptions about nature. Goethe wrote that: ‘Nature has no system; she has – she is – life and development from an unknown centre toward an unknowable periphery’ (Goethe, 1823). This is important because his observations led him to believe that nature’s patterns are not fixed – he was detecting and trying to explain all kinds of transitions both between and within organisms. ‘From first to last, the plant is nothing but leaf’, Goethe writes in his *Italian Journey*, implying that by transformations of the leaf shape (expanding or contracting its parts during development), one might expect to understand how unique shapes of other structures of the same plant are generated (Goethe, 1817). He could see such transitions apply across the different plant species as well, and from such transitions Goethe conceptualizes an archetypal plant, or ‘Urpflanze’, an abstract common morphological denominator of all plants seen and possible, either in the past or in the future. This is still many years before the idea of an archetype takes on an evolutionary meaning, specifically referring to ancestral forms. A century before evolutionary theory, Goethe believed that all living organisms changed under the inner physiognomic ‘drive to formation’ or ‘Bildungstrieb’. In his publication titled *First Sketch*

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**Fig. 1. Connecting the growth and form in morphospace.** (A) D'Arcy Wentworth Thompson circa 1906. Courtesy of University of Dundee Archive Services, UK. (B) Geometric transformations of human heads drawn by artist Albrecht Dürer (Dürer, 1528; Fig. 366 from Thompson, 1917a). (C) Thompson's comparative illustrations of chimpanzee (left) and human (right) cranial ontogenetic shape changes (Figs 405 and 406 from Thompson, 1917a). (D,E) Evolution of the horse skull from *Hyracotherium* (Eocene) to the modern horse, represented as a coordinate transformation and to the same scale of magnitude. (F) Diagram of the Cartesian coordinates projecting shape outlines of skulls in the lineage from *Hyracotherium* to the modern horse. A to H indicate progressive changes in morphology through evolution (Figs 401 and 402 from Thompson, 1961).

of a *General Introduction into Comparative Anatomy, Starting from Osteology*, Goethe deliberated an intrinsic law explaining the balancing action of the *Bildungstrieb* in that: ‘nothing can be added to one part without subtracting from another’ (Goethe, 1795).

Goethe's *Urpflanze*, with its capacity for metamorphosis of (plant) organs, along with the later concepts of Richard Owen (1804–1892) on the animal ‘*Bauplan*’ (body plan) and its archetypal and serial ‘homologies’ became crucial to our ability to relate different species and their individual traits to each other (Owen, 1847, 1848). From a static phenomenon worthy of a simple description, morphology became a dynamic process that needs to be considered both in the ontogenetic (developmental) and phylogenetic (evolutionary) temporal dimensions. Based on morphological observations on the anatomy of modern organisms and their embryos, and fossils of related extinct species, the relationship between ontogeny and phylogeny was very evident to the early evolutionary and developmental biologists alike. First proposed as a simple recapitulation, the ontogeny-phylogeny connection turned out to be a much more complex, multilayered

and mutually interdependent phenomenon. Already back in the late 19th century, it was clear that understanding this relationship held great promise for both nascent fields of embryology and Darwinian evolutionary biology, and deserved the most rigorous investigation. Many researchers of morphology were wondering whether a deeper understanding of biological forms could provide important insight into the developmental and phylogenetic principles and processes that generated the morphology of individuals and whole populations. Such was the intellectual environment in the late 19th and early 20th centuries in which D'Arcy Thompson was developing his ideas.

**On ‘transformation of related forms’ and ‘laws of growth’**

*‘Philosophy [nature] is written in that great book which ever is before our eyes... The book is written in mathematical language, and the symbols are triangles, circles and other geometrical figures, without whose help it is impossible to comprehend a single word of it; without which one wanders in vain through a dark labyrinth.’*

Galileo Galilei (*The Assayer*, 1623)

The problem of shape (in the language of mathematics, shape is form without scale) is as profound in biology today as in the time of Goethe but it often receives less attention than it deserves. In the age of advanced genetics, molecular biology and biochemistry, it is even more important that researchers direct their main efforts to explain biological form rather than focus exclusively on the molecules and genes within it. The properties of biological shapes are still far from completely appreciated at any organizational level, and understanding them remains crucial to studies of the underlying biomechanical and structural properties.

One very important aspect of morphology that Thompson liked to ponder was that studying the natural laws and patterns found among living forms could greatly benefit from the aesthetic awareness and appreciation of nature. Thus, scientific observation of nature is intertwined with the aesthetic experience of things orderly and structured. This is important because in the age of Newtonian physics, Galileo's mathematics and Mendeleev's chemistry, governing natural laws and the resulting order were expected, sought and indeed often found in nature. Thus, morphological studies into natural patterns were a way to 'the discovery of an aesthetic truth' provided for by the underlying natural laws (Brady, 1987). Such an ideology was a major inspiration for D'Arcy Thompson's search for the deeper meaning of complexity and diversity of biological forms. Regarding his aspirations, Thompson wrote: 'We want to see how, in some cases at least, the forms of living things, and of the parts of living things, can be explained by physical considerations, and to realize that in general no organic forms exist save for such as are in conformity with physical and mathematical laws' (p. 10, Thompson, 1917a). *On Growth and Form* is a multifarious writing with parts on the structure and form of cells and tissues, chapters on phyllotaxis and shapes of bird eggs and shells of foraminifera. Thompson searched for and found plentiful examples of correlations between biological forms and mechanical phenomena and used them to emphasize the roles of physical laws and mechanics. This is where Thompson's thinking about morphology echoes the 'functionalism' of Bertrand Russell (1872–1970), a British philosopher and mathematician who searched for physical causes of multiple physiological and behavioural phenomena.

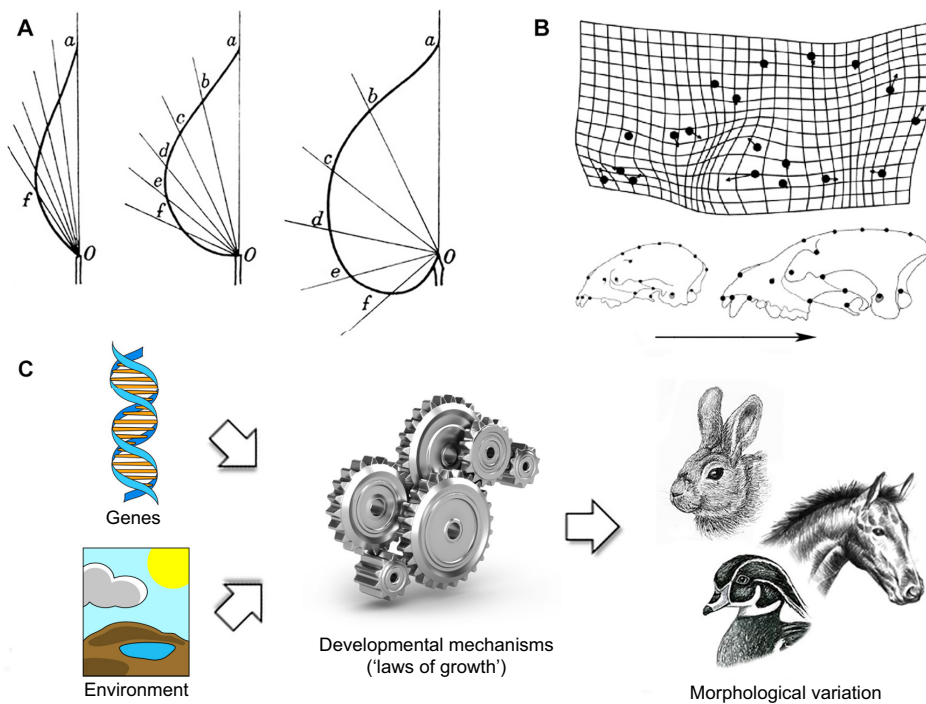
One of the main themes of the book is to argue that the form of any object, including that of the living organism, is a 'diagram of forces' that created and maintained it. Thus, a shape (of an organism, organ or cell) can be seen and studied as an impression of the generative forces that have acted upon it. Such thinking is at the foundation of chemistry, physics, astronomy and other sciences. Modern biology is now moving beyond the notion that observed biological shapes are largely driven by unsystematic processes, such as random mutations and genomic rearrangements, followed by adaptation to rather unpredictable and changing environmental factors. Thompson argued, for example, that shapes of individual cells are produced by surface tension on their membranous walls as if they were bubbles of soap [see Graner and Rivelino (2017) for further discussion of this aspect of Thompson's work]. He discussed the shape of bird eggs in different species (from the spherical owl egg to the pointed guillemot egg) in relation to the process that produces them as they rotate and slowly pass through the oviduct – as described in Thompson's earlier publication in *Nature* titled *On the Shapes of Eggs and the Causes Which Determine Them* (Thompson, 1908). In a series of chapters, Thompson reflected on the role of spiralling forms (in particular the presence of particular types of spirals, such as the equiangular or logarithmic spirals), both in terms of mechanics and construction

under the influence of forces in structures and taxa as varied as the horns of ruminants, claws of birds, and the shells of living and extinct mollusks.

Probably the most famous set of observations in *On Growth and Form* comes from Thompson's attempts to relate biological shapes to each other via geometric transformations. In so doing, he was seeking to find mathematical logic in biological shapes by applying methods developed 400 years earlier by Albrecht Dürer, a German renaissance artist, and described in *De Symetria Partium in Rectis Formis Humanorum Corporum Libri* (Dürer, 1528). To study human proportions, Dürer skilfully used transformations of human heads drawn against a coordinate grid to understand facial variation (Fig. 1B). This was a very powerful way to demonstrate how otherwise disparate shapes can be meaningfully compared. What makes such a method particularly useful for analysing biological shapes is that it allows for continuity, for gradual ontogenetic or phylogenetic transformations of whole organisms and their body parts.

Thompson was not so much interested in capturing a single biological shape as in its relationship with other such shapes. He wrote that: 'Our essential task lies in the comparison of related forms rather than in the precise definition of each; and the deformation of a complicated figure may be a phenomenon easy of comprehension, though the figure itself have to be left unanalysed and undefined' (p. 723, Thompson, 1917a). This statement is important for two reasons. First, the shapes are compared by the method of 'deformation', the point-by-point transformation of one shape into another, which allows for a visual understanding of both objects. When placed on a square grid, such transformation becomes a geometric process that can be described mathematically, both qualitatively and quantitatively (Fig. 1C–F). Second, Thompson compared 'related forms' and insisted on the futility of directly relating shapes of distantly related taxa. Most or all comparisons that Thompson himself made are between individuals of the same species or class of animals or plants. He described his analytic approach: 'This process of comparison, of recognizing in one form the definitive permutation of deformation of another, apart altogether from a precise and adequate understanding of the original type...finds its solution in the elementary use of a certain method of the mathematician. This is the Method of Coordinates, on which is based the Theory of Transformations.' (p. 723, Thompson, 1917a). Comparisons between truly different forms, even if they have similarly named parts, become meaningless as these can no longer be derived from each other either developmentally or evolutionarily. Some species could have features that are missing or have no identifiable counterparts in other species but, in general, related species can be compared. Thompson believed that the very fact that two distinct crustaceans or fishes could relate to each other by a geometric transformation 'will of itself constitute a proof that variation has proceeded on definite and orderly lines, that a comprehensive "law of growth" has pervaded the whole structure in its integrity' (p. 727, Thompson, 1917a). To master evidence, he combined techniques learned from Dürer and Descartes, used proportional drawings of biological forms on a Cartesian grid and subjected them to increasingly complex mathematical transformations.

Mathematical experimentation with biological shapes allowed Thompson to reveal and visualize connections between biological shapes whether during development, such as the growing and maturing skulls of primates or growing plant leaves (Fig. 2A,B), or through evolution (Fig. 1C). One of the most striking (and famous) of Thompson's examples of phylogenetic change in



**Fig. 2. Biological shapes, transformations and the 'laws of growth'.** (A) Geometric shape changes during hyacinth leaf growth, which follows a very specific set of spatial rules, e.g. following particular ratios of radial and tangential growth velocities (Fig. 359 from Thompson, 1917a). (B) Geometric morphometric space describing shape alterations in hyena skulls during development from juvenile to adult (Tanner et al., 2010). (C) The 'laws of growth' interpreted as a broad set of developmental mechanisms translating genetic information and physical forces of the environment into individual biological shapes and contributing to their diversity. Images in C created by Keith Chan; copyright Alexmit ([www.fotosearch.com](http://www.fotosearch.com)); animal images are illustrations from Seton (1898).

shape as a geometric transformation is evolution of the skull shape from an early horse ancestor *Hyracotherium* (which lived in Eocene) to the modern horse *Equus*, represented as a coordinate transformation and to the same scale of magnitude (Fig. 1D-F). The principles and methods he used for this analysis are at the foundation of the modern field of geometric morphometrics (the analysis of 2D and 3D shapes using Cartesian geometric coordinates) (Klingenberg, 2010; Adams et al., 2013). The entire concept of 'morphospace' – mathematical space within which multiple shapes could be placed and compared – was, arguably, invented by Thompson. The diagram of the Cartesian coordinates projecting shape outlines of skulls representing steps in horse evolution onto the same grid (Fig. 1F) allows one to capture and visually demonstrate the continuous and gradual nature of this particular evolutionary story. Later in the 20th century, a more definitive set of approaches was developed, in the form of geometric morphometrics, by paleontologist David Raup and developmental biologist Pere Alberch (Raup, 1961, 1966; Alberch et al., 1979; Oster and Alberch, 1982; Adams et al., 2013). These allowed researchers to address a wide and ever growing range of biological problems from coiling shell shape distributions in extinct gastropods to the developing digits of amphibians and other tetrapods (Oster and Alberch, 1982; Oster et al., 1988; Klingenberg, 2010; Adams et al., 2013).

Using geometric transformations on related organisms, Thompson believed that he was demonstrating that biological forms were, indeed, related and that their shapes were produced by what he called the 'laws of growth'. What are these 'laws' and why might this concept still be important today? Thompson's extensive modelling with biological shapes led him to conclude that the growth of an individual organism can be generalized to all of the individuals within a species, or even a group of related species. Thompson's 'laws of growth' referred to empirically derived and theoretically envisaged principles, which applied to all patterns of biological growth with the resulting shapes molded by development and influenced by the physical environment surrounding the

growing organism (Fig. 2C). Although Thompson never attempted to explicitly explain the ultimate causes for the transformations he so carefully observed, it is clear that he thought every biological shape to be a reflection of the 'diagram of forces' that acted upon it and he believed that these generative forces were largely internal. Thompson wrote: 'The deep-seated rhythms of growth which, as I venture to think, are the chief basis of morphological heredity, bring about similarities of form which endure in the absence of conflicting forces; but a new system of forces, introduced by altered environment and habits, impinging on those particular parts of the fabric which lie within this particular field of force, will assuredly not be long in manifesting itself in notable and inevitable modifications of form' (p. 717, Thompson, 1917a). He was well aware of the science of embryology, its main postulates and advances made by key embryologists of the time, such as Karl Ernst von Baer, Wilhelm Roux and Ernst Haeckel. Embryology (better known as developmental biology today) was already an important scientific field in his day, making a great impact on the minds of biologists and providing clues about the mechanisms generating morphological diversity. However, although the 'laws of growth' were conceptually inspired by these new exciting studies, the exact mechanisms controlling individual development in the early 20th century remained largely unknown. Today, we give a much more mechanistic explanation to Thompson's 'laws of growth', associating them with the entire panoply of developmental processes at all hierarchical levels from gene sequence to cell proliferation, differentiation and signalling, tissue- and organ-level phenomena to full organismal complexity (Fig. 2C).

'I suppose everyone must admit that there are "laws of growth"... but after all one does not feel sure how far this is really admitted', Thompson mused in a letter to a friend (Thompson, 1889). He realized that his 'theory of transformations', despite numerous explained case studies, directly accounted for only a very small fraction of the existing biological diversity. It was also far from clear in Thompson's times how the 'laws of growth' could be related to the Darwinian evolutionary process.

**Pecking for the origins of morphological variation**

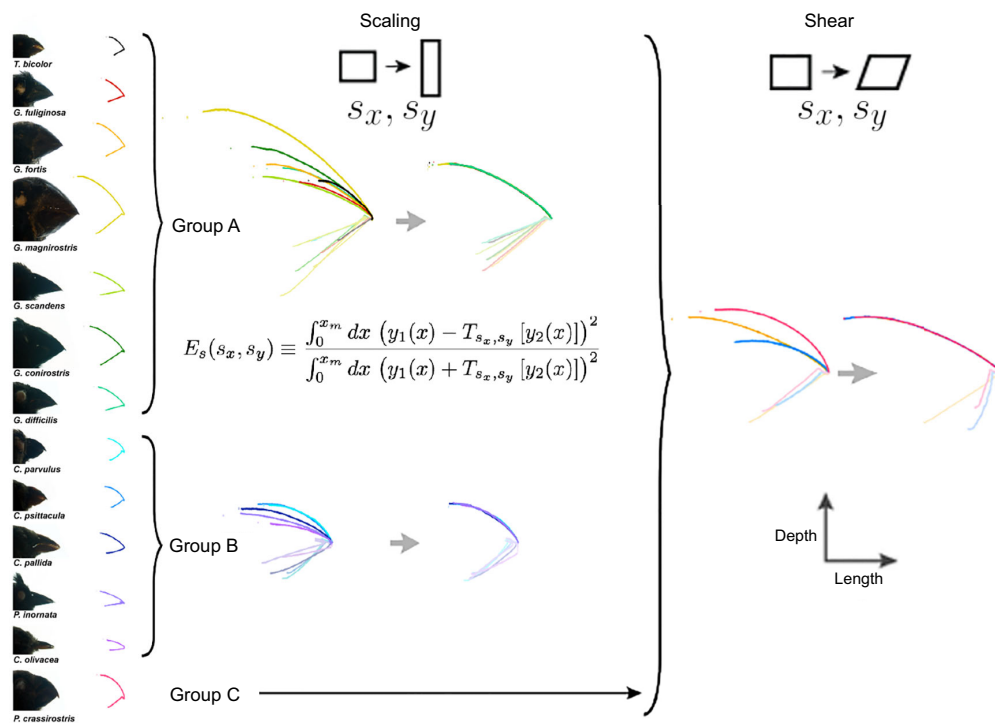
*‘I have stated, that in the thirteen species of ground-finches, a nearly perfect gradation may be traced, from a beak extraordinarily thick, to one so fine, that it may be compared to that of a warbler.’*

Darwin (1839)

Thompson’s work was well ahead of its time in many respects. As already mentioned, it provided a powerful paradigm for the field of geometric morphometrics and it remains the most celebrated attempt to quantify the morphological diversity observed in the natural world (Adams et al., 2004; Arthur, 2006; Slice, 2007; Pappas and Miller, 2013; Polly and Motz, 2017). There have been numerous studies that have successfully applied Thompson’s ideas to a variety of biological forms (e.g. Garnier et al., 2005; Depecker et al., 2006; Bhullar et al., 2012; Drake et al., 2017; Klein and Svoboda, 2017; Fabbri et al., 2017). However, only relatively recently have we begun to connect the ‘theory of transformations’ to phylogenetic studies and developmental genetics and to explain the origins of morphological diversity (Weston, 2003; Larson, 2005; Klingenberg and Zaklan, 2000; Klingenberg, 2010). To be informative, the geometrical transformations related to morphological variation in different species must themselves be related to each other in a way that is meaningful in terms of both phylogeny and the underlying developmental genetics of morphogenesis. Can such connections be shown using modern methods and approaches on specific illustrative case studies? What do they tell us about the role of development in morphological evolution?

A classical textbook example of morphological diversity is Darwin’s finches (Thraupidae), much of whose success can be

attributed to beak shape variation (Darwin, 1845; Lack, 1947; Bowman, 1961; Grant, 1986). These birds inhabit the Galápagos Islands and comprise a monophyletic group of 15–16 closely related species that have been described as case studies on adaptive radiation, niche partitioning, and rapid morphological evolution (Grant and Grant, 2008). In fact, Darwin’s finches occupy ecological niches normally occupied by different families of birds on the mainland, such as warblers, finches, thrushes, grosbeaks and woodpeckers (Grant, 1986). Molecular phylogenies suggest that all members of this group retained and exploited the beak shape that they inherited from the last common ancestor, echoing Charles Darwin, who first speculated that: ‘From an original paucity of birds in this archipelago [Galápagos], one species had been taken and modified for different ends’ (Darwin, 1845). After more than 100 years, morphological and ecological studies have identified key components of bill morphology of Darwin’s finches and established their adaptive significance (Lack, 1947; Bowman, 1961; Grant, 1986, 1999; Herrel et al., 2005; Foster et al., 2008). Recently, their diversity was examined from a different perspective to understand whether there was a mathematical structure underlying divergent bill shapes that can be connected both to their phylogenetic relations and bill developmental genetics (Campàs et al., 2010). Darwin’s finch beaks are known to differ in overall size as well as depth, width and length, so it was hypothesized that bill shapes in these species might differ simply by their scales, and thus it might be possible to superimpose their bill shapes onto a single common shape after normalizing each axis with its corresponding scale. Mathematically, this normalization is equivalent to a scaling transformation, in which each axis is stretched by a constant scaling factor (Fig. 3). When beak shapes of Darwin’s finches were analyzed to determine



**Fig. 3. Geometric relations among the beaks of Darwin’s finches.** (Left) Lateral profiles of beaks of Darwin’s finches. (Centre) Group structure under scaling transformations focusing on the upper beak profile: untransformed shapes and shapes collapsed onto a common shape via scaling transformations. (Right) Collapse of all group shapes onto a common shape via a composition of shear and scaling transformations suggesting a two-tier morphological variation (adapted from Campàs et al., 2010).

whether they are related by a scaling transformation, species clustered according to the similarity of their collapsed profiles (Campàs et al., 2010).

The geometric analysis clearly identified three morphological groups, within which the bill shapes are related through scaling transformations alone. The first group (group A) corresponded to the genus *Geospiza* in addition to the black-faced grassquit (*Tiaris bicolor*), representative of a group basal to Darwin's finches; the second group (group B) corresponded to the tree (*Camarhynchus*), Cocos (*Pinaroloxias inornata*) and warbler (*Certhidea*) finches; whereas the third group (group C) consisted of a single species, the vegetarian finch (*Platyspiza crassirostris*). Thus, scaling transformations accounted for a substantial part of the variation observed in the beak shapes of Darwin's finches by reducing the complexity from 15 original beak shapes to three different (group) shapes. However, the differences between 'group shapes' could not be explained by scaling (Fig. 3). Mathematically, scaling transformations form a subgroup of affine transformations (linear mapping methods that preserve points, lines, curves and planes, allowing one to map points in one shape to points in another), which also includes shear transformations (Campàs et al., 2010). When shear transformation along the bill depth axis was added, all beak shapes of Darwin's finches collapsed onto a single common shape. Thus, remarkably, not only could the diverse beak shapes of Darwin's finches be transformed into each other pairwise, all of them could be transformed into the ancestral shape provided by a molecular phylogeny (Campàs et al., 2010). This geometric analysis demonstrated that the (species- and genus-level) beak shapes of all Darwin's finches are related by affine transformations, characterized by precisely three parameters: the depth and length for the scaling transformation and an additional parameter measuring the degree of shear.

The general significance of such two-tier variation detecting the same pattern of hierarchical collapse of shapes was further confirmed by performing a pairwise comparison of the beak shapes in about 200 bird species spanning a significant section of Passeroidea, including most tanager and cardinal relatives of Darwin's finches (Thraupidae and Cardinalidae) (Fritz et al., 2014). Such a precise morphological pattern echoes the observations of Goethe, who commented that: 'The laws of transformation according to which nature produces one part through another and achieves the most diversified forms through the modification of a single organ' (Goethe, 1790); and suggests a highly structured and versatile generative developmental process.

To explain such morphological diversity at a mechanistic level requires an explicit connection between the genes involved in shaping the beak during development and the parameters characterizing the observed geometric transformations. Analysis of naturally occurring hybrids between species of Darwin's finches and the more recent comparative analysis of genes expressed in the developing beak primordium suggests that avian beak morphology is a polygenic character regulated by multiple developmental genes (Grant, 1993; Grant and Grant, 2002, 2015; Grant and Grant, 2008; Lawson and Petren, 2017). For example, changes in the expression of *Bone morphogenetic protein 4* (*Bmp4*) control the depth and width in the embryonic cartilage component of the upper beak skeleton, which forms first and establishes species-specific beak shape during embryonic development. The *Bmp4* expression level and pattern in the frontonasal mass (upper beak primordium) display a strong correlation with the scaling factors and quantify a large portion of the adult beak morphological diversity (Abzhanov et al., 2004). Other developmental genes, such as *CaM*, *TGFβIIIr*,

*β-catenin* and *Dkk3* form a regulatory network and together explain other scaling parameters, such as beak length or width (Abzhanov et al., 2004, 2006; Mallarino et al., 2011, 2012) (Fig. 4B–D). The necessity of including shear transformations to explain the full morphological variation in the beaks of Darwin's finches suggests the involvement of more significant and as yet unknown developmental changes controlling the exact curvature of beak profiles characteristic of different 'group shapes'. The uncovered hierarchical morphological structure is likely to be related to the hierarchical structure of developmental regulatory networks, which are thought to be the proximate cause of evolutionary changes in morphology. These could include modifications at different stages of embryonic development and the involvement of different types of developmental mechanisms, such as diffusible morphogenetic signals, the pre-patterning of skeletal condensations resulting in distinct morphogenetic maps using transcription factors, and regulation of the planar polarity of cell division during growth.

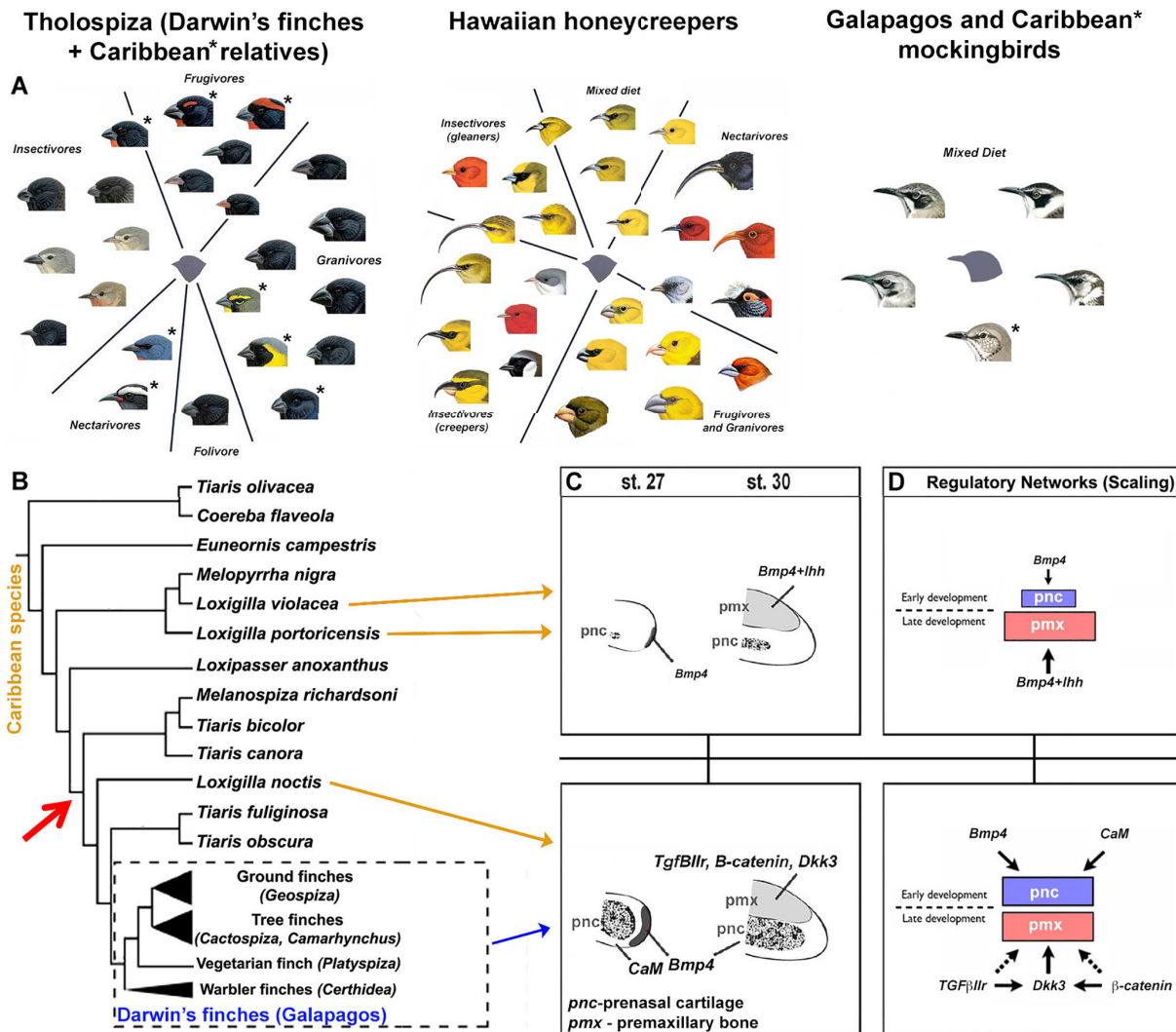
Mechanisms specifically controlling shear transformation are suggested by the developmental strategy by which the beak grows (Fig. 5A). When the primordial beak forms, it contains a large zone of actively proliferating cells, termed a growth zone. As the beak grows, this group of dividing cells is gradually depleted and the growth zone decays at a constant rate until it completely disappears at the end of beak development (Fritz et al., 2014). Thus, the conical shape of the beak (a sectioned parabolic cone to be exact) is produced by an 'envelope' of all of the growth zone shapes observed over developmental time (Fig. 5B). The behaviour of this growth zone determines both the scaling-based and shear-based transformations. While scaling can be explained by diffusing molecules, such as BMP4, signalling to the growth zone from the outside (Campàs et al., 2010), the distinct beak curvatures that distinguish the different beak 'group shapes' may rely on the precise and coordinated internal alignment of the cell division planes of proliferating cells relative to the main axis of growth (Fritz et al., 2014).

### Modularity of the cranial skeleton and evolution of diverse skull shapes

*'We tend, as we analyse a thing into its parts or into its properties, to magnify these, to exaggerate their apparent independence, and to hide from ourselves (at least for a time) the essential integrity and individuality of the composite whole.'*  
(p. 712, Thompson, 1917a)

Studying the vertebrate skull in its full complexity is particularly challenging and intriguing. The vertebrate head is a fascinating part of the body, with its intricate organization and multifunctional design. With a host of taxon-, age- and sex-specific features and highly adaptive characteristics, an image of the vertebrate head with all its attributes can often instantly tell us what species the animal belongs to and provide information about its ecology. The exact anatomy of the head, the overall shape of the skull and shape of the individual skeletal parts and how they are integrated with the brain, eyes and muscles all reveal the animal's natural history. There are now many morphological studies showing how geometric transformations of even anatomically complex multi-part structures – such as tetrapod limbs, vertebral columns and bony crania – allow for direct comparisons in the most morphologically diverse clades, such as cichlid fishes, anole lizards and phyllostomid bats (Cakenberghe et al., 2002; Clabaut et al., 2007; Monteiro and Nogueira, 2011; Muschick et al., 2012; Sanger et al., 2012, 2013; Wilson et al., 2015).

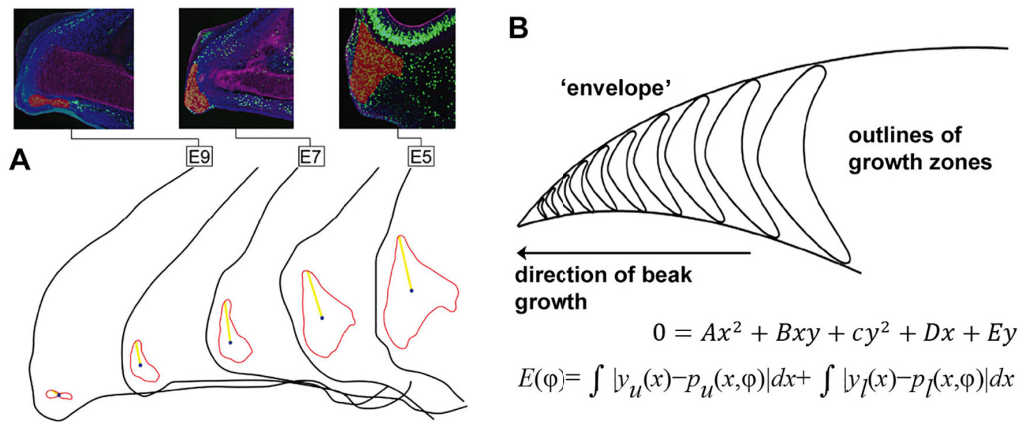
Early in embryonic development, the faces of all amniote vertebrates (mammals, reptiles and birds) are remarkably similar



**Fig. 4. Evolution of beak shape diversity in songbirds and developmental mechanisms for beak morphogenesis.** (A) Exceptionally high diversity of beak shapes in *Tholospiza* (Darwin's finches on Galápagos and endemic Caribbean relatives, marked with an asterisk) and Hawaiian honeycreepers as compared with the much more limited morphological diversity in Galápagos mockingbirds (and a single Caribbean endemic Bahama mockingbird *Mimus gundlachi*, also marked with an asterisk). *Tholospiza* and honeycreepers show much higher degrees of sympatric distribution (related species co-inhabiting the same geographic areas), while Galápagos mockingbirds (and other Galápagos land birds) display allopatric speciation with just four morphologically similar endemic species for the entire Galápagos archipelago. (B) Highly modular multigenic beak developmental programs are found in Darwin's finches and close *Tholospiza* relatives but not in the more basal species (modified after Mallarino et al., 2012). Darwin's finches and the closely related Caribbean species *Loxigilla noctis* deploy multiple regulatory genes to control both prenasal cartilage and premaxillary bone parts of the developing beak, whereas the more basal species use a much more limited set of genes to regulate the shape of premaxillary bone (genes expected to be deployed based on Galápagos species are not expressed). The red arrow in the *Tholospiza* phylogeny points at the phylogenetic position within this group beyond which higher morphological diversification is observed and needs to be explained (phylogeny from Burns et al., 2002; modified after Mallarino et al., 2012). (C) Within Darwin's finches, species with deep beaks have strong expression of *Bmp4*, *TGFβ1lr*, *β-catenin* and *Dkk3*, whereas expression of *CaM* is upregulated in species with elongated beaks, such as *Geospiza scandens* and *Geospiza conirostris*. *BMP4* and *CaM* act independently to alter the growth of the prenasal cartilage and *TGFβ1lr*, *β-catenin*, and *Dkk3* regulate the premaxillary bone. (D) Darwin's finches and the closely related Caribbean *L. noctis* share beak developmental programs, which are highly modular in terms of both tissue and molecular composition, while the more basal species *Loxigilla portoricensis* and *Loxigilla violacea* have simpler beak developmental patterns and represent a simpler starting condition (also found in outgroup species such as zebra finches). Illustrations of the head of each bird species were derived from del Hoyo et al. (2017) with permission from Elisa Badia. Illustrations of Hawaiian honeycreepers are by H. Douglas Pratt (Pratt, 2005).

despite the substantial phenotypic differences observed in adults (Hall, 1996; Raff, 1996). To understand the evolutionary significance of such conservation at the developmental level, geometric morphometric analyses have been conducted on the entire face during the whole developmental trajectory for all major amniote groups (Young et al., 2014). The faces of early embryos appear as an assemblage of protruding tissue buds filled with cells, which need to expand and fuse in a particular order to form the

cranium. This comparative analysis found that the most conserved period of amniote facial shape coincides with the time when fusion of prominences occurs. Next, comparative morphospace was used to infer principles of facial growth and to predict potential but unrealized shapes. Surprisingly, deviations from the conserved early embryonic trajectories resulted in increasing mismatch in the shape and size of craniofacial prominences, which increased the likelihood of clefts (incomplete fusions) and later abnormalities.



**Fig. 5. Principles of beak development in songbirds.** (A) Snapshots of growing beak for embryonic day (E) 5–9, showing developing beak outlines (black), the size of the growth zone (red), its centroid (blue) and the relevant length scale for shaping the upper beak profile (yellow). All measures of the growth zone are derived from midsagittal cross-sections of zebra finch embryo beaks, stained to show cell nuclei (blue) and dividing cells (green). Areas with a high density of dividing cells are defined as the growth zone (red outline). (B) The final conical shape of the beak is given by an ‘envelope’ of the growth zone observed during developmental time, which decays at a constant rate until it shrinks to size zero generating a tip (adapted and modified from Fritz et al., 2014). All beak shapes are well fitted by equations, as shown, that describe beak shape and the profile  $[p_u(x)$  and  $p_l(x)]$  generated by a fixed growth law and growth zone decay, where  $\phi$  is a vector parameterizing the shape and all other free parameters in the problem. The midsagittal sections of songbird beaks are all calculated to be conic sections.

Moreover, experiments on live chicken embryos that aimed to alter the signalling environment in the early face forced the developmental trajectory into the normally unoccupied morphospaces and resulted in abnormalities, such as clefts of the primary palate (Young et al., 2014). It appears that fusion of craniofacial prominences is a strong selective filter against developmental shape variation, explaining morphological conservation at the early stages. Once this critical stage is passed, phenotypic diversity increases sharply. This, in effect, is an example of the powerful, if constraining, role of the intrinsic developmental mechanisms in generating morphological diversity.

What is the role of modularity in the generation of diversity? Recently, a detailed comparative geometric morphometrics analysis was reported of 3D skull shapes in both Darwin’s finches and Hawaiian honeycreepers within the same morphospace using X-ray microcomputed tomography ( $\mu$ CT) scans of their cranial skeletons (Tokita et al., 2017) (Fig. 6A–D). The Hawaiian honeycreepers and Darwin’s finches have both evolved remarkable levels of adaptive cranial morphological variation, and this analysis demonstrated that cranial shapes in both groups are much more diverse than in their respective outgroups (Fig. 4A) (Tokita et al., 2017). The Hawaiian honeycreepers as a group displayed the highest skull shape diversity and disparity of all the bird groups studied. Interestingly, Darwin’s finches showed strong covariation between the shape of the whole skull and those of the upper beak, orbit, palatine and adductor chamber. By contrast, in Hawaiian honeycreepers, the parts of the skull are less strongly coupled with the shape of the whole skull (Fig. 6D). Such results suggest that the high level of disparity in skull morphology observed in Hawaiian honeycreepers is associated with changes in modularity and integration of individual skull elements, allowing for more evolutionary flexibility to explore the morphospace. Modularity here refers to the ability of a biological system to organize individual and discrete units that can increase the overall flexibility of the system. This tends to facilitate selective forces, whereas integration exerts an opposite effect as it works to match and bind the modules together (Hall and Olson, 2001). Similarly, studies on mammalian and fish skulls indicated a significant role for changes in skull integration and

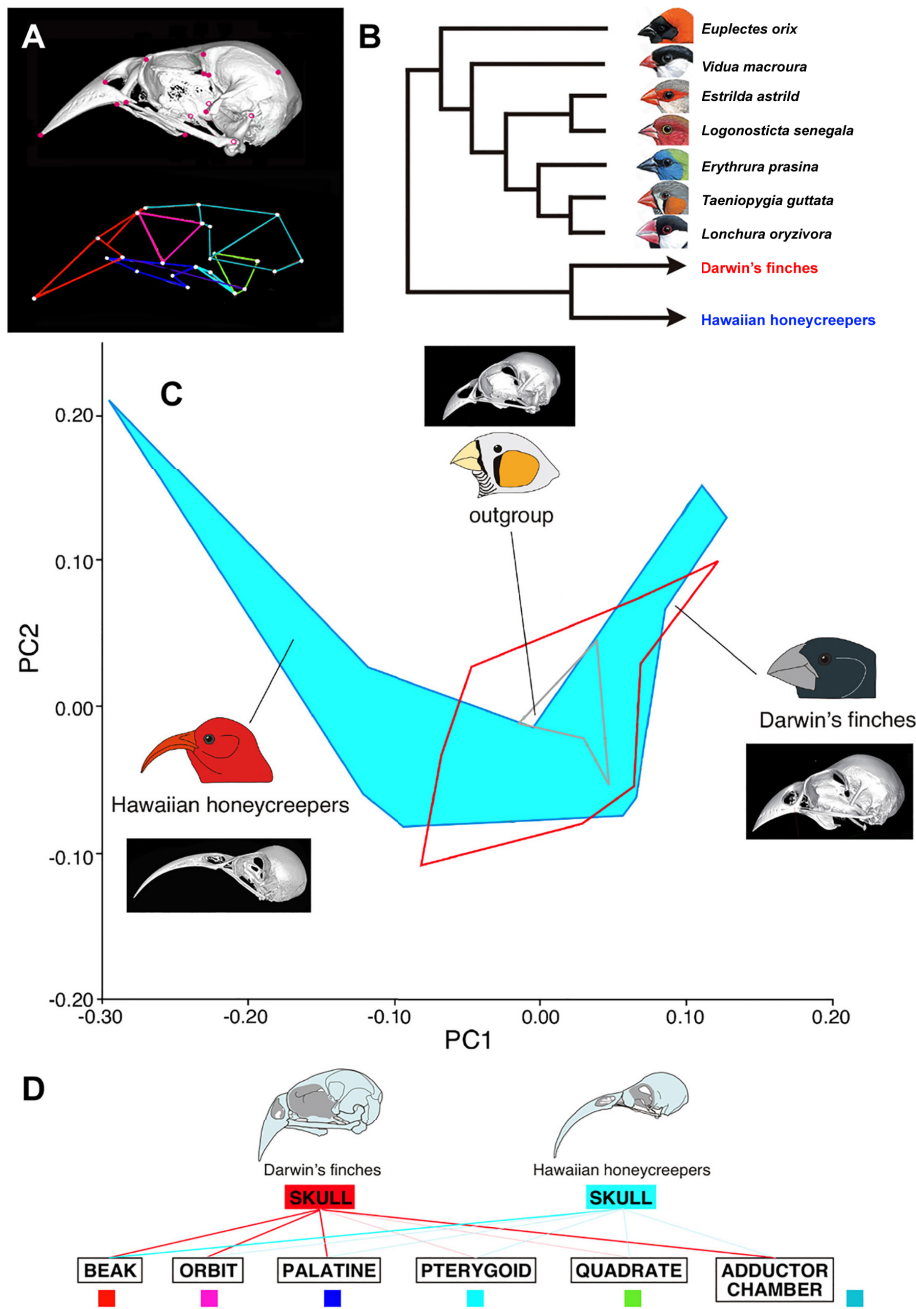
modularity in both the extent and directionality of skull shape changes (Goswami, 2007; Drake and Klingenberg, 2010; Goswami et al., 2014). The exact developmental mechanisms controlling integration and modularity of the skull skeletal elements are not yet known but further studies should reveal how the ‘laws of growth’ actually operate as they shape vertebrate cranial diversity.

#### Geometry of life on a large scale: transformation from reptile to bird

*‘The many diverse forms of Dinosaurian reptiles, all of which manifest a strong family likeness underlying much superficial diversity, furnish us with plentiful material for comparison by the method of transformations.’* (p.754, Thompson, 1917a)

As predicted by D’Arcy Thompson, comparisons based on geometric transformations can be successfully applied to both small and large evolutionary scales with reasonable success. For instance, modern birds represent a surviving group of theropod dinosaurs and their unique skulls are morphologically radically different from those of their reptilian relatives and ancestors and any other vertebrates. Among major innovations of the avian head are the toothless beak derived from the fusion of premaxillary bones, uniquely shaped palatines (bones that form the roof of the mouth), highly reduced face/snout, and a hugely expanded brain and overlying domed cranial roof (Fig. 7A,B). The nature of the reptile-to-bird transition became clearer when a geometric morphometric study was performed integrating developmental, neontological and palaeontological data, which revealed that pedomorphosis, by which descendants resemble the juveniles of their ancestors, was responsible for several major evolutionary transitions in the origin of birds (Bhullar et al., 2012). The same set of variable skull landmarks was analyzed across extant and extinct members of Archosauria (‘ruling reptiles’), from the basalmost taxa such as *Euparkeria* to the early dinosaur *Herrerasaurus*, non-avian theropods (e.g. *Guanlong*), crocodylians, primitive birds (*Archaeopteryx*, *Confuciusornis* and *Yixianornis*) and modern birds (Fig. 7B) (Bhullar et al., 2012). Adult skull shapes were analyzed together with those of juveniles and embryos, wherever



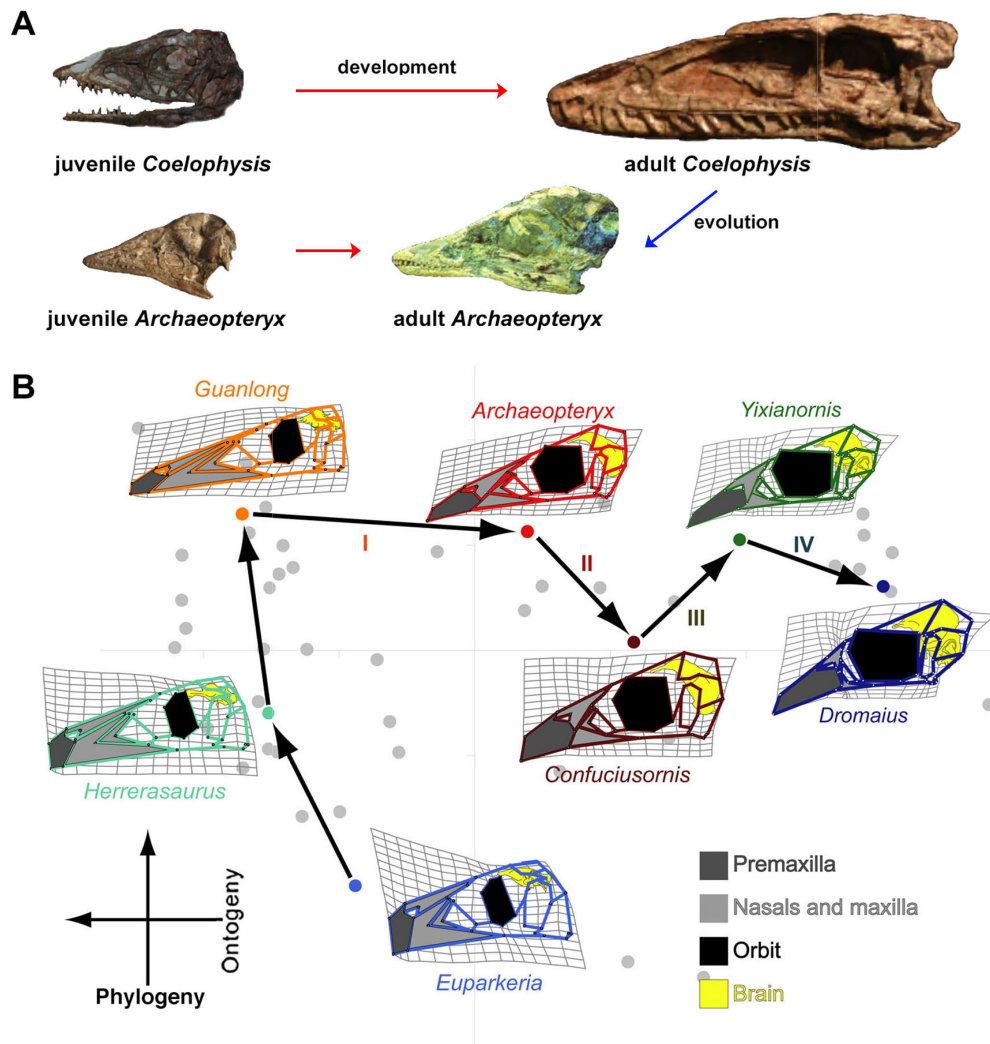


**Fig. 6. High level of morphological disparity in avian skull shapes is associated with increased modularity.** (A) Microcomputed tomography ( $\mu$ CT) scan of a bird skull showing geometric morphometric landmarks (above, red dots on skull scan) and defined modules (beneath, coloured lines). (B) The phylogeny of bird species used for mapping shape data by squared-change parsimony. Representative, more basal, species were used as outgroups. (C) Morphospace occupied by skull shapes. The polygons show parts of the morphospace occupied by different groups revealing that Hawaiian honeycreepers (polygon shaded blue) have some of the most diversified and divergent skulls of all species studied. (D) Darwin's finches show strong covariation between the shape of the whole skull and several skull modules (red thick lines), suggesting strong integration within the skull. By contrast, Hawaiian honeycreepers show strong covariation only between the shape of the whole skull and that of the upper beak (blue thick line), indicating much greater flexibility of evolutionary change. Such a unique pattern of morphological integration in their skulls is likely to reflect an altered and much higher state of developmental modularity within the skull, which contributed to the outstanding level of disparity of skull morphology observed in Hawaiian honeycreepers. Cranial modules in D are colour-coded in the same way as in A. All images adapted and modified from Tokita et al. (2017).

available, within the same morphospace. Basally branching bird relatives and primitive birds clustered with embryos and early juveniles of other archosaurs, indicating paedomorphosis (Fig. 7B). This paedomorphosis is most evident in their relatively shorter face, enormous eyes and enlarged brains (Bhullar et al., 2012). The paedomorphic trend holds even after body size and phylogeny are statistically accounted for: non-avian dinosaurs such as *Compsognathus* are small, yet its skull shape falls within the ancestral adult cluster, while ostrich and emu (*Dromaius*) are very large but their skulls group with other birds. This morphometric analysis revealed at least four paedomorphic episodes (marked I-IV on Fig. 7B) in the history of birds, which connect ancestral skull shapes of early archosaurs through a series of morphological transitions to modern birds (Fig. 7B). This evolutionary story covers over 240 million years and represents one of the most dramatic

morphological transitions in animals yet can be addressed entirely within the framework provided by Thompson's 'theory of transformations'.

Despite the overwhelming imprint of paedomorphosis on the early evolution of the bird skull seen in the collapse of the face and the enlargement of the brain, localized peramorphosis, a trend which is the reverse of paedomorphosis where the descendants mature past the ancestral adulthood condition and evolve previously unseen traits, also occurs later in the bird lineage and explains, for example, the origin of the distinctive avian beak structure (Bhullar et al., 2012, 2015). The avian beak was an evolutionary innovation, formed from the fusion and elongation of premaxillary bones and uniquely shaped palatines, which allow for kinesis (upper beak movement relative to the skull). This 'new snout' of birds, the bill, permitted vast diversification in avian ecology. A combined approach



**Fig. 7. Geometric morphometrics analysis of skull shapes in Archosauria reveals pedomorphosis (retention of juvenile features) at the origin of birds.** (A) Photographs of fossil skulls of the basal theropod dinosaur *Coelophysis* (early juvenile and adult) and first bird *Archaeopteryx* (juvenile and adult). (B) Several transitions are revealed during evolution of birds from non-avian theropod dinosaurs associated with heterochrony (changes in developmental timing). I-IV refer to heterochronic (changes in developmental timing) transitions during evolution of modern avians. Transition I is the most dramatic pedomorphic transition, during which skulls of birds broke the existing trend towards more elongated snouts and acquired juvenile-like shapes. Other transitions (II-IV) produced features found in modern birds, such as toothless beaks, larger brain and eyes. Grey spots show positions of all other archosaur taxa analyzed in this study; only the most important taxa are highlighted. All images modified from Bhullar et al. (2012).

bridging paleontology, comparative anatomy and experimental developmental biology showed that the avian beak occupies a distinctive part of the facial morphospace within the archosaurs. To expose underlying developmental mechanisms, developmental gene expression was studied in the embryonic face (Bhullar et al., 2015). This study revealed a novel mid-facial expression domain of *Fgf8* in early bird embryos and the downstream mid-facial WNT-responsive region at later stages. Altering *Fgf8* expression in chicken embryos using specific antagonists altered later WNT responsiveness to the ancestral pattern. The resulting experimental skeletal phenotypes clustered geometrically with ancestral fossil snouted forms instead of with beaked birds (Bhullar et al., 2015). Other studies have highlighted the roles of other signalling molecules, such as SHH and BMP, in the origin and large-scale evolution of beak shapes (Hu et al., 2015a,b; Smith et al., 2015). These studies are good examples of how the ‘laws of growth’ can be understood in more precise and mechanistic terms.

**Thompson’s ‘laws of growth’ versus Darwin’s natural selection**

*‘I have tried to make it as little contentious as possible. That is to say where it undoubtedly runs counter to conventional Darwinism, I do not rub this in, but leave the reader to draw the obvious moral for himself.’*

D’Arcy Thompson on *On Growth and Form* (Thompson, 1958)

The reception of D’Arcy Thompson’s 1917 book (edited in 1942 and 1961) was extremely wide-ranging as it drew different reactions from a very diverse audience. Developmental biologists were eager to understand the ‘laws of growth’ and were mostly inspired or otherwise influenced in a positive way. Mathematicians and applied physicists found it fascinating, and attempts to perfect Thompson’s approaches continue to this day. It had a great impact on the immunologist Sir Peter Medawar and theoretical biologist Joseph Henry Woodger, philosopher Michael Ruse, architects Philip

Beesley and Sarah Bonnemaison, as well as countless designers and artists who were mesmerized by the idea of organismal transformations (Medawar, 1945; Woodger, 1945). Both Julian Huxley and Stephen J. Gould, famous evolutionary biologists, were motivated by Thompson's ideas to produce their own theories (Huxley, 1932; Gould, 1977, 2002). However, many contemporary evolutionary biologists found it a challenge to accept the concepts explaining biological forms by physical or largely internal biological processes. They thought that the book was arguing against Darwinian evolution, and many believed that by using his famous transformation diagrams, D'Arcy was arguing that 'laws of growth' rather than evolution could be used to explain the different forms of related species. At the British Association meeting in 1894, Thompson gave a lecture titled *Some Difficulties in Darwinism*. It was never published in a journal or a book but was briefly summarized by a *Nature* correspondent: 'He doubts the efficacy of the struggle for existence in the case of humming-birds, etc., and in these cases he regards the profusion of forms, colours, and other modifications as due merely to laws of growth, and thinks that growth may be more exuberant in the absence of struggle and hardship' (Anon, 1894). In other words, the general perception was that Thompson saw natural selection more as an impediment to creating diversity rather than as a generative force, and he was considered a 'stubborn opponent' to Darwinism (Gould, 1971). Was Thompson completely wrong in his conviction?

A century later, this dispute still might not be completely settled. Consider how adaptive radiations are explained in a standard biology textbook (Simpson, 1953; Futuyma, 2009; Zimmer and Emlen, 2012). Adaptive radiation, or the rapid evolution of morphologically and ecologically diverse species from a single ancestor, usually implies two coincidental processes: multiplication of species number (increased taxonomic diversity defined as the 'species richness') and increased phenotypic disparity (defined as 'morphological diversification'). Alternative scenarios include increases in species richness without major morphological diversification, and dramatic morphological changes in few isolated lineages. The importance of adaptive radiation as an evolutionary phenomenon was first recognized by George Gaylord Simpson in *The Major Features of Evolution* (Simpson, 1953). Much of the current species richness, ecological and morphological diversity in such clades as birds, angiosperms and mammals, is the result of multiple radiation events (Moen and Morlon, 2014; Gill, 2007). As already mentioned, some of the best-studied textbook examples of adaptive radiations are found in birds: Darwin's finches, Hawaiian honeycreepers and Madagascar vangas. All of these avian clades display an unusually high degree of beak morphological variation, which is matched by a diversity in diets and feeding behaviours, increased species richness and sympatric distribution of their species (Fig. 4A). Molecular phylogenies suggest that Darwin's finches are part of a larger clade called Tholospiza and that this entire clade should be considered as a single adaptive radiation (Fig. 4A,B) (Burns et al., 2002, 2014). Compared with other related lineages, this group has undergone extensive bill evolution in a relatively short time frame, especially among the Darwin's finches, which demonstrate 'exceptional' rates of diversification (Burns et al., 2002, 2014). These dramatic changes in bill morphology have occurred with little genetic divergence among the species (Burns et al., 2002).

There are two possible explanations for Tholospiza diversity (which are not necessarily mutually exclusive). A model for adaptive radiation developed by Simpson (1953) involved simultaneous divergence of multiple lineages as a consequence of entering new adaptive zones, such as isolated islands or new and

unusual habitats. Thus, the canonical explanation for diversity among Darwin's finches and their Caribbean relatives is that their radiation occurred in response to the niches available to their ancestors invading new island habitats (Losos and Ricklefs, 2009). However, their diversity is both exceptional and unique, as the Galápagos and Caribbean islands are inhabited by representatives of many other families of land birds whose ancestors had the same opportunities for diversification but show much more limited morphological variation and a high degree of allopatry (no more than one species per island). Darwin wrote, about the finches now bearing his name: 'These birds are the most singular of any in the Archipelago' (Darwin, 1839). Indeed, he was right, on Galápagos there are 28 endemic species and 6 endemic subspecies of birds: martins, mockingbirds, owls, hawks, flycatchers, doves, warblers, cuckoos and others. These locally adapted species evolved from 18 different ancestral bird species that colonized the islands over the last 5 million years. All of these other birds display allopatric speciation and low levels of morphological variation, including beak shapes, when compared with Darwin's finches on the same islands. In particular, Galápagos mockingbirds enjoy diverse diets on different islands, which they have colonized for as long as the Darwin's finches, but they remained morphologically conservative and have similar beaks to each other and their American and Caribbean relatives (Fig. 4A) (Arbogast et al., 2006). When Tholospiza family members were compared with the similarly aged and sized groups of tanagers, it was concluded that this clade demonstrated unusually high levels of morphological diversity, even considering their island habitats (Burns et al., 2002). As this study concluded: 'An alternative, more structuralist interpretation is that the ancestor to all of these birds possessed a developmental-genetic architecture (passed on to its descendents) that included a greater variety of regulatory genes controlling nasiocranial development' (Burns et al., 2002).

A similar comparative study with similar results was performed on Hawaiian honeycreepers (Lovette et al., 2002). To understand the origin of their morphological diversity, beak shapes of Hawaiian honeycreepers were contrasted with those of the endemic Hawaiian thrushes. Phylogenetic analyses indicated that the ancestral thrush colonized the Hawaiian islands as early as the common ancestor of the honeycreepers. The similar timing of colonization suggests that the observed differences in diversity between the Hawaiian honeycreeper and thrush clades did not result from the length of time that they spent on the archipelago (Lovette et al., 2002). Morphometric analyses of the clade-specific morphological characteristics associated with rates of diversification demonstrated that the relatives of Hawaiian honeycreepers (Carduelini) displayed significantly greater variation in bill size and shape among species than the Hawaiian thrushes and their non-Hawaiian relatives (Turdinae). In fact, Hawaiian honeycreepers have diversified to fill much of the beak shape morphospace occupied by New World passerine birds in general. Like the study on Darwin's finches, this report concluded that: 'The greater morphometric variation of the carduelines suggests that the ancestor of the honeycreepers may have had an intrinsically higher capacity for morphological change than did the ancestor of the Hawaiian thrushes' and that such 'high bill shape lability in the Carduelini... might therefore represent a key innovation of morphological versatility' (Lovette et al., 2002).

In summary, all of these comparative investigations related to extensive and rapid morphological evolution combined suggest a rather striking picture. First, Darwin's finches and Hawaiian honeycreepers (and their diverse relatives) are the classic examples of adaptive radiation and morphological diversification but their beak and skull diversity cannot be explained by the external factors driving

natural selection alone. For both clades, novel intrinsic mechanisms providing higher capacity for generating morphological diversity have been suggested. Second, as discussed above, beaks of Darwin's finches are controlled by a multigenic modular developmental program, which allows for independent shape changes along individual axes. Third, the follow-up comparative developmental analysis indicated that such a sophisticated beak developmental program is present in Darwin's finches and their closest and morphologically diverse Caribbean relatives but it is not found in the more basal *Tholospiza* species (Fig. 4B–D) (Mallarino et al., 2012). This later observation suggests that the most important innovation in the *Tholospiza* clade was an intrinsic one: the formation of the modular multigenic program that enabled more flexible control over various parameters of beak shape and size. It is not yet clear when this regulatory network expressed in beak cartilages and bones emerged, and further phylogenetically guided developmental studies are needed. In particular, it will be interesting to analyze how the novel gene regulatory network emerged, perhaps with the help of hybridization between rapidly evolving species exchanging beneficial mutations, a phenomenon called 'adaptive introgression'. Finally, the study of diversity in entire skull shapes, described earlier in this Review, indicated that it was high in Darwin's finches and extremely high in Hawaiian honeycreepers and was linked to altered patterns of integration and elevated levels of modularity of skull skeletal elements (Fig. 6D) (Tokita et al., 2017). The developmental mechanisms controlling development of the vertebrate skull are still in their infancy; for instance, little is currently understood about how different parts of the skull interact during development and how such interactions change during evolution.

Taken as a whole, evidence suggests that the internal mechanisms, the famed Thompson's 'laws of growth', indeed exert a huge influence over morphological diversity and may explain much, perhaps most, of the increased generative capacity in certain avian and other animal clades to produce variation. In particular, more research is needed to understand the role of novel developmental changes in clades that are unexpectedly and exceptionally diverse for the conditions that they inhabit. For such groups, the presence of the novel ecological niches would be an important, indeed probably required, condition, but far from sufficient to promote variation at the observed levels. Natural selection would play an optimizing and sieving role for the morphological variants produced at elevated levels. Within this structuralist framework, one can better understand why D'Arcy Thompson was hesitant to explain the 'profusion of forms' in hummingbirds and other birds by the means of natural selection alone.

### Concluding remarks

*'This book [On Growth and Form], at once substantial and stately, is to the credit of British Science and an achievement for its distinguished author to be proud of. It is like one of Darwin's books, well-considered, patiently wrought-out, learned and cautious – a disclosure of the scientific spirit.'*

Thompson (1917b)

Charles Darwin is credited with having recognized natural selection as the fundamental process driving adaptive evolutionary change of organisms. However, it is less well known that his true position was much more nuanced. Darwin wrote a number of passages showing that he did recognize the 'laws of growth' as being a more important evolutionary process than natural selection. In 1872, he wrote about the role of these 'laws' in biological diversity: 'We may easily err in attributing

importance to characters, and in believing that they have been developed through natural selection. We must by no means overlook the effects...of the complex laws of growth, such as correlation, compensation, of the pressure of one part on another' and 'we thus see that...many morphological changes may be attributed to the laws of growth and the interaction of parts, independently of natural selection' (Darwin, 1872). Finally, in a letter to Alpheus Hyatt, Darwin sends an important message: 'I should be inclined to attribute the character in both your cases to the laws of growth and descent, secondarily to Natural Selection. It has been an error on my part, and a misfortune to me, that I did not largely discuss what I mean by laws of growth at an early period in some of my books. I have said something on this head in two new chapters in the last edition of the *Origin*...Endless other changes of structure in successive species may, I believe be accounted for by various complex laws of growth...Therefore I should expect that characters of this kind would often appear in later-formed species without the aid of Natural Selection, or with its aid if the characters were of any advantage' (Darwin, 1872).

Thus, the morphology of biological structures is first created, shaped and transformed by novel alterations in the organism's development by the 'laws of growth', and then resulting modifications become both the source and subject of evolution. Thompson and Darwin might have been singing a similar tune after all. The 'laws of growth' in modern interpretation include developmental genetics and should embrace all interacting ontogenetic processes from the molecular to organismal levels. Many evo-devo studies currently focus on dissecting the relative roles for intrinsic factors in triggering and modulating morphological evolution. Future investigations should test the hypothesis that some of the most famous examples of adaptive radiation coupled with morphological diversification and dramatic large-scale evolutionary transitions are driven primarily by the propagative capacity of novel developmental genetic programs. The origin and evolution of the underlying developmental innovations at the genetic, epigenetic and genomic levels deserve a detailed study as well. It will be important to combine evidence from multiple fields using different methods – geometric morphometrics, comparative embryology and functional experimentation (Mallarino and Abzhanov, 2012). There is substantial benefit in blending such efforts to solve the great puzzle that is the evolution of biological diversity.

As many new research publications show, the legacy of D'Arcy Thompson's greatest book lives on and its ideas and approaches remain surprisingly relevant. The current synergy between morphology/morphometry, developmental genetics and evolutionary biology fields is thriving on many of the ideas first touched on by Thompson. After 100 years, *On Growth and Form* continues to inspire experimentalists and theorists alike and makes us all wonder what the next century of studying biological transformations will bring.

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The author declares no competing or financial interests.

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