

EVOLUTIONARY BIOLOGY

How to build a longer beak

Nipam H. Patel

Evolutionary changes in the beaks of Darwin's finches have been instrumental in the adaptive radiation of these birds. The molecular basis for variation in beak size and shape is opening up to investigation.

A classic illustration of nature's ability to generate morphological diversity comes from the finches that inhabit the Galapagos Islands. The beak shapes of these finches are remarkably diverse, and — as described on page 563 of this issue¹ — Abzhanov and colleagues have uncovered one of the mechanisms involved in achieving this. They have compared beak development of several finch species at the molecular level. In combination with experimental analyses in chickens, they show that changes in calcium-dependent molecular signalling during development are involved in the evolution of beak shape.

When Darwin visited the Galapagos Islands, he collected several birds that are now known as Darwin's finches. There are roughly a dozen species of them, and we recognize today that they are closely related to one another, despite their remarkable differences in beak shape and size, and in eating habits (Fig. 1). Indeed, they are so varied that Darwin did not immediately realize that they were all finches, and did not initially use them to support his emerging theories of evolution.

Subsequently, however, the finches have figured prominently in our understanding of the mechanisms of evolution. In particular, over the past 30 years or more, Peter and Rosemary Grant have shown that variation in the finches is driven by ecological forces, and that the birds' adaptive radiation — their rapid speciation from a common ancestor to fill many ecological niches — has occurred in just the past few million years. The precise dimensions (length, depth and width) of each species' beak are crucial to their lifestyle and survival² (Fig. 1), and fluctuations in the environment lead to selection that changes the relative success of birds with various beak shapes. Indeed, these evolutionary processes are evident in real time on the Galapagos Islands³.

An initial insight into the molecular and genetic underpinning of the different beak morphologies came from Abzhanov and colleagues two years ago⁴. They focused on genes that regulate the skeletal and cartilaginous development of the face in laboratory species such as mice and chickens. Using this 'candidate gene approach', they showed that a gene

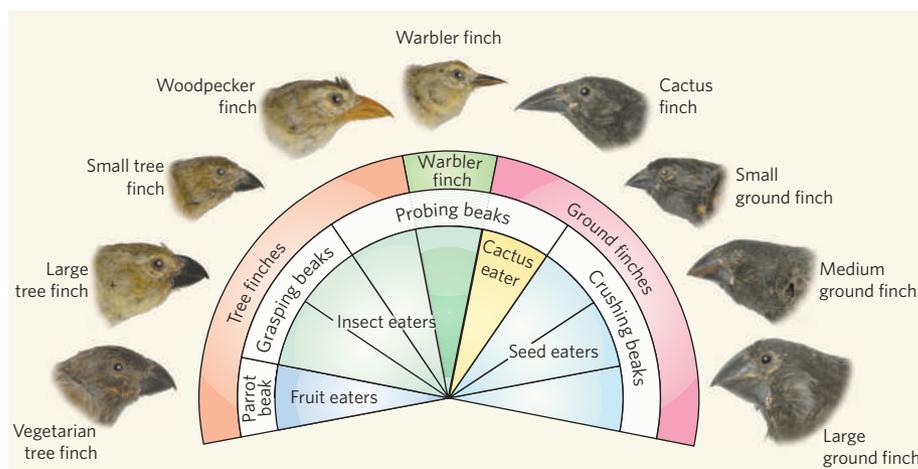


Figure 1 | The evolutionary radiation of Darwin's finches. The species depicted here have all arisen from a common ancestor, but have evolved a remarkable diversity of beak shapes and sizes as they have adapted to exploit different food sources. The work of Abzhanov *et al.*¹ implicates upregulation of the calmodulin-dependent signalling pathway in the evolution of the long, pointed beak of the cactus finch. (Finch specimens provided by the Museum of Vertebrate Zoology, Berkeley.)

encoding a cell–cell signalling protein, known as bone morphogenetic protein 4 (BMP4), was more broadly expressed during the embryonic development of the deep and wide beaks of ground finches than during the development of finches with narrower beaks. To go beyond correlation, they then showed that broadening the expression of the gene encoding BMP4 in chicken embryos resulted in chickens with wider beaks.

The candidate-gene approach, however, is restricted to the relatively few genes known to play a role in facial development. In their latest research¹, Abzhanov *et al.* used a microarray approach to look, in a relatively unbiased manner, for genes that are differentially expressed between species and that are correlated with beak morphology. In this way, they identified a gene that encodes a protein, called calmodulin (CaM), that is expressed at much higher levels in the long and pointed beaks of cactus finch embryos than in the beaks of other finch embryos. CaM mediates calcium signalling in cells, which in turn plays many roles in controlling cell and tissue differentiation and development. Thus, this part of the analysis provided a striking correlation — high levels

of CaM are associated with the long and pointed beaks of cactus finches.

To go beyond correlation, however, Abzhanov *et al.*¹ used the biochemical knowledge of the CaM-dependent signal-transduction pathway. In response to elevated levels of calcium in the cell, CaM is activated, and in turn activates a protein known as CaMKII, which then activates many other known target proteins. Previous studies had identified a mutant form of CaMKII that is constitutively (continuously) active, and by expressing this mutant form in the beak of chicken embryos, Abzhanov and colleagues believed they could generate the same sort of change in signalling that results from raising levels of CaM expression.

When they elevated CaM-dependent signalling in this way, they created chickens with longer, but not wider or deeper, beaks. They were thus able to create a change that reproduced at least part of the evolutionary distinction seen between cactus finches and other finches. Combined with the work on BMP4, these experiments also show that different aspects of beak size (length versus width and depth) are controlled separately at the genetic



50 YEARS AGO

“Nuclear magnetic resonance and electron spin resonance” — It is no new idea that most of the advances in the techniques of chemistry have come from the use of apparatus and methods originally devised by physicists. This is particularly true of spectroscopy, where the main applications associated with the different frequency bands have moved over, one after another, from the pure physicist to the chemist... It would appear that during the past eighteen months a similar move has been taking place with the two new techniques of nuclear magnetic resonance and electron spin resonance... As with all techniques which study the interaction of atoms with external forces, it soon became clear that these new methods also had very great potentialities as tools for chemical investigation, and during the past few years these applications have been brought to light in a very striking way. **D. J. E. Ingram**

From *Nature* 4 August 1956.

100 YEARS AGO

“Strength of a Beetle” — Last night a small beetle (*Aphodius fossor*), the length of which is $\frac{1}{2}$ inch, flew in at my window and alighted on a table next to me. As it buzzed about I put a lid of a tin box over it, but to my surprise the beetle walked about bearing the lid on its back. I then put the tin box on top of the lid, and was absolutely amazed to find that the insect tilted up a corner of the combined box and lid, and nearly escaped. The weight of the beetle when dead was $\frac{1}{2}$ grain, alive I suppose it was a little more; but the box and lid weighed 1758 grains! Assuming that the living insect weighed 1 grain, it must have tilted up 1758 times its own weight! Of course, the strength required to tilt up a box on edge is nothing like so great as that required to actually lift the weight, but nevertheless the feat seems to me sufficiently astounding. The dimensions of the box are $3\frac{1}{8} \times 2\frac{1}{8} \times 1\frac{1}{2}$ inches. From *Nature* 2 August 1906.

level, allowing each dimension to evolve independently.

However, these results do not establish the precise nature of the genetic changes responsible for the differences in morphology. Are the changes in CaM levels between species due to one or more differences in the CaM gene itself — for example in the flanking regulatory regions of the genome that control where and at what rate the gene is transcribed? Or are they due to changes in one or possibly many genes scattered throughout the genome that act upstream of CaM to cause it to be expressed at higher levels in the developing beaks of cactus finches?

Genetic mapping studies in other animals and plants, such as maize (corn) and teosinte (from which maize was domesticated)⁵, suggest that mutations directly affecting the expression level of a single gene have been responsible for some profound evolutionary changes. The application of mapping techniques could

answer this question in Darwin’s finches. Such information would add to the debate over whether evolution proceeds through the accumulation of many mutations of small effect in many genes, or through one or a few mutations of large effect in a single gene. Although it is difficult to generalize from a few examples, Darwin’s finches still have much to tell us about the evolutionary process. ■

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1. Abzhanov, A. et al. *Nature* **442**, 563–567 (2006).
2. Grant, P. R. *The Ecology and Evolution of Darwin’s Finches* (Princeton Univ. Press, 1999).
3. Grant, P. R. & Grant, B. R. *Science* **313**, 224–226 (2006).
4. Abzhanov, A. et al. *Science* **305**, 1462–1465 (2004).
5. Doebley, J., Stec, A. & Hubbard, L. *Nature* **386**, 443–445 (1997).

PARTICLE PHYSICS

A finer constant

Andrzej Czarnecki

For the first time in a decade, the precision of the fine-structure constant — central to understanding the electromagnetic force — has improved. But even greater accuracy is required to test new physics.

How does the colour of a rose relate to the hardness of oak? To physicists, both result from electromagnetism, an interaction whose strength is encoded in one pure number — the fine-structure constant. Appropriately for something introduced at the dawn of quantum mechanics, the fine-structure constant is denoted by the Greek letter alpha (α). It was once believed to be a simple fraction, $1/137$, a circumstance that provoked theorists to search for some deeper meaning to it. Studied closer, the denominator turned out not to be an integer. Writing in *Physical Review Letters*, Gabrielse and colleagues¹ use a measurement of the electron’s magnetic moment reported in a companion paper² to find that $\alpha = 1/137.03599710(96)$, the most accurate value yet. But why is this important — and why is even this accuracy not enough?

Electromagnetism dominates most phenomena at scales larger than the subatomic (which is ruled by nuclear forces) but shorter than the astronomical (the realm of gravity). Thus, α can be measured in many ways, using any system of well-understood electromagnetic nature. When Arnold Sommerfeld first used α in 1915, he named it the fine-structure constant because it described subtle features of the radiation spectrum of the hydrogen atom. Its value was initially best determined by measuring atomic transitions. In the 1970s, more

precise values came from solid-state systems, through the discovery of electrical phenomena such as the Josephson and the quantum Hall effects (Fig. 1).

For the past quarter-century, the world record for the most accurate value of α has been held by amazing experiments performed on a single electron trapped in a vacuum permeated by electric and magnetic fields³. The electron, as a charged and rotating particle, is a tiny magnet with a strength — its magnetic moment — given by $\mu = g(e/2m)s$, where e , s and m are the electron’s charge, spin and mass. The proportionality coefficient g would be 1 for a classical spinning ball. For the point-like electron, relativity theory demands that $g = 2$.

This is not yet the whole story. The physical vacuum, far from being ‘nothing’, vibrates with activity. Elementary particles borrow energy from the vacuum to pop up and disappear again through quantum fluctuations. The electron interacts with such ‘virtual’ particles, mainly photons, and its g -factor is increased slightly by an amount that depends on α . This deviation, known as ‘ g minus two’ ($g - 2$) is among the most precisely calculated quantities in physics. In fact, quantum electrodynamics, the theory of electron interactions with light, was born through efforts to understand its value.

The dream of the theorist is an exact expression for $g - 2$ in terms of α , but that seems as