

## Opinion piece

## Darwin would have loved DNA: celebrating Darwin 200

**Analysis of DNA sequences now plays a key role in evolutionary biology research. If Darwin were to come back today, I think he would be absolutely delighted with molecular evolutionary genetics, for three reasons. First, it solved one of the greatest problems for his theory of evolution by natural selection. Second, it gives us a tool that can be used to investigate many of the questions he found the most fascinating. And third, DNA data confirm Darwin's grand view of evolution.**

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*On the origin of species by means of natural selection, or the preservation of favoured races in the struggle for life* was a best seller (Darwin 1859). It sold out on the day of publication, the second edition sold out six weeks later, and it has remained in print ever since. It is remarkable that a work of science has been continuously in print and widely available in bookshops and libraries for 150 years and is still worth reading for the scientific content, not just for historical interest. *The origin* is ideal popular science: it is presented at an introductory level, yet does not 'talk down' to its reader. It is written in an engaging style, yet is packed with facts, observations and the results of experiments. I recommend *The origin* to my students as one of the best introductory books on evolution. But there is one major respect in which *The origin* is notably dated, and that is the topic of heredity.

Darwin's theory of natural selection relied critically on the continual production of heritable variation in populations. From his own observations he knew that natural populations contained a wealth of variation, and he had a clear view of how these variants would accumulate in populations under the influence of natural selection. But he did not know how variation was generated, or how traits could be inherited. It is remarkable that his theory of evolution was essentially correct despite his lack of knowledge of the causes of heredity.

Because heredity held the key to his theory, Darwin amassed a large amount of evidence on the mode of inheritance, much of which he published in the two-volume *The variation of animals and plants under domestication* (Darwin 1868). He made his own observations in natural communities and conducted experiments around Down House, his home in Kent. He also sent surveys to breeders and had a worldwide network of correspondents offering him their own observations.

The information gathered by Darwin presented a bewildering array of phenomena. For example, Darwin (1868) cites the example of Lord Morton's chestnut mare that, when mated to a quagga (a type of zebra, now extinct), produced a hybrid half-stripy foal. The same mare was then mated to a black Arab stallion, but again her offspring showed evidence of stripes and other quagga-like characters (Morton 1821). To Darwin, this was an important case study 'plainly showing the influence of the first male on the progeny subsequently borne by the mother to other males' (even though foals with 'zebrine' stripes could occasionally appear from a cross between horses, as Darwin himself remarks later in the same chapter).

What conclusions did Darwin draw from his vast catalogue of observations on heredity? In addition to aspects of heredity that are familiar to modern readers, there were two widely reported phenomena that Darwin felt compelled to explain. The first was the inheritance of acquired characteristics. Darwin documents many cases of heritable change arising from the use or disuse of body parts. A typical example illustrates Darwin's *modus operandi* of '... patiently accumulating and reflecting on all sorts of facts which could possibly have any bearing on [the origin of species]' (Darwin 1859): by weighing and tabulating the wing and leg bones of wild and domestic ducks, he found that domestic ducks had lighter wing bones and heavier leg bones than wild ducks. He interpreted this pattern as resulting from 'lessened use of the wings and the increased use of the legs' in domestic ducks (Darwin 1868) and used this evidence to support the claim that 'changed habits produce an inherited effect' (Darwin 1872). Second, Darwin felt he needed to explain how the environment influenced the amount and kinds of variations that arose. Information from his global network of correspondents suggested that developmental responses to environment change could be inherited. In particular, Darwin (1868) gives many examples of characters induced by a change of climate when English domesticated breeds were taken to the colonies.

To explain these and other observed phenomena, Darwin (1868) developed his own theory of heredity, which he referred to as his 'provisional hypothesis of pangenesis'. He speculated that every cell in the body produced tiny informational particles (gemmules) that circulated in the body and collected in buds or gametes before reproduction. These gemmules provided the information needed not only for the development of offspring but also, in some species, for regeneration of lost body parts. Gemmules were produced throughout the life of the organism, so characteristics of the adult body contributed heritable information to its offspring, thus providing a mechanism for the inheritance of acquired characteristics.

Darwin's gemmule theory was complex, but he considered that it answered many of the puzzling observations of heredity. He was at pains to point out that, while it was pure speculation, having a 'provisional hypothesis' was better than having no hypothesis at all, quoting Whewell: 'Hypotheses may often be of service to science, when they involve a certain portion of incompleteness, and even of error' (see Darwin 1868). If the invention of an unobserved particle to

explain observations seems unreasonable, consider the status of the gene in the first half-century of genetics: geneticists inferred the existence of genes purely from observations on heredity, and studied the effect of genes without knowing what they were made of, or how they were passed from one generation to the next. As Thomas Hunt Morgan, one of the founders of modern genetics, said in his Nobel Prize acceptance speech in 1933: 'At the level at which the genetic experiments lie it does not make the slightest difference whether the gene is a hypothetical unit, or whether the gene is a material particle'.

But it is probably fair to say that Darwin convinced few of his theory of pangenesis (possibly not even himself). The theory was criticized by contemporary scientists, including Francis Galton, who transfused blood from a variety of rabbit breeds into a purebred strain and determined that it did not produce mongrel offspring as might be expected if hereditary information was carried in the blood (Galton 1871, but see Darwin 1871*a*). Furthermore, it was argued that blending inheritance, predicted by gemmule theory, would dilute variation with each passing generation, limiting the potential for adaptation (e.g. Jenkin 1867). But the killer argument came from August Weismann, one of the first scientists to be called 'neo-Darwinian' (not a compliment then, and frequently used in the same vein since). From his studies of cell biology and development, combined with observations, experiments and theoretical considerations, Weismann (1893) concluded that heritable characters were not altered during an individual's lifetime. Heritable information was carried in reproductive cells from one generation to the next, essentially unchanged. Along with the Mendelian theory of particulate inheritance, Weismann's theory of 'hard inheritance' formed the basis of modern genetics. But nobody knew why inheritance was particulate and immune to lifetime alteration until the instant revolution brought about by the publication of the structure of DNA by Watson & Crick (1953).

Crick's (1958) 'central dogma' was essentially a biochemical statement of Weismann's theory (figure 1). Information is stored in nucleic acids and copied when an organism reproduces, so barring copy errors or damage, the embryo receives a copy of information that was used to make its parent. When information is needed for growth and development, the relevant instructions are transcribed into RNA and translated into proteins. This resembles Darwin's gemmule theory in many aspects—information particles transferred from parents to offspring and used as instructions for growth and development throughout life—but provides a simpler explanation of the generation and maintenance of variation, because there is no blending of information, the environment does not direct the generation of heritable, adaptive variations, and changes during an individual's lifetime cannot be coded into heritable information. If we could go back in time and take half an hour to explain the central dogma to Darwin, we could save him years of work (which makes you wonder what someone 150 years from now wishes they could come back and explain to us to save us barking up wrong trees).

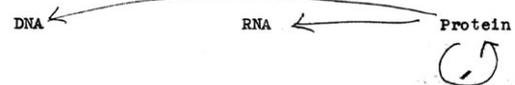
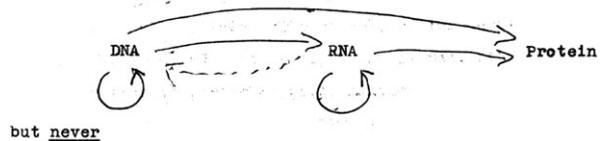
In addition to explaining many of the facts that puzzled Darwin, DNA provides a tool for exploring

#### Ideas on Protein Synthesis (Oct. 1956)

##### The Doctrine of the Triad.

The Central Dogma: "Once information has got into a protein it can't get out again". Information here means the sequence of the amino acid residues, or other sequences related to it.

That is, we may be able to have



where the arrows show the transfer of information.

Figure 1. Francis Crick's statement of the central dogma, from an early draft of Crick (1958), available at [http://profiles.nlm.nih.gov/SC/B/B/F/T/\\_/\\_/scbbft.pdf](http://profiles.nlm.nih.gov/SC/B/B/F/T/_/_/scbbft.pdf).

many of the questions that Darwin was interested in. In particular, DNA has revolutionized the study of sexual selection (Darwin 1871*b*) by illuminating female choice and male reproductive success. With DNA it is possible to tell who has mated with whom to produce offspring, revealing some surprising results. For example, the alpine marmot (*Marmota marmota*) was considered one of the few monogamous mammal species. But DNA investigations reveal that up to a third of litters contain extra-pair offspring, and a fifth of all offspring were fathered by a non-resident male (Goossens *et al.* 1998). DNA exposes a lot more shenanigans than had been suspected on behavioural observations alone.

DNA also sheds light on the origins of species by revealing the relationships between lineages. The origin of whales provides a useful illustration: in order to support his theory of descent with modification, Darwin (1859) was compelled to bridge the gap between whales and their terrestrial relatives with a series of slight changes, each beneficial to its carrier, so he offered the following thought experiment: 'In North America the black bear was seen... swimming for hours with widely open mouth, thus catching, like a whale, insects in the water. Even in so extreme a case as this, if the supply of insects were constant, and if better adapted competitors did not already exist in the country, I can see no difficulty in a race of bears being rendered, by natural selection, more and more aquatic in their structure and habits, with larger and larger mouths, till a creature was produced as monstrous as a whale'. This passage was ridiculed by Darwin's critics (e.g. Owen 1860) and was removed from later editions. Recently, molecular phylogenies have revealed that whales' closest living relatives are the hippos (Gatesy & O'Leary 2001). Darwin might have embraced this 'Whippo hypothesis' because it suggests a possible semi-aquatic stepping stone between terrestrial mammals and fully aquatic whales.

Darwin would also appreciate the way that DNA provides an alternative historical narrative for evolution.

Darwin began as a geologist, and drew upon fossil evidence in support of his evolutionary theory, but he believed it provided a highly incomplete record of the evolutionary past (bearing in mind that the palaeontological record was much patchier in Darwin's day than it is today). Darwin used this position to defend his theory against claims that the fossil record failed to provide evidence of the gradual modifications that he predicted (a debate that continues to this day). Most vexing to Darwin was the sudden start to the animal fossil record, which began with complex and diverse fauna, with no sign of a gradual transformation from a simpler ancestor. This was a serious stumbling block to Darwin's insistence on gradual transformations (*Natura non facit saltum*): 'The case at present must remain inexplicable; and may be truly urged as a valid argument against the views here entertained' (Darwin 1859). Darwin was sure that earlier forms had existed, but were not found as fossils: 'If the theory be true, it is indisputable that before the lowest [Cambrian] stratum was deposited, long periods elapsed, as long as, or probably far longer than, the whole interval from the [Cambrian] age to the present day; and that during these vast periods, the world swarmed with living creatures' (Darwin 1859).

What was needed was a way of probing into deep history that could circumvent any gaps in the fossil record. Since every organism carries a record of its history in its genome, DNA has the potential to provide this alternative historical narrative. Molecular date estimates for the diversification of the animal kingdom suggest that Darwin was right about the animal kingdom having a hidden history, and that the ancestors of modern animals arose at least 50 Myr before the first undisputed fossils (Bromham 2008). These molecular dates are controversial, and much work remains to be done to gauge and improve their reliability, but the prospect of an alternative record of evolution would surely have delighted Darwin.

Perhaps more importantly, molecular analyses confirm Darwin's grand view of evolution, not only in providing evidence for the action of natural selection in populations, but also by illuminating the connection between population-level processes and major evolutionary change. Like Lamarck (1809) before him, Darwin argued that varieties, races and species were essentially arbitrary divisions of a continuous scale of divergence because heritable changes accumulated constantly over the generations. Comparison of DNA sequences confirms this idea. Because nucleic acid genomes are a universal feature of living organisms, we can compare sequences between members of a family, or individuals in a population, or between populations, species, genera, families or kingdoms. Since changes in DNA accumulate constantly, we find greater levels of divergence between evermore distantly related genomes. There is no obvious disjunction that defines the different taxonomic levels, but a sliding scale of genetic distance. Thus, DNA evidence confirms Darwin's central hypothesis: that heritable variation arises continually and is gradually accumulated, making lineages steadily diverge from each other (though not necessarily at a constant rate). This supports Darwin's claim, disputed by his contemporaries and by some biologists in every age since,

that macroevolution (broad-scale patterns in species diversity over time, space and lineages) is the result of the continuous action of microevolution (changes in frequencies of heritable traits in populations).

I would love to be able to go back and tell Darwin that this wonderful new tool we have, DNA analysis, corrects one key idea that he had wrong, sheds light on questions that interested him and confirms that his most important ideas were right.

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- Bromham, L. 2008 *Reading the story in DNA: a beginner's guide to molecular evolution*. Oxford, UK: Oxford University Press.
- Crick, F. H. C. 1958 On protein synthesis. *Symp. Soc. Exp. Biol.* **XII**, 139–163.
- Darwin, C. 1859 *On the origin of species by means of natural selection, or preservation of favoured races in the struggle for life*, 1st edn. London, UK: John Murray.
- Darwin, C. 1868 *The variation of animals and plants under domestication*. London, UK: John Murray.
- Darwin, C. 1871a Pangenesis. *Nature* **3**, 502–503. (doi:10.1038/003502a0)
- Darwin, C. 1871b *The descent of man, and selection in relation to sex*. London, UK: John Murray.
- Darwin, C. 1872 *The origin of species by means of natural selection, or the preservation of favoured races in the struggle for life*, 6th edn. London, UK: John Murray.
- Galton, F. 1871 Experiments in pangenesis, by breeding from rabbits of a pure variety, into whose circulation blood taken from other varieties had previously been largely transfused. *Proc. R. Soc.* **19**, 393–410. (doi:10.1098/rspl.1870.0061)
- Gatesy, J. & O'Leary, M. A. 2001 Deciphering whale origins with molecules and fossils. *Trends Ecol. Evol.* **16**, 562–570. (doi:10.1016/S0169-5347(01)02236-4)
- Goossens, B., Graziani, L., Waits, L. P., Farand, E., Magnolon, S., Coulon, J., Bel, M.-C., Taberlet, P. & Allaine, D. 1998 Extra-pair paternity in the monogamous alpine marmot revealed by nuclear DNA microsatellite analysis. *Behav. Ecol. Sociobiol.* **43**, 281–288. (doi:10.1007/s002650050492)
- Jenkin, F. 1867 [Review of] *The origin of species*. *N. Br. Rev.* **46**, 277–318.
- Lamarck, J. B. 1809 Zoological philosophy. [English transl. by I. Johnston.] See <http://records.viu.ca/~johnstoi/lamarck/tofc.htm>.
- Morton, Right Honourable The Earl Of 1821 A communication of a singular fact in natural history. *Phil. Trans. R. Soc.* **3**, 20.
- Owen, R. 1860 Darwin on the origin of species. *Edinb. Rev.* **111**, 487–532.
- Watson, J. & Crick, F. H. C. 1953 Molecular structure of nucleic acids; a structure for deoxyribose nucleic acid. *Nature* **171**, 737–738. (doi:10.1038/171737a0)
- Weismann, A. 1893 *The germ-plasm: a theory of heredity*. [English translation by W. N. Parker & H. Rönfeldt.] New York, NY: Charles Scribner's Sons.