# Random Chance in Evolution

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## 15 November 2023

Evolution is driven by change – organisms produce offspring that are subtly different, and natural selection then eliminates the least well-adapted. This intuitively leads to the idea that evolution is somehow a steady march of biological improvement – an idea that has been repeatedly hijacked over the last 150 years by those wishing to suggest human 'superiority' over other animals, or even over other humans.

But in fact, nothing could be further from the truth. Natural selection does not have a travel plan – it simply selects the individuals that are best suited to their environment at the time. And, as we will see in this lecture, being 'best suited' is often just a matter of luck…

## Triumph and Disaster

Generally speaking, evolution is slow. Tiny genetic changes result in tiny biological changes which lead to tiny advantages in the struggle for survival and ultimately, over millennia, to the appearance of new species. But sometimes, chance events change the environment so radically that the evolutionary 'rulebook' changes too. Perhaps the most dramatic example of such a chance event is the asteroid strike that is widely accepted to have caused global mass extinctions at the end of the Cretaceous period, 66 million years ago. This massive disruption to global climate is estimated to have wiped out 75% of the animal and plant species alive at the time and brought to an end the domination of the dinosaurs.

But with disaster comes opportunity. The ecological 'niche' vacated by the dinosaurs became occupied by the therapsids – a group of small, largely nocturnal organisms. Free from predation and competition with dinosaurs, this group expanded and diversified, ultimately producing the thousands of species we know as 'mammals' today. And whilst we cannot replay the tape of evolution to test the theory, it seems unlikely that the global expansion of mammals – including ourselves - would have occurred without this improbable, cataclysmic destruction of the dinosaurs.

## Island Isolations

The impact of mass extinctions on evolution is profound but, thankfully, rare. But much smaller scale population 'bottlenecks' can still have major evolutionary consequences. The 'Founder Effect' is one such phenomenon.

Genetic change brought about by mutation or recombination is, in essence, random, and therefore many genes exist as a range of variants, or alleles, in any population. In humans, good examples are features such as eye colour or hair colour, which are caused by different alleles of the same genes. In most cases, this background variation has little evolutionary impact – people with blue eyes or red hair are not dramatically more or less likely to successfully reproduce than those with brown eyes or blonde hair – and therefore the population remains 'polymorphic', with the proportion of brown-eyed or red-haired individuals remaining roughly the same over time.

However, if a new population diverges from a very small number of individuals within such a population, then, by chance, some of these alleles may be missing from the new 'founder' population. Without incoming gene flow (for instance, via people migrating from the original population into the new one) this new population will

expand without those missing alleles and may end up visibly distinct from the original source population – a population without red-haired individuals, for instance.

The founder effect is particularly common on islands, where the original colonising population of a plant or animal may have consisted of only a handful of individuals, washed up on drifting vegetation, for instance. But it can also occur in the absence of geographical isolation – the founder effect requires only genetic isolation, not physical separation. Consequently, founder effects have occurred repeatedly in human societies that practice endogamy (reproducing only with other individuals from within the same group); for instance, in some 'closed' religious communities or within highly stratified cultures in which marriage between different groups is forbidden.

Such founder effects are typically noticed when otherwise rare genetic diseases are observed at much higher frequencies in particular groups. For instance, the neurodegenerative condition Tay-Sachs disease is a genetic disorder caused by a 'faulty' version of the gene hexosaminidase A. Affected patients inherit two copies of this faulty gene, one from each parent. On average, this occurs less than once in every 300 000 births. However, in some human populations that originate from very small 'founder' groups, such as the Old-Order Amish or Ashkenazi Jews, the disease is almost 100 times as common. By chance, the faulty allele was present in some of the small number of individuals within the founder population and has therefore remained common as the population expanded from that early genetic bottleneck. Understanding the basis of founder effects is therefore critical for tackling such genetic diseases in humans, as well as in preventing their occurrence in areas as diverse as endangered species conservation or agricultural crop breeding.

## Drifting and Shifting Across a Genetic Landscape

The outcome of the interaction between an organism and its environment is described as 'fitness' – organisms that are better adapted pass on their genes more successfully and are therefore 'fitter'. In 1932, the pioneering geneticist Sewall Wright proposed a way of thinking about this interaction as a 'fitness landscape' – in essence, a three-dimensional surface in which increased fitness is represented by troughs. In such a landscape, a marble would 'evolve' (roll towards) the nearest low point, whereas maladaptive changes (rolling up a slope towards a peak) would be strongly selected against. Over the last century this metaphor has been hugely useful in explaining several features of evolution – for instance, the occurrence of evolutionary 'traps', in which organisms appear unable to evolve a demonstrably beneficial trait because to do so would necessitate precursor steps that are in themselves disadvantageous. A hypothetical example might be the ability to produce a certain vitamin (a fitness advantage) but which would first necessitate the evolution of a metabolic pathway that produces toxic intermediate compounds (a fitness cost).

One way to overcome such a fitness barrier is to 'leap it' with a dramatic new evolutionary innovation. Such occurrences are vanishingly unlikely and yet – given the vast numbers of organisms on the planet and the vast amounts of time that have elapsed since life began – they are not unheard of. Often they rely on organisms 'importing' a trait from elsewhere in the evolutionary tree via horizontal gene transfer and then repurposing it and a particularly profound example has occurred during the evolution of adaptive immunity.

Classical adaptive immunity – the ability to mount a highly specific immune response and then retain a 'memory' of it to guard against future infections – occurs only in vertebrates. It relies heavily on a phenomenon called V(D)J recombination, which is the process by which the unique specificity of antibodies (and their T-cell equivalent, the T-cell receptor) is produced.

In essence, antibody and T-cell receptor genes are modular, they are composed of different segments, and each segment exists as multiple 'options' within the genome. During development of B and T-cells, the DNA encoding this modular gene is cut and pasted, rearranging different segments together, to create the final, unique protein. An analogy might be assembling a Lego tower by choosing one brick from a bag of different red bricks, then one from a bag of blue bricks and so on.

The enzyme that does this cutting and pasting is called *recombination activating gene*, or RAG. In the tree of life, RAG appears apparently out of nowhere – it is not present in any other branch of the tree, but makes a sudden appearance at the base of the vertebrate branch.

But of course it didn't come from 'nowhere' at all – we now know that a very similar gene exists in a particular family of transposons; mobile chunks of DNA that act a little bit like viruses, hopping around between genomes for their own benefit. We know that such 'mobile genetic elements' sometimes leave chunks of

themselves behind when they hop around, so the most plausible explanation for the evolution of adaptive immunity in vertebrates is an event in which a RAG-like gene from a transposon hopped into a forerunner of the early vertebrates. In doing so, it ultimately conferred the ability to produce multiple versions of an antibody-like protein from a single gene and provided its new host with a remarkable fitness advantage. And thus the entire vertebrate immune system – and consequently the evolutionary success of our own species – owes its existence to an event that was perhaps even more unlikely than a catastrophic asteroid strike.