Adapt first, mutate later

Evolution is meant to start with random mutations. But we may have things the wrong way round, reports Colin Barras

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"TO BE honest, I was intrigued to see if they'd even survive on land," says Emily Standen. Her plan was to drain an aquarium of nearly all the water and see how the fish coped. The fish in question were bichir fish that can breathe air and haul themselves over land when they have to, so it's not as far-fetched as it sounds.

What was perhaps more questionable was Standen's rationale. Two years earlier, in 2006, *Tiktaalik* had become a global sensation. This 360-million-year-old fossil provides a snapshot of the moment our fishy ancestors hauled themselves out of the water and began trading fins for limbs. Standen thought forcing bichir fish to live almost entirely on land could reveal more about this crucial step in our evolution. Even if you were being kind, you might have described this notion as a little bit fanciful.

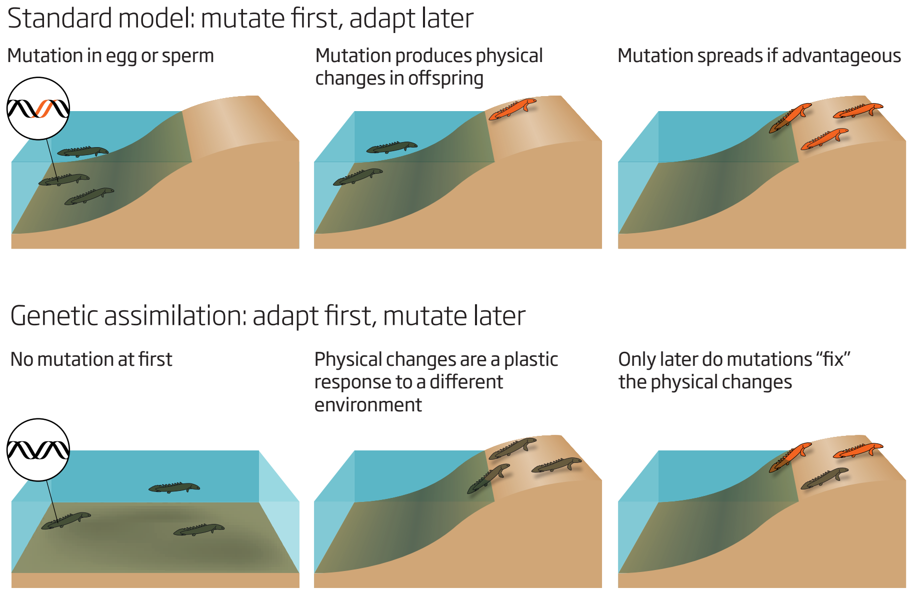
Today, it seems positively inspired. The bichirs did far more than just survive. They became better at "walking". They planted their fins closer to their bodies, lifted their heads higher off the ground and slipped less than fish raised in water. Even more remarkably, their skeletons changed too. Their "shoulder" bones lengthened and developed stronger contacts with the fin bones, making the fish better at press-ups. The bone attachments to the skull also weakened, allowing the head to move more. These features are uncannily reminiscent of those that occurred as our four-legged ancestors evolved from *Tiktaalik*-like forebears.

What is really amazing about this experiment is that these changes did not come about after raising generations of fish on land and allowing only the best walkers to breed. Instead, it happened within the lifetime of individual fish. Simply forcing young fish to live on land for eight months was all it took to produce these quite dramatic changes.

We have long known that our muscles, sinews and bones adapt to cope with whatever we make them do. A growing number of biologists think this kind of plasticity may also play a key role in evolution. Instead of mutating first and adapting later, they argue, animals often adapt first and mutate later. Experiments like Standen's suggest this process could even play a role in major evolutionary transitions such as fish taking to land and apes starting to walk upright.

The idea that plasticity plays a role in evolution goes back more than a century. Some early biologists thought that characteristics acquired during an animal's lifetime could be inherited by their offspring: giraffes got their long necks by stretching to eat leaves, and so on. The French naturalist Jean-Baptiste Lamarck is the best-known advocate of this idea, but Darwin believed something similar. He even proposed an elaborate mechanism to explain how information about changes in the body could reach eggs and sperm, and therefore be passed on to offspring. In this way, Darwin suggested, plasticity produces the heritable ›

Evolving without evolving



variations on which natural selection can work its magic.

With the rise of modern genetics, such notions were dismissed. It became clear that there is no way for information about what animals do during their lifetime to be passed on to their offspring (although a few exceptions have emerged since). And it was thought this meant plasticity has no role in evolution.

Instead, the focus shifted to mutations. By the 1940s, the standard thinking was that animals mutate first and adapt later. A mutation in a sperm cell, say, might produce a physical change in the bodies of some offspring. If the change is beneficial, the mutation will spread through the population. In other words, random genetic mutations generate the variation on which natural selection acts. This remains the dominant view of evolution today.

The dramatic effects of plasticity were not entirely ignored. In the 1940s, for instance, the Dutch zoologist Everhard Johannes Slijper studied a goat that had been born without forelegs and learned to hop around, kangaroo-like, on its rear legs. When Slijper examined the goat after its death, he discovered that the shape of its muscles and skeleton looked more like those of a biped than a quadruped.

Few biologists considered such findings relevant to the evolutionary process. The fact that changes acquired during an animal's lifetime are transient seemed to rule out that possibility. If Standen's better-at-walking fish were bred and the offspring raised in a normal aquarium, for instance, they should look and behave like perfectly ordinary bichirs.

Transient response

But what if the environmental conditions that induce the plastic response are themselves permanent? In the wild, this could happen as a result of alterations in prey animals, or in the climate, for instance. Then all the members of a population would develop in the same, consistent way down the generations. It would look as if the population had evolved in response to an altered environment, but technically it's not evolution because there is no heritable change. The thing is, the only way to tell would be to "test" individuals by raising them in different circumstances.

In this way at least, plasticity can allow animals to "evolve" without evolving. The crucial question, of course, is whether it can lead to actual evolution, in the sense of heritable changes. "You can plastically induce generation after generation," says Standen, who is now at the University of Ottawa in Ontario, Canada. "At some point, can you remove the environmental conditions that induced the change and have the organisms remain changed?"

The answer, surprisingly, seems to be yes. In the 1950s, British biologist Conrad Hal Waddington showed that it is feasible in an experiment involving fruit flies. Waddington found that when pupa are briefly heated, some offspring develop without crossveins in their wings. He then selected and bred those flies. By the 14th generation, some lacked crossveins even when their pupa were not heated. A physical feature that began as a plastic response to an environmental trigger had become a hereditary feature.

How is this possible? Plastic changes occur because an environmental trigger affects a developmental pathway in some way. More of a certain hormone may be produced, or produced at a different time, or genes are switched on that normally remain inactive, and so on. The thing is, random mutations can also have similar effects. So in an environment in which a particular plastic response is crucial for survival, only mutations that reinforce this response, or at least do not impede it, can spread through a population. Eventually, the altered developmental pathway will become so firmly stabilised by a genetic

No coincidence

Can plasticity explain why evolution repeats itself?

During the last ice age, great ice sheets covered much of Eurasia and North America. As they retreated, they left behind lakes and rivers with no native fish.

Marine three-spined sticklebacks were quick to take advantage, repeatedly colonising these new environments and evolving into the freshwater sticklebacks found today (pictured right). What's extraordinary, though, is that freshwater species that evolved entirely independently of each other are often strikingly similar in body shape, and so on.

This is far from the only example. The cichlid fish of Africa's lakes, for instance, have also evolved along parallel lines in many cases.

The standard explanation for this is convergent evolution: even though

scaffolding that it will occur even without the environmental trigger, making it a permanent hereditary feature.

Waddington called this process genetic assimilation. It may sound like Lamarckism, but it is not. The acquired characteristics don't shape the genetic changes directly as Darwin proposed, they merely allow animals to thrive in environments that favour certain mutations when they occur by chance.

Waddington's findings have been regarded as a curiosity rather than a crucial insight. But in the past decade or two, attitudes have begun to change. One reason for this is a growing appreciation of the flexibility of genes. Rather than being rigidly preprogrammed, we now know that the environment influences many aspects of animals' bodies and behaviour.

Such discoveries have led some biologists to claim that developmental plasticity plays a major role in evolution. A few, such as Kevin Laland at the University of St Andrews, UK, even argue that the conventional "mutate first, adapt later" picture of evolution needs a rethink (*Nature*, vol 514, p 161). Most biologists have yet to be convinced.

The sceptics point out that genetic assimilation does not overturn any fundamental principles of evolution – in the long run, evolution is all about the spread of mutations, whether or not plasticity is involved. Yes, say the proponents of plasticity,

"The 'bipedal' mice had features like those in our hominin ancestors"

but the key point is that plasticity can determine which mutations spread (*New Scientist*, 12 October 2013, p 33), so its role should be given the prominence it deserves. "Several major recent evolutionary textbooks do not even mention plasticity," says Laland.

It may play a role occasionally, respond the sceptics, but it's a minor one at best. "There is little debate that genetic assimilation can happen," says Gregory Wray of Duke University in Durham, North Carolina. "But there is unfortunately very little support for its role in nature." This is what makes Standen's work on the bichir so significant. It implicates plasticity in a major evolutionary transition: fish turning into four-legged land animals (*Nature*, vol 513, p 54).

Plasticity will soon be implicated in another major transition too – the one our ancestors made from four legs to two about 7 million years ago. Adam Foster, now at the Northeast Ohio Medical University in Rootstown, has been making mice walk on a treadmill. "I had a custom harness system built so I could modify the load experienced by the hind limbs," he says. Some mice had to walk on their hind limbs, while others walked on all fours. Each mouse exercised on the treadmill for an hour a day for three months, and then Foster examined their skeletons.

He found that the "bipedal" mice had developed longer legs than standard quadrupedal mice, and that their thigh bones had larger femoral heads – the ball in ›

mutations are random, similar environments produce similar evolutionary results. And there is some evidence to support this view, for instance when it comes to the loss of armour plates in freshwater stickleback species (*New Scientist,* 2 April 2011, p 32).

Strikingly similar

But Mary Jane West-Eberhard of the Smithsonian Tropical Research Institute in Costa Rica thinks parallel evolution happens too often for convergence to be the full explanation. In her 2003 book *Environmental Plasticity and Evolution,* she argues that it happens because similar conditions produce a similar plastic response in the ancestral species. Natural selection then reinforces those trajectories.

If West-Eberhard is right, then at least some of the heritable characteristics seen in living animals originated from the plastic changes that occurred as their ancestors moved into new environments. And this is actually a testable prediction when it comes to freshwater sticklebacks; marine three-spined sticklebacks are still around, and have changed little since the ice age.

So Matthew Wund at The College of New Jersey in Ewing decided to put West-Eberhard's ideas to the test. With colleagues at Clark University in Worcester, Massachusetts, he set out to discover whether simply allowing marine sticklebacks to eat a diet similar to those of their freshwater cousins as they grew up would lead them to develop similar body shapes too. And it did.

Marine fish raised on planktonic invertebrates from the upper water of deep lakes developed the long snouts of sticklebacks living in lake surface waters. In contrast, marine fish given large invertebrates found at the bottom of shallow lakes developed the stubby snouts typical of sticklebacks that live there (*The American Naturalist,* vol 172, p 449).

"We subsequently expanded the experiment to consider not only dietary differences but also habitat," says Wund. The results of those experiments, published a couple of years ago, also support the idea that developmental plasticity shaped the evolution of sticklebacks as they invaded the lakes left by the retreating ice sheets.

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the hip joint. Both features are associated with the transition to bipedalism in our hominin ancestors. Foster's results will be published later this year. "I think Adam's research is really compelling," says Jesse Young, an anatomist at Northeast Ohio Medical University. "As he was getting it going, I was a bit sceptical. You couldn't predict it would reveal anything useful."

While the work of Standen and Foster suggests that developmental plasticity could play a role in major evolutionary transitions, it is only suggestive. Indeed, these studies do not even show that the plastic changes seen in the bichir fish and mice can be fixed by mutations. Demonstrating this kind of genetic assimilation would certainly be tricky, says Standen. It would not be practical with the bichir fish she studied. "As wonderful as they are, they're frustrating fish," says Standen. "They take the better part of a decade to mature, and even then they're really difficult to breed in captivity."

The fossil record is usually no help either. It is possible that some of the changes seen as fish colonised the land were a result of plasticity rather than genetics, says Per Ahlberg of the University of Uppsala in Sweden who studies the transition to land. For Ahlberg, the trouble is that there is no way to prove it. "There's no evidence that will allow us to choose between the two," he says.


TOBIAS BERNHARD/GETTY

Fiddler crabs can take either side in the debate about the role of plasticity

More evolvable

Other biologists are more enthusiastic. It has long been suggested that different parts of the skeleton are more plastic and "evolvable" than others, says William Harcourt-Smith of the American Museum of Natural History. "So a foot bone or a hand bone might give you more useful info than a hip bone, for instance."

Work like Foster's could reveal if this is indeed the case and help us interpret the fossil record of human evolution. "These experiments do have validity," Harcourt-Smith says. "They can help us understand whether traits are plastic or not."

Take the honeycomb structure in the heads of our long bones. It is lighter and weaker than it was in our extinct cousins such as the Neanderthals. A study out last month compared the bones of hunter-gatherers and early farmers in North America. It concluded that our bones became weak only when our ancestors' lifestyles changed (*PNAS*, doi.org/xwq). "We could have a skeleton as strong as our prehistoric ancestors," says team member Colin Shaw of the University of Cambridge, UK. "We just don't because we're not as active."

It's possible that similar kinds of skeletal structural change seen in prehistory have been misinterpreted as signs of speciation when they really just reflect developmental plasticity, says Shaw – perhaps especially so in hominin evolution. Humans are unique, he points out. "Our first line of defence against environmental insult is culture. When that's not adequate – for instance if the clothing you can make is not good enough to keep you warm – then arguably the second line of defence is plasticity. Only after that fails might you actually get genetic selection."

All this still leaves open the question of whether genetic assimilation can "fix" traits that first appear as a result of plasticity. A decade ago, Richard Palmer at the University of Alberta in Edmonton, Canada, found a way to search for evidence in the fossil record. Most animals have some asymmetric traits. In our case, it's the position of the heart and other organs, which is encoded in our genes. But in other species, asymmetries are plastic. For instance, the enlarged claw of male fiddler crabs (pictured above) is as likely to be on the left as on the right.

What Palmer showed by examining the fossil record of asymmetry in 68 plant and animal species is that on 28 occasions, asymmetries that are now hereditary and appear only on one side started out as non-hereditary asymmetries that appeared on either side (*Science*, vol 306, p 828). "I think it's one of the clearest demonstrations that genetic assimilation has happened and that it is more common than expected," says Palmer.

There is a caveat here, though. The ancestral non-hereditary asymmetries may have been a result of random genetic noise, says Palmer. So while his work does show genetic assimilation in action, it was not necessarily fixing traits due to developmental plasticity.

There is no simple way to prove the evolutionary importance of developmental plasticity, says Mary Jane West-Eberhard of the Smithsonian Tropical Research Institute in Costa Rica, whose work has been particularly influential. "Evolutionary biology that is concerned with evolution and speciation in nature necessarily depends on indirect proof – an accumulation of facts that support or deny a hypothesis," she says.

At the moment, the facts that are accumulating seem to support the hypothesis. Expect lots more results soon: Standen's success is inspiring others. "I've already had people ask me what other critters we could try this on," says Standen. "Everybody is friendly and excited and interested. It's fun – it's the way science should be." ■

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