15 EVOLUTIONARY GEMS

A resource from *Nature* for those wishing to spread awareness of evidence for evolution by natural selection.

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Most biologists take for granted the idea that all life evolved by natural selection over billions of years. They get on with researching and teaching in disciplines that rest squarely on that foundation, secure in the knowledge that natural selection is a fact, in the same way that the Earth orbits the Sun is a fact.

Given that the concepts and realities of Darwinian evolution are still challenged, albeit rarely by biologists, a succinct briefing on why evolution by natural selection is an empirically validated principle is useful for people to have to hand. We offer here 15 examples published by *Nature* over the past decade or so to illustrate the breadth, depth and power of evolutionary thinking. We are happy to offer this resource freely and encourage its free dissemination.

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GEMS FROM THE FOSSIL RECORD

1 Land-living ancestors of whales

Fossils offer crucial clues for evolution, because they reveal the often remarkable forms of creatures long vanished from Earth. Some of them even document evolution in action, recording creatures moving from one environment to another.

Whales, for example, are beautifully adapted to life in water, and have been for millions of years. But, like us, they are mammals. They breathe air, and give birth to and suckle live young. Yet there is good evidence that mammals originally evolved on land. If that is so, then the ancestors of whales must have taken to the water at some point.

As it happens, we have numerous fossils from the first ten million years or so of whale evolution. These include several fossils of aquatic creatures such as *Ambulocetus* and *Pakicetus*, which have characteristics now seen only in whales — especially in their ear anatomy — but also have limbs like those of the land-living mammals from which they are clearly derived. Technically, these hybrid creatures were already whales. What was missing was the start of the story: the land-living creatures from which whales eventually evolved.

Work published in 2007 might have pinpointed that group. Called raoellids, these now-extinct creatures would have looked like very small dogs, but were more closely related to even-toed ungulates — the group that includes modern-day cows, sheep, deer, pigs and hippos. Molecular evidence had also suggested that whales and even-toed ungulates share a deep evolutionary connection.

The detailed study, by Hans Thewissen at Northeastern Ohio Universities Colleges of Medicine and Pharmacy in Rootstown and his colleagues, shows that one raoellid, *Indohyus*, is similar to whales, but unlike other even-toed ungulates in the structure of its ears and teeth, the thickness of its bones and the chemical composition of its teeth. These indicators suggest that this raccoon-sized creature spent much of its time in water. Typical raoellids, however, had a diet nothing like those of whales, suggesting that the spur to take to the water may have been dietary change.

This study demonstrates the existence of potential transition forms in the fossil record. Many other examples could have been highlighted, and there is every reason to think that many others await discovery, especially in groups that are well represented in the fossil record.

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GEMS FROM THE FOSSIL RECORD

2 From water to land

The animals we are most familiar with are tetrapods — they are vertebrates (they have backbones) and they live on land. That includes humans, almost all domestic animals and most of the wild ones that any child would recognize: mammals, birds, amphibians and reptiles. The vast majority of vertebrates, however, are not tetrapods, but fish. There are more kinds of fish, in fact, than all the species of tetrapods combined. Indeed, through the lens of evolution, tetrapods are just one branch of the fish family tree, the members of which just happen to be adapted for life out of water.

The first transition from water to land took place more than 360 million years ago. It was one of the most demanding such moves ever made in the history of life. How did fins become legs? And how did the transitional creatures cope with the formidable demands of land life, from a desiccating environment to the crushing burden of gravity?

It used to be thought that the first landlubbers were stranded fish that evolved to spend more and more time ashore, returning to water to reproduce. Over the past 20 years, palaeontologists have uncovered fossils that have turned this idea upside down. The earliest tetrapods, such as *Acanthostega* from eastern Greenland around 365 million years ago, had fully formed legs, with toes, but retained internal gills that would soon have dried out in any long stint in air. Fish evolved legs long before they came on land. The earliest tetrapods did most of their evolving in the more forgiving aquatic environment. Coming ashore seems to have been the very last stage.

Researchers suspect that the ancestors of tetrapods were creatures called elpistostegids. These very large, carnivorous, shallow-water fish would have looked and behaved much like alligators, or giant salamanders. They looked like tetrapods in many respects, except that they still had fins. Until recently, elpistostegids were known only from small fragments of fossils that were poorly preserved, so it has been hard to get a rounded picture of what they were like.

In the past couple of years, several discoveries from Ellesmere Island in the Nunavut region of northern Canada have changed all that. In 2006, Edward Daeschler and his colleagues described spectacularly well-preserved fossils of an elpistostegid known as *Tiktaalik* that allow us to build up a good picture of an aquatic predator with distinct similarities to tetrapods — from its flexible neck, to its very limb-like fin structure.

The discovery and painstaking analysis of *Tiktaalik* illuminates the stage before tetrapods evolved, and shows how the fossil record throws up surprises, albeit ones that are entirely compatible with evolutionary thinking.

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GEMS FROM THE FOSSIL RECORD

3 The origin of feathers

One of the objections to Charles Darwin's theory of evolution was the lack of 'transitional forms' in the fossil record — forms that illustrated evolution in action, from one major group of animals to another. However, hardly a year after the publication of *On the Origin of Species*, an isolated feather was discovered in Late Jurassic (about 150 million years old) lithographic limestones of Solnhofen in Bavaria, followed in 1861 by the first fossil of *Archaeopteryx*, a creature with many primitive, reptilian features such as teeth and a long, bony tail — but with wings and flight feathers, just like a bird.

Although *Archaeopteryx* is commonly seen as the earliest known bird, many suspected that it was better seen as a dinosaur, albeit one with feathers. Thomas Henry Huxley, Darwin's colleague and friend, discussed the possible evolutionary link between dinosaurs and birds, and palaeontologists speculated, if wildly, that dinosaurs with feathers might one day be found.

In the 1980s, deposits from the early Cretaceous period (about 125 million years ago) in the Liaoning Province in northern China vindicated these speculations in the most dramatic fashion, with discoveries of primitive birds in abundance — alongside dinosaurs with feathers, and feather-like plumage. Starting with the discovery of the small theropod *Sinosauropteryx* by Pei-ji Chen from China's Nanjing Institute of Geology and Palaeontology and his colleagues, a variety of feather-clad forms have been found. Many of these feathered dinosaurs could not possibly have flown, showing that feathers first evolved for reasons other than flight, possibly for sexual display or thermal insulation, for instance. In 2008, Fucheng Zhang and his colleagues from the Chinese Academy of Sciences in Beijing announced the bizarre creature *Epidexipteryx*, a small dinosaur clad in downy plumage, and sporting four long plumes from its tail. Palaeontologists are now beginning to think that their speculations weren't nearly wild enough, and that feathers were indeed quite common in dinosaurs.

The discovery of feathered dinosaurs not only vindicated the idea of transitional forms, but also showed that evolution has a way of coming up with a dazzling variety of solutions when we had no idea that there were even problems. Flight could have been no more than an additional opportunity that presented itself to creatures already clothed in feathers.

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GEMS FROM THE FOSSIL RECORD

4 The evolutionary history of teeth

One motivation in the study of development is the discovery of mechanisms that guide evolutionary change. Kathryn Kavanagh at the University of Helsinki and her colleagues investigated just this by looking at the mechanisms behind the relative size and number of molar teeth in mice. The research, published in 2007, uncovered the pattern of gene expression that governs the development of teeth — molars emerge from the front backwards, with each tooth smaller than the last.

The beauty of the study lies in its application. Their model predicts the dentition patterns found in mouse-like rodent species with various diets, providing an example of ecologically driven evolution along a developmentally favoured trajectory. In general, the work shows how the pattern of gene expression can be modified during evolution to produce adaptive changes in natural systems.

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GEMS FROM THE FOSSIL RECORD

5 The origin of the vertebrate skeleton

We owe much of what makes us human to remarkable tissue, found only in embryos, called the neural crest. Neural-crest cells emerge in the developing spinal cord and migrate all over the body, effecting a remarkable series of transformations. Without the neural crest, we would not have most of the bones in our face and neck, or many of the features of our skin and sensory organs. The neural crest seems to be unique to vertebrates, and helps to explain why vertebrates have distinctive 'heads' and 'faces'.

Untangling the evolutionary history of the neural crest is especially hard in fossil forms, as embryonic data are obviously absent. One key mystery, for example, is how much of the vertebrate skull is contributed by neural-crest cells and how much comes from deeper layers of tissue.

New techniques have allowed researchers to label and follow individual cells as embryos develop. They have revealed the boundaries of the bone derived from the neural crest, down to the single-cell level, in the neck and shoulders. Tissue derived from the neural crest anchors the head onto the front lining of the shoulder girdle, whereas the skeleton forming the back of the neck and shoulder grows from a deeper layer of tissue called the mesoderm.

Such detailed mapping, in living animals, casts light on the evolution of structures in the heads and necks of animals long extinct, even without fossilized soft tissue such as skin and muscle. Skeletal similarities that result from a shared evolutionary history can be identified from muscle attachments. This allows the tracing of, for example, the location of the major shoulder bone of extinct land vertebrate ancestors, the cleithrum. This bone seems to survive as part of the shoulder blade (scapula) in living mammals.

This kind of evolutionary scan may have immediate clinical relevance. The parts of the skeleton identified by Toshiyuki Matsuoka from the Wolfson Institute for Biomedical Research in London and his colleagues as being derived from the neural crest are specifically affected in several developmental disorders in humans, providing insights into their origins.

Matsuoka's study shows how a detailed analysis of the morphology of living animals, informed by evolutionary thinking, helps researchers to interpret fossilized and now-extinct forms.

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GEMS FROM HABITATS

6 Natural selection in speciation

Evolutionary theory predicts that divergent natural selection will often have a key role in speciation. Working with sticklebacks (*Gasterosteus aculeatus*), Jeffrey McKinnon at the University of Wisconsin in Whitewater and his colleagues reported in 2004 that reproductive isolation can evolve as a by-product of selection on body size. This work provides a link between the build-up of reproductive isolation and the divergence of an ecologically important trait.

The study was done on an extraordinary geographical scale, involving mating trials between fish taken in Alaska, British Columbia, Iceland, the United Kingdom, Norway and Japan. It was underpinned by molecular genetic analyses that provided firm evidence that fish that have adapted to living in streams had evolved repeatedly from marine ancestors, or from fish that live in the ocean but return to fresh water to spawn. Such migratory populations in the study had larger bodies on average than did those living in streams. Individuals tended to mate with fish of a similar size, which accounts well for the reproductive isolation between different stream ecotypes and their close, seafaring neighbours.

Taking into account the evolutionary relationships, a comparison of the various types of stickleback, whether stream or marine, strongly supports the view that adaptation to different environments brings about reproductive isolation. The researchers' experiments also confirmed the connection between size divergence and the build-up of reproductive isolation — although traits other than size also contribute to reproductive isolation to some extent.

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GEMS FROM HABITATS

7 Natural selection in lizards

A popular evolutionary hypothesis is that behavioural shifts in new environments negate the effects of natural selection. But work by Harvard University's Jonathan Losos and his colleagues in 2003 lends little support to this theory. The researchers introduced the large ground-dwelling predatory lizard *Leiocephalus carinatus* to six small islands in the Bahamas, with six other islands serving as controls. They found that the lizard's prey, a smaller lizard called *Anolis sagrei,* spent more time higher up in the vegetation on islands occupied by the larger predator than they did on the islands where *L. carinatus* was absent. But mortality in *A. sagrei* was still much higher on the experimental islands than on control islands.

The presence of the larger predator selected for longer-legged male *A. sagrei* lizards, which can run faster, and also favoured larger females, which are both faster and harder to subdue and ingest. The researchers did not detect any selection on size in males; they suggested that the larger males may have been more vulnerable because of their conspicuous territorial behaviour.

The study shows how the introduction of a predator can cause individuals of a prey species to change their behaviour so as to reduce the risk of predation, but also cause an evolutionary response at the level of the population that differs between the sexes according to their ecology.

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GEMS FROM HABITATS

8 A case of co-evolution

Species evolve together, and in competition. Predators evolve ever deadlier weapons and skills to catch prey, which, as a result of Darwin's canonical 'struggle for existence', become better at escaping them, and so the arms race continues. In 1973, evolutionary biologist Leigh Van Valen likened this to the Red Queen's comment to Alice in Lewis Carroll's *Through the Looking Glass*, "it takes all the running you can do, to keep in the same place. If you want to get somewhere else, you must run at least twice as fast as that!" The 'Red Queen' hypothesis of co-evolution was born.

A problem with studying Red-Queen dynamics is that they can be seen only in the eternal present. Discovering their history is problematic, because evolution has generally obliterated all earlier stages.

Happily, Ellen Decaestecker from the Catholic University of Leuven in Belgium and her colleagues discovered a remarkable exception, in the co-evolutionary arms race between water fleas (*Daphnia*) and the microscopic parasites that infest them; their research was published in 2007. As the water fleas become better at evading parasitism, the parasites become better at infecting them. Both prey and predator in this system can persist in dormant stages for many years in the mud at the bottom of the lake they share. The sediments of the lake can be dated to the year they were formed, and the buried predators and prey can be revived. Thus, their interactions can be tested, against one another, and against predators or prey from their relative pasts and futures.

Confirming theoretical expectations, the parasite adapted to its host over a period of only a few years. Its infectivity at any given time changed little, but its virulence and fitness rose steadily — matched at each stage by the ability of the water fleas to resist them.

This study provides an elegant example in which a high-resolution historical record of the co-evolutionary process has provided an affirmation of evolutionary theory, showing that the interaction of parasites and their hosts is not set in time but is instead the result of a dynamic arms race of adaptation and counter-adaptation, driven by natural selection, from generation to generation.

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GEMS FROM HABITATS

9 Differential dispersal in wild birds

Gene flow caused, for instance, by migration, can disrupt adaptation to local conditions and oppose evolutionary differentiation within and between populations. Indeed, classical population genetics theory suggests that the more that local populations migrate and interbreed, the more genetically similar they will be. This concept seems to accord with common sense, and it assumes that gene flow is a random process, like diffusion. But non-random dispersal can actually favour local adaptation and evolutionary differentiation, as Ben Sheldon of the Edward Grey Institute of Field Ornithology in Oxford, UK, and his colleagues reported in 2005.

Their work was part of a multi-decade study of the great tits (*Parus major*) that inhabit a wood in Oxfordshire, UK. The researchers found that the amount and type of genetic variation in nestling weight in this songbird differs from one part of the wood to another. This pattern of variation leads to varying responses to selection in different parts of the wood, leading to local adaptation. The effect is reinforced by non-random dispersal; individual birds select and breed in different habitats in a way that increases their fitness. The authors conclude that "when gene flow is not homogeneous, evolutionary differentiation can be rapid and can occur over surprisingly small spatial scales".

In another study of great tits on the island of Vlieland in the Netherlands, published in the same issue of *Nature*, Erik Postma and Arie van Noordwijk from the Netherlands Institute of Ecology in Heteren found that gene flow, mediated by non-random dispersal, maintains a large genetic difference in clutch size at a small spatial scale, again illustrating, as these scientists put it, "the large effect of immigration on the evolution of local adaptations and on genetic population structure".

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GEMS FROM HABITATS

10 Selective survival in wild guppies

Natural selection favours traits that increase fitness. Over time, such selection might be expected to exhaust genetic variation by driving advantageous genetic variants to fixation at the expense of less advantageous or deleterious variants. In fact, natural populations often show large amounts of genetic variation. So how is it maintained?

An example is the genetic polymorphism seen in the colour patterns of male guppies (*Poecilia reticulata*). As reported in 2006, Kimberly Hughes from the University of Illinois at Urbana-Champaign and her colleagues manipulated the frequencies of males with different colour patterns in three wild guppy populations in Trinidad. They showed that rare variants have much higher survival rates than more common ones. In essence, variants are favoured when rare, and selected against when common.

Such 'frequency-dependent' survival, in which selection favours rare types, has been implicated in the maintenance of molecular, morphological and health-related polymorphisms in humans and other mammals.

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GEMS FROM HABITATS

11 Evolutionary history matters

Evolution is often thought to be about finding optimal solutions to the problems that life throws up. But natural selection can only work with the materials at hand — materials that are themselves the results of many millions of years of evolutionary history. It never starts with a blank slate. If that were the case, then tetrapods faced with the task of moving on land would not have had their fins transform into legs; they might perhaps have evolved wheels.

A real-life case of the ingenuity of adaptation concerns a moray eel (*Muraena retifera*), a long, snake-like reef predator. Historically, bony fish use suction to catch their prey. A fish approaching food opens its mouth wide to create a large cavity into which prey and water flood. As the excess water leaves through the gills, the fish sucks the prey down into its throat and pharyngeal jaws, a second set of jaws and teeth derived from the skeleton that supports the gills. But morays have a problem because of their elongated, narrow shape. Even with their jaws agape, their mouth cavity is too small to generate enough suction to carry prey to their pharyngeal jaws. The solution to this conundrum was documented in 2007.

Through careful observation and X-ray cinematography, Rita Mehta and Peter Wainwright from the University of California, Davis, discovered evolution's breathtaking solution. Rather than prey coming to the pharyngeal jaws, the pharyngeal jaws move forwards into the mouth cavity, trapping the prey and dragging it backwards. This, the researchers say, is the first described case of a vertebrate using a second set of jaws to both restrain and transport prey, and is the only known alternative to the hydraulic prey transport reported in most bony fish — a major innovation that could have contributed to the success of moray eels as predators.

The mechanics of the moray's pharyngeal jaws are reminiscent of the ratchet mechanisms used by snakes — also long, thin and highly predatory creatures. This is an instance of convergence, the evolutionary phenomenon in which distantly related creatures evolve similar solutions to common problems.

This study demonstrates the contingent nature of evolution; as a process it does not have the luxury of 'designing from scratch'.

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GEMS FROM MOLECULAR PROCESSES

12 Darwin's Galapagos finches

When Charles Darwin visited the Galapagos Islands, he recorded the presence of several species of finch that all looked very similar except for their beaks. Ground finches have deep and wide beaks; cactus finches have long, pointed beaks; and warbler finches have slender, pointed beaks, reflecting differences in their respective diets. Darwin speculated that all the finches had a common ancestor that had migrated to the islands. Close relatives of the Galapagos finches are known from the South American mainland, and the case of Darwin's finches has since become the classic example of how natural selection has led to the evolution of a variety of forms adapted to different ecological niches from a common ancestral species — termed 'adaptive radiation'. This idea has since been reinforced by data showing that even small differences in the depth, width or length of the beak can have major consequences for the overall fitness of birds.

To find out what genetic mechanisms underlie the changes in beak shape that mark each species, Harvard University's Arhat Abzhanov and his colleagues examined numerous genes that are switched on in the developing beaks of finch chicks; their study was published in 2006. The researchers discovered that shape differences coincide with differing expression of the gene for calmodulin, a molecule involved in calcium signalling that is vital in many aspects of development and metabolism. Calmodulin is expressed more strongly in the long and pointed beaks of cactus finches than in the more robust beaks of other species. Artificially boosting the expression of calmodulin in the embryonic tissues that give rise to the beak causes an elongation of the upper beak, similar to that seen in cactus finches. The results show that at least some of the variation in beak shape in Darwin's finches is likely to be related to variation in calmodulin activity, and implicates calmodulin in the development of craniofacial skeletal structures more generally.

The study shows how biologists are going beyond the mere documentation of evolutionary change to identify the underlying molecular mechanisms.

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GEMS FROM MOLECULAR PROCESSES

13 Microevolution meets macroevolution

Darwin conceived of evolutionary change as happening in infinitesimally small steps. He called these 'insensible gradations', which, if extrapolated over long periods of time, would result in wholesale changes of form and function. There is a mountain of evidence for such small changes, called microevolution — the evolution of drug resistance, for instance, is just one of many documented examples.

We can infer from the fossil record that larger species-to-species changes, or macroevolution, also occur, but they are naturally harder to observe in action. That said, the mechanisms of macroevolution can be seen in the here-and-now, in the architecture of genes. Sometimes genes involved in the day-to-day lives of organisms are connected to, or are even the same as, those that govern major features of animal shape and development. So everyday evolution can have large effects.

Sean Carroll from the Howard Hughes Medical Institute in Chevy Chase, Maryland, and his colleagues looked at a molecular mechanism that contributes to the gain of a single spot on the wings of male flies of the species *Drosophila biarmipes*; they reported their findings in 2005. The researchers showed that the evolution of this spot is connected with modifications of an ancestral regulatory element of a gene involved in pigmentation. This regulatory element has, over time, acquired binding sites for transcription factors that are ancient components of wing development. One of the transcription factors that binds specifically to the regulatory element of the yellow gene is encoded by *engrailed*, a gene fundamental to development as a whole.

This shows that a gene involved in one process can be co-opted for another, in principle driving macroevolutionary change.

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GEMS FROM MOLECULAR PROCESSES

14 Toxin resistance in snakes and clams

Biologists are increasingly coming to understand the molecular mechanisms that underlie adaptive evolutionary change. In some populations of the newt *Taricha granulosa*, for example, individuals accumulate the nerve poison tetrodotoxin in their skin, apparently as a defence against garter snakes (*Thamnophis sirtalis*). Garter snakes that prey on the newts that produce tetrodotoxin have evolved resistance to the toxin. Through painstaking work, Shana Geffeney at the Stanford School of Medicine in California and her colleagues uncovered the underlying mechanism; their study was published in 2005. Variation in the level of resistance of garter snakes to their newt prey can be traced to molecular changes that affect the binding of tetrodotoxin to a particular sodium channel.

Similar selection for toxin resistance apparently occurs in softshell clams (*Mya arenaria*) in areas of the North American Atlantic coast, as reported by Monica Bricelj at the Institute for Marine Biosciences in Nova Scotia, Canada, and her colleagues in the same issue of *Nature*. The algae that produce 'red tides' generate saxitoxin — the cause of paralytic shellfish poisoning in humans. Clams are exposed to the toxin when they ingest the algae. Clams from areas subject to recurrent red tides are relatively resistant to the toxin and accumulate it in their tissues. Clams from unaffected areas have not evolved such resistance.

Resistance to the toxin in the exposed populations is correlated with a single mutation in the gene that encodes a sodium channel, at a site already implicated in the binding of saxitoxin. It seems likely, therefore, that the saxitoxin acts as a potent selective agent in the clams and leads to genetic adaptation.

These two studies show how similar selective pressures can lead to similar adaptive responses even in very different taxa.

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GEMS FROM MOLECULAR PROCESSES

15 Variation versus stability

Species can remain mostly unchanged for millions of years, long enough for us to pick up their traces in the fossil record. But they change, too, and often very suddenly. This has led some to wonder whether species — usually those developing along specific tracks — store the potential for sudden change under the hood, unleashing a flood of otherwise hidden variation at times of environmental stress — variation on which selection can act.

This idea of such 'evolutionary capacitance' was first mooted by Suzanne Rutherford and Susan Lindquist in startling experiments on fruitflies. Their idea was that key proteins involved in the regulation of developmental processes are 'chaperoned' by a protein called Hsp90 that is produced more at times of stress. On occasion, Hsp90 is overwhelmed by other processes and the proteins it normally regulates are left to run free, producing a welter of otherwise hidden variation.

Aviv Bergman from the Albert Einstein College of Medicine in New York and Mark Siegal at New York University explored whether evolutionary capacitance is particular to Hsp90 or found more generally; their study was published in 2003. They used numerical simulations of complex gene networks and genome-wide expression data from yeast strains in which single genes had been deleted. They showed that most, and perhaps all, genes hold variation in reserve that is released only when they are functionally compromised. In other words, it looks as if evolutionary capacitance might go wider and deeper than Hsp90.

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