A Theory Evolves

How evolution really works, and why it matters more than ever

BY THOMAS HAYDEN

When scientists introduced the world to humankind's earliest known ancestor two weeks ago, they showed us more than a mere museum piece. Peering at the 7 million-year-old skull is almost like seeing a reflection of our earlier selves. And yet that fossil represents only a recent chapter in a grander story, beginning with the first single-celled life that arose and began evolving some 3.8 billion years ago. Now, as the science of evolution moves beyond guesswork, we are learning something even more remarkable: how that tale unfolded.

Scientists are uncovering the step-by-step changes in form and function that ultimately produced humanity and the diversity of life surrounding us. By now, scientists say, evolution is no longer "just a theory." It's an everyday phenomenon, a fundamental fact of biology as real as hunger and as unavoidable as death.

ILLUSTRATION BY JEFF CROSBY FOR *USN&WR*

Darwin proposed his theory of evolution based on extensive observations and cast-iron logic. Organisms produce more young than can survive, he noted, and when random changes create slight differences between offspring, "natural selection" tends to kill off those that are less well suited to the environment. But Darwin's evidence was fragmentary, and with the science of genetics yet to be invented, he was left without an explanation for how life might actually change.

The "modern synthesis" of genetics and evolutionary theory in the 1940s began to fill that gap. But until recently, much of evolution still felt to nonscientists like abstract theory, often presented in ponderous tomes like paleontologist Stephen Jay Gould's 1,464-page *Structure of Evolutionary Theory,* published shortly before his death this spring. As theorists argued over arcane points and creationists stressed uncertainties to challenge evolution's very reality, many people were left confused, unsure what to believe.

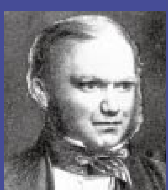
Nuts and bolts. But away from heated debates in schools and legislatures, a new generation of scientists has been systematically probing the fossil record, deciphering genomes, and scrutinizing the details of plant and animal development. They are documenting how evolution actually worked, how it continues to transform our world, and even how we can put it to work to fight disease and analyze the wealth of data from genome-sequencing projects. "The big story," says evolutionary biologist E. O. Wilson of Harvard University, "is not in overarching, top-down theory now, but in the details of research in the lab and in the field."

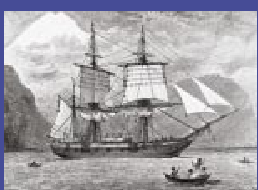
Scientists have confirmed virtually all of Darwin's postulates. For example, Ward Watt of Stanford University has demonstrated natural selection in action. In a hot environment, he found, butterflies with a heat-stable form of a metabolic gene outreproduced their cousins with a form that works well only at lower temperatures. "Darwin was more right than he knew," says Watt. Darwin also held that new species evolve slowly, the result of countless small changes over many generations, and he attributed the lack of transitional forms—missing links—to the spotty nature of the fossil record. By now many gaps have been filled. Dinosaur researchers can join hands with bird experts, for example, their once disparate fields linked by a series of fossils that show dinosaurs evolving feathers and giving rise to modern birds. And last year, paleontologists announced that they had recovered fossils from the hills of Pakistan showing, step by step, how hairy, doglike creatures took to the sea and became the first whales.

But new research also shows that evolution works in ways Darwin did not imagine. Many creatures still appear quite suddenly in the fossil record, and the growing suspicion is that evolution sometimes leaps, rather than crawls. For example, the first complex animals, including worms, mollusks, and shrimplike arthropods, show up some 545 million years ago; paleontologists have searched far and wide

Life of an idea

1831–36 A young Charles Darwin sails aboard the Beagle (below) to Patagonia, Tierra del Fuego, and the Galápagos, making observations that led to his theory.





1859 Darwin publishes *The Origin of Species,* spelling out natural selection as the mechanism behind "descent with modification," or evolution.

1890s Social Darwinism is on the rise, misusing evolutionary ideas to justify the wealth and power of tycoons like Rockefeller and Carnegie.

1896 Henri Becquerel discovers radioactivity, leading to calculations that put Earth's age at billions of years—enough time for Darwinian evolution to work.

1925 John Scopes (left) is tried in Tennessee—and fined $100—for teaching evolution.

1940s The Modern Synthesis of genetics and

MARCH OF TIME. **Paleontologist Whitey Hagadorn in the Mojave Desert, scouting for traces of the first many-celled animals**

for fossil evidence of gradual progress toward these advanced creatures but have come up empty. "Paleontologists have the best eyes in the world," says Whitey Hagadorn of Amherst College, who has scoured the rocks of the Southwest and California for signs of the earliest animal life. "If we can't find the fossils, sometimes you have to think that they just weren't there."

A new understanding of Earth's history helps explain why. Scientists have learned that our planet has been rocked periodically by catastrophes: enormous volcanic eruptions that belched carbon dioxide, creating a super greenhouse effect; severe cold spells that left much of the planet enveloped in ice; collisions with asteroids. These convulsions killed off much of life's diversity. Once conditions improved, says Harvard paleontologist Andy Knoll, the survivors found a world of new opportunities. They were freed to fill new roles, "experimenting" with new body plans and evolving too rapidly to leave a record in the fossils.

We may owe our own dominance to the asteroid impact that killed the dinosaurs 65 million years ago. As mammals, we like to think that we're pretty darned superior. The sad truth: "Mammals coexisted with dinosaurs for 150 million years but were never able to get beyond little ratlike things," says Knoll. "It was only when the dinosaurs were removed that mammals had the ecological freedom to evolve new features."

Whether evolution worked fast or slow, theorists labored to explain how it could produce dramatic changes in body structure through incremental steps. Half an eye would be worse than none at all, creationists were fond of arguing. But "partial" eyes turn out to be common in nature, and biologists can trace eye evolution from the lensless flatworm eyespot to the complex geometry of vertebrate eyes. Now "evo-devo" biologists, who study how fertilized egg cells develop into adults, are discovering powerful new ways evolution can transform organisms. They are finding that changes in a handful of key genes that control development can be enough to drastically reshape an animal.

Master switches. The central discovery of evo-devo is that the development and ultimate shape of animal bodies are orchestrated by a small set of genes called homeotic genes. These regulatory genes make proteins that act as master switches. By binding to DNA, they turn on or shut down other genes that actually make tissues. All but the simplest animals are built in segments (most obvious in creatures like centipedes, but also apparent in human vertebrae), and the Hox family of homeotic genes interacts to determine what each segment will look like. By simple genetic tinkering, evo-devo biologists can tweak the controls, making flies with legs where their antennae should be, or eyeballs on their knees.

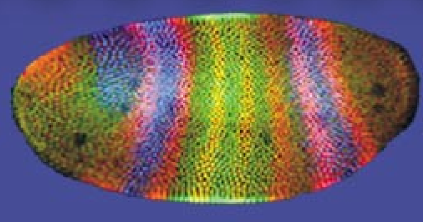
This might seem like little more than a

evolution provides a mechanism for heritable changes.

1975 Sociobiologists stir controversy by suggesting that many human social behaviors, like those in ants, are biological adaptations.

1981 A 65 million-year-old debris layer points to an asteroid impact at the time of the dinosaurs' extinction, confirming the importance of catastrophes in evolution.

1984 Discovery of homeotic genes, which orchestrate embryonic development (bands in the fly embryo at right indicate active genes). Mutations can produce drastic changes in body plan.



1999 Kansas temporarily drops evolution from its high school science curriculum.

TOP: DAVID BUTOW—CORBIS SABA FOR *USN&WR;*
BOTTOM, FROM LEFT: BROWN BROTHERS; CORBIS BETTMANN; BROWN BROTHERS; GERRY ELLIS—MINDEN PICTURES; COURTESY JIM LANGELAND, STEVE PADDOCK, AND SEAN CARROLL

AT THE CONTROLS. **By altering genes that guide embryos' development, biologist Sean Carroll can re-create evolutionary leaps.**

cruel parlor trick, and the resulting monstrosities would never survive in nature. But small changes in these master-switch genes may help explain some major changes in evolutionary history. This past winter, evo-devo biologists showed that an important animal transition 400 million years ago, when many-legged arthropods (think lobsters) gave rise to six-legged insects, was due to just a few mutations in a Hox gene. In the past few months, researchers have found that a change in the regulation of a growth-factor gene could have resulted in the first vertebrate jaw. And, incredibly, researchers reported in the journal *Science* last week that a single mutation in a regulatory gene was enough to produce mice with brains that had an unusually large, wrinkled cerebral cortex resembling our own. (No word, though, on whether the mutant mice gained smarts.)

Some critics of evolution argue that animals are so complex and their parts so interconnected that any change big enough to produce a new species would cause fatal failures. Call it the Microsoft conundrum. But just as Judge Thomas Penfield Jackson managed to delete that company's Web browser on his own computer without crashing the operating system, evo-devo biologists are learning how evolution can tweak one part of an animal while leaving everything else alone. The key to modifying the machine of life while it's running, says biologist Sean Carroll of the University of Wisconsin–Madison, is mutations in the stretches of DNA that homeotic proteins bind to.

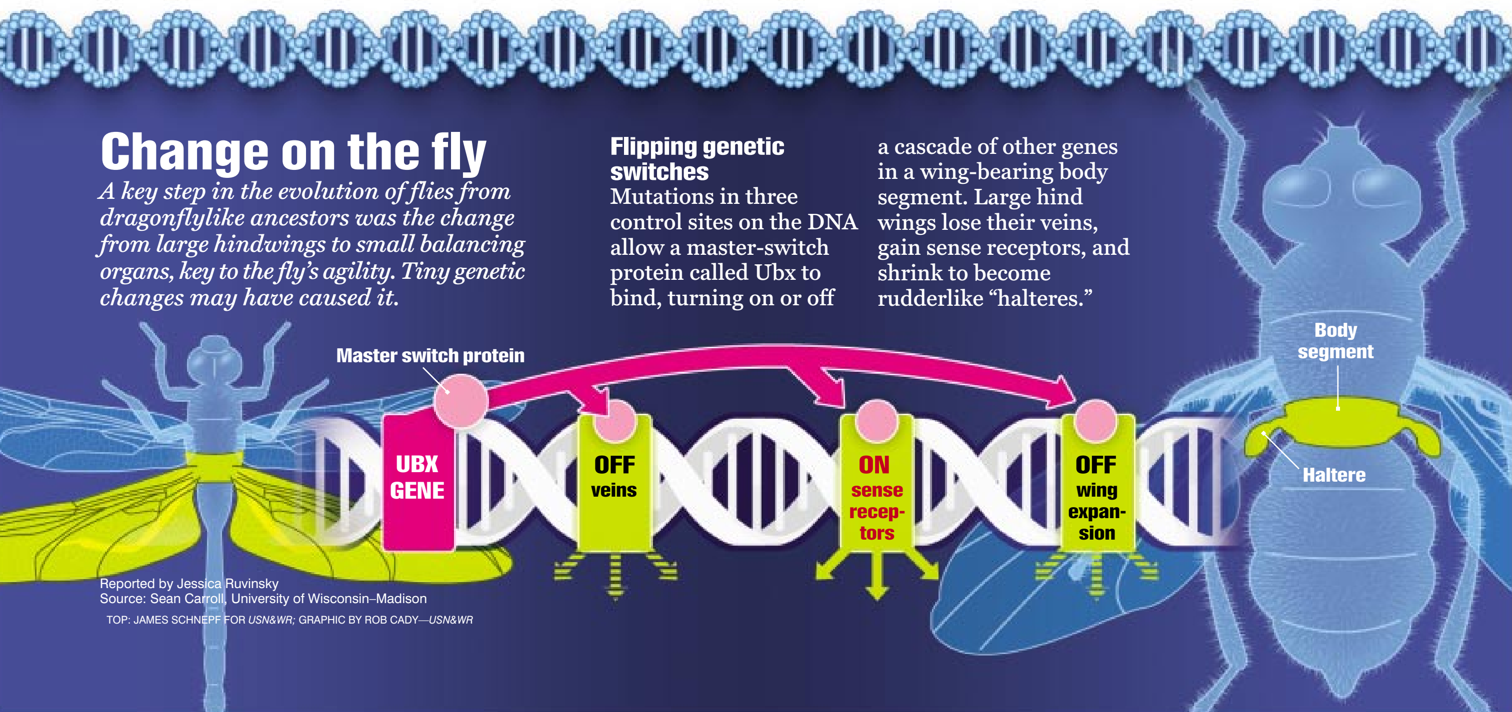
"If you change a Hox protein, you might mess up the whole body," says Carroll. "But if you change a control element, you can change a part as small as a bristle or a fingernail." He explains that genetic accidents can set the stage by duplicating segments, creating spares that are free to evolve while the other segments carry on with their original function. Biologists now believe that appendages like insect wings and the proboscis a mosquito jabs you with evolved from spare leg segments.

Making do. This process may be rapid, but it's not elegant. Instead of inventing new features from scratch, evolution works with what it has, modifying existing structures by trial and error. The result is a messy legacy of complicated biochemical pathways and body parts that

Change on the fly

A key step in the evolution of flies from dragonflylike ancestors was the change from large hindwings to small balancing organs, key to the fly's agility. Tiny genetic changes may have caused it.

Flipping genetic switches
Mutations in three control sites on the DNA allow a master-switch protein called Ubx to bind, turning on or off a cascade of other genes in a wing-bearing body segment. Large hind wings lose their veins, gain sense receptors, and shrink to become rudderlike "halteres."



Reported by Jessica Ruvinsky
Source: Sean Carroll, University of Wisconsin–Madison

TOP: JAMES SCHNEPF FOR *USN&WR*; GRAPHIC BY ROB CADY—*USN&WR*

LADIES' CHOICE. **These male birds of paradise evolved in different directions to suit female fancy, perhaps speeding their split into separate species.**

Species: life's mystery packages

When Darwin published *The Origin of Species,* he left one problem unsolved: the origin of species. He laid out in extraordinary and enduring detail how living things change over time, evolving from common ancestors. "But what is it about life that makes it come in discrete packages?" asks Jerry Coyne, an evolutionary biologist at the University of Chicago. "How do you start with one group and wind up with two?"

Species aren't just things that look different. Broccoli, brussels sprouts, and cabbage are all the same species. Left to their own devices, they'd make perfectly healthy and fertile baby plants. Dogs and cats, on the other hand, don't have kuppies and pittens; the reproductive barriers between them are what make them separate species. Because we know they had common ancestors tens of millions of years ago, we know those ancestors must have split into new species. But how did it happen?

Separation anxiety. "We have lots of ideas—they're good ideas—but we don't actually know what causes most new species to form," says Dolph Schluter, a zoologist at the University of British Columbia. Geographic isolation is a good bet: Give a few finches stranded on an island a few million years, and when they and their cousins from another island next meet, both groups are likely to have changed to the point that they may not even recognize each other as finches, let alone mate.

But you don't need an island or a mountain for isolation, claim some scientists. Mutations that give one group of fruit flies a taste for apples while another sticks with hawthorn fruits may be enough to keep them from mingling, even if they live in the same orchard. Given time, they may split into separate species. What the girls like may also play a role in creating reproductive barriers. Males of one species of bird of paradise in New Guinea perch on a branch and raise their display feathers high, while males of a closely related species actually hang upside down. Some scientists think that such differences in male display—and female preference—could greatly speed up speciation, and maybe even cause it.

All of these mechanisms are now generally acknowledged to be at least possible. But how prevalent each is remains a topic of fierce debate. It's no wonder there's controversy, when even the fastest animal speciation event takes a dozen (or several thousand, depending on who you ask) biologist lifetimes.
–Jessica Ruvinsky

FROM LEFT: TOM MCHUGH—PHOTO RESEARCHERS; GERRY ELLIS—MINDEN; W. PECKOVER—VIREO

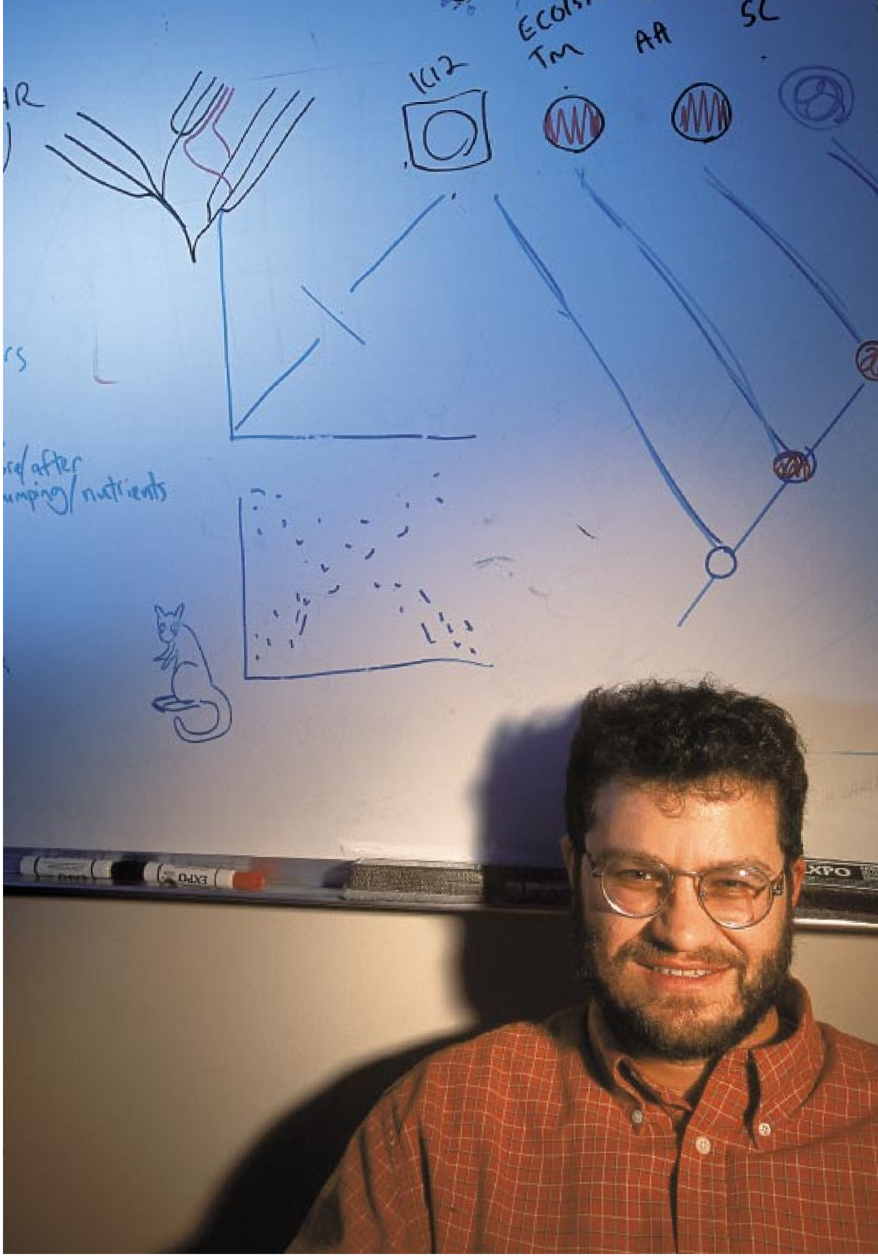
are more serviceable than sleekly designed. Although proponents of intelligent design (story, Page 52) hold that organisms are too "perfect" to have arisen by chance, science shows that organisms don't work perfectly at all; they just work.

While many scientists busy themselves figuring out the history and mechanics of evolution, others are already putting it to use. Jonathan Eisen of the Institute for Genomic Research in Rockville, Md., deciphers the information stored in organisms' genomes for clues to their ancestry and how they function. For him, evolution is as critical a tool as DNA-sequencing machines and supercomputers. "If I didn't approach everything with an evolutionary perspective," says Eisen, "I'd miss out on most of the information."

That's because genomes are the handiwork of evolution, and their origin can be key to making sense of them. Researchers analyzing the human genome, for example, reported finding a series of human genes that were also common in bacteria but absent from invertebrates like fruit flies. They concluded that bacterial genes had infiltrated vertebrate animals, helping to shape our genetic identity. But the explanation turned out to be more mundane. Knowing how evolution often prunes away unneeded genes, Eisen and several others showed most of the suspect genes had simply been dropped during the evolutionary history of flies. The moral of the story: "I'm begging people to treat evolution as a science and not just tack it on as an explanation afterwards," says Eisen.

Arms race. For microbiologist Richard Lenski, evolution is an obvious reality. Since 1988, the Michigan State University professor has been following 12 populations of the bacterium E. coli. With a new generation every 3.5 hours or so, this is evolution on fast-forward. The populations were once genetically identical, but each has adapted in its own way to the conditions in its test-tube home. The same speedy adaptation, unfortunately, can be readily seen in hospitals, where powerful antibiotics provide a major selective advantage for bacteria that evolve resistance. As bacterial evolution outwits one antibiotic after another, notes Harvard evolutionary biologist Stephen Palumbi, treating infections has become an evolutionary arms race. "It's a cycle of escalation, and the entity that can make the last turn of the cycle wins," says Palumbi. "So far, there's no indication that it's going to be us." The answer, he says, is not just new antibiotics but new strategies based on evolution.

"The key is to tip the balance of selec-



FAMILY MAN. **Geneticist Jonathan Eisen compares genomes for clues to how different organisms evolved from common roots.**

tion in favor of mild organisms," says evolutionary biologist Paul Ewald of Amherst College. That can mean measures as simple as having doctors scrub their hands to prevent the spread of the dangerous, antibiotic-resistant strains from their sickest patients. Making life difficult for virulent microbes can actually guide the species' evolution, weeding out the most harmful variants. In the case of malaria, the trick is keeping mosquitoes away from people bedridden with virulent strains. "If you mosquito-proof the houses," says Ewald, "then only people walking around outside can spread the disease, and that will be a mild form."

Evolutionary theorists may be able to guess how specific microbes will evolve, but not the fate of the whole panoply of life. "You can't predict what organisms will look like millions of years from now," says Knoll. Chance events, small and large, make all the difference, as mutations arise at random and unpredictable mass extinctions set life on a new course.

One mass extinction is easy to foresee: the one already underway because of our logging and paving and polluting. Things don't look good for most large mammals—they can't compete with us for space and resources. The outlook is brighter for species that depend on humans, like farm animals and crop plants, as well as rats and cockroaches. But this mass extinction is different from the last, 65 million years ago. "The day after the meteorite hit," says Knoll, "the planet started to heal. The problem now doesn't go away. It gets bad and it stays bad as long as our evolutionary history continues."

God and man. Which brings us to one final result of evolution, the odd, upright, and curiously self-obsessed ape in the mirror. We've turned the tables on evolution, curing diseases and changing our environment to suit us, rather than the other way around. But don't think that frees us from further evolutionary changes. Incurable epidemics that strike the young are still a powerful selective force. A mutation that boosted resistance to HIV, for example, could spread quickly by allowing those who have it to survive and have children. "We continue to accumulate mutations," says Sarah Tishkoff, a geneticist at the University of Maryland. "But we're altering evolution." Assisted reproduction allows some people to beat natural selection, she notes, while birth control gives an evolutionary leg up to those who don't use it.

A quick survey of the human condition reveals any number of desirable improvements—surely evolution could take care of hernias and osteoporosis and the appendix, which serves no greater purpose than to become inflamed? But those annoyances usually don't keep the annoyed from passing on their genes. And with precious little geographic isolation—one of the main drivers of speciation—left in our global village, we'll probably have to wait until a space colony gets cut off for several thousand generations before a new human species evolves.

Of course, it's the idea that human beings themselves are products of evolution that provokes most of the attacks on evolution. Such rejections leave most scientists mystified. "The scientific narrative of the history of life is as exciting and imbued with mystery as any other telling of that story," says Knoll. The evidence against evolution amounts to little more than "I can't imagine it," Ewald adds. "That's not evidence. That's just giving up."

Many researchers simply ignore the debates and press on with their work. But as evolution becomes an applied science, others say it's more urgent than ever to defend its place in the schools. "HIV is one of the world's most aggressively evolving organisms," says Palumbi. If it weren't for the virus's adaptability, which helps it foil the body's defenses and many drugs, "we would have kicked HIV in the teeth 15 years ago." But doctors don't learn about evolution in medical school, he says, leaving them about as well prepared to combat HIV as a flat-Earth astronomer would be to plan a moon shot.

"Somewhere in high school in this country is a student who's going to cure AIDS," Palumbi says. "That student is going to have to understand evolution." |

With Jessica Ruvinsky, Dan Gilgoff, and Rachel K. Sobel

JEFFREY MACMILLAN FOR *USN&WR*