YAHOO! NEWS

Efforts to Resuscitate Extinct Species May Spawn a New Era of the Hybrid

By David Biello | Scientific American – Tue, Mar 26, 2013

WASHINGTON, D.C.—A bird that once darkened the skies of the 19th-century U.S. no longer exists, except as well-preserved museum specimens bearing bits of DNA. An ambitious new effort aims to use the latest techniques of genetic manipulation to bring the passenger pigeon back, as North Dakotan Ben Novak, a would-be de-extinction scientist working on the Revive & Restore project at the Long Now Foundation, told the crowd at the TEDxDeExtinction event here on March 15.

"This [pigeon flock] was a biological storm that was rejuvenating resources and allowing other animals to thrive," Novak said of the storms of *Ectopistes migratorius* feces that used to fall like rain on the landscape of eastern North America. Plus, with the regrowth of forest on the east coast "there is more passenger pigeon habitat every year."

But if a bird looks like an extinct passenger pigeon, has some of the genetic code of the passenger pigeon, but does not act like a passenger pigeon because it is raised by other breeds and few in number: is it a true passenger pigeon? That is just one of the questions posed by the idea of de-extinction—deliberately resurrecting species killed off by human activity or inactivity. And that question may just challenge one of the fundamental concepts of biology: what determines a distinct species.

Welcome to the new era of the hybrid. Species have always been promiscuous and enjoyed porous boundaries, but synthetic

Tainted animals

The bison now repopulating the U.S. West's plains bear the genetic traces of their cattle forebears, residue of an effort that began in the 19th century to breed an animal that could survive the brutal Great Plains winters and drink less water than European cows. Wolves racing through the western landscape with black coats instead of the traditional gray can thank ancestors that got frisky with dogs. And does a Florida panther that carries genes from the Texas cougar count as less of a panther, even if the effort is all that stands between the species and extinction?

"Purity is not found in species," argued Kent Redford, a conservation biologist and former chief scientist at the Wildlife Conservation Society at the DeExtinction event. "We ourselves are not pure," bearing traces of genetic intermixing with Neandertals, Denisovans and perhaps other extinct hominids.

So what counts as a species then? Per the dictionary, a species is "a class of individuals having common attributes or designated by a common name." But biologists more precisely count species as a group of organisms that can interbreed to produce fertile offspring. So the horse and donkey are species, although those aren't their species names, and the mule is—well, it's been a little unclear since Carl Linnaeus came up with the species designation in 1753. As a (usually) sterile hybrid, the mule doesn't count.

But mules certainly do live and cases of mule fertility have been reported from antiquity down to the present day. Mules have even been cloned—and now, with the development of techniques to cut and splice DNA almost at will, scientists might be able to remake the mule into a fertile hybrid. But first they would rather apply the technique to endangered or extinct animals, like the Pyrenean ibex known as the bucardo or the Asian wild cattle called the banteng.

Rise of the hybrid

When a new animal is born it bears a mixture of both parents' genetics. So what then is an animal that has parents from two different species? The term hybrid was first used to describe the offspring of a tame sow and a wild boar. Or, as Redford put it, "something humans wanted." But now hybrids often bear a linguistic taint, neither fish nor fowl—almost as bad as a genetically modified organism, which, of course, all commercial species now are to one extent or another.

But purity still exists in the wild. Or does it? Traffic fatalities have caused swallow wings to shorten to enable quicker takeoffs just as fishing pressure has caused many wild-caught fish species to shrink in size. Bacteria rapidly evolve resistance to our best antibiotics. Humanity directs evolution unconsciously—except when we do it consciously, introducing useful suites of genetic information like the ability to produce a toxin poisonous to insects inserted into crop plants that was originally made by a bacterium.

With crude technologies such as cloning, where an entire cell nucleus is swapped from one species to another, this has already been done to revive an endangered species. An ordinary cow gave birth to a banteng—*Bos javanicus*, a species of wild cattle from Asia—in 2003. Although the scientists involved were worried that the hybrid might look more like an ordinary cow, out popped a banteng that lived at the San Diego Zoo for seven years—a diminished life span but a life nonetheless. "It was surreal to see this exotic animal from the jungles of Southeast Asia born in an Iowa field that reeked of cow manure," recalled Robert Lanza of Advanced Cell Technology, the company that helped achieve the feat.

Now new technologies such as an enzyme that can precisely cut DNA, known as Cas9 (for clustered regularly interspaced short palindromic repeats-associated system 9) and also derived from a bacterium, may enable scientists to stitch strands of DNA in and out of the genetic code. Find the genes that make a mammoth different from an elephant—say, sebaceous glands, hair growth, extra hemoglobin in the blood to withstand cold temperatures, among other traits—insert those into a strand of elephant DNA, and begin to make mammoth sperm and eggs. Then impregnate the mammoth's closest living relative, the Asiatic elephant, and wait for a baby mammoth to be born.

Only it won't be a true mammoth, because its mother will have something to say about how those genes are expressed, from epigenetics to the micro biome. "A gene doesn't tell you how to read it and make an organism," noted biologist David Ehrenfeld of Rutgers University at the DeExtinction event. "The genetic code is more like a database than an instruction manual." In other words, even the best genetic transcript—something still out of reach for many extinct animals and plants—will not provide the detailed source code needed to build version 2.0 of the extinct organism. He added: "All the words of *Hamlet* are in the dictionary, but if I scan the dictionary, *Hamlet* does not fall out of it. A strand of DNA can be read in hundreds or even thousands of ways."

And then there's the danger of the favoritism of humans that could lead some artifact "species" to predominate. "Who would have dreamed that genetic engineering in agriculture would diminish the biodiversity of agriculture? We lost tens of thousands of genome diversity from plants," Ehrenfeld added. As he noted, it's hard to predict the ultimate impact of a given technology.

Different species, different ecology

When he was just 13, Long Now's Novak was already putting together an award-winning science fair project detailing the prospects for cloning the dodo and bringing it back to life. Although that prospect has proved elusive, his passion for bringing back extinct birds remains undiminished. He now hopes to spend his professional life to bringing back some version of *E. migratorius*, a bird once so numerous in the U.S. that no one bothered to count them until the population had collapsed by the end of the 19th century.

The obstacles are many. "We can't clone birds," said developmental biologist Michael McGrew of the University of Edinburgh at the event. The problem is that a bird's egg yolk constitutes one enormous cell. Swapping nucleus at that scale has proved impossible, to date, according to McGrew.

But there is nonetheless reason for Novak to hope. In order to help with the biosecurity of the chicken eggs humanity relies on to manufacture vaccines (as well as eat), the stem cells of chickens have been put into a duck embryo that was bred as an adult with a chicken. The resulting eggs produced live chicks, proof of principle that although birds cannot be cloned, they can be made to carry the genes of other birds, potentially including extinct ones. With enough back breeding, in which bird after bird is bred together to derive a more complete version of the desired genetic code, the passenger pigeon's close relative, the band-tailed pigeon (*Columba fasciata*) might be made to lay eggs that result in passenger pigeon offspring, a generation of replacements.

"Breeding [the passenger pigeon] is the greatest technical challenge," Novak said. But it "pales in comparison to making this a natural passenger pigeon." After all, who will teach this novel baby bird to fly—or all the other roles parents of a given species play?

Novak's solution for that challenge starts with painting domestic homing pigeons—luring yet another pigeon species into boxes and airbrushing them to look like passenger pigeons—as well as building aviaries in the woods of eastern North America to protect the few, rare, newly non-extinct fledglings from predators like falcons. The painted homing pigeons would lead the newly created passenger pigeon replacement young from spot to spot as trained by human handlers, theoretically re-creating the flitting behavior of the extinct flocks. "Eventually, we would witness the passenger pigeon rediscovering itself in the forests of New England and the Great Lakes," Novak enthused.

But will those birds be the same as their ancestors? "The banded pigeons fly differently, mate differently, have different goals," Ehrenfeld said of the new passenger pigeon's putative parents, adding that key traits will be forever lost to this new hybrid creature. Not least of which will be the fact that even a few thousand artifact pigeons would still not match the sheer numbers of their genetic ancestors or even hope to fulfill the role they once played in the bygone forest ecosystems of an earlier North America.

Even sheer numbers still failed to protect the abundant bird from going extinct under hunting pressure, the loss of its habitat as farmers cleared eastern lands of trees, and the terminal decline once its population fell below a certain threshold. The eastern forest is also not the same one the passenger pigeon knew before going extinct. Whereas forest cover has rebounded since the 1920s, the American chestnut is largely gone—a victim of a fungal blight that nearly eliminated the once copious tree. "If you're going to bring back species like the passenger pigeon, what are you bringing them back to?" asked forestry scientist William Powell of the State University of New York College of Environmental Science and Forestry at the DeExtinction talks. "You might want to bring back the chestnut before anything else."

Powell is working on genetically engineering a version of the American chestnut to be resistant to the fungus—but even that new version will be some kind of hybrid, bearing new genetic information either bred into it from its relative the Chinese chestnut or inserted whole by scientists like Powell.

Then there are the risks, such as the restored flocks of hybrid passenger pigeons turning into a new way to spread bird flu. "The passenger pigeon could be the vector for some terrible disease," said Hank Greely, a bioethicist and lawyer at Stanford Law School at the event. "No one wants to be responsible for an avian version of kudzu or, sticking to birds, starlings."

If people do not like squawking, flocking starlings that chew up the landscape, what will they think when a rain of pigeon droppings starts falling on them?

Unique pets

Releasing any replacement hybrid species back into the wild to replace an extinct species or augment the numbers of a threatened species would be another kind of experiment that calls for the invention of an entirely new branch of science, dubbed "resurrection ecology" by Stanley Temple, an ecology professor emeritus from the University of Wisconsin–Madison. "We need to think carefully before the saber-tooth cat is out of the bag," he noted.

So, for example, the pressures that lead to the extinction of the original species in the first place would need to be gone, whether hunting, in the case of the thylacine (Tasmanian tiger), or habitat loss, in the case of the ivory-billed woodpecker.

Candidate species for hybrid replacements will also have to be weighed by specific criteria that might include (for birds like the passenger pigeon, for example) relatively recent extinction, minimal parental care, small egg size and nonmigratory habits. "If you only have one or two and they fly away, you're going to cry," noted ornithologist Susan Haig of the U.S. Geological Survey.

More fundamentally, scientists remain unsure why changing conditions can cause one species to disappear whereas another similarly adapted species flourishes or changes with the times. For example, when the ice age ended, "why do some species like the cave lion go extinct while caribou thrive today?" asked Beth Shapiro, an evolutionary biologist at the University of California, Santa Cruz.

There's also the question of whether such an expensive effort to re-create and reintroduce a once extinct species could divert funds from ongoing conservation efforts to save species still extant but dwindling fast. And the relative expense of this project means it might find its first use creating glorified pets, like the rare animals in zoos. "If it had not been illegal to keep thylacines as pets, then would it be extinct now?" asked paleontologist Michael Archer of the University of New South Wales, who is attempting to resurrect the marsupial tiger. "I'm positive it wouldn't."

Biological control

"By the end of this century we will have much more control over life than we ever dreamed," Greely said at the event—and that seems set to be true, one way or another.

But control is almost as tricky a concept when it comes to science as species. The newly extant hybrid species will need to be further genetically armored against the causes of their extinction, such as American chestnuts or resurrected gastric brooding frogs tweaked to resist fungal threats. Scientists will be making a long-lived commitment to certain species, like the booster shots against West Nile virus that veterinarians still dispense to all captive and pseudo-wild California condors extant. "It's a rather momentous undertaking we have to do," said bird curator Michael Mace of the San Diego Zoo. A similar effort might be needed to bring back a new version of the Hawaii ‘O‘o bird, whose habitat still exists but is now plagued with avian malaria that even a new hybrid bird might not survive.

More philosophically: Is de-extinction a project in search of some artificial stasis, more commonly dubbed a "balance of nature," that has never existed? Will we turn nature into a well-curated museum of artifact creatures while we let other, less glamorous species dwindle and disappear? Or will this new technology be used to preserve those species that perform some critical function, such as the wild bees that pollinate many different species of plant?

And how have we changed? The Carolina parakeet died out in 1918 because it interfered with crops and had the unfortunate behavior of flocking to fallen comrades, enabling hunters to decimate the population. "What we have left is remorse and remains," noted nature artist Isabella Kirkland. That remorse might drive us to use the remains to resurrect lost plants and animals, albeit in a new hybrid form.

Novak, for one, hopes that with enough money and determination a living hybrid passenger pigeon could be created within a decade, a kind of second coming of *E. migratorius*. "We don't have extinct species brought back to life yet," said environmentalist Stewart Brand, an instigator of Revive & Restore who hopes to bring back the passenger pigeon, "but it will be soon." We just don't know what species they will be.

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