GENOMICS

What If Extinction Is Not Forever?

Although new technologies may make it possible to bring extinct species back to life, there are ethical, legal, and social ramifications to be addressed

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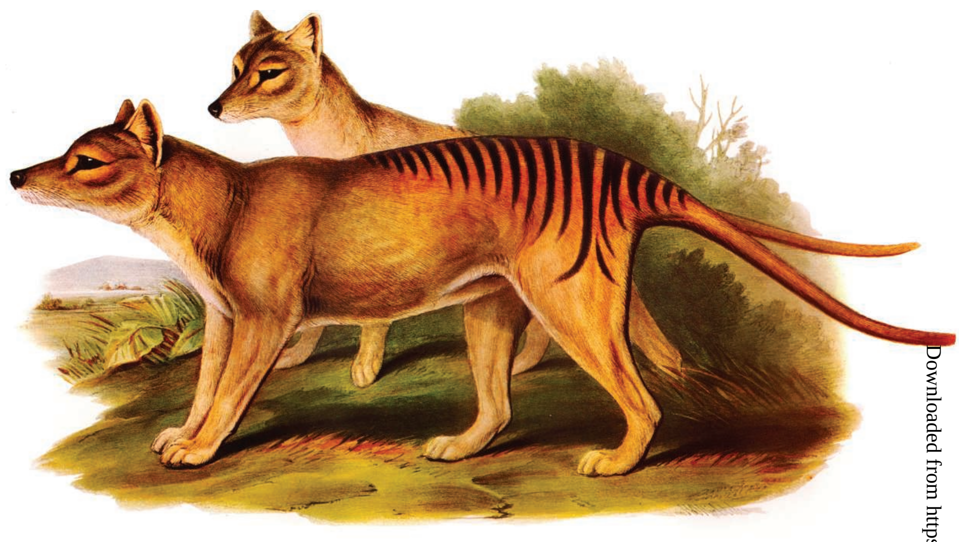
A 1930s film shows a dog running and jumping inside a fenced enclosure (*1*)—except that the dog has a strange-shaped head, odd stripes, and a rigid tail that can only move side-to-side. The "dog" is actually one of the last thylacines, a marsupial predator also called the Tasmanian tiger. The film was taken shortly before humans extinguished the species forever. Or did we? Recently, new technologies have made it plausible to try to revive many recently extinct species. Scientists around the world are discussing, and working toward, "de-extinction" (*2*).

Currently, three approaches to de-extinction seem most likely to succeed: back-breeding, cloning, and genetic engineering. If the extinct species left closely related descendants, it might be possible to use selective breeding to produce progeny with the phenotypes of the extinct species, as the auroch project in Europe has been doing since 2008 (*3*). With newly cheap genome sequencing methods, one might guide back-breeding with genome sequences from samples of the extinct species. Of course, back-breeding will only be possible in situations where the genetic variations of the extinct species survive in the descendant species.

Cloning provides another possibility. Using cryopreserved tissue from the last known Pyrenean ibex, a Spanish group used somatic cell nuclear transfer (SCNT) to revive that extinct subspecies. Out of several hundred efforts, however, only one fetus survived to term, and it died minutes after birth from lung abnormalities (*4*). This example highlights two problems with SCNT: it is neither very safe nor efficient and will only work if viable cell nuclei are available. This will likely be the case in only a few very recent extinctions.

Genetic engineering offers a third approach. Take an extinct species—say, the passenger pigeon—that left sufficient samples to allow high-quality whole-genome sequencing. DNA in cells from a similar living species—perhaps the band-tailed pigeon—could be edited to match the extinct species' genomic sequence. The modified cells could then be used to produce living birds that, genomically, were mainly band-tailed pigeon but partially passenger pigeon (*5*). By using targeted replacement of genomic sequence (*6*) across several loci, much of the extinct genome could be reconstructed within several generations.

Neither the back-breeding nor genetic engineering approaches would yield an animal that had exactly the same genome as any member of the extinct species for many years, if ever. The cloning approach, in the few cases where viable nuclei are available, would produce a genomic twin to one member of the extinct species—but only one. Does one individual (or a set of clones) make a "species"? Even if genomic identity is necessary, is it sufficient? The revived individuals would not have the same epigenetic makeup, microbiome, environment, or even "culture" as their extinct predecessors.



Tasmanian tiger. By the 1930s, settlers, encouraged by government bounties, had hunted the thylacine to extinction in the wild. Well-preserved specimens could pave a way to bringing it back.

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Risks and Objections

Objections to bringing back extinct animals fall into five categories: animal welfare, health, environment, political, and moral.

Animals created in the de-extinction process could end up suffering, either as a result of the processes used or because of their particular genomic variations. We know, for example, that SCNT can lead to high levels of deformity and early death (*7*). The Animal Welfare Act and its institutional animal care and use committees limit precisely this kind of suffering (*8*). Beyond physical suffering, some animal advocates might oppose de-extinction as they oppose zoos—on the grounds that they exploit animals for unimportant human purposes, like entertainment.

Newly de-extinct creatures might prove excellent vectors for pathogens. An extinct animal's genome could also conceivably harbor unrecognized, harmful endogenous retroviruses.

If the species either is released or escapes into the general environment, it might do substantial damage. Even extinct species that were not pests in their past environments could be today. For example, less than 200 years ago, billions of passenger pigeons migrated each year between the eastern United States and Canada. Today, those regions have far more humans, far larger urban centers, very different agriculture, and largely transformed ecosystems. The American chestnut, a main food source for the passenger pigeon, is now nearly extinct in the wild. Even in the same location, the passenger pigeon would today be an alien, and potentially invasive, species—perhaps another starling or even an avian kudzu.

The political risks are considerable,

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too. Current protection of endangered and threatened species owes much to the argument of irreversibility. If extinctions—particularly extinctions where tissue samples are readily available—are not forever, preservation of today's species may not seem as important. Also, genetics and, more broadly, modern bioscience, could face a backlash if citizens perceive public investments in bioscience as being used to revive species rather than cure human disease.

Finally, some people will complain that, whatever its consequences, de-extinction is just wrong—it is "playing god," "reversing natural selection," or an act of hubris. Others may argue that we cannot know enough about the consequences to re-introduce a species. But neither do we know the full consequences of its extinction or its continuing nonexistence.

Benefits

Like the risks or objections to de-extinction, we see the benefits falling into five categories: scientific knowledge, technological advancement, concrete environmental benefits, justice, and "wonder." These benefits are quite similar to the arguments made for preserving currently endangered or threatened species.

De-extinction could allow scientists the unique opportunity to study living members of previously extinct species (or, at least, close approximations to those species), providing insights into their functioning and evolution. Some revived species may be translated into useful products; for example, it is conceivable that new drugs may be derived from extinct plants.

De-extinction could lead to technological advances. The most likely would be improvements in genetic engineering, such as the targeted replacement of large stretches of genomic DNA (*6*).

Some researchers argue that "re-wilding" with existing species, locally extinct in particular habitats, can help restore extinct or threatened ecosystems (*9*). The same can be argued about the restoration of extinct species. The revival of the wooly mammoth as a major grazing animal in the Arctic, for example, might provide substantial benefits by helping restore an arctic steppe in the place of the less ecologically rich tundra (*10*).

Justice is a viscerally attractive argument for de-extinction, at least for species that humans drove to extinction: We killed them. We have the power to revive them. We have a duty to do so. But to whom or what do we owe that duty? Would it apply to all species in whose extinction humans played the sole, the leading, or a substantial role?

The last benefit might be called "wonder," or, more colloquially "coolness." This may be the biggest attraction, and possibly the biggest benefit, of de-extinction. It would surely be very cool to see a living wooly mammoth. And while this is rarely viewed as a substantial benefit, much of what we do as individuals—even many aspects of science—we do because it's "cool."

Legal Issues

We may also need to consider several legal issues. First, would a de-extinct species be "endangered"? The answer is unclear. In the United States, the Endangered Species Act provides for listing as "endangered" any species "over utilized" for scientific purposes, inadequately protected by current regulations, or whose existence is threatened by other "manmade factors" (*11*)—all considerations that would seem to apply to a newly revived species. Ironically, international organizations typically tie endangered status to whether species' population has declined—the opposite of the concern about newly revived species (*12*). Uncertainty about the status of de-extinct species will affect numerous civil, criminal, and international laws.

Second, could a revived species be patented? This answer also seems unclear. The United States and many other countries allow patents on living organisms (*13*). Although "products of nature" cannot be patented, is a revived species a "product of nature" in light of the inevitable differences from its predecessors? Additionally, the "lost arts doctrine" may allow the patenting of previously existing species if they have been completely lost to the public (*14*).

Last, would de-extinction be regulated and if so, how? Again, the answer is unclear. And even if there were no legal regulation, the concerns previously discussed could dampen the enthusiasm for de-extinction by some research entities, such as universities. This could drive the efforts toward less controlled, or constrained, enterprises.

What Should Be Done?

The answer to the question—What to do about de-extinction?—depends in part on closely defining the question. Consider three different "bottom-line" questions.

First, should de-extinction be publicly funded? This answer seems, to us, "largely no." The potential tangible benefits from de-extinction are too small and the potential objections are too serious to justify substantial government expenditure. One might argue that governments fund science projects with similarly small practical relevance, but those "cool" projects, like the Mars rovers, present fewer risks and objections.

Second, should de-extinction be categorically banned? Here the answer seems a fairly clear "no." The risks look fairly small and probably manageable. If people want to devote their own time, money, and efforts to the endeavor, the risks to the world do not seem to justify complete prohibition.

Third, should de-extinction be regulated? Here, we think the answer is "Yes—somewhat." The animal welfare and environmental concerns are real. They could be mitigated by protective action but only if the law requires it. Bringing all de-extinction efforts under something like the Animal Welfare Act and requiring careful environmental assessments before any planned releases (as well as approved precautions against inadvertent release) do seem appropriate. Whether other kinds of regulation are needed is less clear, although there may be some cases, like any attempted revival of extinct hominid species, where special controls, or bans, would be appropriate.

De-extinction is a particularly intriguing application of our increasing control over life. We think it will happen. The most interesting and important question is how humanity will deal with it.

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