Reshaping the Tree of Life

In the Science News article, *The tree of life gets a makeover* much is made of the concept of single-lineage supergroups. But researchers from the University of Colorado, Rutgers University, Chicago Botanic Garden, the Natural History Museum London, Sun Yat-Sen University Institute of Microbiology and the Wuhan Institute of Virology of the Chinese Academy of Sciences recognize that “Systematics as a discipline has not kept pace with microbial discovery and its importance, given that trees continue to reflect lineages evolving in isolation.”

They propose a new paradigm for phylogenetic analysis in *Reshaping Darwin’s Tree: Impact of the Symbiome*.

“Much of the undescribed biodiversity on Earth is microbial… Physically associated and coevolving life forms comprise a symbiome. We propose that systematics research can accelerate progress in science by introducing a new framework for phylogenetic analysis of symbiomes… It has become difficult to work within a 2D space that reflects only genetic distance, time, and single-species terminals. Instead, third and potentially higher dimensions are needed to depict quality, quantity, and
stability (i.e., longevity) of interactions. We envisage multidimensional tree spaces, namely networks, that depict conflicting topologies derived from analysis of different genomic regions: symbiomes resulting from different combinations of parental genomes can—and should—occupy different terminals or perhaps even branches of network space [emphasis added]."

This new multidimensional framework is given the name SYMPHY (symbiome phylogenetics).

The Power to Control Evolution?

In their book, A Crack in Creation: Gene Editing and the Unthinkable Power to Control Evolution, Jennifer Doudna and co-author, Samuel Sternberg, write about the discovery and adaptation of an anti-viral bacterial immune system known by the acronym, CRISPR-Cas9 or CRISPR for short. CRISPR, repurposed as biotechnology, is a very potent way to cut, splice and repair single gene defects.

Recently, researchers used the technology to experimentally repair the single gene defect that causes hypertrophic cardiomyopathy (HCM), a genetic disorder that can cause heart failure. The components of CRISPR-Cas9 were injected into donated eggs simultaneously with donated sperm from a carrier of the HCM defect. The experimental IVF procedure was to test if human embryos with repaired genomes could be created. The test was hailed as a success, because two common problems with the biotechnology were not detected. However, the experiment was not without a surprise: the synthetic gene sequence that was injected was not used by CRISPR. Rather the

"Human embryos grow in a laboratory for a few days after researchers used CRISPR gene editing technology to successfully repair a heart disease-causing genetic mutation." (Oregon Health & Science University via AP)
embryos used the mothers’ healthy genes for the repair.

**A Primer on Anthropocentricity and Unthinking**

The point of this commentary is to use quotations from *Crack in Creation* as a primer on how anthropocentrism, human exceptionalism, and a general disregard for the biospheric context of our existence is all too common in science writing and thinking. It is not to pick on this one book because many other science books, articles and papers would provide similar evidence of unthinking.

“Industrialization has caused climate change that threatens ecosystems around the globe, and this and other human activities have precipitated a surge in species extinction that is ravaging the diverse populations of creatures with which we share this earth. These transformations have prompted geologists to propose that we rename this era the Anthropocene—the human epoch.“ (Kindle 62)

We utterly depend on the Earth to sustain us, but that realization and the contradiction of our continued “ravaging” of our own life-support system is lost or ignored in favor of our supposed “biological mastery” in the Anthropocene. It is odd to point out our extinction of species while speaking of our *sharing* the Earth. The idea of our supposed “biological mastery” is set in the insufficient and outmoded neo-Darwinian explanations of evolution.

“The biological world is also undergoing profound, human-induced changes. For billions of years, life progressed according to Darwin's theory of evolution: organisms developed through a series of random genetic variations, some of which conferred advantages in survival, competition, and reproduction. Up to now, our species too has been shaped by this process; indeed, until recently we were largely at its mercy. When agriculture emerged ten thousand years ago, humans began biasing evolution through the selective breeding of plants and animals, but the starting material—the random DNA mutations constituting the available genetic variations—was still generated spontaneously and randomly.“ (Kindle 65)
Is it possible that Doudna and Sternberg are ignorant of the non-Darwinian processes that are now recognized to drive evolution? There is no mention of symbiogenesis, horizontal gene transfer, interspecific hybridization, whole genome duplication, or the movement of mobile genetic elements (natural genetic engineering) in their book.

What is described in Crack in Creation is a still-imperfect method for editing single-gene defects. Yet, this biotechnology borrowed from bacteria is repeatedly described as providing mastery of evolution.

“Today, things could not be more different. Scientists have succeeded in bringing this primordial process fully under human control [emphasis added]. Using powerful biotechnology tools to tinker with DNA inside living cells, scientists can now manipulate and rationally modify the genetic code that defines every species on the planet, including our own. And with the newest and arguably most effective genetic engineering tool, CRISPR-Cas9 (CRISPR for short), the genome—an organism's entire DNA content, including all its genes—has become almost as editable as a simple piece of text.” (71)

The idea of a gene as that which produces a trait is conflated with the completely different definition of gene as a length of DNA.

“As long as the genetic code for a particular trait is known, scientists can use CRISPR to insert, edit, or delete the associated gene in virtually any living plant's or animal's genome. This process is far simpler and more effective than any other gene-manipulation technology in existence. Practically overnight, we have found ourselves on the cusp of a new age in genetic engineering and biological mastery—a revolutionary era in which the possibilities are limited only by our collective imagination.” (75)

Is our collective imagination—given that significant numbers of us believe in angels, but not global climate change or evolution—what we want to rely on when it comes to “using powerful biotechnology tools to tinker with DNA?”

“The issue is this: For the roughly one hundred thousand years of modern humans' existence, the Homo sapiens genome has been shaped by the twin
forces of random mutation and natural selection. Now, for the first time ever, we possess the ability to edit not only the DNA of every living human but also the DNA of future generations—in essence, to direct the evolution of our own species. This is unprecedented in the history of life on earth. It is beyond our comprehension. And it forces us to confront an impossible but essential question: What will we, a fractious species whose members can't agree on much, choose to do with this awesome power?” (64)

Homo sapiens—like all extant organisms—have been shaped by more than blind chance and natural selection. Should we not expect or require that those who want to develop and use these tools at least be up to date on the subject of evolution, the process they want to direct? There is no question that we are a fractious species. If indeed this power is beyond our comprehension or agreement on its use, is its exercise a choice or compulsion?

“CRISPR is also tucked away inside the genomes of new mosquito strains, part of a plan to rapidly drive new traits into wild mosquito populations. Scientists hope to eventually eradicate mosquito-borne illnesses, such as malaria and Zika, or perhaps even wipe out the disease carrying mosquitoes themselves.” (93)

“Somewhat incredibly, scientists don't seem overly concerned about a world without mosquitoes. As one entomologist put it, "If we eradicated them tomorrow, the ecosystems where they are active will hiccup and then get on with life." If he's right and we could have a world free from the ravages of mosquito-borne illness, can we justify not taking the risk?” (2253)

We want to be careful about wiping out organisms that we view in our ignorance as useless or noxious. Goat grass (Aegilops squarrosa), is such a plant, but when hybridized with a moderately useful plant, emmer wheat (Triticum turgidum) what is produced is the world's most valuable crop plant, bread wheat (Triticum aestivum). This example should tell us that we cannot predict in advance whether a particular organism will be worthless or priceless. At a time when bee populations are in serious
decline, wiping out other pollinators, such as mosquitoes, might not be the first thing we want to risk with “this awesome power.”

“But with CRISPR, gene editing was now so powerful and multifaceted that it was often referred to as genome engineering, a reflection of the supreme mastery that scientists held over genetic material inside living cells.” (1568)

“And in a page taken straight out of a famous book-to-film sci-fi franchise, some laboratories are pursuing a venture known as de-extinction, which is nothing less than the resurrection of extinct species through cloning or genetic engineering.” (1777)

One of the gaps in the thinking about bringing back dinosaurs is how to recreate the lost microbiomes of these extinct holobionts. Crack in Creation predominantly takes a myopic reductionism view of things in isolation rather than the broad view of systems as reflected by the well-known quote of John Muir, “When we try to pick out anything by itself, we find it hitched to everything else in the Universe.”

“Yes, someday soon, CRISPR might be employed to destroy entire species... Some of the efforts in these and other areas of the natural world have tremendous potential for improving human health and well-being. Others are frivolous, whimsical, or even downright dangerous.” (1782)

Even when the biosphere is invoked, a biospheric view is missing. The book reflects a dangerous and shortsighted anthropocentric view that defaults to a definition of good as anything that is seen as “improving human health” or “improving our world [emphasis added].”

“CRISPR gives us the power to radically and irreversibly alter the biosphere that we inhabit by providing a way to rewrite the very molecules of life any way we wish [emphasis added]. At the moment, I don’t think there is nearly enough discussion of
the possibilities it presents—for good, but also for ill. It's a thrilling moment in the life sciences, but we can't let ourselves get carried away. It's important to remember that, while CRISPR has enormous and undeniable potential to improve our world, tinkering with the genetic underpinnings of our ecosystem could also have unintended consequences. We have a responsibility to consider the ramifications in advance and to engage in a global, public, and inclusive conversation about how to best harness gene editing in the natural world, before it's too late.” (1786)

   The difficulty with “unintended consequences” is that their ramifications are by definition not those that are considered in advance.

   The view of bacteria expressed by the authors of Crack in Creation is of organisms simple and primitive. Even though they are immersed in biotechnology—much of which is based in the diverse and wondrous capabilities of bacteria.

   “Sure, genetically modified humans made for great science fiction, and they were a fertile subject for philosophical and ethical musings on the possibility of human 'self-evolution.' But unless the Homo sapiens genome suddenly became as easy to manipulate as the genome of a laboratory bacterium like E. coli, there was little chance of anyone pursuing such Frankenstein schemes anytime soon. Now, we could no longer laugh off this kind of speculation. Making the human genome as easily manipulable as that of a bacterium was, after all, precisely what CRISPR had accomplished.” (2716)

   It is good to keep in mind that CRISPR is a bacterial tool, not something we invented, but one—like much of biotechnology—that we have co-opted. E. coli is described as “easy to manipulate,” but that is due to its resilience and

   “Living systems can synthesize complex molecules, convert light, [chemical energy] or biomass into usable energy, produce high-performance materials, and harness the power of molecular self-assembly and replication.

   Consider the bacterium E. coli. It swims toward things it likes and away from things it doesn't. It communicates with other cells. It synthesizes complicated compounds and replicates itself every 20 minutes. Put another way, E. coli tastes, thinks, talks, listens, and makes things.” source: http://www.gallivanlab.org
versatility which are vastly superior to humans.

"Previous genetic-engineering technologies, including gene therapies and RNA interference, were similarly extolled as pivotal advances that would completely transform medicine, yet hundreds of clinical trials have thrown quite a bit of cold water on that enthusiasm. That's not to say that we're heading for the same sort of rude awakening with gene editing, just that it's important to temper the excitement with realistic expectations, methodical research, and meticulous clinical trials. Only then can we ensure that the first wave of CRISPR-based therapeutics will have the best chance of success and the least risk of dangerous side effects.” (2666)

“As of this writing, the field of gene-editing-based therapies is expanding at a frantic pace, both in the academic and commercial realms [emphasis added]. New studies surface at a rate of more than five per day, on average, and investors have poured well over a billion dollars into the various startup companies that are pursuing CRISPR-based biotechnology tools and medical therapeutics.” (2670)

That every earlier advance in genetic engineering has been “extolled as pivotal” should be viewed as evidence that such claims are routinely overstated. It is already apparent that CRISPR has surprises in store for researchers.

“I think we should refrain from using CRISPR technology to permanently alter the genomes of future generations of human beings, at least until we've given much more thought to the issues that editing germ cells will raise. Until we have a better understanding of all the attendant safety and ethical issues, and until we have given a broader range of stakeholders the opportunity to join the discussion, scientists would do well to leave the germ line alone. But, really, whether we'll ever have the intellectual and moral capacity to guide our own genetic destiny is an open question…” (2673)

There are certainly ample grounds for agreeing that we lack the intellectual and moral capacity to guide our own destiny—genetic or otherwise. One need look no further than our continuing reliance on
fossil fuels in the face of global climate change.

“Robert Sinsheimer, then [1967] a professor of biophysics at Caltech, described human genetic modification as ‘potentially one of the most important concepts to arise in the history of mankind...For the first time in all time a living creature understands its origin and can undertake to design its future [emphasis added].’” (2756)

Nineteenth-century proponents of eugenics were equally sure that mankind understood for the first time how to improve the future of humanity.

“Sinsheimer scoffed at critics who argued that genetic engineering was simply a modern version of the timeless but futile dream to perfect mankind: ‘Man is all too clearly an imperfect, a flawed creature. Considering his evolution, it is hardly likely that he could be otherwise... We now glimpse another route—the chance to ease the internal strains and heal the internal flaws directly—to carry on and consciously to perfect, far beyond our present vision, this remarkable product of two billion years of evolution.’” (2759)

Clearly reductionist neo-Darwinists, such as Sinsheimer, did not have the realistic understanding of our origin, the evolution of life, or a route to healing imperfect, flawed humans, although they were sure that they glimpsed it. This is a perpetual problem: the hubris that says, “As imperfect as we are, now we understand how it all works” or conversely, “Mistakes were made in the past, but we no longer make those kinds of mistakes.”

“Within two decades of the publication of Sinsheimer’s essay, scientists were rapidly mapping the route to perfection he had been able only to glimpse in the late 1960s, By the beginning of the 1990s, gene therapy trials were under way with human patients...” (2760)

Is there a scientific definition of “perfection”? Shall we narrow the biological diversity of our species? Will we be better off becoming more of a monoculture in a constantly changing environment?

“...others welcome human involvement in the works of nature as long as the
goals being pursued are inherently good, such as improved health or fertility.” (3326)

Is it “inherently good” to improve human health and fertility on a planet that cannot sustain its current and still expanding human population? It is difficult to see how healthier and more fertile humans can be seen as “inherently good” in the current biospheric context.

“As NIH director Francis Collins put it, ‘Evolution has been working toward optimizing the human genome for 3.85 billion years. Do we really think that some small group of human genome tinkerers could do better without all sorts of unintended consequences?’” (3331)

When the idea of pure chance and random mutations is reduced—as it is in the new integrative evolutionary synthesis—it is no longer blind. As Denis and Ray Noble have pointed out evolution must be seen as a one-eyed watchmaker.

“What I share the general feeling of unease at the idea of humans taking control of their own evolution, I wouldn't go so far as to say that nature has somehow fine-tuned our genetic composition. Obviously, evolution didn't optimize the human genome for the present era, when modern foods, computers, and high-speed transportation have completely transformed the way we live. And if we look over our shoulders at the course of evolution that has led to this moment, we'll see that it's littered with organisms that certainly didn't benefit from the mutational chaos that underpins evolution. It turns out nature is less an engineer than a tinkerer, and a fairly sloppy one at that. Its carelessness can seem like outright cruelty for those people unlucky enough to inherit genetic mutations that turned out to be suboptimal.” (3337)

What we have above is the outmoded neo-Darwinian notion that evolution is a “mutational chaos,” “sloppy,” or “careless.” When evolution is seen as harnessing stochasticity—as it is when seen through the lens of biological relativity—it turns out that evolution is less the tinkerer than an engineer. Yes, organisms have been eliminated, but this is quality control: natural selection is a necessary curb on fecundity and extinction...
is a curb on overspecialization in a changing environment. The idea that these essential components of the natural world—a system that has preserved life for more than 3800 million years—is bad or cruel is totally anthropocentric and completely at odds with the biospheric system in which we have evolved.

“...while the risk that gene editing will fragment human society seems like a problem for future generations, it looks less remote in light of history.

“Once a game-changing technology is unleashed on the world, it is impossible to contain it. Blindly rushing ahead with new technologies creates problems of its own. ...gene-editing technology gives us the chance to hold an informed public discussion about how we want to use CRISPR's most far-reaching power: the ability to control the future of life [emphasis added]. But if we wait too long, we may find that the reins have slipped from our hands.” (3504)

Technology is hard (impossible?) to leash safely from human misuse. It is we humans who rush ahead with it blindly. It is unlikely that we will ever “control the future of life,” but that is not to say we won’t affect our own future. From a biospheric worldview, the preponderance of evidence about our effects on the Earth cannot be mistaken for stewardship or “control,” and most certainly not “mastery.” James Lovelock quipped that humans are as likely to be stewards of the Earth as goats are to be gardeners.

“Together, we can choose how best to harness this technology. There's simply no way to unlearn this new knowledge, so we must embrace it. But we must do so cautiously, and with the utmost respect for the unimaginable power it grants us.” (3512)

Near the end of the book, the authors say that scientists need “discussion without dictation” when discussing the application of powerful and potentially extremely dangerous technologies with the public. But here there is no choice or discussion.

“For most of our species' history, humans have been subjected to slow, often imperceptible evolutionary pressures exerted by the natural world.
Now we find ourselves in the position of controlling the focus and intensity of those pressures. From here, things will progress much more quickly than either our species or our planet is accustomed to. It's hard to predict what the average human genome will look like just a few decades from now. Who's to say how our species or our world will appear in a few hundred years—or a few thousand?” (3517)

If the above were possible, it would be an extraordinary jump in the speed of organismic change. Who's to say what could possibly go wrong when a bunch of synthetic and/or transgenic organisms are produced and loosed? Like rabbits in Australia.

“Many of these changes will be unequivocally good. CRISPR has such incredible potential to improve our world.” (3522)

Or result in all kinds of unintended consequences. Some which might even impact the microcosmos—imagine something so bad it makes germs sick. More likely we will make ourselves sick. “Few technologies are inherently good or bad; what matters is how we use them. And when it comes to CRISPR, the possibilities of this new technology good and bad—are limited only by our imaginations.” (3526)

When it comes to the possibilities, perhaps more constraint, a slower pace, more methodical, reproducible, carefully monitored and reviewed would be the wise. Always choosing the side of caution. Yeah, like that will happen.

“As a species, we have never done anything like this before—but then again, we have never had the tools to do it. The power to control our
species’ genetic future is awesome and terrifying. Deciding how to handle it may be the biggest challenge we have ever faced. I hope—I believe—that we are up to the task.” (3528)

Awesome and terrifying, yes. Are there long-term, careful studies of the effects of genetically modified and transgenic organisms and their contamination of the natural world? It is human exceptionalism that confuses wielding a technology with control of its effects. Why do we assume that, despite ample evidence that we’ve been error-prone and incautious with previous technologies, this time—with the stakes higher than ever—we will be “up to the task.”

“I have been taken aback by just how intensely competitive the study and use of CRISPR can be and how much it transformed in a matter of years, becoming a global field that touches virtually any researcher studying biology.” (3555)

Science is intensely social and political. Quite the opposite of the mythology of its being dispassionate and objective. There is an endless chasing of celebrity and grants. The three great human motivators, according to Lynn Margulis are “money, power and genital friction.”

“I have also come to appreciate the importance of stepping out of my comfort zone and discussing science with people beyond my circle of specialists.” (3560)

Doudna and Sternberg might want to venture from their silo and professional echo chamber to visit the larger neighboring discipline of evolution. It seems they would discover that the context for their work has undergone a startling paradigm shift to biological relativity.

“Scientists are viewed with increasing distrust by a public that is skeptical about their contributions to society—that is, skeptical about the power of science to describe and improve the world. When people refuse to acknowledge climate change, reject vaccination programs for children, or insist that genetically modified organisms are unfit for human consumption, it signals not only their ignorance about science, but also a breakdown in communication between scientists and the public. The same
can be said of the protest movements against CRISPR that have already sprung up in France and Switzerland to decry the prospect of "GM babies." Unless we can reach these people and others like them, such distrust will spread." (3565)

While there is everything from ignorance and paranoia to denial and well-financed propaganda at work, some of what scientists see as "distrust" is actually a healthy skepticism on the part of the public about accepting on faith that advances in science and technology are "unequivocally good." There is no free lunch. Answers to scientific questions beg more questions. Technologies exact a price. Technological fixes often have a higher biospheric price tag than the problem they address, but they allow us to kick the can down the road. Then there are the genuine scientific SNAFUs like DDT, Thalidomide or CFCs.

"Scientists are partially responsible for this breakdown in communication. ... We need to make sure that knowledge flows just as freely between scientists and the public as it does among the researchers themselves." (3566)

No, scientists are largely responsible for the dearth of communication with the public just as they are for the lack of communication between scientific disciplines. If there were a free flow of knowledge between the sciences, would Doudna and Sternberg still be couching their arguments in neo-Darwinian blind chance? One would hope that the researchers, such as Doudna and Sternberg, who are urging the embrace of this new technology, would be up on the latest information about how genomes work as part of cells and organisms, what Denis Noble has termed biological relativity. That would seem to be a prerequisite for being “up to the task.”

Sinclair Lewis said "It is difficult to get a man to understand something when his salary depends upon his not understanding it!" It appears that scientists have no special immunity to what Whitehead referred to as trained incapacities, those things that you learn not to know.

“Given how radical the implications of gene editing are for our species

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and our planet, opening the lines of communication between science and the public has never been more essential than it is now. Gone are the days when life was shaped exclusively by the plodding forces of evolution. We’re standing on the cusp of a new era, one in which we will have primary authority over life’s genetic makeup and all its vibrant and varied outputs. Indeed, we are already supplanting the deaf, dumb, and blind system that has shaped genetic material on our planet for eons and replacing it with a conscious, intentional system of human-directed evolution. That we are unprepared for such colossal responsibility, I have no doubt.” (3575)

“Given how radical the implications of gene editing are for our species and our planet,” we might want to take a lesson from the “plodding forces of evolution” which have shepherded life through travails for more than 3800 million years. Do we need to set a pace that seen in contrast to deep time is nothing short of “frantic”.

We know next to nothing about what kinds of intelligence or consciousness exists on Earth. We do know that all cells sense and react to their environments to maintain metabolism and avoid harm. Hubris and human exceptionalism would have us mistake all sentient life

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and a living Earth as “deaf, dumb, and blind.” We know that bacteria quorum sense. If bacteria form some sort of global sensorium, we are ignorant of its existence. The authors arrive by circular logic at a determination that a “human-directed evolution” will be “conscious” and “intentional.” What is the evidence to support this claim?

There’s a schizophrenia here: one minute we are “up to the task” and the next we are “unprepared for such colossal responsibility.” The evidence, I submit, would indicate that it is most likely the latter.

Doudna and Sternberg note that scientific and governmental agencies unanimously support an international moratorium on any clinical application of gene editing human embryos. The Obama administration stated that “altering the human germ-line for clinical purposes is a line that should not be crossed at this time.” The NIH does not provide governmental funding for any research involving the gene editing of human embryos. Nonetheless, before Crack in Creation had landed on bookstore shelves, Nature had published the study where CRISPR was used in human embryos, “Correction of a pathogenic gene mutation in human embryos” mentioned earlier. Granted that these embryos, while reportedly viable, were not destined for implantation in a woman to produce a full term pregnancy, but the day they will be—moratorium or no—cannot be far off. —James MacAllister