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Industry 4.0: Gene Editing Is Pollution

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When new technologies are being developed, human imagination is often blindsighted by their revolutionary potential, leaving harms and dangers unpredicted or unnoticed until it is too late to rein them in. Now, industrial-scale biological engineering poses a similar problem. To make sure this technology stays within humane limits, we need to expand the moral circumference of what we see as pollution – i.e., to adopt an outlook that regards non-human organisms as possessing agency, dignity, and purpose.

In 2016, Klaus Schwab announced that we had entered the Fourth Industrial Revolution. This is the era of the industrialization of biology, the leveraging of technologies to modify biological materials to meet human goals. While the first two Industrial Revolutions exploited energy and materials and the Third exploited digital information, the current revolution is a direct manipulation of life-forms and life's substances.

The signature invention of this new era is CRISPR, dubbed "genetic scissors." CRISPR is a ground-breaking method of making precise changes to DNA for a wide range of possible uses, from disease reduction and elimination to the eradication of "pest" species and increases in the productivity of farmed animals. CRISPRs (the best-known system being CRISPR-Cas9) originate in RNA-based bacterial defence systems. Naturally occurring in species of bacteria, the Cas9 enzyme cuts the genomes of bacteriophages (viruses that will attack a bacterium), saving a record for defence against future infections. Scientists realised that this immunological strategy could be coopted to innovate a general tool for cutting DNA.

The optimism among those that seek to utilise these tools has been palpable for some time. As noted by the researchers at the Roslin Institute, creators of Dolly the Sheep, the world's first cloned mammal: "Until recently, we have only been able to dream of…the ability to induce precise insertions or deletions easily and efficiently in the germline of livestock. With the advent of genome editors this is now possible."

But the technologies of this new industrial era present ethical dilemmas and unknown consequences. What will it take to ensure that this revolution avoids worsening the enormous challenges we already face, especially from biodiversity loss and climate change? How can we get the balance right between the benefits and risks of human inventiveness?

Information and power

In the 1980s, tech theorist David Collingridge presented his eponymous dilemma for those seeking to control potentially disruptive technologies. First, there is an “information problem” in which significant impacts are often invisible until the technology is already in use. Second, there is a “power problem” in which the technology becomes difficult to shape, regulate or scale back once it has become integrated into our lives. If we are going to navigate the Fourth Industrial Revolution successfully, we need to examine our use of CRISPR through the Collingridge dilemma.

The investors and engineers of the first industrial revolutions in the nineteenth century provide a vivid example of the information problem. They hoped that innovations like the combustion engine would unlock efficiency across multiple human sectors, from transportation to logistics to tourism. Such optimism was not unwarranted. Yet, as Collingridge’s dilemma suggests, it is easier to picture gains than to predict trouble. Building road systems and infrastructure carved capital movements into the landscape, symbolising freedom and the flow of wealth and creativity.

Yet the striking visual parallels with our circulatory system did not stimulate anyone to forecast the 90 per cent of people today who are exposed to unsafe pollution levels from traffic or the associated health burdens from heart and lung disease to asthma. Nobody then foresaw the yearly deaths of two billion or so non-human vertebrates on our roads today, or that high-traffic areas would cause localised declines in insect abundance of at least a quarter and, in some studies, as much as 80 per cent.

And, of course, most calamitous of all, there is climate change. Traffic emissions account for a fifth of all contributions to global warming. Yet the idea that a profitable and efficient machine like the combustion engine might precede devastating shifts in temperature and weather patterns was scarcely conceivable at the time. Now, it is a near-ubiquitous feature of our understanding of the world.

When it comes to the engineering of biology, a similar information problem arises. Not only is our understanding of biological life incomplete, but we know little about what the industrial processes that we are advancing inside the cells of organisms will do. The changes are both physically and ethically occluded. The ramifications of this and other related biotechnologies are not only rendered uncertain by the inherently complex nature of biological systems but are largely inaccessible to our imaginations.

We must struggle with the radical character of the industrialisation of biology. Gene drives (a tool to increase the likelihood of passing on a gene) can weaponise the bodies and reproductive strategies of organisms to bias evolution in a directed way. Artificial chimeric organisms (those composed of cells from more than one species) mix and match biological traits and functions to bring about beings that wouldn’t occur otherwise, transforming autonomous organisms into useful parts for plug and play. But while evolutionary processes will sift those forms and strategies that most benefit future organisms, our acts of creation primarily benefit us alone. Survival of the fittest gives way to the contrivance of the functional.

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Yet, despite the disruptive nature of these technologies, CRISPR is already entrenched in our research and economic landscape: here is the power problem of our new technology. The efficiency of modern versions of CRISPR has allowed the technology to pick up users fast. It is now a commonplace tool in labs around the world – with uses amplified during the pandemic – and continues to be utilised in ethically provocative trials, including the cloning of mammal species. CRISPR has been normalised by stealth.

This largely uncontested rollout has been enabled by biases in the evaluation of who is at risk. Put bluntly, humans worry about humans, and take risks to non-humans less seriously. As such, there are vastly different acceptance thresholds for certain kinds of uses and these can be exploited by those that seek to deregulate or profit from the technologies.

CRISPR made headlines following the case of He Jiankui, the Chinese scientist who created the first genetically edited babies. Referred to as China's "Dr Frankenstein", he applied CRISPR-Cas9 to their genomes before they were born to remove a particular gene associated with susceptibility to HIV. There was considerable fallout, including the call by the WHO for a global ban on heritable human genome editing. He spent three years in prison as a result.

In comparison, the commentary around genome editing on non-human species is muted. This discrepancy is evident in the anxieties of Jennifer Doudna, one of the Nobel-winning scientists who made the CRISPR breakthrough. In her book, *A Crack in Creation*, she writes of a dream in which Hitler appears to her with the face of a pig and questions her excitedly about the power she has unleashed. Doudna's anxieties relate not to the pigs of her dream (who are subject to a wide range of CRISPR applications) but to the potential of eugenics re-emerging in human societies. Her dream reflects not only the inevitability that any technology such as this will be equal parts destruction to rewards, but also that we must confront uncomfortable ideas about what it is to be a *creature* as much as a creator. Recognising that these technologies work in the bodies of all biological beings, including humans, is a continual assault on the reasoning behind a hard moral border between us and them.

At present, the lives of non-human animals are the experimental landscape for our technologies. Their powerlessness to protest the uses of their bodies, wombs, physical materials, or futures leaves them vulnerable to being the test sites for a wide range of possible human applications. As a direct consequence of the serviceability of the bodies of organisms, CRISPR has been integrated into our world with little fanfare, directly facilitating the power problem that will, eventually, impact us too. Given Collingridge's dilemma, what concepts and strategies could help us reduce the risks from CRISPR?

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Polluting bodies

The first thing we need is a new definition of pollution. When it comes to combustion engines and other technologies of the first industrial revolutions, pollution is by far the most consequential harm. Direct impacts include the release of particulate matter or chemical compounds like nitrogen oxides or carbon dioxide into the atmosphere. Pollution from traffic has an immediate impact, especially 50 to 100 metres from the roadside, with effects that we can measure, such as reduced growth rates or leaf damage in plants, or changes to soil chemistry and nutrient availability. On the other hand, long-term effects of emissions, such as global warming, or the sustained impacts of waste on organisms and ecosystems, have proven tricky to anticipate and even harder to hold in mind.

The most effective environmental laws and ethical guardrails that have been enacted to date have been grounded in the concept of pollution, which both identifies who is responsible and the nature of the harm that should matter to us. The UK's 2021 Environment Act prioritised clean air and rivers, and reforms to the treatment of waste and plastics. Many countries have similar urgencies. Temporary car bans have become commonplace in cities around the world, with Barcelona and Oslo among those considering permanent bans. And there are precedents. The phasing out of leaded petrol from the 1980s onwards or the banning of chlorofluorocarbons (CFCs) that were found to damage the ozone layer offer guides to collective action. But how did the concept of pollution as a normative standard emerge?

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In the 1980s, as the environmental movement gathered momentum, freshwater biologist and oceanographer Michael Champ analysed the etymology and uses of the word "pollution" to guide principles that might assist in mitigating global environmental degradation. Quoting a 1971 review, Champ traced the Latin term "pollutionem", meaning defilement, on to its early English usage as the "defilement of man, his beliefs, or his symbols by physical, moral, or spiritual contamination or uncleanness," through to its modern sense of a human-caused "alteration of the existing environment that adversely affects the natural quality and quantity of the environment for life."

Human-made gene-edits (often trademarked as a product) are importantly different to biological functions that emerge holistically from the organism and their interaction with the environment. This difference allows us to view the genetic edits that are directly engineered into the body of an organism as possible pollutants. By extension, the deliberate integration of engineered organisms into an ecosystem can also be understood as a form of pollution.

This expanded concept of pollution helps identify and legislate against a range of negative consequences. There are known risks from genetic editing and modification techniques. We know, for instance, that even in the bacteria in which CRISPR-Cas9 is native, mistakes can follow. Sometimes there's binding to off-target sites, leading to unwanted mutations. CRISPR-based gene therapies can result in unintended edits to the genome that cause new diseases or even cancers. Other studies consider the implications of high numbers of damaged cells.

Further problems can follow from pleiotropic effects. Pleiotropy is the idea that a gene might influence the phenotype in multiple ways. The complex regulatory activities within cells and between genes make it difficult to engineer a desired trait at the level of the whole organism without incurring considerable risks. These direct effects can be conceptualised both as defilement and contamination. There is also the potential for secondary environmental impacts through unanticipated changes in population dynamics or even localised extinctions of species.

In other words, when viewed through the lens of pollution, we should be able to quantify harm from lots of different angles, including reductions in the health and welfare of individual organisms and spillover impacts on ecosystems, opening the way to litigate those enterprises that seek to exploit genetic technologies without robust justification and public agreement.

As Champ highlighted, pollutants only become *pollution* when the impacts are known and understood to matter to something or *someone*. Our perspectives on what we regard as pollution are constrained by the perceived value of that which has been affected by the introduction of a substance. Clean water and air, for example, matter *relative to us*. The notion of contaminated elements derives from our perspectives as organisms that are interdependent with our environment and thus positively or negatively affected by what we drink and breathe. Key, also, is our experience of our lives as meaningful, and our knowledge not only that wellbeing and flourishing matter to us but that we are the kinds of entities that can act on such knowledge. We are purposeful agents, and as such, we apply the concept of pollution as much to our bodies as to the environment.

It is far rarer, however, to extend the concept of pollution to non-human organisms as individuals with bodily autonomy. That is not because the concept doesn't apply. A new theory of pollution that includes the pollution of the bodies of sentient living beings more broadly could prove one of the most useful ways of weighing justifications for the uses of genetic technologies. Yet we are currently limited in our ability to do this by a formal ambivalence towards the capacities of other organisms, especially a recognition of their agency.

These biases against non-human life may be exacerbated by genetic-engineering technology. Recently, the British biotech firm Oxitec began to sell the eggs of a genetically modified species of mosquito that increases female infertility. The project results in localised reductions in diseases like dengue. This is a compelling achievement given that the biting females of the *Aedes* mosquitoes lead to thousands of human deaths. Oxitec's invention is like a genetic bugspray. What is of note, however, is the branding of a genetically modified animal *as if it is a product*. These are factory-produced living beings, trademarked under the brand "Friendly Aedes". That is a radical remodelling of what it is to be a living entity.

There are also companies like Colossal, which leverages the current interest in biodiversity loss and climate change to accelerate so-called "de-extinction" or "resurrection" technologies by using CRISPR to splice the DNA of an extinct organism with that of a related living animal to create the illusion of a biological revival. These applications overlay the presumption that the substances and processes of life-forms can be repurposed solely for human desire. The ethically thorny, if not indefensible, aspects of such projects – such as using elephants as surrogates for genetically engineered pseudo-mammoths – are obscured by misleading language that encourages people to think we're bringing an animal back from the dead in an act of benevolence. In reality, Colossal is a for-profit company currently valued at 15 billion US dollars.

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Organism over genome

What is curious about the Fourth Industrial Revolution is that while several branches of science are arming us with the evidence that justifies an expansion of the moral circle to encompass a larger range of organisms, other branches are cranking up the objectification and exploitation of life-forms. As a result, there's an obvious gap. Without addressing this, most concepts of pollution will remain anthropocentric. This may prove a critical misstep.

CRISPR is often described as a "dual-use technology", by which commentators mean that it can be used as readily for positive benefits like medical treatments as for aggressive or destructive ones such as novel invasive species. But the chief concern is biowarfare.

We often perceive biowarfare as a weapon analogous to a bomb, which causes direct harm to our bodies. Yet biowarfare also has indirect impacts on the wider environment. As we've seen in Ukraine, environmental destruction can be a weapon of war. We must assume that genetic modification will lead to the innovation of new military or aggressive methods. Some of these might be viewed as weaponised forms of pollution, through the destruction or poisoning of food sources, for example, or the devastation of ecosystems, or the release of a new pathogen that destroys crops.

Ultimately, what we need to secure us all is much more oversight and a tightening of the justified exploitation of non-human life. But to do this, we must acknowledge our biases and the importance of how we frame what's (or who's) at stake. This isn't always an easy task. Focusing only on trade-offs, for example, is inadequate and can skew us towards acceptance of a novel intervention.

An expanded and extended concept of pollution, reinforced by a more robust moral concern for non-human life, could help us both in describing the risks of genetic engineering and building legislation to hold those that trade in the most disruptive aspects of these technologies to account. There are any number of routes to this shift, from the scientific consensus on the capacities and intelligence of other beings, and new conceptualisations of living beings as meaningful agents, to more recent efforts to recognise animals as beings with dignity who are vulnerable to power structures.

Following from this, we need to rethink whose voices are included in the setting of recommendations and the formation of policies. Molecular biologist Natalie Kofler was sufficiently alarmed by the risks and inequities present in research environments around genetic technologies like CRISPR that she formed Editing Nature, a platform to debate future developments and uses, especially on non-human life-forms. Genetic engineering tools have a place in a "healthier planetary future", she wrote in an article for Science, "but only if they are developed with diverse inputs and employed with respect and humility toward a multiplicity of communities."

Beyond the missing voices of some human groups in policy formation, there's a growing movement to acknowledge the troubling absence of non-human life in decision-making. Recently, scholars like Martha Nussbaum, Danielle Celermajer, and Alasdair Cochrane have called for political representation of other species. Animals in the Room, for example, a project I have been involved in founding, designs deliberative processes that include the interests of non-human beings in governance settings precisely because making the realities of other species present helps shape our political choices in surprising ways.

Indeed, when we consider living beings not as entities directed by their genes but as beings whose genes work *for* them, our perspectives can transform. An equally valid interpretation of the science of biology allows us to look on the unique state of being alive as a *purpose-directed* process, replete with morally-relevant agents. Prioritizing the organism rather than their genome offers us a better framework for the recognition of genetic pollution.

And this more capacious definition of pollution can then assist in developing frameworks and ethical principles, and in designing associated laws. A legal system that can adequately capture the deleterious or lasting impacts of CRISPR on another living being's existence or on the environment in which life-forms thrive is warranted.

Ultimately, we must seek to apply the lessons of the past. As Collingridge showed us, we should not allow an absence of information to thwart our attempts to account for the negative consequences of new technologies, and nor should we feel powerless to halt or change direction simply because we have already begun to benefit from a disruptive tool. Future generations of both humans and non-humans alike will thank us for our bravery and foresight.

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