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# The Hope and Challenge of Synthetic Biology

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***Abstract* - Mankind's newfound ability to edit germline codes will soon be widely available. We will also be able to extend the palette of naturally available amino acids for molecular assembly. The opportunity to heal disease, improve memory, increase strength, and extend lifetime is exciting. The threat that an ideological enemy could insert malfeasant and irreversible mutations is frightening. The United States, at least, needs a policy framework that defines and addresses the five key decisions that will determine whether we can leverage the benefits and simultaneously defend against attacks.**

***Keywords - synthetic biology, CRISPR, germline modifications***

## I. Introduction

By far the most important information known to mankind – the human genome – is stored in trillions of containers, inside billions of mobile agents, and dynamically refreshed millions of times per year. Not every new instance is perfect, and miniscule deviations can be healthy or self-destructive. But there are so inconceivably-many copies that, taken in aggregate, new versions eventually break ground along a meandering path that began four thousand millennia ago. Evolution is indifferent to and unencumbered by quarterly reports to an owner; authentic experimental freedom created the best innovation of all: life itself.

Nature organized this chemical database into forty-six (twenty-three paired) units called chromosomes, each written in a deceptively simple four-letter alphabet. Our molecular-scale understanding of the story told in three billion cuneiforms of nucleic acid is only seventy years old, eyeblink short on the time scale it took to create its letter-by-letter assembly. Yet we can already connect some metabolic pathways to their genetic grammar.

In this paper, we consider the implications of the accelerating pace of human germline modification in an historical context. The potential impact and consequences on evolution will be explored and discussed, with particular emphasis on who, from a policy perspective, "owns" the bio threat. Finally, we will describe the relevant policy questions in the context of five imperative decisions.

## II. The New Keyboard of Computational Biology

Until the last century we hardly knew genes existed. Fifty years ago, we began to attach radioactive isotopes to small segments of chromosomes to see where they landed after mitosis. Today we have machines that allow us to actively read-and-write DNA by the base-pair, almost like a modern word processor or software development environment.

In other words, human-made hardware is now capable of changing the somatic software that runs us, like a computer autonomously downloading new apps it finds interesting, or willfully changing its operating system. Germline modification – the ability to permanently change DNA that is transmitted to offspring – is coming soon. It will be inexpensive, reliable, and generally available.

To understand how fast these changes will occur, consider Kevin Drum's animation that starkly demonstrates acceleration at Moore's Law speed of change: doubling something every eighteen months [1]. He pretended to fill Lake Michigan with water, starting with one fluid ounce, and then two fluid ounces a year and a half later, and then four fluid ounces after three years. Seven decades later one can barely detect the results of such make-believe. Yet in only fifteen more years, the lake is full. Put in astronomical context: a little more than a century ago we were in the pre-Kitty Hawk days of heavier-than-air flight; two generations later we took giant leaps on the moon.

Illuminating biological pathways for mischief or profit will occur faster still.

For most of history information exchange, fake or not, depended upon physical access, which became exponentially sweeping with broadcast radio, broadcast television, and most recently with the internet. The adoption of movable type for mechanical printing took almost exactly 400 years, from Bi Sheng's invention to the Gutenberg Bible. The iPhone moved mainstream adoption of smartphones from 5% to 40% – a typical metric of comparison – "in about four years" [2].

None of these advances remotely exploit the taproot of all information, literally encoded in our DNA. We can already manipulate cell-level outcomes by blocking certain functions that result in disease. Tomorrow we will change DNA itself to anthropogenically repair mutations that cause problems in the first place. The day after tomorrow we will manipulate molecularly bio-similar instructions outside of a living organism to produce new non-biological materials with properties we have never seen before, like those reported in November 2017 [3].

A genetic program of (only) three billion instructions can create a human baby in nine months. Now the underlying "technology" that reads the code-script, specifically the ribosomes (software developers would call these compilers) that assemble proteins one amino acid at a time, can be teleologically reverse engineered. Reflect, for example, on the power to genetically modify for strength, intellect, longevity, or control based on the current alphabet of twenty building blocks. Imagine synthetically extending the keyboard to include hundreds, thousands, or hundreds of thousands of new "letters" – new amino acids – for biological and non-biological applications. Truly we are at the incunabula stage – the quiet interregnum between handwritten texts and mass-produced manuscripts – in our ability to print molecular components whose attributes we-ourselves define.

## III. Real World Implications

The public health implications of genetic de-coding are breathtaking. Prophylactic vaccinations against communicable infection coupled to curative therapies for cancer, diabetes, and heart disease mean that many of us, particularly in the developed world, will live longer, healthier, and physiologically safer lives. An individual's opportunity for creative contribution, including especially our collective scientific understanding, will grow exponentially.

Few would want to turn the clock back to an age before anesthetics, x-rays, penicillin, or imatinib [4]. Fewer still can conceive the convergence of carbon-born ethics to silicon-born judgment. Developed-world innovation in artificial intelligence and biochemistry will exacerbate inequality, because those countries are technologically, institutionally, and infrastructurally farther up the acceleration curve.

### *A. Faster Evolution*

The emerging miracles of modern biotechnology and biotech-inspired materials science conceal an existential threat to a fragile balance of international powers, and to our own national security. If not more thoughtfully debated on the global stage and controlled by multi-party agreement, our very existence is challenged by a single laboratory accident or ideologically-driven attack. There are now people in the world who perform scientific experiments that can lead to morally disturbing outcomes. There are now people in the world who aim to demolish the foundational institutions of modern society by any means possible. New systems, especially those that biomimick natural pathogens and cognitive synthesis, will far exceed our governments' ability to control them. Riven enemies can too easily turn them against us and each other; ignorance and prejudice will fuel anger and violence.

Scientific breakthroughs in biochemistry and microbiology will be further advanced by self-reinforcing capabilities of (irreversible) computer-aided decisions. For all the benefits of artificial intelligence (AI) and machine learning (ML) – and there are many – the predictive power of these new technologies is imperfect, and their moral judgment and executive function is nonexistent.

Dan Geer, In-Q-Tel's chief information security officer, told us that, "Our intervention in evolution is just more evolution, but at a faster clock rate. Changes that depend on random perturbations take geologic time, including time to test for side effects. Changes that people design may have just as many unforeseen consequences, but the equilibria they punctuate are of much shorter duration." In other words, machine learning means self-modifying algorithms; it is impossible to ask them how they made their decisions, and their impact is quick and permanent. The problem, Geer explained, is that "nations don't have geological time-scales to cull for fitness of their machine learning stock. What if the current generation of people becomes an experiment in evolution?"

Geoffrey Hinton wisely observed that "the algorithm can solve a case. It cannot build a case" [5]. In other words, AI and ML are great at deciphering the what's, where's, and how's – all questions that are essentially answered by extremely sophisticated pattern recognition – but they cannot begin to understand why, which is the core of the human experience. AI and ML can help experienced professionals avoid poor choices, and they can suggest data-driven hypotheses. But correlation is not causality, and neither can yet replace compassionate bedside manner, values-based judgement, or face-saving diplomatic nuance. AI and ML will continue to make marvelous contributions to diagnosis and classification, but they will not, in our opinion, and certainly not in the near term, be able to harvest social sentiment or connect outcomes to social values [6].

Even in a data drenched world, data scientists are still unable to predict the outcomes of plebiscites or the weather. And no computer would have anticipated the physical fatigue, psychological momentum, or miraculous catch that changed the otherwise prevenient outcome of the final quarter of Super Bowl LI. AI and ML reveal patterns; they cannot ask the right questions, detect insincere answers to national polls, or hypothesize Julian Edelman's hands. There are no silicon- (or even carbon-) based systems that can stop torture, stop ethnic cleansing, or better teach the irrefutable science of climate change.

### *B. Who Owns the Threat?*

Today we are still untangling the engineering problem of cataloging proteomic outcomes to genetic codes, ribosomal assembly, and the restricted spectrum of natural permutations. Soon we will be able to create an editable biochemical code, with an expanded palette of man-made materials. Civil society must demand political leadership engage in open debate to determine if the outcomes are desired or not, for whom, and why. On the one hand we need to agree and establish in international law acceptable scientific methods, ethical norms, and commercial standards; on the other hand, we need to recognize that some governments, and powerful individuals within those governments, will flout them anyway.

There is no single agency in the US government, or any international body, that "owns" the bio threat. This leaves the US wide open to nefarious actors, just as it leaves the civilized world vulnerable to the malevolent, violent, and absent-minded. The confluence of uncharted technical capability and poor prediction is especially serious now, because for the first time we have the capability not only to destroy ourselves on a nuclear scale, we might accidentally change the structure of our embedded software species-wide. The first experiments of so-called germline embryos occurred in China. They were well intended. Soon enough they will be successful and fall into the hands of less altruistic communities. The consequences are even more tragic and destabilizing than a suicide bomber who kills children (as incomprehensible as that is); genetic changes are heritable, persistent, and may be impossible to undo.

Sonal Shah, the executive director of the Beeck Center for Social Impact and Innovation at Georgetown University, said "The convergence of AI with biotechnology is one of the most important social consideration of our times, on par with global warming." This is an important point, because from the scientific perspective, the case of carbon dioxide loading is well decided [7]. General John R. Allen, who commanded coalition forces in Afghanistan, told us that the Department of Defense is investing in technologies that lower our carbon footprint and obviate climate change. "We know how to model the security implications of increasing temperatures," he said, "but the ethical considerations of autonomous systems deciding who to kill in a robot war are new and undecided." LaPointe and Levin made a similar point in Foreign Affairs [8], as did Danzig [9].

There are plenty of examples of our collective inability to cooperate when the physical evidence is clear, for instance in contaminated water, depleted fish stock, and inexorably rising tides. The existential threat of AI-driven biotechnology is abstract to most people, including highly educated policymakers of every color, creed, culture, and continent. But knowhow, like the atmosphere, neither conforms to nor respects international borders.

## IV. The Policy Questions

There are five decisions to make:

First and foremost, we will implicitly choose whether or not to address these discussions openly, transparently, authentically, and democratically. We have already ceded a years-long head start to our friends, rivals, and enemies, primarily because of restrictions on stem-cell research. They are making dramatic progress in artificial intelligence and bio-engineering. So, first, we need to decide to decide.

Second, assuming a more pro-active and deliberate process, the US government needs to dramatically increase funding into the overlapping disciplines of bio-engineering and machine learning. There are, of course, undeniable benefits to an ageing society with a paucity of primary-care physicians. Superior pattern-matching capabilities and front-line decision support to human clinicians will improve quality, lower costs, extend resources, and change lives for the better. Pedro Domingos of the University of Washington expects that AI will help screen drugs for toxicity much faster than human trials. He said, "We know that some medicines may be poison to most people, but can save the lives of a small group of patients; we can use machine learning to safely reach those who will benefit."

The most dire need for focused research is in the area of dementia and Alzheimer's. George Vradenburg, founder of the non-profit USAgainstAlzheimer's, estimates that the global cost to support dementia victims already exceeds $1 trillion, over 1% of global GDP, and is increasing at an accelerating rate. Ironically, nowhere is the need for advances in computer discovery and intelligence more acute than human cognition and rational behavior.

Third, we need to protect what we discover. We blithely live in the shoals of a relentless tsunami of breached personal data. This is a gigantic mistake. Our profligate attitude towards cybersecurity is going to migrate from personal inconvenience to economic intrusion, and from intrusion to physical incursion. We have lit up a fog-shrouded runway for our competitors and adversaries to land on; they do not need an invitation to take the next step. So much of societally beneficial innovation was born in the United States – from satellite navigation to semiconductor design, and from advanced industrial materials to HIV therapies – but we controlled, to a greater or lesser extent, when and how they were deployed [10]. At this point not only do our rivals have a jump, they have an asymmetric advantage because they can see what we are, and are not, doing; they can also engage new technologies anyway they choose.

Fourth, the United States needs to be keenly aware of the research and development efforts of other countries. Some intelligence gathering will inevitably fall on the shoulders of clandestine operations. Some requires more structured and pro-active engagement with globally-minded scientists from other nations, where academic collaboration and technical trust trump selfish commercial impulses (or clumsy friends) that may have detrimental – or what we today perceive as detrimental – effects on national security and economic competitiveness.

Finally, the most difficult question of all: how much should we share? The convergence of scientific discovery (based on advances in the creation and construction of bio-mimicking processes), technological capability (based on advances in AI and ML), and ethical judgment (based on verifiable truthful and fact-based information) can lead to a richer, more peaceful world, or to horrible conflagration. There will be tremendous commercial advantage to the companies, and the nation-states that host or sponsor them, who master the science and technology of the 21st century. Left to their own devices, their human values and political goals will inevitably permeate not just consumer choice, but seats of government. Clearly there is a case for thoughtful dialog, for investment, for protection, and for nourishing communities of aligned and common interests.

## V. Conclusion

Domingos writes [11], "The real story of automation is not what it replaces but what it enables." Technologies that touch the genome shift the ethical, commercial, and global security paradigm in ways that are unprecedented in human history. Unless and until we honestly, methodically, and transparently approach the governance of our new-found powers, we need not fear cyborg domination any time soon, no, just the people who control their software.

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