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2016 : WHAT DO YOU CONSIDER THE MOST INTERESTING RECENT [SCIENTIFIC] NEWS? WHAT MAKES IT IMPORTANT?

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The Race Between Genetic Meltdown and Germline Engineering

The most remarkable breaking news in science is that I exist. Well, not just me. People like me who, without technology, would have died early. Of the roughly 5 ½ billion people who survived past puberty, perhaps only one billion would be here were it not for modern sanitation, medicine, technology, and market-driven abundance. Ancestrally, the overwhelming majority of humans died before they had a full complement of children, often not making it past childhood. For those who live in developed nations, our remodeled lifetables are among the greatest of the humane triumphs of the Enlightenment—delivering parents from the grief of holding most of their children dead in their arms, or of children losing their parents (and then themselves dying from want).

But there is hidden and unwelcome news at the core of this triumph. This arises out of the brutal way natural selection links childbearing to the elimination of genetic disease.

The first thing to recall is that even our barest functioning depends on amazingly advanced organic technology at all scales—technology engineered by selection. For example, our eyes—macroscopic objects—have two million moving parts, and yet individual rods are so finely crafted they can respond to single photons. Successful parents in every species live near spiring summits on adaptive landscapes.

The second thing to remember is that physics is perpetually hurling us off these summits, assaulting the organization that is necessary to our existence. Entropy not only ages and kills us as individuals, but also successfully attacks each parent's germ line. Indeed, the real news is that a number of methods have converged on the estimate that every human child contains roughly 100 new mutations—genetic changes that were not present in their parents. To be sure, many of these occur in inert regions, or are otherwise “silent” and so do no harm. But a few are very harmful individually; and although the remainder are

individually small in effect, collectively they plague each individual with debilitating infirmities.

These recent estimates are striking when one considers how, in an entropy-filled world, we maintained our high levels of biological organization. Natural selection is the only physical process that pushes species' designs uphill against entropy toward greater order (positive selection), or maintains our favorable genes against the downward pull exerted by mutation pressure (purifying selection). If a species is not to melt down under the hard rain of accumulating mutations, the rate at which harmful mutations are introduced must equal the rate at which selection removes them (mutation-selection balance). This removal is self-executing: Harmful genes cause impairments to the healthy design of the individuals they are situated in. These impairments (by definition) are characteristics that reduce the probability that the carrier will reproduce, and thereby reduce the number of harmful genes passed on. For a balance to exist between mutation and selection, a critical number of offspring must die before reproduction—die because they carry an excess load of mutations.

Over the long run, successful parents average a little more than two offspring that survive into parenthood. (The species would go extinct or fill the planet if the average were smaller or greater.) This is as true for humans with our handful of children as it is for an ocean sunfish with a nest full of 300 million. To understand how endlessly cruel the anti-entropic process of selection is, consider a sunfish mother with one nest. On average 299,999,997 of her progeny die, and 2 or 3 become comparable parents. Since the genotypes of offspring are generated randomly, the number of coin flips (in 300 million series) guarantees a lower end of the binomial distribution of mutations that are many standard deviations out. That is, there are two or three who become parents because they received a set of genes that are improbably free of negative mutations. These parents therefore restart the lineage's next generation having shed enough of the mutational load to have rolled back mutational entropy to the parental level. Ancestral humans, with far smaller offspring sets, maintained our functional organization more precariously, having survived over evolutionary time on the edge of a far smaller selective gradient between those children with somewhat smaller sets of impairments and those with somewhat larger sets. Most ancestral humans were fated by physics to be childless vessels whose deaths served to carry harmful mutations out of the species.

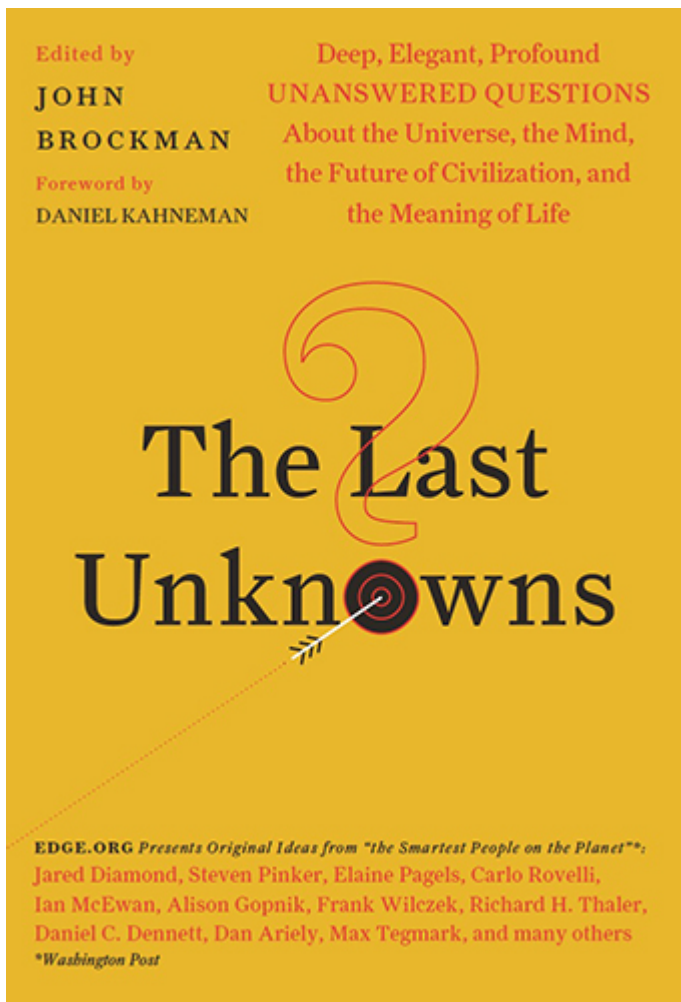
Now, along comes the demographic transition—the recent shift to lower death rates and then lower birth rates. Malthusian catastrophe was averted, but the price of relaxing selection has been moving the mutation-selection balance toward an unsustainable increase in genetic diseases. Various naturalistic experiments suggest this meltdown can proceed rapidly. (Salmon raised in captivity for only a few generations were strongly outcompeted by wild salmon subject to selection.) Indeed, it is possible that the drop in death rates over the demographic transition caused—by increasing the genetic load—the subsequent drop in birth rates below replacement: If humans are equipped with physiological assessment systems to detect when they are in good enough condition to conceive and raise a child, and if each successive generation bears a greater number of micro-impairments that aggregate into, say, stressed exhaustion, then the paradoxical outcome of improving public health for several generations would be ever lower birth rates. One or two children are far too few to shed incoming mutations.

No one could regret the victory over infectious disease and starvation now spreading across the planet. But we as a species need an intensified research program into germline engineering, so that the Enlightenment science that allowed us to conquer infectious disease will allow us to conquer genetic disease (through genetic repair in the zygote,

morula, or blastocyst). With genetic counseling, we have already focused on the small set of catastrophic genes, but we need to sharpen our focus on the extremely high number of subtle, minor impairments that statistically aggregate into major problems.

I am not talking about the ethical complexities of engineering new human genes. Imagine instead that at every locus, the infant received healthy genes from her parents. These would not be genetic experiments with unknown outcomes: Healthy genes are healthy precisely because they interacted well with each other over evolutionary time. Parents could choose to have children created from their healthiest genes, rather than leaving children to be shotgunned with a random and increasing fraction of damaged genes. Genetic repair would replace the ancient cruelty of natural selection, which only fights entropy by tormenting organisms because of their genes.

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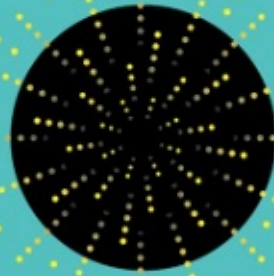


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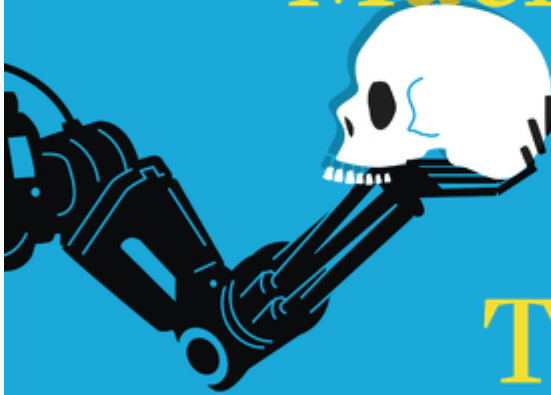
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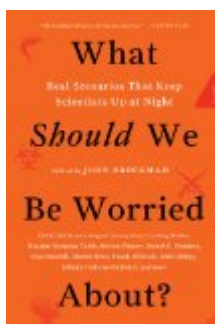
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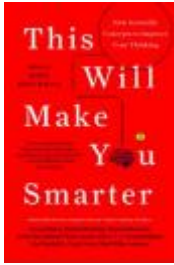
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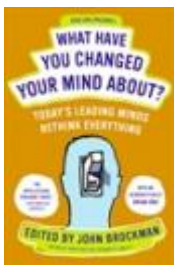
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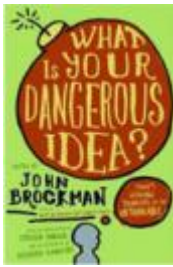


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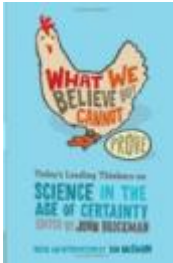


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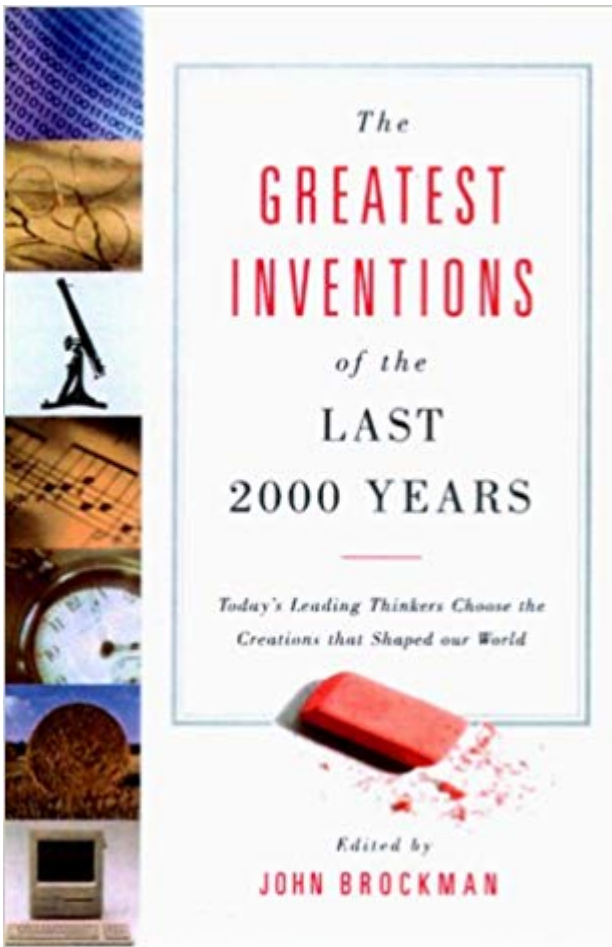
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