#### The Ascent of Man

Tall tales from biology's Wild West by KATHERINE XUE

it together, at least in the public eye, was on June 26, 2000, when Human Genome Project director Francis Collins and Celera Genomics founder Craig Venter joined President Bill Clinton in the White House to declare the draft sequence of the human genome complete. "Without a doubt, this is the most important, most wondrous map ever produced by human-

kind," declared Clinton. "Today, we are learning the language in which God created life." It was a triumph more than a decade, some dozen institutions, and a thousand scientists in the making. Just as importantly, the Human Genome Project represented the fulfillment of an entire biological paradigm—the field of molecular biology—that had begun in 1953 with the discovery of the structure of DNA.

That was then, and this is now. Welcome to the post-genomic age. The idea

of the human genome is obsolete: hard on the heels of the Human Genome Project came the International HapMap Project and then the 1000 Genomes Project, each aiming via its successively more sophisticated technology to assess and record the range of human variation. Genomes are relatively cheap—about \$1,000 for yours or mine—but even one genome per person may not be enough. It's fashionable now to speak of multiple genomes in a single individual, generated by mutations that occur as the body's cells grow and divide. And genomes aren't enough: everything has an "-ome" these days. The epigenome, proteome, microbiome, metabolome, con-

#### Off the Shelf

Recent books with Harvard connections

Women After All: Sex, Evolution, and the End of Male Supremacy, by Melvin Konner, Ph.D. '73, M.D. '85 (Norton, \$26.95). A sweeping, searching argument, from "biology and...the domains of our thoughts and feelings influenced by biology," that "women are not equal to men; they are superior in many ways, and in most ways that will count in the future." The author is an anthropologist, who also engages in neuroscience, at Emory.



Wicked Problems, Workable Solutions, by Daniel Yankelovich '46, G '49, K '96 (Rowman & Littlefield, \$36). Drawing on a life's work investigating American public opinion, the author probes ways to engage citizens in reaching better

public decisions and solutions to intractable issues.

Two useful collections: Byline Richard Wright, edited by Earle V. Bryant, Ph.D. '79 (University of Missouri, \$60). The editor, of the University of New Orleans, has collected and annotated much of the Daily Worker journalism and two New Masses essays that preceded Wright's iconic Native Son and Black Boy. And Edward P. Kohn '90 has edited A Most Glorious Ride (Excelsior Editions/SUNY, \$29.95), Theodore Roosevelt's diaries from 1877 to 1886. Occasional "studying with a will" and much partying, shooting, and recording of "prettiest girls," such as Miss Emily Swan, with whom TR "had several very pleasant rows and rides."

Geek Heresy, by Kentaro Toyama '91 (PublicAffairs, \$27.99). The co-founder of Microsoft Research India, where he studied the intersection of technology with socioeconomic issues among some of the world's poorest people, now writes from the University of Michigan. The rapid spread of digital technology, he observes, has coincided with persistent, and per-

Westward ho! Theodore Roosevelt and brother Elliott en route to TR's first western hunting trip, 1880 haps worsening, poverty. This "recovering technoholic" makes the case for "rescuing social change from the cult of technology."

Biology basics: In Tools for Critical Thinking in Biology (Oxford, \$49.95), venerable teacher Stephen H. Jenkins, Ph.D. '75, now emeritus from the University of Nevada, Reno, attempts to teach the basics through applying the fundamental tenets of the scientific process. The Developing Genome: An Introduction to Behavior Epigenetics, by David S. Moore, Ph.D. '88 (Oxford, \$39.95), is an approachable primer on the frontier field of studying which genes are switched on, and how they are influenced by experience. The author is at Pitzer College and Claremont Graduate University.

Cora Du Bois: Anthropologist, Diplomat, Agent, by Susan C. Seymour, Ph.D. '7I (Nebraska, \$39.50). The author, an anthropologist emerita at Pitzer College, profiles Du Bois, who did pioneering anthropological field work among Native Americans and in Indonesia and Sri Lanka; served in the Office of Strategic Services during World War II; and was appointed to the Zemurray chair at Radcliffe and to tenure in the anthropology department, before presiding over the American Anthropological Association.

The Physicist and the Philosopher, by Jimena Canales, Ph.D. '03 (Princeton, \$35). The author, a University of Illinois historian of science, uses a celebrated debate between Albert Einstein and Henri

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nectome, interactome—each vies to be the next new scientific thing to set the public imagination on fire.

Out of this post-genomic landscape comes Evolving Ourselves: How Unnatural Selection and Nonrandom Mutation Are Changing Life on Earth. Venture capitalists Juan Enriquez '81, M.B.A. '86, and Steve Gullans, formerly a professor at Harvard Medical School and Brigham and Women's Hospital, present a fast-paced, conversational collection of dispatches from biology's frontiers. Captured in the book's title is its thesis: more than ever, human beings are both agents and subjects of biological change. Darwin is dead, and with him the forces of natural

selection and random mutation that built all life on earth.

Instead, the authors articulate a new biological order, founded on two principles: unnatural selection and nonrandom mutation. In the first, humans alter their environment through civilization: the plant and animal domestication that Darwin recognized as artificial selection has been followed by industrialization and now modernization. Agriculture has rearranged ecosystems and propelled select species across the planet, and anthropogenic chemicals have found their way into all the earth's water and air. Human activity exerts subtler selective pressures as well:

Evolving Ourselves: How Unnatural Selection and Nonrandom Mutation Are Changing Life on Earth, by Juan Enriquez '81, M.B.A. '86, and Steve Gullans (Penguin/Random House, \$28.95)

minimum-size requirements on fishing have shrunk sardines, and city-dwelling mice and voles develop bigger brains than their rural cousins. "Unnatural selection" is too dramatic a term here—the fish and rodents are still products of Darwinian evolution—but the authors seek to evoke agency. The biological world, they argue, is increasingly one of our own making.

This expanded agency is at the core of

Bergson about the nature of time to illuminate the colliding worldviews of scientific and humanistic understanding.

Galápagos Regained, by James Morrow, M.A.T. '70 (St. Martin's, \$28.99). In his tenth novel, the author imagines an assistant to Charles Darwin, one Chloe Bathurst, seeking fortune and fame by appropriating and applying his theory of evolution. Those not fond of tortoises, be warned.

Being Nixon: A Man Divided, by Evan Thomas '73 (Random House, \$32). The fluid biographer of Dwight Eisenhower, Robert Kennedy, and others turns his attention to a darker subject, providing amusing reminders of RMN's bipolar attitude toward Harvard and Harvardians ("None of them in the Cabinet, do you understand?")—a good many of whom, like Henry Kissinger and Daniel Patrick Moynihan, he relied upon for the largest matters of his presidency.

A pair of primers. What's Your Future Worth? by Peter Neuwirth '78 (Berrett-Koehler, \$18.95 paper). A consulting actuary advises on balancing time, risk, and money by employing present value; in the author's note, he says the technique figured in his decision about whether to get married. Remember: he's an actuary. Harvard Law student Tyler Vigen amusingly illustrates different and bone-headed analyses in Spurious Correlations (Hachette, \$20), a humorous guide (the first example is the notorious simultaneous

rise of human births and the stork population in late nineteenth-century Holland). If the law doesn't pan out...

The Allure of Order, by Jal Mehta, associate professor of education (Oxford, \$24.95 paper). A sobering history of the "troubled quest to remake American schooling" through attempts to impose external accountability on teaching—most recently, via the No Child Left Behind Act. For an on-the-ground look at

classrooms and students, How Did You Get Here? by Thomas Hehir, Pascucci professor of practice in learning differences, and Laura A. Schifter (Harvard Education Press, \$70 cloth, \$35 paper), tells the stories of 16 students with diverse disabilities who made their way to, and through, Harvard.

Tangible Things: Making History through Objects, by Laurel Thatcher Ulrich, 300th Anniversary University Professor, et alia (Oxford, \$49.95, paper). A quartet of authors and a photographer build upon a 2011 exhibition drawn from Harvard collections to illustrate the importance of materially based history.

The world of work: **Pedigree: How Elite Students Get Elite Jobs,** by Lau-



Among Harvard's tangible things: "Blondie Goes to Leisureland," a comic-based 1940 game, promoting Westinghouse products

ren A. Rivera, Ph.D. '09 (Princeton, \$35). An associate professor of management at Northwestern's Kellogg School shows through sociological research that mobility and merit are hollowing out, as toptier employers gravitate toward affluent, upper-class applicants. In entirely different realms, Harvard Magazine's Craig Lambert '69, Ph.D. '78, who retired as deputy editor (a real job) last year to finish writing a book (another real job), has delivered Shadow Work: The Unpaid, Unseen Jobs That Fill Your Day (Counterpoint, \$26). Odds are, he had to book his own flights and assign his own seats and schlep his own bags on his book tour. For more, see harvardmag.com/lambert-15.

their second theme, "nonrandom mutation," in which humans alter life more or less at will. Much of the book consists of a paean to bioengineering's potential (Enriquez is a TED all-star, and it shows). Synthetic organs—skin, bladder, teeth are gaining in sophistication, and CRIS-PR-Cas is the latest technology to make it easier to modify our genes. Meanwhile, biology intrudes on identity: hormone treatments alter emotions and blur distinctions between the sexes, and in rats, simple memories can be triggered using pulses of light. The field of synthetic biology aims further still, toward a sort of reversal of time (see "Synthetic Biology's New Menagerie," September-October 2014, page 42). Its most audacious, or at least most vocal, proponents imagine "de-extinction," using large-scale DNA synthesis to bring extinct species—the passenger pigeon, the woolly mammoth—back to life.

The authors greet this brave new biological world with relatively untrammeled optimism. They imagine designer organs and cloned humans, genetic engineering akin to plastic surgery. The book's final chapter is devoted to human colonization of space. Short stature might be an advantage in confined extraterrestrial settlements, the authors helpfully advise, and gene variants associated with a cheerier

disposition might not be so bad, either. What's clear to them, at least, is that humanity has reached a technological point of no return. "[W]e have changed the nature of our world to such an extent, and developed such profound capabilities for recrafting our bodies and environment," they write, "that we are birthing our successor species."

When read against the grain, however, Evolving Ourselves gives hint of best-laid plans gone awry. Modernization has its casualties, some just beginning to be known. Enriquez and Gullans open the book with a medical mystery, the skyrocketing incidence of autism in recent years. Changes in diagnosis undoubtedly contribute, but the authors cite studies suggesting that environmental factors are at least partly to blame. "Autism," they write, "maybe be just one harbinger, one symptom, of our radically changing world."

Autism is hardly alone, they add. Various other diseases—obesity, allergies, depression—are on the rise, less-welcome products of the technological progress that has brought about immense lifestyle change, propelling old bodies into a new world. Consider antibiotics. Since their introduction in the mid 1900s, they've saved millions of lives, yet recent research on the

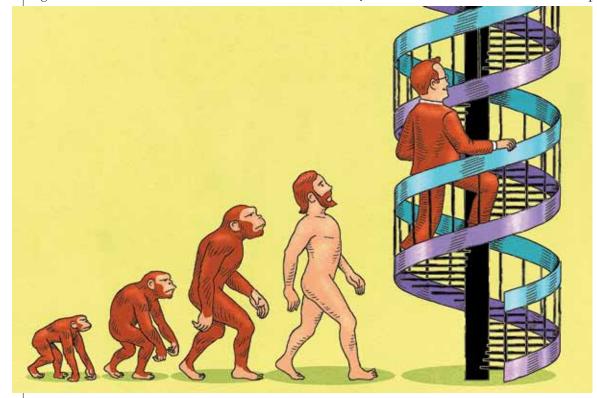
microbiome prompts caution about all-out antimicrobial assault. Our body's resident microbes have important roles to play. They digest nutrients, fend off would-be invaders, and produce chemicals necessary for bodily function. Antibiotic use may in fact be linked to obesity: farmers have long fed their animals low doses of antibiotics to promote weight gain, and it's possible that humans experience similar effects.

These scattered anecdotes form a crosscurrent to the authors' breathless technooptimism, and in the chapter "A Perfectly Modern Pregnancy," the book gives a far more familiar—and telling—snapshot of biotechnology today. When Gullans's expectant daughter asks her father for medical advice, he and she dive into murky waters. Smoking is out, as are most prescription (and recreational) drugs, but right around there, the clear advice ends. A balanced diet is important, but nutritional supplements may be too much. Genetic testing is by and large a no, and likewise analysis of the baby's the epigenome and microbiome. "The methods for analysis aren't robust enough," the authors write, "so the data remains difficult to interpret, leading to more confusion and worry than anything...." Space colonization remains intellectual light-years away.

These discrepancies between current

research and its imagined possibilities are not mere pedantry; on technical points, the book is meticulously cited and largely correct. Still, Evolving Ourselves is best read as a book of tall tales from biology's Wild West. Its stories begin in scientific truth but swiftly shape-shift into myth. Clones, cyborgs, designer babies—as dreams and nightmares, they have been with us for decades, always at the edge of the biological horizon. They are our society's technological visions, ghost stories of Biology Yet to Come.

From the same scientific beginnings, the



# Scientific progress morphs into promises of technologically designed utopia: "Forever Young, Beautiful, and Fearless?"

authors could have chosen different stories to tell. Sequencing the human genome took more than a decade, and beginning to interpret it will take much longer than that. It is easier than ever to read and engineer DNA, but it remains dauntingly difficult to engineer biology, and the two should not be confused. Enriquez and Gullans note that as soon as researchers began scouring the human genome for genes that influence health and disease, they ran up against the problem of so-called missing heritability. Height, for instance, is estimated to be 80 percent genetic, but as of last year, the nearly 700 hundred genes identified in connectionthrough genome-wide studies of a quartermillion individuals, no less—account for about one-fifth of that effect.

If genes seem to lose their luster, there is no shortage of biological paradigms looking to take their place. The authors

describe the epigenome—chemical modifications to DNA that affect when genes are expressed—as each person's "second genome," one subject to heritable change due to environmental effects. As it happens, "Second Genome" is also the name of a company that aims to develop therapeutic interventions for the microbiome, which has been increasingly linked to physical health as well as moods and mental disease. "My microbiome made me do it," one T-shirt proclaims.

It's no surprise that scientists and the media alike embrace these totalizing languages. They have a seductive simplicity. Genomes first or second are reified into biology itself; scientific progress morphs into promises of technologically designed utopia. "Forever Young, Beautiful, and Fearless?" asks one chapter. "The Robot-Computer-Human Interface,"

posits another. It is enough, I hope, to give one pause. Genetic (epigenetic, microbial) engineering could be used for disastrous ends, with or without intent. At the grand-historical scale of the authors' imaginings, technologies alone cleave a Gordian knot, leaving convoluted personal, political, and societal consequences in their wake.

We may submit to these totalizing scientific vocabularies to pursue fantasies of total biological control, but the bargain is Faustian. When scientific concepts become all that is worth knowing, humanity shrinks to fit what can be known. When all aspects of the human experience are fully and scientifically understood—when DNA becomes the language of personality, and hormones, microbes, and electric pulses the substance of emotion—when genes, memories, and thoughts can be generated and manipulated at will—then, will mankind have ascended at last?

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