

BIOMOLECULARIZATION

THE EVOLUTION OF HIGH-RESOLUTION HUMANS

THE CHALLENGE

Adapting our social, medical, and governance systems to a new understanding of humans as microbial ecosystems

THE SHAPE OF TRANSFORMATION

From individually responsible intelligent organisms to complex ecosystems of biologically distributed intelligence

Since the 1735 publication of Linnaeus's *Systema Naturae*, humans have been defined as an anatomically distinct species. And certainly since Darwin's *On the Origin of Species*, humans have pointed to one organ in particular—the brain—as the principal distinguishing feature of our species. We have believed that this brain functions as a central command center to control our behavior and adaptations to our environment. Our human genetic makeup mixes with our lived experiences to determine the person we become.

This is how we have viewed ourselves. Up until now. But thanks to high-resolution tools, we're discovering that our humanness is a very small part of what we call our "beings." At the molecular level, we now know that our human cells make up only a tiny fraction—1% to 10%—of our body's cells and DNA. The rest appear to be bacterial cells of many stripes and colors. We increasingly understand ourselves to be *symbionts*—organisms that only live in symbiosis with others. Furthermore, closer examination of our nervous systems reveals that our "distinguishing intelligence" is actually much more distributed in the system we call our bodies (and their environments) than we imagined. That which we took to be a centralized function in the human body is proving to be much more diffuse.

Over the next century, this high-resolution view of the human system will challenge our social, legal, and medical systems as well as our personal identities. The current health care system will evolve beyond traditional molar medicine based on individual organ systems. A more integrated medicine will seek to create microbial ecosystems that optimize our physical performance, our collective intelligence, and our individual and societal well-being. Our legal system, which relies on definitions of human autonomy and capacity for independent self-control, will be challenged by neurobiological findings that undermine these basic assumptions. And as we begin to optimize our microbial selves, we'll also begin to tinker with these basic building blocks of being, exploring genetic material at an entirely different scale to bacterially bioengineer ourselves for the extreme environments we face.

Perhaps the most fundamental shift by 2100 will track back to our distinguishing intelligence. Rather than seeing ourselves as separate individuals with central command-and-control brains, we'll begin to recognize ourselves in patterns of distributed intelligence that almost certainly extend far beyond our anatomical bodies.

—Rachel Hatch

THE CORE DILEMMA

The core dilemma as we evolve to see ourselves as micro-superorganisms will be managing risk at the level of the individual (and maintaining institutions which serve that model of risk) versus de-individualizing risk and managing it at microbial scales.

Dilemmas typically take shape when short-term benefits mask long-term costs— or when long-term benefits require short-term costs. These are particularly acute when one group experiences the costs while another experiences the benefits.

SHORT TERM

Costs

- Infrastructure investment in developing robust datasets about the microbiome and enterotypes
- Uneven application of neurobiology to case law, yielding legal controversies
- Loss of productivity due to likely surge in bacterial infections as we shift away from antibiotics
- Challenges to core identities based on religion, citizenship, and established health practices

Benefits

- Near-term platforms for innovation of microbial interventions
- Increased real-time, actionable data about antibiotic resistance, enabling rapid response
- Innovations in education and parenting that work with rather than against the limits of the adolescent brain

LONG TERM

Costs

- Aggravated well-being gap between people who can afford high-resolution regimens and those who cannot
- Wild-card potential for pathogenic warfare via bioengineered bacteria

Benefits

- Gains in productivity due to a boost in well-being via microbial interventions
- Potential for higher efficacy in rehabilitation of criminals
- Capacity to leverage our bacterial partners for faster human adaptation to extreme environments

SIGNALS



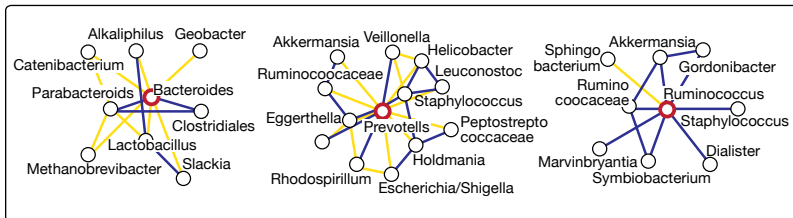
commonfund.nih.gov

The Human Microbiome Project

To get a handle on the more than 100 trillion microbes in our near-field human ecology, a \$115 million National Institutes of Health effort is building on the Human Genome Project to map the microbiome (microbes and their genomes) of the human person, with five parts of the human body as the starting point.

BIOMOLECULARIZATION

Limited application of microbial innovations



Manimozhiyan Arumugam, et al., "Enterotypes in the human gut microbiome." nature.com

What's your enterotype?

Just as human blood types fall into just four distinctive categories (A, B, AB, and O), it appears that the composition of microbial DNA in a human gut forms just three clusters, called enterotypes, that may be used to guide both diagnosis and treatment in the future.

BIOMOLECULARIZATION KEY FRICTIONS

HUMAN IDENTITY

Individuals vs. Symbionts

- A shift from genomics toward metagenomics focuses attention on cross-species functions rather than the structure of individual species.
- Experimentation in microbially optimized environments redefines *wild* and *domestic*.
- Newly revealed connections between the gut and brain challenge long-held ideas about the brain as the center of individual intelligence.
- Controversies arise over attempts to "govern evolution" by bacterially bio- and geoeengineering our habitats and ourselves for extreme environments.
- New global warming debates emerge as a result of impacts of climate change, such as ocean acidification, on the human microbiome.
- Looking to bacterial DNA as building blocks for human beings, scientists experiment with gene-swapping therapies.
- New social platforms support microbe-sharing practices for a new citizen science of the extended self.

HUMAN HEALTH

Superbugs vs. Microbial Ecologies

- Microbial strategies for preventing and treating cancer, heart disease, and obesity compete with clinical infrastructures for chemotherapy and weight management.
- Microbial solutions proliferate beyond conventional probiotics to more controversial treatments such as fecal transplants.
- While some scientists point to a few critical bacteria as defining health or disease, others argue for ecosystem diversity as a precondition for resilience.
- The boundaries between familiar disciplines—for instance, dentistry, cardiology, and gastroenterology—blur as new microbial interventions unite them.
- Superbugs hasten the advent of antibiotic resistance mapping.
- UV and other superbug-killing technologies for hospitals compete with the introduction of "natural" microbes that combat superbugs.
- Defense technologies drive a shift from traditional antibiotic drug delivery toward nanoparticle medication.

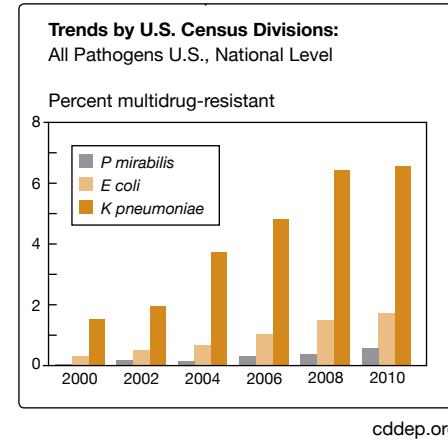
HUMAN ACCOUNTABILITY

Culpability vs. Capability

- Clinical and legal distinctions between neurobiological and psychiatric disorders blur.
- While some courts uphold standard prison terms, others experiment with customized sentencing such as prison terms based on a spectrum of culpability.
- Rehabilitation strategies expand to include probiotic interventions as well as prefrontal cortex "workouts" to strengthen neural pathways for long-term decision making.
- The jury selection process begins to include the neurobiology of decision making.
- Social debates around predictive law and free will come to the forefront.

Antibiotic resistance mapping

Extending the Cure, an initiative of the Center for Disease, Dynamics, Economics, and Policy, is mapping antibiotic resistance—showing what may be exponential increases in multi-drug resistance of three common bacterial threats between 1999 and 2009.



BIOMOLECULARIZATION

Institutional reforms based on microbial evidence

The wild life of our homes

A citizen science project seeks to map the microbes in urban and rural homes across North America, asking volunteers to send samples of their homes in an effort to understand the impacts of our microbial environments on our health and well-being.



yourwildlife.org

10 YEAR FORECAST THE MICRO-SUPERORGANISM

As we humans look at ourselves under a high-resolution, molecular-scale lens, it is already hard to recognize “us” in what we see. Far from describing ourselves in terms of the human genome we first mapped in 2000, we find that our human genetic profiles tell only a fraction of the story of our so-called *individual* bodies. We “each” have a much more complex genetic profile when we include our microbial symbionts. Our genetic fingerprints are shifting configurations of human and microbial cells that govern everything from our weight to our ability to make sound judgments about the world around us. Over the next decade, we will develop “human microbial observatories” such as the Human Microbiome Project to explore this disorienting terrain from new vantage points. And as we do, we will trigger debates in our churches, courtrooms, schools, and hospitals about how to manage the risks of living systems—superorganisms, really—that just happen to have human cells as imperfect and widely distributed guidance systems.

THE SCALE OF RISK: INDIVIDUALS VS. SYMBIONTS

Risk has traditionally been identified and managed at the level of the individual person: The individual consumer. The individual worker. The individual investor. Even the individual soul. And we have built our institutions to manage the personal risks that confront us in each of these risk-laden identities. But now, Carl Zimmer, author of “Our Microbiomes, Ourselves,” tells us that “Microbes simply defy a notion of individuality.” At every scale of human activity, from the micro-processes in our guts to the globally connected networks of people who apparently spread happiness as readily as disease, the boundaries that define the individual look more permeable and even artificial. In this world of permeability, how are we to hold any single individual responsible? This question will be answered as much by scientists studying bacterial “quorum sensing” and social activists seeking legal reform as by actuarial experts plotting broad patterns of human illness, accidents, and behavior.

THE TARGET OF INTERVENTION: SUPERBUGS VS. MICROBIAL ECOLOGIES

In the past decade, our attitudes toward bacteria have shifted. We see not only the pathogenic, but also the beneficial relationships our bacteria have with us, their symbionts. We are already seeing the shift away from antibiotic approaches to medicine, driven by the scourges of superbugs and the realization that those 90%–99% of cells that we call our body are, at any given point in time, a community of bacteria that are not only sometimes beneficial, but essential to our health. In the next decade, we will map the human microbiome, develop baselines such as gut enterotypes, and experiment with interventions designed to create “communities of well-being” at the microbiome scale. From cancer to stress to obesity to depression, we will try to optimize dynamic ecosystems rather than target a single pest for obliteration. We may well expect to see microbe-sharing practices for well-being and even microbially optimized homes and workplaces.

THE RULE OF LAW: CULPABILITY VS. CAPABILITY

In *The Brain on Trial*, David Eagleman asserts: “The crux of the problem is that it no longer makes sense to ask, ‘To what extent was it his biology, and to what extent was it him?’ because we now understand that there is no meaningful distinction between a person’s biology and his decision making.” If our biology is actually a pattern of human DNA, interacting with multiple micro-organisms throughout the body, how do we now define the “reasonable person” that legal practice generally assumes? In the next decade, expect a reframing of the distinction between neurological and psychiatric disorders—“brain problems” versus “mind problems.” We’re learning that our decision making is much more liberally laced with our neurobiology than we previously understood, and this knowledge will spark changes in our legal system, including customized sentencing, the development of a new spectrum of culpability, variable lengths of prison terms, and even jury selection based on our microbiology.