MICROBIOME · LONGEVITY · MEDICINE

THE GUT CODE



How Your Gut Bacteria Decide Your Health, Your Mind, and the Length of Your Life

RADIM KAUFMANN · BERNHARD MANN

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RADIM KAUFMANN
AND
BERNHARD MANN

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DEDICATION

For our families, who taught us that health
is shaped at the table.

And for the patients and readers whose questions,
across the years, gradually became this book.

Authors' Note

A few words on how this book is organised, and on the conventions we have adopted across its twenty-five chapters.

This book is a work of synthesis. The two of us — writing between Prague and Vienna — combine independent research, scientific literature review, and a long interest in microbiome biology. We are not physicians or licensed medical professionals; we are writers and analysts of scientific information. What follows is our reading of what the contemporary literature on the human microbiome has actually established.

The main narrative of each chapter is jointly authored. We passed every chapter back and forth across 2025 and 2026 until the science, the historical scenes, and the practical implications had been treated with the care the subject deserves. The result is a single integrated voice. At the end of each chapter, however, one of us steps forward in a short section called *Author's Words*, alternating across the book, where attribution is given each time.

The book is organised in five Parts: foundations of the microbiome; the body in dysbiosis; what modern civilisation has done to the human microbial ecosystem; the science of longevity and contemporary therapy; and the practical synthesis of how to rebuild a resilient ecosystem over the adult lifespan.

A word on the evidence. Where it is strong, the language here is direct. Where it is suggestive but unsettled, the language reflects that uncertainty. Where it is genuinely contested, we say so. Each chapter ends with numbered Notes documenting the principal scientific sources.

Nothing in this book is medical advice. Readers with specific medical conditions should consult a qualified clinician before acting on anything written here. This book is not a diet plan, not a wellness manifesto, and not a marketing document. It is a map of the territory.

— Radim Kaufmann

— Bernhard Mann

Prague and Vienna, 2026

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INTRODUCTION

You Are Not One Organism

For most of human history, we believed the human body belonged entirely to us. Our thoughts were ours. Our hunger was ours. Our illnesses were ours. Our emotions were ours. Our survival depended on the strength of our organs, the quality of our blood, and the resilience of our minds.

Modern medicine mapped the heart. It mapped the lungs. It mapped the brain. By the end of the twentieth century, it had mapped the human genome itself.[1] And yet, for nearly all of that history, one of the most important systems in the human body remained almost entirely invisible.

Inside every human being lives an enormous ecosystem of bacteria, archaea, fungi, viruses, and microscopic organisms collectively known as the *microbiome*. Most of them live in the gastrointestinal tract — particularly inside the large intestine — where tens of trillions of microbial cells interact, continuously, with the immune system, metabolism, hormones, inflammation, and even the brain.[2]

These organisms are not accidental passengers. They help digest food. They produce vitamins. They regulate inflammation. They shape immune responses. They influence insulin sensitivity. They affect body weight. They communicate chemically with the nervous system. They may influence mood, stress, anxiety, and cognitive decline. Some scientists now believe they may even affect the rate at which human beings age.

In purely numerical terms, the human body is less individual than we once imagined. A healthy adult carries roughly as many bacterial cells as human cells — for years the figure was given as ten bacteria for every one of our own, but a careful 2016 recalculation by Ron Milo's laboratory at the Weizmann Institute revised the ratio downward to something closer to one-to-one.[3] The bacterial *genes* in the gut, however, still outnumber human genes by an extraordinary margin: roughly 150-fold.[4] The ecosystem within the body behaves less like a simple infection to eliminate and more like a rainforest, an ocean, or a planetary biosphere whose balance determines whether the host can survive.

You are not a single organism. You are an ecosystem.



This realization is quietly transforming modern medicine.

For more than a century, medicine viewed bacteria primarily as enemies. The great victories of twentieth-century medicine — antibiotics, sterilization, vaccines, modern surgery — emerged from humanity's war against infectious disease. Millions of lives were saved. Entire civilizations became safer.

But in winning that war, modern civilization may also have damaged part of the biological system that kept human beings healthy for hundreds of thousands of years. Industrial food altered microbial diversity. Urban sanitation changed environmental exposure. Antibiotics disrupted ancient ecosystems inside the gut. Modern stress reshaped hormonal biology. Sleep deprivation, ultra-processed food, alcohol, smoking, obesity, and chronic inflammation began interacting with the microbiome in ways no previous human generation had experienced.

At the same time, the modern world saw explosive growth in diseases that were once comparatively rare: obesity, type 2 diabetes, autoimmune disease, inflammatory bowel disease, allergies, depression, metabolic syndrome, and neurodegenerative disorders. No serious scientist believes the microbiome alone explains all of these conditions. But fewer serious scientists now believe it is unrelated.



The microbiome revolution is still young.

Many claims are exaggerated. Some are commercially manipulated. The wellness industry often moves faster than the evidence. Entire markets now sell "gut health" products built on incomplete, oversimplified, or in some cases simply incorrect science.

This book is not an argument for pseudoscience. It is not a detox manifesto. It is not an anti-medicine ideology. It is an attempt to understand — carefully, and with appropriate humility — one of the most important shifts in modern biology.

The field of microbiome research now sits at the intersection of medicine, neuroscience, immunology, nutrition, aging research, evolutionary biology, metabolism, artificial intelligence, and personalized medicine. The implications are enormous. For the first time in the history of biomedicine, the field is beginning to accept that human health may depend not only on human cells but also on the vast ecological system living within them.



We did not approach this subject as physicians. We are not gastroenterologists. We are not microbiologists. We are not clinical researchers.

Our background comes from a different direction: systems, patterns, complexity, and the observation of how fragile structures fail over time. The deeper we read into modern metabolic disease, inflammation, obesity, diabetes, and aging, the more often one invisible pattern surfaced beneath the surface: the ecosystem itself was changing. The bacteria living inside modern humans were no longer living in the conditions that shaped human biology over evolutionary time. And perhaps modern humans are paying the price.

This book was written for general readers, not specialists. But it was also written with deep respect for scientific rigor. The main narrative is intentionally accessible. The notes and bibliography are not. Throughout the book, the reader will find references to peer-reviewed research, historical medical developments, microbiome sequencing studies, clinical trials, epidemiological observations, and emerging hypotheses from the frontier of longevity science.

Some discoveries discussed here may later prove incomplete. Some may prove revolutionary. Science evolves precisely because certainty is temporary.

But one fact already appears unavoidable: human beings are far less biologically independent than we once believed.

The future of medicine may not begin in the stars, or in artificial intelligence, or even in genetics alone. It may begin inside the invisible civilization already living within us.

AUTHOR'S WORDS

This book is the work of two writers who began circling the same body of research from different sides, and who realised — perhaps later than they should have — that they were trying to tell one story. The story is that of the human microbiome, and of what its discovery has done to medicine, to our self-understanding, and to the practical question of how to live well in a body that is, at the cellular level, much less individual than the language we use about it implies.

The chapters that follow are written in a single voice that we developed together over the course of 2025 and 2026. That voice belongs to neither of us alone; it is the product of a long argument, conducted mostly in writing and across two cities, about what the contemporary literature actually says and what it does not. We have tried to be honest about both. Where the evidence is strong, we have said so plainly. Where the evidence is suggestive but unresolved, we have tried to say that plainly as well. Where the science is genuinely contested, we have said so and named the dispute.

At the end of each chapter, however, one of us steps forward in a short personal section called Author's Words. We alternate across the book, with attribution given each time. These passages are explicitly the view of one author, not both, and they are the place where the more personal — and occasionally more skeptical — voice of each of us is allowed to speak. They are not the central science of the book. They are something more like marginalia: the thoughts that occurred to one of us in the course of writing the chapter, that the other agreed were worth keeping, but that neither of us wanted to put into the joint voice of the main text.

For this introduction, the Author's Words belong to both of us. We wrote it together. What follows in the rest of the book is best read with the understanding that the main narrative is jointly authored, and the closing paragraphs of each chapter are the place where the seam between two writers becomes briefly, deliberately, visible.

— Radim Kaufmann & Bernhard Mann
Prague and Vienna, 2026

NOTES

1. The Human Genome Project announced a draft sequence in June 2000 and published two near-complete drafts in February 2001 (Lander et al., *Nature*; Venter et al., *Science*). A genuinely "telomere-to-telomere" gapless human genome was not completed until 2022 by the T2T Consortium. See Nurk et al., "The complete sequence of a human genome," *Science* 376 (2022).
2. For a readable overview of the microbiome as a system, see Knight, *Follow Your Gut* (2015), and Yong, *I Contain Multitudes* (2016). For a technical synthesis, see Cho and Blaser, "The human microbiome: at the interface of health and disease," *Nature Reviews Genetics* 13 (2012): 260–270.
3. Sender, Fuchs, and Milo, "Revised Estimates for the Number of Human and Bacteria Cells in the Body," *PLOS Biology* 14 (8): e1002533 (2016). The classic 10:1 figure originated in a 1972 estimate by Thomas Luckey and was popularized by Dwayne Savage in the late 1970s; the Milo paper showed that careful counting yields a ratio closer to 1.3:1, which the authors describe as "essentially one-to-one."
4. The 150-fold gene-count ratio comes from the MetaHIT consortium's landmark cataloguing of the human gut microbial gene set: Qin et al., "A human gut microbial gene catalogue established by metagenomic sequencing," *Nature* 464 (2010): 59–65. The catalogue has since expanded considerably; see Almeida et al., *Nature Biotechnology* 39 (2021): 105–114.



CHAPTER ONE

The Forgotten Organ

"I, then, most always saw, with great wonder, that in the said matter there were many very little living animalcules, very prettily a-moving."

— Antonie van Leeuwenhoek, letter to the Royal Society of London, 17 September 1683

In September of 1683, a draper in the Dutch city of Delft sat down at his workbench, lifted a small instrument of his own design toward the light, and turned the focusing screw. The instrument was the size of a postage stamp. It consisted of a single ground-glass lens mounted between two thin brass plates, with a tiny pinhole through which the lens could observe a sample skewered on a needle behind it. The draper, whose name was Antonie van Leeuwenhoek, had built more than two hundred such devices in the back of his shop, and a few of them were so finely ground that they could resolve objects fewer than two thousandths of a millimetre across. No one else in Europe could see what he could see.[1]

That morning, Leeuwenhoek had decided to look at the white matter scraped from between his own teeth. He had been curious about it for years. He noticed it accumulated more rapidly on some mornings than on others. He suspected, correctly, that it was alive.

He pressed a sliver of the material against the needle, brought the lens to his eye, and waited for the focus to settle.

What he saw, he later reported in a careful letter to the Royal Society of London, were "little animals" — what he called *animalcules* — swimming through the watery scrapings of his mouth in vast and improbable numbers. Some moved in slow, dignified arcs. Others "shot through the water like a pike does through it." A third kind spun in tight, energetic circles. The numbers were impossible. He concluded, with the philosophical equanimity of a seventeenth-century shopkeeper, that "there are more animals living in the scum on the teeth in a man's mouth than there are men in a whole kingdom."[2]

It was the first time a human being had ever clearly seen a bacterium.

The Royal Society, when the letter arrived, was not entirely persuaded. They consulted their own microscopists. They asked Leeuwenhoek to send drawings. They sent observers to Delft. Over years of correspondence, they came to accept that Leeuwenhoek was telling the truth: there were living organisms inside the human body too small to see with the naked eye, in numbers no one had previously imagined.

Then, for the next two centuries, almost nothing happened.

It is worth pausing on the strangeness of this fact. Leeuwenhoek had identified a phenomenon that, today, we understand as one of the most important biological systems on Earth. A motivated observer with even modest tools could, in principle, have repeated his work the following year. And yet what we now call microbiology — the systematic study of the organisms Leeuwenhoek saw — would not be invented for nearly two hundred years. The human microbiome, considered as a serious object of medical attention, would have to wait twice that long.

Why?

Partly, the instruments were not yet good enough to make the field productive. Leeuwenhoek's lenses were marvels of craftsmanship, but he refused to share his grinding techniques, and no successor matched his resolution for a

generation. The achromatic microscope — capable of producing colour-corrected images at high magnification — arrived only in the 1820s.[3] Until then, the world Leeuwenhoek had described was, for nearly everyone, hearsay.

But the deeper reason is conceptual. The eighteenth century had no framework for the idea that a healthy human body might be a habitat. Disease was understood as imbalance — of humours, of constitution, of regimen. The word *infection*, in its modern sense, did not yet exist. Bacteria, when they were considered at all, were curiosities; their relationship to illness was unclear, and their relationship to health was simply not a question one was expected to ask.

When the question finally arrived, in the second half of the nineteenth century, it arrived as a war.

THE WAR ON GERMS

Between roughly 1860 and 1900, a handful of figures — Louis Pasteur in France, Joseph Lister in Scotland, Robert Koch in Germany — succeeded in establishing what is now called the *germ theory* of disease. Pasteur demonstrated, with a sequence of beautifully designed experiments on wine spoilage and silkworm pestilence, that specific microbes produced specific effects. Lister translated the principle into surgery, drenching his operating field in carbolic acid and watching post-operative mortality collapse. Koch worked his way down a methodical list of major killers — anthrax, tuberculosis, cholera — and showed that for each one a particular bacillus was responsible. By 1884 he had formalised the famous four postulates that would govern medical microbiology for the next century.[4]

The triumph was so total, so morally clean, and so deserved that it shaped how Western medicine thought about bacteria for the entire twentieth century. Microbes caused disease. Eliminating microbes prevented disease. The microbe was, by default, the enemy.

Within this framework, the idea that a healthy adult might host trillions of bacteria in his or her own intestine — not as a low-grade infection, not as contamination, but as a constitutive part of biology — was difficult to entertain. The framework had no slot for it. When physicians in the late nineteenth century did discover that a healthy human gut was teeming with microbes, the most common interpretation was that those microbes must be doing harm. The German pediatrician Theodor Escherich, who in 1885 first cultured what would later be named *Escherichia coli* from the faeces of healthy infants, was careful to point out that the organism appeared, paradoxically, to coexist with their robust good health.[5] The observation was filed away. It did not change the framework.

The framework did, however, deliver one of the great gifts of the twentieth century. By the 1940s, the germ theory had matured into antibiotic medicine, and the leading killers of human beings — tuberculosis, pneumonia, sepsis, syphilis, gas gangrene — began to retreat in a way that earlier generations would have considered miraculous. Sanitation, vaccination, refrigeration, and chlorination of municipal water added their own enormous contributions. The human lifespan in industrial countries expanded by decades in a single generation.[6]

Almost no one paused, during this great victory, to wonder what else might have been killed along the way.

THE FORGOTTEN DISSENTER

There was one exception, and his name was Élie Metchnikoff.

Metchnikoff, a Russian-born zoologist who eventually became deputy director of the Pasteur Institute in Paris, had spent the 1880s discovering that white blood cells engulf invading microbes — the foundational mechanism of cellular immunity, for which he would share the 1908 Nobel Prize in Physiology or Medicine.[7] But it was Metchnikoff's second career, in the first decade of the twentieth century, that made him the strange grandfather of microbiome science.

Working from a small lab in Paris, Metchnikoff had become obsessed with the question of why some human populations seemed to live extraordinarily long, healthy lives. He was particularly fascinated by Bulgarian peasants, who reportedly produced an unusual number of centenarians and whose diet included a great deal of soured milk. Metchnikoff hypothesised that the lactic acid bacteria in this fermented milk — one of which, *Lactobacillus bulgaricus*, still bears the name of its country of origin — were displacing "putrefactive" bacteria in the colon and reducing what he called *intestinal autointoxication*. The autointoxication theory was wrong in detail. But the underlying intuition — that the bacteria in the human gut might be doing something important, and that what they were doing might be modifiable by diet — was something close to a century ahead of its time.

Metchnikoff laid out the argument in his 1907 book *The Prolongation of Life: Optimistic Studies*.[8] He drank fermented milk every day. He recommended it to his friends. He died in 1916, at seventy-one, of heart failure, having never quite persuaded mainstream medicine that he was onto anything substantial. For most of the twentieth century, he was remembered as the man who discovered phagocytosis. The other half of his life's work was treated as the eccentricity of an aging genius.

It is worth recording that Metchnikoff anticipated, in rough outline and with a single dietary intervention, much of what the past two decades of microbiome research have begun to put on a serious empirical footing: that the gut microbiota matter for systemic health; that they are influenced by the foods we eat; that interventions in early or middle life may affect the trajectory of aging; and that they may be implicated in low-grade inflammation, immune balance, and longevity. He was right about the direction. He was off by a hundred years on the timing.

WHY WE COULD NOT SEE THE RAINFOREST

Even after Metchnikoff, the gut remained, for medicine, a tube. The textbook function of the colon was the absorption of water from undigested food residue and the storage of waste prior to elimination. The bacteria, when they were mentioned at all, were treated either as a sanitary problem or as harmless commensals deserving no particular study.

The intellectual hesitation had a technical accomplice. The bacteria of the human colon are, in the language of microbiology, *obligate anaerobes* — that is, most of them die quickly on exposure to atmospheric oxygen. They cannot be grown on the standard nutrient agar plates that microbiologists use to count other bacteria. Many of them cannot be cultured outside the gut at all. Until the late twentieth century, the most diverse and most abundant microbial community on Earth was, in a practical sense, invisible to laboratory science.[9]

A bacterium that cannot be cultured cannot be studied. It cannot be named. It cannot be classified. It cannot be counted with any confidence. Microbiologists working before about 1990 estimated, on the basis of plate culture, that the human gut contained perhaps a few hundred species of bacteria. The true figure, when it became measurable, would turn out to be more than a thousand — and the difference was not a refinement. It was a different order of magnitude.[10]

HOW WE SEE WHAT WE CANNOT GROW

The single technical advance that opened the gut to scientific view was the application of DNA sequencing to a marker gene called *16S ribosomal RNA*. This gene, present in every bacterium and archaeon, contains regions that are nearly identical across the bacterial world and regions that vary in highly informative ways between species. By extracting all the DNA from a stool sample, amplifying the 16S gene, and sequencing the variable regions, a researcher can produce a census of which microbes are present and in roughly what proportions — without ever culturing a single organism. The method, refined through the 1980s by the American microbiologist Carl Woese and applied to the human gut by Paul Eckburg, David Relman, and colleagues in 2005, is the foundation of nearly everything that follows in this book.[11]

THE WORD ARRIVES

The word *microbiome* entered the scientific vocabulary in 2001, in an essay by the Nobel laureate Joshua Lederberg and his collaborator Alexa T. McCray, who proposed the term to describe "the ecological community of commensal, symbiotic, and pathogenic microorganisms that literally share our body space."[12] The word was new, but the concept that Lederberg meant by it was — finally — old. He was describing the system that Leeuwenhoek had glimpsed three hundred and eighteen years earlier in the scrapings from his teeth.

What followed was an extraordinary decade of scientific catch-up. In 2007 the United States National Institutes of Health launched the Human Microbiome Project, a deliberate sequencing effort modelled, both methodologically and rhetorically, on the Human Genome Project that had been completed earlier in the decade.[13] A parallel European consortium, MetaHIT, sequenced the gut microbiomes of 124 European adults and published, in 2010, a catalogue of 3.3 million distinct microbial genes — roughly a hundred and fifty times the number of genes in the human genome itself.[14] By 2012 the HMP had produced a reference set characterising the bacterial communities of

eighteen body sites in 242 healthy American adults.[15] By 2021, an integrated catalogue assembled from nearly 290,000 microbial genomes had pushed the number of identified bacterial species in the human gut past 4,000.[16]

The numbers will keep moving. They are not the point. The point is the change in framing that they made possible.

For the first time in the history of medicine, it became reasonable to ask what an entire microbial community was *doing*, rather than what a single isolated organism was doing on a Petri plate. The shift sounds modest. In practice, it was the difference between describing a forest by listing the trees one has personally encountered in cleared parkland and describing it by mapping every species in it, including the ones that only live in the deep shade.

AN ORGAN, BY ANY REASONABLE DEFINITION

By the second decade of the twenty-first century, researchers had begun, half-seriously and then increasingly seriously, to refer to the gut microbiome as "the forgotten organ" of the human body.[17] The phrase has a certain rhetorical convenience, but it deserves more than rhetorical use. The argument behind it is worth taking seriously, because if it is correct it changes the way medicine should be practised for the rest of our lives.

An organ, in the conventional sense, is a structure of cells organised to perform identifiable functions for the body as a whole. By that definition, the gut microbiome qualifies. It performs digestion of complex carbohydrates that the human enzymatic apparatus cannot break down on its own. It synthesises vitamins — including most of the B-complex and the bulk of usable vitamin K. It produces short-chain fatty acids that the cells of the colon use as their primary fuel. It maintains the integrity of the intestinal mucosa. It calibrates the maturation of the immune system from infancy through old age. It communicates, by way of metabolites, hormones, and the vagus nerve, with the brain. It

influences the absorption and metabolism of pharmaceuticals. It interacts with circadian rhythms, with stress responses, and with the regulation of body weight. [18]

These are not speculative properties. They are the documented working of a system that — if it were composed of human cells — would be diagrammed in every medical textbook and lectured on for two semesters in every medical school in the country. The reason it is not so diagrammed is partly historical inertia and partly the strangeness of describing an organ that is not made of human tissue, that varies between individuals more than any human organ does, and that can, within hours, be reshaped by a meal.

It is also an organ that can be damaged.

This is the worry that animates much of what follows in this book. If the gut microbiome is, in any meaningful sense, an organ — one that has co-evolved with the human host over hundreds of thousands of years, and that performs functions for which the host has no internal substitute — then the abrupt changes of the past century in human diet, in human medication, in human birth practices, in human exposure to soil and animals, and in the chemical composition of the environment, are not minor lifestyle facts. They are stresses on a system. Some of what has emerged in modern medicine — the rise of autoimmune disease, the obesity epidemic, the increase in chronic inflammation, the doubling and re-doubling of metabolic syndrome — may be downstream of those stresses, in ways that even our best clinical instruments are only beginning to detect.

Or it may not be. The science is not yet settled. But it is now serious enough that no honest account of human health can leave it out.

In the rest of this book, we will walk through the major findings, controversies, and open questions of the field. We will look at what is known about how the microbiome is established in infancy and how it ages across a human life. We will look at its role in the immune system, in metabolism, in mood, in inflammation, and in disease. We will look at what modern life — antibiotics, ultra-processed food, alcohol, chronic stress, sleep deprivation — does to it. We will look, at

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