Interpreting ancient DNA—a scientific approach that has grown powerfully during the past decade—reveals that human history is a story of mixing and migration at a scale and complexity that no one previously imagined. Waves of people and genes have flowed across oceans and continents for millennia, creating a mosaic of admixture. Genetically, “race” is a broken concept, this work shows, because every population is a mixture of other populations—which are themselves mixtures of still earlier populations. The analysis of ancient DNA can nevertheless reveal genetic signatures of people who lived in a particular time and place—proving that today’s inhabitants are not necessarily descended from the inhabitants of thousands of years ago. Britain, for instance, has experienced no fewer than five major waves of migration in the last 10,000 years. Three of these migrations involved near-total replacement of the then-native population.

Genetic studies have also provided objective evidence that has helped answer or refine longstanding questions in archaeology, anthropology, and linguistics. How did farming spread, or Indo-European languages? What happened to the Neanderthals? The research has upended certain theories and affirmed others, as it rapidly matures into a freestanding discipline. In 2010, scientists had assembled just five ancient human genomes, including three Neanderthals.
Today, the lab of professor of genetics and of human evolutionary biology David Reich alone has sequenced more than 16,000 ancient humans from around the world.

Reich, one of the world's preeminent analysts of ancient human DNA, is a leader in establishing an ethical framework for the study of ancient remains, and the source of seemingly endless startling discoveries. In 2006, he led work showing that after the human and chimpanzee lineages diverged from a common ancestor, interbreeding continued for perhaps a million years before a final split. That work got the attention of genetecist Svante Pääbo: he had assembled a complete Neanderthal genome, and invited Reich to study the data. The resulting 2010 analysis yielded a stunning surprise: that modern humans had mated with that archaic lineage, and that the genetic legacy of those encounters remains in the DNA of humans today. Later, Reich's lab turned up interbreeding among modern humans, Neanderthals, and another archaic human, the Denisovans. He expects more human lineages will be found, and more evidence of gene flow among them.

Each of those individuals whose DNA can be interpreted contains multitudes, segments of genes from many ancestors: roughly 1,000 who lived 13 generations ago, and up to 100,000 ancestors who lived 1,400 generations ago. Not all of a person's ancestors contribute to their DNA; at 10 generations back, an individual has 1,024 ancestors, but inherits only about 750 segments of genes from them, so some ancestors are no longer represented in their DNA.

The sample sizes are now large enough that DNA scientists can find cousin relationships among these ancient individuals. From these data, patterns have begun to emerge in the global history of human congress—what happens when two or more populations meet. Sometimes they appear to mix as equals, but more frequently, inequity and sex bias—when males contribute more to an admixture—are evident in the genetic signatures of these encounters. Reich's research has led him to reject genetic determinism as an explanation for the success of some cultures at the expense of others. "I see no evidence that genetic adaptation in human populations have been responsible for expansions of some modern human groups" to the detriment of others. Instead, culture, and how societies are mobilized, says Reich, matter most to the outcome when two peoples meet.

"Cultural differences amongst groups are profound," he continues, and are the primary determinant of what happens when they come into contact. The Romans, for instance, "had a social organization premised on military service to the state, and territorial expansion; this combination became so effective that they ran over their neighbors. That had nothing to do with biological fitness." Reich points to a modern example of two cultures in Sudan, genetically similar and equally sophisticated. The Nuer had a strict bride-price system that required men to pay a large number of cows to the wife's family. Marriage was so expensive that a common practice of young Nuer men was to steal cows from the neighboring Dinka to afford the bride price, often taking women and children captive at the same time. Systematic raiding driven by this cultural difference was one factor that led Nuer territory to expand at the expense of the Dinka in the mid-nineteenth century.

Reading a Genetic History of Slavery

Reich grew up in Chevy Chase, Maryland, just outside Washington, D.C., where his mother is novelist Tova Reich, and his father, the first director of the Holocaust Museum, is a professor at George Washington University. Though Reich and his siblings were not raised to be religious, both his parents grew up in Orthodox Jewish families. Of his four grandparents, three were Jewish refugees from Europe who immigrated to New York, he says, and "come from families that were devastated by persecutions of Jews during the Holocaust. That's a rich and intense part of my family background." Isidor "I. F." Stone, the politically progressive investigative journalist, was a family friend who was "like another grandparent," and Reich admired him for learning Ancient Greek at age 70, and then writing a bestselling book, The Trial of Socrates, about the philosopher's prosecution and death. Stone's late-life reinvention of himself made an impression on Reich that would later lead to the most important collaboration of his career, with mathematician Nicholas Patterson; that in turn helped shape the democratic, team-oriented way he runs his laboratory.

In high school, Reich was interested in many subjects and good at lots of them. Not surprisingly, his path to the genetic study of human history was not straightforward. At Harvard in the class of 1996, he concentrated first in social studies before switching to physics. Although accepted into the physics graduate program at Berkeley, Reich wasn't sure he wanted to pursue a degree in the field, or that he would be successful "at a high level." He thought about medical school, and applied to Balliol College at Oxford, hoping to simultaneously secure a Harvard fellowship that would allow him to earn a second bachelor's degree in biochemistry. He didn't get the fellowship, but Balliol accepted him, and his parents agreed to pay for what was essentially a fifth year of college. But the program didn’t hold his interest for long, and he dropped out, instead moving full-time to an Oxford lab run by American researcher David Goldstein, studying human history through genetic data, as part of a "master's by research"
program that he thought would be a “fun” short-term experience before he returned to training for his career. “That took the pressure off,” he recalls, as he applied to medical school and other positions back in the United States.

After two years, Reich left England, but was told if he just came back the following summer and continued publishing papers, he could earn his Ph.D., so he did. In the meantime, he had applied to Harvard Medical School. He was accepted into the joint (with MIT) Health Sciences and Technology (HST) program, rather than the Ph.D. track. Almost two years into that curriculum, Reich found himself becoming absorbed by the human genetics work he was doing at the Whitehead Institute to fulfill the HST program’s research requirement, deferring the requisite clinical work. As his research took on the momentum of a full-fledged post-doc, he decided to drop out. But when he prepared to leave HST, the two leaders of the program summoned him; failing to persuade him to remain as a student, they even offered him a faculty job. (He decided against that, but did stay at Harvard.)

Reich was hired at the medical school in 2003, where he hunted for genes implicated in disease, successfully identifying several related to prostate cancer. African Americans suffer higher rates of the disease than European Americans, raising the possibility that genetic factors inherited from African ancestors increase disease risk. His approach was to screen through the genomes of African Americans, looking for places where individuals with prostate cancer had a higher probability of inheriting genes from African ancestors. In this way he and his colleagues were able to narrow the search for the genes that lead to greater risk. Without ever planning to, Reich had assembled a powerful portfolio of skills for tracing the narrative of human genes through time. He also confronted in those data the history of slavery in the United States: European ancestry in African Americans has been predominantly contributed by men, reflecting the well-documented history of white male slaveowners exploiting women of African descent.

Sex Bias and the Spread of Indo-European Languages

Power imbalances between the sexes appear to have played a role in the spread of genes in numerous cases throughout pre-history. One of the most unexpected examples of how culture and technology combined to spread genes—and language—involves the Yamnaya, a horse-herding people who lived on the Eurasian steppe during the Bronze Age, 5,000 years ago. The story began to take shape in 2012, when Reich’s lab identified the genetic signature of a ghost population, one that no longer exists in unmixed form.

Left to right: sandblasting a petrous bone to expose the inner ear capsule; removing the surface layer of a specimen, which may contain contaminated DNA; transferring the powdered sample into a tube, prior to mixing it with an enzyme-containing liquid that releases the DNA for analysis

Reich and his colleagues had been assessing the relatedness of different groups of modern humans. When they compared Northern Europeans to Native Americans and Southern Europeans, each of whom have distinctive (but not necessarily functionally important) genetic changes at varying frequencies across their genomes, they observed a powerful statistical signal that Northern Europeans have “a massive contribution of genetic material from a population related to Native Americans.”

“We of course didn’t think that Native Americans sailed across the Atlantic. That seemed implausible,” he says. Instead, he and his colleagues proposed the existence of a population that no longer exists, the “Ancient North Eurasians.” “They would have lived in Siberia, or other parts of northern Eurasia, sometime before 15,000 years ago, and contributed to the ancestors of Native Americans before they crossed the Bering Land bridge into North America.” Then, some time later, genes of the descendants of the Ancient North Eurasians who had not crossed into North America somehow suddenly appeared in populations throughout Eurasia. “The signal” Reich recalls, “was very strong.”
It was a weird observation," he says, because the prevailing model from archaeology in 2012 was that Europeans might very well be mixed between hunter gatherers who were the sole population in Europe before 8,500 years ago, and Anatolian farmers who brought agriculture to Europe after that time. That theory rested on the reasonable—but as it turned out, incorrect—assumption that once farming was established in Europe, allowing highly efficient exploitation of local resources, it would have been difficult for any other group to make a major demographic impact. The discovery of genes related to Native Americans arriving in high proportion after the spread of farming was therefore very surprising. That's why Reich and his close collaborator, research fellow in genetics Nick Patterson, had hypothesized the existence of this third source population, the Ancient North Eurasians.

The problem was that there were no modern populations living in Eurasia that were similar to the Ancient North Eurasians. Reich guessed that the Ancient North Eurasians had been largely displaced in the regions where they once lived by post-Ice Age migrations, and that their ancestry survived in higher proportion today only in Native Americans.

Then, in 2013, bones from a boy who lived near Lake Baikal around 24,000 years ago were sequenced by the Danish geneticist Eske Willerslev and his team, and these matched the genetic profile of the ghost population Reich's group had hypothesized. Immediately, the hunt was on for the genetic signature of these mysterious people in samples of 5,000 year-old human bones and teeth gathered from archaeological sites throughout Eurasia. Gradually, Reich and his ancient-DNA-studying colleagues around the world zeroed in on one group: the Yamnaya.

The Yamnaya were horse-riding steppe pastoralists who shepherded vast herds of animals, setting up mobile wagon camps wherever they found fresh pasturage. Their lifestyle was made possible by the invention of the wheel a few centuries earlier, and the domestication of the horse. With those innovations, and the addition of dairying for sustenance, the vast and dry Eurasian steppe, which stretches thousands of kilometers from Hungary to Mongolia, became a superhighway—and the economic foundation of their success.

David Anthony, a professor of archaeology based at Hartwick College, now emeritus, had previously argued on the strength of linguistic evidence, as well as archaeological traces found on the grasslands of the steppe north of the Black and Caspian seas, that the Yamnaya were the best candidates for the spread of Indo-European languages. Their mobile way of life, he says, made their temporary settlements "archaeologically invisible." Only their burial mounds, which, strikingly, included horses and wheeled vehicles, remain.

In his 2007 book, The Horse, The Wheel, and Language: How Bronze Age Riders from the Eurasian Steppes Shaped the Modern World, Anthony argued that whatever civilization had spread the language ancestral to the Indo-European languages (IEL) that are spoken today (including English), must have known about wheels and axles, pointing to common root words that change over time according to predictable phonological rules. And he noted that these languages were later spoken by militaristic, male-dominated societies with chariots, and that they shared similar mythologies, from Greece to India and Scandinavia.

Anthony had been searching for a civilization that could have spread a proto-Indo-European language for much of his career. When he sifted through the chronological, geographical, material, and linguistic evidence, only the Yamnaya fit all the criteria. And they generated subsequent migrations, undertaken by successor cultures, in the expected directions and sequences.

But even Anthony, now working in retirement with Reich as an associate of the department of human evolutionary biology, did not guess then that the Yamnaya transmitted more than just their language and culture. Their spread, as Reich and his ancient DNA colleagues have now documented, was accompanied by a massive, and previously unknown dissemination of Yamnaya genes.

"Their descendants," Reich says, picking up the story, "continued to spread in the guise of another archaeological culture" known for their "corded ware" pots, achieving a "minimum 70 percent replacement of the population" then living in what is present-day Germany, and "within a hundred years," through another successor "Beaker Bell" population, a "minimum 90 percent replacement of the population of Britain, just after Stonehenge had been built."

(Descendants of some of these groups expanded to the east as well, giving rise to the militaristic, chariot-riding Sintashta culture.)

The spread of steppe genes sometimes came with a strong sex bias, as Bronze Age populations with Yamnaya ancestry spread into South Asia (India) and across Western Eurasia. The male-lineage Y chromosome types carried by these groups were absent in India and Europe before the Bronze age, but are predominant in both places today, Reich says. Much of this ancestry is the result of what is known as a "star cluster," when the genes of one very powerful man appear in millions of descendants. Reich estimates that 20 to 40 percent of Indian men and 30 to 50 percent of Eastern European men descend from a single man who lived between 6,800 and
4,800 years ago. In Iberia, Reich’s team uncovered further evidence of sex bias. By 4,000 years ago, genes spread by the descendants of the steppe people accounted for about 40 percent of the ancestry of those populations, with about 60 percent coming from the local inhabitants who had lived there previously. “But if you look at the Y chromosomes—the DNA that people get from their fathers—it was more or less 100 percent from the steppe. What this means is that the males coming in from this Eastern group had completely displaced the local males through some process.” Was it violence, or mate choice, or something else? Could disease have played a role? What happened is unknown, because these events took place before writing had arrived in this part of world.

An Eclectic Path to Discovery

Reich’s lab is best known for developing analytical tools to study genetic history. Integral to the success of this work has been a unique partnership with a colleague known for his quantitative prowess. The way Reich tells the story, he was giving a lecture at the Whitehead Institute/MIT Center for Genome Research during a postdoctoral fellowship with Eric Lander in 2002. Guessing that Nicholas “Nick” Patterson, a mathematician of legendary reputation as a cryptographer for the British GCHQ who later did cryptographic work in the United States, would be listening, he structured the lecture specifically to engage his interest. Patterson, then on his third career at age 50, had taught himself Ancient Greek one summer, and Reich, recalling I.F. Stone’s late-life transformation, knew this was the kind of person he wanted to work with. (Patterson tells the story slightly differently, both men acknowledge. Frustrated with the poor quality of cancer genomics data he’d been analyzing, and depressed, Patterson says he was walking the halls of the Whitehead when by pure happenstance he heard a lecture going on, and slipped into the back. “The lecture was brilliant,” he recalls; he immediately approached Reich afterward to ask if he could work with him.)

Their subsequent collaboration has been “intense and seamless,” according to Reich. “I don’t know where my work ends, and his begins.” But as their first project together advanced, studying how humans and chimpanzees are related to each other and to gorillas, Reich was intimidated: “He was clearly better at this analysis than I was.” After a lot of soul searching, Reich decided that he wanted to “do the best science” and resolved to “lean into this, and work together with this person and not have normal academic boundaries. I think that’s affected my laboratory ever since,” he says. “There is a hard rule that anybody can work on anything they’re interested in, and you must embrace their contribution. You cannot say, ‘This sample is mine. Don’t touch it.’ Everybody has to be able to comment.

“Since that time,” he continues, “when I’ve encountered people with better data or more interesting ways of looking at data than we have, I’ve tried to listen as hard as I could to those alternative methods and approaches, in order to embrace them, learn from them, and apply them when that makes sense.”

Three months before the pandemic struck, Reich joined the Faculty of Arts and Sciences in human evolutionary biology, splitting his time between his labs in Cambridge and Longwood. Thus, his intellectual contributions to the field now also include the mentoring of undergraduates. Goelet professor of medieval history Michael McCormick describes how “I invited David to come and talk about this experience to one of my College classes. Not about his theories,” but about how he became a scientist. Seeing 30 Harvard undergraduates enthralled by his story was “magnificent, as he spoke about his difficulties choosing a concentration at the College; and figuring out what he was going to do afterwards; and how, step by step, and rather indirectly, he followed none of the paths that had been foreseen for him—not to physics, not to medical school, but to this extraordinary path of discovery,” McCormick continues. “I could actually see them becoming less tense as this brilliant, famous scholar told a story that was so like theirs in terms of the different turns and hesitations and sideways moves to find the path that would prove to be the one that he blazed.”

Reich also mentors graduate students and postdocs, who typically spend two to five years in his lab before moving on. Most academic labs are staffed like this, by a revolving cast of graduate students and postdoctoral fellows, but Reich also maintains a core group of staff scientists, who provide specialized expertise, and valuable continuity. Nick Patterson is one; Nadin Rohland, lab director for more than a decade, is another; and Shop Mallick, bioinformatics director of Reich’s group, is a third. “These are formidable and extraordinary scientists that everybody respects,” and he says they are a key element of the team’s success.

Reich’s lab does no field work, although he and some members of his lab do travel to collect samples. Curators of museum collections around the world, archaeologists, and other ancient DNA specialists partner with him for analysis of their samples. His group has pioneered techniques for processing ancient DNA quickly and inexpensively. The result is that the Reich lab has sequenced DNA from more ancient individuals than all other labs in the world combined. With each new individual sequence, Reich has written, there is an important sense in which the scientific value of all the others increases, as more relationships can be discerned.
Encounters with Archaic Humans

Between about four hundred and seven hundred thousand years ago, a group of archaic humans split from the African lineage that would lead to modern humans, and began living in Eurasia. Heavy-browed and physically powerful, their descendants, the Neanderthals, also had slightly larger brains on average than modern humans. In an environment that was at times cold and hostile, they survived as hunter-gatherers. “They were a highly adapted, impressive, and very capable group,” says Reich. Ever since the skeletons of these human cousins were first discovered, scientists have wondered about the nature of their relationship to *Homo sapiens sapiens*: modern humans. Archaeological work, and radio-carbon dating in the twentieth century, established beyond doubt that Neanderthals lived at the same time as the ancestors of people living today. They made tools, fashioned spear points, and left art. They even occupied the same cave sites at different times.

But archaeology alone could not reveal whether these two groups mixed when they met. So when Reich led the analysis showing that they had mated, and that their genes remain in non-Africans around the world, the news created a sensation.

To understand the nature of the interaction between Neanderthals and modern humans, Reich and his colleagues applied several statistical techniques for studying population history they’d developed. A key tool was the “four population test” (a cousin of the “three population test” they had used to show the Ancient North Eurasian contribution to northern Europeans—the key clue that the Yamnaya had mixed into Europe). Reich and Patterson compared a Neanderthal genome to two modern humans—one African, and one non-African. They compared the two modern humans, and at sites where they differed genetically, they examined which matched the Neanderthal. Had there been no interbreeding, the modern human samples would have differed from the Neanderthal genome at an equal number of sites. But they didn’t. Non-Africans matched the Neanderthal genome at a significantly higher rate, indicating that the two groups interbred. Subsequent recombinations, which break up segments of Neanderthal ancestry in modern humans into smaller and smaller pieces at a predictable rate every generation, date these events to between 54,000 and 49,000 years ago.

What led to the disappearance of Neanderthals is guesswork, but among Neanderthal individuals whose genomes have been sequenced there is “shockingly little variation,” says Reich—so little, in fact, that it suggests a population size that may have become too small to overcome the natural accumulation of newly occurring disease-causing mutations in their DNA. (Since sex results in a random reassortment of genes, it can filter deleterious mutations from a breeding population that is sufficiently large and varied.)

Alternatively, Neanderthals may have been driven to extinction by a more technologically advanced group, or one with different cultural norms. There are numerous examples in ancient history of one group flourishing and abruptly displacing another. “In thinking about what happened in Europe around 40,000 years ago it is natural to focus on the fate of the Neanderthals, because of their biological distinctiveness,” Reich points out. “But that doesn’t mean that modern human pioneer groups who lived at the same time in Europe alongside the Neanderthals were not equally displaced—actually they were, by later waves of modern humans spreading after around 40,000 years ago.”

Later in 2010, Reich and his colleagues shocked the world again when their analysis of DNA extracted from a single juvenile finger bone found in Denisova Cave in the Altai mountains of Siberia revealed the history of an entirely new group of archaic humans, whom they dubbed “Denisovans.” The Denisovans marked the history of one group spreading after around 40,000 years ago.”

But determining the sex bias of the interactions between modern and archaic humans (see sidebar, “Detecting Sex Bias in DNA”) will not be straightforward, says Reich. That’s because when these groups mated, they were “at the edge of biological compatibility.” When that happens, natural selection acts swiftly to eliminate the least fit genes in the mixed offspring, muddying the ability of genetic researchers to detect the presence and direction of any potential sex bias. Was it Neanderthal males mating with modern human females, the reverse, or both?

Reich says there may be other ways to understand the nature of that interaction. For instance, there is full genome ancient DNA from multiple mixed individuals living 40,000 to 50,000 years ago, “so there’s hope that we can learn something about it.”
An Ethical Perspective on Prehistory

IF ANYONE CAN untangle that ancient history, it’s Reich. David Anthony, who continues to work with him to find the original speakers of proto-Indo-European (the Yamnaya are thought to have spread the language, but not to have invented it), describes him as “a remarkable man. Brilliant, and a thoughtful referee when disputes come up,” whether they involve data or an ethical aspect of DNA analysis, an area in which he has been “a leader.”

Maybe contemporary non-Africans are actually Neanderthals... “with 98 percent modern human mixture, or something profoundly philosophically unsettling like that.”

A virtual conference of anthropologists, geneticists, archaeologists, and curators from more than 30 countries that members of the Reich lab co-organized in 2020 led to the 2021 publication in Nature of ethical guidelines for DNA analysis, to address “the social and political impacts of studying ancestry,” the scientist coauthors wrote, and the fact that, among other considerations, “ancient DNA work analyses once-living people who must be respected.” That means treating remains with care, using as little bone or tooth material as possible, ensuring all appropriate permissions for ancient DNA analysis are obtained, and engaging with stakeholders to promote final work that is sensitive to local community perspectives. The paper was translated by the authors into 23 languages, ranging from Swahili to Spanish to Punjabi to Arabic.

Although the genetics of ancient human groups underscore the complex connections that unite humanity, Reich is also keenly aware how overstated claims for the biological fitness of one group over another could lead to the misuse of his research. The scientific racism that fed the rise of Nazism swelled on the idea that a master race called Aryans were the original speakers of Indo-European languages. Given his family’s encounter with the horrors unleashed by those ideas, telling the true story of how Indo-European languages spread comes with a personal stake.

Reich is not resting on his laurels. As the data accumulate, and the tools become more sophisticated and powerful, he has begun revisiting some of his own prior interpretations of human prehistory, and coming to terms with what he describes as “weird signals in the current data.” Mitochondrial DNA shows that modern humans and Neanderthals are much more closely related to each other in the maternal line than either is to Denisovans. The Y chromosomes of modern humans and Neanderthals, passed only in the paternal line, are also much more closely related to each other than to Denisovans. “But then if you look at the whole genome, on average, Neanderthals and Denisovans are more closely related to each other than either one is to modern humans. Having an entirely male line and an entirely female line saying one thing, and then the rest of the genome saying something else, is weird.” The explanation some people give is that there may have been modern human mixture with Neanderthals further back in time than currently understood, somewhere between 250,000 and 400,000 years ago, and that contributed a few percent to the Neanderthal genome. “But it’s very surprising that only a few percent contribution would be the source of both the Y chromosome and mitochondrial DNA for Neanderthals.” Maybe contemporary non-Africans are actually Neanderthals, and later waves of modern human DNA from Africa swamped the rest of non-Africans’ genomes so “non-Africans are best described as Neanderthals, with 98 percent modern human mixture, or something profoundly philosophically unsettling like that,” he says, half seriously.

“There’s going to be a challenging of our understanding of these relationships” in the years ahead, Reich continues, “based on analyzing the data in more sensitive ways and looking at it from new perspectives. We’re taking a couple of steps back and realizing that key events and relationships are different, in a deep way, from the first-pass model we have collectively developed. The model that I’ve had a role in building is teetering. I find that exciting, as well as destabilizing. And I’d like to be part of trying to figure out the truth.”

Jonathan Shaw is managing editor of this magazine.

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