barely a decade after Charles Darwin published *On the Origin of Species*, he and his long-time correspondent Alfred Russel Wallace were engaged in a fierce debate. Darwin said that natural selection had shaped the human species just like any other. But Wallace disagreed, arguing that selection alone could not account for the exceptional capabilities of the human mind. "How could natural selection, or survival of the fittest in the struggle for existence, at all favour the development of mental powers so entirely removed from the material necessities of savage men?," he wrote.

Wallace lost out. By the mid-twentieth century most scientists had agreed that human bodies and minds were the product of genes that had evolved under the pressures of natural selection, just like everything else in the living world. One of the exciting prospects of reading the human genome was that it would reveal the ways in which this had happened — the marks left by evolution as it shaped humans into a species with language, learning and all sorts of other traits peculiarly interesting to it. "The idea was that if we could just identify those few critical genetic differences, we could explain the differences in cognition and language," says Todd Preuss of the Yerkes National Primate Center at Emory University in Atlanta, Georgia.

But today, nearly a decade after the human genome was sequenced, some geneticists are thinking again. Genomics has identified many sequences that are under selection, but it has not provided the simple read-out of human evolutionary history that some had hoped for. Scientists are having to rethink how genomes work, and are now pondering whether genes alone can explain the human animal. They don't think that human biology is incomplete without spirituality, as Wallace did. But they do wonder whether it is incomplete without culture. Because many complex skills and behaviours are being passed on through culture, some researchers are coming around to the view that the species has escaped the need to encode them rigidly in its genome. "Of course the mechanisms of selection are operating," says Ajit Varki, a specialist in human origins at the University of California, San Diego. But perhaps "we don't necessarily fix our behaviours, and we are letting some previously fixed behaviours deteriorate, because we can rely on cultural transmission", he adds.

These ideas are not entirely new. In 1981, geneticists Marcus Feldman and Luca Cavalli-Sforza from Stanford University in California published models to show how human behaviour results from the interaction of biological and cultural evolution. What is new for genome scientists is the realization that they will not be able to interpret the evolutionary marks they have found in the human genome without considering behaviour and environment every step of the way.

**Being human**

The human species has a unique set of features, including a large brain in proportion to the rest of the body; the ability to communicate complex information through symbolic language; and physiological vulnerabilities to Alzheimer's disease, certain cancers and other conditions. Geneticists hoped to explain the evolution of these human attributes with the tools of comparative genomics — the side-by-side comparison of different species' genomes.

Varki was part of a group that pushed hard to sequence the genome of human's closest relative, the chimpanzee, arguing that any genetic differences between human and chimp sequences would lead straight to the heart of humanness. But the chimp sequence, published more than three years ago, hasn't delivered this. One comparison between humans, chimps and mice, for example, showed that the protein-coding sequences of genes expressed

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**THE OTHER STRAND**

Geneticists looked to the human genome to understand human evolution. But it’s hard to interpret without considering the inheritance of culture, finds **Erika Check Hayden**.
Some evolutionary research is leading away from protein-coding genes entirely. In 2006, a team of scientists led by David Haussler at the University of California, Santa Cruz, picked out 49 regions of the human genome that had remained largely untouched throughout the evolution of fish, reptiles, birds and monkeys, and then went into mutational hyperdrive after ancestral humans emerged. The researchers found that the genomic address that has evolved faster than any other codes not for a protein, but for a small piece of RNA — human accelerated region 1 (HAR1) — that is expressed in brain cells during human fetal development. Beyond that, nobody knows what HAR1 does. Its sudden status as a belle at the evolutionary ball underscores the idea that selection could have acted most strongly on sequences outside the bounds of protein-coding genes, leaving Haussler and other researchers to work out what these sequences are doing, and why selection has acted on them. The picture could become even more complicated if, as some recent work has suggested, the statistical tests used to find genes under positive selection are themselves questionable. "There are thousands and thousands of changes to our genomes that have occurred in the past few million years that are still hidden, and the vast majority of those will not be functionally consequential," Haussler says. "So it is an amazingly difficult, needle-in-a-haystack type of search."

The idea was that if we could just identify those few critical genetic differences, we could explain the differences in cognition and language. — Todd Preuss

Genome researchers once expected that most of the genetic differences between humans would be in single letters of DNA, a type of variation called a single nucleotide polymorphism, or SNP. But in the past few years, they have discovered that large chunks of the genome can be duplicated, deleted and otherwise rearranged differently between individuals. In a paper published this week, Eichler’s team analysed the genomes of humans, chimpanzees, orangutans and macaques and found that a burst of duplications appears to have occurred in the last common ancestor of humans and chimpanzees. The question now is why? Such rearrangements risk disrupting essential genes and have been linked to human diseases such as autism and schizophrenia. Varki and Eichler suggest that structural variations may also confer benefits by expanding the range of genetic diversity. The negative side effects might be outweighed by the advantages conferred by new genes or other beneficial arrangements. And the human genome might have been able to tolerate some of the potentially toxic variants thanks to clothing, tools, agriculture and other cultural innovations that allow individuals with these variants to survive. "By allowing individuals to be buffered against natural selection, perhaps culture allows a wider spectrum of genetic diversity to creep in," Eichler says. "Maybe the wider spectrum of diversity allows for more savants and autistic people in the same population."

Researchers have found that the human genome has accumulated more than its fair share of other potentially harmful genetic changes too — in protein-coding regions, promoters and even the loss of entire genes. One explanation is that it is a remnant of the frequent population ‘bottlenecks’ in human history, in which small groups that migrated to new areas established new populations that all carried the founders’ mutations. But another possibility, says statistical geneticist Gilean McVean at the University of Oxford, UK, is that the human ability to learn and adapt has eased the selection pressure that would weed
out some of these changes. “When you look in the human genome, one of the things you see is that it has accumulated a lot of apparently bad mutations, and to some extent humans’ inventive skills might have allowed that,” he says. A modern example, he points out, might be the ability of humans to make spectacles to counteract poor vision.

Anthropologist and neuroscientist Terrence Deacon of the University of California, Berkeley, has long argued that culture could have “relaxed” human selection. Apes, for instance, have lost the ability to make vitamin C because the gene that facilitates this process has broken down. Deacon suggests that the availability of fruit eased the selection pressures working against individuals who couldn’t make their own vitamin C, allowing the relevant gene to accumulate mutations but also making apes dependent on external sources for the nutrient.

The relaxed selection created by human culture similarly could have allowed the evolution of more diversity and complexity, Deacon says, but it has also made humans more reliant on the innovations that freed them from selection in the first place. “We have produced symbolic communication and culture and technology, all of which play a part in shielding us from certain kinds of selective forces,” he says.

Genetic burst

When scrutinizing the genome, some researchers see more dramatic evidence of culture’s influence. In 2007, a team led by anthropologist John Hawks of the University of Wisconsin, Madison, and genome scientist Robert Moyzis of the University of California, Irvine, proposed that culture is hastening human evolution1. The team combed through a set of 3.9 million SNPs from European, African and other ancestral human populations, looking for those that bore a signature of positive selection: they were relatively young, common in individuals from the same population and different from those in the other populations. Such mutations are probably being ‘swept’ to abundance shortly after appearing because they lie in or near pieces of DNA that are beneficial in some way.

The team found that a burst of these SNPs had appeared about 10,000 years ago, suggesting that selection has been causing very rapid genetic change since that time.

The researchers then tested whether evolution had sped along like this throughout human history. If so, then the different ancestral populations should have fairly similar genomes because many mutations and their surrounding regions would have swept throughout the human genome before these populations diverged. But current human populations are much more genetically diverse than this hypothesis predicts, so Moyzis and Hawks have concluded that evolution must have ramped up over the past 40,000 years. They chalk some of this acceleration up to human population growth, which exposed the species to more new mutations and created more raw material for selection. But the other reason, Hawks thinks, is culture — because although the physiology of humans has not changed much in the past 40,000 years, their expansion and migration means that lifestyles, languages and technologies certainly have.

Although not everyone agrees with Hawk’s claims, the best understood example of recent human evolution does seem to fit. Genetic mutations that allow adults to digest lactose, a sugar found in milk, have emerged independently in different populations in response to the same cultural innovation — cattle domestication2. “I don’t see culture as an alternative to genetics, I see culture as being the explanatory factor for these genetic changes,” says Hawks. “There is no explanation for change without the gene–environment interaction.”

Hawks and others are now looking for the beneficial sequences connected with the selected SNPs. But these sequences are hard to pinpoint, and even harder to connect up with a specific human trait. “We know that genes involved in immunity, genes involved in brains, these are showing signals of adaptation in a way that suggests [these traits] have been important,” says McVean. “But that’s kind of obvious — you only have to look at our biology or our physiology or behaviour to see that.”

To Varki and others, the absence of sequences that underlie specific human behaviours could itself testify to the importance of human culture. According to the ‘Baldwin effect’, named after the American psychologist who proposed it in the late 1800s, behaviours crucial to survival will often become ‘hard-wired’ into the genome to ensure that they are not lost. But most human skills are not hard-wired: people who have never lived in the Arctic would have a difficult time figuring out how to hunt a seal,
Agriculture, tools and other cultural innovations may have allowed mutations to accumulate in the human genome.

Long before the next centennial of Darwin’s birth, these data might have closed the book on human evolution. If they do show that culture has shaped the evolution of humans in a way that has no counterpart elsewhere in the animal kingdom, then perhaps Wallace will earn some posthumous credit: this was more than natural-selection-as-usual. But culture cannot have had so strong a role in human evolution without itself being influenced by the results. In the words of Wallace, understanding this interplay will require all of the “mental powers so play will require all of the “mental powers so