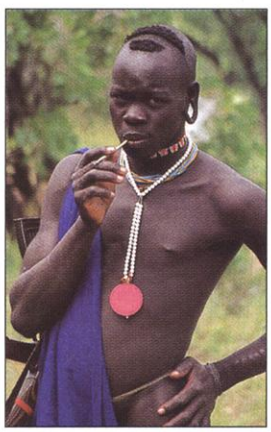
NEWS

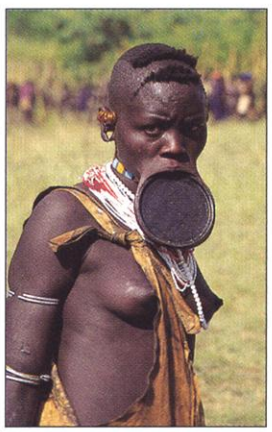
Tracking the Sexes by Their Genes

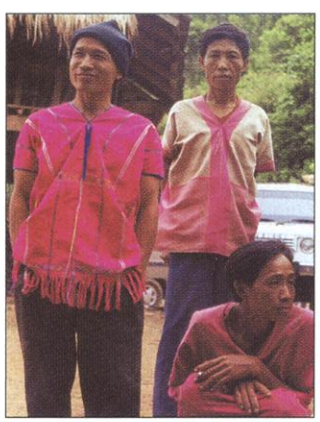
By comparing data from maternally and paternally inherited DNA, researchers are finding that in our ancestral populations, men and women didn't always travel together

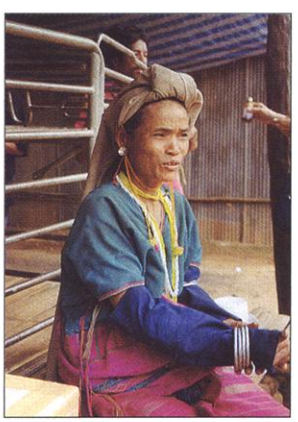
Men aren't really from Mars, nor women from Venus, but even though the two sexes hail from the same planet, they may not share a common homeland. Humans have been on the move for nearly 2 million years, expanding into new areas or retreating to warmer climes, and it would be reasonable to assume that men and women moved together. But molecular anthropologists tracking these ancient travelers by the trails left in their descendents' DNA are finding a surprise: striking differences in how the two sexes traveled about parts of this planet.

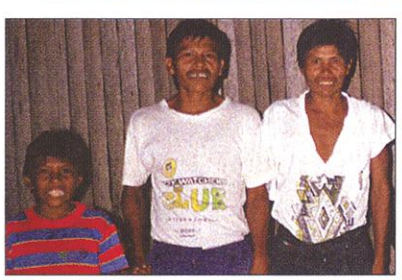
By analyzing and comparing DNA passed on only through either the maternal or paternal lines, researchers can track down each gender's homelands and even trace their movements back hundreds of generations. Much more work needs to be done to ensure that the apparent differences between male and female migrations are real, but a few patterns are already emerging. "It's one of the most exciting things going on right now in [the study of] human evolution," says David Goldstein, a geneticist at University College London (UCL). In some cases, the genes reveal how male explorers or warriors carried their genomes to distant places. But surprisingly, in general females seem to have stirred the genetic melting pot by dispersing their DNA more widely than their brothers dispersed theirs—perhaps as a result of thousands of years of moving to join their husbands' clans.











Who moves most? Maternally and paternally inherited DNA, sampled in people from *(top to bottom)* Africa, Thailand, and South America, helps reveal which sex spreads genes the farthest.

This research took off about 15 years ago, when researchers began studying DNA found in a cellular organelle called the mitochondrion. This mitochondrial DNA (mtDNA) is passed only from mother to child and escapes the mixing and matching that goes on between pairs of chromosomes. By comparing sequence differences among living people, researchers can build family trees that help determine the ancestral group—and the ancestral homeland—of a population. Moreover, based on an estimated average mutation rate, they can get a sense of how long ago a group moved away from its native land. And in the past 5 years or so, molecular explorers have begun probing the Y chromosome, which is found only in men, constructing similar histories traced back through the male line (see Viewpoint on p. 1738).

Now researchers are putting both kinds of analysis together. For example, in one of the first such comparative studies, Svante Pääbo, a geneticist at the Max Planck Institute for Evolutionary Anthropology in Leipzig, Germany, and his colleagues compared molecular markers in groups of Bedouins in the Sinai. Current Bedouin custom dictates that the wife join her husband's group, and in 1996 the DNA studies verified that this so-called patrilocal social structure had indeed been followed faithfully for centuries. Because women and their mtDNA moved about, the mtDNA is well mixed and diverse. "The mtDNA of the Sinai tribes has as much variation as that of all the people in the Nile," Pääbo explains. But the genetic signatures in the Y chromosome data clustered into distinct geographic groups. Thus the study showed that living people's genes can offer a glimpse into the population structure of their ancestors.

Women on the move

Pääbo's results were widely accepted. But the following year, a study by Mark Seielstad, then a biology graduate student at Harvard University, and his collaborators kicked off an intense debate. Seielstad, now an evolutionary geneticist at the Harvard School of Public Health in Boston, looked for similar patterns on a much broader scale. He and his colleagues used an expanding set of Y chromosome studies of native Africans and Europeans that he and L. Luca Cavalli-Sforza's group at Stanford University in Palo Alto, California, had compiled, together with existing mtDNA data gathered over the years by various investigators. The researchers quantified the degree to which different geographic groups shared Y chromosome and mtDNA markers. Their bold conclusion: Over thousands of years, it was women who had dispersed genes most widely, not men as many had assumed (*Science*, 31 October 1997, p. 805).

"There was demonstrably greater geographic structure to the Y chromosome [data] than to [the] mtDNA [data]," Seielstad explains. In one analysis, only 35% of the Y chromosome markers were shared among populations, and men from each location tended to have their own unique markers. That was much less true of mtDNA markers, leading Seielstad to suggest that over the past several thousand years, men have tended to

CREDITS: (AFRICA AND THAILAND) M. SEIELSTAD; (SOUTH AMERICA) ANDRÉS RUIZ-LINARES/UNIVERSITY COLLEGE LONDON

have children near their own birthplaces. In contrast, women were the movers, if not the shakers, of traditional societies, eventually spreading their genes even to different continents. That implies that patrilocal societies like the modern-day Bedouins were common in human ancestry and have dominated during the past several millennia, most likely emerging with the growing dependence on agriculture, says Seielstad.

"We have an image of men being more mobile," Seielstad explains. "That happens, but prior to global exploration, what was more significant, long-range migration of males or day-to-day migration of women? My feeling is that the latter is more important."

With these words, Seielstad threw down the gauntlet to his colleagues. Some applauded his study for its innovative use of the two types of genetic data. But critics felt, as population geneticist Lynn Jorde of the University of Utah in Salt Lake City complains, that "[Seielstad and his collaborators] went way too far in generalizing this to a worldwide pattern." The skeptics also note that mtDNA and Y chromosomes mutate at different rates and are passed along at different frequencies, and Seielstad studied these markers in different-sized populations. Thus, he was "in danger of looking at apples and pears," says Matthew Hurles, a population geneticist at the McDonald Institute for Archeological Research in Cambridge, United Kingdom.

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>
> —Mark Seielstad

Others pointed out that even if the pattern is real, there could be other explanations for it. If, for example, a few men had most of the children, then their Y chromosomes would dominate, making it seem as though few new migrants with different Y chromosomes had entered the population. Recognizing these limitations, Seielstad is now conducting two projects that he hopes will help clarify the effect of polygyny and other marriage mores on the diversity seen in mtDNA and Y chromosome data.

In one, with Daoroong Kangwanpong of Chiang Mai University in Thailand, he is obtaining genetic material from a region where tradition calls for the husband to move in with the wife and her parents. To date they have gathered only Y chromosome data, but as Seielstad predicted, Y chromosome markers from this population are more broadly distributed than those from a nearby region where patrilocality is the rule. Seielstad is also analyzing data collected from several regions of China, looking for the DNA traces of migrants into various communities, whose molecular markers should differ from those of their neighbors. If his hypothesis is correct, more of those migrants are women.

Seielstad's proposal also sent some of his critics scrambling back to their labs to see what their own data had to say about whether the pattern really is worldwide. Some of these efforts do support Seielstad's conclusions. Hurles and his colleagues have looked at single base changes in noncoding regions of both the mtDNA and the Y chromosome of some 25 groups in Europe, gathering both types of genetic data from the same populations and thus addressing a key methodological criticism of Seielstad's study. Their findings so far are "pretty consistent" with Seielstad's, "[even] though we're looking at different loci and different rates," says Hurles, who has yet to publish these results. The same pattern turns up in Asia, adds Hiroki Oota of the University of Tokyo and the Max Planck Institute for Evolutionary Anthropology, who compared his data on the mtDNA of 280 women from China, Vietnam, and Japan with Y chromosome data collected by others.

But other researchers say the pattern is not the worldwide trend Seielstad suggested. It doesn't appear in South America, for example, contend Natalia Mesa and Andrés Ruiz-Linares of the University of Antioquia in Medellín, Colombia, who examined both mtDNA and Y chromosome markers in five Native American populations in Colombia and reviewed existing genetic data on South Amerinds. As they reported in the November 2000 *American Journal of Human Genetics*, they saw roughly equal distributions of diversity in the Y chromosome and mtDNA, suggesting that neither matrilocality nor patrilocality has predominated. Their newer work looking at people from Central and North America yields the same result. "We don't see what Seielstad and Cavalli-Sforza reported," says Ruiz-Linares, who is now based at UCL.

Men from afar

Although the Y chromosome data suggest that men were often geographically restricted, it also reveals some cases in which men were the travelers. For example, for almost 25 years, anthropologists have debated the origins of a group of South Africans called the Lemba. Although the Lemba share the language and looks of the local Bantu people, they also have customs and folklore suggestive of Jewish origins. Early analyses of blood groups and mtDNA detected no difference between the Lemba and other Bantu, but a cursory look at Y chromosome markers hinted at Jewish ancestry.

More recently, in the February 2000 *American Journal of Human Genetics*, UCL's Goldstein and his colleagues described how one of the Lemba clans has the so-called Cohen modal haplotype—a Y chromosome marker found in 10% or more of the men of various Jewish groups but not at all in non-Jews. "It appears that the story these people tell is at least partially true," says Utah's Jorde. Furthermore, "it's the males, not the females, [who] probably came down [from the Middle East] and intermixed with the population" some 3000 to 5000 years ago, as the mtDNA seems to be Bantu-like.

Other populations also reveal traces of long-distance male movement. For example, Jorde has examined the origins of caste populations in southeastern India. As his Utah colleague Mike Bamshad reported at a meeting* in November 2000, they find that the mtDNA in all caste groups is "most similar to [that of] other Asian populations," Jorde says. But the Y chromosome data indicate that males in "the upper castes are more similar to Europeans than to Asians," and that there is "less and less [similarity to Europeans] as you go down the castes." He thinks that about 3500 years ago, immigrant traders, farmers, or warriors from Western Eurasia, likely with few women of their own kind, formed the basis of the upper castes.

Researchers are turning up more and more such tales as they analyze different populations. However, some warn that, like many conclusions about gender differences, the underlying analyses may be shaky, particularly when anthropologists try to step back many thousands of years. Recent events can mask earlier ones, notes Goldstein. And Pääbo worries that over thousands of years, as for example in Seielstad's studies, differences in the mutation rates of the two kinds of genetic markers may throw off the results. For example, a researcher might unknowingly compare a mtDNA pattern from 5000 years ago with a Y chromosome pattern that was 50,000 years in the making. "On a deeper history level, I'm a little more worried" about Y chromosome and mtDNA comparisons, says Pääbo.

But Jorde is less concerned. Researchers now have not just the Y chromosome and mtDNA but also gene sequences inherited from both parents at their fingertips—data that will help them discern whether the suggested differences between men and women are real. And because of that, he points out, "we can be much more secure in our interpretation of human history."

—ELIZABETH PENNISI

* Cold Spring Harbor Millennium Meeting on Human Origins & Disease, 25–29 October 2000, Cold Spring Harbor, New York.