

Worldwide genetic and cultural change in human evolution

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Both genetic variation and certain culturally transmitted phenotypes show geographic signatures of human demographic history. As a result of the human cultural predisposition to migrate to new areas, humans have adapted to a large number of different environments. Migration to new environments alters genetic selection pressures, and comparative genetic studies have pinpointed numerous likely targets of this selection. However, humans also exhibit many cultural adaptations to new environments, such as practices related to clothing, shelter, and food. Human culture interacts with genes and the environment in complex ways, and studying genes and culture together can deepen our understanding of human evolution.

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Introduction

The study of worldwide genetic variation has made great strides in the 25 years since researchers first convened to plan the Human Genome Diversity Panel (HGDP) [1]. The initial analyses of HGDP data showed that the vast majority of genetic variation occurs within human populations; however, the small fraction of between-population genetic variation could be used to characterize clusters of individuals, which generally correspond to geographic regions and can often be further segmented into population-level groups [2]. The data produced as a result of this initiative, combined with the HapMap and 1000 Genomes initiatives and additional samples from modern and ancient populations, continues to shed light on important aspects of human evolution, including demographic

history, migration patterns, admixture between groups, selection pressures, and mutation rates [3^{••},4[•],5–10].

Meanwhile, it has become increasingly clear that human culture interacts with genetic variation in complex ways. Culture can evolve through similar processes to genetic evolution: cultural variants can have differential survival and reproduction, but there are notable differences between cultural transmission, mutation, and inheritance and their genetic analogues [11–13]. Cultural transmission does not obey the precise rules that Mendelian inheritance imposes on single genes, and it may occur between unrelated individuals. Culturally transmitted traits, such as norms and preferences, can change within the course of a human generation, and cultural inheritance may occur over many generations, between groups rather than individuals, and depend on the environmental or social context in which an individual lives. Further, genes and culture often interact: several researchers have suggested that genetic changes, for example those that affect brain architecture, can promote large-scale changes in human culture [14,15], but cultural changes can also alter the selective advantage of genetic mutations, fostering their spread [16–18]. In one classic example, the spread of dairy farming and animal domestication in multiple geographic regions led to a corresponding regional increase in the frequency of genetic variants associated with lactase persistence, allowing more individuals to benefit from drinking milk into adulthood [19,20]. This interaction between genetic and cultural evolution has been studied under several research umbrellas, including gene–culture coevolution, dual inheritance theory, and cultural niche construction [19,21,22]. Here, we review the literature on human genetic and cultural variations, the interactions between them, and the importance of considering both genes and culture in studies of human evolutionary history.

Patterns of worldwide genetic variability and the influence of cultural practices

Geographic patterns of human demographic history have left detectable signatures on the human genome. For example, the human migration out of Africa likely occurred by repeated founder events, in which a small group of people broke away from a larger population to establish a new settlement [23]. Since each subsequent founder event constitutes a sample of the genotypes of the larger group, the serial founder effect model predicts a decrease in genetic diversity with geographic distance from the putative human origin in Africa [24]. Patterns of human

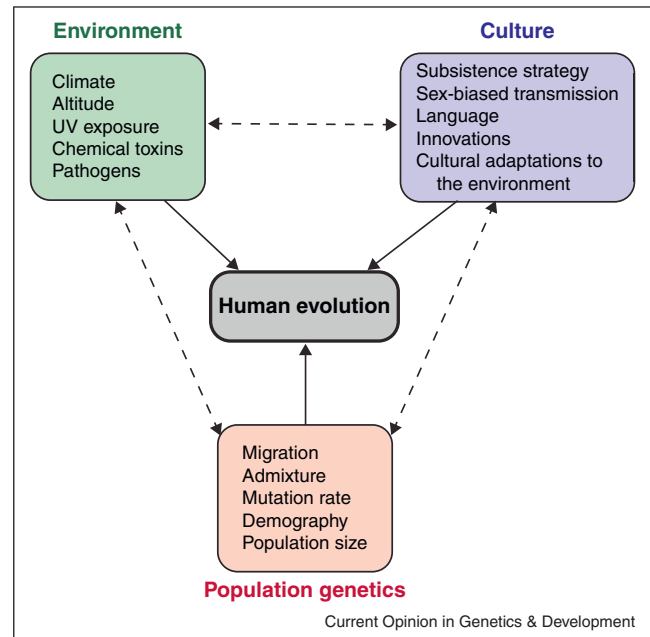
genetic variation have also shed light on the extent of admixture between different populations [25]. This admixture can be a result of relatively recent events in human history, such as colonialism or the advent of technology that facilitates long-distance transportation [4[•],8,25,26]. However, recent studies have illustrated that ancient admixture events, such as between modern humans and Neanderthals or Denisovans, are also detectable in the modern human genome [27^{••},28^{••}].

As researchers accumulate genetic data from more human populations and develop more sophisticated computational techniques, the effects of various forces in population genetics — for example, recent population growth [29], population separation [30[•]], range expansion [31], neutral genetic variation [32,33], and mutational load [34[•]] — can be understood in much greater detail. However, signals of population genetic and demographic processes in the human genome are complicated by cultural factors. For example, runs of homozygosity (ROH) are stretches of the genome where heterozygous nucleotides are absent or extremely rare, indicating that an individual's two chromosomes share a recent ancestor, with the length of each run dependent on the number of generations since the common ancestor [35]. ROH can provide evidence for population bottlenecks and ancestral relationships between populations, but it is important to note that the length of these runs can be dramatically influenced by cultural practices, particularly those surrounding marriages between relatives [35–37]. Indeed, homozygosity-based measurements can be used to estimate inbreeding more accurately than can be achieved with family pedigrees [38], particularly in cases where parental relatedness is elevated for many generations [39]. This inbreeding can, in turn, be negatively associated with phenotypes that are relevant to fitness and health, such as height, educational attainment [40], and hypertension [41].

Consanguinity and the cultural practices surrounding it provide one example of a culturally transmitted behavior that leaves an identifiable signature on the human genome. Other aspects of human culture, such as religion [42,43] and sex-specific demographic features [44] including sex-biased migration and sex-specific definition of cultural belonging, can also shape a population's trajectory of genetic evolution. By separately tracing the evolution of maternally transmitted mitochondrial sequences and paternally transmitted Y chromosomes, researchers can test the genetic effects of cultural practices such as matrilineality and patrilineality [45], as well as other sex-biased patterns of human demography that are culturally determined (Figure 1).

For example, the deep phylogenetic history of mitochondrial DNA sequences suggests that human populations were matrilineally structured before the out-of-Africa

Figure 1



Genetic, environmental, and cultural factors are capable of influencing one another (dashed arrows), and all three have an impact on human evolution (solid arrows).

expansion [46]. A further study of Eurasian and African populations found a discrepancy between the Y chromosome and mitochondrial DNA in the signal of expansion events, implying that male gene flow might have been restricted in some ancestral lineages [47]. Marital practices in which a man relocates to his wife's village upon marriage have left a genetic signature of reduced effective population size and genetic diversity for females in Timor [48]. In contrast, patrilineal societies exhibit male-biased transmission of reproductive success, likely culturally transmitted, which leads to reduced genetic diversity [49]. The sex-specific cultural practices surrounding age of reproduction can also leave a mark on genetic variation, with faster matrilineal genetic evolution in Iceland attributed to a shorter generation interval in women [50]. In the specific example of the Hindu caste system, the cultural tradition of hypergamy, in which women are permitted to marry into a higher social caste in some circumstances but men are not socially mobile, has led to female-specific gene flow and, in some cases, genetic stratification of the populations [51]. Thus, societal systems and cultural norms can have an affect on genetic evolution; however specific cultural events can also leave a mark on the genome. For example, known migration events or significant cultural innovations in human history may correspond to dramatic expansions of the male human lineage, detectable on the Y chromosome [52^{••}]. Although some of the effects of culture on

patterns of genetic diversity are due to the ways in which culturally transmitted practices alter effective population size, others may be due to the spread of the attitudes, preferences, or norms that have no direct demographic impact.

Genetic and non-genetic adaptations to the environment

Underlying these patterns of worldwide genetic variation is a human tendency to explore previously uninhabited geographic regions. As a result of this cultural propensity to migrate to new areas, humans have adapted to differences in climate, altitude, and resource availability. Some of these adaptations to new environments are themselves cultural practices: for example, clothing and foot coverings that are suited to the climate, as well as novel tools and techniques for food acquisition and cultivation. Migration to new environments also alters the selection pressures on the human genome, and comparative genetic studies have pinpointed certain loci that were likely targets of this selection [53,54]. For example, highly pigmented skin protects against skin cancer but reduces the synthesis of vitamin D3 by the skin, so differences in the amount of ultraviolet radiation in the environment place different selection pressures on pigmentation genes [55]. Polymorphic loci in several genes contribute to variation in pigmentation, including *MC1R* and *SLC45A2* in skin [56–59] and *SLC24A4* in the hair and eyes [59], whose effects on health can be modified by clothing and shelter practices.

Migration to high altitude also alters selection pressures, and the mechanism of genetic adaptation to altitude appears to differ among Andean, Tibetan, and Ethiopian highland populations [60]. On the Tibetan Plateau, residents have a decreased hemoglobin phenotype that appears to accommodate the reduced oxygen levels at high altitude; this phenotype is associated with polymorphisms in genes such as *EPAS1* and *EGLN1* [61,62]. Humans have also adapted to local chemical environments; for example, high environmental arsenic levels in the Argentinean Andes have been linked to changes in a putative gene for arsenic metabolism, *AS3MT* [63*]. Evolutionary pressures may change when humans migrate to new climates, but a changing climate also appears to have an impact on human migration: historical fluctuations in climate occurred concurrently with the timing of migration events predicted by analysis of ancient DNA from South America [64].

Whereas older statistical methods were used to evaluate signals of environmental adaptation in single nucleotide polymorphisms and candidate genes, newer Bayesian algorithms have enabled genome-wide scans for adaptation to the local environment [54], with the caveat that results of this type of analysis are more stable when averaged over multiple runs [65]. Across the genome,

climate differences are correlated with polymorphisms in genes related to UV radiation and metabolism of starch and sugar, among others, and cultural practices related to both subsistence strategy and food sources appear to have had measurable genetic effects [66,67]. Diet provides another pathway by which culture can interact with the environment, shaping selection pressures on the human genome [66].

In addition to associations between environmental variables and single gene polymorphisms, recently developed techniques can reveal signatures of local adaptation in phenotypes controlled by more than one gene, for example, a polygenic association between latitude and skin pigmentation [68*]. Another technique, which detects signals of polygenic selection within one population, has shown that genes related to lactose digestion, immune function (HLA), and hair and eye pigmentation have been under selection in the United Kingdom [69]. However, one researcher estimated that ‘local adaptations are over 10-fold more likely to affect gene expression than amino acid sequence’ and found polygenic associations between the local environment and gene expression levels in several pathways, including those involved in response to UV radiation, diabetes, and the immune system [70].

Local adaptation involves responding to selection pressures, not only related to the climate, altitude, and resource availability, but also to the pathogens in the local environment. In fact, the pathogenic environment may play a more important role than climate in driving local adaptation [71]. Further, past adaptive responses to environmental pathogens might have implications for present-day human health: genes found to be linked to pathogen-driven selection were associated with susceptibility to celiac disease, type 1 diabetes, and other autoimmune diseases [71]. Other chronic diseases also show signatures of environmental adaptation, since risk alleles for numerous diseases are significantly associated with environmental variables [72]. For example, risk alleles for asthma were found to be strongly correlated with summer humidity levels, and risk alleles for several autoimmune diseases, such as Crohn’s disease, ulcerative colitis, and systemic lupus erythematosus, appear to be associated with various features of the local climate [72]. In contrast, risk alleles for type 2 diabetes seem to follow the predictions of the serial founder effect model of migration out of Africa, with the frequency of risk alleles decreasing with distance from Africa [72–74].

Patterns of worldwide cultural variation

Human genetic and cultural transmission differ in that culture can be inherited not only from parents but also from teachers and peers, and thus patterns of cultural evolution may often diverge from population genetic histories [11,19]. Even so, some widespread culturally

transmitted phenotypes appear to show geographic signatures of human demographic history [75,76*,77]. Cultural traits can also respond to selection pressures, as genes do; for example, in a study of Polynesian canoes, functional elements evolved more slowly than symbolic elements, suggesting purifying selection on the properties of canoes most relevant to the survival of the human passengers [78]. Since they are transmitted differently but closely linked, cultural and genetic traits can be studied using a coevolutionary framework developed for co-speciating hosts and parasites, as opposed to framing such traits as two sources of data from the same organism [79].

Languages, genes, and geography

Language is a culturally transmitted human characteristic that has been studied for centuries and has recently been considered in the context of genetic variation. In a recent global comparison of genetic variation with inventories of phonemes, the smallest units of sound capable of distinguishing meaning between words, both genetic distance and phonemic distance between populations were significantly correlated with geographic distance [76*]. The pattern of worldwide phonemic variation contains signals of both historical migrations and recent population contact [76*]. However, most studies of regional language and genetic variation highlight local features that are more complex than this global pattern (although some regions, such as Daghestan [80] and New Britain [81], show a relatively straightforward correlation between genetic and linguistic diversity). For example, in Northern island Melanesia [81], North America [82], and northeastern Thailand [83], language boundaries do not appear to act as a barrier to gene flow, so genetic distance does not show a strong association with linguistic distance. In contrast, in Europe [84], the Caucasus [85], the Niger-Congo populations of sub-Saharan Africa [86], and the Kra-Dai linguistic family in Thailand [87], language seems to be a better predictor of genetic differences than geography, so genetic distance shows a stronger association with linguistic than geographic distance.

Language and sex-biased gene flow

Comparisons of linguistic, genetic, and geographic distances can also provide evidence for sex-biased demography. For example, Y-chromosome genetic distance among African populations was reported to be more closely correlated with linguistic distance than with geographic distance [86,88], whereas mtDNA genetic distance was associated with both linguistic and geographic distance [88], suggesting that culturally determined sex-biased demographic patterns, such as patrilocality and male-biased language transmission, could have played a role in the evolution of these populations. In contrast, among a set of Austronesian populations, language was more closely associated with genetic differences in mtDNA than Y-chromosome DNA [89], implying a pat-

tern of sex-biased transmission, such as matrilineality and female-biased language transmission, that differs from the pattern of male-biased transmission suggested by the study of African populations. We can speculate that variation in the extent to which language differences form a barrier to gene flow might be related to child-rearing practices, in particular the transmission of parental attitudes that result in children's lifelong preferences.

Cultural homophily

Human culture can also bias genetic evolution through culturally mediated mating preferences. Through assortative mating or homophily, humans often choose mates who are similar to themselves in certain ways. People assort on numerous phenotypes, from polygenic traits such as eye color [90], height, and IQ [91–93] to behavioral traits such as generosity [94], risk attitude [95], smoking [96], and education level [97*]. This assortment may affect fitness; more similar mates tend to have higher fertility [98]. Further, assortative mating on religion and educational attainment corresponds to differences in the length of runs of homozygosity in homophilic groups [99,100], which could be interpreted as evidence for inbreeding if assortative mating is not taken into account. The tendency for assortative mating can itself be culturally transmitted or may be partially genetic [92], and evolutionary simulations indicate that increased assortative mating can have a strong effect on evolution by facilitating the spread of rare cultural and genetic traits [101,102]. The tendency for culturally similar individuals to come into contact more frequently than by chance was called 'assortative meeting' by Eshel and Cavalli-Sforza; their theoretical analysis showed that such homophily can have a positive effect on the spread of cooperative behavior and that the tendencies to homophily and altruistic behavior may coevolve [103]. Thus, assortative mating represents an important mechanism of interaction between genes and culture that is not often accounted for in genetic studies.

Conclusions

In sum, researchers can better understand evolutionary patterns and human demographic history when both genes and culture are considered. In the 25 years since the Human Genome Diversity Panel was first proposed, our understanding of human population structure, local adaptation, admixture, and gene-culture coevolution has dramatically improved. That said, the juxtaposed study of genes and culture has potential pitfalls when poorly deployed, particularly when researchers fall victim to the use of incomplete data, faulty statistics, or logical fallacies. Recent examples include (1) the assertion by Ashraf and Galor that the high genetic diversity in Africa and low genetic diversity in the Americas are both detrimental to economic development whereas the 'intermediate level' of genetic diversity in Europe is conducive to such economic development [104], and (2) the proposition

by Wade that differences between ‘races’ in wealth, IQ, and societal institutions have a genetic basis [105]; the methods and conclusions of both works have been strongly criticized on biological and anthropological grounds [106–108]. Extreme care is needed here to guard against the erroneous conclusion that the genetic diversity of a population in any sense determines whether members of that population are subject to a lack of wealth or intelligence; such claims run the risk of providing pseudo-scientific support for those seeking to justify economic or social policies such as ethnic cleansing, systematically mistreating immigrants, or halting humanitarian aid. With these caveats in mind, and in light of increased genetic sampling and improved analysis techniques, the next 25 years hold great promise for the study of human evolution by considering both its genetic and cultural components.

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References and recommended reading

Papers of particular interest, published within the period of review, have been highlighted as:

- of special interest
- of outstanding interest

1. Cavalli-Sforza LL: **The human genome diversity project: past, present and future.** *Nat Rev Genet* 2005, **6**:333-340 <http://dx.doi.org/10.1038/nrg1579>.
2. Rosenberg Na, Pritchard JK, Weber JL, Cann HM, Kidd KK, Zhivotovsky La *et al.*: **Genetic structure of human populations.** *Science* 2002, **298**:2381-2385 <http://dx.doi.org/10.1126/science.1078311>.
3. Gamba C, Jones ER, Teasdale MD, McLaughlin RL, Gonzalez-Fortes G, Mattiangeli V *et al.*: **Genome flux and stasis in a five millennium transect of European prehistory.** *Nat Commun* 2014, **5**:5257 <http://dx.doi.org/10.1038/ncomms6257>.
This paper presents a time series of ancient genomes from the same location across 5000 years: Neolithic, Copper, Bronze, and Iron Age burial sites in the Great Hungarian Plain. The earliest Neolithic sample, which was taken from an agricultural settlement, is genetically similar to ancient hunter-gatherers, and the latest Iron Age sample shows genetic similarity with Eastern Eurasian populations, consistent with predicted cultural influences from the Steppe during this time.
4. Hellenthal G, Busby GBJ, Band G, Wilson JF, Capelli C, Falush D *et al.*: **A genetic atlas of human admixture history.** *Science* 2014, **343**:747-751 <http://dx.doi.org/10.1126/science.1243518>.
This paper presents a technique called chromosome painting to assess which human populations mixed at which points in history. This approach predicts the genetic signatures of known phenomena, such as the Bantu expansion and European colonialism, as well as previously unreported admixture events.
5. Aghakhanian F, Yunus Y, Naidu R, Jinam T, Manica A, Hoh BP *et al.*: **Unravelling the genetic history of Negritos and indigenous populations of Southeast Asia.** *Genome Biol Evol* 2015, **7**:1206-1215 <http://dx.doi.org/10.1093/gbe/evv065>.
6. Friedlaender JS, Friedlaender FR, Reed Fa, Kidd KK, Kidd JR, Chambers GK *et al.*: **The genetic structure of Pacific Islanders.** *PLoS Genet* 2008, **4**:e19 <http://dx.doi.org/10.1371/journal.pgen.0040019>.
7. Rosenberg N, Mahajan S: **Low levels of genetic divergence across geographically and linguistically diverse populations from India.** *PLoS Genet* 2006:2 <http://dx.doi.org/10.1371/journal.pgen.0020215>.
8. Tishkoff Sa, Reed Fa, Friedlaender FR, Ehret C, Ranciaro A, Froment A *et al.*: **The genetic structure and history of Africans and African Americans.** *Science* 2009, **324**:1035-1044 <http://dx.doi.org/10.1126/science.1172257>.
9. Wang S, Lewis CM, Jakobsson M, Ramachandran S, Ray N, Bedoya G *et al.*: **Genetic variation and population structure in native Americans.** *PLoS Genet* 2007, **3**:e185 <http://dx.doi.org/10.1371/journal.pgen.0030185>.
10. Skoglund P, Malmstrom H, Raghavan M, Stora J, Hall P, Willerslev E *et al.*: **Origins and genetic legacy of neolithic farmers and hunter-gatherers in Europe.** *Science* 2012, **336**:466-469 <http://dx.doi.org/10.1126/science.1216304>.
11. Cavalli-Sforza L, Feldman MW: *Cultural Transmission and Evolution.* Princeton University Press; 1981.
12. Mesoudi A: **Cultural evolution: a review of theory, findings and controversies.** *Evol Biol* 2015 <http://dx.doi.org/10.1007/s11692-015-9320-0>.
13. Mesoudi A: **Cultural evolution: integrating psychology, evolution and culture.** *Curr Opin Psychol* 2016, **7**:17-22 <http://dx.doi.org/10.1016/j.copsyc.2015.07.001>.
14. Klein RG: *The Dawn of Human Culture.* John Wiley & Sons; 2002.
15. Vallender EJ, Mekel-Bobrov N, Lahn BT: **Genetic basis of human brain evolution.** *Trends Neurosci* 2008, **31**:637-644 <http://dx.doi.org/10.1016/j.tins.2008.08.010>.
16. Richerson PJ, Boyd R: *Not by Genes Alone: How Culture Transformed Human Evolution.* University of Chicago Press; 2008.
17. Laland KN, Odling-Smee J, Myles S: **How culture shaped the human genome: bringing genetics and the human sciences together.** *Nat Rev Genet* 2010, **11**:137-148 <http://dx.doi.org/10.1038/nrg2734>.
18. Fisher SE, Ridley M: **Evolution. Culture, genes, and the human revolution.** *Science* 2013, **340**:929-930 <http://dx.doi.org/10.1126/science.1236171>.
19. Boyd R, Richerson PJ: *Culture and the Evolutionary Process.* Chicago University Press; 1985.
20. Ranciaro A, Campbell MC, Hirbo JB, Ko WY, Froment A, Anagnostou P *et al.*: **Genetic origins of lactase persistence and the spread of pastoralism in Africa.** *Am J Hum Genet* 2014, **94**:496-510 <http://dx.doi.org/10.1016/j.ajhg.2014.02.009>.
21. Cavalli-Sforza LL, Feldman MW: *Cultural Transmission and Evolution: A Quantitative Approach.* Princeton University Press; 1981.
22. Odling-Smee J, Laland KN, Feldman MW: *Niche Construction: The Neglected Process in Evolution.* Princeton University Press; 2003.
23. Henn BM, Cavalli-Sforza LL, Feldman MW: **The great human expansion.** *Proc Natl Acad Sci* 2012, **109**:17758-17764 <http://dx.doi.org/10.1073/pnas.1212380109>.
24. Ramachandran S, Deshpande O, Roseman CC, Rosenberg Na, Feldman MW, Cavalli-Sforza LL: **Support from the relationship of genetic and geographic distance in human populations for a serial founder effect originating in Africa.** *Proc Natl Acad Sci* 2005, **102**:15942-15947 <http://dx.doi.org/10.1073/pnas.0507611102>.
25. Pickrell JK, Pritchard JK: **Inference of population splits and mixtures from genome-wide allele frequency data.** *PLoS Genet* 2012, **8**:e1002967 <http://dx.doi.org/10.1371/journal.pgen.1002967>.
26. Kidd JM, Gravel S, Byrnes J, Moreno-Estrada A, Musharoff S, Bryc K *et al.*: **Population genetic inference from personal genome data: impact of ancestry and admixture on human genomic variation.** *Am J Hum Genet* 2012, **91**:660-671 <http://dx.doi.org/10.1016/j.ajhg.2012.08.025>.
27. Vernot B, Tucci S, Kelso J, Schraiber JG, Wolf AB, Gittelman RM *et al.*: **Excavating Neandertal and Denisovan DNA from the genomes of Melanesian individuals.** *Science* 2016, **9416**:1-9 <http://dx.doi.org/10.1126/science.aad9416>.
This paper provides evidence that humans and Neanderthals appear to have intermixed multiple times after the human migration out of Africa,

whereas in this sample only Oceanian populations retain genes from an ancient admixture event with Denisovans.

28. Sankararaman S, Mallick S, Dannemann M, Prüfer K, Kelso J, Pääbo S *et al.*: **The genomic landscape of Neanderthal ancestry in present-day humans.** *Nature* 2014, **507**:354-357 <http://dx.doi.org/10.1038/nature12961>.
- In this study, the authors systematically detect Neanderthal ancestry across the genomes of 1004 humans and predict that Neanderthal alleles have both costs and benefits in modern humans. There appears to have been selection to eliminate Neanderthal genetic material from the human genome, particularly in genes that could be linked to male fertility; in contrast, Neanderthal alleles affecting skin and hair appear to have conferred a benefit to humans adapting to environments outside of Africa.
29. Lohmueller KE: **The impact of population demography and selection on the genetic architecture of complex traits.** *PLoS Genet* 2014;10 <http://dx.doi.org/10.1371/journal.pgen.1004379>.
30. Schiffels S, Durbin R: **Inferring human population size and separation history from multiple genome sequences.** *Nat Genet* 2014, **46**:919-925 <http://dx.doi.org/10.1038/ng.3015>.
- This paper presents an approach to investigate human evolutionary history at deep timescales using the multiple sequentially Markovian coalescent (MSMC), which analyzes mutation patterns across individuals. Using this technique, the authors suggest, for example, that the genetic separation between West African and European samples predates the out-of-Africa migration.
31. Sousa V, Peischl S, Excoffier L: **Impact of range expansions on current human genomic diversity.** *Curr Opin Genet Dev* 2014, **29**:22-30 <http://dx.doi.org/10.1016/j.gde.2014.07.007>.
32. MacLeod IM, Hayes BJ, Goddard ME: **The effects of demography and long-term selection on the accuracy of genomic prediction with sequence data.** *Genetics* 2014, **198**:1671-1684 <http://dx.doi.org/10.1534/genetics.114.168344>.
33. Coop G, Pickrell JK, Novembre J, Kudaravalli S, Li J, Absher D *et al.*: **The role of geography in human adaptation.** *PLoS Genet* 2009;5 <http://dx.doi.org/10.1371/journal.pgen.1000500>.
34. Henn BM, Botigué LR, Peischl S, Dupanloup I, Lipatov M, Maples BK *et al.*: **Distance from sub-Saharan Africa predicts mutational load in diverse human genomes.** *Proc Natl Acad Sci* 2015;201510805 <http://dx.doi.org/10.1073/pnas.1510805112>.
- This paper brings together a new dataset of genomes from seven world-wide populations and a spatially explicit model of mutation load to examine the distribution of deleterious mutations across human populations. The authors find a signal of purifying selection; however, many mutations that are predicted to be deleterious appear to evolve as though they were neutral during the human migration out of Africa.
35. Kirin M, McQuillan R, Franklin CS, Campbell H, Mckeigue PM, Wilson JF: **Genomic runs of homozygosity record population history and consanguinity.** *PLoS One* 2010, **5**:1-7 <http://dx.doi.org/10.1371/journal.pone.0013996>.
36. Pemberton TJ, Absher D, Feldman MW, Myers RM, Rosenberg NA, Li JZ: **Genomic patterns of homozygosity in worldwide human populations.** *Am J Hum Genet* 2012, **91**:275-292 <http://dx.doi.org/10.1016/j.ajhg.2014.02.009>.
37. Henn BM, Gignoux CR, Jobin M, Granka JM, Macpherson JM, Kidd JM *et al.*: **Hunter-gatherer genomic diversity suggests a southern African origin for modern humans.** *Proc Natl Acad Sci U S A* 2011, **108**:5154-5162 <http://dx.doi.org/10.1073/pnas.1017511108/-/DCSupplemental>. www.pnas.org/cgi/doi/10.1073/pnas.1017511108.
38. Kardos M, Luikart G, Allendorf FW: **Measuring individual inbreeding in the age of genomics: marker-based measures are better than pedigrees.** *Heredity (Edinb)* 2015, **115**:63-72 <http://dx.doi.org/10.1038/hdy.2015.17>.
39. Ben Halim N, Nagara M, Regnault B, Hsouna S, Lasram K, Kefi R *et al.*: **Estimation of recent and ancient inbreeding in a small endogamous Tunisian community through genomic runs of homozygosity.** *Ann Hum Genet* 2015, **79**:402-417 <http://dx.doi.org/10.1111/ahg.12131>.
40. Verweij KJH, Abdellaoui A, Vejjala J, Sebert S, Koiranen M, Keller MC *et al.*: **The association of genotype-based inbreeding coefficient with a range of physical and psychological human traits.** *PLoS One* 2014;9 <http://dx.doi.org/10.1371/journal.pone.0103102>.
41. Yang H-C, Li H-W: **Analysis of homozygosity disequilibrium using whole-genome sequencing data.** *BMC Proc* 2014, **8**:S15 <http://dx.doi.org/10.1186/1753-6561-8-S1-S15>.
42. Haber M, Gauguier D, Youhanna S, Patterson N, Moorjani P, Botigué LR *et al.*: **Genome-wide diversity in the levant reveals recent structuring by culture.** *PLoS Genet* 2013, **9**:e1003316 <http://dx.doi.org/10.1371/journal.pgen.1003316>.
43. Behar DM, Metspalu E, Kivisild T, Rosset S, Tzur S, Hadid Y *et al.*: **Counting the founders: the matrilineal genetic ancestry of the Jewish Diaspora.** *PLoS One* 2008;3 <http://dx.doi.org/10.1371/journal.pone.0002062>.
44. Heyer E, Chaix R, Pavard S, Austerlitz F: **Sex-specific demographic behaviours that shape human genomic variation.** *Mol Ecol* 2012, **21**:597-612 <http://dx.doi.org/10.1111/j.1365-294X.2011.05406.x>.
45. Underhill Pa, Kivisild T: **Use of Y chromosome and mitochondrial DNA population structure in tracing human migrations.** *Annu Rev Genet* 2007, **41**:539-564 <http://dx.doi.org/10.1146/annurev.genet.41.110306.130407>.
46. Behar DM, Villems R, Soodyall H, Blue-Smith J, Pereira L, Metspalu E *et al.*: **The dawn of human matrilineal diversity.** *Am J Hum Genet* 2008, **82**:1130-1140 <http://dx.doi.org/10.1016/j.ajhg.2008.04.002>.
47. Aime C, Heyer E, Austerlitz F: **Inference of sex-specific expansion patterns in human populations from Y-chromosome polymorphism.** *Am J Phys Anthropol* 2015, **157**:217-225 <http://dx.doi.org/10.1002/ajpa.22707>.
48. Tumonggor MK, Karafet TM, Downey S, Lansing JS, Norquest P, Sudoyo H *et al.*: **Isolation, contact and social behavior shaped genetic diversity in West Timor.** *J Hum Genet* 2014, **59**:494-503 <http://dx.doi.org/10.1038/jhg.2014.62>.
49. Heyer E, Brandenburg JT, Leonardi M, Toupanç B, Balaresque P, Hegay T *et al.*: **Patrilineal populations show more male transmission of reproductive success than cognatic populations in Central Asia, which reduces their genetic diversity.** *Am J Phys Anthropol* 2015, **157**:537-543 <http://dx.doi.org/10.1002/ajpa.22739>.
50. Helgason A, Hrafnkelsson B, Gulcher JR, Ward R, Stefánsson K: **A population wide coalescent analysis of Icelandic matrilineal and patrilineal genealogies: evidence for a faster evolutionary rate of mtDNA lineages than Y chromosomes.** *Am J Hum Genet* 2003, **72**:1370-1388 <http://dx.doi.org/10.1086/375453>.
51. Bamshad MJ, Watkins WS, Dixon ME, Jorde LB, Rao BB, Naidu JM *et al.*: **Female gene flow stratifies Hindu castes.** *Nature* 1998, **395**:651-652 <http://dx.doi.org/10.1038/27103>.
52. Poznik GD, Xue Y, Mendez FL, Willems TF, Massaia A, Wilson Sayres MA *et al.*: **Punctuated bursts in human male demography inferred from 1,244 worldwide Y-chromosome sequences.** *Nat Genet* 2016. advance online publication.
- This paper investigates variation in the human Y chromosome using data from the 1000 Genomes project. By generating a time-calibrated phylogeny, the authors predict that large expansions in the male population size have occurred at multiple points in human history, particularly at times corresponding to cultural innovations and migration events.
53. Akey JM, Zhang G, Zhang K, Jin L, Shriver MD: **Interrogating a high-density SNP map for signatures of natural selection.** *Genome Res* 2002, **12**:1805-1814 <http://dx.doi.org/10.1101/gr.631202>.
54. Coop G, Witonsky D, Di Rienzo A, Pritchard JK: **Using environmental correlations to identify loci underlying local adaptation.** *Genetics* 2010, **185**:1411-1423 <http://dx.doi.org/10.1534/genetics.110.114819>.
55. Jablonski NG: **The evolution of human skin and skin color.** *Evol Anthropol* 2004, **33**:585-623 <http://dx.doi.org/10.1146/annurev.anthro.33.070203.143955>.
56. Rana BK, Hewett-Emmett D, Jin L, Chang BHJ, Sambuughin N, Lin M *et al.*: **High polymorphism at the human melanocortin 1 receptor locus.** *Genetics* 1999, **151**:1547-1557.

57. Norton HL, Kittles RA, Parra E, McKeigue P, Mao X, Cheng K *et al.*: **Genetic evidence for the convergent evolution of light skin in Europeans and East Asians.** *Mol Biol Evol* 2007, **24**:710-722 <http://dx.doi.org/10.1093/molbev/msl203>.
58. Sulem P, Gudbjartsson DF, Stacey SN, Helgason A, Rafnar T, Magnusson KP *et al.*: **Genetic determinants of hair, eye and skin pigmentation in Europeans.** *Nat Genet* 2007, **39**:1443-1452 <http://dx.doi.org/10.1038/ng.2007.13>.
59. Norton HL, Edwards M, Krithika S, Johnson M, Werren EA, Parra EJ: **Quantitative assessment of skin, hair, and iris variation in a diverse sample of individuals and associated genetic variation.** *Am J Phys Anthropol* 2015 <http://dx.doi.org/10.1002/ajpa.22861>.
60. Beall CM: **Andean, Tibetan, and Ethiopian patterns of adaptation to high-altitude hypoxia.** *Hum Biol* 2006, **46**:18-24 <http://dx.doi.org/10.1093/icb/icj004>.
61. Yi X, Liang Y, Huerta-Sanchez E, Jin X, Cuo ZX, Pool JE *et al.*: **Sequencing of 50 human exomes reveals adaptation to high altitude.** *Science* 2010, **329**:75-78 <http://dx.doi.org/10.1126/science.1190371>.
62. Simonson TS, Yang Y, Huff CD, Yun H, Qin G, Witherspoon DJ *et al.*: **Genetic evidence for high-altitude adaptation in Tibet.** *Science* 2010, **329**:72-75 <http://dx.doi.org/10.1126/science.1189406>.
63. Schlebusch CM, Gattepaille LM, Engstrom K, Vahter M, Jakobsson M, Broberg K: **Human adaptation to arsenic-rich environments.** *Mol Biol Evol* 2015, **32**:1544-1555 <http://dx.doi.org/10.1093/molbev/msv046>.
- Many studies of local adaptation focus on broad characteristics of the environment such as climate and altitude. This study examines the genetic effects of an aspect of the chemical environment: in areas of the Andes with elevated arsenic levels in the environment, inhabitants have developed a unique pathway to metabolize arsenic.
64. Fehren-Schmitz L, Haak W, Mächtle B, Masch F, Llamas B, Cagigao ET *et al.*: **Climate change underlies global demographic, genetic, and cultural transitions in pre-Columbian southern Peru.** *Proc Natl Acad Sci* 2014, **111**:9443-9448 <http://dx.doi.org/10.1073/pnas.1403466111>.
65. Blair LM, Granka JM, Feldman MW: **On the stability of the Bayenv method in assessing human SNP-environment associations.** *Hum Genomics* 2014, **8**:1 <http://dx.doi.org/10.1186/1479-7364-8-1>.
66. Hancock AM, Witonsky DB, Ehler E, Alkorta-Aranburu G, Beall C, Gebremedhin A *et al.*: **Colloquium paper: human adaptations to diet, subsistence, and ecoregion are due to subtle shifts in allele frequency.** *Proc Natl Acad Sci* 2010, **107**(Suppl.):8924-8930 <http://dx.doi.org/10.1073/pnas.0914625107>.
67. Hancock AM, Witonsky DB, Alkorta-Aranburu G, Beall CM, Gebremedhin A, Sukernik R *et al.*: **Adaptations to climate-mediated selective pressures in humans.** *PLoS Genet* 2011:7 <http://dx.doi.org/10.1371/journal.pgen.1001375>.
68. Berg JJ, Coop G: **A population genetic signal of polygenic adaptation.** *PLoS Genet* 2014, **10**:e1004412 <http://dx.doi.org/10.1371/journal.pgen.1004412>.
- This paper presents a method for identifying polygenic traits that have adapted to local environments; the study of local adaptation had been previously limited to single locus variants. The authors present numerous polygenic signals of adaptation, including an association between latitude and skin pigmentation.
69. Field Y, Boyle EA, Telis N, Gao Z, Gaulton KJ: **Detection of human adaptation during the past 2,000 years.** *bioRxiv* 2016:1-18 <http://dx.doi.org/10.1101/052084>.
70. Fraser HB: **Gene expression drives local adaptation in humans.** *Genome Res* 2013, **23**:1089-1096 <http://dx.doi.org/10.1101/gr.152710.112>.
71. Fumagalli M, Sironi M, Pozzoli U, Ferrer-Admetlla A, Pattini L, Nielsen R: **Signatures of environmental genetic adaptation pinpoint pathogens as the main selective pressure through human evolution.** *PLoS Genet* 2011:7 <http://dx.doi.org/10.1371/journal.pgen.1002355>.
72. Blair LM, Feldman MW: **The role of climate and out-of-Africa migration in the frequencies of risk alleles for 21 human diseases.** *BMC Genet* 2015, **16**:81 <http://dx.doi.org/10.1186/s12863-015-0239-3>.
73. Corona E, Chen R, Sikora M, Morgan AA, Patel CJ, Ramesh A *et al.*: **Analysis of the genetic basis of disease in the context of worldwide human relationships and migration.** *PLoS Genet* 2013:9 <http://dx.doi.org/10.1371/journal.pgen.1003447>.
74. Chen R, Corona E, Sikora M, Dudley JT, Morgan AA, Moreno-Estrada A *et al.*: **Type 2 diabetes risk alleles demonstrate extreme directional differentiation among human populations, compared to other diseases.** *PLoS Genet* 2012:8 <http://dx.doi.org/10.1371/journal.pgen.1002621>.
75. Mateos P: *Ethnicity and Populations: Tracing Identity in Space.* Springer; 2014.
76. Creanza N, Ruhlen M, Pemberton TJ, Rosenberg NA, Feldman MW, Ramachandran S: **A comparison of worldwide phonemic and genetic variation in human populations.** *Proc Natl Acad Sci U S A* 2014, **112**:1265-1272 <http://dx.doi.org/10.1073/pnas.1424033112>.
- This paper presents an analysis of the geographic patterns in large sets of genetic and phonemic data in worldwide human populations. The authors predict that migration within geographic regions shapes phoneme evolution, although human expansion out of Africa has not left a strong signature on phonemes.
77. Ingram CJ, Liebert A, Swallow DM: **Population genetics of lactase persistence and lactose intolerance.** *eLS* 2012 <http://dx.doi.org/10.1002/9780470015902.a0020855.pub2>.
78. Rogers DS, Ehrlich PR: **Natural selection and cultural rates of change.** *Proc Natl Acad Sci* 2008, **105**:3416-3420 <http://dx.doi.org/10.1073/pnas.0711802105>.
79. Tehrani JJ, Collard M, Shennan SJ: **The cophylogeny of populations and cultures: reconstructing the evolution of Iranian tribal craft traditions using trees and jungles.** *Philos Trans R Soc B* 2010, **365**:3865-3874 <http://dx.doi.org/10.1098/rstb.2010.0020>.
80. Karafet TM, Bulayeva KB, Nichols J, Bulayev OA, Gurgenova F, Omarova J *et al.*: **Coevolution of genes and languages and high levels of population structure among the highland populations of Daghestan.** *J Hum Genet* 2015:1-11 <http://dx.doi.org/10.1038/jhg.2015.132>.
81. Hunley K, Dunn M, Lindström E, Reesink G, Terrill A, Healy ME *et al.*: **Genetic and linguistic coevolution in Northern Island Melanesia.** *PLoS Genet* 2008, **4**:e1000239 <http://dx.doi.org/10.1371/journal.pgen.1000239>.
82. Hunley K, Long JC: **Gene flow across linguistic boundaries in Native North American populations.** *Proc Natl Acad Sci* 2005, **102**:1312-1317 <http://dx.doi.org/10.1073/pnas.0409301102>.
83. Kutanan W, Ghirotto S, Bertorelle G, Srithawong S, Srithongdaeng K, Pontham N *et al.*: **Geography has more influence than language on maternal genetic structure of various northeastern Thai ethnicities.** *J Hum Genet* 2014, **59**:1-9 <http://dx.doi.org/10.1038/jhg.2014.64>.
84. Longobardi G, Ghirotto S, Guardiano C, Tassi F, Benazzo A, Ceolin A *et al.*: **Across language families: genome diversity mirrors linguistic variation within Europe.** *Am J Phys Anthropol* 2015, **157**:630-640 <http://dx.doi.org/10.1002/ajpa.22758>.
85. Barbujani G, Whitehead G, Bertorelle G, Nasidze I: **Testing hypotheses on processes of genetic and linguistic change in the caucasus.** *Hum Biol* 1994, **66**:843-864.
86. De Filippo C, Barbieri C, Whitten M, Mpoloka SW, Gunnarsdóttir ED, Bostoen K *et al.*: **Y-chromosomal variation in sub-Saharan Africa: insights into the history of Niger-Congo groups.** *Mol Biol Evol* 2011, **28**:1255-1269 <http://dx.doi.org/10.1093/molbev/msq312>.
87. Srithawong S, Srikumool M, Pittayaporn P, Ghirotto S, Chantawannakul P, Sun J *et al.*: **Genetic and linguistic correlation of the Kra-Dai-speaking groups in Thailand.** *J Hum Genet* 2015, **60**:1-10 <http://dx.doi.org/10.1038/jhg.2015.32>.

88. Wood ET, Stover Da, Ehret C, Destro-Bisol G, Spedini G, McLeod H *et al.*: **Contrasting patterns of Y chromosome and mtDNA variation in Africa: evidence for sex-biased demographic processes.** *Eur J Hum Genet* 2005, **13**:867-876 <http://dx.doi.org/10.1038/sj.ejhg.5201408>.
89. Kayser M, Choi Y, Van Oven M, Mona S, Brauer S, Trent RJ *et al.*: **The impact of the Austronesian expansion: evidence from mtDNA and Y chromosome diversity in the Admiralty Islands of melanesia.** *Mol Biol Evol* 2008, **25**:1362-1374 <http://dx.doi.org/10.1093/molbev/msn078>.
90. Laeng B, Mathisen R, Johnsen JA: **Why do blue-eyed men prefer women with the same eye color?** *Behav Ecol Sociobiol* 2007, **61**:371-384 <http://dx.doi.org/10.1007/s00265-006-0266-1>.
91. Cavalli-Sforza LL, Bodmer WF: *The Genetics of Human Populations*. Courier Corporation; 1999.
92. Tenesa A, Rawlik K, Navarro P, Canela-Xandri O: **Genetic determination of height-mediated mate choice.** *Genome Biol* 2016, **16**:1-8 <http://dx.doi.org/10.1186/s13059-015-0833-8>.
93. Keller MC, Garver-Apgar CE, Wright MJ, Martin NG, Corley RP, Stallings MC *et al.*: **The genetic correlation between height and IQ: shared genes or assortative mating?** *PLoS Genet* 2013:9 <http://dx.doi.org/10.1371/journal.pgen.1003451>.
94. Tognetti A, Berticat C, Raymond M, Faurie C: **Assortative mating based on cooperativeness and generosity.** *J Evol Biol* 2014, **27**:975-981 <http://dx.doi.org/10.1111/jeb.12346>.
95. Bacon PM, Conte A, Moffatt PG: **Assortative mating on risk attitude.** *Theory Decis* 2014, **77**:389-401 <http://dx.doi.org/10.1007/s11238-014-9448-x>.
96. Treur JL, Vink JM, Boomsma DI, Middeldorp CM: **Spousal resemblance for smoking: underlying mechanisms and effects of cohort and age.** *Drug Alcohol Depend* 2015, **153**:221-228 <http://dx.doi.org/10.1016/j.drugalcdep.2015.05.018>.
97. Domingue BW, Fletcher J, Conley D, Boardman JD: **Genetic and educational assortative mating among US adults.** *Proc Natl Acad Sci* 2014, **111**:7996-8000 <http://dx.doi.org/10.1073/pnas.1321426111>.
- This paper examines assortative mating in humans by calculating genetic similarity between spouses and comparing it to educational similarity. On average, spouses are more genetically similar than two individuals selected at random, but this effect of assortative mating is much stronger for educational similarity.
98. Thiessen D, Gregg B: **Human assortative mating and genetic equilibrium: an evolutionary perspective.** *Ethol Sociobiol* 1980, **1**:111-140 [http://dx.doi.org/10.1016/0162-3095\(80\)90003-5](http://dx.doi.org/10.1016/0162-3095(80)90003-5).
99. Abdellaoui A, Hottenga J-J, Xiao X, Scheet P, Ehli EA, Davies GE *et al.*: **Association between autozygosity and major depression: stratification due to religious assortment.** *Behav Genet* 2013, **43**:455-467 <http://dx.doi.org/10.1007/s10519-013-9610-1>.
100. Abdellaoui A, Hottenga JJ, Willemsen G, Bartels M, Van Beijsterveldt T, Ehli EA *et al.*: **Educational attainment influences levels of homozygosity through migration and assortative mating.** *PLoS One* 2015, **10**:1-14 <http://dx.doi.org/10.1371/journal.pone.0118935>.
101. Creanza N, Fogarty L, Feldman MW: **Models of cultural niche construction with selection and assortative mating.** *PLoS One* 2012, **7**:e42744 <http://dx.doi.org/10.1371/journal.pone.0042744>.
102. Creanza N, Feldman MW: **Complexity in models of cultural niche construction with selection and homophily.** *Proc Natl Acad Sci* 2014, **111**(Suppl.):10830-10837 <http://dx.doi.org/10.1073/pnas.1400824111>.
103. Eshel I, Cavalli-Sforza LL: **Assortment of encounters and evolution of cooperativeness.** *Proc Natl Acad Sci* 1982, **79**:1331-1335 <http://dx.doi.org/10.1073/pnas.79.4.1331>.
104. Ashraf Q, Galor O: **The "Out of Africa" hypothesis, human genetic diversity, and comparative economic development.** *Am Econ Rev* 2013, **103**:1-46 <http://dx.doi.org/10.1257/aer.103.1.1>.
105. Wade N: *A Troublesome Inheritance: Genes, Race and Human History*. Penguin; 2014.
106. Guedes J, d'Alpoim, Bestor TC, Carrasco D, Flad R, Fosse E, Herzfeld M *et al.*: **Is poverty in our genes?** *Curr Anthropol* 2013, **54**:71-79 <http://dx.doi.org/10.1371/journal.pgen.1004817>.
107. Rosenberg NA, Kang JTL: **Genetic diversity and societally important disparities.** *Genetics* 2015, **201**:1-12 <http://dx.doi.org/10.1534/genetics.115.176750>.
108. Feldman M: **Echoes of the past: hereditarianism and a troublesome inheritance.** *PLoS Genet* 2014, **10**:10-12 <http://dx.doi.org/10.1371/journal.pgen.1004817>.