

The future of the Eurasian past: highlighting plotoles and pillars of human population movements in the Late Pleistocene

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Summary - *The major genetic divergences among non-Africans took place within a relatively short period of time, between 50 and 40 thousand years ago. These events shaped human diversity worldwide and set the basis for our current understanding of demographic history, patterns of adaptation and genetic burden across human populations. While the global picture appears already set, with the main human expansion Out of Africa inferred to have occurred between 60 and 70 thousand years ago and the main separation between contemporary East and West Eurasian to have taken place at around 40 thousand years ago, several finer details remain unresolved, including the whereabouts of such expansions and the dynamics of their interactions with archaic hominins and the interplay between environmental, cultural and demographic effectors. Here we review the major events that characterize human movements across and beyond Eurasia until the last glacial maximum and, at the end of each paragraph, spell out in italics the major questions that remain unsolved and that may provide major breakthroughs in the field in the upcoming years.*

Keywords - *Palaeolithic eurasia, Ancient DNA, Open questions.*

To fully understand the events that led to the peopling of Eurasia, one should step back in Africa, where the journey began. An early expansion Out of Africa (OoA) likely occurred before 100 kya as suggested by numerous remains excavated in Levant and Arabia between 130 and 90 kya (Groucutt et al. 2018; Grün et al. 2005) such an expansion could have reached as far as China and South East Asia, where numerous sites dated between 100 and 50 kya have been found (Cai et al. 2017; Liu et al. 2015; Shackelford et al. 2018; Westaway et al. 2017), and Australia, where archaeological remains that have been dated around 65 kya (Clarkson et al. 2017) have been recovered. The reliability of many of these dates, however, have been contested in recent years both for Asia (Michel et al. 2016; Sun et al. 2021) and Oceania (McCull et al. 2018) but counter arguments have been presented (Higham and Douka 2021; Martínón-Torres et al. 2021) and the debate is far from being closed (Hublin 2021).

On the other hand, genetic evidence shows that all present day non Africans share a single, recent origin (Bergström et al. 2021; Posth et al. 2016) and date the bottleneck (Schiffels and Durbin, 2014) associated with the Out of Africa between 70 kya (Malaspinas et al. 2016; Mallick et al. 2016; Soares et al. 2012) and 65 kya (Pagani et al. 2015). This suggests that, if Homo sapiens had reached East Asia after an earlier expansion, they became extinct before the ancestors of modern East Asians reached the area; an exception to that might be represented by populations from Papua New Guinea, for which a ~2% contribution from a population that left Africa before 100 kya was suggested (Pagani et al. 2016), although the matter is currently debated (Bergström et al. 2020).

Even though the human expansions Out of Africa that took place significantly earlier than 70kya may not have contributed any genome to contemporary populations, the questions remain open with respect to their contribution

to the uniparental and autosomal genome of archaic humans (Neanderthal and Denisovans) who were certainly inhabiting Eurasia at that time. In accordance with the existence of multiple climatic windows of opportunity to leave Africa (Beyer et al. 2021; Groucutt et al. 2021); recent papers have highlighted how the Africa/Eurasia boundary was not impermeable to gene flow, as Neanderthals appear to have inherited mtDNA and chrY haplogroups from a lineage leading towards *Homo sapiens*, between 400 and 200 kya (Petr et al. 2020; Posth et al. 2017). A similar, although much more subtle signature was reported for the autosomes, both within the aforementioned timeframe (Peyrégne et al. 2022) and more recently around 100 kya (Kuhlwilm et al. 2016).

- Demography driven accumulation of deleterious variants in the uniparental (Petr et al. 2020; Posth et al. 2017)) and perhaps autosomal Neanderthal genome have been proposed as the main mechanism driving these extensive genetic turnover, although recent selective sweeps along the sapiens lineage cannot be excluded as a potential driver for the surprising success of these introgressed haplotypes. Furthermore, whether the populations whose remains were retrieved on both shores of the Mediterranean sea (e.g. Jebel Irhoud (Hublin et al. 2017), Apidima (Harvati et al. 2019), Misliya (Hershkovitz et al. 2018) and Skhul (Grün et al. 2005)) might have played a role in the inferred gene flow is still an open question (Fig. 1A).

Shortly after leaving Africa, the ancestor of all non Africans hybridized with Neanderthals (Green et al. 2010), with the date of introgression estimated between 65 and 47 kya (Sankararaman et al. 2012), 54 and 41 kya (Moorjani et al. 2016) or 60-50 kya (Fu et al. 2014). The latter in particular shows that the event must have occurred before ~45 kya, since the Siberian Ust'Ishim individual analysed there already displays Neanderthal ancestry. The analysis of introgressed Neanderthal haplotypes in various non African populations revealed that the gene flow

took place before they further divided into sub-populations, and showed that, on average, 2 to 4 Neanderthal founding haplotypes (i.e. 2-4 events of successful interspecies mating) are sufficient to explain the diversity of Neanderthal haplotypes in non Africans, but in certain genomic loci more than 20 are needed (Bergström et al. 2020). This should, however, be considered as a lower bound for the actual number of mating events between Neanderthals and sapiens, considering the low genetic diversity of Neanderthals (Prüfer et al. 2014), the fact that fitness and fertility of hybrids were likely reduced (Harris and Nielsen 2016) and the existence of human lineages that experienced additional Neanderthal admixture but did not contribute to the gene pool of modern populations (Fu et al. 2015; Hajdinjak et al. 2021).

- Moreover, it is important to note that, while admixture with Neanderthals has generally been considered as a single pulse event, it has been recently shown that the data and methods currently available do not have the power to distinguish between this model and a slower but continuous gene flow that took place over many generations (Iasi et al. 2021), a scenario that must be kept into consideration and needs to be addressed by future studies given the attested presence of Neanderthals in the Middle East until at least 41 kya (Heydari-Guran et al. 2021) (Fig. 1B).

As a result of the interbreeding, non-African *Homo sapiens* all carry genomic segments introgressed from Neanderthals. These regions are not uniformly distributed along the genome and have since been a major target for natural selection; primarily purifying selection which reduced the frequency of Neanderthal alleles up to the point that in certain regions named archaic deserts no contribution from Neanderthals can be detected (Sankararaman et al. 2014). In some cases, however, the Neanderthal variants are thought to have played a role in accelerating the adaptation to the new environmental conditions through a process known as adaptive introgression (Jagoda et al. 2017; Racimo et al. 2015) and increased in frequency as a result.

- While more and more regions of Neanderthal origin have been associated with specific phenotypes (Dannemann and Kelso 2017; McArthur et al. 2021), our understanding of the molecular mechanism and exact genes involved, as well as the selective pressure acting on them is still lagging behind. An example of this is represented by the Neanderthal derived haplotype detected along chromosome 3 and at high frequency in South Asians, which is associated with a more severe response to Sars Cov-2 infection (Zeberg and Pääbo 2020). Such a genotype-phenotype link has only been unlocked by the recent Covid-19 pandemic, hence highlighting the importance of further research to fully appreciate the biological contribution of Neanderthals to our genome (Fig. 1B).

Neanderthals are not the only archaic hominin that interbred with *Homo sapiens* after the Out of Africa; Denisovans also left a genetic trace in the genomes of human populations from Asia and Oceania (Reich et al. 2010). Knowledge about Denisovans is still scarce compared to what we know about Neanderthals; sites with fossils certainly attributable to Denisovans account so far just to a handful of sites in the Altai mountains (Brown et al. 2016; Krause et al. 2010; Reich et al. 2010; Sawyer et al. 2015; Slon et al. 2017), Tibetan Plateau (Chen et al. 2019) and Laos (Demeter et al. 2022). To make this population even more elusive, Denisovan ancient DNA (aDNA) has been successfully recovered just from some individuals from the Denisova Cave (Altai), including the genome of a first generation hybrid of a Neanderthal mother and a Denisovan father (Slon et al. 2018). This sparse record leaves open the question of the geographical range occupied by Denisovans, especially when considering that modern population residing in the areas where Denisovans were excavated and, more broadly, in East Asia, South Asia and the Americas, do show a contribution from Denisovans that is much smaller than the one displayed by populations from Insular South East Asia, Melanesia and Oceania (Sankararaman et al. 2016). Additionally, and in contrast with the scenario of the admixture with Neanderthals, several studies highlighted

that multiple and highly structured populations of Denisovans existed and contributed differentially to different East Eurasian and Oceanian populations (Browning et al. 2018; Jacobs et al. 2019), suggesting the presence of several geographically isolated Denisovan groups that admixed with the incoming sapiens as they came into contact. Since the contribution from some of these Denisovan groups has been detected exclusively in human populations from the Philippines (Larena et al. 2021) and Papua New Guinea (Choin et al. 2021; Jacobs et al. 2019) it seems likely that Denisovans occupied these lands too.

- Further excavation in these regions, as well as the thorough reassessment of the East Asian fossil record with uncertain or debated taxonomy (Athreya and Wu 2017; Ji et al. 2021; Li et al. 2017; Stringer 2012; Wu et al. 2019; Xing et al. 2015), potentially supported by aDNA analysis or paleoproteomic, will certainly prove invaluable in refining our understanding of the range, demography and biology of archaic Asian hominins (Fig. 1C).

Going back to the main backbone of the human dispersal OoA, it is noteworthy to stress that, as the genetic divergence between East and West Eurasian macropopulations started only around 45-40 kya (Choin et al. 2021; Malaspinas et al. 2016; Pagani et al. 2015; Schiffels and Durbin 2014), there seem to have been a delay between this major event and the OoA bottleneck before 60kya. One might speculate that this time was necessary for the first Eurasian settlers to adapt to the new Eurasian environment and to recover from the effect of the OoA bottleneck, or that geoclimatic or ecological barriers prevented them from rapidly colonizing the remainder of the continent.

- Anyhow, this delay implies that for several millennia the ancestors of all modern-day Eurasians were part of a single population living somewhere outside of Sub Saharan Africa. Potential regions that might have hosted this population during this timeframe include most of the Middle East and North Africa, but a more

precise localization is currently lacking and is likely to be the topic of future studies (Fig. 1D).

The population in which the ancestors of East Asians and Europeans lived after the Out of Africa but before they diverged has been named Hub in a recent paper (Vallini et al. 2022), which also showed that the broader colonization of Eurasia occurred through multiple expansions from the Hub that were chronologically, genetically and culturally distinct. According to this scenario, a massive expansion, genetically represented by individuals from Ust’Ishim (Fu et al. 2014), Bacho Kiro (Hajdinjak et al. 2021), Tianyuan (Yang et al. 2017) and Oase1 (Fu et al. 2015), and associated with Initial Upper Paleolithic (IUP) techno complexes, took place around 45 kya and colonized most of Eurasia and potentially Oceania. It then became largely extinct in Europe after ~40 kya and thrived elsewhere, being virtually in continuity with present day local populations. Europe was instead almost completely recolonized by a new wave of expansion out of the Hub sometimes before 38 kya by individuals associated with technocomplexes broadly labeled as Upper Paleolithic (UP) and genetically represented by Kostenki14 (Seguin-Orlando et al. 2014) and Sunghir (Sikora et al. 2017), that admixed with members of the previous expansion while moving through Siberia, as shown by the admixed ancestry profile of individuals like Yana (Sikora et al. 2019) and Mal’ta (Raghavan et al. 2014), but did not penetrate into East Asia. Before these events and before 45 kya, an earlier expansion that did not leave any trace in the gene pool of subsequent populations and whose range is unknown is currently represented by a single individual from Zlatý kůň, Czech Republic (Prüfer et al. 2021). On one hand, this emerging scenario helps placing several genetic and archaeological evidence within a unified, broad picture. On the other, it highlights long standing questions that still need to be clarified.

- The availability of the Zlatý kůň genome leads the way towards further investigations aimed at characterizing other short lived expansion across

paleolithic Europe that may put within a broader demographic picture remains that largely predate the ones we just described (Slimak et al. 2022) and techno complexes that present a marked discontinuity with the preceding or coeval lithics such as the Uluzzian in Southern Europe (Benazzi et al. 2011; Marciari et al. 2020). Future studies aimed at a multidisciplinary understanding of these early expansions may also help clarify the causal connections between paleoclimatic changes, demography, and cultural and genetic adaptation to new environments (Fig. 1E).

- While the presence of an East Asian genetic component, associated with IUP, largely faded in Europe after 40 kya; two individuals from Belgium and Bulgaria dated a few millennia afterwards were still carrying a minor genetic component linked to it, and subsequently their legacy has been partly attested in post LGM individuals of the El Mirón cluster in Iberia (Fu et al. 2016). To what extent this ancestry was an ephemeral phenomena and how much of its legacy was passed on to the subsequent inhabitants of the continent both before and after the LGM is not clear and only a denser spatiotemporal sampling of Europe will tell (Fig. 1F).

- To what extent the various streams that contributed to the colonization of Asia can be considered as actual independent peopling event? Can the diversity of the Denisova genomic segments that were embedded during these expansions provide a clue to elucidate the routes taken by these human populations as they expanded east- and south-ward? (Fig. 1G)

- The position of populations inhabiting Near Oceania has long been debated, with genomic evidence leveraging frequentist approaches advocating for a close relationship between them and contemporary East Asians (Mallick et al. 2016; Wall 2017), while analyses based on site frequency spectra indicating a more basal position of Oceanians with respect to both West and East Eurasians (Choin et al. 2021; Malaspina et al. 2016), yet requiring subsequent gene flow from

East Asians towards Oceanians. The reported connection between Papuan genomes and the broad IUP expansion across Eurasia (Vallini et al. 2022) may seem to strengthen the former view, however a likely scenario awaiting to be clarified involves paleolithic interactions between the early, basal settlers of Oceania and subsequent streams from the East of Eurasia (Fig. 1H).

- As our understanding of the early relationship between East and West Eurasian genetic components is getting clearer and clearer, a lot is yet to be done to clarify the genetic makeup and the whereabouts of the so-called Basal Eurasian populations (Lazaridis et al. 2016). Such a term has been coined to identify groups that likely diverged soon after the Out of Africa movement from the mainstream of Eurasian populations and who idled somewhere before being incorporated into post glacial West Eurasian populations. Putative hideouts for Basal Eurasians have been hypothesized in North Africa or Arabia (Pagani and Crevecoeur 2019) or in the Persian Gulf (Ferreira et al. 2021), nevertheless the refinement of the Hub whereabouts and the recent improvement in aDNA recovery techniques from warm climates (Slon et al. 2022) may soon improve our understanding of this elusive population (Fig. 1I).

Fast forwarding on the fate of the population expansions explored so far, it is noticeable to see how West and East Eurasia apparently seem to have followed a similar trajectory with the approaching of the Last Glacial Maximum (LGM), circa 25-19 kya. Paleogenomic evidence available to date clearly show that LGM triggered a turnover in West Eurasia (Fu et al. 2016; Marchi et al. 2022), with UP groups being assimilated or completely replaced by other populations (dubbed “Villabruna” from one of the earliest sites associated with this genetic contribution and broadly associated with Late Epigravettian technocomplexes (Bortolini et al. 2021)). A similar scenario can be observed in East Eurasia, with pre-LGM groups from North East Asia being only distantly related to

the individuals that occupied the same region starting from at least 19 kya (Kılınç et al. 2021; Mao et al. 2021). The LGM likely had an impact in positively selecting adaptive variants like the derived form of the EDAR gene (Fujimoto et al. 2008; Tan et al. 2013), that has high frequency in modern and post LGM ancient East Asian but has not yet been documented before 19 kya; even though the limited number of genomes older than that might hinder our ability to correctly time the selective sweep. Importantly, the post LGM turnover in both areas was fundamental if examined at a local scale, but it simply substituted a West Eurasian group with another and an East Eurasian group with another if looked at a pan-Eurasian scale.

- The unveiled extent of post LGM replacement across Eurasia revives the long-standing question about the role of glacial refugia as a reservoir for the local diversity or as springs for subsequent replacements as seen in both West and East Eurasia (Fig. 1J).

Within this broader picture, the Siberian landscape appears instead not to have been extremely affected by the last LGM, with individuals genetically affine to Mal'ta (Raghavan et al. 2014) (bearer of the so called Ancestral North Eurasian, or ANE, legacy) found all the way to the Bronze Age (Zhang et al. 2021) and as also partly recapitulated by metagenomic analyses (Moodley et al. 2021). The ANE legacy also took part, together with additional East Asian influxes (Raghavan et al. 2015), to the colonization of the Americas (Raghavan et al. 2014), aided in crossing the Bering strait by the LGM favorable conditions. The prolonged permanence and far-reaching expansion of the ANE legacy across both shores of the Bering strait instead teaches us a lesson about the unpredictability of the success of a given genomic component over another. Here, a hunter gatherer population hitchhiked from Central Siberia all the way to the continent edge and, after further mixing with East Asians, colonized the whole of the Americas. The debate on how many more

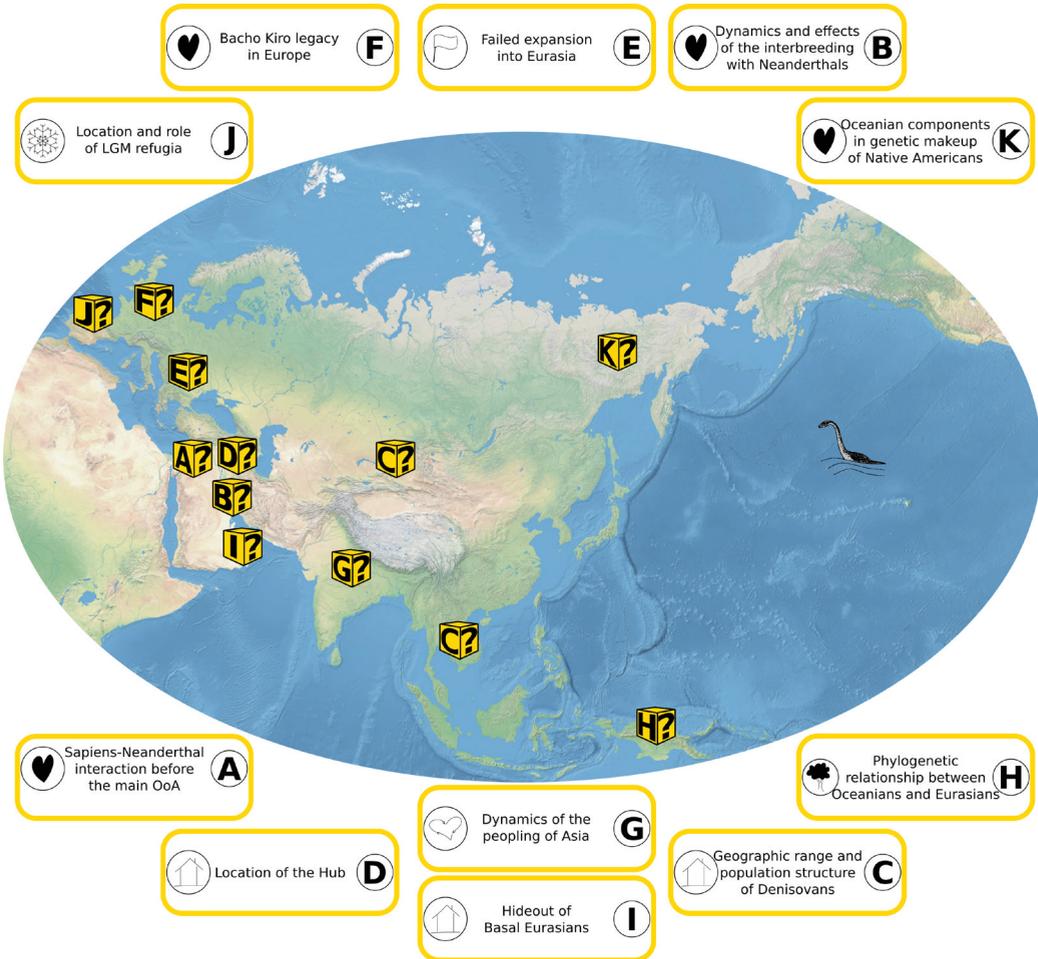


Fig. 1 - A summary of the open questions outlined in the current review, schematized by an icon and labelled with progressive letters for ease of referencing in the main text.

population waves entered the Americas and mixed, especially in the north, with pre-existing groups is not over yet (Moreno-Mayar et al. 2018; Scheib et al. 2018), but it is unlikely to profoundly reshape what we currently understood about the settling of the last continent that was colonized by our species during the paleolithic. More intriguing scenarios may instead be unveiled when the genetic affinity for Papuan components displayed by a few South American populations (Skoglund et al. 2015) will be further explored.

- Were the Amazons and Near Oceania linked by the aftermaths of the post Neolithic Austronesian expansion (Skoglund et al. 2016)? Or should we contemplate paleolithic contacts between Oceanian and East Asians, soon before the settlement of the Americas? (Fig. 1K)

One thing is for certain: the availability of additional ancient genomes from tropical areas around the globe will increase the surface of what we can claim we understood and extend the perimeter of what we will realize we still need to dig out.

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