OLLI SG 497
Ancient DNA

Session 3 - October 12, 2022

Recap

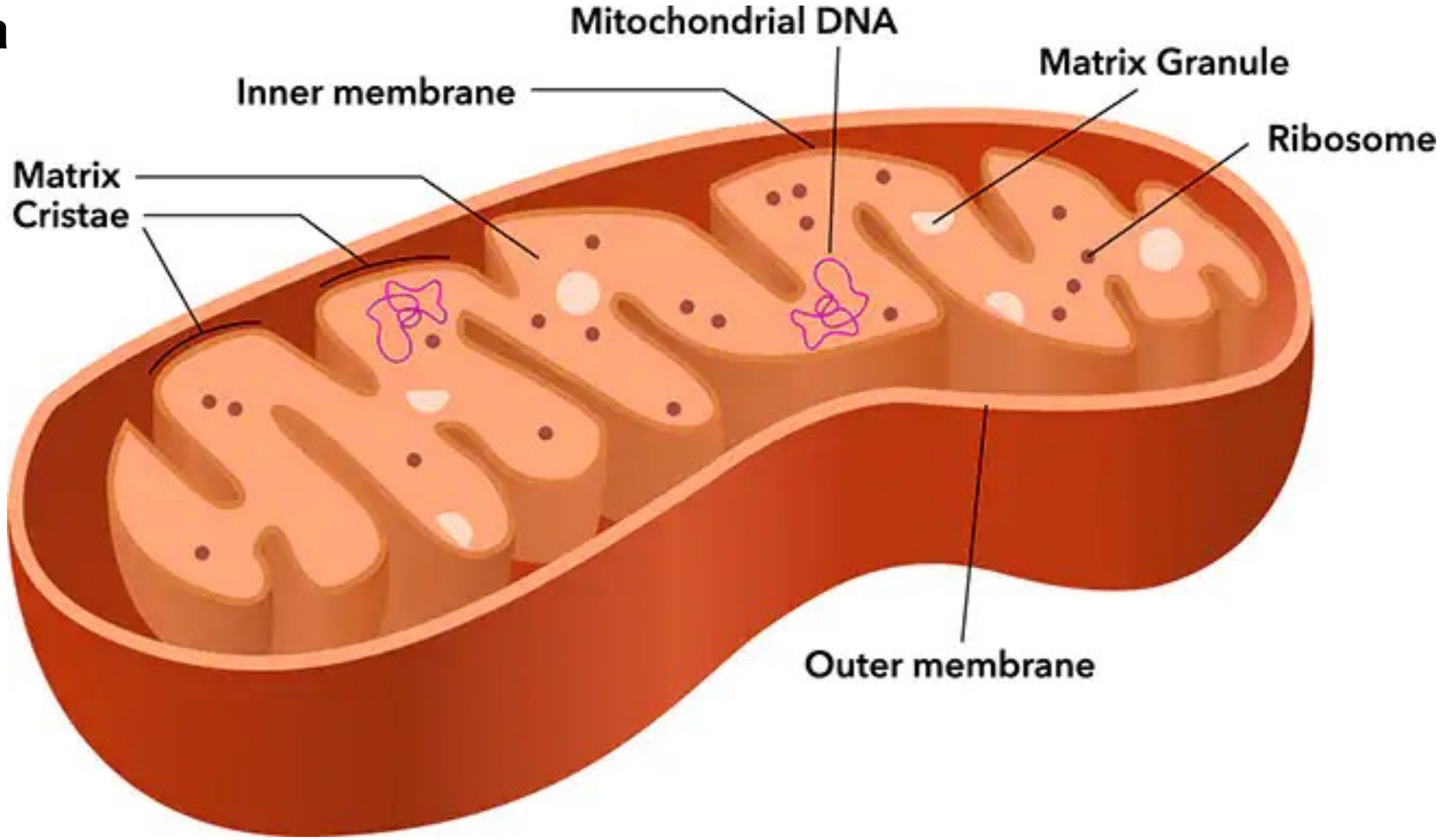
- Recombination and meiosis.
- Overview of statistical genetics, Principal Component Analysis, and Reich's methodology.
- Overview of the laboratory methodology for extracting, purifying and sequencing ancient DNA.
- Reich's view on how we can use the genome to explain who we are - our deep history.

Today’s Meeting

- Mitochondrial Eve and Y-Chromosome Adam.
- One hundred thousand Adams and Eves.
- Natural selection on advantageous mutations.
- Neanderthal interbreeding with modern humans.
- Why so little Neanderthal DNA in contemporary modern human DNA?

Mitochondrial Eve

Mitochondria



mtDNA: 16 kilobases,
37 genes

Mitochondrial Eve

Haplogroups

- A haplotype is a group of alleles inherited from a single parent.
- A haplogroup is a group of similar haplotypes that share a common ancestor with a SNP mutation.
- Haplogroups are identified by an initial letter, e.g., L, followed by numbers/letters to identify subgroups or refinements, e.g., L-1a.
- In human genetics, the haplogroups most commonly studied are the Y-chromosome (Y-DNA) haplogroups, and the mitochondrial DNA (mtDNA) haplogroups.

Mitochondrial Eve

Haplofroups

- Each of these haplogroups can be used to define genetic populations.
- Y-DNA and mtDNA change only by chance mutation at each generation.
  - mtDNA is not subject to recombination during meiosis.
  - For Y-DNA, 95% of the Y chromosome never experiences recombination.
- mtDNA mutation rate is estimated to be one mutation per 8000 years.
- Wikipedia articles on Mitochondrial Eve, and on Y-Chromosome Adam.
- Wikipedia article on haplogroups.

Mitochondrial Eve

Haplogroups

From Wikipedia article on Haplogroups:

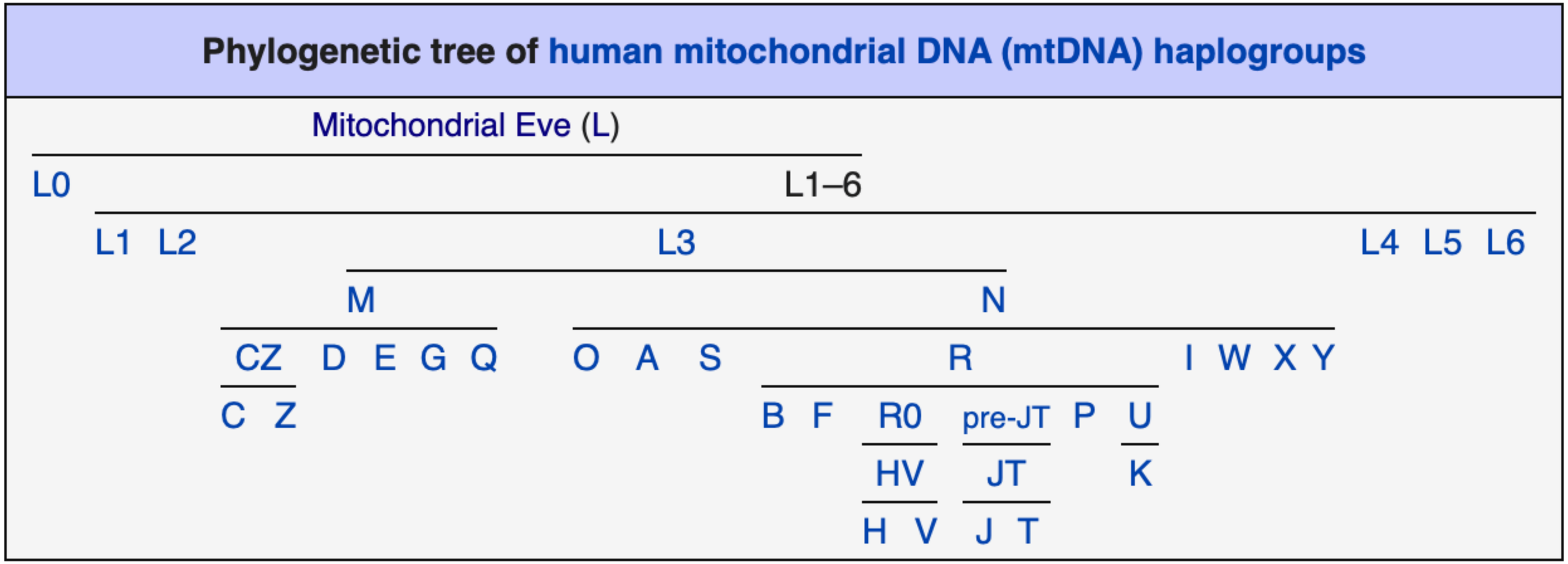
The special feature that both Y chromosomes and mtDNA display is that mutations can accrue along a certain segment of both molecules and these mutations remain fixed in place on the DNA. Furthermore, the historical sequence of these mutations can also be inferred. For example, if a set of ten Y chromosomes (derived from ten different men) contains a mutation, A, but only five of these chromosomes contain a second mutation, B, then it must be the case that mutation B occurred after mutation A.

Furthermore, all ten men who carry the chromosome with mutation A are the direct male line descendants of the same man who was the first person to carry this mutation. The first man to carry mutation B was also a direct male line descendant of this man, but is also the direct male line ancestor of all men carrying mutation B. Series of mutations such as this form molecular lineages. Furthermore, each mutation defines a set of specific Y chromosomes called a haplogroup.

All men carrying mutation A form a single haplogroup, and all men carrying mutation B are part of this haplogroup, but mutation B also defines a more recent haplogroup (which is a subgroup) of its own to which men carrying only mutation A do not belong. Both mtDNA and Y chromosomes are grouped into lineages and haplogroups; these are often presented as tree like diagrams.

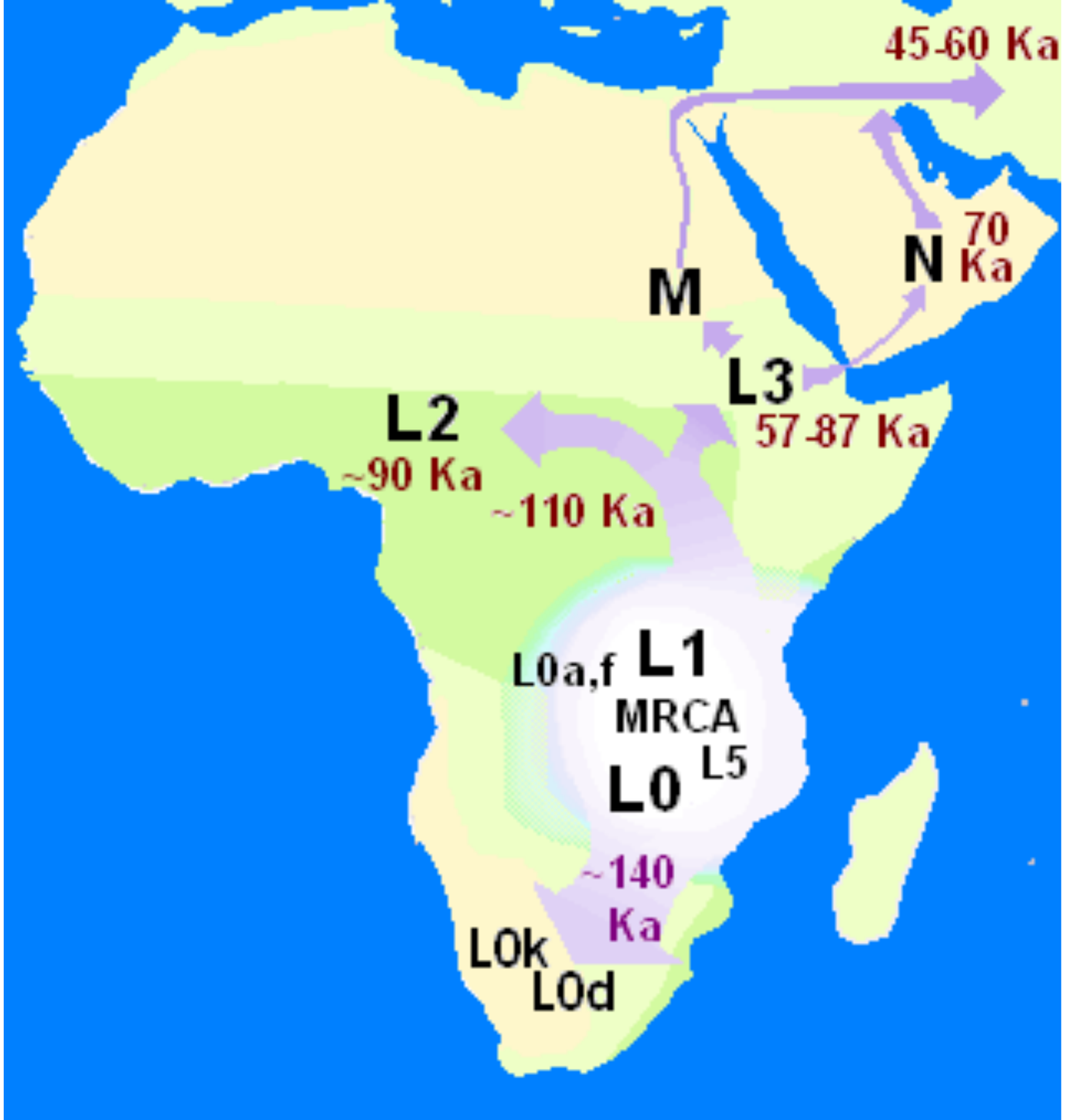
Mitochondrial Eve

Haplogroups

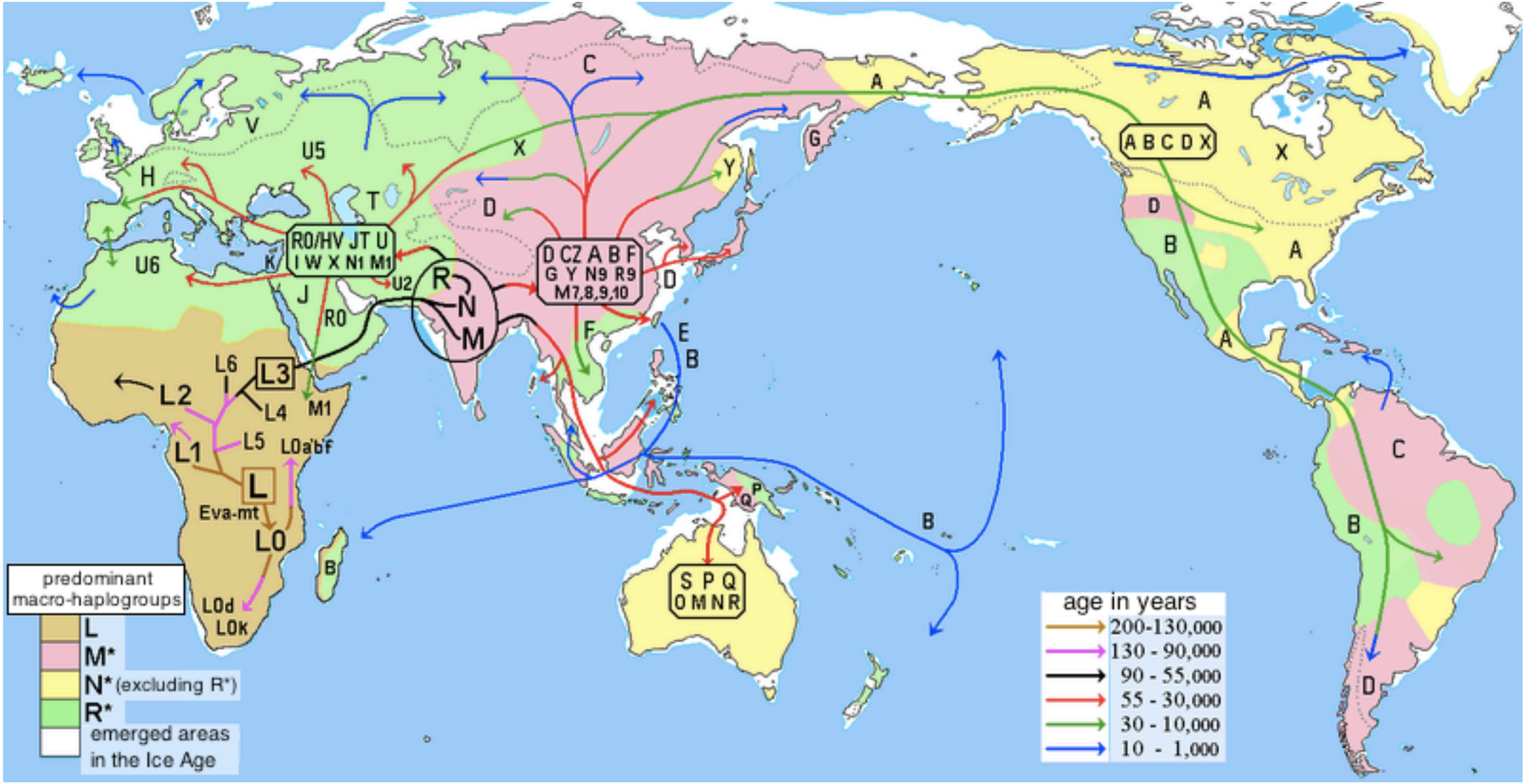


Mitochondrial Eve

Haplogroup Distribution in Africa

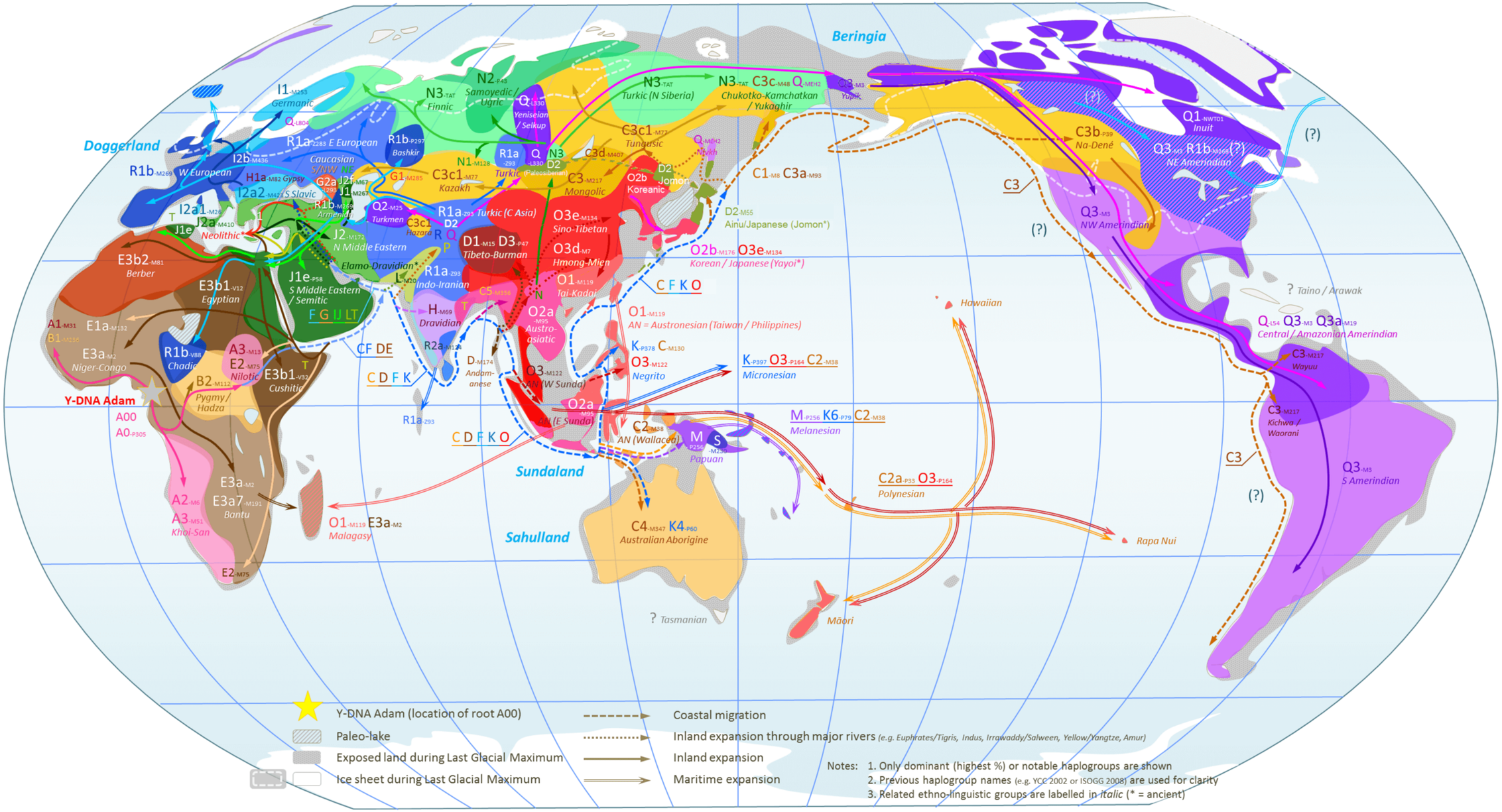


mtDNA Haplogroups and Migration Pattern



World Map of Y-DNA Haplogroups

Dominant Haplogroups in Native Populations with Possible Migration Routes



tree: **Y-DNA Adam** → A B DE C F F → G H IJ K K → LT NO MS P(→Q R)

Mitochondrial Eve

Allan Wilson's Study

- Sequenced a few hundred letters of mitochondrial DNA from diverse people from around the world.
- Compared mutations among these sequences. Constructed a "family tree" of maternal relationships.
- Branch that left the main trunk of this tree earliest is found today only in people of sub-Saharan Africa. All non-Africans today descended from a later branch of the tree.
- Supported the theory that all modern humans descend from ancestors who lived in Africa.
- Based on mutation rate, estimated that the most recent common ancestor of all the branches, "Mitochondrial Eve", lived after 200,000 (new est. 160,000) years ago.

One Hundred Thousand Adams and Eves

- “Mitochondrial Eve” is misleading, fostered the mistaken impression that all of our DNA comes from precisely two ancestors.
- In reality, chromosomes are “mosaics”, the result of recombination during meiosis, a splicing together of both parents chromosomes.
- On average, females produce 45 new splices when producing eggs, and males produce 26 new splices when producing sperm, for a total of 71 new splices per generation.
- A person’s genome is derived from 47 stretches of DNA (the 46 chromosomes and mtDNA). One generation back, a person’s genome is derived fro 118 stretches of DNA transmitted by his or her parents. And so forth for each generation back.

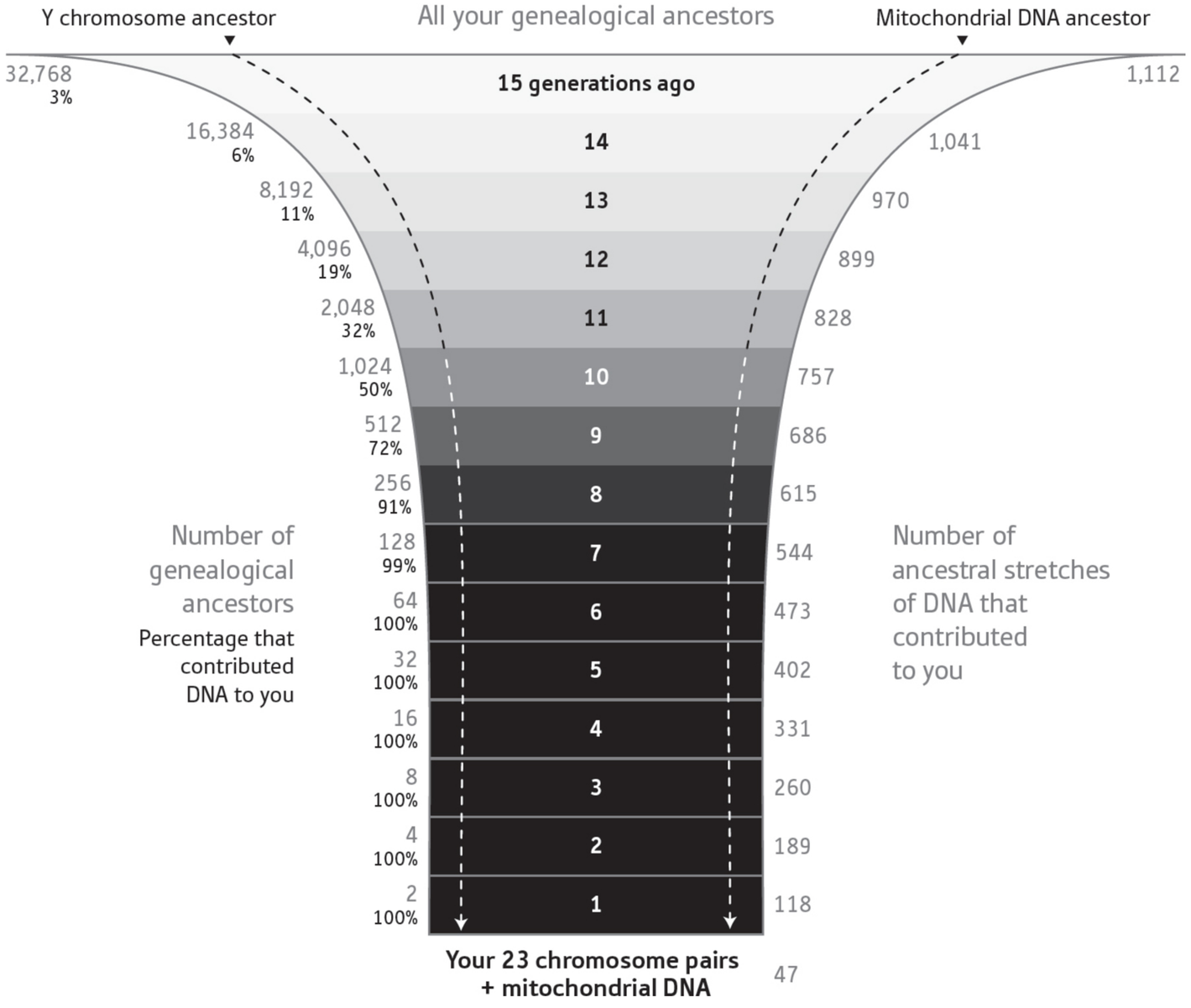
One Hundred Thousand Adams and Eves

- Number of DNA stretches inherited from ancestors increases arithmetically, but the number of ancestors increases exponentially.
- Twenty generations in the past, the number of ancestors is a thousand times greater than the number of ancestral stretches of DNA in a person's genome, so it is a certainty that each person has not inherited any DNA from the great majority of his or her ancestors.
- No "Mitochondrial Eve", no "Y-Chromosome Adam".
- Tracing back fifty thousand years… We inherit DNA from nearly everyone in our ancestral population who had a substantial number of offspring.

One Hundred Thousand Adams and Eves

The Far Richer Story Told by the Whole Genome

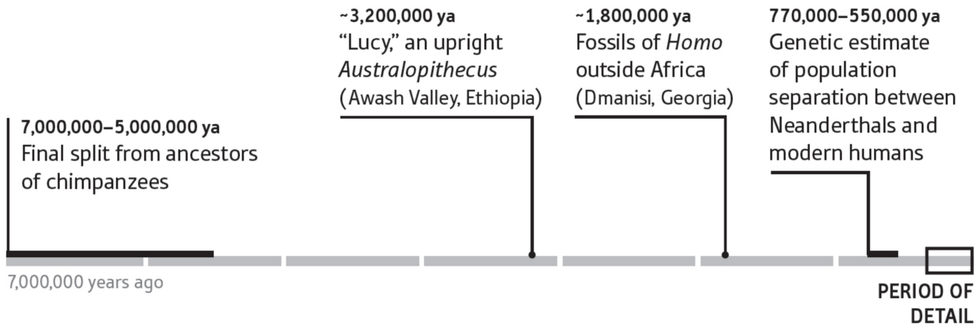
Y chromosomes and mitochondrial DNA reflect information only from the entirely male or entirely female lineages (dashed lines). The whole genome carries information about tens of thousands of others.

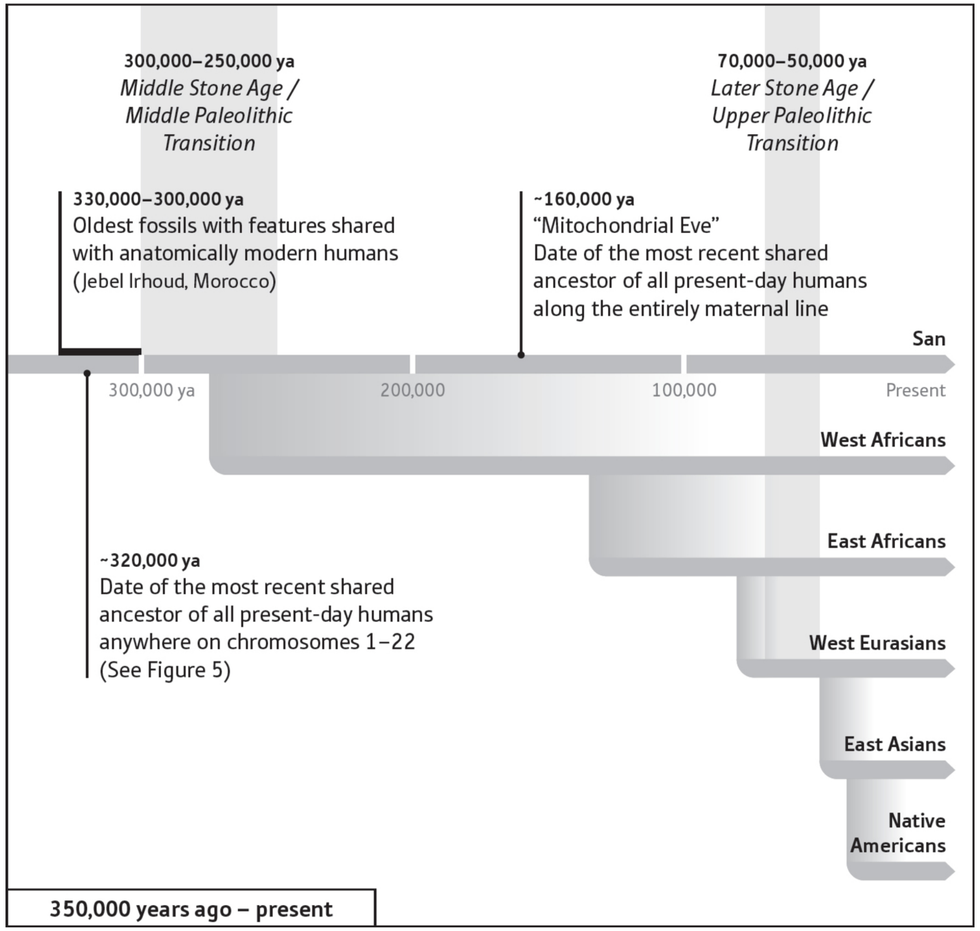


One Hundred Thousand Adams and Eves

“Figure 4. The number of ancestors you have doubles every generation back in time. However, the number of stretches of DNA that contributed to you increases by only around seventy-one per generation. This means that if you go back eight or more generations, it is almost certain that you will have some ancestors whose DNA did not get passed down to you. Go back fifteen generations and the probability that any one ancestor contributed directly to your DNA becomes exceedingly small.”

The Age of Modern Humans





Population Bottleneck

Li and Durbin's Study

- Insight: we carry two genomes, one from our mother and one from our father. Counting the mutations in each genome makes it possible to determine when the parents shared a common ancestor at each location.
- Li and Durbin were thus able to establish the size of the ancestral population at different times.
- Found that after the separation of non-African and African populations, there was an extended period when non-African populations were small; a population "bottleneck event."

Natural Selection

Prezeworski's Limit

- With getting the ability to sequence the genome, researchers attempted to identify genes, or small clusters of genes, responsible for traits or diseases, and that have been operated on by natural selection.
- Molly Prezeworski in a 2006 study that genome scans of present-day humans will miss most instances of natural selection because they lacked the statistical power needed to detect it.
- And in a 2011 study, she showed that only a small fraction of advantageous mutations involved natural selection - Prezeworski"s Limit.
- Mutations, such as allowing digestion of milk in adults, are the exception, rather than the rule.

Natural Selection

Prezeworski's Limit

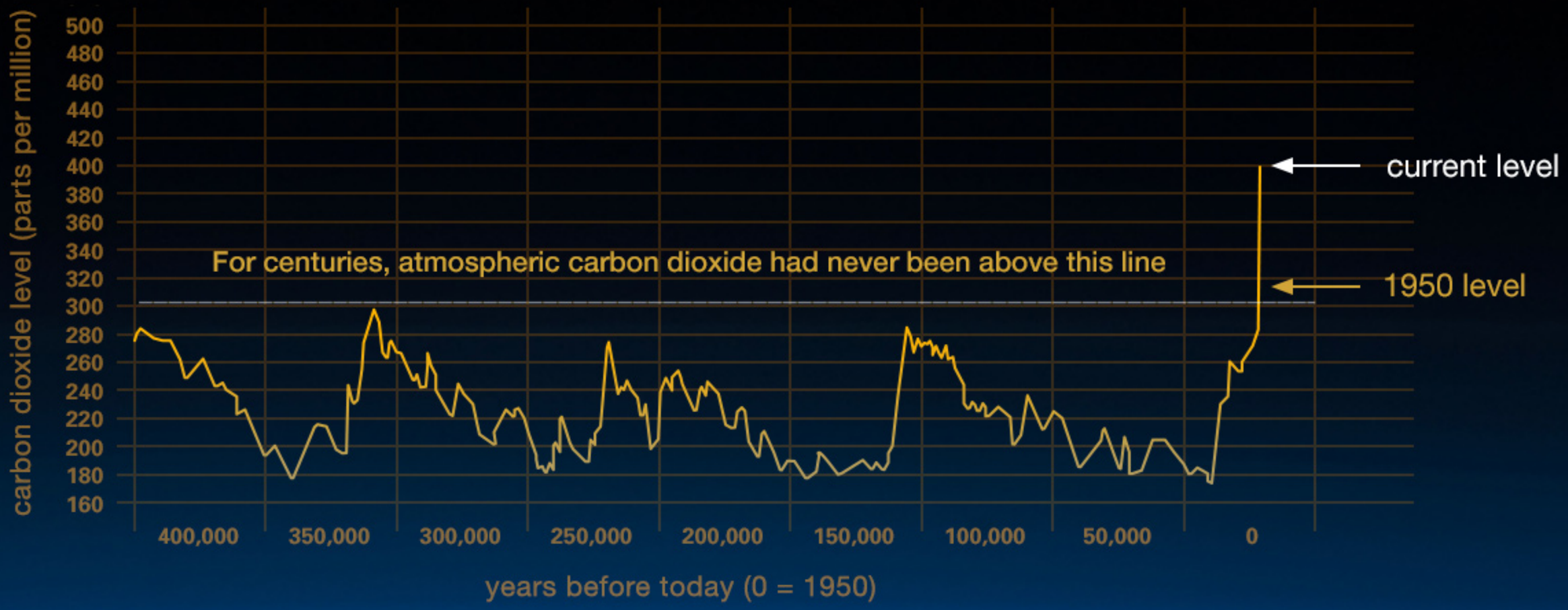
- Reich cites two studies:
  - 2010 study that showed there are 180 independent genetic changes that are more common in shorter people.
  - 2015 study using DNA data from 230 ancient Europeans, showed that there was natural selection for decreased height among southern European farmers.
- Reich's conclusion: By leveraging the power of **whole genome** to analyze thousands of independent positions in the genome simultaneously, it is possible to overcome Prezeworski"s Limit.

Neanderthals

Introduction

- Sophisticated human species that evolved in Europe from archaic human species, probably *Homo Heidelbergensis.*
- May have been capable of speech. Have the unique throat bone that enables speech in *Homo Sapiens*.
- Survived multiple advances and retreats of glaciation. Advances and retreats of glaciers correlates to the fluctuations in CO_2 in the atmosphere.
- Suggested reading: Kindred: Neanderthal Life, Love, Death and Art by Rebecca Wragg Sykes.

Periods of Glaciation - NASA graph from Vostok Lake Cores



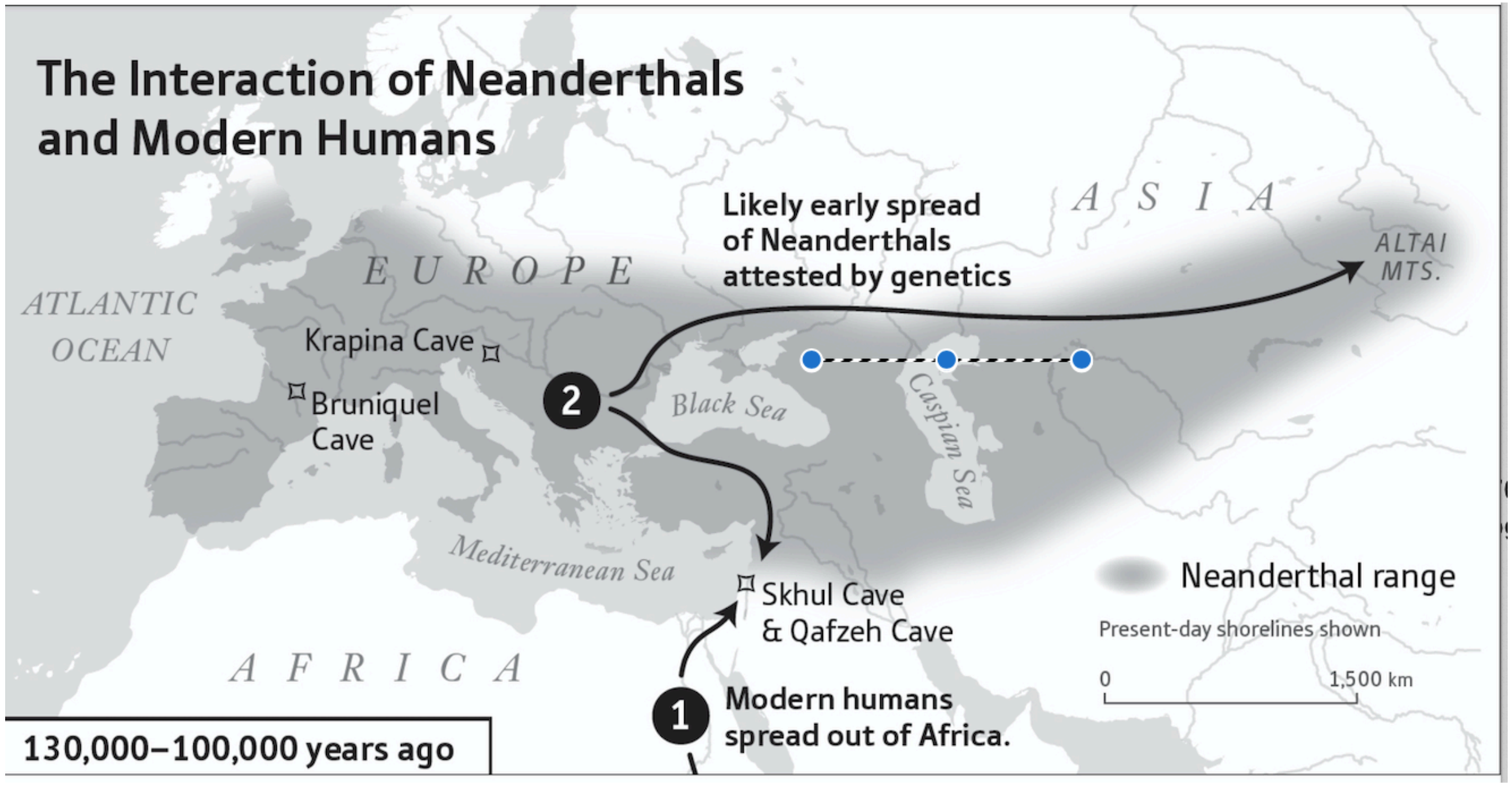
Neanderthals and Modern Humans

Opportunities for Contact

- Near East occupied by modern humans between 130,000 and 100,000 years ago.
- Neanderthals re-entered the region between 60,000 and 48,000 years ago.
- Two opportunities for modern humans to interbreed with Neanderthals.
- Did they interbreed?

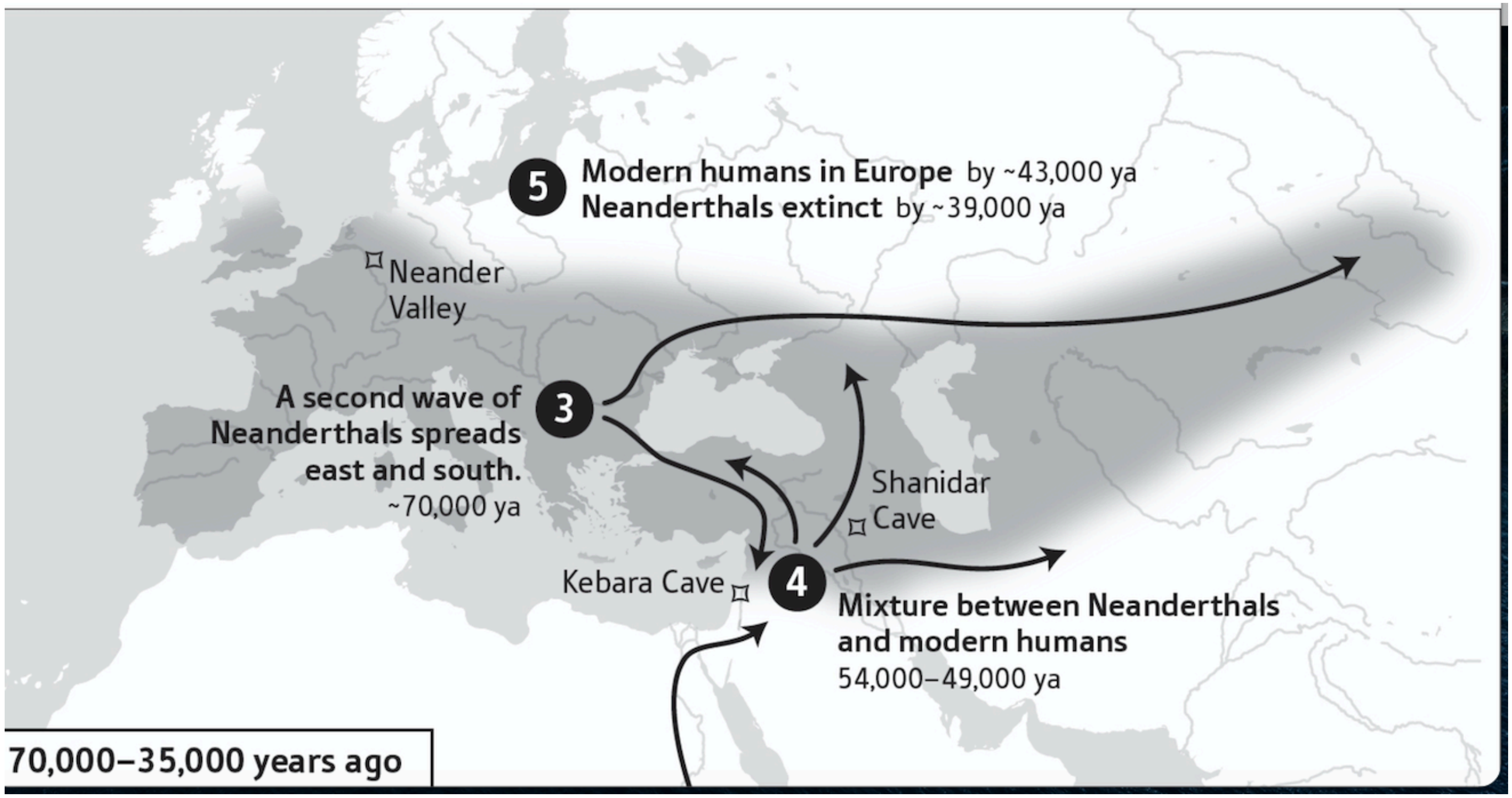
Neanderthals and Modern Humans

Opportunities for Contact



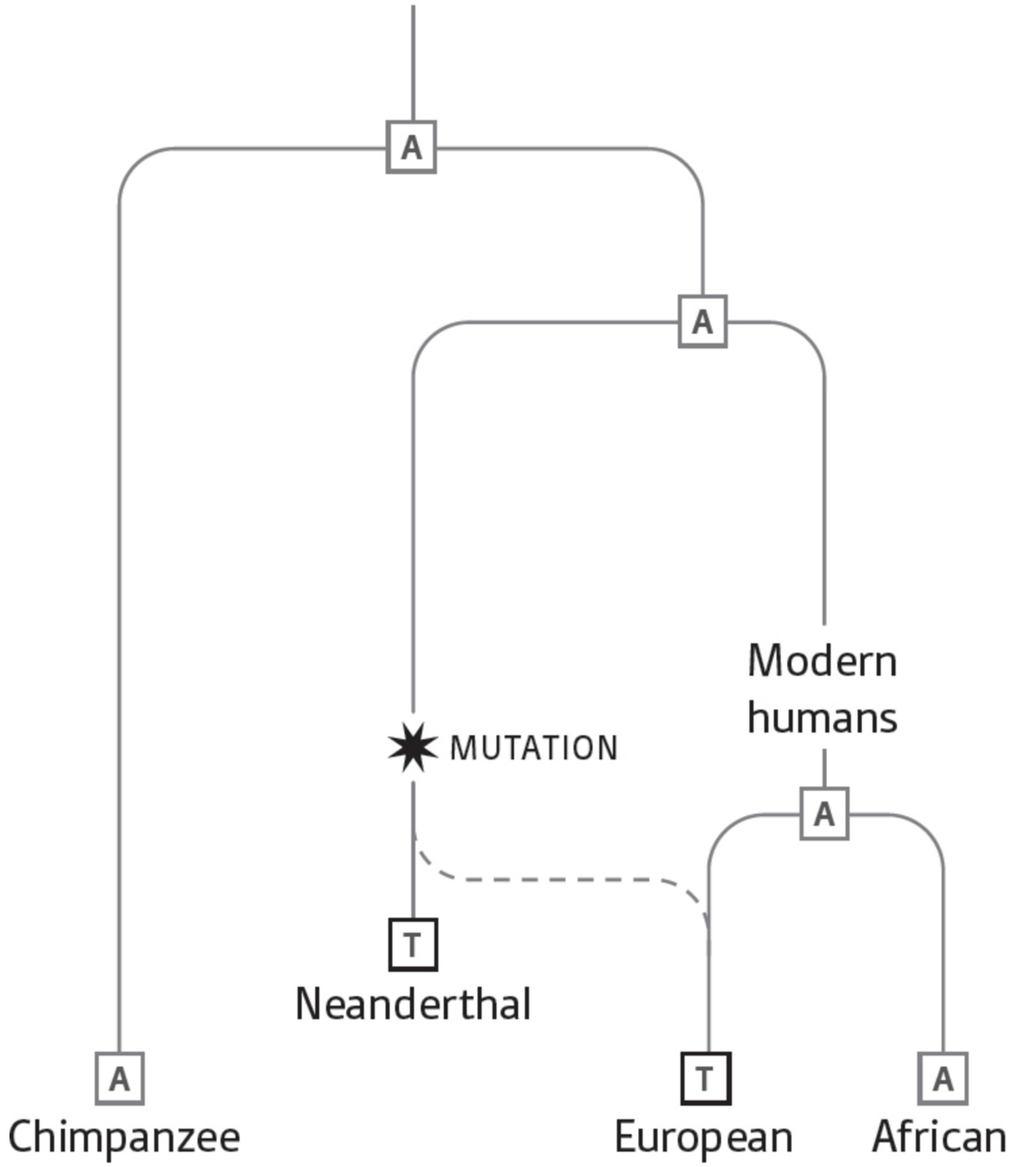
Neanderthals and Modern Humans

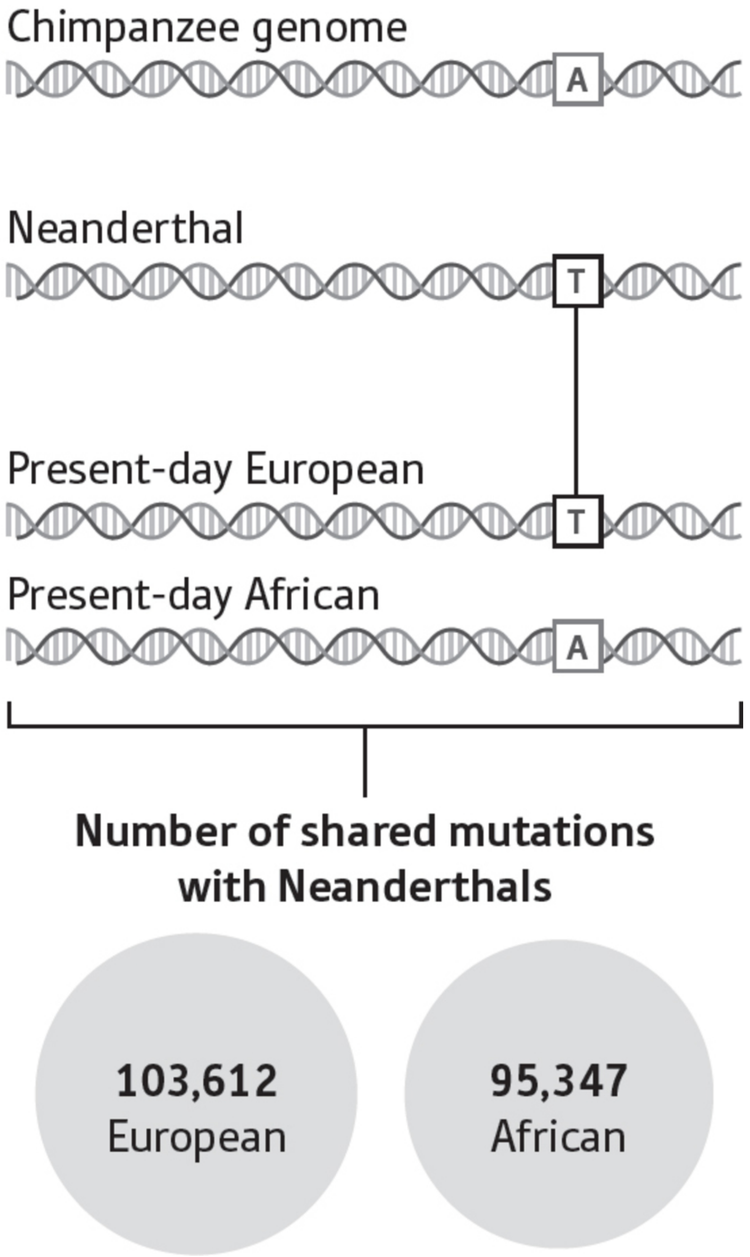
Opportunities for Contact



Neanderthals and Modern Humans

Evidence for Interbreeding





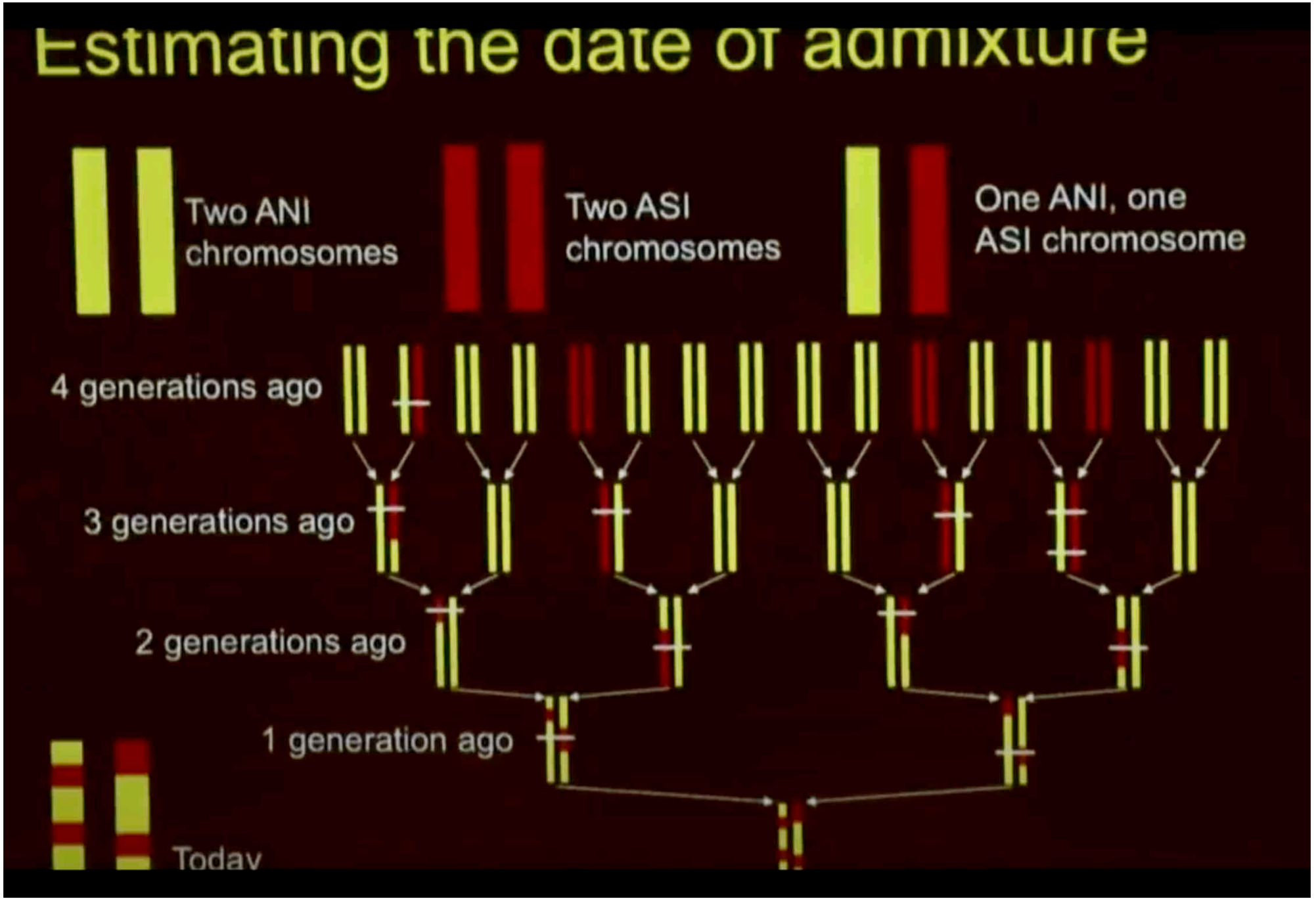
Neanderthals and Modern Humans

Evidence for Interbreeding

“Figure 7. We can evaluate whether two populations are consistent with descending from a common ancestral population through the “Four Population Test.” For example, consider a mutation that occurred in the ancestors of the Neanderthal (letter T, above) that is not seen in chimpanzee DNA. There are about 9 percent more of these mutations shared with Europeans than with African genomes, reflecting a history of Neanderthal interbreeding into the ancestors of Europeans.”

Neanderthals and Modern Humans

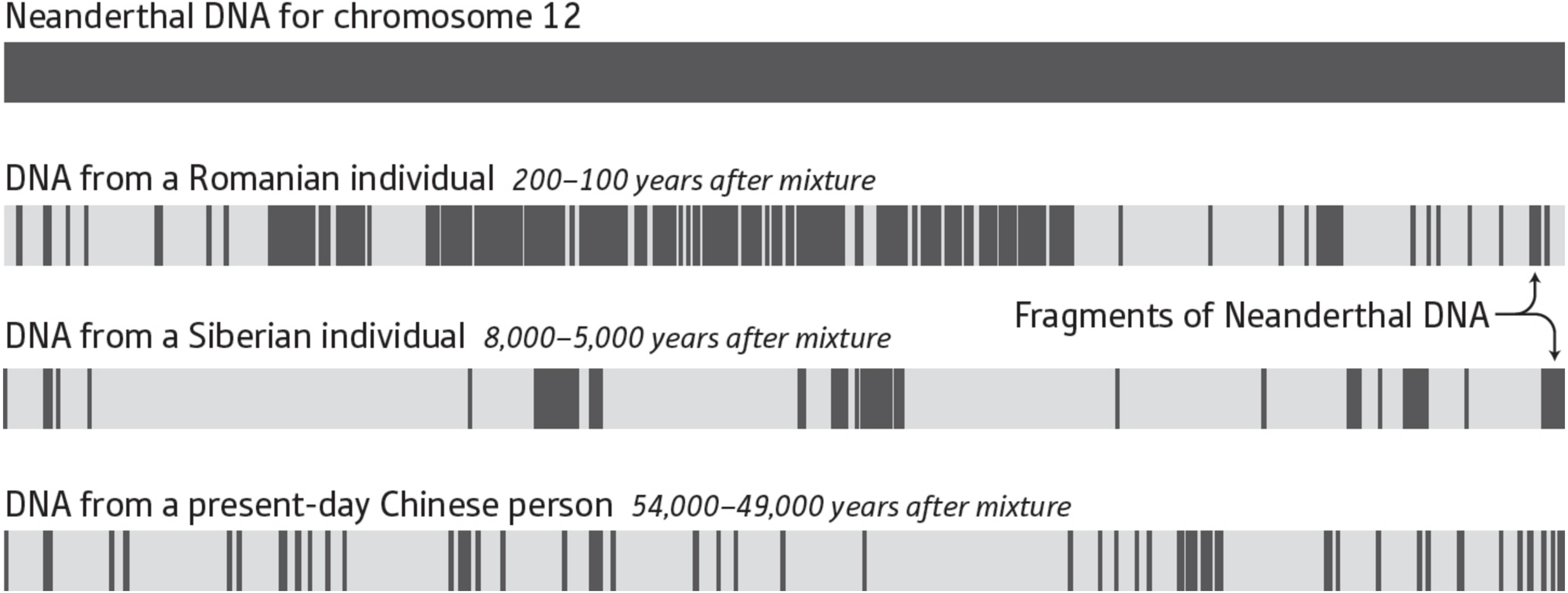
Evidence for Interbreeding



Neanderthals and Modern Humans

Evidence for Interbreeding

. . . provides a clock for dating mixture events.



Neanderthals and Modern Humans

Evidence for Interbreeding

“Figure 8. When a person produces a sperm or an egg, he or she passes down to the next generation only one chromosome from each of the twenty-three pairs he or she carries. The transmitted chromosomes are spliced-together versions of the ones inherited from the mother and father (facing page). This means that the sizes of the bits of Neanderthal DNA in modern human genomes became smaller as the time since mixture increased (above, real data from chromosome 12).”

Neanderthals and Modern Humans

Evidence for Interbreeding

- Why so little Neanderthal DNA in contemporary modern human DNA?
  - Dilution.
  - Low fertility rate of hybrids.
  - Widespread natural selection against Neanderthal DNA.

Up Next

- Chapter 3: Ancient DNA Opens the Floodgates.
- Chapter 4: Humanity’s Ghosts.