

Minireview

'Chumanzee' evolution: the urge to diverge and merge

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Abstract

A recent analysis of the human and chimpanzee genomes compared with portions of other primate genomes suggests that the divergence of the human and chimpanzee lineages beginning around 6 million years ago was not a simple clean split.

The popular and scientific press gave extensive coverage to the recent analysis by Patterson *et al.* [1] of the human and chimpanzee genomes, in which they conclude that after initially splitting, our lineage continued to hybridize with chimpanzees for more than a million years. While the *Washington Post* noted that "Human ancestors may have interbred with chimpanzees" [2], Slate.com asked more bluntly: "Did humans mate with chimps? And are we their offspring?" [3].

Given the extraordinary similarity of the chimpanzee and human genomes, scientists and the public alike have often asked such questions. An extensive review of the literature has yet to turn up a credible report of such crosses. In the 1920s, a Soviet scientist, Il'ya Ivanovich Ivanov, with the assistance of the Institut Pasteur at one of their field stations in French Guinea, unsuccessfully artificially inseminated three chimpanzees with human sperm [4]. He then tried to continue his experiments at the primate center at Sukhum in the then Soviet Republic of Georgia, where he intended to artificially inseminate human volunteers with ape sperm. He was arrested by the Soviet secret police on charges unrelated to this project and was never able to carry it out [4].

Through their own sequencing efforts and data mining, Patterson *et al.* [1] have put together an alignment of human, chimpanzee, gorilla, orangutan, and macaque sequences that covers almost 20 Mb, which is 800 times larger than any previous analysis. But it is not just the size of the dataset that is important, it is the phylogenetic distribution. Most recent analyses of the human and chimpanzee genomes compare them with the mouse genome, which seems to be evolving at

a different rate and under different constraints. By adding the very closely related gorilla, moderately close orangutan, and somewhat more distant macaque, the timing and processes of primate evolution can be more effectively studied. It is difficult, to nearly impossible, to infer whether an evolutionary event occurred on the human or chimpanzee lineage unless relatively closely related primate sequences are available for comparison.

Because our genomes are not inherited clonally, but in pieces from each of our parents, each independent region of the genome can have its own slightly different history. The different segments may be inherited from ancestors from different geographic regions of the world, making one's ancestry an amalgam of different histories. The same is true at the species level - different regions of the genome will have different evolutionary histories. Furthermore, the various regions of the genome evolve at different rates and have different selective constraints. Thus, when comparing two DNA sequences, you are not necessarily measuring the species-level differences between their owners (Figure 1). The best way to measure the overall difference between two species is through the analysis of many different regions of the genome. This is exactly what Patterson *et al.* [1] did.

They found a considerable amount of variation in the amount of divergence among different regions of the genomes of humans and chimpanzees. Applying molecular dating techniques to each of these regions, they inferred that human and chimpanzee speciation occurred less than 6.3 million years ago. Depending on the calibration points used to estimate this date, it could be as recent as 5.4 million

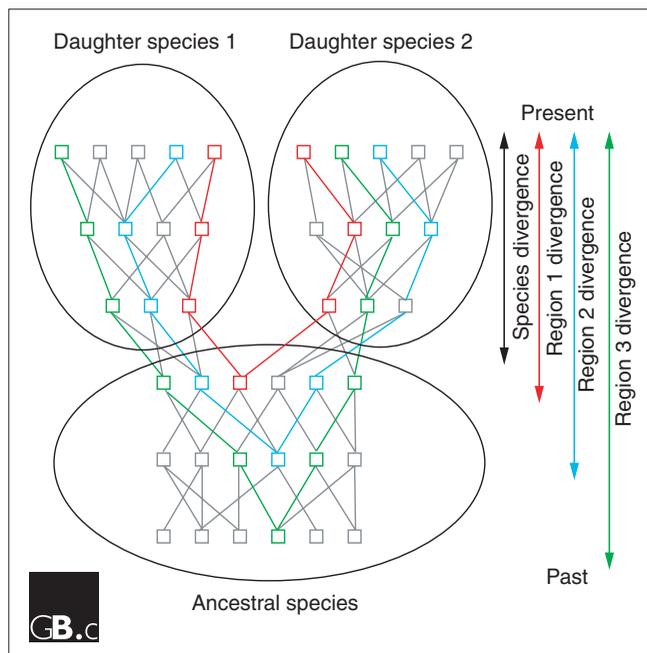


Figure 1
Genetic divergence times can vary across different regions of a genome. Individuals within each generation are represented by open squares, connecting lines represent the transmission of alleles from one generation to the next. While full speciation occurs when members of the daughter populations no longer interbreed (black divergence time), individual regions of the genome in the two daughter species (for example, the green, blue and red regions) may share more ancient relationships, as indicated by the corresponding red, blue, and green divergence times on the right. Adapted from Hennig [11].

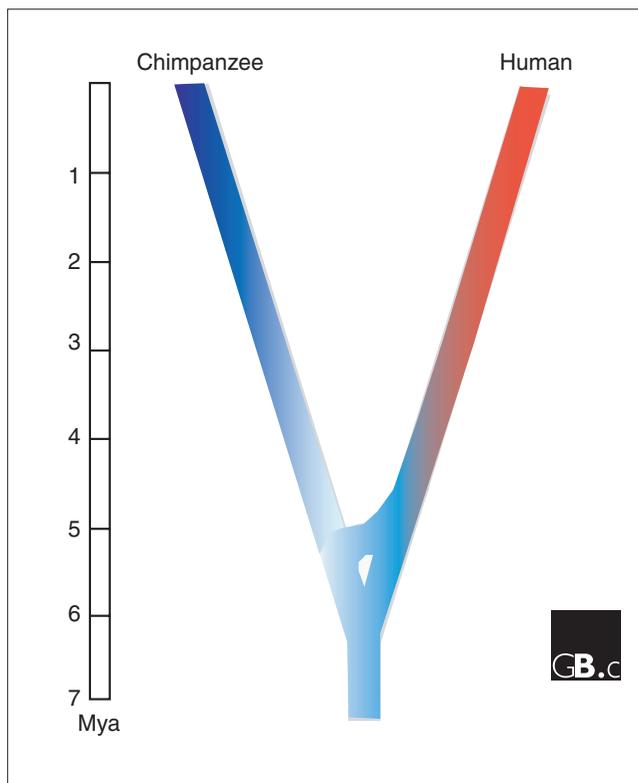


Figure 2
The scenario proposed by Patterson *et al.* [1] for the human-chimpanzee split. An initial divergence between the human and chimpanzee lineages was followed by a period of hybridization and, eventually, by full speciation. Mya, million years ago.

years ago. This could be important if the current most favored interpretation of the fossil record holds up. In this interpretation, the fossil species *Sahelanthropus tchadensis*, dated to 6.5 to 7.4 million years ago, is considered to be a hominin [5]. That is, it falls on the human lineage after the divergence of chimpanzees and humans. It has dental features similar to other fossil hominins and is inferred to be bipedal like all other hominins, and unlike chimpanzees. Another fossil species, *Orrorin tugenensis*, is also inferred to be a bipedal hominin dating to around 5.8 million years ago. Thus, if either or both of these species are indeed true hominins, they would contradict a 6.3 million year or younger date for the split between humans and chimpanzees. However, the hominin status of these fossils is not absolutely certain and several researchers dispute their bipedality.

More interestingly, Patterson *et al.* [1] found that the amount of molecular divergence (the proportion of nucleotides differing between human and chimpanzees) between any region varied between 84% and 147% of the overall average level of divergence. Furthermore, they found that the sequences from the X chromosome diverged from each other by only 83.5% of the average overall divergence, instead of the approximately 93% divergence they inferred from their

modeling of the X chromosome. A smaller degree of divergence is expected in sequences on the X chromosome because the number of copies of the X chromosome in a population of any primate species is only three quarters of the number of copies of any autosome. The smaller effective population size of the X chromosome will only be able to generate and maintain a smaller amount of variation. The same is true, but even more so, for the Y chromosome and the mitochondrial genome, whose effective population sizes are only a quarter those of the autosomes. Peterson *et al.* [1] interpret this reduced amount of variation on the X chromosome to mean that humans and chimpanzees were still exchanging X chromosomes 1.2 million years after the species split (Figure 2). Hence the headlines of ancestral chimpanzees and humans mating.

If chimpanzees and humans were hybridizing for over a million years after their 'split', this might imply that the early human lineage still maintained the $2n = 48$ karyotype found among all the great apes (modern humans have $2n = 46$). Such a speculation might also explain the apparent lack of hybridization found between modern humans and the very closely related extinct Neanderthals [6]. If the population leading to the modern human lineage

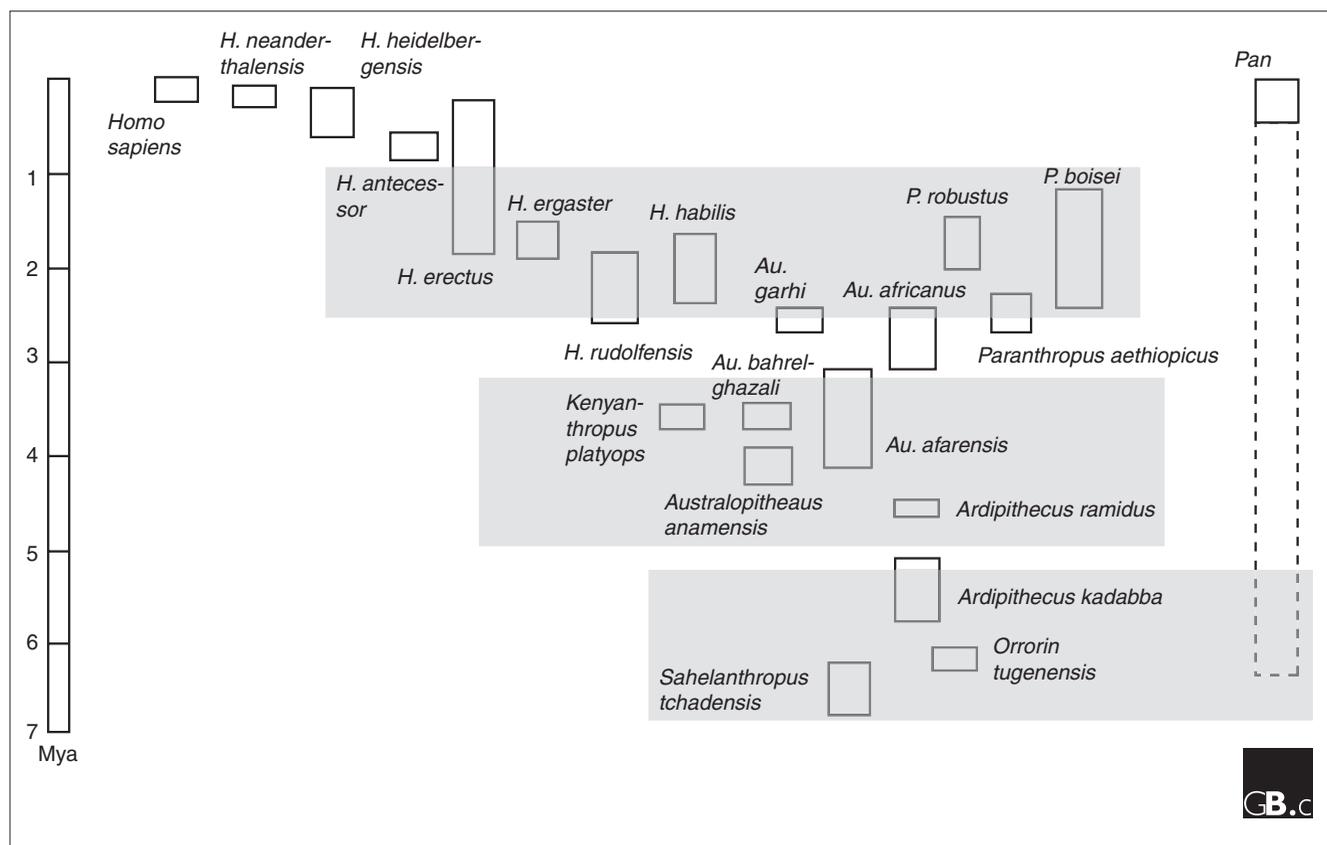


Figure 3
Hominin evolution. The boxes represent the time periods over which the indicated species is thought to have existed. Three hypothetical 1.5-million-year windows of potential interbreeding between hominin species are indicated by gray shading. Adapted from Wood [12].

subsequently underwent a chromosomal fusion event, giving us our $2n = 46$ karyotype, while the Neanderthal lineage retained $2n = 48$, perhaps modern humans could not successfully interbreed with Neanderthals.

Back on firmer ground, a potentially messy split between humans and chimpanzees should not be surprising given other examples from the order Primates. Interspecies crosses and hybrids are very common among the Old World monkeys. For instance, the species *Macaca arctoides* may have formed by the hybridization of two other species, *Macaca fascicularis* and the species that gave rise to *M. thibetana* and *M. assamensis* [7]. The different species of baboons, which initially split nearly two million years ago, regularly hybridize in the wild wherever their adjacent ranges meet [8], and almost all possible combinations of crosses are known. Fertile intergeneric hybrids are also known. In one case, the offspring of a *Theropithecus gelada* and a *Papio hamadryas* baboon subsequently produced offspring in a zoo setting and such hybrids are also known to occur naturally [9]. Even more distant crosses between *Papio hamadryas* and *Macaca mulatta* have been purposely produced in captivity, but the resulting offspring, while

healthy, were infertile [10]. Thus, the potential hybridization of two newly split lineages, even if they belong to two different genera, should not be so shocking. What is more interesting is why lineages do not merge, rather than continuing on their own separate evolutionary trajectories.

It has been proposed that many members of the hominin adaptive radiation (species more closely related to humans than to chimpanzees) would have been capable of interbreeding. This would be especially likely for lineages that had recently split or that share ancestry within a range of, say, two million years, like the baboons [8]. Imagining potential interbreeding within a sliding one- or two-million-year window of divergence may become more common than assuming that species somehow split cleanly and nearly instantaneously (Figure 3), even though it will give big headaches to those trying to precisely delineate and name such species.

The conclusions drawn from the analysis of Patterson *et al.* [1] now await testing with the completion of additional primate genomes. Sequencing of the genomes of a gorilla, orangutan, gibbon, baboon, marmoset and bushbaby is

planned or in the works. However, improving on our theories of human evolutionary history also requires the continued discovery of new fossils and better ways of interpreting them. Inferences extrapolating backwards in time not only require fossils to calibrate the molecular clocks used, but can also be tested by the only hard evidence we have for ancient events, the bones and teeth of the ancestors we are hypothesizing.

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