Soft sweeps predominate recent positive selection in bonobos (*Pan paniscus*) and chimpanzees (*Pan troglodytes*)

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Abstract

Two modes of positive selection have been recognized: 1) hard sweeps that result in the rapid fixation of a beneficial allele typically from a *de novo* mutation and 2) soft sweeps that are characterized by intermediate frequencies of at least two haplotypes that stem from standing genetic variation or recurrent *de novo* mutations. While many populations exhibit both hard and soft sweeps throughout the genome, there is increasing evidence that soft sweeps, rather than hard sweeps, are the predominant mode of adaptation in many species, including humans. Here, we use a supervised machine learning approach to assess the extent of completed hard and soft sweeps in the closest living relatives of humans: bonobos and chimpanzees (genus *Pan*). We trained convolutional neural network classifiers using simulated data and applied these classifiers to population genomic data for 71 individuals representing all five extant *Pan* lineages, of which we successfully analyzed 60 individuals from four lineages. We found that recent adaptation in *Pan* is largely the result of soft sweeps, ranging from 73.1 to 97.7% of all identified sweeps. While few hard sweeps were shared among lineages, we found that between 19 and 267 soft sweep windows were shared by at least two lineages. We also identify novel candidate genes subject to recent positive selection. This study emphasizes the importance of shifts in the physical and social environment, rather than novel mutation, in shaping recent adaptations in bonobos and chimpanzees.

Keywords: adaptation, convolutional neural network, diploS/HIC, selective sweep, supervised machine learning

Introduction

The identification of adaptative traits and their genetic basis is one of the central goals of evolutionary biology. Two approaches, top-down and bottom-up, have been used to accomplish this goal; the latter of which leverages population-level data to recognize the genomic signatures of positive selection (Barrett and Hoekstra 2011). At the genomic level, the process of adaptation results in a window of reduced variation that erodes over time. As these signatures do not persist, they can only be used to infer selection over a particular time scale in a population. In most species, this time frame is restricted to a few thousand generations, roughly ~ 200,000 years in humans (Oleksyk et al. 2010). The classic model for positive selection for a given locus proposes that a single, novel mutation, that confers a fitness advantage (i.e., a beneficial allele) will rapidly spread in a population and eventually reach fixation (Maynard Smith and Haigh 1974). Neutral polymorphism adjacent to the novel allele will 'hitchhike', resulting in a distinct pattern of reduced genomic diversity at the locus and surrounding sites. The term 'hard sweep' has been used to identify this pattern and process.

'Soft sweeps' describe the presence of two or more haplotypes that occur at intermediate frequencies (Hermisson and Pennings 2005). Thus, the signature of a soft sweep is intermediate to those of neutral or 'background' genomic variation and the signature of a hard sweep. This pattern can result from recurrent *de novo* mutations following positive selection. Alternatively, soft sweeps can also result from positive selection on standing genetic variation where alleles were already present in a population before selection. This variation may be the result of independent mutations (multiple origin soft sweep) or when an adaptive allele arose before selection, but multiple copies have subsequently swept through the population (single origin soft sweep). Soft sweeps are often incorrectly viewed synonymously with standing genetic variation;

hard sweeps can emerge from standing genetic variation if a single copy of the beneficial allele was the ancestor of all beneficial alleles in a sample (Hermisson and Pennings 2017).

Hard and soft sweeps are locus-specific and, thus, not mutually exclusive across a genome. Unsurprisingly, soft sweeps are also much more difficult to recognize than hard sweeps because their genomic patterns are intermediate. Additionally, the identification of selective sweeps, hard or soft, is further complicated by the possibility that neutral loci linked to either soft or hard sweeps may produce a false signature similar to that of a sweep (Schrider et al. 2015; Kern and Schrider 2018).

With these challenges in mind, a considerable amount of work has been dedicated to both developing robust methods to identify selective sweeps and also understanding the evolutionary parameters that determine hard or soft sweeps. Mutation-limited scenarios are expected to exclusively produce hard sweeps because beneficial alleles rarely occur (Hermisson and Pennings 2017). Thus, the most important parameter for estimating the likelihood of hard vs soft sweeps is the population-scaled mutation rate: $\Theta = 4N_e\mu$, where N_e is the effective population size and μ is the mutation rate. However, this single parameter can vary widely depending on the advantage of the beneficial allele, the effective population size, the size of the mutational target, and the timescale for adaptation (Messer and Petrov 2013; Hermisson and Pennings 2017). Therefore, adaptation across the genome for a given population can be simultaneously mutation-limited and non-mutation-limited (B.A. Wilson et al. 2014). While it has become clear that most populations will likely exhibit a mosaic of hard and soft sweeps (Hermisson and Pennings 2017), additional data on sweep type frequencies in various species are sorely needed to better tease apart which parameters may determine each of those frequencies.

Both species of the *Pan* genus represent important evolutionary models due to their phylogenetic proximity to humans. *Homo* and *Pan* diverged ~ 5 to 7 Ma (Sarich and Wilson 1967; Bradley 2008; Scally et al. 2012; Besenbacher et al. 2019) and the most recent estimates for the divergence of bonobos and chimpanzees range between 1 and 2 Ma (Prüfer et al. 2012; de Manuel et al. 2016). Four extant chimpanzee subspecies evolved from a chimpanzee common ancestor that split ~ 600 Ka with both subsequent lineages further splitting: one ~ 250 Ka and the other ~ 160 Ka (de Manuel et al. 2016). These two species exhibit stark differences in aspects of their morphology, physiology, behavior, and ecology (Susman 1984; Goodall 1986; Wrangham 1986; Kano 1992; White 1996; Furuichi 2011; Nishida 2011; Stumpf 2011; Behringer et al. 2014; Turley and Frost 2014; M.L. Wilson et al. 2014). Many of these distinguishing traits are inferred to have occurred shortly after divergence, while much less is known about recent evolutionary processes in these lineages.

Understanding recent positive selection in *Pan* is intriguing because of the dynamic physical and social environments in which they evolved. Climatic variation across Africa is well-documented for the Pleistocene and has been proposed to drive the evolution of early *Homo* (Potts 1998; Antón et al. 2014), and such variation probably impacted other taxa throughout the Pleistocene, including the genus *Pan*. Chimpanzee populations living in more stable environments that were closer to Pleistocene refugia were recently described to exhibit less behavioral diversity than chimpanzees living in more seasonal habitats that are more distant to forest refugia (Kalan et al. 2020). While the formation of these refugia may have resulted in periods of habitat stability for some bonobo and chimpanzee populations during glacial periods (Takemoto et al. 2017; Barratt et al. 2020), climatic fluctuations throughout the Pleistocene likely affected both the physical environment—via changes in habitat structure and type—and

the social environment—via changes in the frequency of dispersal and intergroup encounters. Further, evidence of admixture within extant and between extant and extinct members of the *Pan* genus adds even more variation to the social environments in which these apes evolved (Hey 2010; Wegmann and Excoffier 2010; de Manuel et al. 2016; Kuhlwilm et al. 2019). A dynamic environment may result in selection for multiple existing alleles, resulting in a greater frequency of soft sweeps than in a more stable environment where one would expect a greater frequency of hard sweeps.

In this study, we apply a recently developed supervised machine-learning approach to population-level genomic data for bonobos (*Pan paniscus*) and chimpanzees (*Pan troglodytes*) to assess the extent of different completed sweep types in these species. While a few studies have examined recent positive selection in bonobos and chimpanzees (e.g., Cagan et al. 2016; Han et al. 2019; Schmidt et al. 2019; Kovalaskas et al. 2020; Nye et al. 2020), the role of hard and soft sweeps in shaping their adaptations is currently unknown. We sought to categorize genomic regions as subject to recent hard or soft sweeps, as linked to recent hard or soft selective sweeps, or as evolving neutrally. Data from simulations have predicted that hard sweeps would be common in humans because of our overall low mutation rate (Hermisson and Pennings 2017). Under this "mutation limitation hypothesis" and given the similarity in mutation rate between *Homo* and *Pan*, one could predict that bonobos and chimpanzees should also exhibit a high degree of hard sweeps. However, hard sweeps have been thought and observed to be quite rare in recent human evolution (Hernandez et al. 2011; Schrider and Kern 2017), although this perspective is debated (Jensen 2014; Harris et al. 2018). This could be explained by several non-mutually exclusive alternatives including demographic effects. Larger populations can have more standing variation for selection to act on (Hermisson and Pennings 2005) which may result

in more soft sweeps, whereas bottlenecks can result in drift and thus potentially more hard sweeps if intermediate frequency haplotypes are lost (B.A. Wilson et al. 2014). For example, humans have experienced recent demographic changes (e.g., Schiffels and Durbin 2014), including a bottleneck upon leaving Africa (e.g., Henn et al. 2012). Indeed, Schrider and Kern (2017) found that hard sweeps were more frequent in non-African than African populations. Chimpanzees and bonobos have also experienced recent demographic changes, including in effective population size, within the time frame (< 200 Ka) for selective sweeps, based on PSMC analyses (Prado-Martinez et al. 2013; de Manuel et al. 2016). Three of the five lineages appear to have declined, whereas the other two have increased and then decreased. Under such changes in population size, the strength of selection plays a strong role in the likelihood of soft sweeps (B.A. Wilson et al. 2014). We therefore predicted that we would observe a higher frequency of soft sweeps in *Pan*, but that lineage-specific population histories might affect the degree to which soft sweeps dominate.

Methods

Genomic Data

We retrieved raw short read data on bonobos and all four chimpanzee subspecies from the Great Ape Genome Project (GAGP) (Prado-Martinez et al. 2013). This dataset contained high coverage genomes (Figures S1, S2) from 13 bonobos (*P. paniscus*), 18 central chimpanzees (*P. troglodytes troglodytes*), 19 eastern chimpanzees (*P. t. schweinfurthii*), 10 Nigeria-Cameroon chimpanzees (*P. t. ellioti*), and 11 western chimpanzees (*P. t. verus*) (File S1).

Read Mapping and Variant Calling

Initial quality assessments in fastqc (Andrews 2010) and multiqc (Ewels et al. 2016) indicated a number of quality issues, including failed runs, problematic tiles, and substantial variation in base quality. We removed adapters and trimmed all reads for quality with BBduk (https://sourceforge.net/projects/bbmap/). For trimming, we used the parameters “ktrim=r k=21 mink=11 hdist=2 qtrim=rl trimq=15 minlen=50 maq=20” for all reads and added “tpo and tpe” for paired reads.

We used XYalign (Webster et al. 2019) to create versions of the chimpanzee reference genome, panTro6 (Kronenberg et al. 2018), for male- and female-specific mapping. Specifically, the version of the reference for female mapping has the Y chromosome completely masked, as its presence can lead to mismapping (Webster et al. 2019). We then mapped reads with BWA MEM (Li, unpublished data) and used SAMtools (Li et al. 2009) to fix mate pairs, sort BAM files, merge BAM files per individual, and index BAM files. We use Picard (Broad Institute 2018) to mark duplicates with default parameters, before calculating BAM statistics with SAMtools. We next measured depth of coverage with mosdepth (Pedersen and Quinlan 2018), removing duplicates and reads with a mapping quality less than 30 for calculations. Visualizations for coverage and demography (see Generation of Simulated Chromosomes below) were created in R, version 3.5.2 (R Core Team 2020), using ‘ggplot2’ (Wickham 2016).

We used GATK4 (Poplin et al. 2018) for joint variant calling across all samples. We used default settings for all steps—HaplotypeCaller, CombineGVCFs, and GenotypeGVCFs—with three exceptions. First, we turned off physical phasing for computational efficiency and downstream VCF compatibility with filtering tools. Second, because multiple samples in this dataset suffer from contamination from other samples both within and across taxa (Prado-Martinez et al. 2013), we employed a contamination filter to randomly remove 10% of reads

during variant calling. This should have the effect of reducing confidence in contaminant alleles. Finally, we output non-variant sites to allow equivalent filtering of all sites in the genome and more accurate assessments of callability.

The above quality control, assembly, and variant calling steps are all contained in an automated Snakemake (Köster and Rahmann 2012) available on Github (https://github.com/thw17/Pan_reassembly). The repository also contains a Conda environment with all software versions and origins, most of which are available through Bioconda (Grüning et al. 2018).

Variant Filtration and Genome Accessibility

We considered only autosomes for this analysis as the X and Y chromosome violate many of the assumptions for the following methods (Webster and Wilson Sayres 2016). We also excluded unlocalized scaffolds (N = 4), unplaced contigs (N = 4,316), and the mitochondrial genome from any downstream analyses. Additional filtration steps were completed using bcftools (Li 2011); command line inputs are provided in parentheses. Given our focus on selective sweeps, we only included single nucleotide variants (SNVs) ("-v snps") that were biallelic ("-m2 -M2"). On a per sample basis within each site, we marked genotypes where sample read depth was less than 10 and/or genotype quality was less than 30 as uncalled ("-S . -i FMT/DP ≥ 10 && FMT/GT ≥ 30"). To ensure that missing data did not bias our results, we further excluded any sites where less than ~ 80% of individuals (N = 56) were confidently genotyped ("AN ≥ 112"). We also removed any positions that were monomorphic for either the reference or alternate allele ("AC > 0 && AC ≠ AN"). These filtrations steps yielded 41,869,892 SNVs for our downstream analyses (Table S1).

We considered sites in our sample with low to no coverage to be 'inaccessible' in the reference genome. Using the output of mosdepth (see Read Mapping and Variant Calling above), we identified and filtered sites exhibiting low coverage as defined above. We used the 'maskfasta' function in bedtools (Quinlan and Hall 2010) to mark these sites (N) in the pantro6 FASTA, featuring only the autosomes, for use in downstream analyses. This resulted in 86.3% of the assembled autosomes as accessible (File S2).

Generation of Simulated Chromosomes

We used the software 'discoal' to generate simulated chromosomes on which we trained a classifier per lineage (Kern and Schrider 2016). We generated a matching number of simulated haploid chromosomes for the sample size of each *Pan* lineage (i.e., 26 chromosomes for 13 *P. paniscus*, 20 chromosomes for 10 *P. t. ellioti*, etc.). Simulated chromosomes were set to 1.1 Mb in length and divided into 0.1 Mb subwindows for a total of 11 subwindows. These simulations included a population-scaled mutation rate ($4N\mu L$), where N is the effective population size, μ is the per base pair per generation mutation rate, and L is the length of the simulated chromosome. We used the median of the previously reported effective population size range per lineage (Prado-Martinez et al. 2013). As estimates of genome-wide mutation rates vary considerably and are complicated in that mutation rates vary across individual genomes, we based our parameter on a mutation rate of 1.6×10^{-8}, which falls between estimates from genome-wide data and phylogenetic estimates (Narasimhan et al. 2017). We introduced some variation in this rate by setting a lower and upper-bound to 1.5 and 1.7×10^{-8} and sampled a new mutation rate per simulation drawing from this uniform prior. All simulations also included a population-scaled recombination rate ($4NrL$), where r is the recombination rate per base pair per generation, again

calculated from the median effective population size for each lineage from Prado-Martinez et al. (2013) and a recombination rate drawn from a uniform prior of 1.1 - 1.3 x 10^{-8}, based on the mean genome-wide rate (1.2 x 10^{-8}) reported for bonobos, chimpanzees, and gorillas (Stevison et al. 2015). Recent results from a different selective sweep classifier, Trendsetter, suggest that including a range of recombination rates is important to reducing misclassification (Mughal and DeGiorgio 2019). We note that while some of the estimated recombination rates in bonobos and chimpanzees are beyond the uniform distribution used in our simulations, many of these values are the high rates present in the telomeres, regions that generally exhibit lower or no coverage and thus will be largely if not entirely masked from this analysis (see Variant Filtration and Genome Accessibility above). We also included a demographic string reflecting approximate changes in population size for each lineage between ~ 0.05 and 2 Ma. Changes in population size were set in units of $4N_0$ generations, N_0 was set to the approximate median effective population size from (Prado-Martinez et al. 2013) and we used a generation time of 25 years (Langergraber et al. 2012). Population size changes for this time period were drawn from a previous PSMC analysis (de Manuel et al. 2016) (Figure S3). While this is only one study from which to draw demographic information and reconstructions of *Pan* demography vary widely across studies, the downstream program used to classify genomic windows, diploS/HIC, is robust to demographic misspecification (Kern and Schrider 2018). We generated 2 x 10^3 simulations using these parameters as a set of simulations under neutral evolution per lineage.

Hard and soft selective sweeps were simulated with all of the aforementioned parameters and using a uniform prior of population-scaled selection coefficients ($\alpha = 2Ns$) derived from each lineage's median effective population size (Prado-Martinez et al. 2013) and moderately weak to moderately strong selection coefficients between 0.02 and 0.05. Sweeps also included a

parameter (τ) for the time to fixation of the beneficial allele over a uniform range in units of 4N generations. This value ranged from 0 to 0.001 for all lineages. Linked-hard and linked-soft sweeps were generated by placing the selected site at the center of each of the 10 subwindows flanking the center (6^{th}) subwindow. Additionally, we included a uniform prior on the frequency at which a mutation is segregating at the time it becomes beneficial for soft and linked-soft sweeps, setting this range from 0 to 0.2. We generated 1×10^3 simulations per subwindow for linked-hard and linked-soft sweeps (N = 10) and 2×10^3 simulations for hard and soft sweeps. This resulted in a total of 2×10^3 hard, 1×10^4 hard-linked, 2×10^3 soft, and 1×10^4 soft-linked simulated sweeps. Parameters for these simulations are presented in File S3.

Calculation of Simulation Feature Vectors and Classifier Training

We calculated feature vectors from these simulated chromosomes using the 'fvecSim' function in the program diploS/HIC (Kern and Schrider 2018). Briefly, diploS/HIC calculates 12 summary statistics for all 11 subwindows: π, Watterson's θ, Tajima's D, the variance, skew, and kurtosis of genotype distance (g_{kl}), the number of multilocus genotypes, J_1, J_{12}, J_2/J_1, unphased Z_{ns}, and the maximum value of unphased ω. Collectively, these summary statistics capture information about the site frequency spectrum (SFS), haplotype structure, and linkage disequilibrium (LD). diploS/HIC uses a convolutional neural network (CNN) to capture essential aspects of a feature (the feature vector) by sliding a receptive field over the image to compute dot product between the original filter and the convolutional filter. In diploS/HIC, the CNN uses three branches of a CNN, of which each has two dimensional convolutional layers with ReLu activations followed by max pooling. This is followed by a dropout layer to control for model overfitting. Outputs from all three units are fed into two fully connected dense layers, which also

use dropout layers, before arriving at a softmax activation that outputs the probability for each categorical class (hard, hard-linked, neutral, soft-linked, or soft). Complete details for this procedure can be found in Kern and Schrider (2018).

When calculating feature vectors for the simulated chromosomes, we used the optional arguments for the 'fvecSim' function to mask each simulation with 110,000 bp segment randomly drawn from our masked FASTA where > 0.25 of SNVs in a subwindow were accessible (i.e., not marked by Ns). This enabled us to train our classifiers on simulated data featuring the same patterns of inaccessible genomic regions that the classifier would encounter in the empirical data.

We created a balanced set with equal representation (2×10^3) of all five classes via sampling without replacement in which to train the classifier using diploS/HIC's 'makeTrainingSets' function. These were divided into 8,000 training examples, 1,000 validation examples, and 1,000 testing examples to test the accuracy of the classifier via the 'train' function in diploS/HIC. We built ten classifiers per lineage and selected the one with the highest accuracy to apply to the empirical data (File S4).

A second, independent set of simulated chromosomes was generated per lineage using the same parameters. We then calculated feature vectors and created another balanced training set with 2×10^3 chromosomes per class (hard, linked-hard, neutral, linked-soft, and soft). We used diploS/HIC's 'predict' function by applying each trained classifier to all five classes separately per lineage. In other words, we ran each classifier on 2000 simulated hard sweeps, 2000 simulated linked-hard sweeps, 2000 simulated neutral regions, 2000 simulated linked-soft sweeps, and 2000 simulated soft sweeps and for each lineage. We used a binary classification scheme, where the identification of a sweep (hard or soft) was considered to be positive and

linked or neutral regions were negative, to assess the true positive rate, false positive rate, and obtain a second estimate of accuracy for each trained classifier (Tables S2 - S5). We also calculated class-specific accuracy, by summing the number of instances per lineage where the predicted class matched the simulated class divided by the total (1×10^4) (Tables S2 - S5).

Empirical Data Feature Vectors and Prediction

Upon achieving > 0.8 accuracy, each trained classifier was applied to its respective *Pan* lineage. Each autosome was analyzed separately and feature vectors calculated using diploS/HIC's 'fvecVcf' function. We supplied this function with the masked FASTA for that chromosome and discarded windows where any subwindow had < 0.25 unmasked sites following Schrider and Kern (2017) (File S5). This step reduces the potential effect of the number of SNVs in a given window on sweep classification. Finally, the trained classifier was applied to the feature vector files using the 'predict' function.

Sweep Identification, Potential Target Genes, and Gene Ontology

As diploS/HIC outputs the probability for each sweep class, we first report the class inferred to be the most likely. However, as the difference between the most likely class and the next most likely may be small, we further report windows where the sweep class probability is > 0.5, > 0.75, and > 0.9 (File S6). We also examined our data for spatial patterns. Windows classified as immediately abutting other windows with the same sweep type for hard and soft sweeps were considered to be a single sweep. Unique sweep windows and those shared between two or more lineages were visualized using UpSet plots (Lex et al. 2014) in R (R Core Team 2020).

We examined what genes lie in the windows identified as being subject to a recent selective sweep by extracting the genomic coordinates of all autosomal coding regions for the longest transcript per gene (N = 20,119 genes) in the panTro6 genome via the panTro6 gff (retrieved from: https://www.ncbi.nlm.nih.gov/genome/202?genome_assembly_id=380228). We used the bedtools 'intersect' function (Quinlan and Hall 2010) to identify overlap between coding regions and candidate sweep windows after converting both CDS and sweep window coordinates to 0-start, half-open format. As some coding sequences may have been masked (see Variant Filtration and Genome Accessibility above), we extracted FASTAs for each coding sequence using bedtools 'getfasta' function (Quinlan and Hall 2010) and used a custom R script to calculate the percent of each gene that was masked. Overall, 66.2% of all coding sequence was unmasked. We excluded listing genes for candidate sweep regions if > 50% of the total coding sequence per gene was masked. Thus, we considered 13,228 genes as potential targets for selective sweeps (File S7).

We investigated the enrichment of particular pathways by performing a gene ontology analysis using the Functional Annotation Tool in DAVID (Huang et al. 2008; Huang et al. 2009). We used the custom background described above (genes whose total coding sequence was > 50% unmasked) rather than all pantro6 genes to ensure our analysis was not underpowered. DAVID does not allow for official gene symbols to be used in a background list, so we converted gene symbols to Entrez gene IDs. As not all gene symbols have a corresponding Entrez gene ID, we removed genes for which there was no Entrez gene ID (N = 98 in background list). We collated genes for both hard and soft sweeps into a single input per lineage. We evaluated statistical significance for biological process gene ontology terms via p-values adjusted using the Benjamini-Hochberg method (Benjamini and Hochberg 1995).

Scripts for all data analyses are available on Github (https://github.com/brandcm/Pan_Selective_Sweeps).

Results

We generated four classifiers that reached an acceptable level of accuracy for bonobos (*P. paniscus*), central chimpanzees (*P. t. troglodytes*), eastern chimpanzees (*P. t. schweinfurthii*), and Nigeria-Cameroon (*P. t. ellioti*) chimpanzees. These classifiers ranged in accuracy from 85.6% (Nigeria-Cameroonian chimpanzees) to 93.9% (central chimpanzees) (File S4). We could not produce a sufficiently accurate classifier using realistic parameters for western chimpanzees (*P. t. verus*); therefore, they were excluded from downstream analyses. Our trained classifiers had considerable statistical power (1 - false positives) ranging from 96.6 to 99.2% and a low false positive rate (false positives / false positives + true negatives) that ranged from 1.4 to 4.3% across all four classifiers (Tables S2 - S5). When considered separately—i.e., true positives only included one sweep type (hard or soft) rather than both—we had greater power to detect hard sweeps than soft sweeps, averaging 99% and 96.9% across lineages, respectively (Tables S2 - S5). Accuracy (true positives + true negatives / total) for identifying sweep regions vs non-sweep regions ranged from 94.1 to 98.3% while a second estimate (in addition to the first accuracy estimate that resulted from the construction of the classifiers) of class-specific accuracy ranged from 81.6 to 92.1% (Tables S2 - S5).

We classified ~ 91.6% of the assembled autosomes in each lineage (Table 1, File S8), even after masking for inaccessible regions and excluding windows with few SNVs. We found that soft sweeps were abundant in all four lineages, accounting for > 73% of all individual sweeps, whereas hard sweeps were relatively rare (Table 1, File S8). This pattern held true even

when more stringent posterior probabilities were applied to consider a region a sweep and at least 30% of hard sweep windows and 76% of soft sweep windows were called with 50% or greater posterior probability (File S6). Genomic regions linked to sweeps were also quite pervasive in all four lineages (Table 1); particularly among eastern chimpanzees, where roughly 86% of the genome was classified as linked to selective sweeps.

We examined overlap in windows classified as either a hard or soft sweep across lineages, which may reflect either ancestral or parallel adaptation. Most hard sweep windows were unique to each lineage; however, we did find some shared windows across lineages (Figure 1). Central and Nigeria chimpanzees shared the highest number of sweep windows (N = 33) but when weighted by the total possible number of windows, the highest overlap for hard sweeps was between eastern and Nigeria chimpanzees (7/32 or ~ 0.21). No hard sweeps windows were shared across all lineages. Like hard sweeps, most soft sweep windows were also unique to each lineage (Figure 2). Among pairs of lineages there was remarkable consistency in the number of shared windows (N = 111-147), even when the total possible number of shared windows is considered. One exception is eastern and central chimpanzees who shared nearly twice the number of soft sweep windows (N = 267). The highest number of shared soft sweep windows between three lineages occurred in the three chimpanzee subspecies (N = 80). Only 19 windows were shared across all four lineages.

After excluding genes that were > 50% masked, we identified 1,671 candidate genes in bonobo hard and soft sweeps, 1,761 genes in central chimpanzee sweeps, 1,372 genes in eastern chimpanzee sweeps, and 1,844 genes in Nigeria-Cameroonian chimpanzee sweeps (File S9). After correcting for multiple testing, across all lineages, we identified only two significantly

enriched pathways in central chimpanzees: nervous system development and central nervous system development (File S10).

Discussion

Our study contributes to the emerging picture of recent evolution in *Pan* and adaptation more broadly. Contrary to the predictions of a mutation-limitation hypothesis, yet concordant with recent results for humans (e.g., Hernandez et al. 2011; Schrider and Kern 2017) and flies (Garud et al. 2015), we find soft sweeps to overwhelmingly predominate regions of the genome experiencing selective sweeps in both bonobos and the three chimpanzee subspecies we could analyze. These results confirm the prediction from Schmidt et al. (2019) who speculated that soft sweeps played a major role in the evolution of eastern and central chimpanzees. Those authors also posit that hard sweeps should be more frequent in western chimpanzees relative to other subspecies because of their low effective population size. While western chimpanzees are estimated to have the lowest effective population size, it is estimated to be only slightly lower than that of bonobos for which we found a high number (95.1%) of soft sweeps (e.g., Prado-Martinez et al. 2013; de Manuel et al. 2016). It is curious that Nigeria-Cameroon chimpanzees exhibit the most hard sweeps in this analysis. While this could be the result of a multitude of factors, it is particularly curious because this lineage has experienced a rather stable effective population size in recent evolutionary time as estimated by PSMC (Prado-Martinez et al. 2013; de Manuel et al. 2016), whereas a scenario with dramatic population decline would be expected to “harden” soft sweeps as haplotypes are stochastically lost, resulting in more hard sweeps (B.A. Wilson et al. 2014).

Our analysis of shared hard and soft sweeps found that most sweeps of both types were unique to each lineage. However, there was a high number of hard sweep windows shared between central and Nigeria-Cameroon chimpanzees as well as between eastern and Nigeria-Cameroon chimpanzees when the total possible number of shared sweeps was considered. Further, there were nearly twice the number of shared soft sweep windows shared between eastern and central chimpanzees. These results are similar to other recent findings (Nye et al. 2020). It is impossible to discern whether or not the overlap in hard sweeps between central and Nigeria-Cameroon chimpanzees and the overlap in soft sweeps for eastern and central chimpanzees is the result of shared ancestry and/or similar environmental conditions because both pairs of lineages share a geographic boundary: the Ubangi river for eastern and central chimpanzees and Sanaga river for central and Nigeria-Cameroon chimpanzees. The overlap in hard sweeps between eastern and Nigeria-Cameroon chimpanzees is more puzzling because they are not sister taxa and share a common ancestor ~ 600 Ka. Therefore, parallel adaptation via similar physical and/or social environments may serve as a more likely hypothesis. While the lowest in overall frequency, we also identified a number of soft sweep windows that were shared across three lineages as well as 19 windows that occurred in all four. Future work should further investigate these shared sweep windows.

As mentioned above, soft sweeps are not exclusively the result of selection on standing genetic variation (Pennings and Hermisson 2006a; Pennings and Hermisson 2006b). However, given the mutation rates estimated for bonobos and chimpanzees, it appears unlikely that recurrent *de novo* mutations explain the majority of these soft sweeps. We did not explicitly model for different types of soft sweeps in our analysis. However, while soft sweeps from standing genetic variation and *de novo* mutations may exhibit similar genomic signatures, the

hypothesis that these processes result in similar genomic signatures must be tested before any additional conclusions are drawn. Hartfield and Bataillon (2020) recently suggested differences in diversity (as measured by π) at the selected locus may be used to differentiate soft sweep types, although this may be more difficult to accomplish in outcrossing species. Nonetheless, our results reveal a major role of standing genetic variation, and thus changes in the physical and social environment, in driving recent adaptations in *Pan*.

A few recent studies have considered the impact of effective population size on adaptive evolution in the great apes (Cagan et al. 2016; Nam et al. 2017). Theory predicts that the rate of adaptive evolution should be positively correlated with effective population size when $N_e s$ is >> 1 (Gossmann et al. 2012). Both Cagan et al. (2016) and Nam et al. (2017) found a positive association between effective population size and the rate of adaptive evolution, measured by proportion of adaptive substitutions and the number of selective sweeps, respectively. However, we observed no clear linear relationship between the number of sweeps (hard, soft, or both) estimated from this analysis and the estimated effective population sizes for these four lineages (see File S3 for population sizes). This descriptive result should be considered cautiously because of the limited number of lineages analyzed here and the potential confounding effect of phylogeny. It is possible that this relationship may not be driven by the number of sweeps, but rather the strength of sweeps a population experiences (Nam et al. 2017). Estimates of selection strength are generally lacking for the great apes so this relationship remains a question for further study.

In addition to characterizing broad patterns in the genomic landscape for bonobos and chimpanzees, the results of this study also highlight thousands of candidate regions and genes for further analysis. We also find additional support for previous selection candidates. For example,

449 disease has been long thought to shape evolution in primates (Nakajima et al. 2008; van der Lee
450 et al. 2017). The potential for disease transmission between non-human primates and humans has
451 also prompted much research, particularly focusing on the genomic underpinnings of host
452 responses to lentiviruses, which include HIV and SIV (Gao et al. 1999; Van Heuverswyn et al.
453 2006; Compton et al. 2013; Nakano et al. 2020). Cagan and colleagues (2016) found evidence of
454 recent positive selection within *IDO2*, a T-cell regulatory gene, among all four-chimpanzee
455 subspecies and bonobos. We identified a candidate soft sweep region for eastern chimpanzees
456 that overlaps this gene. However, this window had one of the lowest posterior probabilities in
457 this lineage (49.7%) and there was a nearly equally high probability that this window was linked
458 to a soft sweep (43.8%). Clearly, additional work is needed to understand the potential role of
459 *IDO2* in *Pan* evolution. Schmidt et al. (2019) recently described three chemokine receptor
460 genes—*CCR3*, *CCR9*, and *CXCR6*—had a significant number of highly differentiated SNVs in
461 central chimpanzees. We could evaluate all three of these genes in our analysis but only one fell
462 within a candidate sweep window: *CXCR6*. The window containing this gene was confidently
463 called as a soft sweep with a posterior probability of 85.5%. It is not known as to whether or not
464 SIV_{cpz} uses *CXCR6* to enter chimpanzee host cells (Wetzel et al. 2018). However, multiple lines
465 of evidence for selection either at this locus or within the window overlapping this gene prompt a
466 closer examination of this genomic region. Finally, *TRIM5* fell within a hard sweep window in
467 central chimpanzees. *TRIM5* is a well-known retrovirus restriction factor that appears subject to
468 ancient, multi-episodic positive selection in primates (Sawyer et al. 2005).

469 Recent attention has focused on admixture between lineages in the genus *Pan* and the
470 potential adaptiveness of introgressed genomic elements. de Manuel and colleagues (2016)
471 identified 221 genes that fell within putatively introgressed elements in central chimpanzees

472 from admixture with bonobos. Some of this admixture is estimated to occur < 200 Ka, thus
473 within the timeframe that the present analysis can detect selective sweeps. While we could not
474 evaluate six of these 221 genes, five fell within candidate sweep regions in central chimpanzees
475 from our study: *CDK8*, *EIF4E3*, *GRID2*, *PTPRM*, and *TRIM5*. As described above, *TRIM5* was
476 unique to central chimpanzees. We found *CDK8* in sweep windows for bonobos, eastern
477 chimpanzees, and Nigeria-Cameroon chimpanzees. In humans, *CDK8* mutations have been
478 associated with multiple phenotypic effects including hypotonia, behavioral disorders, and facial
479 dysmorphism (Calpena et al. 2019). We also identified *EIF4E3* in candidate sweeps for bonobos
480 whereas *GRID2* and *PTPRM* were found in eastern chimpanzees. *EIF4E3* is a translation
481 initiation factor (Osborne et al. 2013) while *PTPRM* is a member of the protein phosphatase
482 family (PTP) and has multiple functions including cell proliferation and differentiation (Sun et
483 al. 2012). *GRID2* generates ionotropic glutamate receptors and mutations have been associated
484 with abnormalities of the cerebellum (Lalouette et al. 1998).

485 The gene ontology analysis produced only two statistically significant terms, nervous
486 system development and central nervous system development, for a single *Pan* lineage: central
487 chimpanzees. While cognitive and neurological differences are widely considered to differentiate
488 bonobos and chimpanzees (e.g., Rilling et al. 2012; Stimpson et al. 2016; Staes et al. 2019), we
489 are unaware of any studies that investigate variation among chimpanzee subspecies that may
490 explain enrichment for nervous system and central nervous system development related genes
491 specifically in central chimpanzees. We note that compared to other gene ontology analyses, our
492 level of enrichment is quite low. While we excluded a large number of genes from our analysis
493 due to poor coverage, our use of a custom background should increase, rather than decrease,
494 statistical power.

The results from our analysis should be interpreted with some caution. First, while our classifiers achieved a high degree of accuracy, it is possible that some selective sweeps in each lineage were not detected or regions were incorrectly identified as such (Tables S2 - S5). We also note that we did not model small selection coefficients ($s < 0.02$) as we could not accurately classify sweeps under weak selection, which may be the result of the large window size (1.1 Mb) used here. One consequence may be that if weakly beneficial hard sweeps are present in the empirical data, they may have been sometimes classified as soft (Harris et al. 2018). Nonetheless, our classifiers were overall quite good at identifying moderately selected hard and linked-hard sweeps with both at approximately 95% accuracy across all lineages. Neutral and linked-soft regions were the most difficult to recognize with neutral regions typically being classed as soft-linked when they did not appear neutral. This suggests that the neutral portion of the genome for each lineage is slightly underestimated here. Finally, some moderately selected soft sweeps were identified as hard sweeps in each of our classifiers, suggesting that some portion of identified hard sweeps in each lineage are, in fact, soft sweeps. The low false positive rates demonstrate the overall accuracy of the observed genomic patterns (i.e., the proportion of hard and soft sweeps) for these taxa. However, this point underscores the need to conduct subsequent analyses of the candidate regions and genes to confirm such the proposed mode of adaptation and investigate any functional consequences of that adaptation. In the ‘era of -omics’, the generation of candidate regions for any type of selection across populations and species appears to overwhelmingly outpace the confirmation of such patterns. Avenues of research that investigate these candidate genes in more detail are thus well poised to provide a deeper and more accurate understanding of lineage-specific adaptations.

Second, background selection, the loss of a linked neutral site from purifying selection on a deleterious allele, can potentially mimic patterns of selective sweeps and thus may impact the results of this study (Charlesworth et al. 1993). We did not explicitly model background selection in our analysis, however, evidence from simulations in various taxa demonstrate that this pattern of selection does not substantially increase the rate of false positives in selective sweep analyses (Schrider and Kern 2017; Schrider 2020). Further, Nam et al. (2017) considered the effect of background selection on genomic diversity in extant apes, including all five *Pan* lineages, and note that background selection alone does not produce the observed diversity reduction near genic regions in these lineages. While background selection may not largely affect certain selective sweep analyses, it may impact estimations of demography that are inferred using PSMC/MSMC approaches (Johri, Riall, et al. 2020; Johri, Charlesworth, et al. 2020). The demographic strings calculated from PSMC used in this analysis also broadly agree in population size shape with other demographic estimates generated using other methods (e.g., Becquet and Przeworski (2007); Hey (2010)), therefore, background selection unlikely affects the demographic models used in analysis. Yet, this issue should be strongly considered in future studies where demography is only inferred from PSMC/MSMC.

Further, sampling bias can reduce the accuracy of identifying selective sweeps. If multiple haplotypes are present in a population but only individuals sharing one haplotype are sampled, then the sweep would be classified as a hard sweep when it is a soft sweep. However, this scenario would only underestimate the degree of recent adaptation from soft sweeps. Therefore, if this sampling bias is present in this analysis, then soft sweeps may predominate recent *Pan* evolution to an even larger degree than described here. Population structure adds further complications to the classification of hard sweeps. Parallel adaptation produces multi-

origin soft sweeps at the global population level that would appear to be hard in local populations, although even local samples may sometimes appear to be soft sweeps (Ralph and Coop 2010). Thus, if samples stemmed from one or few local populations then global soft sweeps may be misclassified as hard. A previous analysis estimated the geographic origin of individuals used in this analysis (de Manuel et al. 2016). These authors found that individuals from both eastern and central chimpanzee populations were sampled from multiple countries across the geographic range for both subspecies. Therefore, any hard sweeps detected in these populations are likely accurate at the subspecies level. Geographic origin could not be assessed for any of the bonobos or all of the Nigeria-Cameroon chimpanzees used in this analysis (de Manuel et al. 2016). As such, sampling or geographic bias may partially explain the high degree of hard sweeps observed in Nigeria-Cameroon chimpanzees, if they were sampled from a smaller geographic area than the other subspecies. We encourage future studies to consider this potential bias when hard sweeps are encountered in existing data and during study design.

This analysis focuses on signatures of positive selection at single loci. However, there is theoretical and empirical evidence that a number of adaptive traits have a complex, multilocus architecture (Pritchard et al. 2010; Yang et al. 2017; Bergey et al. 2018). For these polygenic traits, shifts in the physical or social environment might result in allele frequency changes at many loci, of which, according to models, few to none of which would reach fixation (Pritchard et al. 2010). This may, in part, explain why hard sweeps appear to be rare in humans and other species if it represents a dominant mode of adaptation in these taxa. Unfortunately, at this point, we lack the data and methods to investigate the extent of polygenic selection across the genome in many non-model taxa such as *Pan*. Another factor to consider is dominance. Here, we assumed advantageous alleles were codominant, however, there is evidence that dominance may

influence patterns of selective sweeps when variants occur via *de novo* mutation or recurrent mutation (Hartfield and Bataillon 2020). It is also worthwhile to address that this analysis explicitly focused on modelling very recent completed selective sweeps. Another future avenue of study in these lineages is the identification of incomplete or partial sweeps using existing approaches (Ferrer-Admetlla et al. 2014; Vy and Kim 2015) as well as explicitly modelling both incomplete and complete sweeps to address potential "temporal misclassification" (Zheng and Wiehe 2019).

Finally, while our approach to identifying hard and soft sweeps is a logical first step, future work should consider sweeps within subspecies to assess population-level (i.e., local), rather than lineage-specific (i.e., global) adaptations. This is underscored by the extensive phenotypic variation among chimpanzees, particularly that of behavioral variation, which includes key characteristics that are often used to dichotomize bonobos and chimpanzees (Wilson et al. 2014). Further investigation is also clearly warranted in bonobos, whose overall phenotypic variation is likely underappreciated compared to chimpanzees (Hohmann and Fruth 2003; Sakamaki et al. 2016; Beaune et al. 2017; Wakefield et al. 2019).

Conclusion

This study highlights the importance of changes in physical and/or social environment via soft selective sweeps in the recent evolution of our closest living relatives, chimpanzees and bonobos. Our results also yield further support for the ubiquity of soft, rather than hard, sweeps in adaptation. We contribute candidate regions and genes that may help identify unique phenotypes in each *Pan* lineage. Our findings also prompt many new questions including the estimation of selection strength coefficients and the degree of haplotypic diversity in candidate

sweep regions. While our study focuses on these lineages broadly, this point also underscores the need for high-coverage genomic data collected using non-invasive methods at more local geographies.

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References

Andrews S. 2010. FASTQC. A quality control tool for high throughput sequence data. Available from: http://www.bioinformatics.babraham.ac.uk/projects/fastqc

Antón SC, Potts R, Aiello LC. 2014. Evolution of early *Homo*: An integrated biological perspective. Science 345:1236828.

Barratt CD, Lester JD, Gratton P, Onstein RE, Kalan AK, McCarthy MS, Bocksberger G, White LC, Vigilant L, Dieguez P, et al. 2020. Late Quaternary habitat suitability models for chimpanzees (*Pan troglodytes*) since the Last Interglacial (120,000 BP). *bioRxiv* [Internet]. Available from: http://biorxiv.org/content/early/2020/05/25/2020.05.15.066662

Barrett RDH, Hoekstra HE. 2011. Molecular spandrels: tests of adaptation at the genetic level. *Nat Rev Genet.* 12:767–780.

612 Beaune D, Hohmann G, Serckx A, Sakamaki T, Narat V, Fruth B. 2017. How bonobo
613 communities deal with tannin rich fruits: Re-ingestion and other feeding processes. *Behav*
614 *Process.* 142:131–137.

615 Becquet C, Przeworski M. 2007. A new approach to estimate parameters of speciation models
616 with application to apes. *Genome Res.* 17:1505–1519.

617 Behringer V, Deschner T, Deimel C, Stevens JMG, Hohmann G. 2014. Age-related changes in
618 urinary testosterone levels suggest differences in puberty onset and divergent life history
619 strategies in bonobos and chimpanzees. *Horm Behav.* 66:525–533.

620 Benjamini Y, Hochberg Y. 1995. Controlling the false discovery rate: a practical and powerful
621 approach to multiple testing. *J R Stat Soc Series B Stat Methodol* 57:289–300.

622 Bergey CM, Lopez M, Harrison GF, Patin E, Cohen JA, Quintana-Murci L, Barreiro LB, Perry
623 GH. 2018. Polygenic adaptation and convergent evolution on growth and cardiac genetic
624 pathways in African and Asian rainforest hunter-gatherers. *Proc Natl Acad Sci USA.*
625 115:E11256.

626 Besenbacher S, Hvilsom C, Marques-Bonet T, Mailund T, Schierup MH. 2019. Direct estimation
627 of mutations in great apes reconciles phylogenetic dating. *Nat Ecol Evol.* 3:286–292.

628 Bradley BJ. 2008. Reconstructing phylogenies and phenotypes: a molecular view of human
629 evolution. *J Anat.* 212:337–353.

630 Broad Institute. 2018. Picard Tools. Available from: http://broadinstitute.github.io/picard/

631 Cagan A, Theunert C, Laayouni H, Santpere G, Pybus M, Casals F, Prüfer K, Navarro A,
632 Marques-Bonet T, Bertranpetit J, et al. 2016. Natural selection in the great apes. *Mol Biol*
633 *Evol.* 33:3268–3283.

634 Calpena E, Hervieu A, Kaserer T, Swagemakers SMA, Goos JAC, Popoola O, Ortiz-Ruiz MJ,
635 Barbaro-Dieber T, Bownass L, Brilstra EH, et al. 2019. De novo missense substitutions in
636 the gene encoding CDK8, a regulator of the mediator complex, cause a syndromic
637 developmental disorder. *Am J Hum Genet.* 104:709–720.

638 Charlesworth B, Morgan MT, Charlesworth D. 1993. The effect of deleterious mutations on
639 neutral molecular variation. Genetics 134:1289–1303.

640 Compton AA, Malik HS, Emerman M. 2013. Host gene evolution traces the evolutionary history
641 of ancient primate lentiviruses. *Philos Trans R Soc B.* 368:20120496.

642 Ewels P, Magnusson M, Lundin S, Käller M. 2016. MultiQC: summarize analysis results for
643 multiple tools and samples in a single report. Bioinformatics 32:3047–3048.

644 Ferrer-Admetlla A, Liang M, Korneliussen T, Nielsen R. 2014. On detecting incomplete soft or
645 hard selective sweeps using haplotype structure. *Mol Biol Evol.* 31:1275–1291.

646 Furuichi T. 2011. Female contributions to the peaceful nature of bonobo society. *Ev Anth.*
647 20:131–142.

648 Gao F, Bailes E, Robertson DL, Chen Y, Rodenburg CM, Michael SF, Cummins LB, Arthur LO,
649 Peeters M, Shaw GM, et al. 1999. Origin of HIV-1 in the chimpanzee *Pan troglodytes*
650 *troglodytes*. Nature 397:436–441.

651 Garud NR, Messer PW, Buzbas EO, Petrov DA. 2015. Recent selective sweeps in North
652 American *Drosophila melanogaster* show signatures of soft sweeps. *PLoS Genet.*
653 11:e1005004.

654 Goodall J. 1986. The chimpanzees of Gombe: Patterns of behavior. Cambridge, MA: Belknap
655 Press.

656 Gossmann TI, Keightley PD, Eyre-Walker A. 2012. The Effect of Variation in the Effective
657 Population Size on the Rate of Adaptive Molecular Evolution in Eukaryotes. *Genome*
658 *Biol Evol.* 4:658–667.

659 Grüning B, Dale R, Sjödin A, Chapman BA, Rowe J, Tomkins-Tinch CH, Valieris R, Köster J,
660 The Bioconda Team. 2018. Bioconda: sustainable and comprehensive software
661 distribution for the life sciences. *Nat Methods* 15:475–476.

662 Han S, Andrés AM, Marques-Bonet T, Kuhlwilm M. 2019. Genetic variation in *Pan* species is
663 shaped by demographic history and harbors lineage-specific functions. *Genome Biol*
664 *Evol.* 11:1178–1191.

665 Harris RB, Sackman A, Jensen JD. 2018. On the unfounded enthusiasm for soft selective sweeps
666 II: Examining recent evidence from humans, flies, and viruses. *PLoS Genet.*
667 14:e1007859.

668 Hartfield M, Bataillon T. 2020. Selective sweeps under dominance and inbreeding. G3 10:1063.

669 Henn BM, Cavalli-Sforza LL, Feldman MW. 2012. The great human expansion. *Proc Natl Acad*
670 *Sci USA.* 109:17758.

671 Hermisson J, Pennings PS. 2005. Soft sweeps: Molecular population genetics of adaptation from
672 standing genetic variation. Genetics 169:2335–2352.

673 Hermisson J, Pennings PS. 2017. Soft sweeps and beyond: understanding the patterns and
674 probabilities of selection footprints under rapid adaptation. *Methods Ecol Evol.* 8:700–
675 716.

676 Hernandez RD, Kelley JL, Elyashiv E, Melton SC, Auton A, McVean G, Project 1000 Genomes,
677 Sella G, Przeworski M. 2011. Classic selective sweeps were rare in recent human
678 evolution. Science 331:920–924.

679 Hey J. 2010. The divergence of chimpanzee species and subspecies as revealed in
680 multipopulation isolation-with-migration analyses. *Mol Biol Evol.* 27:921–933.

681 Hohmann G, Fruth B. 2003. Culture in bonobos? Between□species and within□species variation
682 in behavior. *Curr Anthropol.* 44:563–571.

683 Huang DW, Sherman BT, Lempicki RA. 2008. Bioinformatics enrichment tools: paths toward
684 the comprehensive functional analysis of large gene lists. *Nucleic Acids Res.* 37:1–13.

685 Huang DW, Sherman BT, Lempicki RA. 2009. Systematic and integrative analysis of large gene
686 lists using DAVID bioinformatics resources. *Nat Protoc.* 4:44–57.

687 Jensen JD. 2014. On the unfounded enthusiasm for soft selective sweeps. *Nat Commun.* 5:5281.

688 Johri P, Charlesworth B, Jensen JD. 2020. Toward an evolutionarily appropriate null model:
689 Jointly inferring demography and purifying selection. Genetics 215:173.

690 Johri P, Riall K, Becher H, Charlesworth B, Jensen JD. 2020. The impact of purifying and
691 background selection on the inference of population history: problems and prospects.
692 *bioRxiv*:2020.04.28.066365.

693 Kalan AK, Kulik L, Arandjelovic M, Boesch C, Haas F, Dieguez P, Barratt CD, Abwe EE,
694 Agbor A, Angedakin S, et al. 2020. Environmental variability supports chimpanzee
695 behavioural diversity. *Nat Commun.* 11:4451.

696 Kano T. 1992. The last ape: Pygmy chimpanzee behavior and ecology. Stanford: Stanford
697 University Press.

698 Kern AD, Schrider DR. 2016. Discoal: flexible coalescent simulations with selection.
699 Bioinformatics 32:3839–3841.

700 Kern AD, Schrider DR. 2018. diploS/HIC: An updated approach to classifying selective sweeps.
701 G3 8:1959–1970.

702 Köster J, Rahmann S. 2012. Snakemake—a scalable bioinformatics workflow engine.
703 Bioinformatics 28:2520–2522.

704 Kovalaskas S, Rilling JK, Lindo J. 2020. Comparative analyses of the Pan lineage reveal
705 selection on gene pathways associated with diet and sociality in bonobos. *Genes Brain*
706 *Behav.* n/a:e12715.

707 Kronenberg ZN, Fiddes IT, Gordon D, Murali S, Cantsilieris S, Meyerson OS, Underwood JG,
708 Nelson BJ, Chaisson MJP, Dougherty ML, et al. 2018. High-resolution comparative
709 analysis of great ape genomes. Science [Internet] 360. Available from:
710 https://science.sciencemag.org/content/360/6393/eaar6343

711 Kuhlwilm M, Han S, Sousa VC, Excoffier L, Marques-Bonet T. 2019. Ancient admixture from
712 an extinct ape lineage into bonobos. *Nat Ecol Evol.* 3:957–965.

713 Lalouette A, Guénet J-L, Vriz S. 1998. Hotfoot mouse mutations affect the δ2 glutamate receptor
714 gene and are allelic to lurcher. Genomics 50:9–13.

715 Langergraber KE, Prüfer K, Rowney C, Boesch C, Crockford C, Fawcett K, Inoue E, Inoue-
716 Muruyama M, Mitani JC, Muller MN, et al. 2012. Generation times in wild chimpanzees
717 and gorillas suggest earlier divergence times in great ape and human evolution. *Proc Natl*
718 *Acad Sci USA.* 109:15716.

719 Lex A, Gehlenborg N, Strobelt H, Vuillemot R, Pfister H. 2014. UpSet: Visualization of
720 intersecting sets. *IEEE Transactions on Visualization and Computer Graphics* 20:1983–
721 1992.

722 Li H. 2011. A statistical framework for SNP calling, mutation discovery, association mapping
723 and population genetical parameter estimation from sequencing data. Bioinformatics
724 27:2987–2993.

725 Li H, unpublished data, https://arxiv.org/abs/1303.3997

726 Li H, Handsaker B, Wysoker A, Fennell T, Ruan J, Homer N, Marth G, Abecasis G, Durbin R,
727 1000 Genome Project Data Processing Subgroup. 2009. The sequence alignment/map
728 format and SAMtools. Bioinformatics 25:2078–2079.

729 de Manuel M, Kuhlwilm M, Frandsen P, Sousa VC, Desai T, Prado-Martinez J, Hernandez-
730 Rodriguez J, Dupanloup I, Lao O, Hallast P, et al. 2016. Chimpanzee genomic diversity
731 reveals ancient admixture with bonobos. Science 354:477–481.

732 Maynard Smith J, Haigh J. 1974. The hitch-hiking effect of a favourable gene. *Genet Res.* 23:23–
733 35.

734 Messer PW, Petrov DA. 2013. Population genomics of rapid adaptation by soft selective sweeps.
735 *Trends Ecol Evol.* 28:659–669.

736 Mughal MR, DeGiorgio M. 2019. Localizing and classifying adaptive targets with trend filtered
737 regression. *Mol Biol Evol.* 36:252–270.

738 Nakajima T, Ohtani H, Satta Y, Uno Y, Akari H, Ishida T, Kimura A. 2008. Natural selection in
739 the TLR-related genes in the course of primate evolution. Immunogenetics 60:727–735.

740 Nakano Y, Yamamoto K, Ueda MT, Soper A, Konno Y, Kimura I, Uriu K, Kumata R, Aso H,
741 Misawa N, et al. 2020. A role for gorilla APOBEC3G in shaping lentivirus evolution
742 including transmission to humans. *PLoS Pathog.* 16:e1008812.

743 Nam K, Munch K, Mailund T, Nater A, Greminger MP, Krützen M, Marquès-Bonet T, Schierup
744 MH. 2017. Evidence that the rate of strong selective sweeps increases with population
745 size in the great apes. *Proc Natl Acad Sci USA.* 114:1613–1618.

746 Narasimhan VM, Rahbari R, Scally A, Wuster A, Mason D, Xue Y, Wright J, Trembath RC,
747 Maher ER, Heel DA van, et al. 2017. Estimating the human mutation rate from
748 autozygous segments reveals population differences in human mutational processes. *Nat*
749 *Commun.* 8:1–7.

750 Nishida T. 2011. Chimpanzees of the lakeshore: Natural history and culture at Mahale.
751 Cambridge: Cambridge University Press.

752 Nye J, Mondal M, Bertranpetit J, Laayouni H. 2020. A fully integrated machine learning scan of
753 selection in the chimpanzee genome. *NAR Genom Bioinform.* [Internet] 2. Available
754 from: https://doi.org/10.1093/nargab/lqaa061

755 Oleksyk TK, Smith MW, O'Brien SJ. 2010. Genome-wide scans for footprints of natural
756 selection. *Philos Trans R Soc B.* 365:185–205.

757 Osborne MJ, Volpon L, Kornblatt JA, Culjkovic-Kraljacic B, Baguet A, Borden KLB. 2013.
758 eIF4E3 acts as a tumor suppressor by utilizing an atypical mode of methyl-7-guanosine
759 cap recognition. *Proc Natl Acad Sci USA.* 110:3877.

760 Pedersen BS, Quinlan AR. 2018. Mosdepth: quick coverage calculation for genomes and
761 exomes. Bioinformatics 34:867–868.

762 Pennings PS, Hermisson J. 2006a. Soft sweeps II—Molecular population genetics of adaptation
763 from recurrent mutation or immigration. *Mol Biol Evol*. 23:1076–1084.

764 Pennings PS, Hermisson J. 2006b. Soft sweeps III: The signature of positive selection from
765 recurrent mutation. *PLoS Genet.* 2:e186.

766 Poplin R, Ruano-Rubio V, DePristo MA, Fennell TJ, Carneiro MO, Van der Auwera GA, Kling
767 DE, Gauthier LD, Levy-Moonshine A, Roazen D, et al. 2018. Scaling accurate genetic
768 variant discovery to tens of thousands of samples. *bioRxiv*:201178.

769 Potts R. 1998. Variability selection in hominid evolution. *Ev Anth.* 7:81–96.

770 Prado-Martinez J, Sudmant PH, Kidd JM, Li H, Kelley JL, Lorente-Galdos B, Veeramah KR,
771 Woerner AE, O'Connor TD, Santpere G, et al. 2013. Great ape genetic diversity and
772 population history. Nature 499:471–475.

773 Pritchard JK, Pickrell JK, Coop G. 2010. The genetics of human adaptation: Hard sweeps, soft
774 sweeps, and polygenic adaptation. *Curr Biol.* 20:R208–R215.

775 Prüfer K, Munch K, Hellmann I, Akagi K, Miller JR, Walenz B, Koren S, Sutton G, Kodira C,
776 Winer R, et al. 2012. The bonobo genome compared with the chimpanzee and human
777 genomes. Nature 486:527–531.

778 Quinlan AR, Hall IM. 2010. BEDTools: a flexible suite of utilities for comparing genomic
779 features. Bioinformatics 26:841–842.

780 R Core Team. 2020. R: A Language and Environment for Statistical Computing. Vienna,
781 Austria: R Foundation for Statistical Computing Available from: https://www.R-
782 project.org/

783 Ralph P, Coop G. 2010. Parallel adaptation: One or many waves of advance of an advantageous
784 allele? Genetics 186:647–668.

785 Rilling JK, Scholz J, Preuss TM, Glasser MF, Errangi BK, Behrens TE. 2012. Differences
786 between chimpanzees and bonobos in neural systems supporting social cognition. *Soc*
787 *Cogn Affect Neurosci.* 7:369–379.

788 Sakamaki T, Maloueki U, Bakaa B, Bongoli L, Kasalevo P, Terada S, Furuichi T. 2016.
789 Mammals consumed by bonobos (*Pan paniscus*): new data from the Iyondji forest,
790 Tshuapa, Democratic Republic of the Congo. Primates 57:295–301.

791 Sarich VM, Wilson AC. 1967. Immunological time scale for hominid evolution. Science
792 158:1200.

793 Sawyer SL, Wu LI, Emerman M, Malik HS. 2005. Positive selection of primate *TRIM5α*
794 identifies a critical species-specific retroviral restriction domain. *Proc Natl Acad Sci*
795 *USA.* 102:2832.

796 Scally A, Dutheil JY, Hillier LW, Jordan GE, Goodhead I, Herrero J, Hobolth A, Lappalainen T,
797 Mailund T, Marques-Bonet T, et al. 2012. Insights into hominid evolution from the
798 gorilla genome sequence. Nature 483:169–175.

799 Schiffels S, Durbin R. 2014. Inferring human population size and separation history from
800 multiple genome sequences. *Nat Genet.* 46:919–925.

801 Schmidt JM, Manuel M de, Marques-Bonet T, Castellano S, Andrés AM. 2019. The impact of
802 genetic adaptation on chimpanzee subspecies differentiation. *PLoS Genet.* 15:e1008485.

803 Schrider DR. 2020. Background selection does not mimic the patterns of genetic diversity
804 produced by selective sweeps. Genetics 216:499–519.

805 Schrider DR, Kern AD. 2017. Soft sweeps are the dominant mode of adaptation in the human
806 genome. *Mol Biol Evol.* 34:1863–1877.

807 Schrider DR, Mendes FK, Hahn MW, Kern AD. 2015. Soft shoulders ahead: Spurious signatures
808 of soft and partial selective sweeps result from linked hard sweeps. Genetics 200:267–
809 284.

810 Staes N, Smaers JB, Kunkle AE, Hopkins WD, Bradley BJ, Sherwood CC. 2019. Evolutionary
811 divergence of neuroanatomical organization and related genes in chimpanzees and
812 bonobos. Cortex 118:154–164.

813 Stevison LS, Woerner AE, Kidd JM, Kelley JL, Veeramah KR, McManus KF, Great Ape
814 Genome Project, Bustamante CD, Hammer MF, Wall JD. 2015. The time scale of
815 recombination rate evolution in great apes. *Mol Biol Evol.* 33:928–945.

816 Stimpson CD, Barger N, Taglialatela JP, Gendron-Fitzpatrick A, Hof PR, Hopkins WD,
817 Sherwood CC. 2016. Differential serotonergic innervation of the amygdala in bonobos
818 and chimpanzees. *Soc Cogn Affect Neurosci.* 11:413–422.

819 Stumpf RM. 2011. Chimpanzees and bonobos: Inter- and intraspecies diversity. In: Campbell CJ,
820 Fuentes A, MacKinnon KC, Bearder SK, Stumpf RM, editors. Primates in perspective.
821 New York: Oxford University Press. p. 340–356.

822 Sun P-H, Ye L, Mason MD, Jiang WG. 2012. Protein tyrosine phosphatase μ (PTP μ or
823 PTPRM), a negative regulator of proliferation and invasion of breast cancer cells, is
824 associated with disease prognosis. *PLOS ONE* 7:e50183.

825 Susman RL ed. 1984. The pygmy chimpanzee: Evolutionary biology and behavior. New York:
826 Springer.

827 Takemoto H, Kawamoto Y, Higuchi S, Makinose E, Hart JA, Hart TB, Sakamaki T, Tokuyama
828 N, Reinartz GE, Guislain P, et al. 2017. The mitochondrial ancestor of bonobos and the
829 origin of their major haplogroups. *PLOS ONE* 12:e0174851.

830 Turley K, Frost SR. 2014. The appositional articular morphology of the talo-crural joint: The
831 influence of substrate use on joint shape. *Anat Rec.* 297:618–629.

832 Van Heuverswyn F, Li Y, Neel C, Bailes E, Keele BF, Liu W, Loul S, Butel C, Liegeois F,
833 Bienvenue Y, et al. 2006. SIV infection in wild gorillas. Nature 444:164–164.

834 van der Lee R, Wiel L, van Dam TJP, Huynen MA. 2017. Genome-scale detection of positive
835 selection in nine primates predicts human-virus evolutionary conflicts. *Nucleic Acids Res.*
836 45:10634–10648.

837 Vy HMT, Kim Y. 2015. A composite-likelihood method for detecting incomplete selective
838 sweep from population genomic data. Genetics 200:633.

839 Wakefield ML, Hickmott AJ, Brand CM, Takaoka IY, Meador LM, Waller MT, White FJ. 2019.
840 New observations of meat eating and sharing in wild bonobos (*Pan paniscus*) at Iyema,
841 Lomako Forest Reserve, Democratic Republic of the Congo. *Fol Primatol*. 90:179–189.

842 Webster TH, Couse M, Grande BM, Karlins E, Phung TN, Richmond PA, Whitford W, Wilson
843 MA. 2019. Identifying, understanding, and correcting technical artifacts on the sex
844 chromosomes in next-generation sequencing data. Gigascience [Internet] 8. Available
845 from: https://academic.oup.com/gigascience/article/8/7/giz074/5530326

846 Webster TH, Wilson Sayres MA. 2016. Genomic signatures of sex-biased demography: progress
847 and prospects. *Curr Opin Genet.* 41:62–71.

848 Wegmann D, Excoffier L. 2010. Bayesian inference of the demographic history of chimpanzees.
849 *Mol Biol Evol.* 27:1425–1435.

Wetzel KS, Yi Y, Yadav A, Bauer AM, Bello EA, Romero DC, Bibollet-Ruche F, Hahn BH, Paiardini M, Silvestri G, et al. 2018. Loss of CXCR6 coreceptor usage characterizes pathogenic lentiviruses. *PLoS Pathog.* 14:e1007003.

White FJ. 1996. *Pan paniscus* 1973 to 1996: Twenty-three years of field research. *Ev Anth.* 5:11–17.

Wickham H. 2016. ggplot2: Elegant Graphics for Data Analysis. New York: Springer-Verlag Available from: https://ggplot2.tidyverse.org

Wilson BA, Petrov DA, Messer PW. 2014. Soft selective sweeps in complex demographic scenarios. Genetics 198:669.

Wilson ML, Boesch C, Fruth B, Furuichi T, Gilby IC, Hashimoto C, Hobaiter CL, Hohmann G, Itoh N, Koops K, et al. 2014. Lethal aggression in *Pan* is better explained by adaptive strategies than human impacts. Nature 513:414–417.

Wrangham RW. 1986. Ecology and social relationships in two species of chimpanzee. In: Rubenstein DI, Wrangham RW, editors. Ecological aspects of social evolution: Birds and mammals. Princeton, NJ: Princeton University Press. p. 352–378.

Yang J, Jin Z-B, Chen J, Huang X-F, Li X-M, Liang Y-B, Mao J-Y, Chen X, Zheng Z, Bakshi A, et al. 2017. Genetic signatures of high-altitude adaptation in Tibetans. *Proc Natl Acad Sci USA.* 114:4189.

Zheng Y, Wiehe T. 2019. Adaptation in structured populations and fuzzy boundaries between hard and soft sweeps. *PLoS Comput Biol.* 15:e1007426.

872 Table 1. Selective sweep summary per population.

	Number / Percent of Windows per Class Type						Number and Percent of Sweep Type		
Lineage	Hard	Linked-hard	Neutral	Linked-soft	Soft	Total	Hard	Soft	Total
P. paniscus	85 (0.4%)	1,576 (6.5%)	7,488 (30.8%)	13,168 (54.1%)	2,002 (8.2%)	24,319	81 (4.9%)	1,585 (95.1%)	1,666
P. t. ellioti	573 (2.4%)	6,358 (26.1%)	1,389 (5.7%)	14,498 (59.6%)	1,505 (6.2%)	24,323	488 (26.9%)	1,323 (73.1%)	1,811
P. t. schweinfurthii	32 (0.1%)	696 (2.9%)	1,835 (7.5%)	20,179 (83.0%)	1,581 (6.5%)	24,323	32 (2.3%)	1,376 (97.7%)	1,408
P. t. troglodytes	224 (0.9%)	1,746 (7.2%)	5,483 (22.5%)	15,121 (62.2%)	1,749 (7.2%)	24,323	184 (10.6%)	1,557 (89.4%)	1,741

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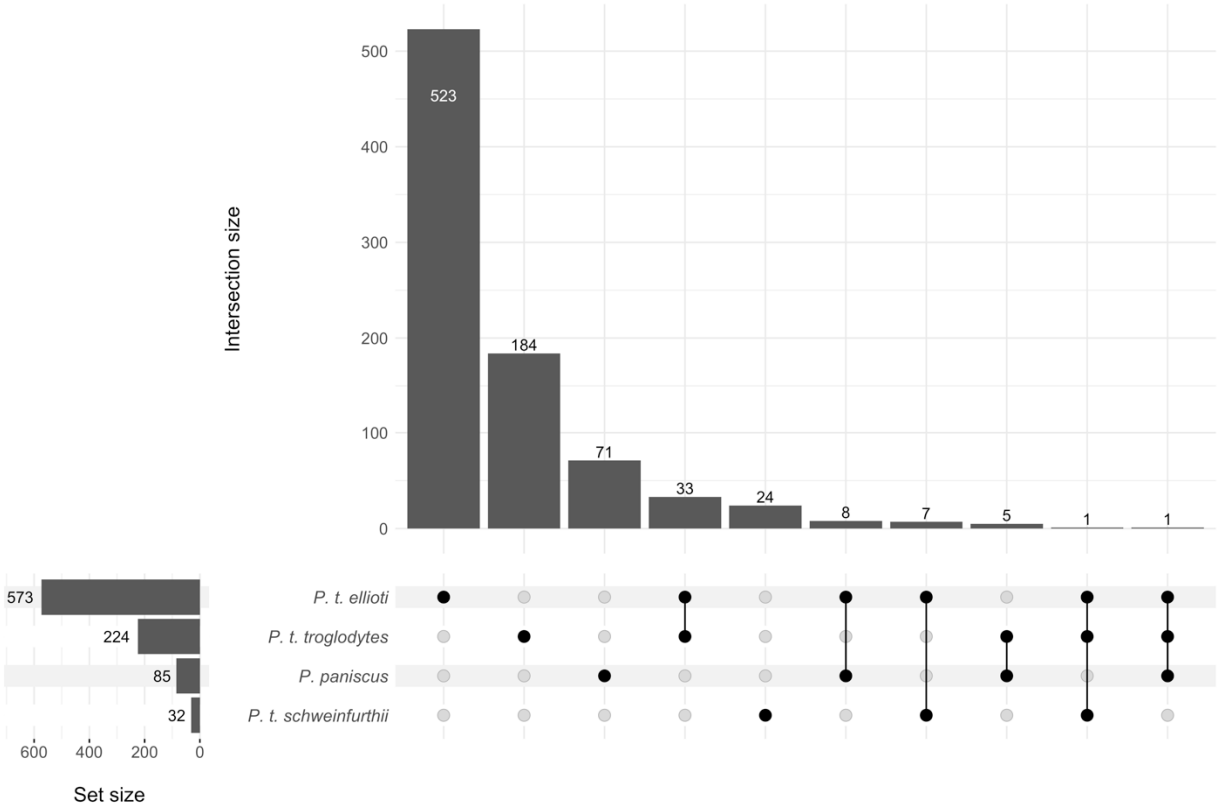
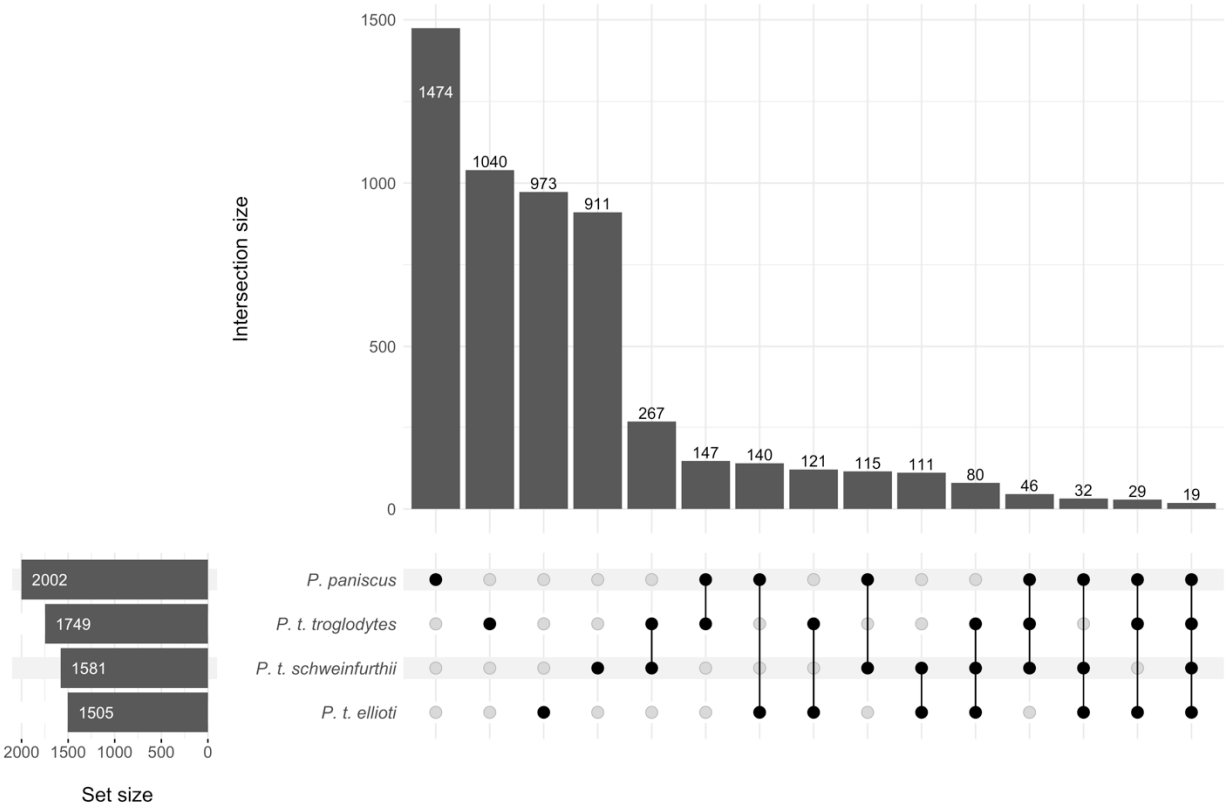
875 Figure 1. Unique and shared hard sweep windows. The frequency of windows shared by two or
876 more lineages should be considered relative to the total possible number of shared windows (i.e.,
877 the set size of the lineage with the smallest set size).



878

879 Figure 2. Unique and shared soft sweep windows. The frequency of windows shared by two or
880 more lineages should be considered relative to the total possible number of shared windows (i.e.,
881 the set size of the lineage with the smallest set size).



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Supplements.

- Main Supplemental File: Figures S1 - S3, Tables S1-S4.
- File S1. Sample information. (File name: File_S1_sample_information.xlsx)
- File S2. Genome accessibility information. (File name: File_S2_genome_accessibility.xlsx)
- File S3. Discoal parameter information. (File name: File_S3_discoal_input_summary.xlsx)
- File S4. Classifier trial information. (File name: File_S4_diploshic_classifier_summary.xlsx)
- File S5. Unmasked SNV count/fraction per window for VCF feature vectors. (File name: File_S5_fvec_vcf_unmaskedsnpcount_unmaskedfrac_summary)
- File S6. Number of hard and soft sweep windows using higher probability thresholds. (File name: File_S6_sweeptype_probability_cutoff_summary.xlsx)
- File S7. Genes included in sweep analysis (File name: File_S7_genes_to_include.xlsx)
- File S8. Sweep information. (File name: File_S8_selective_sweep_summary.xlsx)
- File S9. List of genes in hard and soft sweeps. (File name: File_S9_gene_lists.xlsx)
- File S10. Gene ontology analysis. (File name: File_S10_gene_ontology.xlsx)