



Julie Edwards/Stockimo/Alamy

Whole-genome sequencing of Neanderthals and Denisovans has shown that modern humans contain genetic material from these archaic hominins. Methods to detect introgression (genetic exchange by hybridization and backcrossing) either involve comparison with a reference genome or are reference-free. Now, Browning *et al.* report the development of an improved reference-free method to detect archaic introgression.

The new method, SPrime (S'), is similar to the S^* statistic, which is an established reference-free method to identify introgressed sequences. Comparing the performance of S' and two versions of the S^* statistic using simulated data confirmed that S' had a better detection frequency for the same level of accuracy and is suitable for use with large, genome-wide data sets. There are a number of possible reasons for this improved performance: unlike S^* , S' avoids windowing (analysis of discrete blocks of sequence), so its power increases with the size of the introgressed region; S' uses a different scoring function; and S' performs simultaneous analysis of more individuals than S^* . Additionally, the accuracy of S' is maintained in the face of a wide range of mutation rates, allele frequencies and demographic histories.

To identify putative archaic alleles in modern humans, the authors applied S' to whole-genome sequences of 5,639 individuals from Eurasia and Oceania, which were obtained from a number of genome sequencing projects (for example, the 1,000 Genomes Project and the UK10K study). Across all populations analysed, 1.36 Gb of the genome was covered with putative introgressed segments, and the introgression rates detected were similar to other studies.

The authors then compared the putative archaic introgressed segments to the genomes of Neanderthals and Denisovans. The results of this analysis are consistent with at least one wave of admixture of modern humans with Neanderthals and imply that there were at least two waves of admixture with Denisovans. Interestingly, there seemed to be positive selection of some introgressed regions, all of which were from Neanderthals, and several of which contained genes involved in pigmentation and immunity.

The S' method should prove useful for mapping introgressed archaic hominin sequences in the genome of modern humans, owing to its computational efficiency and its availability in the free SPrime software package.

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ORIGINAL ARTICLE Browning, S. R. *et al.* Analysis of human sequence data reveals two pulses of archaic Denisovan admixture. *Cell* <https://doi.org/10.1016/j.cell.2018.02.031> (2018)
WEB SITE <http://faculty.washington.edu/browning/sprime.html>