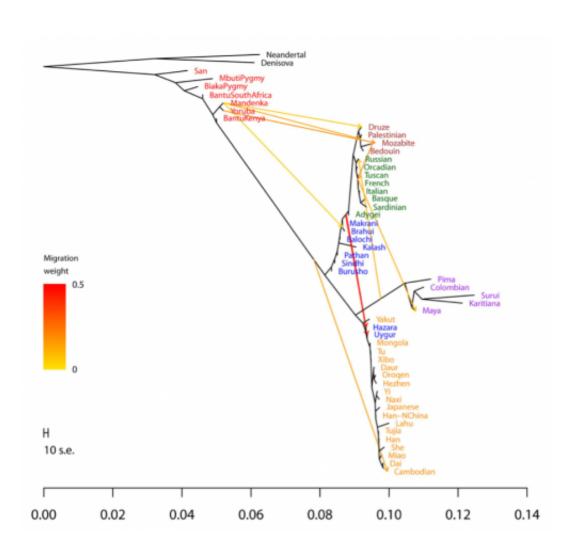


A history lesson from genes: Using DNA to tell us how populations change

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This is a graph produced by the TreeMix software showing human population splits and migration events. Credit: Jonathan Pritchard



When Charles Darwin first sketched how species evolved by natural selection, he drew what looked like a tree. The diagram started at a central point with a common ancestor, then the lines spread apart as organisms evolved and separated into distinct species.

In the 175 years since, scientists have come to agree that Darwin's original drawing is a bit simplistic, given that multiple species mix and interbreed in ways he didn't consider possible (though you can't fault the guy for not getting the most important <u>scientific theory</u> of all time exactly right the first time). Using a tree-like structure is a great way to show the history of the evolution of a species, or its phylogeny. But it's not so great for showing the population history of groups within a single species, such as humans, who can move around and interbreed with each other.

Jonathan Pritchard, PhD, professor in the department of human genetics, studies the nature of these human genetic variations by combining methods from evolutionary biology and statistics. Intrigued by recent research on the Neanderthal genome that suggests more interbreeding with Homo sapiens than previously thought, Pritchard wanted to develop a general method for estimating gene flow between different groups within the same species over time. In a recent paper published in PLOS Genetics, he and Joseph Pickrell, a former University of Chicago researcher now at Harvard, described a software model they developed that can infer the history of population splits and mixtures within a species based on modern DNA.

"If you try to make a tree of <u>population histories</u> within a species, there's always the possibility that you've got genes flowing from one branch to another," Pritchard said. "The populations can interbreed, so if they're geographically together or if there's movement from one place to another, then this tree representation is not necessarily going to be a good way of representing history. The goal of this research is to learn



more about departures from 'tree-ness.'"

Pritchard and Pickrell developed software called TreeMix that compares how often variants of a particular gene from different populations appear in the same species. It then calculates how closely groups are related, and when in their history they separated to form a genetically distinct population or breed.

The resulting graph looks less like tree branches and more like a tangled shrub or mass of vines. The trunk of the shrub represents the major relationships between the groups, and the largest branches represent distinct populations as they develop over time from left to right on the graph. But those tangled vines that crisscross the branches are the key, showing migration events where a previously separate population mixed with another, rejoining to form a new group at a later point in time.

Pritchard and Pickrell tested the model using DNA from 55 human populations and 82 dog breeds, and already found some interesting results. For example, boxer and basenji breeds of dogs trace a large portion of their DNA (nine percent and 25 percent, respectively) back to wolves after domestication, meaning that these breeds interbred with wolves again after humans had begun to domesticate dogs.

"What I like about this is that it's starting to give us some resolution on relationships that are just much more complicated than you can capture using the standard tree approach," Pritchard said.

He gave another example of the Mozabite people who live in Algeria. Their DNA is largely a mixture of European and Middle Eastern ancestry, but they also mixed with sub-Saharan African ancestors at various points in their history. The new model can represent the complex relationships among all of these backgrounds, whereas the traditional tree-based method would just show a primary relationship to Middle



Easterners.

Another group of researchers has already used Pritchard's software to show a link between Denisovans, an extinct relative of Neanderthals found in Siberia, and Papuans in the South Pacific. It doesn't make geographic sense right away, but such a finding forces researchers to ask more questions about how these groups migrated and changed over time. Much like DNA evidence has revolutionized criminal investigations, often negating assumptions based on physical evidence, advanced genetic analysis like Pritchard's can change what we think about human history as well.

Provided by University of Chicago Medical Center

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