

Shifting from Pure Theory



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John Novembre analyzes data to understand patterns of genetic variation in humans, such as the geographic spread of a rare genetic mutation that provides resistance to HIV (far right).

By Aaron Dalton

If you met someone from Europe who was tall, blond and fair-skinned, you might not have too much trouble deducing that your new acquaintance originally hailed from Scandinavia or elsewhere in Northern Europe.

But would you be able to pinpoint this person’s ancestral home to an accuracy of a few hundred miles?

In 2008, UCLA assistant professor of ecology and evolutionary biology John Novembre led a team of researchers in publishing a *Nature* article demonstrating how DNA analysis of hundreds of thousands of points on the human genome could identify a person’s geographic homeland. Novembre’s main contribution was on the analytical side; working with colleagues at Cornell, GSK, and the University of Chicago, Novembre developed the algorithm that crunched the data on the variation of DNA from the genomes of 3,200 Europeans and placed 90 percent of them within about 500 miles of the center of their country-of-origin.

As Europeans migrate around the European Union, Novembre admits that it will be challenging to use genetic data as a sort of birthplace GPS. But for the purposes of understanding the evolutionary history of human beings, the individuals included in the study provide a window into the past.

“The genetic patterns that are specific to particular regions will be lost over time, but for most of human history, individuals had very localized mating patterns,” said Novembre. The study revealed how subtle patterns of genetic variation exist within Europe, with differences tied much more tightly to specific geographic locations than to broad linguistic regions (Germanic, Romance, Slavic, etc.).

But outside of being able to determine that a random European acquaintance came from a specific location, what implications does Novembre’s study of human population genetics have for the rest of us? A deep knowledge of the variation in genetic populations is crucial when it comes to untangling the genetic basis of complex diseases.

As an example, for researchers who are trying to isolate some genetic risk factors for heart disease by looking at one group of people who have heart disease and another group that don’t, Novembre’s research suggests it is more important than previously supposed to have both groups of patients come from the same geographic area.

“This is an exciting time to be doing research on population genetics,” said Novembre. “For the first time, technological developments are making it feasible to look at large-scale genetic variation in humans.”

Indeed, the new technological tools are taking theoretical population genetics out of the realm of pure theory and mathematical modeling and allowing researchers to compare their models against thousands of real-world human gene sequences.

These interests are not new for Novembre—he describes himself in high school as a “computer programming geek” who found himself intellectually intrigued by biology. As a college undergraduate, Novembre became interested in molecular evolution and found that computer programming was an important skill in that field. Population genetics gave him a chance to combine his fascination with biology with his enjoyment of the day-to-day challenges of computer programming.

“For someone like me, UCLA is a very exciting place,” said

to the Real World

Biologist John Novembre uses new tools to create advances in the study of the genetics of human populations.

Novembre in explaining his choice to join the university two years ago. “Few universities have on one campus such strong departments of human genetics, evolutionary biology, biomathematics, and anthropology. We have strong statistical geneticists and bioinformaticians across multiple departments, and a Center for Society and Genetics. I interact with a lot talented people.”

Since arriving at UCLA, Novembre has had the opportunity to branch out from human population genetics to work with fellow evolutionary biologist Bob Wayne on the genetic analysis of wolves and other canids. Together, Wayne and Novembre recently published a paper in the journal *Nature* showing gene-based evidence that most dog breeds appear to be originally domesticated from wolves in the Middle Eastern region.

Novembre has also been working with Ken Lange in human genetics and Lange’s student David Alexander to develop a faster method for determining the geographic backgrounds of people with mixed ancestry. For instance, Latino populations often have ancestors who came from Europe mixed in with indigenous Native American ancestry.

Such analyses typically try to determine what percentage of a person’s genetic makeup comes from ancestral African, European or Native American sources. In the past, the analyses were based on relatively small data sets—perhaps just ten locations on the genome. But recent technological advances allow researchers to analyze literally hundreds of thousands of locations on the genome.

With such vast amounts of data, “you can identify patterns that you had no hint of before,” said Novembre. However, given the size of the new data sets, the old methods of analysis were no longer practical. So Novembre, Lange, and Alexander developed a new and much faster way to analyze the data while maintaining the high levels of statistical sophistication from the previous model. Excitingly, other researchers have already begun using this new method of data analysis.

Novembre’s work has him looking at a number of interesting issues. He is involved in the genetic analysis of people like Sorbs and Sardinians who are believed to have been relatively genetically isolated for hundreds to thousands of years. Meanwhile, he and Wayne will continue their work on dogs and wolves. They have assembled a team to sequence the wolf genome and compare it to the dog genome to see the differences that changed dogs from aggressive predators into the fuzzy little partners and friends of man that we know today.

Since genetic research is applicable to every corner of the animal kingdom, Novembre will also be working with

Thomas Smith from ecology and evolutionary biology on collecting data from migratory birds, tracing the birds back to their breeding ranges in the far reaches of North America. The resulting analysis should reveal migration patterns that could ultimately prove useful for both bird conservation and monitoring the spread of bird-borne disease such as avian flu.

Birds, canids and people—we all have genetic data that constitutes a rich gold mine of information. It’s a treasure that researchers are beginning to bring to light with the help of mathematical models like those that John Novembre continues to develop and improve. [UCLA](#)

