

# Genomic analysis in snakes shows link between neutral, functional genetic diversity

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As part of this work, Gibbs' lab was the first to sequence the genome of the Eastern massasauga rattlesnake, which was listed as threatened under the Endangered Species Act in 2016 because of loss and fragmentation of its wetland habitat. Credit: Scott Martin

In the world of threatened and endangered species conservation, the

genomic revolution has raised some complicated questions: How can scientists justify assessing species genetic diversity without consulting entire genomes now that they can be sequenced? But then again, how can scientists justify the time and expense of genome sequencing when age-old measures of neutral genetic diversity are much cheaper and easier to obtain?

A new study suggests making a transition from "old school" genetics to "new school" genomics for [species](#) conservation purposes probably isn't necessary in all cases.

Researchers found the functional genetic [diversity](#) they detected by analyzing [gene variations](#) in fully sequenced genomes of 90 Eastern massasauga rattlesnakes correlated nicely with the neutral genetic diversity seen across broad sections of those same genomes containing no [protein-coding genes](#)—similar to the type of genetic material historically used to assess genetic diversity.

"If we're worried about the genetic health of populations, neutral diversity can give us a pretty good answer, as has long been argued. We have directly tested that for this species," said H. Lisle Gibbs, professor of evolution, ecology and organismal biology at The Ohio State University and senior author of the study.

"Hopefully for many other small species that live in small, isolated populations, it's a good news story in that neutral genetic diversity measured using much less expensive and more easily accessible techniques than sequencing their whole genomes gives us important information about their genetic health."

The results are published in the journal [\*Proceedings of the National Academy of Sciences\*](#).

The point of assessing genetic diversity in a small, isolated animal (or plant) population is to get an idea of how well its members are able to adapt to changing conditions through their "good" [mutations](#), and determining the level of need for [conservation measures](#) that will give them a fighting chance to carry on. Other species are deemed threatened or endangered because the inbreeding that happens in a small population is expected to let damaging ("bad") gene mutations pile up, lowering chances for species survival.

Historically, genetic diversity has been estimated by searching easy-to-measure DNA regions unrelated to protein-coding genes. A higher level of diversity in these regions suggests more [genetic variation](#) in genes that encode proteins—a sign, but not firm evidence, that the species' genes are changing to allow for adaptation to future [environmental changes](#).

"With genomic information, we can now for the first time do things like go after specific variants in specific genes across the entire [genome](#), which we've never been able to do before. And that's what we were able to do," Gibbs said. "There's no expectation that this be done for every single species—that would be cost prohibitive and impossible. So we are trying to provide a model for how one can do these things in any [endangered species](#)."

As part of this work, Gibbs' lab was the first to sequence the genome of the Eastern massasauga rattlesnake, which was listed as threatened under the Endangered Species Act in 2016 because of loss and fragmentation of its wetland habitat. They then compared 90 of those sequences to sequenced genomes of 10 Western massasauga rattlesnakes, a common species with no limitations on breeding opportunities and large populations.

For this study, the researchers made use of that analysis to create two "boxes" in which to classify Eastern massasauga functional mutations:

gene changes seen in massasaugas that implied either strong positive selection, and therefore contained beneficial mutations, or strong negative selection, and, accordingly, contained deleterious mutations. For comparison, the region they assigned as neutral consisted of sections of the genome located far away from functional genes.

"Those were our three types of variation. The prediction is that if measuring the neutral variation is accurate, then if there's lots of neutral variation, then there should be lots of good variation present in the population and not very much bad variation," Gibbs said. "And that's because in big populations, [natural selection](#) is efficient, leading to all the bad stuff being purged and the good stuff retained.

"But then bad things happen when populations shrink because [genetic drift](#), and random processes, start to become important and interfere with how effectively natural selection can purge things, allowing bad mutations to increase in frequency or maintain high frequencies of good mutations. So that's the model that we have for how population size affects how evolution acts on these two kinds of mutations."

There is a caveat to the finding, he said, They also show evidence that neutral [genetic diversity](#) may not be so useful for predicting the future because conditions on the ground aren't yet captured in species' [genes](#).

"When we study patterns of diversity that we see in nature, we're looking at what I call the ghost of evolution past over many previous generations. But humans have started to have an impact within the last 200 years, so when you do genetics and conservation, you have to be aware of this lag," he said. "The patterns may no longer be relevant to what is going to happen in the future. You can still use neutral variation, but be aware it may not be as predictive as it used to be."

Co-authors include former Ohio State postdoctoral scholars Samarth

Mathur and Andrew Mason and Gideon Bradburd of the University of Michigan.

**More information:** Samarth Mathur et al, Functional genomic diversity is correlated with neutral genomic diversity in populations of an endangered rattlesnake, *Proceedings of the National Academy of Sciences* (2023). [DOI: 10.1073/pnas.2303043120](https://doi.org/10.1073/pnas.2303043120)

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