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## Non-coding DNA adapts

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Much of the "junk" DNA in *Drosophila* shows signs of either negative or positive selection, according to a [study](#) in this week's *Nature*. An analysis by [Peter Andolfatto](#) of the University of California, San Diego, reveals that around half of non-coding *Drosophila* DNA is evolutionarily constrained and that much of the remaining divergent DNA has undergone adaptive evolution. Both types of selection show that "this non-coding DNA actually has functional importance to the organism," said Andolfatto.

"We've known for a while that it was possible you'd see constraint—essentially, negative selection—on non-coding regions," said [Gerald Wyckoff](#) of the University of Missouri-Kansas City, who was not involved in the study, "but his methodology makes it so clear that this type of selection is abundant."

During the study, Andolfatto analyzed polymorphisms in 35 coding fragments and 153 non-coding fragments scattered across the *Drosophila melanogaster* X chromosome. He compared these data with *D. melanogaster*'s close relative, *D. simulans*.

Andolfatto used synonymous mutations—mutations in coding DNA that do not cause changes in amino acid sequence—as markers of neutral evolution. By comparing the rate at which synonymous mutations accumulate to the rate of mutations in non-coding DNA, Andolfatto found that most non-coding DNA in *D. melanogaster* evolves appreciably slower—with fewer polymorphisms and less divergence—than neutrally evolving synonymous sites. He estimated that levels of constraint are 40% for introns, 50% for intergenic regions, and 60% for untranslated regions (UTRs).

Although reduced levels of polymorphism and divergence are consistent with negative selection, it remains possible that non-coding DNA simply has a lower mutation rate, Andolfatto said. However, he also found that individual polymorphisms in non-coding DNA tended to appear at low frequency in the population, exactly the pattern expected under negative selection. "There's much more constraint there than we thought previously," Andolfatto said.

Since non-coding DNA sequences showed so much evidence of negative selection, Andolfatto thought that this sequence conservation could be hiding increased divergence at some sites—the hallmark of adaptive evolution. To filter out some effects of negative selection, he excluded rare polymorphisms from his analysis, because they "are more likely to be targets of ongoing negative selection than polymorphisms at higher frequencies," Andolfatto told *The Scientist*. "With the effects of negative selection minimized, the signature of positive selection is more apparent."

He found unexpectedly high divergence between *Drosophila* species in UTRs, introns, and intergenic DNA, which suggests that this non-coding DNA was driven to fixation by positive selection. Using statistical tests, he estimated that about 20% of nucleotide divergence in introns and intergenic DNA and 60% of UTR divergence was driven to fixation by positive selection.

Andolfatto's paper shows that "the methodologies that we've been using to detect positive selection are very conservative—more conservative than we even thought they were," Wyckoff told *The Scientist*.

"Positive selection—which is interesting, because that's the hallmark of adaptation—is actually more abundant than we thought."

According to an accompanying [News & Views article](#) by Alexey S. Kondrashov of the NIH's National Center for Biotechnology Information in Bethesda, Md., Andolfatto's findings do not completely demolish the [neutral theory](#) of genome evolution. While this theory, which says that most non-coding DNA is functionless and ignored by evolution, may not be relevant to *Drosophila*, it still works for mammals and other vertebrates, Kondrashov writes.

"It could well be that large parts of the mammalian genome are truly junk" and therefore undergo neutral evolution, Andolfatto said. Mammalian non-coding DNA may contain positively selected sites, he said, but, "if your positively selected sites are buried in junk, they're more difficult to find."

Since most animals possess far more non-coding than coding DNA, even a small amount of non-coding adaptation may contribute greatly to genome function, Andolfatto said. "The signature of positive selection is weaker in non-coding DNA, but there's much more non-coding DNA than coding DNA," Andolfatto said. "So if you sum over the whole genome...you realize that perhaps protein evolution isn't so important after all."

## References

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