

Researchers create a neural network for genomics that explains how it achieves accurate predictions

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An artist's rendition of a biochemical model inspired by an interpretable neural network. Credit: Elizabeth Speiser



A team of New York University computer scientists has created a neural network that can explain how it reaches its predictions. The work reveals what accounts for the functionality of neural networks—the engines that drive artificial intelligence and machine learning—thereby illuminating a process that has largely been concealed from users.

The breakthrough centers on a specific usage of <u>neural networks</u> that has become popular in recent years—tackling challenging biological questions. Among these are examinations of the intricacies of RNA splicing—the focal point of the study—which plays a role in transferring information from DNA to functional RNA and protein products.

"Many neural networks are <u>black boxes</u>—these algorithms cannot explain how they work, raising concerns about their trustworthiness and stifling progress into understanding the underlying biological processes of genome encoding," says Oded Regev, a computer science professor at NYU's Courant Institute of Mathematical Sciences and the senior author of the paper, which was published in the <u>Proceedings of the National</u> <u>Academy of Sciences</u>.

"By harnessing a new approach that improves both the quantity and the quality of the data for machine-learning training, we designed an interpretable neural network that can accurately predict complex outcomes and explain how it arrives at its predictions."

Regev and the paper's other authors, Susan Liao, a faculty fellow at the Courant Institute, and Mukund Sudarshan, a Courant doctoral student at the time of the study, created a neural network based on what is already known about RNA splicing.

Specifically, they developed a model—the data-driven equivalent of a high-powered microscope—that allows scientists to trace and quantify the RNA splicing process, from input sequence to output splicing



prediction.

"Using an 'interpretable-by-design' approach, we've developed a <u>neural</u> <u>network</u> model that provides insights into RNA splicing—a fundamental process in the transfer of genomic information," notes Regev. "Our model revealed that a small, hairpin-like structure in RNA can decrease splicing."

The researchers confirmed the insights their model provides through a series of experiments. These results showed a match with the model's discovery: Whenever the RNA molecule folded into a hairpin configuration, splicing was halted, and the moment the researchers disrupted this hairpin structure, splicing was restored.

More information: Susan E. Liao et al, Deciphering RNA splicing logic with interpretable machine learning, *Proceedings of the National Academy of Sciences* (2023). DOI: 10.1073/pnas.2221165120

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