

New AI tool captures top players' strategies in RNA video game

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Solving an RNA design problem. Predicted fold of an RNA chain as an Eterna videogame player changes its sequence to eventually arrive at a target fold. Credit: Koodli et al.

A new artificial-intelligence tool captures strategies used by top players of an internet-based videogame to design new RNA molecules. Rohan Koodli and colleagues at the Eterna massive open laboratory present the tool, called EternaBrain, in *PLOS Computational Biology*. Eterna is directed by the lab of Prof. Rhiju Das at the Stanford University School of Medicine in California.

Found naturally in all living cells, RNA molecules perform essential biological functions. Recent years have seen strong interest in designing new RNA structures for use in cancer treatment, CRISPR gene editing, and more. However, every RNA <u>structure</u> consists of a long sequence of four <u>building blocks</u>, and determining the precise sequence needed to build a given structure can be computationally difficult.

In the new study, Koodli, Das, and colleagues carried out research through the Eterna internet-based videogame, a citizen-science initiative to tackle the computational challenges of RNA design. Eterna presents each player with a target RNA structure, and the player attempts to discover an RNA sequence that allows the finished molecule to fold into the desired shape. Some players outperform the best computerautomated methods in solving these challenges.

Using a dataset of 1.8 million design choices made by Eterna players, the researchers discovered an artificial neural network that captures some of the predilections and strategies of these experts. Called EternaBrain, this approach can predict the choices of the best players with significantly better accuracy than achieved by random guessing. An extended



EternaBrain algorithm performs similarly or better than previously developed algorithms in solving Eterna challenges.

"Our findings suggest that it should be possible to create automatic algorithms for computer RNA design that emulate or outperform human RNA designers," Das says. "But we're not there yet; we still have a lot to learn from both gamers and AI researchers."

Next, the researchers will see if they can outperform top players by integrating EternaBrain with other computational approaches to RNA design. "We also hope to apply EternaBrain to more complicated problems being tackled by Eterna players, including the design of RNA computers and 3-D machines, and the learning of design rules from actual wet-lab data," Das says.

More information: Rohan V. Koodli et al, EternaBrain: Automated RNA design through move sets and strategies from an Internet-scale RNA videogame, *PLOS Computational Biology* (2019). <u>DOI:</u> <u>10.1371/journal.pcbi.1007059</u>

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