

# Building a better protein

February 23 2009

---

Proteins are widely viewed as a promising alternative to synthetic chemicals in everything from medications to hand lotion. The naturally occurring molecules have been shown to be more efficient and effective than many of the most sophisticated chemical compounds on the market. But outside the controlled confines of the lab bench, proteins quickly change structure, causing irreversible damage to their functionality and often safety.

Scientists are now searching for ways to increase the stability of proteins. In new research published Feb. 5 in the online *Early Edition of the Proceedings of the National Academy of Sciences (PNAS)*, Rensselaer Senior Constellation Professor George Makhatadze and his colleagues detail a targeted strategy to substantially increase the thermodynamic stability of nearly any protein, while preserving its unique function. Their redesign technique creates proteins that remain stable at temperatures 10 degrees Celsius higher than normal.

To achieve these results, the researchers used high-powered computers to create new and improved versions of two human enzymes. The enzymes are specific types of protein. The two enzymes in the study vary widely in size and functionality, yet both showed substantial increases in stability without loss of function in the body. This supports the idea that the stability of many other proteins could also be greatly stabilized, according to Makhatadze. The researchers are now looking to use the technique to improve that stability of specific proteins with strong industrial and drug development applications.

They developed a computational approach that altered the proteins' structure and tested it for increased stability. "Our experimental validation of computational results is actually motivated by Thomas Edison, who wrote, 'Until man duplicates a blade of grass, nature will laugh at his so-called scientific knowledge,'" Makhatadze said.

"There are several viable approaches to optimize proteins," Makhatadze added. "Many researchers seek to optimize the protein by changing all types of physical interactions within the computer model at once. Instead, we felt that if we could understand one interaction, we could then use it to our advantage to build on the algorithm and then experimentally prove that that property really exists in the real protein system."

The interaction the researchers focused on was the surface charge of the protein. The investigation of the importance of protein surface structure is a growing area of research within the field. In fact, a 2006 paper in the journal *Biochemistry*, published by Makhatadze supporting the importance of protein surface structure on stability, was the one of the top five most cited and downloaded papers from the journal that year.

In addition to important potential industrial applications, Makhatadze also believes the research sheds some light on the evolution of proteins. The researchers compared the mutations that they made within the proteins in order to optimize the protein's performance with the mutations naturally occurring in the proteins from the evolutionary distant organisms. Instead of seeing more mutations along with increased performance as with most evolutionary adaptations, the researchers saw that less frequent mutations resulted in a more stable protein. "This suggests that the stability of proteins might not be evolutionarily important," he said. "It appears that as soon as the protein is able to function in given conditions and is stable at a given temperature, anything above that is not really necessary."

Source: Rensselaer Polytechnic Institute

Citation: Building a better protein (2009, February 23) retrieved 26 April 2024 from <https://phys.org/news/2009-02-protein.html>

This document is subject to copyright. Apart from any fair dealing for the purpose of private study or research, no part may be reproduced without the written permission. The content is provided for information purposes only.