Cold-adapted enzymes can transform at room temperature

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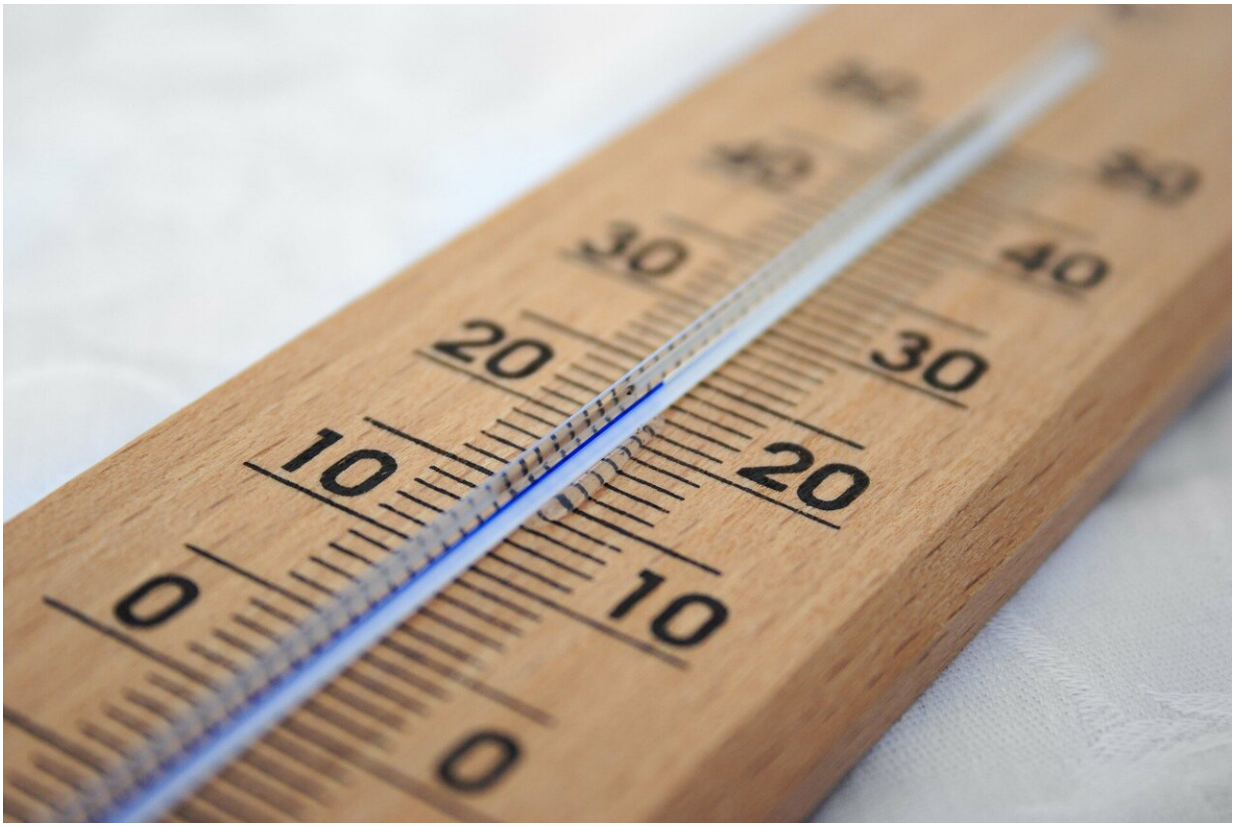

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Enzymes from cold-loving organisms that live at low temperatures, close to the freezing point of water, display highly distinctive properties. In a new study published in *Nature Communications*, scientists at Uppsala

University have used large-scale computations to explain why many cold-adapted enzymes stop functioning at around room temperature.

Enzymes are the "machines" that maintain metabolism in all living cells, but unfortunately all biochemical reactions normally stop at low temperatures. Evolution has solved this problem by developing cold-adapted enzymes in species whose internal cell temperature is the same as in the cold external environment. This applies to countless organisms, from bacteria to certain plants and cold-blooded vertebrates, such as fish that live in very cold water. These cold-adapted enzymes have special thermodynamic properties that enable them to function in freezing conditions. Evidently, they also melt at lower temperatures than ordinary enzymes; but it makes no difference if they melt at approximately 40 degrees Celsius, since they never need to work in such a warm environment.

However, one major unsolved enigma has been why many cold-adapted enzymes stop functioning even at around room temperature, long before they start melting. Researchers Jaka Socan, Miha Purg and Johan Åqvist have now, for the first time, succeeded in explaining this by means of extensive computer simulations.

The scientists simulated the chemical reaction in a starch-degrading enzyme from an Antarctic bacterium at various temperatures, and compared this with calculations relating to the same enzyme from an ordinary, warm-blooded pig. The Antarctic enzyme then proved to start breaking up locally even at room temperature, and this defect makes the starch molecules adhere much less well to the enzyme. This phenomenon gives rise to a maximum reaction speed at 25 degrees Celsius, and takes place at some 15 degrees Celsius below the melting point. In the pig enzyme, on the other hand, the reaction speed just keeps increasing until the enzyme finally melts at roughly 60 degrees Celsius.

With computer calculations, it is thus possible to identify which parts of the cold-adapted enzymes give rise to their special properties.

"Both our new results and earlier ones from computer simulations of various cold-adapted enzymes, and their mutants, show that we've now reached a stage where one can rationally redesign enzymes to change their properties in a predictable way. This approach has long been an aim, but to date it hasn't been able to compete with random laboratory evolution of enzymes, for which Frances Arnold was awarded the Nobel Prize in 2018," says Johan Åqvist, Professor of Theoretical Chemistry at the Department for Cell and Molecular Biology, Uppsala University.

More information: Jaka Sočan et al, Computer simulations explain the anomalous temperature optimum in a cold-adapted enzyme, *Nature Communications* (2020). DOI: 10.1038/s41467-020-16341-2

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