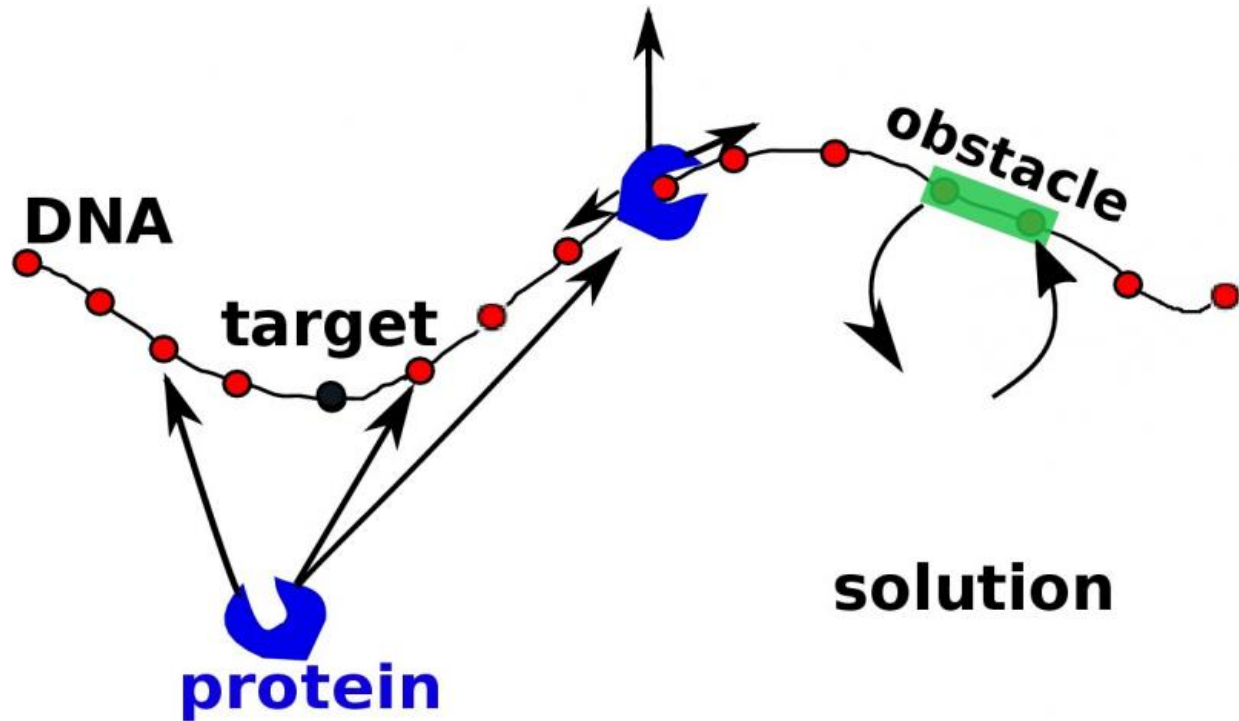


Obstacles not always a hindrance to proteins

December 10 2015



Obstacles can help proteins if they have less space to search for genetic targets on DNA. Rice researchers found that obstacles can both help and hurt proteins carry out their tasks. Credit: Alexey Shvets

Proteins are little Olympians in the games of life, racing around cells to trigger critical processes through interactions with specific genes. Sometimes they're sprinters, sometimes hurdlers. But they generally find their genetic targets, whatever the obstacles.

A new theoretical study by Rice University scientists looks at the roles of those obstacles, and how they hinder – and sometimes help – proteins in finding their targets along strands of DNA.

In doing so, Rice biophysicist Anatoly Kolomeisky and his team said they are helping to resolve seeming conflicts between other studies on how proteins carry out their biological tasks.

The study appears in the American Chemical Society's *Journal of Physical Chemistry*.

The authors, including Rice postdoctoral researcher Alexey Shvets and graduate student Maria Kochugaeva, set out to see how proteins actively seeking a target deal with blocking proteins.

In computer simulations, they established cases where the obstacle is static on DNA, a hurdle to be overcome, and others where the obstacle is dynamic, repeatedly landing on and disassociating from the strand.

"Most previous theories assume there's only DNA and the [protein](#), but there's no obstruction between the protein and its target," Kolomeisky said. "In reality, there are obstructions, and a lot of them. Cells are very crowded systems. The surprising thing is that a protein still manages to find its target sequence efficiently. But how?"

"We decided to look at these things because the literature has theoretical studies with contrary results," he said. "One says obstacles are good; another says obstacles are bad. What we're saying in unifying them is that, yes, sometimes they're good and sometimes bad. People were looking at specific regimes or parameters and thinking theirs was a general case."

The Rice researchers attacked the challenge in stages.

In their simplest simulation, the seeker protein is a sprinter, alighting on DNA and probing for its target, usually finding it in milliseconds. If the target is on the other side of an obstacle, the seeker becomes a hurdler: It eventually disassociates and continues searching. But if it falls within a segment shortened by an obstacle, the seeker finds it faster.

"This was a surprise, that the presence of the obstacle is not always a bad thing," Kolomeisky said.

"But in reality, obstacles are not static," he said. "Taking things step by step, we went to the next, where obstacles bind and unbind to the same place on DNA."

Even in these more-complex models, seeker proteins found benefits, he said. "Dynamic obstacles are generally better than static because sometimes they go away."

Kolomeisky said the fundamental paper should be of interest to anyone who studies gene transcription, signaling pathways or drug design.

"This process of proteins finding a target on DNA is the beginning of all biological processes," he said. "Activating a gene means a protein binds somewhere on DNA and starts a cascade. If they don't do it well, you might have a problem—so it's important to understand how and why the process works."

Kolomeisky said the study serves as a baseline for the lab, which will now turn its attention to a more complex scenario in which obstacles can also sprint along DNA, like a moving hurdle.

More information: Alexey Shvets et al. The Role of Static and Dynamic Obstacles in the Protein Search for Targets on DNA, *The Journal of Physical Chemistry B* (2015). [DOI: 10.1021/acs.jpcb.5b09814](https://doi.org/10.1021/acs.jpcb.5b09814)

Provided by Rice University

Citation: Obstacles not always a hindrance to proteins (2015, December 10) retrieved 10 April 2024 from <https://phys.org/news/2015-12-obstacles-hindrance-proteins.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.