Important new model shows how proteins find the right DNA sequences

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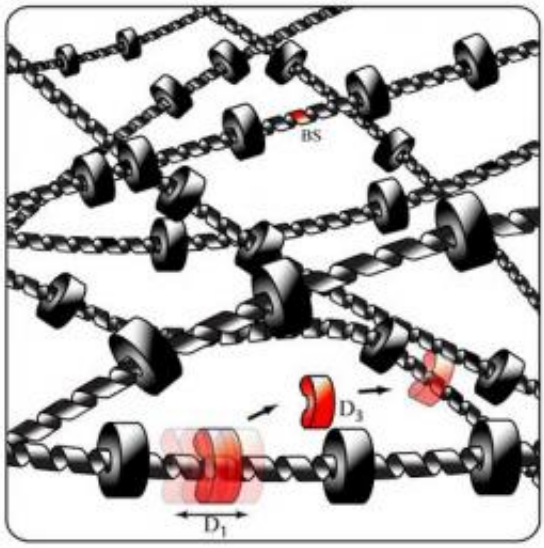

Illustration of how proteins find the right DNA sequences.

(PhysOrg.com) -- Researchers at Uppsala University and Harvard University have collaboratively developed a new theoretical model to explain how proteins can rapidly find specific DNA sequences, even though there are many obstacles in the way on the chromosomes. The findings are being published today in the scientific journal *Nature Physics*.

In living cells, DNA-binding proteins regulate the activity of various genes so that different cells carry out the right tasks at the right time. For

this to work, the DNA-binding proteins need to find the right DNA site sufficiently quickly. The research team behind the new study has previously succeeded in determining that it takes only a few minutes for an individual protein molecule to look through the millions of nearly identical binding alternatives and find the right place to bind. This is nevertheless slower than what is predicted by the established theoretical model for how DNA-binding proteins find their way to the proper place by alternating between diffusing in the cell cytoplasm and along DNA strands.

"By also taking into consideration the fact that there are many obstacles in the way when proteins are to diffuse along DNA strands, we can now calculate more exactly how long it takes them to find their way," says Johan Elf, associate professor of molecular biotechnology at the Center for Bioinformatics.

Besides offering a more precise prediction regarding the time needed to find the right site on DNA, the new theoretical model explains why there is an optimal total concentration of DNA-binding proteins. If there were more, it would simply be impossible for them to find a binding place in a reasonable time, since the proteins would be in each other's way. If there were fewer it would go slower as well, since not enough proteins would be searching. Finally, the new model provides an explanation why so many DNA-binding proteins also bind auxiliary binding sites close to the regulatory site, thus forming DNA loops. It turns out that this can shorten the time to find the right sites.

"This more detailed understanding of gene regulation is important, since it can ultimately provide a better understanding of diseases that occur as a result of problems in the control functions of cells, such as in cancer" says Johan Elf.

More information: Read the article on the Nature Physics Web site.

Source: Uppsala University