

Statistics are insufficient for study of proteins' signal system

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Ten years ago great attention was attracted by the discovery that it was possible to demonstrate signal transfer in proteins using statistical methods. In an article in the journal *Proceedings of the National Academy of Science* Uppsala researchers are now presenting results of experiments that contradict the theory.

Proteins govern nearly all chemical processes in the body's cells. A fundamental property of proteins is their ability to transfer signals – both within and between proteins. It is known, for example, that such signal transfer is vital to haemoglobin, which transports oxygen in the body. In that instance the mechanism has largely been clarified.

"But in other instances very little is known about the mechanisms or whether such signal transfer even occurs," says Per Jemth, who together with his research group at Uppsala University is studying whether signal transfer also occurs in small proteins.

Nearly ten years ago great attention was attracted by an article published in *Science* that described a method of demonstrating signal transfer in proteins by comparing their amino acid sequence. The authors recorded a statistical method of showing how certain parts of proteins change together through evolution, i.e. if a change had taken place in one part a change simultaneously took place in another part of the protein. One thus found a network of parts that seemed to belong together, and within this network signal transfer was deemed to take place.

But the Uppsala researchers saw several things that were not right about the results in the much discussed article, and by means of experiments they can now show that no more signals occur in this network than with other parts of the protein. They instead found, completely logically, that nearby parts of the protein interact more with each other than parts that are a long way apart.

"Our results thus question whether statistical methods can demonstrate signal transfer within proteins, and emphasise the importance of precise experiments to substantiate computer-based methods in protein chemistry," says Per Jemth.

The ability to predict proteins' function down to the smallest detail on the basis of their amino acid sequence is a goal that has preoccupied many researchers ever since human DNA became known. This study emphasises that experiments are needed to improve and refine the computerised methods currently in use.

"When theory, computer simulation and experiments provide the same answers the long-term goal has been attained, but there's still a long way to go."

Source: Uppsala University

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