**DETECTION OF SIMILAR PROTEINS BY THE INVERSE-FOLDING PROTOCOL.**

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Method for evaluating protein structure (3D) - sequence (1D) compatibility (threading) have been developed in these years. The protocol in which a sequence recognizes its compatible structure in the structural library,*i.e*., the fold recognition or the forward-folding search, is available for the structure prediction of new proteins. However, the reverse protocol in which a structure recognizes its homologues in a sequence database, called the inverse-folding protocol, is known difficult in practice. In this study, we have challenged the feasibility of the latter approach.

A structural library composed of about 400 structures that are well resolved and are mutually dissimilar in the sequence, was prepared. Of them, 160 proteins have their remote homologues in the library, and it was examined if they could correctly seek their homologues by both the forward- and inverse-folding searches.

The results showed that the inverse-folding protocol is more effective rather than the forward-folding protocol, once the reference states of the compatibility functions are appropriately adjusted. This adjustment little affect the ability of the forward-folding search. Also noticed was that the procedure in which a query sequence is re-mounted onto a structure according to the 3D-1D alignment determined by the dynamic programming method is only effective in the forward-folding protocol, but not in the inverse-folding protocol. Namely, the inverse-folding search works significantly better in use of the 3D-1D alignment score*per se*, rather than that obtained by the re-mounting. The implications of these results are discussed.

**References**

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