Predicting the structure of membrane porins

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Presently two types of membrane protein structures are known at atomic resolution: the alpha helical proteins of the cytoplasmic membrane and the beta barrel proteins of the bacterial outer membrane. The topography and topology of alpha helical transmembrane (TM) helices (H) can be predicted with good accuracy and several web servers are available for TMH prediction (1). However this is not so for the second type of membrane proteins due to the difficult task of predicting beta strands and particularly those of membrane proteins. Beta barrel structures are presently also believed to form the transbilayer pore of the voltage dependent anion channels in the outer membrane of mitochondria from different species. For these proteins, barely homologous to the outer membrane porins, several sequences are available and modeling is required. Moreover recently it has been recognized that other proteins of the outer membrane are also endowed with beta barrel structures, anchoring the protein to the membrane. It seems therefore that modeling of the beta barrel structures is as important as that of the TMHs. Modeling requires a correct prediction of the protein regions generating the beta barrel.
We developed a neural network based predictor to locate putative beta strands adopting the TM beta barrel structure starting from the protein sequence. The predictor is trained and cross validated using the six porins presently known at atomic resolution in the PDB database. These proteins, albeit characterized by the same 3D structure, have very low sequence identity. Network outputs are then filtered with a Hidden Markov Model procedure (2) to avoid spurious assignments and to select the beta barrel-forming beta strands. The predictor accuracy scores as high as 73% and its performance is higher than that previously obtained with other statistical and empirical methods.

1. B. Rost, Marrying structure and genomics, Structure 6: 259-263 (1998)
2. R. Durbin, S.R. Eddy, A. Krogh, and G. Mitchison, Biological Sequence Analysis, Cambridge Univers ity Press, Cambridge (1998).