

## **Fishing new outer membrane proteins with neural networks**

P.L. Martelli, P. Fariselli, G.L. Tasco, E. Capriotti, R. Casadio

Università di Bologna

As a result of large sequencing projects, data banks of protein sequences and structures are growing rapidly and whole genomes are available from different organisms. One major problem is however the annotation of those genes which have no counterpart in the database of presently known sequences with a given function. We focused on the membrane proteins of the outer membrane of gram-negative bacteria, such as *Escherichia coli*, and posed the question: is it possible to filter the proteome in order to distinguish globular from membrane proteins, and among membrane proteins fishing those interacting with the outer membrane (the so called beta barrel membrane proteins)?.

In our lab tools have been developed in order to bridge the gap between sequence and protein 3D structure based on the notion that information is to be retrieved from the databases and that knowledge-based methods can help in approaching a solution of the protein-folding problem. To this aim our group has implemented neural network based predictors capable of performing with some success in different tasks, including predictions of the secondary structure of globular and membrane proteins, of the topology of membrane proteins and porins, of stable alpha helical segments suited for protein design and the probability of finding a cysteine in a disulphide bridge. All our predictors take advantage of evolution information derived from the structural alignments of homologous proteins and derived from the sequence and structure databases.

Recently we integrated our tools in a program (HUNTER), which takes as input the bacterial proteome and clusters globular, inner and outer membrane proteins. Hunter, which includes also a signal peptide predictor, scores as high as 96% when it is tested on some 2920 well or partially annotated proteins of *E.coli*. When the remaining non-annotated proteins are filtered (1253), Hunter predicts 154 new membrane proteins, 18 of which are classified as outer membrane proteins.