

Predicting the antibody VH/VL packing angle from interface residues

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Abstract:

The antibody packing angle is defined as the angle at which the variable region light chain (VL) and heavy chain (VH) pack with one another. Variability in this angle will affect the topography of the antigen combining site. Getting the angle correct is therefore important in modelling antibodies and, if specific residues are important in defining the packing angle, these must be included in humanization of mouse antibodies.

We have assessed the variability in the packing angle and find that it varies by up to 30 degrees. We hypothesize that residues in the VH/VL interface determine the packing angle and have tried to identify important interface residues.

Neural networks were used to predict packing angle from a description of residues in the VH/VL interface. Since the number of potential interface residues is very large compared with the limited data available for training the neural network, we performed feature selection using a genetic algorithm in which the penalty function is the performance of the neural network.