How to improve the modelling of proteins mutations? A preliminary assessment

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Several programs have been developed that are able to replace a residue with another one in a protein structure, but usually they are not able to simulate the short- and long-range effects of a real single point mutation. We tested if the approach of re-modelling the entire protein structure of a mutant protein using the wild type structure as a template can correctly reproduce the structural features of mutant proteins. To do this, we selected a benchmark of 4 different families of proteins for which a large group of mutants are available in the PDB database and we used MODELLER by applying different modelling strategies.

Our results showed that different starting templates of the same wild type protein can affect the structures of the mutants, and that often structural peculiarities attributed to the effect of the mutations are strictly related to low quality electron density or alterations in the quality parameters used to evaluate the proteins. In general, the standard modelling procedure allows creating mutants more similar to the wild type protein than to the mutant one, but we devised possible suggestions to improve the ability of this approach to predict the effects of mutations on protein structure.

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