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Predicting non-functional mutations in protein complexes[1]
CASEY BEARD, JAGDISH PATEL, JAMES VANLEUVAN, LUANN SCOTT, MILLER CRAIG, HOLLY WICHMAN, F. MARTY YTREBERG, University of Idaho — Robust methods to predict the effects of mutation upon protein free energy have many important applications in understanding the consequences of real-time viral evolution. In our research, we seek to develop an effective computational approach for narrowing down the list of viable mutations. We have chosen the bacteriophage φX174 as a model to develop this computational approach. Specifically, we focused on mutations within the spike protein, G, located on the viral capsid. Using snapshots generated via molecular dynamics simulations, we predicted the biophysical effects of all possible single mutations within the G protein using FoldX. FoldX has a semi-empirical scoring function that requires a minimum of computational resources, allowing calculation of all possible stability changes to binding and folding among the G pentamer, as well as the binding between protein G and the viral capsid protein, F. We then compared these calculated values to empirically-derived results for a subset of the mutations to protein G. Statistical analysis revealed a relationship between simulated free energy changes and the experimentally-determined viability of the mutation, allowing us to separate viable from nonviable mutants.

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