Database Pipeline Local Pipeline Input: Input: PDB [+ target sequences] Uniprot ID + mutation(s) **Previously** Now + mutations Run Provean to construct a Sequence Do we have a multiple sequence Provean MSA for alignment for the specified Input: fasta file with domain sequence this protein? protein. DB **Output:** provean supporting set Create and mutate .mutate(mutation): to compute sequence-**Sequence** objects based features of a mutation. Run Modeller to create Do we have homology models for all homology models for all domains in domains in this protein. DB Model this protein? **Input:** fasta file with target sequences, pdb yes. file of the template Create and mutate Output: Homology model + model 3. **Model** objects Run Modeller to create Do we have properties homology models of all pairs homology models of domains mediating .mutate(mutation): to compute sequencefor all interactions interactions involving this involving this based features of a mutation. protein. DB protein? yes J Does the specified **Predictor** Return None. mutation fall no **ELASPIC** only works for Input: DataFrame of all features, with one inside a domains mutations that fall inside for which we have Compute ΔΔG mutation per row (as if pulled out from the domains. a structural database) template? **Output:** ddG predictions yes, Run FoldX and other programs and internal scripts to calculate all the features Have the features and ΔΔG values required by the machine learning classifier. Run the been calculated classifier to predict a value of for the specified DB mutation(s)? $\Delta\Delta G$ for every mutation and every domain / domain pair. Results yes

Success!
Return the predicted ΔΔG caused
by the mutation for all domains and
domain-domain interactions