Abstract Submitted
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Predicting the conformational preferences of proteins using a physics-based free energy method[1] ARIJIT ROY, ALBERTO PEREZ, JUSTIN MACCALLUM, KEN A. DILL, Laufer Center for Physical and Quantitative Biology, Stony Brook University — Protein molecules often undergo conformational changes. In order to get insights about the forces that drive such changes, it would be useful to have a method that computes the per-residue contributions to the conversion free energy. Here, we will describe the "Confine-Convert-Release" (CCR) method which is applicable to large conformational changes of proteins. CCR correctly predicts the stable states of several "chameleon" sequences that have previously been challenging for molecular simulations. CCR can often discriminate better from worse predictions of native protein models in CASP. We will show how the total conversion free energies can be parsed into per-residue free-energy components. Such parsing gives insights into which amino acids are most responsible for given transformations. For example, we are able to "reverse-engineer" the known design principles of the chameleon proteins. This opens up the possibility for systematic improvements in structure-prediction scoring functions, in the design of protein conformational switches, and in interpreting protein mechanisms at the amino-acid level.

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