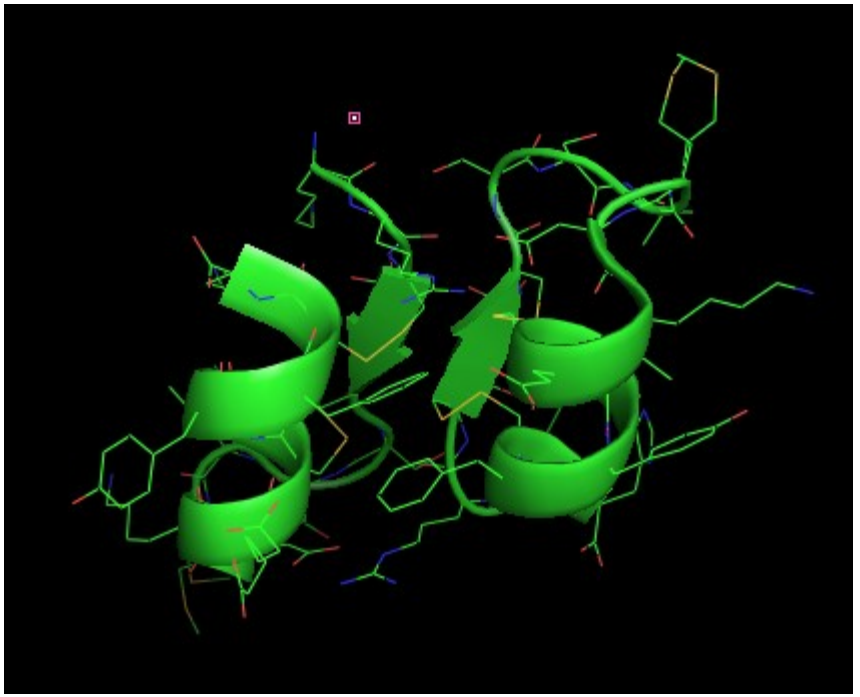
A machine learning based approach to sidechain optimization



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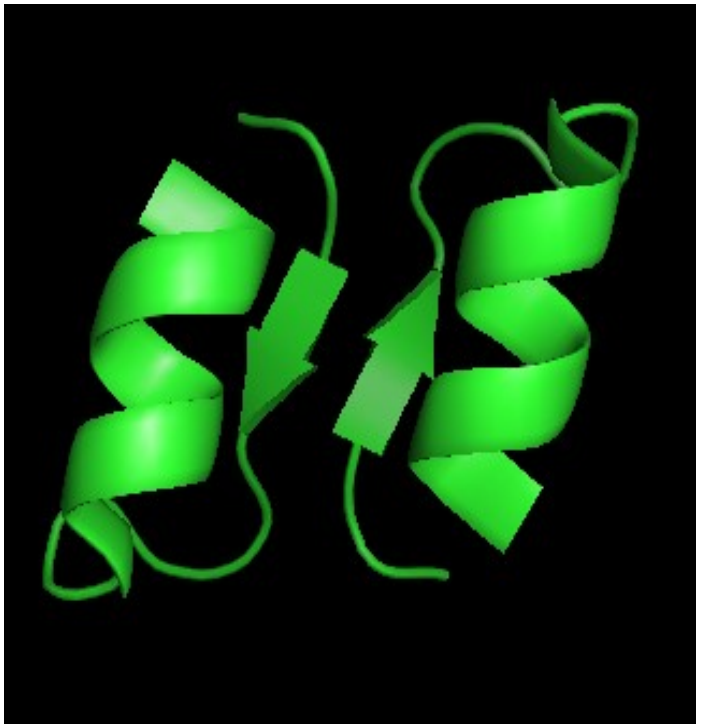
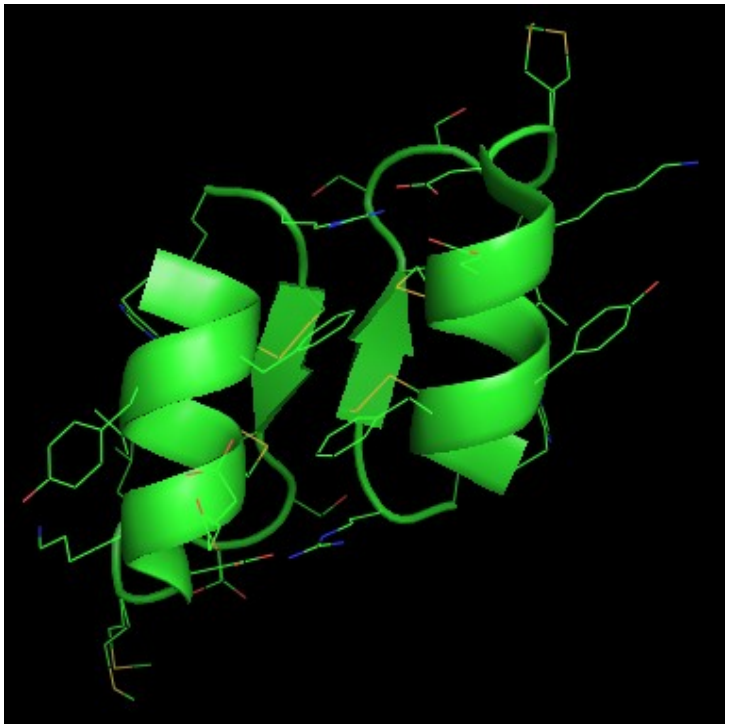
Sidechain Optimization

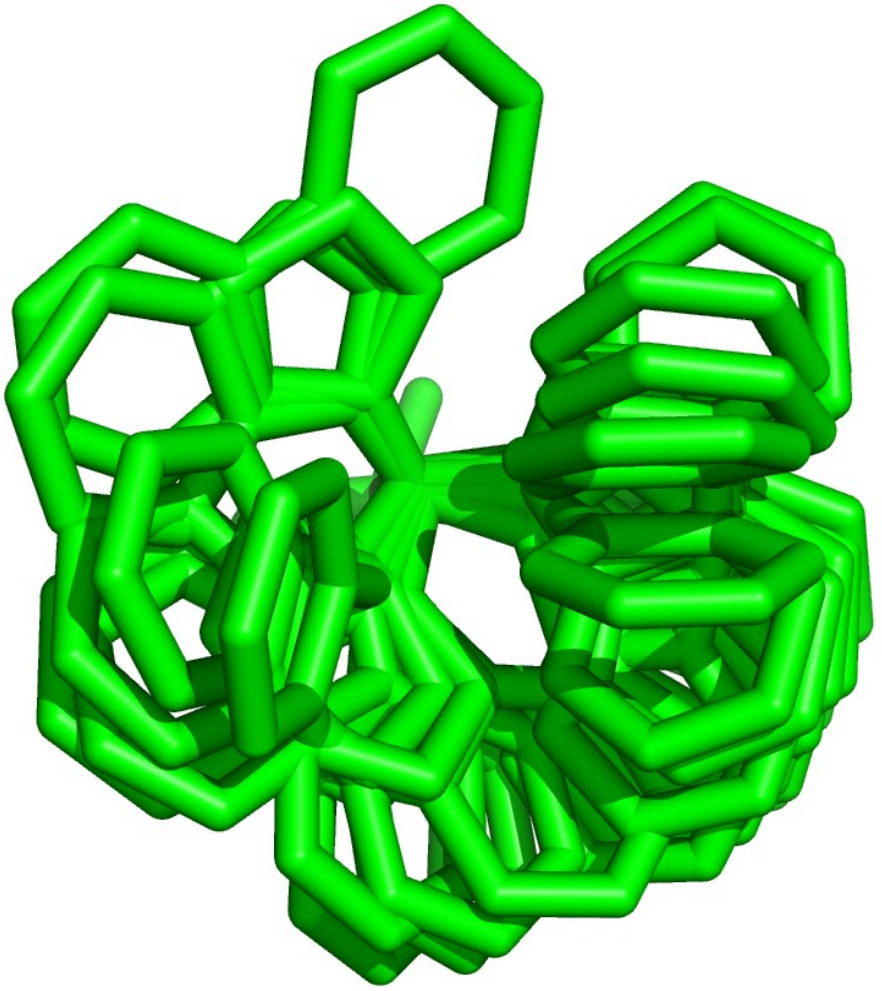




Backbone

Add sidechains to achieve minimum energy configuration

Conformer Library

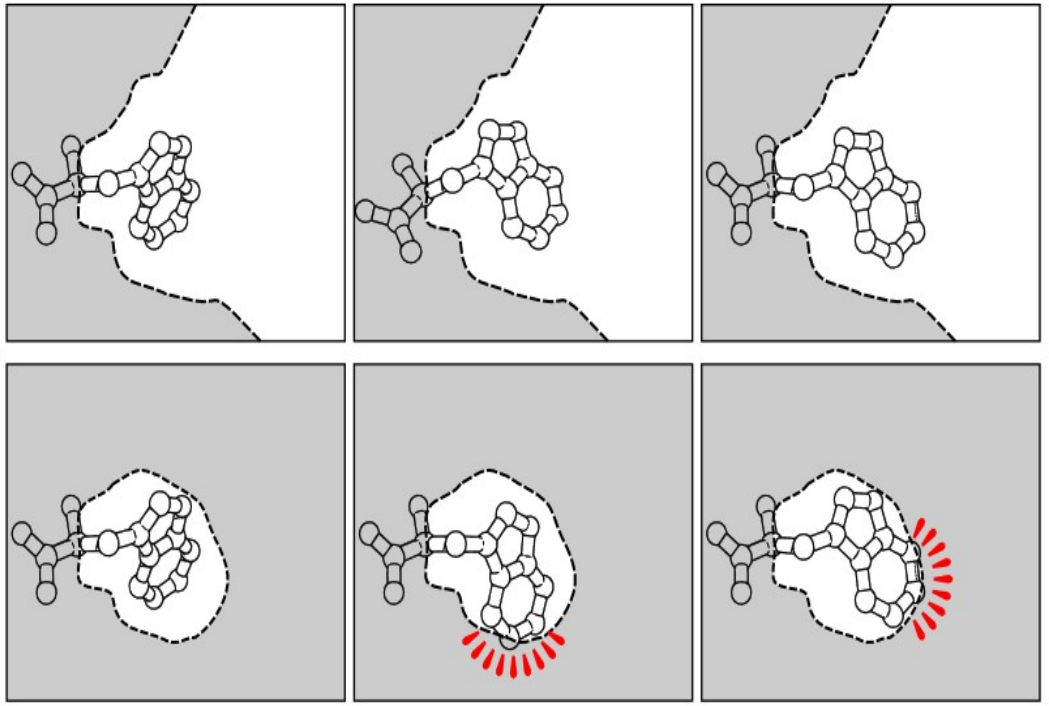


Computational Complexity - Combinatorial

10 3 **10** 3 **10** 9

possible conformations = 10 * 3 * 10 * 3 * 10 * 9 = 81000

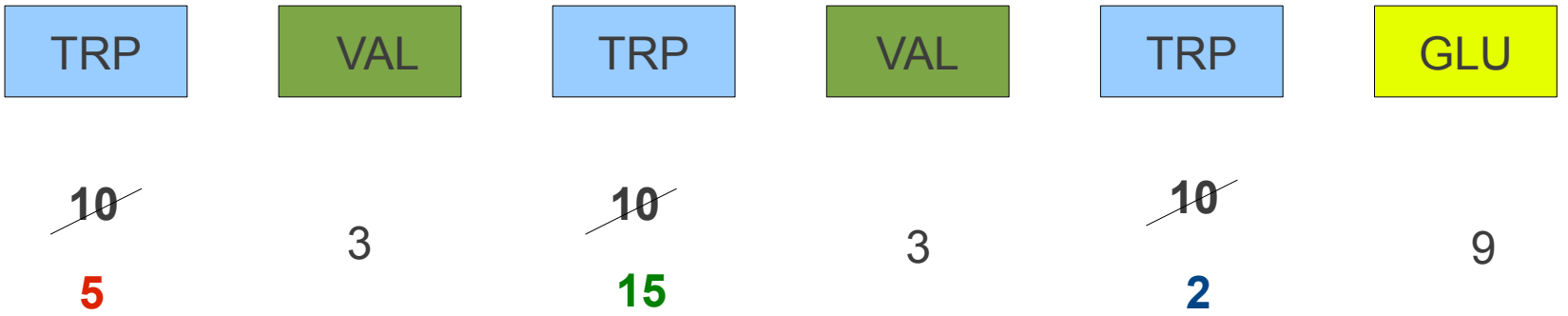
Varying sampling requirements



Exposed sidechain
Many isoenergetic
Conformations - Easy

Buried sidechain
Fewer isoenergetic
Conformations - Hard

Reduced Search Space and/or Better Energies



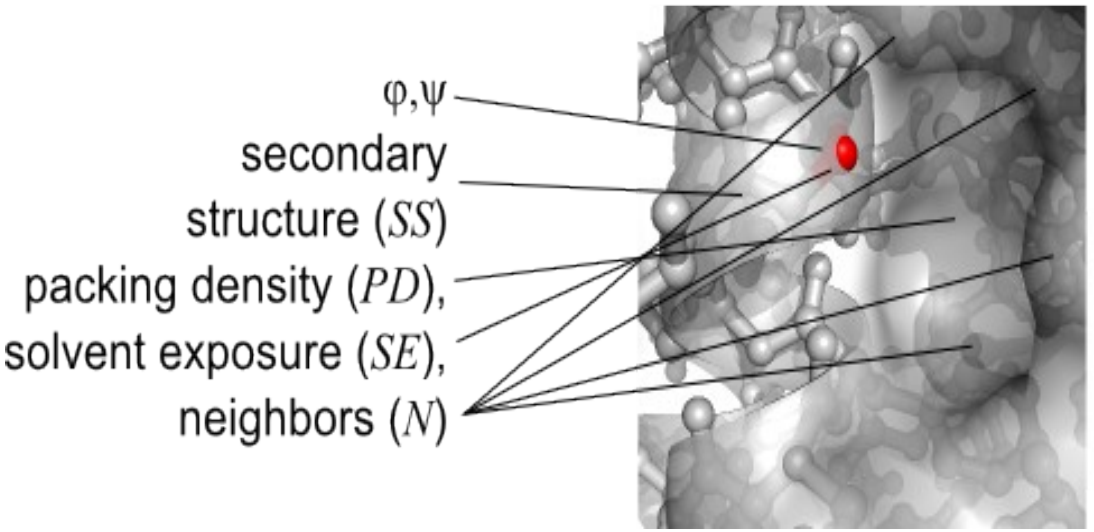
possible conformations = 5 * 3 * 15 * 3 * 2 * 9 = 12150

By moving sampling from the easy positions to the hard ones, we could be more efficient (fast) and/or achieve better energies

But, can we predict if a position is easy or hard?

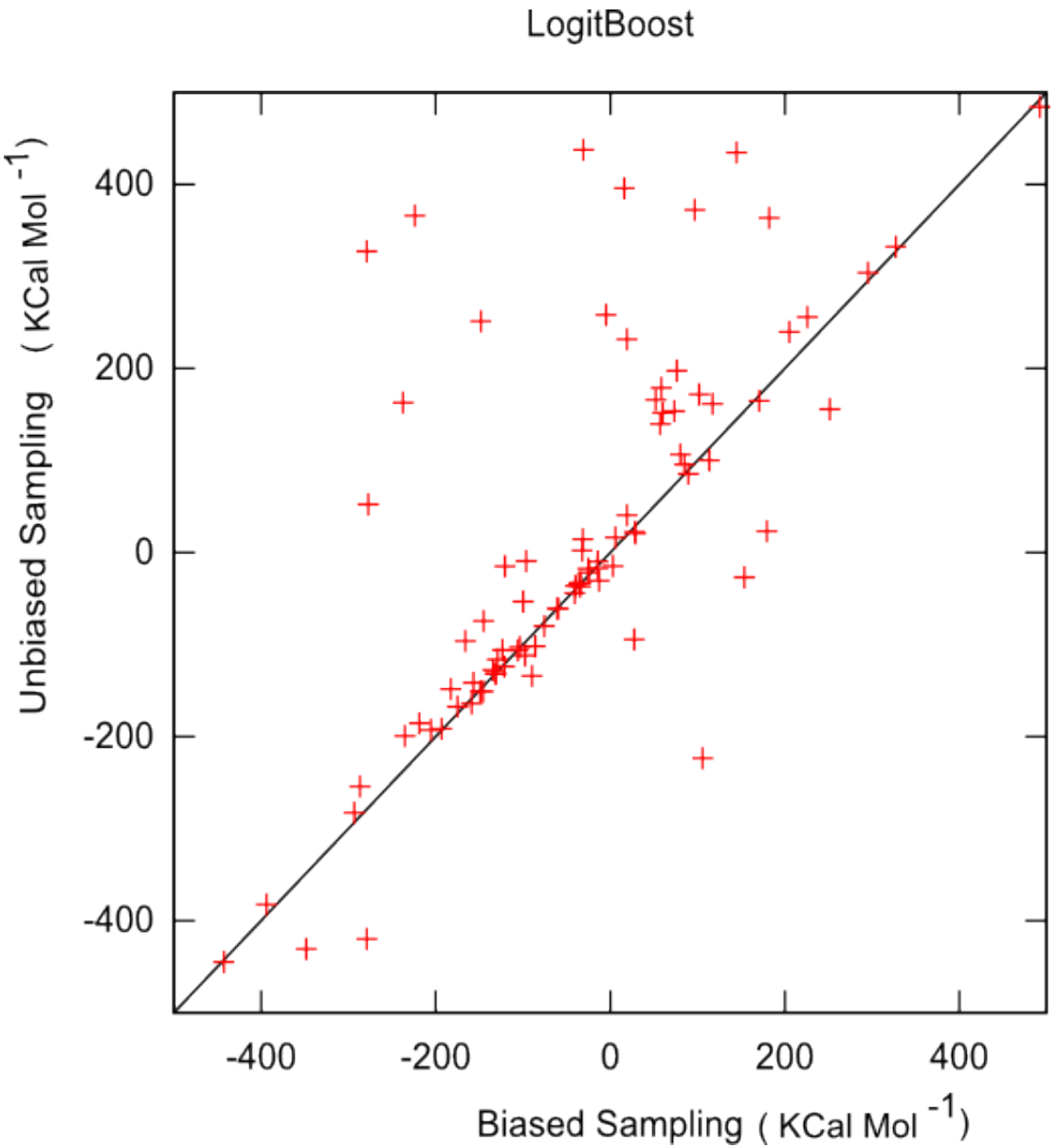
Yes, use machine learning

Associate each sidechain in the database with a feature vector $\boldsymbol{X}$ and a label $\boldsymbol{Y}$



$\boldsymbol{X}$ = {φ, ψ, *SS*, *SE*, *PD*, *N*, ...}
$\boldsymbol{Y}$ = {Hard, Medium, Easy}

Achieve better energies



The biased sampling scheme using machine learning achieves better energies on majority of the proteins

Thank You !!