# Increasing accuracy of energy calculations of lattice models by adjusting the potentials

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**Introduction:** Lattice models of proteins can approximate off-lattice structures to arbitrary precision with RMS deviations roughly equal to half the lattice spacing[1,2]. However, even small distortions in the positions of chain links lead to significant errors in lattice based energy calculations[3]. These errors arise mainly from rigid interactions (such as steric repulsion) which change their energies considerably at a range which is much smaller than the usual accuracy of lattice modelling (~1.0Å or more). To reduce this error we suggest a procedure of adjusting energy functions to a given lattice.

**Method:** The lattice adjusted potential for (particles) residues α and β has the following form[4]:

$$\tilde{\varepsilon}_{\alpha\beta}(l) = \sum_{\{r\}} W_{\alpha\beta}(r/l)\,\varepsilon_{\alpha\beta}(r) ,$$

where $W_{\alpha\beta}(r/l)$ is the probability that an off-lattice distance between particles α and β is ***r*** when the distance between their corresponding positions on the lattice is ***l***.

To determine the $W_{\alpha\beta}$'s we used two different approaches. In the first one we used statistics of inter-residue contacts in known proteins and their 3D lattice models. The second approach is based one an "a priori" physical estimation based on quasi-Boltzmann statistics in proteins[5].

**Application and Results:** These methods are illustrated using a set of energy calculations based on pairwise potentials by Kolinski et al[6] and lattices with spacings ranging from 0.5Å to 3.8Å. These calculations show that the lattice-adjusted potentials improve the accuracy of lattice based energy calculations as well as the correlations between off-lattice and on-lattice energies. The improvement is particularly essential for coarse lattices: while the energy calculation based upon the original potentials have no correlation with the off-lattice energies when lattice spacing exceeds 1.5Å, the accuracy of energy calculations on a lattice of 2.0Å spacing with adjusted potentials is the same as on a lattice of 1.0Å spacing with the original potentials. Figure 1. shows an example of improvement in accuracy of energy differences calculations for lattice models of the folded and the extended conformation of the α-chymotrypsin inhibitor. The best improvement in accuracy is obtained with the statistically adjusted potentials.

The method of energy function adjustment is simple and general. It can be applied to any off-lattice energy functions and will improve the accuracy of any discrete modeling procedures.

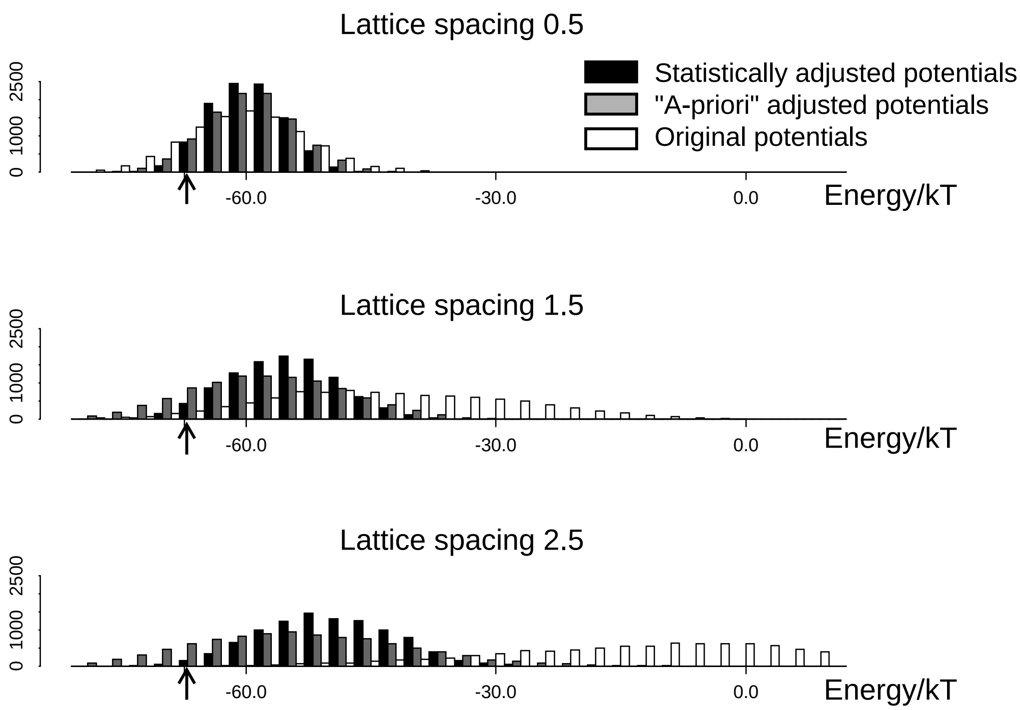


Figure 1: Histogram of energy differences between lattice models of the folded and the extended conformation of the α-chymotrypsin inhibitor (1acb). 100 lattice models of both conformations provided with 10,000 energy differences. The arrows indicate the off-lattice energy difference (-67.4).

## References


1 Rykunov D.S., Reva B.A., Finkelstein A.V. *Accurate general method for lattice approximation of three-dimensional structure of a chain molecule*. Proteins. **22**:, 100-109, 1995.

2 Reva B.A., Rykunov D.S., Olson A.J., Finkelstein A.V. *Constructing of lattice models of protein chains with side groups*. J.Com.Biol., in press, 1995.

3 Reva B.A., Sanner M.F., Olson A.J., Finkelstein A.V. *Lattice modelling: accuracy of energy calculations*. J.Comp.Chem., in press, 1996

4 Reva B.A., Finkelstein A.V., Sanner M.F., Olson A.J., *Adjusting potential energy functions for lattice modeling of chain molecules*. submitted in Proteins, 1995

5 Finkelstein A.V., Gutin A.M., Badretdinov A.Ya. *Why do protein architectures have Boltzmann-like statistics?*. Proteins, in press, 1996.

6 Kolinski A., Godzik A., Skolnick J. *A general method for the prediction of the three dimensional structure and folding pathway of globular proteins: Application to designed proteins*. J.Chem.Phys. **98**:1-14, 1993.