

Atomic Contact Energies

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1 Introduction

Energy functions are used to model protein 3D structures. Aspects that influence the free energy of proteins are van-der-Waals forces, electrostatics, dipole interactions, and torsions. The free desolvation energy describes the required energy for the trans-location of in water solvated atoms to the interior of a protein (Zhang et al., 1997), which therefore is measure for the stability of a structure. Zhang et al. (1997) described a method to approximate the desolvation energy based on atom contacts, rather than residue interactions, as proposed by Miyazawa and Jernigan (1996).

Their approach is to assign one of 18 atom types to each heavy atom. Based on these types, the energetic contribution of each contact pair to the overall energy is derived. A contact pair is defined by Zhang et al. (1997) as two atoms that have a distance below 6 Å and that are at least ten covalent bonds away from each other. The covalent distance is approximated with respect to connectivity classes without considering bonds in side-chains.

Here, we implement this algorithm and assess its quality on various protein prediction data sets.

2 Material and Methods

We implemented the algorithm in the Python language. In addition, we used Biopython’s pdb processing functionality (Hamelryck and Manderick, 2003).

The pairwise contact energies were adopted from Zhang et al. (1997). We used the author’s cutoff distance of 6 Å, because we were able to verify this value based on the atomic packaging of a large set of non-homologous experimental protein structures (see Figure 3)

The performance of the implemented function was assessed on a subset of the submissions to the eleventh CASP competition (Critical Assessment

Table 1: For the dataset T0784 and T0769, the tables show the computed contact energies and the RMSD counterparts sorted by energies (left) and by RMSD (right).

T0784	Energy in $\frac{kcal}{mol}$	RMSD	T0784	Energy in $\frac{kcal}{mol}$	RMSD
T0784TS156.1	-130.48	1.15	T0784TS117.1	-230.12	1.73
T0784TS420.1	-127.74	1.17	T0784TS008.1	-203.16	1.86
T0784TS499.1	-149.46	1.18	T0784TS251.1	-193.6	1.63
T0784TS237.1	-139.99	1.22	T0784TS038.1	-162.31	1.38
T0784TS268.1	-160.82	1.28	T0784TS268.1	-160.82	1.28

T0769	Energy in $\frac{kcal}{mol}$	RMSD	T0769	Energy in $\frac{kcal}{mol}$	RMSD
T0769TS241.1	-59.34	2.67	T0769TS442.1	-90.73	16.72
T0769TS368.1	-66.75	3.16	T0769TS155.1	-90.62	17.12
T0769TS258.1	-74.39	4.37	T0769TS044.1	-84.32	10.38
T0769TS361.1	-79.04	4.41	T0769TS169.1	-81.02	10.39
T0769TS186.1	-79.97	4.51	T0769TS317.1	-80.61	6.89

of protein Structure Prediction)¹. The datasets in question were T0762, T0769, T0776, T0784. We evaluated each prediction by superimposing its backbone C α atoms onto the reference and computing the RMSD values, which we compared to the RMSD numbers listed on the CASP website². Afterwards, we investigated correlations between the RMSD and the computed energies whereby the implementations of the Pearson and the Spearman correlation coefficients from the python package SciPy (Oliphant, 2007) were used.

3 Results

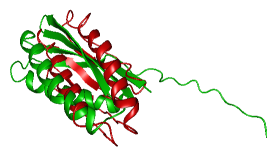
For every target structure, we visualized the prediction with the lowest RMSD and the one with the lowest free contact energy in BALLView (Moll et al., 2006). Representative visualizations for the datasets T0679 and T0784 are shown in Fig. 1

The relationship between ranked contact energy prediction and the RMSD are shown in Fig. 2.

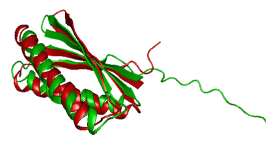
Pearson’s correlation coefficients between the free contact energies and the RMSD ranged from 0.19 to 0.44. In contrast to these values, Spearman’s rank correlation coefficients were lower, in a range from 0.15 to 0.33 (Table 1). A comparison of the C α superimposed RMSD values with the reference values from CASP an high degree of similarity.

¹<http://www.predictioncenter.org/casp11> (last accessed: June 17, 2015)

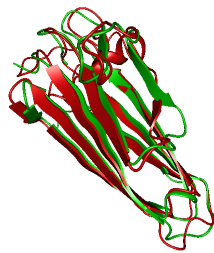
²http://www.predictioncenter.org/casp11/local_acc_plot.cgi?target=T0762-D1 (last accessed: June 17, 2015)



(a) T0769 442



(b) T0769 241



(c) T0784 117



(d) T0784 156

Figure 1: Best scoring predictions of T0769 and T0784 evaluated using (a,c) atomic contact energies and (b,d) the RMSD between prediction and experimental structure. green: target experimental structure. red: predicted structure.

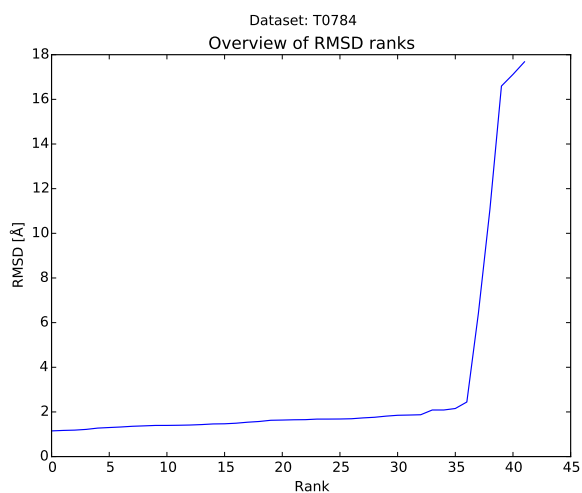


Figure 2: Calculated RMSD values are plotted against the rank of the corresponding prediction for the target set T0784.

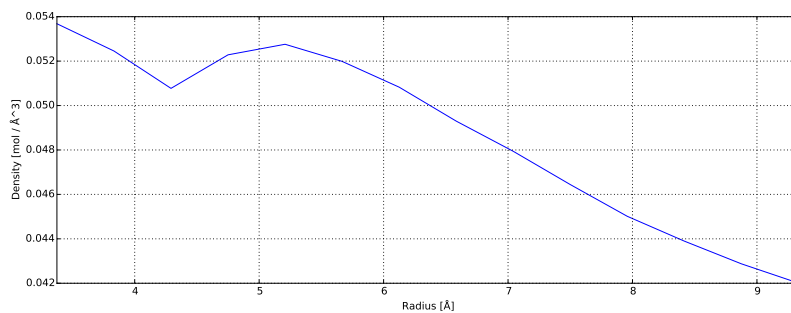


Figure 3: Shown is the atomic packaging estimated by the number density according to a radius around an interior atom. An atom is considered to be buried if the accessible surface area (SAS) is zero.

4 Discussion

After implementing the algorithm of Zhang et al. (1997), we were able to reproduce the threshold value of 6 Å on a non-homologous structure set. A relative increase of density for radii around this value was observable (see Figure 3) which could be due to the relevance for atomic contacts. The correlation metrics Pearson and Spearman did not indicate a linear correlation between RMSD and the computed energies. However, visual inspections of the RMSD distribution suggest that these metrics are bound to fail, because significant changes were only observed for the lower ranking third of the predicted structures. The original CASP11 evaluations take this property of RMSD into account, as they utilize a multitude of other quality measures.

Although the correlation coefficients are low, plots of the superimposed structures show trends of consensus with the reference structures.

Since the overall energy is derived from the sum of contact energies, the implemented algorithm just took a few minutes on the whole dataset. Therefore, we suggest that the energy function of Zhang et al. (1997) is suitable to quickly assess the quality of folds, even though the resulting values will not be able to compete with more current free desolvation energy functions.

References

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