Supplementary Material

What Are the Preferred Horizontal Displacements of Aromatic-Aromatic Interactions in Proteins? Comparison with Calculated Benzene-Benzene Potential Energy Surface

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Data from Protein Data Bank

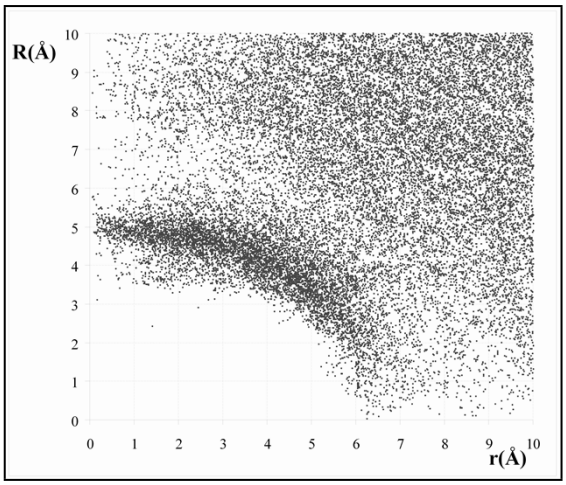


Fig. S1 The correlation of the normal distance (R) with the offset values (r) ; R< 10 Å and r < 10 Å.

The PDB search yielded 24 002 contacts in which centre of the phenyl ring from phenylalanine residue was found to be within the area that corresponds to R< 10 Å and r < 10 Å around another phenylanine ring. The data suggest that two interacting rings form ellipsoid on diagram. The final number of 6 919 structures were extracted from initial set of structures using equation of an ellipsoid $(x/a)^2 + (y/b)^2 = 1$ where a=(r)=7Å and b=(R)=6Å.

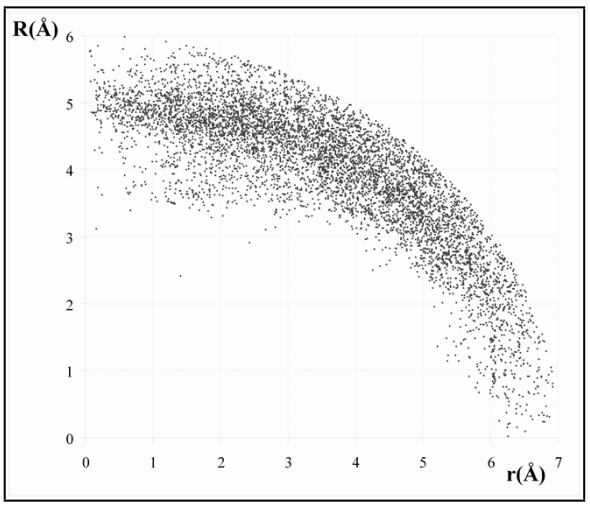
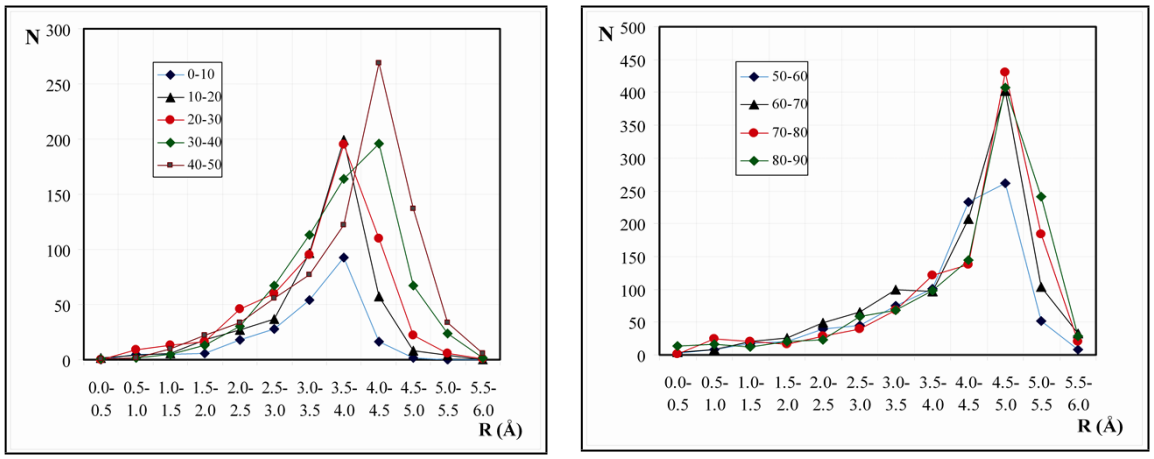


Fig. S2 The correlation of the normal distance (R) with the offset values (r) for ellipsoid with R= 6 Å and r=7 Å



a) b)

Fig. S3 Distributions of normal distance R for various tilt angles a) for the tilt P_1/P_2 angle in the range 0-50º b) for the tilt P_1/P_2 angle in the range 50-90º

For the tilt angle P_1/P_2 in the range 0-30º (Figure S3a) the distribution shows large number of interactions with R value in the range of 3.5-4.0 Å. These R values are typical for stacking interaction. The values of R increase with the tilt angles increase and reach its maximum in the range of 4.5-5.0 Å, for the torsion angles larger than 50º (Figure S3b).

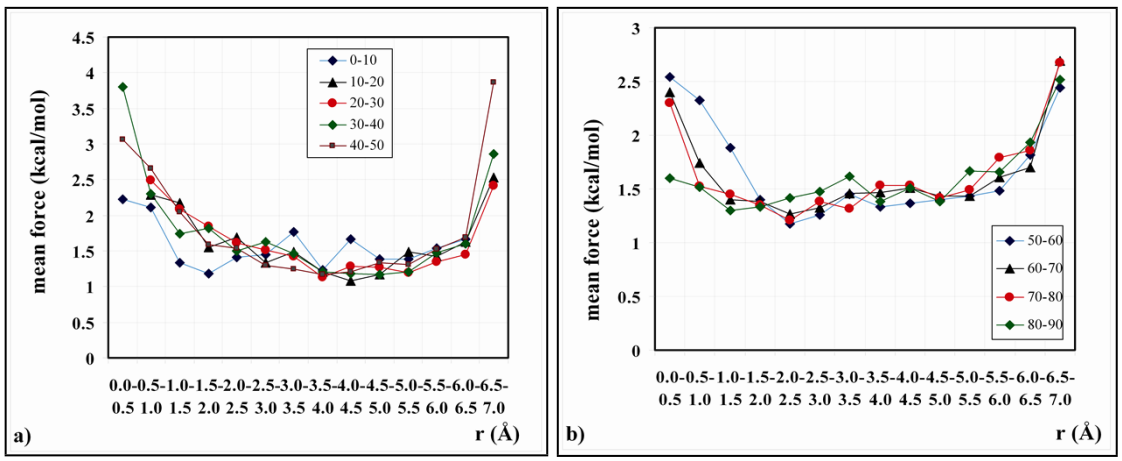


Fig. S4 The mean force (according to Boltzmann law)[**S1**] for different r values a) for the tilt P_1/P_2 angle in the range 0-50º b) for the tilt P_1/P_2 angle in the range 50-90º

Results of Calculations

The geometry of isolated benzene molecule was optimized using B2PLYP-D2/def2-TZVP method. The optimized benzene geometry is a planar regular hexagonal ring, with a C-C bond of 1.392 Å and a C-H bond of 1.082 Å.

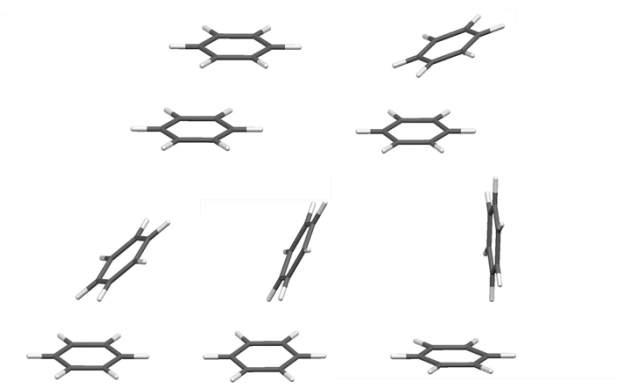
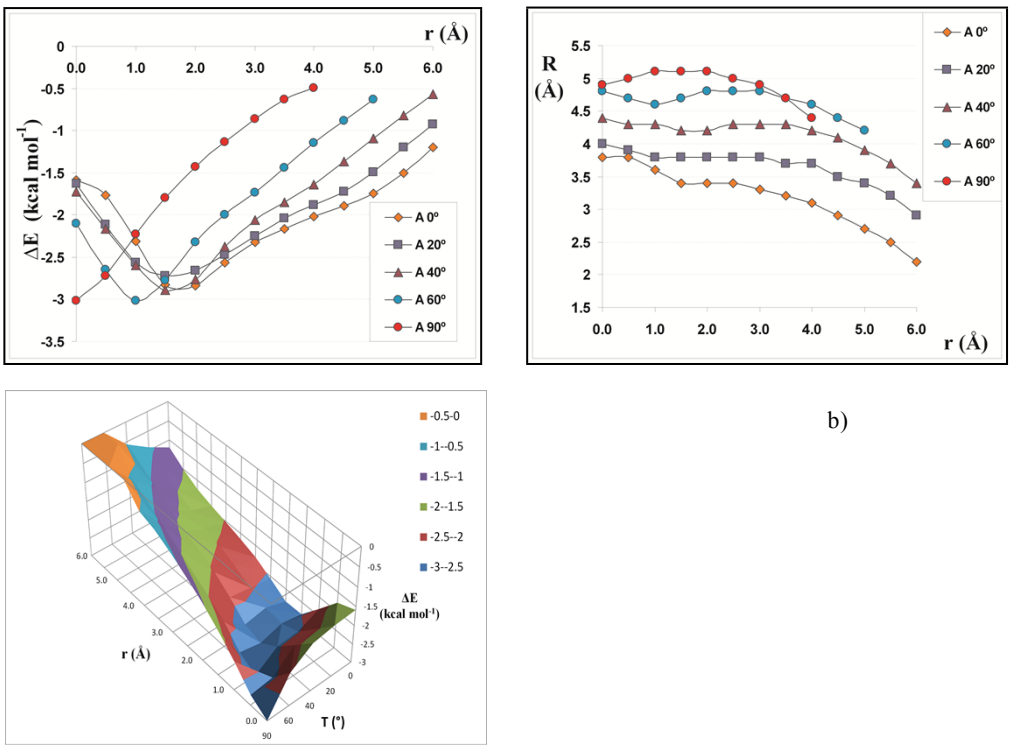


Fig. S5 The side view of the A orientation at different values of tilt angles (0º, 20º, 40º, 60º and 90º) for the offset *r* of 1.5Å.



a) b)

Fig. S6 a) Calculated interaction energies (ΔE) presented on 2-D (up) and 3-D (down) diagrams; b) the optimal normal distances (R) of orientation A (Figure S4) for values of tilt P_1/P_2 angle of 0º, 20º, 40º, 60º and 90º. The values for angle 0º are obtained in previous work[15]

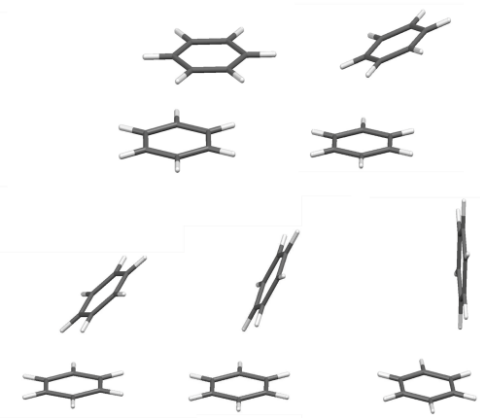
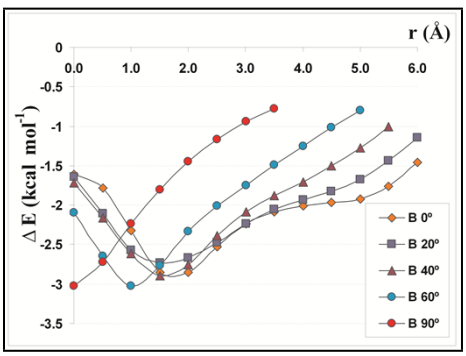
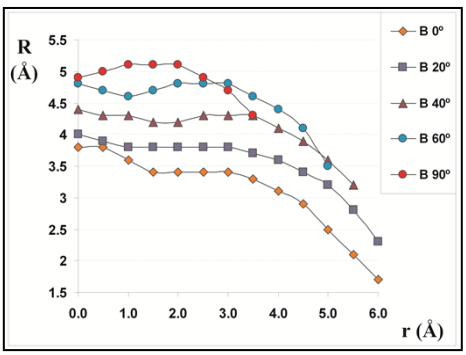
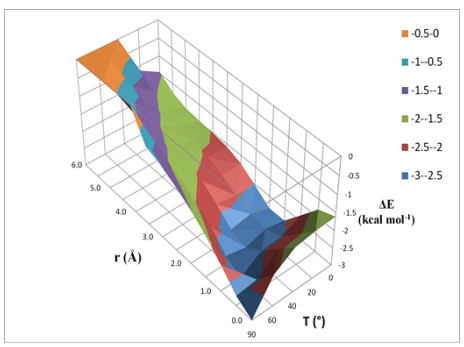


Fig. S7 The side view of the B orientation at different values of tilt angles (0º, 20º, 40º, 60º and 90º) for the offset *r* of 1.5Å.





b)



a)

Fig. S8 a) Calculated interaction energies (ΔE) presented on 2-D (up) and 3-D (down) diagrams; b) the optimal normal distances (R) of orientation B (Figure S6) for values of tilt P_1/P_2 angle of 0º, 20º, 40º, 60º and 90º. The values for angle 0º are obtained in previous work[15]

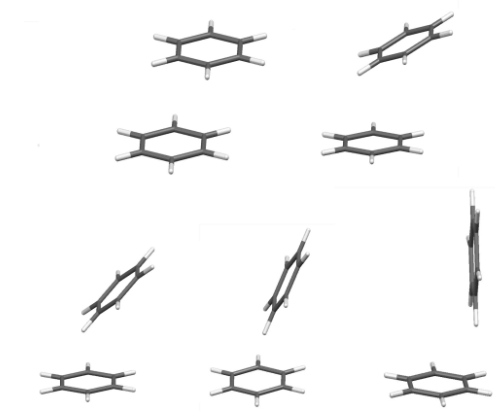
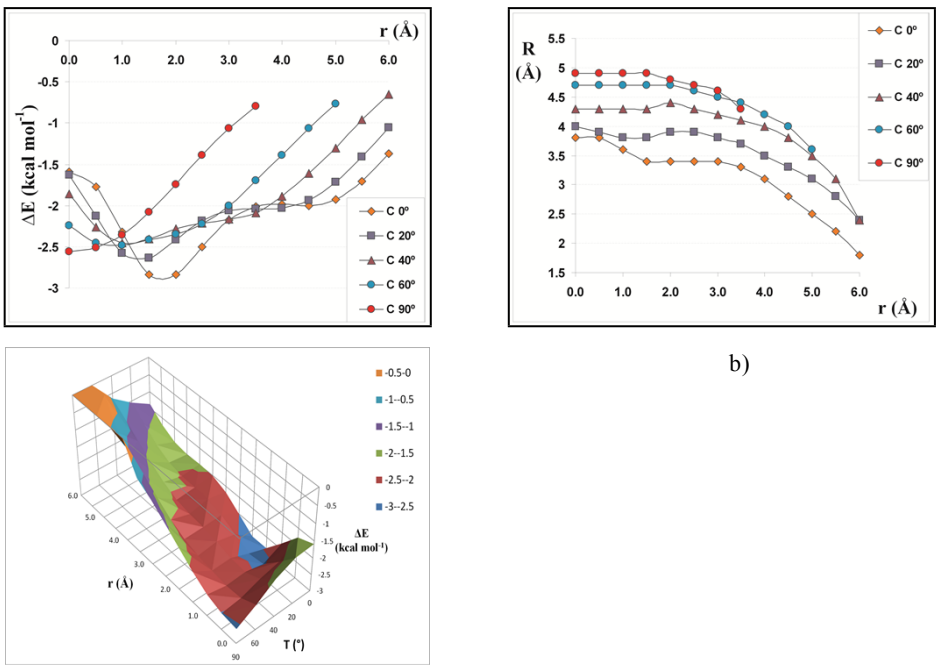


Fig. S9 The side view of the C orientation at different values of tilt angles (0º, 20º, 40º, 60º and 90º) for the offset *r* of 1.5Å.



b)

a)

Fig. S10 a) Calculated interaction energies (ΔE) presented on 2-D (up) and 3-D (down) diagrams; b) the optimal normal distances (R) of orientation C (Figure S8) for values of tilt P_1/P_2 angle of 0º, 20º, 40º, 60º and 90º. The values for angle 0º are obtained in previous work[15]

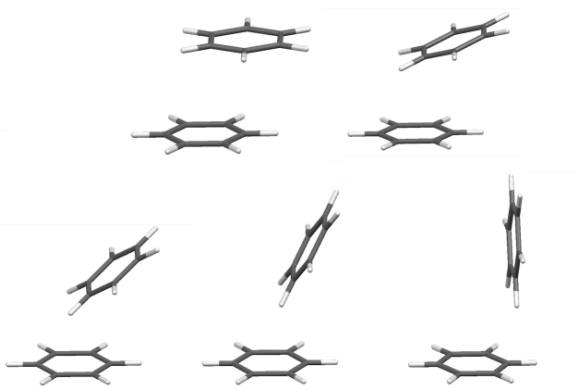
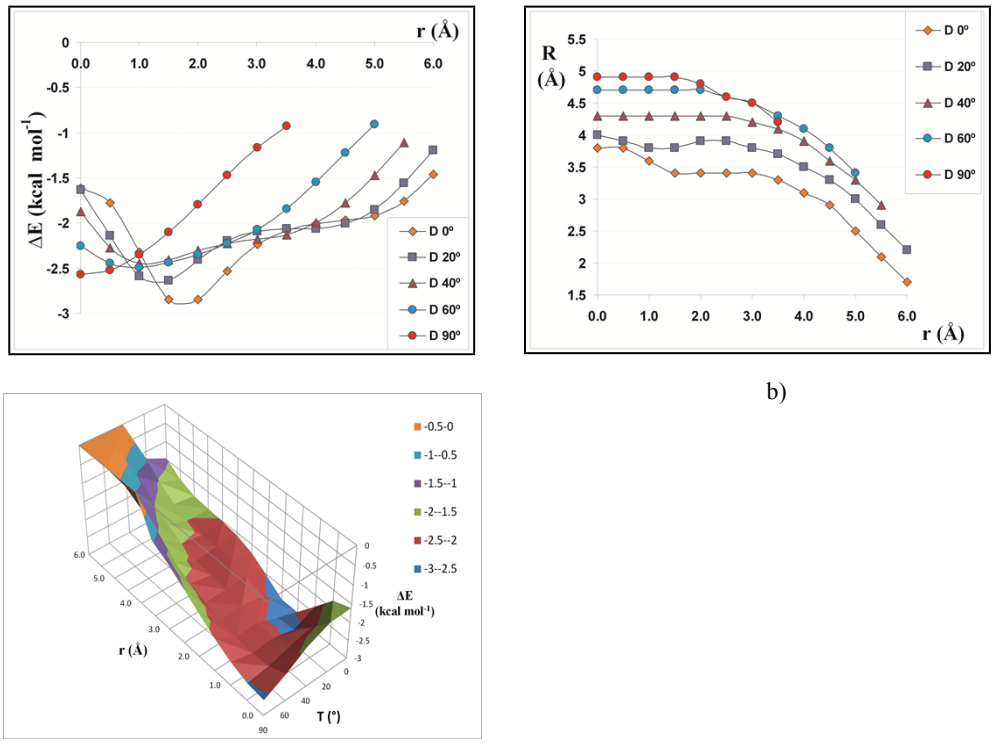


Fig. S11 The side view of the D orientation at different values of tilt angles (0º , 20º, 40º, 60º and 90º) for the offset *r* of 1.5Å.



a) b)

Fig. S12 a) Calculated interaction energies (ΔE) presented on 2-D (up) and 3-D (down) diagrams; b) the optimal normal distances (R) of orientation D (Figure S10) for values of tilt P_1/P_2 angle of 0º, 20º, 40º, 60º and 90º. The values for angle 0º are obtained in previous work[15]

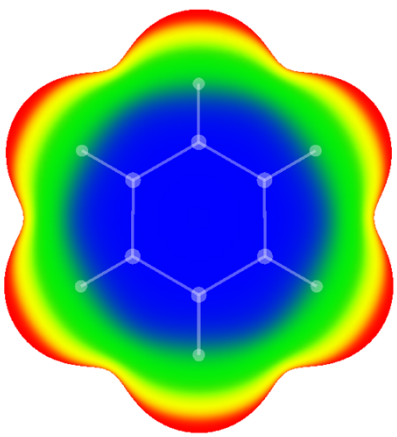


Fig.S13 The view of electrostatic potential map of benzene, C_6H_6 ; electrostatic potential increases from blue (V(r) < -8.9 kcal/mol) and green (V(r) = -8.9 to 0.0 kcal/mol) to yellow (V(r) = 0.0 to +6.7 kcal/mol) and red (V(r) > +6.7 kcal/mol); grey dots and lines represent atoms and bonds.

[**S1**] Manfred J. Sippl, *J.Mol.Biol.*,1990, **213**, 859.

[**S2**] F. A. Bulat and A. Toro-Labbe, 'WFA: A suite of programs to analyse wavefunctions', unpublished ; F. A. Bulat, A. Toro-Labbe, T. Brinck, J. S. Murray, P. Politzer, *J. Mol. Model.*,2010, **16**,1679.