Comparative analysis of hydrogen bond energy between protein-ssDNA and protein-dsDNA complexes

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Introduction

Protein-DNA interactions are essential to a number of key biological processes such as DNA replication, repair ,gene transcription, and genome integrity.

These interactions typically occur between proteins and DNA of two distinct structural types, double-stranded DNA (dsDNA) and single-stranded DNA (ssDNA), and are mediated by weak intermolecular forces including hydrogen bonds.

Each DNA type has unique structural and functional properties that are further influenced by varying levels of binding specificity, from nonspecific to highly specific.

Previous studies have demonstrated that hydrogen bonds play a crucial role in protein interactions[1], with protein-DNA complexes exhibiting a unique distribution of hydrogen bond energy compared to other protein-ligand complexes[2].

This study aims to quantitatively assess hydrogen bond energy distributions of dsDNA and ssDNA complexes with respect to varying levels of binding specificity in order to gain insights into the role of hydrogen bonds between different DNA types.

Methods

A nonredundant dataset composed of complexes with varying levels of binding specificity and DNA type was used.

	protein-dsDNA	protein-ssDNA
SP	126	17
NS	41	27

REDUCE[3] was used to add hydrogen atoms to crystallography files, FIRST[4] was used to calculate hydrogen bond energy based on the following criteria.

$$E_{HB} = V_0\left\{5\left(\frac{d_0}{d}\right)^{12} - 6\left(\frac{d_0}{d}\right)^{10}\right\} F(\theta, \phi, \varphi)$$

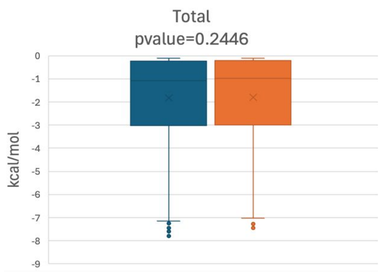
Hydrogen bonds were grouped into 3 categories Backbone-Backbone (BB-BB), Sidechain-Base (SC-Base), and Mixed.

Mann-Whitney U test was used to compare continuous distributions of hydrogen bond energy based on DNA type and binding specificity.

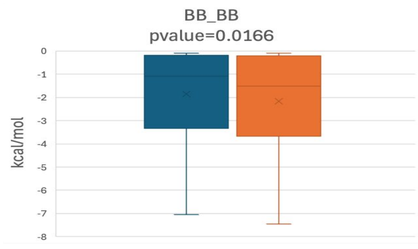
Results

protein-dsDNA

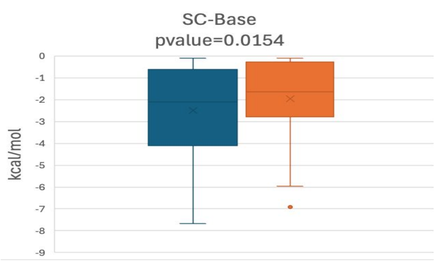
Figure 1: Comparison of Binding Specificity in protein-dsDNA – SP (Blue) vs NS (Orange)



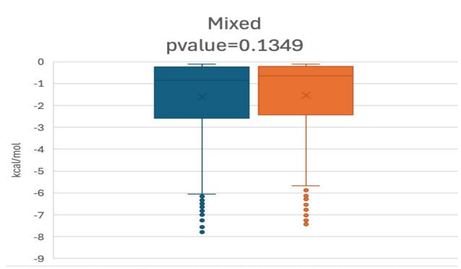
A. No significant difference in all hydrogen bonds



B. Significant difference in distributions of BB-BB interactions



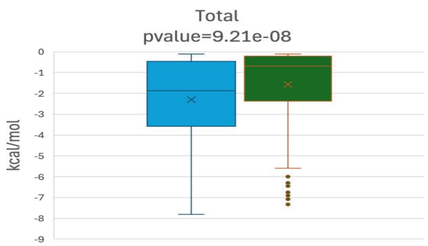
C. Significant difference in distributions of SC-Base interactions



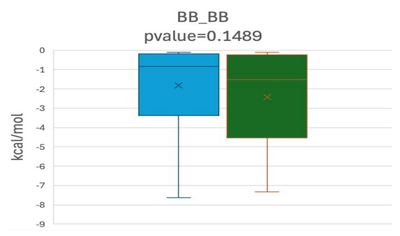
D. No significant difference in distributions of Mixed Interactions

protein-ssDNA

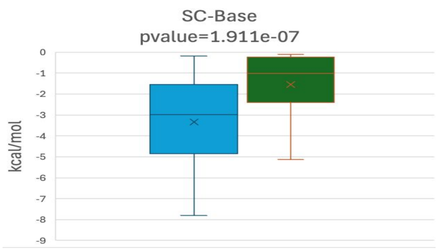
Figure 2: Comparison of Binding Specificity in protein-ssDNA – SP (Blue) vs NS (Green)



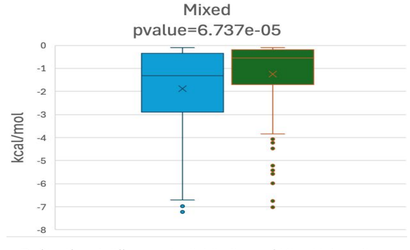
A. Significant difference in all hydrogen bonds.



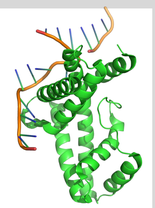
B. No significant difference in distributions of BB-BB interactions



C. Significant difference in distributions of SC-Base interactions



D. Significant difference in distributions of Mixed interactions.



Results

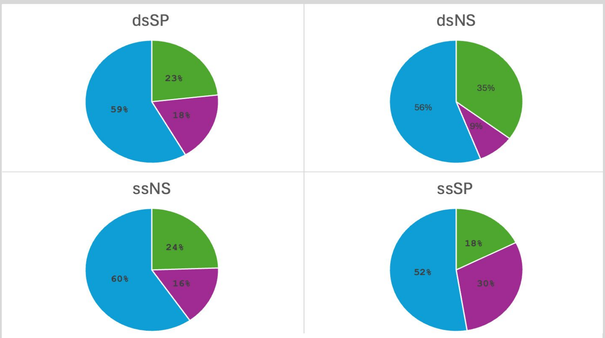


Figure 3 - Distribution of hydrogen bonds(<-0.1 kcal/mol) for interaction type BB-BB(Green), SC-Base (Purple), Mixed (Blue) among different types of complexes

	ssDNA-SP	dsDNA-NS
dsDNA-SP	1.049e-06	2.2e-16
ssDNA-NS	1.229e-10	1.415e-07

Table 1 Chi-square goodness of fit test comparing distribution of interaction types

Conclusion

Comparisons in protein-dsDNA complexes reveal no difference in overall distribution of hydrogen bond energies but a significant difference in interaction types between different specificity types. NS complexes are composed of more backbone-backbone interactions whereas SP complexes favor SC-Base and Mixed interactions.

Comparisons in protein-ssDNA complexes reveal a significant difference in overall distribution of hydrogen bond energies with SP complexes having stronger hydrogen bonds and having a larger composition of SC-Base interactions

References

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