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Abstract

Motivation. Hydrogen bonds belong to the most important interactions in the biopolymer structure. Up to now, due to the dimension of the biopolymers and to the limited computer resources, only geometrical criteria were used to identify possible candidates for an attractive interaction (see the Hbexplore and HBplus programs). We have proposed the Mulliken overlap population (OP) as a quantitative quantum chemical criterion, not only for the identification of possible interactions, but also for the evaluation of their relative strength.

Method. An original program SHB_interactions was developed to identify and to analyze intermolecular interactions in biopolymers. Mulliken overlap population values are calculated with the Extended Hückel (EH) method. This method, due to its simplicity, offers the possibility to perform such calculations for a large set of biopolymer structures in a relative short time. The program uses PDB files containing NMR structures, builds a possible interaction table with all the residue pairs that have atoms placed at a distance less than 3.5 Å, cuts off from the structure the corresponding residue pairs, adds hydrogen atoms to satisfy the oxygen and phosphorus valences, and performs EH calculation of the overlap population values. Although SHB_interactions was initially developed for the nucleic acid structures, it can be applied to proteins as well. The application of SHB_interactions is described for the 1g70 structure, an RNA/protein complex of HIV–1 RRE–IIB RNA with the peptide RSG–1.2.

Results. A comparison between the results obtained for 1g70 and those obtained using geometrical criteria (HBexplore) was made. 56 DNA and 22 RNA NMR structures from Protein Data Bank have been scanned in order to identify and to analyze the hydrogen bond intermolecular interactions using the OP criterion. Our results show that there is a clear delimitation between H–bond overlap population values when the acceptor is an oxygen atom and those when the acceptor is a nitrogen atom. This is evidence for the capability of the overlap population to make distinction between different H–bond types, and allows comparative analysis of the results for the same type of H–bonds. For classical H–bonds interactions ($r > 1.7$ Å) the overlap population values are in the range 0.01 – 0.15. The OP criterion allows makes possible the detection of weaker H–bonds.

Conclusions. In spite of the limitations of the EH method, the results obtained with SHB_interactions allow a rationalization of the H–bonds in nucleic acids as well as in protein structures. The results obtained outline the capability of the OP criterion to substitute all of the five geometrical parameters used by HBexplore. In addition, the use of the overlap population as a quantum selection criterion presents the advantage to detect not only the weaker H–bonds like C–H…A, but also any other atom–atom intermolecular interactions.

Availability. The source code for SHB_interactions, written in C, instructions and some examples are available at http://gw–chimie.math.unibuc.ro/staff/cbendic/shb/SHB_interactions.html.

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Keywords. SHB_interactions; hydrogen bonds; nucleic acids; overlap population.

Abbreviations and notations	
A, acceptor	OP, Overlap Population
D, donor	PDB, Protein Data Bank
DNA, deoxyribonucleic acid	RNA, ribonucleic acid
EH, Extended Hückel	SHB, Search for Hydrogen Bonds

1 INTRODUCTION

The hydrogen bonds are one of the most important intra– and inter–molecular interactions in biological macromolecules [1], and are responsible for the structural and functional differences in RNA and DNA. A new and fundamental, but unanswered question of biochemistry could be considered: are there differences between DNA and RNA hydrogen bonds?

Much of our current understanding of hydrogen bonds of DNA and RNA is extrapolated from small molecule studies. Measurements of hydrogen bonds in nucleic acids have been difficult due to the interference of other weak interactions such as base stacking [2–4].

Recently, through a combination of direct experimental measurements on DNA and RNA, and *ab initio* calculations, it was shown that N3–H3…N1 hydrogen bonds of A:U base pairs in RNA duplexes are stronger than those of A:T base pairs in DNA. The observed differences in hydrogen bond strengths is consistent with an average shorter H–bond length in RNA of only a few hundredths of an Ångström [5,6].

Existing tools for H–bond analysis, like the corresponding modules in structure determination or modeling packages, do not have the required flexibility. Even complex programs such as HBexplore [7] and HBPLUS [8] are limited to a selection of potential H–bonds using only geometrical criteria, followed by a classification and a statistical analysis.

In order to identify and to analyze intermolecular interactions, an original program called SHB_interactions [9], was especially developed. This program is based on Extended Hückel (EH) calculation [10] and uses the Mulliken overlap population [11] as a quantitative quantum chemical criterion, able to measure the strength of hydrogen bonds, and of other atom–atom intermolecular interactions. Differing from the previous HBexplore [7] program, which outlines only the potential hydrogen bonds, this program allows an estimate of the contribution of every atom–atom intermolecular interaction to the stabilization of the biopolymers and their complexes with different ligands.

The purposes of the present paper are: (*a*) to make a comparative analysis between the results obtained using OP as quantum criterion and the results based only on geometrical criteria (HBexplore), and (*b*) to analyze the hydrogen bonding patterns for a large sets of DNA and RNA structures using this quantum chemical criterion.

2 MATERIALS AND METHODS

Mulliken overlap population values were calculated with the Extended Hückel method [10] using SHB_interactions [9]. The simplicity of this method offers the possibility to perform, due to our algorithm, such calculations for a large set of biopolymer structures in a relative short time, and to obtain the electronic structure properties of huge molecules like nucleic acids.

The choice of the overlap population as a quantitative quantum chemical criterion, able to measure the strength of atom–atom intermolecular interactions, is justified qualitatively: the more positive is the electronic population of atomic overlap distribution $\chi_A^*\chi_B$ (A and B are two neighboring nuclei), the greater the overlap distribution contributes to atom–atom interaction [12]. The chemical bond is a classical example.

The use of the EH method is also justified because it is the only semiempirical method that does not use the ZDO approximation and allows the direct calculation of Mulliken overlap population. The simplicity of this method and the approximations that are made are compensated by the use of overlap population as a relative criterion in the interpretation of the results.

Although the SHB_interactions program was initially developed for the nucleic acid structures, it can be applied to proteins as well. Therefore, the application of SHB_interactions and the comparative analysis with HBexplore is described for the RNA/protein complex of HIV–1 RRE–IIB RNA with the peptide RSG–1.2 (PDB code: 1g70).

A set of 56 DNA and 22 RNA NMR structures from Protein Data Bank has been scanned in order to identify and to analyze the hydrogen bond intermolecular interactions using the SHB_interactions program.

DNA PDB codes: 103d, 107d, 132d, 140d, 141d, 142d, 143d, 170d, 171d, 175d, 177d, 179d, 185d, 186d, 193d, 199d, 1a6h, 1a83, 1a84, 1a8n, 1a8w, 1ac7, 1afz, 1ag3, 1ag5, 1agh, 1agk, 1ago, 1agz, 1al9, 1amd, 1ao1, 1ao9, 1ap1, 1at4, 1au5, 1au6, 1aul, 1ax6, 1ax7, 1axo, 1axp, 1axu, 1b6x, 1b6y, 1bae, 1b5k, 1b60, 1axv, 1b0s, 1b3p, 1b4y, 1bcb, 1bce, 1bdz, and 1be5.

RNA PDB codes: 176d, 17ra, 1a3m, 1a4d, 1a4t, 1a51, 1a60, 1a9l, 1afx, 1ajl, 1ajt, 1al5, 1am0, 1anr, 1aqo, 1atv, 1atw, 1b36, 1bau, 1bgz, 1bj2, and 1bn0.

NMR structures often contain more than one model. In such cases only model 1 was used for the analysis.

2.1 Computer Software

The source code for SHB_interactions, written in C, can be obtained on request from the author, and is available at http://gw–chimie.math.unibuc.ro/staff/cbendic/shb/SHB_interactions.html. The source code can be modified and any other desired method that permits the overlap population

calculation can be added and used instead of the EH method.

The SHB_interactions program requires structural information in the PDB format [13]. The positions of the H atoms are usually not given for the structures determined by diffraction methods. Therefore, the program in the present form can use only NMR structures that contain also the coordinates of hydrogen atoms. An alternative way, which allows X–ray structures to be used, is to add hydrogen atoms with a protein–nucleic acid manipulation program.

The program uses as input file a PDB file: pdbxxxx (xxxx is the PDB code) scans it and creates a file xxxx. This file contains a possible interaction table with all the pairs of the residue numbers that correspond to the different residues (nucleotide–nucleotide, ligand–nucleotide, molecule–molecule etc.) that possess atoms placed at a distance less than 3.5 Å. These residues can be considered to interact with each other.

Using this table of residue numbers, SHB_interactions cuts off from the PDB structure the corresponding residue pairs, adds hydrogen atoms to satisfy the oxygen and phosphorus valence, and performs EH calculation of the overlap population. Finally, the program lists all the atom pairs with overlap population values greater than 0.0005 and creates files that contains H–bonds sorted according to the residue types (base–base, backbone–backbone, backbone–base, etc.)

More details about how to use the program and some samples are delivered together with the source code and the make file [9].

3 RESULTS AND DISCUSSION

The application of SHB_interactions is described for the 1g70 structure, a RNA/protein complex of HIV–1 RRE–IIB RNA with the peptide RSG–1.2. This RNA/protein complex provides a good example to illustrate the capability of SHB_interactions to identify and to analyze the H–bonds not only in nucleic acids, but also in proteins.

The overlap population values corresponding to the principal covalent bonds for this structure, calculated with SHB_interactions, are presented in Table 1.

Table 1. The Overlap Population Values of the Covalent Bonds in DNA and RNA

Bond	*r* (Å)	Overlap population
C – H	1.05–1.11	0.451–0.756
N – H	1.01–1.02	0.560–0.668
O – H	0.96–1.10	0.363–0.431
C – C	1.49–1.56	0.636–1.607
C – O	1.41–1.46	0.717–1.214
C – N	1.46–1.49	0.571–0.812
C = O	1.20–1.23	1.441–2.087
C = C, C ≕ C	1.34–1.45	0.868–2.170
C = N, C ≕ N	1.29–1.39	1.029–2.798

These results show that covalent bonds (bond length up to 1.6 Å) have overlap population values in the range 0.3 – 2.8, whereas for the intermolecular interactions (r > 1.7 Å) the overlap population is at least an order of magnitude lower. Similar results were obtained for the previously investigated Actinomycin D–DNA complexes and 1rnk RNA structure reported elsewhere [15,16].

The results obtained for 1g70 structure are summarized in Tables 2–4 in Appendix 1. In these tables the overlap population values between hydrogen atoms and different acceptors are listed in an increasing order. The last five columns of the tables contain the geometrical parameters used by HBexplore for the selection of these hydrogen bonds. It can be observed that all base–base H–bonds (Table 2, Appendix 1) selected using HBexplore geometrical criteria were found by SHB_interactions, with overlap population values in the range 0.004–0.078, except 2H6:A A73 – O6:G A46 H–bond. In this case A A73 and G A46 are located in two different planes, and although geometrical criteria were fulfilled, SHB_interactions rejected this bond because a negative value of the overlap population was obtained for it and therefore, the interaction between 2H6 and O6 is not possible.

In the case of backbone–backbone and backbone–base H–bonds the correspondence between the results obtained using geometrical and OP criteria is not relevant. This is due to the differences in the H–atom positions used as input data for sp^3 donor atoms: the SHB_interactions program uses H–atoms positions from PDB files, whereas HBexplore calculates the H–atom coordinates for the position corresponding to the minimum H…A distance, considering a free rotation around the C – D bond. The overlap population for this kind of H–bond is in the range 0.005–0.073 (Table 3, Appendix 1).

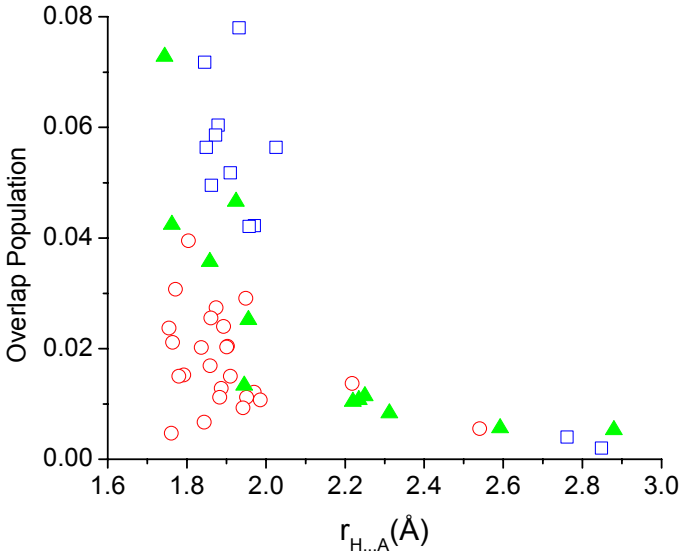

Figure 1. Overlap population for H–bonds *vs*. H…A distance for 1g70 RNA; □ – D – H…N hydrogen bonds; o – D – H…O base–base; ▲ – backbone–backbone hydrogen bonds;

An interesting result is outlined in Figure 1 that presents the H–bond overlap population as a function of the hydrogen–acceptor distance (r_{HA}) for 1g70 RNA structure. It may be observed that there is a clear delimitation between H–bond overlap population values when the acceptor is an oxygen atom and those when the acceptor is a nitrogen atom. In addition, D – H…N bonds have OP values greater than D – H…O bonds for the same distance between hydrogen and acceptor atom.

The examination of the data in Figure 1 also outlines that the OP values for the backbone–backbone H–bonds are intermediate between D – H…N and D – H…O base–base H–bonds. This is an evidence for the capability of the overlap population to make distinction between different H–bond types, and allows comparative analysis of the results.

Major differences are observed for protein–protein and protein–base H–bond due to the fact that HBexplore program does not consider the amidic N–atom as a possible H–acceptor, a possibility that is taken into account by other protein manipulation programs (*e.g.*, HyperChem, Sibyl). For these H–bonds, the SHB_interactions program finds OP values in the same range as H–bonds having nitrogen, respectively oxygen atom as acceptor (Table 4, Appendix 1).

The results obtained outline the capability of the overlap population to substitute all the five geometrical parameters used by HBexplore. Moreover, the use of the overlap population as a quantum selection criterion presents the advantage to offer the possibility to evaluate the relative strength of different H–bonds of the same type, and also to detect the weaker H–bonds that where rejected by geometrical criteria. These H–bonds are presented at the end of Table 2.

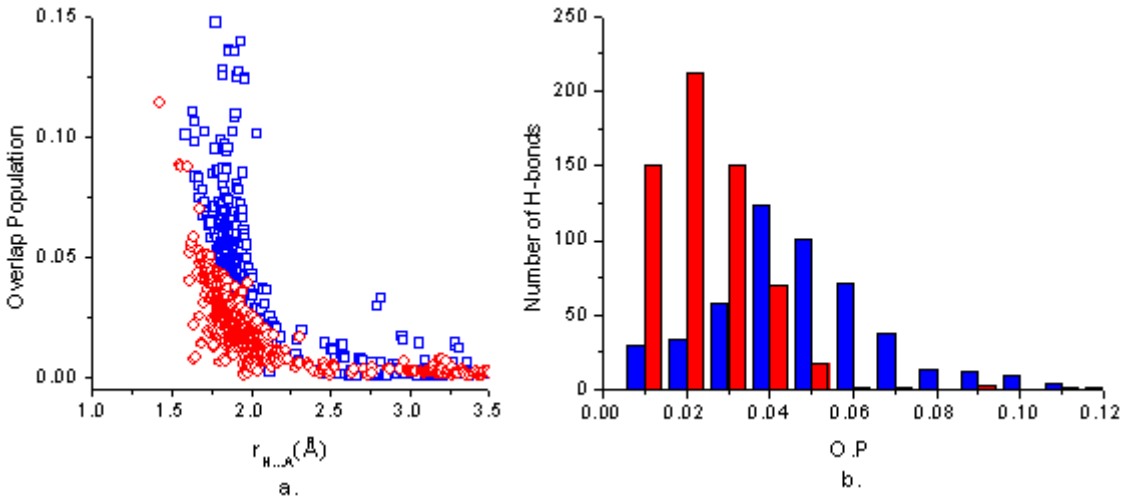

Figure 2. Base-base H-bonds for DNA structures: a. overlap population *vs.* H…A distance; b. OP distribution; □, ▮ – D – H…N hydrogen bonds; o, ▮ – D – H…O hydrogen bonds.

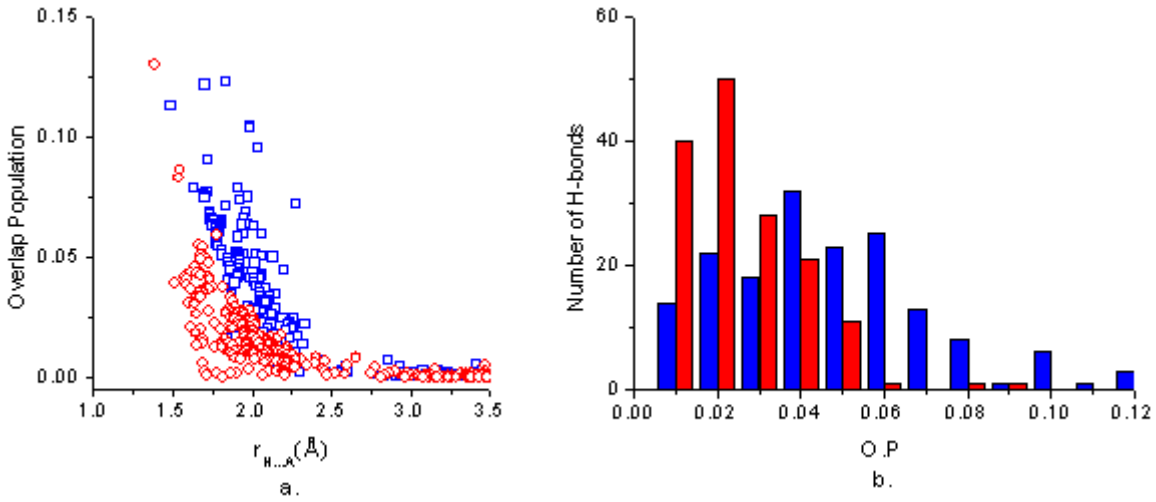

Figure 3. Base–base H–bonds for RNA structures: a. overlap population *vs*. H…A distance; b. OP distribution; □, ▮ – D – H…N hydrogen bonds; o, ▮ – D – H…O hydrogen bonds.

In order to obtain the hydrogen bonding patterns in nucleic acids, 56 DNA and 22 RNA structures were scanned and the hydrogen bond intermolecular interactions analysis was performed using SHB_interactions. Even though we have not included all DNA and RNA NMR structures, this set is large enough to be considered as representative for NMR structures currently known.

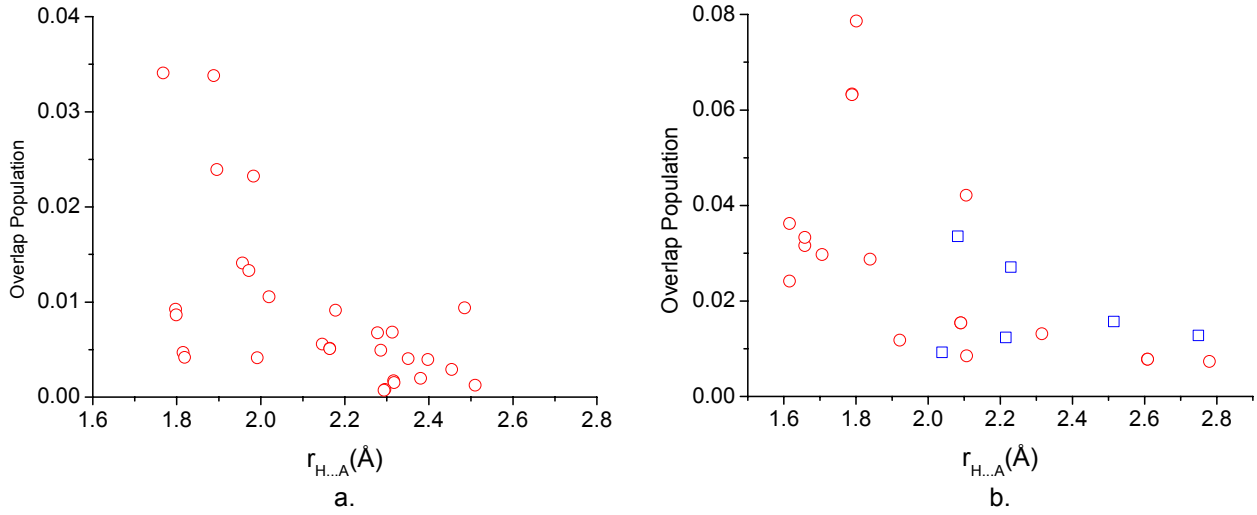

Figure 4. Overlap population for the backbone–base H–bonds *vs*. H…A distance: a. DNA structures; b. RNA structures; □ – D – H…N hydrogen bonds; o – D – H…O hydrogen bonds.

The OP values corresponding to the base–base H–bonds as a function of the H…A distance and the OP distribution are presented in Figures 2a,b and 3a,b for the DNA and respectively RNA structures. In both cases the majority of the H–bonds, with OP greater than 0.01, is placed in the same range of distances 1.5–2.3 Å. The clear delimitation between H–bond OP values when the acceptor is oxygen and those when the acceptor is nitrogen, observed for 1g70, can be also observed for all investigated structures.

Furthermore, for the two H–bond types there is a difference between the OP distribution in the range 0.005–0.120: the OP distribution for the D – H…O bond has a distinct maximum between 0.015 and 0.025, whereas for the D – H…N bond this maximum is shifted to a larger value, *i.e.*, between 0.035–0.045.

The other types of the H–bonds (backbone–base and backbone–backbone) are much less frequent both in the DNA and RNA structures, as it is depicted in Figures 4a,b and 5. However, these types of H–bonds are very important for the RNA structure, especially for the unusual structures like the pseudoknot that have a larger number of H–bonds implying backbone atoms.

The majority of these bonds have oxygen atom as the principal acceptor: O4* for DNA, and O2* for RNA in the case of the backbone–base H–bonds, and O4* and O5* for RNA in the backbone–backbone ones. The OP values for the backbone–base H–bonds are lower than the OP values for the base–base H–bonds in a range up to 0.04 and 0.08 for DNA, respectively RNA. Although more frequent in the case of the RNA structure (Figure 5), the backbone–backbone H–bonds are practically inexistent in DNA structures.

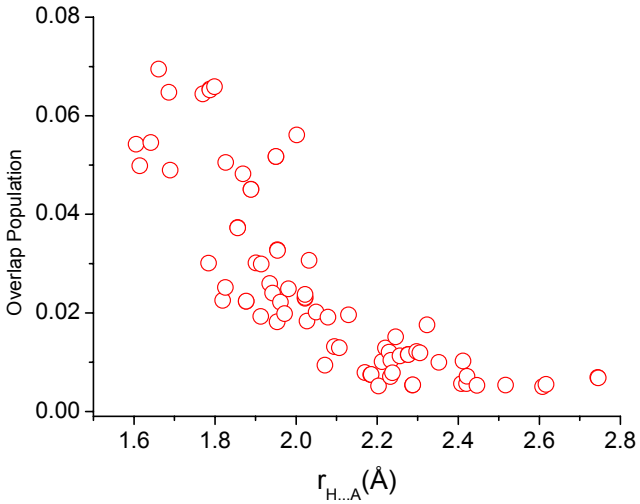

Figura 5. Overlap population for the backbone– backbone H–bonds in the RNA structure *vs*. H…A distance; o – D – H…O hydrogen bonds.

The SHB_interactions program allows also an analysis of the contribution of the potential hydrogen bonds and other atom–atom intermolecular interactions to the stability of the nucleic acids complexes with different ligands, as well as of the weaker H–bonds like C – H…A bonds. It is interesting to note that the interactions involving the C–H group as a potential hydrogen donor with different acceptor atoms correspond to OP values up to 0.025, *i.e.*, in a range where classical hydrogen bonds and other atom–atom intermolecular interactions are also observed [16].

Quantum chemical studies on small molecules suggest that C–H···O interactions can be considered as weak hydrogen bonds [17,18]. There is an increasing awareness that this type of interactions may also be relevant to biopolymer structure. The contribution of C–H···X (O, N)

hydrogen bonds to the stability of different biological macromolecules was recently discussed in literature [19–22].

Up to now these interactions have been identified as possible candidates for attractive interactions in the biopolymers, only on the base of geometrical criteria. We consider that the overlap population can be a useful tool not only for their identification, but also for their classification according to the strength and allows an estimate of their contribution to the stability of the different complexes.

4 CONCLUSIONS

The SHB_interactions program is especially developed to identify and to analyze intermolecular interactions in biopolymers using the Mulliken overlap population as a quantitative quantum chemical criterion.

In spite of the limitations of the EH method, the results obtained with SHB_interactions allow a rationalization of the H–bonds in nucleic acid, as well as in protein structures. A comparative analysis with HBexplore is described for the RNA/protein complex (PDB code 1g70). The results obtained outline the capability of the overlap population criterion to substitute all the five geometrical parameters used by HBexplore. Differences have been observed for backbone–backbone and backbone–base H–bonds, as well as for protein–protein and protein–base H–bonds. These differences are due either to the different H–atom positions used as input data for sp^3 donor atoms, or to the fact that the SHB_interactions program considers not only the oxygen as a possible H–acceptor, but also the amidic N–atom.

56 DNA and 22 RNA NMR structures were investigated and the hydrogen bond intermolecular interactions analysis was performed using SHB_interactions. Even though we have not included all known DNA and RNA NMR structures, this set is large enough to be considered as representative for NMR structures currently known.

Our results suggest that the overlap population criterion has the capacity to make distinction between different H–bond types, and allows comparative analysis of the results for the same type of H–bonds. For classical H–bonds interactions ($r > 1.7$ Å) the OP values are in the range 0.01 – 0.15. SHB_interactions can detect the weaker H–bonds that are rejected by common geometrical criteria.

In addition, the use of the overlap population as a quantum selection criterion presents the advantage to detect not only the weaker H–bonds like C–H…A, but also any other atom–atom intermolecular interactions [16].

Appendix 1

Table 2. Base–base Hydrogen Bonds of 1g70 Found by SHB_interactions

Type	H atom	Acceptor	OP	Geometrical criteria (HBexplore)				
				rHA	rDA	aDHA	aHAA1 (aHAAm)	aDAA1 (aDAAm)
D – H…N	H3 U A 45	N1 A A 75	0.0780	1.932	2.942	174.4	165.5	167.2
	H1 G A 67	N3 C A 51	0.0718	1.845	2.836	166.2	179.1	179.3
	H1 G A 76	N3 C A 44	0.0604	1.879	2.884	168.7	176.4	178.7
	H1 G A 46	N3 C A 74	0.0586	1.873	2.827	155.2	175.3	177.8
	H1 G A 47	N1 A A 73	0.0564	2.026	3.000	156.5	173.7	178.7
	H1 G A 64	N3 C A 54	0.0564	1.849	2.836	161.9	173.9	175.2
	H1 G A 50	N3 C A 69	0.0518	1.910	2.894	163.2	167.2	172.6
	H1 G A 70	N3 C A 49	0.0495	1.862	2.819	156.4	177.1	179.7
	H1 G A 41	N3 C A 79	0.0479	1.935	2.863	150.6	171.8	172.4
	H3 U A 66	N1 A A 52	0.0422	1.971	2.907	152.5	168.3	170.9
	H1 G A 42	N3 C A 78	0.0421	1.958	2.928	160.1	171.2	174.3
D – H…O	H1 G A 77	O2 U A 43	0.0395	1.804	2.81	170.7	129.9	127.8
	2H2 G A 46	O2 C A 74	0.0307	1.771	2.78	168.8	123.9	121.9
	H1 G A 63	O2 U A 60	0.0291	1.949	2.736	130.5	132.8	148.6
	H3 U A 43	O6 G A 77	0.0274	1.874	2.868	165	131.3	128.3
	2H2 G A 70	O2 C A 49	0.0255	1.861	2.864	169.6	121.2	119.2
	2H2 G A 64	O2 C A 54	0.0240	1.893	2.853	148.3	122.8	125.7
	2H4 C A 49	O6 G A 70	0.0237	1.755	2.764	177.4	115.9	115.9
	2H2 G A 50	O2 C A 69	0.0211	1.764	2.745	159.1	108.2	114.4
	2H2 G A 67	O2 C A 51	0.0204	1.903	2.901	163.2	111.5	115.1
	2H2 G A 76	O2 C A 44	0.0203	1.901	2.906	173.2	124.7	123.6
	H1 G A 71	O6 G A 48	0.0202	1.837	2.788	153.2	103.1	112.0
	2H2 G A 41	O2 C A 79	0.0183	1.923	2.808	134.8	126.2	128.2
	1H6 A A 52	O4 U A 66	0.0169	1.859	2.861	166.2	135.5	131.3
	2H4 C A 54	O6 G A 64	0.0152	1.792	2.778	155.5	125.0	126.4
	2H2 G A 42	O2 C A 78	0.0150	1.910	2.887	156.8	110.9	115.6
	2H4 C A 44	O6 G A 76	0.0150	1.780	2.782	167.8	125.0	124.1
	2H2 G A 71	O6 G A 48	0.0137	2.218	3.041	137.5	150.7	150.9
	2H4 C A 78	O6 G A 42	0.0128	1.887	2.874	163.1	114.3	118.2
	H1 G A 48	O6 G A 71	0.0121	1.970	2.958	164.6	104.2	108.9
	2H4 C A 74	O6 G A 46	0.0112	1.883	2.895	178.8	115.7	115.9
	2H4 C A 51	O6 G A 67	0.0112	1.951	2.911	151.9	107.8	114.1
	2H4 C A 69	O6 G A 50	0.0107	1.986	2.973	162.6	107.5	112.5
	1H4 C A 62	O2P U A 61	0.0104	2.220	2.912	170.6	127.3	124.6
	1H4 C A 44	O4 U A 72	0.0093	1.942	2.911	161.8	110.9	116.2
	1H6 A A 75	O4 U A 45	0.0067	1.844	2.788	145.1	100.2	110.6
	1H6 A A 73	O6 G A 47	0.0047	1.761	2.687	141.2	115.6	124.6
	2H6 A A 73	**O6 G A 46**	**–0.0038**	2.445	2.892	102.7	122.2	102.2
	H3 U A 60	O2 C A 62	0.0061	2.406	3.213	135.5	92.3	79.6
	2H2 G A 48	O6 G A 71	0.0055	2.540	3.379	140.3	152.0	146.2

*D, donor; A, acceptor; H, hydrogen; A1, Am bonded neighbors of A; rHA, distance H…A; rDA, distance D…A; aHAA1(Am), angle HAA1(Am); aDAA1(Am), angle DAA1(Am) [7]

Table 3. Backbone–backbone and Backbone–base Hydrogen Bonds of 1g70 Found by SHB_interactions

Type*	H atom				Acceptor				rHA	O. P
Bk–Bk	2HO*	U	A	43	O4*	C	A	44	1.744	0.0728
	2HO*	G	A	47	O5*	G	A	48	1.762	0.0424
	2HO*	U	A	72	O2P	A	A	73	1.858	0.0357
	2HO*	U	A	60	O5*	U	A	61	1.945	0.0133
	2HO*	G	A	50	O5*	C	A	51	2.250	0.0114
	2HO*	C	A	51	O5*	A	A	52	2.235	0.0107
	2HO*	G	A	48	O5*	C	A	49	2.312	0.0083
	2HO*	G	A	46	O5*	G	A	47	1.804	0.0070
	2HO*	A	A	52	O4*	C	A	54	2.592	0.0056
	2HO*	G	A	46	O4*	G	A	47	2.880	0.0053
Bk–b	2HO*	G	A	71	N7	G	A	70	1.9241	0.0466
	2HO*	U	A	61	N7	G	A	63	1.9558	0.0252
	1H4	C	A	62	O2P	U	A	61	2.2196	0.0104

*Bk–Bk, backbone–backbone; Bk–b, backbone–base

Table 4. Protein–protein and protein–base H–bonds of 1g70 found by SHB_interactions

Type*	H atom				Acceptor				rHA	O. P
P–P N–H…N bonds	H	ALA	B	19	N	ARG	B	18	2.384	0.0496
	H	GLU	B	13	N	ALA	B	12	2.406	0.0485
	H	ALA	B	21	N	ALA	B	20	2.204	0.0428
	H	ARG	B	16	N	ARG	B	15	2.555	0.0398
	H	ALA	B	20	N	ALA	B	19	2.352	0.0381
	H	ARG	B	17	N	ARG	B	16	2.405	0.0346
	H	ARG	B	18	N	ARG	B	17	2.569	0.0254
	H	ARG	B	15	N	ARG	B	14	2.780	0.0238
	H	ALA	B	22	N	ALA	B	21	2.588	0.0231
	H	ARG	B	14	N	GLU	B	13	2.642	0.0222
P–P N–H…O bonds	H	ALA	B	22	O	ARG	B	18	1.9583	0.0274
	H	ALA	B	12	O	SER	B	10	1.9439	0.0147
	H	ARG	B	16	O	ALA	B	12	2.0528	0.0141
	H	ARG	B	15	O	GLY	B	11	2.2645	0.0101
	H	ALA	B	20	O	ARG	B	16	2.2261	0.0096
	H	SER	B	10	O	PRO	B	9	3.1154	0.0055
P–b	H	ALA	B	12	N7	G	A	46	2.177	0.0335
	3HB	ALA	B	12	N7	G	A	46	2.606	0.0118
	1HH2	ARG	B	8	N7	G	A	64	2.981	0.0050
	HE	ARG	B	8	N7	G	A	64	3.062	0.0039
	H	SER	B	7	N7	G	A	64	2.985	0.0037
	1H6	A	A	73	NH1	ARG	B	15	3.629	0.0036
	2HH1	ARG	B	15	N7	A	A	73	2.744	0.0036

*P–P, Protein–protein H–bonds; P–b, protein–base H–bonds

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