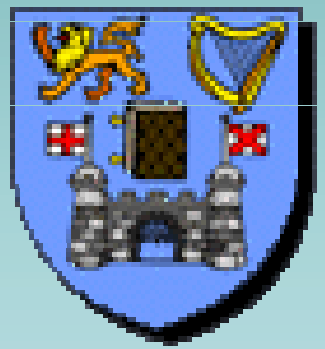
Hydrogen Bonding and Other Interactions in Biological Systems



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Hydrogen Bonding and Other Interactions in Biological Systems: RNA bases and amino acid models

- RNA performs essential and diverse functions within the cell (gene replication and expression) → interaction with proteins.

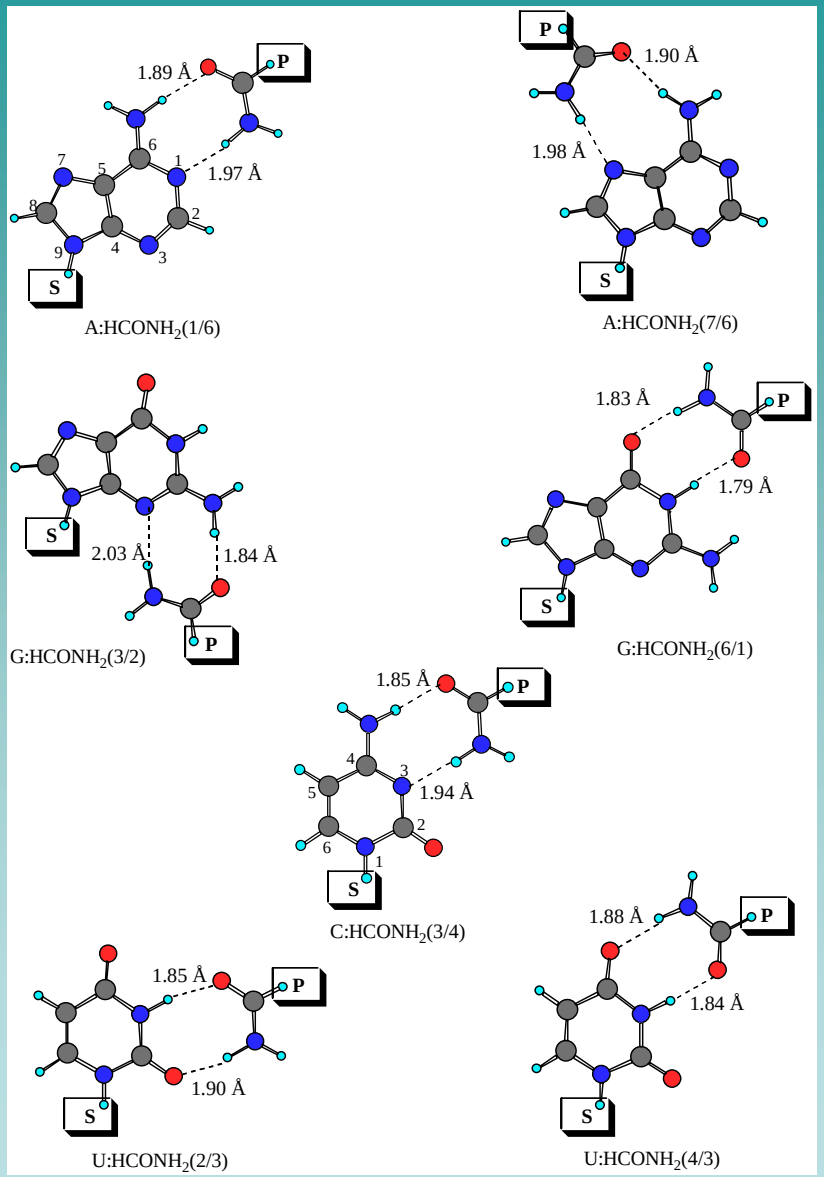
- The most important interaction established between the RNA bases and amino acids is through HBs: Glutamic acid and Asparagine show a good number of HB contacts with the RNA bases (mostly with Guanine and Uracil).

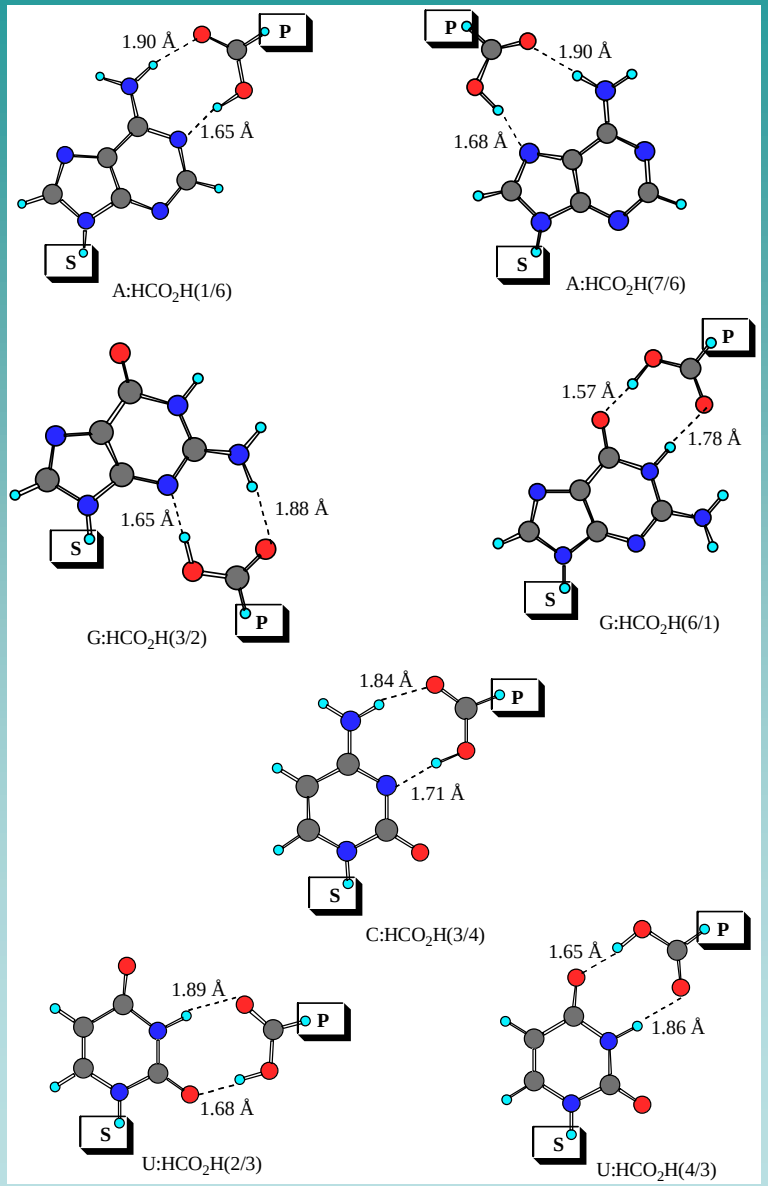
- Donor-acceptor arrangements of the Nucleic bases → many possible interactions.

- The ability to form HB of amino acid → three types of small ligands:

  Acceptor/acceptor HB groups such as carboxylate (Glu & Asp)
  Donor/acceptor HB groups such as formamide (Gln & Asn)
  Donor/donor HB groups such as guanidinium (Arg)

Hydrogen Bonding and Other Interactions in Biological Systems: RNA bases and amino acid models, donor-acceptor cases

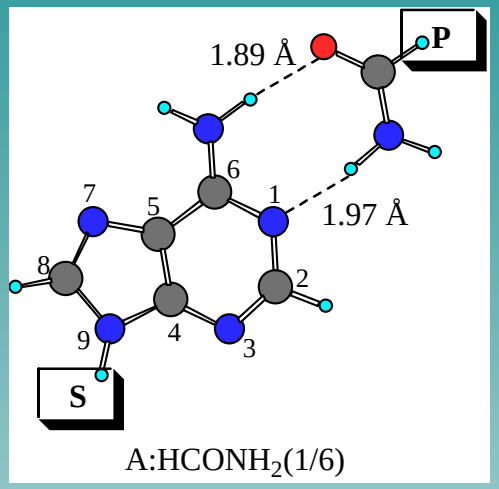




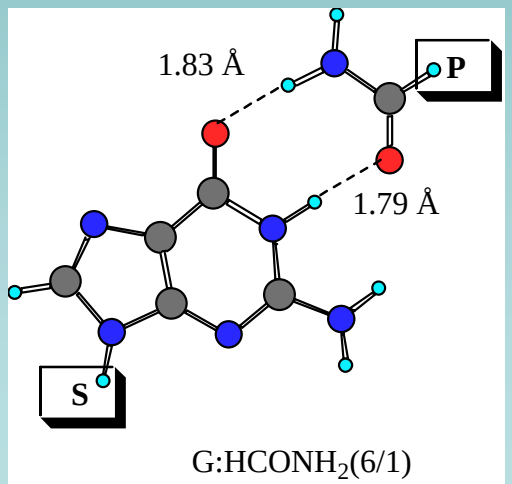
Hydrogen Bonding and Other Interactions in Biological Systems: RNA bases and amino acid models, donor-acceptor cases

B3LYP/6-31+G**, AIM, NBO

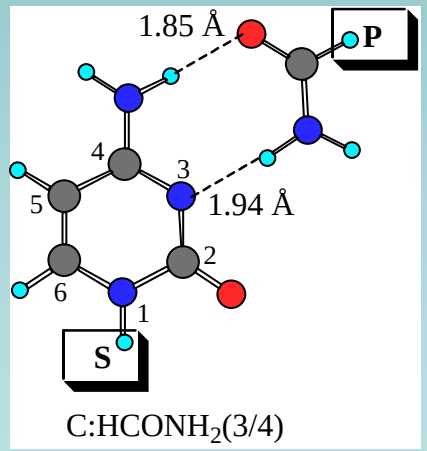
	E_{I+BSSE} kcal/mol	ρ(bcp)	$\nabla^2\rho$(bcp)	Q transf.	*E(2)*
A:$HCONH_2$(1/6)	–11.57	0.0293 0.0292	0.0819 0.0688	–0.005	11.84 17.38
G:$HCONH_2$(6/1)	–18.08	0.0374 0.0336	0.1044 0.0950	0.011	18.83 14.15
C:$HCONH_2$(3/4)	–15.24	0.0320 0.0303	0.0900 0.0743	–0.005	13.90 17.88
U:$HCONH_2$(4/3)	–11.48	0.0321 0.0291	0.0905 0.0855	0.013	14.17 9.60



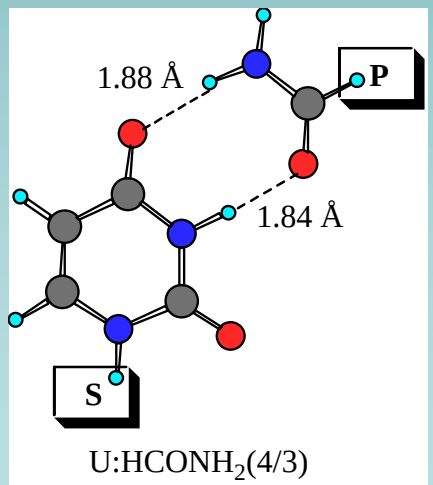
A:$HCONH_2$(1/6)



G:$HCONH_2$(6/1)



C:$HCONH_2$(3/4)



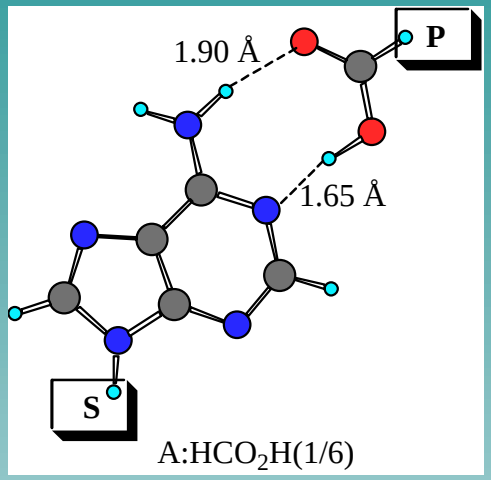
U:$HCONH_2$(4/3)

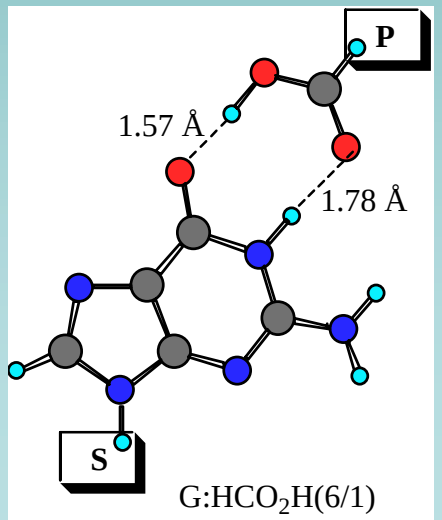
Rozas, Alkorta, Elguero, *J. Phys. Chem. B*, 3335, *108* (**2004**)

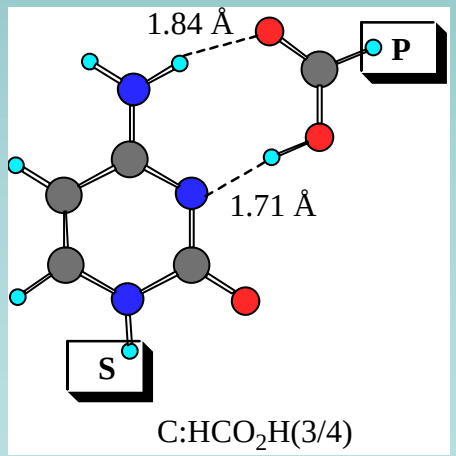
Hydrogen Bonding and Other Interactions in Biological Systems: RNA bases and amino acid models, donor-acceptor cases

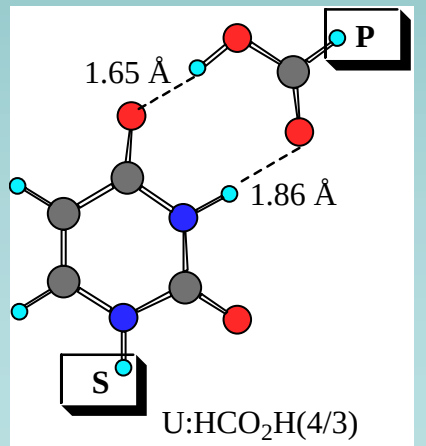
B3LYP/6-31+G**, AIM, NBO

	E_{I+BSSE} kcal/mol	ρ(bcp)	$\nabla^2\rho$(bcp)	Q transf.	E(2)
A:HCO_2H(1/6)	–15.07	0.0285 0.0599	0.0815 0.1040	–0.065	10.41 44.94
G:HCO_2H(6/1)	–19.08	0.0375 0.0614	0.1076 0.1524	–0.037	18.17 37.96
C:HCO_2H(3/4)	–16.46	0.0326 0.0518	0.0943 0.1011	–0.046	13.35 37.76
U:HCO_2H(4/3)	–13.37	0.0302 0.0489	0.0867 0.1408	–0.026	11.77 25.34



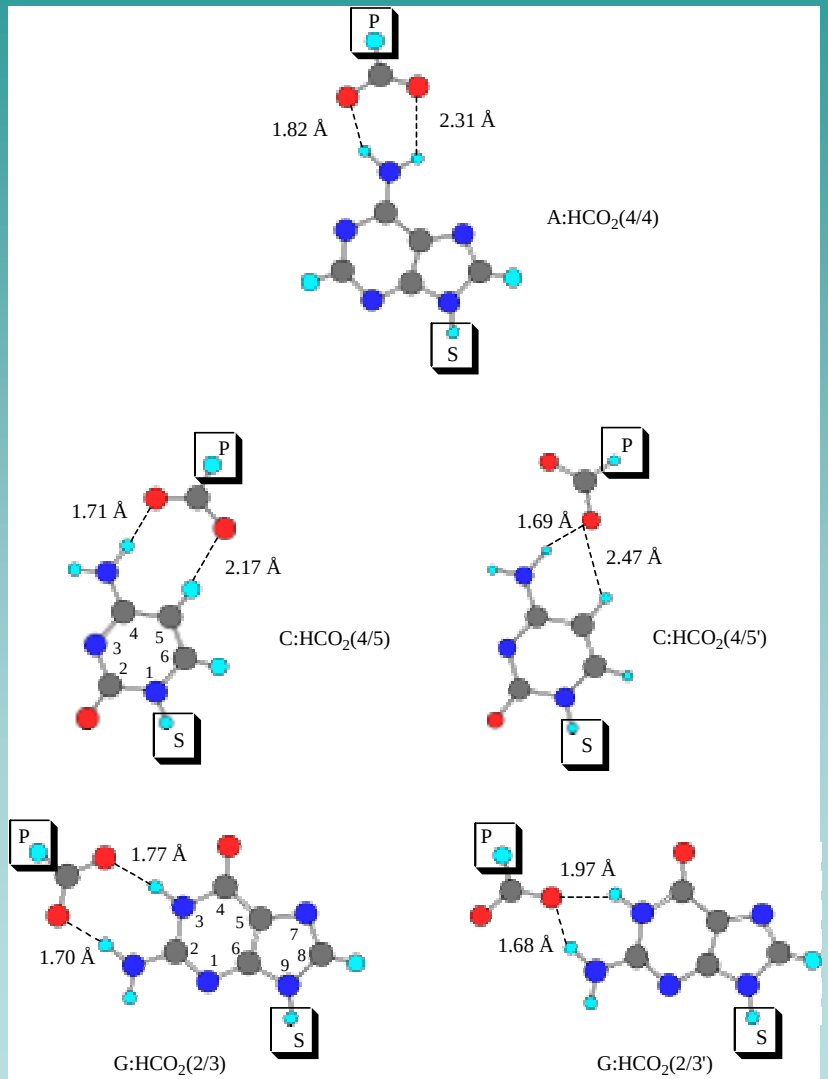


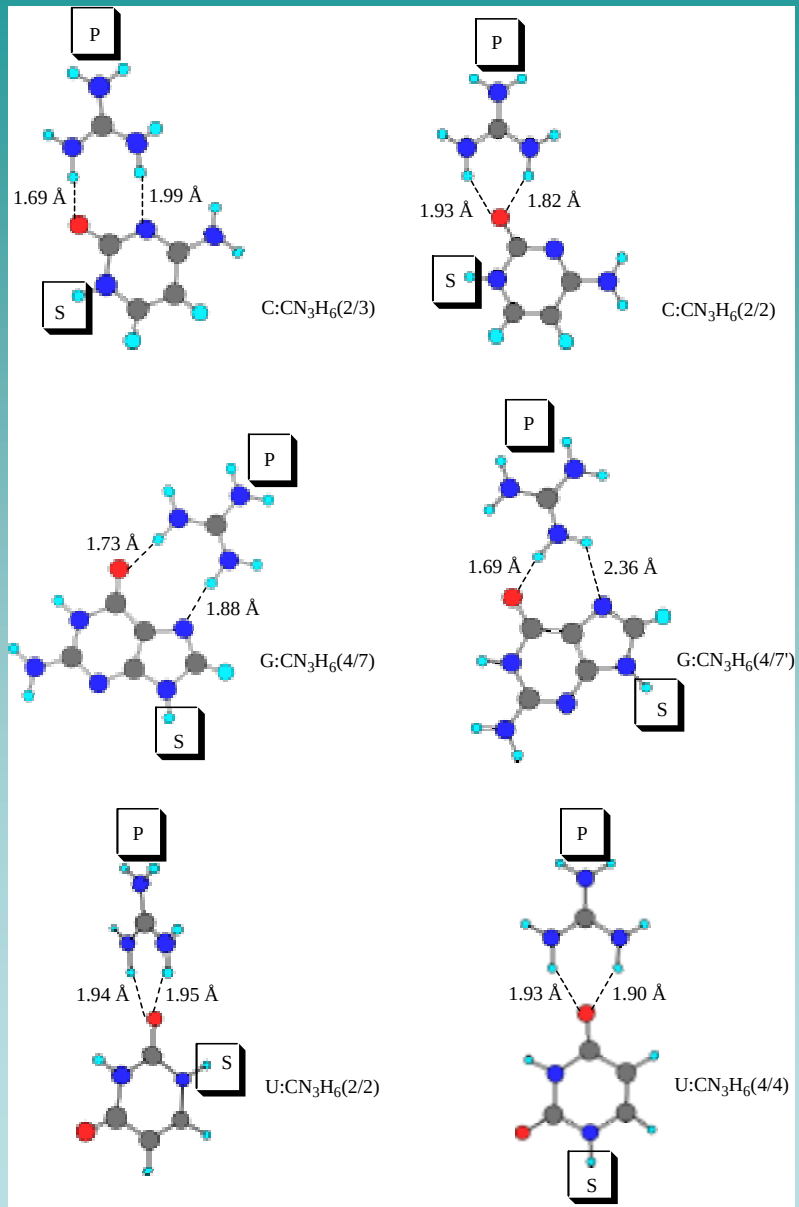




Rozas, Alkorta, Elguero, *J. Phys. Chem. B*, 3335, *108* (**2004**)

Hydrogen Bonding and Other Interactions in Biological Systems: RNA bases and amino acid models, donor/donor-acceptor/acceptor cases

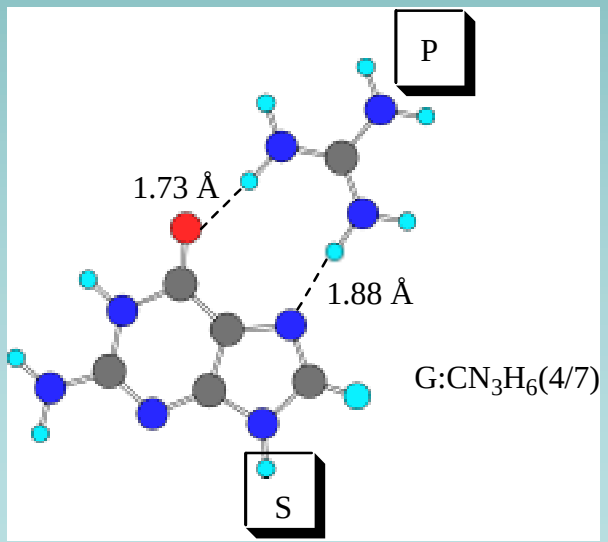


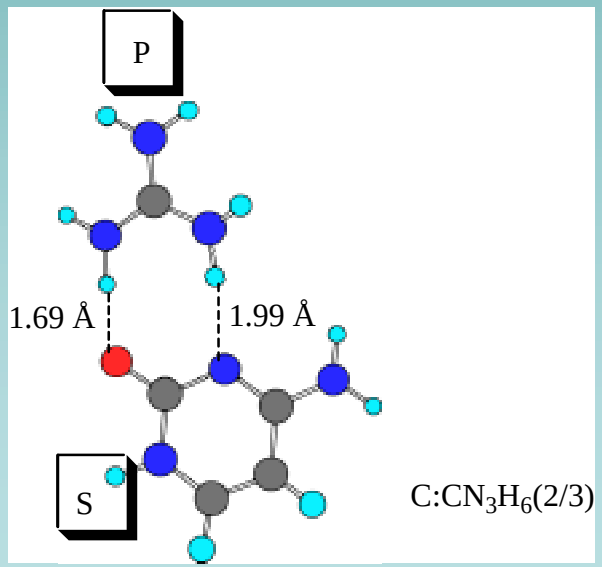


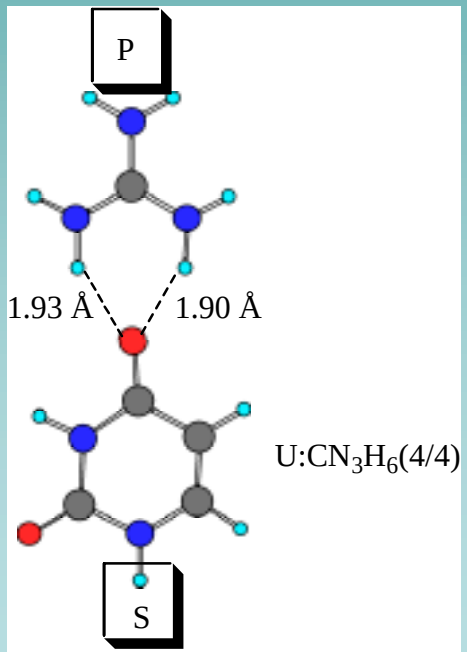
Hydrogen Bonding and Other Interactions in Biological Systems: RNA bases and amino acid models, acceptor-acceptor case

B3LYP/6-31+G**, AIM, NBO

	E_{I+BSSE} kcal/mol	ρ(bcp)	$\nabla^2\rho$(bcp)	Q transf.	*E(2)*
G:CN_3H_6(4/7)	-37.75	0.0460 0.0158	0.1311 0.0488	0.113	17.88 23.61
C:CN_3H_6(2/3)	-35.04	0.0447 0.0275	0.1342 0.0652	0.114	21.63 16.21
U:CN_3H_6(4/4)	-23.07	0.0274 0.0251	0.0855 0.0811	0.059	8.25 7.76





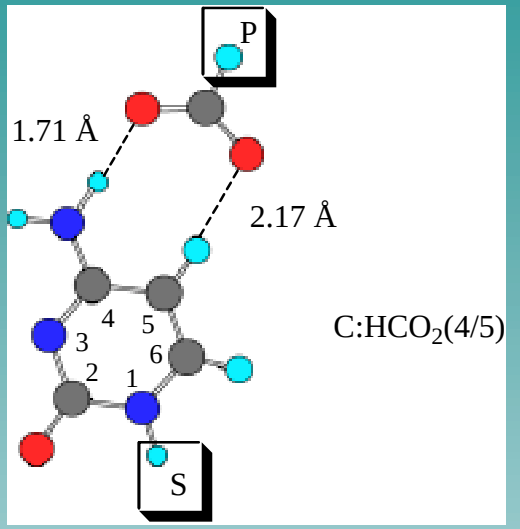


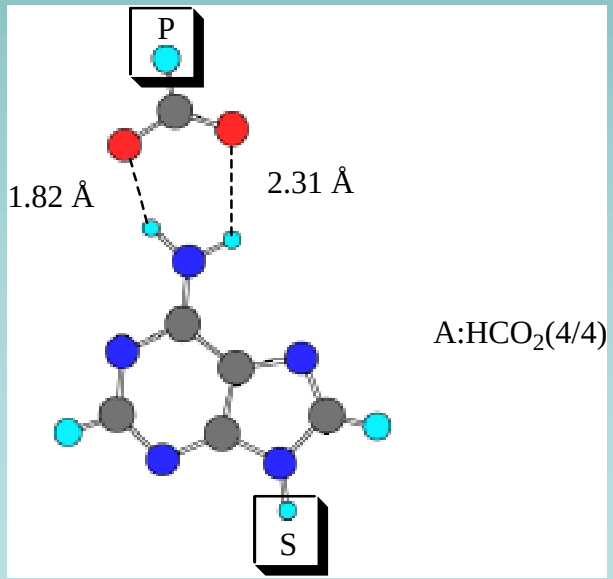
Rozas, Alkorta, Elguero, *Org. Biomol. Chem.*, 366, *3* (**2005**)

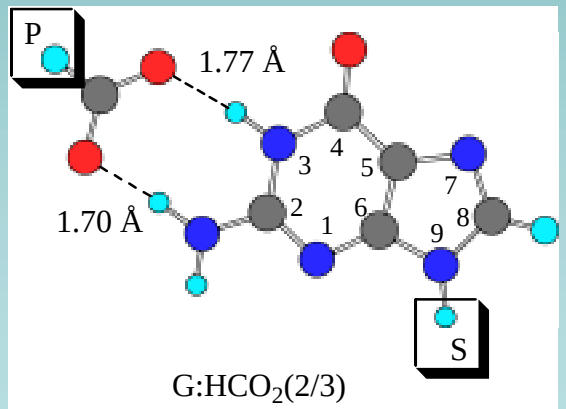
Hydrogen Bonding and Other Interactions in Biological Systems: RNA bases and amino acid models, acceptor-acceptor case

B3LYP/6-31+G**, AIM, NBO

	E_{I+BSSE} kcal/mol	ρ(bcp)	$\nabla^2\rho$(bcp)	Q transf.	*E(2)*
A:HCO_2(4/4)	-19.10	0.0360 0.0144	0.0956 0.0470	-0.075	17.32 2.45
G:HCO_2(2/3)	-36.95	0.0467 0.0384	0.1229 0.1047	-0.151	21.23 27.74
C:HCO_2(4/5)	-29.85	0.0451 0.0181	0.1230 0.0469	-0.106	26.85 5.69







Rozas, Alkorta, Elguero, *Org. Biomol. Chem.*, 366, *3* (**2005**)

Conclusions

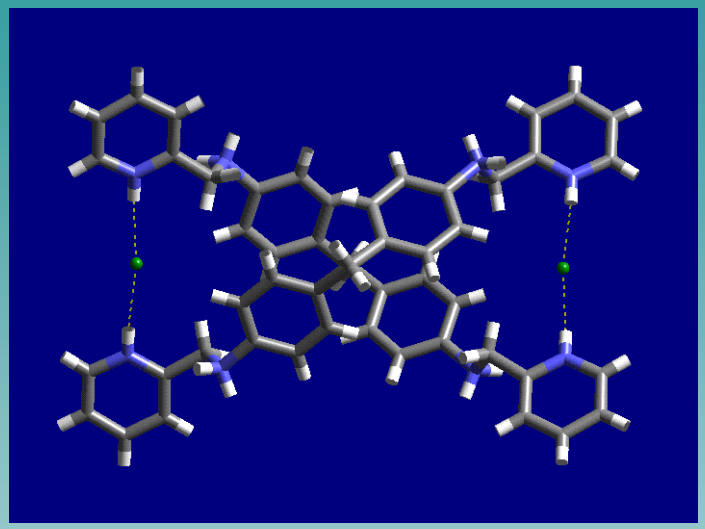
- The E_Is of the donor-donor and acceptor-acceptor complexes are larger than those of the donor-acceptor complexes → influence of the charged monomers

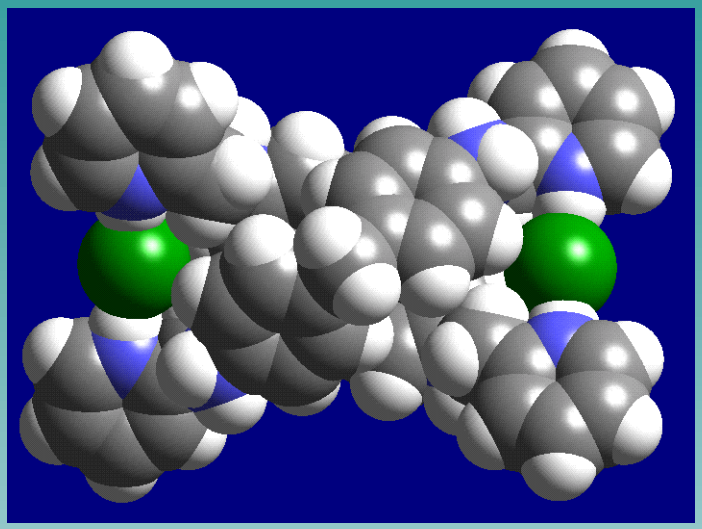
- Several good correlations were found between HB distances and ρ(bcp) and $\nabla^2\rho$(bcp) and as well a correlation was found between the orbital energy *E(2)* and ρ(bcp)

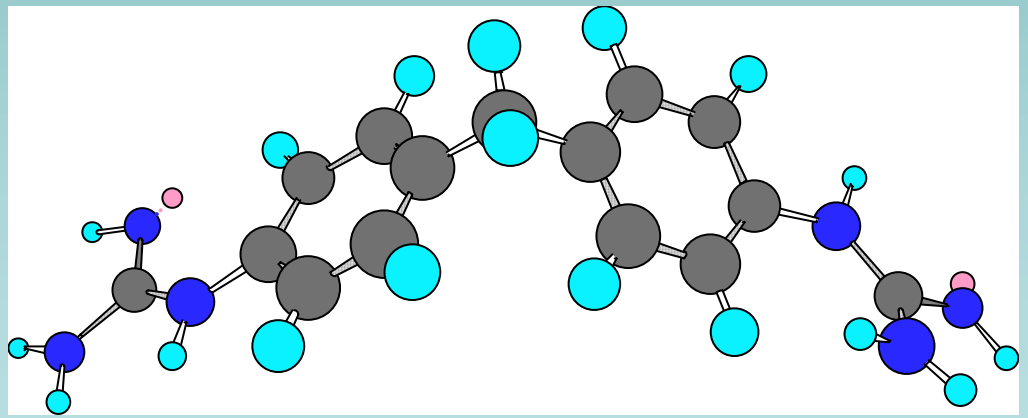
E(2) = 929.90ρ(bcp) – 15.08, R^2= 0.9, n= 27
HB acceptor is an O atom: *E(2)*= 796.98ρ(bcp) – 12.36, R^2=0.98, n=20
HB acceptor is an N atom: *E(2)* = 898.73 ρ(bcp) - 8.67, R^2 = 0.99, n= 7

E(2) = 708.71ρ(bcp) – 7.27, R^2= 0.92, n= 22
HB acceptor is an O atom: *E(2)* = 716.99ρ(bcp) – 8.14, R^2= 0.95, n= 19

Hydrogen Bonding and Other Interactions in Biological Systems: supramolecular systems





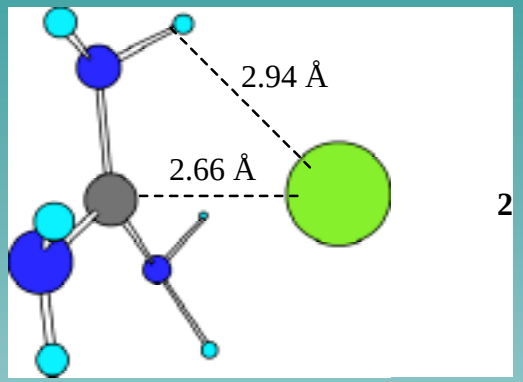


Keegan, Kruger, Nieuwenhuyzen, O'Brien, Martin, *Chem. Commun.*, 2192 (**2001**)

Hydrogen Bonding and Other Interactions in Biological Systems: Guanidinium vs Chloride and Sulfate anions

MP2/6-31+G*, AIM, NBO

	E_I kcal/mol	ρ(bcp)	$\nabla^2\rho$(bcp)	Q transf.	*E(2)*
1	-109.32	0.0369	0.0982	0.231	28.31
2	-98.71	0.0307	0.0742	0.251	137.67
3	-150.76	0.0235	0.0713	0.098	9.09



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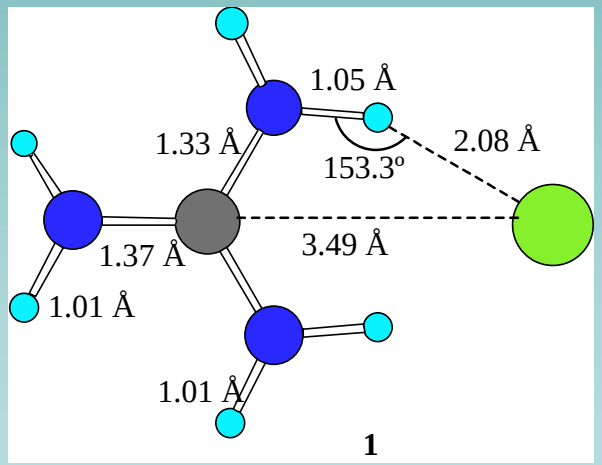

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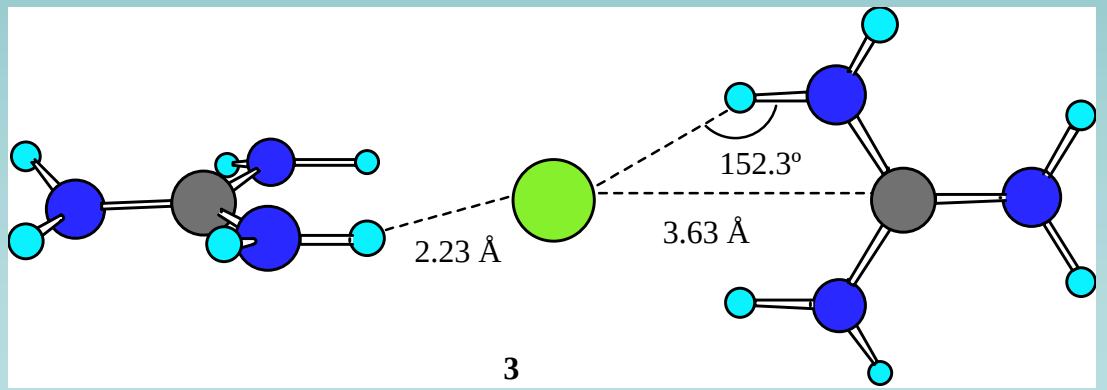

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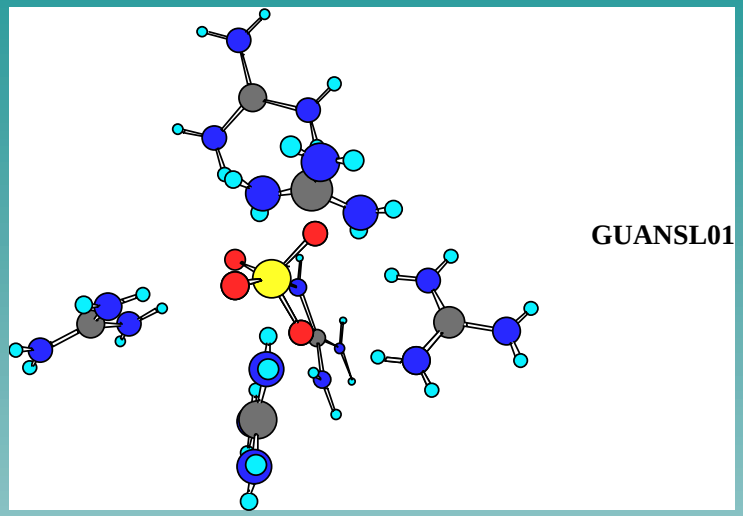
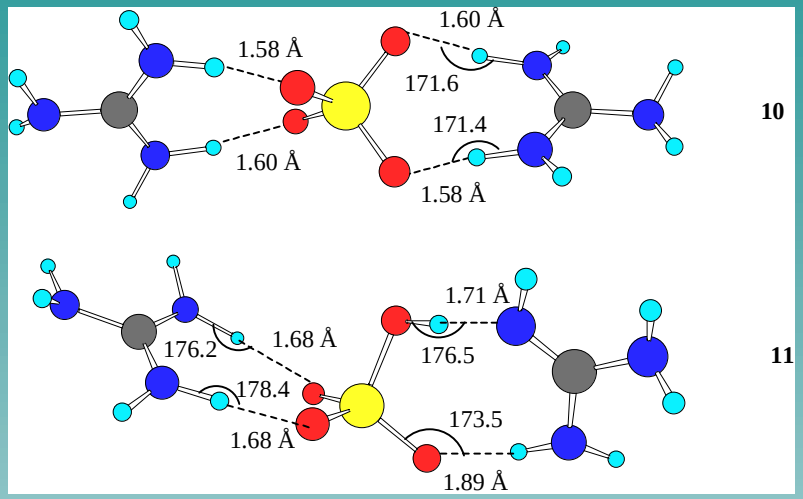
Rozas, Kruger, *J. Chem. Theory Comput.*, in press (**2005**)

Hydrogen Bonding and Other Interactions in Biological Systems: Guanidinium vs Chloride and Sulfate anions

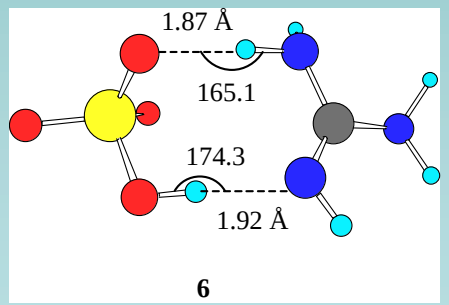


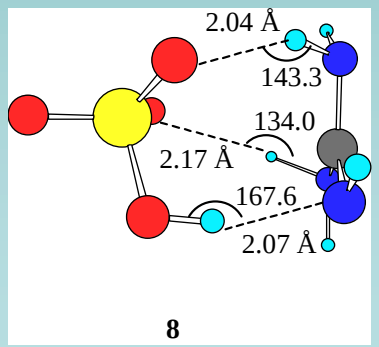
GUANSL01

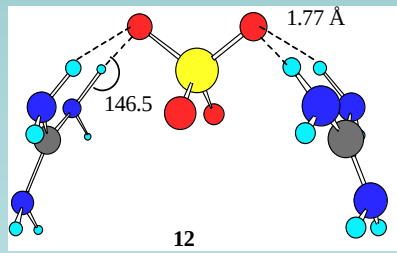
E_I → -15.27 / -21.56 kcal/mol

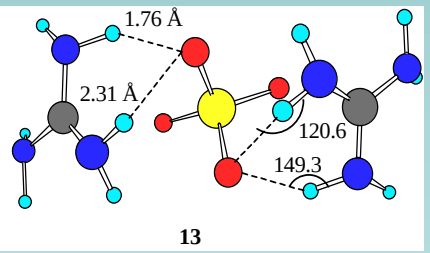


E_I → -102.08 / -327.84 kcal/mol









Rozas, Kruger, *J. Chem. Theory Comput.*, in press (**2005**)

Conclusions

- The E_Is are very large → influence of the charged monomers

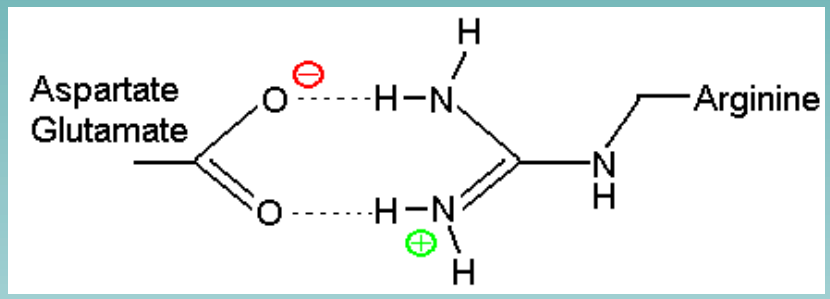
- Several good correlations were found between HB distances and ρ(bcp) and $\nabla^2\rho$(bcp) and as well a correlation was found between the orbital energy *E(2)* and ρ(bcp)

E(2) = 815.92 ρ(bcp) - 11.46, R^2= 0.90, n= 25.
HB acceptor is an N atom: *E(2)* = 1310.60ρ(bcp) - 24.26, R^2= 0.99 n=4
HB acceptor is an O atom: *E(2)* = 763.63ρ(bcp) - 10.65, R^2= 0.92 n= 21

Hydrogen Bonding and Other Interactions in Biological Systems: Hydrogen bond vs. Electrostatic interactions

- Very high E_Is in complexes with charged monomers… could be a consequence of the method used???

- Hydrogen bonds in biological ligand-receptor complexes are usually enhanced/supplemented by electrostatic forces

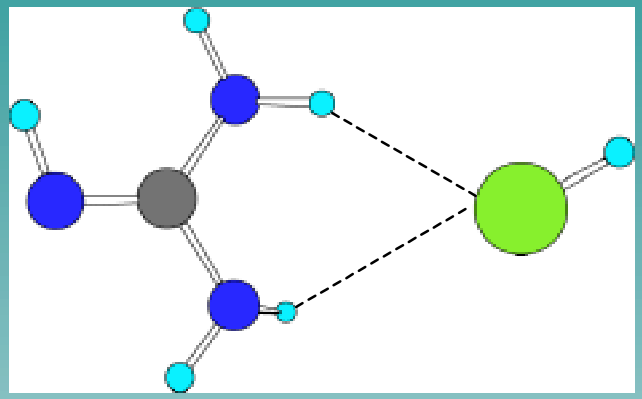


- Are the two different forces working at the same time but independently???

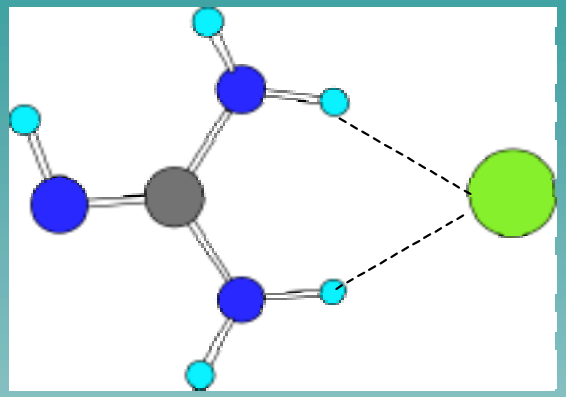
- Are HBs enhanced??? Do they really become stronger??? How much???

Hydrogen Bonding and Other Interactions in Biological Systems: Hydrogen bond vs. Electrostatic interactions

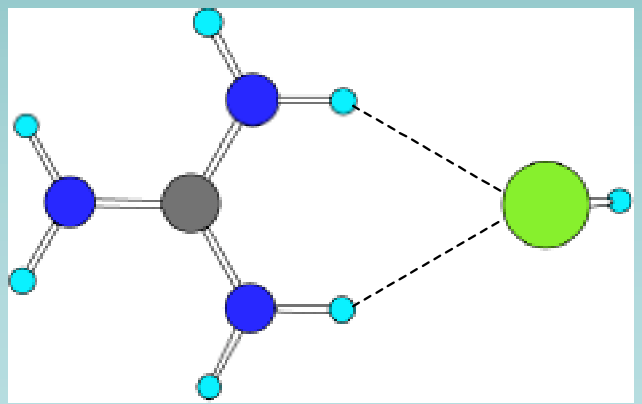
Systems:



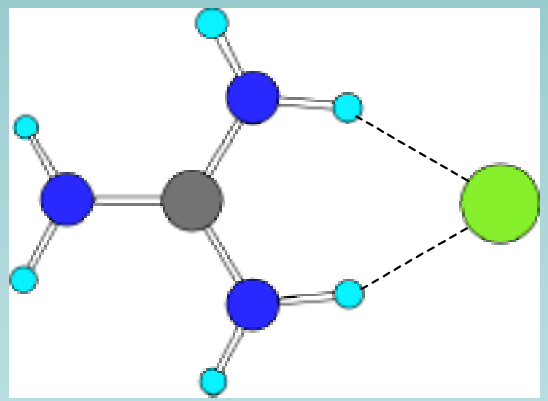
neutral



minus
Negative charge assisted HB



plus
Positive charge assisted HB



Plusminus
Positive/negative charge assisted HB

Methods & Basis:

B3LYP/6-31+G*

B3LYP/TZVP

MP2/6-31+G*

MP2/6-311++G**

MP2/aug-cc-pVDZ

CBS-QB3

G3MP2

AIM, NBO

Hydrogen Bonding and Other Interactions in Biological Systems: Hydrogen bond vs. Electrostatic interactions

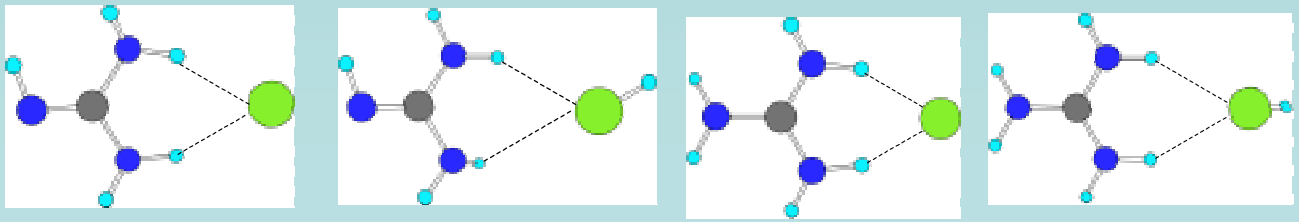
Interaction energies (kcal/mol)

	minus	neutral	plusminus	plus
B3LYP/ 6-31G*	*23.24*	*2.48*	107.73	*5.84*
B3LYP/ TZVP	27.66	*2.33*	115.18	*6.03*
MP2/ 6-31G*	25.56	4.32	109.32	7.23
MP2/ 6-311++G**	26.57	4.44	*113.71*	7.36
MP2/ aug-cc-pVDZ	26.12	4.24	*113.13*	8.02
CBS-QB3	*24.73*	*2.44*	*113.23*	*6.45*
G3MP2	*24.42*	*2.60*	*112.23*	*5.99*

Hydrogen Bonding and Other Interactions in Biological Systems: Hydrogen bond vs. Electrostatic interactions

HB distances (Å) and electron density characteristics at the bcps

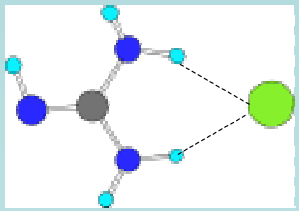
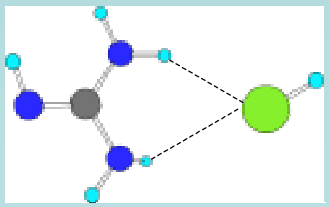
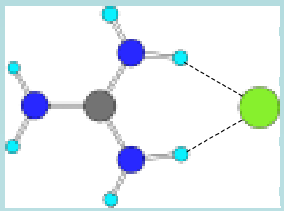
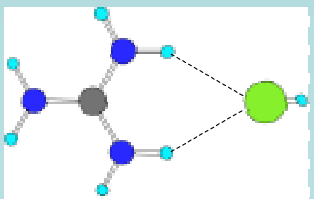
		minus	neutral	plusminus	plus
B3LYP/ 6-31G*	d(HB) ρ(bcp) $\nabla^2\rho$(bcp)	2.33 2.39 0.0208 0.0181 0.0595 0.0543	2.82 0.0064 0.0248	***2.04*** ***0.0377*** ***0.0866***	2.65 0.0092 0.0350
B3LYP/ TZVP	d(HB) ρ(bcp) $\nabla^2\rho$(bcp)	2.28 2.33 0.0224 0.0201 0.0598 0.0559	2.85 3.29 0.0060 0.0045 0.0192 0.0166	***2.01*** ***0.0414*** ***0.0756***	2.63 0.0094 0.0316
MP2/ 6-31G*	d(HB) ρ(bcp) $\nabla^2\rho$(bcp)	2.30 2.36 0.0217 0.0190 0.0635 0.0579	2.68 3.30 0.0085 0.0054 0.0340 0.0185	***2.04*** ***0.0369*** ***0.0892***	2.59 0.0103 0.0398
MP2/ 6-311++G**	d(HB) ρ(bcp) $\nabla^2\rho$(bcp)	2.24 2.31 0.0241 0.0208 0.0644 0.0591	2.69 3.36 0.0082 0.0053 0.0284 0.0183	***1.94*** ***0.0484*** ***0.0712***	2.57 0.0106 0.0368
MP2/ aug-cc-pVDZ	d(HB) ρ(bcp) $\nabla^2\rho$(bcp)	2.26 2.32 0.0234 0.0210 0.0598 0.0541	2.67 3.22 0.0090 0.0069 0.0278 0.0214	***1.99*** ***0.0427*** ***0.0912***	2.54 0.0122 0.0349



Hydrogen Bonding and Other Interactions in Biological Systems: Hydrogen bond vs. Electrostatic interactions

Atomic charges calculated with NBO and AIM methods

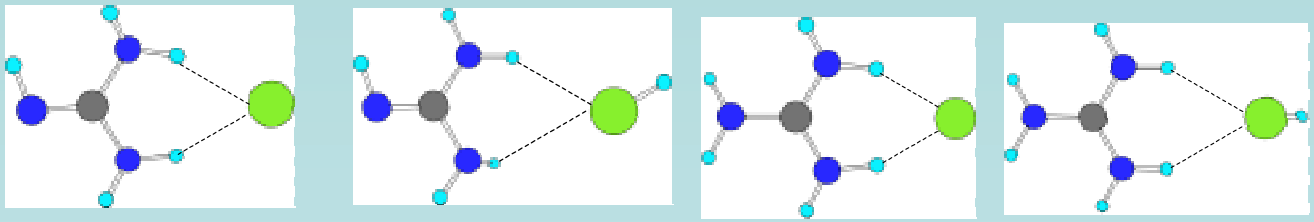
		minus	neutral	plusminus	plus
B3LYP/ 6-31G*	Cl H H	-0.91 -0.89 0.44 0.45 0.44 0.46	-0.29 -0.26 0.41 0.40 0.42 0.41	-0.78 -0.79 0.45 0.52 0.45 0.52	-0.30 -0.27 0.46 0.48 0.46 0.48
B3LYP/ TZVP	Cl H H	-0.92 -0.89 0.42 0.44 0.42 0.44	-0.26 -0.25 0.37 0.37 0.38 0.38	-0.78 -0.78 0.44 0.50 0.44 0.50	-0.28 -0.27 0.43 0.46 0.43 0.46
MP2/ 6-31G*	Cl H H	-0.91 -0.90 0.44 0.48 0.44 0.48	-0.28 -0.27 0.41 0.42 0.42 0.43	-0.79 -0.81 0.46 0.55 0.46 0.55	-0.30 -0.29 0.46 0.51 0.46 0.51
MP2/ 6-311++G**	Cl H H	-0.91 -0.89 0.41 0.45 0.42 0.46	-0.24 -0.25 0.37 0.38 0.38 0.40	-0.75 -0.78 0.43 0.52 0.43 0.52	-0.26 -0.27 0.43 0.47 0.43 0.47
MP2/ aug-cc-pVDZ	Cl H H	-0.90 -0.90 0.43 0.51 0.43 0.51	-0.26 -0.27 0.39 0.44 0.40 0.45	-0.76 -0.81 0.45 0.58 0.45 0.58	-0.29 -0.30 0.45 0.52 0.45 0.52

Hydrogen Bonding and Other Interactions in Biological Systems: Hydrogen bond vs. Electrostatic interactions

Atomic energy calculated with AIM method

		minus	neutral	plusminus	plus
B3LYP/ 6-31G*	Cl H H	-461.27 -0.41 -0.46	-461.27 -0.45 -0.44	-461.35 -0.36 -0.36	-461.31 -0.40 -0.40
B3LYP/ TZVP	Cl H H	-460.77 -0.43 -0.43	-460.66 -0.48 -0.47	-460.81 -0.39 -0.39	-460.70 -0.43 -0.43
MP2/ 6-31G*	Cl H H	-460.15 -0.40 -0.39	-460.17 -0.44 -0.43	-460.23 -0.34 -0.34	-460.21 -0.39 -0.39
MP2/ 6-311++G**	Cl H H	-459.90 -0.43 -0.42	-460.03 -0.47 -0.46	-460.07 -0.37 -0.37	-460.05 -0.42 -0.42
MP2/ aug-cc-pVDZ	Cl H H	-459.72 -0.38 -0.37	-459.97 -0.42 -0.42	-459.82 -0.33 -0.33	-459.98 -0.38 -0.38



Conclusions (so far …)

- Large E_Is for plusminus >> minus >> positive > neutral
- At all levels of calculation, correlations were found between HB distances and ρ(bcp) and $\nabla^2\rho$(bcp) as well as correlations between the orbital energy *E(2)* and ρ(bcp)
- Large decrease in Cl- atomic charge in plusminus complex >> minus > plus > neutral
- Positive/negative charge assisted HBs (plusminus) are the strongest in terms of electron density characteristics at the bcp and distances >> minus >> plus > neutral

Hydrogen Bonding and Other Interactions in Biological Systems: Acknowledgments

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