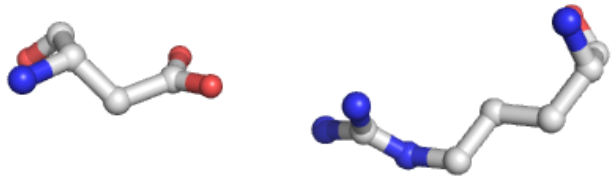
Knowledge-based potential for partial covalent interactions (PCI-KBP)

Steven Combs

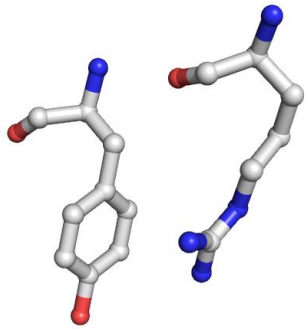
Partial Covalent Interactions (PCI)

- An interaction between an e^- deficient atom to a slightly positive atom
  - Cation-pi
  - Pi-pi
  - Salt bridge
  - Hydrogen Bonds

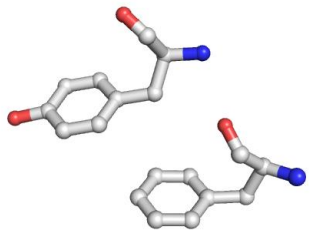
Hydrogen Bonds / Salt bridges



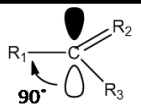
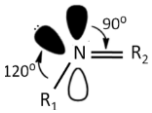
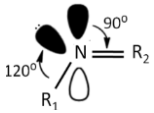
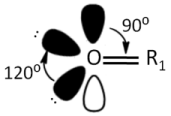
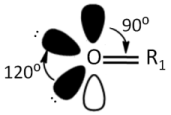
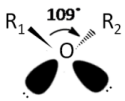
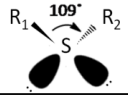
Cation-π

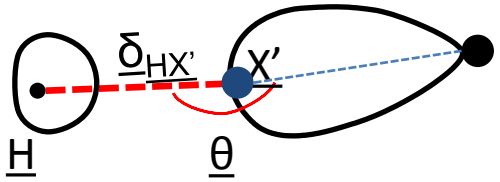


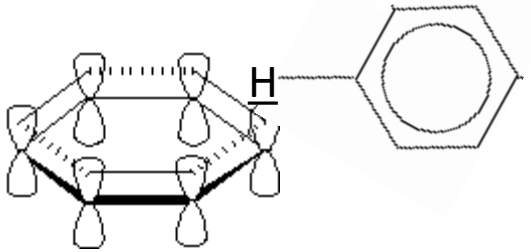
π - π



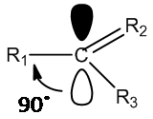
Placement of Orbitals on Atoms Allows for an Accurate Description of PCIs

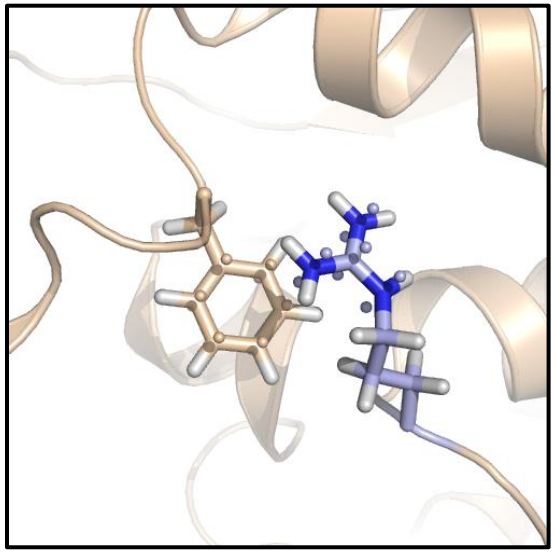
Orbital Type Name	Hybridization	Atom Type	Example	Picture
C.pi.sp2	sp2	aroC COO CNH2	Tyr, Trp, Phe Asp, Glu Asn, Gln	
N.pi.sp2	sp2	Ntrp Narg Nhis NH20	Trp Arg His Asn, Gln	
N.p.sp2	sp2	Nhis	His	
O.pi.sp2	sp2	ONH2 OOC	Asn, Gln Asp, Glu	
O.p.sp2	sp2	ONH2 OOC	Asn, Gln Asp, Glu	
O.p.sp3	sp3	OH	Ser, Thr, Tyr	
S.p.sp3	sp3	S	Cys, Met	

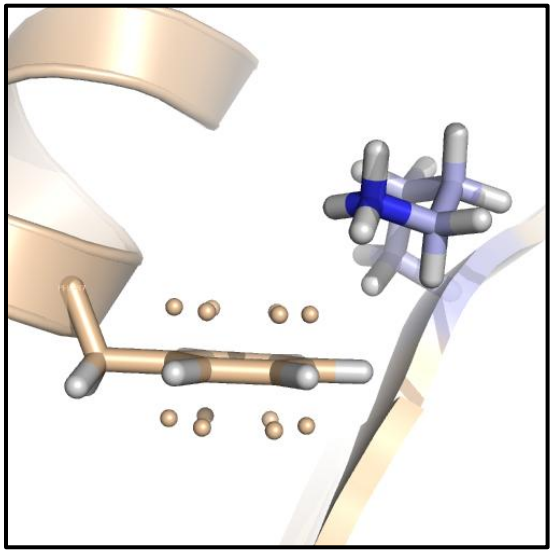


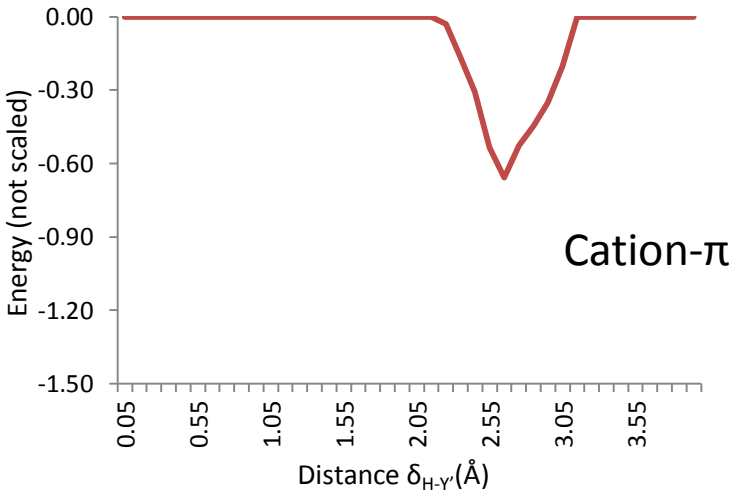


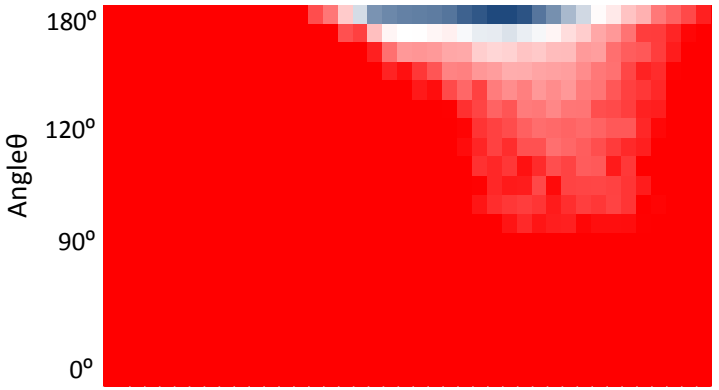
Orbital Placement Improves Sharpness and Depth of Energy Wells

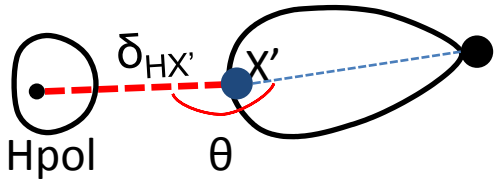
Rosetta Orbital Type Name	Rosetta Orbital Type	Hybridization	Rosetta Atom Type	Picture
C.pi.sp2	pi	sp2	aroC COO CNH2	



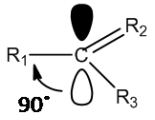


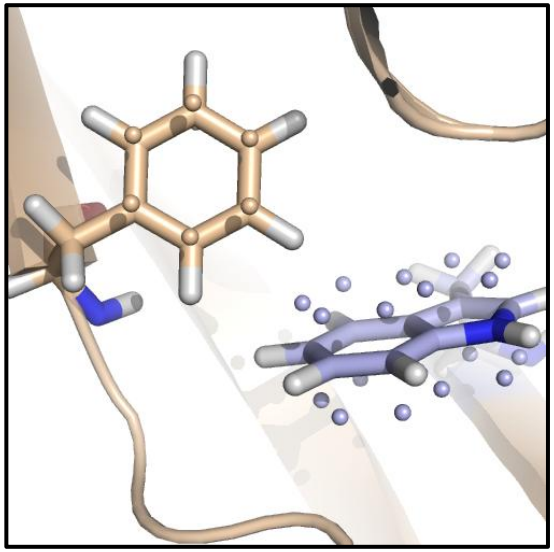


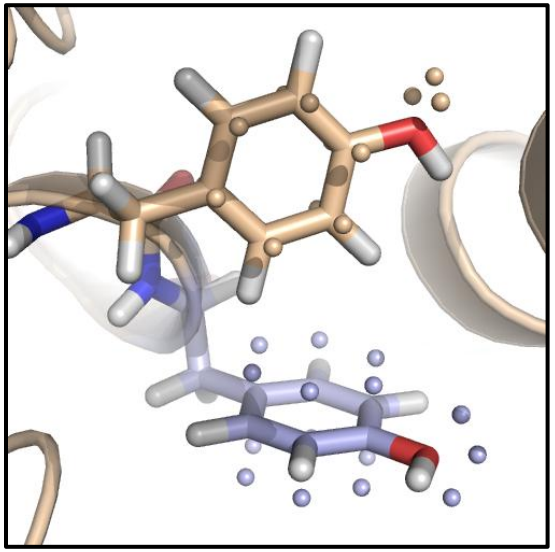


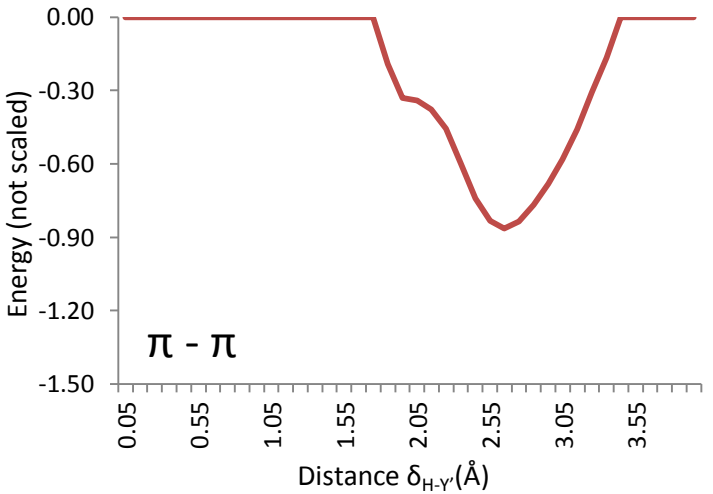


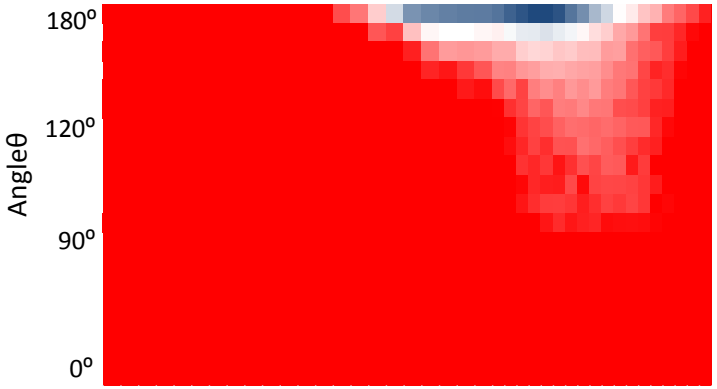
Orbital Placement Improves Sharpness and Depth of Energy Wells

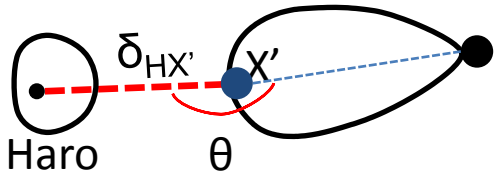
Rosetta Orbital Type Name	Rosetta Orbital Type	Hybridization	Rosetta Atom Type	Picture
C.pi.sp2	pi	sp2	aroC COO CNH2	



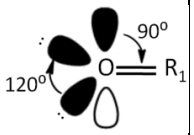


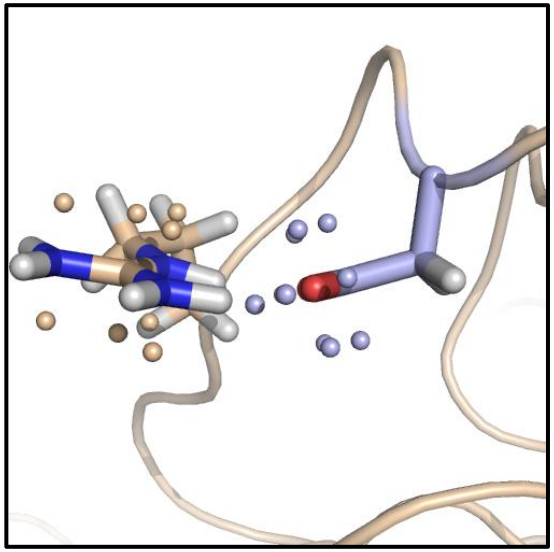


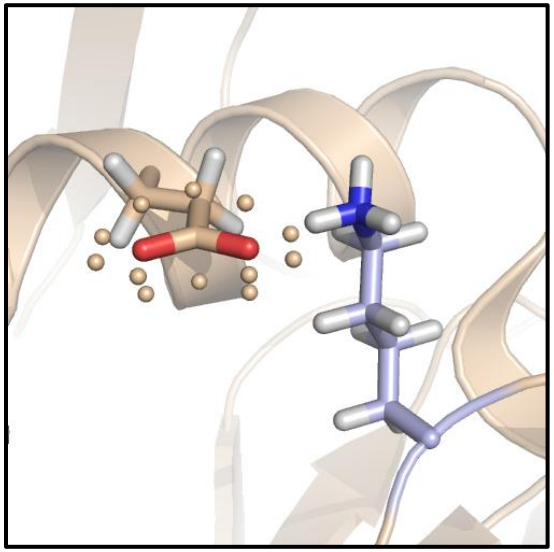


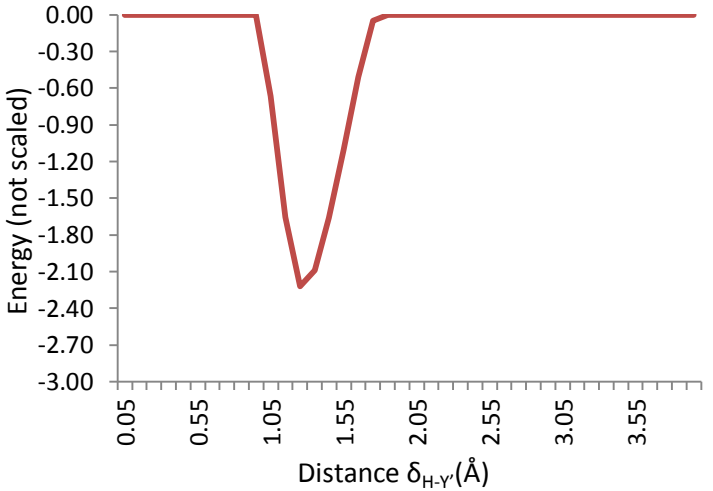


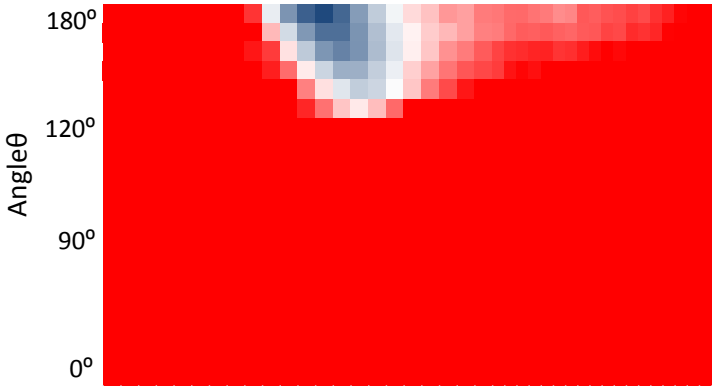
Orbital Placement Improves Sharpness and Depth of Energy Wells

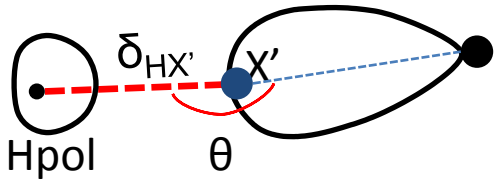
Rosetta Orbital Type Name	Rosetta Orbital Type	Hybridization	Atom Type	Picture
O.p.sp2	p	sp2	ONH2 OOC	



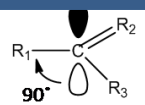
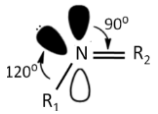
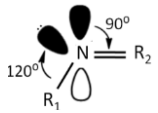
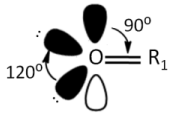
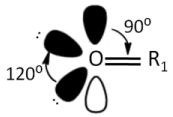
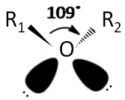
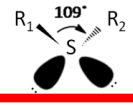








The PCI-KBP Is Divided into Two Scoring Terms

Orbital Type Name	Hybridization	Atom Type	Example	Picture
C.pi.sp2	sp2	aroC COO CNH2	Tyr, Trp, Phe Asp, Glu Asn, Gln	
N.pi.sp2	sp2	Ntrp Narg Nhis NH20	Trp Arg His Asn, Gln	
N.p.sp2	sp2	Nhis	His	
O.pi.sp2	sp2	ONH2 OOC	Asn, Gln Asp, Glu	
O.p.sp2	sp2	ONH2 OOC	Asn, Gln Asp, Glu	
O.p.sp3	sp3	OH	Ser, Thr, Tyr	
S.p.sp3	sp3	S	Cys, Met	

orbitals_haro

orbitals_hpol

Weights Used During Optimization

Score12

Score Term	Description
Fa_atr	Attractive portion of LJ
Fa_rep	Repulsive portion of LJ
Fa_sol	Implicit solvation potential
Fa_intra_rep	Intra-residue repulsion
Pro_close	Close the proline ring
Hbond	Hydrogen bond potential
Dslf	Disulphide potential
Rama	Phi-psi angles in ramachandran plot
Fa_dun	Dunbrack rotamer library
P_aa_pp	Probability of an amino acid given phi-psi angle

	Free	Removed
1.	hbond_sc, pair, sol	
2.	hpol, haro, sol	pair, hbond_sc
3.	hpol, haro, bb_hpol, sol	pair, hbond_sc, hbond_bb_sc

Benchmark Set-up

- Dataset from et al Grishin 2001
- Better than 1.8A
- 100-500 Residues
- Monomeric
- No ligands
- Complete Side chains

Introduction of Partial Covalent Interactions within Rosetta Improves Protein Metrics

Score12

Location	% SR
Buried	63
Surface	31
Overall	46

Location	% PSSM
Buried	72
Boundary	73
Surface	73
Overall	72

Packstats	0.60

Score 12 Optimized

Location	% SR
Buried	65
Surface	35
Overall	49

Location	% PSSM
Buried	77
Boundary	74
Surface	76
Overall	76

Packstats	0.63

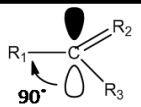
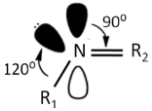
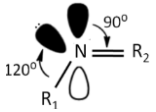
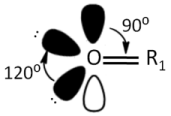
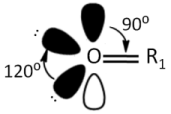
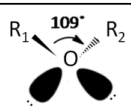
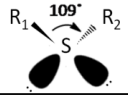
Orbitals

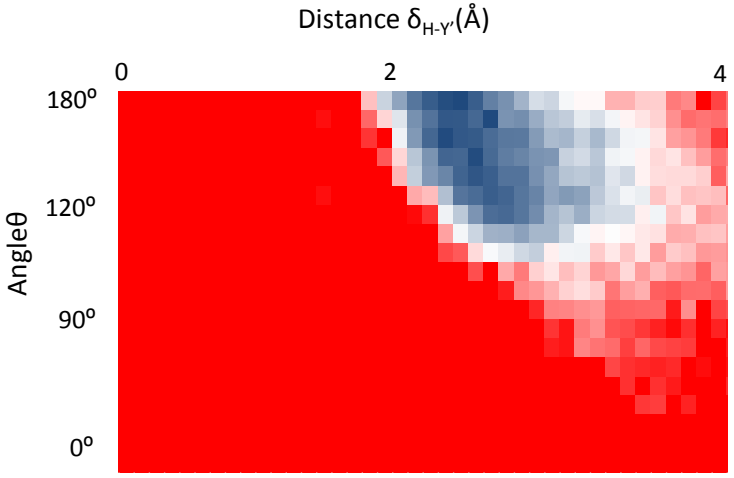
Location	% SR
Buried	69
Surface	36
Overall	52

Location	% PSSM
Buried	78
Boundary	78
Surface	77
Overall	78

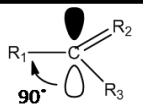
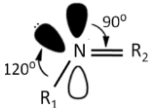
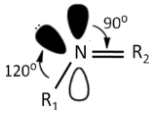
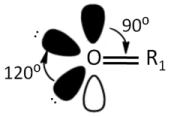
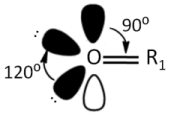
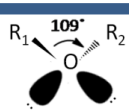
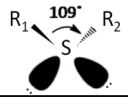
Packstats	0.68

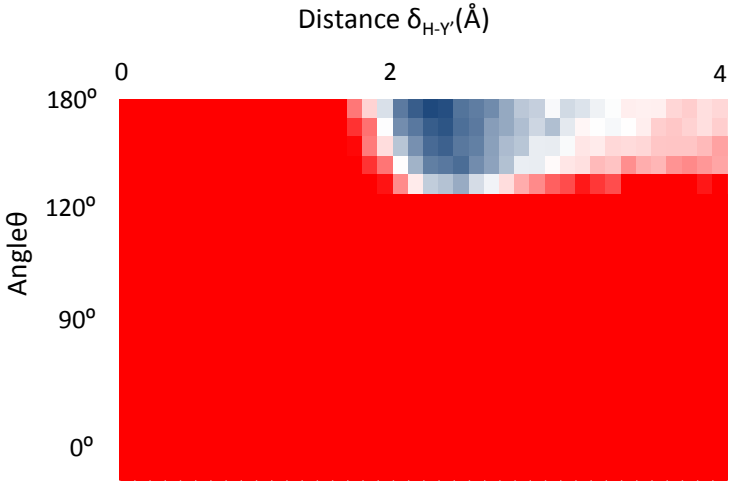
Identifying non-Classical PCIs
Sulfur-Aromatic

Orbital Type Name	Hybridization	Atom Type	Example	Picture
C.pi.sp2	sp2	aroC COO CNH2	Tyr, Trp, Phe Asp, Glu Asn, Gln	
N.pi.sp2	sp2	Ntrp Narg Nhis NH20	Trp Arg His Asn, Gln	
N.p.sp2	sp2	Nhis	His	
O.pi.sp2	sp2	ONH2 OOC	Asn, Gln Asp, Glu	
O.p.sp2	sp2	ONH2 OOC	Asn, Gln Asp, Glu	
O.p.sp3	sp3	OH	Ser, Thr, Tyr	
S.p.sp3	sp3	S	Cys, Met	



Identifying non-Classical PCIs
Anion-Pi

Orbital Type Name	Hybridization	Atom Type	Example	Picture
C.pi.sp2	sp2	aroC COO CNH2	Tyr, Trp, Phe Asp, Glu Asn, Gln	
N.pi.sp2	sp2	Ntrp Narg Nhis NH20	Trp Arg His Asn, Gln	
N.p.sp2	sp2	Nhis	His	
O.pi.sp2	sp2	ONH2 OOC	Asn, Gln Asp, Glu	
O.p.sp2	sp2	ONH2 OOC	Asn, Gln Asp, Glu	
O.p.sp3	sp3	OH	Ser, Thr, Tyr	
S.p.sp3	sp3	S	Cys, Met	



Conclusions

- Orbital placement allows for accurate description of residue interactions
- PCI-KBP can perform as well as score12
- New interactions are captured by PCI-KBP

Future Work

- Extend PCI-KBP to ligands/DNA/RNA
- Improve geometry of interactions
- Fix little bugs/memory leaks/speed

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