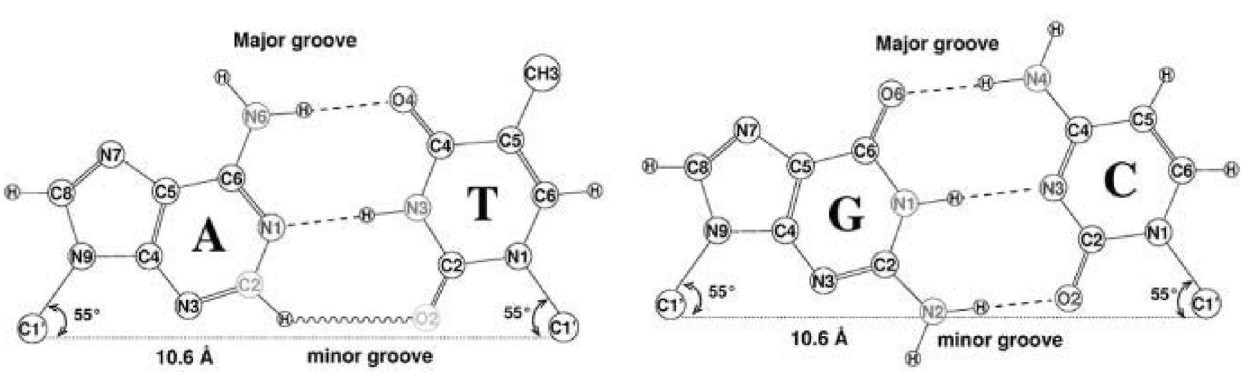
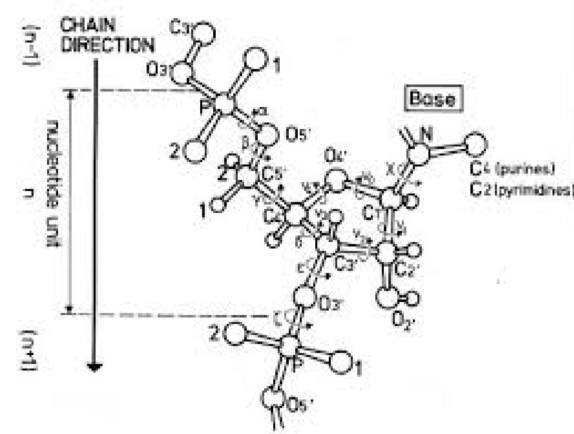
Bio 5357 Tutorial on Base Pairing (10 12 2021)

Most people are familiar with the AT and GC Watson Crick base pairs, with 2 and 3 H-bonds respectively, and probably wonder why it was so hard for Watson and Crick to figure out the structure of native duplex DNA. Actually, the DNA bases are capable of many more pairing interactions than the Watson Crick base pairs, and these additional base pairing interactions underlie much of the complexity and fascinating structures of folded DNA and RNA molecules. To begin to appreciate this complexity and anticipate the ways in which nucleic acid strands can interact, you will explore all the possible types of base pairing interactions.

A·T and G·C Watson–Crick Base Pairs

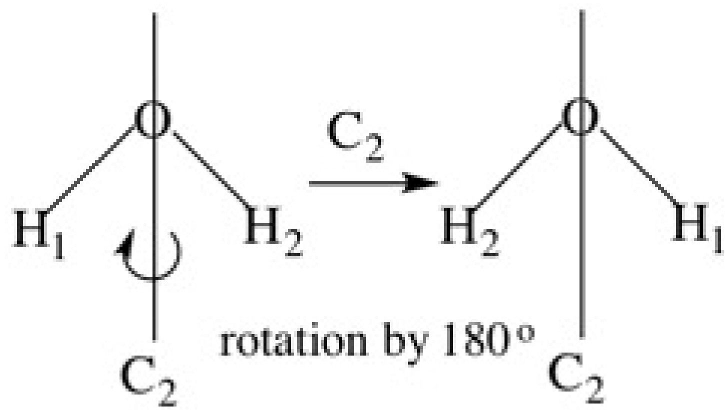




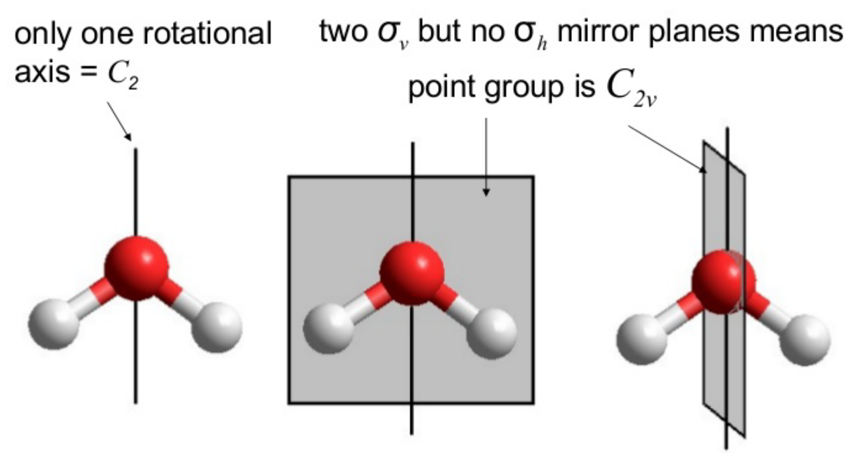
The bases are flat aromatic compounds (3.4 A thick) with N-H bonds and lone pairs in the plane of the base. A good H-bond in a base pair is a linear arrangement of an N-H bond vector and a lone pair orbital vector (N-H-----:O or N-H ---- :N), and having two H-bonds in parallel makes the interaction between bases even stronger. The bases are attached to a sugar phosphate backbone with a phosphate linkage between the 5’-OH and 3’-OH. The Watson Crick base pairing face points away from the sugar phosphate backbone (anti conformation) in B form duplex DNA.

Puzzle: How many ways are there to make base pairs with 2 or more parallel (or roughly parallel) in line H-bonding interactions?

1. How many homo-pyrimidine pairs, i.e., between C-C, T-T? Homo-purine A-A, G-G?
2. How many hetero-pyrimidine? i.e., T-C, Hetero-purine, A-G?
3. How many purine-pyrimidine? i.e., A-T, A-G, G-T, G-C?
4. Which base pairs were symmetric? I.e., have a plane of symmetry or a C-2 rotation axis of symmetry?
5. Which base pairs would result in a parallel duplex if propagated perpendicular to the plane of the base pair? Which ones are antiparallel? (If the same end is present it is parallel).
6. Bonus question: Can you make any base triples? Quadruples? More? Hint: Purines (A and G) have two faces that can make two or more in line H-bonds.



A C2 axis of symmetry is when you can rotate about a line through the object and get back the same structure. The C2-axis in water is in the plane of the molecule.

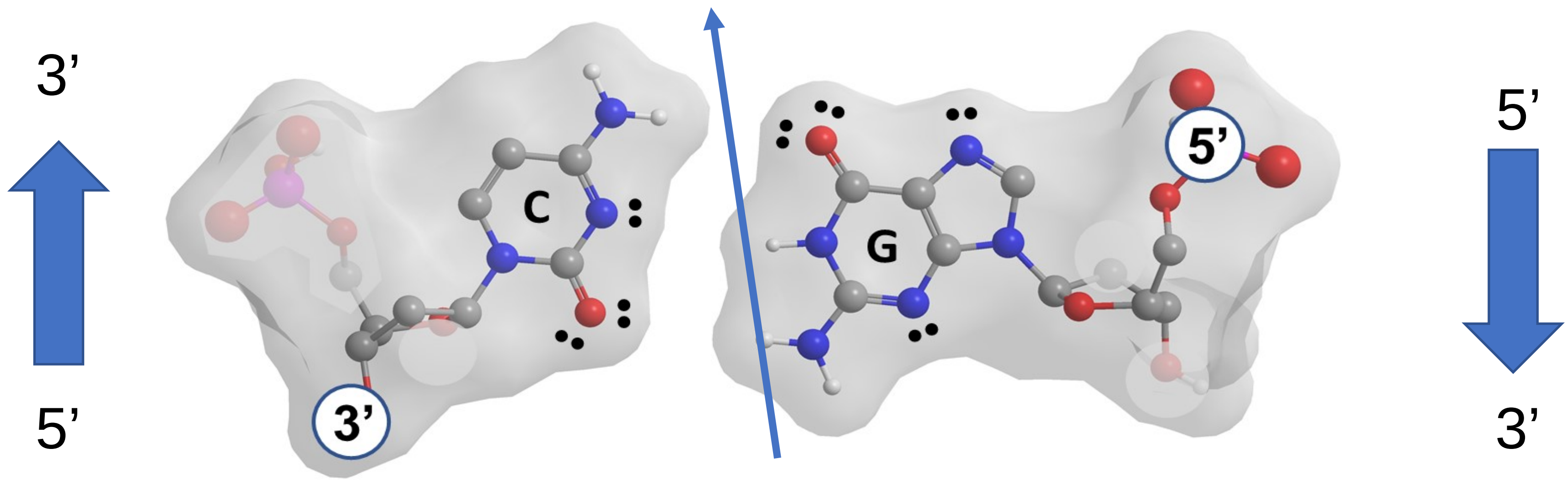


Water also has 2 planes of symmetry.

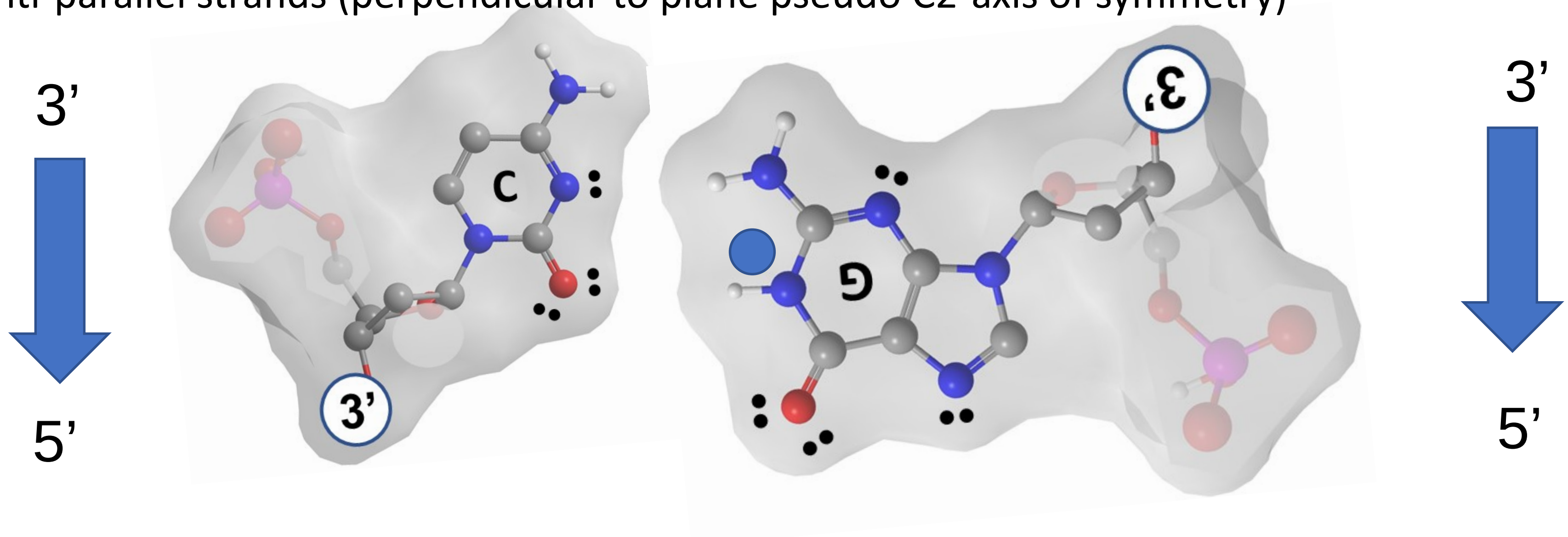
Determining relative strand orientation:

If the same end is up, then the strands would be parallel, if opposite ends, antiparallel.
The arrows show the direction as viewed from the side of the base pair

Parallel strands (in plane pseudo C2-axis of symmetry)



Anti-parallel strands (perpendicular to plane pseudo C2-axis of symmetry)



Solution: Use the templates (next pages) for the bases A, C, G and T with an attached sugar phosphate backbone to explore possible base pairing schemes. Polar H’s are white balls, oxygens are red, and nitrogens are blue. Only the in-plane lone pairs are shown. Groups that are behind the plane of the base are faded, those in front, such as the 5’- or 3’-ends are not.

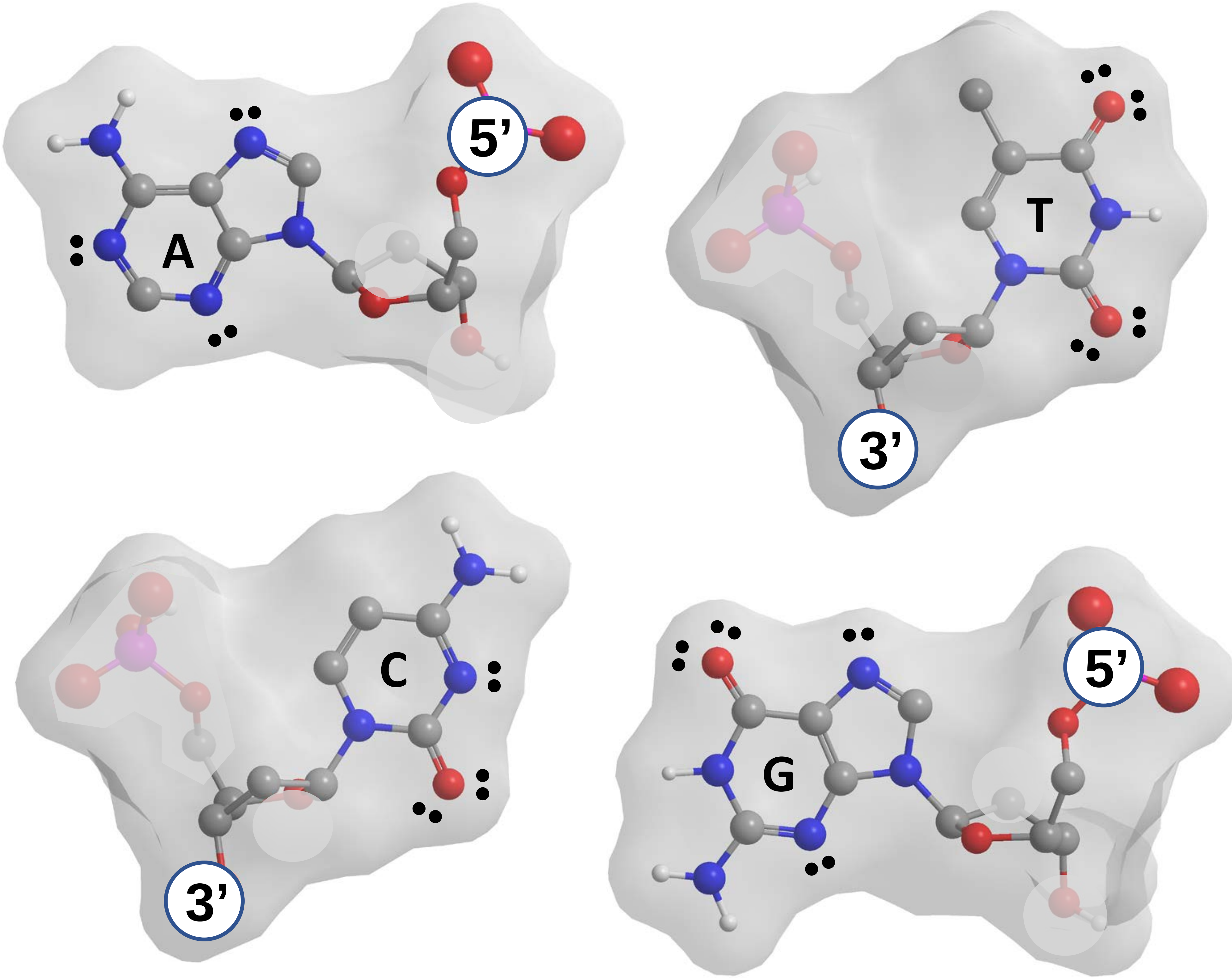
1. Print the first template slide on cardstock (this is a stiff paper used to make greeting cards). If you don’t have any print on normal paper.
2. Take the printed paper and put it back in the printer so that the second template slide will print on the other side (On my inkjet printer I simply take the printed paper out of the output tray and re-insert it into the paper tray without turning it over or turning it around. You may have to experiment with your printer.
3. Cut around the grey area which represents the molecular surface of the nucleotide.
4. Repeat, so that you have two of each nucleotide.
5. Try orienting the nucleotides in different ways, and flipping one of them, to see how many ways you can make two or more parallel H-bonds between nucleotides.

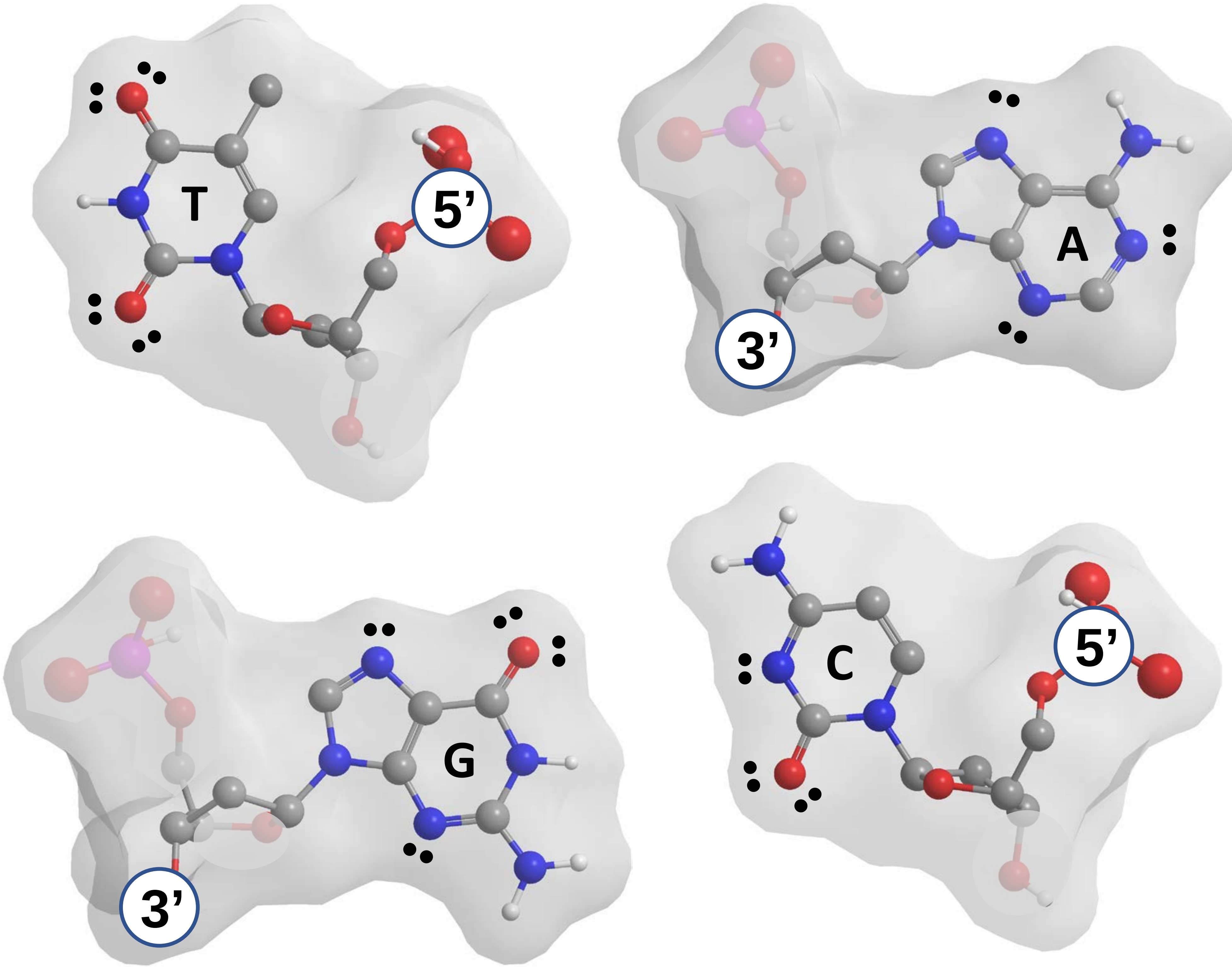
Alternate methods for preparing stiff templates

If your printer cannot accommodate cardstock, but can accommodate the more flexible Avery labels, you could print onto a full page label, then cut them out and affix them to both sides of piece of cardstock, cereal box cardboard, or corrugated cardboard from a box, and then cut around them with scissors. If you use foamboard you may have to use a box cutter (be careful!). Alternatively, simply print out the templates on regular paper and glue them to a stiffer material.

Fill in answers here

		symmetric	un-symmetric	parallel	anti-parallel
Homo--pyrimidine	C-C				
	T-T				
Homo-purine	A-A				
	G-G				
hetero-pyrimidine	C-T				
hetero-purine	A-G				
purine-pyrimidine	A-C				
	A-T				
	G-C				
	G-T				


A
5’
T
3’
C
3’
G
5’



T
5’
A
3’
G
3’
C
5’

Extra questions:

1. Draw a geometrically correct structure of a non-Watson Crick A-T base pair. Use your models to get the right alignment.

2. Draw the structure of a symmetric homo-pyrimidine base pair. What type of symmetry does it have? Will it form a parallel or anti parallel helix?

3. For each of the four deoxynucleosides dA, dC, dG and dT:

a) Draw in all the lone pairs for each base and indicate what type of orbital they are in (s, p, sp, sp^2, or sp^3). To help you decide, determine the hybridization state of the atom to which they are attached. When given a choice pick the hybridization that maximizes resonance.

b) Circle the lone pair orbitals that are perpendicular to the plane of the base. Put a triangle around those that are in the plane of the base.