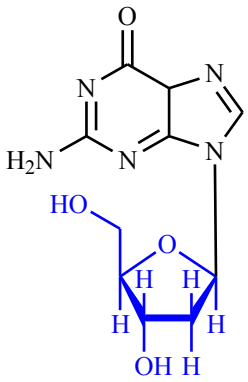
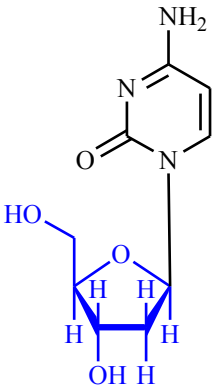
Answers to end-of-chapter questions

1) Proflavine contains a planar, heteroaromatic, tricyclic ring which can slip between the base pairs of DNA and interact with these base pairs through van der Waals interactions. The amino groups are likely to be ionised at physiological pH and can form ionic bonds with the charged phosphate groups of the DNA sugar phosphate backbone (see also section 9.1).
The drug is unlikely to show any selectivity between the DNA of bacteria and the DNA of human cells. Therefore, it cannot be used systemically.

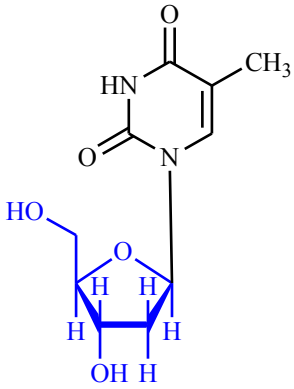
2) The nucleosides which are mimiced are deoxyguanosine, deoxycytidine and deoxythymidine respectively (see also section 20.6.1).



Deoxyguanosine

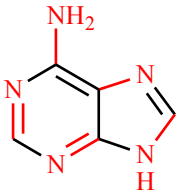


Deoxycytidine



Deoxythymidine

3) It is possible to identify five CN fragments within the skeleton of adenine as shown below.



4) The table in appendix 2 can be used to answer this question. A change in Z is least likely to result in a change of amino acid. For example, CUU, CUC, CUA and CUG all code for leucine.

5)
AGU to ACU
This changes serine to threonine. Both these molecules contain an alcohol functional group in their side chain, and so it is possible that the receptor would still be functional. The increased bulk of threonine might have an effect on the range of ligands which could bind.

AGU to GGU

Serine is changed to glycine. Glycine has no side chain and so an important binding group is lost. The receptor is unlikely to be functional.

AGU to AGC
Serine is retained. The identical receptor will result.

GAAto GAU
Glutamate is changed to aspartate. Both residues contain a carboxylate group that can interact through ionic interactions. It is likely that the mutated receptor will still be functional. However, the relative activity of different ligands may alter since the aspartate residue is shorter than the glutamate residue.

GAA to AAA
Glutamate is changed to lysine. If lysine is ionised, it will have a positive charge rather than a negative charge. The same binding interactions are not possible and so the receptor is unlikely to be functional with existing ligands.
However, it is conceivable that the receptor might be active with ligands bearing a carboxylate group since this would permit an ionic interaction to take place.

GAA to GUA
Glutamate is changed to valine. Valine has an alkyl side chain. An important ionic binding interaction is lost and the receptor is likely to be non functional.

UUU to UUC
Phenylalanine is retained. The receptor is unaffected.

UUU to UAU
Phenylalanine is changed to tyrosine. Tyrosine is very similar to phenylalanine and contains an aromatic ring. Therefore, there is a good chance that the receptor will still be functional.

UUU to AUU
Phenylalanine is changed to isoleucine. Isoleucine contains an alkyl side chain and no aromatic ring. Both groups can interact with hydrophobic groups on ligands through van der Waals interactions, but it is likely that the mutation will have an effect on receptor activity due to the different sizes and shapes of the side chains. The aromatic ring of phenylalanine is planar, whereas the alkyl side chain of isoleucine is branched and bulky. The receptor may still be functional, but it is likely that the relative activity of ligands would be significantly affected.