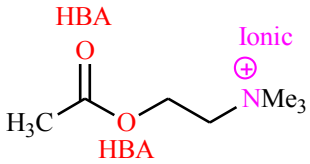
Answers to end-of-chapter questions

1) A binding site is a hollow or cleft on the surface of a receptor protein into which a chemical messenger can fit and bind.
A binding region is a specific region of that binding site, which is important in the binding process. It may contain a functional group capable of forming a specific bonding interaction with a functional group present on the guest molecule or ligand. Alternatively, it may be a hydrophobic region that can form van der Waals interactions with a hydrophobic region of the ligand.

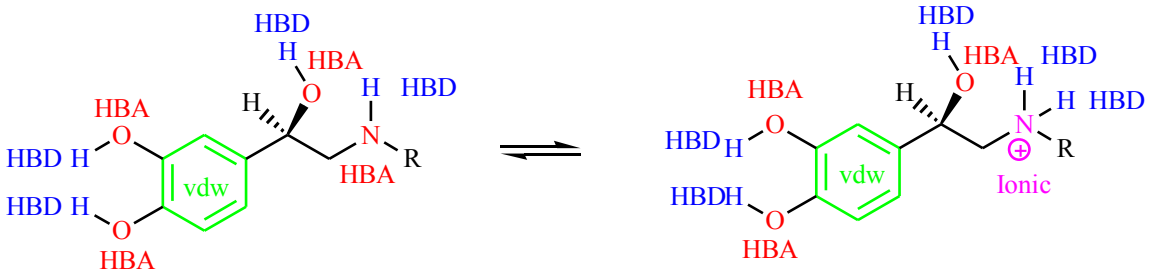
2) The possible binding interactions for the functional groups in each molecule are shown as HBD (hydrogen bond donor), HBA (hydrogen bond acceptor), ionic and vdw (van der Waals interactions). It should also be noted that van der Waals interactions involving alkyl groups or alkyl chains are possible.
The following amino acids have side chains which could interact by hydrogen bonding: Ser, Thr, Tyr, Asn, Gln, Asp and Glu
The following amino acids have side chains which could interact by ionic interactions: Asp, Glu, His, Lys, Arg
The following amino acids have aromatic or heteroaromatic groups in their side chains which could interact by van der Waals interactions; Phe, Tyr, Try
The following amino acids contain alkyl side chains which could interact by van der Waals interactions; Val, Leu, Ile, Met, Pro
In addition, the peptide links between amino acids in the binding site can interact with ligands by hydrogen bonding.

<u>Acetylcholine</u>



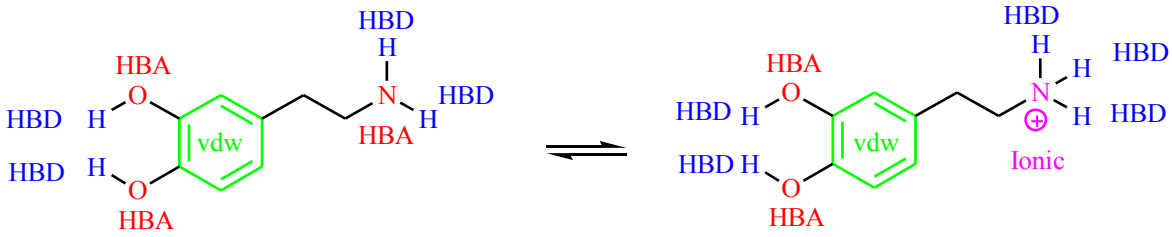
It is also known that three of the four methyl groups fit into hydrophobic pockets and participate in van der Waals interactions (see also sections 22.5 and 17.14.1). Note also that the carbonyl oxygen is the stronger HBA of the two oxygen atoms present.

<u>Noradrenaline and adrenaline</u>



The amine group of both noradrenaline and adrenaline can exist as the free base or as the protonated, ionised form. Note that the nitrogen can act as a HBA in the free base, but not when it is ionised. The phenolic oxygen atoms are also likely to be relatively weak HBAs. Further details on the binding interactions of noradrenaline and adrenaline can be found in sections 17.14.1, 23.8 and 23.9.

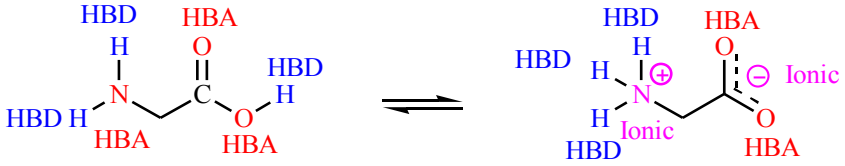
Dopamine



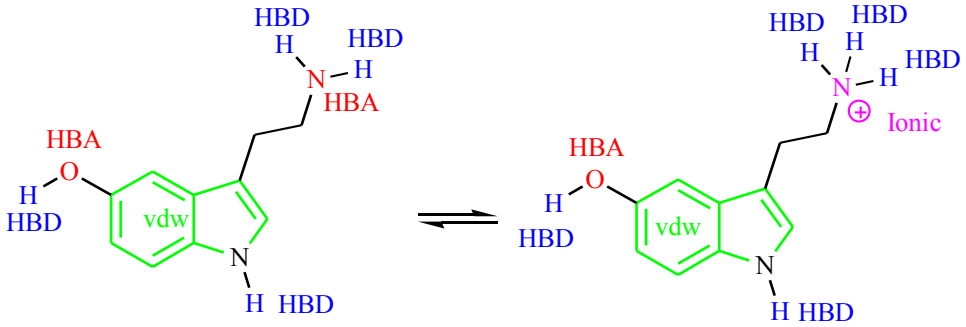
The amine group of dopamine can exist as the free base or as the protonated, ionised form. Note that the nitrogen can act as a HBA in the free base, but not when it is ionised. The phenolic oxygen atoms are also likely to be relatively weak HBAs. Further details on the binding interactions of dopamine can be found in section 17.14.1.

Glycine

Glycine is an amino acid which is more likely to exist as the zwitterion with both the amine and carboxylic acid groups being ionised. There is no side chain.

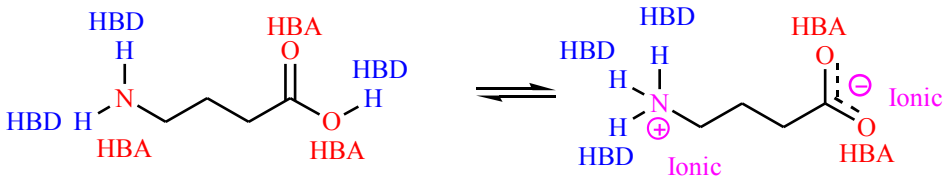


Serotonin

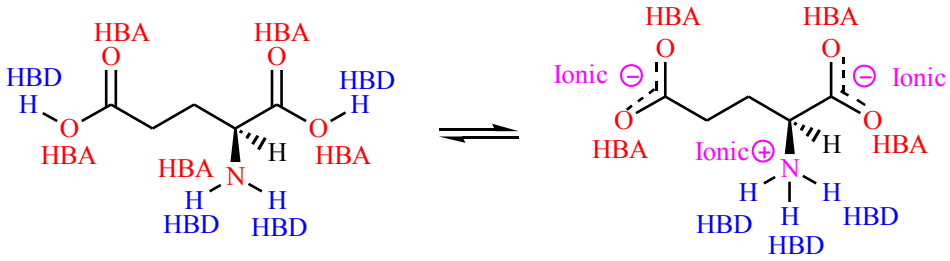


The amine group of serotonin can exist as the free base or as the protonated, ionised form. Note that the nitrogen can act as a HBA in the free base, but not when it is ionised. Note also that the heterocyclic nitrogen is unlikely to be a good HBA since its lone pair interacts with the ring's π system. The phenolic oxygen is also likely to be a relatively weak HBA. Further details on the binding interactions of serotonin can be found in section 17.14.1.

γ-Aminobutyric acid

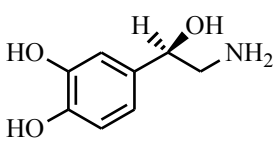


Glutamic acid

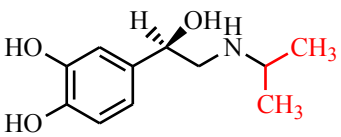


Glutamic acid is an amino acid where the head group is more likely to be present as a zwitterion. The side chain can also be ionised to form the glutamate ion.

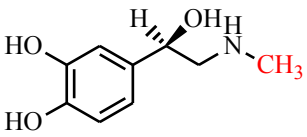
3) The differences between noradrenaline, isoprenaline and adrenaline are highlighted below. Noradrenaline has a primary amine group, whereas the other two structures have secondary amine groups with *N*-alkyl substituents.



Noradrenaline



Isoprenaline



Adrenaline

The difference in receptor selectivities observed between these three compounds indicates that an *N*-alkyl substituent has a role to play in receptor selectivity. Increasing the size and bulk of the *N*-alkyl substituent results in loss of potency at the α-receptor, but an increase in potency at β-receptors. These results indicate that the β-adrenoceptor has a hydrophobic pocket into which a bulky alkyl group can fit, whereas the α-adrenoceptor does not (see also sections 13.3.1.1 and 23.9.2).

4) In an α-helix, the NH and C=O of each peptide link forms hydrogen bonds within the centre of the helix such that these groups do not have to interact with the hydrophobic centre of the cell membrane. The α-helix also positions the side chains (which are mostly hydrophobic) to the exterior of the helix where they can interact with the hydrophobic centre of the cell membrane (see also section 2.2).