NEUTRAL GUEST BINDING

Non-covalent interactions available for ligand design:

H-bonding: strongly directional to give specificity.

π-π stacking: between aromatic groups.

Hydrophobic effects: exclusion of non-polar groups or molecules from aq. solution

1. Complementarity in H-bonding: Principles

- Host / Receptor has multiple H-bonding groups which are complementary to the guest.
- H-bonding groups are pre-organised and rigidly held within receptor molecule so that directionality in interaction with guest is retained.

Barbiturate binding: strength of binding dependent upon number of H-bonds.

2. π-π stacking Interactions in Peptides

Attraction between negatively charged π-electron cloud of an aromatic system with positively charge δ- framework of neighbouring aromatic molecule

- 2 configurations: a) Face to Face: parallel ring systems seperated by ca. 3.5 Å. Aligned so centre of one lies over corner of other
  b) Edge to Face: H atom from one ring interacts in a perpendicular orientation with centre of π-cloud of second ring.

EXAMPLE: Molecular hinge - π-π stacking of naphthalene with thymine