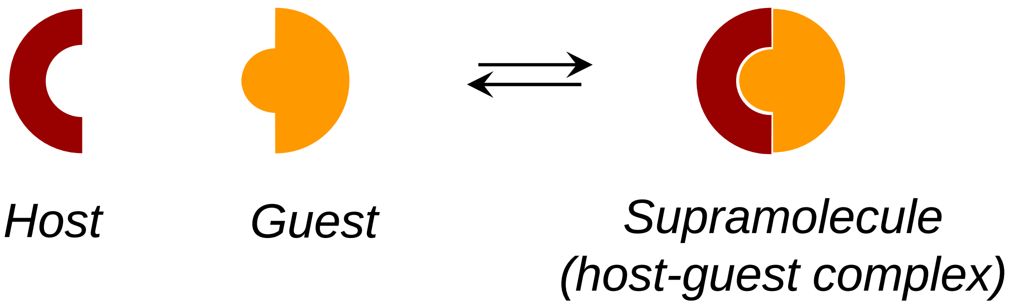
Molecular recognition



The first (and original) goal of Supramolecular Chemistry is to design and realize a receptor (**host**) capable to use the intermolecular interactions in order to selectively and reversibly bind (**recognize**) a selected molecule (**guest**) from a solution.

The concept of molecular recognition hence imply **reversible equilibrium**:

$$K = \frac{[Supramolecule]}{[Host][Guest]}$$

Association and dissociation constants

$$Host + Guest \rightleftharpoons Host \cdot Guest$$

$K_a = \frac{[H \cdot G]}{[H][G]}$	Association constant, units: M^{-1}	(Chemists)
$K_d = \frac{[H][G]}{[H \cdot G]}$	Dissociation constant, units: M (mM, μM)	(Biochemists)

In reality, equilibrium constants are defined as ratios of activities, which are dimensionless values . Consequentely, also equilibrium constants are dimensionless. Assumption that concentrations are close to acitivies leads to the use of units.

$$a_H = \frac{\gamma[H]}{[H_0]}$$

Solvent is ignored since solvatation effects are included in the relative stabilities of the species involved. Binding constants should be always tabulated reporting the sovent and temperature.

Thermodynamics of binding

$$K_a = \frac{[H \cdot G]}{[H][G]} \qquad \Delta G_0 = -RTln(K_a)$$

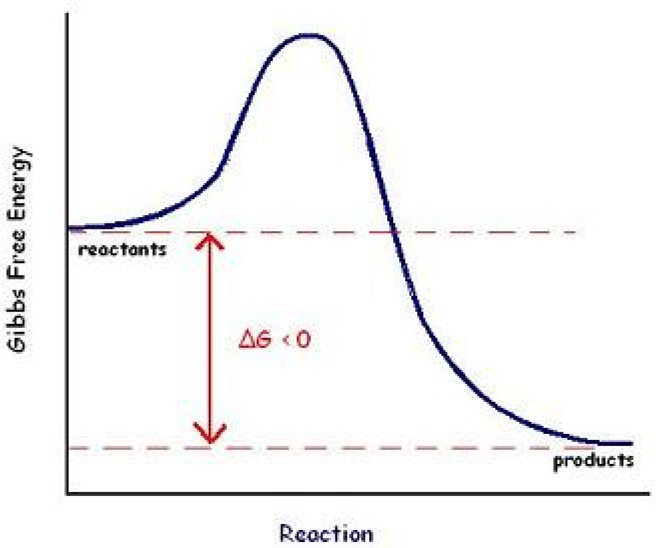
$K_a = 10\ M^{-1}$ ⇒ $\Delta G = 1.36$ Kcal/mol

$K_a = 100\ M^{-1}$ ⇒ $\Delta G = 2.73$ Kcal/mol

$K_a = 1000\ M^{-1}$ ⇒ $\Delta G = 4.09$ Kcal/mol

T = 298 K

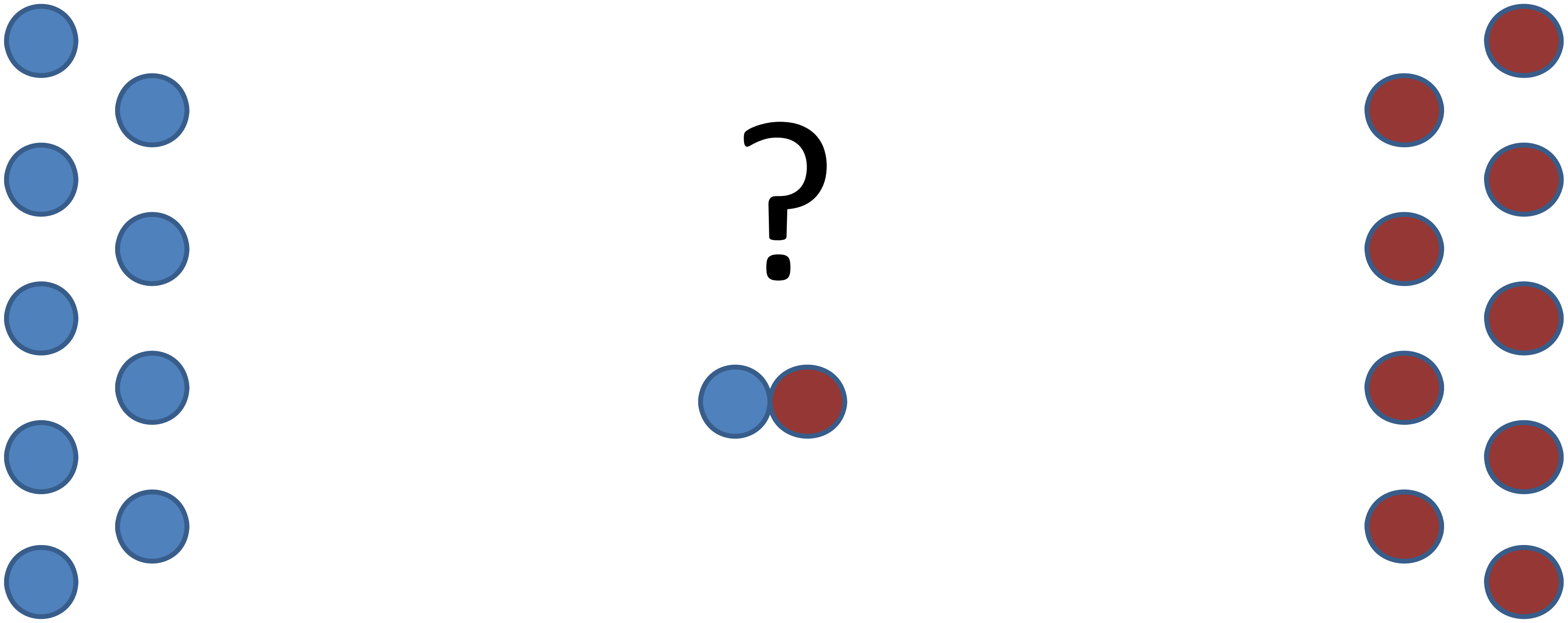
1.36 Kcal (2.3RT) every 10-fold K_a increase



Exoergonic reaction
Spontaneus

Binding at play

$K_a = 10\ M^{-1}$



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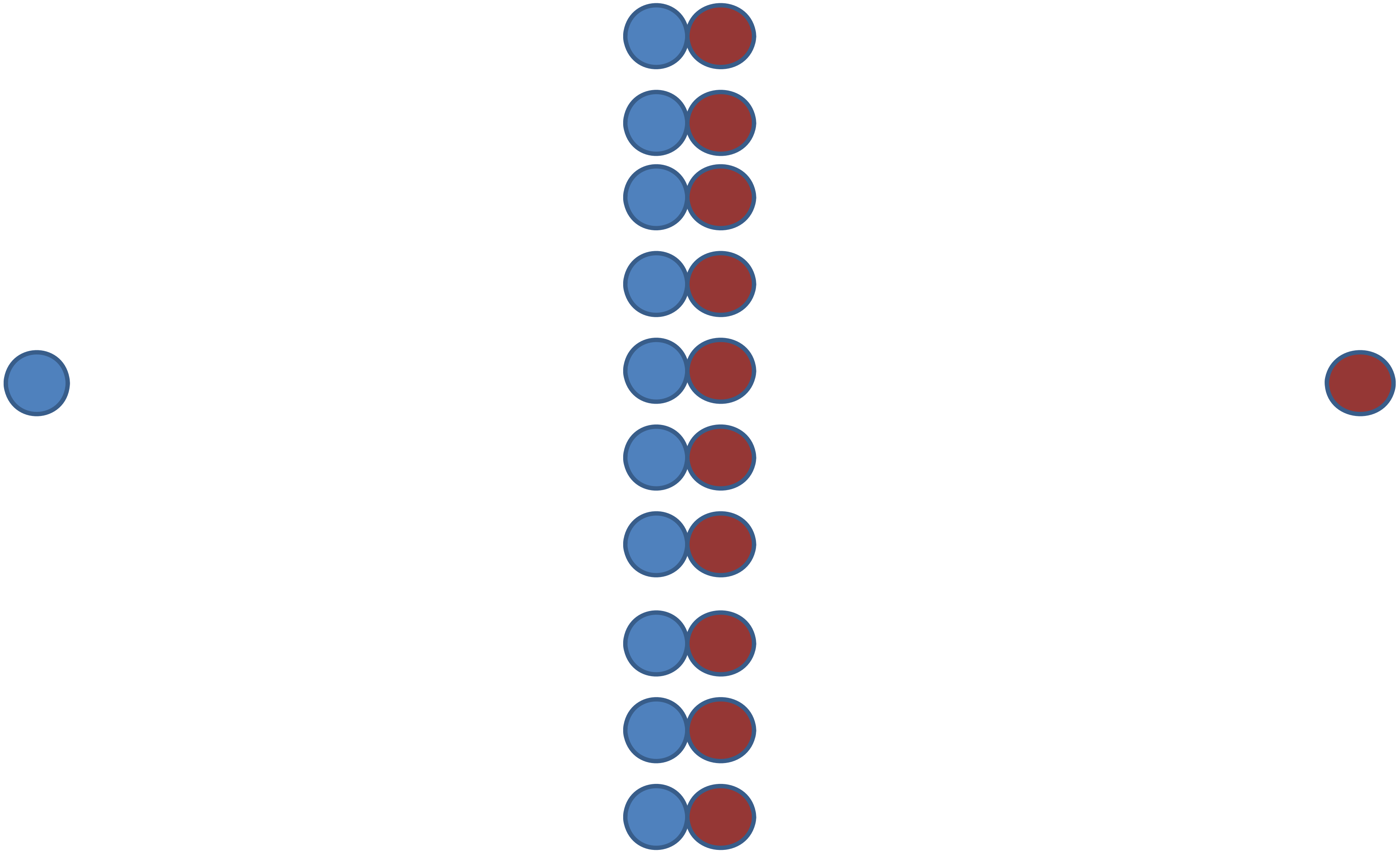
Binding at play

$K_a = 10\ M^{-1}$



Binding at play

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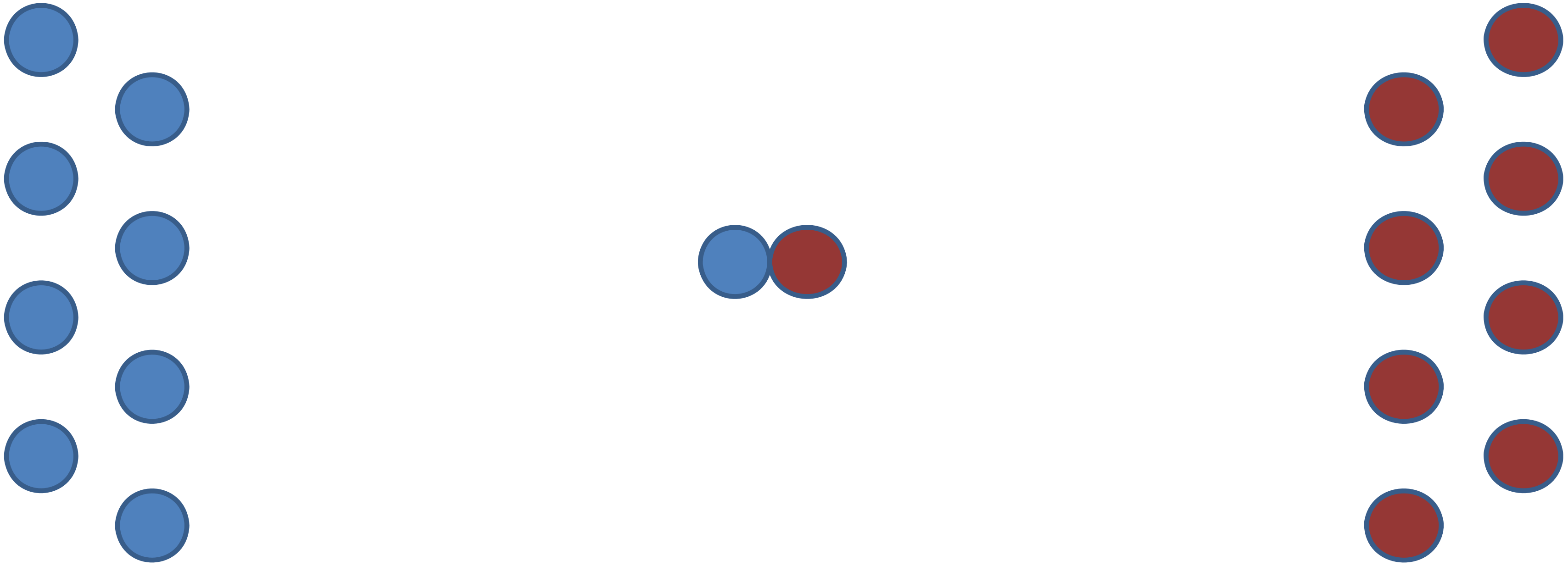
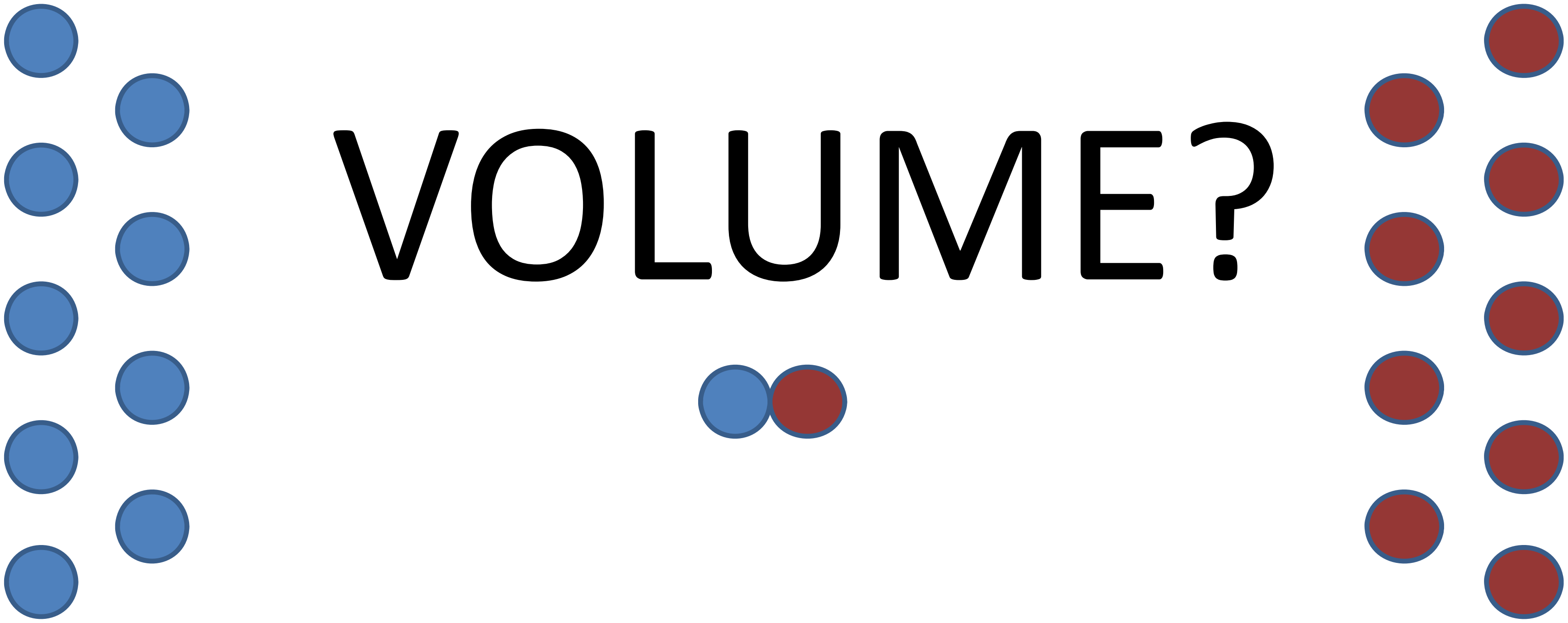


Binding at play

$K_a = 10\ M^{-1}$



VOLUME?

Binding at play

$$K_a[G]^2+(K_a[H]_0 - K_a[G]_0 + 1) - [G]_0 = 0$$

$$[G] = \frac{-1 \pm \sqrt{1 - 4K_a[G]_0}}{2K_a}$$

$K_a = 10\ M^{-1}$

Initial concentrations:

[H] = 10 mM, [G] = 10 mM

Final concentrations:

[H] = 9.2 mM, [G] = 9.2 mM, [HG] = 0.84 mM

Initial concentrations:

[H] = 1 M, [G] = 1 M

Final concentrations:

[H] =0.27 M, [G] = 0.27 M, [HG] = 0.73 M

Initial concentrations:

[H] = 100 M, [G] = 100 M

Final concentrations:

[H] =3.1 M, [G] = 3.1 M, [HG] = 96.9 M

Binding at play

Initial concentrations:

[H] = 10 mM, [G] = 10 mM

$K_a = 10\ M^{-1}$
$K_d = 100\ mM$

Final concentrations:

[H] = 9.2 mM, [G] = 9.2 mM, [HG] = 0.84 mM

$K_a = 100\ M^{-1}$
$K_d = 10\ mM$

Final concentrations:

[H] =6.2 mM, [G] = 6.2 M, [HG] = 3.8 mM

$K_a = 1000\ M^{-1}$
$K_d = 1\ mM$

Final concentrations:

[H] =2.7 mM, [G] = 2.7 mM, [HG] = 7.3 mM

Influence of dilution on equilibrium

$$K_a = \frac{[H \cdot G]}{[H][G]}$$

$$K_a = \frac{\left(\frac{n_{H \cdot G}}{V}\right)}{\left(\frac{n_H}{V}\right)\left(\frac{n_G}{V}\right)} = \left(\frac{V n_{H \cdot G}}{n_H n_G}\right)$$

When the volume (V) increases, n_H and n_G must increase more than n_{HG} to keep the ratio constant.

Dilution causes dissociation

Thermodynamics of binding

Why an exoergonic equilibrium is shifted toward products at high dilutions?

$$\mu_H = \mu^0 + RTln(a_H)$$

$$\Delta G = \Delta G^0 + RTln\left(\frac{a_{HG}}{a_H a_G}\right)$$

$$\Delta G^0 = -RTln\left[\left(\frac{\gamma_{HG}[HG]}{\gamma_H[H]\gamma_G[G]}\right)\left(\frac{[H]_0[G]_0}{[HG]_0}\right)\right]$$

$$\Delta G^0 = -RTln\left[K_a\left(\frac{[H]_0[G]_0}{[HG]_0}\right)\right]$$

If $K_a = 10^6$ M^{-1}, ΔG^0 = -8.16 Kcal/mol, when the standard states refer to 1 M concentrations , but ΔG^0 = 8.16 Kcal/mol, if the standard states refer to 10^{-12} M concentrations.

The ΔG^0 value misure the position of the equilibrium of the standard states