Two molecules A and B form the dimers AA, AB and BB. Concentrations are at a steady state determined by the law of mass action according to this reaction network:
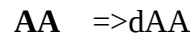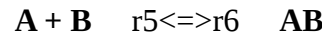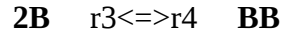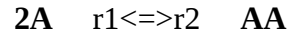
$$=>sA \quad \mathbf{A} \quad =>dA$$

$$=>sB \quad \mathbf{B} \quad =>dB$$

$$\mathbf{2A} \quad r1<=>r2 \quad \mathbf{AA}$$

$$\mathbf{2B} \quad r3<=>r4 \quad \mathbf{BB}$$

$$\mathbf{A + B} \quad r5<=>r6 \quad \mathbf{AB}$$

$$\mathbf{AA} \quad =>dAA$$

$$\mathbf{BB} \quad =>dBB$$

$$\mathbf{AB} \quad =>dAB$$
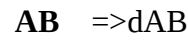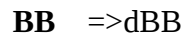
where s_A, s_B are synthesis rates (units of concentration * time^-1), r_1, r_3, r_5 are dissociation rates (units of time^-1), r_2, r_4, r_6 are association rates (units of concentration^-1 * time^-1), and $d_A, d_{AA}, d_{AB}, d_{BA}, d_{BB}, d_B$ are degradation rates (units of time^-1).

Let $c_A, c_{AA}, c_{AB}, c_{BB}, c_B$ denote the concentrations of the five molecular species.

Because the concentration of A is constant:
Equation 1: $s_A + 2r_1 c_{AA} + r_5 c_{AB} = d_A c_A + 2r_2 c_A^2 + r_6 c_A c_B$

Because the concentration of AA is constant:
Equation 2: $r_2 c_A^2 = d_{AA} c_{AA} + r_1 c_{AA}$

Because the concentration of AB is constant:
Equation 3: $r_6 c_A c_B = d_{AB} c_{AB} + r_5 c_{AB}$

A/B symmetry: The reaction network is symmetric with respect to the two lists of variables $[c_A, c_{AA}, s_A, d_A, r_1, r_2, d_{AA}]$ and $[c_B, c_{BB}, s_B, d_B, r_3, r_4, d_{BB}]$. This means that any equation will remain true if we simultaneously replace each of these parameters by the corresponding parameter from the other list.

Starting from equation 1, we can get an expression for c_{AA}:

$$s_A + 2r_1 c_{AA} + r_5 c_{AB} = d_A c_A + 2r_2 c_A^2 + r_6 c_A c_B$$

$$c_{AA} = \frac{d_A c_A + 2r_2 c_A^2 + r_6 c_A c_B - s_A - r_5 c_{AB}}{2r_1}$$

Starting from equation 2, we can get another expression for c_{AA} :

$$r_2 c_A^2 = d_{AA} c_{AA} + r_1 c_{AA}$$

$$c_{AA} = \frac{r_2}{d_{AA} + r_1} c_A^2$$

With k_{AA} defined as $\frac{r_2}{d_{AA} + r_1}$:

$$c_{AA} = k_{AA} c_A^2$$

By equating these two expressions of c_{AA} , we can get an expression for c_{AB} :

$$k_{AA} c_A^2 = \frac{d_A c_A + 2r_2 c_A^2 + r_6 c_A c_B - s_A - r_5 c_{AB}}{2r_1}$$

$$2r_1 k_{AA} c_A^2 = d_A c_A + 2r_2 c_A^2 + r_6 c_A c_B - s_A - r_5 c_{AB}$$

$$r_5 c_{AB} = d_A c_A + 2r_2 c_A^2 + r_6 c_A c_B - s_A - 2r_1 k_{AA} c_A^2$$

$$r_5 c_{AB} = d_A c_A + 2(r_2 - r_1 k_{AA}) c_A^2 + r_6 c_A c_B - s_A$$

$$c_{AB} = \frac{d_A c_A + 2(r_2 - r_1 k_{AA}) c_A^2 + r_6 c_A c_B - s_A}{r_5}$$

From the definition $k_{AA} = \frac{r_2}{d_{AA} + r_1}$, we get $r_2 - r_1 k_{AA} = d_{AA} k_{AA}$ and therefore:

$$c_{AB} = \frac{d_A c_A + 2 d_{AA} k_{AA} c_A^2 + r_6 c_A c_B - s_A}{r_5}$$

Starting from equation 3, we can get another expression for c_{AB} :

$$r_6 c_A c_B = d_{AB} c_{AB} + r_5 c_{AB}$$

$$c_{AB} = \frac{r_6}{d_{AB} + r_5} c_A c_B$$

With k_{AB} defined as $\frac{r_6}{d_{AB} + r_5}$:

$$c_{AB} = k_{AB} c_A c_B$$

By equating these two values of c_{AB} , we can get an expression for c_B :

$$k_{AB} c_A c_B = \frac{d_A c_A + 2 d_{AA} k_{AA} c_A^2 + r_6 c_A c_B - s_A}{r_5}$$

$$r_5 k_{AB} c_A c_B = d_A c_A + 2 d_{AA} k_{AA} c_A^2 + r_6 c_A c_B - s_A$$

$$(r_5 k_{AB} - r_6) c_A c_B = d_A c_A + 2 d_{AA} k_{AA} c_A^2 - s_A$$

$$c_B = \frac{d_A c_A + 2 d_{AA} k_{AA} c_A^2 - s_A}{(r_5 k_{AB} - r_6) c_A}$$

From the definition $k_{AA} = \dfrac{r_6}{d_{AB} + r_5}$, we get $r_6 - r_5 k_{AB} = d_{AB} k_{AB}$ and therefore:

$$c_B = \frac{d_A c_A + 2 d_{AA} k_{AA} c_A^2 - s_A}{- d_{AB} k_{AB} c_A}$$

By applying the A/B symmetry to this equation, we can get another expression for c_B :

$$c_A = \frac{d_B c_B + 2 d_{BB} k_{BB} c_B^2 - s_B}{- d_{AB} k_{AB} c_B}$$

where k_{BB} is defined as $\dfrac{r_4}{d_{BB} + r_3}$

$$- d_{AB} k_{AB} c_B c_A = d_B c_B + 2 d_{BB} k_{BB} c_B^2 - s_B$$

$$0 = (d_B + d_{AB} k_{AB} c_A) c_B + 2 d_{BB} k_{BB} c_B^2 - s_B$$

$$0 = 2 d_{BB} k_{BB} c_B^2 + (d_B + d_{AB} k_{AB} c_A) c_B - s_B$$

Applying the quadratic formula:

$$c_B = \frac{-b \pm \sqrt{b^2 - 4ac}}{2a} = \frac{-(d_B + d_{AB} k_{AB} c_A) \pm \sqrt{(d_B + d_{AB} k_{AB} c_A)^2 + 8 d_{BB} k_{BB} s_B}}{4 d_{BB} k_{BB}}$$

In the formula above, the coefficients are such that $a > 0$, $b \geq 0$, $c \leq 0$ and thus $b \leq \sqrt{b^2 - 4ac}$. It follows that $-b + \sqrt{b^2 - 4ac}$ is non-negative, while $-b - \sqrt{b^2 - 4ac}$ is non-positive. We therefore choose $-b + \sqrt{b^2 - 4ac}$ to obtain a non-negative value of c_B .

$$c_B = \frac{-(d_B + d_{AB} k_{AB} c_A) + \sqrt{(d_B + d_{AB} k_{AB} c_A)^2 + 8 d_{BB} k_{BB} s_B}}{4 d_{BB} k_{BB}}$$

By equating the two expressions that we obtained for c_B, we get:

$$\frac{d_A c_A + 2 d_{AA} k_{AA} c_A^2 - s_A}{-d_{AB} k_{AB} c_A}$$
$$=$$
$$\frac{-(d_B + d_{AB} k_{AB} c_A) + \sqrt{(d_B + d_{AB} k_{AB} c_A)^2 + 8 d_{BB} k_{BB} s_B}}{4 d_{BB} k_{BB}}$$

$$\frac{s_A - d_A c_A - 2 d_{AA} k_{AA} c_A^2}{d_{AB} k_{AB} c_A}$$
$$=$$
$$\frac{-(d_B + d_{AB} k_{AB} c_A) + \sqrt{(d_B + d_{AB} k_{AB} c_A)^2 + 8 d_{BB} k_{BB} s_B}}{4 d_{BB} k_{BB}}$$

Taking $x = d_{AA} k_{AA}$, $y = d_{BB} k_{BB}$ and $z = d_{AB} k_{AB}$, we obtain:

$$\frac{s_A - d_A c_A - 2 x c_A^2}{z c_A} = \frac{-(d_B + z c_A) + \sqrt{(d_B + z c_A)^2 + 8 y s_B}}{4 y}$$

$$4 y s_A - 4 y d_A c_A - 8 y x c_A^2 = -d_B z c_A - z^2 c_A^2 + \sqrt{(d_B z c_A + z^2 c_A^2)^2 + 8 y s_B z^2 c_A^2}$$

$$(d_B z c_A + z^2 c_A^2) + (4 y s_A - 4 y d_A c_A - 8 y x c_A^2) = \sqrt{(d_B z c_A + z^2 c_A^2)^2 + 8 y s_B z^2 c_A^2}$$

$$\left((d_B z c_A + z^2 c_A^2) + (4 y s_A - 4 y d_A c_A - 8 y x c_A^2)\right)^2 = (d_B z c_A + z^2 c_A^2)^2 + 8 y s_B z^2 c_A^2$$

$$2(d_B z c_A + z^2 c_A^2)(4 y s_A - 4 y d_A c_A - 8 y x c_A^2)$$
$$+$$
$$(4 y s_A - 4 y d_A c_A - 8 y x c_A^2)^2$$
$$=$$
$$8 y s_B z^2 c_A^2$$

$$8d_B s_A y z c_A - 8d_A d_B y z c_A^2 - 16d_B x y z c_A^3 + 8s_A y z^2 c_A^2 - 8d_A y z^2 c_A^3 - 16x y z^2 c_A^4$$
$$+$$
$$16s_A^2 y^2 - 16s_A d_A y^2 c_A - 32s_A x y^2 c_A^2 - 16s_A d_A y^2 c_A + 16d_A^2 y^2 c_A^2 + 32d_A x y^2 c_A^3$$
$$- 32s_A x y^2 c_A^2 + 32d_A x y^2 c_A^3 + 64x^2 y^2 c_A^4$$
$$=$$
$$8 y s_B z^2 c_A^2$$

$$8d_B s_A y z c_A - 8d_A d_B y z c_A^2 - 16d_B x y z c_A^3 + 8s_A y z^2 c_A^2 - 8d_A y z^2 c_A^3 - 16x y z^2 c_A^4$$
$$+$$
$$16s_A^2 y^2 - 16s_A d_A y^2 c_A - 32s_A x y^2 c_A^2 - 16s_A d_A y^2 c_A + 16d_A^2 y^2 c_A^2 + 32d_A x y^2 c_A^3$$
$$- 32s_A x y^2 c_A^2 + 32d_A x y^2 c_A^3 + 64x^2 y^2 c_A^4 - 8y s_B z^2 c_A^2$$
$$=$$
$$0$$

Dividing by y :

$$8d_B s_A z c_A - 8d_A d_B z c_A^2 - 16d_B x z c_A^3 + 8s_A z^2 c_A^2 - 8d_A z^2 c_A^3 - 16x z^2 c_A^4$$
$$+$$
$$16s_A^2 y - 16s_A d_A y c_A - 32s_A x y c_A^2 - 16s_A d_A y c_A + 16d_A^2 y c_A^2 + 32d_A x y c_A^3$$
$$- 32s_A x y c_A^2 + 32d_A x y c_A^3 + 64x^2 y c_A^4 - 8s_B z^2 c_A^2$$
$$=$$
$$0$$

Dividing by 8:

$$d_B s_A z c_A - d_A d_B z c_A^2 - 2d_B x z c_A^3 + s_A z^2 c_A^2 - d_A z^2 c_A^3 - 2x z^2 c_A^4$$
$$+$$
$$2s_A^2 y - 2s_A d_A y c_A - 4s_A x y c_A^2 - 2s_A d_A y c_A + 2d_A^2 y c_A^2 + 4d_A x y c_A^3$$
$$- 4s_A x y c_A^2 + 4d_A x y c_A^3 + 8x^2 y c_A^4 - s_B z^2 c_A^2$$
$$=$$
$$0$$

$$0 = (8x^2y - 2xz^2)c_A^4 + (8d_Axy - 2d_Bxz - d_Az^2)c_A^3$$
$$+ (s_Az^2 - d_Ad_Bz - 8s_Axy + 2d_A^2y - s_Bz^2)c_A^2 + (s_Ad_Bz - 4s_Ad_Ay)c_A + 2s_A^2y$$

$$0 = 2x(4xy - z^2)c_A^4 + (d_A(8xy - z^2) - 2d_Bxz)c_A^3$$
$$+ (2yd_A^2 + s_A(z^2 - 8xy) - d_Ad_Bz - z^2s_B)c_A^2 + s_A(d_Bz - 4d_Ay)c_A + 2s_A^2y$$

Dividing by z :

$$0 = 2x\left(4\frac{xy}{z} - z\right)c_A^4 + \left(d_A\left(8\frac{xy}{z} - z\right) - 2d_Bx\right)c_A^3$$
$$+ \left(\frac{2yd_A^2}{z} + s_A\left(z - 8\frac{xy}{z}\right) - d_Ad_B - zs_B\right)c_A^2 + s_A\left(d_B - 4d_A\frac{y}{z}\right)c_A + 2s_A^2\frac{y}{z}$$

Eliminating x , y and z using their definitions $x = d_{AA}k_{AA}$, $y = d_{BB}k_{BB}$ and $z = d_{AB}k_{AB}$, we obtain:

$$0$$
$$=$$
$$2d_{AA}k_{AA}\left(4\frac{d_{AA}k_{AA}d_{BB}k_{BB}}{d_{AB}k_{AB}} - d_{AB}k_{AB}\right)c_A^4$$
$$+$$
$$\left(d_A\left(8\frac{d_{AA}k_{AA}d_{BB}k_{BB}}{d_{AB}k_{AB}} - d_{AB}k_{AB}\right) - 2d_Bd_{AA}k_{AA}\right)c_A^3$$
$$+$$
$$\left(\frac{2d_{BB}k_{BB}d_A^2}{d_{AB}k_{AB}} + s_A\left(d_{AB}k_{AB} - 8\frac{d_{AA}k_{AA}d_{BB}k_{BB}}{d_{AB}k_{AB}}\right) - d_Ad_B - d_{AB}k_{AB}s_B\right)c_A^2$$
$$+$$
$$s_A\left(d_B - 4d_A\frac{d_{BB}k_{BB}}{d_{AB}k_{AB}}\right)c_A$$
$$+$$
$$2s_A^2\frac{d_{BB}k_{BB}}{d_{AB}k_{AB}}$$

This formula can be used to compute the values of the coefficients of the 4th degree polynomial given the values of the chemical parameters. The resulting values of the coefficients can then be used by a numerical solver to compute the 4 possible values of c_A (the 4 roots of the polynomial). The

corresponding steady-state concentrations of the other molecular species can then be computed using the formulas derived above.

$$c_B = \frac{d_A c_A + 2d_{AA} k_{AA} c_A^2 - s_A}{-d_{AB} k_{AB} c_A} = \frac{s_A - 2d_{AA} k_{AA} c_A^2 - d_A c_A}{d_{AB} k_{AB} c_A} = \frac{s_A / c_A - 2d_{AA} k_{AA} c_A - d_A}{d_{AB} k_{AB}}$$

$$c_{AA} = k_{AA} c_A^2 = \frac{r_2}{d_{AA} + r_1} c_A^2$$

$$c_{BB} = k_{BB} c_B^2 = \frac{r_4}{d_{BB} + r_3} c_B^2$$

$$c_{AB} = k_{AB} c_A c_B = \frac{r_6}{d_{AB} + r_5} c_A c_B$$

Among the 4 possible values of c_A, the one that results in positive values for the concentrations of all five molecular species is the physically correct solution.