Appendix S . Calculation of dimensionless partition function for A population ith distribution of valence

The -th equation in this appendix is numbered as (S1-). For example, the first equation is numbered as (S1-1). All the other equations mentioned in the following derivations refer to equations in the main body of the article.

To include the participation of monovalent LAT in LAT aggregation, the factor $(1+\beta)$ in our previous paper [1] has to be replaced by $(1+\beta+\ )$. The term is included to take into account the possible binding of a monovalent LAT to a binding site on a Grb2 molecule, which is part of a Grb2-S S1-Grb2 complex, with the other Grb2 in the complex being bound to another LAT molecule with valency greater than one. Incorporating the bivalent LAT species into the aggregates is more tricky. We make the ansatz that in order to include bivalent LAT in the cross-linking species, one should replace in the expression of q, the dimensionless concentration of the Grb2-S S1-Grb2 species ($c = 2K\ \ C$) by c^0, where c^0 is the sum of c and the dimensionless concentration of all linear chains of bivalent LAT molecules bridged by the Grb2-S S1-Grb2 complex and having Grb2-S S1-Grb2 moieties at either end. The sum of the concentrations of all such chains can be written as
$(2K\ \ C)\ D + (2K\ \ C)\ (2\overline{K}\ \ D)D + (2K\ \ C)\ (2\overline{K}\ \ D)\ D + ...$
$= D(2K\ \ C)\ /(1 - 2K\ \ C2\overline{K}\ \ D)$. Hence, we can write c^0 as

$$c^0 = c + \frac{2\overline{K}\ \ D(2K\ \ C)}{1 - (2K\ \ C)(2\overline{K}\ \ D)}. \tag{S1-1}$$

Replacing $2K\ \ C$ by c from Eq. (8) and $2\overline{K}\ \ D$ by d (Eqs. (4) and (6)), the above equation can be re-written as

$$c^0 = c + \frac{dc}{1 - c\ d} = \frac{c}{1 - cd}. \tag{S1-2}$$

In terms of c^0, we define

$$q^0 = \frac{-\delta^0 w}{1 - 2\delta^0 w}, \tag{S1-3}$$

where

$$\delta^0 = \frac{\alpha c^0}{(1+\beta+\ )}, \tag{S1-4}$$

and

$$w = (1+\beta+\ )\ . \tag{S1-5}$$

Following the procedure in Goldstein et al. [2], it can be shown that the second term on the RHS of Eq. (14) can be written as

$$q\ \ = 4q\ \ \mathsf{X}^{1}\ \ \frac{(1/2)...(1/2-m)}{(m+1)}(-4q\ \ )\ \ \frac{\gamma}{(m+2)}, \tag{S1-6}$$

where

$$\gamma = \frac{1}{(3w/2)}. \tag{S1-7}$$

By virtue of its definition, the term q^0 represents the dimensionless partition function for all linear chains composed of bivalent and trivalent LAT molecules in which the terminal LAT molecules are trivalent. Replacing q by q^0 in Eq. (S1-6) will account for all LAT aggregates with only trivalent LAT molecules in the terminal positions. We observe that we can include the concentrations of LAT aggregates, which have

$$q_{uv}^{(ii)} = \left[4(2KK_xDX_T)^2 S_U^2 S_V\right] / \left[1-(2KK_xDX_T)^2(4S_US_V)\right], \tag{S3-16}$$

and

$$q_{uv}^{(iii)} = \left[4(2KK_xDX_T)^2 S_U S_V^2\right] / \left[1-(2KK_xDX_T)^2(4S_US_V)\right]. \tag{S3-17}$$

In order to obtain the total partition function for all linear chains in which receptors are cross-linked by both bivalent and trivalent ligands, we should consider the set of elements of the U sequence, connected only by bivalent ligands. Such elements comprise the set $\{UU, UUU, UUUU, ...\}$ and the sum of the concentrations of the elements of this sequence is denoted by S_U. Moreover, we have to incorporate elements of this sequence into the chains in each of sets (i)-(iii). It can be shown that on incorporating the elements of this set into the sets (i), (ii) and (iii), the corresponding partition functions $q_{uv}^{(i)}$, $q_{uv}^{(ii)}$ and $q_{uv}^{(ii)}$ are modified to yield

$$q_{uv}^{(i)} = [4(2KK_xDX_T)(S_U+S_{UU})S_V] / \left[1-(2KK_xDX_T)^2\{4(S_U+S_{UU})S_V\}\right], \tag{S3-18}$$

$$q_{uv}^{(ii)} = \left[4(2KK_xDX_T)^2(S_U+S_{UU})^2 S_V\right] / \left[1-(2KK_xDX_T)^2\{4(S_U+S_{UU})S_V\}\right], \tag{S3-19}$$

and

$$q_{uv}^{(iii)} = \left[4(2KK_xDX_T)^2(S_U+S_{UU})S_V^2\right] / \left[1-(2KK_xDX_T)^2\{4(S_U+S_{UU})S_V\}\right]. \tag{S3-20}$$

Then, we can express the partition function of all chains (including the free receptor), which have a free receptor site at either end as

$$q_f = S_U + S_{UU} + S_V + q_{uv}^{(i)} + q_{uv}^{(ii)} + q_{uv}^{(iii)}, \tag{S3-21}$$

which reduces to

$$\begin{aligned} q_f &= (S_U + S_{UU} + S_V) \\ &+ [4(2KK_xDX_T)(S_U+S_{UU})S_V(1+(2KK_xDX_T)(S_U+S_{UU}) \\ &+ (2KK_xDX_T)S_V)]/[1-(2KK_xDX_T)^2\{4(S_U+S_{UU})S_V\}]. \end{aligned} \tag{S3-22}$$

Now S_U is the same as $q_f^{(a)}$ in Eq. (S3-12) and S_V is the same as $q_f^{(3)}$ in Eq. (S3-13). We can obtain an expression for S_{UU} in the following fashion. Let us consider the sequence of all linear chains which have a free receptor site at either end, cross-linked only by bivalent ligands and containing at least two receptors. The sum of concentrations of the elements in this sequence is given by

$$S_V - x = \alpha\Delta x^2/(1-\alpha\Delta x). \tag{S3-23}$$

In order to obtain an expression for S_{UU}, we should replace the reduced receptor concentration x by in the above equation by the dimensionless sum of concentrations of all linear chains comprising of receptors cross-linked only by trivalent receptors. This latter sum is thus the same as S_U. Thus,

$$S_{UU} = \alpha\Delta(\alpha\chi x^2/(1-\alpha\chi x))^2/(1-\alpha\Delta(\alpha\chi x^2/(1-\alpha\chi x))), \tag{S3-24}$$

so that,

$$\begin{aligned} S_U + S_{UU} &= \alpha\chi x^2/(1-\alpha\chi x) \\ &+ \alpha\Delta(\alpha\chi x^2/(1-\alpha\chi x))^2/(1-\alpha\Delta(\alpha\chi x^2/(1-\alpha\chi x))) \\ &= \alpha\chi x^2/(1-\alpha\chi x-\alpha^2\chi\Delta x^2). \end{aligned} \tag{S3-25}$$

In terms of $(S_U + S_{UU})$ and S_V, q_f can be re-written as

$$q_f = [(S_U + S_{UU}) + S_V + 2\alpha\Delta(S_U + S_{UU})S_V]/(1 - (\alpha\Delta)^2(S_U + S_{UU})S_V). \tag{S3-26}$$

Substituting the values of $(S_U + S_{UU})$ from Eq. (S3-25), and S_V (which is the same as $q_f^{(3)}$) from Eq. (S3-13) into the above equation, we get

$$q_f = x/(1 - \alpha\chi x - \alpha\Delta x) = (\frac{x}{1 - \alpha\Delta x})/(1 - \frac{\alpha\chi x}{1 - \alpha\Delta x}), \tag{S3-27}$$

which is the same as Eq. (S3-14).

The factor $(1 + \chi)^2$ on the RHS of $q_0 = q_f(1 + \chi)^2$ in Goldstein et al. [1] has to be replaced by $(1 + \chi + 2\Delta + \mu)^2$ to account for the bivalent and monovalent ligands which can occupy the end positions of the chains. Hence, the dimensionless partition function for all linear chains (including the free receptor) is given by

$$q_0 = \left[(\frac{x}{1 - \alpha\Delta x})/(1 - \frac{\alpha\chi x}{1 - \alpha\Delta x})\right](1 + \chi + 2\Delta + \mu)^2. \tag{S3-28}$$

Since it is the ligand and not the receptor that has variable valency, Eq. (S3-1) holds for the q_0 in Eq. (S3-28).

References

1. Goldstein B, Perelson AS (1984) Equilibrium theory for the clustering of bivalent cell surface receptors by trivalent ligands: Application to histamine release from basophils. Biophys J 45: 1109-1123.