Supporting information for [Kinetics of a Multilamellar Lipid Vesicle Ripening: Simulation and Theory]

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I The detailed kinetics equations for the aging of lipid multilamellar vesicles.

To simplify the equations, the flip-flop between the hemileaflets of the vesicle bilayer is ignored. And the number of two single layers consisting of a bilayer are assumed to be equal, i.e., $N_{i,out} = N_{i,in} = 0.5 N_i^{||}$ (*i*=1, 2,…, *n*-1, *n*). The number of molecules changes in every layer regarding as a component with a specific radius. We set $4\pi r^2 = N^{||} a/2$, where *r* is the mean radius of one of vesicles in MLV, $N^{||}$ is the number of lipids in the vesicle bilayer, and a is the area per lipid in the bilayer film. Therefore the radius *r* is equal to $\sqrt{\frac{a}{8\pi} N^{||}}$. Introducing the letter Λ, which is equal to $\frac{4}{3}\pi \left(\frac{a}{8\pi}\right)^{\frac{3}{2}}$, the volume $\frac{4}{3}\pi r^3$ can be described as $\Lambda \left(N^{||}\right)^{\frac{3}{2}}$. Therefore, the kinetic function of each bilayer can be combined and simplified. The detailed model can be written as follows:

$$\frac{dN_i^{||}}{dt} = 0.5\left(\frac{1}{\Lambda} k_{i,out}^{on} \left(\frac{N_{i-1}^{aq}}{A - \left(N_i^{||}\right)^{\frac{3}{2}}}\right) - k_{i,out}^{off} + \frac{1}{\Lambda} k_{i,in}^{on} \left(\frac{N_i^{aq}}{\left(N_i^{||}\right)^{\frac{3}{2}} - B}\right) - k_{i,in}^{off}\right) N_i^{||}$$

$$\text{when} \begin{cases} i = 1,\ A = V' \text{ and } B = \left(N_{i+1}^{\|}\right)^{\frac{3}{2}} \\ i = n,\ A = \left(N_{i-1}^{\|}\right)^{\frac{3}{2}} \text{ and } B = 0 \\ i = others,\ A = \left(N_{i1}^{\|}\right)^{\frac{3}{2}} \text{ and } B = \left(N_{i+1}^{\|}\right)^{\frac{3}{2}} \end{cases}, \tag{s1}$$

$$\frac{dN_i^{aq}}{dt} = 0.5\left(k_{i,in}^{off} - \frac{1}{\Lambda}k_{i,in}^{on}\left(\frac{N_i^{aq}}{\left(N_i^{\|}\right)^{\frac{3}{2}} - B}\right)\right)N_i^{\|} + 0.5\left(k_{i+1,out}^{off} - \frac{1}{\Lambda}k_{i+1,out}^{on}\left(\frac{N_i^{aq}}{A - \left(N_{i+1}^{\|}\right)^{\frac{3}{2}}}\right)\right)N_{i+1}^{\|}$$

$$\text{When} \begin{cases} i = 0,\ N_i^{\|} = 0,\ A = V' \\ i = n,\ N_{i+1}^{\|} = 0,\ B = 0 \\ i = others,\ A = \left(N_i^{\|}\right)^{\frac{3}{2}} \text{ and } B = \left(N_{i+1}^{\|}\right)^{\frac{3}{2}} \end{cases}, \tag{s2}$$

Based on Arrhenius equation, the rate constant of dissociation of the lipids can be written as Eq. (s3).

$$\begin{aligned} k &= A^{off} \exp\left[-\frac{\Delta E_0 - \alpha_{in/out} \exp\left[-\frac{\left(c - x_c\right)^2}{2w^2} \right]}{RT} \right] \\ &= A^{off} \exp\left[-\frac{\Delta E_0}{RT} \right] \exp\left[\frac{\alpha_{in/out}}{RT} \exp\left[-\frac{\left(N^{\|-0.5} - \sqrt{\frac{a_h}{8\pi}} x_c \right)^2}{2w^2 \frac{a_h}{8\pi}} \right] \right] \end{aligned} \tag{s3}$$

Here, α is the coefficient to distinguish the inner and outer layer of the bilayer, c is the curvature of the vesicle, and ΔE_0 is a constant. a is 0.65 nm^2, the universal gas constant R is 8.314 J/mol•K and the temperature T is 315 K. Bringing the rate constants into Eq. (s1) and (s2), the rate equations can be obtained.

Ⅱ The detailed kinetics equations for the aging of two ULVs with different size.

For the two ULVs, the thickness of bilayer is ignored and the numbers of lipids in the inner and outer hemileaflets of a bilayer are equal. Based on the kinetics model of MLV ripening, the kinetics equations of aging of two ULVs with different size can be described as follow:

$$\frac{dN_1^{ll}}{dt}=\frac{1}{2}\left(k_{1,out}^{on}\frac{N_0^{aq}}{V_0^{aq}}+k_{1,in}^{on}\frac{N_1^{aq}}{V_1^{aq}}-k_{1,out}^{off}-k_{1,in}^{off}\right)N_1^{ll}, \tag{s4}$$

$$\frac{dN_2^{ll}}{dt}=\frac{1}{2}\left(k_{2,out}^{on}\frac{N_0^{aq}}{V_0^{aq}}+k_{2,in}^{on}\frac{N_2^{aq}}{V_2^{aq}}-k_{2,out}^{off}-k_{2,in}^{off}\right)N_2^{ll}, \tag{s5}$$

$$\frac{dN_0^{aq}}{dt}=\frac{1}{2}\left(k_{1,out}^{off}-k_{1,out}^{on}\frac{N_0^{aq}}{V_0^{aq}}\right)N_1^{ll}+\frac{1}{2}\left(k_{2,out}^{off}-k_{2,out}^{on}\frac{N_0^{aq}}{V_0^{aq}}\right)N_2^{ll}, \tag{s6}$$

$$\frac{dN_1^{aq}}{dt}=\frac{1}{2}\left(k_{1,in}^{off}-k_{1,in}^{on}\frac{N_1^{aq}}{V_1^{aq}}\right)N_1^{ll}, \tag{s7}$$

$$\frac{dN_2^{aq}}{dt}=\frac{1}{2}\left(k_{2,in}^{off}-k_{2,in}^{on}\frac{N_2^{aq}}{V_2^{aq}}\right)N_2^{ll}, \tag{s8}$$

where N_i^{ll} is the number of lipids in the *i*th bilayer. V_0^{aq} is the volume of aqueous phase outside the two ULVs and its value is equal to the volume of simulation box minus that of two ULVs ($V_0^{aq}=V-4\pi r_1^3/3-4\pi r_2^3/3$ where *V* is the simulated space and r_i is the mean radius of the *i*th vesicle). V_i^{aq} is the volume of aqueous phase in the *i*th ULV ($V_i^{aq}=4\pi r_i^3/3$). N_0^{aq} are the number of free lipids outside the two ULVs. N_i^{aq} is number of free lipids inside the *i*th ULV. $k_{i,out}^{off}$ is the dissociation rate constant of lipids from the outer layer to the aqueous solution, and $k_{i,out}^{on}$ is the binding rate constant of free lipids from the solution to the outer layer.