Birthing of a daughter vesicle in a model system for self-reproduction vesicles

Petch Khunpetch\textsuperscript{a}, Yuka Sakuma, Masayuki Imai, and Toshihiro Kawakatsu

Department of Physics, Tohoku University, Aoba, Aramaki, Aoba-ku, Sendai 980-8578, Japan

Received: date / Revised version: date

Abstract. Sakuma and Imai [Phys. Rev. Lett. 107, 198101 (2011)] established a temperature-controlled cyclic process for a model system of self-reproducing vesicles without feeding. The vesicle generates a smaller inclusion vesicle called “daughter vesicle” inside the original vesicle (we call this “mother vesicle”) and then the daughter vesicle is expelled through a small pore on the mother vesicle. This self-reproducing process is called birthing. In the present study we present theoretical model on the birthing process of a single, rigid daughter vesicle through a pore. By using a simple geometric picture, we derive the free energy constituting the material properties of the bending, stretching and line tension moduli of the mother vesicle, as a function of the distance between the centers of the daughter and mother vesicles, and the size of the daughter vesicle. We see clearly the disappearance of the energy barrier by selecting appropriate moduli. The dynamics of the system is studied by employing the Onsager principle. The results indicate that translocation time decreases as the friction parameter decreases, or the initial size of the daughter vesicle decreases.

PACS. PACS-key discribing text of that key – PACS-key discribing text of that key

1 Introduction

Vesicles assembled from the amphiphilic molecules are considered as the important step in the transition pathway from molecular assembly to cellular life \cite{1}. A vesicle can be regarded as a container for a virtual cell called a protocell which is composed of three fundamental components \textit{i.e.} a metabolism, genes, and a container \cite{2–4}. Developing self-reproducing vesicles coupled with the metabolic system is a step forward to protocell \cite{5,6}. Previous successful studies in developing model systems for self-reproducing vesicles \cite{7–10} have shown that the molecules of membrane precursor turn to assemble an inclusion vesicle called daughter vesicle inside the mother vesicle with the help of catalyst. When the daughter vesicle grows to certain size, the daughter vesicle is then expelled through the small pore on the mother vesicle in the process called “birthing”.

Sakuma and Imai developed a model system for self-reproduction of giant unilamellar vesicle (GUV) without adding molecules \cite{11}. In their system, the vesicle with a composition of inverse-cone-shaped lipid having a small head group and bulky tails \cite{1, 2-dilauroyl-sn-glycero-3-phosphoethanolamine (DLPE)}/cylinder-shaped lipids \cite{1, 2-dipalmitoyl-sn-glycero-3-phosphocholine (DPPC)}=3/7 has a spherical shape at 35°C. DPPC and DLPE have melting temperatures $T_{m}^{\text{DPPC}}$= 41°C and $T_{m}^{\text{DLPE}}$= 29°C, respectively. By increasing temperature from 35°C to 42°C, above $T_{m}^{\text{DPPC}}$, surface area of vesicle increases, and the GUV deforms to a stomatocyte shape. The stomatocyte vesicle then forms an inclusion vesicle inside it by plucking off the invagination neck. When the temperature is decreased to 35°C, the surface area of the mother vesicle decreases. This causes an increase in the surface tension of the mother vesicle. To release this tension, the mother vesicle produces a pore and, then, the daughter vesicle is expelled through the pore. Driven by the line tension around the pore, the mother GUV recovers a spherical shape by closing the pore after the birthing. The observed pathway and the schematic diagram for birthing process in self-reproducing vesicles are shown in fig. 1.

A coarse-grained description can give a reasonable parameterization of the complexity of specific chemical compounds that constitute the vesicles in terms of mechanical characteristics such as bending and stretching moduli. This approach is successful in the study of, for example, the problem of encapsulation of a rigid spherical particle by a vesicle \cite{12,13}, and translocation of a vesicle through a narrow pore \cite{14,15}. In the present study, we propose a theoretical model on the birthing process of a single, rigid daughter vesicle through a pore on the mother GUV. By using a simple geometric picture, we first derive the free energy within the framework of the Helfrich theory constituting the material properties of the mother vesicle, \textit{i.e.}, bending, stretching and line tension moduli, as a function of the distance between centers of the daughter vesicle.
and mother vesicles, and the size of the daughter vesicle. For studies of a closed vesicle, the contribution from the Gaussian curvature in the Helfrich free energy is just a constant and can then be omitted from the theory. However, when a pore is presented, the Gaussian curvature term cannot be neglected. We have evaluated the integral of the Gaussian curvature explicitly by using differential geometry of curved surface for the non-preserved topology of the mother vesicle. The theoretical study of pored vesicle is scarce. The stability of a budding pore with the meta-stable state is probably hard to observe experimentally by Yao et al. [16]. The pored membrane is modelled as a spherical cap combined with a catenoid, where the boundary of a pore is located on the waist of the catenoid. The budding pore which has a meta-stable state is found as a spherical cap combined with a catenoid, where the boundary of a pore is located on the waist of the catenoid. The budding pore which has a meta-stable state is probably hard to observe experimentally because the energy barrier is very shallow and the range of the values of the line tension energy is very narrow. Experimental evidence that shows a pored vesicle is studied by Karatekin et al. [17]. By using visible light to increase the membrane tension, the vesicle is stretched until the membrane responds by opening a pore. The size of the pores are several microns but only a single pore can be observed at a time. As the inner liquid leaks out, the pores are transient which are driven to close by the line tension within a few seconds. Other experiment that shows the transient pores in GUVs has done by Ro-
vesicle with radius $R$ is modeled by a simple geometric ansatz as illustrated in fig. 2. We neglect the thickness of the membrane of the mother vesicle. The distance between the center of the mother vesicle ($C_{M}$) and that of the daughter vesicle ($C_{d}$) is denoted by $z_{d}$. During the birthing process, the pore on the surface of the mother vesicle gradually expands and then shrinks due to the line tension energy. We have assumed that the pore has a circular shape with radius $a$ where its center is located on the straight line connecting the centers of the mother and daughter vesicles. We introduce the angle $\theta$ defined by the line joining the centers of the mother and daughter vesicles, and the line between the center of the mother vesicle and the edge of the hole (see fig. 2). We assume that during the birthing process there is no liquid leaks out from the mother vesicle and that the daughter vesicle moves very slowly. The volume between the mother and daughter vesicles, which is conserved during the birthing process, is the only one independent variable that describes the system. Since, the amount of the liquid in the volume between the two vesicles is preserved, it leads to another constraint as

$$\Delta V = \left\{ \frac{4}{3} \pi R^3 - \pi b^2 [(R \cos \theta - z_{d}) + b] ight. \left. + \frac{\pi}{3} [(R \cos \theta - z_{d})^3 + b^3] \right. \\
- \pi R^3 (1 - \cos \theta) + \frac{\pi R^3}{3} (1 - \cos^3 \theta) \right\} \\
- \left\{ \frac{4}{3} \pi R_0^3 - \pi b^2 [(R_0 \cos \theta_0 - z_{d,0}) + b] \\
+ \frac{\pi}{3} [(R_0 \cos \theta_0 - z_{d,0})^3 + b^3] \\
- \pi R_0^3 (1 - \cos \theta_0) + \frac{\pi R_0^3}{3} (1 - \cos^3 \theta_0) \right\} \\
= 0,$$

where the first and the second parentheses account for the present and the initial volume of the liquid.

2.2 The free energy

We have assumed that, at equilibrium, the mother vesicle has a spherical shape. The total free energy of the system is given by

$$F = \frac{\kappa}{2} \int (2H - c_0)^2 dA + \kappa_G K dA + \frac{\lambda}{2} \left( \frac{A - A_{eq}}{A_{eq}} \right)^2 + \sigma \int dl.$$  

The first two terms on the right hand side of eq. (4) are the bending energy which is harmonic in the mean curvature $H$, where $H$ is defined by $H \equiv (1/R_1 + 1/R_2)/2$ ($R_1$ and $R_2$ stand for the radii of principal curvatures,) and $c_0$ is the spontaneous curvature, which is zero when there is no asymmetry between the inner and outer leaflets of the bilayer. Since the mother vesicle does not preserve its topology, the Gaussian curvature, $K \equiv 1/(R_1 R_2)$, needs to be taken into account. $\kappa$ and $\kappa_G$ are the local bending and the Gaussian bending rigidity, respectively. Typically, the bending modulus $\kappa$ is of the order of $10 k_BT$ for fluid membranes and the experimental techniques to measure this bending modulus and its reported values are given in
Helfrich free energy is given by
\[ F_b = \kappa \left( 1 + \cos \theta \right) \left( \frac{2}{R} - \kappa_0 \right)^2 + 2\pi \kappa_0 \left( 1 + \cos \theta \right) \left( \frac{2}{R} - \kappa_0 \right)^2 + \frac{2\kappa_0}{\kappa} \],
(9)
where the mean curvature \( H \) and the Gaussian curvature \( K \) for the sphere with radius \( R \) are \( 1/R \) and \( 1/R^2 \), respectively and the spontaneous curvature is \( \kappa_0 \). Using eq. (2), we can eliminate \( \cos \theta \). Then, we obtain the Helfrich free energy in terms of the parameters \( R, z_d, \) and \( b \) as
\[ F_b = \pi \kappa \left( 1 + \frac{R^2 + z_d^2 - b^2}{2z_d R} \right) \left( \frac{2}{R} - \kappa_0 \right)^2 + \frac{2\kappa_0}{\kappa} \). \]
(10)

In order to obtain the stretching contribution, we must calculate the surface area of the mother vesicle subtracted by the area of the circular pore which is already given by eq. (8). Then, the stretching energy can be written as
\[ F_s = \frac{\lambda}{2} \frac{(\Delta A)^2}{A_{eq}} \]
where \( \lambda = \frac{\pi \lambda}{2R_{eq}^2} \) is of the order of \( 10^4 \pi k_B T/\mu \text{m}^2 \). Here we should note that \( R \) is not independent of \( z_d \). As we have assumed that during the birthing process the volume
of the region between the mother and the daughter vesicles shown in the shaded region in fig. 2 is preserved. Then, $R$ can be determined by the volume constraint eq. (3) together with geometric constraint eq. (2). Finally, the free energy eq. (15) is a function of $z_d$ and $b$ only.

2.3 The energy dissipation function

When the daughter vesicle is moving through the pore, the energy dissipation is caused mostly at the pore. In the limit of small Reynolds number, the dissipation function for the daughter vesicle is given by

$$\Phi = \frac{1}{2} \zeta z_d^2,$$  

(16)

where $\zeta$ is the friction coefficient. Generally, the friction coefficient is a function of the slow variables and it can be derived from the Stokesian hydrodynamics. In this work, for simplicity, we assume that the friction coefficient is a constant which is proportional to the radius of the pore $a$. As we assume that the daughter vesicle is a rigid body, there is no liquid flow inside of the daughter vesicle. Thus, the friction is generated at the perimeter of the pore only and can be written as

$$\zeta = 2 \pi \alpha a = 2 \pi \alpha R \sin \theta,$$  

(17)

where $\alpha$ is related to the dynamic viscosity and has the unit of kg m$^{-1}$ s$^{-1}$. The estimated order of magnitude of $\alpha$ for $b = 10 \mu m$, the translocation time of the daughter vesicle $t_{\text{trans}} \approx 1.0 s$, and $\lambda = 1.0 \times 10^6 k_B T / \mu m^2$, is around $10^4$ kg m$^{-1}$ s$^{-1}$ (see Appendix A.). Please note that the dynamic viscosity of water is around $8.90 \times 10^{-4}$ kg m$^{-1}$ s$^{-1}$ at $25^\circ C$ [37], while, in our assumption, there is no water layer between the daughter vesicle and the perimeter of the mother vesicle’s pore.

2.4 The equation of motion

The Rayleighian of the system is given by

$$\mathcal{R} = \Phi + \dot{\Phi} = \frac{1}{2} \zeta z_d^2 + \frac{dF(z_d)}{dt} = \frac{1}{2} \zeta z_d^2 + \frac{dF}{dz_d} \dot{z}_d.$$  

(18)

By minimizing $\mathcal{R}$ with respect to $\dot{z}_d$, i.e., $\partial \mathcal{R} / \partial \dot{z}_d = 0$, we obtain the equation of motion for the daughter vesicle

$$\dot{z}_d = -\frac{1}{\zeta} \frac{dF}{dz_d}.$$  

(19)

Fig. 3. The change in the free energy landscapes when the bending modulus $\kappa$ changes. The stretching and line tension moduli are fixed at $\lambda = 1.0 \times 10^6 k_B T / \mu m^2$ and $\sigma = 0.7 \times 10^6 k_B T / \mu m$, respectively. The $\kappa/\kappa_G$ ratio is $-1$. The size of the daughter vesicle is $b = 10 \mu m$, while the equilibrium size of the mother vesicle is $R_{eq} = 38 \mu m$. The initial size of the mother vesicle is $R_0 = 40 \mu m$. The spontaneous curvature $c_0$ is set as zero. The plots are shown for the entire landscapes (a) and at very small scale (b).

3 Results and discussions

We present our results by first discussing the explicit free energy landscapes when the bending, stretching, and line tension moduli are changed, while the daughter vesicle size is constant. Later, the kinetics of birthing will be discussed when the friction coefficient is changed or the size of the daughter vesicle is varied.

3.1 Free energy landscapes

Representative results of the free energy landscapes over $z_d$ when the bending, stretching, and line tension moduli change are shown in figs. 3, 4, and 5.

All plots in figs. 3, 4, and 5 are evaluated when the size of the daughter vesicle is fixed at $b = 10 \mu m$, while the equilibrium size of the mother vesicle is taken to be $R_{eq} = 38 \mu m$. The initial size of the mother vesicle is $R_0 = 40 \mu m$. The initial size means the state that the daughter vesicle is discharged from the mother vesicle completely, the pore has already been opened. When the daughter vesicle is slightly expelled from the mother vesicle, where the pore has already been opened, the daughter vesicle is discharged from the mother vesicle completely, the pore shrinks and eventually closes, and the mother vesicle recovers its spherical shape.
Please give a shorter version with: \authorrunning and \titlerunning prior to \maketitle

Fig. 4. The free energy landscapes with the variation of the stretching modulus $\lambda$. The bending and line tension moduli are fixed at $\kappa = 20k_BT$, $\kappa_G = -20k_BT$, and $\sigma = 0.7 \times 10^8 k_BT/\mu m$, respectively. The equilibrium size of the mother vesicle is $R_{eq} = 38 \mu m$. The initial size of the mother vesicle is $R_0 = 40 \mu m$. The size of the daughter vesicle is $b = 10 \mu m$. The initial distance that separates the mother and the daughter is $z_{d,0} = 32 \mu m$. The spontaneous curvature $c_0 = 0$.

Figure 4(a) shows that all curves for each fixed value of $\kappa$ almost coincide, where the stretching and line tension moduli are fixed at $\lambda = 1.0 \times 10^8 k_BT/\mu m^2$ and $\sigma = 0.7 \times 10^8 k_BT/\mu m$, respectively, and $\kappa/\kappa_G = -1$. Increasing of the free energy when the bending modulus $\kappa$ increases can be seen in fig. 4(b) at very small scale. All graphs show that there is no energy barrier and the daughter vesicle succeeds in the birthing process at $z_d < 50 \mu m$. As the initial size of the mother vesicle is $40 \mu m$ and the size of the daughter vesicle is $10 \mu m$, we have set up the initial distance that separates the mother and the daughter as $z_{d,0} = 32 \mu m$ and we found that the final value of $z_d$ is less than $50 \mu m$. This means that, at the equilibrium final state, the mother vesicle reduces its size due to the stretching energy. From the result, it seems that changes in bending modulus does not affect the free energy landscapes significantly. Theoretical study done by Brochard-Wyart et al. \[58\] and experimental works of Karatekin et al. \[17\] and Rodriguez et al. \[18\] for pored vesicles have suggested that the transient pores observed in stretched vesicles are driven by the competition between the surface tension and the line tension that our results would confirm their studies as we will show in the following.

In contrast to changes in the bending modulus, as we discussed above, figs. 4(a) and (b) show the effect of varying the stretching modulus $\lambda$ on the free energy landscapes. In this figure, the bending and line tension moduli are fixed at $\kappa = 20k_BT$, $\kappa_G = -20k_BT$, and $\sigma = 0.7 \times 10^8 k_BT/\mu m$, respectively. In the range of $z_d$ where the tangent to the plot of $F/bT$ has a positive slope, the system shows the energy barrier. Increasing $\lambda$ will reduce the height of the barrier where the maximum point moves more and more closer to $z_{d,0}$ (fig. 4(a)). The barrier disappears and the whole range of $z_d$ has a negative slope which means the daughter vesicle is discharged completely at $\lambda = 1.0 \times 10^8 k_BT/\mu m^2$. However, increasing $\lambda$ further, the system shows the metastable state where the daughter vesicle is trapped in its vicinity as we can see in the curve of $\lambda = 1.6 \times 10^8 k_BT/\mu m^2$ (fig. 4(b)).

The free energy landscapes when the line tension modulus $\sigma$ changes are shown in figs. 5(a) and (b). The bending and stretching moduli are fixed at $\kappa = 20k_BT$, $\kappa_G = -20k_BT$, and $\lambda = 1.0 \times 10^8 k_BT/\mu m^2$, respectively. We see clearly the decreasing in the energy barrier when $\sigma$ decreases. The daughter vesicle has succeeded in the birthing at $\sigma = 0.7 \times 10^8 k_BT/\mu m$ when the energy barrier disappears (fig. 5(a)). Further reducing $\sigma$, the plot of $F/bT$ has a stagnant point at $z_d = 45.95 \mu m$ on the curve of $\sigma = 0.51 \times 10^8 k_BT/\mu m$ and has a negative slope everywhere else. Continuously reducing $\sigma$, the plot of the free energy has a dip where the bottom of the dip corresponding to the metastable state is at $z_d = 43.29 \mu m$, as seen clearly in the curve of $\sigma = 0.40 \times 10^8 k_BT/\mu m$ (fig. 5(b)).
Further investigating the metastable states as seen in figs. 4(b) and 5(b) suggests that their origin is from the competition between the stretching energy and the line tension energy. The metastable state refers the state of the system other than the state with the least energy, where the daughter vesicle is trapped in the basin of this state. The stretching free energy penalty which is assumed to be the quadratic form in the change of the mother vesicle’s surface area can be found to be minimized when the surface area of the mother vesicle subtracted by the area of the pore is minimum. While the line tension energy that attempts to decrease the edge length of the pore reaches the maximum value where the pore size opens maximally, by definition, and the daughter vesicle passes through the pore almost half of its volume. As we have already seen that, in our model, the bending energy did not play a significant role, the competition between the two energies gives rise the metastable state.

Experimentally, it is rather difficult to directly measure the line tension modulus $\sigma$ of the membrane due to the instability of a pore. The reported value is rare. Our simulations suggest that $\sigma$ is to be of around the order of $10^8$ $k_BT/\mu m$ for the successful birthing process with $\kappa, \kappa_G, \lambda$ and $\alpha$ are from the references as given above. While, the reported value of $\sigma$ is found to be $10^3 - 10^4$ $k_BT/\mu m$ for DOPC vesicle [17] which is inconsistent with our finding value. The value of the obtained line tension $\sigma$ in our model seems to be determined by the balance between the stretching energy and the line tension energy only where the bending energy did not play a role. Somehow, our results support the study of pore dynamics by Brochard-Wyart et al. [38] in which the kinetic of a pore is driven by the two forces. Nevertheless, let us make some notes.

1) In their consideration, the Gaussian rigidity $\kappa_G$ did not appear, but we are. And the authors have assumed that the pore is much smaller than the whole vesicle which seems to be inconsistent with experimental observations.

2) The leak-out of the internal liquid has been considered in their model, while we did not investigate it. Experimental observations by Karatekin et al. [17] and Rodriguez et al. [18] have been shown the leakage of the liquid through the pore during the open-closed states of the pore. This is presumably the origin of our discrepancy.

### 3.2 Kinetics of birthing

The free energy landscapes when $\kappa = 20$ $k_BT$, $\kappa_G = -20$ $k_BT$, $\lambda = 1.0 \times 10^8$ $k_BT/\mu m^2$, and $\sigma = 0.7 \times 10^8$ $k_BT/\mu m$ are used to verify the kinetic of the birthing process at $T = 35^\circ C$. By solving eq. (19) numerically, we obtain the trajectory of the daughter vesicle when the dynamic viscosity $\alpha$ is changed as shown in fig. 6. As the friction coefficient $\zeta$ decreases (by decreasing $\alpha$), the result shows clearly that the daughter vesicle has succeeded in the birthing with less translocation time. The daughter vesicle spends less distance to detach itself from the mother when its velocity increases as well. In fig. 6, we have selected the values for $\alpha$ ranging from $1.0 \times 10^3$ kg·(ms)$^{-1}$ to $1.0 \times 10^4$ kg·(ms)$^{-1}$. While, in our estimation, $\alpha$ is around $2.1 \times 10^3$ kg·(ms)$^{-1}$ for the same values of $\lambda$ and $b$ (see Appendix A.). Figure 7 shows that $\alpha = 1.0 \times 10^3$ kg·(ms)$^{-1}$ yields the translocation time around 1.8 s which is close to the translocation time 19 used in our estimation for $\alpha$. Note that our estimated $\alpha$ is directly obtained by knowing only the stretching modulus $\lambda$ with there is no information about $\kappa, \kappa_G,$ and $\sigma$ included.

At $R_{eq} = 38 \mu m$ and $R_0 = 40 \mu m$, fig. 7 shows the trajectory of the daughter vesicle with different size $b$, when $\kappa/\kappa_G = -1$, $\lambda = 1.0 \times 10^8$ $k_BT/\mu m^2$, and $\sigma = 0.7 \times 10^8$ $k_BT/\mu m$ are kept constant. The dynamic viscosity is fixed at $\alpha = 5.0 \times 10^3$ kg·(ms)$^{-1}$ and $T = 35^\circ C$. The result indicates that, for the bigger daughter vesicle, the mother vesicle has more potential energy and, consequently, the mother tries to release the energy by expelling the daughter vesicle with a higher velocity than that of the smaller daughter vesicle in the initial stage. However, in the intermediate stage, the velocity is reduced due to the barrier from the line tension energy. The velocity of the daughter vesicle is growing up again due to the decrease of line energy and, finally, the daughter vesicle is expelled completely from the mother vesicle. Also, the result shows that the smaller daughter takes less translocation time as expected.

### 4 Conclusions

In this work, we have proposed a simple geometric ansatz to study the birthing of the daughter vesicle in the model.
Please give a shorter version with: \authorrunning and \titlerunning prior to \maketitle

The effect of barrier from the line tension energy in the later time. In our model, the specific details regarding the chemical properties of the vesicle are parametrized in terms of the material parameters such as bending, stretching, and line tension moduli for the purpose of investigating the large scale properties of the birthing process. The model suggests that the line tension modulus is of the order of ca. $10^4 k_B T / \mu m$ for the successful birthing process, where we keep the bending and stretching moduli in accordance with the experimental reports. While, Karatekin et al. reports that the value of the line tension is of the order of ca. $10^3 - 10^4 k_B T / \mu m$ for single component membrane composed of cylinder-shaped lipid molecules (DOPC vesicle). Nevertheless, we would argue that our model is just a simple and first theoretical model to study the escape of a vesicle from a pore. In order to eliminate the discrepancy, we might need to consider the leakage of the liquid through the pore during the birthing process as observed by Karatekin et al. and Rodriguez et al. We will leave the improvement for our next work. However, in this work, we believe that our simple and handleable model captures the characteristic features of the birthing mechanism insightfully and it is a good starting point to study the vesicle discharged from the pore.

This work is supported by PCoMS-IPD program at Tohoku University and the Grant-in-Aid for Scientific Research (Grant Number 26287096 and 16K13844) from The Ministry of Education, Culture, Sports, Science and Technology (MEXT), Japan.

5 Authors contributions

TK initiated this collaboration of the authors. PK performed research and calculations under the guidance of TK, and wrote the manuscript. YS and MI provided the experimental data. All the authors were involved in the preparation of the manuscript. All the authors have read and approved the final manuscript.

Appendix A. Estimation of the dynamic viscosity $\alpha$

In order to estimate the order of magnitude of $\alpha$, we have modelled the birthing of the daughter vesicle passing through the pore of radius $a$ by using a rigid sphere flowing through a tube with a diameter $2b$ as shown in fig. 8.

The pressure force acting on the sphere is

$$F = PA,$$

where $P$ is the pressure difference between the lower and upper regions of the tube, and $A = \pi b^2$ is a crosssection area of the tube. Assuming the friction coefficient $\xi$ at the

\begin{figure}[h]
\centering
\includegraphics[width=0.5\textwidth]{fig7}
\caption{The trajectory of the daughter vesicle with different size $b$. The bending, stretching, and line tension moduli are fixed at $\kappa/\kappa_G = -1$, $\lambda = 1.0 \times 10^4 k_B T / \mu m^2$, and $\sigma = 0.7 \times 10^4 k_B T / \mu m$, respectively. The dynamic viscosity $\alpha$ is fixed at $5.0 \times 10^4 \text{kg} \cdot (\text{ms})^{-1}$. The result is evaluated at $T = 35^\circ C$, $R_{eq} = 38 \mu m$, $R_0 = 40 \mu m$, and $c_0 = 0$.}
\end{figure}
contact line, the steady-state velocity of the sphere $v$ is given by

$$F = \xi v,$$  \hspace{1cm} (A.2)

where the unit of $\xi$ is kg s$^{-1}$. Combining these two equations, we obtain

$$v = \frac{PA}{\xi}. \hspace{1cm} (A.3)$$

The translocation time $t_{\text{trans}}$ is estimated by the time when the sphere migrates by a distance $2b$ with the speed $v$ as

$$t_{\text{trans}} = \frac{2b}{v} = \frac{2b}{PA}. \hspace{1cm} (A.4)$$

Here, $\xi$ is given by

$$\xi = \alpha L = 2\pi\alpha b,$$  \hspace{1cm} (A.5)

where $\alpha$ has the unit of kg m$^{-1}$ s$^{-1}$. Substituting eq. (A.5) and $A = \pi b^2$ into eq. (A.4), we obtain

$$t_{\text{trans}} = \frac{4\alpha}{P}. \hspace{1cm} (A.6)$$

Then, we evaluate the pressure difference between the inner and outer regions of the vesicle, $P$. The stretching energy $F_s$ is defined as

$$F_s = \frac{\lambda}{2} \left(\frac{\Delta A}{A_{\text{eq}}}\right)^2,$$  \hspace{1cm} (A.7)

where $A_{\text{eq}}$ is the equilibrium area of the vesicle and $\Delta A$ is the excess area due to the stretching. Equation (A.7) can be rewritten as

$$F_s = \frac{\lambda}{2} \left(\frac{\Delta A}{A_{\text{eq}}}\right)^2 = A_{\text{eq}} \frac{\lambda}{2} \left(\frac{A - A_{\text{eq}}}{A_{\text{eq}}}\right)^2,$$  \hspace{1cm} (A.8)

where this expression means that the stretching energy is given by the square of the local strain $\Delta A/A_{\text{eq}}$ integrated over the whole vesicle surface which gives the factor $A_{\text{eq}}$.

Using the method of virtual work, this stretching energy $F_s$ can be given by an integral of the surface tension $\Sigma$ with respect to the excess area $\Delta A$ as

$$F_s = \int \Sigma d(\Delta A),$$ \hspace{1cm} (A.9)

and, therefore,

$$\Sigma = \frac{\partial F_s}{\partial (\Delta A)} = \lambda \frac{\Delta A}{A_{\text{eq}}}. \hspace{1cm} (A.10)$$

Then, the pressure difference $P$ can be given by Laplace law as

$$P = \frac{2\Sigma}{b} = \frac{2\lambda}{b} \frac{\Delta A}{A_{\text{eq}}}. \hspace{1cm} (A.11)$$

Substituting eq. (A.11) into eq. (A.6), we obtain

$$t_{\text{trans}} = \frac{2\alpha b A_{\text{eq}}}{\lambda \Delta A}. \hspace{1cm} (A.12)$$

Thus,

$$\frac{\alpha b}{\lambda} = \frac{t_{\text{trans}} \Delta A}{2 A_{\text{eq}}}. \hspace{1cm} (A.13)$$

Experiments show that $t_{\text{trans}} \approx 1.0 \text{ s}$ \textsuperscript{[19]} and $\Delta A/A_{\text{eq}} = 0.1$. Substituting $b = 10 \mu m$ and $\lambda = 1.0 \times 10^8 k_B T/\mu m^2$ into eq. (A.13), we, then, obtain

$$\alpha \approx 2.1 \times 10^3 \text{ kg m}^{-1}\text{s}^{-1}. \hspace{1cm} (A.14)$$

References

1. Y. Sakuma, M. Imai, Life 5, 651 (2015).
2. P.L. Luisi, \textit{The Emergence of Life: From Chemical Origins to Synthetic Biology} (Cambridge University Press, Cambridge, 2006).
3. S. Rasmussen, M.A. Bedau, L. Chen, D. Deamer, D.C. Krakauer, N.H. Packard, P.F. Stadler, Eds.; \textit{Protocells: Bridging Nonliving and Living Matter} (The MIT Press, Cambridge, 2009).
4. D. Deamer, J.W. Szostak, Eds.; \textit{The Origins of Life} (Cold Spring Harbour Laboratory Press, New York, 2010).
5. D.W. Deamer, J.P. Dworkin, Top. Curr. Chem. \textbf{259}, 1 (2005).
6. P. Walde, Orig. Life Evol. Biosph. \textbf{36}, 109 (2006).
7. M.M. Hanczyz, S.M. Fujikawa, J.W. Szostak, Science \textbf{302}, 618 (2003).
8. K. Takakura, T. Toyota, T. Sugawara, J. Am. Chem. Soc. \textbf{125}, 8134 (2003).
14. H.R. Shojaei, M. Muthukumar, J. Phys. Chem. B, 120, 6102 (2016).
15. P. Khunpetch, X. Man, T. Kawakatsu, M. Doi, J. Chem. Phys. 148, 134901 (2018).
16. Z. Yao, R. Sknepnek, C.K. Thomas, M.O. de la Cruz, Soft Matter 8, 11613 (2012).
17. E. Karatekin, O. Sandre, H. Guitouni, N. Borghi, P.H. Puech, F. Brochard-Wyart, Biophys. J. 84, 1734 (2003).
18. N. Rodriguez, S. Cribier, F. Pincet, Phys. Rev. E 74, 061902 (2006).
19. Y. Sakuma, The resealing time of the pore (translocation time of detached daughter vesicle) is measured in the developed model system for self-reproduction DLPE/DPPC vesicle. Since the pore opens and completely closes, the measure indicates that the translocation time is around a second with the diameter of the mother and daughter vesicles are 28.2 µm and 13.1 µm, respectively.
20. L. Onsager, Phys. Rev. 37, 405 (1931).
21. L. Onsager, Phys. Rev. 38, 2265 (1931).
22. M. Doi, Soft Matter Physics (Oxford University Press, Oxford, 2013).
23. M. Doi, J. Phys.: Condens. Matter 23, 284118 (2011).
24. M. Doi, Chin. Phys. B 24, 020505 (2015).
25. M. Doi, J. Phys. Soc. Jpn. 78, 052001 (2009).
26. A. Onuki, Phase Transition Dynamics (Cambridge University Press, Cambridge, 2002).
27. N.S. Wingreen, K.C. Huang, Annu Rev Microbiol. 69, 361 (2015).
28. W. Rawicz, K.C. Olbrich, T. McIntosh, D. Needham, E. Evans, Biophys. J. 79, 328 (2000).
29. P. Wiggins, R. Phillips, Biophys. J. 88, 880 (2005).
30. D. Marsh, Chem. Phys. Lipids 144, 146 (2006).
31. M. Hu, J.J. Briguglio, M. Deserno, Biophys. J. 102, 1403 (2012).
32. T. Baumgart, S. Das, W.W. Webb, J.T. Jenkins, Biophys. J. 89, 1067 (2005).
33. U. Seifert, Adv. Phys. 46, 13 (1997).
34. H. Gluck, The gauss-bonnet theorem. https://www.math.upenn.edu/~shiydong/Math501X-7-GaussBonnet.pdf.
35. E. Evans, W. Rawicz, Phys. Rev. Lett. 64, 2094 (1990).
36. R. Phillips, T. Ursell, P. Wiggins, P. Sens, Nature 459, 379 (2009).
37. J.R. Rumble, editor, CRC Handbook of Chemistry and Physics (Boca Raton, FL: CRC Press, 2018).
38. F. Brochard-Wyart, P.G. de Gennes, O. Sandre, Physica A 278, 32 (2000).