Hard rod and frustum model of two-dimensional vesicles
Ryota Morikawa, Yukio Saito

To cite this version:

HAL Id: jpa-00247945
https://hal.archives-ouvertes.fr/jpa-00247945
Submitted on 1 Jan 1994

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L’archive ouverte pluridisciplinaire HAL, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d’enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.
Classification

Physics Abstracts
87.20 — 36.20C — 05.20

Hard rod and frustum model of two-dimensional vesicles

Ryota Morikawa and Yukio Saito

Department of Physics, Keio University, 3-14-1 Hiyoshi, Kohoku-ku, Yokohama 223, Japan

(Received 12 July 1993, accepted in final form 13 October 1993)

Abstract. — A two-dimensional vesicle of hard rods subject to a shadowing interaction is analyzed by Monte Carlo simulations. From the mode analysis of the shape fluctuation of the vesicle, the bending rigidity is estimated microscopically and the relation between the rod length and the bending rigidity is studied. A scaling relation of a mean square radius of gyration is investigated and compared with that proposed by Leibler, Singh and Fisher. Increasing osmotic pressure a vesicle performs a shape transition from a circular to bi-lobocyte shape. A vesicle with a spontaneous curvature is also studied by using molecules of a frustum shape.

1. Introduction.

It is widely known that natural and artificial membrane vesicles can change their shapes under various conditions [1-3]. A typical example is the red blood cell of a closed membrane or vesicle which deforms by varying temperature, pH of the solution, osmotic pressure, and so on. In order to understand a mechanism and the relevant physical quantities governing these shape transformations, a continuous elastic model is widely in use [4-6]. The so-called spontaneous-curvature model [7] proposed by Helfrich [5] has the curvature elastic energy per unit area of a fluid membrane in the form as:

\[ g_c = \frac{1}{2} \kappa_c (c_1 + c_2 - c_0)^2 + \bar{\kappa}_c c_1 c_2 \]  \hspace{1cm} (1)

where \( \kappa_c \) and \( \bar{\kappa}_c \) are the curvature elastic modulus (bending rigidity) and Gaussian curvature elastic modulus, \( c_1 \) and \( c_2 \) are the two principal curvatures, and \( c_0 \) is the spontaneous curvature. Under an external field such as an osmotic pressure difference \( \Delta P \) between the outside and the inside of the vesicle, the total free energy of the vesicle is represented as

\[ F_c = \int g_c dS + \int \Delta P dV, \]  \hspace{1cm} (2)

where the first and the second integrals are taken over the surface and the volume of the vesicle, respectively. By minimizing \( F_c \) for a given surface area \( S \), various shapes of the vesicle, which
have been observed in experiments, are realized. Though this and the related models [8, 9] explain shapes of the vesicle in real systems, effects of the thermal noise and shape fluctuation are not taken into consideration.

Thermal noise has been taken into account by means of Monte Carlo simulation of microscopic models such as tethered hard spheres in three dimensions [10, 11]. Scaling laws for the mean radius of gyration under various conditions and crumpling phenomenon have been found. Since the simulation of the tethered membrane in three dimensions needs a long CPU time, Leibler, Singh, Fisher (LSF) have studied a tethered ring in two dimensions [12-16] in detail.

Albeit with all these success of continuum and tethered ring models, they are still inadequate when we want to understand microscopic effects such as the individual shapes of the molecules or interactions between them. For example, in real system, phospholipid molecules which construct the biological membranes together with protein molecules [17] are anisotropic and have polar hydrophilic heads and oily hydrophobic tails. The origin of the lipid bilayer formation is believed to be a hydrophobic interaction [18]. Hydrophobic chains of phospholipids lead configurational ordering in the surrounding water molecules and cause an entropy reduction and the free energy increase. For detailed understanding of the microscopic properties of the membrane, the hydrophobic effect is indispensable. The bending elasticity is believed to be induced by such an anisotropy of the molecule [19], and the spherical molecule as in the tethered membrane model is insufficient. In addition, in describing shape transformations accompanied by topological changes such as endocytosis or exocytosis, tethered membrane model needs an artificial bond recombination [20].

Taking account of an anisotropy of phospholipid molecules and microscopic interactions between them, we have recently proposed a simple model [21], in which a pair of phospholipid molecules in both layers is regarded as a single hard rod. These hard rods cohere and form lamellars or vesicles by the attractive interaction, which mimics the hydrophobic interaction. Here we describe the extended investigation on various shapes of a ring vesicle in a two-dimensional system. We estimate the bending rigidity from microscopic interactions between rod molecules instead of treating it as an a priori given parameter as in LSF model. We also study topological changes of the membrane induced by the spontaneous curvature in two dimensions. Since in LSF model there is an assumption of the connectivity between hard spheres, topological changes of the vesicle are not allowed and effects of the spontaneous curvature for the thermodynamic properties of the model only leads to trivial energy shift [1]. In our model, on the contrary, the cohesion of rod molecules are caused by a caricature hydrophobic interaction or “shadowing interaction”, and the topological changes of the vesicle are permitted. We introduce a spontaneous curvature into our model by changing the shape of a molecule from a rod to a frustum.

In section 2 the model is explained in detail and is studied by the Monte Carlo simulation at finite temperatures. From the simulation results, a bending rigidity of a continuum elastic model is estimated. We also investigate scaling relations of a mean square radius of gyration and of a mean area of vesicles, and compare the results with those proposed by LSF. When an osmotic pressure is applied on the vesicle, a shape transition of a vesicle from circular to bilobocyte is expected according to LSF. This effect of the osmotic pressure on vesicles is studied in section 3. In section 4 the model with a spontaneous curvature is studied by using molecules of a frustum shape and observe topological change of vesicular shape. Final summary and conclusion is given in section 5.

2.1 A model with shadowing interaction. — We consider a hard-rod system in two dimensions as is shown in figure 1. Each rod has a hard core to prevent rods from crossing each other, and the minimum distance between two rods is set \( a \). To stabilize the membrane structure, we introduce an attractive shadowing interaction to mimic the hydrophobic interaction [18]. When a rod \( i \) is isolated, both of its sides are naked and face water such that the ordering is induced in the surrounding water molecules with an energy cost \( J \) per length. When another rod \( j \) stays close to the rod \( i \), part of the rod \( i \) is covered by the shadow of the rod \( j \) projected on rod \( i \) and is shielded from the water (Fig. 1). We assume that only the remaining naked part of the rod \( i \) causes the energy increase. Therefore the "hydrophobic" energy is written as

\[ E_h = J \sum l_{nt,i} \]  

where \( l_{nt,i} \) is a total length of the naked part in rod \( i \), and the summation is taken over all rods. Compared to the hard-rod diameter \( a \), the length of the rod \( l \) is set long enough to yield sufficient cohesion.

The shielding is most effective when the neighboring \( i \) and \( j \) rods are parallel with each other, and perpendicular to the vector \( r_{ij} \), connecting the mass centers of the two rods. Since we do not know precisely how far the ordering of water molecules extends or how it decays, we simply assume here that the effect of the screening extends uniformly in the shielding region, and vanishes outside of a cutoff. The shielding region is rather arbitrary chosen as a rectangle with a height \( 2l \) and a width \( 2r_c \) around the rod as is shown in figure 1. When two widely separated rods are tilted against each other, the projected length is short and the shielding

Fig. 1. — Lipid bilayer is regarded as a hard rod. Hard rod interact with shadowing attraction, modeling the hydrophobic interaction.
becomes less effective. When shadows from different rods overlap, they cannot contribute to the shielding additively, and thus the present interaction is not a simple two-body force but a many-body one.

When $N$ rods form a ring, the ground state configuration is a circle with an allowed minimum radius such that every rod points out radially with the neighboring inner ends being in contact. The radius in the ground state is calculated to be $R_0 = (l + a/\sin(\pi N^{-1}))/2$ with an energy $E_0 = 2NJ(R_0 + l/2)(1 - \cos(2\pi N^{-1}))$. At a finite temperature the ring deforms to gain the orientational entropy of each rod and the configurational entropy associated with the global shape variation. To allow for the deformation, the radius of the ring increases at finite temperatures. The shape of a vesicle is described by a contour line connecting the mass centers of rod molecules. By assuming that the shape variation of the vesicle takes place very slowly compared to the adjustment of the rod orientation to the normal direction of the shape, the energy for a given vesicle shape is represented as

$$E_h \approx J \sum_i \left( \frac{\Delta s_i}{\sin(\Delta \phi_i/2)} \right) + l \left( 1 - \cos \Delta \phi_i \right),$$

(4)

where $\Delta s_i$ is the separation between the mass centers of the rods $i$ and $i + 1$, and $\Delta \phi_i$ is a difference of the orientations of rods $i$ and $i + 1$. With the assumption that the separations between neighboring rods are all equal as $\langle \Delta s \rangle = s/N$ for a total perimeter length $s$, and that the angle difference $\Delta \phi$ is small, the energy (4) is written in a continuum limit as

$$E_h \approx \frac{J\langle \Delta s \rangle}{2} \int H^2 ds + J\langle \Delta s \rangle \int |H| ds,$$

(5)

where $H = \lim_{\Delta s \to 0} \Delta \phi / \Delta s$ is the curvature. For a singly connected ring with a positive curvature, i.e. an oval, the integral of curvature $|H|$ along the closed contour is constant to be $2\pi$ and the second term gives a trivial contribution. Then the energy $E_h$ reduces to the elastic energy of a continuum theory in two dimensions;

$$E_c = \frac{\kappa}{2} \int H^2 ds,$$

(6)

with the curvature elastic modulus or the bending rigidity $\kappa$ estimated as

$$\kappa = J\langle \Delta s \rangle.$$

(7)

At higher temperatures, where fluctuations cannot be neglected any more, the estimation (7) may be insufficient, and we estimate $\kappa$ from the undulation of the contour of the vesicle. For a shape described by a polar coordinate as $r = r(\theta)$, the undulations of the vesicle shape are decomposed into Fourier modes [22] as

$$r = \frac{s}{2\pi} \left[ 1 + \sum u_n \exp(-in\theta) \right].$$

(8)

When the perimeter length $s$ is fixed and the equipartition of energy among different modes is adopted, the amplitude is obtained to be [21]

$$\langle |u_n|^2 \rangle = \frac{k_BT s}{8\pi^2 \kappa (n^2 - 1)^2}.$$

(9)

By using equation (9), we may estimate accurately the bending rigidity $\kappa$ by obtaining mode amplitudes $\langle |u_n|^2 \rangle$ and the perimeter length $s$ from the simulation.
2.2 Simulation. — In order to understand the thermodynamic behaviors in detail, as in the case when the shape deviates largely from the circle at high temperatures, we have to rely on Monte Carlo method because of the complexity of our microscopic system.

In a Monte Carlo trial, a rod is chosen randomly. Its center of mass and orientation are tried to be shifted randomly. These trials are accepted or rejected according to the Boltzmann weight \( \exp(-\Delta E/k_BT) \), which is calculated from the associated energy change \( \Delta E \) and the temperature of the system \( k_BT \) in order to satisfy the detailed balance. The maximum shift and rotation sizes are so chosen that about fifty percent of the trials are accepted.

In the simulation, the rod length \( l \) is taken to be 10 times of the hard core radius \( a \), and the attraction range \( r_c \) is set \( 3a \). As an initial configuration we prepare \( N=100 \) rods in a circular ring of the ground state configuration in an infinitely extended space. The radius in the ground-state is \( R_0=20.9a \) and the energy per rod is \( E_0/NJa=0.102 \). This energy is quite low compared to the value of 20 when the rod is isolated. Simulations are run up to \( 1 \times 10^6 \) Monte Carlo steps (MCS) for every rod at various temperatures.

At low temperatures, \( k_BT/Ja \leq 1.1 \), the ring vesicle is stable (Fig. 2a). At \( k_BT/Ja \approx 1.3 \sim 3 \) the ring breaks apart at one or few points to form fragments (Fig. 2b). At still higher temperatures the system breaks down to a collection of isolated rods, as shown in figure 2c. At a temperature \( k_BT_c/Ja=1.2 \), we obtain a precursory behavior of phase transition such that a rod leaves and returns to the vesicle. At low temperatures, \( T < T_c \), where the vesicle is stable, the energy \( E_h/NJa \) is found to be proportional to the temperature \( k_BT/Ja \), and the specific heat \( C/N = (\langle E_h^2 \rangle - \langle E_h \rangle^2)/Nk_BT^2 \) remains constant about unity. The specific heat obtained by the energy fluctuation is compatible with that obtained by the temperature derivative of the energy, indicating that an equilibrium is reached in the simulation. Since our Monte Carlo simulation does not contain the kinetic energy contribution, the value unity of the specific heat can be interpreted that there are essentially two vibrational degrees of freedom in our ring vesicle. These two degrees of freedom may be the vibration of the rod orientation and that of the mass center of the rod normal to the ring, or of the shape fluctuation.

![Fig. 2. — Energy per rod \( \langle E_h \rangle/JaN \) versus temperature and snapshot of the configuration of 100 rods at (a) \( k_BT/Ja = 0.5 \), (b) 1.6 and (c) 3.0.](image-url)
2.3 Estimate of bending rigidity. — Bending rigidity $\kappa$ in the microscopic model can be estimated by using the shape fluctuation, equation (9). The inverse root square of the mode amplitude $1/\sqrt{\langle |u_n|^2 \rangle}$ is obtained from the simulation, and the result is plotted in figure 3 against the mode number $n^2 - 1$ at various temperatures for the system with $N = 100$. At low temperatures the deviation of the vesicle shape from the circle is small and relation (9) is found to be satisfied. From the slope of figure 3, the bending rigidity $\kappa$ is estimated by the least square fit to equation (9). $\kappa$ is found to increase at relatively low temperatures, $k_B T/J_a < 0.2$, but remains almost constant at $\kappa/J_a^2 \approx 32$ at $k_B T/J_a \approx 0.2 - 0.6$ as is shown in figure 4. Estimation by equation (7) yields $\kappa/J_a^2 \approx 24$ in agreement of the order. The difference may be due to the neglect of the separation fluctuation in the estimation (7).

For $k_B T/J_a > 0.6$, the linearity of $\langle |u_n|^2 \rangle^{-1/2}$ to $n^2 - 1$ becomes poor, and the estimation of the bending rigidity $\kappa$ is not fully confidential. Here the fluctuation $\langle |u_n|^2 \rangle$ of the mode with small $n$ is expected to become large, but the neighboring inner ends of hard rods may contact each other, and the hard core repulsion between them reduces the fluctuation from the expected value. Also the contribution of the total curvature in equation (5) may stiffen the vesicle when the fluctuation becomes large.

According to the rough estimate equation (7) of the bending rigidity, $\kappa$ should be insensitive to the system size for large $N$, since the average separation of the two neighboring rods $\langle \Delta s \rangle$ is determined by the local interaction of the hard core repulsion and the shadowing attraction. Simulation shows the systematic increase of $\kappa/J_a^2$ when $N$ increases from 40 to 100, but it seems to converge to an asymptotic constant value at $k_B T/J_a \leq 0.6$ for large $N$ as shown in figure 4. For the system with 40 rods $\kappa$ deviates largely from the asymptotics. Since the effect of the molecular size limits the shape fluctuation of the vesicle, the smallness of the system

![Fig. 3 - Mode amplitude $\langle |u_n|^2 \rangle^{-1/2}$ versus mode number $n^2 - 1$, at various temperatures. The lines represent least square fits and from the slopes the bending rigidity is estimated.](image)

![Fig. 4 - Bending rigidity $\kappa$ estimated from equation (9) versus temperature for systems containing various numbers of rods $N$.](image)
size affects strongly in the estimation of the bending rigidity even at low temperatures.

Another characteristic of \( \kappa \) expected from equation (7) is its dependence on the length of the rod \( l \). At zero temperature \( \Delta s \) is proportional to the rod length \( l \) as \( \Delta s_0 = a + l \sin \pi/N \). Therefore, the bending rigidity \( \kappa \) is a quadratic function of \( l \) at \( k_B T/Ja = 0 \). At finite temperatures, \( k_B T/Ja = 0.05, 0.1 \) and \( 0.5 \), we obtained \( \kappa \) from simulations of systems with various rod lengths as is shown in figure 5. \( \kappa \) is well fitted to be a quadratic function of \( l \), as is drawn by the lines in figure 5. The result is consistent with that of the mean separation \( \langle \Delta s \rangle \), which can be well fitted by the linear law in \( l \) as

\[
\langle \Delta s(T, l) \rangle = \bar{a}(T) + l \bar{b}(T).
\]  

(10)

\( \kappa \) and \( \langle \Delta s \rangle \) satisfies the relation

\[
\kappa = Jl \langle \Delta s(T, l) \rangle \Theta(T),
\]  

(11)

with a parameter \( \Theta(T) \) being independent of the rod length \( l \).

We also find that the stability of a vesicular shape depends strongly on the rod length \( l \). At \( k_B T/Ja = 0.5 \) the vesicle is stable when \( l \geq 5a \), but torn off when \( l \leq 4a \). Destabilization of a vesicle for a small aspect ratio \( l/a \) is well expected, since for a system with \( l = 0 \) the model reduces to a simple hard-core system and no cohesion is expected at zero pressure. Even at the lowest temperature as \( k_B T/Ja = 0.01 \), a system with \( l = a \) can not keep a ring form stably but breaks up at one point. At \( k_B T/Ja = 0.2 \) all the rods become isolated. This represents the importance of a large aspect ratio \( l/a \) for the formation of a stable layer structure.

2.4 SCALING FORMS. — For a polymer chain connected with \( N \) monomers, many universal laws have been derived by applying the theory of a self-avoiding walk [23]. One of them is the scaling relation between the Flory radius \( R_F \) and the degree of polymerization \( N \) as \( R_F \sim N^\nu \). The Flory exponent \( \nu \) is independent of the details of the monomer structure. For a membrane,
scaling laws for the square radius of gyration $\langle R_G^2 \rangle$ and the mean area $\langle A \rangle$ have been studied in detail by using LSF [12-14], or Ostrowsky and Peyraud [15] model in two dimensions. We expect that the same scaling laws are satisfied in our model of a vesicle constructed by hard rods.

Due to the bending energy cost, thermal fluctuation is restricted to modes with wavelength longer than the rigidity length:

$$ l_\kappa = \kappa / k_B T. \quad (12) $$

In our model, with $N = 100$, the rigidity length $l_\kappa$ decrease from 480a at $k_B T / J a = 0.05$ to 40a at $k_B T / J a = 1.1$. If the system size $s$ is smaller than $l_\kappa$, or the dimensionless quantity

$$ y = s / l_\kappa \quad (13) $$

is less than unity, we expect a circular vesicle, and square radius of gyration $\langle R_G^2 \rangle$ and mean area $\langle A \rangle$ are then proportional to $s^2$. On the other hand, at high temperatures when $l_\kappa$ becomes smaller than $s$, we may expect a fractal shape of a vesicle. Then $\langle R_G^2 \rangle$ and $\langle A \rangle$ may have the scaling relation [13];

$$ \langle R_G^2 \rangle = \left( \frac{s}{2\pi} \right)^2 U(y), \quad \langle A \rangle = \frac{s^2}{4\pi} V(y), \quad (14, 15) $$

with scaling forms $U(y)$ and $V(y)$ with $U(0) = V(0) = 1$, and $U(y) \sim V(y) \sim y^{-2(1-\nu)} = y^{-1/2}$ for $y \gg 1$. Here $\nu$ is expected to be $3/4$ in two dimension.

By linear mode analysis, we calculate $U(y)$ and $V(y)$ up to the first order of $y$ for small $y$;

$$ U(y) = 1 - \left( \frac{17}{32\pi^2} - \frac{1}{24} \right) y \quad (16) $$

$$ V(y) = 1 - \frac{3}{16\pi^2} y. \quad (17) $$

Both analyses are valid for $y < 1$ where the higher order terms of $u_n$ are negligible.

The scaling (14) and (15) are investigated for systems with $N = 40, 60, 80, 100$. We observe a stiff region where $\langle A \rangle \sim \langle R_G^2 \rangle \sim s^2$ for $y \ll 1$, and the linear mode analysis (16, 17) yields satisfactory fit to the data for $y \leq 1$. However, the soft region with behaviors $\langle A \rangle \sim \langle R_G^2 \rangle \sim s^{2\nu}$ with the Flory exponent $\nu = 3/4$ is not obtained. Instead, at high temperatures with $y \gg 1$, thermal fluctuation is too wild to destroy the vesicular conformation itself (Fig. 1). To observe the soft region with large $y$, we have to simulate a large system, which is out of our present capability.

3. Osmotic pressure effect.

3.1 Transition to bi-lobocyte. — In a real system, osmotic pressure of the vesicle plays an important role to the deformation of the shape. With the curvature elastic model (2), the bending rigidity $\kappa_c$, the spontaneous curvature $c_0$ and the osmotic pressure $\Delta P$ control the vesicle shapes such as discocyte, stomatocyte, dumbbell and so on [6]. In LSF model [12, 13], the circular vesicle is transformed into bi-lobocyte by osmotic pressure, and a phenomenon of nonlinear flickering is also observed. We expect a similar shape transition in our model caused by external or osmotic pressure applied to the vesicle.
The osmotic pressure is defined by a pressure difference between the interior and the exterior of the vesicle:

$$\Delta P \equiv P_{\text{ex}} - P_{\text{in}}.$$  \hfill (18)

In Monte Carlo simulation, the energy of the system is chosen as

$$E_{\text{hp}} = E_h + \Delta PA,$$  \hfill (19)

where $A$ is an area enclosed by the connecting line of the mass centers of the consecutive rods. Therefore, when the vesicle breaks apart or some rods change their position in the vesicle, our simulation loses the validity.

First we carry out the simulation with $N = 100$ rods at $k_B T/\mu_a = 0.5$. Figure 6 depicts the variation of vesicular shape as a function of an external over pressure, $\Delta P > 0$. It shows the superposition of the center of mass of each rod at various time steps at various pressures. When $\Delta P$ is small, the shape of the vesicle is circular and does not differ much from that at zero pressure (Fig. 6a). At $\Delta Pa/J = 0.006$, a fluctuation of the vesicle shape becomes very large (Fig. 6b), and for higher pressure $\Delta Pa/J \geq 0.008$, the vesicle collapses into bi-lobocyte (Fig. 6c). The compressibility for the vesicle is obtained from the area fluctuation as

$$\gamma_T = \frac{\langle A^2 \rangle - \langle A \rangle^2}{\langle A \rangle k_B T}.$$  \hfill (20)

$\gamma_T$ has a maximum at $\Delta Pa/J = 0.006$ (in Fig. 6) associated with the shape transition. A reduced area $4\pi (A)/s^2$ also reflects the shape transition, as is shown in figure 6. It is almost constant for $\Delta Pa/J \leq 0.005$, but decreases sharply when the vesicle takes a bi-lobocyte shape for large $\Delta P$.

For large pressure difference, $\Delta Pa/J > 0.01$, two concave sides of bi-lobocyte contact with each other, and some rod molecules change their concave sides. Thus with a very large $\Delta P$, the area of the vesicle cannot be defined appropriately with our algorithm and the simulation has to be terminated.
3.2 Linear Stability Analysis of the Shape. — Here we analyze the stability of the vesicle shape by means of a mode analysis. The energy of the system is written in the continuum theory as

\[ E_{\text{cp}} = E_{\text{c}} + \Delta P \int dA. \tag{21} \]

By decomposing the vesicle shape in the Fourier modes as in equation (8), and expanding the energy up to the second order of mode amplitudes, we obtain the thermal average of the mode amplitude as

\[ \langle |u_n|^2 \rangle = \frac{k_B T s}{8\pi^2 \kappa (n^2 - 1) \{n^2 - 1 - \Delta P s^3/(2\pi)^3 \kappa \}} \tag{22} \]

From equation (22), the amplitude \( u_2 \) of the mode number \( n = 2 \) is found to diverges at \( \Delta P_c \equiv 24\pi^3 \kappa / s^3 \). For the present case at \( k_B T / Ja = 0.5 \), parameters are estimated roughly as \( s/a = 220 \) and \( \kappa / Ja^2 = 30 \). Therefore we expect that at \( \Delta P a/J \approx 0.002 \), the vesicle should become unstable and collapse into bi-lobocyte. The order of this estimation agrees to the result of simulations, showing that the shape transition occurs at \( \Delta Pa/J \approx 0.006 \). The discrepancy may be attributed to the term \( J(\Delta s) \int |H| ds \) in equation (5), since the shape of the vesicle is no longer oval near the instability point and the total curvature \( \int |H| ds \) varies over \( 2\pi \). For large pressure difference, the effect of the total curvature in equation (5) increases and restrains the shape from transforming into non-oval shape, i.e. bi-lobocyte. Therefore larger pressure difference \( \Delta P a/J \approx 0.006 \) is required in the simulation than the theoretical expectation \( \Delta P a/J \approx 0.002 \) to the transformation into bi-lobocyte.

The reciprocal of the mode amplitude \( R_n = 1/\langle |u_n|^2 \rangle (n^2 - 1) \rangle \) is plotted against the mode number \( n^2 - 1 \) for various pressures as shown in figure 7. For \( \Delta Pa/J < 0.006 \), \( R_n \) is linearly proportional to \( n^2 - 1 \) and the slopes do not vary much as pressure varies. Hence from equation (22), the bending rigidity is almost independent of the osmotic pressure \( \Delta P \). In figure 7, the

![Figure 7](image-url)

**Fig. 7.** — Reciprocal mode amplitude \( \langle |u_n|^2 \rangle (n^2 - 1)^{-1} \) versus mode number \( n^2 - 1 \), at various pressures. The solid line represents a theoretical expectation (23) when the divergence of mode amplitude occurs at \( n = 2 \).
data of \( R_n \) for \( \Delta Pa/J < 0.006 \) stay above the critical line;

\[
\frac{1}{\langle |u_n|^2 \rangle (n^2 - 1)} \equiv \frac{8\pi^2 \kappa}{k_B T s} (n^2 - 4)
\]

(23)

where the instability of the second mode, \( n = 2 \), takes place. For \( \Delta Pa/J \geq 0.006 \), the vesicular shape deviates largely from a simple circle and the value of \( R_n \) becomes small except \( n = 3 \), indicating that the relation (22) completely breaks down.

The linear mode analysis of the reduced area \( 4\pi \langle A \rangle/s^2 \), equation (17), can be extended for the present case with pressure difference. It is expected to satisfy the relation

\[
\frac{4\pi \langle A \rangle}{s^2} = 1 - \frac{y}{4\pi^2} Z(\omega),
\]

(24)

where \( Z(\omega) \) is a scaling form

\[
Z(\omega) = \frac{1 - 3\omega^2}{2\omega^2(1 - \omega^2)} - \frac{\pi}{2\omega} \cot \pi \omega,
\]

(25)

with a dimensionless parameter \( \omega \) defined as

\[
\omega \equiv \sqrt{1 + \frac{3\Delta P}{\Delta P_c}}.
\]

(26)

The relation (25) is shown by a solid curve in figure 8. When \( \omega \to 1 \) or \( \Delta P \to 0 \), \( Z(1) = 3/4 \) and equation (24) reduces to equation (17). When \( \omega \to \omega_c = 2 \) or \( \Delta P \to \Delta P_c \), the scaling form \( Z(\omega) \) diverges. However since the reduced area \( 4\pi \langle A \rangle/s^2 \) should be positive, the scaling form \( Z(\omega) \) should be less than \( 4\pi^2/y \) which is about 12 for \( n = 100 \) and \( l = 10a \) for instance. Linear analysis becomes meaningless around \( \omega = 2 \).

In the present system, we expect the universality of the scaling form \( Z(\omega) = 4\pi^2(1 - 4\pi \langle A \rangle/s^2)/y \) against scaling parameter \( \omega \). The parameter \( \omega \) depends not only on \( \Delta P \) but also

\[\begin{array}{c}
\text{N}=100, \text{Va}=10 \\
\text{N}=100, \text{Va}=8 \\
\text{N}=100, \text{Va}=6 \\
\text{N}=80, \text{Va}=10
\end{array}\]

Fig. 8. — Scaling form \( Z(\omega) \) versus scaling parameter \( \omega \). A solid curve represents the results of the linear mode analysis of \( Z(\omega) \) in equation (25).
on the bending rigidity $\kappa$ and the perimeter length $s$. These parameters $\kappa$ and $s$ depends on the rod length $l$. Therefore, we vary parameter $\omega$ either by varying the over pressure $\Delta P$ or the rod length $l$. The system investigated have the combination of the number of rods $N$ and the rod length $l/a$ as $(N, l/a) = (100, 10), (100, 8), (100, 6)$ and $(80, 10)$ at $k_B T / J a = 0.5$. The results show that $Z(\omega)$ increases very slowly at $\omega < 2.9$, but rapidly at $\omega > 2.9$ as is shown in figure 10. Hence the critical parameter $\omega_c$ may take the value around 2.9.

The simulation results of the LSF model [12, 13] can be interpreted with the present parametrization that the fluctuations become anomalously large at $\omega = 2.0 \sim 2.4$ and then a new type of shape as bi-lobocyte appears when $\omega \geq 3.4$. The critical parameter $\omega_c \approx 2.9$ in our model is not much different from $\omega = 2.0 \sim 2.4$ in LSF model. We also observe the critical behavior similar to “flickering” found in LSF model around $\omega_c$.

4. A frustum system for vesicles.

4.1 Spontaneous curvature in two dimensions. — To investigate shapes of the vesicle in three dimensions, the spontaneous curvature in equation (1) plays an important role in a continuum theory [6]. It is connected to the asymmetry of the inner and the exterior of the lipid bilayer membrane. The difference of two layers may be due to the chemical difference, to the different number of lipids, or to the difference in the environment. In two dimensions, the energy of a vesicle with a spontaneous curvature $H_0$ without the osmotic pressure is written as

$$E_{cs} = \frac{\kappa}{2} \int (H - H_0)^2 ds. \quad (27)$$

As long as we consider a single vesicle, $H_0$ gives a trivial contribution [1]. But when the topology of a vesicle changes, $H_0$ plays a crucial role. When there are $m$ vesicles in the system, the geometrical relation yields the integral:

$$\int H ds = 2\pi m. \quad (28)$$

Then equation (27) is written as

$$E_{cs} = \frac{\kappa}{2} \int H^2 ds + \frac{\kappa H_0^2}{2} \int ds - 2\pi \kappa H_0 m, \quad (29)$$

where the integral is over total perimeter of vesicles. The second term in equation (29) has the same form of the interfacial tension of vesicles. The topological contribution to the energy $E_{cs}$ is realized by the third term, and it produces a discrete variation in the energy by varying the number of vesicles $m$.

4.2 A frustum model. — The effect of spontaneous curvature can be introduced into the microscopic model by changing a shape of the molecule from a rod into a frustum, which is shown in figure 9. The physical or biological meanings of such a model are as follows. In a binary mixture of an amphiphilic molecule with cosurfactant, membrane may be constructed from a triple of two main lipids and one cosurfactant [1]. We may regard this triplet as a frustum shaped particle. Also one of the pair of anionic phospholipids which form membrane, is kept in contact with divalent cations, the latter reduce a repulsive radius of the polar head effectively [18], and thus the pair of anionic phospholipids becomes asymmetric and can be modeled by a frustum.
In figure 9, both sides of the frustum, each having length $l$, make an angle $\theta_s$ with each other. When they are naked, each side cost an energy $Jl$ as before. The attractive and repulsive interaction between the frustum shaped molecules are essentially the same as between the rod shaped molecules. In order to prevent the inversion of a frustum or, in a real bilayer system, to prevent the exchange of molecules between two monolayers, we introduced additional restriction on the interaction such that when the direction $n_i$ of the $i$-th frustum is opposite to that, $n_j$, of the neighboring $j$-th frustum, i.e. $n_i \cdot n_j \leq 0$, they are ineffective to shield each other. This restriction keeps the bigger end of the frustum exterior of the membrane. In the Monte Carlo simulation we never encounter this inversion so far.

An energy of a vesicle constructed by $N$ frustums is estimated as following at low temperature. The shape of a vesicle is described by the contour lines connecting the centers of frustum molecules with a total perimeter $s$. By assuming that the average orientation of the frustum molecule is in normal direction of the shape, the energy between a frustum $i$ and $i + 1$ is represented as

$$\varepsilon_{hs,i} = J(l + \delta_i) \{1 - \cos(\theta_s - \Delta \phi_i)\}$$

with

$$\delta_i = \frac{\Delta s_i - l \sin((\theta_s/2) \cos(\Delta \phi_i/2))}{|\sin((\theta_s - \Delta \phi_i)/2)|},$$

where $\Delta s_i$ is the separation between the centers of the frustums $i$ and $i + 1$, and $\Delta \phi_i$ is the
angle difference of the normals of the frustums $i$ and $i + 1$. Inner ends of the neighboring frustums are closer than the outer ends for $\Delta \phi_i > \theta_s$, while outer ends are closer than the inner ends for $\Delta \phi_i < \theta_s$. At $\Delta \phi_i = \theta_s$, a vesicle is the most stable.

The total energy of the vesicle $E_{hs}$ is derived from equation (30) as

$$E_{hs} = \sum_i J l \{1 - \cos(\theta_s - \Delta \phi_i)\}$$
$$\quad + \sum_i 2 \left(\Delta s_i - l \sin \frac{\theta_s}{2} \cos \frac{\Delta \phi_i}{2}\right) \left|\sin \frac{\theta_s - \Delta \phi_i}{2}\right|.$$  \hspace{1cm} (32)

Assuming that the frustums are separated equidistantly as $(\Delta s) = s/N$, and that the angle $\Delta \phi_i$ and $\theta_s$ are small, the average energy for a given vesicle shape in a continuum limit is approximated as

$$E_{hs} = \frac{J l (\Delta s)}{2} \int (H - H_0)^2 ds + J (\Delta s) \left(1 - \frac{H_0 l}{2}\right) \int |H - H_0| ds$$ \hspace{1cm} (33)

with a spontaneous curvature $H_0$:

$$H_0 = \theta_s/(\Delta s).$$  \hspace{1cm} (34)

The first term in equation (33) corresponds to equation (27) and representation of the bending rigidity is the same as that of the rod model shown in equation (7). The spontaneous curvature $H_0$ is found to be related to the asymmetry $\theta_s$ of the exterior and interior size of a molecule. The second term in equation (33) is similar to the total curvature term $J \langle \Delta s \rangle \int |H| ds$ in equation (5). Except $H \approx H_0$, the sign of $H - H_0$ remains definite for small configurational fluctuation, and the second term may be negligible. However, when the topology of the vesicle changes, this term also gives a discrete variation additional to the contribution given as equation (29).

4.3 SIMULATION. — To realize the topological change of the membrane, we simulate the frustum model at finite temperature by the Monte Carlo method. First, we prepare the ring-shaped vesicle constructed by $N = 100$ frustums and carry out the simulation for various $\theta_s$ at $k_B T/Ja = 0.5$. On increasing $\theta_s$ from 0 to 0.04$\pi$, the fluctuation of the area of the vesicle is enhanced and the compressibility $\gamma_T$ in equation (20) has maximum around $\theta_s = 0.04\pi$. The enhancement may be caused by the fact that the vesicle with $N = 100$ is metastable at $\theta_s = 0.04\pi = 2\pi/(N/2)$ and try to split into two. On further increasing $\theta_s$, the average curvature $\langle H \rangle = 2\pi/N$ differs largely from $H_0$, and the energy increase associated with a small deformation or curvature change $\delta H$ becomes very large to suppress the shape fluctuation. This fluctuation suppression happens for $0.06\pi \leq \theta_s \leq 0.14\pi$, and at $\theta_s = 0.14\pi$ fluctuation vanishes eventually. For $\theta_s$ larger than 0.14$\pi$, the vesicle "ruptures" and breaks into many smaller vesicles. The stiffening for $0.04\pi \leq \theta_s$ is also observable in the reduced area $4\pi \langle A \rangle/s^2$. It approaches unity for large $\theta_s$, indicating that the shape of the vesicle becomes circular at large $\theta_s$ like a stiff vesicle at $y \ll 1$ (in Sect. 2.4).

The energy per frustum $E_{hs}/N$ for various sizes of vesicle ($N = 20, 25, 100$) is obtained by simulation at $k_B T/Ja = 0.5$ and is shown in figure 10. It looks a quadratic function of $\theta_s$ with a minimum depending on the number $N$ of frustums. Accordingly, a vesicle constructed by $N = 100$ frustums with $\theta_s = 0.1\pi$, for example, has a high energy, and gains energy by splitting into several smaller vesicles. The minimum energy state is a collection of 5 vesicles, each of which is constructed by 20 frustums.

We simulate this relaxation process of vesicle splitting by using Monte Carlo simulation. Initially we prepare $N = 100$ frustums in a circular ring and then gradually increase the
Fig. 10. — Energy per frustum \( \langle E_{\text{hs}} \rangle / JaN \) versus angle of frustum \( \theta_s/\pi \), at \( k_BT/Ja = 0.5 \) for various sizes of vesicles; \( N = 20, 25 \) and 100.

Fig. 11. — Variation of the energy per frustum \( \langle E_{\text{hs}} \rangle / JaN \) against Monte Carlo step (MCS) at \( k_BT/Ja = 0.9 \) for a system with \( \theta_s = \pi/10 \), \( N = 100 \). Inserts show the topological changes of a vesicle; (a) “heart”-shape of the torn vesicle which is the final configuration at \( k_BT/Ja = 0.8 \), and (b)-(c) the process of “furling”.

A connected vesicle is overheated above \( k_BT/Ja = 0.5 \) to remain in a metastable state. At \( k_BT/Ja = 0.8 \) the closed vesicle tears off at a point and the broken ends curl inside to form like a “heart” (Fig. 11a). This state is very unstable, and at a higher temperature \( k_BT/Ja = 0.9 \), two edges of the torn vesicle “furl” (Fig. 11b) and new smaller vesicles are born one by one (Fig. 11c). Finally, there appear 4 vesicles. During this rupture process, the energy per frustum is lowered from \( E_{\text{hs}}/NJa \approx 1.535 \) (at \( k_BT/Ja = 0.8 \)) to \( E_{\text{hs}}/NJa \approx 1.153 \)(at \( k_BT/Ja = 0.9 \)), as shown in figure 11. The number of the newly born vesicles, four, in the
simulation differs from the expected number, five, in the ground state due to the energy barrier associated with the rupture kinetics.

5. Summary.

Hard rods with shadowing interactions are found to align in a ring vesicular form at low temperatures. From the shape fluctuation the bending rigidity $\kappa$ of the continuum elastic model is estimated. The gyration radius or the area of vesicles are found to satisfy the scaling relation in their size dependence in the stiff region. If an extremely large system were simulated, we would have got the scaling laws even in the soft region, but this expectation cannot be tested due to the CPU time limitation. Pressure difference between the inside and outside of a vesicle is shown to induce the collapse of the shape from circular to bi-lobocyte, as was already obtained by LSF.

For the macroscopic aspects, our microscopic model leads the same behavior with the LSF model. Our present model furthermore reveals the microscopic foundation of the macroscopic parameters. For the cohesion of molecules and for the bending rigidity $\kappa$ of a vesicle, the aspect ratio of the molecule is found to be very important. Another effect considered is the asymmetry of a molecule, which is represented as a frustum shape. The asymmetric shape leads to the spontaneous curvature, and on varying temperature topological changes of membrane vesicles is caused in two dimensions.

Recently, a few researches are started on a topological change of membranes in three dimensions. By simulating fluid membranes with a boundary line tension by the Monte Carlo method, a phase transition from open to closed topology has been found at finite temperatures [20]. A construction of a membrane and a vesicle from microscopic elements has been proposed by using molecular dynamics simulations [24]. In this model, orientation-dependent interaction and the "hydrophobic" cohesive interaction was introduced in addition to hard-core interaction. Though our microscopic model can simulate a vesicle only in two dimensions, we hope that it will be extended for the study of three-dimensional membranes.

Acknowledgements.

We acknowledge the discussion with Prof. H. Hyuga, Prof. K. Kinosita Jr. and Dr. H. Miyata. R.M. is also grateful to Dr. S. Komura, Dr. T. Kawakatsu and Dr. T. Yamaguchi who have made useful comments during the course of this work. This work was supported by Grant-in-Aid for Scientific Research on Priority Areas from the Ministry of Education, Science and Culture under Contract N°03247223.

References