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ARTICLE

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A relationship between membrane properties forms the basis of a selectivity mechanism for vesicle self-reproduction

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Abstract Self-reproduction and the ability to regulate their composition are two essential properties of terrestrial biotic systems. The identification of non-living systems that possess these properties can therefore contribute not only to our understanding of their functioning but also hint at possible prebiotic processes that led to the emergence of life. Growing lipid vesicles have been previously established as having the capacity to self-reproduce. Here it is demonstrated that vesicle self-reproduction can occur only at selected values of vesicle properties. We treat as an example a simple vesicle with membrane elastic properties defined by a membrane bending modulus κ and spontaneous curvature C_0, whose volume variation depends on the membrane hydraulic permeability L_p and whose membrane area doubles in time T_d. Vesicle self-reproduction is described as a process in which a growing vesicle first transforms its shape from a sphere into a budded shape of two spheres connected by a narrow neck, and then splits into two spherical daughter vesicles. We show that budded vesicle shapes can be reached only under the condition that $T_d L_p \kappa C_0^4 \geq 1.85$. Thus, in a growing vesicle population containing vesicles of different composition, only the vesicles for which this condition is fulfilled can increase their number in a self-reproducing manner. The obtained results also suggest that at times much longer than T_d the number of vesicles with their properties near the "edge" in the system parameter space defined by the minimum value of the product $T_d L_p \kappa C_0^4$, will greatly exceed the number of any other vesicles.

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Introduction

Vesicles can be formed from a variety of lipids that constitute contemporary biological membranes (Lasic 1993), as well as from other amphiphilic molecules such as surfactants (Marques 2000) and block copolymers (Discher and Eisenberg 2002). They are relatively stable macroscopic assemblies; during long incubation they either equilibrate at radii corresponding to the asymmetry between the outer and the inner parts of their membrane (Marques 2000; Jung et al. 2001) or, equally well, may stay for a long time trapped in one of their non-equilibrium configurations (Marques 2000). Under conditions that allow growth, vesicles exhibit the phenomenon of fission, with an accompanying increase in number (Berclaz et al. 2001). The main elements of the latter experiments have recently been captured in terms of phenomenological kinetic equations which simulate different phases of the vesicle formation process (Bolton and Wattis 2003). Here we focus on the mechanical aspects of vesicle self-reproduction related to the formation of budded vesicle shapes which supposedly precede the vesicle fission process. Vesicle budding has been well characterized both theoretically and experimentally (Svetina and Žekš 1989; Miao et al. 1991; Döbereiner et al. 1993).

The specific consequence of the following work is the demonstration that, for the vesicles to exhibit self-reproduction behaviour, some of their physical properties have to be interrelated. Our aim is to present the basic principle underlying this feature of the system. For this reason we have modelled vesicle self-reproduction as an ideal process in which a vesicle, in the first step, grows from a sphere into a shape composed of two spheres connected by a narrow neck. Vesicle fission is assumed to be the second phase of the process, in which the neck breaks and the vesicle splits into two separate vesicles. In the following analysis of the first step of this process we shall employ a macroscopic description of vesicle behaviour, based on the elastic properties of its membrane and on membrane hydraulic permeability. We shall, as an example, treat a possible simple hypothetical system in which an asymmetrical vesicle membrane separates the inner and outer aqueous media, with the latter also containing the compounds that constitute the membrane.

A model for the shape behaviour of growing vesicles

Vesicle growth is considered as the consequence of the continuous insertion of new molecules or molecular aggregates into the vesicle membrane, with consequent increase in its area. For the sake of simplicity, it is assumed that the rates of release of membrane constituents back into the medium are negligible. If the composition of the external solution does not change with time, the rate at which different compounds are incorporated into a given vesicle membrane is expected to be proportional to its area A, so that:

$$\frac{dA}{dt} = \frac{\ln 2}{T_d} A \tag{1}$$

where t is time, and T_d the time taken for the membrane to double its area. The vesicle volume (V) changes with time because of the net flow of water across the membrane, and is given by:

$$\frac{dV}{dt} = L_p A \Delta P \tag{2}$$

where L_p is the hydraulic permeability and ΔP is the difference between the pressures outside and inside the vesicle.

At given membrane area A and volume V, a vesicle assumes the shape that corresponds to the minimum elastic energy of its membrane (reviewed in Seifert 1997; Svetina and Žekš 2002). Membranes composed of amphiphilic molecules generally behave, in the plane of the membrane, as incompressible liquids; however, energy is needed for their bending deformation. A suitable model for the membrane bending elasticity is the spontaneous curvature model (Helfrich 1973) which, for instance, accounts well for the equilibrium size distribution of different catanionic vesicles (Jung et al. 2001). Although the membrane in the spontaneous curvature model is considered as a single layer system, the model can be applied also to multilamellar membranes under conditions that allow for rapid equilibration of membrane constituents between different layers. The elastic energy of the spontaneous curvature model includes (1) a membrane bending energy term which is the integral over the membrane area (A):

$$W_b = \frac{1}{2}\kappa \int (C_1 + C_2 - C_0)^2 dA \tag{3}$$

where κ is the bending modulus, C_1 and C_2 the two principal curvatures, and C_0 the spontaneous membrane curvature, and (2) a Gaussian bending energy term which is expressed as:

$$W_{b,G} = \kappa_G \int C_1 C_2 \, dA \tag{4}$$

where κ_G is the saddle-splay modulus. For an arbitrary closed surface of genus n, the Gaussian bending energy contributes a constant value $n 4\pi\kappa_G$ to the membrane energy. It has therefore to be considered only when shape transformations involve change of vesicle topology. Because bending energy is scale invariant, vesicle shapes as deduced theoretically by minimization of Eq. (3) (Deuling and Helfrich 1976; Svetina and Žekš 1989; Seifert et al. 1991) depend essentially only on the reduced (dimensionless) spontaneous curvature $c_0 = C_0 R$, where R is the radius of the sphere with area A ($A = 4\pi R^2$), and the reduced vesicle volume $v = 6\sqrt{\pi} V / A^{3/2}$. Vesicle shape behaviour can thus be represented in the c_0–v phase diagram (Fig. 1a) characterized by different lines that represent borders between shapes of different symmetries. Because the bending constant κ appears in Eq. (3) as a constant factor, it is appropriate to express the bending energy also in a reduced form. This is customarily done by dividing the bending energy (W_b) by the bending energy of a sphere for $c_0 = 0$, i.e. by $8\pi\kappa$, giving rise to the reduced bending energy $w_b(c_0, v) = W_b(c_0, v)/8\pi\kappa$.

Membrane bending energy depends on volume; therefore equilibrium can be established for a flaccid vesicle ($v < 1$) at a given v if the difference between the outside and inside vesicle pressures is $\Delta P = -\partial W_b/\partial V$. In the case of a spherical vesicle shape, the pressure difference (ΔP) can be smaller than $(-\partial W_b/\partial V)|_{v=1}$ because the equilibrium state can be established by the increase of the membrane lateral tension. Because $(-\partial W_b/\partial V)|_{v=1} = 2\kappa(6 - C_0 R)/R^3$, we have (Ou Yang and Helfrich 1989):

$$\Delta P - \frac{2\kappa(6 - C_0 R)}{R^3} < 0 \tag{5}$$

Taking into consideration the described basic properties of the spontaneous curvature model, Eqs. (1) and (2) can now be written specifically for this model. Because vesicle shapes depend only on the reduced variables c_0 and v, it is appropriate to replace the variables A and V by them. Since the reduced spontaneous curvature is directly proportional to the square root of the membrane area ($c_0 = C_0 (A/4\pi)^{1/2}$), dc_0/dt equals $(C_0/4(\pi A)^{1/2})$ ($d\,A/d\,t$), and Eq. (1) can be simply replaced by:

$$\frac{dc_0}{dt} = \frac{\ln 2}{T_d}\frac{c_0}{2} \tag{6}$$

The time dependence of the reduced spontaneous curvature, obtained by integrating Eq. (6) and taking $c_0(0)$ for the initial value of the spontaneous curvature, is then given by:

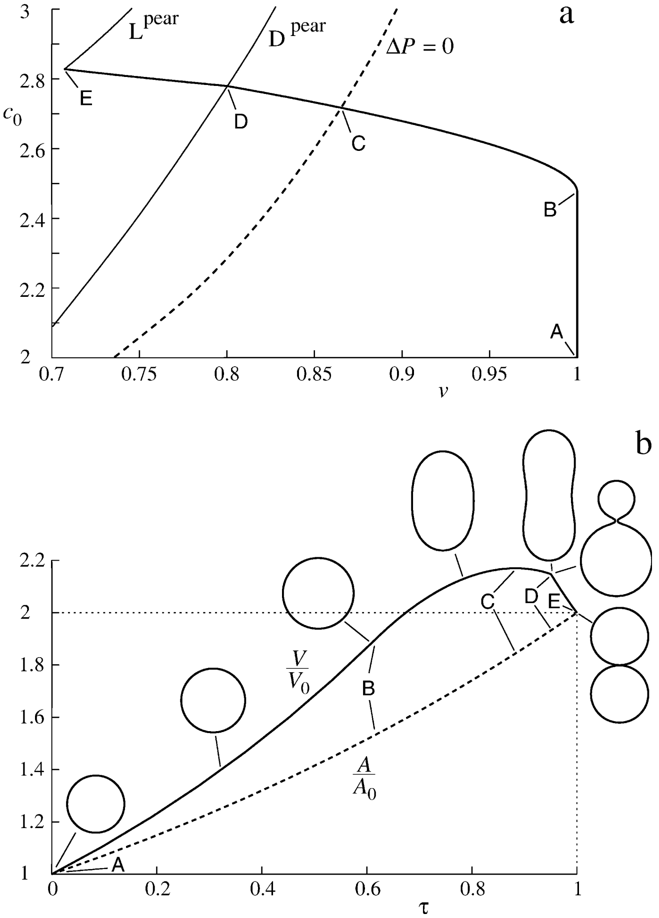

Fig. 1a, b Two representations of the vesicle shape transformation from a sphere (*point A*) to a shape composed of two equal spheres connected by a narrow neck (*point E*). The meaning of the intermediate points *B* to *D* is described in the text. (**a**) The pathway of the treated shape transformation in the c_0–v phase diagram. The reduced spontaneous curvature $c_0 = 2$ corresponds to the radius of a sphere with zero bending energy, $R_0 = 2/C_0$. The *dashed line* ($\Delta P = 0$) connects points which, at each value of c_0, are the maximum values of the bending energy. The line D^{pear} (obtained from fig. 10 in Seifert et al. 1991) denotes a discontinuous transition from axisymmetric prolate shapes that exhibit equatorial mirror symmetry to the pear-like shapes. The line L^{pear} (eq. 5.4 in Seifert et al. 1991) denotes the $v(c_0)$ dependence of shapes composed of two spheres connected by a narrow neck. The shape transformation pathway (*bold line*) begins at *point A* ($c_0 = 2$, $v = 1$) and ends at point $E\left(c_0 = 2\sqrt{2},\ v = 1/\sqrt{2}\right)$. (**b**) The dependence of the relative vesicle volume (*full line*, V/V_0 where $V_0 = 4\pi R_0^3/3$) and the relative membrane area (*dashed line*, A/A_0 where $A_0 = 4\pi R_0^2$) on the reduced time ($\tau = t/T_d$). Axial cross-sections of some characteristic shapes are also shown. Shapes are determined by solving numerically the shape equation that was obtained by minimizing the bending energy (Deuling and Helfrich 1976)

$$c_0(\tau) = c_0(0)2^{\tau/2} \tag{7}$$

where $\tau = t/T_d$ is the reduced time.

To derive the equation which will replace Eq. (2), we have to take into consideration that growth of the membrane area (Eq. 1) can cause two different types of vesicle shape transformation. In the case of a sufficiently slow rate of membrane growth, the vesicle grows as a sphere. At larger rates of membrane growth, above a certain critical value, the flow of solvent into the vesicle is not sufficiently fast, and the shape must deviate from the sphere. We have thus first to derive the condition which has to be satisfied for spherical vesicle growth. By assuming such a growth, it is possible to derive from Eqs. (1) and (2) the pressure difference across the membrane. On the basis of the relationship between the volume and area of a sphere ($V = A^{3/2}/6\sqrt{\pi}$), the derivative of the volume with respect to time in Eq. (2) can be replaced by $(A^{1/2}/4\sqrt{\pi})(\mathrm{d}\ A/\mathrm{d}\ t)$. Then, by comparing Eqs. (1) and (2), the expression for the pressure difference follows as:

$$\Delta P = \frac{\ln 2R}{2T_d L_p} \tag{8}$$

By inserting the result in Eq. (8) into Eq. (5), we obtain, as the condition for spherical vesicle growth expressed in terms of the reduced spontaneous curvature $c_0 = C_0 R$, the expression:

$$1 - 4\frac{\eta}{\ln 2c_0^4}(6 - c_0) < 0 \tag{9}$$

where the constant η is expressed in terms of all other parameters of the system as:

$$\eta = T_d L_p \kappa C_0^4 \tag{10}$$

Because the pressure difference in Eq. (8) is proportional to the radius of the vesicle and because $(-\partial W_b/\partial V)|_{v=1}$ decreases on increasing the radius, the shape of a growing vesicle will eventually have to deviate from that of a sphere. For a given value of the constant η, the critical radius and the corresponding critical reduced spontaneous curvature ($c_{0,\mathrm{cr}}$) can be obtained by exchanging the inequality in Eq. (9) by the equality.

In the regime of spherical vesicle growth we have $v = 1$, and the time dependence of vesicle properties is determined by the time dependence of c_0 as given by Eq. (7). When the vesicle shape deviates from spherical and we have $v < 1$, the time dependence of the reduced volume v is obtained from Eqs. (1) and (2) by taking:

$$\frac{\mathrm{d}V}{\mathrm{d}t} = \frac{\mathrm{d}\left(vA^{3/2}/6\sqrt{\pi}\right)}{\mathrm{d}t} \tag{11}$$

and by taking into consideration that both v and A depend on time. We obtain:

$$\frac{1}{\ln 2}\frac{\mathrm{d}v}{\mathrm{d}\tau} = -\frac{3}{2}v - \frac{18\eta}{\ln 2c_0^4}\frac{\partial \mathrm{w_b}(c_0,v)}{\partial v} \tag{12}$$

where $\partial w_b(c_0,v)/\partial v = (R^3/6\kappa)\partial W_b(c_0,v)/\partial V$. The first term on the right-hand side of Eq. (12) represents the effect on the reduced volume v due to the increasing the membrane area, whereas the second term, which has its origin in the right-hand side of Eq. (2), reflects the effect on v due to water flow through the membrane. In this regime the reduced volume can be obtained by the integration of Eq. (12) in which Eq. (7) is inserted for

$c_0(\tau)$. It is to be noted that the only parameter on which the behaviour of the system described by Eq. (12) depends is the constant η. The function $\partial w_b(c_0,v)/\partial v$ is known because it is an inherent property of the spontaneous curvature model.

The condition for vesicle self-reproduction

In this section we shall derive the condition under which vesicle growth brings about shape transformations that ultimately lead to a vesicle shape that is composed of two spheres connected by a narrow neck. Such budded vesicle shapes are commonly observed in vesicle suspensions (Döbereiner et al. 1993), and their existence is understood on the basis of membrane elastic properties (Svetina and Žekš 1989; Miao et al. 1991). Vesicle self-reproduction is assumed to be the consequence of breaking the neck that connects the spherical parts of the budded vesicle. After splitting, the two daughter vesicles grow independently and the cycle can be repeated, giving rise to an exponential increase of the vesicle number. Vesicle splitting is an energetically favourable process because of the release of the neck energy. If it is assumed that the bending energy can be approximated by Eqs. (3) and (4) also in extremely curved membrane regions, the neck energy corresponds to the change of the Gaussian bending energy (Eq. 4). The latter is equal to $4\pi\kappa_G$ and is negative because values of κ_G are normally negative. It has to be realized that the breaking of the neck is not an obvious process because it can only occur by considerable structural rearrangements of the membrane in the neck region (Kozlovsky and Kozlov 2003). However, it can be assumed that at some conditions, e.g. in some turbulent environments, the splitting of vesicles that contain narrow necks is a highly probable process. Then, to foresee the vesicle self-reproduction process, it only remains to be demonstrated under what conditions a growing, initially spherical vesicle attains the budded shape.

In the c_0–v phase diagram (Fig. 1a) the budded shapes lie on the line L^{pear} (eq. 5.4 in Seifert et al. 1991). The lowest point on this line at $c_0 = 2\sqrt{2}$ and $v = 1/\sqrt{2}$ is the symmetrical shape composed of two equal, connected spheres. Otherwise the radii of the two spherical vesicle parts are different. In the following procedure we choose an initially spherical vesicle shape, and for a given value of the constant η integrate Eq. (12) and thus obtain the pathway in the c_0–v phase diagram. Depending on the value of the constant $\eta = T_d L_p \kappa C_0{}^4$, this pathway can either end or not end on the line L^{pear}. If η is relatively small, according to Eq. (9) the vesicle deviates from a sphere at too low a $c_{0,\mathrm{cr}}$ value and can fail to hit the L^{pear} line. Such vesicles are expected to continue their growth, without forming a budded shape, into rather elongated shapes (Seifert et al. 1991, fig. 12), and are lost to the process of self-reproduction. It can thus be reasoned that there is a minimal value of the constant η needed for self-reproduction to occur. The minimal value of η corresponds to hitting the lowest point on the curve L^{pear} which corresponds to the symmetrical case where the vesicle makes a shape transformation from a sphere corresponding to $c_0 = 2$ and $v = 1$ to the double sphere at $c_0 = 2\sqrt{2}$ and $v = 1/\sqrt{2}$. Vesicle splitting then gives rise to two equal vesicles, equal in size to the initial vesicle. According to Eq. (7), this shape transformation happens at time $\tau = 1$. The value of the constant η at which this shape transformation is realized is found to be 1.85. Consequently, for self-reproduction to occur, the system parameters that appear in Eq. (10) must satisfy the condition:

$$T_d L_p \kappa C_0^4 \geqslant 1.85 \tag{13}$$

For $\eta = 1.85$, we show in Fig. 1a the corresponding shape pathway in the c_0–v phase diagram, and in Fig. 1b the time dependence of the vesicle volume and the membrane area. Both representations show that vesicle growth occurs in two distinct phases. A vesicle begins its growth as a sphere with zero bending energy and radius $R_0 = 2/C_0$. It continues to grow as a sphere until the left-hand side of Eq. (9) becomes zero, which for $\eta = 1.85$ occurs at $c_{0,\mathrm{cr}} = 2.475$ (point B). The second phase is non-spherical growth, which can also be subdivided into sub-phases defined by lines $\Delta P = 0$, D^{pear} and L^{pear} (Fig. 1a). Between points B and C, growth is characterized by increase of the vesicle volume and decrease of the reduced volume, because during this phase the pressure inside the vesicle is smaller than the outside pressure, demanding flow of water into the vesicle. Vesicle shapes are axisymmetric and have an equatorial mirror symmetry. At point C, where the vesicle reaches the maximum of the bending energy, the pressure difference changes sign. Between points C and D, vesicles retain their symmetries; however, here the bending energy decreases and therefore the pressure inside the vesicles is larger than the outside pressure, which causes water to flow out. Point D indicates a discontinuous transformation into a shape without equatorial mirror symmetry, characterized by a rather narrow neck. Between point D and point E this neck narrows further and the difference between the sizes of the two vesicle parts decreases. At point E, both vesicle parts are spherical and have the same radius, and the neck is predicted to be infinitesimally small.

Vesicles with $\eta > 1.85$ also exhibit self-reproducing behaviour. Their shape pathway in the c_0–v phase diagram ends higher up on the line L^{pear}, where budded shapes are compositions of two different spheres connected by an infinitesimally thin neck. On splitting, the resulting two vesicles have different sizes. They grow independently, but because they have the same value of the constant η, they eventually reach the same budded shape. The only difference between the fates of these two daughter vesicles is that the larger one needs less time to reach $c_{0,\mathrm{cr}}$ than the smaller one. To illustrate this behaviour, we show in Fig. 2, for each value of the con-

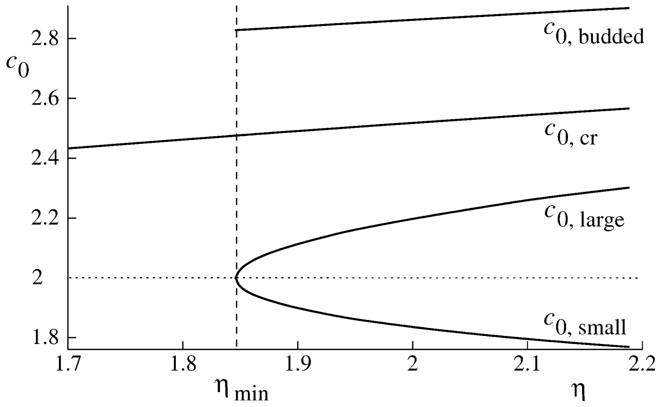

Fig. 2 The dependence of the reduced spontaneous curvature ($c_0 = C_0 R$) on the constant $\eta = T_d L_p \kappa C_0^4$. R is the radius of the sphere with the area A. $c_{0,\text{budded}}$ is the reduced spontaneous curvature for the budded shapes, $c_{0,\text{cr}}$ is the critical reduced spontaneous curvature obtained by setting Eq. (9) to zero, and $c_{0,\text{large}}$ and $c_{0,\text{small}}$ are the reduced spontaneous curvatures of the daughter vesicles. $\eta_{\min}$ denotes the minimum value of the constant η at which the budding occurs

stant η, the critical spontaneous curvature ($c_{0,\text{cr}}$) obtained by Eq. (9) set to zero, the reduced spontaneous curvature at which the budded shape is reached ($c_{0,\text{budded}}$), and the reduced spontaneous curvatures of the larger and smaller daughter vesicles, $c_{0,\text{large}}$ and $c_{0,\text{small}}$. Figure 3 shows as a function of the constant η the mean vesicle number doubling time, which in this case is the mean of the times in which the larger and the smaller vesicles reach the budded shape.

Discussion

The main implication of the present analysis is that growing vesicles may exhibit self-reproduction behaviour only if a certain combination of their material constants matches the growth rate of their membranes. In the case of vesicles that behave according to the spontaneous curvature model, the condition for self-reproduction behaviour can be expressed as the inequality of Eq. (13). The resulting requirement for vesicle material constants suggests a selectivity mechanism for the respective membrane properties. Vesicles formed in an environment that brings about a constant increase of the area of their membranes are in general expected to grow into a population exhibiting a very large variety of vesicle sizes and compositions (Segre et al. 2001). The present analysis suggests that each vesicle whose membrane material properties and membrane area growth rate satisfy Eq. (13), and grows in an environment that stimulates vesicle fission, produces a pair of daughter vesicles. The number of such vesicles would thus increase exponentially and could therefore greatly exceed the number of vesicles that do not self-reproduce. There is also a distinction between self-reproducing vesicles. Those that have larger doubling times would increase their number at a slower rate than faster reproducing vesicles. Consequently, in the long term, the number of vesicles which increase their number with a doubling time just above T_d would greatly exceed the number of more slowly duplicating vesicles. Eventually, the vesicles that have their properties interrelated in accordance with the near equality version of the condition of Eq. (13) would become the most numerous. It can thus be anticipated that the corresponding membrane composition is a selected membrane composition, in contrast to all other vesicle membrane compositions.

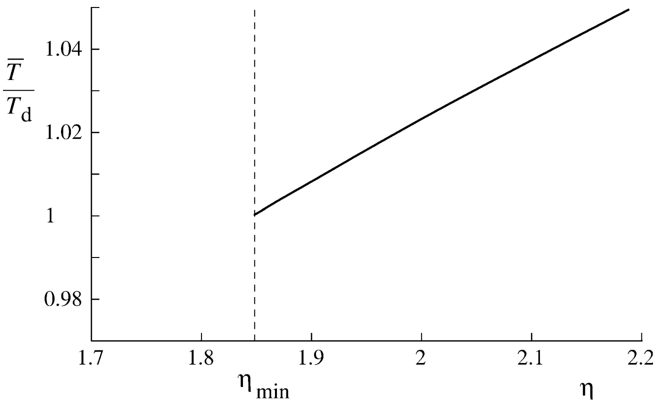

Fig. 3 The dependence of the mean vesicle number doubling time of two daughter vesicles divided by the time taken for the membrane to double its area ($\overline{T}/T_d$) on the constant η. $\eta_{\min}$ denotes the minimum value of the constant η at which the budding occurs

In the present analysis we employed a simple spontaneous curvature model characterized by membrane material properties that do not depend on vesicle size and shape. In particular, the membrane spontaneous curvature (C_0) does not change during vesicle growth. The spontaneous curvature model has been successfully applied in studies of the shape behaviour of many different vesicular systems, and has been directly verified in the case of catanionic vesicles (Jung et al. 2001). The structural parameter of the spontaneous curvature model is the membrane spontaneous curvature. It can arise as a consequence, for instance, of differences in the properties of the outside and inside solutions, of an asymmetric distribution of the membrane constituents in between the two leaflets of the bilayer membrane of mixed composition, or of asymmetrically shaped transmembrane membrane-embedded constituents. Vesicle sizes obtained by inserting values of some known membrane material properties into Eq. (13) accord with the sizes of commonly observed vesicles; for a typical phospholipid membrane, with a water permeability coefficient of 100 μm/s (Olbrich et al. 2000) and bending modulus 10^{-19} J (Rawicz et al. 2000), the predicted equilibrium radii of vesicles, corresponding to doubling times of between 10 minutes and one day, range between 150 nm and 500 nm. In a simple spontaneous curvature model the membrane is supposed to be laterally homogeneous. However, this model was also shown to be effectively valid when membrane curvature affects the local composition of the vesicle membrane (Seifert 1993; Kralj-Iglič et al. 1996). Altogether, all quoted reasons support the use of the spontaneous curvature model in the investigations of the mechanical aspects of the process of vesicle self-reproduction. Moreover, this model is also an appropriate choice to demonstrate theoretically the basics of the self-reproducing behaviour of vesicular systems because of its well-documented shape behaviour (Deuling and Helfrich 1976; Seifert et al. 1991).

In the treated simple model of vesicle self-reproduction we certainly did not include all properties of different vesicular systems that could have a role in this process. Possible generalizations of the described model may involve a more complex description of the membrane mechanical properties due to, for instance, an effect of membrane curvature on the membrane spontaneous curvature C_0, alternative driving forces for the flow of solvent through the membrane, and the dependence of the uptake of membrane constituents on the vesicle shape or on membrane composition. The corresponding more complex, growing vesicular systems would require different treatments of their shape transformations. It is nevertheless reasonable to assume that such systems would exhibit a similar qualitative behaviour, the only difference being in the detailed expressions for the criterion (13) and for the rate equations such as Eqs. (6) and (12). Namely, the main conclusion of the model presented here, that vesicle self-reproduction can occur only for selected values of the membrane material constants, is a consequence of the limitations in the system to exhibit the vesicle budding. In this respect it has to be noted that the property of shape phase diagrams to exhibit budded shapes is a more general property of vesicular systems than it appears to be in the spontaneous curvature model in which it is the consequence of the dependence of the bending energy on the membrane spontaneous curvature. In particular, in systems with membranes that are composed of layers, the budding occurs due to interlayer geometrical constraints independently of their molecular details (Svetina and Žekš 1989). It can thus be anticipated that there is a variety of possible vesicular systems for which a relationship between vesicle physical properties could be found, analogous to Eq. (13).

Vesicles could have existed in the primordial aqueous environment which contained lipid and other amphiphilic molecules, either produced by synthesis or acquired by deposition of extraterrestrial material (Deamer 1997). It has already been suggested that vesicle physical properties may have played a role in the prebiotic evolution of cellular life (Morowitz et al. 1988; Deamer 1997; Norris and Raine 1998; Luisi et al. 1999; Segre et al. 2001). The recently verified (Berclaz et al. 2001) ability of vesicles to self-reproduce is certainly such a property. Our analysis, based on a plausible model of vesicle fission, indicates that the ability of vesicles to self-reproduce is also inherently related to the requirement to select the composition of their membranes. This property of the system can be ascribed to the general shape behaviour of vesicular systems and it is therefore justifiable to assume that it could have been exhibited also by prebiotic vesicles. The possible consequent accumulation of large amounts of vesicles with a rather narrow variation in their composition could then have served as an efficient template for other processes that led to the emergence of a cell.

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