Deformability of Multilamellar Vesicles*

M. Richterová and V. Lisý

Department of Biophysics, Institute of Physics, P. J. Šafárik University, Košice, Slovakia
E-mail: richterova@fyzika.utc.sk

Abstract. Although a free unilamellar vesicle has zero or almost zero genuine surface tension, the multilamellar vesicle ("onion") exhibits a nonzero effective surface tension σ_{eff}. The expression for σ_{eff} used in the literature is $\sigma_{\text{eff}} \sim \sqrt{\kappa B/d_0}$, where B is the interaction modulus between the vesicle bilayers, d_0 the repeating distance between the bilayers in the droplet, and κ their bending rigidity. In this paper we calculate the contributions to the effective surface tension of a lamellar droplet in the case when the layers interact with one another and when they are free. It is shown that the interaction contribution to the surface tension is small and σ_{eff} is determined mainly by κ, the radius of the droplet R_0, and the number of the shape undulation modes $l_{\max}$. A nonzero surface tension of the layers is also included in the calculation which is necessary when the vesicle membrane is stressed in the complex of other membranes.

Key words: Multilamellar vesicle — Effective surface tension — Deformation energy

Introduction

It is now widely accepted in the literature that the density of the surface energy of a lipid-bilayer membrane of vesicles or a surfactant monolayer of microemulsion droplets can be expressed in the form (Canham 1970; Helfrich 1973)

$$\varepsilon = \sigma + \frac{1}{2}\kappa\left(\frac{1}{R_1} + \frac{1}{R_2} - \frac{2}{R_s}\right)^2 + \frac{\bar{\kappa}}{R_1 R_2} \tag{1}$$

where σ is the microscopic surface tension, R_i are the local curvature radii, and κ and $\bar{\kappa}$ are the bending and Gaussian rigidity, respectively (Borkovec 1992). For vesicles it is assumed (Seifert 1997) that the vesicle has no genuine surface tension, i.e. $\sigma = 0$. However, the situation changes in the case of multilamellar droplets. It

Correspondence to: Vladimír Lisý, Department of Biophysics, Institute of Physics, P. J. Šafárik University, Jesenná 5, 041 54 Košice, Slovakia. E-mail: lisy@upjs.sk

* The results were presented on 1st Symposium of Slovak Biophysical Society (Herľany, Slovakia, September 12–15, 2004).

has been shown by van der Linden and Dröge (1993) that such a vesicle exhibits an effective surface tension (σ_{eff}) which is nonzero even if the bilayers themselves have zero surface tension. The vesicle was modeled by a system of large number of concentric membranes of small thickness d. The membranes are separated by water layers of thickness $d_w \gg d$. Such layers in a solvent deform due to the fluctuations in the shape. Another contribution to the deformations of the layers is connected with the interaction between the layers. From the comparison of the deformation energy with the energy of deformation as it would be for a layer changing its surface area and exhibiting the surface tension σ_{eff}, the latter effective parameter has been determined (van der Linden and Dröge 1993; van der Linden et al. 1996),

$$\sigma_{\text{eff}} = \left[\frac{l\,(l+1)}{(l-1)\,(l+2)}\frac{\kappa B}{d_0}\right]^{1/2} \tag{2}$$

Here B is a constant of interaction between the layers, $d_0 = d + d_w$, and the index $l = 2, 3, \ldots$ numbers the deformation modes. For large l, Eq. (2) becomes identical with the result for planar symmetry of the lamellar phase (de Gennes 1974). The conclusion that the effective surface tension of the multilamellar vesicle is nonzero even for zero surface tension of the bilayer is true. In the following we, however show, that σ_{eff} considerably differs from Eq. (2). This is a consequence of the bending energy contribution to the deformation energy (not considered by van der Linden and Dröge 1993; van der Linden et al. 1996), as it follows from Eq. (1), and a very large number of deformation modes, $l_{\max}$, for large lamellar droplets. Since the result of Eq. (2) is often used in the literature (for recent papers see: Courbin et al. 2001; Leng et al. 2001; Soubiran et al. 2001; Versluis et al. 2001; Gradzielski 2003), e.g. in the calculations of the size of lamellar droplets (van der Linden et al. 1996) or modeling the forces exerted on a vesicle under stress (Berni et al. 2002), a discussion on the appropriate expression for the σ_{eff} is of interest. In the next section we present the calculation of the effective surface tension of a unilamellar vesicle with zero microscopic surface tension. Then the case of multilamellar droplets is considered. As distinct from the work by van der Linden and Dröge (1993), we do not assume the zero surface tension of the layers. This assumption is valid for a free vesicle but does not hold in the case when the membrane is a part of a more complex structure, in particular, when it is stretched between bulky aggregates of membranes (Lebedev and Muratov 1989).

Methods

Calculations of the effective surface tension

Let us first consider a unilamellar spherical vesicle of the equilibrium radius R_0. Its surface energy density is assumed to be given by Eq. (1) with $\sigma = 0$ and $R_s = \infty$. The deviation from the spherical equilibrium shape is described by the multipole

expansion (Bohr and Mottelson 1975) in spherical harmonics,

$$R(\vartheta,\varphi) - R_0 = \sum_{lm} u_{lm} Y_{lm}(\vartheta,\varphi) \tag{3}$$

with $0 \le l \le l_{\max}$ and m changing from $-l$ to l. The number of the modes can be estimated as $l_{\max} \sim R_0/a$, where a is a typical molecular diameter (Sparling and Sedlak 1989; Palmer and Morse 1996). The deformation energy (E_s) expressed through the fluctuation amplitudes (u_{lm}) is (Sparling and Sedlak 1989)

$$\Delta E_S = \frac{1}{2R_0^2} \sum_{l\neq 0,m} \kappa l(l+1)(l-1)(l+2)\left|u_{lm}\right|^2 \tag{4}$$

This change of the vesicle free energy due to the deviation from the spherical shape is connected to the change of the surface area (A) of the droplet (keeping the vesicle volume constant),

$$\Delta A = \frac{1}{2} \sum_{l\neq 0,m} (l-1)(l+2)\left|u_{lm}\right|^2 \tag{5}$$

The effective surface tension is thus

$$\sigma_{\text{eff}} = \frac{\Delta E_S}{\Delta A} = \frac{1}{R_0^2}\left[\sum_{l\neq 0,m} \kappa l(l+1)(l-1)(l+2)\left|u_{lm}\right|^2\right] \cdot \left[\sum_{l\neq 0,m} (l-1)(l+2)\left|u_{lm}\right|^2\right]^{-1} \tag{6}$$

Often only the most dominant ellipsoidal mode (giving the main contribution to the thermodynamic quantities) is considered; then $\sigma_{\text{eff}} \approx 6\kappa/R_0^2$. However, it is not correct to consider an arbitrary individual mode (l) to calculate from Eqs. (4) and (5) the quantities $\Delta E_{S,l}$ and ΔA_l, and to combine $\sigma_{eff,l}$ depending on the mode number l as it was done by van der Linden et al. (1996). In general, one must start with the whole sums determining the quantities $\Delta E_{S,l}$ and ΔA_l. The question arises how to use the above expressions to estimate the effective surface tension when all the modes contribute in Eqs. (4) and (5). We use here the estimation that consists in replacing $|u_{lm}|^2$ by their averages over the thermal fluctuations (Borkovec 1992):

$$\left\langle \left|u_{lm}\right|^2 \right\rangle = \left\langle u_{l0}^2 \right\rangle \approx \frac{k_B T}{\alpha_l (l-1)(l+2)} \quad \alpha_l \equiv \sigma + \frac{2\kappa}{R_s^2} - \frac{4\kappa}{R_s R_0} + \frac{\kappa l(l+1)}{R_0^2} \tag{7}$$

For true vesicles, the expression for α_l simplifies since we have $\sigma = 0$ and $R_s = \infty$. Substituting Eq. (7) into (4) and (5), one obtains the change in the free energy of the droplet and the corresponding change of the droplet surface area. This gives for the estimation of the effective surface tension

$$\sigma_{\text{eff}} \approx \left[\frac{k_B T}{2}\sum_{l=2}^{l_{\max}} (2l+1)\right]\left[\frac{k_B T R_0^2}{2\kappa}\sum_{l=2}^{l_{\max}}\left(\frac{1}{l}+\frac{1}{l+1}\right)\right]^{-1} \approx \frac{\kappa}{2R_0^2}\frac{l_{\max}^2}{\ln l_{\max}} \tag{8}$$

assuming very large $l_{\max}$ that holds for vesicles having a typical radius of 10^4 Å.

Results

Multilamellar vesicles ($\sigma = 0$)

The same method of calculation can be applied to the case of multilamellar vesicles assuming zero surface tension of its layers (van der Linden and Dröge 1993). If there is no interaction between the layers, the effective surface tension of the droplet is that given in the preceding section since only the outer layer is observed. When the layers interact, one proceeds similarly as van der Linden et al. (1996). The deformation of the n^{th} layer is

$$R_n(\vartheta,\varphi) = r_n\left[1 + \sum_{lm} a_{lm,n} Y_{lm}(\vartheta,\varphi)\right] \tag{9}$$

The coefficients $a_{lm,n}$ are dimensionless since $u_{lm,n} = r_n a_{lm,n}$ depend on the radius r_n of the layer in equilibrium. We express $a_{lm,n}$ through $a_{lm}^{(0)}$ in the absence of interaction, which are the same for all independent layers,

$$a_{lm,n} = R(r_n)\, a_{lm}^{(0)} \tag{10}$$

The unknown function R describes the spatial correlation between the layers due to interaction. The deformation energy for the l^{th} mode is then

$$\begin{aligned}\Delta E_{SI} &= \frac{1}{2}\kappa l(l+1)(l-1)(l+2)\sum_m \left|a_{lm}^{(0)}\right|^2 R^2(r_n) = \\ &= \frac{\kappa}{2d_0} l(l+1)(l-1)(l+2)\int_0^{R_0} \mathrm{d}r R^2\left(r\sum_m \left|a_{lm}^{(0)}\right|^2\right)\end{aligned} \tag{11}$$

the second equation being written in the continuum limit ($d_0/R_0 \ll 1$). The interaction energy is (de Gennes 1974)

$$\Delta E_I = \frac{1}{2}B\int\left[\nabla_r R(r)\, r\sum_m a_m^{(0)} Y_{lm}(\vartheta,\varphi)\right]^2 r^2 \mathrm{d}r\mathrm{d}\Omega \tag{12}$$

After the integration over the spatial angle Ω we have

$$\Delta E_I = \frac{1}{2}B\sum_m \left|a_{lm}^{(0)}\right|^2 \int_0^{R_0} \mathrm{d}r\left\{R^2 r^2 + 2RR' r^3 + R'^2 r^4\right\} \tag{13}$$

The function R is now found minimizing the total change of the energy $\Delta E = \Delta E_{SI} + \Delta E_I$. This is done using the variational principle. The Euler–Lagrange equation is

$$r^4 R'' + 4r^3 R' + \left(2r^2 - \lambda_l^2\right) R = 0 \qquad \lambda_l^2 \equiv \frac{\kappa}{d_0 B} l(l+1)(l-1)(l+2) \tag{14}$$

The solution of this equation, after the exclusion of the singularity at $r = 0$, is

$$R(r) = \frac{R_0}{r} \exp\left(-\frac{\lambda_l}{r} + \frac{\lambda_l}{R_0}\right) \tag{15}$$

This solution describes how the deformation of the outer layer is transferred to inner layers. The full energy for the l^{th} mode is thus, using Eqs. (11) and (13),

$$\Delta E = \frac{1}{2} B \lambda_l R_0^2 \sum_m \left|a_{lm}^{(0)}\right|^2 \tag{16}$$

If only the most dominant $l = 2$ mode is considered, we would have, using the expression for the change of the surface area at deformation,

$$\Delta A = \frac{R_0^2}{2} (l-1)(l+2) \sum_{lm} \left|a_{lm}^{(0)}\right|^2 \tag{17}$$

and the effective surface tension due to interaction is

$$\sigma_{\text{eff,int}} = \left[\frac{l(l+1)}{(l-1)(l+2)} \frac{\kappa B}{d_0}\right]^{1/2} = \left[\frac{3}{2} \frac{\kappa B}{d_0}\right]^{1/2} \tag{18}$$

The result is the same as that found by van der Linden and Dröge (1993), if the incorrect factor 1/2 is dropped out. In a more correct approach the contributions of all modes should be summed, which gives for the total energy change ΔE

$$\Delta E = \frac{R_0^2}{2} \sum_{l \neq 0, m} \lambda_l |a_{lm}^{(0)}|^2 \tag{19}$$

Here $\lambda_l \sim l^2$ for large l, while the corresponding term in the energy of the outer layer that does not interact with other layers,

$$\Delta E_S = \frac{1}{2} \sum_{l \neq 0, m} \kappa l (l+1)(l-1)(l+2) |a_{lm}^{(0)}|^2 \tag{20}$$

behaves as $\sim l^4$. For large l (the case considered by van der Linden and Dröge (1993)) the latter contribution becomes more important than the contribution (19) given by the interaction. In fact, for a typical onion (see below after Eq. (22)) already for $l = 14$ one finds that $\Delta E \approx \Delta E_S$. To estimate the total sums we again use the mean

$$\left\langle \left|a_{lm}^{(0)}\right|^2 \right\rangle = \frac{k_B T}{\kappa l (l+1)(l-1)(l+2)} \tag{21}$$

so that the effective surface tension due to interaction is

$$\sigma_{\text{eff,int}} \sim \sum_l (2l+1) \sqrt{\frac{B}{d_0 \kappa l (l+1)(l-1)(l+2)}} \Bigg/ \sum_l \frac{2l+1}{\kappa l (l+1)} \sim \sqrt{\frac{B\kappa}{d_0}} \tag{22}$$

and it is independent of $l_{\max}$, which is very large for multilamellar vesicles. Using the parameters of a "typical onion" (van der Linden and Dröge 1993) ($R_0 \sim 10^{-6}$ m, $B \sim 10^2$ Jm^{-3}, $\kappa \sim 50 k_B T$, and $d_0 \sim 12$ nm), one estimates at room temperatures $\sigma_{\text{eff,int}} \sim 5 \cdot 10^{-5}$ Nm^{-1}, and for σ_{eff} without interaction, Eq. (8), $\sigma_{\text{eff},0} \sim \left(l_{\max}^2 / \ln l_{\max}\right) \cdot 10^{-7}$ Nm^{-1}. A rough estimate of the maximum number of modes can be done assuming that the total number of undulation modes within $2 \leq l \leq l_{\max}$, which is $n - 4 = (l_{\max} + 3)(l_{\max} - 1) \approx l_{\max}^2$, is determined by the surface area A and the area a^2 *per* independent degree of freedom as $n = A/a^2$ (Palmer and Morse 1996). Taking $a = 10$ Å, one has $l_{\max}$ of order 10^3 so that $\sigma_{\text{eff},0}$ is some three orders larger than $\sigma_{\text{eff,int}}$. The estimation shows that the effective surface tension of multilamellar vesicles is given mainly by the bending energy of the outer layer and not by the interaction energy between the layers, as it is believed in the literature.

Multilamellar vesicles ($\sigma \neq 0$)

As mentioned in Introduction, vesicle membranes in a lamellar droplet can have a nonzero surface tension σ. A generalization of the above results to this case is straightforward. One has just to replace the deformation energy for the l^{th} mode due to the interaction, Eq. (11), by a more general expression

$$\Delta E_{SI} = \frac{1}{2d_0} (l-1)(l+2) \int_0^{R_0} \mathrm{d}r \left[\sigma r^2 + \kappa l (l+1)\right] R^2(r) \sum_m \left| a_{lm}^{(0)} \right|^2 \tag{23}$$

and the deformation energy of the outer layer, in the absence of interaction, is

$$\Delta E_S = \frac{R_0^2}{2} \left[\sigma + \frac{\kappa l (l+1)}{R_0^2}\right] (l-1)(l+2) \sum_m \left| a_{lm}^{(0)} \right|^2 \tag{24}$$

The interaction energy is the same as in Eq. (13). The function $R(r)$ is found minimizing the energy $\Delta E_{SI} + \Delta E_I$ with respect to R, i.e. from the variation of the functional

$$\begin{aligned} F(R, R', r) &= \int_0^{R_0} \mathrm{d}r \left\{ \left[\lambda_l^2 + (\sigma_l / R_0)^2 r^2\right] R^2(r) + r^2 (R + rR')^2 \right\} \\ \sigma_l^2 &\equiv \frac{\sigma R_0^2}{d_0 B} (l-1)(l+2) \end{aligned} \tag{25}$$

The corresponding Euler–Lagrange equations are

$$r^4 R'' + 4r^3 R' + \left[\left(2 - \sigma_l^2 / R_0^2\right) r^2 - \lambda_l^2\right] R = 0 \tag{26}$$

When $\sigma = 0$, we return to the case considered in the preceding section. For $\lambda_l = 0$, the solution is

$$R(r) = r^{\nu_l - 3/2} \quad \nu_l \equiv (1/2) \sqrt{1 + 4 (\sigma_l / R_0)^2} \tag{27}$$

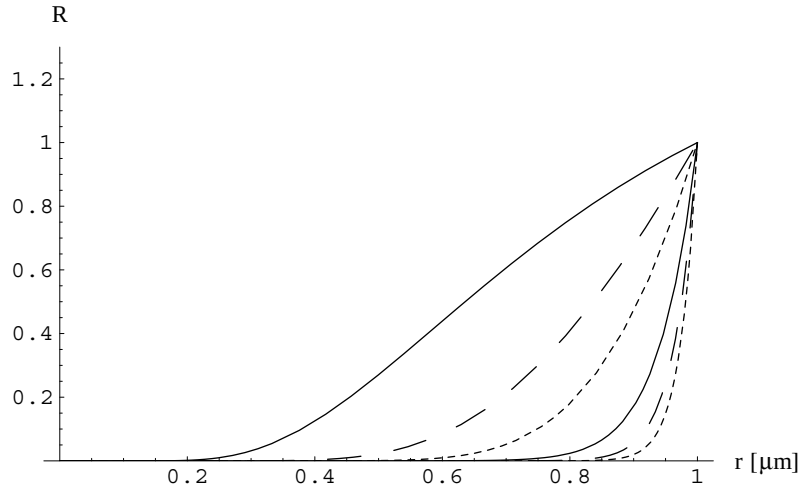

Figure 1. The function $R(r)$ describing the spatial correlation between the layers of a multilamellar vesicle due to the interaction, shown for the lowest deformation modes $l = 2$ (—), 3 (– – –), and 4 ($\cdots$). The upper three curves correspond to zero surface tension of the layers (van der Linden and Dröge 1993), Eq. (15), the lower curves are calculated from Eq. (28) for small σ (10^{-3} mN/m). The graph illustrates the difference between the two approaches for the same vesicle parameters ($R_0 \sim 10^{-6}$ m, $B \sim 10^2$ Jm^{-3}, $\kappa \sim 50 k_B T$, and $d_0 \sim 12$ nm).

Here it is taken into account that R must be finite as $r \to 0$, which requires also the condition $\sigma_l / R_0 \geq \sqrt{2}$. When both σ and λ_l are nonzero, the solution can be expressed through the modified Bessel function I_μ, $\mu \equiv -\nu_l$,

$$R(r) = \left(\frac{R_0}{r}\right)^{3/2} I_\mu\left(\frac{-\lambda_l}{r}\right) I_\mu^{-1}\left(\frac{-\lambda_l}{R_0}\right) \tag{28}$$

Numerical representations of this solution are shown in Figure 1. A notable difference from Eq. (15) is seen even for a very small (on the level of detectability by the current experimental techniques) surface tension σ.

Discussion

Amphiphilic molecules, because of their solubility properties, aggregate into molecularly ordered structures which often take form of bilayers. The resulting aggregates for curve bilayers are called vesicles, widely used as mimics of biological membranes. The vesicle phase can consist of unilamellar or multi lamellar vesicles. When the amphiphilic molecules are phopholipids, the vesicles are known as liposomes. Liposomes, due to their unique properties, such as encapsulation, permeability, and

similarity to biological systems, have received considerable attention and are candidates for novel applications, e.g. in drug delivery, biochemical catalysis and cosmetics (Lasic 1993). The vesicles are known to display complex physical behaviors, some of which are only now beginning to understand (Pozo-Navas et al. 2003). A number of questions is to be answered, in particular the mechanism for the shear-induced change in conformation from sheet-like lamellae into the onion-like droplets and the exact nature of these droplets (Berni et al. 2002). The physical properties of these systems are essentially determined by the properties of the droplet membranes and, in the case of multilamellar vesicles, the interactions between the bilayers together with the effects of the bilayer undulations have to be considered. In the present paper simple but very successful phenomenological theory by Canham (1970) and Helfrich (1973) has been applied to a particular problem of the effective surface tension of multilamellar vesicles. The result that can be found in the literature (van der Linden and Dröge 1993; van der Linden et al. 1996) is based on the calculation of the deformation energy due to interaction between the layers. Only one deformation mode l is considered and the surface tension of individual membranes is assumed to be zero. The effective surface tension σ_{eff} is then obtained from this deformation energy and the change of the surface, for very large l. We have shown that this approach should be corrected in several points. First, for large l, the contribution of the Helfrich bending energy of the membrane is important and can be even dominant in σ_{eff}. Moreover, the membrane stressed in the complex of other membranes should exhibit also a nonzero surface tension. This must be taken into account in the consideration of the vesicle deformability. We have shown that this influences the effective interaction between the membranes and the exact formula for the transfer of the deformation between the layers has been obtained. The found results can be applied e.g. in modeling the properties of "onions" and interpretation of rheometry experiments (Bergenholtz and Wagner 1996), where σ_{eff} is used to construct the balance between a viscous force exerted by the flow field and an elastic force (determined by σ_{eff}) required to maintain a vesicle at a given size.

References

Bergenholtz J., Wagner N. J. (1996): Formation of AOT/Brine multilamellar vesicles. Langmuir **12**, 3122—3126

Berni M. G., Lawrence C. J., Machin D. (2002): A review of the rheology of the lamellar phase in surfactant systems. Adv. Coll. Interface Sci. **98**, 217—243

Borkovec M. (1992): Phenomenological theories of globular microemulsions. Adv. Coll. Interface Sci. **37**, 195—217

Bohr A., Mottelson B. R. (1975): Nuclear Structure, Volume II: Nuclear Deformations. W. A. Benjamin Inc., New York

Canham P. B. (1970): The minimum energy of bending as a possible explanation of the biconcave shape of the human red blood cell. J. Theor. Biol. **26**, 61—81

Courbin L., Cristobal G., Rouch J., Panizza P. (2001): Closed compact Taylor's droplets in a phase-separated lamellar-sponge mixture under shear flow. Europhys. Lett. **55**, 880—886

de Gennes P. G. (1974): The Physics of Liquid Crystals (1st ed.), Oxford University Press
Gradzielski M. (2003): Vesicles and vesicle gels – structure and dynamics of formation. J. Phys.: Condens. Matter **15**, R655—697
Helfrich W. (1973): Elastic properties of lipid bilayers: theory and possible experiments. Z. Naturforsch., C **28**, 693—703
Lasic D. D. (1993): Liposomes. From Physics to Application. Elsevier, New York
Lebedev V. V., Muratov A. R. (1989): Dynamics of micelles and vesicles. Sov. Phys. JETP **68**, 1011—1022
Leng J., Nallet F., Roux D. (2001): Anomalous elasticity of an ordered lamellar liquid foam. Eur. Phys. J. E, Soft Matter **4**, 337—341
Palmer K. M., Morse D. C. (1996): Statistical mechanics of microemulsions: Droplet phases and macroscopic interfaces. J. Chem. Phys. **105**, 11147—11174
Pozo-Navas B., Raghunathan V. A., Katsaras J., Rappolt M., Lohner K., Pabst G. (2003): Discontinuous unbinding of lipid multibilayers. Phys. Rev. Lett. **91**, Art. No. 028101
Seifert U. (1997): Configurations of fluid membranes and vesicles. Adv. Phys. **46**, 13—137
Soubiran L., Staples E., Tucker I., Penfold J., Creeth A. (2001): Effects of shear on the lamellar phase of a dialkyl cationic surfactant. Langmuir **17**, 7988—7994
Sparling L. C., Sedlak J. E. (1989): Dynamic equilibrium fluctuations of fluid droplets. Phys. Rev., A **39**, 1351—1364
van der Linden E., Dröge J. H. M. (1993): Deformability of lamellar droplets. Physica A **193**, 439—447
van der Linden E., Hogervorst W. T., Lekkerkerker H. N. W. (1996): Relation between the size of lamellar droplets in onion phases and their effective surface tension. Langmuir **12**, 3127—3130
Versluis P., van de Pas J. C., Mellema J. (2001): Influence of salt concentration and surfactant concentration on the microstructure and rheology of lamellar liquid crystalline phases. Langmuir **17**, 4825—4835

Final version accepted: October 21, 2004