Calculating the bending moduli of the Canham–Helfrich free-energy density from a particular potential

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Abstract
The Canham–Helfrich free-energy density for a lipid bilayer involves the mean and Gaussian curvatures of the midsurface of the bilayer. The splay and saddle-splay moduli $\kappa$ and $\bar{\kappa}$ regulate the sensitivity of the free-energy density to changes of these curvatures. Seguin and Fried derived the Canham–Helfrich energy by taking into account the interactions between the molecules comprising the bilayer, giving rise to integral representations for the moduli in terms of the interaction potential. In the present work, a specific potential is chosen and the integrals are evaluated to yield explicit expressions for the moduli—which are found to depend on two parameters associated with the potential. Adjusting these parameters yields values for $\kappa$ and $\bar{\kappa}$ consistent with most values reported in the literature.

Keywords: interaction potential; lipid molecules; splay modulus; saddle-splay modulus; biomembrane; vesicle; curvature elasticity

1 Introduction

Biomembranes are ubiquitous in nature. An essential element of a biomembrane is a lipid bilayer, which is composed of phospholipid molecules. These molecules have hydrophilic head groups and a pair of hydrophobic tails. Due to these properties, when a large number of lipid molecules are placed in a solution they self assemble, under suitable conditions, into two-dimensional structures consisting of two leaflets (or monolayers). The lipid molecules are oriented so that the tails of the molecules in each leaflet are in contact with each other, while the head groups are in contact with the suspending solution; see, for example, Lasic [13]. These two-dimensional structures often close to form vesicles and are usually between 50 nanometers and tens of micrometers in diameter but only a few nanometers thick, as observed by Luisi and Walade [15]. Due to these dimensions, lipid bilayers are usually modeled as surfaces.

An accepted expression for the free-energy density of a lipid bilayer takes the form

$$\psi = \frac{1}{2} \kappa (H - H_0)^2 + \bar{\kappa} K,$$

where $H$ and $K$ denote the mean and Gaussian $K$ curvatures of the midsurface of the bilayer, $\kappa$ and $\bar{\kappa}$ are the splay and saddle-splay moduli, respectively, and $H_0$ is the spontaneous mean-curvature,
which describes the natural, local shape of the bilayer. While Helfrich [11] first suggested (1.1) as a model for lipid bilayers, Canham [4] previously proposed (1.1) with $H_0 = 0$ as a model for red blood cells. The expression (1.1) is therefore commonly called the Canham–Helfrich free-energy density.

Most often, $\kappa$ and $\bar{\kappa}$ are viewed as constant material parameters, as is $H_0$, and this view is adopted here. Whereas $\kappa$ is always positive and can be measured in numerous ways, including, for example, flicker spectroscopy (Brochard and Lennon [3], Schneider, Jenkins and Webb [17]) and x-ray scattering (Liu and Nagle [14], Tristram-Nagle and Nagle [21]), $\bar{\kappa}$ is more difficult to quantify. Part of the problem in determining $\bar{\kappa}$ is related to the Gauss–Bonnet theorem (do Carmo [5]), which states that the integral of the Gaussian curvature $K$ over a surface depends only on the topology and boundary of that surface. Granted that $\bar{\kappa}$ is constant and that the bilayer is closed, the second term on the right-hand side of (1.1) therefore plays a role only in particular processes, such as fusion and fission events.

Despite this difficulty, experimental and numerical strategies for obtaining $\bar{\kappa}$ do exist. As $\kappa$ is relatively easily obtained, it is convenient to specify $\bar{\kappa}$ through the ratio $\bar{\kappa}/\kappa$. This ratio is typically found to be negative, with magnitude depending on the constitution of the bilayer. While experiments conducted by Baumgart, Das, Webb and Jenkins [1] and by Lorzen, Servuss and Helfrich [16] delivered values close to −1 (namely $−0.9 \pm 0.38$ and $−0.83 \pm 0.12$, respectively), experiments conducted by Semrau et al [20] delivered values between $−0.63$ and $−0.31$. Course-grained numerical simulations performed by Hu, Brigugli and Deserno [8] and Hu et al [9] yielded values $−0.95 \pm 0.1$ and $−1.04 \pm 0.03$, respectively.

A derivation of the Canham–Helfrich free-energy density based on considering the interactions between the lipid molecules that comprise the bilayer was carried out by Seguin and Fried [18]. That derivation provides integral representations for the moduli in terms of a generic interaction potential. In the present work, a particular interaction potential is chosen and the integrals are evaluated to obtain $\kappa$ and $\bar{\kappa}$. Before performing these calculations, two simplifying postulates are imposed: the lipid molecules comprising the bilayer are assumed to be (a) identical and (b) uniformly distributed. The resulting moduli are given in terms of five parameters. Aside from the molecular number density, two of these parameters are determined by the dimensions of the lipid molecules and the remaining two appear in the interaction potential. It is shown that the two parameters coming from the interaction potential can be chosen so that the resulting moduli take values consistent with those appearing in the current literature.

The paper is organized as follows. Synopses of the salient features of surface geometry and the derivation of Seguin and Fried [18] appear in Sections 2 and 3, respectively. Section 4 contains two parts, the first devoted to introducing the particular potential used here and the second devoted to determining and interpreting the associated splay and saddle splay moduli $\kappa$ and $\bar{\kappa}$.

## 2 Geometry of surfaces

Consider a smooth, orientable surface $S$ in a three-dimensional Euclidean point space. Let $n$ denote a smooth mapping that determines a unit-normal at each point of the surface. Given a mapping $h : S \rightarrow W$ defined on the surface that takes values in some vector space $W$, the surface gradient $\nabla^Sh$ of $h$ can be defined by

\[
\nabla^Sh := \nabla_x h^\circ(1 - n(x) \otimes n(x)) \quad \text{for all } x \in S,
\]

where $h^\circ$ is an extension of $h$ to a neighborhood of $x$ and $\nabla_x h^\circ$ is the classical three-dimensional gradient of this extension at $x$. Importantly, it can be shown that the definition of the surface gradient is independent of the extension appearing on the right-hand side of (2.1).
Of particular interest is the negative \( L := -\nabla^S n \) of the surface gradient \( \nabla^S n \) of \( n \)—called the curvature tensor, which is a second-order tensor field defined on \( S \). The tensor \( L \) is symmetric and has two scalar invariants: the mean curvature \( H \) and Gaussian curvature \( K \), as defined by

\[
H := \frac{1}{2} \text{tr} L \tag{2.2}
\]

and

\[
K := \frac{1}{2} \left[ (\text{tr} L)^2 - \text{tr}(L^2) \right]. \tag{2.3}
\]

If \( \kappa_1 \) and \( \kappa_2 \) are the two nontrivial eigenvalues of \( L \), often called the principle curvatures, then (2.2) and (2.3) yield

\[
H = \frac{1}{2}(\kappa_1 + \kappa_2) \quad \text{and} \quad K = \kappa_1 \kappa_2. \tag{2.4}
\]

3 Recapitulation of the derivation of the Canham–Helfrich free-energy density

The derivation of Seguin and Fried [18] rests on four assumptions:

(i) the thickness of the bilayer is small relative to its average diameter;

(ii) the (phospholipid) molecules can be modeled as one-dimensional rigid rods;

(iii) the molecules do not tilt relative to the orientation of the bilayer;

(iv) interactions between the bilayer and the solution are negligible.

Assumption (i), which is often made in models for lipid bilayers (Luisi and Walade [15]), allows the lipid bilayer to be identified with its midsurface \( S \). This surface may adopt a large variety of shapes; however, being made up of molecules of a finite size, it cannot support arbitrarily large curvatures. Let \( \ell \) denote the smallest stable radius of curvature that \( S \) may exhibit.

For each leaflet \( i = 1, 2 \) of the bilayer, introduce a molecular number density \( W_i \) defined on \( S \) and measured per unit area of \( S \). Let \( da_y \) denote the area element on \( S \). The total number of molecules in leaflet \( i = 1, 2 \) is then given by the integral

\[
\int_S W_i(y) \, da_y. \tag{3.1}
\]

Taking \( W_i \) to be defined on \( S \) amounts to assuming that the centers of the lipid molecules of both leaflets lie on \( S \), which is consistent with assuming that the bilayer is thin relative to its average diameter. In general, the number densities of the leaflets may differ.

On the basis of Assumption (ii), the configuration of each molecule in the bilayer may be described by a point on \( S \) and a unit-vector-valued director, with the point representing the center of the rod and the director representing the orientation of the rod. Without loss of generality, it is assumed that the director tips point toward the headgroups of the molecules. It is further assumed that the interaction between a pair of molecules at two different points on \( S \) is governed by a potential that depends on a vector connecting the points and the directors at the points and is restricted such that only molecules separated by distances less than some fixed cutoff distance \( d \) may interact. Moreover, the cutoff distance \( d \) is required to be small relative to the smallest radius of curvature \( \ell \) the bilayer can support, so that \( d \ll \ell \) or, equivalently,

\[
\epsilon := \frac{d}{\ell} \ll 1. \tag{3.2}
\]
As will be discussed in the next section, instead of possessing a cutoff distance many potentials decay rather rapidly as the distance between the interacting molecules increases. For such potentials, it is sometimes possible to define an effective cutoff distance beyond which the interaction is negligible and, thus, may be neglected.

Choose points \(x\) and \(y\) on \(\mathcal{S}\) and consider a molecule at \(x\) with orientation \(e\) and a molecule at \(y\) with orientation \(f\). Suppose that interactions between the molecules at \(x\) and \(y\) are governed by a potential \(\Phi\), with dimensions of energy, depending on the vectors \(r = x - y\), \(e\), and \(f\). Granted that \(\Phi\) is frame-indifferent, its dependence on these quantities must reduce to dependence on the scalars \(r \cdot r\), \(r \cdot e\), \(r \cdot f\), and \(e \cdot f\). Assume that this dependence takes the form
\[
\Phi(r, e, f) = \phi(\epsilon^{-2} r \cdot r, r \cdot e, r \cdot f, e \cdot f),
\]
where \(\phi\) satisfies
\[
\phi(s, a, b, c) = 0 \quad \text{if } s \geq \ell \quad \text{for all } (a, b, c) \in \mathbb{R} \times \mathbb{R} \times [-1, 1].
\]
The stipulation (3.4) ensures that the molecules at \(x\) and \(y\) interact only if the distance \(r = |r|\) between \(x\) and \(y\) obeys
\[
r < d = \epsilon \ell.
\]
In contrast to \(\Phi\), \(\phi\) is independent of \(d\). Importantly, the interaction energy \(\phi\) between two molecules can change on flipping the head group and tails of one of the molecules. Interaction potentials of this form may therefore account for differences between the polarities of the head group and tails of a lipid molecule. Taking \(\Phi\) to depend on the cutoff distance \(d\) as indicated in (3.3) is motivated by the work of Keller and Merchant [12].

Aside from potentials \(\Phi_{11}\) and \(\Phi_{22}\) that account for interactions between molecules in each leaflet, it is generally necessary to consider a potential \(\Phi_{12} = \Phi_{21}\) that accounts for interactions between molecules belonging to different leaflets. Although the particular forms of the potentials \(\Phi_{11}, \Phi_{22},\) and \(\Phi_{12} = \Phi_{21}\) may differ, they share the same general properties to the extent that they satisfy (3.3) and (3.4).

Without loss of generality, orient \(\mathcal{S}\) with a unit-normal field that points into the region adjacent to the head groups of leaflet 1 and denote that field by \(n\). On the basis of Assumption (iii), it follows that the directors of molecules in leaflets 1 and 2 coincide with \(n\) and \(-n\), respectively. Bearing in mind the cutoff property (3.4), define \(\mathcal{S}_d(x)\) by
\[
\mathcal{S}_d(x) := \{y \in \mathcal{S} : |x - y| \leq d\}.
\]
Seguin and Fried [18] argued that the interactions between the lipid molecules making up the bilayer contribute to the free-energy density \(\phi\) through the four terms
\[
\psi_{11}(x) := \int_{\mathcal{S}_d(x)} \Phi_{11}(x - y, n(x), n(y)) W_1(x) W_1(y) \, da_y, \quad \text{(3.7)}
\]
\[
\psi_{22}(x) := \int_{\mathcal{S}_d(x)} \Phi_{22}(x - y, -n(x), -n(y)) W_2(x) W_2(y) \, da_y, \quad \text{(3.8)}
\]
\[
\psi_{12}(x) := \int_{\mathcal{S}_d(x)} \Phi_{12}(x - y, n(x), -n(y)) W_1(x) W_2(y) \, da_y, \quad \text{(3.9)}
\]
\[
\psi_{21}(x) := \int_{\mathcal{S}_d(x)} \Phi_{21}(x - y, -n(x), n(y)) W_2(x) W_1(y) \, da_y. \quad \text{(3.10)}
\]

\footnote{In the work of Seguin and Fried [18], the integrals in (3.7)–(3.10) were scaled by \(\epsilon^{-2}\), following the lead of Keller and Merchant [12]. However, upon evaluating these integrals for a particular potential, it transpires that the results scale more appropriately if the factor of \(\epsilon^{-2}\) is dropped.}
The integral in (3.7) represents the contribution to the free-energy density coming from the interactions between the molecules in leaflet 1 at \( x \) and all other molecules in leaflet 1. The integral in (3.8) is an analogous contribution involving leaflet 2. The integral in (3.9) accounts for the interactions between the molecules in leaflet 1 at \( x \) and all other molecules in leaflet 2. The integral in (3.10) is analogous to that in (3.9), but with the roles of the two leaflets interchanged. By Assumption (iv), these integrals sum to yield the net free-energy density \[ \psi = \psi_{11} + \psi_{22} + \psi_{12} + \psi_{21}. \] (3.11)

On substituting (3.7)–(3.10) into the right-hand side of (3.11), \( \psi \) can be expanded in powers of \( \epsilon \) up to order \( \epsilon^4 \) with the objective of capturing dependence on the curvature of \( S \). This expansion takes the form \[ \psi = \psi_0 + \frac{1}{2} \kappa (H - H_o)^2 + \bar{\kappa} (K - K_o), \] (3.12)

where \( \psi_0, \kappa, \bar{\kappa}, H_o, \) and \( K_o \) are given in terms of \( \Phi_{ij} \) and \( W_i \). In particular, \( \kappa \) and \( \bar{\kappa} \) are of order \( \epsilon^4 \) and terms of order \( o(\epsilon^4) \) are neglected. The quantities \( \phi_0, \kappa, \bar{\kappa}, H_o, \) and \( K_o \) generally depend on the point \( x \) in \( S \). Thus, \( \psi \) may depend on \( x \) through not only the mean and Gaussian curvatures of \( S \) at \( x \) but also through the values of splay and saddle-splay moduli and the spontaneous mean and Gaussian curvatures at \( x \). As Seguin and Fried [18] mentioned, the term \( \psi_0 \) is independent of the shape of the membrane and is not part of the Canham–Helfrich free-energy density. However, due to implicit dependence of the number densities on temperature, concentration, and relevant electromagnetic fields, that term encompasses effects associated with ambient temperature, concentration, and electromagnetic conditions.

Suppose now that:

1. the molecules making up the leaflets of the bilayer are uniformly distributed;
2. all of the molecules comprising the bilayer are identical.

As a consequence of Item 1, there is a constant \( W \) such that \[ W = W_1(x) = W_2(x) \quad \text{for all} \quad x \in S. \] (3.13)

Further, as a consequence of Item 2, there is a potential \( \Phi \) such that \[ \Phi = \Phi_{11} = \Phi_{22} = \Phi_{12} = \Phi_{21}. \] (3.14)

Thus, granted (3.13) and (3.14), the spontaneous curvatures vanish and (3.12) takes the form \[ \psi = \psi_0 + \frac{1}{2} \kappa H^2 + \bar{\kappa} K. \] (3.15)

To provide detailed expressions for \( \psi_0, \kappa, \) and \( \bar{\kappa} \), it is convenient to first introduce the notational conventions \[ \phi_0(s, a) := \phi(s^2, 0, 0, a) \] (3.16)

and \[ \phi_k(s, a) := \frac{\partial \phi(\xi_1, \xi_2, \xi_3, \xi_4)}{\partial \xi_k} \bigg|_{(\xi_1, \xi_2, \xi_3, \xi_4) = (s^2, 0, 0, a)}, \quad k \in \{1, 2, 3, 4\}. \] (3.17)

The term \( \psi_0 \) in (3.15) is given by \[ \psi_0 := 4\pi \epsilon^2 \int_0^\ell \left[ \phi_0(r, 1) + \phi_0(r, -1) \right] W^2 r \, dr \] (3.18)
and the bending moduli \( \kappa \) and \( \bar{\kappa} \) are given by
\[
\kappa := 8(B + C) \quad (3.19)
\]
and
\[
\bar{\kappa} := -2B, \quad (3.20)
\]
with \( B \) and \( C \) defined according to
\[
B := \pi \varepsilon ^4 \int _0 ^\ell \left[ \phi _0 (r, 1) - \phi _4 (r, 1) + \phi _0 (r, -1) + \phi _4 (r, -1) \right] W^2 r^3 \, dr \quad (3.21)
\]
and
\[
C := \frac{3 \pi \varepsilon ^4}{8} \int _0 ^\ell \left[ \phi _1 (r, 1) + \phi _1 (r, -1) \right] W^2 r^5 \, dr. \quad (3.22)
\]

The signs of \( \kappa \) and \( \bar{\kappa} \) are often set by the signs of \( \phi _0, \phi _1, \) and \( \phi _4, \) which are determined by the properties of the potential \( \phi. \) In particular, the sign of \( \phi _1 \) is linked to whether \( \phi \) is attractive or repulsive:

- if the potential is attractive, then \( \phi _1 (r, \pm 1) \geq 0 \) for all \( r; \)
- if the potential is repulsive, then \( \phi _1 (r, \pm 1) \leq 0 \) for all \( r. \)

Potentials may, of course, possess attractive and repulsive domains, as is the case for the Gay–Berne \( \phi _{GB} \) potential \( \phi _{GB}, \) for which the sign of \( \phi _{GB} (r, \pm 1) \) depends on \( r. \) If \( \phi \) obeys (3.4) and is attractive (repulsive), then \( \phi _0 \leq 0 \) (\( \phi _0 \geq 0 \)). Evaluating the potential and its partial derivatives at the values \( (s^2, 0, 0, \pm 1) \) (see (3.16)–(3.18) and (3.21)–(3.22)) is akin to considering side-by-side configurations for the molecules. In particular, the sign of \( \phi _4 (r, \pm 1) \) is linked to whether such a configuration is favorable:

- if side-by-side configurations are favorable, then \( \phi _4 (r, 1) \leq 0 \) and \( \phi _4 (r, -1) \geq 0 \) for all \( r; \)
- if side-by-side configurations are unfavorable, then \( \phi _4 (r, 1) \geq 0 \) and \( \phi _4 (r, -1) \leq 0 \) for all \( r. \)

In view of (3.19)–(3.22) and the foregoing observations, \( \kappa \geq 0 \) and \( \bar{\kappa} \leq 0 \) for a repulsive potential that favors side-by-side configurations but \( \kappa \leq 0 \) and \( \bar{\kappa} \geq 0 \) for an attractive potential that does not favor side-by-side configurations. Since \( \kappa \leq 0 \) is physically unsound, using an attractive potential that does not favor side-by-side configurations is unreasonable. If the potential is neither attractive nor repulsive, then determining the signs of \( \kappa \) and \( \bar{\kappa} \) is more involved.

4 Calculations using a particular potential

In this section, \( \psi _0 \) and the bending moduli \( \kappa \) and \( \bar{\kappa} \) are computed using a given potential and the results are discussed. Prior to this, a few words on the choice of the potential seem appropriate.

4.1 Choosing a potential

The literature is replete with potentials designed to describe the interactions between molecules. Of interest here are potentials appropriate to molecules that resemble one-dimensional rods in the sense that they possess an axis of symmetry and are relatively long in the direction of that axis.

It is possible to consider two categories of pair potentials: those with hard cores and those with soft cores. The energy of a hard-core potential becomes infinite as the distance between the
interacting molecules approaches zero. This property reflects the impossibility of molecular overlap. For a soft-core potential, the energy tends to a finite value as the distance between the molecules approaches zero.

Many potentials for axisymmetric particles exhibit a multiplicative decomposition in which one factor, referred to as the strength parameter, is independent of the distance between the molecules but the other factor depends on the distance and tends to zero as that distance approaches infinity. To illustrate the properties of such a potential, consider axisymmetric particles at \( x \) and \( y \) with respective directors \( \mathbf{d} \) and \( \mathbf{e} \). Introduce the unit vector
\[
\hat{\mathbf{r}} = \frac{\mathbf{r}}{|\mathbf{r}|}, \quad r = |\mathbf{r}|, \tag{4.1}
\]
in the direction of \( \mathbf{r} = x - y \neq \mathbf{0} \). A potential \( \Phi \) manifesting the aforementioned multiplicative decomposition can be written in the form
\[
\Phi(\mathbf{r}, \mathbf{d}, \mathbf{e}) = S(\hat{\mathbf{r}}, \mathbf{d}, \mathbf{e})\Sigma(\mathbf{r}, \mathbf{d}, \mathbf{e}), \tag{4.2}
\]
where \( S \) is the strength parameter\(^2\) and \( \Sigma \) satisfies
\[
\lim_{r \to \infty} \Sigma(\mathbf{r}, \mathbf{d}, \mathbf{e}) = 0. \tag{4.3}
\]
If there is a \( d \) such that
\[
\Sigma(\mathbf{r}, \mathbf{d}, \mathbf{e}) = 0 \quad \text{for all } \mathbf{r} \text{ satisfying } r > d, \tag{4.4}
\]
then \( d \) is the cutoff distance of the potential. If a potential does not possess a cutoff distance but decays rapidly enough in the limit \( (4.3) \), then it is possible to define an effective cutoff distance. If two molecules are separated by a distance greater than an effective cutoff distance, then the interaction is negligibly small. The technique of truncating a potential in this way is described by Earl \[6\]. Whereas the strength parameter \( S \) controls the maximal strength of the interaction, the factor \( \Sigma \) controls the range of the interaction. If \( \Phi \) is a hard-core potential, then
\[
\lim_{r \to 0} \Sigma(\mathbf{r}, \mathbf{d}, \mathbf{e}) = \infty. \tag{4.5}
\]
However, if \( \Phi \) is a soft-core potential, then
\[
\lim_{r \to 0} \Sigma(\mathbf{r}, \mathbf{d}, \mathbf{e}) < \infty. \tag{4.6}
\]

For particles with an axis of symmetry, it is common to consider “Gaussian” potentials. A short survey of such potentials is given by Walmsley \[22\], who observes that for a Gaussian potential it is common to choose \( \Sigma \) to be of the form
\[
\Sigma(\mathbf{r}, \mathbf{d}, \mathbf{e}) = f(r^{-1}\sigma(\hat{\mathbf{r}}, \mathbf{d}, \mathbf{e})), \tag{4.7}
\]
where the range parameter \( \sigma \) is defined to ensure that \( f \) achieves a minimum if \( r = \sigma(\hat{\mathbf{r}}, \mathbf{d}, \mathbf{e}) \). Not all potentials are of type described by \( (4.7) \). A noteworthy exception is due to Gay and Berne \[7\], who use \( \sigma \) but choose an expression for \( \Sigma \) not contained within the class considered by Walmsley \[22\].

In the present work, a soft-core potential of the form \( (4.7) \) is used. This is because the model for the lipid bilayer considered here is continuous rather than discrete. To compute the bending moduli \( \kappa \) and \( \bar{\kappa} \), the interactions between molecules arbitrarily close together must be considered. As a

\(^2\) The strength parameter is commonly denoted by \( \epsilon \), but that symbol has already been used with a different meaning in this work.
consequence of the property (4.5), using a hard-core potential would result in an infinite bending moduli, which is certainly not useful.

For the strength parameter \( S \), an expression proposed by Gay and Berne [7] is used. This expression has the form

\[
S(\hat{r}, d, e) := S_0 S_1(d, e)\nu S_2(\hat{r}, d, e)^\mu,
\]

where \( S_0, \nu, \) and \( \mu \) are parameters to be chosen and where \( S_1 \) and \( S_2 \) are given by

\[
S_1(d, e) := \frac{1}{(1 - \chi(d \cdot e)^2)^{1/2}}
\]

and

\[
S_2(r, d, e) := 1 - \frac{\chi'}{2} \left( \frac{(\hat{r} \cdot d + \hat{r} \cdot e)^2}{1 + \chi'(d \cdot e)} + \frac{\hat{r} \cdot d - \hat{r} \cdot e)^2}{1 - \chi'(d \cdot e)} \right),
\]

with \( \chi \) and \( \chi' \) defined in accord with

\[
\chi := \frac{\rho^2 - 1}{\rho^2 + 1} \quad \text{and} \quad \chi' := \frac{1 - (\epsilon_E/\epsilon_S)^{1/\mu}}{1 + (\epsilon_E/\epsilon_S)^{1/\mu}},
\]

where \( \rho \) is the aspect ratio (length divided by diameter) of a molecule and \( \epsilon_E \) and \( \epsilon_S \) are the strength parameters for side-to-side and end-to-end interactions, respectively. For slender molecules, \( \rho \) is positive and closer to 1 than to 0.

Following Berne and Pechuckas [2], \( \Sigma \) is taken to be of the form

\[
\Sigma(r, d, e) := e^{-\frac{d^2}{\sigma_0 r^2}},
\]

with the range parameter \( \sigma \) given by

\[
\sigma(\hat{r}, d, e) := \frac{\sigma_0}{\left[ 1 - \frac{\chi}{2} \left( \frac{(\hat{r} \cdot d + \hat{r} \cdot e)^2}{1 + \chi(d \cdot e)} + \frac{\hat{r} \cdot d - \hat{r} \cdot e)^2}{1 - \chi(d \cdot e)} \right) \right]^{1/2}},
\]

where, on using \( D \) to denote the diameter of a molecule,

\[
\sigma_0 := \sqrt{2}D.
\]

The particular choice (4.12) of \( \Sigma \) leads to a potential that does not have a cutoff distance. However, as Earl [6] observes, since the potential decays exponentially as the ratio \( r/\sigma_0 \) becomes large, it is reasonable to define an effective cutoff distance

\[
d = 3\sigma_0.
\]

Looking at (3.18)–(3.22), the interaction potential \( \phi \) only enters \( \psi_0 \) and the bending moduli \( \kappa \) and \( \bar{\kappa} \) through the expressions

\[
\phi_0(r, \pm 1) = \frac{S_0}{(1 - \chi^2)^{\nu/2}} e^{-\frac{d^2}{\ell^2 \sigma_0^2}},
\]

\[
\phi_1(r, \pm 1) = -\frac{S_0 d^2}{\ell^2 \sigma_0^2 (1 - \chi^2)^{\nu/2}} e^{-\frac{d^2}{\ell^2 \sigma_0^2}},
\]

\[
\phi_4(r, \pm 1) = \frac{S_0 \nu \chi^2}{(1 - \chi^2)^{1+\nu/2}} e^{-\frac{d^2}{\ell^2 \sigma_0^2}}.
\]
From (4.16)–(4.18) it is clear that \( \psi_0, \kappa, \) and \( \bar{\kappa} \) can be determined without reference to the values of \( \mu \) and \( \chi' \). The values of \( \psi_0, \kappa, \) and \( \bar{\kappa} \) are, however, influenced by \( \nu, S_0, \sigma_0, \) and \( \chi \). As it transpires that working with \( \sigma_0 \) and \( \chi \) is more convenient than working with \( \rho \) and \( D \), only \( \sigma_0 \) and \( \chi \) will be used hereafter.

Notice that of \( \phi_0(r,a), \phi_1(r,a), \) and \( \phi_4(r,a) \) only \( \phi_4(r,a) \) is sensitive to whether \( a = 1 \) or \( a = -1 \). This observation can be interpreted once it is taken into consideration that \( \phi_2(r,a) = \phi_3(r,a) = 0 \) and, as Seguin and Fried [19] found, that the force \( f \) and couple \( C \) exerted on a molecule at \( x \) with director \( e \) from a molecule at \( x + r \) with director \( d \) are given respectively by

\[
f = -2e^{-2}\phi_1r - \phi_2d - \phi_3e \tag{4.19}
\]

and

\[
C = -\phi_2d \land r - \phi_4d \land e. \tag{4.20}
\]

The insensitivity of \( \phi_0 \) and \( \phi_1 \) to whether \( a = 1 \) or \( a = -1 \) implies that the interaction energy and forces between molecules in side-by-side configurations are the same regardless of whether the molecules are oriented in the same direction. However, since \( \phi_4(r,a) \) is sensitive to whether \( a = 1 \) or \( a = -1 \), in side-by-side configurations the couple exerted by one molecule on another is influenced by how the molecules are orientated.

The sign of the parameter \( \nu \) deserves some discussion. The absolute value of \( \nu \) encompasses the extent to which the strength of the interaction between molecules is effected by their relative orientation. Whereas, parallel configurations of molecules are preferred for \( \nu < 0 \), perpendicular configurations are preferred for \( \nu > 0 \). Molecular orientation does not influence the strength of the interaction if the orientation strength vanishes. Since the lipid molecules comprising the bilayer prefer to be parallel, a negative value of the orientation strength is appropriate.

### 4.2 Computation of bending moduli and discussion

On using the potential given in the previous subsection with the effective cutoff distance \( 4.15 \), the formulas (3.18)–(3.22) can be used to compute \( \psi_0 \) and the bending moduli \( \kappa \) and \( \bar{\kappa} \). With the aid of Mathematica and retaining only two significant figures, the computations yield

\[
\psi_0 = \frac{13S_0\sigma_0^2W^2}{(1 - \chi^2)^{\nu/2}}, \tag{4.21}
\]

\[
\kappa = \frac{6.4(1 - \chi^2 - 3.9\chi^2\nu)S_0\sigma_0^4W^2}{(1 - \chi^2)^{1+\nu/2}}, \tag{4.22}
\]

\[
\bar{\kappa} = \frac{6.3(1 - \chi^2 - \chi^2\nu)S_0\sigma_0^4W^2}{(1 - \chi^2)^{1+\nu/2}}. \tag{4.23}
\]

Since \( \chi > 0 \) and \( \nu < 0 \), (4.22) and (4.23) imply that \( \kappa > 0 \) and \( \bar{\kappa} < 0 \). In view of the discussion in the final paragraph of Section 3, this is unsurprising as the chosen potential is repulsive and favors side-by-side configurations. The ratio \( \bar{\kappa}/\kappa \) of the bending moduli is given by

\[
\frac{\bar{\kappa}}{\kappa} = -\frac{0.98(1 - \chi^2 - \chi^2\nu)}{1 - \chi^2 - 3.9\chi^2\nu}. \tag{4.24}
\]

Plots of this ratio as a function of \( \nu < 0 \) for various values of \( \chi \) are provided in Figure 1. In view of (4.11), there is a one-to-one correspondence between the value of \( \chi \) and the aspect ratio \( \rho \) of the lipid molecules. The aspect ratio increases as \( \chi \) approaches 1. For \( \chi < 1 \), (4.24) implies that \( \bar{\kappa}/\kappa \) may take any value in the interval \((-1, -0.25)\). On performing these calculations for different
Figure 1: Plot of the ratio $\bar{\kappa}/\kappa$ as a function of the orientation strength $\nu$ for different choices of the parameter $\chi$ defined in terms of the molecular aspect ratio $\rho$ in (4.11). The solid, long-dashed, medium-dashed, and short-dashed lines correspond respectively to $\chi = 0.6$, $\chi = 0.7$, $\chi = 0.8$, and $\chi = 0.9$ or, equivalently, $\rho = 2.0$, $\rho = 2.4$, $\rho = 3.0$, and $\rho = 4.4$.

effective cutoff distances, it is found that the effect of increasing the effective cutoff distance $d$ defined in (4.15) on the expressions (4.21)–(4.24) is negligible. This indicates that the chosen cutoff distance $3\sigma_0$ is reasonable.

The results (4.22) and (4.23) agree with most of what appears in the literature in the sense that the interaction potential parameters $S_0$ and $\nu$ may be selected to ensure that the resulting values for the moduli $\kappa$ and $\bar{\kappa}$ are consistent with those obtained through experimental measurements and numerical simulations. To confirm this assertion, notice first that $S_0$ can be chosen so that the splay modulus $\kappa$ can take any positive value. To match the saddle-splay modulus, it is convenient to consider the expression (4.24) for the ratio $\bar{\kappa}/\kappa$. By choosing an appropriate value for $\nu$, that ratio can be made to match the experimental results of Lorzen, Servuss and Helfrich [16], Baumgart, Das, Webb and Jenkins [1], and Semraru Idema, Holtzer, Schmidt and Storm [20] as well as the ratio found through simulations by Hu, Brigugli and Deserno [8]. It is important to keep in mind that the studies just mentioned consider different types of lipid bilayers and, hence, yield different values for the ratio $\bar{\kappa}/\kappa$ of the bending moduli. See the tabulated values compiled by Hu, Brigugli and Deserno [8]. Notice, however, that the prediction that $\bar{\kappa}/\kappa$ should be strictly less than $-1$ arising from the simulations of Hu, de Jong, Marrink and Deserno [9] is not encompassed by the model considered here. It is possible that the inability to match the results of Hu, de Jong, Marrink and Deserno [9] is due to the choice of potential, rather than the overall model for a lipid bilayer. To verify this would likely require an in-depth study of the most appropriate form for the potential governing the interaction between lipid bilayers. Specifically, while the particular expressions for $S$ and $\Sigma$ chosen in Section 4.1 are well-known in the literature, these choices are unlikely to be optimal for describing the interactions between lipid molecules. Moreover, it seems likely that superior choices for these quantities remain undetermined.

Taking into account experimental error, Baumgart, Das, Webb and Jenkins [1] found values in the interval $(-1.28, -0.52)$. The results obtained here encompass most of the values in that interval.

Taking into account numerical error, Hu, Brigugli and Deserno [8] found values in the interval $(-1.05, -0.85)$. The results obtained here are also encompass most of the values in that interval.
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