

MEMBRANE ELASTICITY AND MEDIATED INTERACTIONS IN CONTINUUM THEORY: A DIFFERENTIAL GEOMETRIC APPROACH

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2.1. INTRODUCTION: BIOPHYSICS AND SCALE SEPARATION

Biomembranes are fantastically complex systems [1–4]: hundreds of different lipid and protein species self-assemble into a large two-dimensional aggregate of locally complex and laterally inhomogeneous structure, and a globally potentially daunting topology. Thermal motion of this elastically soft system contributes prominently to its properties, and active processes constantly drive it away from equilibrium. How can we ever hope to learn something quantitative about such a complicated thing?

The route to success lies — as so often in physics — in the observation that we can frequently study different aspects of the problem largely independently. For instance, if a system spans many orders of magnitude in spatial scales, chances are that on the large scales it is perfectly well described by an effective Hamiltonian, whose small number of phenomenological parameters depend on — and can in principle be determined from — the underlying microscopic physics. Yet, establishing this micro–macro relation is not prerequisite to a successful and productive effective macroscopic description, since these phenomenological parameters can alternatively be measured experimentally on the macroscopic level. Often several such coarsening steps can be performed, thus constructing a hierarchy of scales with much beautiful physics in the different tiers. For instance, the laws of quantum mechanics explain everything about water that we need to know — e.g., how water structure and hydrogen bonds give rise to many of water’s anomalies — but we can often just describe it effectively as a substance with some

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measurable material parameters, such as density, heat of vaporization, melting point, and compressibility. And even of these parameters many become irrelevant if we're only interested in large-scale fluid motion, for which density and viscosity are often the only relevant properties. Having gotten so used to this separability, we sometimes even forget that the success of physics as a science rests entirely on it. If phenomena on different scales could not be disentangled, we would for instance not be able to describe the motion of the liquid in a stirred cup of coffee without a thorough appreciation of its atomic structure. Or, maybe we'd even need to understand quarks? Or strings? The fact that for all intents and purposes we can master our surrounding world quite well, *without* knowing what the ultimate structure of matter and the form of a Grand Unified Theory is, provides a vivid proof for the power of scale separation.

However, the ease with which this program can be implemented depends crucially on how well scales actually separate. For instance, the size of a water molecule ($\sim \text{\AA}$) is about 10 orders of magnitude smaller than ordinary human scales (m) and 16 orders of magnitude smaller than scales characterizing, say, the Gulf stream (1000 km); and its vibration frequencies (~ 100 THz) are 14 orders of magnitude away from human scales (\sim s) and 24 orders of magnitude away from the times characterizing deep sea ocean currents (~ 1000 yr). Hence, scale separation for water works extremely well. In contrast, many systems studied in soft matter physics show relaxation times that easily extend beyond hours, days, and years — even if their constituents are only two orders of magnitude larger than water molecules! In these cases more effort is required to understand such complex matter, the techniques are more specialized, and tend to be tailored to the specific system in question (e.g., liquid crystals, polymers, colloids, ...) [5]. But the benefits to be reaped are the same: a quantitative phenomenology based on a small set of measurable parameters describes much of the meso- or macroscopic behavior.

Is scale separation possible in biology? The success of the medical sciences suggests a cautious “yes.” We are evidently able to understand enough about how organisms function to be able to “fix” them when certain (simple) things go wrong.¹ Nevertheless, biology is more complicated in many ways. First of all, most of the materials that nature uses are soft, so “trivial” scale separation hardly ever works and we must resort to the more sophisticated techniques developed in soft matter physics. However, biology is more than soft matter. It is never in equilibrium while alive. No living system is isolated from its outside world. Every living system is here for a purpose (namely, to carry its genes into the future), for which it has to compete or cooperate with other organisms, owing to limited resources. Every organism is evolutionarily optimized to do just that. Such concepts don't resonate easily with our classical physical approach to the world, but this should not aggrieve us to the point of giving up the program. The complexity of nature is sometimes used to argue that simplifications are impossible. If that were true, biological science would not be possible either. Quite to the contrary, given the complexity of nature and our inability to grasp it all at once, we depend more than ever on techniques that promise a reliable, systematic, and quantitative phenomenological approach. Moreover, despite its astounding complexity, biology is full of simple laws. Here's one: the metabolic rate of an organism scales like its weight to the power of $3/4$ — a law that holds over *more than 20 orders of magnitude in weight* [6]. Such relations must be explicable on very fundamental general principles, and indeed convincing explanations for this law (and others) have been proposed [7].

In this book we are concerned with only a small aspect of nature: biomembranes. Still, they are already sufficiently complex such as to necessitate a hierarchical treatment — as nicely illustrated by the scope spanned by the different chapters. In the present chapter we will set out to

look at membranes from a comparatively large scale, where continuum elastic treatments become meaningful. Admittedly, membrane elasticity as such might not at first be perceived as a frontier in biosciences, and indeed the basic equations are more than three decades old by now [8,9]. However, it still fits within the context for the following reasons:

- Whether old or not, it is the mesoscopic scale on which a lot of cellular physics happens, and it therefore remains a crucial contribution in the mix of techniques useful to elucidate cellular behavior.
- Continuum elasticity theory provides a close and very natural link to stresses transmitted in membranes, and as such it constitutes an ideal framework for all situations in which such stresses play an important role, e.g., in morphology changes, protein interactions, or locomotion.
- Recent theoretical developments have provided new tools with which membrane stresses can be described in very geometrical (and thus often very *intuitive*) ways.
- Years of careful simulation work have begun to establish a systematic coarse-graining sequence through which microscopic membrane properties can be quantitatively linked to the phenomenological parameters on larger scales (see, e.g., the chapters by Hoopes et al., Vattulainen, and Tieleman in this volume). Continuum theory is thus bound even more tightly to the finer levels. In particular, its phenomenological parameters have become *predictable*.

2.2. CONTINUUM THEORY FOR MEMBRANES: A FIRST LOOK

Lipids are the major structural component of most biomembranes. These are typically two-tailed amphiphiles, and as such they prefer to aggregate into lamellar phases. This alone already has one remarkable consequence: as classical micellization theory shows, the size distribution of aggregates depends crucially on their morphology [5]. Spherical micelles tend to be very monodisperse, having a size distribution peaked around some particular mean value that accommodates the spontaneous curvature of the surfactants. In contrast, cylindrical micelles have a much wider exponential size distribution with a mean length that scales with the square root of surfactant concentration. Lamellar-forming amphiphiles differ even more strongly: it turns out that they follow a distribution that, even though initially exponentially decaying, again peaks at the size corresponding to a *single aggregate containing all amphiphiles*. Hence, bilayers have an intrinsic tendency to be “infinite.” In consequence, it is only too natural to apply continuum theory to them: the mechanism of self-assembly transforms individual entities, only a couple of nanometers big, into bilayer sheets extending over many microns. This extremely large aspect ratio also points toward the proper effective theory that would need to be developed on the micron scale: membranes are essentially two-dimensional surfaces.

Let us begin to develop a model for bilayer elasticity. The simplest deformation we can do to a bilayer is stretch it. Experiments of this type can be done with very high accuracy using micropipette techniques [10,11]. The idea is essentially this: grab a large vesicle (many microns in size) with a micropipette (having a bore on the order of a micrometer) and gently suck the vesicle in, thereby putting it under tension. Since one can measure both the pressure difference between inside and outside and relative area changes and the vesicle size very accurately, one can accurately probe the stress–strain relation. Neglecting fluctuations, which are important at

low tension, one finds that the bilayer can essentially be stretched like a harmonic spring, obeying a stretching energy of the form

$$E_{\text{stretch}} = \frac{1}{2} K_{\text{stretch}} \frac{(A - A_0)^2}{A_0}. \quad (2.1)$$

Here, K_{stretch} is the stretching modulus. Typical values valid for phospholipids are on the order of 250 mN/m [11]. Notice that the membrane tension σ is given by the derivative of the energy with respect to the area (at constant number of lipids, N):

$$\sigma = \left(\frac{\partial E_{\text{stretch}}}{\partial A} \right)_N = K_{\text{stretch}} \frac{A - A_0}{A_0} = K_{\text{stretch}} u, \quad (2.2)$$

where $u = (A - A_0)/A_0$ is the dimensionless (relative) *strain*. In other words, what we have here is nothing but Hooke's law: *a linear stress–strain relation*.

What happens now if we bend such a membrane? Since the membrane has a finite thickness, bending implies that the “outside” part of the bilayer will be stretched a little bit while the inside part will be compressed a little bit. The total energy of the bent membrane can then be obtained by a volume integral of the stretching energy of infinitesimal volume elements comprising the bilayer. The full calculation can for instance be found in Landau and Lifshitz [12]. Here we will restrict ourselves to a simplified presentation of the matter.

In order to understand the stretching behavior of volume elements, we will use an energy identical in spirit to Eq. (2.1): a deviation from a given volume will cost quadratically in energy:

$$E_{\text{stretch}} = \frac{1}{2} Y \frac{(V - V_0)^2}{V_0}, \quad (2.3)$$

where Y is called *Young's modulus*. Let us consider a quadratic membrane patch of side length L and thickness h and bend it along one direction into an arc of curvature radius R , measured from the midplane of the membrane, also known as the *neutral surface* (see Fig. 2.1). Assuming that the stretching along the x -direction will only change the shape of an infinitesimal cube along the same direction (and not shrink it, for instance, in a direction perpendicular to x), we see that the length dx is stretched by a factor $(R + z)/R = 1 + z/R$, where z is the perpendicular distance of that cube from the neutral surface. Hence, the stretching energy of this cube is given by

$$\frac{1}{2} Y \frac{(dx' dy' dz' - dx dy dz)^2}{dx dy dz} = \frac{1}{2} Y \frac{(dx(1 + z/R) dy dz - dx dy dz)^2}{dx dy dz} = \frac{1}{2} Y \frac{z^2}{R^2} dx dy dz, \quad (2.4)$$

so that the total stretching/compression energy of the membrane patch is given by

$$E_{\text{bend}} = \frac{Y}{2R^2} \int_{-L}^L dx \int_{-L}^L dy \int_{-h/2}^{h/2} dz z^2 = \frac{L^2 Y h^3}{24 R^2}. \quad (2.5)$$

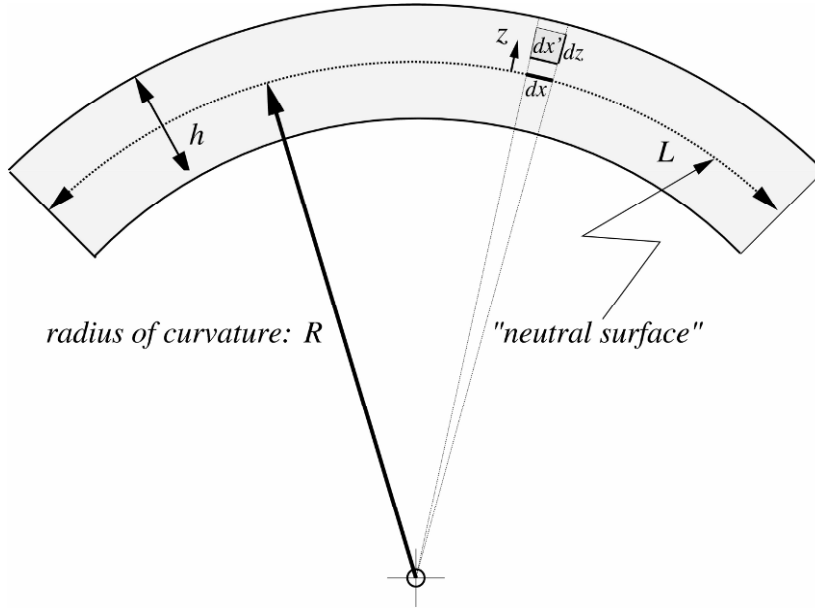


Figure 2.1. How to derive bending energy from stretching. A thin elastic sheet is bent along one direction into an arc of curvature radius R , measured from the neutral surface. A small volume element a distance z from that neutral surface is stretched along the x -direction if it is on the outer side, and compressed if it is on the inner side.

This implies a bending energy density per unit area of

$$e_{\text{bend}} = \frac{E_{\text{bend}}}{L^2} = \frac{1}{24} Y h \left(\frac{h}{R} \right)^2. \quad (2.6)$$

At this point several comments are in order:

1. For simple dimensional reasons, Young's modulus, stretching modulus, and membrane thickness are related by $K_{\text{stretch}} = Yh$.
2. Since typically $h \ll R$, i.e., the radius of curvature is much larger than the membrane thickness, the bending energy per unit area can be quite small even if the stretching modulus is large. This is why we can make soft springs out of rather stiff metal: by making them thin enough.
3. The bending energy scales as the square of the curvature. Using the abbreviation $\kappa = \frac{1}{12} Y h^3 = \frac{1}{12} K_{\text{stretch}} h^2$, we can then write the bending energy density as

$$e_{\text{bend}} = \frac{1}{2} \kappa \frac{1}{R^2}. \quad (2.7)$$

It should be noted that, even though this looks like a simple quadratic elastic theory ("Hooke's law for curvatures"), curvature is not just another form of strain, and this theory is subtly different from standard elastic theories.²

4. Since lipid membranes are composed of two monolayers that can slide past each other, no transversal stress can be transmitted across the neutral surface. In consequence, the stretching and compression of the outer and inner monolayer will be smaller than if both leaflets were rigidly coupled, as Figure 2.2 illustrates. It is in fact more appropriate to describe the overall deformation energy as two times the deformation of a monolayer that has half the thickness of the membrane. These two factors of 2 do not cancel, since the thickness enters not linearly but cubically in the bending energy. We should therefore expect

$$e_{\text{bend, bilayer}}(h) = 2 \times e_{\text{bend, monolayer}}(h/2) = \frac{1}{96} Yh \frac{h^2}{R^2}. \quad (2.8)$$

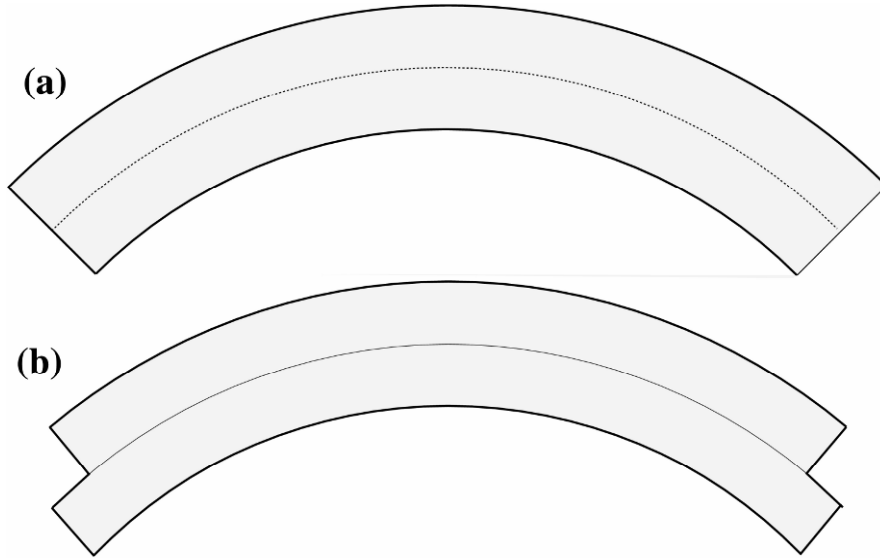


Figure 2.2. Monolayer sliding and bending stress. Since the two monolayers of a lipid bilayer can slide past each other, no stress can be transmitted across the midplane of the membrane. The resulting strain in both leaflets due to stretching or compression is therefore smaller (b) than if the monolayers were rigidly coupled (a).

5. We have simplified the discussion by assuming that a stretched piece of membrane will not shrink in the direction perpendicular to the applied strain, but there is no principal justification for this. In fact, taking a piece of material of length L and width w , a longitudinal strain $u = \Delta L / L$ also implies a transversal relative width change $\Delta w / w = -\nu u$, where $-1 \leq \nu \leq \frac{1}{2}$ is *Poisson's ratio* [12]. If the material shows no transverse response to a longitudinal strain, as we have pretended so far, we have the special case $\nu = 0$. It is also easy to see that in the limit of an incompressible material, where the transverse shrinking has to compensate for the longitudinal extension, we must have $\nu = \frac{1}{2}$.³ It may be shown that Poisson's ratio

modifies our formulas by effecting the replacement $Y \rightarrow Y/(1-\nu^2)$ [12]. Hence, a better formula for the bending modulus than the one we have initially written down would be

$$\kappa = \frac{K_{\text{stretch}} h^2}{48(1-\nu^2)}. \quad (2.9)$$

This includes the “bilayer = 2 monolayers” correction discussed above.

6. Let us put it in numbers: using Eq. (2.9) in the limit of an incompressible material ($\nu = \frac{1}{2}$, such that the prefactor 48 turns into 36) and taking typical values for the stretching modulus ($K_{\text{stretch}} = 250 \text{ mN/m}$) and the bilayer thickness ($h = 4 \text{ nm}$) we arrive at $\kappa = 27k_{\text{B}}T_{\text{r}}$, where $k_{\text{B}}T_{\text{r}} \approx 4.1 \times 10^{-21} \text{ J} \approx 0.6 \text{ kcal/mol}$ is the thermal energy at room temperature. This is quite a typical value for phospholipids, maybe a bit on the large side [11]. But beyond that actual number, what really matters is the fact that it is a *fair* amount larger than thermal energy, so fluctuations do not tear the bilayer into bits and pieces, while it is not *tremendously* much larger than thermal energy, so nanoscopic sources of energy, provided, e.g., by adhering proteins or ATP hydrolysis, are capable of deforming the lipid membrane.

2.3. CURVATURE ELASTICITY

Based on what we have learned in the previous section, we suspect that bilayer elasticity will turn out to be a “curvature squared theory,” where the elastic constants — e.g., κ — might even be derivable from other known elastic constants (such as Young’s modulus and Poisson’s ratio). However, we have actually only looked at a rather simple deformation: homogeneous bending into one direction. While it is possible to extend this line of reasoning to more complicated deformations — details can be found in Landau and Lifshitz [12] — it proves more instructive to “derive” a phenomenological curvature-based theory from scratch. Based only on the expected symmetries and the knowledge that the shape of the deformed surface will matter, one can essentially write down the correct Hamiltonian. The most transparent way to do this is within a differential geometric framework. In order to clarify the notation, we will first and very briefly revisit a few basic points. These can by no means replace a good introduction into the field, and the reader is encouraged to consult, for instance, the classical texts by do Carmo [13], Spivak [14], or Kreyszig [15].

2.3.1. Differential Geometry *in nuce*

Let us consider a two-dimensional surface embedded into three-dimensional Euclidean space \mathbf{R}^3 . We can locally describe it by a parametrization, which for now we will take to be a mapping from a two-dimensional region of \mathbf{R}^2 into \mathbf{R}^3 , given by the function $\mathbf{x} = \mathbf{X}(u^1, u^2)$, where the two parameters u^a ($a \in \{1, 2\}$) are the (curvilinear) surface coordinates. Using the embedding function \mathbf{X} , we can define tangent and normal vectors on the surface:

$$\mathbf{e}_a = \frac{\partial \mathbf{X}}{\partial u^a} = \partial_a \mathbf{X}, \quad (2.10)$$

$$\mathbf{n} = \frac{\mathbf{e}_1 \times \mathbf{e}_2}{|\mathbf{e}_1 \times \mathbf{e}_2|}. \quad (2.11)$$

Notice that while the normal vector \mathbf{n} is indeed normalized to unit length, the tangent vectors \mathbf{e}_a are in general neither normalized nor perpendicular to each other.⁴

With these vectors we are now in the position to define two important tensors on the surface: the metric tensor g_{ab} and the (extrinsic) curvature tensor K_{ab} :

$$g_{ab} = \mathbf{e}_a \cdot \mathbf{e}_b, \quad (2.12)$$

$$K_{ab} = \mathbf{e}_a \cdot \partial_b \mathbf{n} = -\mathbf{n} \cdot \partial_b \mathbf{e}_a = -\mathbf{n} \cdot \partial_a \partial_b \mathbf{X}. \quad (2.13)$$

As the definitions show, both tensors are symmetric. The metric will be concerned with scalar products and thus distance information on the surface. Consider for instance two vectors $\mathbf{v} = \sum_{a=1,2} v^a \mathbf{e}_a \equiv v^a \mathbf{e}_a$ and $\mathbf{w} = w^b \mathbf{e}_b$ defined at the *same* point of the surface. Their scalar product is then given by

$$\mathbf{v} \cdot \mathbf{w} = (v^a \mathbf{e}_a) \cdot (w^b \mathbf{e}_b) = v^a w^b \mathbf{e}_a \cdot \mathbf{e}_b = v^a w^b g_{ab} = v^a w_a, \quad (2.14)$$

where we also have shown how indices can be lowered by the metric. Indices can also be raised with the tensor g^{ab} , whose components are defined such that the following holds:

$$g^{ab} g_{bc} = \delta_c^a, \quad (2.15)$$

where δ_c^a is the Kronecker-delta, which is 1 if both indices are identical and zero if they are different. So g^{ab} is essentially the inverse of g_{ab} . Lower indices are referred to as “covariant coordinates,” while upper indices are “contravariant coordinates.” The determinant of the metric is abbreviated as $g = \det(g_{ab})$ and can also be expressed as $|\mathbf{e}_1 \times \mathbf{e}_2|^2$. From this we see immediately that the proper area element on the surface is given by $dA = \sqrt{g} du^1 du^2$.

The curvature tensor K_{ab} measures local *extrinsic curvature*, i.e., bending of the two-dimensional surface into the third space dimension. This is intuitively reasonable, since it monitors how the normal vector changes as we move along the surface. If it stays constant, the surface is flat; if it is not, the surface must be curved. Raising one index of the curvature tensor gives the matrix $K_a^b = K_{ac} g^{cb}$, whose eigenvalues are the *principal curvatures*, and whose eigenvectors point into the *principal directions*. The *trace* of the curvature tensor is called the total extrinsic curvature, $K = \text{Tr}(K_{ab}) = g^{ab} K_{ab} = K_a^a$. The determinant of the matrix K_a^b is called the Gaussian curvature, $K_G = \det(K_a^b)$. Notice that in the present case of 2×2 matrices it can also be written as $K_G = \frac{1}{2}(K^2 - K_{ab} K^{ab})$, which is (half) the difference between the square of the trace and the trace of the square of the extrinsic curvature tensor.

Since the surface coordinates are curvilinear, they depend on position. Hence, the ordinary partial derivative of surface vectors or tensors will, via the product rule, also contribute terms from the positional dependence of the local basis. This ultimately implies that, for instance, $\partial_a v_b$ is *not* a tensor of second rank, since these additional terms spoil the transformation law. It is, however, possible to restore this property by defining a covariant derivative ∇_a that incorporates the additional terms. When acting on scalars, it is identical to the usual partial derivative

(since scalars do not involve the position-dependent basis!), while its action on co- or contravariant vectors is given by

$$\nabla_a v_c = \partial_a v_c - \Gamma_{ac}^b v_b, \quad (2.16)$$

$$\nabla_a v^c = \partial_a v^c + \Gamma_{ab}^c v^b. \quad (2.17)$$

The new object Γ_{ab}^c is called the *Christoffel symbol* (of second kind) and is defined as

$$\Gamma_{ab}^c = \frac{1}{2} g^{cd} (\partial_a g_{bd} + \partial_b g_{da} - \partial_d g_{ab}). \quad (2.18)$$

Observe that Γ_{ab}^c is symmetric in its two lower indices. We also have a Christoffel symbol of the first kind, $\Gamma_{abc} = g_{cd} \Gamma_{ab}^d$. Since it's the “job” of the Christoffel symbols to “undo” the non-tensor character of the partial derivative, they cannot be tensors themselves.⁵ Covariant derivatives of objects with more than one co- or contravariant index follow the same pattern as seen in Eqs. (2.16) and (2.17), i.e., each covariant index necessitates the subtraction of a Christoffel symbol term, and each contravariant index necessitates its addition (the placement of the indices on the Christoffel symbol is always obvious).

It turns out that the metric is constant with respect to the covariant derivative, $\nabla_a g_{bc} = 0$, a fact known as the Lemma of Ricci. The practically extremely convenient consequence is that *raising and lowering of indices commutes with the process of covariant differentiation*.

On the downside: covariant derivatives no longer commute! Instead, we have

$$(\nabla_a \nabla_b - \nabla_b \nabla_a) v_c = R_{abcd} v^d, \quad (2.19)$$

a relation which defines the Riemann tensor R_{abcd} , whose components — from Eq. (2.19) — can be worked out to be

$$R_{abcd} = \partial_c \Gamma_{bda} - \partial_d \Gamma_{bca} + \Gamma_{bd}^e \Gamma_{eca} - \Gamma_{bc}^e \Gamma_{eda}. \quad (2.20)$$

The contraction of the Riemann tensor with respect to the first and third index is called the *Ricci tensor*:

$$R_{bd} = g^{ac} R_{abcd}, \quad (2.21)$$

whose repeated contraction gives the Ricci scalar:

$$R = g^{bd} R_{bd}. \quad (2.22)$$

In general, the Riemann tensor has more independent components than the Ricci tensor, which in turn has more independent components than the Ricci scalar.⁶ However, for two-dimensional surfaces all of the three tensors have exactly one independent component, and so the Riemann tensor is completely determined by the Ricci scalar, namely via

$$R_{abcd} = \frac{1}{2} R (g_{ac} g_{bd} - g_{ad} g_{bc}) \quad (\text{only in two dimensions!}). \quad (2.23)$$

Finally, it turns out that there are integrability conditions to be satisfied (e.g., $\partial_a \partial_b \mathbf{e}_c = \partial_b \partial_a \mathbf{e}_c$), which link the extrinsic geometry associated with the curvature tensor with the intrinsic geometry associated with the metric.⁷ These are called the equations of Gauss-Codazzi-Mainardi, and they state the following:

$$\nabla_a K_{bc} - \nabla_c K_{ab} = 0, \quad (2.24)$$

$$K_{ac} K_{bd} - K_{ad} K_{bc} = R_{abcd}. \quad (2.25)$$

If we contract Eq. (2.25) with respect to ac , we find

$$K K_{bd} - K_{ad} K_b^a = R_{bd}. \quad (2.26)$$

Contracting it once more with respect to bd , we find the truly remarkable result

$$2K_G = K^2 - K^{ab} K_{ab} = R. \quad (2.27)$$

This final equation states that the Gaussian curvature K_G , which has been defined using the *extrinsic* curvature tensor (i.e., by making use of a normal vector pointing into the third space dimension!), can in fact be expressed by the Ricci scalar curvature, which originates from the entirely *intrinsic* Riemann tensor (i.e., without any reference to an embedding into 3-space). Hence, the Gaussian curvature can be obtained exclusively from distance measurements *within* the surface. This discovery is due to Gauss, who was so much impressed by it that he called it the *Theorema Egregium*. He then went on to execute a precision triangulation measurement of a triangle formed by three mountaintops near Göttingen (namely Hohenhagen, Brocken, and Inselberg). He wanted to check whether the Euclidean result that the sum of the interior angles must be 180° is satisfied, because he realized that *the Euclidean geometry of space is an empirical question, subject to verification or disproof by measurement* [16].

This should suffice for now as a minute survey of differential geometry. Since none of these formulas have been properly derived here and mathematical subtleties have been nonchalantly swept under the rug, the interested reader is highly encouraged to look up the details in [13–15]. This section should rather be seen as a convenient introduction of the geometric *dramatis personae* as well as a quick reference for some useful formulas that will be needed below. They are typically applied extensively throughout all calculations, but luckily, when the dust has settled, most of the final formulas will express relations between extremely intuitive geometric quantities and not complicated tensors. So even if one is unwilling to delve into differential geometry, one will be able to make use of many of its beautiful results.

2.3.2. Curvature Elasticity from a Formal Point of View

As Eqs. (2.7) and (2.8) suggest, the key physical characteristic of bending elasticity is its proportionality to squared curvature. The prefactor κ measures the corresponding bending rigidity, which can be linked to other (maybe more fundamental) material properties, such as for instance Young's modulus. This step, however, requires both modeling and certain non-obvious assumptions (concerning, for instance, the homogeneity of the material or the lateral stress profile). We might thus alternatively consider κ as a phenomenological modulus that can be determined in experiment. If we take this point of view, we may more generally view the surface energy density as reflecting the first terms of an expansion of the generalized elastic energy in surface scalars, ordered by dimensionality, each term multiplied by a phenomenological modulus. Which terms one can write down depends on the available fields and symmetries. In the simplest case we have only the geometry of the membrane, fully determined by the two tensors

g_{ab} and K_{ab} . The first few terms have been discussed for instance by Capovilla, Guven, and Santiago [17], and we briefly review their results:

- The simplest scalar that can be constructed from them is $g_a^a = 2$, just a number. The corresponding surface integral gives the surface area, and the corresponding “modulus” is the surface tension.
- The next simplest scalar — of dimension $(\text{length})^{-1}$ — is $K_a^a = K$, the total extrinsic curvature. Since K depends on the orientation of the normal vector, it can only appear in a physical Hamiltonian if the surface in question is in some way asymmetric with respect to its two sides. The appearance of a linear term is therefore typically associated with the existence of a spontaneous curvature, but it can even matter for symmetric membranes by virtue of the following observation: the variation of the local area element is proportional to the local value of the curvature. It follows that the *difference in area* between the two close but not identical surfaces representing the two leaflets of the membrane is proportional to the *surface integral over K* . If for some reason the area of these two surfaces is *individually* conserved (for instance, because lipids might not have sufficient time to flip between the two leaflets during the timescale of observation), one can enforce this constraint by an additional term in the Hamiltonian that is proportional to K and whose prefactor is the Lagrange multiplier enforcing this constraint. More details on this, and its relation to so-called “area difference elasticity” can be found in [18].
- For dimension $(\text{length})^{-2}$ we have two independent scalars: the square of the trace and the trace of the square, $K^2 = K_a^a K_b^b$ and $K_a^b K_b^a$, but it proves more convenient to use K^2 and the linear combination $R = K^2 - K_a^b K_b^a = 2K_G$ to work with. The reason is that the Gaussian curvature integrates to a topological invariant (by virtue of the Gauss-Bonnet theorem [13–15]) and can thus often (but by no means always!) be neglected in the description.
- On order $(\text{length})^{-3}$ we have three independent terms, which can for instance be chosen to be K^3 , KR , and $K^{ab}R_{ab}$. More terms could be written down, but these would no longer be independent. For instance, by using the Codazzi-Mainardi equations, it is easy to see that $K_a^b K_b^c K_c^a = K^3 - KR - K^{ab}R_{ab}$, and thus no new invariant results.
- On order $(\text{length})^{-4}$ it happens for the first time that the independent terms are not of the same order in surface derivatives. An independent set would for instance be K^4 , K^2R , R^2 , and $(\nabla_a K)(\nabla^a K)$. While the first three terms are of order curvature in terms of surface derivatives, the fourth term contains the derivative of curvature.

Stopping at this order, the energy density can be written as

$$\begin{aligned}
 e_{\text{surface}} = & \sigma \\
 & + \kappa_1 K \\
 & + \frac{1}{2} \kappa K^2 + \frac{1}{2} \bar{\kappa} R \\
 & + \frac{1}{3} \kappa_3 K^3 + \kappa_{3\times} KR + \kappa_{3R} K^{ab} R_{ab} \\
 & + \frac{1}{4} \kappa_4 K^4 + \kappa_{4\times} K^2 R + \frac{1}{2} \bar{\kappa}_2 R^2 + \frac{1}{2} \kappa_{\nabla} (\nabla_a K)(\nabla^a K).
 \end{aligned} \tag{2.28}$$

Typically, the linear term is incorporated in the quadratic one by defining a spontaneous curvature K_0 and writing $\frac{1}{2}\kappa(K-K_0)^2$. Up to a constant (which enters the surface tension) this amounts to the choice $\kappa_1 = \kappa K_0$.

Terms such as the ones featured in Eq. (2.28) — as well as more complicated ones — have been used to model corrugated (“egg-carton”) surfaces [19]. However, for most applications going up to quadratic order is fully sufficient. In fact, probably the most important subset of terms from Eq. (2.28) is the quadratic order without linear term (i.e., for up-down symmetric surfaces):

$$e_{\text{Helfrich}} = \sigma + \frac{1}{2}\kappa K^2 + \frac{1}{2}\bar{\kappa} R. \quad (2.29)$$

This Hamiltonian (actually, including the spontaneous curvature) was originally proposed by Wolfgang Helfrich as a suitable model for bilayer elasticity [9], after Canham [8] had three years earlier suggested a Hamiltonian with only one bending term (of the form $K_{ab}K^{ab}$ in our notation).

2.3.3. Additional Fields

Curvature elasticity involves energetic changes of a surface due to deformation of its *shape*. However, other sources of energy are possible if additional fields “live” on the membrane. For instance, a lipid membrane might consist of different types of lipids. If these completely phase separate, then the membrane consists of patches that differ in their elastic properties. However, if these components mix — not necessarily ideally, though — a scalar concentration field ϕ may be defined on the membrane whose local value will generally influence the (free) energy.⁸ This can happen in different ways:

- The elastic constants become functions of the concentration; e.g., the bending modulus might depend on the local lipid composition: $\kappa = \kappa(\phi)$.
- New scalars can be constructed by using the geometric variables and non-geometric fields. For instance, a term of the form $\frac{1}{2}\kappa(K - \phi c_0)^2$, where ϕ is a composition field and c_0 the spontaneous curvature at $\phi = 1$, creates a composition-dependent spontaneous curvature. Of course, one might alternatively look at this as a ϕ -dependent linear K -coupling ($\kappa_1 = \kappa\phi c_0$) combined with a ϕ -dependent extra surface tension ($\sigma \rightarrow \sigma + \frac{1}{2}\kappa c_0^2 \phi^2$), but the spontaneous curvature interpretation is more natural in this case.
- The field itself contributes to the overall free energy (e.g., in the form of energy/entropy of mixing). The most obvious examples would be a Ginzburg-Landau type functional of the form $V(\phi) + \frac{1}{2}\eta(\nabla_a \phi)(\nabla^a \phi)$, where $V(\phi)$ is a potential and the second term the covariant generalization of a squared gradient.

These examples all involve a single scalar field ϕ . However, one might have more than one field. Or one might have a vector field. A good example for the latter would be *lipid tilt*. This could be described by the average projection of a lipid into the membrane plane. Without tilt, lipids always point into the same direction as the membrane normal; with tilt they acquire a tangential component that can be expanded in the local tangential frame: $\mathbf{m} = m^a \mathbf{e}_a$. The associated field (components) m^a can again give rise to energy contributions. Since these have to be scalar, one either must construct scalars from these vectors (e.g., $m_a m^a$, $\nabla_a m^a$,

$(\nabla_a m^b)(\nabla_b m^a)$), for which one already needs the metric, or one involves the curvature tensor (e.g., $K_{ab} m^a m^b$). Evidently many more possibilities exist, but these are also strongly restricted by symmetry considerations. An insightful discussion of this has been presented by Nelson and Powers [20,21].

Frequently such fields are “excited” by proteins embedded in the membrane. Rather than guessing the phenomenological form or strength of this coupling, one can try to construct a more detailed approach to describe the local physics. The chapter by Frischknecht in this book provides an example of how this can be done.

2.4. MEMBRANE STRESSES AND SHAPE EQUILIBRIA

The total elastic energy of a membrane is the surface integral over its energy density — containing all contributions discussed so far, geometric or field-derived. In mechanical equilibrium⁹ the membrane will choose a configuration that minimizes this overall energy. This naturally leads to a functional minimization problem and corresponding Euler-Lagrange differential equations for the membrane shape and all fields defined on it. But there is also a different way to look at this: in equilibrium all stresses have to balance, meaning that there ought to be a local stress tensor that is divergence-free. Indeed, these two ways of looking at things are closely related, and the divergence of the stress tensor indeed turns out to be nothing but the Euler-Lagrange derivative. Yet, looking at the problem from a point of stresses might provide complementary insight that the usual energy approach does not necessarily offer. This is all the more true as it turns out that the stress tensor in question can be expressed *completely* in terms of the local deformations, thus establishing a strong link between the geometry of a deformed membrane and the forces it transmits. This approach has been pioneered in a series of papers by Capovilla and Guven [17,22–26], and we will in the following summarize some of their key findings.

2.4.1. The Membrane Stress Tensor

If we think about surface stresses, we invariably first think of surface tension. Yet, this easiest of stresses is way too special to serve as a generic guidance: the stress in a soap bubble or in the surface of a pending water droplet is constant over the surface, always tangential, and locally isotropic. In general, however, stresses can vary from place to place, also point out of the surface plane, and depend on the direction at which one places a fictitious cut through the surface. Instead of the standard constant scalar surface tension σ , we have a tensor f^{ai} , where $a \in \{1,2\}$ describes the direction in the two-dimensional surface (along \mathbf{e}_1 or \mathbf{e}_2) and $i \in \{1,2,3\}$ numbers the directions in three-dimensional space. This description in terms of a 2×3 matrix is a bit unhandy, though, and it turns out to be more convenient to combine the i -components into a vector that gets one surface index: \mathbf{f}^a . The interpretation is that \mathbf{f}^1 is the force per unit length along a cut in the 1-direction and \mathbf{f}^2 the force per unit length along a cut in the 2-direction. If we want, we can expand the stress tensor into its tangential and normal components:

$$\mathbf{f}^a = f^{ab} \mathbf{e}_b + f^a \mathbf{n}. \quad (2.30)$$

The link to ordinary surface tension is quite simple: in this case the stress is purely tangential, isotropic, and constant, hence f^{ab} must be proportional to the metric — and the constant of proportionality is precisely (minus) the surface tension σ — and the normal component f^a vanishes:

$$\mathbf{f}^a = -\sigma g^{ab} \mathbf{e}_b = -\sigma \mathbf{e}^a \text{ (for surface tension) .} \quad (2.31)$$

The minus sign is ultimately a convention. Here it is chosen like this: place a cut along a surface and locally define a unit vector \mathbf{l} that is normal to the curve of the cut but tangential to the surface (hence we can expand it as $\mathbf{l} = l^a \mathbf{e}_a$). The cut locally separates the surface into two regions — A and B , say — and let us assume that \mathbf{l} points from the A to the B -side. Then the contraction $l_a \mathbf{f}^a$ denotes the *force per unit length that the A -side exerts on the B -side*. For the case of ordinary surface tension we have $l_a \mathbf{f}^a = -\sigma l_a \mathbf{e}^a = -\sigma \mathbf{l}$, and the minus sign convention becomes understandable: surface tension is *pulling*.

The concept of the stress tensor is so useful because, as has just been mentioned, one can write down the stress tensor also for more complicated surface Hamiltonians. There are several ways to see how this comes about. One possibility is to recognize its existence as a consequence of Noether's theorem: Every continuous symmetry implies a conservation law “on shell,” i.e., a law satisfied by the solutions of the corresponding Euler-Lagrange equations. Since the Hamiltonian of a membrane — or in fact any purely surface bound Hamiltonian — is evidently invariant with respect to translations of the entire surface, this implies a conserved Noether current, which indeed turns out to be the stress tensor. This line of reasoning has been outlined by Capovilla and Guven [22]. Later Guven has presented an alternative derivation, which provides a technically very powerful approach to the variation problem of a geometric functional [25]. We will briefly illustrate the main point of this second approach.

What makes the variation of geometric surface Hamiltonians so tedious is that the observables on which the energy density depends most directly — metric, metric determinant, curvature trace, etc. — are fairly involved and indirect functions of the embedding function $\mathbf{X}(u^1, u^2)$. It would be much easier if one could directly vary the functional with respect to, say, the curvature tensor or the metric. However, these “high-end” observables are not independent: they are related by integrability conditions, as we have seen above. However, it turns out that these complications can be accounted for by enforcing all the interrelations that geometry requires in the form of *constraints* to the functional. This is most directly done by enforcing the very *definitions* of the respective geometric objects and thus look at an amended functional of the following form [25]:

$$\begin{aligned} H_{\text{constraint}} = \int dA \{ & \mathcal{H}(g_{ab}, K_{ab}) \\ & + \mathbf{f}^a \cdot (\mathbf{e}_a - \nabla_a \mathbf{X}) + \lambda_{\perp}^a (\mathbf{e}_a \cdot \mathbf{n}) + \lambda_n (\mathbf{n}^2 - 1) \\ & + \lambda^{ab} (\mathbf{e}_a \cdot \mathbf{e}_b - g_{ab}) + \Lambda^{ab} (\mathbf{e}_a \cdot \nabla_b \mathbf{n} - K_{ab}) \}. \end{aligned} \quad (2.32)$$

Here, $\mathcal{H}(g_{ab}, K_{ab})$ is a Hamiltonian density depending explicitly only on the two surface tensors g_{ab} and K_{ab} . The terms in the second line define the local coordinate system, and the terms in the third line define the two surface tensors themselves. Notice that all constraints are at most quadratic. Moreover, the embedding function $\mathbf{X}(u^1, u^2)$ only appears at *one* place in the entire functional, namely at the constraint defining the tangent vectors. Varying this constraint functional

with respect to the embedding function (and partially integrating once) yields the following very simple Euler-Lagrange equation:

$$\frac{\delta H_{\text{constraint}}}{\delta \mathbf{X}} = 0 \Rightarrow \nabla_a \mathbf{f}^a = 0. \quad (2.33)$$

This proves instantly that there must exist some quantity that is covariantly conserved: the Lagrange multiplier \mathbf{f}^a that pins the tangent vectors to the surface. This turns out to be the stress tensor, as is carefully explained in [27]. The other variations (with respect to \mathbf{e}_a , \mathbf{n} , g_{ab} , and K_{ab}) help to identify \mathbf{f}^a in terms of the surface geometry. One easily finds [25]

$$\mathbf{f}^a = (T^{ab} - \mathcal{H}^{ac} K_c^b) \mathbf{e}_b - (\nabla_b \mathcal{H}^{ab}) \mathbf{n}, \quad (2.34)$$

where we have also defined the two additional surface tensors

$$T^{ab} = -\frac{2}{\sqrt{g}} \frac{\delta(\sqrt{g} \mathcal{H})}{\delta g_{ab}}, \quad (2.35)$$

$$\mathcal{H}^{ab} = \frac{\delta \mathcal{H}}{\delta K_{ab}}. \quad (2.36)$$

Remarkably, the overall *structure* of the stress tensor as given in Eq. (2.34) is completely independent of the surface Hamiltonian. The latter only enters in the specific form of the two tensors \mathcal{H}^{ab} and T^{ab} (the latter is sometimes also termed *metric stress*). If \mathcal{H} does not explicitly depend on derivatives of metric or curvature tensor, the respective functional derivatives reduce to partial ones. In that case the metric stress tensor can also be written as $T^{ab} = -\mathcal{H} g^{ab} - 2\partial \mathcal{H} / \partial g_{ab}$, where we made use of the formula $\partial g / \partial g_{ab} = g g^{ab}$. The fact that the metric stress has two contributions results from the fact that not just the Hamilton density $\mathcal{H}(g_{ab}, K_{ab})$ but also the area element $dA = \sqrt{g} du^1 du^2$ depends on the metric.

That the stress tensor is divergence-free — Eq. (2.33) — is *almost* equivalent to the Euler-Lagrange equation. Almost, because $\nabla_a \mathbf{f}^a = 0$ really constitutes *three* equations, while the vanishing of the (scalar!) Euler-Lagrange derivative is only a single equation. Where do two additional equations come from? The answer is that the actual Euler-Lagrange derivative only corresponds to the *normal component* of $\nabla_a \mathbf{f}^a = 0$, since this is the one related to normal variations of the surface [22]. In contrast, tangential variations only correspond (in first order) to reparametrizations of the surface [17] and will thus only result in *consistency conditions* for the stress tensor components. Using the expansion of \mathbf{f}^a into tangential and normal components introduced in Eq. (2.30), this can be written as [22]

$$\begin{aligned} 0 &= \nabla_a f^{ab} + K_a^b f^a \quad (\text{tangential}), \\ \mathcal{E}(\mathcal{H}) &= \nabla_a f^a - K_{ab} f^{ab} \quad (\text{normal}), \end{aligned} \quad (2.37)$$

where $\mathcal{E}(\mathcal{H})$ is the scalar Euler-Lagrange derivative that vanishes in equilibrium. Notice that the tangential projection vanishes even if $\mathcal{E}(\mathcal{H})$ does not — it has nothing to do with equilibrium and energy minimization.

If we consider a *closed* surface, there will generally be a pressure difference P between the inside and outside. From a point of view of forces, it is clear that this will act as a source of constant normal stress. In consequence, the Euler-Lagrange derivative is not zero in equilibrium but equal to this pressure difference [22]:

$$\mathcal{E}(\mathcal{H}) = P. \quad (2.38)$$

The easiest way to see this formally is to add a term $-PV$ to the energy functional, which may be viewed either as a Lagrange multiplier to fix the internal volume or as a Legendre transform to an ensemble of constant pressure difference between the two sides. Since the volume V of some region \mathcal{R} can be expressed as

$$V = \int_{\mathcal{R}} dV = \frac{1}{3} \int_{\mathcal{R}} dV \nabla \cdot \mathbf{X} = \frac{1}{3} \int_{\partial \mathcal{R}} dA \mathbf{n} \cdot \mathbf{X}, \quad (2.39)$$

it can be written as a surface integral and thus be included in the above formalism.

Now that we know how to express the Euler-Lagrange derivative in terms of the stress tensor, we can work it out in terms of the surface geometry. The only remaining bits of help we need are the equations of Gauss and Weingarten, $\nabla_a \mathbf{e}_b = -K_{ab} \mathbf{n}$ and $\nabla_a \mathbf{n} = K_a^b \mathbf{e}_b$, which tell us how the local coordinate system moves if we move along the surface (they are the surface analogs of the Frenet-Serret formulas for curves [13–15]). Using this, and the normal part of Eq. (2.37), we arrive at

$$(P =) \mathbf{n} \cdot \nabla_a \mathbf{f}^a = \mathcal{E}(\mathcal{H}) = -K_{ab} T^{ab} + (K_{ac} K_b^c - \nabla_a \nabla_b) \mathcal{H}^{ab}. \quad (2.40)$$

2.4.2. Three Examples

To illustrate the above abstract formalism, let us now look at three specific examples of increasing complexity (in terms of the Hamiltonian density). We will look at the stresses and field equations they imply and later use them to learn about mediated interactions between objects that couple to these fields.

2.4.2.1. Scalar Field

The first example we will look at is a simple scalar field ϕ defined on the membrane, which is characterized by a Ginzburg-Landau (free) energy [28] of the form

$$\mathcal{H}(\phi) = \frac{1}{2} \eta (\nabla_a \phi) (\nabla^a \phi) + V(\phi). \quad (2.41)$$

The only complication here is that we replaced the conventional gradient term $(\nabla \phi)^2$ by its covariant version (which we will subsequently take the liberty to again abbreviate as $(\nabla \phi)^2$). The field equation for ϕ for such a Hamiltonian can be obtained by a simple variation with respect to ϕ , and we obtain

$$0 = \mathcal{E}(\mathcal{H}) = -\eta \Delta \phi + V'(\phi), \quad (2.42)$$

where $\Delta = \nabla_a \nabla^a$ is the covariant Laplacian and V' is the derivative of V with respect to its argument. Using Eq. (2.34), we equally quickly find the associated stress tensor [24]:

$$\mathbf{f}^a = \left[\eta (\nabla^a \phi) (\nabla^b \phi) - \left(\frac{1}{2} \eta (\nabla \phi)^2 + V(\phi) \right) g^{ab} \right] \mathbf{e}_b. \quad (2.43)$$

This “Ginzburg-Landau stress” is of course not new. It has been used frequently in the past within the context of statistical field theory, specifically for the treatment of forces induced by critical fluctuations (the Casimir effect) [29–33].

Since we will ultimately need projections of the stress tensor normal to some arbitrary cut through the surface, let us introduce a local coordinate system that is adapted to such a cut. Assume we have a curve with some local normalized tangent vector $\mathbf{t} = t^a \mathbf{e}_a$ and that perpendicular to this curve we have a normal vector $\mathbf{l} = l^a \mathbf{e}_a$ (still tangent to the surface, of course). Hence, $(\mathbf{l}, \mathbf{t}, \mathbf{n})$ is a convenient local orthonormal basis, which we furthermore choose to be right-handed. Notice that for reasons of completeness we also have $l_a l_b + t_a t_b = g_{ab}$. Using this coordinate system, the important normal projection of the stress tensor (2.43) is readily found to be

$$l_a \mathbf{f}^a = \left[\frac{1}{2} \eta \left((\nabla_\perp \phi)^2 - (\nabla_\parallel \phi)^2 \right) - V(\phi) \right] \mathbf{l} + \eta (\nabla_\perp \phi) (\nabla_\parallel \phi) \mathbf{t}, \quad (2.44)$$

where we also defined the two directional derivatives

$$\nabla_\perp = l_a \nabla^a, \quad \nabla_\parallel = t_a \nabla^a. \quad (2.45)$$

Given that the surface Hamiltonian (2.41) is purely intrinsic, we are not surprised that the corresponding stress is purely tangential. However, contrary to the case of a simple surface tension, it is no longer isotropic, since it contains the term $(\nabla^a \phi) (\nabla^b \phi)$ that is not proportional to g^{ab} .

2.4.2.2. Vector Field

As explained above, a good example of a vector field on a lipid membrane is *lipid tilt*. Let us describe this by the tangential surface vector $\mathbf{m} = m^a \mathbf{e}_a$ (which is not necessarily normalized). In this case we already have quite a number of possibilities to create a scalar energy density from this, even at minimal coupling to the geometry (i.e., $\partial_a \rightarrow \nabla_a$). A fairly general case is studied in [27]; here we will restrict to the simpler example

$$\mathcal{H}(m^a) = \frac{1}{2} \lambda M^2 + V(m^2), \quad \text{with} \quad M = \text{div}(m^a) = \nabla_a m^a. \quad (2.46)$$

The Euler-Lagrange equation for the field m^a is found to be

$$0 = \mathcal{E}(\mathcal{H}) = -\lambda \nabla_a M + 2V'(m^2) m_a, \quad (2.47)$$

and the stress tensor is given by [27]

$$\mathbf{f}^a = \left[\left(\frac{1}{2} \lambda M^2 + \lambda m^c \nabla_c M - V(m^2) \right) g^{ab} - 2V'(m^2) m^a m^b \right] \mathbf{e}_b, \quad (2.48)$$

which is again tangential but not isotropic. Notice, however, that while in the scalar case the *gradient* term gave rise to the anisotropic stress, here it is the *potential* term. In (\mathbf{l}, \mathbf{t}) coordinates the projection on l_a reads

$$l_a \mathbf{f}^a = \left[\frac{1}{2} \lambda M^2 + \lambda (m_\perp \nabla_\perp + m_\parallel \nabla_\parallel) M - V(m^2) - 2V'(m^2) m_\perp^2 \right] \mathbf{l} - 2V'(m^2) m_\perp m_\parallel \mathbf{t} . \quad (2.49)$$

Curiously, a vector field leads to a substantially more complicated stress than a scalar field. If we include all possible quadratic gradient terms, it becomes even more daunting [27].

2.4.2.3. Membrane Shape

In some sense, we can think of membrane shape as a tensor field, since the membrane is characterized by the two tensors g_{ab} and K_{ab} . However, as has been mentioned repeatedly, these tensors are not independent, since they both have to correspond to one and the same surface.

Once shape and tensors are involved, a large number of scalars is possible, but from a physical point of view only a few of them will usually contribute to the energy. As we have discussed above when we generalized the naïve bending expressions (2.7) or (2.8), one can systematically construct a shape-based surface density by expanding it in scalar invariants — allowed by symmetry and ordered by dimensionality. In this context the by far most-frequent Hamiltonian in use is the symmetric quadratic energy expression due to Helfrich, Eq. (2.29). We will only look at this example.

Since $K = g^{ab} K_{ab}$, we easily find $\partial K / \partial K_{ab} = g^{ab}$ and $\partial K / \partial g_{ab} = -K^{ab}$. For the latter we need to remember that $\partial g^{ab} / \partial g_{cd} = -\frac{1}{2} (g_{ac} g_{bd} + g_{ad} g_{bc})$. Writing $R = K^2 - K_{ab} K^{ab}$, we can also calculate that $\partial R / \partial K_{ab} = 2(K g^{ab} - K^{ab})$ and $\partial R / \partial g_{ab} = -2(K K^{ab} + K_c^a K^{bc}) = -2R^{ab}$, where the second step follows from Eq. (2.26).¹⁰ We now only need to know two more things: (i) the Einstein tensor $G_{ab} = R_{ab} - \frac{1}{2} R g_{ab}$ vanishes identically in two dimensions (a simple consequence of Eq. (2.23)); and (ii) the tensor $K g^{ab} - K^{ab}$ is divergence-free, as follows from a contraction of Eq. (2.24). Putting all this together, we arrive at

$$\mathbf{f}^a = \left[\kappa K (K^{ab} - \frac{1}{2} K g^{ab}) - \sigma g^{ab} \right] \mathbf{e}_b - \kappa (\nabla^a K) \mathbf{n} . \quad (2.50)$$

Unlike the scalar- and vector-example from above, this tensor is no longer tangential: it has a normal component proportional to the gradient of the curvature. Moreover, the tangential part f^{ab} is again not isotropic — its eigenvectors coincide with those of the curvature tensor; it is thus diagonal in a coordinate system aligned with the principal directions. Notice finally that the Gaussian modulus $\bar{\kappa}$ has dropped out: *the Gaussian curvature term does not contribute to curvature stress.*

Performing the projection on (\mathbf{l}, \mathbf{t}) coordinates, we find

$$l_a \mathbf{f}^a = \left[\frac{1}{2} \kappa (K_\perp^2 - K_\parallel^2) - \sigma \right] \mathbf{l} + \kappa K K_{\perp\parallel} \mathbf{t} - \kappa (\nabla_\perp K) \mathbf{n} , \quad (2.51)$$

where we also introduced the coordinate-adapted components of the curvature tensor

$$K_\perp = l^a l^b K_{ab}, \quad K_\parallel = t^a t^b K_{ab}, \quad K_{\perp\parallel} = l^a t^b K_{ab} . \quad (2.52)$$

Observe the reappearance of the “ $\perp^2 - \parallel^2$ ” motif that we’ve already seen in the scalar case.

From the divergence of the stress we obtain the shape equation. For a closed vesicle it reads

$$P = \mathcal{E}(\mathcal{H}) = \mathbf{n} \cdot \nabla_a \mathbf{f}^a = \kappa \left[K (R - \frac{1}{2} K^2) - \Delta K \right] + \sigma K . \quad (2.53)$$

We see that this Euler-Lagrange equation contains (i) a cubic of the curvature and (ii) its (surface) Laplacian. The tension enters linearly in the curvature. If we set the bending rigidity to zero, we arrive at the well-known Young-Laplace law $P = \sigma K$, relating the excess pressure inside a water droplet or a soap bubble to its curvature and surface tension. In fact, for a *spherical* vesicle this equation *also* reduces to $P = \sigma K$, since in this case both $R - \frac{1}{2}K^2 = 0$ and $\Delta K = 0$; as far as bending goes, spherical surfaces do not create a normal force density.¹¹

2.5. MEMBRANE-MEDIATED INTERACTIONS

The idea that interactions between membrane-associated proteins can be created by membrane-based fields (provided that the proteins somehow “couple” to these fields) is a very fruitful and well-studied one. In 1984 Mouritsen and Bloom introduced the mattress model, in which elastic stretching and compression of the lipid bilayer due to hydrophobically mismatched proteins creates interactions between these proteins and affects their phase behavior [34]. Their treatment was later refined by several other groups [35–39]. Coupling to a composition field was investigated in the context of wetting [40–43] and charge-demixing [44–46]. Goulian, Bruinsma, and Pincus first studied interactions mediated by curvature [47,48], a subject taken up by many other groups [27,49–63].

After having introduced the concept of a stress tensor, membrane-mediated interactions between bound particles can be described in a remarkably clear way: the forces between these particles are encoded in the stress tensors pertaining to the field(s) to which the particles couple. And just as in classical three-dimensional elasticity theory, the total force on a particle can be identified with the flux of stress through a closed surface (here: loop) around that particle. However, before this can be exploited, one more subtle point must be clarified.

If several such particles indeed exert forces onto each other, this will generally induce them to *move*. In this case the situation is no longer static, and we would for instance also have to consider viscous stresses. In order to avoid this complication we will assume that the relative positions of the particles are fixed. There are still membrane-mediated forces, but they are now counterbalanced by the constraints. Or, conversely, *the constraints act as sources of stress* for the membrane that can be picked up by closed loop integrals, such that the force on particle i can be written as

$$\mathbf{F}_i = -\oint_i ds \, l_a \mathbf{f}^a, \quad (2.54)$$

where the loop encircles exclusively particle i .

Below we will look at examples of mediated interactions for different fields, but always the same overall geometry: two identical particles are separated a distance d from each other, and their membrane perturbation is such that mirror symmetry with respect to the plane between them holds (see Fig. 2.3). The force on, say, the left particle can then most conveniently be obtained via a contour that passes exactly along the symmetry curve between the particles, while the three remaining branches — 2, 3, and 4 — are drawn out to infinity, since there the stress tensor either vanishes or is at least very simple.

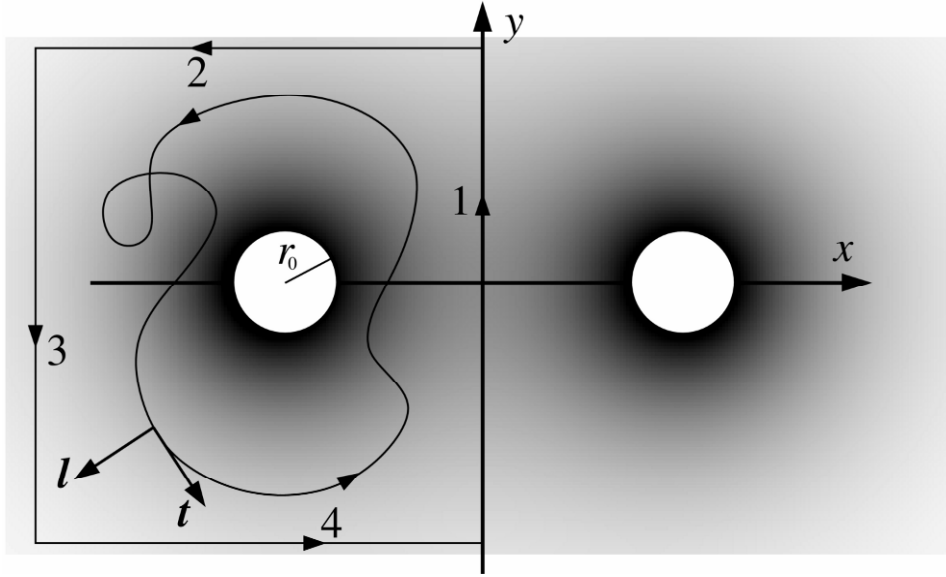


Figure 2.3. Mediated interactions via stress tensor integrals. Two circular particles of radius r_0 and mutual separation d locally disturb a field and thus interact. The force on, say, the left particle can then be obtained by a closed-loop integral of the flux of stress. Let this loop locally have a tangent vector $\mathbf{t} = l^a \mathbf{e}_a$ and an outward-pointing unit normal vector $\mathbf{l} = l^a \mathbf{e}_a$. Since the stress tensor away from external perturbations is divergence-free, the contour can be conveniently deformed such as to conform to the existing mirror symmetry. Furthermore, branches 2, 3, and 4 can then be drawn out to infinity, where the stress tensor typically assumes a very simple form.

The route to interactions à la stresses then proceeds along the following two steps:

1. Simplify the stress integral as far as possible by exploiting all available symmetries. This leads to an exact analytical connection between field and force.
2. Solve the field equation for the two particles and insert into the previously obtained force formula. This, of course, is the hard part. Below we will restrict to linearized situations and superposition approximations. It should be noted, however, that the usefulness of the stress tensor approach does not rest on these approximations. For instance, the exact analytical formula can unveil interesting information about the force even in the absence of a solution to the field equation.

2.5.1. Exact Analytical Interaction Formulas

2.5.1.1. Scalar Field

For the scalar field ϕ we need to integrate the stress flux from Eq. (2.44) along branches $1 \rightarrow 2 \rightarrow 3 \rightarrow 4$. If far away from the two particles the field approaches the value $\phi = 0$, and if furthermore $V(\phi = 0) = 0$, the stress flux vanishes on branches 2, 3, and 4. We then readily find

$$\mathbf{F} = - \int_1 ds \left\{ \frac{1}{2} \eta \left[(\nabla_{\perp} \phi)^2 - (\nabla_{\parallel} \phi) \right] - V(\phi) \right\} \mathbf{l} . \quad (2.55)$$

Moreover, since mirror symmetry holds, $\nabla_{\perp}\phi$ vanishes on branch 1. We hence obtain for the force on the left particle

$$\mathbf{F} = \int_1 ds \left\{ \frac{1}{2} \eta (\nabla_{\parallel}\phi)^2 + V(\phi) \right\} \mathbf{l} . \quad (2.56)$$

If $V(\phi) \geq 0$, we see that the force is attractive, since \mathbf{l} always points in the positive x -direction (i.e., for the left particle that we're concerned about it points toward the right particle). This result holds true no matter how complicated $V(\phi)$ is otherwise, i.e., no matter how nonlinear and intractable the field equations are.

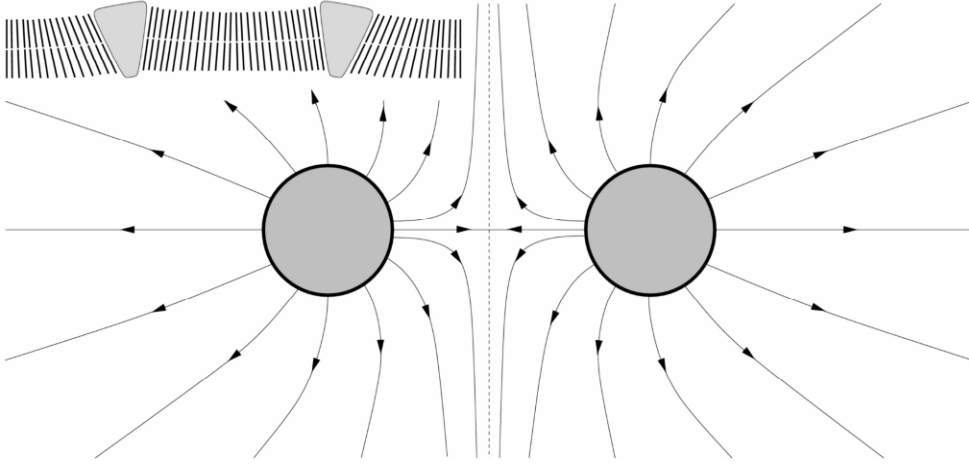


Figure 2.4. Lipid tilt field lines. Two-lipid tilt imposing circular particles symmetrically inserted into a bi-layer gives rise to tilt field lines as qualitatively illustrated in this sketch. A visual analogy to electrostatics suggests that in this situation the two particles should repel — a suspicion confirmed by the actual calculation, see Eq. (2.69). Reprinted with permission from [27]. Copyright © 2005, American Physical Society.

2.5.1.2. Vector Field

For the vector field m^a we need to look at the stress (2.49). We will make the same assumption as for the scalar field, namely that m^a and $V(m^2)$ vanish far away from the perturbations, such that we again only need to consider branch 1. The stress tensor is a fair bit more complicated than in the scalar case, but mirror symmetry will save the day: most terms vanish. To understand why this is so, it is helpful to visualize the situation, which is done in Figure 2.4.

To begin with, $m_{\perp} = l^a m_a$ must vanish on the axis, since a vector field that has a mirror symmetry with respect to some plane must on that plane have a vanishing normal component. This alone removes three of the terms in Eq. (2.49). Next, the term $m_{\parallel} \nabla_{\parallel} M$ can be rewritten as $\nabla_{\parallel}(m_{\parallel} M) - M \nabla_{\parallel} m_{\parallel}$. Here, the total derivative is *along* the direction of integration and will thus only contribute two boundary terms — but these vanish if the field vanishes at the boundaries

(which we took to be infinitely far away). Since furthermore we have $M = \nabla_{\perp} m_{\perp} + \nabla_{\parallel} m_{\parallel}$, we readily find

$$\mathbf{F} = - \int_1 ds \left\{ \frac{1}{2} \lambda \left[(\nabla_{\perp} m_{\perp})^2 - (\nabla_{\parallel} m_{\parallel})^2 \right] - V(m^2) \right\} \mathbf{1} . \quad (2.57)$$

Notice that despite a substantially different stress tensor the structure of this term is vexingly similar to the general scalar expression in Eq. (2.55). However, in this case the \perp -term does *not* drop out: Even though m_{\perp} vanishes on the mid-curve, $\nabla_{\perp} m_{\perp}$ generally does not. And since this term has the opposite sign compared to the two other terms, the *overall* sign of the interaction (i.e., attraction vs. repulsion) is no longer obvious. Notice, again, the appearance of the “ $\perp^2 - \parallel^2$ ” motif.

2.5.1.3. Membrane Shape

The relevant stress tensor is now the one from Eq. (2.51). In this case we have to be a bit careful, because even though the curvatures will approach zero far away from the perturbation (since we have an asymptotically flat membrane in mind), the surface tension σ will not vanish. However, it is easy to see what its contribution is: branches 2 and 4 will cancel against each other. On branches 1 the direction is always in the *positive* x -axis (in particular, it has no vertical component, since the surface on that branch is horizontal in x -direction for symmetry reasons). On branch 3 the direction is always in the *negative* x -axis. The only difference of these two branches is a difference in the *length* of the integration contour: While branch 3 is a straight line, branch 1 is generally curved, since the surface close to the membrane-deforming objects is not flat. There will thus be an *extra length* ΔL by which branch 1 is longer than branch 3,¹² thus implying an extra force $\sigma \Delta L$ in the positive x -direction (i.e., a tension-mediated attraction). As far as curvatures are concerned, both $KK_{\perp\parallel}$ and $\nabla_{\perp} K$ are zero on branch 1. The first one vanishes because branch 1 is a *line of curvature* on which the off-diagonal element of the curvature tensor, $K_{\perp\parallel}$, is equal to zero; the second vanishes obviously for reasons of mirror symmetry. We therefore arrive at the curvature-mediated force

$$\mathbf{F} = \sigma \Delta L \mathbf{x} - \frac{1}{2} \kappa \int_1 dx \left\{ K_{\perp}^2 - K_{\parallel}^2 \right\} \mathbf{x} . \quad (2.58)$$

There it is again: the “ $\perp^2 - \parallel^2$ ” motif in the mediated force, and again the fact that it’s the *difference* between squares that matters prevents a simple determination of the sign of the interaction. While the surface tension term and the \parallel -derivative drive an attraction, the \perp -derivative drives a repulsion.

We can, however, specialize to a case in which the sign becomes clear. Think of two very long particles of length L that lie parallel to each other, e.g., two actin bundles adsorbed on a membrane. In the limit in which we can ignore end-effects (say, $L \gg d$, where d is their mutual separation), this becomes a quasi-one-dimensional problem, because the translationally invariant direction along the particles drops out, and we need to look at a *force per length*, F/L , between these particles. There is still an excess length ΔL , but it does not scale with the particle length, so its contribution to the force per length vanishes for large L . Something similar happens with the K_{\parallel} -contribution: it no longer scales with the length of the particle, because it is only different from zero at the two ends — between the ends branch 1 is essentially a straight

line. In consequence, the K_{\parallel} contribution per length also vanishes in the limit of long particles. However, the K_{\perp} -contribution does not vanish: In fact, K_{\perp} will have some constant value anywhere between the ends of the long particles, and the deviations at the ends will again vanish in the limit. Hence, in the long-particle limit we arrive at

$$\mathbf{F}/L = -\frac{1}{2}\kappa K_{\perp}^2 \mathbf{x} \quad (\text{long particles, } L \gg d), \quad (2.59)$$

and we immediately see that we have a repulsion. It should be pointed out that even though this formula no longer seems to contain the tension σ , this does by no means imply that the force is independent of it: it enters implicitly by codetermining the curvature K_{\perp} on branch 1, since the tension σ has of course *not* dropped out of the shape equation.

2.5.2. Interaction Forces for Simple Linearized Situations

In the previous section we have discussed ways to derive interaction forces in terms of simple integrals over the stress tensor. These furnish tight connections between geometry and forces and often have a remarkably simple structure. They are analytically exact, but they are also formal, since one cannot extract actual numbers out of them without knowing the values for the respective fields. The latter requires one to solve the shape equations, and this is generally difficult, because for curved surfaces they are invariably nonlinear.

However, in order to illustrate the usefulness of the approach, we will now derive explicit force formulas between two particles for situations in which the shape equations can indeed be solved — for instance, by restricting to scalar or vector fields on flat membranes, or to small deviations from flatness such that the Hamiltonian can be linearized.

It should also be remarked that even if the differential equation is linear, solving it in the absence of sufficient symmetry can be quite a task. The reason is that boundary conditions need to be adjusted at the surfaces of two particles. One might want to object that the superposition principle should still hold — and of course it does — but what is sometimes not sufficiently well appreciated is how this principle may (or rather: may not) be used if the sources of fields are *not* point particles. One needs to write the general solution as a superposition of, say, eigenfunctions of the differential operator and *the boundary conditions need to be applied to the superposition*. It'd be so much easier if one could instead look at a single particle — a much more symmetric situation! — adjust the boundary conditions, and then superimpose two such solutions belonging to two different particles. But, alas, after boundary conditions have been fixed, one can no longer superimpose the solutions, because solution 1 of particle 1 added up onto solution 2 of particle 2 will destroy the boundary conditions at particle 2, which only went into the construction of solution 2 (and, of course, vice versa). But be this as it may, this incorrect superposition can still be a good *approximation* to the two-particle solution, and this “cheat” is more politely termed “superposition approximation” or “Nicolson approximation” [64]. For the sake of clarity we will employ this shortcut here, since we are more interested in illustrating the geometry–force relation rather than how to solve partial differential equations with tedious boundary conditions. Under what conditions a superposition approximation gives at least the correct far-field behavior is a nontrivial question that we will not delve into here.

2.5.2.1. Scalar Field

The treatment of the scalar field theory on a membrane we have provided above is valid for arbitrarily curved membranes. Remember that the curvature enters into the covariant gradient. It results in a Laplace operator in the field equation that in truth is the curvilinear Laplace-Beltrami operator, and it ends up having the metric tensor appear in the stress tensor.¹³ So, even if the scalar field theory is quadratic, the resulting field equation may be very difficult because the Laplace-Beltrami operator is nonlinear.

To avoid all these complications, let us therefore restrict to a situation in which the surface on which the field lives is in fact flat. Hence, the geometry becomes trivial, but of course the forces do not. The Euler-Lagrange Eq. (2.42) becomes $-\eta\Delta\phi + V'(\phi) = 0$, where Δ now is the “ordinary” Laplacian in the plane. For the simple quadratic case $V(\phi) = \frac{1}{2}t\phi^2$ we therefore get the Helmholtz equation

$$(\Delta - \ell^{-2})\phi = 0, \quad \text{with } \ell = \sqrt{\eta/t}. \quad (2.60)$$

Let us assume that a circular particle of radius r_0 has adsorbed onto the surface, which locally fixes the value of the scalar field ϕ to the value ϕ_0 . The problem then acquires cylindrical symmetry, and Eq. (2.60) can be rewritten as

$$\tilde{r}^2\phi'' + \tilde{r}\phi' - \tilde{r}^2\phi = 0, \quad \text{with } \tilde{r} = r/\ell \quad \text{and} \quad ' = \partial/\partial\tilde{r}. \quad (2.61)$$

This is a modified Bessel equation, whose general form is $x^2y'' + xy' - (x^2 - n^2)y = 0$. The solution of this equation are the modified Bessel functions of first and second kind, $I_n(x)$ and $K_n(x)$, respectively [65]. At large argument the former asymptotically scale like $I_n(x) \approx e^x/\sqrt{2\pi x}$ and the latter like $K_n(x) \approx \pi e^{-x}/\sqrt{2\pi x}$. The solution of the field equation which satisfies the boundary condition $\phi(r_0) = \phi_0$ at the rim of the particle and which vanishes at $r \rightarrow \infty$ is therefore given by

$$\phi(r) = \phi_0^* K_0(r/\ell), \quad \text{with } \phi_0^* = \phi_0/K_0(r_0/\ell). \quad (2.62)$$

We see that the field decays essentially exponentially with a characteristic length ℓ determined by the (square root of the) ratio between the two coupling constants η and t entering the Hamiltonian.

If we now have two such particles at a center-to-center distance d , and if we use the superposition approximation, the total field ends up being the sum of two such decaying Bessel functions, centered at the respective particles. We can then insert that field into the interaction equation (2.56) and obtain, after a little bit of algebra, the following expression for the force:¹⁴

$$\begin{aligned} F(d) &= 2t\ell \phi_0^{*2} \int_{-\infty}^{\infty} d\xi \left\{ \frac{\xi^2 K_1^2\left(\sqrt{\xi^2 + (d/2\ell)^2}\right)}{\xi^2 + (d/2\ell)^2} + K_0^2\left(\sqrt{\xi^2 + (d/2\ell)^2}\right) \right\} \\ &= 2\pi t\ell \phi_0^{*2} K_1(d/\ell). \end{aligned} \quad (2.63)$$

The pair potential is then the integral over this force:

$$U(d) = -2\pi\eta\phi_0^{*2} K_0(d/\ell). \quad (2.64)$$

Just like the field itself, the interaction decays like the modified Bessel function of second kind and order 0, and thus essentially exponentially with length scale ℓ .

Notice that ℓ diverges as $t \rightarrow 0$, and the interaction thus becomes logarithmic and very long ranged. However, two cautionary remarks should be made then:

1. The potential $V(\phi)$ will most likely have higher-order terms (since in the spirit of a Landau theory we think of it as an expansion in the field). Likely this might be a term of quartic order. This will change the naïve solution obtained for $t \rightarrow 0$, but it is hard to calculate this because then the differential equation is no longer linear.
2. As is well known, a potential $V(\phi) = \frac{1}{2}t\phi^2 + \frac{1}{4}u\phi^4$ (with $u > 0$) approaches its critical point in the limit $t \rightarrow 0$ [28]. This also means that critical fluctuations will become important, and they of course must also contribute to the interaction, in the spirit of a Casimir force [29–33]. Since for a simple scalar field theory the upper critical dimension is $d = 4$, this means that for $d < 4$ the fluctuation part to the free energy at the critical point will be more important than the mean field contribution [28]. Hence, even though our calculation for the interaction force becomes large and significant in this limit, it also becomes questionable, because the critical contribution must be expected to be larger.

2.5.2.2. Vector Field

Restricting again to the case of a planar surface, the Euler-Lagrange equation (2.47) for the vector field m^a that belongs to the Hamiltonian density (2.46) simplifies to

$$-\lambda\nabla(\nabla \cdot \mathbf{m}) + 2V'(m^2)\mathbf{m} = 0, \quad (2.65)$$

where we now use the terminology \mathbf{m} to describe the two-dimensional vector field in the plane. Notice that the two del-operators in a row are “grad-div” and not “div-grad”, i.e., they are *not* the Laplacian of the vector \mathbf{m} . Assuming a quadratic potential $V(m^2) = \frac{1}{2}tm^2$, this equation becomes

$$-\nabla(\nabla \cdot \mathbf{m}) + \ell^{-2}\mathbf{m} = 0 \quad \text{with} \quad \ell = \sqrt{\lambda/t}, \quad (2.66)$$

where the characteristic length ℓ is again the square root of the ratio of the two moduli that define the Hamiltonian.

Restricting again to axisymmetry and writing $\mathbf{m}(r) = m(r)\mathbf{e}_r$, this equation becomes

$$\tilde{r}^2 m'' + \tilde{r} m' - (\tilde{r}^2 + 1)\phi = 0, \quad \text{with} \quad \tilde{r} = r/\ell \quad \text{and} \quad ' = \partial/\partial\tilde{r}. \quad (2.67)$$

After what we have learned from the scalar case, this is readily recognized again as a modified Bessel equation, this time however of order 1. The radially symmetric solution that imposes the boundary condition $m(r_0) = m_0$ at the rim of a circular tilt-imposing particle of radius r_0 and that vanishes at infinity is given by

$$m(r) = m_0^* K_1(r/\ell), \quad \text{with} \quad m_0^* = m_0/K_1(r_0/\ell). \quad (2.68)$$

This looks similar to the scalar case, but here it is the modified Bessel function of second kind and order 1 that solves the problem. Still, the tilt again decays essentially exponentially with characteristic length ℓ .

Two such particles at a center-to-center distance d , within superposition approximation, create a total field that can be inserted into interaction equation (2.57). Once more a little straightforward algebra is required and one obtains

$$\begin{aligned} F(d) &= 4t\ell m_0^{*2} \int_{d/2\ell}^{\infty} d\xi \frac{\left(\xi^2 - 2(d/2\ell)^2\right) K_0(\xi)K_2(\xi) + \left(\xi^2 - (d/2\ell)^2\right) K_1^2(\xi)}{\xi \sqrt{\xi^2 - (d/2\ell)^2}} \\ &= -2\pi t\ell m_0^{*2} K_1(d/\ell). \end{aligned} \quad (2.69)$$

While the integral looks substantially different from the scalar case, the final result is almost identical — *with one absolutely crucial difference*: there is an additional minus sign out front, which means that the interaction is this time *repulsive*! Integrating the force, we find the pair potential for the symmetric tilt-mediated interaction to be

$$U(d) = 2\pi\lambda m_0^{*2} K_0(d/\ell). \quad (2.70)$$

As has been pointed out above, the Hamiltonian (2.46) for the vector field is not the most general possible. Even if we restrict to the quadratic level, there are two more first-derivative terms possible that would consequently enter into the stress tensor and the Euler-Lagrange equation. Remarkably, it turns out that they hardly change the interaction formula (2.70): all that happens is that the modulus λ is replaced by the expression $\lambda + 2\mu$, where μ is a second modulus, multiplying the quadratic term $M_{ab}M^{ab}$ in the extended Hamiltonian, where $M_{ab} = \frac{1}{2}(\nabla_a m_b + \nabla_b m_a)$ is the *symmetrized* derivative of the vector field. The modulus ν of a third term $\frac{1}{4}\nu F_{ab}F^{ab}$, where $F_{ab} = \nabla_a m_b - \nabla_b m_a$ is the *antisymmetrized* derivative, does not enter the force at all. This is discussed in detail in [27].

It is indeed curious to see that the form of the interaction potential compares in every detail to the scalar case — except the sign. This shows that any plausibility argument concerning the question of whether membrane-perturbing particles attract or repel should be eyed with some suspicion. Apparently, a good sanity check is this: would the prediction of one's favorite argument depend on whether the particles perturb a scalar or a vector field?

2.5.2.3. Membrane Shape

The last case we would like to look at is curvature elastic membranes. In this case the surface of course cannot be assumed to be flat, and in order to arrive at tractable equations, we need to at least expand the integrand of the Helfrich functional up to quadratic order. The well-known result is

$$E_{\text{curv.lin}} = \frac{1}{2} \int dx dy \left\{ \kappa (\Delta h(x,y))^2 + \sigma (\nabla h(x,y))^2 \right\}, \quad (2.71)$$

where $h(x,y)$ now describes the surface by its deviation from the flat reference state $h = 0$ and Δ is once more the ordinary planar Laplacian. This simplified version of the energy functional is good as long as gradients are small, i.e., as long as we have $|\nabla h| \ll 1$.

The easiest way to obtain the Euler-Lagrange equations for this expanded functional is to actually vary it directly. One quickly obtains the result

$$\Delta(\Delta - \ell^{-2})h = 0 \quad \text{with} \quad \ell = \sqrt{\kappa/\sigma}, \quad (2.72)$$

showing that the solutions will be the eigenfunctions of the Laplacian with eigenvalues 0 and ℓ^{-2} . Hence, in the axisymmetric situation the general solution can be written as

$$h(r) = c_1 + c_2 \ln(r/\ell) + c_3 K_0(r/\ell) + c_4 I_0(r/\ell). \quad (2.73)$$

The solution which does not diverge at infinity and which would be created by a circular particle of radius r_0 , which at its rim imposes a nonzero membrane angle α , is then given by

$$h(r) = \alpha^* \ell (K_0(r_0/\ell) - K_0(r/\ell)) \quad \text{with} \quad \alpha^* = \alpha / K_1(r_0/\ell). \quad (2.74)$$

The two-particle solution is again obtained approximately via superposition of two such one-particle solutions. Knowing the shape, we can then insert it into the interaction formula (2.58). For this we need to know that $K_{\perp} = \partial^2 h / \partial x^2|_{x=0}$ and $K_{\parallel} = \partial^2 h / \partial y^2|_{x=0}$. Also, the excess length is obtained by integrating $\sqrt{1 + (\partial h / \partial y)^2} - 1 \approx \frac{1}{2} (\partial h / \partial y)^2$ along the line with $x = 0$. Working out all these derivatives is a bit tedious, but after the necessary algebra we end up with the interaction force

$$\begin{aligned} F(d) = 4\sigma\ell \alpha^{*2} \int_0^\infty d\xi \left\{ \frac{\left(\xi^2 - (d/2\ell)^2 \right) K_0\left(\sqrt{\xi^2 + (d/2\ell)^2} \right) + \xi^2 K_1^2\left(\sqrt{\xi^2 + (d/2\ell)^2} \right)}{\xi^2 + (d/2\ell)^2} \right. \\ \left. + \frac{2\left(\xi^2 - (d/2\ell)^2 \right) K_0\left(\sqrt{\xi^2 + (d/2\ell)^2} \right) K_1\left(\sqrt{\xi^2 + (d/2\ell)^2} \right)}{\left(\xi^2 + (d/2\ell)^2 \right)^{3/2}} \right\} \\ = -2\pi \sigma \ell \alpha^{*2} K_1(d/\ell). \end{aligned} \quad (2.75)$$

After having recovered from the amazement that such complicated Bessel integrals have such simple solutions, we see that the force is again repulsive. The interaction potential is then found to be

$$U(d) = 2\pi\kappa \alpha^{*2} K_0(d/\ell), \quad (2.76)$$

and is — again! — of the same structural form as all the other equations for the other fields that we have obtained so far.

However beautiful, the result in Eq. (2.76) should be viewed with a bit of skepticism: this is a situation where the superposition approximation really becomes questionable. The reason is, among other things, that in the presence of two curvature creating particles there is one important “mode” with which the particles can react to their neighbor: They can *tilt* toward or away from each other. This process, if it happens, will clearly lower the overall free energy and

thereby have an impact on the interaction. In order to account for this, one needs to do better than a simple superposition approximation, and consequently the treatment becomes significantly more involved. Yet, the calculation has been performed by Weikl, Kozlov, and Helfrich [51], even for the case of different local curvature imprints (i.e., different detachment angles α_1 and α_2 at the two particles). Since satisfying the boundary conditions exactly is extremely cumbersome, they instead expand the solution in powers of r_0/ℓ and determine the correct conditions up to this order. Setting $\alpha_1 = \alpha_2 = \alpha$, their result for the first two nontrivial orders becomes

$$U_{\text{WKH}}(d) = 2\pi\kappa \left(\frac{\alpha r_0}{\ell} \right)^2 \left\{ K_0(d/\ell) + \left(\frac{r_0}{\ell} \right)^2 K_2(d/\ell) \right\}. \quad (2.77)$$

This indeed looks fairly different from Eq. (2.76). Does it at least in some limit approach our formula? Yes, but two conditions are required: first, if $\ell \gg r_0$ we can make use of the small argument asymptotics $K_1(x) = 1/x + O(\ln(x))$ to see that $\alpha^* \rightarrow \alpha r_0/\ell$, the prefactor in (2.77). Second, if $d \gg \ell$, the second term in Eq. (2.77) will vanish compared to the first one. So, both results coincide in the fairly restrictive regime $d \gg \ell \gg r_0$. Unfortunately, this regime does not include the interesting zero-tension limit $\ell \rightarrow \infty$ at fixed separation d . Our formula in this limit again reduces to a logarithm, while the result of Weikl, Kozlov, and Helfrich becomes

$$\lim_{\ell \rightarrow \infty} U_{\text{WKH}}(d) = 8\pi\kappa\alpha^2 \left(\frac{r_0}{d} \right)^4, \quad (2.78)$$

which is the well-known correct expression. Our simple result in Eq. (2.76) does evidently *not* have this property, thus warning us against a too-confident use of the superposition approximation.

As a final side note, it might be worth pointing out that Eq. (2.78) did have a convoluted history, though. The fact that tensionless membranes mediate interactions was first shown by Goulian, Bruinsma, and Pincus [47]. These authors indeed find a $(r_0/d)^4$ decay, but with a prefactor of $-4\pi(2\kappa + \bar{\kappa})\alpha^2$. Since for reasons of mechanical stability $2\kappa + \bar{\kappa}$ must always be positive,¹⁵ the minus sign out front implied an *attraction*. In an Erratum, which appeared soon after [48], they corrected the minus sign. Later, other researchers pointed out that the dependence on the Gaussian modulus $\bar{\kappa}$ is also erroneous, since by virtue of the Gauss-Bonnet theorem [13–15] the Gaussian curvature contribution must drop out of the problem [50,51]. One then ends up at Eq. (2.78).

2.6. SUMMARY

In this chapter we have seen how membrane-mediated interactions of various types can be studied in a continuum treatment of the lipid bilayer. While the Helfrich Hamiltonian itself has been known and studied for more than three decades, the differential geometric techniques — specifically the stress tensor — are more modern or, in any case, have not been widely used. This is to some degree understandable, since this approach requires a familiarity with nonstandard mathematics. However, the remarkable geometric insight that they provide more often than not seems worth the effort. For instance, the combination of a differential geometric framework,

variational calculus, and the stress tensor language proves singularly suitable for the treatment of boundary conditions of adhering or contacting surfaces [23,66]. Notice also that recently a discussion of the stress tensor in the more familiar Monge gauge has been presented [67].

Besides exact but formal expressions, we have also derived several explicit force formulas. In order to do this analytically, we had to make certain approximations (linearization, superposition) to avoid obfuscating the line of thought. It ought to be noted that these formulas are therefore not as fundamental and trustworthy as what can in principle be achieved with the stress tensor approach. Ultimately one needs to use some kind of numerics in order to solve what invariably ends up being partial nonlinear differential equations with difficult boundary conditions. But even then the stress approach will be advantageous, since it might, for instance, be numerically more stable to determine the force by a line integral over the final numerically determined solution, rather than to obtain the energy as a function of distance as a surface integral and then numerically differentiate. Notice also that a stress analysis based on membrane shape is of course not restricted to shapes calculated mathematically. One can just as well attempt to analyze shapes determined *experimentally*, for instance, using fluorescent microscopy or various cryo-EM tomography techniques. The challenge then would be to determine these shapes accurately enough such that stresses can be extracted. In other words, one needs to be able to differentiate the shape function *three times* to get the stresses and *still* have a meaningful signal left. Such a strategy holds the potential to offer unique insights into the stresses acting in living cells, and attempts to realize such a program are currently underway [68].

Everything we have talked about in this chapter was ground state theory. No fluctuations were considered. We have seen that they might in certain cases be important — maybe more important than the ground state itself — and so one continuously needs to keep them in mind. However, even then the approach to forces via stresses is very transparent, as a recent publication by Fournier and Barbetta illustrates, in which the contribution to the lateral mechanical tension of a membrane due to its fluctuations is determined by averaging the fluctuating stress tensor [69].

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NOTES

1. In many other cases we at least *know* what needs to be fixed, but we are too clumsy to actually do it. For instance, the “trivial” solution to any cancer is to eliminate all the bad cancer cells, and we can tell quite confidently which are the bad ones when we see them; but sadly, they are so difficult to hunt down among the healthy ones.

2. Some people prefer to restrict the word “elastic” to the context of a “gradient-square theory.” Bending turns out to be a “Laplacian-square-theory.” To keep the terminology comparable but emphasize the difference, one can speak of “curvature-elasticity.”

3. If Poisson’s ratio is negative, this means that a stretched material expands in the perpendicular direction. Remarkably, $\nu < 0$ is thermodynamically permissible, but such materials (called *auxetics*) are extremely rare.

4. For obvious reasons we require them to *not* be parallel at any point: they would otherwise not span a surface there.

5. Whatever “transformational mess-up” the expression $\partial_a v_c$ suffers from, the correction term $-\Gamma_{ac}^b v_b$ must show an opposite mess-up in order to cancel the first one. Hence, if $\partial_a v_c$ is no tensor, $-\Gamma_{ac}^b v_b$ cannot be a tensor either, for otherwise their *combination* could not be a tensor. Moral: not everything that has a bunch of indices is a tensor.

6. Our world, as we know it, depends on that! In four dimensions — relevant for space-time! — the Riemann tensor has 20 components, but the Ricci tensor has only 10. Einstein’s field equations uniquely determine the Ricci tensor in terms of the energy momentum tensor of matter (e.g., the mass distribution). Hence, inside the Earth the Ricci tensor has some nontrivial value, while outside the Earth it is essentially zero. If the Ricci and Riemann tensor had the same number of components, then Ricci would uniquely determine the Riemann. But then the Riemann tensor would also vanish outside the Earth. Since a vanishing Riemann tensor implies a flat space-time, there would be no gravitational field outside the Earth — or *any* mass distribution for that matter! Curiously enough, in *three* dimensions the Ricci and Riemann tensor do have the same number of components. Gravity in three dimensions is therefore something quite different from what we know from our four-dimensional world.

7. The origin of these integrability conditions is connected with the following question: If we randomly pick a metric g_{ab} and a curvature tensor K_{ab} , will these two tensor fields describe a surface? The answer is generally “no.” Unlike for the one-dimensional case, where every choice of a curvature and a torsion function leads to a well-defined curve (even unique up to translations and rotations, if we neglect subtleties with segments where the curvature vanishes), the same does not hold for surfaces. There is just too much freedom of choice with two tensor fields. One thus needs to make sure that the intrinsic geometry, dictated by the metric, is compatible with the extrinsic geometry, encoded by the curvature tensor. That’s ultimately what the integrability conditions ensure.

8. Membrane patches resulting from a liquid–liquid coexistence in ternary lipid mixtures have been studied with great intensity in the context of “lipid rafts.” The chapter by McConnell in this book provides a historical overview.

9. Notice the important distinction between *mechanical equilibrium* and *thermal equilibrium*: in mechanical equilibrium all stresses balance and the membrane finds the shape that minimizes the Hamiltonian. One might alternatively call this the ground state. In thermal equilibrium the membrane will additionally fluctuate, leading to additional free energy contributions and possibly shifts in ground-state properties. Owing to the softness of bending modes, such fluctuations always have the potential of being relevant, yet in the present chapter we will only consider questions pertaining to mechanical equilibrium.

10. Since $R = R^{ab} g_{ab}$, we might naïvely have expected $\partial R / \partial g_{ab} = R^{ab}$, but this is wrong: R^{ab} itself depends also on the metric and needs to be differentiated. In fact, looking at the definition of the Riemann tensor, Eq. (2.20), we see that it depends in a very complicated way on the

metric, and a purely intrinsic calculation is quite involved. Remarkably, the extrinsic detour is *significantly* less painful.

11. This is also related to the *scale invariance* of the bending energy, i.e., its independence of absolute size. If a spherical vesicle had a normal force density that would like to move the surface, it would have to be the same everywhere (since all points on a sphere are equivalent). But this would correspond to a tendency to uniformly expand or shrink the sphere. But since uniform scaling does not change the energy, the force must indeed vanish.

12. If the reader is concerned by the fact that both branch 1 and branch 3 will have infinite length once the contour has been extended to infinity, it might be advisable to calculate the difference in length *before* that limit is performed. It is then easy to see that since both branch 1 and 3 become straight lines far away from the curvature perturbation; the excess length is indeed a well-defined quantity.

13. This is in fact the only way in which the curved geometry enters. Nowhere does a curvature tensor explicitly show up. Hence, the nontrivial geometry affects the physics in the smallest possible way, and this is sometimes referred to as “minimal coupling to curvature.”

14. While it is not hard to derive the integral, solving it is quite a task! The author has to confess ashamedly that he was unable to formally derive the solution. Instead, he essentially *guessed* the answer (after noticing striking similarities in the series expansion of the integral) and then confirmed it numerically up to machine precision. The same is true for the even more formidable Bessel integrals that will occur in Eqs. (2.69) and (2.75).

15. If the two principal curvatures are c_1 and c_2 , we have $K = c_1 + c_2$ and $K_G = c_1 \cdot c_2$. The Helfrich Hamiltonian (density) is then $\mathcal{H} = \frac{1}{2}\kappa K^2 + \bar{\kappa} K_G = \frac{1}{2}(c_1; c_2) \cdot \begin{pmatrix} \kappa & \kappa + \bar{\kappa} \\ \kappa + \bar{\kappa} & \kappa \end{pmatrix} \cdot \begin{pmatrix} c_1 \\ c_2 \end{pmatrix}$. Requiring (the matrix of) this quadratic form to be positive definite gives rise to the conditions $2\kappa > -\bar{\kappa} > 0$.

PROBLEMS

- 2.1. Prove Ricci's lemma, namely, that both $\nabla_a g_{bc} = 0$ and $\nabla_a g = 0$.
- 2.2. Prove that the Gaussian curvature can be written as $K_G = \frac{1}{2}(K^2 - K_{ab}K^{ab})$.
- 2.3. Show that the metric determinant is indeed given by the square of the modulus of the cross-product between the two tangent vectors, i.e., $g = |\mathbf{e}_1 \times \mathbf{e}_2|^2$.
- 2.4. Why is it true that $\mathbf{e}_a \cdot \partial_b \mathbf{n} = -\mathbf{n} \cdot \partial_b \mathbf{e}_a$?
- 2.5. Given that the stretching modulus of typical phospholipid bilayers is $K_{\text{stretch}} \approx 250 \text{ mN/m}$, what value for Young's modulus of the membrane interior would this imply, if we make the simplifying assumptions that such an identification is permissible? Is that value reasonable?
- 2.6. Show that Poisson's ratio for an incompressible material has the value $\nu = \frac{1}{2}$.

FURTHER STUDY

The topics covered in this chapter spanned from membrane biology up to differential geometry, and naturally there's no single book to study all of this. All biological aspects are nicely summarized in many excellent textbooks on molecular cell biology, such as the ones by Lodish et al. [1] or Karp [2]. Physical and in particular thermodynamic properties of membranes are covered in the book by Heimburg [3]. Much about the physics of membranes viewed as curvature-elastic fluctuating surfaces can be learned in the comprehensive review article by Seifert [18] or in the excellent *Proceedings of the Fifth Jerusalem Winter School on the Statistical Mechanics of Membranes and Surfaces*, which have recently appeared in a substantially extended second edition [70]. Differential geometry — as far as it is needed here — is best learned in the older texts such as the classical ones by do Carmo [13], Spivak [14], or Kreyszig [15]. The reader will find a more modern and abstract introduction, but with physicists in mind, in the book by Frankel [71]. The union of differential geometry and variational calculus is the topic of a beautiful book by Lovelock and Rund [72]. The stress tensor, as it has been discussed in this chapter, has been introduced by Capovilla and Guven, and their series of publications is highly recommended by virtue of being both succinct and clear. In [22] the tensor is first introduced and its existence is connected to Noether's famous theorem. A technically very different but highly efficient method both for doing the variation as well as for identifying the stress tensor has later been proposed by Guven [25] (this is the route I indicated in this chapter). An excellent coverage of the topics discussed in this chapter can also be found in the thesis by Müller, which is available online [73].

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