ON THE GEOMETRY OF SOFT MATTER OBJECTS POSSESSING DIFFERENT ORDERS OF COMPLEXITY GOVERNED BY THE SURFACE TENSION, CURVATURE ELASTICITY AND THE INTERACTION WITH THE SOLID SUPPORTS

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Abstract

In this paper we consider the interplay between the surface tension, bending elasticity and geometrical curvature of soft matter objects in rising order of complexity, namely, from water microdroplets to model lipid membranes (vesicles) and cells (erythrocytes) contacting artificial solid surfaces.

1. Introduction

In the hierarchy of biological complexity, the lipid bilayer membranes are the most ‘simple’ liquid crystal systems capable to self-organize in water in a large variety of shapes starting from planar lamellae, vesicles (closed membrane shells encapsulating water with dissolved components) (Fig.1a) to hexagonal phase (Fig.1b) and lipid nanotubes (LNT) (the cylindrical structures shown on Fig.1c, respectively). Owing to their amphiphilic nature, lipid molecules assemble into bilayer in water in order to minimize the contact of hydrophobic chains to the surrounding water.

These objects attracted experimental and theoretical attention since the lipid bilayer forms a supporting matrix for the proteins in living cell membranes and plays an important role in the maintaining of the cellular shape. Free-standing or supported lipid bilayers (SLB), both in planar and closed shape geometry, are intensively studied [1-13,16-19,21,22,24-30] since they serve as a convenient model system mimicking basic properties of biological membrane. These systems demonstrate a wide area of practical applications ranging from search of new functional food components [14] to micro-bioreactors for the surface and curvature-controlled reactions [19-21,24-30]. Other newly developed systems, the so-called liquid marbles, allow the construction of micro-bioreactors in a larger scale (> 100 microns) [15,31-34].

Geometry of the elastic lipid membranes plays an essential role in self-organization of biomimetic reactors and networks [24-30]. In particular, the formation of surface-immobilized lipid vesicles interconnected with hollow water-filled lipid nanotubes with controlled geometry has been reported in [24-26].
Lipid nanotubes (LNT) or lipid tethers are water-filled cylindrical vesicles of radius between 300 nm – 500 nm formed spontaneously in lipid aggregates or pulled out from bilayer vesicles by various techniques [24-27]. The lipid membrane nanotubes demonstrate peculiar micromechanical behaviour. Besides practical applications, these model systems enable fundamental studies of curvature elasticity role in cell membrane dynamics, reactions and transport phenomena in a nanometer scale.

![Fig.1](image)

Fig.1. (a) A sketch of lipid bilayer vesicle, a container with encapsulated water and microcomponents; (b) a hexagonal phase (upper cylinder) and (c) a lipid nanotube (LNT); (d) a micro-bioreactor of larger scale (a liquid marble of radius ~ 100 μm composed of a microdroplet of blood enwrapped with hydrophobic powder) for rapid blood typing measurements (reprinted from [15] with permission).

The red blood cell (RBC) is considered as a ‘primitive’ cell since it has a simple inner architecture of the cell - without organelles (nucleus and mitochondria). In thermodynamic and rheological studies, the red blood cell is viewed as a droplet of a complex fluid demonstrating non-Newtonian viscosity. Being adsorbed on surfaces, red blood cells may easily change their shapes. Since the RBC membrane contains no special focal adhesion proteins normally present in other type of cells [37], the RBC adsorption is considered as a passive adhesion. The interaction of RBC with hydrophobic or hydrophilic polymer supports is a crucial factor in biomedical applications in particular, for the blood-contacting materials and devices [45]. Visible geometry of cells is the sensor response of the cell membrane to the interaction with surfaces.

The shape transformation of cells on a supportive surface indicates a favorable or unfavorable thermodynamic state of the system. The equilibrium shape of membrane corresponds to the minimum of the free elastic energy of the membrane [3-10]. In a large number of theoretical works [1-5,], the shape and dynamics of RBC and lipid vesicles on supports has been modelled on the basis of curvature elasticity model (the so-called Helfrich [5] or Canham-Helfrich theory [4,5]) with the adhesion strength included for the membrane-support interaction [6-13].

In this paper we represent the resulting geometry and shape of objects (in rising order of complexity) on solid supports after the application of mechanical (shear) stress to the i) microdroplets of water; ii) lipid dispersion in buffer solution; iii) lipid myelin shapes; iv) lipid ‘pearling’; v) supported lipid containers and networks with LNTs; and vi) the shape of red blood cells contacting a polymer surface. In these different soft matter objects the common point is the interplay between the surface tension, adhesion, membrane elasticity and effects of curvature.
1. Water.

Starting from the most ‘simple’ however fundamental element in soft and biological systems (water), we investigated the mechanics and geometrical shape of a water droplet onto the hydrophobic-hydrophilic surface of (Fig.2a-c) polymer fibres and (Fig.2e-f) of ultrathin water film hydrophilic microscopy glass. The mechanical force exerted on water microdroplet by using a surface smearing technique, produced the film stretching. The contraction of the film under the action of surface tension opposing the mechanical stretching and the evaporation of water at heating of the film surface, created highly non-equilibrium conditions resulted in the formation of cusps (fingering or viscous ‘legs’), i.e. regions of curvature singularities of the liquid front. The experimentally observable effect is a consequence of non-homogenous distribution of the film surface density. Similar phenomena has been analyzed in [23] in terms of Marangoni-driven curvature flows in a low viscous complex fluid. For the comparison, we present the shape of a water droplet in the standard WOC measurement on the surface of a hydrophobic polymer support (polyurethane microfibres) treated with the oxygen plasma to make the polymer surface more hydrophilic (Fig.2a-c).

![Fig.2](image)

Fig.2 . The water droplet on the hydrophobic-hydrophilic surfaces of polyurethan (experimental: electrospun polyurethane fibrous network; WOC measurements. (a) Hydrophobic response on pristine electrospun fibre membrane. (b) Hydrophilic response on oxygen treated fibres during the dynamic wetting process 10 s after drop has been deposited on the surface. (c) Advancing and receding angle from progressing drop on tilted oxygen treated fibres (reproduced from [37] with permission). (e)Thin (distilled) water film stretched onto the surface of hydrophilic glass (Microscopy: 40x objective, phase contrast, Zeiss Axiovert 200); (f) zoomed fragment of (e).

2. Lipids dispersion in water: curvature elasticity and the shape of aggregates.

Owing to their amphiphilic nature, lipid molecules assemble into bilayer in water in order to minimize the contact of hydrophobic chains to the surrounding water. Lipid dispersions in water demonstrate rich phase behaviour depending on temperature conditions (thermotropic liquid crystals (LC) properties) and the content of water (lyotropic LC properties) [1]. Lipid molecules in water solutions spontaneously form liquid crystalline structures of various
shapes – lamellae, spheres (micelles and vesicles), cylindrical structures (straight lipid tubes or tethers), myelin forms and helicoidal surfaces (Fig.2c). The cylindrical structures (tethers) and myelin forms (Fig.2b) are also observed in red blood cells.

The application of similar mechanical stress as described in section (1), produced 2D patterns with the regions of sign varying curvature of the lipid film fronts (Fig.3a). The dark lines show the streamlines of lipid microscopic colloidal particles dragged by the hydrodynamic flows arising during the lipid material redistribution at rapid in-plane liquid film motion.

Fig. 3. (a) The pattern shows the curvature of the lipid film after the application of mechanical stretching (the microdroplet of lipid dispersion was prepared from soy bean lecithin powder, Merck, quickly dispersed in water solution with added 50% of alcohol for the rapid evaporation of the solvent; the lipid film was prepared by the surface smearing technique. Microscopy: 40x objective, phase contrast, Zeiss Axiovert 200). (b) The self-assembled lipid forms (myelin lipid structures) spontaneously organized in a dense solution of lipids in buffer; (lipids: soy bean lecithin powder, Merck; PBS standard buffer solution). The arrow points a twizzler\(^1\) form of lipids (see a zoomed fragment in (c)).

The equilibrium shape of spontaneously formed lipid structures in water and other solvents can be described within the curvature elasticity anzats suggested by Wolfgang Helfrich [5]. According to this theory, the equilibrium shape of lipid membranes corresponds to the minimum of the free energy of elasticity:

\[
F_M = \frac{K_C}{2} \int (C_1 + C_2 - C_0)^2 \, dA + \Delta P \int dV + \lambda \int dA \quad (1)
\]

where \(C_1\) and \(C_2\) correspond to the principal curvature(s) of the membrane surface, \(C_0\) is the so-called spontaneous curvature of membrane, \(A\) is the surface area of the membrane and \(V\), is the volume, \(K_C\) is the modulus of membrane bending. The Lagrange multipliers \(\Delta P\) and \(\lambda\) correspond to the hydrostatic pressure difference and surface tension, \(\sigma\), respectively [5].

For the surface–bounded vesicles the adhesion strength (or contact potential \(W_C\)) must be added [6-13]:

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\(^1\) Tweezler is a type of helicoidal CMC (constant mean curvature) surface; a special type of Delaunay surfaces.
\[ F = \frac{k_c}{2} \sqrt{(c_1 + c_2 - c_0)^2} dA + \sigma \cdot A + F_{\text{contact}}, \quad (2) \]

\[ F_{\text{contact}} = -W_c A_c. \]

with \( A_c \) introduced for the contact surface area of membrane. The shapes of vesicles on adhesive surfaces are shown schematically on Fig. 4 (a-d), respectively.

Fig. 4. Illustration of surface-bound vesicles on adhesive surfaces: (a) intact shape of a spherical vesicle with a minimal contact area (on a surface of vanishing contact potential); (b-d) surface adhesion of vesicles to (picture is a courtesy of Roger Karlsson, Göteborg University). (e) One of the first publications reporting vesicles' decomposition after adhesion on SiO2 surface (while remaining intact in shape on an oxidized gold) and formation of planar lipid bilayers [16] opened a new way for the surface functionalization of solid supports (now one of the SLB [17-19] techniques).

The application of mechanical force to the lipid membrane may essentially change the system geometry. Fig. 5 shows the system of lipid vesicles interconnected with a common lipid tether formed at the application of mechanical stress to the system (a surface smearing technique).

Fig. 5. (a) Micrograph of a ‘pearls-on-a-string’ formed in a self-organized network of lipid vesicles connected via a common lipid tether – a cylindrical tube coming through the chain of vesicles. (b) a zoomed fragment of (a) showing the catenoid \(^2\) shape of junction between the vesicle body and the ‘string’- a lipid tether or tube. The micrograph clearly shows that the lipid tether is continuous, both outside and inside the vesicle (Experimental: Lipid vesicles prepared from soybean lecithin powder, Merck, by swelling in PBS buffer; the lipid vesicles

\(^2\) Catenoid is a type of minimal surface of rotation
‘pearls-on-string’ was formed after the application of mechanical stress; method: a surface smearing technique. Microscopy: 40x objective, phase contrast, Zeiss Axiovert 200).

3. Surface-immobilized lipid vesicles interconnected via common LNTs
The membrane tether (LNT) can be pulled off from vesicle [24,25,26] by applying a gentile negative pressure to the micropipette (Fig.6a). An opening where the cylinder tether joins the patch of membrane surface, or junction, has a generalized catenoidal form. It was found, that the membrane tubule can vary in length and diameter. The neck of the nanotube has a similar to the fusion pore geometrical features however (yet) exhibiting different microstructure during its formation (e.g., contains no stalk). The nanofabrication of the network of lipid vesicles interconnected via common lipid nanotubes (LNT) has been reported in the pioneer research paper [24]. It was shown for the first time that the network can be created and its mechanical behaviour can be manipulated in a controlled way (Fig.6a and 6b). In later publications, the lipid transport along the nanotube has been studied by means of application of mechanical stress to the system of lipid vesicles. Namely, the mechanical pinching of one of the lipid vesicle (a ‘container’”) created a surface tension gradient along the tube [25]. This discovery opened a way for the micromanipulation method for producing and controlling lipid vesicle networks consisting of LNTs connecting lipid bilayer ‘containers’- surface immobilized vesicles.

The peculiar diffusion of microparticles transported via lipid nanotubes was found as a response to the application of mechanical stress to the vesicles. Experiments show [25,26] that the variation in the surface tension in the membrane led to the mechanical motion of water and dissolved microparticles in the tube. Later experiments [28,29] revealed the crucial role of the geometry of junctions between the lipid vesicles and connecting tubes influencing the lipid membrane transport. The experimentally observed transport of microparticles between lipid bilayer containers via a common nanotube in the system depicted on Fig.6a has been described in terms of Marangoni-driven lipid flow [30].

Fig 6. (a) Built-up network of surface-immobilized lipid vesicles connected with lipid tethers (LNTs) (micrograph is reprinted from the article [26] with permission). (b) two vesicles- containers with a common LNT (picture is a courtesy of Roger Karlsson, Göteborg University).

4. Lipid transport in the system of LNTs - lipid containers.
The energy of the cylindrical lipid tube of radius $R_e$ and of length $L$ pulled from lipid vesicle with the external force $f$ is given by expression [27]:

\[ E = fL - \frac{1}{2} \rho g R_e^2 L \]
As pointed out in [27], \( \sigma \) reduces \( R_t \) while bending elasticity \( K_C \) expands \( R_t \). The equilibrium radius \( R_{t0} \) of the tube is given by minimum of energy (3):

\[
R_{t0} = \sqrt{\frac{K_C}{2\sigma}}
\]

(4)

The Laplace pressure in the system of two vesicles-containers of radius \( R_1 \) and \( R_2 \), is given by \( P_1 = 2\sigma_1/R_1 \) and \( P_2 = 2\sigma_2/R_2 \), respectively.

The mechanical deformation of membrane surface (for example, pinching one of the vesicles) produces a flow of lipid fluid in lateral direction toward the higher tension point [25,26] due to the gradient of surface concentration of lipid material. We assume that:

i) Lipid membrane is fluidic in the lateral plane and lipid flow velocity is equal everywhere for the configurations (6a-b).

ii) The ‘necks’ (or junction elements) between the vesicle and the lipid tube are resistive elements and characterized by coefficient of friction (or viscous resistance value(s)).

Let us introduce the following notions:

iii) \( \nu_L \) - lipid flow velocity (mean velocity)

iv) \( \sigma \) - lipid membrane tension

v) \( \eta_L \) - viscous resistance (a friction coefficient)

Then, for the configuration shown on Fig.6b, we found:

\[
\nu_{L}^{(1)} = \nu_L = \frac{(\sigma_1-\sigma_2)}{\eta_{L1}}
\]

(5)

\[
\nu_{L}^{(2)} = \nu_L = \frac{(\sigma_2-\sigma_1)}{\eta_{L1}}
\]

(6)

By assuming that \( \eta_{L1} = \eta_{L2} = \eta_L \), from (5),(6) one can get for the velocity of the lipid flow induced by the difference in membrane surface tension \( \Delta \sigma \):

\[
\nu_L = \frac{1}{2} \frac{(\sigma_1-\sigma_2)}{\eta_L}
\]

(7)

In the equivalent electrical circuit model, the electrical current \( J \) is an analogy of the lipid flux \( J_L = 2\pi R_t \nu_L \), the voltage difference \( \Delta \phi \) is an analogy of the membrane surface tension, \( \Delta \sigma \), and the friction coefficient (or viscous resistance ) \( \eta_L \) corresponds to the electrical resistance in the circuit. Providing the analogy between these two kinetic processes, one can consider the expression (7) as an analogy of the Ohm law for the membrane transport in the network of vesicles-containers connected with LNTs.
The reason for the high viscous resistance in the LNT junction elements in such a system can be a viscous friction coupling between monolayers in the bilayer (considering a junction curvature and a so-called surface viscosity value). A detailed analysis of the surface viscosity of lipid bilayer membrane and the calculation of the friction coefficient is presented in the paper [42].

This effect of the so-called Marangoni motion of the lipid layer which arises due to the gradient of surface tension along the lipid tube connecting two vesicles-containers, can be analysed also within the standard fluid mechanics scheme [20]. Considering two reservoirs (vesicles 1 and 2) joined with a common lipid film, the change in the surface concentration of lipids $\partial \alpha / \partial t$ with time is given by the equation [20]:

$$\partial \alpha / \partial t + \partial (\alpha v_x) / \partial x + \partial (\alpha v_y) / \partial y = 0 \quad (8)$$

with the surface tension for the vesicles–containers $\sigma(\alpha_x) \equiv \sigma_1$ and $\sigma(\alpha_y) \equiv \sigma_2$. For the steady flow, the straightforward calculation of the lipid flow velocity gives us the following expression:

$$v_L \approx A \frac{\Delta \sigma}{\eta \Delta t} \quad (9)$$

with the coefficient $A \sim 1$. Comparing the results (7) and (9), one can estimate the friction coefficient in (7).

The Marangoni effect, or the effect of adsorbed films on the motion of a liquid [38], has been studied also for the liquid marbles [39] systems. The liquid marbles [31-34,43] represent a class of liquid droplets packed into the shell of microparticles of different nature, for example, mineral dust or polymer microparticles and adsorbed onto the hydrophilic, hydrophobic and superhydrophobic supports [31,32,33,34,43]. Further study of the interplay between the interfacial forces phenomena changing visible geometry of the object and the hydrodynamics of the adsorbed shell (lipid bilayer in case of vesicle and film of microparticles coating a water droplet in liquid marbles) can provide a deep insight into the general mechanisms of hydrophilic–hydrophobic interactions of artificial and biological surface in contact with water [34].

Marangoni effect in LNT-based lipid vesicles can be used for the direct delivery of compounds (e.g., drugs, proteins and microparticles) between lipid containers. Instead of mechanical pinching, the difference in a surface density in the vicinity of main phase transition of the constituting lipids may lead to Marangoni lipid flow between the interconnected vesicles. In a suggested experiment, the local hyperthermia of one of the containers (with $T > T_C$) may be created, for example, by point laser irradiation, while the other lipid container remains at $T < T_C$ temperature. The Marangoni effect in liquid marbles
covered with CNTs has been studied in recent work [39]. In this study, the local heating of the droplet coating (CNTs) was created with the help of near infrared radiation (NIR).

5. Geometrical factors: the surface topography.

Two parameters – the adhesion strength (or the contact potential) and the geometry of the contact surface play a key role in the cell-surface interaction. Experimental trends in healthcare materials for regenerative medicine based on blood cells -nanoparticles interaction [15,41] and nanofibers usage [40] emphasize the importance of size, shape and geometry of contact surfaces. In this direction, further development in the theory can be useful for the quantitative explanation of visible shapes of cells on surfaces with given topographical profile. Recently, a theoretical work based on a generalized Helfrich model with curvature flows calculations [45] aiming to model the dynamic interaction of vesicles and red blood cells with surfaces of varying contact potential and different geometrical shape has been started [37,45]. In particular, it was shown that at some values for the contact potential, the membrane of vesicles wrapped over the curved areas of the contact surface. Experimentally, this phenomenon has been observed for lipid vesicles (bending of lipid membranes onto the highly curved or folded regions in a topographic polymer coating visible on Fig.7a) and for the red blood cells onto the surface of (polyurethane) microfibers of cylindrical geometry (Fig. 7b). The new trends in microscopy (a confocal and digital holography microscopy, as an example [35-37]) allow researchers to study the interaction of membranes and surfaces in 3D and to monitor the process of cell or vesicle ‘landing’ during its sedimentation in real time.

![Fig.7. (a) Lipid vesicles network with common LNTs on topographic polymer-coated (SU8) substrate (fluorescent microscopy, a view from above; micrograph is reproduced from the paper [44], with permission); (b) The shape of red blood cells contacting a polymer surface of a cylindrical geometry; a zoomed fragment of RBC leaned over the cylindrical polymer fiber (Confocal microscopy of blood cells on electrospun oxygen treated polyurethane fibers).](image)

To conclude, we have brought together surface-related physical effects in different soft matter systems, demonstrating the common features in the hierarchy levels of complexity – from liquid droplets to vesicles and red blood cells. We show that the interplay between the varying surface tension, curvature effects and adhesion strength enables various shapes formation. The theoretical description and mathematical modelling provide a deep insight into the unified physical mechanism of tension-induced dynamic phenomena in these objects,
in particular, Marangoni-driven flows, and deliver the mathematical formulation of the relations between the mechanical and thermodynamical parameters of the systems.

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References


4-210