Modelling and Analysis of Lipid membranes subject to intra-membrane viscous flows and membrane-substrate interactions

by

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Abstract

The mechanical responses of the lipid membranes and their mechanisms are of importance in the understanding of essential cellular functions such as budding, fission and vesicle formations. Inside the lipid bilayers, viscous flows play vital roles since they can influence the transportations of elements, the shapes of the lipid membranes and various cellular processes. Within the description of the continuum setting, lipid membranes can be idealized as continuous bilayer sandwich structures. Based on nonlinear elastic thin-film theory, this thesis presents the continuum-based models of lipid membranes subjected to intra-membrane viscous flows as well as interactions with the elliptical-cross-section substrates. The corresponding boundary conditions and shape equations of the membranes are formulated based on the principles of energy equilibrium law and virtual work statement. A careful derivation of the model is presented and utilized to obtain the exact analytical solutions. The solutions of the obtained shape equations in the form of Partial Differential Equations (PDEs) are obtained by using eigenfunction expansion and Mathieu function in the elliptical domain. This thesis also investigates the morphologies of lipid membranes impacted by the uniform, non-uniform and mixed types of viscous flows by modifying the obtained equilibrium equations. Finally, the thickness distension of membranes is considered, and the corresponding analytical solutions are obtained.

Preface

This main body of the thesis is composed of two peer-reviewed papers and one project.

Chapter 2 is mainly from the published paper Kim, C. I., & Zhe, L. Mechanics of Lipid Membranes under the Influence of intra-membrane Viscosity. *Math. Probl. Eng.* (2019).

Chapter 3 is mainly from the published paper Zhe, L. & Kim, C. I. Deformation analysis of lipid membranes subjected to general forms of intra-membrane viscous flow and interactions with an elliptical-cross-section substrate. *Sci. Rep.* **10**(1), 1-19 (2020).

Chapter 4 is mainly from the ongoing project related to the thickness distension of lipid membrane.

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Contents

LIST OF FIGURES

LIST OF SYMBOLS

ω: the two-dimensional surface we studied

θ^1, θ^2: the embedded surface coordinate

r: the parametric position vector of a point on the surface $r = r(\theta^\alpha)$

$\mathbf{n}$: the unit normal vector to the deformed elastic surface

$\mathbf{a}_\alpha$, $\mathbf{a}_\beta$: the associated tangent vectors of the surface

$a_{\alpha\beta}$: the surface metric/the first fundemental form

$b_{\alpha\beta}$: the surface metric/the first fundemental form

$a^{\alpha\beta}$: the dual metric component of $a_{\alpha\beta}$.

$b^{\alpha\beta}$: the dual metric component of $b_{\alpha\beta}$.

a: $a = det(a_{\alpha\beta})$

H: the Mean curvature of surface

K: the Gaussian curvature of surface

$\tilde{b}^{\alpha\beta}$: the cofactor of the curvature

$\mathbf{T}^\alpha$: the stress vector

F: the energy density per unit mass of the surface

W: the energy density per unit area of the surface

CHAPTER 1

INTRODUCTION AND BACKGROUND

Lipid membranes are vital cellular tissues, which protect cell organelles, regulate the materials entering/exiting the cell, and facilitate the signalling among cells. The researches on the mechanical responses of the lipid membranes subjected to forces and flows are of much importance in the understanding of the mechanisms of such cellular activities. Since lipid membranes are very thin and fragile, experimental studies are very limited. Thus, mathematical models describing the mechanical responses of lipid bilayers can be effective alternatives. Due to the complex nature of lipid membranes, various interdisciplinary concepts and methods such as differential geometry, continuum mechanics, nonlinear surface theory, virtual work statement and energy minimizing principles are adopted in the mathematical modelling of lipid membranes.

1.1 Introduction

1.1.1 Lipid membrane

Lipid membranes (or lipid bilayers) are thin polar membranes composed of two layers of lipid molecules [1]. They form continuous barriers (typically between

5 and 10 nanometers) and separate the interior of the cells from the outside environments. The lipid bilayers can mediate cellular processes by regulating substances entering and leaving cells. They can also carry markers that allow cells to recognize each other and pass signals to other cells through receptors [2]. Furthermore, the lipid bilayer compositions of biomembranes are important for the distributions, organizations, and functions of membrane proteins and thus for various cellular functions [3].

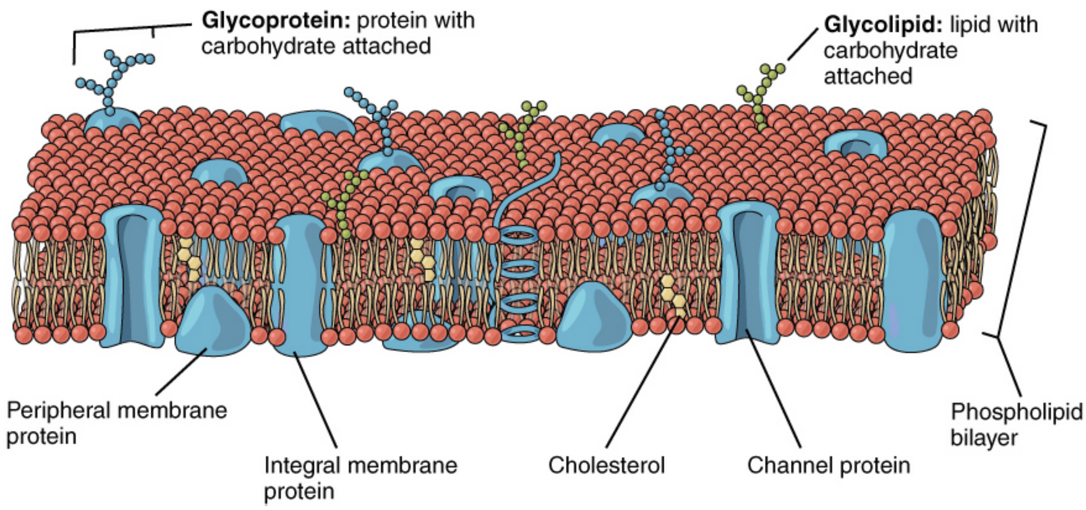

Figure 1.1: The schematic picture of a fluid membrane model of the phospholipid bilayer. (*Picture taken from*: © *2013 OpenStax College*)

As Figure 1.1 shows, the structure of the lipid membranes consists of the double layers of phospholipids with embedded, integral and peripheral proteins. The phospholipids are amphiphilic and have hydrophilic phosphate heads and hydrophobic tails consisting of two fatty acid chains. The packing of lipids within the membranes also influence their mechanical properties, including their resistances to stretching and bending [4]. Various proteins and lipid structures are embedded peripheral or inside the membrane, such as glycoprotein, glycolipid, integral membrane proteins and cholesterols [5].

1.1.2 Intracellular fluid

The intracellular fluids, also known as cytosols, are the fluids contained inside the cells [6]. They are complex liquids comprising varying amounts of proteins, macromolecules, and electrolytes [7]. The intracellular fluids impact the morphologies of the lipid membranes in the processes of osmoses because of the osmotic pressures and viscosity forces.

1.1.3 Membrane Transport

Membrane transports refer to the processes that solutes (e.g., ions, small particles) are conveyed across biological membranes through the regulations of a series of membrane mechanisms such as active and passive transports [8]. A characteristic of lipid membrane - selective membrane permeability plays a vital role in the regulation of membrane transport because it enables membranes to separate substances of different chemical properties [8].

There are two main types of membrane transports: passive transport and active transport. Passive transport is the process that the elements (icons, molecules, proteins) pass through the lipid membrane without energy input. It is the

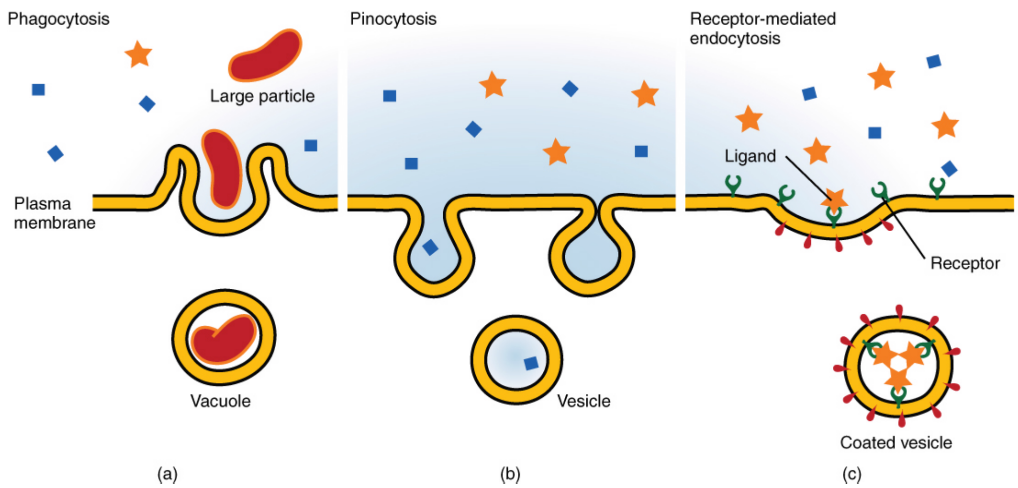

Figure 1.2: The schematic picture of a fluid membrane model of the phospholipid bilayer. (*Picture taken from*: © *2013 OpenStax College*)

spontaneous phenomenon which decreases the free energy and increases the entropy of the cellular system. The organizations and properties of the membrane lipids and proteins affect the permeability of the cell membranes and furtherly the rate of passive transport. Diffusion, facilitated diffusion, osmosis and filtration are the four most common types of passive transport [9]. In contrast, the processes that the particles move across or through membranes from the lower concentration regions to the higher concentration regions are referred to as active transports. Cellular energy is required to achieve active transport [10]. There are two types of active transport, which are primary active transport and secondary active transport. The primary active transport utilizes a source of chemical energy (e.g., Adenosine Triphosphate (ATP)) as the power source, while the secondary active transport utilizes an electrochemical gradient [10].Endocytosis is also a form of membrane active transport. It refers to the substances transporting process in which cell membranes engulf the transported particles. The target particle to be internalized is surrounded by a part of the cell lipid membrane. Then, a vesicle enclosing the ingested particle is formed through the budding of the cell. As Figure 1.2 illustrates, endocytosis includes pinocytosis (cell drinking) and phagocytosis (cell eating) [11].

1.2 Background and motivation

From the discussions in the previous sections, it is apparent that the lipid membranes are critically important tissues in various cellular activities. The mechanical properties of the lipid membranes are affected by internal/external conditions, including the intra-membrane viscous flows, proteins or molecules interactions and various forces generated from the processes of different cellular activities. To understand the mysteries of the related cellular processes, it is necessary and vital to research on the mechanical properties and morphologies of the lipid membranes.

To understand the mechanisms of various essential cellular processes such as budding, fission and fusion [12]-[16], the mechanics of the lipid membranes has consistently been the popular research area. Since lipid membranes are negligibly thin (typically 5-10nm) and fragile, the study of various aspects of lipid bilayers is often achieved by employing mathematical models in order to overcome the formidable difficulties of experimental studies. Because lipid membranes are very densely distributed, they can be idealized as thin elastic films. Within this context, the development of theoretical models describing the behavior of lipid bilayers has greatly benefited from the differential geometry of a surface and the theory of an elastic surface such that the deformation energy of a thin membrane can be expressed by the mean and Gaussian curvatures of a surface [17]-[18]. In particular, Helfrich proposed a well-known Helfrich energy potential [12] which addresses the symmetry of lipid bilayers and further ensures the resulting equilibrium state to be energy minimizing [19]. This, together with the use of variational principle, and the virtual-work statement, furnish the Euler-Lagrange equations also known as "membrane shape equations", which have been successfully adopted in a wide range of problems (see, for example, [20]-[22]). The variations of the classical Helfrich model have been continuously investigated in order to provide more efficient descriptions of lipid membranes' morphology induce by various cellular activities, such as distensions [21], tilts [23], buddings [24]-[25], spontaneous curvatures [20] and substrate interactions [26]-[28].

To investigate the impacts of the intra-membrane viscous flows on the essential cellular functions, including budding, fission and vesicle formations [29]-[32], the study of the mechanical responses of lipid membranes subjected to intra-membrane viscous flows is necessary. The authors in [33] have established the theoretical framework of the lipid membranes incorporating the effects of intra-membrane viscosity. In there, authors reveal that the dynamics of the membrane system is notably influenced by the presence of intra-membrane viscous flow. The authors in [34] developed the integrated non-linear model of membranes incorporating the effects of intra-membrane viscosity from the theory of elastic surfaces [35]-[36]. Besides, a compatible linear model within the setting of superposed incremental deformations is presented by [37]. However, to obtain a mathematically tractable system, the analysis in [37] is limited to certain types of problems where viscous flow is characterized as either constant or simple linear functions, and the interaction occurs through a circular contact region. In contrast, the realistic lipid membrane system involves more complex environments [15]-[16], such as the non-circular contaction domain, multi-source viscous flow and membrane thickness distension. Therefore, the development of a more comprehensive model considering these processes may be necessary to promote researches in the related subjects. In this respect, the authors in [38] derived the membrane model, considering the distension phenomenon induced by possible external forces. The authors in [39] developed the nonlinear model of lipid membrane employing the thickness distension. However, considering the complexity of the realistic membrane system, the models that incorporate both viscosity and thickness distension are necessary to provide more general and precise descriptions of lipid membranes.

1.3 Aims and Scope

This thesis aims to develop the theoretical models to predict the morphologies of lipid membranes subjected to intra-membrane viscous flows and interactions with elliptical-cross-section substrates. In addition, the thickness distensions of the bilayers' surfaces will be considered and analyzed. Throughout careful derivations, the theoretical model of the inviscid fluid membrane will be developed. Then the model of the lipid membranes subjected to intra-membrane viscous flows and interactions with elliptical-cross-section substrates will be developed by incorporating the viscous stress and other interdisciplinary methods. The shape equations and corresponding boundary conditions of the membranes will be formulated and then solved analytically and numerically. After obtaining the exact solutions, we will input different types of viscous flows to the obtained solutions to investigate the detailed influences of the viscous flows on the morphologies of lipid membranes. The solutions and the associated morphologies of lipid membranes will be presented both in circular and elliptical domains and compared to the existed results. Lastly, the thickness distensions of membranes will be considered, and the corresponding analytical solutions will be obtained.

1.4 Structure of the thesis

This thesis consists of five main chapters. It is composed as follows. Chapter one is the introduction to introduce the research topic, background, aim and scope of this thesis. Chapter two is the chapter to develop the nonlinear model for the mechanical responses of the inviscid fluid membranes. Chapter three discusses the model which predicts the responses of lipid membranes subjected to intermembrane viscous flows and interactions with the elliptical-cross-section substrates. The theoretical solutions for this model are obtained, plotted and analyzed. Chapter four is the chapter to study the thickness distension phenomena of the lipid membranes. The conclusions of this research and future works are presented in Chapter five.

Throughout all chapters, we make use of several well-established symbols and conventions. Therefore, unless otherwise stated, Greek indices take the values in $\{1, 2\}$ and, when repeated, are summed over their ranges. Finally, $(*)_{,\alpha}$ expresses the derivative of '$*$' concerning a coordinate θ^{α} and W_K stands for the derivatives of a scalar-valued function $W(K)$ concerning the parameter K.

CHAPTER 2

INVISCID FLUID MEMBRANES

In this chapter, we present the prerequisite knowledge of differential geometry and develop the underlying theoretical model of inviscid fluid membrane for further researches on the intra-membrane viscosity. By combining the theory of elastic surfaces, the membrane equilibrium equations and the corresponding projections on normal and tangential directions are formulated via rigorous derivations. The deformation energy of the membrane is accounted for by means of the Mean and Gaussian curvatures of the surface which are the functions of the first and second fundamental forms.

2.1 Introduction

In 1920s, E. Gorter and F. Grendel [40] found that the cell membranes are composed of lipid molecules (phospholipids) which are generally divided into two important groups: the hydrophilic head parts and hydrophobic tail groups. Later, in 1959, David Robertson [41] identified that the bilayer structure is characteristic of all biological membranes (biomembranes). The microstructures (lipid molecules) of lipid membranes are unique in that they are aligned to the normal direction of the membrane prior to the deformations. Within this prescription, lipid membranes can be regarded as a simple fluid membrane where its free energy is expressed as a function of Mean and Gaussian curvatures via the first ($a_{\alpha\beta}$) and second ($b_{\alpha\beta}$) fundamental forms. The concept has been widely and successfully adopted in the relevant subject of problems [42]-[45] where the microstructures of materials dominate the general mechanical responses.

In this chapter, we develop the underlying theoretical model of inviscid fluid membrane for further researches on the intra-membrane viscosity. In section 2.2, we present the basic formulations related to surface geometry (e.g., surface metric, coordinate configurations, definitions of curvatures) as the prerequisite knowledge of this modelling. Then the detailed derivations of this model are presented in section 2.3. Starting from the stress equilibrium equation, we obtain the membrane shape equations and their projections on normal and tangential directions via rigorous derivations. The deformation energy of the membrane is accounted for by means of the Mean and Gaussian curvatures of the surface which are the functions of the first and second fundamental forms.

2.2 Basic formulations related to surface geometry

The present modelling incorporates the configuration of differential geometry [46] regards to the morphology analysis of fluid membrane. In this framework, the two-dimensional surface we studied is defined by ω (see Figure 2.1). Then it is parameterized by the embedded surface coordinate (θ^1, θ^2). Therefore the parametric position vector $r \in R^3$ of a point on the surface can be defined by the projection $r = r(\theta^\alpha)$. The coordination of the elastic surface is then given by $\mathbf{n}(\theta^\alpha) = (1/2)\varepsilon^{\alpha\beta}\mathbf{a}_\alpha \times \mathbf{a}_\beta$, where $\mathbf{n}$ is the unit normal vector to the deformed elastic surface ω, and $\mathbf{a}_\alpha$ and $\mathbf{a}_\beta$ are the associated tangent vectors defined as $r_{,\alpha}(\theta^\alpha, t) = \partial r/\partial\theta^\alpha = \mathbf{a}_\alpha$; $\varepsilon^{\alpha\beta} = e^{\alpha\beta}/\sqrt{a}$ represents the two-dimensional permutation tensor with $a = det(a_{\alpha\beta})$. $e^{\alpha\beta}$ can be evaluated as $e^{11} = e^{22} = 0$, $e^{12} = -e^{21} = 1$. Besides, $a_{\alpha\beta}$ is the induced surface metric with the relation $a_{\alpha\beta} = \mathbf{a}_\alpha \cdot \mathbf{a}_\beta$,where the dot represents the Euclidean inner product. The matrix $a_{\alpha\beta}$ of the surface metric is a non-negative definite in general, with relation $a^{\alpha\beta} = (a_{\alpha\beta})^{-1}$, where $a^{\alpha\beta}$ is the matrix of dual metric components. The symmetric coefficients of the second fundamental form on ω is defined as $b_{\alpha\beta} = \mathbf{n} \cdot \mathbf{a}_{\alpha,\beta}$, from which we can obtain the dual metric of $b_{\alpha\beta}$ as $b^{\alpha\beta} = \mathbf{a}^{\alpha\lambda}\mathbf{a}^{\beta\mu}b_{\lambda\mu}$.

The formulations of Mean and Gaussian curvatures of surfaces are given as $H = \frac{1}{2}a^{\alpha\beta}b_{\alpha\beta}$ and $K = \frac{1}{2}\varepsilon^{\alpha\beta}\varepsilon^{\lambda\mu}b_{\alpha\lambda}b_{\beta\mu}$, where $\tilde{b}^{\alpha\beta}$ is the cofactor of the curvature with the relation: $\tilde{b}^{\alpha\beta} = 2Ha^{\alpha\beta} - b^{\alpha\beta}$.

2.3 Modelling process

The surface covariant differentiation defined by [46] is

$$\mathbf{a}_{\alpha;\beta} = \mathbf{a}_{\alpha,\beta} - \Gamma^\lambda_{\alpha\beta}\mathbf{a}_\lambda, \tag{2.1}$$

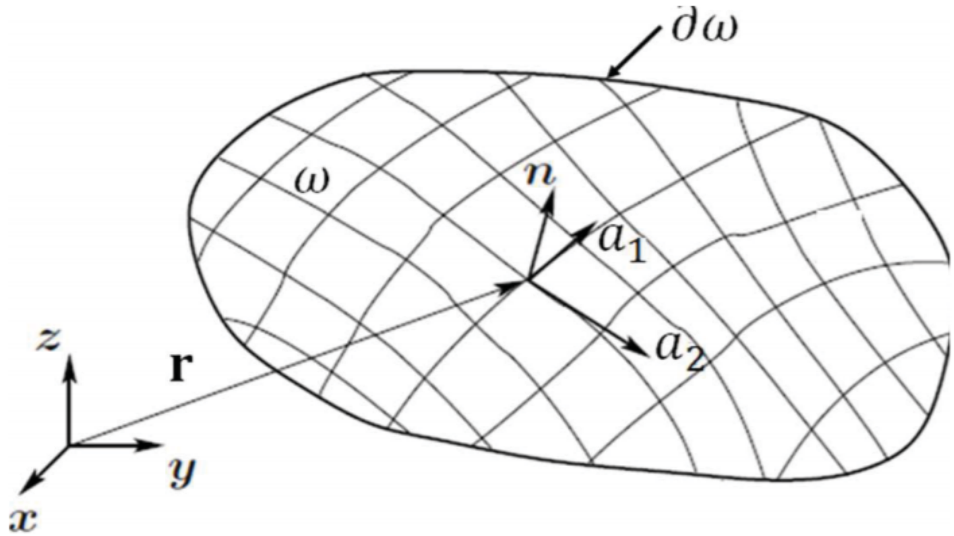

Figure 2.1: The schematic of the membrane surface. (*Picture taken from*: *Belay, T. 2016*)

where $\Gamma^{\lambda}_{\alpha\beta} = \mathbf{a}_{\alpha,\beta} \cdot \mathbf{a}^{\lambda}$ are the Christoffel symbols induced by the local surface coordinate on ω and $\mathbf{a}^{\lambda}$ is the dual basis, defined as

$$\mathbf{a}^{\alpha} = a_{\alpha\beta}\mathbf{a}_{\beta}. \tag{2.2}$$

Equations (2.1) and (2.2) furnish well know Gauss-Weigard equation:

$$\mathbf{a}_{\alpha,\beta} = (\mathbf{a}_{\alpha,\beta} \cdot \mathbf{a}^{\lambda})\mathbf{a}_{\gamma} + (\mathbf{a}_{\alpha,\beta} \cdot \mathbf{n})\mathbf{n} = \Gamma^{\lambda}_{\alpha\beta}\mathbf{a}_{\gamma} + b_{\alpha\beta}\mathbf{n}; b_{\alpha\beta} = \mathbf{a}_{\alpha,\beta} \cdot \mathbf{n}(\text{Gauss}), \text{ and} \tag{2.3}$$

$$\mathbf{n}_{,\alpha} = (\mathbf{n}_{,\alpha} \cdot \mathbf{a}_{\beta})\mathbf{a}^{\beta} + (\mathbf{n}_{,\alpha} \cdot \mathbf{n})\mathbf{n} = -b_{\alpha\beta}\mathbf{a}^{\beta}; b_{\alpha\beta} = -\mathbf{n}_{,\alpha} \cdot \mathbf{a}_{\beta}(\text{Weingarten}), \tag{2.4}$$

where $b_{\alpha\beta}$ are the coefficient of the second fundamental form (curvature) and their symmetric properties can be seen as

$$b_{\alpha\beta} = -\mathbf{n}_{,\alpha} \cdot \mathbf{a}_{\beta} = \mathbf{a}_{\beta,\alpha} \cdot \mathbf{n} = b_{\beta\alpha}. \tag{2.5}$$

Also, the contravariant cofactor of the curvature tensor is given by [46]

$$\tilde{b}^{\alpha\beta} = \varepsilon^{\alpha\lambda}\varepsilon^{\beta\gamma}b_{\lambda\gamma} \tag{2.6}$$

which is again symmetric (i.e., $\tilde{b}^{\alpha\beta} = \tilde{b}^{\beta\alpha}$) from the result of (2.5). We note here that (2.5) is valid for the sufficient smoothness of r up to the second-order (i.e., $r \in C$). Also, substituting (2.3) into (2.1) yields

$$\mathbf{a}_{\alpha;\beta} = b_{\alpha\beta}\mathbf{n}. \tag{2.7}$$

Within this prescription, the equilibrium state of a purely elastic surface, subjected to normal pressure p, is given by [35]

$$\mathbf{T}^{\alpha}_{;\alpha} + p\mathbf{n} = 0, \tag{2.8}$$

where $\mathbf{T}^{\alpha}_{;\alpha}$ and $\mathbf{n}$ are the stress vectors and the local surface unit normal, respectively. Further, the associated deformation energy of the surfaces can be expressed by the two primary parameters: the coefficient of the first fundamental form $a_{\alpha\beta}$ (the surface metric) and the second fundamental form $b_{\alpha\beta}$ (the curvature). In the case of fluid films whose energy density per unit mass of the surface is $F = F(a_{\alpha\beta}, b_{\alpha\beta})$, T^{α} takes the following compact form [35]:

$$\mathbf{T}^{\alpha} = (\sigma^{\beta\alpha} + b^{\beta}_{\mu}M^{\mu\alpha})\mathbf{a}_{\beta} - M^{\alpha\beta}_{;\beta}\mathbf{n}, \tag{2.9}$$

and

$$\begin{aligned} \sigma^{\beta\alpha} &= \rho(\frac{\partial F}{\partial a_{\alpha\beta}} + \frac{\partial F}{\partial a_{\beta\alpha}}) \\ M^{\beta\alpha} &= \frac{\rho}{2}(\frac{\partial F}{\partial b_{\alpha\beta}} + \frac{\partial F}{\partial b_{\beta\alpha}}). \end{aligned} \tag{2.10}$$

In a typical environment, where fluid films are subjected to morphological transitions, the reference velocity of the system is low and therefore the corresponding Reynolds numbers are sufficiently small [15], [16]. Further, it is widely accepted that lipid membranes are relatively stiff against areal dilation in comparison with bending or shear motions [13], [14]. This implies that deformations preserve surface area. In other words, fluid films are subjected to the two-dimensional incompressibility $J = 1$ which can be incorporated by replacing F as [35]

$$F = \overline{F} - \frac{\gamma}{\rho}, \tag{2.11}$$

where $\overline{F}$, ρ, and γ are, respectively, a constitutive function, mass density, and the Lagrange-multiplier field associated with surface pressure;

$$\gamma = \rho^2 F_\rho. \tag{2.12}$$

The energy density per unit area of the surface ω is then defined by [34]

$$W(H, K, \rho; a_{\alpha\beta}, b_{\alpha\beta}) = \rho\overline{F}, \tag{2.13}$$

where the expressions of Mean and Gaussian curvatures of surfaces (i.e., H and K) are given explicitly as [46]

$$H = \tfrac{1}{2} a^{\alpha\beta} b_{\alpha\beta} \quad \text{and} \quad K = \tfrac{1}{2}\varepsilon^{\alpha\beta}\varepsilon^{\lambda\mu} b_{\alpha\lambda} b_{\beta\mu}. \tag{2.14}$$

In particular, K satisfies

$$b^\alpha_\mu \tilde{b}^{\mu\beta} = K a^{\alpha\beta}, \tag{2.15}$$

which can be easily seen from (2.6). Therefore, we find $F = 1/\rho(W-\gamma)$ and subsequently obtain from (2.10) that

$$\begin{aligned} \sigma^{\beta\alpha} &= \rho(\frac{\partial(1/\rho)(W-\gamma)}{\partial a_{\alpha\beta}} + \frac{\partial(1/\rho)(W-\gamma)}{\partial a_{\beta\alpha}}) \\ \text{and } M^{\beta\alpha} &= \frac{\rho}{2}(\frac{\partial(1/\rho)(W-\gamma)}{\partial b_{\alpha\beta}} + \frac{\partial(1/\rho)(W-\gamma)}{\partial b_{\beta\alpha}}). \end{aligned} \tag{2.16}$$

Using chain rules, we evaluate

$$\begin{aligned} \rho(\frac{\partial(1/\rho)(W-\gamma)}{\partial a_{\alpha\beta}}) &= \rho[-\rho^{-2}\frac{\partial\rho}{\partial a^{\alpha\beta}}W + \frac{1}{\rho}(W_\rho\frac{\partial\rho}{\partial a_{\alpha\beta}} + W_H\frac{\partial H}{\partial a_{\alpha\beta}} \\ &\quad +W_K\frac{\partial K}{\partial a_{\alpha\beta}}) + \rho^{-2}\frac{\partial\rho}{\partial a_{\alpha\beta}}\gamma - \frac{1}{\rho}\frac{\partial\gamma}{\partial\rho}\frac{\partial\rho}{\partial a_{\alpha\beta}}], \end{aligned} \tag{2.17}$$

where $W_H = \partial W/\partial H$ and similarly for other terms. The derivatives of ρ, H and K with respect to $a_{\alpha\beta}$ can be evaluated as [35]

$$\begin{aligned} \frac{\partial\rho}{\partial a_{\alpha\beta}} &= -\frac{\rho}{2}a^{\alpha\beta}, \\ \frac{\partial H}{\partial a_{\alpha\beta}} &= -\frac{1}{2}b^{\alpha\beta} \\ \text{and } \frac{\partial K}{\partial a_{\alpha\beta}} &= -Ka^{\alpha\beta}, \end{aligned} \tag{2.18}$$

Accordingly, (2.17) reduces to (e.g., $-\rho^{-2}(\partial\rho/\partial a_{\alpha\beta})W = -\rho^{-2}(-(\rho/2)a^{\alpha\beta})W$, etc.)

$$\begin{aligned} \rho(\frac{\partial(1/\rho)(W-\gamma)}{\partial a_{\alpha\beta}}) &= \rho[\frac{1}{2\rho}a^{\alpha\beta}W - \frac{1}{2}a^{\alpha\beta}W_\rho - \frac{1}{2\rho}b^{\alpha\beta}W_H \\ &\quad -\frac{1}{\rho}W_K K a^{\alpha\beta} - \frac{1}{2\rho}a^{\alpha\beta}\gamma + \frac{1}{2}\gamma_\rho a^{\alpha\beta}]. \end{aligned} \tag{2.19}$$

Also from (2.12) and (2.13), F_ρ can be computed as $F_\rho = (W/\rho - \gamma/\rho)_{,\rho} = W_\rho/\rho - W/\rho^2 - \gamma_\rho/\rho + \gamma/\rho^2$, and thus it yields

$$W_\rho = \rho F_\rho + \frac{W}{\rho} + \gamma_\rho - \frac{\gamma}{\rho} \tag{2.20}$$

Substituting (2.20) into (2.19) furnishes

$$\begin{aligned}
\rho(\frac{\partial(1/\rho)(W-\gamma)}{\partial a_{\alpha\beta}}) &= [-\frac{1}{2}b^{\alpha\beta}W_H - W_K K a^{\alpha\beta} - \frac{1}{2}a^{\alpha\beta}\rho^2 F_\rho] \\
&= -\frac{1}{2}\gamma a^{\alpha\beta} - (W_H H + W_K K)a^{\alpha\beta} + \frac{1}{2}W_H \tilde{b}^{\alpha\beta}, \quad (2.21)
\end{aligned}$$

In the above we make use of the identity $b^{\alpha\beta} = 2Ha^{\alpha\beta} - \tilde{b}^{\alpha\beta}$ from the Cayley-Hamilton theorem and $\rho^2 F_\rho = \gamma$ (see (2.12)). Therefore, from (2.21) and the symmetry of $a^{\alpha\beta}$ and $\tilde{b}^{\alpha\beta}$, $(2.10)_1$ becomes

$$\sigma^{\beta\alpha} = (\lambda + W)a^{\alpha\beta} - (2W_H H + 2W_K K)a^{\alpha\beta} + W_H \tilde{b}^{\alpha\beta}, \quad (2.22)$$

where

$$\lambda = -(\gamma + W). \quad (2.23)$$

Now, we evaluate $\rho(\partial(1/\rho)(W-\gamma)/\partial b_{\alpha\beta})$ as

$$\begin{aligned}
\rho(\frac{\partial(1/\rho)(W-\gamma)}{\partial b_{\alpha\beta}}) &= \rho[-\rho^{-2}\frac{\partial\rho}{\partial b^{\alpha\beta}}W + \frac{1}{\rho}(W_p\frac{\partial\rho}{\partial b_{\alpha\beta}} + W_H\frac{\partial H}{\partial b_{\alpha\beta}} \\
&\quad + W_K\frac{\partial K}{\partial b_{\alpha\beta}}) + \rho^{-2}\frac{\partial\rho}{\partial b_{\alpha\beta}}\gamma - \frac{1}{\rho}\frac{\partial\gamma}{\partial\rho}\frac{\partial\rho}{\partial b_{\alpha\beta}}]. \quad (2.24)
\end{aligned}$$

Since,

$$\begin{aligned}
\frac{\partial\rho}{\partial b_{\alpha\beta}} &= 0, \\
\frac{\partial H}{\partial b_{\alpha\beta}} &= \frac{1}{2}a^{\alpha\beta} \quad (2.25) \\
\text{and } \frac{\partial K}{\partial b_{\alpha\beta}} &= \tilde{b}^{\alpha\beta},
\end{aligned}$$

Equation (2.24) becomes (e.g., $W_H(\partial H/\partial b_{\alpha\beta}) = W_H(1/2)a^{\alpha\beta}$)

$$\frac{\partial(1/\rho)(W-\gamma)}{\partial b_{\alpha\beta}} = \frac{1}{2}W_H a^{\alpha\beta} + W_K \tilde{b}^{\alpha\beta}. \quad (2.26)$$

Invoking (2.26) and $(2.10)_2$ furnishes

$$M^{\beta\alpha} = \frac{1}{2} W_H a^{\alpha\beta} + W_K \tilde{b}^{\alpha\beta}, \tag{2.27}$$

where $b_{\alpha\beta} = b_{\beta\alpha}$ from (2.5).

Further, by combining (2.8) and (2.9), we find

$$\begin{aligned} 0 &= (\sigma^{\beta\alpha} + b^\beta_\mu M^{\mu\alpha})_{;\alpha} \mathbf{a}_\beta + (\sigma^{\beta\alpha} + b^\beta_\mu M^{\mu\alpha}) \mathbf{a}_{\beta;\alpha} \\ & -(M^{\alpha\beta}_{;\beta})_{;\alpha} \mathbf{n} - M^{\alpha\beta}_{;\beta} \mathbf{n}_{,\alpha} + p\mathbf{n}. \end{aligned} \tag{2.28}$$

Finally, we project (2.28) into normal direction by applying dot product of unit normal $\mathbf{n}$ and subsequently obtain

$$\begin{aligned} 0 &= (\sigma^{\beta\alpha} + b^\beta_\mu M^{\mu\alpha})_{;\alpha} \mathbf{a}_\beta \cdot \mathbf{n} + (\sigma^{\beta\alpha} + b^\beta_\mu M^{\mu\alpha}) \mathbf{a}_{\beta;\alpha} \cdot \mathbf{n} \\ & -(M^{\alpha\beta}_{;\beta})_{;\alpha} \mathbf{n} \cdot \mathbf{n} - M^{\alpha\beta}_{;\beta} \mathbf{n}_{,\alpha} \cdot \mathbf{n} + p\mathbf{n} \cdot \mathbf{n}. \end{aligned} \tag{2.29}$$

But, since $a_\beta \cdot n = 0, (n \cdot n)_{,\alpha} = 0$, and $a_{\alpha;\beta} = b_{\alpha\beta}\mathbf{n}$ (see (2.7)), the above reduces to

$$(\sigma^{\beta\alpha} + b^\beta_\mu M^{\mu\alpha}) b_{\alpha\beta} - (M^{\alpha\beta}_{;\beta})_{;\alpha} + p = 0. \tag{2.30}$$

Similarly, for tangential projection (e.g., $a_\beta \cdot a^\alpha = \delta^\alpha_\beta, a_{\beta;\alpha} \cdot a^\alpha = b_{\alpha\beta} n \cdot a^\alpha = 0$, etc.), we have

$$(\sigma^{\beta\alpha} + b^\beta_\mu M^{\mu\alpha})_{;\alpha} - M^{\alpha\mu}_{;\mu} b^\beta_\alpha + p = 0. \tag{2.31}$$

where $n_{,\alpha} \cdot a^\beta = -b_{\alpha\gamma} a^\gamma \cdot a^\beta = -b_{\alpha\gamma} a^\gamma \cdot a^\beta = -b_{\alpha\gamma} a^{\gamma\beta} = -b^\beta_\alpha$ from Weingarten equation.

CHAPTER 3

MODELLING OF LIPID MEMBRANES AFFECTED BY GENERAL FORMS OF INTRA-MEMBRANE VISCOUS FLOWS AND INTERACTIONS WITH ELLIPTICAL-CROSS-SECTION SUBSTRATES

In this chapter, we study the morphologies of lipid membranes subjected to intra-membrane viscous flows and interactions with elliptical cylinder substrates. Based on the non-linear elastic surface theory, the linearized shape equations and admissible boundary conditions are formulated in the elliptical domain via the Monge representation of a surface. In particular, the intra-membrane viscosity terms are linearized and mapped into the elliptic coordinates in order to accommodate more general forms of viscous flows. The assimilated viscous flows are characterized by the potential functions which satisfy the continuity condition. A complete solution regarding Mathieu function is then obtained within the prescription of incremental deformations superposed on large. The results describe smooth morphological transitions over the domain of interest and, more importantly, predict wrinkle formations in the presence of intra-membrane viscous flows in the surface. Lastly, *the obtained solution accommodates the results from the circular cases in the limit of vanishing eccentricity and intra-membrane viscous flow.*

3.1 Introduction

In this chapter, we study the deformations of lipid bilayers subjected to the intra-membrane viscous flows and the interactions of elliptical cylinder substrates. Utilizing the Monge parameterization of a surface and general curvilinear coordinates, the expressions of linearized shape equations and associated boundary conditions are obtained from the non-linear theory [34]. The intra-membrane viscosity terms are formulated by means of 'admissible linearization' and successively transformed into elliptical coordinates to assimilate more general types of viscous flow. More importantly, we obtained a complete analytic solution by employing adapted iterative reduction and the method of eigenfunction expansion [47]-[49], which describes the deformations of lipid membranes when interacting with intra-membrane viscous flows and elliptical-cross-section substrates. It is found that intra-membrane viscosity induces wrinkle formations of the lipid membranes, and the corresponding number of wrinkles exhibits sensitivity to both the radius of the ellipse and the intensity of viscous flows. Comparisons with phenomenologically compatible cases such as a circular substrate-membrane interaction and capillary wrinkle of polymer films, are made where the proposed model successfully reproduces the results from [37], [50] in the limit of vanishing eccentricity of an ellipse.

Further, we obtain solutions corresponding to the case of a lipid membrane subjected to non-uniform viscous flows and dual source flows. This is facilitated by the relaxed form of the prescribed tangential and normal force, and the condition of continuity along and within the elliptical boundaries, unlike those arising in circular boundaries where the admissible set of viscous flows are strictly uniform in one of the coordinate directions [37]. The resulting deformation fields show clear signs of dual source interference in that both the radial and circumferential wave forms are simultaneously predicted. Case studies vis a vis morphologically similar results of shape memory films [51] are presented to investigate the potential applicabilities of the proposed model in the analysis of different types of membranes. In particular, it is found that the principles of superposition from linear elasticity remains valid, even in the presence of general forms of dual source viscous potentials. That is, the solution of a dual source problem can be directly obtained by adding solutions of two single source problems. The solutions presented here are of more practical interest in that, essentially, they lead to solutions of problems in which the viscosity effects are characterized by a wide class of potential functions and so can accommodate a correspondingly large set of physically relevant problems. For example, potential applications may be expected in the study of wrinkle-caused disease (e.g., a macular epiretinal membrane [52]) and the influences of membrane viscosity on various cellular functions such as fusion, fission and budding [53]. Further, the presented solution reproduces the existing results

[26] when viscosity effects are removed, and does incorporate the solution of the classical membrane-substrate interaction problem [20] in the limit of vanishing eccentricity. In fact, the classical solution obtained directly from the proposed model produces more accurate predictions by identifying the additional Bessel functions, which is reduced from the Mathieu potentials.

This chapter is composed as follows. In section 3.2, we develop the normal and tangential equations of motion of viscous lipid membranes and derive the incompressible condition of viscous fluids. In section 3.3, by employing Monge representation of a surface and admissible linearization, we linearize the membrane shape equations and the corresponding boundary conditions and transform them into the elliptical domain. Then, in section 3.4, a complete solution regarding Mathieu function is obtained by employing adapted iterative reduction and the method of eigenfunction expansion. Various types of viscous flows (uniform, non-uniform and dual source types) are studied and discussed in section 3.4.1, 3.4.2 and 3.4.3. Lastly, we reduce the obtained solutions to the circular domain in section 3.4.4.

3.2 Viscous lipid membranes

The viscous stress induced by the straining effects of the fluid is given by [54]

$$\sigma^{\alpha\beta} = (\lambda + W)a^{\alpha\beta} + \nu a^{\alpha\lambda} a^{\beta\mu} \dot{a}_{\lambda\mu}, \tag{3.1}$$

where ν is the intra-membrane shear viscosity and

$$\dot{a}_{\lambda\mu} = (\mathbf{a}_\lambda \cdot \mathbf{a}_\mu)^{\dot{}} = \dot{\mathbf{a}}_\lambda \cdot \mathbf{a}_\mu + \mathbf{a}_\lambda \cdot \dot{\mathbf{a}}_\mu \tag{3.2}$$

is the time derivative of the evolving surface metric. Thus, in order to compute viscous stress, it is required to compute $\dot{\mathbf{a}}_\mu$, which can be obtained via the material time derivative of a position vector $\mathbf{r}$ [35]:

$$\mathbf{u} = \dot{\mathbf{r}} = \frac{\partial \mathbf{r}}{\partial t} + \frac{\partial \mathbf{r}}{\partial \theta^\alpha}\frac{\partial \theta^\alpha}{\partial t} = \mathbf{r}_t + \mathbf{a}_\alpha v^\alpha. \tag{3.3}$$

Accordingly, it is found that

$$\begin{aligned} \dot{\mathbf{a}}_\lambda &= \mathbf{u}_{,\lambda} = (v^\alpha \mathbf{a}_\alpha + w\mathbf{n})_{,\lambda} = v^\alpha_{,\lambda}\mathbf{a}_\alpha + v^\alpha \mathbf{a}_{\alpha,\lambda} + w_{,\lambda}\mathbf{n} + w\mathbf{n}_{,\lambda} \\ &= (v_{\alpha;\lambda} - w b_{\alpha\lambda})\mathbf{a}^\alpha + (v^\alpha b_{\alpha\lambda} + w_{,\lambda})\mathbf{n}. \because v_{\alpha;\beta} = v_{\alpha,\beta} - v_\beta \Gamma^\lambda_{\alpha\beta}, \end{aligned} \tag{3.4}$$

and

$$\dot{a}_{\lambda\mu} \overset{\text{(Eqs. 3.2\&3.4)}}{=} v_{\mu;\lambda} + v_{\lambda;\mu} - 2wb_{\lambda\mu}, \tag{3.5}$$

where $v^\alpha = \partial\theta^\alpha/\partial t$, and $\mathbf{r}_t = |\mathbf{r}_t|\,\mathbf{n} = w\mathbf{n}$ are respectively the tangential and normal velocities of a material point on the initial surface ([35], [54] and [55]).

It is now straightforward to show from Eqs. (2.22),(3.1) and (3.5) that,

$$\begin{aligned} \sigma^{\beta\alpha} &= (\lambda + W)a^{\beta\alpha} - 2(W_H H + W_K K)a^{\beta\alpha} + W_H \tilde{b}^{\beta\alpha} \\ &\quad + \nu[a^{\beta\lambda}a^{\alpha\mu}(v_{\mu;\lambda} + v_{\lambda;\mu}) - 4wHa^{\beta\alpha} + 2w\tilde{b}^{\beta\alpha}], \end{aligned} \tag{3.6}$$

which is the expression of the viscous stress.

Thus, by means of Eqs. (2.27), (2.15) and (3.6), and applying the conventional Euclidean dot product in normal $\mathbf{n}$ direction, Eq. (2.8) becomes [34]

$$\begin{aligned} p &= W_H(2H^2 - K) + 2H(W_K K - W) - 2\lambda H + \Delta(\frac{1}{2}W_H) \\ &\quad +(W_K)_{;\alpha\beta}\tilde{b}^{\alpha\beta} - 2\nu[\frac{1}{2}b^{\alpha\beta}(v_{\alpha;\beta} + v_{\beta;\alpha}) - 2w(2H^2 - K)], \end{aligned} \tag{3.7}$$

which serves as the equation of motion (normal direction) of the lipid membrane in the presence of intra-membrane viscosity effects. Further, Δ is the Laplace-Beltrami operator (i.e. $\Delta\phi = \phi_{;\alpha\beta}a^{\alpha\beta}$) on the surface Ω. Consequently, by projecting Eq. (2.8) onto the basis coordinate plane of $\mathbf{a}_\alpha$, the following tangential equations of motion can be obtained:

$$\lambda_{,\alpha} - 4vwH_{,\alpha} + 2\nu[\frac{1}{2}a^{\lambda\mu}(v_{\mu;\alpha} + v_{\alpha;\mu})_{;\lambda} - w_{,\lambda}b^{\lambda}_{\alpha}] = 0. \tag{3.8}$$

Much of literature on the mechanics of lipid membranes has revealed that a bilayer membrane can be regarded as a continuous two-dimensional elastic surface where the response functions are governed by the well-known Helfrich energy potential [12]. The model has been widely adopted in various subjects within bilayer membrane mechanics (see, for example, [20], [21] and [24], and the references therein). Following the study of [34], in this paper, we consider the symmetric membrane of the Helfrich type (i.e. $W(H,\,K) = W(-H,\,K)$), subjected to the membrane-substrate interactions and the effects of intra-membrane viscosity. The corresponding free-energy density function is defined by [12]

$$W = kH^2 + \bar{k}K, \tag{3.9}$$

where k and $\bar{k}$ are empirical bending constants, which pertain to lipid membranes with uniform properties. Thus, from Eq.(3.9), Eq. (3.7) becomes

$$
\begin{aligned}
p &= k[\Delta H + 2H(H^2 - K)] - 2\lambda H - 2\nu[\frac{1}{2}b^{\alpha\beta}(v_{\alpha;\beta} + v_{\beta;\alpha}) \\
&\quad -2w(2H^2 - K)], \qquad (3.10)
\end{aligned}
$$

while the tangential equations (Eq. (3.8)) remain intact.

Lastly, by invoking Eq. (3.5), the condition of an incompressible fluid $\dot{J}/J = \frac{1}{2}a^{\alpha\beta}\dot{a}_{\alpha\beta} = 0$ can be obtained as [56]

$$
v^{\alpha}_{;\alpha} - 2wH = 0, \qquad (3.11)
$$

where $H = \frac{1}{2}a^{\alpha\beta}b_{\alpha\beta}$.

3.3 Incremental deformations of lipid membranes

The use of Monge parameterization and admissible linearization is a widely adopted methodology for lipid membrane analysis, and the associated procedures are well documented in the literature (see, for example, [20], [24] and [27]). Here, we reformulate the results for the sake of completeness. Under the Monge parameterization, material points on the membrane surface Ω is defined by

$$
\mathbf{r}(\theta^{\alpha}, t) = \boldsymbol{\theta} + z(\boldsymbol{\theta},\ t)\mathbf{k}, \qquad (3.12)
$$

where $\boldsymbol{\theta}(\theta^{\alpha})$ is position on a plane p with unit normal $\mathbf{k}$. The problem of determining the membranes' deformed configuration is then reduced to solving a single function $z(\boldsymbol{\theta},\ t)$. In the cases of Cartesian coordinates, we have

$$\boldsymbol{\theta} = \theta^{\alpha}\mathbf{e}_{\alpha}, \tag{3.13}$$

where $\{\mathbf{e}_{\alpha}\}$ is an orthonormal basis for the plane and, the subscripts of the surface coordinates are dropped and replaced by $1 = x$, $2 = y$, unless otherwise specified. Accordingly, we compute

$$\begin{aligned}
\mathbf{r}_{,t} &= z_{,t}\mathbf{k},\ \mathbf{a}_{\alpha} = \mathbf{e}_{\alpha} + z_{,\alpha}\mathbf{k},\ a = \det(a_{\alpha\beta}) = [1 + (z_{,1})^2 + (z_{,2})^2], \\
a^{\alpha\beta} &= \delta_{\alpha\beta} + z_{,\alpha}z_{,\beta}, H = \frac{\left(1 + z_{,2}^2\right) z_{,11} + \left(1 + z_{,1}^2\right) z_{,22} - 2z_{,1}z_{,2}z_{,12}}{2a^{3/2}}, \\
K &= \frac{\left(z_{,11}z_{,22} - z_{,12}^2\right)}{a^2}, \mathbf{n} = \frac{(\mathbf{k} - \nabla z)}{\sqrt{a}}, \\
\mathbf{b} &= b_{\alpha\beta}(\mathbf{a}^{\alpha} \otimes \mathbf{a}^{\beta}) = \frac{z_{,\alpha\beta}}{\sqrt{a}}(\mathbf{a}^{\alpha} \otimes \mathbf{a}^{\beta}).
\end{aligned} \tag{3.14}$$

Here, $\nabla z = z_{,\alpha}\mathbf{e}_{\alpha}$ is surface gradient, $\delta_{\alpha\beta}$ is Kronecker delta and $\mathbf{b}$ is the curvature tensor. Further, the expressions of the dual basis and the Christoffel symbols are obtained as

$$\begin{aligned}
\Gamma^{\lambda}_{\alpha\beta} &= z_{,\lambda}z_{,\alpha\beta}/\sqrt{a}, \\
\mathbf{a}^1 &= \frac{1}{a}\left[\left(1 + z_{,2}^2\right)(\mathbf{e}_1 + z_{,1}\mathbf{k}) - z_{,1}z_{,2}\left(\mathbf{e}_2 + z_{,2}\mathbf{k}\right)\right], \text{and} \\
\mathbf{a}^2 &= \frac{1}{a}\left[\left(1 + z_{,1}^2\right)(\mathbf{e}_2 + z_{,2}\mathbf{k}) - z_{,1}z_{,2}\left(\mathbf{e}_1 + z_{,1}\mathbf{k}\right)\right].
\end{aligned} \tag{3.15}$$

In the incremental deformation analysis, it is assumed that the gradient of $z(\theta^{\alpha}, t)$ of all orders are 'small' so that their products can be neglected. The procedure is commonly referred to as admissible linearization through which the geometrical and kinematical quantities associated with the surface (Eq. (3.8)) can be approximated as

$$a \simeq 1,\ w \simeq z_t,\ \mathbf{n} = \mathbf{k} - \nabla_p z,\ \mathbf{a}^\alpha \simeq \mathbf{a}_\alpha = \mathbf{e}_\alpha + z_{,\alpha}\mathbf{k},\ \Gamma^\lambda_{\alpha\beta} \simeq 0,$$
$$\mathbf{n}\cdot\mathbf{r} \simeq z - z_{,\alpha}\theta^\alpha, \mathbf{b} \simeq\ \nabla_p^2 z,\ H \simeq \frac{1}{2}\Delta_p z \text{ and } K \simeq 0, \tag{3.16}$$

where the subscript $(*)_p$ refers to the projected counterparts of $(*)$ on the coordinate plane ω_p, $\nabla_p^2 z = z_{,\alpha\beta}\ \mathbf{e}_\alpha \otimes \mathbf{e}_\beta$ is the second gradient, and $\Delta_p z = tr(\nabla_p^2 z)$ is the corresponding Laplacian, respectively.

3.3.1 Linearization of the intra-membrane viscosity terms

In the forthcoming derivations, we present the linearization procedures for the terms associated with the intra-surface viscous flow, which arise in the formulation of membrane equilibrium equations. To proceed, we express the surface gradient of the viscous flow fields and the curvature tensor as

$$\begin{aligned} \nabla\mathbf{v} &= \nabla(v_\alpha \mathbf{a}^\alpha) = (v_{\alpha,\beta}\mathbf{a}^\alpha + v_\alpha \mathbf{a}^\alpha_{,\beta}) \otimes \mathbf{a}^\beta \overset{\text{(Eqs.2.1-2.3)}}{=} v_{\alpha;\beta}\mathbf{a}^\alpha \otimes \mathbf{a}^\beta, \text{and} \\ \mathbf{b} &= b^{\alpha\beta}(\mathbf{a}_\alpha \otimes \mathbf{a}_\beta). \end{aligned} \tag{3.17}$$

We then compute their traces to obtain

$$tr(\mathbf{b}(\nabla\mathbf{v})^T) + tr(\mathbf{b}(\nabla\mathbf{v})) = b^{\alpha\beta}(v_{\alpha;\beta} + v_{\beta;\alpha}), \tag{3.18}$$

where $\mathbf{a}_\alpha \cdot \mathbf{a}^\beta = \delta_\alpha^\beta$. Also, from the results in Eq. (3.16), Eq. (3.17) can be approximated, up to the leading order, to

$$\begin{aligned} v_{\alpha;\beta}(\mathbf{a}^\alpha \otimes \mathbf{a}^\beta) &= (v_{\alpha,\beta} - v_\lambda \Gamma^\lambda_{\alpha\beta})[(\mathbf{e}_\alpha + z_{,\alpha}\mathbf{k}) \otimes (\mathbf{e}_\beta + z_{,\beta}\mathbf{k})] \\ &\simeq (v_{\alpha,\beta})(\mathbf{e}_\alpha \otimes \mathbf{e}_\beta), \text{and} \\ \mathbf{b} &= b_{\lambda\gamma} a^{\lambda\alpha} a^{\gamma\beta}(\mathbf{a}_\alpha \otimes \mathbf{a}_\beta) \\ &= b_{\lambda\gamma}(\delta_{\lambda\alpha} + z_{,\lambda} z_{,\alpha})(\delta_{\gamma\beta} + z_{,\gamma} z_{,\alpha\beta})(\mathbf{a}_\alpha \otimes \mathbf{a}_\beta) \\ &\simeq z_{,\alpha\beta}\mathbf{e}_\alpha \otimes \mathbf{e}_\beta. \end{aligned} \tag{3.19}$$

Now, combining Eqs. (3.18) and (3.19), we find that,

$$\begin{aligned} tr(\mathbf{b}(\nabla \mathbf{v})^T) &= [v_{\alpha,\beta}(\mathbf{e}_\alpha \otimes \mathbf{e}_\beta) z_{,\lambda\gamma}(\mathbf{e}_\gamma \otimes \mathbf{e}_\lambda)] \simeq v_{\alpha,\beta} z_{,\alpha\beta} \\ tr(\mathbf{b}(\nabla \mathbf{v})) &\simeq v_{\beta,\alpha} z_{,\alpha\beta}. \end{aligned} \tag{3.20}$$

Thus, Eq. (3.18) simplifies to

$$b^{\alpha\beta}(v_{\alpha;\beta} + v_{\beta;\alpha}) \simeq z_{,\alpha\beta}(v_{\alpha,\beta} + v_{\beta,\alpha}). \tag{3.21}$$

However, since $z_{,\alpha\beta} = z_{,\beta\alpha}$, the above can be re-written as

$$z_{,\alpha\beta}(v_{\alpha,\beta} + v_{\beta,\alpha}) = 2 z_{,\alpha\beta} v_{\alpha,\beta}. \tag{3.22}$$

To obtain the simplified expression of incompressibility condition (3.11), we evaluate the surface divergence of the viscous flow field as

$$\operatorname{div} \mathbf{v} = tr(\nabla(v_\alpha \mathbf{a}^\alpha)) \overset{(\text{Eqs.3.17})}{=} tr[v_{\alpha;\beta}\mathbf{a}^\alpha \otimes \mathbf{a}^\beta] = v_{\alpha;\beta} a^{\alpha\beta} = v^\alpha_{;\alpha}, \tag{3.23}$$

where $\mathbf{a}^\alpha \cdot \mathbf{a}^\beta = \mathbf{a}_\lambda a^{\lambda\alpha} \cdot \mathbf{a}_\gamma a^{\lambda\alpha} = a_{\lambda\gamma} a^{\lambda\alpha} a^{\lambda\alpha} = a^{\alpha\beta}$. Substituting the above into Eq. (3.11), and further invoking Eq. (3.3), we arrive at

$$v^\alpha_{;\alpha} - 2wH = \operatorname{div}\mathbf{v} - 2(\frac{z_{,t}}{\sqrt{a}})H. \tag{3.24}$$

Thus, from Eq. (3.16), the leading order approximation of the above can be found as

$$v^\alpha_{;\alpha} - 2wH = (\operatorname{div}\mathbf{v})_P = v_{\alpha,a}, \tag{3.25}$$

where $(\operatorname{div}\mathbf{v})_P$ is the divergence of the projected coordinate plane Ω_p.

Consequently, substitution of these linearized expressions, (Eqs. (3.16),(3.22) and (3.25)), into Eqs. (3.8) and (3.10-3.11) delivers the following normal and tangential equations, and incompressibility conditions:

$$\begin{aligned} \frac{1}{2}k\Delta_p(\Delta_p z) - \lambda\Delta_p z - 2\nu z_{,\alpha\beta} v_{\alpha,\beta} &\simeq p,\ (\lambda + P)_{,\alpha} + v\Delta_p v_\alpha \simeq 0 \\ \text{and } v_{\alpha,\alpha} &\simeq 0 \end{aligned} \tag{3.26}$$

Here, $P = P(\theta^\alpha, t)$ is understood as a sequence of prescribed surface pressure (see, [34]) from the admissible set of boundary forces which satisfy

$$\begin{aligned} f_\tau &= \nu(v_{\alpha,\beta} + v_{\beta,\alpha})(\tau_\beta\gamma_\alpha)_p \simeq 0 \text{ and} \\ f_\gamma &= -P \simeq \lambda + \nu(v_{\alpha,\beta} + v_{\beta,\alpha})(v_\beta\gamma_\alpha)_p, \end{aligned} \tag{3.27}$$

where $\boldsymbol{\gamma} \times \boldsymbol{\tau} = \mathbf{n}$. In particular, the compatible linear forms for the moments and normal interaction forces are given by [20]

$$f_n \simeq \overline{k}\nabla_p[\boldsymbol{\tau}_p \cdot (\nabla^2_p z)\boldsymbol{\gamma}_p] \cdot \boldsymbol{\tau}_p - k\boldsymbol{\gamma}_p \cdot \nabla_p H = \sigma, \tag{3.28}$$

where $\tau'(S) = \frac{d\tau}{dS} = \frac{d\tau}{d\boldsymbol{\theta}} \cdot \frac{d\boldsymbol{\theta}}{dS} = \nabla_p \tau \cdot \boldsymbol{\tau}_p$ and σ are the arc length derivative on the projected curve, and the empirical constant accounting for the wetting of the interacting boundary, respectively. Hence, the solution of Eq. (3.26) can be determined by imposing the admissible boundary conditions, Eqs. (3.27) and (3.28).

3.3.2 Formulations in the elliptical coordinates

We consider the cases when lipid membranes interact through the elliptical contact domain of a transmembrane substrate, and are subjected a general class of intra-membrane viscous flow (see, Fig. 3.1.).The deformations of lipid membranes

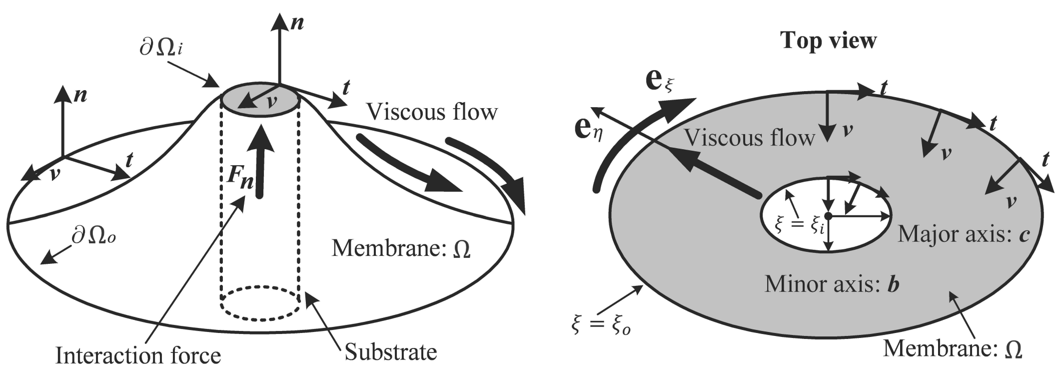

Figure 3.1: Schematic of an elliptical cylinder substrate-membrane system.

defined on an elliptical domain can be examined by using the mapping,

$$x + iy = c\cosh(\xi + i\eta), \tag{3.29}$$

such that

$$x = c\cosh(\xi)\cos(\eta) \text{ and } y = c\sinh(\xi)\sin(\eta), \tag{3.30}$$

through which the rectangular Cartesian coordinates (x, y) are mapped to the elliptical coordinates (ξ, η). The semi focal length c is defined by $c = \sqrt{a^2 - b^2}$ and $\xi \in [0, \infty)$, and $\eta \in [0, 2\pi]$ are respectively the radial and angular coordinates. Accordingly, Eqs. (3.29-3.30) furnish the gradient and Laplacian in elliptical coordinates as

$$\nabla = \frac{1}{\sqrt{c^2(\cosh^2\xi - \cos^2\eta)}}(\frac{\partial}{\partial\xi}\mathbf{e}_\xi, \frac{\partial}{\partial\eta}\mathbf{e}_\eta), \tag{3.31}$$

$$\Delta = \frac{1}{c^2(\cosh^2\xi - \cos^2\eta)}(\frac{\partial^2}{\partial\xi^2} + \frac{\partial^2}{\partial\eta^2}). \tag{3.32}$$

The condition of incompressibility (i.e. $v_{\alpha,\alpha} = 0$) then yields

$$\frac{1}{\sqrt{c^2(\cosh^2\xi - \cos^2\eta)}}(v_{\xi,\xi} + v_{\eta,\eta}) = 0, \tag{3.33}$$

from which the admissible set of viscous flow field is found to be

$$\begin{aligned} v_\xi &= \int w(\xi, \eta) d\xi + C_1\eta \\ v_\eta &= \int -w(\xi, \eta) d\eta + C_2\xi, \end{aligned} \tag{3.34}$$

so that Eq. (3.33) is satisfied (i.e. $v_{\xi,\xi} + v_{\eta,\eta} = w(\xi, \eta) - w(\xi, \eta) = 0$). In the analysis, we assume $C_1 = C_2 = 0$ for the sake of simplicity. The cases of non-zero coefficients can be easily accommodated via the principles of superposition which will be discussed in the later section.

The membrane-substrate interaction occurs through the wall of the elliptical substrate where the corresponding domain of interest, Ω, and interacting boundary, $\partial\Omega$, are defined respectively as

$$\begin{aligned} \Omega &= \xi_i \leqslant \xi \leqslant \xi_o \text{ (elliptical annulus), and} \\ \partial\Omega &= \xi = \xi_i \text{ (interacting boundary).} \end{aligned} \tag{3.35}$$

Using the mapping functions in Eqs. (3.29-3.30), the associated boundary conditions can be obtained from Eqs. (3.27) such that

$$\begin{aligned} 0 &\simeq \frac{\nu}{\sqrt{c^2(\cosh^2\xi - \cos^2\eta)}}(v_{\alpha,\beta} + v_{\beta,\alpha})(\tau_\beta \gamma_\alpha)_p, \text{ and} \\ -\lambda - P &\simeq \frac{\nu}{\sqrt{c^2(\cosh^2\xi - \cos^2\eta)}}(v_{\alpha,\beta} + v_{\beta,\alpha})(\gamma_\beta \gamma_\alpha)_p. \end{aligned} \tag{3.36}$$

Here, the repeated indices, α and β, when summed over their ranges $\{1, 2\}$, refer to ξ and η in elliptic coordinates. On the boundaries (i.e. $\xi = \xi_o$ and $\xi = \xi_i$), we find

$$\boldsymbol{\tau} = \mathbf{e}_\eta = \text{and } \boldsymbol{\gamma} = -\mathbf{e}_\xi, \tag{3.37}$$

and thereby reduce Eq. (3.36) to

$$\begin{aligned} 0 &\simeq \frac{\nu}{\sqrt{c^2(\cosh^2\xi - \cos^2\eta)}}(v_{\xi,\eta} + v_{\eta,\xi}), \text{ and} \\ -\lambda - P &\simeq \frac{\nu}{\sqrt{c^2(\cosh^2\xi - \cos^2\eta)}}(2v_{\xi,\xi}). \end{aligned} \tag{3.38}$$

In particular, since the membrane-substrate interaction condition (i.e. $\mathbf{n} - \nabla z = \mathbf{k}$, see, [20] and [22]) requires $\nabla z = 0$ at the inner boundary ($\xi = \xi_i$), the normal force (Eq. (3.28)) becomes

$$f_n \simeq -k\boldsymbol{\gamma}_p \cdot \nabla_p H = \sigma. \tag{3.39}$$

We continue by rewriting $\nabla_p H$ using Eq. (3.31) and subsequently reduce Eq. (3.39) to

$$\frac{1}{h(\xi,\eta)}\frac{\partial H}{\partial \xi} = \frac{\sigma}{k}, \quad \text{on } \partial w \text{ (i.e. at } \xi = \xi_i), \tag{3.40}$$

where,

$$h(\xi,\eta) = \sqrt{c^2(\cosh^2\xi - \cos^2\eta)}. \tag{3.41}$$

Further, applying the similar schemes as in the above, it is not difficult to show

$$z_{,\alpha\beta}\nu_{\alpha,\beta} = \frac{1}{h^3(\xi,\eta)}\,[z_{,\xi\xi}v_{\xi,\xi} + z_{,\xi\eta}v_{\eta,\xi} + z_{,\xi\eta}v_{\xi,\eta} + z_{,\eta\eta}v_{\eta,\eta}]. \tag{3.42}$$

Consequently, by combining the above results, we reformulate Eq. (3.26) and the associated boundary conditions as

$$\frac{1}{2}k\Delta(\Delta z) - \lambda\Delta z - \frac{2v}{h^3(\xi,\eta)}(z_{,\xi\xi}v_{\xi,\xi} + z_{,\xi\eta}v_{\eta,\xi} + z_{,\xi\eta}v_{\xi,\eta} + z_{,\eta\eta}v_{\eta,\eta}) = 0, \tag{3.43}$$

subjected to

$$z(\xi_i,\eta) = 0,\ \nabla z(\xi_i,\eta) = 0 \text{ and } \frac{1}{h}\frac{\partial}{\partial\xi}H(\xi_i,\eta) = \frac{\sigma}{k}. \tag{3.44}$$

Remark. 1.

It should be noted that the restrictions on the continuity conditions ($\mathrm{div}(\mathbf{v}) = 0$) and the prescribed tangential ($f_\tau = 0$) force can be relaxed along and within the elliptical boundaries unlike those arising in circular cases where the admissible set of viscous flows are required to be strictly uniform in one of the coordinate directions (i.e. either $v_r = const$ or $v_\theta = const$) to satisfy the constraints [37]. This is mainly due to the confined descriptions of the circular interaction boundary where the rate of change in the unit normal and tangent on the circular boundary remains constant so that the associated normal velocity fields v_r always points to the center of a circular substrate. Thus, v_r is required to be vanished by its gradient $v_{r,r}$ or gradient of tangential velocity $v_{\theta,\theta}$ to satisfy the continuity condition; i.e.,

$$\text{div}(\mathbf{v}) = v_{r,r} + \frac{v_{\theta,\theta}}{r} + \frac{v_r}{r} = 0. \tag{3.45}$$

Such restriction can be relaxed in the case of the elliptic interaction boundary, since the rate of change in local coordinate is not necessarily constant, yet they vary with respect to the coordinates ξ and η (see, Eqs. (3.31)-(3.32)). This further suggests that the normal velocity field v_ξ does not necessarily points to the center of an elliptical substrate (see, Fig. 3.1.) and therefore no restrictions are necessary for v_ξ. In results, the associated flow fields (v_ξ and v_η) can accommodate more general forms such as non-uniform viscous flows and periodic wave form of viscous flows (no need to be strictly constant) without violating the aforementioned constitutive restrictions. Examples regarding these cases will be discussed in the following section.

Lastly, Eqs. (3.43-3.44) serve as the linearized shape equation system which describes the morphology of lipid membranes under the influences of membrane-substrate interactions and general forms of viscous flows. In the analysis, we also impose $z(\xi_i, \eta) = 0$ for the purpose of comparison with the existing literature.

3.4 Solutions to the linearized systems

It can be seen from Eqs. (3.31), (3.32), and (3.43) that the gradient, Laplacian and the resulting PDEs in elliptical curvilinear coordinate continuously vary with respect to the material points ($\xi = \xi_o, \eta = \eta_o$) on the membrane surface, where ξ_o and η_o denote a particular configuration of the surface. In other words, the associated tangential and normal velocities are simultaneously updated as material points move over the membrane surface. Therefore, the solution of the Eq. (3.43), which is coupled with the viscous velocity fields, cannot be accommodated by the conventional separation variable method of modified Helmholtz equation. In this section, we combine the method of adoptive iteration and the principle of eigenfunction expansions [47]-[49], and obtained the complete expression of the membrane's shape function $z(\xi, \eta)$.

To proceed, we solve the homogenous sections of the Eq. (3.43) ($\frac{1}{2}k\Delta(\Delta z) - \lambda\Delta z = 0$), which is a special type of Laplace equation. The solution is obtained as

$$z(\xi, \eta) = \frac{2}{\mu^2}H(\xi, \eta) + B_m + \varphi(\xi, \eta). \tag{3.46}$$

Here, $\varphi(\xi, \eta)$ is the plane harmonic function, which is chosen as

$$\varphi(\xi, \eta) = C_m \log(e^{\xi}/e^{\xi_0}) + D_m \sum_{m=0}^{\infty} e^{-\xi} ce_m(\eta, q) \tag{3.47}$$

to accommodate the desired behavior (i.e. $|\nabla z| \to 0$) as approaching the boundary. In particular, the unknown potential $H(\xi, \eta, q)$ can be expressed as [57]

$$H(\xi, \eta) \equiv \sum_{m=0}^{\infty}\sum_{n=0}^{\infty} A_m Ke_m(\xi, q) ce_n(\eta, q) T_{mn}(\xi, \eta), \tag{3.48}$$

where $ce_n(\eta, q)$ and $Ke_m(\xi, q)$ are the modified Mathieu functions of the first and second kind, respectively, and q ($q > 0$) is the associated parameter (see, for example [58]).

Now, by substituting Eqs. (3.34) and (3.48) into Eq. (3.43), and invoking the orthogonal properties of the Mathieu function,

$$\int_0^{2\pi} ce_m(\eta, q) ce_n(\eta, q) d\eta = \int_0^{2\pi} Ke_m(\xi, q) Ke_n(\xi, q) d\xi = \pi\delta_{mn}, \text{and} \tag{3.49}$$

$$\int_0^{2\pi}\int_0^{2\pi} Ke_m(\xi, q) ce_n(\eta, q) Ke_k(\xi, q) ce_l(\eta, q) d\xi d\eta = \pi\delta_{mk}, \tag{3.50}$$

we obtain the following expressions for T_{mn}:

$$\begin{aligned} T_{mn}(\xi, \eta) \quad = \quad & \int_0^{2\pi}\int_0^{2\pi} \sum_{m=0}^{\infty}\sum_{n=0}^{\infty} - \frac{\nu}{\lambda\pi^2 h^3(\xi, \eta)} * \\ & [-e^{-\xi} ce'_m(\eta, q) Ke_m(\xi, q) ce_n(\eta, q)(\frac{\partial \int w(\xi, \eta) d\xi}{\partial \eta} \\ & + \frac{\partial \int -w(\xi, \eta) d\eta}{\partial \xi}) + \{e^{-\xi}\pi Ke_m(\xi, q) + e^{-\xi} ce''_m(\eta, q) * \\ & Ke_m(\xi, q) ce_n(\eta, q)\} w(\xi, \eta)] d\xi d\eta. \end{aligned} \tag{3.51}$$

The detailed procedures which can be found in [47]-[49] are omitted here for the sake of brevity.

Consequently, the general solution in Eq. (3.46) can be found in the form

$$\begin{aligned} z(\xi, \eta) \quad = \quad & \frac{2}{\mu^2}\sum_{m=0}^{\infty}[A_m Ke_m(\xi, q) ce_m(\eta, q) T_{mn}(\xi, \eta) \\ & + B_m + C_m \log(e^{\xi}/e^{\xi_0}) + D_m e^{-\xi} ce_m(\eta, q)], \end{aligned} \tag{3.52}$$

where $\mu = \sqrt{2\lambda/k}$ is the natural length scale which is commonly adopted in the membrane studies (see, for example, [20], [23] and [34]). Details regarding the dimensionless variables adopted in the present work will be discussed in later section. The unknown constants A_m, B_m, C_m and D_m can be completely determined by imposing the admissible boundary conditions. For instance, the substrate-membrane interaction conditions (3.44) require

$$\frac{\partial}{\partial \xi} z(\xi_i, \eta) = 0,\ \frac{\partial}{\partial \eta} z(\xi_i, \eta) = 0,\ z(\xi_i, \eta) = 0 \text{ and } \frac{1}{h(\xi_i, \eta)} \frac{\partial}{\partial \xi} H(\xi_i, \eta) = \frac{\sigma}{k}, \quad (3.53)$$

on the boundary from which we find that,

$$A_m = \sum_{m=0}^{\infty} \frac{\sigma h(\xi_i, \eta)}{k(Ke_m(\xi_i, q)ce_m(\eta, q)T'_\xi(\xi_i,\eta) + ce_m(\eta, q)Ke'_m(\xi_i, q)T_{mn}(\xi_i, \eta))}$$

$$\begin{aligned} B_m \;&=\; \sum_{m=0}^{\infty} [\frac{2h(\xi_i, \eta)\sigma}{ce'_m(\eta, q)k\mu^2} * \\ &\frac{Ke_m(\xi_i, q)ce_m(\eta, q)T'_\eta(\xi_i, \eta) + Ke_m(\xi_i, q)ce'_m(\eta, q)T_{mn}(\xi_i, n)}{Ke_m(\xi_i, q)T'_\xi(\ell, \eta) + Ke'_m(\xi_i, q)T_{mn}(\xi_i, \eta)} \\ &- \frac{2\sigma Ke_m(\xi_i, q)h(\xi_i, \eta)T_{mn}(\xi_i, \eta)}{k\mu^2(Ke_m(\xi_i, q)T'_\xi(\xi_i, \eta) + Ke'_m(\xi_i, q)T_{mn}(\xi_i, \eta))}], \end{aligned}$$

$$\begin{aligned} C_m \;&=\; \sum_{m=0}^{\infty} [-\frac{2\sigma h(\xi_0, \eta)}{k\mu^2} - \frac{2\sigma h(\xi_i, \eta)}{ce'_m(\eta, q)k\mu^2} \\ &\frac{Ke_m(\xi_i, q)ce_m(\eta, q)T'_\xi(\xi_i, \eta) + Ke_m(\xi_i, q)ce'_m(\eta, q)T_{mn}(\xi_i, \eta)}{Ke_m(\xi_i, q)T'_\xi(\xi_i, \eta) + Ke'_m(\xi_i, q)T_{mn}(\xi_0, \eta)}], \end{aligned}$$

and

$$\begin{aligned} D_m \;&=\; \sum_{m=0}^{\infty} -\frac{2\sigma h(\xi_i, \eta)e^{\xi_i}}{ce'_m(\eta, q)k\mu^2} * \\ &\frac{Ke_m(\xi_i, q)ce_m(\eta, q)T'_\eta(\xi_i, \eta) + Ke_m(\xi_i, q)ce'_m(\eta, q)T_{mn}(\xi_i, \eta)}{Ke_m(\xi_i, q)ce_m(\eta, q)T'_\eta(\xi_i, \eta) + ce_m(\eta, q)Ke'_m(\xi_i, q)T_{mn}(\xi_i, \eta)} \end{aligned} \quad (3.54)$$

where

$$
\begin{aligned}
Ke'_m(\xi, q) &= \frac{\partial Ke_m(\xi, q)}{\partial \xi},\ ce'_m(\eta, q) = \frac{\partial ce_m(\eta, q)}{\partial \eta}, \\
T'_\xi(\xi, \eta) &= \frac{\partial T_{mn}(\xi, \eta)}{\partial \xi}, T'_\eta(\xi, \eta) = \frac{\partial T_{mn}(\xi, \eta)}{\partial \eta}, \\
T'_\xi(\xi_i, \eta) &= \left[\frac{\partial T_{mn}(\xi, \eta)}{\partial \xi}\right]_{\xi=\xi_i},\ T'_\eta(\xi_i, \eta) = \frac{\partial T_{mn}(\xi_i, \eta)}{\partial \eta}.
\end{aligned}
\tag{3.55}
$$

As Fig 3.2 illustrates, the viscous flows on the membranes' surfaces can impact the morphologies of lipid membranes due to the viscous impact forces, frictional forces and the gravity of flows. The viscous impact forces are aligned with the flows' directions because of the inertia of fluid. The frictional forces are tangential to the membranes' surfaces and point to the opposite directions of the speed vectors of the viscous flows. Further, gravity points vertically downwards because of the law of attraction. When the viscous flows start to flow on the membranes' surfaces, the wrinkles appear due to the small stiffness of membranes, the frictional forces, and the gravity of flows. Then the viscous impact forces help the spreading of the wrinkles on the membranes' surfaces.

3.4.1 Constant viscous flow potential: $w(\xi, \eta) = A$

The membrane systems may be exposed to the constant viscous flow within a cell such as the selective transport of molecules inside the lipid bilayers where the molecules travel with the constant flow from one side of the membrane to the objective protein [59]. To assimilate such constant viscous flow, we consider the

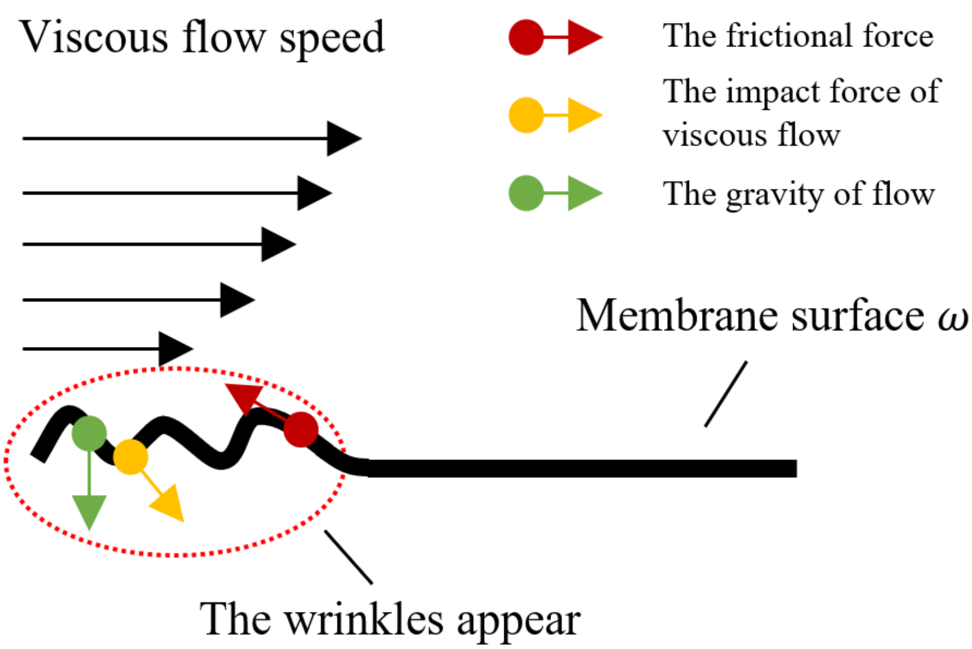

Figure 3.2: Schematic of the forces on the membrane's surface when viscous flows go through

case when $w(\xi,\eta) = A$, and thereby reduce Eq. (3.51) to

$$\begin{aligned} T_{mn}(\xi,\eta) &= \int_0^{2\pi}\int_0^{2\pi}\sum_{m=0}^{\infty}\sum_{n=0}^{\infty} -\frac{1}{\lambda\pi^2}\frac{\nu A e^{-\xi} Ke_m(\xi,q)}{h^3(\xi,\eta)}[\pi \\ &+ \frac{\partial^2 ce_m(\eta,q)}{\partial\eta^2} ce_n(\eta,q)]d\xi d\eta. \end{aligned} \tag{3.56}$$

Eqs. (3.52), (3.54) and (3.56) then deliver

$$\begin{aligned} z(\xi,\eta) &= \sum_{m=0}^{\infty}[\frac{2\sigma h(\xi,\eta) ce_m(\eta,q)}{\sigma_1}\{Ke_m(\xi,q)T_{mn}(\xi,\eta) - Ke_m(\xi_0,q)T_{mn}(\xi_0,\eta)\} \\ &-(\frac{2h\sigma}{k\mu^2} + \frac{2\sigma ce_m^2(\eta,q)h(\xi,\eta)Ke_m(\xi_0,q)}{\sigma_1} * \\ &\frac{T'_\eta(\xi_0,\eta) + T_{mn}(\xi_0,\eta)}{ce'_m(\eta,q)})\log(\frac{e^{\xi}}{e^{\xi_i}})], \end{aligned} \tag{3.57}$$

where

$$\sigma_1 = k\mu^2[Ke_m(\xi_i, q)ce_m(\eta, q)dT\xi(\xi_i, \eta, q) + ce_m(\eta, q)dKe_m(\xi_i, q)T_{mn}(\xi_i, \eta, q)]. \quad (3.58)$$

The resulting function $z(\xi, \eta)$ in Eq. (3.57) describes the morphology of a lipid membrane when subjected to membrane-substrate interactions and the effects of uniform intra-membrane viscous flow. The associated results are presented in Figs. 3.1, 3.3 and 3.4. In the assimilation, we adopt the value of intra-membrane surface viscosity $\nu = 10^{-4}pN\cdot s/nm$ and the flexural modulus of the membrane $k = 82pN\cdot nm$ from the work of [60] and [61]. The Lagrange multiplier λ is dependent on membrane systems in consideration and usually do not have definite range of values. The values of λ commonly used in the literatures is about $\lambda \propto 10^{-4}pN/nm$. In the present study, we assimilate data under the normalized setting using the aforementioned values. The dimensionless parameters used in the simulations are adopted from the works [20], [23] and [34] as;

$$\mu = \sqrt{2\lambda/k}\text{: natural length scale (e.g., } \mu a\text{: radius of a circular membrane),}$$
$$\sigma/\lambda\text{: force scale (e.g., } f_n = \sigma/\lambda\text{: interaction force).} \quad (3.59)$$

We have found that the viscous flow gives rise to wrinkle phenomena, when the normalized magnitude of viscous flow is greater than the critical number (i.e. $\frac{A\nu}{\lambda} \geq 10^{-15}$). Especially, the number of radial wrinkles with respect to the intra-membrane viscous flows (A) and the radius of the inner ellipse (μc) are illustrated in Fig. 3.3. The top two figures indicate that, with the same inner ellipse, the number of wrinkles reduce as the magnitude of viscous flow decreases from 10^{-5} to 10^{-7}. Further, the right and/or left two figures shows that the number of wrinkles increase as the inner radius of an ellipse increase from 0.3 to 0.6 while the magnitude of the viscous flow remains the same (i.e. $A = 10^{-5}$ (left) and $A = 10^{-7}$(right)). Phenomenologically compatible results can be found in the relevant works such as circular substrate-membrane interactions [37], capillary wrinkles on thin polymer films [50] and theoretical study on an elastic surface [62], where the number of radial wrinkles depends upon the size of the inner radius and membrane thickness. The proposed model successfully reproduces the reported results under physically similar/compatible settings (see Fig. 3.3 and 3.4). The solutions presented in [37] are the special case of the presented solution (see, Fig. 3.4-3.5.) in the limit of vanishing eccentricity of elliptical domains (i.e. $h(\xi_i, \eta) = a(1 - e^2 \cos^2 \eta)^{1/2} = a$ for $e \to 0$.). Lastly, we note here that the predicted wrinkle cases are unique and steady, since the proposed model satisfies strict quasi-convexity through the minimization of membranes' strain-energy potentials (see, for example, [62]-[63]).

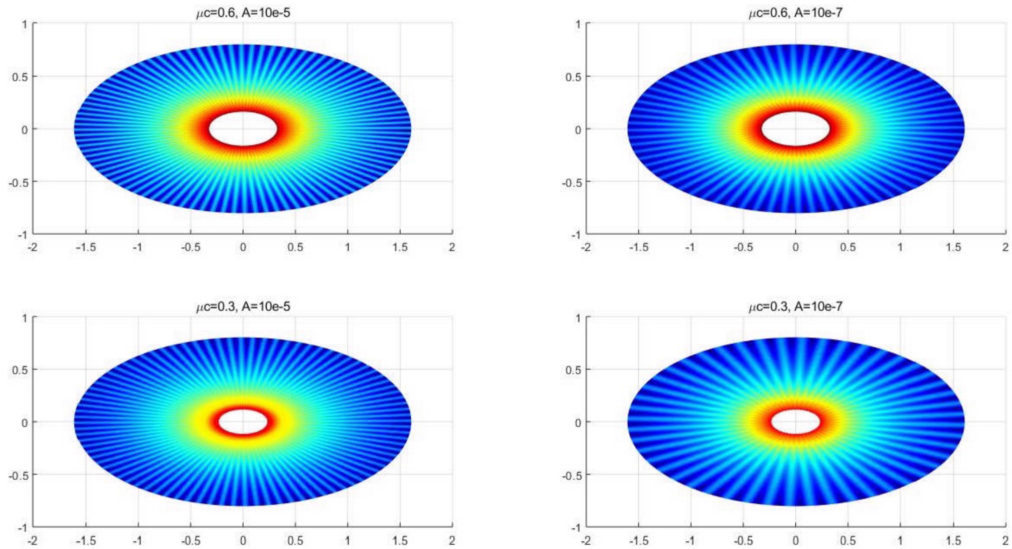

Figure 3.3: Number of wrinkles with respect to A and μc (inner radius: major axis).

3.4.2 Non-uniform viscous flow potential: $w(\xi, \eta) = A \sin \xi \cos \eta$ (waveform)

In this section, we consider membrane systems with non-uniform viscous flow. The non-uniform cases can be observed in various cellular activities such as the transportation of the intracellular membrane and the transmembrane proteins induced by the viscous flow with tension gradient [64]. In this case, the viscous flow field becomes non-uniform due to the interactions with tension gradient field.

Membranes subjected to the waveform of non-uniform viscous flows can be examined by introducing the following potential function,

$$w(\xi, \eta) = A \sin(E\xi) \cos(F\eta), \tag{3.60}$$

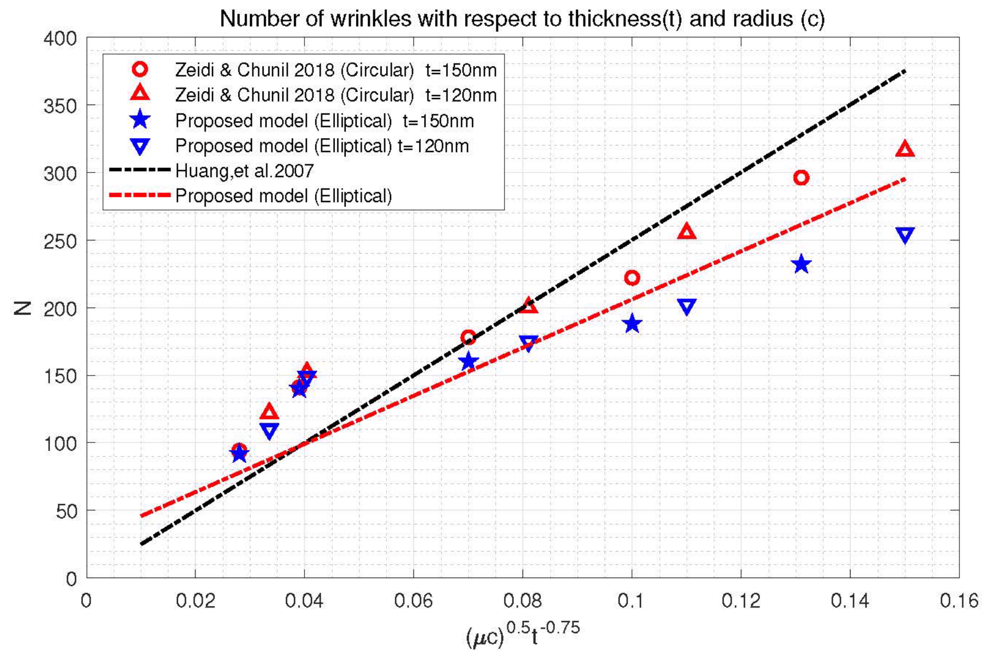

Figure 3.4: Comparisons:Number of wrinkles on thin polymer films. (*Picture taken from*: *Huang, J., et al. 2007*)

where the intensity of wavy flow can be controlled by the parameters E and F. In the assimilation, we set $E = F = 1$ for simplicity. Accordingly, from Eq. (3.51), we obtain the following expression of $T_{mn}(\xi, \eta)$, addressing the viscous effects,

$$
\begin{aligned}
T_{mn}(\xi,\eta) \quad = \quad & \int_0^{2\pi}\int_0^{2\pi}\sum_{m=0}^{\infty}\sum_{n=0}^{\infty} - \frac{1}{\pi^2\lambda}\frac{\nu A \sin\xi \cos\eta e^{-\xi} K e_m(\xi,q)}{h^3(\xi,\eta)} \; * \\
& [\pi + \frac{\partial^2 ce_m(\eta,q)}{\partial\eta^2} ce_n(\eta,q)] d\xi d\eta. \qquad (3.61)
\end{aligned}
$$

Combining (3.52), (3.54) and (3.61), the complete solution describing the mem-

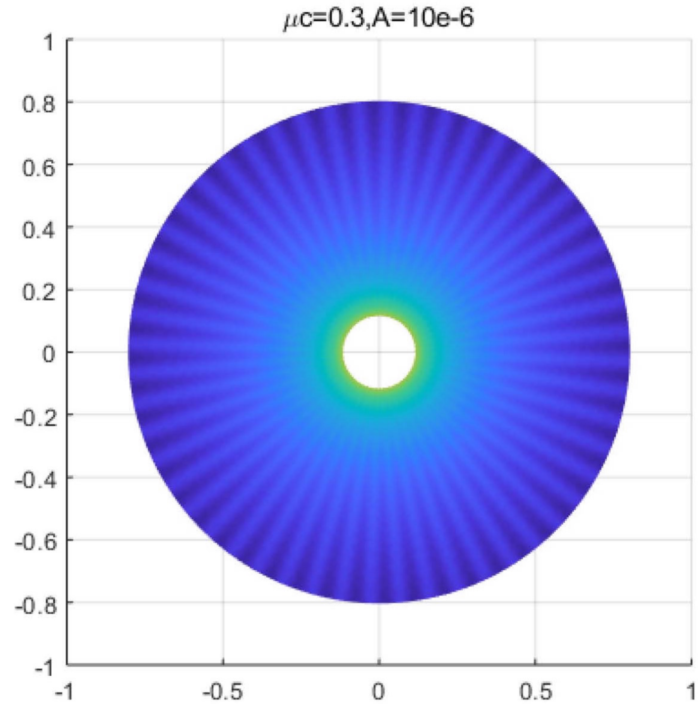

Figure 3.5: Comparison with circular case (47 wrinkles in total). (*Picture taken from*: *Zeidi, M., et al. 2018*)

branes' morphology can then be found as

$$\begin{aligned} z(\xi,\eta) &= \sum_{m=0}^{\infty}[\frac{2h\sigma ce_m(\eta,q)}{\sigma_1}\{Ke_m(\xi,q)T_{mn}(\xi,\eta)-Ke_m(\xi_i,q)T_{mn}(\xi_i,\eta)\} \\ &\quad -(\frac{2h\sigma}{k\mu^2}+\frac{2\sigma ce_m(\eta,q)h(\xi,\eta)Ke_m(\xi_i,q)}{\sigma_1} \\ &\quad \frac{ce_m(\eta,q)T'_\eta(\xi_i,\eta)+ce'_m(\eta,q)T_{mn}(\xi_i,\eta)}{ce'_m(\eta,q)})\log(\frac{e^\xi}{e^{\xi_i}})] \end{aligned} \tag{3.62}$$

where σ_1 is defined in Eq. (3.58). Similar to the constant viscous cases, the resulting deformation fields (radial wave deformations) are sensitive to both the dimension of an inner ellipse and the intensity of viscous flow; i.e., the number of waves reduces as A decreases from 10^{-5} to 10^{-7} (See. Fig. 3.6.). But, more importantly, the transverse wave deformations of the membrane and the corresponding vertical deflections die out as they approach the remote boundary. As a result, the corresponding boundary remains intact and stable (See. Fig. 3.7.). In the case of vanishing A, the wave deformations are completely removed from the entire domain of interest so that the vertical deformation profile reduces to the results in [26], where the authors present the analysis of elliptical substrate-membrane interaction problems without the considerations of viscosity effects (See. Fig. 3.7). Also, Fig. 3.8. shows that the obtained solution accommodates the results of circular substrate-membrane interaction problems in [37] when the eccentricity converges to zero (i.e. $e \to 0$.). In fact, the solutions in Figs. 3.7 and 3.8 become essentially identical for sufficiently small value of A; i.e., $A \leq 10^{-16}$ for case in Fig. 3.7 and $A \leq 10^{-8}$ and $A \leq 10^{-10}$ for the cases in Fig. 3.8. In the assimilations, the classical solutions obtained from the proposed model are intentionally reproduced at $A = 10^{-15}$, $A = 10^{-7}$ and $A = 10^{-9}$ for the purpose of visual demonstration.

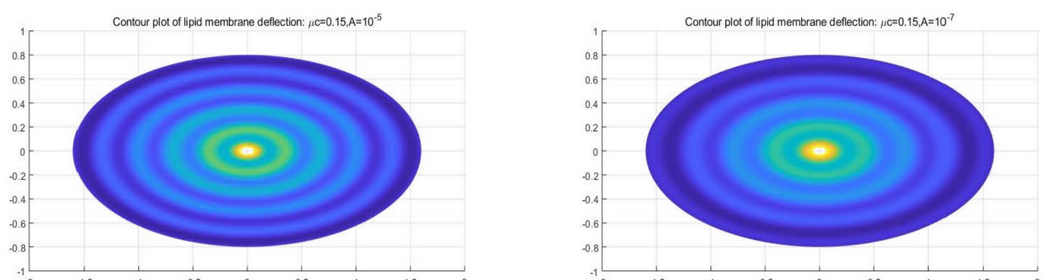

Figure 3.6: Wave deformations of lipid membrane with respect to A.

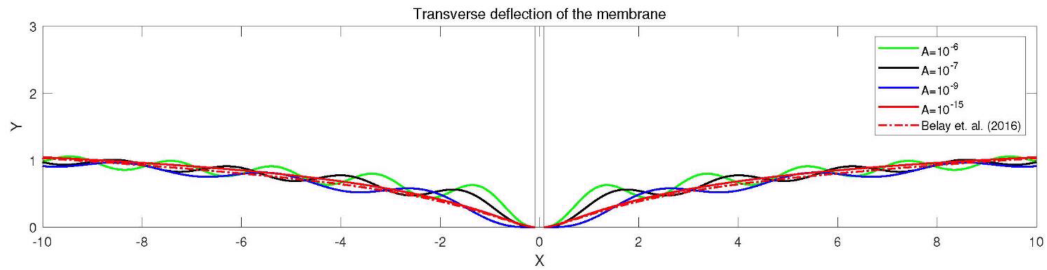

Figure 3.7: Transverse deflections of lipid membrane with respect to intra-membrane viscous flows.

3.4.3 Dual source problems: $w(\xi, \eta) = A + A\sin\xi\cos\eta$

The proposed model is sufficiently general in that the viscous effects from both radial and circumferential directions can be simultaneously considered. To demonstrate this, we introduce the following dual source potential

$$w(\xi, \eta) = A + A\sin\xi\cos\eta, \tag{3.63}$$

and subsequently obtain from Eq. (3.51) that

$$\begin{aligned} T_{mn}(\xi, \eta) &= \int_0^{2\pi}\int_0^{2\pi}\sum_{m=0}^{\infty}\sum_{n=0}^{\infty} -\frac{1}{\lambda\pi^2}\frac{\nu A(1+\sin\xi\cos\eta)e^{-\xi}Ke_m(\xi, q)}{h^3(\xi, \eta)} \\ &\quad *[\pi + e^{-\xi}\frac{\partial^2 ce_m(\eta, q)}{\partial\eta^2}ce_n(\eta, q)]d\xi d\eta. \end{aligned} \tag{3.64}$$

Thus, from Eqs. (3.52) and (3.54), the deformation mapping function $z(\xi, \eta)$ can be obtained in the same manner as in the single source cases.

Figure 3.9 illustrates the deformation configuration of the membranes under the influence of dual source viscous flow. It is shown that both the radial and circumferential wave patterns are simultaneously observed. Morphologically similar cases are reported in the work of [51] where the authors examined the wrinkle

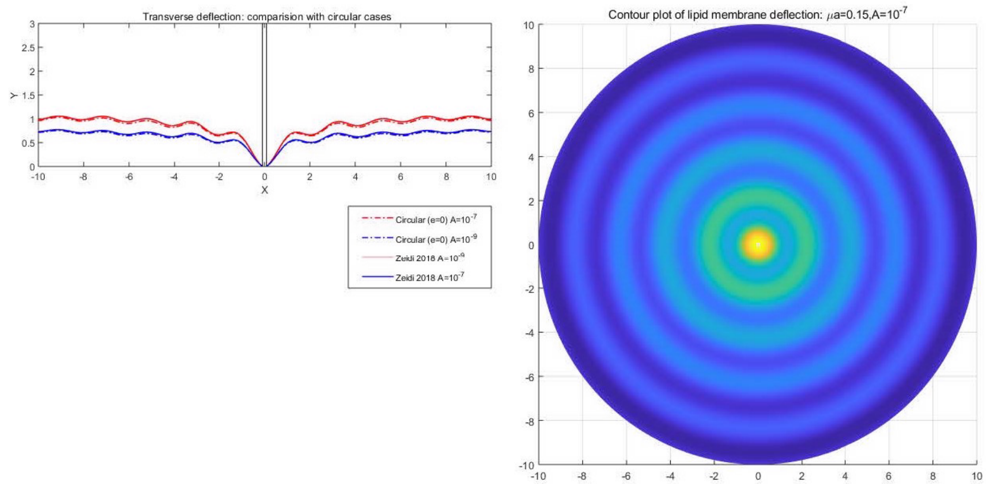

Figure 3.8: Comparison with circular case. (*Picture taken from*: *Zeidi, M., et al. 2018*)

phenomena of a thin gold layer ($10nm$ in thickness) when subjected to thermal stresses from the adjoined polymer substrate. In cases of thin membranes, thermal stresses may be understood as a particular type of the surface stress [65], [66]. Therefore, the results may bear close resemblance with the present case where the membrane's deformations are induced by the surface interaction forces which are transmitted from the acting viscous flows. The obtained solution assimilates the experimental results in [51] when compatible conditions are applied (see, Figs. 3.10 and 3.11). This further suggests that the proposed model may be of practical interest in the morphological study of thin film structures. Such investigations are, however, limited in the present study due to the lack of available data.

Remark. 2.

The results in Fig. 3.9 further indicates that the principle of superposition remains valid in the present cases. The principle is widely adopted in various engineering problems with simple initial and/or boundary value problems of both first (Dirichlet) and second (Neumann) types [67]-[69]. However, such practices are largely absent in the membrane studies due the complexity of mixed boundary conditions (i.e. both the Dirichlet and Neumann boundary conditions are prescribed on the boundaries), and the limited access for the solutions of membrane systems subjected to coupled-physics environment. In the present case, the solutions of single source problems (i.e. $w = A$ and $w = A \sin\xi \cos\eta$) can be obtained from Eqs. (3.56), (3.57), (3.61) and (3.62) that

$$\begin{aligned} T_{mn}(\xi,\eta) &= \int_0^{2\pi}\int_0^{2\pi}\sum_{m=0}^{\infty}\sum_{n=0}^{\infty} - \frac{1}{\lambda\pi^2}\frac{\nu A e^{-\xi} Ke_m(\xi,q)}{h^3(\xi,\eta)} \\ &\quad [\pi + \frac{\partial^2 ce_m(\eta,q)}{\partial\eta^2} ce_n(\eta,q)] d\xi d\eta, \end{aligned} \tag{3.65}$$

$$\begin{aligned} z(\xi,\eta) &= \sum_{m=0}^{\infty}[\frac{2\sigma h(\xi,\eta) ce_m(\eta,q)}{\sigma_1}\{Ke_m(\xi,q)T_{mn}(\xi,\eta) - Ke_m(\xi_0,q)T_{mn}(\xi_0,\eta)\} \\ &\quad -(\frac{2h\sigma}{k\mu^2} + \frac{2\sigma ce_m(\eta,q)h(\xi,\eta)Ke_m(\xi_0,q)ce_m(\eta,q)}{\sigma_1} * \\ &\quad \frac{T'_\eta(\xi_0,\eta) + T_{mn}(\xi_0,\eta)}{ce'_m(\eta,q)}) \log(\frac{e^{\xi}}{e^{\xi_i}})], \end{aligned} \tag{3.66}$$

for uniform flow $w = A$ and

$$\begin{aligned} T_{mn}(\xi,\eta) &= \int_0^{2\pi}\int_0^{2\pi}\sum_{m=0}^{\infty}\sum_{n=0}^{\infty} - \frac{1}{\pi^2\lambda}\frac{\nu A \sin\xi\cos\eta e^{-\xi} Ke_m(\xi,q)}{h^3(\xi,\eta)} \\ &\quad * [\pi + \frac{\partial^2 ce_m(\eta,q)}{\partial\eta^2} ce_n(\eta,q)] d\xi d\eta, \end{aligned} \tag{3.67}$$

$$
\begin{aligned}
z(\xi,\eta) &= \sum_{m=0}^{\infty}[\frac{2h\sigma ce_m(\eta,q)}{\sigma_1}\{Ke_m(\xi,q)T_{mn}(\xi,\eta)-Ke_m(\xi_i,q)T_{mn}(\xi_i,\eta)\} \\
&\quad -(\frac{2h\sigma}{k\mu^2}+\frac{2\sigma ce_m(\eta,q)h(\xi,\eta)Ke_m(\xi_i,q)}{\sigma_1} * \qquad (3.68) \\
&\quad \frac{ce_m(\eta,q)T'_\eta(\xi_i,\eta)+ce'_m(\eta,q)T_{mn}(\xi_i,\eta)}{ce'_m(\eta,q)})\log(\frac{e^{\xi}}{e^{\xi_i}})],
\end{aligned}
$$

for non-uniform flow $w = A\sin\xi\cos\eta$. It is clear from Eqs. (3.66)-(3.68) that the structure of the solution $z(\xi,\eta)$ remains intact. In fact, only $T_{mn}(\xi,\eta)$ part of the solutions (i.e. Eqs. (3.65) and (3.67)) are affected with respect to the varying viscous flows. In particular, by adding Eqs. (3.65) and (3.67), we find

$$
\begin{aligned}
T_{mn}(\xi,\eta) &= \int_0^{2\pi}\int_0^{2\pi}\sum_{m=0}^{\infty}\sum_{n=0}^{\infty}-\frac{1}{\lambda\pi^2}\frac{\nu A(1+\sin\xi\cos\eta)e^{-\xi}Ke_m(\xi,q)}{h^3(\xi,\eta)} \\
&\quad *[\pi+e^{-\xi}\frac{\partial^2 ce_m(\eta,q)}{\partial\eta^2}ce_n(\eta,q)]d\xi d\eta. \qquad (3.69)
\end{aligned}
$$

The above is the same as the solution obtained from the dual source problem (Eq. (3.64) and Fig. 3.9). This, in turn, suggests that the solutions of dual source problems can be obtained directly from the solutions of single source problems (see, also, Figs. 3.9 and 3.12) via simple summations. In other words, the principle of superposition remains valid even with the presence of intra-membrane viscous flows and interaction forces. The result may further promote the study of various different influences of viscous flows onto membrane-substrate systems by minimizing computational complexities and resources.

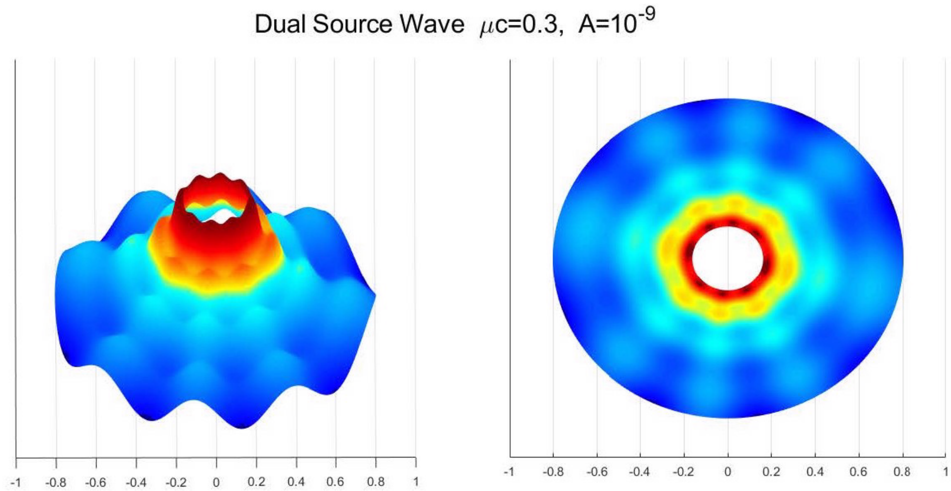

Figure 3.9: Membrane shape evolutions with dual source viscous effects: $w(\xi, \eta) = A + A \sin \xi \cos \eta$

3.4.4 Reduction to the circular lipid membrane problems

The solution of a classical membrane-substrate problem [20] can also be obtained directly from the present model. To demonstrate this, we evaluate (when $e = 0$)

$$\begin{aligned} h(\xi_i, \eta) &= a(1 - e^2 \cos^2 \eta)^{\frac{1}{2}} = a, \; ce_m(\eta, q) = \frac{1}{\sqrt{2}} \text{ (for } m = 0), \\ ce_m(\eta, q) &= \cos m\theta \text{ (for } m \neq 0) \qquad (3.70) \\ Ke_m(\eta, q) &= G_m K_m(\mu r) \text{ and } Ke'_m(\eta, q) = \mu G_m K'_m(\mu r), \end{aligned}$$

where a, m, and $K_m(\mu\rho)$ are the radius of the inner circle, the separation constant and the modified Bessel function of second kind of order m, respectively. Also, $r = ce^{\xi}/2$ and G_m are arbitrary constants with respect to the order m.

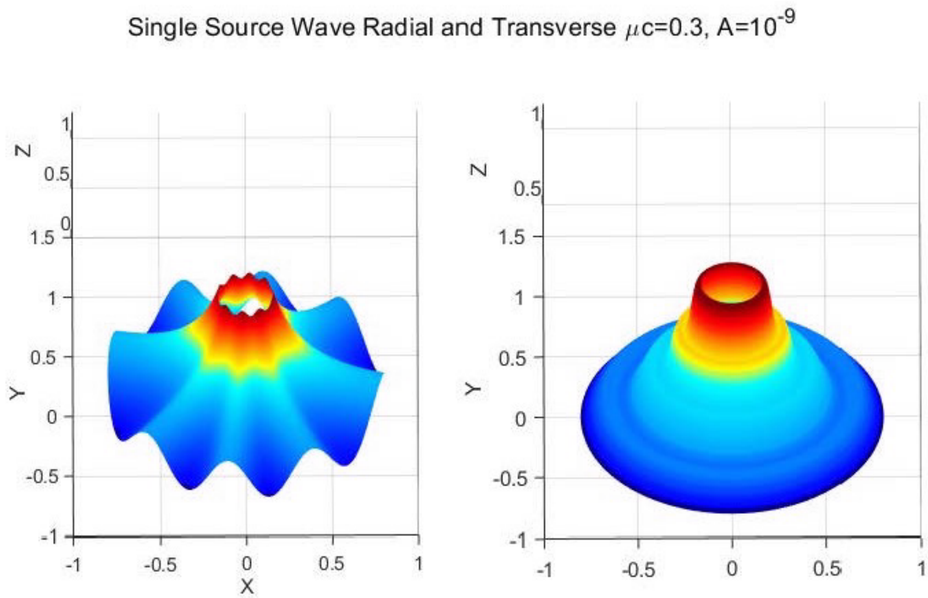

Figure 3.10: Decomposed solutions of the shape evolution: $w = A$ (Left); $w = A \sin \xi \cos \eta$ (Right)

Now, substituting the above into Eq. (3.51) yields

$$T_{mn}(\xi, \eta) = T_m(\mu a) = G_m \frac{\nu}{\pi^2 \lambda} \frac{1}{a^3} \; [-\pi \frac{1}{a} K_m(\mu r) + \frac{1}{a} K_m(\mu r)] \equiv \frac{1}{a} \mathbf{A} G_m, \quad (3.71)$$

where we define $\mathbf{A} = \frac{\nu}{\pi^2 \lambda} \frac{1}{a^3} \; K_m(\mu r)[1 - \pi]$. Thus, from Eqs. (3.57) and (3.71) we find

$$\begin{aligned} z(\xi, \eta) \quad = \quad z(r) &= \frac{2\sigma a G_m}{k \mu^3 G_m K'_m(\mu a)} [K_m(\mu r) - K_m(\mu a)] \\ &- (\frac{2\sigma}{k\mu^2} + \frac{2\sigma K_m(\mu a) G_m}{k \mu^3 \frac{1}{\rho_0} G_m K'_m(\mu a)}) \log(\frac{r}{a}). \end{aligned} \quad (3.72)$$

But, since $G_m / G_m = 1$, Eq. (3.71) further reduces to

$$z(r) = \frac{2\sigma}{k\mu^2} [(\frac{K_m(\mu r) - K_m(\mu a)}{\mu K'_m(\mu a)}) a - (1 + \frac{K_m(\mu a) a}{\mu K'_m(\mu a)}) \log(\frac{r}{a})]. \quad (3.73)$$

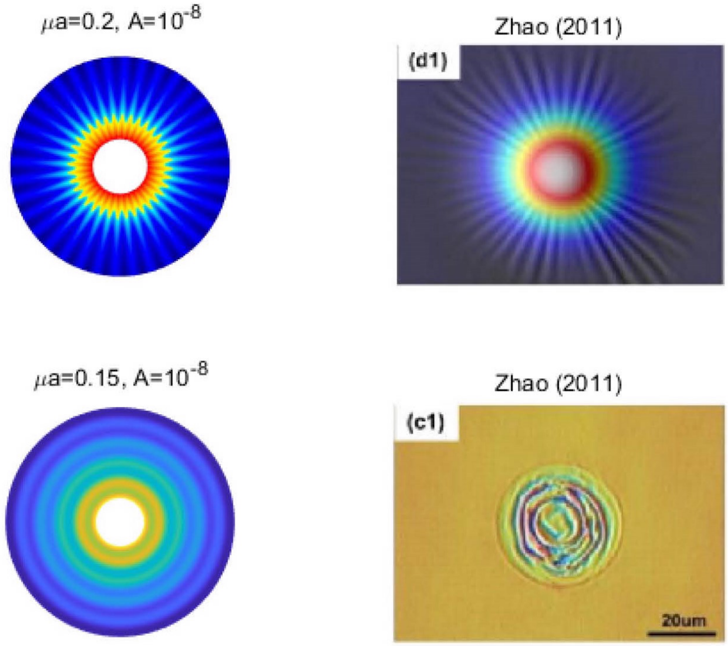

Figure 3.11: Case study (Single source problem): experimental results comparisons. (*Picture taken from*: *Zhao, Y., et al. 2011*)

Finally, we substitute $\mu^2 = 2\lambda/k$ in the above and thereby obtain

$$z(r) = \frac{2\sigma a}{k\mu^3 K_0'(\mu a)}[K_0(\mu r) - K_0(\mu a)] - \frac{\sigma a}{\lambda}(1 + \frac{K_0(\mu a)}{\mu K_0'(\mu a)})\log(\frac{r}{a}). \qquad (3.74)$$

The obtained solution in Eq. (3.74) is the same as in [20](Eq. 135), except the Bessel terms associated with the logarithmic function (i.e. $\frac{K_0(\mu a)}{\mu K_0'(\mu a)}\log(\frac{r}{a})$).

Remark. 3.

The method proposed in the present study is unique in that it utilizes both the iterative reduction scheme and the method of eigenfunction expansions while invoking the orthogonal properties of the Mathieu function. This further allows one to identify more wide class of potential functions of Mathieu type that the

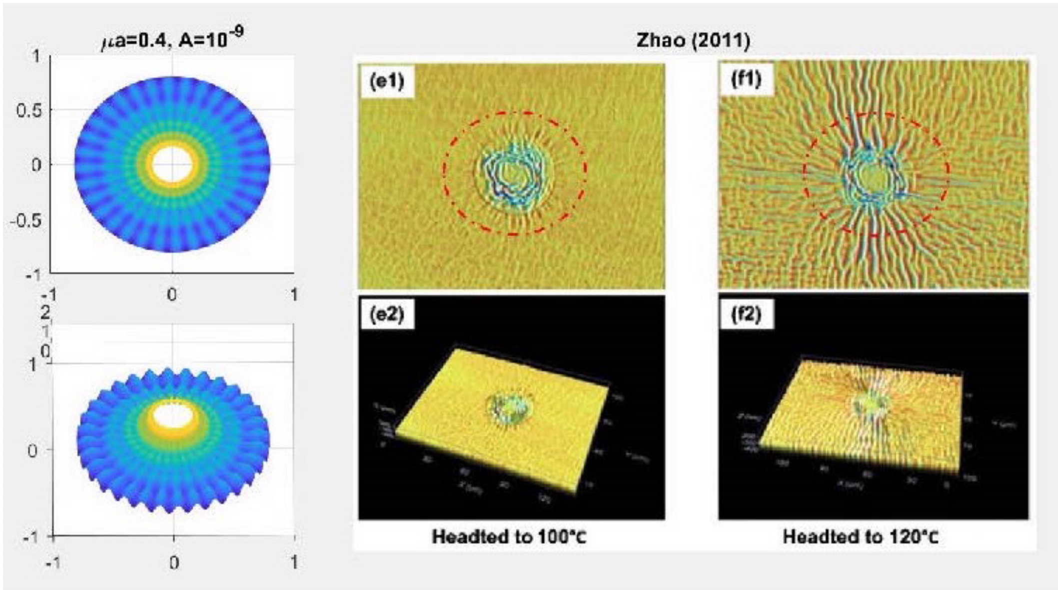

Figure 3.12: Case study (Dual source problem): experimental results comparisons. (*Picture taken from*: *Zhao, Y., et al. 2011*)

traditional method is limited in prediction. Further, since the Mathieu potential reduces to the Bessel function at the particular configuration of $e = 0$; i.e.,

$$Ke_m(\eta, q) = G_m K_m(\mu r) \text{ and } Ke'_m(\eta, q) = \mu G_m K'_m(\mu r) \text{ for } e = 0, \tag{3.75}$$

the solutions of circular substrate interaction problems [20] and [27] can be accommodated by the proposed model as a special case (i.e. $e = 0$, see, Fig. 3.8 and 3.13.). In fact, Eq. (3.74) yields better predictions (slightly more resemble to the non-linear solution) when compared with the existing results (see, Fig. 3.13). This is due the presence of additionally predicted Bessel terms which cannot be obtained by the classical Helmholtz equations defined in the circular system. This further allows one to consider more general, and perhaps more realistic classes of viscous flows especially those arising in circular boundaries. For example, in circular problems, the generalization of the viscous potential Eq. (3.35) and the implementation of dual source flow Eq. (3.63) is no longer possible due to the confined descriptions of the associated circular boundary (see. Remark. 1.). Such difficulties can be overcome by creating desired forms of viscous flows in an elliptic coordinate where the corresponding continuity equation is the same form as in the Cartesian coordinate (i.e. $v_{\xi,\xi} + v_{\eta,\eta} = 0$, see, Eq. (3.34)), and reducing the obtained solutions to the circular cases where the transition is always possible since the conformal mapping of an ellipse to a circle exists [70].The results obtained in

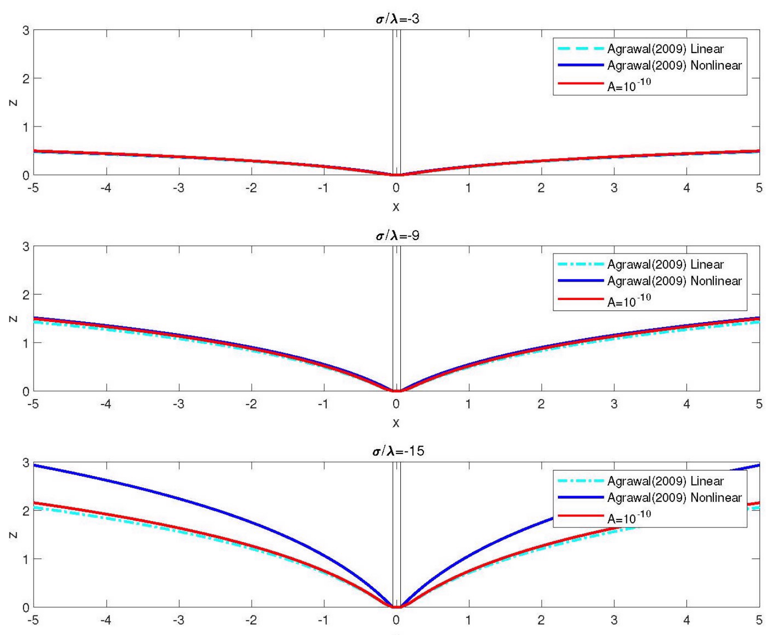

Figure 3.13: Comparison with existing models: membrane-circular substrate interaction problem. (*Picture taken from*: *Agrawal, A., et al. 2009*)

the present study are of more practical interest in that, when used in conjunction with the principle of superposition (see. Remark. 2.), they essentially lead to the solution of a class of problems in which the viscous effects are characterized by a much wider and more realistic class of functions. Potential applications may be extended to retina clinical study of wrinkle-caused vision impairment [52] and the effects of viscous flows on essential cellular functions such as fusion, fission and vesicle formation [53], [71] and [72]. For example, the idiopathic epiretinal membranes (iERMs) is a common pathology which have been observed in more than 20% of eyes from elderly person [52] and [73]. When iERMs are thicker with contractile properties, they cause surface wrinkling of the retina resulting impaired vision (a macular epiretinal membrane) [52] and [74]. Such wrinkle formations are most often induced by the interactions between the posterior vitreous cortex and the retina [75]. Since nearly all the emmetropic retinas are oblate in shape in both transverse axial and sagittal sections [76], the wrinkle formations on the retina may share close similarity to the elliptical membrane-substrate systems examined by the proposed model. In addition, wrinkle involved deformations and the directional elongation of the vesicle are often caused by the viscous shear flows and/or directional viscous flows [71]-[72]. Therefore, the proposed model may be employed to study the morphological transitions of cell membranes associated with those cellular activities.

CHAPTER 4

MODELLING OF LIPID MEMBRANES AFFECTED BY GENERAL FORMS OF INTRA-MEMBRANE VISCOUS FLOWS, INTERACTIONS WITH ELLIPTICAL-CROSS-SECTION SUBSTRATES AND THICKNESS DISTENSIONS

In this chapter, we develop a theoretical model of lipid membranes subjected to intra-membrane viscous flows, interactions of elliptical-cross-section substrates and thickness distensions. Starting from the purely elastic surface theory, we introduce the distension terms and new energy density functions and implement them in the following derivations. Rigorous derivations are made to obtain the membrane shape equations and the corresponding boundary conditions. Then, we employ the admissible linearization techniques for the systems of membrane shape equations and boundary conditions and transform them into the elliptical domain. Lastly, by employing adapted iterative reduction and the method of eigenfunction expansion, we solve the systems of equations (membrane shape equations and boundary con-

ditions) and obtain the corresponding analytical solutions in the forms of Mathieu functions.

4.1 Introduction

In this chapter, we develop a theoretical model of lipid membranes subjected to intra-membrane viscous flows, interactions of elliptical-cross-section substrates and thickness distensions. In section 4.2, we introduce the distension terms and new energy density functions and utilize them in the following derivations. Then we incorporate the viscous effects and obtain the membrane shape equations and corresponding boundary conditions in section 4.3. In section 4.4.1, we linearize the nonlinear systems of equations obtained (membrane shape equations and boundary conditions) via Monge parameterization and admissible linearization. They are successively transformed into the elliptical domain in section 4.4.2. Lastly, by employing the adaptive iteration reduction and the principle of eigenfunction expansion, we obtain an analytical solution in the forms of Mathieu functions in section 4.4.3.

4.2 Inviscid lipid membranes with thickness distensions

To accommodate distension effects, we introduce

$$\nabla\phi(\theta^\alpha) = \phi_{,\alpha}\mathbf{a}^\alpha \text{ and } G^2 = \nabla\phi \cdot \nabla\phi = a^{\alpha\beta}\phi_{,\alpha}\phi_{,\beta}, \tag{4.1}$$

where ϕ is the lipid distension in the current membrane surface ω, $G = |\nabla\phi|$ and $\nabla\phi$ is the gradient of ϕ and

$$\lambda = -q\phi(\theta^\alpha), \tag{4.2}$$

where λ is a constitutively indeterminate Lagrange-multiplier field related to the lipid membrane surface area constraint [77], q is the Lagrange multiplier field related to the incompressiblity constraint.

Then, we propose the energy density function as

$$W = W(H,\ K,\ \phi,\ G;\ a_{\alpha\beta},\ b_{\alpha\beta}). \tag{4.3}$$

Since $\phi(\theta^\alpha)$ is depends specifically on the surface coordinates θ^α (i.e. $W_\phi \frac{\partial\phi}{\partial a_{\alpha\beta}} = 0$), we evaluate

$$\begin{aligned} \rho\frac{\partial\frac{1}{\rho}(W-\gamma)}{\partial a_{\alpha\beta}} &= \rho[-\rho^{-2}\frac{\partial\rho}{\partial a_{\alpha\beta}}W + \frac{1}{\rho}(W_\rho\frac{\partial\rho}{\partial a_{\alpha\beta}} + W_H\frac{\partial H}{\partial a_{\alpha\beta}} \\ &\quad + W_K\frac{\partial K}{\partial a_{\alpha\beta}} + W_G\frac{\partial G}{\partial a_{\alpha\beta}}) + \rho^{-2}\frac{\partial\rho}{\partial a_{\alpha\beta}}\gamma - \frac{1}{\rho}\frac{\partial\gamma}{\partial\rho}\frac{\partial\rho}{\partial a_{\alpha\beta}}]. \end{aligned} \tag{4.4}$$

The derivatives of ρ, H, K and G with respect to $a_{\alpha\beta}$ can be evaluated as [35]

$$\frac{\partial\rho}{\partial a_{\alpha\beta}} = -\frac{\rho}{2}a^{\alpha\beta},\ \frac{\partial H}{\partial a_{\alpha\beta}} = -\frac{1}{2}b^{\alpha\beta} \text{ and } \frac{\partial K}{\partial a_{\alpha\beta}} = -Ka^{\alpha\beta}, \tag{4.5}$$

In particular, we find

$$\frac{\partial G^2}{\partial a_{\alpha\beta}} = \frac{\partial a^{\lambda\mu}\phi_{,\lambda}\phi_{,\mu}}{\partial a_{\alpha\beta}}, \tag{4.6}$$

using Chain rule, the above becomes

$$\frac{\partial G^2}{\partial a_{\alpha\beta}} = 2\frac{\partial G^2}{\partial G}\frac{\partial G}{\partial a_{\alpha\beta}} = \phi_{,\lambda}\phi_{,\mu}\frac{\partial a^{\lambda\mu}}{\partial a_{\alpha\beta}} = \phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta}). \tag{4.7}$$

Thus we obtain

$$\frac{\partial G}{\partial a_{\alpha\beta}} = -\frac{1}{2} G^{-1} \phi_{,\lambda} \phi_{,\mu} (\varepsilon^{\lambda\alpha} \varepsilon^{\mu\beta} - a^{\lambda\mu} a^{\alpha\beta}). \tag{4.8}$$

Accordingly, Eq. (4.4) reduces to

$$\begin{aligned} \rho \frac{\partial \frac{1}{\rho}(W-\gamma)}{\partial a_{\alpha\beta}} &= \rho[\frac{1}{2\rho} a^{\alpha\beta} W - \frac{1}{2} a^{\alpha\beta} W_\rho - \frac{1}{2\rho} b^{\alpha\beta} W_H \\ &\quad - \frac{1}{\rho} W_K K a^{\alpha\beta} - \frac{1}{2\rho} W_G G^{-1} \phi_{,\lambda} \phi_{,\mu} (\varepsilon^{\lambda\alpha} \varepsilon^{\mu\beta} - a^{\lambda\mu} a^{\alpha\beta}) \\ &\quad - \frac{1}{2\rho} a^{\alpha\beta} \gamma + \gamma_\rho \frac{1}{2} a^{\alpha\beta}]. \end{aligned} \tag{4.9}$$

Now using $F_\rho = (W/\rho - \gamma/\rho)_{,\rho}$ (i.e. $W_\rho = \rho F_\rho + \frac{W}{\rho} + \gamma_\rho - \frac{\gamma}{\rho}$), we obtain

$$\begin{aligned} \rho \frac{\partial \frac{1}{\rho}(W-\gamma)}{\partial a_{\alpha\beta}} &= [-\frac{1}{2} b^{\alpha\beta} W_H - W_K K a^{\alpha\beta} \\ &\quad - \frac{1}{2} W_G G^{-1} \phi_{,\lambda} \phi_{,\mu} (\varepsilon^{\lambda\alpha} \varepsilon^{\mu\beta} - a^{\lambda\mu} a^{\alpha\beta}) - \frac{1}{2} a^{\alpha\beta} \rho^2 F_\rho] \\ &= -\frac{1}{2} \gamma a^{\alpha\beta} - (W_H H + W_K K) a^{\alpha\beta} \\ &\quad - \frac{1}{2} W_G G^{-1} \phi_{,\lambda} \phi_{,\mu} (\varepsilon^{\lambda\alpha} \varepsilon^{\mu\beta} - a^{\lambda\mu} a^{\alpha\beta}) + \frac{1}{2} W_H \tilde{b}^{\alpha\beta}, \end{aligned} \tag{4.10}$$

where F_ρ is defined via the relation $\rho^2 F_\rho = \gamma$ [35] and $b^{\alpha\beta} = 2H a^{\alpha\beta} - \tilde{b}^{\alpha\beta}$. Thus,

$$\begin{aligned} \sigma^{\beta\alpha} &= (\lambda + W) a^{\alpha\beta} - (2 W_H H + 2 W_K K) a^{\alpha\beta} \\ &\quad + W_G G^{-1} \phi_{,\lambda} \phi_{,\mu} (\varepsilon^{\lambda\alpha} \varepsilon^{\mu\beta} - a^{\lambda\mu} a^{\alpha\beta}) + W_H \tilde{b}^{\alpha\beta}, \end{aligned} \tag{4.11}$$

and

$$\lambda = -(\gamma + W). \tag{4.12}$$

Similarly, by using

$$\frac{\partial \rho}{\partial b_{\alpha\beta}} = 0, \ \frac{\partial H}{\partial b_{\alpha\beta}} = \frac{1}{2} a^{\alpha\beta}, \ \frac{\partial K}{\partial b_{\alpha\beta}} = \tilde{b}^{\alpha\beta}, \tag{4.13}$$

and

$$\frac{\partial G^2}{\partial b_{\alpha\beta}} = \frac{\partial a^{\lambda\mu}\phi_{,\lambda}\phi_{,\mu}}{\partial b_{\alpha\beta}} = 0 \ (\because \frac{\partial a^{\lambda\mu}}{\partial b_{\alpha\beta}} = 0 \text{ and } \frac{\partial \phi_{,\mu}}{\partial b_{\alpha\beta}} = 0) \text{ Thus } \frac{\partial G}{\partial b_{\alpha\beta}} = 0. \quad (4.14)$$

We evaluate

$$\frac{\partial \frac{1}{\rho}(W-\gamma)}{\partial b_{\alpha\beta}} = W_H \frac{\partial H}{\partial b_{\alpha\beta}} + W_K \frac{\partial K}{\partial b_{\alpha\beta}} + W_G \frac{\partial G}{\partial b_{\alpha\beta}} = \frac{1}{2} W_H a^{\alpha\beta} + W_K \tilde{b}^{\alpha\beta}, \quad (4.15)$$

and subsequently obtain from Eq. (2.26) and $(2.10)_2$ that

$$M^{\beta\alpha} = \frac{1}{2} W_H a^{\alpha\beta} + W_K \tilde{b}^{\alpha\beta}. \quad (4.16)$$

4.3 Viscous lipid membranes with thickness distensions

Combining Eqs. (4.11-4.12), (3.1) and (3.5), we find

$$\begin{aligned} \sigma^{\beta\alpha} &= (\lambda + W)a^{\beta\alpha} - (2W_H H + 2W_K K)a^{\beta\alpha} \\ &+ W_G G^{-1}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta}) \\ &+ W_H \tilde{b}^{\beta\alpha} + \nu[a^{\beta\lambda}a^{\alpha\mu}(v_{\mu;\lambda} + v_{\lambda;\mu}) - 4wHa^{\beta\alpha} + 2w\tilde{b}^{\beta\alpha}]. \quad (4.17) \end{aligned}$$

In terms of the distension term $W_G G^{-1}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta})$, we evaluate

$$[W_G G^{-1}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta})]b_{\beta\alpha} = W_G G^{-1}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta})b_{\beta\alpha}, \quad (4.18)$$

Since $\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta}b_{\beta\alpha} = \tilde{b}^{\lambda\mu}$ and $a^{\lambda\mu}a^{\alpha\beta}b_{\beta\alpha} = b^{\lambda\mu}$, the above equation can be derived as

$$\begin{aligned} W_G G^{-1}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta})b_{\beta\alpha} &= W_G G^{-1}\phi_{,\lambda}\phi_{,\mu}(\tilde{b}^{\lambda\mu} - b^{\lambda\mu}) \\ &= W_G G^{-1}\phi_{,\alpha}\phi_{,\beta}(\tilde{b}^{\alpha\beta} - b^{\alpha\beta}). \quad (4.19) \end{aligned}$$

Substituting Eqs. (4.16), (4.17) and (4.19) into Eq. (2.30), we obtain the normal equation of motion as

$$\begin{aligned} p &= -(\lambda + W)a^{\beta\alpha}b_{\beta\alpha} + (W_H H + W_K K)a^{\beta\alpha}b_{\beta\alpha} \\ &\quad + G^{-1}W_G\phi_{,\alpha}\phi_{,\beta}(\tilde{b}^{\alpha\beta} - b^{\alpha\beta}) \\ &\quad - \frac{1}{2}W_H\tilde{b}^{\beta\alpha}b_{\beta\alpha} + [\frac{1}{2}(W_H)_{;\beta}a^{\beta\alpha} + (W_K)_{;\beta}\tilde{b}^{\beta\alpha}]_{;\alpha} \\ &\quad - \nu[a^{\beta\lambda}a^{\alpha\mu}(v_{\mu;\lambda} + v_{\lambda;\mu}) - 4wHa^{\beta\alpha} + 2w\tilde{b}^{\beta\alpha}]b_{\beta\alpha}. \end{aligned} \tag{4.20}$$

Utilizing the identities $H = \frac{1}{2}a^{\alpha\beta}b_{\alpha\beta}$, $b_{\beta\alpha} = b^{\mu}_{\alpha}a_{\mu\beta}$, $a^{\alpha\lambda}a_{\lambda\beta} = \delta^{\alpha}_{\beta}$ and $a^{\beta\alpha}K = b^{\beta}_{\mu}\tilde{b}^{\mu\alpha}$ and combining the fact that covariant derivatives of the dual metric and the covariant cofactor identically vanish (i.e. $a^{\alpha\beta}_{;\beta} = 0$, $\tilde{b}^{\alpha\beta}_{;\beta} = 0$), the above equation further reduces to

$$\begin{aligned} p &= W_H(2H^2 - K) + 2H(W_K K - W) + G^{-1}W_G\phi_{,\alpha}\phi_{,\beta}(b^{\alpha\beta} - \tilde{b}^{\alpha\beta}) \\ &\quad - 2\lambda H + \Delta(\frac{1}{2}W_H) + (W_K)_{;\alpha\beta}\tilde{b}^{\alpha\beta} \\ &\quad - 2\nu[\frac{1}{2}b^{\alpha\beta}(v_{\alpha;\beta} + v_{\beta;\alpha}) - 2w(2H^2 - K)], \end{aligned} \tag{4.21}$$

where Δ is the Laplace-Beltrami operator (i.e. $\Delta\phi = \phi_{;\alpha\beta}a^{\alpha\beta}$) defined on the surface.

In order to obtain the tangential equation of motion, we compute

$$\begin{aligned} (\sigma^{\beta\alpha})_{;\alpha} &= [(\lambda + W)a^{\beta\alpha} - (2W_H H + 2W_K K)a^{\beta\alpha} \\ &\quad + W_H\tilde{b}^{\beta\alpha}]_{;\alpha} - [W_G G^{-1}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta})]_{;\beta}, \end{aligned} \tag{4.22}$$

Since

$$\varepsilon^{\lambda\alpha}_{;\beta} = 0 \text{ and } a^{\lambda\mu}_{;\beta} = 0, \tag{4.23}$$

We find

$$
\begin{aligned}
(\sigma^{\beta\alpha})_{;\alpha} &= (\lambda_{,\alpha} + W_{,\alpha})a^{\beta\alpha} - [2(W_H)_{;\alpha}H + 2W_H H_{,\alpha} + 2(W_K)_{;\alpha}K \\
&\quad +2W_K K_{,\alpha}]a^{\beta\alpha} + (W_H)_{;\alpha}\tilde{b}^{\beta\alpha} \\
&\quad -[(W_G G^{-1})_{;\beta}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta}) \\
&\quad +W_G G^{-1}(\phi_{,\lambda})_{;\beta}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta}) \\
&\quad +W_G G^{-1}\phi_{,\lambda}(\phi_{,\mu})_{;\beta}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta})],
\end{aligned} \tag{4.24}
$$

By substituting Eqs. (4.16) and (4.24) into Eq. (2.31), we obtain

$$
\begin{aligned}
0 &= -(\gamma_{,\alpha} + W_K K_{,\alpha} + W_H H_{,\alpha})a^{\beta\alpha} - (W_G G^{-1})_{;\beta}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta}) \\
&\quad -2W_G G^{-1}(\phi_{,\lambda})_{;\beta}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta} - a^{\lambda\mu}a^{\alpha\beta}) - 4\nu w H_{,\alpha}a^{\beta\alpha} \\
&\quad +2\nu[\frac{1}{2}a^{\beta\lambda}a^{\alpha\mu}(v_{\mu;\lambda} + v_{\lambda;\mu})_{;\alpha} - w_{,\alpha}b^{\beta\alpha}],
\end{aligned} \tag{4.25}
$$

where $(v_{\mu;\lambda} + v_{\lambda;\mu})_{;\alpha} = (v_{\mu;\lambda} + v_{\lambda;\mu})_{,\alpha} - (v_{\beta;\lambda} + v_{\lambda;\beta})\Gamma^{\beta}_{\mu\alpha} - (v_{\beta;\mu} + v_{\mu;\beta})\Gamma^{\beta}_{\lambda\alpha}$. Invoking $b^{\beta\alpha} = b^{\alpha}_{\lambda}a^{\lambda\beta}$ and $\gamma_{,\alpha} = -\lambda_{,\alpha} - W_K K_{,\alpha} - W_H H_{,\alpha}$, Eq. (4.25) further reduces to

$$
\begin{aligned}
0 &= a^{\beta\alpha}[-(W_G G^{-1})_{;\beta}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta}a_{\beta\alpha} - a^{\lambda\mu}) \\
&\quad -2W_G G^{-1}(\phi_{,\lambda})_{;\beta}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta}a_{\beta\alpha} - a^{\lambda\mu})] \\
&\quad a^{\beta\alpha}[\lambda_{,\alpha} - 4vwH_{,\alpha} + 2\nu\{\frac{1}{2}a^{\lambda\mu}(v_{\mu;\alpha} + v_{\alpha;\mu})_{;\lambda} - w_{,\lambda}b^{\lambda}_{\alpha}\}].
\end{aligned} \tag{4.26}
$$

In the above derivation, we also used $a^{\beta\alpha}a_{\beta\alpha} = (a^{\beta\alpha})^{-1}a_{\beta\alpha} = 1$. Since $a^{\beta\alpha} \neq 0$, the above equation becomes

$$
\begin{aligned}
0 &= \lambda_{,\alpha} - 4vwH_{,\alpha} - (W_G G^{-1})_{;\beta}\phi_{,\lambda}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta}a_{\beta\alpha} - a^{\lambda\mu}) \\
&\quad -2W_G G^{-1}(\phi_{,\lambda})_{;\beta}\phi_{,\mu}(\varepsilon^{\lambda\alpha}\varepsilon^{\mu\beta}a_{\beta\alpha} - a^{\lambda\mu}) \\
&\quad +2\nu[\frac{1}{2}a^{\lambda\mu}(v_{\mu;\alpha} + v_{\alpha;\mu})_{;\lambda} - w_{,\lambda}b^{\lambda}_{\alpha}],
\end{aligned} \tag{4.27}
$$

which serves as the tangential equation of motion.

The energy density W of uniform membranes of the Helfrich type is given by [39] as

$$W = kH^2 + \bar{k}K + F(\phi) + \sigma G^2, \tag{4.28}$$

where k and $\bar{k}$ are empirical constants (the bending moduli). Subsequently, invoking Eq. (4.28), Eq. (4.21) yields

$$
\begin{aligned}
p &= k[\Delta H + 2H(H^2 - K)] - 2\lambda H \qquad (4.29) \\
&\quad -2v[\frac{1}{2}b^{\alpha\beta}(v_{\alpha;\beta} + v_{\beta;\alpha}) - 2w(2H^2 - K)] \\
&\quad -2\sigma HG^2 + 2\sigma\phi_{,\alpha}\phi_{,\beta}(b^{\alpha\beta} - \tilde{b}^{\alpha\beta}),
\end{aligned}
$$

while Eq. (4.27) remains intact. Substituting Eq.(4.2) into Eq.(4.29) furnishes

$$
\begin{aligned}
p &= k[\Delta H + 2H(H^2 - K)] + 2q\phi H - 2v[\frac{1}{2}b^{\alpha\beta}(v_{\alpha;\beta} + v_{\beta;\alpha}) \qquad (4.30) \\
&\quad -2w(2H^2 - K)] - 2\sigma HG^2 + 2\sigma\phi_{,\alpha}\phi_{,\beta}(b^{\alpha\beta} - \tilde{b}^{\alpha\beta}).
\end{aligned}
$$

In addition, the incompressibility condition of viscous flow is given from the Chapter 3 (see Eq. (3.11)) as

$$v^{\alpha}_{;\alpha} - 2wH = 0. \tag{4.31}$$

The Euler equation related to distension is given by [39] as

$$W_{\varphi} - q = (G^{-1} W_G a^{\alpha\beta} \phi_{,\beta})_{;\alpha}. \tag{4.32}$$

4.4 Linear Analysis

4.4.1 Linearization of the terms related to thickness distension

We plug Eq. (3.16) and Eq. $(4.1)_2$ into the distension terms $(-2\sigma H G^2 + 2\sigma \phi_{,\alpha}\phi_{,\beta}(b^{\alpha\beta} - \tilde{b}^{\alpha\beta}))$ of Eq. (4.30) and obtain

$$\begin{aligned} -2\sigma H G^2 + 2\sigma \phi_{,\alpha}\phi_{,\beta}(b^{\alpha\beta} - \tilde{b}^{\alpha\beta}) &= -\sigma \phi_{,\alpha}\phi_{,\beta} a^{\alpha\beta} \Delta z \\ &\quad + 2\sigma \phi_{,\alpha}\phi_{,\beta}(b^{\alpha\beta} - \tilde{b}^{\alpha\beta}), \end{aligned} \tag{4.33}$$

Then, by substituting the linearized expressions (Eqs. (3.16),(3.22),(3.25) and (3.58)) into Eqs. (4.32), (4.30), (4.31) and (4.27), we obtain:

$$\begin{gathered} \frac{1}{2} k \Delta_p(\Delta_p z) + q\varphi \Delta_p z - 2\upsilon z_{,\alpha\beta}\, \nu_{\alpha,\beta} - \sigma \phi_{,\alpha}\phi_{,\beta} a^{\alpha\beta} \Delta z + 2\sigma b^{\alpha\beta} \phi_{,\alpha}\phi_{,\beta} \simeq p, \\ (\lambda + P)_{,\alpha} + \upsilon \Delta_p v_\alpha \simeq 0,\ v_{\alpha,\alpha} \simeq 0 \text{ and } 2\sigma a^{\beta\alpha} \phi_{,\beta\alpha} \simeq 0. \end{gathered} \tag{4.34}$$

4.4.2 Formulations in the elliptical coordinates

Invoking Eqs. (3.31), (3.32) and (3.42), Eq. (4.34) can be transformed into the elliptical domain as

$$
\begin{aligned}
0 &= \frac{1}{2}k\Delta(\Delta z) + q\phi\Delta z + \frac{\sigma}{h^2(\xi,\eta)}(\phi_{,\xi}\phi_{,\xi} + \phi_{,\eta}\phi_{,\eta})\Delta z + \\
&\quad \frac{2\sigma}{h^4(\xi,\eta)}(\phi_{,\xi}\phi_{,\xi}z_{,\xi\xi} + 2\phi_{,\xi}\phi_{,\eta}z_{,\xi\eta} + \phi_{,\eta}\phi_{,\eta}z_{,\eta\eta}) \\
&\quad -\frac{2\upsilon}{h^3(\xi,\eta)}(z_{,\xi\xi}\,\nu_{\xi,\xi} + 2z_{,\xi\eta}\,\nu_{\xi,\eta} + z_{,\eta\eta}\,\nu_{\eta,\eta}), \\
0 &= \frac{2\sigma}{h^2(\xi,\eta)}[\phi_{,\xi\xi} + \phi_{,\eta\eta}], \qquad (4.35)
\end{aligned}
$$

subjected to (the associated boundary conditions remain the same as the boundary conditions in Chapter 3)

$$z(\xi_0,\eta) = 0,\ \nabla z(\xi_0,\eta) = 0 \text{ and } \frac{1}{h}\frac{\partial}{\partial\xi}H(\xi_0,\eta) = \frac{\sigma}{k}. \qquad (4.36)$$

Here, Eqs. (4.35-4.36) serve as the linearized shape equation system which describes the morphologies of lipid membranes subjected to general forms of intramembrane viscous flows, membrane-substrate interactions and thickness distensions.

4.4.3 Solutions to the linearized systems

Similar to the methods utilized in section 3.3.4 (Chapter 3), the form of the solution $z(\xi,\eta)$ is obtained as

$$z(\xi,\eta) = \frac{2}{\mu^2}H(\xi,\eta) + B_m + \varphi(\xi,\eta), \qquad (4.37)$$

and $\varphi(\xi,\eta)$ is chosen as

$$\varphi(\xi,\eta) = C_m \log(e^{\xi}/e^{\xi_0}) + D_m \sum_{m=0}^{\infty} e^{-\xi} ce_m(\eta,\underline{q}), \tag{4.38}$$

to meet the boundary conditions from Eq. (4.36). The unknown potential $H(\xi,\eta)$ can be expressed as [57]

$$H(\xi,\eta) \equiv \sum_{m=0}^{\infty}\sum_{n=0}^{\infty} A_m Ke_m(\xi,\underline{q}) ce_n(\eta,\underline{q}) T_{mn}(\xi,\eta), \tag{4.39}$$

where $ce_n(\eta,\underline{q})$ and $Ke_m(\xi,\underline{q})$ are the even modified Mathieu functions of the first and second kind, respectively, and the associated parameter $\underline{q}$ [58] is of the form

$$\underline{q} = \frac{c^2[q\phi + \frac{\sigma}{h^2}(\phi_{,\xi}\phi_{,\xi} + \phi_{,\eta}\phi_{,\eta})]}{4k}, \tag{4.40}$$

Now, we substitute Eqs. (3.34) and (4.39) into Eq. $(4.35)_1$ and simplify it based on the orthogonality properties of the Mathieu function; i.e.

$$\int_0^{2\pi} ce_m(\eta,\underline{q}) ce_n(\eta,\underline{q}) d\eta = \int_0^{2\pi} Ke_m(\xi,\underline{q}) Ke_n(\xi,\underline{q}) d\xi = \pi\delta_{mn}, \text{and}$$
$$\int_0^{2\pi}\int_0^{2\pi} Ke_m(\xi,\underline{q}) ce_n(\eta,\underline{q}) Ke_k(\xi,\underline{q}) ce_l(\eta,\underline{q}) d\xi d\eta = \pi\delta_{mk}, \tag{4.41}$$

the expression of T_{mn} can be derived as

$$\begin{aligned} T_{mn}(\xi,\eta) \;=\; & \int_0^{2\pi}\int_0^{2\pi}\sum_{m=0}^{\infty}\sum_{n=0}^{\infty} - \frac{2\sigma}{\pi h^4(\xi,\eta)[2q\phi + \frac{2\sigma}{h^2}(\phi_{,\xi}\phi_{,\xi} + \phi_{,\eta}\phi_{,\eta})]}(\phi_{,\xi}\phi_{,\xi} z_{,\xi\xi} \\ & + 2\phi_{,\xi}\phi_{,\eta} z_{,\xi\eta} + \phi_{,\eta}\phi_{,\eta} z_{,\eta\eta}) Ke_m(\xi,\underline{q}) ce_n(\eta,\underline{q}) \\ & + \frac{4\upsilon}{\pi h^3(\xi,\eta)[2q\phi + \frac{2\sigma}{h^2}(\phi_{,\xi}\phi_{,\xi} + \phi_{,\eta}\phi_{,\eta})]} * \\ & [(-e^{-\xi}\frac{\partial ce_m(\eta,\underline{q})}{\partial\eta} Ke_m(\xi,\underline{q}) ce_n(\eta,\underline{q}))(\frac{\partial \int w(\xi,\eta) d\xi}{\partial\eta} \\ & + \frac{\partial \int -w(\xi,\eta) d\eta}{\partial\xi}) + \{e^{-\xi}\pi Ke_m(\xi,\underline{q}) \\ & + e^{-\xi}\frac{\partial^2 ce_m(\eta,\underline{q})}{\partial\eta^2} Ke_m(\xi,q) ce_n(\eta,q)\} w(\xi,\eta)] d\xi d\eta. \end{aligned} \tag{4.42}$$

Consequently, by combining the Eqs. (4.37),(4.38)-(4.39) and (4.42), the general solution is obtained as

$$\begin{aligned} z(\xi,\eta) &= \frac{2}{\mu^2}\sum_{m=0}^{\infty}[A_m Ke_m(\xi,\underline{q})ce_m(\eta,\underline{q})T_{mn}(\xi,\eta)+B_m \\ &\quad +C_m\log(e^{\xi}/e^{\xi_0})+D_m e^{-\xi}ce_m(\eta,\underline{q})], \end{aligned} \tag{4.43}$$

where A_m, B_m, C_m and D_m are

$$A_m = \frac{4(-1)^{\frac{m-1}{2}}\sigma\cos(\frac{m\pi}{20}\xi)h(\xi_0,\eta)}{m\pi k(Ke_m(\xi_0,\underline{q})ce_m(\eta,\underline{q})T'_\xi(\xi_0,\eta)+ce_m(\eta,\underline{q})Ke'_m(\xi_0,\underline{q})T_{mn}(\xi_0,\eta))},$$

$$B_m = \sum_{m=0}^{\infty}\frac{8\sigma(-1)^{\frac{m-1}{2}}\cos(\frac{m\pi}{20}\xi)ce_m(\eta,\underline{q})h(\xi_0,\eta)Ke_m(\xi_0,\underline{q})T'_\eta(\xi_0,\eta)}{m\pi kce'_m(\eta,\underline{q})\mu^2(Ke_m(\xi_0,\underline{q})T'_\xi(\xi_0,\eta)+Ke'_m(\xi_0,\underline{q})T_{mn}(\xi_0,\eta))},$$

$$\begin{aligned} C_m &= \sum_{m=0}^{\infty}8\sigma(-1)^{\frac{m-1}{2}}\cos(\frac{m\pi}{20}\xi)Ke_m(\xi_0,\underline{q})h(\xi_0,\eta)\{ce_m(\eta,\underline{q})T'_\eta(\xi_0,\eta) \\ &\quad +ce'_m(\eta,\underline{q})T_{mn}(\xi_0,\eta)\} * \\ &\quad \{-\mu^2+2Ke_m(\xi_0,\underline{q})e^{\xi_0}T'_\xi(\xi_0,\eta)+2Ke'_m(\xi_0,\underline{q})e^{\xi_0}T_{mn}(\xi_0,\eta)\} \\ &\quad /[m\pi kce'_m(\eta,\underline{q})\mu^4\{Ke_m(\xi_0,\underline{q})T'_\xi(\xi_0,\eta)+Ke'_m(\xi_0,\underline{q})T_{mn}(\xi_0,\eta)\}], \end{aligned}$$

and

$$\begin{aligned} D_m &= -\frac{8\sigma(-1)^{\frac{m-1}{2}}\cos(\frac{m\pi}{20}\xi)Ke_m(\xi_0,\underline{q})h(\xi_0,\eta)e^{\xi_0}}{m\pi kce'_m(\eta,\underline{q})\mu^2} \\ &\quad \frac{ce_m(\eta,\underline{q})T'_\eta(\xi_0,\eta)+ce'_m(\eta,\underline{q})T_{mn}(\xi_0,\eta)}{Ke_m(\xi_0,\underline{q})ce_m(\eta,\underline{q})T'_\xi(\xi_0,\eta)+ce_m(\eta,\underline{q})Ke'_m(\xi_0,\underline{q})T_{mn}(\xi_0,\eta)}, \end{aligned} \tag{4.44}$$

where

$$\begin{aligned} Ke'_m(\xi,\underline{q}) &= \frac{\partial Ke_m(\xi,\underline{q})}{\partial\xi},\ ce'_m(\eta,\underline{q}) = \frac{\partial ce_m(\eta,\underline{q})}{\partial\eta} \\ T'_\xi(\xi,\eta) &= \frac{\partial T_{mn}(\xi,\eta)}{\partial\xi},\ T'_\eta(\xi,\eta) = \frac{\partial T_{mn}(\xi,\eta)}{\partial\eta} \\ T'_\xi(\xi_0,\eta) &= \left[\frac{\partial T_{mn}(\xi,\eta)}{\partial\xi}\right]_{\xi=\xi_0} \text{ and } T'_\eta(\xi_0,\eta) = \frac{\partial T_{mn}(\xi_0,\eta)}{\partial\eta}. \end{aligned}$$

The general solution is obtained as

$$\begin{aligned} z &= \sum_{m=0}^{\infty} \frac{4}{m\pi}(-1)^{\frac{m-1}{2}} \cos(\frac{m\pi}{20}\xi)\{\frac{2\sigma h(\xi_0,\eta)}{\mu^2 k\sigma_2}(Ke_m(\xi,\underline{q})T_{mn}(\xi,\eta) \\ &\quad -Ke_m(\xi_0,\underline{q})T_{mn}(\xi_0,\eta)) - (\frac{2h(\xi_0,\eta)\sigma}{\mu^2 k} \\ &\quad +\frac{2\sigma h(\xi_0,\eta)(Ke_m(\xi_0,\underline{q})ce_m(\eta,\underline{q})T'_\eta(\xi_0,\eta) + Ke_m(\xi_0,\underline{q})ce'_m(\eta,\underline{q})T_{mn}(\xi_0,\eta))}{\mu^2 kce'_m(\eta,\underline{q})\sigma_2}) \\ &\quad \log(e^{\xi}/e^{\xi_0})\}, \end{aligned} \tag{4.45}$$

where

$$\sigma_2 = [Ke'_m(\xi_0,\underline{q})T_{mn}(\xi_0,\eta) + Ke_m(\xi_0,\underline{q})T'_\xi(\xi,\eta)].$$

CHAPTER 5

CONCLUSIONS AND FUTURE WORK

5.1 Conclusion

In this thesis, we develop a continuum-based theoretical model to analyze the mechanical responses of lipid membranes subjected to specific practical factors (intra-membrane viscous flows, membrane-substrate interactions, thickness distensions). Starting from the modelling of the inviscid fluid membrane, we add the considerations of intra-membrane viscous flows and thickness distensions. Interdisciplinary concepts and methods (e.g., eigenfunction expansion, the theory of elastic surface) are adopted to obtain the constitutive equations of the membranes and their solutions within the framework of the present study. In particular, this research illustrates the appearance of the wrinkling phenomena under the impacts of uniform, non-uniform and dual source types of viscous flows. We find that uniform, non-uniform types of viscous flows give rise to wrinkles phenomena in radial and transverse directions on the membranes' surfaces, respectively. When we input dual source types of viscous flows into the proposed solutions, both radial and transverse wrinkles are observed, which illustrates that the principle of superposition remains valid. We find that the intensity of viscous flows and the radius of the inner ellipse of membranes are the key factors to impact the vertical length of the induced wrinkles. More importantly, the proposed solutions are able to accommodate various types of viscous flows, which means the class of membrane-substrate interaction problems subjected to viscous flows can be solved utilizing the proposed solutions. This thesis initializes from a practical physical problem (membrane-substrate interaction) and then ends up as a series of complex mathematical problems (e.g., differential geometry, PDEs), which indicates the great power of mathematics and human wisdom. The highest difficulties in this thesis are the solving of the membrane shape equations and the plotting of the obtained solutions because they all contain the computations among a number of long functions and complicated terms. To overcome these difficulties, we develop our own solving strategies and utilize a series of accessible computing resources.

In chapter two, we present the prerequisite knowledge of differential geometry and develop the underlying theoretical model of inviscid fluid membrane for further researches on the intra-membrane viscosity. By combining the theory of elastic surfaces, the membrane equilibrium equations and the corresponding projections on normal and tangential directions are formulated via rigorous derivations. The deformation energy of the membrane is accounted for by means of the Mean and Gaussian curvatures of the surface which are the functions of the first and second fundamental forms.

In chapter three, we study the deformations of lipid bilayers subjected to the intra-membrane viscous flows and the interactions of elliptical cylinder substrates. Utilizing the Monge parameterization of a surface and general curvilinear coordinates, the expressions of linearized shape equations and associated boundary conditions are obtained from the non-linear theory. The intra-membrane viscosity terms are formulated by means of 'admissible linearization' and successively transformed into elliptical coordinates to assimilate more general types of viscous flow. More importantly, we obtained a complete analytic solution by employing adapted iterative reduction and the method of eigenfunction expansion, which describes the deformations of lipid membranes when interacting with intra-membrane viscous flows and elliptical-cross-section substrates. It is found that intra-membrane viscosity induces wrinkle formations of the lipid membranes, and the corresponding number of wrinkles exhibits sensitivity to both the radius of the ellipse and the intensity of viscous flows. Comparisons with phenomenologically compatible cases such as a circular substrate-membrane interaction and capillary wrinkle of polymer films, are made where the proposed model successfully reproduces the existed results in the limit of vanishing eccentricity of an ellipse. Further, we obtain solutions corresponding to the case of a lipid membrane subjected to non-uniform viscous flows and dual source flows. This is facilitated by the relaxed form of the prescribed tangential and normal force, and the condition of continuity along and within the elliptical boundaries, unlike those arising in circular boundaries where the admissible set of viscous flows are strictly uniform in one of the coordinate directions. The resulting deformation fields show clear signs of dual source interference in that both the radial and circumferential wave forms are simultaneously predicted. Case studies vis a vis morphologically similar results of shape memory films are presented to investigate the potential applicabilities of the proposed model in the analysis of different types of membranes. In particular, it is found that the principles of superposition from linear elasticity remains valid, even in the presence of general forms of dual source viscous potentials. That is, the solution of a dual source problem can be directly obtained by adding solutions of two single source problems. The solutions presented here are of more practical interest in that, essentially, they lead to solutions of problems in which the viscosity effects are characterized by a wide class of potential functions and so can accommodate a correspondingly large set of physically relevant problems. For example, potential applications may be expected in the study of wrinkle-caused disease (e.g., a macular epiretinal membrane) and the influences of membrane viscosity on various cellular functions such as fusion, fission and budding. Further, the presented solution reproduces the existing results when viscosity effects are removed, and does incorporate the solution of the classical membrane-substrate interaction problem in the limit of vanishing eccentricity. In fact, the classical solution obtained directly from the proposed model produces more accurate predictions by identifying the additional Bessel functions, which is reduced from the Mathieu potentials.

In chapter four, we develop a theoretical model of lipid membranes subjected to intra-membrane viscous flows, interactions of elliptical-cross-section substrates and thickness distensions. Starting from the purely elastic surface theory, we introduce the distension terms and new energy density functions and implement them in the following derivations. Rigorous derivations are made to obtain the membrane shape equations and the corresponding boundary conditions. Then, we employ the admissible linearization techniques for the systems of membrane shape equations and boundary conditions and transform them into the elliptical domain. Lastly, by employing adapted iterative reduction and the method of eigenfunction expansion, we solve the systems of equations (membrane shape equations and boundary conditions) and obtain the corresponding analytical solutions in the forms of Mathieu functions.

We discover that the viscous flow gives rise to the wrinkle phenomena of the lipid membranes. The membrane systems may be exposed to the constant viscous flow (viscous flow potential $w(\xi, \eta) = A$) within a cell such as the selective transport of molecules inside the lipid bilayers where the molecules travel with the constant flow from one side of the membrane to the objective protein. In this case, we find that the wrinkling phenomenon in the radial direction of the membrane starts to appear when the normalized magnitude of viscous flow is greater than the critical number (i.e. $\frac{A\nu}{\lambda} \geq 10^{-15}$). The number of radial wrinkles is sensitive to the magnitude of intra-membrane viscous flow (A) and the radius of the inner ellipse (μc). In detail, the number of radial wrinkles is positively correlated with the intra-membrane viscous flows (A) and the radius of the inner ellipse (μc). With the identical radius of the inner ellipse (μc), the number of wrinkles reduces as the magnitude of viscous flow (A) decreases. The number of wrinkles increases as the inner radius of the inner ellipse (μc) increases when the magnitude of the viscous flow (A) remains the same. Phenomenologically compatible results can be found in the related researches such as circular substrate-membrane interactions, capillary wrinkles on thin polymer films and theoretical study on an elastic surface, where the number of radial wrinkles depends upon the size of the inner radius and membrane thickness. The proposed model successfully reproduces the reported results under the physically similar/compatible settings (see Figs. 3.4 and 3.5).

The cases of non-uniform viscous flows (when the viscous flow potential $w(\xi, \eta) = A\, sin\, \xi \cos \eta$) can be observed in various cellular activities such as the transportations of the intracellular membranes and the transmembrane proteins induced by the viscous flows with tension gradient. In this case, the viscous flow field becomes non-uniform due to the interactions with the tension gradient field. Similar to the constant viscous cases, the resulting deformation fields (radial wave deformations) are sensitive to both the dimension of an inner ellipse (μc) and the intensity of viscous flow (A); i.e., the amount of waves decreases as A drops from 10^{-5} to 10^{-7} (See. Fig. 3.6). But, more importantly, the transverse wave deformations of the membrane and the corresponding vertical deflections die out as they approach the remote boundary, which ensures the intactness and stabilization of the corresponding boundary conditions (see. Fig. 3.7). In the event of vanishing A, the wave deformations are completely removed from the entire domain of interest so that the vertical deformation profile reduces to the reported results (see. Fig. 3.7). Also, Fig. 3.8. shows that the obtained solution accommodates the reported results of circular substrate-membrane interaction problems when the eccentricity converges to zero (i.e. $e \rightarrow 0$).

When the viscous flow potential $w(\xi, \eta) = A + A\, sin\, \xi \cos \eta$, we find that both the radial and circumferential wave patterns are simultaneously observed (see. Fig. 3.9). Morphologically similar cases are reported in the existed works where the authors examined the wrinkle phenomena of a thin gold layer (10 nm in thickness) when subjected to thermal stresses from the adjoined polymer substrate. The results in Fig. 3.9 further indicates that the principle of superposition remains valid in the present cases. The principle is widely adopted in various engineering problems with simple initial and/or boundary value problems of either first (Dirichlet) or second (Neumann) type.

The results obtained in this thesis are of more practical interest in that, when used in conjunction with the principle of superposition (see. Remark. 2.), they essentially lead to the solution of a class of problems in which the viscous effects are characterized by a much wider and more realistic class of functions. Potential applications may be extended to retina clinical study of wrinkle-caused vision impairment and the effects of viscous flows on essential cellular functions such as fusion, fission and vesicle formation. For example, the idiopathic epiretinal membranes (iERMs) is a common pathology which have been observed in more than 20% of eyes from elderly person. When iERMs are thicker with contractile properties, they cause surface wrinkling of the retina resulting impaired vision (a macular epiretinal membrane). Such wrinkle formations are most often induced by the interactions between the posterior vitreous cortex and the retina. Since nearly all the emmetropic retinas are oblate in shape in both transverse axial and sagittal sections, the wrinkle formations on the retina may share close similarity to the elliptical membrane-substrate systems examined by the proposed model. In addition, wrinkle involved deformations and the directional elongation of the vesicle are often caused by the viscous shear flows and/or directional viscous flows. Therefore, the proposed model may be employed to study the morphological transitions of cell membranes associated with those cellular activities.

5.2 Future Work

The proposed model can accommodate more terms regarding different cellular activities to provide more general and precise descriptions of lipid membranes. For example, we can consider analyzing the deformations of the lipid membranes concurrently affected by cell buddings, intra-membrane non-uniform viscous flows, large-scale interactions and thickness distensions. Ideally, we can extend this model to simultaneously accommodate all the main cellular activities such that the predictions for the morphologies of the lipid membranes will be very realistic and accurate. Further, various nonlinear analysis techniques (e.g., finite element method, numerical method) can be employed to generate more accurate results within the framework of the proposed model. Lastly, we can add more general structures of cell membranes (e.g., the embedded proteins, glycolipid, cholesterol) into the analysis of the proposed model.

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Appendix A. Copyright Demonstration

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