Modeling and simulation of cells and tissues as active fluids

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Abstract

Within cells, the cytoskeleton organizes into polymer networks with unique properties. At short time-scales, they behave elastically. However, due to molecular turnover, at longer time-scales they behave like viscous fluids in low Reynold limit. In addition to this, they are capable of actively developing tension, thanks to molecular motors using chemical energy. At the tissue scale, epithelial cell formed by monolayers can exhibit, in some regimes, a similar active fluid behavior. Contractile forces play a key role in tissue, for example, in organ development, wound healing, remodeling of the newly synthesized connective tissue, and in sub-cellular level like cell elongation, contraction, rearrangements, cell adhesion, division, cell migration and furrow construction in cytokinesis. Furthermore, as a part of optogenetic technique, the doped epithelial tissues experience contractility upon illumination. Motivated by this, in the present work we considered a monolayer of cells with illumination as an external power input defined as a tension pattern in space and time to engineer contractility patterns to transport material from one part of the tissue to another or to engineer morphogenesis. Altogether, for the system at low Reynold’s limit, governing equations of this compressible active visco-elastic model are developed using traditional continuum approach and Onsager’s variational principle and solved using linear finite elements. The system is non-dimensionalized and the effect of each independent parameter on the system is analyzed. Finally, this model helps in examining the principles that govern the ability to remodel the material by applying space-time patterns of activity.
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Chapter 1

Introduction

1.1 Motivation

Epithelia are biological tissues formed by a monolayer of cells [53]. These tissues support the structure of organs, such as gut, and developing embryos. Viewed from the top, epithelia look like a disorder crystal made of cells. This structure has remarkable mechanical properties. In particular, due to the continuously death and division of the cells in the structure, along with the rearrangement of their junctions, epithelia can be regarded as viscoelastic fluids. Furthermore, epithelia generate an internal active stress due to regulation of acto-myosin networks within cells.

As an example of the fluid and active nature of this material, we can look at organ development, such as the wing development in Drosophila [43], where cells undergo rearrangements to generate the final shape of the wing (see figure 1.1). These rearrangements involve continuous contractions, elongations and orientations which can be understood as the continuous flow of cells in a viscous fluid from one region to the other due to active forces generated by morphogenesis.

Contractile forces plays a key role in tissue, for example, in organ development [43], wound healing [45], remodeling of the newly synthesized connective tissue [46], and in sub-cellular level like cell elongation, contraction [49], rearrangements, cell adhesion [48], division, cell migration [47] and furrow construction in cytokinesis [52].

(a) 15h After Puparium Formation

(b) 32h After Puparium Formation

Figure 1.1: Rearrangements in wing development of Drosophila [43]
Furthermore, optogenetic techniques can be used to control the contractility at a cellular level. Valon, Léo, et al. [42] showed experimentally that doped epithelial tissues experience contractility upon illumination (see figure 1.2). This technique opens door to engineering contractility patterns to transport material from one part of the tissue to another or to engineer morphogenesis.

Motivated by this, in this work we want to study through a simple mathematical model, and finite element simulation, how contractile forces within tissues can generate space-time mobility patterns and transport material from one place of the tissue to another. We consider a monolayer of cells shown in the figure 1.3 with illumination as an external power input defined as an tension $\sigma^{act}$ pattern in space and time. The model is two-dimensional as the thickness $\tau$ of the monolayer is very small compared to its length $l_t$.

Due to the contractility behaviour of the cortex, the network of cells can flow by inducing in-plane active forces. Altogether, for the system at low Reynold’s limit, governing equa-
tions of this compressible active visco-elastic model are developed and solved using linear finite elements. This model can also be developed using Onsager variational principle [13, 31, 32, 29]. The system is non-dimensionalized and the effect of each independent parameter on the system is analyzed. Finally, this model helps in examining the principles that govern the ability to remodel the material by applying space-time patterns of activity.

1.2 Outline

This report is structures as follows. The chapter 2 details the developed continuum model for the compressible active visco-elastic fluid. Further, the discretization of the governing equations is presented in chapter 3. Finally numerical examples are collected in the chapter 4. The drawn conclusions are listed in the chapter 5. Towards the end, in the appendix A, we have presented that this model can be derived using Onsager’s variational principle.
Chapter 2

Continuum mechanics model

In this work, we model an epithelial tissue as a two-dimensional compressible active visco-elastic fluid lying on a substrate (see Fig. 2.1). In this kind of material, viscous and elastic forces dominate over inertia, and thus we neglect inertial forces. The stress $\sigma$ in such a system can be written as the sum of three contributions: (1) a viscous stress, (2) an elastic stress and (3) an active stress. Note that, for a two-dimensional system, the stress has units of N·m$^{-1}$. To model the viscous interactions within the tissue caused by the relative movement of cells with respect to each other, we consider the rheology of the tissue to be of Newtonian nature, so that the viscous part of the stress can be written as

$$\sigma^{\text{visc}} = 2\mu d,$$  \hspace{1cm} (2.1)

where $\mu$ is the shear viscosity of the fluid, $d$ is the rate of deformation tensor $d = \nabla^sv$, and $\nabla^sv = \frac{1}{2} (\nabla v + \nabla v^T)$ stands for the symmetrized gradient of the velocity field $v$ of the tissue.

When looking at long time-scales, epithelial tissues behave as fluids, which cannot sustain shear stress at equilibrium. This is due to the rearrangements of cell-cell junctions when subjected to a shear deformation. Thus, we model the elasticity of an epithelial tissue through an isotropic stress $\sigma^{\text{elast}} = \sigma^{\text{elast}} I$ with $I$ the identity tensor, which only depends
on the density of the monolayer $\rho$,

$$\sigma^{\text{elast}} = \frac{k}{2} \left[ 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right].$$

where $\rho_0$ is the equilibrium density of the monolayer and $k$ is the bulk modulus of the tissue. This kind of stress appears as a reaction to density imbalances within the tissue. The active part of the stress appears due to the internal activity of molecular motors, which is powered by ATP consumption. This part of the stress is characteristic of active (living) matter and distinguishes it from other soft matter systems. In a basic model of the stress generated by this internal activity, we consider an isotropic stress $\sigma^{\text{act}} = \sigma^{\text{act}} I$.

Altogether, the stress in the system is

$$\sigma = \sigma^{\text{visc}} + [\sigma^{\text{elast}} + \sigma^{\text{act}}] I = 2\mu d + \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma^{\text{act}} \right] I. \quad (2.2)$$

Thus, this stress is equivalent to that of a Newtonian fluid with an internal pressure (tension) generated by an equation of state (elastic part) and an active contribution. Conservation of linear momentum within this tissue can be written as

$$\nabla \cdot \mathbf{\sigma} + \mathbf{b} = 0, \quad (2.3)$$

where $\mathbf{b}$ describes the body forces of the system. In this case, as it is a two-dimensional model, the body forces have units of traction. Here we consider that $\mathbf{b}$ is characterized by the viscous dragging caused by the relative slippage of the monolayer and the substrate, which we assume to be at rest,

$$\mathbf{b} = -\eta \mathbf{v}. \quad (2.4)$$

Substituting (2.2) and (2.4) into (2.3), we get

$$2\mu \nabla \cdot \nabla \cdot \mathbf{v} - k \left( \frac{\rho}{\rho_0} \right) \left( \nabla \frac{\rho}{\rho_0} \right) + \nabla \sigma^{\text{act}} - \eta \mathbf{v} = 0. \quad (2.5)$$

The time-evolution of the density field $\rho$ can be characterized through conservation of mass, which takes the form

$$\partial_t \rho + \nabla \cdot (\rho \mathbf{v}) = 0. \quad (2.6)$$

Altogether, we have the system of equations

$$2\mu \nabla \cdot \nabla \cdot \mathbf{v} - k \left( \frac{\rho}{\rho_0} \right) \left( \nabla \frac{\rho}{\rho_0} \right) + \nabla \sigma^{\text{act}} - \eta \mathbf{v} = 0, \quad (2.7)$$

$$\partial_t \rho + \nabla \cdot (\rho \mathbf{v}) = 0.$$
Chapter 3

Space and time discretization

3.1 Time discretization

To integrate Eq. (2.7) numerically, we discretize it both in space and time. Let us first consider the time discretization of the equations. We discretize time in a given grid \((t^{(1)}, t^{(2)}, \ldots, t^{(N)})\), with \(N\) the total number of time-steps. The (possibly time-dependent) time-step is then given by \(\Delta t^{(n)} = t^{(n+1)} - t^{(n)}\). We employ a staggered approach. Let us assume that the solution for \(\rho\) at time \(t^{(n)}\) is given by \(\rho^{(n)}\), then we solve (2.5) to obtain \(v^{(n+1)}\) as

\[
2\mu \nabla \cdot \nabla \rho^{(n)} - k \left( \frac{\rho^{(n)}}{\rho_0} \right) \left( \frac{\nabla \rho^{(n)}}{\rho_0} \right) + \nabla \sigma_{\text{act}} - \eta \rho^{(n+1)} = 0. \tag{3.1}
\]

Then, using \(v^{(n+1)}\) we solve Eq.(2.6) to obtain \(\rho^{(n+1)}\) using a backward Euler approximation

\[
\frac{\rho^{n+1} - \rho^n}{\Delta t^n} + \nabla \rho^{n+1} \cdot v^{n+1} + \rho^{n+1} \nabla \cdot v^{n+1} = 0. \tag{3.2}
\]

We can then continue with the next time-step. This way we generate the sequence of density field \(\rho^{(n)}\) and velocity fields \(v^{(n)}\) in the time grid.

3.2 Spatial discretization

3.2.1 Conservation linear momentum

Weak form

The test function \(w\) is multiplied to (2.3) to obtain the weak form,

\[
\int_{\Omega} w \cdot (\nabla \sigma + b) \, d\Omega = 0
\]
Considering the Dirchlet boundary condition, $v = 0$ on $\partial \Omega$,
\[
\int_{\Omega} (- \nabla w : \sigma + w \cdot b) \, d\Omega = 0
\]
\[
\int_{\Omega} \left( 2 \mu (\nabla^s w : \nabla^s v^{n+1}) + \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma^{\text{act}} \right] \nabla \cdot w + \eta v^{n+1} \cdot w \right) \, d\Omega = 0 \tag{3.3}
\]

Spatial discretization

In order to discretize the computational domain $\Omega$, we consider a linear triangular elements $\Omega^e$ and the approximation $v^h$ lies in $S^h := \{ v \in H^1(\Omega) \mid v|_{\Omega^e} \in P_1(\Omega^e) \forall e \text{ and } v = v_D \text{ on } \Gamma_D \}$ with the precision given by the characteristic mesh size $h$. The Galerkin formulation is obtained by restricting the weak form (3.3) to the finite element spaces, namely, find $v^h \in S^h$ such that
\[
\int_{\Omega^e} \left( 2 \mu (\nabla^s w^h : \nabla^s (v^h)^{(n+1)}) + \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma^{\text{act}} \right] \nabla \cdot w^h + \eta (v^h)^{(n+1)} \cdot w^h \right) \, d\Omega^e = 0
\]
for all $w^h \in S^h$. At this point the computational domain $\Omega$ is discretized into the linear elements $\Omega^e$, the approximation $v^h(x)$ and test function $w^h$ can be written as,
\[
(v^h)^{(n+1)}(x) = \sum_m v^{(n+1)}_m N_m(x)
\]
\[
w^h(x) = N_m(x) \begin{bmatrix} 1 \\ 0 \end{bmatrix}
\]
where $N_m$ is the shape function associated with node number $m$ and $v^{(n+1)}_m$ is the nodal unknown. Thus after substitution, the discrete equation leads to
\[
\sum_{m,n} \int_{\Omega^e} \left( 2 \mu v^{(n+1)}_{m,i} (\nabla^s N_m : \nabla^s N_n) + \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma^{\text{act}} \right] (\nabla N_n)_i + \eta v^{(n+1)}_{m,i} N_m N_n \right) \, d\Omega^e
\]
Finally the linear system of equations can be written in matrix form as,
\[
K v^{(n+1)} = b
\]
where,
\[
K_{mn} = \int_{\Omega^e} \left( 2 \mu (\nabla^s N_m : \nabla^s N_n) + \eta N_m N_n \right) \, d\Omega^e
\]
\[
b_{ni} = - \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma^{\text{act}} \right] (\nabla N_n)_i
\]
3.2.2 Conservation of mass

Weak form

The test function \( w \) is multiplied to the time discretized mass conservation equation (3.2) to obtain weak form,

\[
\int_{\Omega} w\rho^{n+1} + \Delta t^n (w \nabla \rho^{n+1} \cdot \mathbf{v}^{n+1} + w\rho^{n+1} \nabla \cdot \mathbf{v}^{n+1}) \, d\Omega = \int_{\Omega} w\rho^n \, d\Omega \quad \forall w
\]

Spatial discretization

Galerkin method presents serious deficiencies with convection dominated problems. These deficiencies can be counterbalanced by following the Petrov-Galerkin method in which additional term called stabilization term is added through the weight function to the weak form. This stability term controls the convective term of the transport problem by adding some numerical diffusion controlled by the SUPG parameter \( \gamma \) [51]. Considering SUPG method and discretizing computational domain \( \Omega \) into the linear elements \( \Omega_e \), the approximation of unknown nodal solution \( \rho^h(x) \) and weight function \( w^h \) is,

\[
\rho^{(n+1)}_m = \sum_m \rho^{(n+1)}_m N_m(x) \\
w^h = N_n(x) + \gamma \Delta t \nabla \cdot \nabla N_n(x)
\]

where \( N_m(x, y) \) is the basis function associated to the node number \( m \). After discretization, then the weak form is

\[
\int_{\Omega_e} N_n(x) N_m(x) + \Delta t(N_n \nabla N_m(x) \cdot \mathbf{v}^{n+1} + N_n N_m \nabla \cdot \mathbf{v}) \, d\Omega + \int_{\Omega_e} \gamma \Delta t [N_m \mathbf{v}^{n+1} \cdot \nabla N_n(x) + \Delta t(\mathbf{v}^{n+1} \cdot \nabla N_n(x) \cdot \mathbf{v}^{n+1} + \mathbf{v}^{n+1} \cdot \nabla N_n(x) N_m(x) \nabla \cdot \mathbf{v}^{n+1})] \, d\Omega] \rho^{(n+1)}_m = \\
\int_{\Omega_e} (N_n(x) + \gamma \Delta t \mathbf{v}^{n+1} \cdot \nabla N_n(x)) \rho^n \, d\Omega
\]

As a linear system of equations it can rewritten as,

\[
A_{mn} \rho^{(n+1)}_m = F_n
\]

with,

\[
A_{mn} = \int_{\Omega_e} N_n(x) N_m(x) + \Delta t(N_n \nabla N_m(x) \cdot \mathbf{v}^{n+1} + N_n N_m \nabla \cdot \mathbf{v}) \, d\Omega + \int_{\Omega_e} \gamma \Delta t [N_m \mathbf{v}^{n+1} \cdot \nabla N_n(x) + \Delta t(\mathbf{v}^{n+1} \cdot \nabla N_n(x) \cdot \mathbf{v}^{n+1} + \mathbf{v}^{n+1} \cdot \nabla N_n(x) N_m(x) \nabla \cdot \mathbf{v}^{n+1})] \, d\Omega \]

\[
F_n = \int_{\Omega_e} N_n(x) \rho^n \, d\Omega
\]
\[
F_n = \int_{\Omega_n} (N_n(x) + \gamma \Delta t \, v^{n+1} \cdot \nabla N_n(x)) \rho^n \, d\Omega
\]

For detailed derivation see appendix B.3. Upon obtaining all the system of equations, now we have all the ingredients ready for the computational analysis. The following chapter details various numerical examples with three different space and time patterns of tension gradient. This study helps in understanding the material behaviour with different parameters discussed in the section 4.1.
Chapter 4

Numerical examples

This chapter is devoted to present various numerical examples which help in understanding the response of the model as compressible active visco-elastic fluid activated using tension patterns in space and time. In the present work three different space-time patterns, described in the section 4.2, are chosen to study the displacement and velocity achieved by the particles (cells) in the monolayer upon illumination. Before presenting the examples, the model is non-dimensionalized and the three space-time patterns of tension are defined using different parameters are discussed in detail. Finally, the examples are presented which helps in understanding how the particles behave while varying parameters and justified with explanations.

4.1  Non-dimensionalization of the model

From the governing equation we can understand that, dimensionally this model depends on four variables: bulk modulus ($k$), shear viscosity ($\mu$), friction coefficient ($\eta$) and tension pattern ($\sigma$). The dimension of these variables are,

$$k = \frac{[\text{Energy}]}{[\text{Length}]^2}, \quad \sigma = \frac{[\text{Energy}]}{[\text{Length}]^2},$$

$$\mu = \frac{[\text{Energy}][\text{Time}]}{[\text{Length}]^2}, \quad \eta = \frac{[\text{Energy}][\text{Time}]}{[\text{Length}]^4}.$$

The time- length- and energy-scales of the system are given by

$$t_1 = \frac{\mu}{k}, \quad t_2 = \frac{\mu}{\sigma}, \quad l = \sqrt{\frac{\mu}{\eta}}, \quad e = k\frac{\mu}{\eta}.$$

Setting $t_1 = 1, l = 1, e = 1$, that is $k = \mu = \eta = 1$, we are left with

$$t_2 = \frac{t_1}{\sigma}.$$
and the length and time scales are given by the movement of laser, which is elaborated in the section 4.2. Here, we can observe that this model has two different time scales. First one depends on the bulk modulus ($k$) and it is called as the relaxation time scale $t_{\text{relax}} = \frac{\mu}{k}$ as it is taken into account during the time gap between consecutive illuminations. Second one depends on the tension pattern ($\sigma$) and it is called as the activation time scale $t_{\text{act}} = \frac{\sigma}{k}$ as it is taken into account during illumination. Upon dimensionalizing the system, we can write the velocity of the particle as

$$v_{\text{particle}} = X \frac{[\text{length}]}{[\text{time}]} = X \frac{\sigma}{\sqrt{\mu \eta}}.$$

Mathematically, we can say that velocity of the particle has strong dependency on the tension pattern. With the set of numerical examples presented in this chapter shows how the tension pattern effects the model based on displacements and velocity.

### 4.2 Space-time patterns

In the present work the tension pattern $\sigma$ is defined as the Gaussian function which is defined in space and time as shown in figure 4.2. Tension pattern depends on four different parameters namely: (1) tension strength ($\sigma_0$) decides the amount of contractility material through intensity of laser beam, (2) Activation time ($t_0$) is the time taken to finish one cycle. (3) Gaussian function radius ($l_0$) is the radius of the laser beam, (4) tension length ($l_y$) is the length on the distance traveled by the laser beam. These parameters are pictorially illustrated in the figure 4.1. The velocity of the moving tension pattern can be defined in terms of distance covered by the laser beam in specific time as $v_{\text{laser}} = \frac{l_y}{t_0}$

![Figure 4.1: Model parameters](image)

It is necessary to understand the behaviour of particle during activation (when the tissue is exposed to laser beam) and relaxing (when the illumination is turned off). Hence three
different tension patterns are considered in space and time: pattern I is an activation with forward stroke and then allowing certain time for relaxation, pattern II is an activation with continuous forward and backward strokes and pattern (III) is an activation with continuous forward strokes.

The three different space-time patterns of tension are illustrated graphically in the figure 4.2. Additionally, the y-positions of lagrangian particle which is orginally at [0,0] is also presented. In all the three cases, the displacement of the particle is exactly same at the end of first forward stroke, that is at $t = 0.5$. In pattern I, the system is allowed to relax after the first forward stroke. So the particle tends to go back to its original position.
Whereas, in pattern II, the system is not allowed to relax and instead tries to follow the backward motion of the laser beam leading to a position closer to its original location. In pattern III, unlike other two cases, the particle keeps moving forward as the tension pattern is given as a continuous forward stroke. Among these three cases, at the end of every cycle, the better displacements are observed in the patterns I and III. However, within the cycle, the maximum displacement can be achieved from the pattern II.

As we are dealing with a transient problem, it is necessary to the steady state after few number of cycles. Therefore, computations are performed for longer simulation time to know when the solution does not significantly vary from previous cycle. This cycle is called limit cycle of the system. For the three space-time patterns, shown in the figure 4.3 (right), we can observe that, after sixth cycle, that is \( t = 6 \), the displacement at the
end of the cycle doesn’t significantly vary. Hence this is the limit cycle of this system and it can be considered for further computations to ensure the steady state.

Considering an appropriate cycle, that is greater than or equal to the limit cycle, for three different tension patterns in space-time are compared on the basis of displacements at the end of 12 cycles. The color map in the figure 4.3 (left) shows the velocity magnitude, the colored spheres represents the final position of the particles at nine different location, \([0,0], [0.2,0], [0.2,0.2], [0,0.2], [-0.2,0.2], [-0.2,0], [-0.2,-0.2], [0,-0.2] \) and \([0.2,-0.2] \) with respective coloured lines illustrating the path followed to reach the final position.

In all the cases, the illumination starts from \([0,-0.2] \). The particle at the illumination are subjected to contraction and as it is a network of cells it tried to pull the other cells surrounding it leading to movement of other particles. But, as the laser beam moves forward, they try to follow with the beam. So, the particles at the center in the path of illusion ends up oscillating up or down along with the movement of laser beam. Whereas the particles at the sideways try to move towards the illumination. This behaviour is observed in all the three cases. However, the path and final displacement achieved by the particle varies with the tension pattern. Comparing the three patterns, we can observe that higher displacements can be achieved with the help of the tension pattern III or I. It is well noted by looking at the lagrangian y-position at the end of each cycle (see figure 4.4).

Figure 4.4: Lagrangian Y-position of the particle \([0,0] \) at the end of each cycle for the space-time patterns I, II and III.

From the velocity magnitude colour maps, we can say that only in the pattern I, the velocities are almost zero because the particles are allowed to relax between the cycles and we are looking at the end of each cycle. However, compared to pattern III, that is continuous forward and backward strokes, the pattern I achieves reasonable displacements. In the present work, the pattern I and III are mainly considered to study as they deliver more displacements at the end of each cycle.
4.3 Convergence of the numerical method

In order to examine the convergence of the numerical method, the obtained particle displacement is compared with two levels of refinement of previously used unstructured mesh and also for a regular mesh. In the figure 4.5, we compute the difference in the displacement between the reference solution, that is solution of the finest mesh $n_3$ (307376 elements). This analysis shows that the difference between the meshes $n_1$ (19211 elements) and $n_3$ is higher than that between $n_2$ (76844 elements) and $n_3$ which is expected due to convergence.

![Figure 4.5: Convergence of the numerical method](image)

For the time-step validation, we have computed and compared the displacements corresponding to decreasing time-step of the simulation 4.5. Care should be taken care while choosing the time step of the simulation because the SUPG stabilization term depends on the time-step and it creates oscillations or unnecessary disturbances for inappropriate time steps. From this analysis we understood that the displacements does not significantly vary after $\Delta t = 0.001$ and hence it can be considered for the further computations.
4.4 Varying tension strength

One of the important parameters of the Gaussian function is the tension strength, which can be understood as intensity of the contractile force induced by the illumination. In this section we presented few examples which helps in understanding the displacement of the particles with varying tension strength.

Figure 4.6: Eulerian tracking(left) of different particles using pattern III and log-log and (right) plot of displacement of a particle at \([0,0]\) which is activated with tension pattern in space-time pattern I and III.

For the tension pattern III, that is continuous forward stroke, we can observe that the displacement increases almost exponentially with increasing tension strength (see figure 4.6). The particle tracking clearly shows that for very small tension strength the displacement is almost zero and for the higher tension strengths the displacement goes upto 1.5% of the domain length, that is \([1 \times 1]\). Similar behaviour is observed in the case of the tension pattern I.
4.5 Varying activation time

The activation time is another important parameter to be understood in order to obtain desired displacement. In this section we present the how the velocity of tensor pattern or laser beam effects the velocity of the particle. The velocity of the laser is rate of the movement of laser beam over the monolayer. In the case of the tension pattern III, that is with the continuous forward stroke, the velocity of the particle decreases with the decreasing laser velocity (see figure 4.7).

![Graph showing velocity of laser vs velocity of particle]

Figure 4.7: Velocity of laser Vs velocity of particle due to the tension pattern III and colour maps showing velocity and particle displacement

Carefully observing the colour maps of velocity magnitude, we can see that the velocity in the A is greater than B. However, the distance traveled by the particle is much higher in A compared to B. So, it is necessary to know specific velocity of laser in order to achieve desired displacement of particles.
Whereas for the tension pattern I, totally different behaviour was observed. As the velocity of laser decreases, the velocity of the particle increases till a point and then decreases. Upon further decrease in laser velocity does not significantly vary the velocity of the particle. This tells us that, in order to achieve maximum displacement using pattern I, then it is necessary to chose this peak point as the velocity of laser $4.7$.

### 4.6 Varying domain length

We have looked at how the parameters, tension strength $\sigma_0$ and activation time $t_0$ effects the model. Now we are left out with two other parameters, Gaussian radius $l_0$ and tension length $l_y$. In this section, we present an example to show how these parameters effect the model. Considering different domain length $l_t$ and further by changing these parameters accordingly, we have observed that the displacement of the particles increases with increasing domain length till certain point, that is $l_t = 20$. 

![Velocity of laser Vs velocity of particle due to the tension pattern I and colour maps showing velocity and particle displacement](image)
The displacement of the particle is almost same for other domain lengths. This is due to the faster displacement of the particle out of the illumination and therefore the effect of illumination does not effect the particle.
Chapter 5

Conclusion

We have derived a simple mathematical model and finite element simulation to understand how contractile forces within tissues can generate space time mobility patterns and transport material from one place to another. More precisely,

- We have addressed and examined an important problem in biology, namely the flow generated by active processes in epithelial tissues.

- We have developed a two-dimensional continuum mechanics framework to study this problem. This model is based on viscous, elastic and active stresses along with friction with a substrate.

- We have developed a numerical framework for the simulation of the model based on finite elements.

- We have studied the different length and time-scales of the problem and nondimensionalize it.

- We have studied particular examples of active tension patterns in space and time that lead to flow of material. We have presented, how the velocity of the particles (cells) in the material depend on different parameters of the model.

In summary, we have formulated a minimalistic continuum model to examine the principles that govern the ability to remodel the material by applying space-time patterns of activity.
Onsager’s variation principle

A.1 Introduction

The variation principles have been used in many mechanical and thermodynamic theories. It is a general framework which provides both a systematic approach to generate variational time-integrators [1], to understand Noether’s theorem and to provide body of theory like governing equations to support it. The Onsager’s variational principle [2, 3] is an extension of Rayleigh’s principle of the least energy dissipation [15, 16]. This Rayleigh’s principles are usually used in various linear systems such as Viscous flow in Newtonian fluid [5], irreversible thermodynamics [6, 7] and electrical current in Ohmic devices. However, Doi [13] mentioned that Onsager’s principle provide nonlinear time evolution equations [18, 19, 20]. Therefore, the Onsager’s variational principle are applicable to describe non-linear systems. He presented that this principle is a solid general basis for soft matter physics by deriving many equations which describe the nonlinear and non-equilibrium phenomena such as phase separation kinetics [8], gel dynamics [9, 10], molecular modeling for viscoelasticity behavior of soft matter [11, 12]. This concept was extended to derive the geometrically non-linear equations for an inter-facial fluid in which the bending rigidity is coupled to a bulk viscous fluid [21] and to derive the governing equations for a phase-field model of membranes coupled to a bulk viscous fluid [22]. This principle assumes negligible inertia effect [23] in case of slow kinetics and constant temperature of the system in case of isothermal systems.

The Onsager’s variation principle was widely implemented in solid mechanics also. In specific it is used for time-incremental discretized principles to generate algorithms [24] and to develop mathematical analysis [25, 26]. In a similar fashion, Otto et al. [27, 28] illustrated a variational formulation for diffusion equations as gradient flows of entropy functionals with a mathematical and physical insight and emphasized the importance of parameterizing the processes that modify the state of the system. This drove to development of further formalization of Onsager’s variational principle with the introduction of process operators by Peletier [29]. These were independently used by Doi [13] to model the viscoelastic fluids [11, 12] and by Rahimi and Arroyo [30] to derive the equations of a non-linear dynamical model for lipid bilayers. The gradient structure of reaction-diffusion systems were depicted [25] which helps in coupling such problems with other phenomena.
through Onsager’s principle. Very recently, this idea was implemented by Arroyo et al. [32] in describing the reaction-diffusion-elasticity problem associated to the adsorption of curving molecules onto lipid bilayers using Onsager’s principle. They have also presented a general framework for modeling dissipative systems such as lipid bilayers based on the Onsager’s variational principle [31]. This framework is exploited in the present work to develop a two-dimensional active-viscous-compressible flow which illustrates the effect of cortex mechanics in the movement of the cell. Before looking into the application of the Onsager’s Variational principle to the present model, it is introduced and explained with simple models using the nomenclature popularized by Doi [14] in the following sections.

A.2 Elementary energy-dissipative systems

In this section, the Onsager’s principle is explained with an elementary model and viscous compressible fluid in Euclidean space. Initially a simple one-dimensional example is considered to show that the Onsager’s principle provides a systematic approach to derive the governing equations for systems with the help of energetic and dissipative information. In the second example a compressible Newtonian fluid in the low Reynolds number limit is considered to show how the Onsager’s principle can be applied to compressible viscous fluids. In addition to this, the derivation of variational time-integrators is also presented as given in [31]. One of the key aspect of this method is that it does not depend on the formulation of the strong form of the problem and can be readily discretized with finite elements. These models helps in understanding the general framework and also provides background for the derivation of the two-dimensional active-viscous-compressible fluid equations.

A.2.1 One-dimensional spring-dashpot

A spring of elastic constant $k$ coupled in parallel with a dashpot of drag coefficient $\eta$ and under the action of a force $F$ as shown in the figure A.1. Though it might seem abstract to implement Onsager’s principles to derive such a simple model, it helps in understanding the physical picture and essential ingredients. Also, it can be observed that the complex systems follow similar approach.

The displacement of the spring with respect to its natural elongation $x$, characterizes the state of the system. The conservative force generated by the spring is

$$F_{cons} = -kx \tag{A.1}$$

There is a viscous force that is opposing the motion of the spring which is given as,

$$F_{visc} = -\eta v \tag{A.2}$$

where $v = \dot{x}$. The inertia can be neglected if the drag is sufficiently large. Then the balance of forces can be given as

$$F_{cons} + F_{visc} + F = 0 \tag{A.3}$$
which further gives,

\[ \eta \dot{x} + kx = F \]  \hspace{1cm} (A.4)

Figure A.1: A spring with constant \( k \) is in parallel with a dashpot with drag coefficient \( \eta \) and a force \( F \) is applied. The system is characterized by the displacement of the point of application of the force from its equilibrium position, \( x \)

As this is an ordinary differential equation, it can be easily integrated in time to get the \( x \) with provided initial condition. But looking at the structure of the equation, one can say that the equation follows from a variational principle. The spring and external forces can be written as a derived from a potential which includes the stored elastic energy in the spring and the potential for the external force,

\[ F_{\text{cons}} + F = -\frac{dF}{dx} \]  \hspace{1cm} where  \hspace{1cm} \( F(x) = \frac{k}{2}v^2 - Fx \)

Similarly, the viscous forces can also be derived from a potential (dissipative or Rayleigh dissipation function) depending on \( v \),

\[ F_{\text{visc}} = -\frac{\partial D}{\partial v} \]  \hspace{1cm} where  \hspace{1cm} \( D(v) = \frac{\eta}{2}v^2 \)

The rate of change of energy (\( \dot{F} \)) depends on the state of the system \( x \) and on the rate of change of the state \( v \). It can be written as,

\[ \frac{dF(x(t))}{dt} = \frac{dF(x(t))}{dx} \dot{x}(t) = (kx - F)v \]

The process operator relates the rate of change of state variable and process variable. In this case, the relation \( v = \dot{x} \) acts as the process operator. Finally the Rayleigh function can be defined as,

\[ R(x,v) = \dot{F}(x,v) + D(v) = (kx - F)v + \frac{\eta}{2}v^2 \]

As mentioned in [31], the equilibrium equation (A.4) can be obtained by minimizing this Rayleigh function with respect to rate of change of the system \( v \). That is,

\[ \frac{\partial R}{\partial v} = 0 \quad \implies \quad kx - F + \eta v = 0 \]
This is Onsager’s variational principle. By implementing this principle, the governing equations can be obtained by minimizing the Rayleigh function $\mathcal{R}(x, v)$ of the system that is,

$$v = \arg \min_w \mathcal{R}(x, w)$$

In this case, in contrast to the classical equilibrium principle of minimum potential, the minimization is performed over the rate of change of the system $v$ instead of state of the system $x$. This is due to the flexibility of the principle to establish a competition between the energy release rate and dissipation. From this linear response theory, Onsager principle showed it holds for generic irreversible process with the following assumptions,

- Dissipation dominated over the inertia
- Viscous forces are derived from a dissipation potential

However, this principle is still valid if $\mathcal{F}$ or $\mathcal{D}$ are general non-hormonic potentials for the spring or for the dashpot.

### A.2.2 Compressible Stokes flow

In this example, a compressible Newtonian fluid with low Reynolds number is considered in the Eulerian domain. As the fluid is compressible, it is necessary to find the densities and equation of state that characterizes the dependency of the free energy on the densities. Here, we considered a free energy as a quadratic potential of densities.

$$\mathcal{F}[\rho] = \int_{\Omega} \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 d\Omega$$

where $k$ is the bulk modulus, $\rho$ is density and $\rho_0$ is the equilibrium density. As the fluid is considered in the Eulerian domain, the free energy depends on the material domain evolving with time. Then the free energy in terms of material domain $\Omega_t$ with $\Omega_0 = \Omega$ is,

$$\mathcal{F}[\rho, \Omega_t] = \int_{\Omega_t} \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 d\Omega$$

In the previous example, $v = \dot{x}$ is defined as the process operator to relate the rate of change of state variable and process variables. Similarly, there is a need for the process operator in this example to relate the rate of change of the state variable, that is density $\rho$ and process variable, that is $v$. This can be achieved using continuity equation,

$$\frac{\partial \rho}{\partial t} + v \cdot \nabla \rho + \rho \nabla \cdot v = 0 \quad (A.5)$$

This equation should be completed with a boundary condition for density $\rho$ at the in-flow boundary.

$$\rho(x) = c(x) \quad \text{on } \Gamma_f$$
where $\Gamma_I = x \in \Gamma : \mathbf{v}(x) \cdot c(x) < 0$ and $c(x)$ is given. The rate of change of free energy, $\dot{\mathcal{F}}$, involves time differentiation of the integral over moving domain $\Omega_t$ and at $t = 0, \Omega_0 = \Omega$.

$$\dot{\mathcal{F}}[\rho; \partial_t \rho] = \frac{d}{dt} \int_\Omega \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 d\Omega$$

Applying Reynold’s transport theorem, at $t = 0$,

$$\dot{\mathcal{F}}[\rho; \partial_t \rho] = \int_\Omega k \left( \frac{1}{\rho_0} \right) \left( \frac{\rho}{\rho_0} - 1 \right) \frac{\partial \rho}{\partial t} d\Omega + \int_\partial \Omega k \left( \frac{\rho}{\rho_0} - 1 \right)^2 \mathbf{v} \cdot \mathbf{n} dl$$

Implementing the (A.10) and then further simplifying the terms (detailed in Appendix B.1) we get,

$$\dot{\mathcal{F}}[\rho; \partial_t \rho] = \int_\Omega \frac{k}{2} \left[ 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right] \nabla \cdot \mathbf{v} d\Omega$$

Considering the energy dissipated in the viscous fluid by shear, the dissipation potential can written as,

$$D_s[\mathbf{v}] = \int_\Omega \mu \|d^2\| d\Omega \quad (A.6)$$

where $d$ is the strain tensor $(\nabla^s \mathbf{v} = \frac{1}{2}(\nabla \mathbf{v} + (\nabla \mathbf{v})^T))$ and $\mu$ is the shear viscosity of the fluid. The boundary is split into the essential or Dirichlet boundary ($\Gamma_D$), where the velocity field $\mathbf{v}(x)$ is imposed and the natural or Neumann boundary conditions ($\Gamma_N$) where a traction $t(x)$ is applied. The Neumann condition can be implemented as a power generator in terms of traction and velocity filed.

$$P_N[\mathbf{v}] = \int_{\Gamma_N} t \cdot \mathbf{v} d\Gamma \quad (A.7)$$

In this example, the energy ingredient is not considered and hence the system is not concerned to any variable involved int he state of the system. Thus the Rayleighian of the system can be written as the sum of rate of change of free energy and dissipation potential,

$$\mathcal{R}[\rho, \mathbf{v}] = \dot{\mathcal{F}}[\rho; \partial_t \rho] + D_s[\mathbf{v}] + P_N[\mathbf{v}]$$

$$\mathcal{R}[\rho, \mathbf{v}] = \int_\Omega \frac{K}{2} \left[ 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right] \nabla \cdot \mathbf{v} d\Omega + \int_\Omega (\mu (\nabla^s \mathbf{v} : \nabla^s \mathbf{v}) (\nabla \cdot \mathbf{v})) d\Omega + \int_{\Gamma_N} t \cdot \mathbf{v} d\Gamma$$

As per Onsager’s variational principle, the system dynamics follows,

$$\mathbf{v} = \arg\min_w \mathcal{R}(\rho, w)$$

Considering the variations of velocity field $\partial \mathbf{v}(x)$ consistent with Dirichlet boundary conditions, that is $\partial \mathbf{v}(x) = 0$ at $\partial_D \Omega$ leads to stationary condition,

$$\int_\Omega \frac{k}{2} \left[ 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right] \nabla \cdot \partial \mathbf{v} d\Omega + \int 2\mu \; d : \nabla \partial \mathbf{v} d\Omega - \int_{\Gamma_N} t \cdot \partial \mathbf{v} d\Gamma = 0 \quad (A.8)$$
Using the relations,
\[
\frac{k}{2} \left[ 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right] \nabla \cdot \partial v = \nabla \cdot \left( \frac{k}{2} \left[ 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right] \partial v \right) - \nabla \left( \frac{k}{2} \left[ 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right] \right) \cdot \partial v
\]
\[
d : \nabla \partial v = \nabla \cdot (\partial v \cdot d) - \nabla \cdot d \cdot \partial v
\]
the equation \((A.8)\) can be rewritten as,
\[
\int_{\Omega} \left( \nabla (-p \partial v) + \nabla p \cdot \partial v + 2\mu [\nabla \cdot (d \partial v) - \nabla \cdot d \cdot \partial v] \right) \, d\Omega - \int_{\Gamma_N} t \cdot \partial v \, d\Gamma = 0
\]
with \(-p = \frac{k}{2} \left[ 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right] \). Further simplifying it, we get,
\[
\int_{\Gamma} (-p + 2\mu d) \partial v \hat{n} \, d\Gamma + \int_{\Omega} \nabla p \partial v - 2\mu (\nabla \cdot d) \cdot \partial v \, d\Omega - \int_{\Gamma_N} t \cdot \partial v \, d\Gamma = 0
\]
The strong form after integration by parts is obtained as,
\[
\nabla \cdot \sigma = 0 \quad \text{in} \, \Omega,
\]
\[
\partial_t \rho + \nabla \cdot (\rho v) = 0 \quad \text{in} \, \Omega,
\]
\[
v = u \quad \text{on} \, \Gamma_D
\]
\[
\sigma \cdot \hat{n} = 0 \quad \text{on} \, \Gamma_N
\]
\[
\rho = c \quad \text{on} \, \Gamma_I
\]
where \(\sigma = -p I + 2\mu d\). By following Onsager’s variational principle we have obtained the system coupling an elliptic PDE, requires mechanical equilibrium and a hyperbolic PDE, modeling mass conservation and subjected to in-flow Dirichlet boundary conditions.

### A.3 General Framework of Onsager’s principle

Following The main ingredients in Onsager’s modeling framework are,

1. The state variable which describes the state of the system such as \(x\) in the case of spring-dashpot example and \(\rho\) in the case of compressible stokes flow problem.

2. The free energy \(F\) which depends on the state variables.

3. The process variables which shows how the system changes its state and creates dissipation.

4. The process operator relates the rate of change of the state variables and the process variables. In the case of simple one-dimensional example the process operator is \(v = \dot{x}\), where in compressible stokes flow the \(\partial_t \rho\) term in continuity equation gives the process opertator.
5. The dissipation potential $D$ which measures the energy dissipated by process variables, external power supplies and constraints such as incompressibility condition.

In conclusion, the abstract statement of Onsager’s variational principle, in the terminology used by Mark [29], is as follows. A dissipative system is described using state variables $X(t)$ which evolve in suitable space, a free energy $F(x)$, process variables $V$, a dissipation potential $D(X; V)$ and a potential for external power supply $P(X; V)$. The dissipation potential needs few assumptions such as: it should be non-negative, $D(X; 0) = 0$, it is a convex function of $V$, it is differentiable (considered in the case of soft and biological matter as it is usually wet and rate-dependent).

The rate of change of energy is required to evaluate the Rayleighian. This can obtained by the chain rule,

$$\dot{F}(X; \partial_t X) = \frac{d}{dt}[F(X(t))] = D F(X) \partial_t X$$

where $DF(X)$ denotes the derivative of the free energy. The process operator expresses the rate of change of the system $\partial_t X$ in terms of the process variable $V$ as

$$\partial_t X = P(X) V$$

and thus Rayleighian as

$$R(X : V) = D F(X) P(X) V + D(X; V) + P(X; V)$$

Onsager’s variation principle states that the system evolves such that

$$V = \arg\min_W R(X; W)$$

subject to the constraints on $W$.

From these examples [13, 31], it can be observed that the Onsager’s variational principle helps in obtaining dynamics due to the forces from both free energy and dissipation. This formulation assumes negligible inertia forces. In conclusion, the Onsager’s variation principle has several advantages over the traditional approach, it provides a systematic framework, gains more information about the nature of solution like stability, assures more robust algorithms that use the information about variation nature of the problem and ensures both conceptual and algorithm benefits.

### A.4 Model for active fluid

As the active fluid is compressible with low Reynolds number it is mandatory to track the densities. Thus, the state of the monolayer of cells is characterized by the density $\rho$ at a given time $t$. Thus the density of the cells or tissue is the state variable of the active fluid. The process variable characterizing the effect of system on rate of change of the state variable. Here, the rate of change of state variable, that is density $\rho$ is related using continuity equation,

$$\frac{\partial \rho}{\partial t} + v \cdot \nabla \rho + \rho \nabla \cdot v = 0$$

(A.10)

Thus the velocity $v$ of the cells or tissue is considered as the process variable.
A.4.1 Energy

It is also necessary to define an equation of state that characterizes the dependency of the free energy on densities. In the present work, a simple quadratic elastic energy [30, 39] is considered as free energy $\mathcal{F}$ similar compressible stokes problem in section A.2.2.

$$\mathcal{F}[\rho] = \int_{\Omega} \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 d\Omega$$

where $k$ is the bulk modulus, $\rho$ is density and $\rho_0$ is the equilibrium density. As the fluid is considered in the Eulerian domain, the free energy depends on the material domain evolving with time. The free energy,

$$\mathcal{F}[\rho, \Omega_t] = \int_{\Omega_t} \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 d\Omega$$

is written in terms of material domain $\Omega_t$ with $\Omega_0 = \Omega$.

A.4.2 Dissipation

Three major dissipation mechanisms are taken into account according to the active fluid behaviour. First, the energy dissipation due to viscous fluid by shear is considered as shown in the section A.2.2. The shear dissipation potential is,

$$\mathcal{D}_s [v] = \int_{\Omega} \mu ||d^2|| d\Omega \quad (A.11)$$

where $d = \nabla^s v$ is the rate-of-deformation or strain tensor and $\mu$ is the shear viscosity of the fluid. In addition to this, the flow is created using divergence operator over the velocity $v$ and it can be scaled and manipulated using tension parameter $\sigma$. This can be considered an external power input in the case of optogenetical study [42].

$$\mathcal{D}_p [v] = \int_{\Omega} \sigma (\nabla \cdot v) d\Omega \quad (A.12)$$

where $\sigma$ is the tension function which can be defined in space-time. Finally the energy dissipated due to the friction caused by the slipping of the monolayer over the substrate is,

$$\mathcal{D}_f [v] = \int_{\Omega} \eta ||v||^2 d\Omega \quad (A.13)$$

where $\eta$ is the friction coefficient. Thus, the total dissipation is written as the sum of all the three (A.11),(A.12) and (A.13). The total dissipation,

$$\mathcal{D} [v] = \mathcal{D}_s [v] + \mathcal{D}_p [v] + \mathcal{D}_f [v] \quad (A.14)$$

Rewriting it in terms of strain tensor, $(\nabla^s v$,

$$\mathcal{D} [v] = \int_{\Omega} (\mu (\nabla^s v : \nabla^s v) d\Omega + \int_{\Omega} \sigma (\nabla \cdot v) d\Omega + \int_{\Omega} \eta ||v||^2 d\Omega \quad (A.15)$$

which depends on the material parameters.
A.4.3 Governing equations

The required data to form Rayleighian, that is free energy and dissipation, were presented in the previous sections. Now, following the general framework, we can write Rayleighian as,

\[ \mathcal{R}[\rho; \partial_t \rho, \mathbf{v}] = \partial_t \mathcal{F}[\rho; \partial_t \rho, \mathbf{v}] + \mathcal{D}[\mathbf{v}] \]

The rate of change of free energy, \( \partial_t \mathcal{F} \) involves time differentiation of the integral over moving domain \( \Omega_t \) and at \( t = 0, \Omega_0 = \Omega \).

\[ \partial_t \mathcal{F}[\rho; \partial_t \rho, \mathbf{v}] = \frac{d}{dt} \int_{\Omega} \left( \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right) \right)^2 d\Omega \]

Applying Reynold’s transport theorem, at \( t = 0, \)

\[ \partial_t \mathcal{F}[\rho; \partial_t \rho, \mathbf{v}] = \int_{\Omega} \left( \frac{1}{\rho_0} \right) \left( \frac{\rho}{\rho_0} - 1 \right) \frac{\partial \rho}{\partial t} \left( \frac{\rho}{\rho_0} - 1 \right)^2 \mathbf{v} \cdot \mathbf{n} \, dl \]

Implementing the (A.10) and then further simplifying the terms (detailed in Appendix B.1) we get,

\[ \partial_t \mathcal{F}[\rho; \mathbf{v}] = \int_{\Omega} \left( \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) \right) \nabla \cdot \mathbf{v} \, d\Omega \]

Substituting the obtained rate of change of free energy and sum of all dissipations gives the Rayleighian as,

\[ \mathcal{R}[\rho; \mathbf{v}] = \int_{\Omega} \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) \nabla \cdot \mathbf{v} \, d\Omega + \int_{\Omega} \left( \mu (\nabla^s \mathbf{v} : \nabla^s \mathbf{v}) + \sigma (\nabla \cdot \mathbf{v}) \right) \, d\Omega + \int_{\Omega} \eta ||\mathbf{v}||^2 \, d\Omega \]

Following Onsager’s variational principle the system follows from

\[ \{ \mathbf{v} \} = \text{argmin} \mathcal{R}[\rho; \mathbf{v}] \quad \text{(A.16)} \]

and gives us the governing equation which is directly used in later section for spatial discretization in order to implement Galerkin finite element method. Rewriting the Rayleighian function (A.17) in terms of velocity potentials \( \nabla^s \mathbf{v} = \frac{1}{2} (\nabla \mathbf{v} + \nabla \mathbf{v}^T) \), we obtain

\[ \mathcal{R}[\rho; \mathbf{v}] = \int_{\Omega} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \nabla \cdot \mathbf{v} \, d\Omega + \int_{\Omega} \frac{\mu}{4} \left[ \nabla \mathbf{v} : \nabla \mathbf{v} + \nabla \mathbf{v} : \nabla \mathbf{v}^T + \nabla^T \mathbf{v} : \nabla \mathbf{v} + \nabla \mathbf{v}^T : \nabla \mathbf{v}^T \right] \, d\Omega \]

\[ + \int_{\Omega} \eta (\mathbf{v} \cdot \mathbf{v}) \, d\Omega \quad \text{(A.17)} \]
Check the appendix B.1 for more detailed explanation of getting the above equation. Finally we need to solve,

$$\{v\} = \arg\min_{[v]} \mathcal{R}[\rho; v]$$ \tag{A.18}

$$\frac{\partial \rho}{\partial t} = -(v \cdot \nabla \rho + \rho \nabla \cdot v)$$ \tag{A.19}

where everything is written in terms of velocity potential. This is a mixed system of elliptic and hyperbolic PDEs. Before looking into methods of computing the derived governing equations, the parameters involved in the model with their dimensions are presented in the next section.

### A.4.4 Boundary conditions - Open patch

Let us consider a patch of monolayer with boundary denoted as $\partial \Gamma$. Here, we do not consider membranes with a physical boundary. The boundary delimits the region of study by considering it to be relatively larger. We consider that this patch is stationary in parametric space, which is Eulerian approach. Dirichlet boundary condition is defined at the boundary,

$$v = 0 \quad \text{on } \partial \Gamma$$

This boundary condition doesn’t effect or eliminate any terms in the governing equation of the system as it doesn’t have any boundary terms.

### A.5 A computational framework for the simulation

The computational framework for the simulation developed using Onsager’s variational principle is exactly same as the continuum model, however, the discretization of Rayleighian function differs as it does not require weak form and can directly used for discretization. In this section we will present the discretization of Rayleighian function using Galerking method and conclude the linear systems to be solved.

### A.6 Spatial discretization of Rayleighian function

The Rayleighian function is an elliptic equation. Therefore Galerkin method is used for the domain $\Omega$ discretization. However, the process operator, that is mass conservation equation is an hyperbolic equation after implementing the backward difference based time discretization. Hence, Galerkin approach is often characterized by a lack of sufficient stability [51]. Thus, other upwind type methods like SUPG are better adapted for the spatial discretization.

In order to discretize the computational domain $\Omega$, we consider a linear triangular elements and the approximation $v^h$ lies in $\mathcal{S}^h := \{v \in \mathcal{H}^1(\Omega) | v|_{e} \in \mathcal{P}_m(\mathcal{O}^e) \forall e \text{ and } v = v_D \text{ on } \Gamma_D\}$
with the precision given by the characteristic mesh size \( h \). The Galerkin formulation is obtained by restricting the Rayleighian function (A.17) to the finite dimensional spaces, namely, find \( v^h \in \mathcal{S}^h \) such that

\[
\mathcal{R}[\rho; v^h] = \int_{\Omega} \left[ \frac{k}{2} \left(1 - \left(\frac{\rho}{\rho_0}\right)^2\right) + \sigma \right] \nabla \cdot v^h \, d\Omega + \int_{\Omega} \frac{\mu}{4} \left[ \nabla v^h : \nabla v^h + \nabla v^h : (\nabla v^h)^T + (\nabla v^h)^T : \nabla v^h \right] \, d\Omega + \int_{\Omega} \eta (v^h \cdot v^h) \, d\Omega \tag{A.20}
\]

At this point the computational domain \( \Omega \) is discretized into the linear elements \( \Omega_e \), the approximation \( v^h(x) \) can be written as,

\[
v^h(x) = \sum_m v^m N^m(x, y) \tag{A.21}
\]

where \( N^m \) is the shape function associated with node number \( m \) and \( v^m \) is the nodal unknown. Thus after substitution of (A.21) into (A.20), we obtain the discrete equation

\[
\mathcal{R}^m[\rho; v^m, N^m] = \sum_m \int_{\Omega_e} \left[ \frac{k}{2} \left(1 - \left(\frac{\rho}{\rho_0}\right)^2\right) + \sigma \right] \nabla N^m \cdot v^m \, d\Omega + \sum_{m,n} \int_{\Omega_e} \frac{\mu}{2} \left[ ((v^m)^T (\nabla N^m \cdot \nabla N^n) I_2 v^n) + \frac{1}{2} \left( ((v^m)^T (\nabla N^m \otimes \nabla N^n) v^n) + \left( (v^m)^T (\nabla N^m \otimes \nabla N^n) v^n) \right) \right] \, d\Omega + \sum_{m,n} \int_{\Omega_e} \eta ((v^m)^T N^m N^n v^n) \, d\Omega
\]

For elaborative description of discretization look into appendix B.2.1. On assembling the element contribution to this Rayleighian function, we obtain the algebraic system governing the nodal values of the discrete solution. After inclusion of the Dirichlet boundary conditions, this system take the matrix form,

\[
\mathcal{R}[\rho; v] = f v + \frac{1}{2} v^T [D + C + B] v
\]

where,

\[
f = \sum_m \int_{\Omega_e} \left[ \frac{k}{2} \left(1 - \left(\frac{\rho}{\rho_0}\right)^2\right) + \sigma \right] \nabla N^m \, d\Omega
\]
\[
D = \sum_{m,n} \int_{\Omega} \mu (\nabla N^m \cdot \nabla N^n) I_2 d\Omega \\
C = \sum_{m,n} \int_{\Omega} \frac{\mu}{2} \left( (\nabla N^m \otimes \nabla N^n)^T + (\nabla N^m \otimes \nabla N^n) \right) d\Omega \\
B = \sum_{m,n} \int_{\Omega} 2\eta (N^m N^n) d\Omega
\]

Following Onsager’s principle performing,
\[
\{v\} = \arg\min_{\{v\}} R[\rho; v]
\]
that is minimizing \(R\) with respect to \(v\) gives the following linear system of equations,
\[
[D + C + B] v = f
\]
Here, the initial density \(\rho\) is given in the \(n\)th step as \(\rho^n\) and upon solving this system we obtain velocity field in \((n + 1)\)th step. So, this equation can be re-written as,
\[
[D + C + B] v^{(n+1)} = f
\]  
\[\text{(A.22)}\]
with
\[
f = \sum_m \int_{\Omega} \left( \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho^{(n)}}{\rho_0} \right)^2 \right) + \sigma \right] \nabla N^m \right) d\Omega
\]
\[
D = \sum_{m,n} \int_{\Omega} \mu (\nabla N^m \cdot \nabla N^n) I_2 d\Omega \\
C = \sum_{m,n} \int_{\Omega} \frac{\mu}{2} \left( (\nabla N^m \otimes \nabla N^n)^T + (\nabla N^m \otimes \nabla N^n) \right) d\Omega \\
B = \sum_{m,n} \int_{\Omega} 2\eta (N^m N^n) d\Omega
\]

### A.7 Time and spatial discretization of mass conservation

Though we are deriving the model using Onsager variational principle, the time and space discretization of conservation of mass equation is same as presented in continuum model. So we are not going to repeat it again here and witting down the final discretized equations in time (using backward Euler 3.1)

\[
\frac{\rho^{n+1} - \rho^n}{\Delta t} + \nabla \rho^{n+1} \cdot v^{n+1} + \rho^{n+1} \nabla \cdot v^{n+1} = 0.
\]  
\[\text{(A.23)}\]
and space (using SUPG 3.2.2) are,

\[ A_{mn}\rho_m^{(n+1)} = F_n \]  \hspace{1cm} (A.24)

with,

\[
A_{mn} = \int_{\Omega_e} N_n(x)N_m(x) + \Delta t(N_n \nabla N_m(x) \cdot \mathbf{v}^{n+1} + N_m \mathbf{v} \cdot \nabla N_n(x) \cdot \mathbf{v}) d\Omega + \int_{\Omega_e} \gamma \Delta t[N_m \mathbf{v}^{n+1} \cdot \nabla N_n(x) + \Delta t(\mathbf{v}^{n+1} \cdot \nabla N_n(x) \cdot \mathbf{v}^{n+1} + \mathbf{v}^{n+1} \cdot \nabla N_n(x) \mathbf{v} \cdot \mathbf{v}^{n+1})] d\Omega d\Omega
\]

\[ F_n = \int_{\Omega_e} (N_n(x) + \gamma \Delta t \mathbf{v}^{n+1} \cdot \nabla N_n(x))\rho_n d\Omega \]

### A.8 Final system of equations

Finally, we have to solve Eq. (A.22),

\[ [D + C + B] \mathbf{v}^{(n+1)} = f \]  \hspace{1cm} (A.25)

using \( \rho^{(n)} \) to obtain \( \mathbf{v}^{(n+1)} \). Then, we solve Eq. (A.24),

\[ A_{mn}\rho_m^{(n+1)} = F_n \]  \hspace{1cm} (A.26)

using the obtained \( \mathbf{v}^{(n+1)} \), to get \( \rho^{(n+1)} \) which is used in next step as an initial density \( \rho^n \). This way we are generated a sequence of density field \( \rho \) and velocity field \( \mathbf{v} \) in the time grid.
Appendix B

Detailed derivations

B.1 Rate of change of free energy

The free energy,

\[ F[\rho] = \int_{\Omega} \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 d\Omega \]

which is associated to changes in density with a quadratic potential is considered. As the fluid is considered in the Eulerian domain, the free energy depends on the material domain evolving with time. Then the free energy in terms of material domain \( \Omega_t \) with \( \Omega_0 = \Omega \) is,

\[ F[\rho, \Omega_t] = \int_{\Omega_t} \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 d\Omega \]

In order to follow the general framework described in the section A.3, we need to compute the rate of change of the above described free energy. The rate of change of free energy involves time differentiation of the integral over moving domain \( \Omega_t \) and at \( t = 0, \Omega_0 = \Omega \).

\[ \dot{F}[\rho; \partial_t \rho] = \frac{d}{dt} \int_{\Omega} \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 d\Omega \]

Applying Reynold’s transport theorem, at \( t = 0 \),

\[ \dot{F}[\rho; \partial_t \rho] = \int_{\Omega} k \left( \frac{1}{\rho_0} \right) \left( \frac{\rho}{\rho_0} - 1 \right) \frac{\partial \rho}{\partial t} d\Omega + \int_{\partial \Omega} \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 v \cdot n dl \]

From the continuity equation (A.10), we can write,

\[ \frac{\partial \rho}{\partial t} = -\nabla \cdot (\rho v) = -(v \cdot \nabla \rho + \rho \nabla \cdot v) \]
Dissipation potential $\mathcal{D}$ is written in terms of the process variable $v$. So, the rate of change of free energy can also be written in terms of $v$ by replacing $\partial_t \rho$ from above equation.

$$
\dot{F}[\rho; \partial_t \rho] = - \int_{\Omega} \frac{k}{\rho_0} \left( \frac{\rho}{\rho_0} - 1 \right) (v \cdot \nabla \rho + \rho \nabla \cdot v) d\Omega + \int_{\Omega} \nabla \cdot \left( \frac{k}{2} \left( \frac{\rho}{\rho_0} - 1 \right)^2 v \right) d\Omega
$$

$$
\dot{F}[\rho; \partial_t \rho] = - \int_{\Omega} \left( \frac{k}{\rho_0} \left( \frac{\rho}{\rho_0} - 1 \right) \right) v \cdot \nabla \rho d\Omega - \int_{\Omega} K \left( \frac{\rho}{\rho_0} - 1 \right) \nabla \cdot v d\Omega + \int_{\Omega} \left( \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) \right) \nabla \cdot v d\Omega
$$

Now, the rate of change of free energy $\dot{F}$ in terms of process variable obtained as,

$$
\dot{F}[\rho; \partial_t \rho] = \int_{\Omega} \left( \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) \right) \nabla \cdot v d\Omega
$$

### B.2 Spatial discretization

#### B.2.1 Rayleighian function

The Rayleighian Function($R$) of active Visco-elastic compressible fluid is given by,

$$
R[\rho; v] = \int_{\Omega} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) \nabla \cdot v \right] d\Omega + \int_{\Omega} \left( \mu (\nabla^s v : \nabla^s v) + \sigma (\nabla \cdot v) \right) d\Omega + \int_{\Omega} \eta ||v||^2 d\Omega
$$

The strain tensor can be written as,

$$
\nabla^s v = \frac{1}{2} (\nabla v + \nabla v^T)
$$

$$
\nabla^s v : \nabla^s v = \frac{1}{2}(\nabla v + \nabla v^T) : \frac{1}{2}(\nabla v + \nabla v^T)
$$

$$
= \frac{1}{4}(\nabla v : \nabla v) + \frac{1}{4}(\nabla v : \nabla v^T) + \frac{1}{4}(\nabla v^T : \nabla v) + \frac{1}{4}(\nabla v^T : \nabla v^T)
$$

By substituting them in the Rayleighian function we get,

$$
R[\rho; v] = \int_{\Omega} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \nabla \cdot v d\Omega
$$
\[ \int_\Omega \mu \left[ \frac{1}{4} (\nabla v : \nabla v) + \frac{1}{4} (\nabla v : \nabla v^T) + \frac{1}{4} (\nabla v^T : \nabla v) + \frac{1}{4} (\nabla v^T : \nabla v^T) \right] d\Omega + \int_\Omega \eta (v \cdot v) d\Omega \]

\[ \mathcal{R}[\rho; v] = \int_\Omega \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \nabla \cdot v d\Omega + \int_\Omega \frac{\mu}{4} \left[ \nabla v : \nabla v + \nabla v : \nabla v^T + \nabla v^T : \nabla v + \nabla v^T : \nabla v^T \right] d\Omega + \int_\Omega \eta (v \cdot v) d\Omega \]

Considering a linear triangular elements and the approximation \( v^h \),

\[ \mathcal{R}[\rho; v^h] = \int_\Omega \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \nabla \cdot v^h d\Omega + \int_\Omega \frac{\mu}{4} \left[ \nabla v^h : \nabla v^h + \nabla v^h : (\nabla v^h)^T + (\nabla v^h)^T : \nabla v^h + (\nabla v^h)^T : (\nabla v^h)^T \right] d\Omega + \int_\Omega \eta (v^h \cdot v^h) d\Omega \quad (B.1) \]

\[ \mathcal{R}[\rho; v^h] = \int_{\Omega_e} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \nabla \cdot v^h \, d\Omega + \int_{\Omega_e} \frac{\mu}{4} \left[ \sum_m v^m \cdot \nabla N^m + \sum_m v^m N^m \cdot \nabla N^m \right] \, d\Omega + \int_{\Omega_e} \eta (v^h \cdot v^h) \, d\Omega \quad (B.2) \]

\[ \mathcal{R}[\rho; v^h] = \int_{\Omega_e} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \left( \sum_m v^m \right) \cdot \nabla N^m \, d\Omega + \int_{\Omega_e} \frac{\mu}{4} \left[ \sum_m v^m N^m : \sum_n v^n N^n + \sum_m v^m N^m : \sum_n \nabla N^m v^n \right] + \int_{\Omega_e} \eta (v^h \cdot v^h) \, d\Omega \quad (B.3) \]

Considering Galerkin method and discretizing computational domain \( \Omega \) into the linear elements \( \Omega_e \), the approximation \( v^h(x) \) as,

\[ v^h(x) = \sum_m v^m N^m(x, y) \]

\[ \nabla \cdot v^h(x) = \sum_m v^m \cdot \nabla N^m \]

\[ \nabla v^h = \sum_m v^m \otimes \nabla N^m \]

\[ (v^h)^T = \sum_m (v^m)^T N^m \]

\[ (\nabla v^h)^T = \sum_m \nabla N^m v^m \]

where \( N^m(x, y) \) is the basis function associated to the node number \( m \) and \( v^m \) is the nodal unknown.

Substituting the above discretizations into the Rayleighian function \( \mathcal{R} \), it can be rewritten in a discrete form as,

\[ \mathcal{R}^m[\rho; v^m, N^m] = \int_{\Omega_e} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \left( \sum_m v^m \right) \cdot \nabla N^m \, d\Omega + \int_{\Omega_e} \frac{\mu}{4} \left[ \sum_m v^m N^m : \sum_n v^n N^n + \sum_m v^m N^m : \sum_n \nabla N^m v^n \right] + \]
\[
\left( \sum_m \nabla N^m \mathbf{v}^m : \sum_n \mathbf{v}^n \nabla N^n : \right) + \left( \sum_m \nabla N^m \mathbf{v}^m : \sum_n \nabla N^n \mathbf{v}^n \right) d\Omega + \\
\int_{\Omega_e} \eta \left( \sum_m \mathbf{v}^m N^m \right) \cdot \left( \sum_n \mathbf{v}^n N^n \right) d\Omega \\
= \sum_m \int_{\Omega_e} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \left( \nabla N_i^m \mathbf{v}^m \right) d\Omega + \sum_m \int_{\Omega_e} \frac{\mu}{4} \left( \mathbf{v}^m_i N_j^m \nabla v^m_i N_j^m \right) d\Omega + \\
\sum_{m,n} \int_{\Omega_e} \eta \left( \mathbf{v}^m_i N_j^m \nabla v^m_i N_j^m \right) d\Omega \\
= \sum_m \int_{\Omega_e} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \nabla N^m d\Omega + \\
\left( (\mathbf{v}^m)^T \left( \nabla N^m \otimes \nabla N^m \right) \mathbf{v}^n \right) + \left( (\mathbf{v}^m)^T \left( \nabla N^m \otimes \nabla N^n \right) \mathbf{v}^n \right) + \\
\left( (\mathbf{v}^m)^T I_2 \left( \nabla N^m \cdot \nabla N^n \right) \mathbf{v}^n \right) d\Omega + \sum_{m,n} \int_{\Omega_e} \eta \left( (\mathbf{v}^m)^T N^m N^n \mathbf{v}^n \right) d\Omega \\
= \sum_m \int_{\Omega_e} \left[ \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right] \nabla N^m d\Omega + \\
\sum_{m,n} \int_{\Omega_e} \frac{\mu}{2} \left[ \left( (\mathbf{v}^m)^T \left( \nabla N^m \cdot \nabla N^n \right) I_2 \mathbf{v}^n \right) + \\
\frac{1}{2} \left( (\mathbf{v}^m)^T \left( \nabla N^m \right)^T \nabla \mathbf{v}^n \right) + \left( (\mathbf{v}^m)^T \left( \nabla N^m \otimes \nabla N^n \right) \mathbf{v}^n \right) \right] d\Omega +
\]
\[
\sum_{m,n} \int_{\Omega_e} \eta ((\mathbf{v}^m)^T N^m N^n \mathbf{v}^n) \, d\Omega
\]

Therefore, \( \mathcal{R} \) can be written in matrix form as,
\[
\mathcal{R}[\rho; \mathbf{v}] = f \mathbf{v} + \frac{1}{2} \mathbf{v}^T [\mathbf{D} + \mathbf{C} + \mathbf{B}] \mathbf{v}
\]

where,
\[
f = \sum_m \int_{\Omega_e} \left( \frac{k}{2} \left( 1 - \left( \frac{\rho}{\rho_0} \right)^2 \right) + \sigma \right) \nabla N^m \, d\Omega
\]
\[
\mathbf{D} = \sum_{m,n} \int_{\Omega_e} \mu (\nabla N^m \cdot \nabla N^n) \mathbf{I}_2 \, d\Omega
\]
\[
\mathbf{C} = \sum_{m,n} \int_{\Omega_e} \frac{\mu}{2} ((\nabla N^m \otimes \nabla N^n)^T + (\nabla N^m \otimes \nabla N^n)) \, d\Omega
\]
\[
\mathbf{B} = \sum_{m,n} \int_{\Omega_e} 2\eta ((N^m N^n) \, d\Omega)
\]

### B.3 SUPG stabilization method

The time discretized continuity equation is a reaction convection problem in \( \rho^{n+1} \). The weak form can be written as,
\[
\int_{\Omega} w \rho^{n+1} + \Delta t^n (w \nabla \rho^{n+1} \cdot \mathbf{v}^{n+1} + w \rho^{n+1} \nabla \cdot \mathbf{v}^{n+1}) \, d\Omega = \int_{\Omega} w \rho^n \, d\Omega \quad \forall w
\]

To deal with convection term appropriately, the following test function is used which contains the stability term.

\[
(\rho^{(n+1)})^h = \sum_m \rho_m^{(n+1)} N_m(x)
\]
\[
w^h = N_n(x) + \gamma \Delta t \frac{\mathbf{v}^{n+1} \cdot \nabla N_n(x)}{
\text{Stabilization term}}
\]

where \( N_m(x,y) \) is the basis function associated to the node number \( I \). Then the weak form becomes,
\[
\int_{\Omega_e} N_n(x) N_m(x) + \Delta t (N_n \nabla N_m(x) \cdot \mathbf{v}^{n+1} + N_n N_m \nabla \cdot \mathbf{v}) \, d\Omega + \int_{\Omega_e} \gamma \Delta t [N_m \mathbf{v}^{n+1} \cdot \nabla N_n(x) +
\Delta t (\mathbf{v}^{n+1} \cdot \nabla N_n(x) \cdot \nabla N_n(x) \cdot \mathbf{v}^{n+1} + \mathbf{v}^{n+1} \cdot \nabla N_n(x) N_m(x) \nabla \cdot \mathbf{v}^{n+1})] \, d\Omega] \rho_m^{(n+1)} =
\]
\[ \int_{\Omega_e} (N_n(x) + \gamma \Delta t \, \mathbf{v}^{n+1} \cdot \nabla N_n(x)) \rho^n \, d\Omega \]

\[
\sum_{m,n} \int_{\Omega_e} N_n(x) \rho_m^{(n+1)} N_m(x) + \Delta t (N_n \nabla N_m(x) \cdot \mathbf{v}^{n+1} \rho_m^{(n+1)} + N_n N_m \nabla \cdot \mathbf{v}^{n+1} \rho_m^{(n+1)}) \, d\Omega + \int_{\Omega_e} \gamma \Delta t [N_m \mathbf{v}^{n+1} \cdot \nabla N_n(x) + \Delta t (\mathbf{v}^{n+1} \cdot \nabla N_n(x) \mathbf{v}^{n+1} + \mathbf{v}^{n+1} \cdot \nabla N_n(x) \mathbf{v} \cdot \mathbf{v}^{n+1})] \, d\Omega = \\
\sum_{m,n} \int_{\Omega_e} (N_n(x) + \gamma \Delta t \mathbf{v}^{n+1} \cdot \nabla N_n(x)) \rho^n \, d\Omega
\]

\[
\Delta t (\mathbf{v}^{n+1} \cdot \nabla N_n(x) \cdot \nabla N_n(x) \cdot \mathbf{v}^{n+1} + \mathbf{v}^{n+1} \cdot \nabla N_n(x) N_m(x) \mathbf{v} \cdot \mathbf{v}^{n+1})] \, d\Omega
\]

This can also be written as a linear system of equations,

\[ A_{mn} \rho_m^{(n+1)} = F_n \]

with,

\[
A_{mn} = \int_{\Omega_e} N_n(x) N_m(x) + \Delta t (N_n \nabla N_m(x) \cdot \mathbf{v}^{n+1} + N_n N_m \nabla \cdot \mathbf{v}^{n+1}) \, d\Omega + \int_{\Omega_e} \gamma \Delta t [N_m \mathbf{v}^{n+1} \cdot \nabla N_n(x) + \Delta t (\mathbf{v}^{n+1} \cdot \nabla N_n(x) \mathbf{v}^{n+1} + \mathbf{v}^{n+1} \cdot \nabla N_n(x) \mathbf{v} \cdot \mathbf{v}^{n+1})] \, d\Omega
\]

\[ F_n = \int_{\Omega_e} (N_n(x) + \gamma \Delta t \mathbf{v}^{n+1} \cdot \nabla N_n(x)) \rho^n \, d\Omega \]
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