Tissue Interaction Model for Skin Pattern Formation

Atusi Tani [*]

Department of Mathematics, Keio University

[*]3-14-1 Hiyoshi, Yokohama 223-8522, Japan

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Soft Matter Physics.

I.

Mathematical modelling of the generation and onset of spatial patterns in the early stages of embryonic development
— reaction-diffusion equations, chemotaxis equations, mechanochemical force balance equations.

S. F. Gilbert (1988): the communication between different groups of cell and tissue types plays a crucial role during morphogenesis.

Most of the models are concerned only with very specific tissues;
little attention to modelling tissue interaction.

Focus: two aspects of tissue interaction
– two different models for vertebrate skin pattern formulation:

(i) model by Cruywagen–Murray (1992) [3, 10]:
Patterns and structure observed in animals develop from a homogeneous mass of cells seen in the early embryo. This process - morphogenesis - consists of a complex interaction of chemical, mechanical, and electrical phenomena.
Uniform skin tissue can only be excited into spatial structure in the presence of tissue interaction;

(ii) model by Shaw–Murray (1990) [12]:
the interaction mechanism is not crucial for simple pattern formulation, however it can excite the skin tissue into producing far more complex patterns normally exhibited by such models.

II. Tissue interaction

Vertebrate skin is composed two layers: the **epidermis** and the **dermis**.

epidermis – a sheet of tightly packed epithelial cells exhibiting viscoelastic properties;

dermis – mesenchymal cells which can move in the extracellular matrix, an array of fibres and collagen.

These layers are separated by a thin sheet of tissue called **basal lamina**.

Pattern formation – almost simultaneously in both layers and in both dermis and epidermis due to the active communication between the layers.

Theoretical scenario of the dermal-epidermal communication based upon the experimental results due to Chuong–Edelman:
The actual factors (**chemicals**) are produced by the cells in the respective layers
and diffuse across the basal lamina, which are **mechanical signals** with active stresses
→ a major effect on cell behavior;

electrical signals.

III (i). Full tissue interaction system

The **epidermis** is modelled as a **viscoelastic sheet** by a **mechanochemical** system and by the **conservation of the epithelial cell**;

The mechanochemical system = a **force balance equation** describing the **passive viscoelastic stresses** present in the tissue and a traction term responsible for the **active tissue stresses** which depends on a chemical signal received from the dermis.

The **dermis** is modelled as a **cell chemotaxis** since cells in the dermal layer are more loosely arranged and are motile and by the **conservation of the dermal cell**;

The chemo-attractant is induced by the signal received from the epidermal layer.

Epidermal cell equations:

$N = N(x, t) =$ the epithelial (cell) density at (x, t),

$\mathbf{u} = \mathbf{u}(x, t) =$ displacement in the epithelial layer at (x, t),

$\hat{e} = \hat{e}(x, t) =$ epidermal concentration of a signal morphogen, produced in the epidermis, at (x, t),

$\hat{s} = \hat{s}(x, t) =$ epidermal concentration of a signal morphogen, received from the dermis, at (x, t).

$$\nabla \cdot \left[\frac{E}{1 + \nu} \left(\mathcal{E} - \beta_1 \nabla^2 \mathcal{E} + \nu'(\text{tr}\mathcal{E} - \beta_2 \nabla^2 \text{tr}\mathcal{E})\mathcal{I} \right) + \frac{\partial}{\partial t} \left(\mu_1 \mathcal{E} + \mu_2(\text{tr}\mathcal{E})\mathcal{I} \right) + \tau \mathcal{I} \right]$$

$$= \varrho \mathbf{u}, \quad [\text{mechanochemical force balance}] \tag{0.1}$$

$$\frac{\partial N}{\partial t} = -\nabla \cdot \left(N \frac{\partial \mathbf{u}}{\partial t} \right), \quad [\text{epithelial cell conservation}] \tag{0.2}$$

where

$E = E(\hat{s}) =$ the passive elastic modulus,

$\nu = \nu(\hat{s}) =$ Poisson's ratio, $\quad \nu' = \nu/(1 - 2\nu)$,

$(\mu_1, \mu_2) = (\mu_1, \mu_2)(\hat{s}) =$ the first (shear), second (bulk) viscosities,

$\varrho =$ the strength of the attachments of the epidermis to the surrounding tissue,

β_1, $\beta_2 =$ the strength of the effect of long-range elastic forces,

$\mathcal{E} = (\nabla \mathbf{u} + (\nabla \mathbf{u})^{\text{T}})/2 =$ strain tensor,

$\tau = \tau(\hat{s}) =$ the traction, *e.g.*, $\tau(\hat{s}) = k_1 \hat{s}^2/(1 + k_2 \hat{s}^2)$.

Epidermal morphogen equations:

$$\frac{\partial \hat{e}}{\partial t} = \hat{D}_e \nabla^2 \hat{e} + f(N, \hat{s}) - P_e(\hat{e} - e) - \hat{\gamma}\hat{e}, \tag{0.3}$$

$$\frac{\partial \hat{s}}{\partial t} = \hat{D}_s \nabla^2 \hat{s} + P_s(s - \hat{s}) - \hat{\nu}N\hat{s}, \tag{0.4}$$

where

$\hat{D}_e$ = the epidermal diffusion coefficient,

f = production of $\hat{s}$ by N,

P_e = the rate of diffusion across the basal lamina,

$\hat{\gamma}$ = a measure of degradation rate.

Dermal chemotaxis equation:

$n = n(x, t)$ = density of mesenchymal cells at (x, t),

$s = s(x, t)$ = dermal concentration of a signal morphogen, produced in the dermis, at (x, t),

$e = e(x, t)$ = dermal concentration of a signal morphogen, received from the epidermis, at (x, t).

$$\frac{\partial n}{\partial t} = \nabla \cdot (D(e)\nabla n) - \nabla \cdot (n\alpha(e)\nabla e) + rn(\bar{n} - n), \tag{0.5}$$

where

$\bar{n}$ = the normal uniform cell density,

last term in RHS represents mitosis.

Dermal morphogen equations:

$$\frac{\partial e}{\partial t} = D_e \nabla^2 e + P_e(\hat{e} - e) - \gamma ne, \tag{0.6}$$

$$\frac{\partial s}{\partial t} = D_s \nabla^2 s + g(n, e) - P_s(s - \hat{s}) - \nu s. \tag{0.7}$$

III (ii). Complex pattern formation and tissue interaction

the tissue interaction model + two well-known pattern generating mechanism.

The epithelial pattern formation model – Schnakenberg reaction-diffusion system.

Assumption: Hypothetical chemicals provide *positional information* for epithelial morphogenesis due to Wolpert.

Mechanochemical model for dermis:

   a force balance equation for forces within the extracellular matrix
   + conservation equations for dermal density & for the extracellular matrix density.

Schnakenberg reaction-diffusion system:

$$\frac{\partial V}{\partial t} = A - V + V^2 W + D_V \nabla^2 v - \delta \, \nabla \cdot \mathbf{u}, \tag{0.8}$$

$$\frac{\partial W}{\partial t} = B - V^2 W + D_W \nabla^2 W, \tag{0.9}$$

where

   V, W = the concentration of the chemicals,

   A, B = production and kinetics of the chemicals,

   last term in RHS of (0.8) = the dermal to epidermal tissue interaction,

   δ = the strength of the coupling betweens the layers.

Conservations of cell and matrix:

$$\frac{\partial n}{\partial t} + \nabla \cdot \left(n \frac{\partial \mathbf{u}}{\partial t} \right) = 0, \tag{0.10}$$

$$\frac{\partial \varrho}{\partial t} + \nabla \cdot \left(\varrho \frac{\partial \mathbf{u}}{\partial t} \right) = 0, \tag{0.11}$$

where

   n = the dermal cell density,

   ϱ = the extracellular matrix density,

   $\mathbf{u}$ = the displacement of matrix.

Matrix force balance equation:

$$\nabla \cdot \left[\frac{E}{1+\nu} \left(\mathcal{E} + \nu'(\mathrm{tr}\mathcal{E})\mathcal{I} \right) + \frac{\partial}{\partial t} \left(\mu_1 \mathcal{E} + \mu_2 (\mathrm{tr}\mathcal{E})\mathcal{I} \right) \right.$$

$$\left. + \tau(n)n \left(\varrho + \beta \nabla^2 \varrho \right) \left(1 + \gamma(V - \bar{V}) \right) \mathcal{I} \right] = s\varrho \mathbf{u}, \tag{0.12}$$

where

$\tau = \tau(n) =$ the traction per unit length per cell, *e.g.*, $\tau(n) = k_1/(1 + k_2 n^2)$,

$k_1 =$ the strength of the active traction,

$k_2 =$ the cell-cell contact inhibition in high cell populations,

$\beta =$ the strength of long-range traction,

$\bar{V} =$ the uniform steady state of the chemical V,

$\gamma =$ the strength of the dermal to epidermal interaction.

Here we assume that the cell-matrix composite is attached to some external substratum (for example the sub-dermal layer in the chick skin) by tethers that may be modelled by a linear spring. Such a body force may be given by $s\mathbf{u}$ with s being the positive spring constant which reflects the attachment of ECM to the surrounding tissue.

Note that (ii) contains the patterned solutions in the absence of tissue interaction unlike the model (i). However, adding the effect of tissue interaction dramatically changes the nature of these patterned solutions ([10]).

III (iii). Mechanical models for biological pattern formation ([13])

Morphogenetic process of skin primordia development, where mesenchymal cells and cross-linked collagen fibers (extracellular matrix) play important roles. In the development of spatial pattern, mesenchymal cells move through the fibrous component of extracellular matrix. These cells posess finger-like filopodia which enable them to grab onto adhesive sites and move within and recognize the extracellular matrix. The coordinated movement of mesenchymal cells and tissue deformation give rise to the heterogeneous distributions of cell density which forms a spatial pattern in the developing skin.

cell conservation equation:

$$\frac{\partial n}{\partial t} = \nabla \cdot \left(-D\nabla^2 n + n\dot{\mathbf{u}} + \alpha n \nabla \varrho \right) + M(n), \tag{0.13}$$

where

$\mathbf{u}$ = displacement vector of extracellular matrix (ECM) at (x, t),

n = mesenchymal cell density at (x, t),

ϱ = ECM density at (x, t),

$M(n)$ = cell mitosis, *e.g.*, $\quad M(n) = rn(\bar{n} - n)$,

α = haptotaxis coefficient,

$\bar{n}$ = homogeneous cell density,

the overdot represents the total derivative with respect to t.

matrix conservation equation:

$$\frac{\partial \varrho}{\partial t} = -\nabla \cdot (\varrho \dot{\mathbf{u}}) + S(n, \varrho, \mathbf{u}), \tag{0.14}$$

where

$S(n, \varrho, \mathbf{u})$ = the secretion/degradation of ECM from/by cells,
$\quad$ *e.g.*, $\quad S(n, \varrho, \mathbf{u}) = \gamma n \varrho(\bar{\varrho} - \varrho)$, $\quad \bar{\varrho}$ = the homogeneous ECM density.

cell-matrix mechanical interaction equation:

$$\nabla \cdot \left[\frac{E}{1+\nu} \left(\mathcal{E} + \nu'(\mathrm{tr}\mathcal{E}\,\mathrm{tr}\mathcal{E})\mathcal{I} \right) + \frac{\partial}{\partial t} \left(\mu_1 \mathcal{E} + \mu_2(\mathrm{tr}\mathcal{E})\mathcal{I} \right) + \tau n(\varrho + \beta\nabla^2\varrho)\mathcal{I} \right]$$

$$= \varrho\mathbf{f}, \tag{0.15}$$

where

$\mathbf{f}$ = body force such as a resistive force arising from the fibrous tendrils which attach to the subdermal layer, *e.g.*, $\quad \mathbf{f} = s\mathbf{u}$, s = an elastic constant.

Viscoelasticity

Hooke (1660) – Hooke's law,   **Newton** (1687) – Principia,

Young (1807) – Young's modulus,

Navier (1821, 1826) – elasticity, viscous hydrodynamics,

Cauchy (1828) – Cauchy's tensor,   **Poisson** (1829) – Poisson ratio,

Stokes (1845, 1847) –   ,   , viscous hydrodynamics,

Maxwell (1868) – stress relaxation theory,   **Saint Venant** (1870) – ideal plasticity,

Kelvin (1875) – viscoelasticity,   **Boltzmann** (1876) – viscoelasticity,

Reynolds (1885) – dilatancy,   **Voigt** (1890) – viscoelasticity = Kelvin's,

Bingham (1919) – Bingham's plasticity, rheology.

Jeffreys (1929): $\mathcal{M}$ – extra stress tensor, $\mathcal{D}(\mathbf{w})$ – rate of strain tensor

$$\lambda_1 \frac{\mathrm{D}\mathcal{M}}{\mathrm{D}t} + \mathcal{M} = 2\eta \left[\mathcal{D}(\mathbf{w}) + \lambda_2 \frac{\mathrm{D}}{\mathrm{D}t}\mathcal{D}(\mathbf{w}) \right],$$

where

$$\frac{\mathrm{D}\mathcal{M}}{\mathrm{D}t} = \frac{\mathrm{d}\mathcal{M}}{\mathrm{d}t} - \mathcal{W}\mathcal{M} + \mathcal{M}\mathcal{W} - a(\mathcal{D}\mathcal{M} + \mathcal{M}\mathcal{D}), \quad \mathcal{W} = \frac{1}{2}(\nabla\mathbf{w} - \nabla\mathbf{w}^{\mathrm{T}}), \quad a = const.$$

$\lambda_2 = 0 \Rightarrow$ Maxwell model; $\lambda_1 = 0 \Rightarrow$ Kelvin-Voigt model.

Integral form: Boltzmann model, generalization of Boltzmann model

$$\mathcal{M} = \int_0^\infty G(t - \tau)\mathcal{D}(\mathbf{w})\,\mathrm{d}\tau, \quad \mathcal{M} = 2\mu\mathcal{D}(\mathbf{w}) + \int_0^\infty G(t - \tau)\mathcal{D}(\mathbf{w})\,\mathrm{d}\tau.$$

Viscoelastic body: $\mathcal{P} = \mathcal{P}^{(\mathrm{vis})} + \mathcal{P}^{(\mathrm{el})}$,

$$\mathcal{P}^{(\mathrm{vis})} = -p\mathcal{I} + 2\mu\mathcal{D}(\mathbf{v}) + \mu'\mathrm{tr}(\mathcal{D}(\mathbf{v}))\mathcal{I}, \quad \mathcal{P}^{(\mathrm{el})} = 2\lambda\mathcal{D}(\mathbf{u}) + \lambda'\mathrm{tr}(\mathcal{D}(\mathbf{u}))\mathcal{I},$$

thermo-elastic $\Rightarrow$

$$\mathcal{P}^{(\mathrm{el})} = -\beta\theta\mathcal{I} + 2\lambda\mathcal{D}(\mathbf{u}) + \lambda'\mathrm{tr}(\mathcal{D}(\mathbf{u}))\mathcal{I}, \quad \beta = \left(\lambda' + \frac{2}{3}\lambda\right)\alpha,$$

(α = coefficient of expansion).

Mathematical analysis of 1D model system for complex skin patterns

Atusi Tani

Department of Mathematics, Keio University

1 Introduction

A central issue in developmental biology is the formation of spatial pattern and form in the early embryo. Various models and mechanisms have been proposed to describe the pattern formation process, such as those based on the reaction-diffusion theory of Turing [25] involving chemicals called morphogens.

An alternative approach to morphogenetic pattern formation is based on the mechano-chemical interaction of mesenchymal cells with the extracellular matrix (ECM) – a complex of cross-linked collagen fibres and glycosaminoglycans – on which they move. This approach to pattern formation has been applied to several widely studied phenomena in developmental biology, such as the formation of feather germ primordia in chicks and cartilage formation in chick and amphibian limbs.

However, to date, little attention has been given to modelling tissue interaction between different groups of cells and tissue types. Here, we shall consider a tissue interaction model because it has far reaching consequences for explaining morphogenetic structure formation ([22], [16]). Thus we shall couple the above two well-known pattern generating mechanisms and discuss it mathematically.

2 Mathematical Issues

2.1 The model equations for Pattern Formation

Vertebrate skin is composed of two layers, the epidermis and the dermis. The epidermis consists of a sheet of tightly packed epithelial cells which exhibits viscoelastic properties. The dermis, on the other hand, is made up of mesenchymal cells which can move in ECM - essentially an array of fibers and collagen. These layers are separated by a thin sheet of tissue called the basal lamina.

A variety of model mechanisms have been proposed for explaining pattern formation in either of these two layers. However, not only does pattern formation appear to occur almost simultaneously in both layers, biological evidence indicates that there is, in fact, active communication between the layers and that, furthermore, pattern formation can only occur in the presence of both dermis and epidermis.

We focus on a mechanochemical model of the dermis proposed by Shaw and Murray [24] (see also [14, 15, 17, 18, 19, 20, 21, 22, 27]). It consists of three equations: two conservation

equations for mesenchymal cell density $n(x, t)$ and ECM density $\rho(x, t)$ at the position x and the time t, and a force balance equation for the mechanical interaction of cells with the matrix which determines the displacement vector $\mathbf{u}(x, t)$ of a material point of ECM located at position x. Each governing equation is as follows.

The rate of change in cell density is equal to cell flux and cell mitosis:

$$\frac{\partial n}{\partial t} = -\nabla \cdot \mathbf{J} + M(n), \tag{2.1}$$

where $\mathbf{J}$ is the cell flux assumed here, for simplicity, to consist of three terms,

$$\mathbf{J} = \mathbf{J}_{diffusion} + \mathbf{J}_{haptotaxis} + \mathbf{J}_{convection}.$$

Here $\mathbf{J}_{diffusion} = -d_n \nabla n$ is due to diffusion of a random cell motion, $\mathbf{J}_{haptotaxis} = \alpha n \nabla \varrho$ is due to haptotaxis representing cells moving up a gradient of adhesive sites, and $\mathbf{J}_{convection} = n\dot{\mathbf{u}} \equiv n\mathbf{v}$ is due to convection representing cells passively carried by other moving cells or convected with the deforming ECM (the overdot represents the total derivative with respect to t). $M(n)$ represents cell mitosis. The parameters d_n and α are the diffusion coefficient and the haptotaxis coefficient, respectively. With these equation (2.1) can be written as

$$\frac{\partial n}{\partial t} = -\nabla \cdot [-d_n \nabla n + \alpha n \nabla \varrho + n\mathbf{v}] + M(n). \tag{2.2}$$

The rate of change of ECM density which is equal to the convective flux caused by forces exerted by cells:

$$\frac{\partial \varrho}{\partial t} = -\nabla \cdot (\varrho \mathbf{v}) + S(n, \varrho, \mathbf{u}), \tag{2.3}$$

where $S(n, \varrho, \mathbf{u})$ is the secretion/degradation of ECM from/by cells.

By basing on the experimental results examined the role of tissue interaction during chick feather germ morphogenesis by Chuong and Edelman [1, 2] and Gallin $et\ al.$ [10], the mechanochemical force balance equation between cells and matrix is

$$\nabla \cdot \mathcal{P} + \varrho \mathbf{f} = 0, \tag{2.4}$$

where $\mathcal{P}$ is a stress tensor and matrix is $\mathbf{f}$ is an external body force. The stress tensor $\mathcal{P}$ is composed of two components:

$$\mathcal{P} = \mathcal{P}_{matrix} + \mathcal{P}_{cell-matrix}.$$

We model the matrix as a linear, isotropic visco-elastic continuum material with stress tensor

$$\mathcal{P}_{matrix} = \mathcal{P}_{matrix}^{(vis)} + \mathcal{P}_{matrix}^{(el)},$$

$$\mathcal{P}_{matrix}^{(vis)} = -p\mathcal{I} + 2\mu\mathcal{D} + \mu'(\mathbf{tr}\mathcal{D})\mathcal{I}, \qquad \mathcal{P}_{matrix}^{(el)} = 2\lambda\mathcal{E} + \lambda'(\mathbf{tr}\mathcal{E})\mathcal{I},$$

where $\mathcal{D} = \mathcal{D}(\mathbf{v}) = \frac{1}{2}(\nabla\mathbf{v} + \nabla\mathbf{v}^{\mathrm{T}})$ is the velocity deformation tensor, $\mathcal{E} = \mathcal{E}(\mathbf{u}) = \frac{1}{2}(\nabla\mathbf{u} + \nabla\mathbf{u}^{\mathrm{T}})$ is the displacement deformation tensor, $\mathcal{I}$ is the unit tensor, μ, μ' are the viscosities and λ, λ' are Lamé coefficients satisfying $\mu > 0$, $3\mu' + 2\mu \geq 0$, $\lambda > 0$, $3\lambda' + 2\lambda \geq 0$ in three dimensional case (see, for example [13]).

Mesenchymal cells can exert large traction forces by attaching to the matrix. We model the stress due to this cell-matrix interaction by

$$\mathcal{P}_{cell-matrix} = \tau(n)\, n\, (\varrho + \beta\,\nabla^2\varrho)(1 + \gamma(V - \bar{V}))\mathcal{I},$$

where $\tau(n)\,(> 0)$ is the traction per unit length per cell. Traction term accounts for cell-cell contact inhibition in populations of hight cell density; it also depends on the local matrix density ϱ (short-range traction) and nonlocal matrix density $\beta\nabla^2\varrho$ (long-range traction), where $\beta > 0$ measures the strength of this long-range traction. The dermal to epidermal interaction is introduced through the $\gamma(V - \bar{V})$ term, where $\bar{V}$ is the uniform steady state of the chemical V and γ is a measure of the strength of the interaction.

The body force can be considered as a resistive force arising from the fibrous tendrils which attach to the subdermal layer, $\mathbf{f} = -s\mathbf{u}$ with an elastic constant s.

Hence equation (2.4) can be rewritten as

$$\nabla \cdot [-p\mathcal{I} + 2\mu\mathcal{D} + \mu'(\mathbf{tr}\mathcal{D})\mathcal{I} + 2\lambda\mathcal{E} + \lambda'(\mathbf{tr}\mathcal{E})\mathcal{I} \qquad (2.5)$$

$$+ \tau(n)\, n\, (\varrho + \beta\,\nabla^2\varrho)(1 + \gamma(V - \bar{V}))\mathcal{I}] = s\varrho\mathbf{u}.$$

The epithelial pattern formation is modelled by the Schnakenberg reaction-diffusion system ([23]). It is assumed that hypothetical chemicals provide *positional information* ([26]) for epithelial morphogenesis. If we represent the concentration of the two chemicals by V and W, the system can be written as

$$\frac{\partial V}{\partial t} = A - c_1 V + c_2 V^2 W + d_V\,\nabla^2 V - \delta\,\nabla \cdot \mathbf{u}, \qquad (2.6)$$

$$\frac{\partial W}{\partial t} = B - c_3 V^2 W + d_W\,\nabla^2 W, \qquad (2.7)$$

where d_V and d_W are the positive diffusion rates and, A and B are positive constants related to the production and kinetics of the chemicals. Note that an additional term, $-\delta\nabla \cdot \mathbf{u}$, has been added to the first equation to account for the dermal to epidermal tissue interaction. The variable $\nabla \cdot \mathbf{u}$ denotes the dermal cell dilation and δ reflects the strength of the coupling between the layers.

In this paper we consider only the *one-dimensional* situation:

$$
\begin{cases}
\dfrac{\partial n}{\partial t} = d_n \dfrac{\partial^2 n}{\partial x^2} - \dfrac{\partial}{\partial x}\left(\alpha n \dfrac{\partial \varrho}{\partial x}\right) - \dfrac{\partial}{\partial x}(nv) + M(n), \\[2ex]
\dfrac{\partial \varrho}{\partial t} + v\dfrac{\partial \varrho}{\partial x} = -\varrho\dfrac{\partial v}{\partial x} + S(n, \varrho, u), \\[2ex]
\dfrac{\partial}{\partial x}\left[-p(\varrho) + (2\mu + \mu')\dfrac{\partial v}{\partial x} + (2\lambda + \lambda')\dfrac{\partial u}{\partial x} \right. \\[2ex]
\qquad\qquad \left. +\tau(n)n\left(\varrho + \beta\dfrac{\partial^2 \varrho}{\partial x^2}\right)(1 + \gamma(V - \bar{V}))\right] = s\varrho u, \\[2ex]
\dot{V} = A - c_1 V + c_2 V^2 W + d_V \dfrac{\partial^2 V}{\partial x^2} - \delta\dfrac{\partial u}{\partial x}, \\[2ex]
\dot{W} = B - c_3 V^2 W + d_W \dfrac{\partial^2 W}{\partial x^2}, \\[2ex]
v = \dot{u}.
\end{cases}
\tag{2.8}
$$

These equations are studied in the domain $x \in (0, 1)$, $t > 0$.

2.2 Initial Conditions and Boundary Conditions

For the system mentioned above, we need to assign appropriate initial and boundary conditions. In this paper, the initial conditions are given by

$$
(n, \varrho, u, V, W)|_{t=0} = (n_0, \varrho_0, u_0, V_0, W_0)(x), \quad x \in (0, 1).
\tag{2.9}
$$

The boundary conditions for v are supposed to be

$$
\left(v, \dfrac{\partial^2 v}{\partial x^2}\right)\Bigg|_{x=0,1} = (0, 0),
\tag{2.10}
$$

and also for n, V, W

$$
\left(\dfrac{\partial n}{\partial x}, \dfrac{\partial V}{\partial x}, \dfrac{\partial W}{\partial x}\right)\Bigg|_{x=0,1} = (0, 0, 0).
\tag{2.11}
$$

2.3 Setting up the problem

Let us introduce the Lagrangian coordinate. For arbitrary fixed point $(x, t) \in (0, 1) \times (0, \infty)$, we consider the solution curve $X(\tau; x, t)$ of the Cauchy problem

$$
\begin{cases}
\dfrac{\mathrm{d}X(\tau; x, t)}{\mathrm{d}\tau} = v(X(\tau; x, t), \tau), \quad \text{for } 0 < \tau, \\[2ex]
X(t; x, t) = x.
\end{cases}
$$

The unique existence of such a solution curve is guaranteed from the fundamental existence theorem of ordinary differential equation as long as v is suitably smooth. Let $X(0; x, t) = \xi$. Then this is uniquely solvable in x:

$$
x = \xi + \int_0^t v(X(\tau; \xi, 0), \tau)\,\mathrm{d}\tau \equiv \xi + \int_0^t \widehat{v}(\xi, \tau)\,\mathrm{d}\tau \equiv X_{\widehat{v}}(\xi, t).
\tag{2.12}
$$

It is well known that this mapping $(x, t) \longmapsto (\xi, t)$ is one-to-one from $(0, 1) \times (0, \infty)$ onto $(0, 1) \times (0, \infty)$.

Since it follows from (2.12) that

$$\frac{\partial}{\partial x} = \frac{1}{1 + \displaystyle\int_0^t \widehat{v}_\xi(\xi, \tau)\, \mathrm{d}\tau} \frac{\partial}{\partial \xi} \equiv \mathrm{D}_{\widehat{v}}$$

$((\cdot)_\xi$ and $(\cdot)_t$ represent the partial derivatives with respect to ξ and t, respectively), by denoting $w(x, t) = w(X_{\widehat{v}}(\xi, t), t) = \widehat{w}(\xi, t)$, (2.8) becomes

$$\begin{cases}
\widehat{n}_t = d_n \mathrm{D}_{\widehat{v}}^2 \widehat{n} - \mathrm{D}_{\widehat{v}}\left(\alpha\, \widehat{n}\, \mathrm{D}_{\widehat{v}}\, \widehat{\varrho}\right) - \widehat{n}\, \mathrm{D}_{\widehat{v}}\, \widehat{v} + M(\widehat{n}), \\[2mm]
\widehat{\varrho}_t = -\widehat{\varrho}\, \mathrm{D}_{\widehat{v}}\, \widehat{v} + S(\widehat{n}, \widehat{\varrho}, \widehat{u}), \\[2mm]
\mathrm{D}_{\widehat{v}}\left[-p(\widehat{\varrho}) + (2\mu + \mu')\, \mathrm{D}_{\widehat{v}}\, \widehat{v} + (2\lambda + \lambda')\, \mathrm{D}_{\widehat{v}}\, \widehat{u} \right. \\[2mm]
\qquad \left. + \tau(\widehat{n})\widehat{n}\, (\widehat{\varrho} + \beta \mathrm{D}_{\widehat{v}}^2\, \widehat{\varrho}) \left(1 + \gamma\left(\widehat{V} - \bar{V}^{(\widehat{v})}\right)\right)\right] = s\, \widehat{\varrho}\, \widehat{u}, \\[2mm]
\widehat{V}_t = A^{(\widehat{v})} - c_1 \widehat{V} + c_2 \widehat{V}^2 \widehat{W} + d_V \mathrm{D}_{\widehat{v}}^2 \widehat{V} - \delta \mathrm{D}_{\widehat{v}}\, \widehat{u}, \\[2mm]
\widehat{W}_t = B^{(\widehat{v})} - c_3 \widehat{V}^2 \widehat{W} + d_W \mathrm{D}_{\widehat{v}}^2 \widehat{W}, \\[2mm]
\widehat{v} = \widehat{u}_t,
\end{cases} \qquad (2.13)$$

where

$$\left(\bar{V}^{(\widehat{v})}, A^{(\widehat{v})}, B^{(\widehat{v})}\right)(\xi, t) = \left(\bar{V}, A, B\right)(X_{\widehat{v}}(\xi, t), t).$$

The initial and boundary conditions become

$$\left(\widehat{n},\ \widehat{\varrho},\ \widehat{u},\ \widehat{V},\ \widehat{W}\right)\Big|_{t=0} = (n_0,\ \varrho_0,\ u_0,\ V_0,\ W_0)(\xi), \qquad (2.14)$$

$$\left(\widehat{v},\ \widehat{v}_{\xi\xi} - \frac{\widehat{v}_\xi}{1 + \displaystyle\int_0^t \widehat{v}_\xi\, \mathrm{d}\tau} \int_0^t \widehat{v}_{\xi\xi}\, \mathrm{d}\tau,\ \widehat{n}_\xi,\ \widehat{V}_\xi,\ \widehat{W}_\xi\right)\Bigg|_{\xi=0,1} = (0, 0, 0, 0, 0). \qquad (2.15)$$

Equations $(2.13)_2$ and $(2.13)_6$ are easily solved as

$$\widehat{\varrho}(\xi, t) = \frac{\varrho_0(\xi)}{1 + \displaystyle\int_0^t \widehat{v}_\xi(\xi, \tau)\, \mathrm{d}\tau}\, \exp\left(\int_0^t \widetilde{S}(\widehat{n}, \widehat{\varrho}, \widehat{u})(\xi, \tau)\, \mathrm{d}\tau\right), \quad \widetilde{S} \equiv \frac{S(\widehat{n}, \widehat{\varrho}, \widehat{u})}{\widehat{\varrho}}, \qquad (2.16)$$

and

$$\widehat{u}(\xi, t) = u_0(\xi) + \int_0^t \widehat{v}(\xi, \tau)\, \mathrm{d}\tau, \qquad (2.17)$$

respectively.

Further, using (2.16), we can rewrite problem (2.13)-(2.15) as

$$
\begin{cases}
\widehat{n}_t - d_n\,\widehat{n}_{\xi\xi} = d_n\left(\mathrm{D}_{\widehat{v}}^2 - \partial_\xi^2\right)\widehat{n} - \mathrm{D}_{\widehat{v}}\left(\alpha\,\widehat{n}\,\mathrm{D}_{\widehat{v}}\,\widehat{\varrho}\right) - \widehat{n}\,\mathrm{D}_{\widehat{v}}\,\widehat{v} + M(\widehat{n}), \\[2mm]
(2\mu + \mu')\,\phi_t - \beta\,n_0\,\tau(n_0)\,\phi_{\xi\xi} = -(2\mu + \mu')\left(\mathrm{D}_{\widehat{v}}^2 - \partial_\xi^2\right)\widehat{v} \\[2mm]
\qquad - \beta\left[\mathrm{D}_{\widehat{v}}\left(\widehat{n}\,\tau(\widehat{n})\,\mathrm{D}_{\widehat{v}}^2\,\widehat{\varrho}\left(1 + \gamma\left(\widehat{V} - \bar{V}^{(\widehat{v})}\right)\right)\right) - n_0\,\tau(n_0)\int_0^t \partial_\xi^4 \widehat{v}\,\mathrm{d}\tau\right] \\[2mm]
\qquad - \mathrm{D}_{\widehat{v}}\left[-p(\widehat{\varrho}) + (2\lambda + \lambda')\,\mathrm{D}_{\widehat{v}}\,\widehat{u} + \widehat{n}\,\tau(\widehat{n})\,\widehat{\varrho}\left(1 + \gamma\left(\widehat{V} - \bar{V}^{(\widehat{v})}\right)\right)\right] + s\,\widehat{\varrho}\,\widehat{u}, \\[2mm]
\widehat{V}_t - d_V\,\widehat{V}_{\xi\xi} = A^{(\widehat{v})} - c_1\widehat{V} + c_2\widehat{V}^2\widehat{W} + d_V\left(\mathrm{D}_{\widehat{v}}^2 - \partial_\xi^2\right)\widehat{V} - \delta\mathrm{D}_{\widehat{v}}\,\widehat{u}, \\[2mm]
\widehat{W}_t - d_W\,\widehat{W}_{\xi\xi} = B^{(\widehat{v})} - c_3\widehat{V}^2\widehat{W} + d_W\left(\mathrm{D}_{\widehat{v}}^2 - \partial_\xi^2\right)\widehat{W}
\end{cases}
\tag{2.18}
$$

with

$$
\int_0^t \widehat{v}_{\xi\xi}(\xi,\tau)\,\mathrm{d}\tau = \phi(\xi,t),
\tag{2.19}
$$

$$
\left(\widehat{n},\ \phi,\ \widehat{V},\ \widehat{W}\right)\Big|_{t=0} = (n_0,\ 0,\ V_0,\ W_0)(\xi),
\tag{2.20}
$$

$$
\left(\widehat{n}_\xi,\ \widehat{V}_\xi,\ \widehat{W}_\xi\right)\Big|_{\xi=0,1} = (0,0,0), \quad \phi\,|_{\xi=0,1} = \frac{\widehat{v}_\xi}{1 + \displaystyle\int_0^t \widehat{v}_\xi\,\mathrm{d}\tau}\int_0^t \phi\,\mathrm{d}\tau\,\Bigg|_{\xi=0,1}.
\tag{2.21}
$$

It is easily seen that equation (2.19) and boundary condition (2.15) imply

$$
\widehat{v}(\xi,t) = -\xi\int_0^1 \mathrm{d}\xi'\int_0^{\xi'}\phi_t(\xi'',t)\,\mathrm{d}\xi'' + \int_0^\xi \mathrm{d}\xi'\int_0^{\xi'}\phi_t(\xi'',t)\,\mathrm{d}\xi''.
\tag{2.22}
$$

The aim of this paper is to prove an unique existence theorem of local in time solution to the nonlinear problem (2.13)-(2.15), that is, (2.16)-(2.22) in Sobolev-Slobodetskiĭ spaces.

Here we only state the main theorem, which is the improved version of the result in [11].

3   Main Results

Before describing the main theorem in this paper we introduce the Sobolev-Slobodetskiĭ spaces.

Let Ω be a finite open interval in $\mathbb{R}$ and l be a non-negative number. By $W_2^l(\Omega)$ we denote the space of functions $u(x)$ equipped with the standard norm:

$$
\|u\|_{W_2^l(\Omega)}^2 = \sum_{k<l}\left\|\mathrm{D}_x^k u\right\|_{L_2(\Omega)}^2 + \|u\|_{\dot{W}_2^l(\Omega)}^2,
$$

where

$$\|u\|^2_{\dot{W}^l_2(\Omega)} = \begin{cases} \left\|\mathrm{D}^l_x u\right\|^2_{L_2(\Omega)} & \text{if } l \text{ is an integer,} \\[2mm] \displaystyle\int_\Omega \int_\Omega \frac{|\mathrm{D}^{[l]}_x u(x) - \mathrm{D}^{[l]}_y u(y)|^2}{|x-y|^{1+2(l-[l])}}\, \mathrm{d}x \mathrm{d}y & \text{if } l \text{ is not an integer.} \end{cases}$$

Here $[l]$ is an integral part of l, $\mathrm{D}^k_x = \mathrm{d}^k/\mathrm{d}x^k$ and $\|\cdot\|_{L_2(\Omega)}$ is the standard norm in $L_2(\Omega)$.

The anisotropic space $W^{l,l/2}_2(Q_T)$ in the cylindrical domain $Q_T = \Omega \times (0,T)$ is defined by $L_2(0,T; W^l_2(\Omega)) \cap L_2(\Omega; W^{l/2}_2(0,T))$, whose norm is introduced by the formula

$$\|u\|^2_{W^{l,l/2}_2(Q_T)} = \int_0^T \|u\|^2_{W^l_2(\Omega)}\, \mathrm{d}t + \int_\Omega \|u\|^2_{W^{l/2}_2(0,T)}\, \mathrm{d}x \equiv \|u\|^2_{W^{l,0}_2(Q_T)} + \|u\|^2_{W^{0,l/2}_2(Q_T)},$$

where $W^{l,0}_2(Q_T) = L_2(0,T; W^l_2(\Omega))$ and $W^{0,l/2}_2(Q_T) = L_2(\Omega; W^{l/2}_2(0,T))$.

We enumerate the assumptions:

Assumptions

1. d_n, d_V, d_W and β are positive constants;

2. α, γ, s, δ, c_1, c_2 and c_3 are constants;

3. μ, μ', λ and λ' are constants satisfying $2\mu + 2\mu' > 0$ and $2\lambda + \lambda' > 0$;

4. A, $B \in L_2((0,1) \times (0,T)) \cap L_\infty(0,T; L_2(0,1))$,
   $\bar{V} \in L_2((0,T); W^1_2(0,1)) \cap L_\infty(0,T; W^1_2(0,1))$, $\bar{V}_{xx} \in L_\infty((0,1) \times (0,T))$;

5. $(n_0, \varrho_0, u_0, V_0, W_0) \in W^2_2(0,1) \times W^2_2(0,1) \times W^3_2(0,1) \times W^1_2(0,1) \times W^1_2(0,1)$,
   $0 < \underline{n}_0 \le n_0 \le \overline{n}_0$, $0 < \underline{\varrho}_0 \le \varrho_0 \le \overline{\varrho}_0$;

6. $\widetilde{S} \in C^3(\mathbb{R}_+ \times \mathbb{R}_+ \times \mathbb{R})$, p, M, $\tau \in C^1(\mathbb{R}_+)$, $\tau(n) > 0$ for any $n \in \mathbb{R}_+$.

Now the following is our main theorem.

Theorem 3.1 *Under the above assumptions there exists $T^* \in (0,T)$ such that the problem (2.16)-(2.22) has a unique solution $(\widehat{n}, \phi, \widehat{V}, \widehat{W}) \in W^{3,3/2}_2((0,1) \times (0,T^*)) \times W^{2,1}_2((0,1) \times (0,T^*)) \times W^{2,1}_2((0,1) \times (0,T^*)) \times W^{2,1}_2((0,1) \times (0,T^*))$ and $\widehat{v} \in W^{2,0}_2((0,1) \times (0,T^*))$.*

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