

Review Article

Stability Analysis, Dispersion Relation and Pattern Formation of Damaged Cells on Biological Tissues in the Body of Living Organisms

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Abstract

This study is geared towards investigating stability analysis, dispersion relation and pattern formation potential of damage in the body of living organisms using 3-coupled nonlinear system of partial differential equations (PDEs). Obviously, this study proved that there are possibilities of asymptomatic stage of the damage with the first equilibrium point and the second is symptomatic stage of damaged cells at equilibrium which is usually and physically experienced in diabetic patients. The second equilibrium point predicts initiation of damaged cells, progression or inhibitions for healing. The stability analysis revealed steady state solutions with the exudation surface activated by the stress, temperature and viscous terms causing increased growth rate of damaged cells in the body of the organism. The solutions of dispersion relations is an archetype of spatial heterogeneous and homogeneous solutions of the linear biological systems with unbalanced and exponential growth term linearly (linear growth rate of damaged cells and its wave vector k) with respect to time. The study identified that the quadratic nature of $\Psi(k^2)$ would lead the system to bounded finite amplitude. The study explored into complex dispersion relations and ascertained some special cases where one or more parameters affected damaged cells mechanically at equilibrium with bifurcation surface between spatial homogeneity and heterogeneity. Here, the bifurcation parameter τ increases monotonically beyond the critical value and renders $B(k^2)$ zero and the uniform steady state bifurcates to a spatial unstable state. This study showed pattern formation potentials are quadratic and bounded domain of the injured cells, spatial pattern of random and viscous initial damaged cell densities and patterning process of no uniform damaged cell density due cell traction is bigger than the critical value of cell traction which is the resistance of the extracellular matrix and spatial non-homogeneities activates which grows out of bounded region for some k . The study used partial Differential equation and determinant methods to proffer the solutions. Among others, this study recommends that the affected individuals should explore the use of antioxidants as to combat with the out growing inbuilt stress called oxidative stress which is activator of damaged cells densities in the body of the organisms.

Keywords

Biological Tissues, Body, Damage, Dispersion Relation, Living Organisms, Pattern Formation, Stability Analysis

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1. Introduction

Stability analysis, dispersion relations and pattern formation potential in living tissues, particularly in the perspective of damage and wound healing are analyzed using mathematical frameworks like reaction-diffusion-advection systems and mechanical continuum models. These techniques explain how homogeneous tissues (or uniform wound sites) can break symmetry to form structured, non-uniform patterns like scars, lesions or specific wound healing morphologies. Stability analysis body tissue damage determines whether a system returns to its original equilibrium (stable) or forms a new structure (unstable) after perturbation. Linear stability analysis is adopted where small perturbations are introduced to the equilibrium solutions like normal tissue state and the eigenvalues of the Jacobian matrix are analyzed. If the equilibrium is stable under a reaction-only model (ordinary differential equation system), spatial diffusion and chemotaxis may not necessarily destabilize it [14, 15].

However, in body tissue damage situations, coupling reaction terms (chemical signaling) with diffusion (cell movement) and non-linear damage variables often causes a diffusion-driven unsteadiness. In cases of chronic wound healing, if the basic reproduction number (R_0) of a disease or damage process is greater than 1, then the system will move to a non-trivial (endemic equilibrium) it indicates a sustained, damaged pattern rather than healing [17]. The dispersion relation connects the growth rate of perturbations (Ψ) to their spatial frequency (wave number, k). It defines the conditions under which patterns emerge. Patterns arise when the dispersion relation $\Psi(k)$ is positive for a range of $k > 0$, meaning perturbations with certain wavelengths grow for Turing stability. In dermal damage models, the spatial arrangement of myofibroblasts and collagen leads to specific damage patterns, such as the dendritic (branching) patterns in dendritic keratitis that is driven by cytokine-induced instabilities for specific tissue patterns. The mechanical models of extracellular matrix (ECM) suggests that fluid-like (viscoelastic) models, such as the Maxwell or Jeffrey models, exhibit a higher pattern formation potential compared to strictly solid-like models [9, 11].

The potential for pattern formation in damaged tissues is driven by the interaction of mechanical forces, chemical signals and cellular behaviors. Chronic damage leads to uncontrolled extracellular matrix (ECM) deposition forming scars (fibrosis) [4]. The "bin or basket weave" pattern of normal tissue breaks down, replaced by aligned collagen fibers that form non-functional structured tissue. The interaction between damaged cells and macrophages can create localized inflammatory spots or waves, analyzed through reaction-diffusion systems. In damage models, the stress-strain state coupled with damage parameters ($d \in [0, 1]$) influences cellular response [5, 6]. High mechanical stress can either facilitate repair or if beyond thresholds, lead to further tissue damage (necrosis) or apoptosis. Generally, damage occurs to both living and non-living organisms. But this study focuses on tissues in

living organisms.

Various researchers added knowledge to this same direction of study were [3, 9] who carried out their study on mechanical models of pattern and form in biological tissues and the role of stress-strain constitutive equations with findings; that linear stability analysis showed conditions for appearance of pattern and mechanical feedback can influence morphogenesis. The methods used were finite element and ALE methods. Another study on mechanochemical pattern formation in simple models of active viscoelastic fluids and solids was done by the following researchers in the reference number [2, 16, 26] and they came up with the resolution that damaged cells formed voids at on set, later become densely packed as a result of the viscous properties of the cells when evaluated analytically. However, the study of [11, 17, 20, 24] on confinement-induced transition between wavelike collective cell migration modes revealed that the wave vectors was in quadratic form when simulated. In the same vein, the scientists [15, 19, 22, 23] did a study on structure and function of living organisms using the Turing model for biological pattern formation. The results supported that fluid-like constitutive models like Maxwell and Jeffrey models have a pattern formation potential higher than solid-like models of the Kelvin-Voigt model. Therefore, to have more knowledge of this title, the readers would explore these studies [1, 5-8, 12, 13, 18, 21, 25].

2. Materials and Methods

2.1. Assumption

The study considered the general characteristic behaviours of soft tissues in biological systems which Wertheim, (1847) presented force-elongation data for various tissues including arteries and veins that soft tissues do not obey Hooke's law (i.e. a linear relation between Cauchy stress and a linearized measure of strain). Roy, (1880) detected that arteries exhibit an anisotropic response in an 'elastic after-action' or creep which signifies a viscoelastic character and a thermo elastic behaviour similar to rubber. He added that the material properties of arteries differ with radial location within the wall-a local heterogeneity and along the vascular tree-a regional heterogeneity, that they change with exercise, age, disease and time post-mortem, and even that they differ with gender. This implies that most soft tissues exhibit a nonlinear, inelastic, heterogeneous, anisotropic character that varies from point to point, from time to time and from individual to individual.

From the above structures of soft tissues, the study is looking at stability analysis of damage in the body of living organisms in the area of viscoelastic and thermo elastic constitutive relationship. However, the parameters to be considered are: stress damage relation, strain –damage coupled with constitutive equation and law of elasticity coupled with damage, viscoelastic tensor equation, mechanotaxis equation with mitosis

M and conservation equation for the matrix material. From all indications, the model equation will show three equations such as the Force Balance Equation, Cell Conservation Equation and Matrix Conservation Equation respectively.

2.2. Formulation of the Model

Based on the above expositions and assumptions about soft biological tissues, we considered Cell – Matrix Mechanical

$$\nabla \cdot \sigma + CF = 0 \text{ (this is called equilibrium force equation)} \quad (1)$$

Where F = the body forces acting on the matrix and σ is the stress tensor. All the equations in this study has its functional space as position x and time t i.e (x, t) . Now the model of stress tensor consists of the ECM and the cell parts; that is

$$\sigma = \sigma_{ECM} + \sigma_{Cell} \quad (2)$$

where σ = stress tensor, σ_{ECM} ExtraCellular Matrix part of

Interaction Equation which is the mechanical interaction between the cells, matrix and their mechanical damage or deformations. Thus, this model will comprise of material of the cells plus matrix plus cell traction minus body forces as a linear isotropic viscoelastic continuum as functions of the stress tensor $\sigma = \sigma(x, t)$. Believing that the traction forces generated by the cells are in mechanical equilibrium with the elastic restoring forces developed in the matrix and the body forces; then the mechanical cell – matrix equation becomes:

the stress and σ_{Cell} Cell part of the stress.

For soft tissues, a linear viscoelastic material gives the stress–strain constitutive relation below (Landau and Lifshitz 1970);

$$\sigma_{ECM} = (\text{viscous part}) + (\text{elastic part}) \text{ i.e.} \quad (3)$$

$$\sigma_{ECM} = (\mu_1 \varepsilon_t + \mu_2 \theta_t) + E'(\varepsilon + v' \theta I) \text{ (Viscous part)} \quad (4)$$

$$\sigma = -\mu_1 k(x_i - kt) - 3k\mu_2 I(x_i - kt) + \frac{E}{1+v}(x_i - kt) + \frac{E}{1+v} \left(\frac{3vI(x_i - kt)}{1-2v} \right)$$

Where $E' = \frac{E}{1+v}$, $v' = \frac{v}{1-2v}$ Hence (5) is the Extra-Cellular Matrix part of the stress.

Thus, the subscript t denotes partial differentiation with respect to time, I is the unit tensor, μ_1 and μ_2 are the shear and bulk viscosities of the ECM respectively, ε is the strain tensor i.e $\varepsilon = \frac{1}{2}(\nabla u + \nabla u^T)$; where u is the displacement, θ is

the dilation and E and v are the Young's modulus and Poisson ratio respectively. Modeling in place of the elastic contribution in equation (3) since fibrous materials are also characterized by nonlocal elastic interaction and fibres can also transmit stress between points in the ECM we have the anisotropic effect and nonlocal effect which can be modeled by writing in place of the elastic contribution in equation [17].

$$\sigma_{ECM} = E' \dot{\theta}(\varepsilon + \beta_1 \nabla^2 \varepsilon + v'(\theta + \beta_2 \nabla^2 \theta)I) \text{ Elastic part} \quad (5)$$

Where $E' = \frac{E}{1+v}$, $v' = \frac{v}{1-2v}$ and β_1 and β_2 are parameters for long range effects.

If $\beta_1 = \beta_2 = 0$.

Exhibiting the contributions of cell tractions to the stress tensor σ_{Cell} . This study shows that more cells the greater the traction force; that is to say that cell-cell contact activation while the traction force increases for large damage cell densities. Assuming that the cell traction forces, $\tau(n)$ per unit mass of matrix, initially increases with m and increases with m for very large m ; gives:

$$n\tau = \frac{n\tau}{1+\lambda n^2} \quad (6)$$

where τ is the traction force generated by the cell, n is the number of cells in the matrix and λ is the measure of force activation resulting from the neighbouring cells. For the cell traction stress (σ_{Cell}) we have:

$$\sigma_{Cell} = n\tau C(N - n)I \quad (7)$$

where τ is the cell traction, I is the unit tensor, C is the cell density, $n = n(x, t)$ is the number of damage cells transported or pack in an injured area and N (injured steady state) controls the activation of cell traction as the cell density increases. For this study, considering the contribution of σ_{cell} to stress tensor [12] yields;

$$\sigma_{Cell} = \frac{n\tau}{1+\lambda n^2} (C + \gamma \nabla^2 C)I \quad (8)$$

where $\gamma > 0$ is the measure of the nonlocal long range cell – ECM interactions. Considering that the cancer cells are densely packed equation (9) becomes

$$\sigma_{Cell} = \frac{\tau C}{1+\lambda n^2} (n + \gamma \nabla^2 n)I \quad (9)$$

$\sigma = \frac{\tau C}{1+\lambda(x_i - kt)^2} (I(x_i - kt) + 3\gamma I(x_i - kt)^2)$ is the Stress in the cell

Considering the body force F in equation (1) which is the activating forces as the body forces are proportional to the

density of the ECM and the displacement of the matrix by the numerous injured cells from its strained position to unstrained position gives;

$$F = -su \quad (10)$$

$$\nabla \cdot \{\mu_1 \varepsilon_t + \mu_2 \theta_t I + E'(\varepsilon + v'\theta) + n\tau(1 + \lambda n^2)^{-1}(m + \gamma \nabla^2 C)I\} - Csu = 0 \quad (11)$$

Model equation (11) shows that there are two other equations that could help in proffering solutions since it has to do with soft tissue and damaged cells in it. Such equations are the cell conservation equation and the matrix conservation equation will be of immense help to this study. Thus, the general form of cell conservation equation is given by

$$\frac{\partial C}{\partial t} = -\nabla J + M \quad (12)$$

where C is the cell density, J is the flux (instability of the soft tissue damaged cells) of cells, i.e. the number crossing a unit area in a unit time and M is the mitotic or cell proliferation rate. For the damaged cell growth (Mitosis, M) we have

$$M = nr(N + n) \quad (13)$$

where r is the proliferation rate, $n = n(x, t)$ is the number of damaged cells in the tissue cell of the organism and N (injured cells) is the maximum cell density. For the convective flux contribution J_c with $u(x, t)$ as the displacement vector of the ECM is given by

$$J_c = n \frac{\partial u}{\partial t} \quad (14)$$

Where $\frac{\partial u}{\partial t}$ is the velocity of deformation of the matrix and, n is the number of damaged cells transported with gross movement of the tissue. We considered that cells disperse in a steady state in an inhomogeneous isotropic medium. Thus, classical diffusion contributes a flux term ($D_1 \nabla n$) which models the random (travelling wave motion) motion in which the cells respond to local variations in the cell density and tend

$$\frac{\partial C}{\partial t} = \nabla \cdot \left(n \frac{\partial u}{\partial t} \right) + \nabla \cdot (D_1 \nabla n + D_2 \nabla(\nabla^2 n)) + \nabla n(a_1 \nabla C + a_2 \nabla^3 C) + nr(N - n) \quad (17)$$

Where D_1, D_2, a_1, a_2, r and N are positive parameters, and $C(x, t)$ is the cell density.

Finally for the third equation is the conservation equation for the matrix material $m(x, t)$ which is the matrix density is given by

$$\frac{\partial m}{\partial t} + \nabla \cdot (mu_t) = S(C, m, u) \quad (18)$$

Where $s > 0$ is an elastic parameter characterising the damaged cells or substrate attachments in the body of the organisms giving the model for the force balance equation in (1) as

to move down the density gradient. This brings in the usual diffusion term as ($D_2 \nabla^2 n$) to the conservation equation which represents local or short range motion. Hence, the flux of the cells is given by

$$J_D = D_1 \nabla n + D_2 \nabla(\nabla^2 \cdot n) \quad (15)$$

Where $D_1 > 0$ is the usual Fickian or short range diffusion coefficient and $D_2 > 0$ is the long range diffusion coefficient and $n = n(x, t)$ is the number of damaged cells. The long range diffusion gives rise to a biharmonic term in equation (15) above.

However, this soft tissue also exhibits a haptotaxis or mechanotaxis movement which is the traction exerted by the cells on the matrix generating gradients in the matrix density $m(x, t)$. Considering the density of the matrix with that of adhesive sites for the cell lamellapodia to get hold of the cells free to move in an adhesive gradient tend to move up since the cells can get a stronger grip on the denser matrix. This results to a net flux of cells up the gradient which is assumed to be proportional to $(n \nabla C)$ [7, 10, 13]. Because of the physical properties of the matrix and nonlocal sensing properties of the cells we bring in a long range effect as in equation (15) above, then the mechanotaxis flux becomes

$$J_h = n(a_1 \nabla C + a_2 \nabla^3 C) \quad (16)$$

Where $a_1 > 0$ and $a_2 > 0$ are the long range effect coefficients.

Based on the above elucidations and substitution the cell conservation equation is;

$$\frac{\partial m}{\partial t} + \nabla \cdot (mu_t) = 1 - v\theta \quad (19)$$

Where matrix flux is taken to be through convection and $S(C, m, u) = 1 - v\theta$ is taken to be the rate of secretion or spread in matrix by the damaged cells. Upon expansion with the product rules for vector calculus the model equations becomes:

$$\mu_1 \frac{\partial^2 \varepsilon}{\partial x_i \partial t} + \mu_2 I \frac{\partial^2 \theta}{\partial x_i \partial t} + \frac{\partial \varepsilon}{\partial x_i} + v' I \frac{\partial \theta}{\partial x_i} + \frac{\left(\frac{\partial C}{\partial x_i}\right) I \tau \left(\frac{\partial n}{\partial x_i}\right)}{(1+\lambda n^2)} + \frac{\tau \left(\frac{\partial n}{\partial x_i}\right) I \gamma \left(\frac{\partial C}{\partial x_i}\right)}{(1+\lambda n^2)} = s C u \quad (20)$$

$$\frac{\partial C}{\partial t} = D_1 \left(\frac{\partial^2 n}{\partial x^2} \right) - D_2 \left(\frac{\partial^4}{\partial x^4} \right) - 1_2 \left(\frac{\partial n}{\partial x} + \frac{\partial C^2}{\partial x^2} \right) + a_2 \left(\frac{\partial n}{\partial x} + \frac{\partial^4 C}{\partial x^2} \right) - \nabla \cdot (n u_t) + n r (N - n)$$

$$\frac{\partial m}{\partial t} + u_t (\nabla \cdot m) + m \cdot \nabla u_t = 1 - v \theta$$

The three system of equations for the study model comprises the cell conservation equation which is cell density $C(x, t)$; the displacement, $u(x, t)$ and the equation for the matrix material $m(x, t)$ which is the matrix density.

3. Model Analysis

3.1. Equilibrium Analysis

The uniform steady state solutions of (20) are $C = u = m = 0$ and $C = m = 1, u = 1$ and the equilibrium analysis is evaluated by equating the three nonlinear partial differential equations to zero as

$$D_1 \nabla^2 n - D_2 \nabla^4 n - \nabla \cdot \{a_1 n \nabla C - a_2 n \nabla (\nabla^2 C)\} - \nabla \cdot (n u_t) + r n (N - n) = 0$$

$$\nabla \cdot \left\{ (\mu_1 \varepsilon_t + \mu_2 \theta_t I) + (\varepsilon + v' \theta I) + \frac{n \tau}{1 + \lambda n^2} (C + \gamma \nabla^2 C) I \right\} - s u = 0 \quad (21)$$

$$1 - v \theta - \nabla \cdot (C \mu_t) = 0$$

$$1 - m \theta = 0 \Rightarrow m = \frac{1}{v \theta} \quad (26)$$

$$\frac{\partial C}{\partial t} = C_t = 0, \frac{\partial u}{\partial t} = C_t = 0, \frac{\partial \varepsilon}{\partial t} = \varepsilon_t = 0$$

$$C = a_1 = a_2 = D_1 = D_2 = 0, \frac{\partial \theta}{\partial t} = \theta_t = 0, \text{ and}$$

$$C = m = u = 1. \text{ So that } n r (N - n) = 0 \quad (22)$$

To resolve this system of non-linear algebraic equations, we put C_e, u_e and m_e to be the equilibrium solutions for the cell density, displacement and matrix density respectively, then put $n = C_e$, in equation (22) we have:

$$r C_e (N - C_e) = 0 \Rightarrow C_e = 0, C_e = N \quad (23)$$

$$\nabla \cdot \left\{ (\varepsilon + v' \theta I) + \frac{I \tau}{1 + \lambda} \right\} - s u_e = 0 \quad (24)$$

$$u_t = \frac{\nabla \cdot \varepsilon + v' I \nabla \cdot \theta + \nabla \cdot I \tau (1 + \lambda)^{-1}}{s} \quad (25)$$

$$u_t = \frac{\nabla \cdot \varepsilon + v' I \nabla \cdot \theta}{s}$$

From (21) considering the fact that matrix has viscous part gives

The other equilibrium solution shows the existence of both cell density and displacement with matrix density satisfied as:

$$(C_e, u_e, m_e) = (0, 0, 0) \quad (27)$$

$$(C_e, u_e, m_e) = \left(N, \frac{\nabla \cdot \varepsilon + I v \nabla \cdot \theta}{s}, \frac{1}{v \theta} \right) \quad (28)$$

3.2. Stability Analysis

In solving for the stability, this can be determined by performing a linearization. Considering the complexity in damaged cells reproduction and proliferation in this nonlinear systems of equation by finding the rate of spread, Ψ of damaged cells in the body of the organisms, traction term A, stress term B, diffusion term C, haptotaxis or mechanical term D (movement of the damaged cells) and the secretion term E; all are functions of wave vector in the model equations. Hence, the linear stability of the solution is obtained by seeking solutions of the linearised equations (20) and writing it in the corresponding variables as below gives.

$$(C_t - D_1 \nabla^2 n + D_2 \nabla^4 n - r N n + r n^2) C + (a_1 n \nabla^2 m + a_2 n \nabla^4) m + (\nabla \cdot (n u_t)) u \quad (29)$$

$$\left(\frac{\tau \rho \nabla \cdot n}{1 + \lambda n^2} \right) C + \left(\frac{n \tau \nabla \cdot m I}{1 + \lambda n^2} + \frac{n \tau \gamma \nabla^3 m I}{1 + \lambda n^2} \right) m + (\mu_1 \nabla \cdot \varepsilon_t + \mu_2 \nabla \cdot \theta_t I + \nabla \cdot \varepsilon + v' \nabla \cdot \theta I - s C u) u = 0 \quad (30)$$

$$(v\theta - 1)C + (\rho_t)m + (\nabla \cdot (Cu_t))u = 0 \quad (31)$$

$$\frac{\partial}{\partial t} = \Psi, \nabla = ik, C = 1, m = 1, u = 1, I = 1, \quad (32)$$

Since this study is in three dimensional space, we will limit the analysis to x_i direction because we are considering the growth rate Ψ and destruction rate of damaged cells, k . Where $C_t, \theta_t, u_t, m_t, \varepsilon_t$ are in their partial derivatives form and are equal to Ψ ,

$$\tau_1 = \frac{\tau}{1+\lambda}, \tau_2 = \frac{\tau}{1+\lambda n^2}, \mu_1 + \mu_2 = \mu \quad (33)$$

Thus, considering $C - 1, m - 1$ and u small, upon substituting into the nonlinear system of equation and keeping the linear terms in $C - 1, m - 1$ and $u, \lambda < 1, \tau_2 > 0$, and λ is a measure of cell-cell contact activation of cancer cells and also nonnegative. Setting the solutions the linearized equations to be

$$(C, m, u) \propto e^{(\Psi t + ik \cdot r)} \quad (34)$$

Where k is the wave vector k and Ψ is the linear growth term. Thus, the dispersion relation $\Psi = \Psi(k^2)$ is solutions of the polynomial in Ψ given by the determinant in (39).

Thus, the Jacobian matrix of the model and their derivatives in the linear system of equations above becomes:

$$J(C, m, u) = \begin{pmatrix} C_t - D_1 \nabla^2 n + D_2 \nabla^4 n - rNn + rn & a_1 \nabla^2 C & \nabla \cdot u_t \\ \tau_2 \nabla \cdot nI & \tau_1 \nabla \cdot CI + \gamma \tau_1 \nabla^3 \cdot CI & \mu_1 \nabla \varepsilon_t + \mu_2 \nabla \cdot \theta_t I + \nabla \cdot \varepsilon + v' \nabla \cdot \theta - su \\ v\theta - 1 & m_t & \nabla \cdot (Cu_t) \end{pmatrix} \begin{pmatrix} C \\ m \\ u \end{pmatrix} \quad (35)$$

Upon substitution gives:

$$(\Psi + D_1 k^2 + D_2 k^4 - rN +)C + (a_1 k^2 - a_2 k^4)m + (ik\Psi)u = 0 \quad (36)$$

$$(\tau_2 ik)C + (\tau_1 ik - \tau_1 \gamma ik^3)m - (2\mu k^2 \Psi + (1 + v')k^2 + s)u \quad (37)$$

$$(v\theta - 1)C + (\Psi)m + (ik\Psi)u = 0 \quad (38)$$

where Ψ is the growth rate (linear growth term) and k is the wavevector. In solving the equations we have to use determinant method which yields:

$$\begin{vmatrix} \Psi + D_1 k^2 + D_2 k^4 + r & -a_1 k^2 + a_2 k^4 & ik\Psi \\ ik\tau_2 & ik\tau_1 - ik^3 \gamma \tau_1 & -\mu k^2 \Psi - (1 + v')k^2 - s \\ 0 & \Psi & ik\Psi \end{vmatrix} = 0 \quad (39)$$

In the determinant above, we considered our solutions in the growth rate Ψ as a function of rate of destruction of cells k^2 , traction factor A , stress term B , diffusion term C , haptotaxis or mechanical term D (movement of the cells) and the secretion term E in the model equations. Thus, putting

$$A = \tau_1 - \gamma \tau_1 k^2, B = (1 + v'), C = D_1 + D_2 k^2,$$

$$D = k^2(a_2 - a_1) \text{ and } E = (v\theta - 1)$$

so that equation (39) yields:

$$(\Psi C k^2 - rN + r)\{(-Ak^2 \Psi) - (-2\mu k^2 \Psi^2 - Bk^2 \Psi - \Psi s)\} = 0$$

$$Dk^2(-\tau_2 k^2 \Psi + 2\mu k^2 E \Psi + BEk^2 + sE) = 0$$

$$E(-2D\mu k^4 \Psi - DBk^4 - sDk^2 + Ak^2 \Psi) = 0 \quad (40)$$

$$Ak^2(ik\Psi^2 + C ik^2 \Psi - rN ik \Psi + irk \Psi - ikE \Psi)$$

$$(-2\mu k^2 \Psi - Bk^2)(\Psi^2 - C \Psi k^2 - rN \Psi + r\Psi - BDk^2) = 0$$

$$\Psi(\Psi s - Ak^2 \Psi - 2\mu k^2 \Psi^2 - Bk^2 \Psi) \quad (41)$$

From equation (40)

Similarly,

$$Ck^2(\Psi s - Ak^2\Psi - 2\mu k^2\Psi^2 - Bk^2\Psi) = (rN - r - \Psi)(\Psi s - Ak^2\Psi - 2\mu k^2\Psi - Bk^2\Psi) \quad (42)$$

$$C = rN - r - \Psi \quad (43)$$

$$C = \frac{rN - r - \Psi}{k^2} \quad (44)$$

For $N = 0$ implies that it is not yet an open wound gives the equation below:

$$C(k^2) = -(\Psi + r) \Rightarrow C = \frac{-(\Psi + r)}{k^2} \quad (45)$$

From equation (40)

$$Dk^2(-\tau_2 k^2\Psi + 2\mu k^2 E\Psi + BEk^2 + sE) = 0$$

$$D(0) = 0 \text{ and } D(k^2) = \frac{\tau_2 k^2\Psi + BEk^2 - sE}{2E\mu k^2\Psi}$$

$$D = \frac{\tau_2\Psi + BE - sEk^{-2}}{2E\mu k^2\Psi} \quad (46)$$

From equation (40)

$$(-2\mu k^2\Psi - Bk^2 - s)(\Psi^2 + Ck^2\Psi - rN\Psi + r\Psi - BDk^2) = 0$$

$$(-2\mu k^2\Psi - Bk^2 - s)(\Psi^2 + Ck^2\Psi - rN\Psi + r\Psi - Dk^2(v\theta - 1)) = 0$$

$$B(k^2) = \frac{-(2\Psi\mu k^2 + s)(\Psi^2 + Ck^2\Psi + r\Psi + Dk^2)}{\Psi^2 + Ck^2\Psi + r\Psi} \quad (49)$$

Similarly, expressing (40) in a quadratic form gives

$$\Psi(k^2) = \frac{-A(k^2) \pm \sqrt{A^2(k^2) - 4\mu k^2 B(k^2)}}{2\mu k^2} \quad (50)$$

$$\text{If } \mu k^2\Psi^2 + A(k^2)\Psi + B(k^2) = 0$$

$$\Psi = -\frac{(A+B)}{\mu} \quad (51)$$

Equations (42), (43) with Ψ , (50) and (51) gives us steady state solutions which means that the secretion surface is activating the rate of growth or damaged cells in the body of the organism. This stable solution is an indication of the presence of damaged cells which is in a steady state growth showing that the dead cells have defiled all medications because of the action of the oxidative stress. These results also established that there is presence of oxidative stress in the injured area which is also acting as an activator to the spread of the injured cells showing that the immune system is becoming weak. This results are in conformity with [21, 23, 24].

Similarly,

$$E(-2D\mu k^4\Psi - DBk^4 - sDk^2 + Ak^2\Psi) = 0$$

$$E(0) = 0 \text{ and } E(k^2) = \frac{DBk^2 + sDk^2 - Ak^2\Psi}{2D\mu k^2\Psi} \quad (47)$$

$$E = \frac{DB + sD - A\Psi}{2D\mu k^2\Psi}$$

From equation (40) the traction term A and stress term B yield

$$A(k)\{ik\Psi^2 + Cik^3\Psi - rNik\Psi - ik\Psi(v\theta - 1)\} = 0$$

$$A(k^2) = \frac{-ik^2\Psi^2 - rNk^2\Psi + irk^2\Psi(v\theta - 1)}{iCk^4\Psi}$$

$$A = \frac{-\Psi^2 - rN\Psi + r\Psi}{Ck^2\Psi} \quad (48)$$

4. Dispersion Relations

4.1. The Spatial Heterogeneous and Homogeneous Solutions of the Linear System

The spatial heterogeneous solutions of the linear system are categorised by a dispersion relation.

$\Psi(k^2)$. From (34) and (41) where $k = |k|$ and the algebra gives $\Psi(k^2)$ as the solutions of

$$\Psi\{\mu k^2 \Psi^2 + B(k^2)\Psi + C(k^2)\} = 0$$

$$B(k^2) = \mu D_2 k^6 + (\mu D_1 + \gamma \tau_1) k^4 + (1 + \mu r - \tau_1 - \tau_2) k^2 + s$$

$$C(k^2) = \gamma \tau_1 D_2 k^8 + (\gamma \tau_1 D_1 - \tau_2 D_2 - D_2 - a_2 \tau_1) k^6 + (D_1 + s D_2 - \tau_1 D_1 + \gamma \tau_1 r - a_1 \tau_2) k^4$$

$$+ (r + s D_1 - r \tau_1) k^2 + rs \quad (52)$$

Put $\mu = \mu_1 + \mu_2$ and τ_1, τ_2, μ and s to replace $\tau_1/(1+v'), \tau_2/(1+v'), \mu/(1+v')$ and $s/(1+v')$.

Lemma 1: If $\Psi(k^2)$ is the dispersion relation and solutions of (50) with the largest $\text{Re } \Psi \geq 0$, then we need $\text{Re } \Psi(k^2) > 0$ for $k^2 \neq 0$.

Proof: $\Psi(k^2)$ is the dispersion relation and solutions of (50) with the largest $\text{Re } \Psi \geq 0$. Expressing (39), in a quadratic form in terms of $\Psi(k^2)$ i.e.

$$\Psi\{\mu k^2 \Psi^2 + B(k^2)\Psi + C(k^2)\} = 0 \text{ gives}$$

$$\Psi(k^2) = \frac{-B(k^2) + [B^2(k^2) - 4\mu k^2 C(k^2)]^{\frac{1}{2}}}{2\mu k^2}$$

$$B(k^2) = \mu D_2 k^6 + (\mu D_1 + \gamma \tau_1) k^4 + (1 + \mu r - \tau_1 - \tau_2) k^2 + s \Rightarrow$$

$$B(0) = s > 0$$

$$C(k^2) = \gamma \tau_1 D_2 k^8 + (\gamma \tau_1 D_1 - \tau_2 D_2 - D_2 - a_2 \tau_1) k^6$$

$$+ (D_1 + s D_2 - \tau_1 D_1 + \gamma \tau_1 r - a_1 \tau_2) k^4 \quad (54)$$

$$+ (r + s D_1 - r \tau_1) k^2 + rs \Rightarrow C(0) = rs > 0$$

are the sufficient conditions for all the parameters are positive. Since $\Psi\{\mu k^2 \Psi^2 + B(k^2)\Psi + C(k^2)\} = 0$; Thence, $\Psi = \frac{-C}{B} < 0$ and the stability is achieved. Thus we two required and satisfied conditions are:

- i). $\Psi(k^2) > 0$ to exists at least for some $k^2 \neq 0$.
- ii). $\Psi(k^2) > 0$ to exists at least for some $k^2 = 0$.

The solutions of (34) with the wave vectors, k are linearly unstable and grow exponentially with respect to time. Similarly, it is expected that these unstable heterogeneous linear solutions will evolve into finite amplitude due to the quadratic curvature which spatially structured solutions. Experientially, it is obvious that the nonlinear system of equations in (20) with exponentially growth solutions will be bounded due to the quadratic term in the logistic growth equations and the mitotic

$$\Psi(k^2) = \frac{-B(k^2)}{2\mu k^2}, \text{ if } C(k^2) \equiv 0 \quad (53)$$

This is the necessary conditions needed for $\text{Re } \Psi(k^2) > 0$ for $k^2 \neq 0$.

Lemma 2: If $\Psi(k^2)$ has $\text{Re } \Psi(0) \leq 0$ and this exhibits a range of unstable modes with $\Psi(k^2) > 0$ for $k^2 \neq 0$.

Proof: From (40) if $k^2 = 0$, then the spatial homogeneous case from

rate is set to zero. Therefore the contact inhibition term in the displacement model, u will ensure that the solutions are bounded. This solution is in line with the result obtained from [25, 26].

4.2. Complex Dispersion Relations

This section is considering some special cases where one or more factors affecting cell motion or mechanical equilibrium are assumed to be negligible. This can done by setting various parameters to zero and evaluate the result of dispersion relation in (54). Such parameters as:

(i). $D_1 = 0, D_2 = 0, a_1 = 0, a_2 = 0$; there is no cell diffusion and haptotaxis, $r = 0$: no cell division. The model mechanism (20) becomes;

$$C_t \nabla \cdot (C u_t) = 0$$

$$\nabla \cdot \left\{ (\mu_1 \varepsilon_t + \mu_2 \theta_t I) + (\varepsilon + v' \theta I) + \frac{n\tau}{1+\lambda n^2} (C + \gamma \nabla^2 C) I \right\} = \rho s u \quad (55)$$

$$m_t + \nabla \cdot (m \mu_t) = 0$$

The implication of simple conservation equations for C and m is that the cells and matrix are simply convected by the matrix which is the major transport process and it is seen in network formation. Thus, the one-dimensional form of the model mechanism gives;

$$C_t + (Cu_t)_x = 0$$

$$\mu u_{xxt} + u_{xx} + \left[\frac{\tau C}{1+\lambda C^2} (m + \gamma m_{xx}) \right]_x = smu \quad (56)$$

$$m_t + (mu_t)_x = 0$$

Put $\mu = (\mu_1 + \mu_2)/(1 + v')$, $\tau = \tau(1 + v')$, $s = s(1 + v')$ which linearizes the system to

$$C_t + u_{tx} = 0$$

$$B(k^2) = \gamma \tau_1 k^4 + (1 - \tau_1 - \tau_2) k^2 + s \Rightarrow B_{min} = s - \frac{(\tau_1 + \tau_2 - 1)^2}{4\gamma \tau_1} \quad (59)$$

In terms of τ, γ, λ and s becomes;

$$\tau^2 - \tau(1 + \lambda)^2 [1 + \gamma s(1 + \lambda)] + \frac{1}{4} (1 + \lambda)^4 > 0 \quad (60)$$

This implies that spatial pattern will evolve if and only if

$$\tau > \tau_c = \frac{1}{2} (1 + \lambda)^2 [1 + \gamma s(1 + \lambda)] + \{[1 + \gamma s(1 + \lambda)]^2 - 1\}^{\frac{1}{2}} > 0 \quad (61)$$

Thus, the root $\tau_1 + \tau_2 < 1$ is not relevant so $B(k^2) > 0$ is for all k. hence, the surface $\tau = \tau_c(\lambda, \gamma, s)$ is the bifurcation surface between homogeneity and heterogeneity. In view of the role of cell traction and the form of traction against time and the simulations would be captured in part two of this study.

5. Pattern Formation Potentials

This sector is discussed using the results from the dispersion relation in terms of the linear growth rate Ψ , and wave vector k^2 , traction force term A, and diffusion term C respectively. Case 1: $\text{Re } \Psi(k^2) > 0$ for $k^2 \neq 0$ from lemma 1.

The implication of case 1 is that the spatial frequency or pattern of damaged cells repeats per unit distance in the body of living organisms. Thereby creating a of being spread in a region. Here, the pattern formation is quadratic in nature of (54) showing the bounded domain of the injury.

Case 2: $\Psi(k^2) > 0$ for some $k^2 = 0$ from lemma 2.

This implies that for some $k^2 = 0$ there exist a spatial pattern of random initial cell densities which increases and later tends to stabilise the effect of viscous terms in the solutions. This also implies a reduction in the pattern formation of damaged cells.

Case 3: That spatial pattern will evolve if and only if $\tau >$

$$\mu u_{xxt} + u_{xx} + [\tau_1 m + \tau_2 C + \tau_1 \gamma m_{xx}]_x = su \quad (57)$$

$$m_t + u_{tx} = 0$$

From (20) and (52), replacing $\tau_1 = \tau/(1 + v')$, $\tau_2 = \tau(1 - \lambda)/(1 + \lambda)^2$, $\mu/(1 + v')$ and $s/(1 + v')$.

From (54) $C(k^2) \equiv 0$, so the dispersion relation gives

$$\Psi(k^2) = \frac{-B(k^2)}{\mu k^2},$$

$$B(k^2) = \gamma \tau_1 k^4 + (1 - \tau_1 - \tau_2) k^2 + s \quad (58)$$

For $\text{Re} \Psi > 0$, $B(k^2) < 0$ for some $k^2 > 0$ requires $\tau_1 + \tau_2 > 1$ from (58)

τ_c in (61).

This implies that the patterning process of damage is nonuniform cell density which proves that cell traction is greater than the critical value of cell traction which is the resistance of the extracellular matrix and spatial inhomogeneities begins in which the dispersion relation starts to growth out of bounded region. However, this section and the simulations would be captured in part two of this study.

6. Conclusion

Conclusively, the first model analysis showed two equilibria points of trivial case and semi trivial case of which two dependent variables are both coexisting in the tissue of living organisms nevertheless there was no matrix wall of expansion. This implies that the likelihoods of healing is there. The linear solution of the system revealed spatial heterogeneous solutions by the dispersion term $\Psi(k^2)$ with $\text{Re } \Psi(0) \leq 0$ and inhibits range of unstable modes with $\text{Re } \Psi(0) > 0$ for $k^2 \neq 0$. If $k^2 = 0$, it exhibits a spatial homogeneous case with all parameters positive stability is achieved. However, exploring into the complex dispersion, showed a bifurcation surface between spatial homogeneity and heterogeneity. The study

shown that as the bifurcation parameter τ increases monotonically beyond the critical value renders $B(k^2)$ zero and the uniform steady state bifurcates to a spatial unstable state. The results from this study supports the results of [1-3]. In this study, cell traction, oxidative stress and mechanical terms are the activators of damaged cell that increases the density of the ECM. This study has part A which is the present paper while part B would be the continuation of dispersion relations, pattern formations, bifurcation analysis and numerical simulations.

Abbreviations

ODE	Ordinary Differential Equations
ECM	Extra-Cellular Matrix
PDE	Partial Differential Equation

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Conflicts of Interest

The authors declare no conflicts of interest.

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