

# Numerical Study of Effects of Adrenal Hormones on Lymphocytes



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**Abstract** Lymphocytes play significant defensive role to keep the body healthy. However, there is substantial evidence that adrenal hormones such as epinephrine, norepinephrine, and cortisol generated by psychological stress suppress the activities of the immune system or alter the activation and mobilization several immune cells particularly lymphocytes during infections. Glucocorticoid receptors expressed by the immune cells makes binding those hormones possible. This work formulates a mathematical model to examine the impact of adrenal hormones on the immune system with respect to time evolution and spatial distribution cells in response to hormones concentration. The steady state of the model is studied and found to be uniformly and asymptotically stable subject to the secretion and decay rates of hormones. The numerical experiments using the free diffusion equations further investigates the dynamic behaviour of the “bound” lymphocytes secretion rate of the adrenal hormones induced by psychological stress.

**Keywords** Reaction–diffusion equations · Lymphocytes · Adrenal hormones · Mathematical model

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## 1 Introduction

The adrenal hormones are known to influence the activities of immune system in human and other animals. People exposed to life threatening issues are prone to chronic and persistent stress. For instance, a person diagnosed with any terminal disease such as HIV infection or cancer faces social and emotional challenges. Psychological stress that comes with the diagnosis of such illnesses often requires as much attention as the infection [1]. Lymphocytes are specialized white blood cells whose function is to identify and destroy invading antigens [2, 3].

The lymphocytes are vital components of the immune system alongside with macrophages, antigen receptors and antigen-presenting cells [4, 5]. Psychological stress is an unpleasant state of emotional and physiological arousal that people experience in situations that they perceive as dangerous or threatening to their well-being [6]. Psychological stress gets inside the body through the brain by the influence of the impulses via the nerve fibres that descend from the brain into the bone marrow and thymus, spleen and lymph nodes that connect with lymphoid tissues. These fibres release adrenal hormones such as epinephrine, norepinephrine, and cortisol that bind on the receptors on lymphocytes thereby changing the functionality immune system [7]. When psychological stress is excessive, prolonged and chronic, it breaks down the body's defense mechanism and leaves the body vulnerable to infections [8].

In light of the above, we propose a deterministic mathematical model to study the temporal-spatial dynamics of lymphocytes and Adrenal Hormones interaction via numerical experimentation inspired by [9, 10]. The secretions of adrenal hormones during chronic and persistent stress cases are separately examined. The rest of the paper is organized thus. In the second section, the mathematical model is proposed which is followed by tabular description of each equation. In the same section, the stability of the diffusion free system is investigated; equilibrium point obtained and studied. In addition, some estimates of the full diffusion model are also examined in appropriate Sobolev spaces. In section three, the diffusion free model is solved using classical Runge-Kutta method while the full diffusion model is solved by explicit forward in time, central in space (FTCS) method with appropriate stability condition of the scheme and the corresponding results are presented alongside. The last section is concluding remarks.

## 2 Formulation and Analysis of the Model Equations

### 2.1 Model Formulation

In these model equations, the diffusions of the respective component are modelled using Laplace operator. The zero flux boundary conditions are imposed on the system to study the phenomenon in bounded two dimensional domain  $\Omega$ .  $u_1(x, t)$  represents the density of normal lymphocytes at time  $t$ ;  $u_2(x, t)$  : The concentration of adrenal

**Table 1** Biological meaning of the system

Equation	Terms description	
Eq. (1)	$D_1 \Delta u_1$ : diffusion term for normal cells	$\delta$ : source term for normal cells
	$\beta u_3$ : proportion of bound cells that revert to normal	$-\alpha_1 u_1 u_2$ : Proportion of normal cells upon which adrenal hormone bound
	$-\mu_1 u_1$ : proportion of dead normal cells	
Eq. (2)	$D_2 \Delta u_2$ : diffusion term for adrenal hormones	$\alpha_2 u_2$ : natural secretion of adrenal hormones
	$-\mu_2 u_2$ : decay term for adrenal hormones	$\varepsilon(x, t)$ : secretion of adrenal hormones by psychological stress
Eq. (3)	$D_3 \Delta u_3$ : diffusion term for bound cells	
	$-(\beta + \mu_3)u_3$ : sum of proportions of dead bound cells and those that revert to normal	$\alpha_1 u_1 u_2$ : proportions cells bound by natural and stress induced secretions

hormones at time  $t$ ;  $u_3(x, t)$ : The density of bound lymphocytes at time  $t$ .

$$\frac{\partial u_1}{\partial t} = D_1 \Delta u_1 + \delta + \beta u_3 - \alpha_1 u_1 u_2 - \mu_1 u_1 \tag{1}$$

$$\frac{\partial u_2}{\partial t} = D_2 \Delta u_2 + \alpha_2 u_2 - \mu_2 u_2 + \varepsilon(x, t) \tag{2}$$

$$\frac{\partial u_3}{\partial t} = D_3 \Delta u_3 + \alpha_1 u_1 u_2 - (\beta + \mu_3)u_3 \tag{3}$$

$$u_1(\cdot, 0) = u_1^0, u_2(\cdot, 0) = u_2^0, u_3(\cdot, 0) = u_3^0, \text{ in } \Omega$$

$$\frac{\partial u_1}{\partial n} = \frac{\partial u_2}{\partial n} = \frac{\partial u_3}{\partial n} = 0 \text{ on } \partial \Omega$$

where  $\alpha_1, \alpha_2, \beta, \mu_1, \mu_2, \mu_3 > 0, D_1, D_2, D_3 \geq 0, \varepsilon(x, t) \rightarrow 0$  as  $t \rightarrow \infty$ .

We described system, Eqs. (1)–(3) term by term in Table 1 and parameter values given in Table 2.

### 2.2 Model Analysis

Here, the steady state solutions of the ODE system is obtain and the system linearize around the equilibrium point. The eigenvalues of the associated matrix of the linearized system determines stability as in [14]. In the case of the PDE, we obtained  $L^2$  and  $L^\infty$  estimates.

**Table 2** Parameter values

Symbol	Description	Values
$\alpha_1$	Binding rate of adrenal hormones on lymphocytes	0.002/day
$\alpha_2$	Natural secretion rate of adrenal hormones	0.04/day [11]
$\delta$	Source term form lymphocytes	3.63E02cells [12]
$\beta$	Rate bound lymphocytes revert to normal	0.001/day
$\mu_1$	Death rate of normal lymphocytes	0.06/day [12]
$\mu_2$	The adrenal hormone decay rate	0.1/day [11]
$\mu_3$	Death rate of bound lymphocytes	0.06/day
$\varepsilon(x, t)$	Secretion of adrenal hormones induced by psychological stress	
$D_1$	Diffusion coefficient of lymphocytes	0.0045 mm <sup>2</sup> /day [13]
$D_2$	Diffusion coefficient of adrenal hormones	0.0052 mm <sup>2</sup> /day
$D_3$	Diffusion coefficient of bound lymphocytes	0.0045 mm <sup>2</sup> /day [13]

**Theorem 1** For  $\mu_2 > \alpha_2$  and  $\frac{\varepsilon^*}{\mu_2 - \alpha_2} \geq \frac{\mu_1}{\alpha_1}$ , the system, Eqs. (1)–(3) admits a spatially homogeneous steady state  $\wp(u_1^*, u_2^*, u_3^*)$ .

*Proof* Assume that diffusion of the component decrease slowly to a negligible value, then at equilibrium state, set  $\frac{\partial u_1}{\partial t} = \frac{\partial u_2}{\partial t} = \frac{\partial u_3}{\partial t} = 0$ , we have

$$0 = \delta + \beta u_3 - \alpha_1 u_1 u_2 - \mu_1 u_1, \tag{4}$$

$$0 = \alpha_2 u_2 - \mu_2 u_2 + \varepsilon^*, \tag{5}$$

$$0 = \alpha_1 u_1 u_2 - (\beta + \mu_3) u_3, \tag{6}$$

Solving Eqs. (4)–(6) simultaneously, we obtain positive equilibrium values

$$u_1^* = \frac{\delta(\beta + \mu_3)}{(\beta + \mu_3)(\alpha_1 u_2^* - \mu_1) + \beta \alpha_1 u_2^*}, \tag{7}$$

$$u_2^* = \frac{\varepsilon^*}{\mu_2 - \alpha_2}, \tag{8}$$

$$u_3^* = \frac{\delta \alpha_1 u_2^*}{(\beta + \mu_3)(\alpha_1 u_2^* - \mu_1) + \beta \alpha_1 u_2^*}. \tag{9}$$

provided  $\mu_2 > \alpha_2$  and  $\frac{\varepsilon^*}{\mu_2 - \alpha_2} \geq \frac{\mu_1}{\alpha_1}$ , hence the proof.

**Theorem 2** Let  $u' = Ju$  be a linearized system of Eqs. (11)–(13). Suppose that the Jacobian matrix  $J$  is a constant matrix, with eigenvalues  $\lambda_1, \lambda_2, \lambda_3$  and  $Re(\lambda_i) < 0$

for all  $i = 1, 2, 3$ , then the spatially homogeneous steady state  $\wp(u_1^*, u_2^*, u_3^*)$  of Eqs. (1)–(3) is uniformly and asymptotically stable.

*Proof* Now, let the kinetic parts of Eqs. (1)–(3) be expressed as below:

$$\begin{aligned} \varphi_1 &= \delta + \beta u_3 - \alpha_1 u_1 u_2 - \mu_1 u_1, \varphi_2 = \alpha_1 u_2 - \mu_2 u_2 + \varepsilon(x, t), \\ \varphi_3 &= \alpha_1 u_1 u_2 - (\beta + \mu_3) u_3. \end{aligned}$$

Then, the Jacobian matrix evaluated at  $(u_1^*, u_2^*, u_3^*)$  is given by

$$J(u_1^*, u_2^*, u_3^*) = \begin{pmatrix} -\alpha_1 u_2 - \mu_1 & -\alpha_1 u_1 & \beta \\ 0 & \alpha_1 - \mu_2 & 0 \\ \alpha_1 u_2 & \alpha_1 u_1 & -(\beta + \mu_3) \end{pmatrix}.$$

Now, we solve for the eigenvalues from the characteristics equation as follows:

$$|J(u_1^*, u_2^*, u_3^*) - \lambda I| = \begin{vmatrix} -\alpha_1 u_2^* - \mu_1 - \lambda & -\alpha_1 u_1^* & \beta \\ 0 & \alpha_1 - \mu_2 - \lambda & 0 \\ \alpha_1 u_2^* & \alpha_1 u_1^* & -(\beta + \mu_3) - \lambda \end{vmatrix} = 0, \tag{10}$$

where  $\lambda$  is the eigenvalues while  $I$  is the  $3 \times 3$  identity matrix. This leads to the characteristic equation

$$(\alpha_1 - \mu_2 - \lambda)(\lambda^2 - (A_1 + A_2)\lambda + A_1 A_2 + A_3) = 0, \tag{11}$$

where  $A_1 = -\alpha_1 u_2^* - \mu_1, A_2 = -(\beta + \mu_3), A_3 = -\beta \alpha_1 u_2^*$ .

Solving (11), we obtained the following eigenvalues

$$\begin{aligned} \lambda_1 &= \alpha_1 - \mu_2, \lambda_2 = \frac{(A_1 + A_2) - \sqrt{(A_1 + A_2)^2 - 4(A_1 A_2 + A_3)}}{2}, \\ \lambda_3 &= \frac{(A_1 + A_2) + \sqrt{(A_1 + A_2)^2 - 4(A_1 A_2 + A_3)}}{2} \end{aligned} \tag{12}$$

It remains to check whether the real parts of Eq. (12) are negative. Clearly,  $\lambda_1$  and  $\lambda_2$  are both negative but  $\lambda_3 < 0$  if and only if

$$(A_1 + A_2) > \sqrt{(A_1 + A_2)^2 - 4(A_1 A_2 + A_3)}. \tag{13}$$

This suffices to show that  $(A_1 A_2 + A_3) > 0$

$$A_1 A_2 + A_3 = \alpha_1(\beta + \mu_3)u_2^* + \mu_1(\beta + \mu_3) - \beta \alpha_1 u_2^* \tag{14}$$

Since  $u_2^* > 0$  and  $\beta, \mu_3$  are positive constants, therefore

$$A_1A_2 + A_3 > \beta\alpha_1u_2^* - \beta\alpha_1u_2^* + \mu_1(\beta + \mu_3) = \mu_1(\beta + \mu_3) > 0, \Rightarrow \lambda_3 < 0. \tag{15}$$

Since all the eigenvalues Eq. (12) are negative, the system is uniformly and asymptotically stable around the equilibrium point  $(u_1^*, u_2^*, u_3^*)$  and this completes the proof.

Now, we define the time dependent Sobolev spaces to enable us obtain the estimates.

**Definition 3** [15]: let  $X$  be a generic nonempty set and  $1 \leq p < \infty$

$$C([0, T]; X) := \{u|u : [0, T] \rightarrow X \text{ continuous} \}, \tag{16}$$

$$L^p(0, T; X) := \left\{ u|u \text{ measurable, } \int_0^T \|u(t)\|^p dt < \infty \right\}. \tag{17}$$

For an integer  $m > 0$  and real  $p$  with  $1 \leq p < \infty$  and  $X = \Omega \subset \mathbb{R}^2$ , we define the Sobolev space

$$W^{m,p}(\Omega) = \{u \in L^p(\Omega) | D^\alpha u \in L^p(\Omega) \forall |\alpha| \leq m\} \tag{18}$$

equipped with the following norms

$$u_{W^{m,p}(\Omega)} := \begin{cases} \left( \sum_{|\alpha| \leq m} \int_{\Omega} |D^\alpha u|^p dx \right)^{1/p} & 1 \leq p < \infty, \\ \sum_{|\alpha| \leq m} \text{ess sup}_{\Omega} |D^\alpha u| & p = \infty, \end{cases} \tag{19}$$

$$|u|_{W^{m,p}(\Omega)} := \left( \sum_{|\alpha|=m} \int_{\Omega} |D^\alpha u|^p dx \right)^{1/p} \quad 1 \leq p < \infty. \tag{20}$$

Now, for  $p = 2$ , a Hilbert space is defined  $W^{m,2}(\Omega) = H^m(\Omega)$  with the inner product

$$(u, v)_{m,\Omega} = \sum_{|\alpha| \leq m} (D^\alpha u, D^\alpha v)_{0,\Omega}. \tag{21}$$

$$H_0^1(\Omega) = \{u \in H^1 | u = 0 \text{ on } \partial\Omega\} \text{ with dual } H^{-1}(\Omega).$$

**Theorem 4** Let  $u_1^0, u_2^0, u_3^0 \in L^2(\Omega)$  and  $(x, t) \in L^2(0, T; L^2(\Omega))$ , then  $u_1, u_2, u_3 \in L^2(0, T; H_0^1(\Omega))$  with  $\frac{\partial u_1}{\partial t}, \frac{\partial u_2}{\partial t}, \frac{\partial u_3}{\partial t} \in L^2(0, T; H_0^{-1}(\Omega))$ , furthermore the estimates

$$\left( \begin{array}{l} \|u_1(t)\|_{L^2(H_0^1)} \\ \|u_2(t)\|_{L^2(H_0^1)} \\ \|u_3(t)\|_{L^2(H_0^1)} \end{array} \right) \text{ and } \left( \begin{array}{l} \|u_1(t)\|_{L^\infty(L^2)} \\ \|u_2(t)\|_{L^\infty(L^2)} \\ \|u_3(t)\|_{L^\infty(L^2)} \end{array} \right)$$

are bounded by the data.

*Proof* Multiplying Eq. (1) by  $u_1$  and integrating over the domain, we have

$$\int_{\Omega} \frac{\partial u_1}{\partial t} u_1 = D_1 \int_{\Omega} \Delta u_1 u_1 + \int_{\Omega} \delta u_1 + \beta \int_{\Omega} u_3 u_1 - \alpha_1 \int_{\Omega} u_1 u_2 u_1 - \mu_1 \int_{\Omega} u_1 u_1 \quad (22)$$

Using the Young’s inequality, integrating the first term on the right hand side by parts, applying the boundary condition and dropping the negative terms, we have

$$\frac{1}{2} \frac{\partial}{\partial t} \int_{\Omega} u_1^2 + D_1 \int_{\Omega} \nabla u_1 \cdot \nabla u_1 \leq \frac{1}{2} \int_{\Omega} \delta u_1^2 + \frac{\beta}{2} \int_{\Omega} (u_3^2 + u_1^2), \quad (23)$$

$$\frac{1}{2} \frac{\partial}{\partial t} \|u_1(t)\|_{L^2}^2 + D_1 \|u_1(t)\|_{H_0^1}^2 \leq \frac{\delta + \beta}{2} \|u_1(t)\|_{L^2}^2 + \frac{\beta}{2} \|u_3(t)\|_{L^2}^2 \quad (24)$$

In the same manner for Eqs. (2) and (3), we have

$$\frac{1}{2} \frac{\partial}{\partial t} \|u_2(t)\|_{L^2}^2 + D_2 \|u_2(t)\|_{H_0^1}^2 \leq \frac{\alpha_2}{2} \|u_2(t)\|_{L^2}^2 + \|\varepsilon(\cdot, t)\|_{L^2} \|u_2(t)\|_{L^2} \quad (25)$$

$$\frac{1}{2} \frac{\partial}{\partial t} \|u_3(t)\|_{L^2}^2 + D_3 \|u_3(t)\|_{H_0^1}^2 \leq \frac{\alpha_1}{2} (\|u_1(t)\|_{L^2}^2 + \|u_2(t)\|_{L^2}^2 + \|u_3(t)\|_{L^2}^2) \quad (26)$$

Writing Eqs. (24)–(26) in vector form, we realize

$$\frac{1}{2} \frac{\partial}{\partial t} \begin{pmatrix} \|u_1(t)\|_{L^2}^2 \\ \|u_2(t)\|_{L^2}^2 \\ \|u_3(t)\|_{L^2}^2 \end{pmatrix} + \begin{pmatrix} \|u_1(t)\|_{H_0^1}^2 \\ \|u_2(t)\|_{H_0^1}^2 \\ \|u_3(t)\|_{H_0^1}^2 \end{pmatrix} \leq M \begin{pmatrix} \|u_1(t)\|_{L^2}^2 \\ \|u_2(t)\|_{L^2}^2 \\ \|u_3(t)\|_{L^2}^2 \end{pmatrix} + \begin{pmatrix} 0 \\ \|\varepsilon(\cdot, t)\|_{L^2} \|u_2(t)\|_{L^2} \\ 0 \end{pmatrix} \quad (27)$$

$$M = \max\left(\frac{\delta + \alpha_1 + \beta}{2}, \frac{\alpha_1 + \alpha_2}{2}, \frac{\alpha_1 + \beta}{2}\right) = \frac{\delta + \alpha_1 + \beta}{2}.$$

Now integrating in time and using of Cauchy-Schwarz inequality leads to

$$\frac{1}{2} \begin{pmatrix} \|u_1(T)\|_{L^2}^2 \\ \|u_2(T)\|_{L^2}^2 \\ \|u_3(T)\|_{L^2}^2 \end{pmatrix} - \frac{1}{2} \begin{pmatrix} \|u_1^0\|_{L^2}^2 \\ \|u_2^0\|_{L^2}^2 \\ \|u_3^0\|_{L^2}^2 \end{pmatrix} + \begin{pmatrix} \|u_1(t)\|_{L^2(H_0^1)}^2 \\ \|u_2(t)\|_{L^2(H_0^1)}^2 \\ \|u_3(t)\|_{L^2(H_0^1)}^2 \end{pmatrix}$$

$$\leq M \left( \begin{array}{c} \|u_1(t)\|_{L^2(L^2)}^2 \\ \|u_2(t)\|_{L^2(L^2)}^2 \\ \|u_3(t)\|_{L^2(L^2)}^2 \end{array} \right) + \left( \begin{array}{c} 0 \\ \|\varepsilon(\cdot, t)\|_{L^2(L^2)} \|u_2(t)\|_{L^2(L^2)} \\ 0 \end{array} \right) \tag{28}$$

Using Poincare’s inequality on the right hand side of Eq. (28) and that

$$\left( \begin{array}{c} \|u_1(t)\|_{L^2(H_0^1)} \\ \|u_2(t)\|_{L^2(H_0^1)} \\ \|u_3(t)\|_{L^2(H_0^1)} \end{array} \right) \leq C \left\{ \left( \begin{array}{c} 0 \\ \|\varepsilon\|_{L^2(L^2)} \\ 0 \end{array} \right) + \left( \begin{array}{c} \|u_1^0\|_{L^2}^2 \\ \|u_2^0\|_{L^2}^2 \\ \|u_3^0\|_{L^2}^2 \end{array} \right) \right\} < \infty \tag{29}$$

$$\left( \begin{array}{c} \|u_1(t)\|_{L^\infty(L^2)} \\ \|u_2(t)\|_{L^\infty(L^2)} \\ \|u_3(t)\|_{L^\infty(L^2)} \end{array} \right) \leq C \left\{ \left( \begin{array}{c} 0 \\ \|\varepsilon\|_{L^2(L^2)} \\ 0 \end{array} \right) + \left( \begin{array}{c} \|u_1^0\|_{L^2}^2 \\ \|u_2^0\|_{L^2}^2 \\ \|u_3^0\|_{L^2}^2 \end{array} \right) \right\} < \infty \tag{30}$$

### 3 Numerical Solution

#### 3.1 Diffusion Model

Assuming the diffusions of respective interacting components decrease to zero; we solve the resulting system of ordinary differential equations using classical Runge-Kutta method:

$$\frac{du_1}{dt} = \delta + \beta u_3 - \alpha_1 u_1 u_2 - \mu_1 u_1 \tag{31}$$

$$\frac{du_2}{dt} = \alpha_2 u_2 - \mu_2 u_2 + \varepsilon(t) \tag{32}$$

$$\frac{du_3}{dt} = \alpha_1 u_1 u_2 - (\beta + \mu_3) u_3 \tag{33}$$

$$u_1(0) = u_1^0, u_2(0) = u_2^0, u_3(0) = u_3^0,$$

Now, let  $u = (u_1, u_2, u_3)$  and  $t_{n+1} = t_n + h, n = 0, 1, 2 \dots$ , the fourth order Runge-Kutta [16]

$$u_{n+1} = u_n + \frac{1}{6}(k_1 + 2k_2 + 2k_3 + k_4)$$

$$k_1 = f(t_n, u_n)$$



$$k_2 = f\left(t_n + \frac{h}{2}, u_n + \frac{h}{2}k_1\right)$$

$$k_3 = f\left(t_n + \frac{h}{2}, u_n + \frac{h}{2}k_2\right)$$

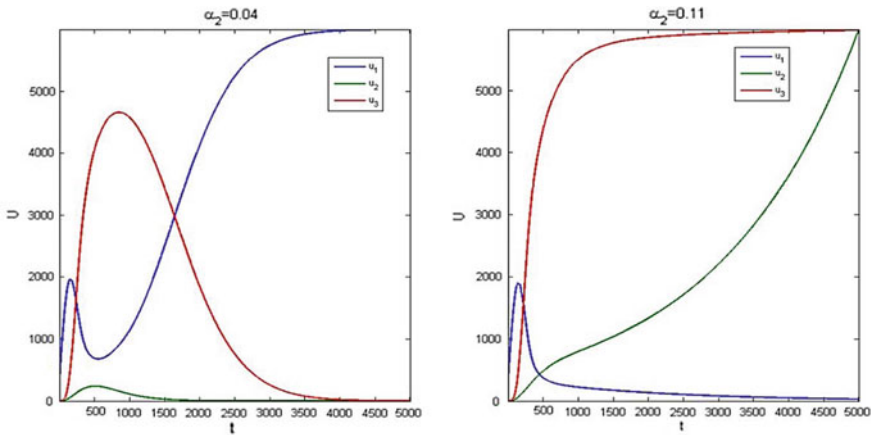
$$k_4 = f(t_n + h, u_n + hk_3)$$

### 3.1.1 Chronic Stress

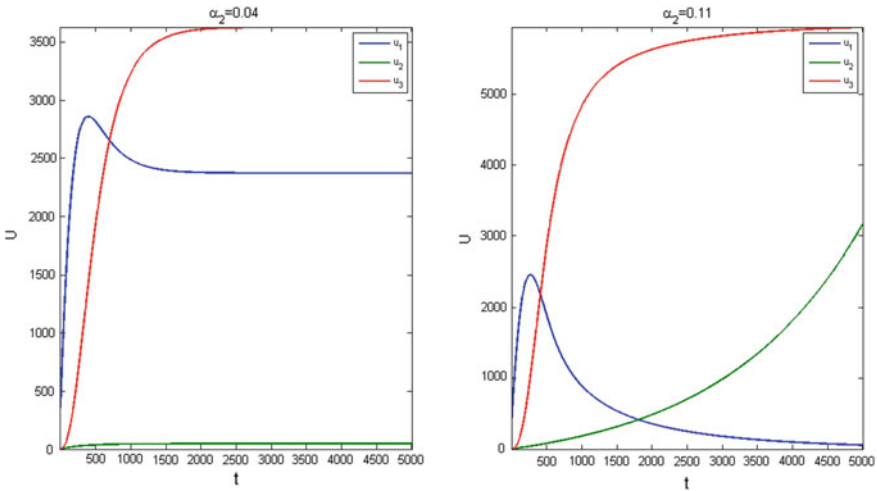
Using the initial values  $u_1(0) = 3.6E02, u_2(0) = 2.8, u_3(0) = 0$  and parameter values in Table 1. In case of chronic stress transient function

$$\varepsilon(t) = t^2 e^{-0.15t}$$

We infer from Fig. 1 below that, in the scenario where  $\alpha_2 = 0.04, \mu_2 = 0.1$ , in line the stability condition  $\mu_2 > \alpha_2$ , the density of normal lymphocytes (blue line) struggled initially but eventually recover from stress induced secretion of adrenal hormones. The second scenario is when  $\mu_2 < \alpha_2$  which is against the stability condition. Here, the escalation of concentration of adrenal hormones leads to exponential increase of number of bound lymphocytes which spell abnormal immune response or reaction. This causes activation or inhibition depending on the particular hormone and lymphocyte involved. This will lead to chronic stress related complications such



**Fig. 1** Density of normal lymphocytes  $u_1(x, t)$  (blue); the concentration of adrenal hormones  $u_2(x, t)$  (green) during chronic stress; the density of bound lymphocytes  $u_3(x, t)$  (red) for  $\alpha_2 = 0.04$  and  $\alpha_2 = 0.11$



**Fig. 2** Density of normal lymphocytes  $u_1(x, t)$  (blue); the concentration of adrenal hormones  $u_2(x, t)$  (green) during persistent stress; the density of bound lymphocytes  $u_3(x, t)$  (red) for  $\alpha_2 = 0.04$  and  $\alpha_2 = 0.11$

as high blood pressure, hypertension and diabetes. However, the second scenario can be explored to treat hyper immune reaction related diseases.

### 3.1.2 Persistent Stress

Here, a constant function is used with the same value as the initial value i.e.  $\varepsilon(t) = 2.8$ . This is to emphasize that the fact, the initial concentration of adrenal hormones persisted for a period of time. The numerical results shown in Fig. 2, further illustrated that, even when the stability condition  $\mu_2 > \alpha_2$  is satisfied with  $\mu_2 = 0.1, \alpha_2 > 0.04$ , the normal lymphocytes cannot recover back to original density. In case of  $\mu_2 < \alpha_2$ , the density of normal lymphocytes crashed. The two cases will lead to stress related complications.

## 3.2 Full Diffusion Model

We use an explicit forward in time, central in space (FTCS) method [17] to solve the system. Let the compact form Eqs. (1)–(3) be given as

$$\frac{\partial U}{\partial t} = D\Delta U + F(U), \tag{34}$$

such that the two dimensions discretize form of Eq. (34) reduces to

$$\frac{U_{ij}^{n+1} - U_{ij}^n}{\Delta t} = D \left( \underbrace{\frac{U_{i+1j}^n - 2U_{ij}^n + U_{i-1j}^n}{\Delta x^2} + \frac{U_{ij+1}^n - 2U_{ij}^n + U_{ij-1}^n}{\Delta y^2}}_{\tilde{\Delta}u_{ij}^n} \right) + F(U^n) \tag{35}$$

This scheme has the stability condition [15]

$$\Delta t \leq \frac{\Delta x^2 \Delta y^2}{2D(\Delta x^2 + \Delta y^2)}$$

$$u_{1ij}^{n+1} = u_{1ij}^n + \Delta t \left( D_1 \tilde{\Delta}u_{1ij}^n + \delta + \beta u_{3ij}^n - \alpha_1 u_{1ij}^n u_{2ij}^n - \mu_1 u_{1ij}^n \right) \tag{36}$$

$$u_{2ij}^{n+1} = u_{2ij}^n + \Delta t \left( D_2 \tilde{\Delta}u_{2ij}^n + (\alpha_2 - \mu_2) u_{2ij}^n + \varepsilon(x_n, y_n, t_n) \right) \tag{37}$$

$$u_{3ij}^{n+1} = u_{3ij}^n + \Delta t \left( D_3 \tilde{\Delta}u_{3ij}^n + \alpha_1 u_{1ij}^n u_{2ij}^n - (\beta + \mu_3) u_{3ij}^n \right) \tag{38}$$

In Theorem 1, this two conditions  $\mu_2 > \alpha_2$  and  $\frac{\varepsilon^*}{\mu_2 - \alpha_2} \geq \frac{\mu_1}{\alpha_1}$  must be satisfied for the positivity of the solution. The parameter values are taken from Table 2 and we used the initial conditions

$$u_1(x, y, 0) = e^{-0.7(x+2)^2 - 0.7(y+2)^2}, u_2(x, y, 0) = 2.8, u_3(x, y, 0) = 0 \tag{39}$$

Note that, from the initial conditions, it is assumed that, in a square domain  $\Omega = [-4, 4]^2$  the initial population of normal lymphocytes is densed at  $x = -2, y = -2$  and the average concentrations adrenal hormone is constant. Also, it is assume that the secretion of adrenal hormones induced by psychological stress is transient given by

$$\varepsilon(x, y, t) = \cos\left(\frac{\pi x}{2}\right) \cos\left(\frac{\pi y}{2}\right) t^2 e^{-0.15t} \tag{40}$$

It is observed from Sect. 3.1 that, the system is highly sensitive to the net secretion rate of the adrenal hormone. Here, a dynamic behaviour is also observed in Figs. 3, 4 and 5 shown at  $t = 1.25$  and  $t = 2.5$  for each component. Particularly, our light is beamed on the density of bound lymphocytes. It is inferred in Fig. 5 that, bound lymphocytes are more densed at areas of high concentration of adrenal hormones. Indeed, this is in consonance with previous results on cortisol association with T cell activation during HIV infection [9].

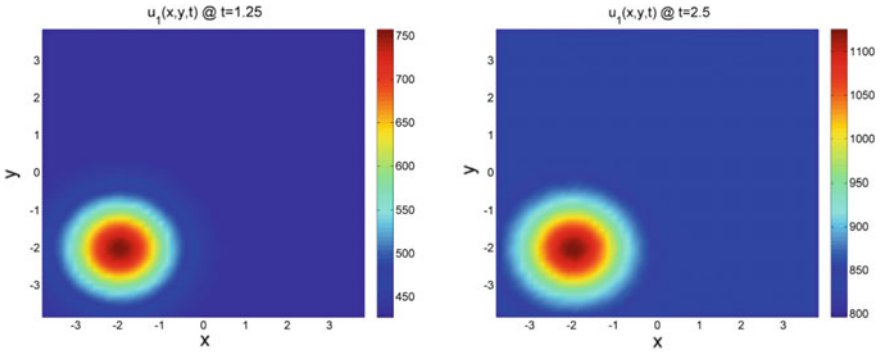


Fig. 3 Density of normal lymphocytes  $u_1(x, t)$  at  $t = 1.25$  and  $t = 2.5$

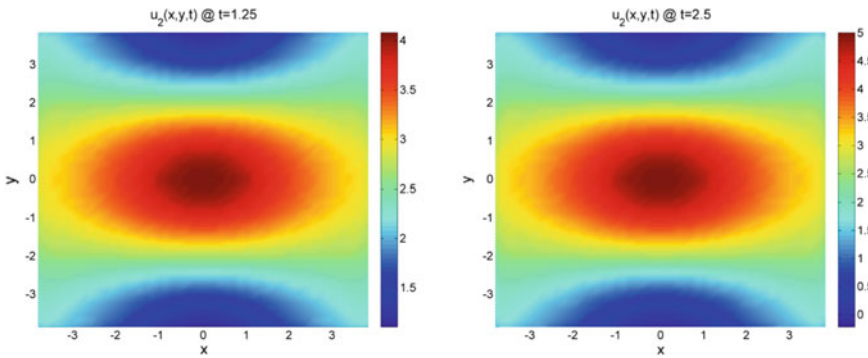


Fig. 4 The concentration of adrenal hormones  $u_2(x, t)$  at  $t = 1.25$  and  $t = 2.5$

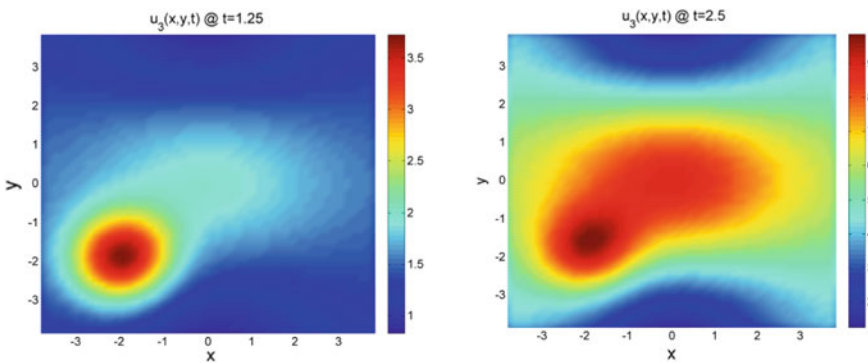


Fig. 5 The density of bound lymphocytes  $u_3(x, t)$  at  $t = 1.25$  and  $t = 2.5$

## 4 Conclusion

In this paper, a coupled system of reaction-diffusion equations to study the interaction of adrenal hormones induced by psychological stress on the human immune system has been formulated. The system has only one critical point which is proved to be uniformly and asymptotically stable (UAS) under certain prescribed constraints  $\mu_2 > \alpha_2$  and  $\frac{\varepsilon^*}{\mu_2 - \alpha_2} \geq \frac{\mu_1}{\alpha_1}$ . Numerical solutions have further shown that, increase in net secretion rate of stress absorbing hormones has great negative effect on the human immune cell. Further research can be carried out in connection with other terminal disease models such as cancer and HIV.

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