# IN-HOST MODELING OF THE SPATIAL DYNAMICS OF HIV

by

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**ABSTRACT**

The well-known three-compartment model which describes the spatially homogeneous dynamics of HIV *in-vivo* is adapted to account for spatial heterogeneity by considering diffusion of populations and spatially varying parameters. The new system of nonlinear parabolic PDEs is analyzed in detail. Specifically, local and global existence, uniqueness and high-order regularity of solutions is proven. We also determine the global asymptotic behavior of the model in certain biologically relevant regimes and compare our findings with the analogous results for the spatially homogeneous model. In doing so, we discuss existence and stability of viral extinction and viral persistence steady states in different cases. Finally, the system is simulated using a semi-implicit finite difference method with the goal of verifying the analysis.

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# CHAPTER 1
# INTRODUCTION

The Human Immunodeficiency Virus (HIV) is a deadly, infectious virus which primarily utilizes $CD4^+$ T cells, a white blood cell useful in directing the adaptive immune response in the body, to reproduce. The course of the infection within a host is characterized by depletion of these cells. With this decrease in the $CD4^+$ T cell population, the immune system is left dangerously compromised and when such cells reach low enough levels in an HIV infected patient, the patient is diagnosed with AIDS. The infection and depletion process can range from a few months to several years. For a biological description of infection dynamics, see [6]. We summarize the very basics here. HIV particles (called *virions*) attach to T cells, enter the cell and release the contents of their genetic information. The process of reverse transcription in the cell copies the viral RNA into the DNA of the cell. The cell then manufactures new strands viral RNA and proteins which form into new virons and separate from the cell (a process called *budding*). The infection will eventually cause the cell to die which results in a burst of virions into its immediate surroundings. The function of $CD4^+$ T cells (also called *helper* T cells) is to "mark" infected cells and virions by secreting proteins which activate the immune system. The components of the immune system work to kill and clear infected cells and virions. If the T cell count remains relatively high, then the immune system will be able to locate and flush out harmful cells. However, with the T cell population depleted, the immune system receives less direction and the HIV virus and other debilitating pathogens are allowed to run rampant.

There have been several efforts to mathematically model the battle between the immune system and HIV within an infected host. Perelson and Nelson [1] provide an overview of some common models which have been used. The most basic and ubiquitous model, discussed, for example, in [4], is concerned with three quantities: $T(t)$, the density of uninfected $CD4^+$ cells, $I(t)$, the density of infected $CD4^+$ cells and $V(t)$, the density of free virions. The corresponding dynamical system is:

$$\left.\begin{aligned} \frac{dT}{dt} &= \lambda - \mu_T T - kTV, && T(0) = T_0, \\ \frac{dI}{dt} &= kTV - \mu_I I, && I(0) = I_0, \\ \frac{dV}{dt} &= N\mu_I I - \mu_V V, && V(0) = V_0. \end{aligned}\right\} \tag{1.1}$$

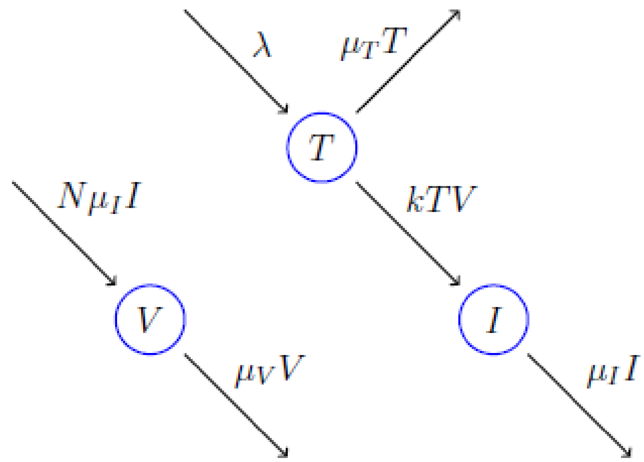


Figure 1: Transfer diagram for (1.1)

Here, all parameters are taken to be positive. The value $\lambda$ represents the natural constant regeneration rate of T cells while $\mu_T, \mu_I$ and $\mu_V$ are death/clearance rates which correspond to cells naturally dying, being killed by virions or the immune response or being cleared by the immune system. The parameter $k$ is an infection rate; note that healthy T cells become infected at a rate proportional to the product of the density of T cells and the density of free virions. This is essentially an application of the mass-action principle. Finally, $N$ is the bud/burst rate which models output of virions from an infected cell. Many sources ([2], [3], [7]) group $N\mu_I$ into a single constant. When the two are kept separate, we can see the term $N\mu_I I$ as representing the total average production of virions by an infected T cell over the course of its lifespan.

More sophisticated versions of this model (those which take into account viral production, drug therapy, drug resistant strains of the virus, etc.) can be found in [1]. However, these models assume spatial homogeneity as do those considered in [2], [3] and [4]. Spatially homogeneous (or *lumped*) models have some advantages. For example, they are simpler in some respects than spatially heterogeneous models and capture some of the asymptotic behavior of the infection (as noted by Brauner et al. [5]).

By contrast, there are also several shortcomings of lumped models. For example, the dynamics of HIV can vary wildly in different compartments of the human body. Also, virions may preferentially infect nearby cells. These considerations are unaccounted for in spatially homogeneous models.

Accordingly, there have been a few efforts to construct spatially heterogeneous models, some of which are discussed in [8]. A common approach (used for example by Funk et al. [7]) is to add discrete spatial aspects to (1.1). Another approach is to consider virions which are bound to cells and virions which are free as separate populations; in this case, free virions must be allowed to diffuse [10]. Further, Stancevic et al. [9] introduce a two-dimensional spatial model with diffusion and a chemotaxis term which accounts for chemical attractors, though their work focuses on simulation and stability of equilibria rather than analysis and estimation of solutions.

In this document, we introduce a new spatial model with diffusion of populations and spatially dependent parameters. Specifically, we assume that the regeneration of T cells does not occur uniformly throughout the body or tissue (i.e., $\lambda = \lambda(x)$). We study the model in $n$ spatial dimensions and time with the goal of proving many classical results for partial differential equations (existence, uniqueness and regularity) and determining some large time asymptotic behavior.

# CHAPTER 2
# WELL-POSEDNESS

We consider the system

$$\left.\begin{aligned}
(\partial_t - D_T\Delta)T &= \lambda(x) - \mu_T T - kTV, && T(x,0) = T_0(x),\\
(\partial_t - D_I\Delta)I &= kTV - \mu_I I, && I(x,0) = I_0(x),\\
(\partial_t - D_V\Delta)V &= N\mu_I I - \mu_V V, && V(x,0) = V_0(x),
\end{aligned}\right\} \tag{2.1}$$

for $x \in \Omega \subset \mathbb{R}^n$, $t \in (0, t^*]$, $t^* > 0$ where $k, N, \mu_T, \mu_I, \mu_V, D_T, D_I, D_V$ are all real, nonnegative constants and $\lambda$ is a nonnegative function of spatial variables. Here, we could have two different cases, but the analysis remains largely the same in each case. First, we may take $\Omega = \mathbb{R}^n$ in which case we also assume that

$$\lim_{|x|\to\infty} \frac{\partial T}{\partial n}(x,t) = \lim_{|x|\to\infty} \frac{\partial I}{\partial n}(x,t) = \lim_{|x|\to\infty} \frac{\partial V}{\partial n}(x,t) = 0, \ \ t \in (0, t^*].$$

In the second case, we take $\Omega$ to be a bounded, open subset of $\mathbb{R}^n$ with boundary $\partial\Omega$ and in this case, we assume that

$$\frac{\partial T}{\partial n}(\cdot,t)\bigg|_{\partial\Omega} = \frac{\partial I}{\partial n}(\cdot,t)\bigg|_{\partial\Omega} = \frac{\partial V}{\partial n}(\cdot,t)\bigg|_{\partial\Omega} = 0, \quad t \in (0, t^*].$$

We also note here that throughout this document, we will impose various restrictions on our initial conditions. In a bounded domain, it is enough to take $T_0, I_0, V_0 \in C\left(\overline{\Omega}\right)$. In addition, they will always be positive. However, for much of the analysis these assumptions are superfluous. As necessary, we will mention the restrictions we are imposing on $T_0, I_0, V_0$. Similarly, we will require $\lambda$ to have certain properties at different junctures so it is convenient to consider $\lambda$ to be a smooth function. Accordingly, we take $\lambda \in H^\infty(\Omega)$; this will play a key role later in this section.

A model similar to ours was considered by [5]. Those authors also introduced diffusion. However, they neglected T cell diffusion. Their assumption was that, under normal conditions, T cells do not move whereas the virions are still active. Accordingly, they set $D_T = D_I = 0$. Our model is slightly more robust since we do not assume this.

## 2.1 Existence and Uniqueness of Solutions

To analyze (2.1), we consider the inhomogeneous and autonomous, vector heat equation given by

$$\left.\begin{aligned} (\partial_t - D_{\mathbf{u}}\Delta)\mathbf{u} = \mathbf{f}(\mathbf{u}), \;\; x \in \Omega, \;\; t \in [0, t^*], \\ \mathbf{u}(x,0) = \mathbf{u}_0(x), \;\; x \in \Omega. \end{aligned}\right\} \tag{2.2}$$

We note that (2.1) can be written in this form by setting $\mathbf{u} = [T \; I \; V]^T$ and letting $\mathbf{f}$ be prescribed by the right hand side of (2.1). We will require later that that $\mathbf{f} : \mathbb{R}^3 \to \mathbb{R}^3$ be a locally Lipschitz function; indeed, we demonstrate that our $\mathbf{f}$ satisfies this requirement. We see that for (2.1)

$$\mathbf{f}(\mathbf{u}) = \begin{bmatrix} f_1(u_1, u_2, u_3) \\ f_2(u_1, u_2, u_3) \\ f_3(u_1, u_2, u_3) \end{bmatrix} = \begin{bmatrix} \lambda - \mu_T u_1 - k u_1 u_3 \\ k u_1 u_3 - \mu_I u_2 \\ N \mu_I u_2 - \mu_V u_3 \end{bmatrix}.$$

The derivatives of each component are

$$\nabla f_1 = \begin{bmatrix} -\mu_T - k u_3 \\ 0 \\ -k u_1 \end{bmatrix}, \quad \nabla f_2 = \begin{bmatrix} k u_3 \\ -\mu_I \\ k u_1 \end{bmatrix}, \quad \nabla f_3 = \begin{bmatrix} 0 \\ N \mu_I \\ -\mu_V \end{bmatrix},$$

each of which remains bounded on compact subsets of $\mathbb{R}^3$. Thus, each of $f_1, f_2, f_3$ is locally Lipschitz and so $\mathbf{f}$ is locally Lipschitz as well.

By Duhamel's principle, we know that the solution to (2.2) is given by

$$\mathbf{u}(x,t) = \int_0^t \int_\Omega \Phi(x-y, t-s)\mathbf{f}(\mathbf{u}(y,s))dyds + \int_\Omega \Phi(x-y,t)\mathbf{u}_0(y)dy,$$

where $\Phi$ is the Green's function for the heat operator in the domain $\Omega$ with Neumann boundary condition; i.e., $\Phi$ satisfies

$$\begin{aligned} &(\partial_t - D_{\mathbf{u}}\Delta)\Phi = 0, \;\; (x,t) \in \Omega \times (0, t^*], \\ &\Phi(x,0) = \delta(x), \\ &\frac{\partial \Phi}{\partial n}(\cdot, t)\bigg|_{\partial\Omega} = 0. \end{aligned}$$

We note, for example, that if $\Omega = \mathbb{R}^n$ then $\Phi$ is the heat kernel given by

$$\Phi(x,t) = \frac{1}{(4D_{\mathbf{u}}\pi t)^{n/2}} \exp\left\{ -\frac{|x|^2}{4D_{\mathbf{u}}t} \right\}, \;\; x \in \Omega, \;\; t > 0, \tag{2.3}$$

which is a particularly nice function. In any case, the heat operator admits only smooth Green's functions, so $\Phi$ is smooth. As a result of this, we can ensure that

$$\int_{\Omega} \Phi(x,t)dx = 1,$$

for all $t > 0$. Lastly, in the sense of distributions, $\Phi$ tends to the Dirac delta as $t \to 0$. That is,

$$\lim_{t\to 0} \int_{\Omega} \Phi(x-y,t)\mathbf{F}(y)dy = \mathbf{F}(x)$$

for any continuous $\mathbf{F}$ defined for $x \in \Omega$. We seek to prove existence and uniqueness of solutions to (2.2).

**Lemma 2.1 (Local Existence)**. If $\mathbf{f} : \Omega \to \mathbb{R}^3$ is a locally Lipschitz function and $\mathbf{u}_0 : \Omega \to \mathbb{R}^3$ is continuous, then there is an $a > 0$ such that (2.2) has a unique solution for $t \in [-a, a]$.

**Proof.** Let $a, \varepsilon > 0$ and define $V = \{\mathbf{v} \in C(\Omega \times [-a,a]) : ||\mathbf{v} - \mathbf{u}_0||_\infty < \varepsilon\}$. Define a linear operator $K$ on $V$ by

$$K\mathbf{u}(x,t) = \int_0^t \int_{\Omega} \Phi(x-y,t-s)\mathbf{f}(\mathbf{u}(y,s))dyds + \int_{\Omega} \Phi(x-y,t)\mathbf{u}_0(y)dy$$

for all $\mathbf{u} \in V$ where $\mathbf{f}, \mathbf{u}_0$ are as in (2.2) and $\Phi$ is the Green's function for the heat operator in $\Omega$.We are assuming that $\mathbf{f}$ is locally Lipschitz and has Lipschitz constant $L$ in the $\varepsilon$-neighborhood of $\mathbf{u}_0$.

By the Banach fixed point theorem (contraction mapping principle), to prove that our system has a unique solution, it will suffice to prove that if we take $a$ sufficiently small, then $K : V \to V$ and that

$K$ is a contraction. To prove the latter, take $\mathbf{u}, \mathbf{v} \in V$ and consider for all $(x,t) \in \Omega \times [-a,a]$,

$$\begin{aligned}
|K\mathbf{u}(x,t) - K\mathbf{v}(x,t)| &= \left| \int_0^t \int_\Omega \Phi(x-y,t-s)\left(\mathbf{f}(\mathbf{u}(y,s)) - \mathbf{f}(\mathbf{v}(y,s))\right) dyds \right| \\
&\leq \int_0^{|t|} \int_\Omega \Phi(x-y,t-s)\left|\mathbf{f}(\mathbf{u}(y,s)) - \mathbf{f}(\mathbf{v}(y,s))\right| dyds \\
&\leq L \int_0^{|t|} \int_\Omega \Phi(x-y,t-s)\left|\mathbf{u}(y,s) - \mathbf{v}(y,s)\right| dyds \\
&\leq L\,||\mathbf{u}-\mathbf{v}||_\infty \int_0^{|t|} \int_\Omega \Phi(x-y,t-s) dyds \\
&= L\,||\mathbf{u}-\mathbf{v}||_\infty\,|t| \leq aL\,||\mathbf{u}-\mathbf{v}||_\infty .
\end{aligned}$$

Since this holds for all $(x,t) \in \Omega \times [-a,a]$, we have an upper bound for $|K\mathbf{u}(x,t) - K\mathbf{v}(x,t)|$. The supremum over all such $(x,t)$ is the least upper bound so we find

$$||K\mathbf{u} - K\mathbf{v}||_\infty \leq aL\,||\mathbf{u}-\mathbf{v}||_\infty$$

for all $\mathbf{u}, \mathbf{v} \in V$. Thus taking $a < 1/L$ will ensure that $K$ is a contraction mapping.

It remains to prove that $K : V \to V$; that is, we must show that for any $\mathbf{u} \in V$, we have $K\mathbf{u} \in V$. Since $\Phi, \mathbf{f}, \mathbf{u}_0$ are continuous, we know that $K\mathbf{u}$ is continuous for any $\mathbf{u} \in V$. Also,

$$\begin{aligned}
|K\mathbf{u}(x,t) - \mathbf{u}_0(x)| &= \left| \int_0^t \int_\Omega \Phi(x-y,t-s)\mathbf{f}(\mathbf{u}(y,s))dyds + \right. \\
&\qquad \left. + \int_\Omega \Phi(x-y,t)\mathbf{u}_0(y)dy - \mathbf{u}_0(x) \right| \\
&\leq \left| \int_0^t \int_\Omega \Phi(x-y,t-s)\mathbf{f}(\mathbf{u}(y,s))dyds \right| + \\
&\qquad + \left| \int_\Omega \Phi(x-y,t)\mathbf{u}_0(y)dy - \mathbf{u}_0(x) \right| \\
&\leq \int_0^{|t|} \int_\Omega \Phi(x-y,t-s)\left|\mathbf{f}(\mathbf{u}(y,s))\right| dyds + \\
&\qquad + \left| \int_\Omega \Phi(x-y,t)\mathbf{u}_0(y)dy - \mathbf{u}_0(x) \right|.
\end{aligned}$$

Since $\Phi$ tends to the Dirac delta as $t \to 0$, we know there is $\delta > 0$ such that

$$0 < |t| \leq \delta \quad \Longrightarrow \quad \left| \int_\Omega \Phi(x-y,t)\mathbf{u}_0(y)dy - \mathbf{u}_0(x) \right| < \tfrac{\varepsilon}{2}.$$

We can ensure that $|t| < \delta$ by taking $a < \delta$. Next,

$$\begin{aligned}
&\int_0^{|t|} \int_\Omega \Phi(x-y,t-s)\, |\mathbf{f}(\mathbf{u}(y,s))|\, dyds \\
&\qquad \le \int_0^{|t|} \int_\Omega \Phi(x-y,t-s)\, (|\mathbf{f}(\mathbf{u}(y,s)) - \mathbf{f}(\mathbf{u}_0(y))| + |\mathbf{f}(\mathbf{u}_0(y))|)\, dyds \\
&\qquad \le \int_0^{|t|} \int_\Omega \Phi(x-y,t-s)\, (L\, ||\mathbf{u}-\mathbf{u}_0||_\infty + ||\mathbf{f}||_\infty)\, dyds \\
&\qquad \le a\, (L\, ||\mathbf{u}-\mathbf{u}_0||_\infty + ||\mathbf{f}||_\infty) < a\, (L\varepsilon + ||\mathbf{f}||_\infty)\, .
\end{aligned}$$

Thus we can force this term to be less than $\frac{\varepsilon}{2}$ by taking $a < \frac{\varepsilon}{2\left(L\varepsilon + ||\mathbf{f}||_\infty\right)}$.

Thus far we have enforced three separate bounds on $a$. To satisfy all three, we may take $a < \min\left\{\frac{1}{L},\ \delta\ ,\ \frac{\varepsilon}{2\left(L\varepsilon+||\mathbf{f}||_\infty\right)}\right\}$. Under this condition,

$$|K\mathbf{u}(x,t) - \mathbf{u}_0(x)| < \tfrac{\varepsilon}{2} + \tfrac{\varepsilon}{2} = \varepsilon, \quad \text{for all } (x,t) \in \Omega_0.$$

Again, since this holds for all $(x,t)$, we have

$$||K\mathbf{u} - \mathbf{u}_0||_\infty < \varepsilon \quad \Longrightarrow \quad K\mathbf{u} \in V.$$

Thus, for sufficiently small $a$, $K$ is a contraction and $K : V \to V$ so by the Banach fixed point theorem, there is a unique solution to (2.2) for $t \in [-a, a]$. ■

From here, we wish to prove that the solution guaranteed by the above lemma will exist globally under certain assumptions. To that end, we prove a few things about the inhomogeneous scalar heat equation which we can then apply to the equations for $T, I, V$ given in (2.1).

We consider the equation

$$\left.\begin{aligned}
&(\partial_t - D_u\Delta)u = g(x,t), && (x,t) \in \Omega \times (0,t^*], \\
&u(x,0) = u_0(x), && x \in \Omega.
\end{aligned}\right\} \tag{2.4}$$

**Lemma 2.2 (Positivity).** Assume that $u$ satisfies (2.4) and that $g(x,t) \ge 0$ for all $(x,t) \in \Omega\times[0,t^*]$ and $u_0(x) > 0$ for all $x \in \Omega$. Then $u(x,t) \ge 0$ for all $(x,t) \in \Omega \times (0,t^*]$. That is, the operator

$(\partial_t - D_u\Delta)$ preserves positivity.

**Proof.** Here, the proof is straightforward if $\Omega = \mathbb{R}^n$. In that case, we write

$$u(x,t) = \int_0^t \int_\Omega \Phi(x-y,t-s)g(y,s)dyds + \int_\Omega \Phi(x-y,t)u_0(y)dy,$$

where $\Phi$ is the heat kernel given by (2.3). We see that $\Phi(x-y,t-s) \geq 0$, so the product $\Phi(x-y,t-s)g(y,s) \geq 0$. This means that the first integral above must be nonnegative. Also $u_0(y) \geq 0$ and $\Phi(x-y,t) \geq 0$. Thus the product $\Phi(x-y,t)u_0(y) \geq 0$ and so the second integral above is nonnegative and we have reduced $u(x,t)$ to a sum of two nonnegative terms. We conclude that $u(x,t) \geq 0$ for all $(x,t) \in \Omega \times (0,t^*]$, and the theorem is proven.

In the case that $\Omega$ is a bounded domain, we recall the definitions of the positive and negative parts of $u$:

$$u_+(x,t) = \max\{0, u(x,t)\} \quad \text{and} \quad u_-(x,t) = -\min\{0, u(x,t)\}.$$

Then $u = u_+ - u_-$. With this in mind, we multiply (2.4) by $u_-$ and integrate in both time and space. Then the left hand side is given by

$$LHS = \int_0^s \int_\Omega u_- \partial_t u \, dxdt - c\int_0^s \int_\Omega u_- \Delta u \, dxdt := I + II,$$

where $s \in (0,t^*]$. Now if we define $\Omega_s^- = \{(x,t) \in \Omega \times (0,s] : u(x,t) \leq 0\}$, then $u_-$ is zero outside of $\Omega_s^-$ so we see

$$I = \int_{\Omega_s^-} u_- \partial_t u \, dxdt.$$

However, on this set $u = -u_-$ so

$$I = -\int_{\Omega_s^-} u_- \partial_t u_- \, dxdt = -\frac{1}{2}\int_{\Omega_s^-} \partial_t \left(u_-^2\right) \, dxdt.$$

However, since $u_-$ is zero outside of $\Omega_s^-$, integrating over $\Omega_s^-$ is the same as integrating over $\Omega \times (0,s]$. Thus

$$I = -\frac{1}{2}\int_\Omega \int_0^s \partial_t \left(u_-^2\right) \, dtdx = -\frac{1}{2}\int_\Omega \left[u_-(x,s)^2 - u_-(x,0)^2\right] dx.$$

Finally, $u_0 \geq 0$ implies that $u_-(x,0) \equiv 0$ so we find $I = -\frac{1}{2}\,||u_-(s)||_2^2 \leq 0$.

We use a similar set of steps for $II$:

$$\begin{aligned} II &= -D_u \int_0^s \int_\Omega u_- \Delta u \, dx dt \\ &= D_u \int_{\Omega_s^-} u_- \Delta u_- \, dx dt \\ &= -D_u \int_{\Omega_s^-} \nabla u_- \cdot \nabla u_- \, dx dt + D_u \int_0^s u_- \frac{\partial u_-}{\partial n}\bigg|_{\partial\Omega} dt. \end{aligned}$$

Enforcing the homogeneous boundary condition gives

$$II = -D_u \int_0^s \int_\Omega |\nabla u_-(x,t)|^2 \, dx dt \leq 0.$$

Thus we have

$$LHS = I + II \leq 0.$$

Next, considering the right hand side under the same operations, we have

$$RHS = \int_0^s \int_\Omega g(x,t) u_-(x,t) \, dx dt.$$

But both $g$ and $u_-$ are nonnegative so $RHS \geq 0$.

To recap, LHS is non-positive and equals RHS which is non-negative. Thus both must be zero. If LHS is zero, then both $I$ and $II$ are zero and we conclude

$$||u_-(s)||_2 = 0.$$

This is only possible if $u_-(x,s) \equiv 0$. However, $s$ was an arbitrary element of $(0, t^*]$ and so $u_-(x,t) \equiv 0$ for all $(x,t) \in \Omega \times (0, t^*]$. But if $u_- = 0$, then $u = u_+ \geq 0$ which completes the proof. ■

Now we would like to prove that $u(x,t)$ remains bounded in some way by the initial data and the forcing function. We can do this by establishing some corollaries to Lemma 2.2.

**Corollary 2.2.1** If $u(x,t)$ satisfies (2.4), then

$$||u(t)||_\infty \leq ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau, \quad \text{for all } t \in [0, t^*].$$

**Proof.** Define a new function

$$v(x,t) = \left( ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau \right) - u(x,t).$$

Then we notice that

$$(\partial_t - D_u \Delta) v = ||g(t)||_\infty - (\partial_t - D_u \Delta) u = ||g(t)||_\infty - g(x,t).$$

But $g(x,t)$ is always bounded by its supremum norm with respect to $x$, so we see

$$(\partial_t - D_u \Delta) v = G(x,t)$$

where $G(x,t) \geq 0$ for all $(x,t) \in \Omega \times [0, t^*]$. Also

$$v(x,0) = ||u_0||_\infty - u(x,0) = ||u_0||_\infty - u_0(x).$$

Again, $u_0(x)$ is bounded by its supremum norm, so we have $v(x,0) = v_0(x)$ where $v_0(x) \geq 0$. Then by Lemma 2.2, $v(x,t) \geq 0$ for $(x,t) \in \Omega \times [0, t^*]$ so

$$0 \leq \left( ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau \right) - u(x,t) \quad \Longrightarrow \quad u(x,t) \leq ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau,$$

for all $(x,t) \in \Omega \times [0, t^*]$. Taking the supremum over $x$ gives

$$||u(t)||_\infty \leq ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau,$$

for all $t \in [0, t^*]$ which completes the proof. ∎

**Corollary 2.2.2** Assume that $u(x,t)$ satisfies the differential inequality

$$(\partial_t - D_u\Delta)u \leq g(x,t), \qquad (x,t) \in \Omega \times (0,t^*],$$
$$u(x,0) = u_0(x), \qquad\qquad x \in \Omega.$$

Then $u(x,t)$ satisfies the same inequality as in Corollary 2.2.1. That is,

$$||u(t)||_\infty \leq ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau, \quad \text{for all } t \in [0,t^*].$$

**Proof.** We use the same technique as was used in the proof of Corollary 2.2.1. Define $v(x,t)$ by

$$v(x,t) = \left( ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau \right) - u(x,t).$$

Then

$$(\partial_t - D_u\Delta)v = ||g(t)||_\infty - (\partial_t - D_u\Delta)u \geq ||g(t)||_\infty - g(x,t) \geq 0$$

and

$$v(x,0) = ||u_0||_\infty - u(x,0) = ||u_0||_\infty - u_0(x) \geq 0.$$

Again the result follows from Lemma 2.2. ■

With these results in mind, we now consider our particular system. Throughout the remainder of this document $C$ will be a positive constant which may change from line to line. Sometimes the constant may be accompanied by a subscript to denote which quantities it depends on; e.g. $C_{t^*}$.

**Theorem 2.3 (Global Existence)**. Suppose $T, I, V$ satisfy (2.1) and $T_0(x), I_0(x), V_0(x)$ are positive for all $x \in \Omega$. Then for any $b > 0$, $T(x,t), I(x,t), V(x,t) > 0$ for all $x \in \Omega$ and all $t \in (0,b]$. Further $||T(t)||_\infty, ||I(t)||_\infty, ||V(t)||_\infty$ remain bounded for $t \in (0,b]$.

**Note:** What this theorem tells us in essence is that the $t^* > 0$ we choose for (2.1) is arbitrary.

**Proof.** We first establish the property for *some* time interval $(0,b]$, then extend the proof to an arbitrary interval.

Consider the $T$ equation:

$$\left.\begin{aligned} &(\partial_t - D_T\Delta)T = \lambda(x) - \mu_T T(x,t) - kT(x,t)V(x,t), \quad (x,t) \in \Omega \times (0,t^*], \\ &T(x,0) = T_0(x), \quad x \in \Omega. \end{aligned}\right\} \tag{2.5}$$

Since we have assumed positivity of initial conditions, there must be some $b > 0$ such that $T(x,t), I(x,t), V(x,t)$ are positive for all $x \in \Omega$ and $t \in [0,b]$. On this interval,

$$(\partial_t - D_T\Delta)T + \mu_T T \leq \lambda(x).$$

Multiplying through by the integrating factor $\zeta_T(t) = e^{\mu_T t}$ gives

$$\zeta_T(t)\partial_t T + \mu_T\zeta_T(t)T - D_T\zeta_T(t)\Delta T \leq \lambda(x)\zeta_T(t).$$

Since $\zeta_T(t)$ is independent of space, it can slide inside the Laplacian operator. This gives

$$(\partial_t - D_T\Delta)\{\zeta_T(t)T\} \leq \lambda(x)\zeta_T(t).$$

Further, $\zeta_T(0)T(x,0) = T_0(x) > 0$. Then by Corollary 2.2,

$$\left|\left|T(t)e^{\mu_T t}\right|\right|_\infty \leq ||T_0||_\infty + \int_0^t ||\lambda||_\infty e^{\mu_T t} dt.$$

However, the exponential is independent of the sup-norm with respect to space. Thus we find

$$||T(t)||_\infty \leq ||T_0||_\infty e^{-\mu_T t} + \frac{||\lambda||_\infty}{\mu_T}\left(1 - e^{-\mu_T t}\right).$$

In particular, there is constant bound for $T$ which is uniform in time; we call this constant $T_M$.

Next we look at the $I$ equation and $V$ equation. Consider

$$\left.\begin{aligned} &(\partial_t - D_I\Delta)I = kT(x,t)V(x,t) - \mu_I I(x,t), \quad (x,t) \in \Omega \times (0,b], \\ &I(x,0) = I_0(x), \quad x \in \Omega. \end{aligned}\right\} \tag{2.6}$$

On the interval $(0,b]$, we have $(\partial_t - D_I\Delta)I \leq kT(x,t)V(x,t)$. Using Corollary 2.2, we can say that

$$\begin{aligned}
||I(t)||_\infty &\le ||I_0||_\infty + k\int_0^t ||T(\tau)V(\tau)||_\infty \, d\tau \\
&\le ||I_0||_\infty + k\int_0^t ||T(\tau)||_\infty \, ||V(\tau)||_\infty \, d\tau \\
&\le ||I_0||_\infty + kC\int_0^t T_M \, ||V(\tau)||_\infty \, d\tau \\
&\le T_M \left(1 + \int_0^t ||V(\tau)||_\infty \, d\tau\right). \qquad (2.7)
\end{aligned}$$

Further

$$\left.\begin{aligned}
&(\partial_t - D_V\Delta)V = N\mu_I I(x,t) - \mu_V V(x,t), \quad (x,t) \in \Omega \times (0,t^*], \\
&V(x,0) = V_0(x), \quad x \in \Omega,
\end{aligned}\right\} \qquad (2.8)$$

and so

$$(\partial_t - D_V\Delta)V \le N\mu_I I(x,t)$$

for $t \in [0,b]$. Corollary 2.2 gives

$$\begin{aligned}
||V(t)||_\infty &\le ||V_0||_\infty + N\mu_I \int_0^t ||I(\tau)||_\infty \, d\tau \\
&\le C\left(1 + \int_0^t ||I(\tau)||_\infty \, d\tau\right). \qquad (2.9)
\end{aligned}$$

To proceed, we define $\phi(t) = ||I(t)||_\infty + ||V(t)||_\infty, \ \ t \in [0,b]$. Then by adding (2.7) and (2.9), we see

$$\phi(t) \le T_M\left(1 + \int_0^t \phi(\tau)d\tau\right), \quad t \in [0,b].$$

By Gronwall's Inequality, we can conclude that

$$\phi(t) \le T_M e^t, \quad t \in [0,b].$$

Thus both $||I(t)||_\infty$ and $||V(t)||_\infty$ are bounded by an exponential for $t \in (0,b]$.

We have proven boundedness and positivity of solutions on the interval $(0,b]$ for some $b > 0$. We attempt to establish the property for any positive time. We note that at this $b$, $T, I, V$ are positive and continuous so there is some $c > 0$ such that $T, I, V$ remain positive for $t \in (b, b+c]$.

We establish a time-shifted diffusion system given by

$$\left.\begin{aligned}(\partial_t - D_T\Delta)T &= \lambda(x) - \mu_T T - kTV, & T(x,b) &= T_b(x),\\ (\partial_t - D_I\Delta)I &= kTV - \mu_I I, & I(x,b) &= I_b(x),\\ (\partial_t - D_V\Delta)V &= N\mu_I I - \mu_V V, & V(x,b) &= V_b(x),\end{aligned}\right\} \tag{2.10}$$

for $x \in \Omega$ and $t \in (b, b+c]$. By slightly modifying the above proofs, we can again prove that (2.10) has solutions and those solutions remain positive and bounded on $(b, b+c]$. Repeating this argument indefinitely, we arrive at a maximal interval of existence for the solution. If we assume this interval is finite, then we may say the interval is $(0, s]$, where

$$s = \sup\{t^* \in \mathbb{R} \ : \ T(x,t), I(x,t), V(x,t) > 0 \text{ for all } t \in [0,t^*]\} < \infty.$$

On the interval $(0, s]$, the solutions will remain positive and bounded. However, by definition of $s$, one of $T(x,s), I(x,s), V(x,s)$ must be equal to zero or else, by continuity, $s$ would not be the supremum of the set. Thus we see that our solutions are positive on the closed interval $(0, s]$ and yet one of the solution must equal zero at $s$. This provides a contradiction so we see that this interval must be infinite.

Therefore, we conclude that our solutions remain positive and bounded for all positive time. That is, for any $b > 0$, $T(x,t), I(x,t), V(x,t) > 0$ for all $x \in \Omega$ and all $t \in (0, b]$ and $||T(t)||_\infty$, $||I(t)||_\infty$, $||V(t)||_\infty$ remain bounded for $t \in (0, b]$. ■

### 2.2 Regularity of Solutions

Now that we have established global existence of solutions, we note that generally, the heat operator has a smoothing effect, so we expect some gain in regularity. That is, assuming our initial data is in $L^2(\Omega)$, we expect that our solutions not only remain in $L^2(\Omega)$ but actually have derivatives which are square integrable as well. Indeed, this is the case.

**Lemma 2.4** (Low Order Regularity). If $T, I, V$ satisfy (2.1) and $T_0, I_0, V_0 \in L^2(\Omega)$, then $T(\cdot,t)$, $I(\cdot,t)$, $V(\cdot,t) \in L^2(\Omega)$ for all $t \in (0,t^*]$. Further, $\nabla T(\cdot,t)$,$\nabla I(\cdot,t)$, $\nabla V(\cdot,t) \in L^2(\Omega)$ for all

$t \in (0, t^*]$.

**Proof**. From (2.5), we multiply through by $T$ and integrate over $\Omega$ to arrive at

$$\frac{1}{2}\frac{d}{dt}\left|\left|T(t)\right|\right|_2^2 - D_T\int_\Omega T\Delta T = \int_\Omega \lambda(x)T - \mu_T\left|\left|T(t)\right|\right|_2^2 - k\int_\Omega T^2V.$$

Integrating by parts on the left (the boundary term goes to zero because of our boundary conditions), using the Cauchy-Schwarz inequality, and replacing $V$ by its supremum, we see

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\left|\left|T(t)\right|\right|_2^2 + D_T\left|\left|\nabla T(t)\right|\right|_2^2 &\leq \left|\left|\lambda\right|\right|_2\left|\left|T(t)\right|\right|_2 - \mu_T\left|\left|T(t)\right|\right|_2^2 + k\left|\left|V(t)\right|\right|_\infty\left|\left|T(t)\right|\right|_2^2\\ &\leq \tfrac{1}{2}\left(\left|\left|\lambda\right|\right|_2^2 + \left|\left|T(t)\right|\right|_2^2\right) - \mu_T\left|\left|T(t)\right|\right|_2^2 + k\left|\left|V(t)\right|\right|_\infty\left|\left|T(t)\right|\right|_2^2,\end{aligned}$$

where

$$\left|\left|\nabla T(t)\right|\right|_2^2 = \int_{\mathbb{R}^3}\left|\nabla T(x,t)\right|^2 dx.$$

Finally we arrive at

$$\frac{d}{dt}\left|\left|T(t)\right|\right|_2^2 \leq C_{t^*}\left(1 + \left|\left|T(t)\right|\right|_2^2\right) - 2D_T\left|\left|\nabla T(t)\right|\right|_2^2. \tag{2.11}$$

From (2.5) again, we take the gradient of the equation and then take the inner product of the resulting equation with $\nabla T$ to arrive at

$$\frac{1}{2}\partial_t\left|\nabla T\right|^2 - D_T\nabla T\cdot\nabla\Delta T = \nabla T\cdot\nabla\lambda - \mu_T\left|\nabla T\right|^2 - k\nabla T\cdot\left(V\nabla T + T\nabla V\right).$$

Integrating over spatial variables and using integration by parts on the left hand side gives

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\left|\left|\nabla T(t)\right|\right|_2^2 + D_T\left|\left|\Delta T(t)\right|\right|_2^2 &= \int_\Omega \nabla T\cdot\nabla\lambda - \mu_T\left|\left|\nabla T(t)\right|\right|_2^2 - k\left(\int_\Omega V\left|\nabla T\right|^2 + T\nabla T\cdot\nabla V\right)\\ &\leq \tfrac{1}{2}\left(\left|\left|\nabla T(t)\right|\right|_2^2 + \left|\left|\nabla\lambda\right|\right|_2^2\right) - \mu_T\left|\left|\nabla T(t)\right|\right|_2^2 + k\left(\left|\left|V(t)\right|\right|_\infty\left|\left|\nabla T(t)\right|\right|_2^2 +\right.\\ &\quad\left. + \tfrac{1}{2}\left|\left|T(t)\right|\right|_\infty\left(\left|\left|\nabla T(t)\right|\right|_2^2 + \left|\left|\nabla V(t)\right|\right|_2^2\right)\right),\end{aligned}$$

whence

$$\frac{d}{dt}\left|\left|\nabla T(t)\right|\right|_2^2 \leq C_{t^*}\left(1 + \left|\left|\nabla T(t)\right|\right|_2^2 + \left|\left|V(t)\right|\right|_2^2\right) - 2D_T\left|\left|\Delta T(t)\right|\right|_2^2. \tag{2.12}$$

We deal with equation (2.6) similarly. Multiplying through by $I$ and integrating gives

$$
\begin{aligned}
\frac{1}{2}\frac{d}{dt}\left|\left|I(t)\right|\right|_2^2 + D_I\left|\left|\nabla I(t)\right|\right|_2^2 &= k\int_\Omega TIV - \mu_I\left|\left|I(t)\right|\right|_2^2 \\
&\leq \left|\left|V(t)\right|\right|_\infty \int_\Omega TI - \mu_I\left|\left|I(t)\right|\right|_2^2 \\
&\leq \tfrac{1}{2}\left|\left|V(t)\right|\right|_\infty \left(\left|\left|T(t)\right|\right|_2^2 + \left|\left|I(t)\right|\right|_2^2\right) - \mu_I\left|\left|I(t)\right|\right|_2^2.
\end{aligned}
$$

From this we see

$$
\frac{d}{dt}\left|\left|I(t)\right|\right|_2^2 \leq C_{t^*}\left(\left|\left|T(t)\right|\right|_2^2 + \left|\left|I(t)\right|\right|_2^2\right) - 2D_I\left|\left|\nabla I(t)\right|\right|_2^2. \tag{2.13}
$$

Next, taking the gradient of equation (2.6) and then the inner product of the resulting equation with $\nabla I$, we see

$$
\frac{1}{2}\partial_t\left|\nabla I\right|^2 - D_I\nabla I\cdot\nabla\Delta I = k\nabla I\cdot(V\nabla T + T\nabla V) - \mu_I\left|\nabla I\right|^2.
$$

Integrating over $\Omega$ yields

$$
\begin{aligned}
\frac{1}{2}\frac{d}{dt}\left|\left|\nabla I(t)\right|\right|_2^2 + D_I\left|\left|\Delta I(t)\right|\right|_2^2 &= k\left(\int_\Omega V\nabla I\cdot\nabla T + \int_\Omega T\nabla I\cdot\nabla V\right) - \mu_I\left|\left|\nabla I(t)\right|\right|_2^2 \\
&\leq k\left(\left|\left|V(t)\right|\right|_\infty\int_\Omega \nabla I\cdot\nabla T + \left|\left|T(t)\right|\right|_\infty\int_\Omega \nabla I\cdot\nabla V\right) - \mu_I\left|\left|\nabla I(t)\right|\right|_2^2 \\
&\leq C_{t^*}\left(\tfrac{1}{2}\left(\left|\left|\nabla I(t)\right|\right|_2^2 + \left|\left|\nabla T(t)\right|\right|_2^2\right) + \tfrac{1}{2}\left(\left|\left|\nabla I(t)\right|\right|_2^2 + \left|\left|\nabla V(t)\right|\right|_2^2\right)\right) \\
&\qquad - \mu_I\left|\left|\nabla I(t)\right|\right|_2^2.
\end{aligned}
$$

This produces the inequality

$$
\frac{d}{dt}\left|\left|\nabla I(t)\right|\right|_2^2 \leq C_{t^*}\left(\left|\left|\nabla T(t)\right|\right|_2^2 + \left|\left|\nabla I(t)\right|\right|_2^2 + \left|\left|\nabla V(t)\right|\right|_2^2\right) - 2D_I\left|\left|\Delta I(t)\right|\right|_2^2. \tag{2.14}
$$

Likewise, from equation (2.8), we multiply through by $V$ and integrate to get

$$
\begin{aligned}
\frac{1}{2}\frac{d}{dt}\left|\left|V(t)\right|\right|_2^2 + D_V\left|\left|\nabla V(t)\right|\right|_2^2 &= N\mu_I\int_\Omega IV - \mu_V\left|\left|V(t)\right|\right|_2^2 \\
&\leq \frac{N\mu_I}{2}\left(\left|\left|I(t)\right|\right|_2^2 + \left|\left|V(t)\right|\right|_2^2\right) - \mu_V\left|\left|V(t)\right|\right|_2^2 \\
&\leq C_{t^*}\left(\left|\left|I(t)\right|\right|_2^2 + \left|\left|V(t)\right|\right|_2^2\right).
\end{aligned}
$$

This yields

$$\frac{d}{dt}\left|\left|V(t)\right|\right|_2^2 \leq C_{t^*}\left(\left|\left|I(t)\right|\right|_2^2 + \left|\left|V(t)\right|\right|_2^2\right) - 2D_V\left|\left|\nabla V(t)\right|\right|_2^2. \tag{2.15}$$

Next, from (2.8), we also see

$$\frac{1}{2}\partial_t\left|\nabla V\right|_2^2 - D_V\nabla V\cdot\nabla\Delta V = N\mu_I\nabla I\cdot\nabla V - \mu_V\left|\nabla V\right|_2^2.$$

Integrating gives

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\left|\left|\nabla V(t)\right|\right|_2^2 + D_V\left|\left|\Delta V(t)\right|\right|_2^2 &= N\mu_I\int_\Omega \nabla I\cdot\nabla V - \mu_V\left|\left|\nabla V(t)\right|\right|_2^2\\ &\leq \frac{N\mu_I}{2}\left(\left|\left|\nabla I(t)\right|\right|_2^2 + \left|\left|\nabla V(t)\right|\right|_2^2\right) - \mu_V\left|\left|\nabla V(t)\right|\right|_2^2\\ &\leq C_{t^*}\left(\left|\left|\nabla I(t)\right|\right|_2^2 + \left|\left|\nabla V(t)\right|\right|_2^2\right),\end{aligned}$$

from which it follows that

$$\frac{d}{dt}\left|\left|\nabla V(t)\right|\right|_2^2 \leq C_{t^*}\left(\left|\left|\nabla I(t)\right|\right|_2^2 + \left|\left|\nabla V(t)\right|\right|_2^2\right) - 2D_V\left|\left|\Delta V(t)\right|\right|_2^2. \tag{2.16}$$

Finally, let $D = \min\{D_T, D_I, D_V\}$ and for $t \in (0, t^*]$, define

$$M(t) = \phi_0(t) + Dt\phi_1(t),$$

where

$$\begin{aligned}\phi_0(t) &= \left|\left|T(t)\right|\right|_2^2 + \left|\left|I(t)\right|\right|_2^2 + \left|\left|V(t)\right|\right|_2^2,\\ \phi_1(t) &= \left|\left|\nabla T(t)\right|\right|_2^2 + \left|\left|\nabla I(t)\right|\right|_2^2 + \left|\left|\nabla V(t)\right|\right|_2^2.\end{aligned}$$

By adding equations (2.11),(2.13) and (2.15), we see

$$\phi_0'(t) \leq C_{t^*}\left(1 + \phi_0(t)\right) - 2D\phi_1(t)$$

and by adding equations (2.12), (2.14) and (2.16), we see

$$\phi_1'(t) \leq C_{t^*}(1 + \phi_1(t)) - 2D\Big(\left|\left|\Delta T(t)\right|\right|_2^2 + \left|\left|\Delta I(t)\right|\right|_2^2 + \left|\left|\Delta V(t)\right|\right|_2^2\Big).$$

Then, letting $\phi_2(t) = ||\Delta T(t)||_2^2 + ||\Delta I(t)||_2^2 + ||\Delta V(t)||_2^2$, we arrive at

$$\begin{aligned} M'(t) &= \phi_0'(t) + D\phi_1(t) + Dt\phi_1'(t) \\ &\le C_{t^*}\left(1 + \phi_0(t)\right) - 2D\phi_1(t) + D\phi_1(t) + Dt\Big(C_{t^*}(1 + \phi_1(t)) - 2\phi_2(t)\Big) \\ &\le C_{t^*}\big(1 + \phi_0(t) + Dt\phi_1(t)\big) - D\phi_1(t) - 2Dt\phi_2(t). \end{aligned}$$

Realizing that $\phi_1$ and $\phi_2$ are nonnegative, we may then say

$$M'(t) \le C_{t^*}\big(1 + M(t)\big).$$

From this, an application of Gronwall's inequality tells us that

$$\begin{aligned} M(t) &\le C_{t^*}\big(1 + M(0)e^t\big) \\ &\le C_{t^*}(1 + M(0)) \qquad \text{for } t \in (0, t^*]. \end{aligned}$$

We note here that by assumption

$$M(0) = ||T_0||_2^2 + ||I_0||_2^2 + ||V_0||_2^2$$

is finite and thus $M(t)$ remains finite on the interval. In particular, this implies that $\phi_0(t)$ remains finite, and from this we conclude that $||T(t)||_2^2$, $||I(t)||_2^2$ and $||V(t)||_2^2$ are finite for $t \in (0, t^*]$. Thus

$$T(\cdot, t),\ I(\cdot, t),\ V(\cdot, t) \in L^2(\Omega)$$

for all $t \in (0, t^*]$.

The bound on $M(t)$ also implies that

$$Dt\phi_1(t) \le C_{t^*}(1 + M(0)) \quad \Longrightarrow \quad \phi_1(t) \le \frac{C_{t^*}}{Dt}(1 + M(0)),\ \ t \in (0, t^*].$$

That is, for any $t \in (0, t^*]$, $\phi_1(t)$ will remain finite. However, each of $||\nabla T(t)||_2^2$, $||\nabla I(t)||_2^2$, $||\nabla V(t)||_2^2$ is bounded by $\phi_1(t)$. Thus these norms remain finite for $t \in (0, t^*]$. and

$$\nabla T(\cdot, t),\ \nabla I(\cdot, t),\ \nabla V(\cdot, t) \in L^2(\Omega)$$

for any $t \in (0, t^*]$. ■

Next we seek to extend the lemma to higher orders of regularity using similar methods.

**Theorem 2.5** (High Order Regularity). Assume that $T, I, V$ satisfy (2.1) and $T_0, I_0, V_0 \in L^2(\Omega)$. Then for all $m \in \mathbb{N} \cup \{0\}$, $T(\cdot,t), I(\cdot,t), V(\cdot,t) \in H^m(\Omega)$ for all $t \in (0, t^*]$.

**Note.** This theorem holds for $\Omega \subset \mathbb{R}^n$ and can be proven using the methods below. However, the proof becomes laborious when $n$ gets larger. Accordingly, we prove the theorem in $\mathbb{R}^3$, point out where the difficulty arises for larger $n$ and suggest how the proof could be amended.

Also, many of the manipulations in this proof are rather formal. Indeed, taking arbitrary spatial derivatives of (2.5), (2.6) and (2.8) may not seem legal but it can be made mathematically rigorous. To do this, we would, for example, approximate $T$ by a sequence $\{T_j\}_{j\in\mathbb{N}}$ of Schwarz class functions which converges uniformly to $T$ in $\Omega$. We would prove the bounds for each member of the sequence and then pass to the limit as $j \to \infty$.

As a final note, several times throughout this proof, we use (without pausing to mention it) the assumption that $\lambda \in H^\infty(\Omega)$; this assumption was heretofore unnecessary, but plays a key role in our argument for regularity.

**Proof** (for $\Omega \subset \mathbb{R}^3$). We prove the theorem by induction on $m$, following a method presented by Pankavich and Michalowski [12], [13]. First, note that the cases $(m = 0, 1)$ have been proven in Lemma 2.4; these will constitute the base case. As an inductive hypothesis, we assume that for some $m \geq 2$, we have $T(\cdot,t), I(\cdot,t), V(\cdot,t) \in H^\ell(\Omega)$ for $0 \leq \ell \leq m-1$. From this, we must prove that $T(\cdot,t), I(\cdot,t), V(\cdot,t) \in H^m(\Omega)$.

Before we prove increased regularity, we must establish some bounds on the quantities $||T(t)||^2_{H^\ell}$, $||I(t)||^2_{H^\ell}$, $||V(t)||^2_{H^\ell}$ for $\ell \in \mathbb{N}$, where $||\cdot||_{H^\ell}$ denotes the norm in

$$H^\ell(\Omega) = \left\{u \in L^2(\Omega) : \partial_x^\alpha u \in L^2(\Omega) \text{ for multi-indices } \alpha \text{ with } |\alpha| \leq \ell\right\}.$$

That is, $||u||_{H^\ell}^2 = \sum_{|\alpha|\leq\ell} ||\partial_x^\alpha u||_2^2$. To this end, define

$$\phi_\ell(t) = ||T(t)||_{H^\ell}^2 + ||I(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2, \quad 0 \leq \ell \leq m, \quad t \in (0, t^*].$$

Note that the definition for $\phi_\ell$ here differs slightly from the definitions of $\phi_1, \phi_2$ in the proof of low order regularity but is very similar (this definition does agree with the previous $\phi_0$). We first seek to prove that

$$\frac{d}{dt}\phi_\ell(t) \leq C_{t^*}\left(1 + \phi_\ell(t)\right) - D\xi_\ell\phi_{\ell+1}(t), \quad 0 \leq \ell \leq m, \quad t \in (0, t^*] \tag{2.17}$$

where $\xi_\ell > 1$ and $D = \min\{D_T, D_I, D_V\}$. Again, we note that (2.17) has been proven for $m = 0, 1$ with $\xi_0 = \xi_1 = 2$ (to see this, add the $\phi_0$ and $\phi_1$ from the low order regularity proof to construct the $\phi_1$ defined above). We now seek to prove the same for $m \geq 2$. First, assume $m \geq 5$; we address the cases that $m = 2, 3, 4$ individually later. For the case that $m \geq 5$, we let $\alpha$ be an arbitrary multi-index of order $\ell \leq m$ and let $\partial_x^\alpha$ be the spatial derivative corresponding to $\alpha$.

Starting from (2.5), we apply $\partial_x^\alpha$ to the equation and then multiply by $\partial_x^\alpha T$ and integrate to arrive at

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}||\partial_x^\alpha T(t)||_2^2 + D_T\,||\partial_x^\alpha \nabla T(t)||_2^2 = &\int_\Omega \partial_x^\alpha \lambda \partial_x^\alpha T(t) - \mu_T\,||\partial_x^\alpha T(t)||_2^2 \\ &- k\sum_{j=0}^{\ell}\sum_{\substack{|\beta|=j\\ \beta+\gamma=\alpha}}\binom{\alpha}{\beta}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t).\end{aligned} \tag{2.18}$$

On the right hand side of (2.18), we handle the first two terms in predictable ways (Cauchy-Schwarz Inequality then Cauchy's Inequality). It remains to discuss the integrals in the sum term; that is, we look for bounds for

$$\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t), \quad |\beta| = 0, 1, \ldots, \ell.$$

We see that when $|\beta| = 0$, we have

$$\begin{aligned}\int_\Omega T(t)\partial_x^\alpha T(t)\partial_x^\alpha V(t) \leq ||T(t)||_\infty \int_\Omega \partial_x^\alpha T(t)\partial_x^\alpha V(t) &\leq \frac{||T(t)||_\infty}{2}\left(||\partial_x^\alpha T(t)||_2^2 + ||\partial_x^\alpha V(t)||_2^2\right) \\ &\leq C_{t^*}\left(||T(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\right).\end{aligned}$$

Similarly, when $|\beta| = \ell$, we have

$$\int_\Omega V(t) \left[\partial_x^\alpha T(t)\right]^2 \leq ||V(t)||_\infty \, ||\partial_x^\alpha T(t)||_2^2 \leq C_{t^*} \, ||T(t)||_{H^\ell}^2 .$$

For the other terms, $|\beta|, |\gamma| < \ell$ so we recall the Sobolev embedding theorem.

**Theorem (Sobolev Embedding).** Let $\Omega \subset \mathbb{R}^n$ and $s > \frac{n}{2}$. Then

$$H^s(\Omega) \subset C^0\left(\overline{\Omega}\right).$$

Further, in the case the $\Omega = \mathbb{R}^n$, we have

$$H^s(\mathbb{R}^n) \subset C_0^0(\mathbb{R}^n),$$

where

$$C_0^0(\mathbb{R}^n) = \left\{ f \in C^0(\mathbb{R}^n) \, : \, \lim_{|x| \to \infty} f(x) = 0 \right\}.$$

**Note.** The full version of the Sobolev embedding theorem is quite a bit more robust. It says for example that under the correct conditions, the injection from $H^s \to C^0$ is compact and makes stronger claims about $W^{m,p}$ spaces. For a full treatment and a proof of the theorem, one could look to Brezis' text [14].

In particular the Sobolev embedding theorem tells us that if $f \in H^s(\Omega)$ with $s > \frac{n}{2}$, then $f$ remains bounded on $\overline{\Omega}$.

Here we have assumed that $T(\cdot, t), V(\cdot, t) \in H^{m-1}(\Omega)$ with $\Omega \subset \mathbb{R}^3$. We note that $\ell \leq m$ and so $\min\{|\beta|, |\gamma|\} \leq \lfloor m/2 \rfloor$; i.e., one of the partial derivatives $\partial_x^\beta, \partial_x^\gamma$ has order less than or equal to $m/2$. If $|\beta| \leq m/2$, we see that $\partial_x^\beta T(\cdot, t) \in H^{m-1-|\beta|}(\Omega)$ where, for even $m$, we have $m - 1 - |\beta| \geq m - 1 - m/2 = m/2 - 1 > \frac{3}{2}$, and for odd $m$, we get $m - 1 - |\beta| \geq m - 1 - m/2 - 1/2 = (m-1)/2 > \frac{3}{2}$. (Note: here we used the assumption that $m \geq 5$). Thus, in both cases, $\partial_x^\beta T$ remains bounded and we may take its supremum and remove it from the integral, yielding

$$\begin{aligned}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) &\leq \left|\left|\partial_x^\beta T(t)\right|\right|_\infty \int_\Omega \partial_x^\alpha T(t)\partial_x^\gamma V(t)\\ &\leq \frac{\left|\left|\partial_x^\beta T(t)\right|\right|_\infty}{2}\left(||\partial_x^\alpha T(t)||_2^2 + ||\partial_x^\gamma V(t)||_2^2\right)\\ &\leq C_{t^*}\left(||T(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\right).\end{aligned}$$

Likewise, when $|\gamma| \leq \lfloor m/2 \rfloor$, we may say

$$\begin{aligned}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) &\leq \frac{||\partial_x^\gamma V(t)||_\infty}{2}\left(||\partial_x^\alpha T(t)||_2^2 + \left|\left|\partial_x^\beta T(t)\right|\right|_2^2\right)\\ &\leq C_{t^*}\,||T(t)||_{H^\ell}^2\\ &\leq C_{t^*}\left(||T(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\right).\end{aligned}$$

Thus each term in the sum is bounded by $C_{t^*}\left(||T(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\right)$ and so the whole sum is bounded by another constant multiple of the same quantity. Further, for the terms in (2.18) which are not in the sum, we see

$$\begin{aligned}\int_\Omega \partial_x^\alpha \lambda \partial_x^\alpha T(t) - \mu_T\,||\partial_x^\alpha T(t)||_2^2 &\leq \frac{1}{2}(||\partial_x^\alpha \lambda||_2^2 + ||\partial_x^\alpha T(t)||_2^2) - \mu_T\,||\partial_x^\alpha T(t)||_2^2\\ &\leq C_{t^*}\left(1 + ||\partial_x^\alpha T(t)||_2^2\right)\\ &\leq C_{t^*}\left(1 + ||T(t)||_{H^\ell}^2\right).\end{aligned}$$

Combining all of this into (2.18) and rearranging gives

$$\frac{d}{dt}\,||\partial_x^\alpha T(t)||_2^2 \leq C_{t^*}\big(1 + ||T(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\big) - 2D_T\,||\partial_x^\alpha \nabla T(t)||_2^2.$$

Summing over all multi-indices of order less than or equal to $\ell$ gives that

$$\frac{d}{dt}\,||T(t)||_{H^\ell}^2 \leq C_{t^*}\big(1 + ||T(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\big) - 2D_T\,||T(t)||_{H^{\ell+1}}^2, \quad 0 \leq \ell \leq m, \quad t \in (0, t^*]. \tag{2.19}$$

A detail here: in the sum, we have replaced

$$\sum_{|\alpha|\leq \ell} ||\partial_x^\alpha \nabla T(t)||_2^2$$

with $||T(t)||^2_{H^{\ell+1}}$. However, the two are not the same since the former does not contain the norm $||T(t)||_2^2$. To remedy this, we can add and subtract $D_T\,||T(t)||_2^2$ and group the term we added into $C_{t^*}\left(1+||T(t)||^2_{H^\ell}+||V(t)||^2_{H^\ell}\right)$.

Next, apply $\partial_x^\alpha$ to (2.6), multiply through by $\partial_x^\alpha I$ and integrate to see

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\,||\partial_x^\alpha I(t)||_2^2+D_I\,||\partial_x^\alpha \nabla I(t)||_2^2 = k\sum_{j=0}^{\ell}\sum_{\substack{|\beta|=j\\ \beta+\gamma=\alpha}}\binom{\alpha}{\beta}\int_\Omega \partial_x^\alpha I(t)\partial_x^\beta T(t)\partial_x^\gamma V(t)\\ -\mu_I\,||\partial_x^\alpha I(t)||_2^2.\end{aligned} \tag{2.20}$$

We deal with the sum in (2.20) in a method nearly identical to the one used to deduce (2.19). When $|\beta|=0$, we have

$$\begin{aligned}\int_\Omega T(t)\partial_x^\alpha I(t)\partial_x^\alpha V(t) &\le ||T(t)||_\infty\int_\Omega \partial_x^\alpha I(t)\partial_x^\alpha V(t)\\ &\le C_{t^*}\left(||\partial_x^\alpha I(t)||_2^2+||\partial_x^\alpha V(t)||_2^2\right)\\ &\le C_{t^*}\left(||I(t)||^2_{H^\ell}+||V(t)||^2_{H^\ell}\right).\end{aligned}$$

Again, when $|\beta|=\ell$, we have

$$\begin{aligned}\int_\Omega V(t)\partial_x^\alpha T(t)\partial_x^\alpha I(t) &\le ||V(t)||_\infty\int_\Omega \partial_x^\alpha T(t)\partial_x^\alpha I(t)\\ &\le C_{t^*}\left(||\partial_x^\alpha T(t)||_2^2+||\partial_x^\alpha I(t)||_2^2\right)\\ &\le C_{t^*}\left(||T(t)||^2_{H^\ell}+||I(t)||^2_{H^\ell}\right).\end{aligned}$$

In all other cases, we turn again to Sobolev's embedding theorem. When $|\beta|\le\lfloor m/2\rfloor$, we see

$$\begin{aligned}\int_\Omega \partial_x^\alpha I(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) &\le \left|\left|\partial_x^\beta T(t)\right|\right|_\infty\int_\Omega \partial_x^\alpha I(t)\partial_x^\gamma V(t)\\ &\le \frac{\left|\left|\partial_x^\beta T(t)\right|\right|_\infty}{2}\left(||\partial_x^\alpha I(t)||_2^2+||\partial_x^\gamma V(t)||_2^2\right)\\ &\le C_{t^*}\left(||I(t)||^2_{H^\ell}+||V(t)||^2_{H^\ell}\right)\end{aligned}$$

and when $|\gamma| \leq \lfloor m/2 \rfloor$,

$$\begin{aligned}\int_\Omega \partial_x^\alpha I(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) &\leq ||\partial_x^\gamma V(t)||_\infty \int_\Omega \partial_x^\alpha I(t)\partial_x^\beta T(t) \\ &\leq \frac{||\partial_x^\gamma V(t)||_\infty}{2}\left(||\partial_x^\alpha I(t)||_2^2 + \left|\left|\partial_x^\beta T(t)\right|\right|_2^2\right) \\ &\leq C_{t^*}\left(||T(t)||_{H^\ell}^2 + ||I(t)||_{H^\ell}^2\right).\end{aligned}$$

Thus every member of the sum is bounded by $C_{t^*}\left(||T(t)||_{H^\ell}^2 + ||I(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\right)$ and so the sum is bounded by another multiple of this term. Combining this bound with (2.20) gives

$$\frac{d}{dt}\,||\partial_x^\alpha I(t)||_2^2 \leq C_{t^*}\big(\,||T(t)||_{H^\ell}^2 + ||I(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\,\big) - 2D_I\,||\partial_x^\alpha \nabla I(t)||_2^2\,.$$

Summing over all $|\alpha| \leq \ell$ yields,

$$\begin{aligned}\frac{d}{dt}\,||I(t)||_{H^\ell}^2 \leq C_{t^*}\big(\,||T(t)||_{H^\ell}^2 + ||I(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\,\big) - 2D_I\,||I(t)||_{H^{\ell+1}}^2\,, \\ 0 \leq \ell \leq m,\ t \in (0, t^*].\end{aligned} \tag{2.21}$$

Finally, starting from (2.8), we apply $\partial_x^\alpha$ then multiply through by $\partial_x^\alpha V$ and integrate, yielding

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\,||\partial_x^\alpha V(t)||_2 + D_V\,||\partial_x^\alpha \nabla V(t)||_2 &= N\mu_I \int_\Omega \partial_x^\alpha V(t)\partial_x^\alpha I(t) - \mu_V\,||\partial_x^\alpha V(t)||_2^2 \\ &\leq \frac{N\mu_I}{2}\left(||\partial_x^\alpha I(t)||_2^2 + ||\partial_x^\alpha V(t)||_2^2\right) - \mu_V\,||\partial_x^\alpha V(t)||_2^2 \\ &\leq C_{t^*}\big(\,||\partial_x^\alpha I(t)||_2^2 + ||\partial_x^\alpha V(t)||_2^2\,\big).\end{aligned} \tag{2.22}$$

Rearranging (2.22) and summing over all $|\alpha| \leq \ell$ produces,

$$\frac{d}{dt}\,||V(t)||_{H^\ell}^2 \leq C_{t^*}\big(\,||I(t)||_{H^\ell}^2 + ||V(t)||_{H^\ell}^2\,\big) - 2D_V\,||V(t)||_{H^{\ell+1}}\,,\quad 0 \leq \ell \leq m,\quad t \in (0, t^*]. \tag{2.23}$$

Adding (2.19),(2.21) and (2.23), yields

$$\frac{d}{dt}\phi_\ell(t) \leq C_{t^*}(1 + \phi_\ell(t)) - 2D\phi_{\ell+1}(t),\ \ell \leq m,\ t \in (0, t^*].$$

Thus, for $m \geq 5$, (2.17) is proven with $\xi_\ell = 2$ for all $\ell$.

It remains to prove (2.17) for $m = 2, 3, 4$. These are the cases in which Sobolev's embedding theorem cannot immediately help since we are not guaranteed that $m - 1 - \lfloor m/2 \rfloor > \frac{3}{2}$. However, we only required this condition to deduce the bounds for $T$ and $I$. Thus we need only reconsider those equations. In all cases, the derivations of bounds for $V$ are all identical as above and thus (2.23) still holds for $m = 2, 3, 4$.

This is why the proof becomes more difficult in $\mathbb{R}^n$ when $n$ is large. For $n = 3$, we need consider 3 special cases: $m = 2, 3, 4$. In general, the special cases will be those $m \geq 2$ such that $m - 1 - \lfloor m/2 \rfloor \leq \frac{n}{2}$. It is easily checked that for odd $n$, there are $n$ special cases to consider and for even $n$ there are $n + 1$ special cases. These can be handled in the manner presented below. However, even in $\mathbb{R}^3$ it becomes quite tedious.

We begin with $m = 2$. Since the bound has already been proven when $\ell = 0, 1$, we need only consider $\ell = m = 2$. Let $\alpha$ be a multi-index of order $\ell = 2$. Then, starting from (2.5), we get

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\,||\partial_x^\alpha T(t)||_2^2 + D_T\,||\partial_x^\alpha \nabla T(t)||_2^2 \leq &\frac{1}{2}\left(||\partial_x^\alpha \lambda||_2^2 + ||\partial_x^\alpha T(t)||_2^2\right) - \mu_T\,||\partial_x^\alpha T(t)||_2^2 \\ &- k\sum_{j=0}^{2}\sum_{\substack{|\beta|=j\\ \beta+\gamma=\alpha}}\binom{\alpha}{\beta}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t).\end{aligned} \tag{2.24}$$

Again we look for bounds on the integrals in the sum. We see that when $|\beta| = 0$ or $|\beta| = 2$, we may deal with integral in the exact same way as above. The trouble occurs when $|\beta| = |\gamma| = 1$. In this case, we integrate by parts to see

$$\begin{aligned}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) &= -\int_\Omega T(t)\partial_x^\beta\left(\partial_x^\alpha T(t)\partial_x^\gamma V(t)\right) \\ &= -\left(\int_\Omega T(t)\left[\partial_x^{\alpha+\beta}T(t)\partial_x^\gamma V(t) + \partial_x^\alpha T(t)\partial_x^\alpha V(t)\right]\right) \\ &\leq T_M\left(\int_\Omega \partial_x^{\alpha+\beta}T(t)\partial_x^\gamma V(t) + \int_\Omega \partial_x^\alpha T(t)\partial_x^\alpha V(t)\right),\end{aligned} \tag{2.25}$$

where $T_M$ is the uniform bound for $T$ we found earlier. Having converted this into two integrals, we deal with each separately. For the second, we simply note that

$$\int_\Omega \partial_x^\alpha T(t)\partial_x^\alpha V(t) \leq \frac{1}{2}\left(||\partial_x^\alpha T(t)||_2^2 + ||\partial_x^\alpha V(t)||_2^2\right).$$

We take more care with the first term. We may still use the Cauchy-Schwarz Inequality to arrive at

$$\int_\Omega \partial_x^{\alpha+\beta} T(t) \partial_x^\gamma V(t) \le \left|\left|\partial_x^{\alpha+\beta} T(t)\right|\right|_2 ||\partial_x^\gamma V(t)||_2 .$$

Next we apply Young's Inequality, with arbitrary $\eta > 0$ to see

$$\begin{aligned}\int_\Omega \partial_x^{\alpha+\beta} T(t) \partial_x^\gamma V(t) &\le \frac{\eta \left|\left|\partial_x^{\alpha+\beta} T(t)\right|\right|_2^2}{2} + \frac{||\partial_x^\gamma V(t)||_2^2}{2\eta} \\ &\le \frac{\eta\, ||\partial_x^\alpha \nabla T(t)||_2^2}{2} + \frac{||\partial_x^\gamma V(t)||_2^2}{2\eta}.\end{aligned}$$

We will choose $\eta$ later. Then combining these bounds with (2.24) gives

$$\frac{d}{dt} ||\partial_x^\alpha T(t)||_2^2 \le C_{t^*}\left(1 + ||T(t)||_{H^2}^2 + ||V(t)||_{H^2}^2\right) - \left(2D_T - \frac{k\eta T_M}{2} \sum_{|\beta|=1} \binom{\alpha}{\beta}\right) ||\partial_x^\alpha \nabla T(t)||_2^2 ,$$

where all sufficiently low order derivatives have been grouped into the $H^2-$norms. Now to fulfill (2.17) we need

$$2D_T - \frac{k\eta T_M}{2} \sum_{|\beta|=1} \binom{\alpha}{\beta} > D.$$

It is sufficient to require that

$$\eta < \frac{2D}{kT_M \sum_{|\beta|=1} \binom{\alpha}{\beta}}.$$

Choosing such $\eta$, we may conclude that

$$\frac{d}{dt} ||\partial_x^\alpha T(t)||_2^2 \le C_{t^*}\left(1 + ||T(t)||_{H^2}^2 + ||V(t)||_{H^2}^2\right) - D\xi_2\, ||\partial_x^\alpha \nabla T(t)||_2^2 , \quad t \in (0, t^*],$$

for some $\xi_2 > 1$. Summing over all such multi-indices $|\alpha| \le 2$, we arrive at

$$\frac{d}{dt} ||T(t)||_{H^2}^2 \le C_{t^*}\left(1 + ||T(t)||_{H^2}^2 + ||V(t)||_{H^2}^2\right) - D\xi_2\, ||T(t)||_{H^3}^2 , \quad t \in (0, t^*]. \tag{2.26}$$

Next, we consider (2.6). From (2.20), we easily deduce

$$\begin{aligned}\frac{1}{2}\frac{d}{dt} ||\partial_x^\alpha I(t)||_2^2 + D_I\, ||\partial_x^\alpha \nabla I(t)||_2^2 = k \sum_{j=0}^{2} \sum_{\substack{|\beta|=j \\ \beta+\gamma=\alpha}} \binom{\alpha}{\beta} \int_\Omega \partial_x^\alpha I(t) \partial_x^\beta T(t) \partial_x^\gamma V(t) \\ - \mu_I\, ||\partial_x^\alpha I(t)||_2^2 .\end{aligned} \tag{2.27}$$

Again, the goal is to bound the integral

$$\int_\Omega \partial_x^\alpha I(t)\partial_x^\beta T(t)\partial_x^\gamma V(t)$$

in the case that $|\beta| = |\gamma| = 1$. We do this with a method similar to that used above:

$$\begin{aligned}\int_\Omega \partial_x^\alpha I(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) &= -\int_\Omega T(t)\partial_x^\beta\big(\partial_x^\alpha I(t)\partial_x^\gamma V(t)\big)\\ &= -\left(\int_\Omega T(t)\big[\partial_x^{\alpha+\beta} I(t)\partial_x^\gamma V(t) + \partial_x^\alpha I(t)\partial_x^\alpha V(t)\big]\right)\\ &\leq T_M\left(\int_\Omega \partial_x^{\alpha+\beta} I(t)\partial_x^\gamma V(t) + \int_\Omega \partial_x^\alpha I(t)\partial_x^\alpha V(t)\right).\end{aligned}$$

Using the same methods as we did above (Young's Inequality, etc) and recombining with results from (2.20), we derive

$$\frac{d}{dt}\,||\partial_x^\alpha I(t)||_2^2 \leq C_{t^*}\big(\,||T(t)||_{H^2}^2 + ||I(t)||_{H^2}^2 + ||V(t)||_{H^2}^2\,\big) - \left(2D_I - \frac{k\eta T_M}{2}\sum_{|\beta|=1}\binom{\alpha}{\beta}\right)||\partial_x^\alpha \nabla I(t)||_2^2\,,$$

where $\eta$ is another an arbitrary positive number we may choose. In fact, using the same choice for $\eta$, and summing over all $\alpha$ gives

$$\frac{d}{dt}\,||I(t)||_{H^2}^2 \leq C_{t^*}\big(\,||T(t)||_{H^2}^2 + ||I(t)||_{H^2}^2 + ||V(t)||_{H^2}^2\,\big) - D\xi_2\,||I(t)||_{H^3}^2\,,\quad t\in(0,t^*] \tag{2.28}$$

for some $\xi_2 > 1$. Adding (2.23),(2.26) and (2.28) gives that

$$\frac{d}{dt}\phi_2(t) \leq C_{t^*}\,(1+\phi_2(t)) - D\xi_2\phi_3(t), \quad t\in(0,t^*].$$

Then since the analagous equations for $\ell = 0, 1$ hold, this proves (2.17) for $m = 2$.

For $m = 3$, to prove the proposition for each $\ell \leq m$, it suffices to look at $\ell = 3$. The instances when $\ell = 0, 1, 2$ follow from the above work. We proceed as usual, letting $|\alpha| = 3$:

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\,||\partial_x^\alpha T(t)||_2^2 + D_T\,||\partial_x^\alpha \nabla T(t)||_2^2 \leq &\frac{1}{2}\left(||\partial_x^\alpha \lambda||_2^2 + ||\partial_x^\alpha T(t)||_2^2\right) - \mu_T\,||\partial_x^\alpha T(t)||_2^2\\ &- k\sum_{j=0}^{3}\sum_{\substack{|\beta|=j\\ \beta+\gamma=\alpha}}\binom{\alpha}{\beta}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t).\end{aligned} \tag{2.29}$$

In this situation there are two troubling cases: $|\beta| = 1, |\gamma| = 2$ and $|\beta| = 2, |\gamma| = 1$; the other cases ($|\beta| = 0, |\beta| = 3$) can be handled as above. If $|\beta| = 1$, we perform steps identical to (2.25) to arrive at

$$\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) \leq ||T(t)||_\infty \left(\int_\Omega \partial_x^{\alpha+\beta} T(t)\partial_x^\gamma V(t) + \int_\Omega \partial_x^\alpha T(t)\partial_x^\alpha V(t)\right).$$

Further, we restrict the second integral above by

$$\int_\Omega \partial_x^\alpha T(t)\partial_x^\alpha V(t) \leq \frac{1}{2}\left(||\partial_x^\alpha T(t)||_2 + ||\partial_x^\alpha V(t)||_2\right),$$

as before. For the first integral, we again use Young's Inequality to see

$$\begin{aligned}\int_\Omega \partial_x^{\alpha+\beta} T(t)\partial_x^\gamma V(t) &\leq \frac{\eta\left|\left|\partial_x^{\alpha+\beta} T(t)\right|\right|_2^2}{2} + \frac{||\partial_x^\gamma V(t)||_2^2}{2\eta}\\ &\leq \frac{\eta\,||\partial_x^\alpha \nabla T(t)||_2^2}{2} + \frac{||\partial_x^\gamma V(t)||_2^2}{2\eta}.\end{aligned}$$

Thus in this case we may choose $\eta$ very similarly. Using (2.29), we arrive at

$$\frac{d}{dt}||\partial_x^\alpha T(t)||_2^2 \leq C_{t^*}\left(1 + ||T(t)||_{H^3}^2 + ||V(t)||_{H^3}^2\right) - \left(2D_T - \frac{k\eta\,||T(t)||_\infty}{2}\sum_{|\beta|=1}\binom{\alpha}{\beta}\right)||\partial_x^\alpha \nabla T(t)||_2^2$$

so we require

$$\eta < \frac{2D}{kT_M\sum_{|\beta|=1}\binom{\alpha}{\beta}}$$

In the case that $|\gamma| = 1$, we use the same technique. Again, we are only truly concerned with bounding the term

$$\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t).$$

But now, when we integrate by parts, we must choose to remove $\partial_x^\gamma$ from $V$:

$$\begin{aligned}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) &= -\int_\Omega V(t)\partial_x^\gamma\left(\partial_x^\alpha T(t)\partial_x^\beta T(t)\right)\\ &\leq ||V(t)||_\infty\left(\int_\Omega \partial_x^{\alpha+\gamma} T(t)\partial_x^\beta T(t) + \int_\Omega \partial_x^\alpha T(t)\partial_x^\alpha T(t)\right).\end{aligned}$$

Then, following through, we see

$$\begin{aligned}\int_\Omega \partial_x^{\alpha+\gamma}T(t)\partial_x^\beta T(t) &\leq \frac{\eta\left|\left|\partial_x^{\alpha+\gamma}T(t)\right|\right|_2^2}{2} + \frac{\left|\left|\partial_x^\beta T(t)\right|\right|_2^2}{2\eta} \\ &\leq \frac{\eta\,||\partial_x^\alpha \nabla T(t)||_2^2}{2} + \frac{\left|\left|\partial_x^\beta T(t)\right|\right|_2^2}{2\eta},\end{aligned}$$

for yet another arbitrary $\eta > 0$. Here we require that

$$\eta < \frac{2D}{kV_M \sum_{|\beta|=2}\binom{\alpha}{\beta}},$$

where $V_M = \sup_{t\in(0,t^*]} ||V(t)||_\infty$. We note that the supremum is finite since $||V(t)||_\infty$ remains bounded on the interval. Thus, having enforced two bounds on $\eta$, we may take the minimum of the two in order to satisfy both. Compiling all of this into (2.29) yields

$$\frac{d}{dt}\,||\partial_x^\alpha T(t)||_2^2 \leq C_{t^*}\left(1 + ||T(t)||_{H^3}^2 + ||V(t)||_{H^3}^2\right) - D\xi_3\,||\partial_x^\alpha \nabla T(t)||_2^2\,, \quad t\in(0,t^*],$$

and summing over all $|\alpha| \leq 3$ gives

$$\frac{d}{dt}\,||T(t)||_{H^3}^2 \leq C_{t^*}\left(1 + ||T(t)||_{H^3}^2 + ||V(t)||_{H^3}^2\right) - D\xi_3\,||T(t)||_{H^4}^2\,, \quad t\in(0,t^*]. \tag{2.30}$$

Following the procedure, we see that

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\,||\partial_x^\alpha I(t)||_2^2 + D_I\,||\partial_x^\alpha \nabla I(t)||_2^2 = k\sum_{j=0}^{3}\sum_{\substack{|\beta|=j\\ \beta+\gamma=\alpha}}\binom{\alpha}{\beta}\int_\Omega \partial_x^\alpha I(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) \\ - \mu_I\,||\partial_x^\alpha I(t)||_2^2\,,\end{aligned} \tag{2.31}$$

and we must bound the integral

$$\int_\Omega \partial_x^\alpha I(t)\partial_x^\beta T(t)\partial_x^\gamma V(t)$$

in the case that $|\beta| = 1$ or $|\beta| = 2$. We do this in a predictable way: if $|\beta| = 1$ we integrate by parts to remove $\partial_x^\beta$ from $T$ and if $|\beta| = 2$ we integrate by parts to remove $\partial_x^\gamma$ from $V$. Performing these steps, we eventually come to

$$\frac{d}{dt}\,||\partial_x^\alpha I(t)||_2^2 \leq C_{t^*}\left(||T(t)||_{H^3}^2 + ||I(t)||_{H^3}^2 + ||V(t)||_{H^3}^2\right) - D\xi_3\,||\partial_x^\alpha \nabla I(t)||_2^2\,, \quad t\in(0,t^*],$$

which, after summing over $\alpha$, leads to

$$\frac{d}{dt}\,||I(t)||^2_{H^3} \leq C_{t^*}\big(\,||T(t)||^2_{H^3} + ||I(t)||^2_{H^3} + ||V(t)||^2_{H^3}\,\big) - D\xi_3\,||\nabla I(t)||^2_{H^3}\,, \quad t \in (0, t^*]. \tag{2.32}$$

Adding (2.23),(2.30),(2.32) yields

$$\frac{d}{dt}\phi_3(t) \leq C_{t^*}\left(1 + \phi_3(t)\right) - D\xi_3\phi_4(t), \quad t \in (0, t^*],$$

which proves (2.17) for $m = 3$.

Finally we address the case that $m = 4$. Here we need only consider $\ell = 4$ since the derivation for $\ell = 0, 1, 2, 3$ follow directly from the above work. When $\ell = 4$, we have

$$\begin{aligned}\frac{1}{2}\frac{d}{dt}\,||\partial_x^\alpha T(t)||_2^2 + D_T\,||\partial_x^\alpha \nabla T(t)||_2^2 \leq &\frac{1}{2}\left(||\partial_x^\alpha \lambda||_2^2 + ||\partial_x^\alpha T(t)||_2^2\right) - \mu_T\,||\partial_x^\alpha T(t)||_2^2 \\ &- k\sum_{j=0}^{4}\sum_{\substack{|\beta|=j\\ \beta+\gamma=\alpha}}\binom{\alpha}{\beta}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t).\end{aligned} \tag{2.33}$$

Attempting to bound the integrals, we see that when $|\beta| = 0, 4$, we can simply take the supremum of the term without a derivative and bound the remaining integral as before. When $|\beta| = 1, 3$, we see that either $m - 1 - |\beta| > \frac{3}{2}$ or $m - 1 - |\gamma| > \frac{3}{2}$. In either case, we may use the Sobolev embedding theorem and proceed as before. There is only trouble when $|\beta| = |\gamma| = 2$. In this case, we bound the integral

$$\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t).$$

To do so we integrate by parts to get

$$\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) = -\int_\Omega \partial_x^{\beta-1}T(t)\partial_x^1\big[\partial_x^\alpha T(t)\partial_x^\gamma V(t)\big],$$

where $\partial_x^1, \partial_x^{\beta-1}$ are the first order spatial derivatives such that $\partial_x^\beta = \partial_x^1\partial_x^{\beta-1}$. Now $|\beta - 1| = 1$ so $m - 1 - |\beta - 1| = 2 > \frac{3}{2}$ and, by the Sobolev embedding theorem, $\partial_x^{\beta-1}T(t)$ remains bounded. Thus

$$\begin{aligned}\int_\Omega \partial_x^\alpha T(t)\partial_x^\beta T(t)\partial_x^\gamma V(t) &\leq \left|\left|\partial_x^{\beta-1}T(t)\right|\right|_\infty \int_\Omega \partial_x^1\big[\partial_x^\alpha T(t)\partial_x^\gamma V(t)\big] \\ &= \left|\left|\partial_x^{\beta-1}T(t)\right|\right|_\infty \left(\int_\Omega \partial_x^{\alpha+1}T(t)\partial_x^\gamma V(t) + \int_\Omega \partial_x^\alpha T(t)\partial_x^{\gamma+1}V(t)\right).\end{aligned}$$

We treat the two integrals separately as before. For the latter, we use

$$\int_\Omega \partial_x^\alpha T(t) \partial_x^{\gamma+1} V(t) \le \frac{1}{2}\left( ||\partial_x^\alpha T(t)||_2^2 + \left|\left|\partial_x^{\gamma+1} V(t)\right|\right|_2^2 \right),$$

while for the former, we take $\eta > 0$ and use

$$\int_\Omega \partial_x^{\alpha+1} T(t) \partial_x^\gamma V(t) \le \frac{\eta \left|\left|\partial_x^{\alpha+1} T(t)\right|\right|_2^2}{2} + \frac{\partial_x^\gamma V(t)}{2\eta} \le \frac{\eta \, ||\partial_x^\alpha \nabla T(t)||_2^2}{2} + \frac{\partial_x^\gamma V(t)}{2\eta}.$$

Combining all of this with (2.33) and rearranging terms gives

$$||\partial_x^\alpha T(t)||_2^2 \le C_{t^*} \left( 1 + ||T(t)||_{H^4}^2 + ||V(t)||_{H^4}^2 \right) - D\xi_4 \, ||\partial_x^\alpha \nabla T(t)||_2^2$$

where

$$\xi_4 \ge \left( 2 - \frac{k\eta \left|\left|\partial_x^{\beta-1} T(t)\right|\right|_\infty}{2D} \sum_{|\beta|=2} \binom{\alpha}{\beta} \right).$$

Thus to force $\xi_4 > 1$, we take

$$\eta < \frac{2D}{\left[\sup_{t\in(0,t^*]} \left|\left|\partial_x^{\beta-1} T(t)\right|\right|_\infty\right] k \sum_{|\beta|=2} \binom{\alpha}{\beta}}.$$

For such $\eta$, we sum over all $|\alpha| \le 4$ to get

$$\frac{d}{dt} ||T(t)||_{H^4}^2 \le C_{t^*} \left( 1 + ||T(t)||_{H^4}^2 + ||V(t)||_{H^4}^2 \right) - D\xi_4 \, ||T(t)||_{H^5}^2, \quad t \in (0, t^*]. \tag{2.34}$$

We turn again to (2.6) and derive

$$\frac{1}{2}\frac{d}{dt} ||\partial_x^\alpha I(t)||_2^2 + D_I \, ||\partial_x^\alpha \nabla I(t)||_2^2 = k \sum_{j=0}^{4} \sum_{\substack{|\beta|=j \\ \beta+\gamma=\alpha}} \binom{\alpha}{\beta} \int_\Omega \partial_x^\alpha I(t) \partial_x^\beta T(t) \partial_x^\gamma V(t) - \mu_I \, ||\partial_x^\alpha I(t)||_2^2. \tag{2.35}$$

We realize again that, in bounding the integrals, we only run into trouble with $|\beta| = |\gamma| = 2$. In this case, we use the same method as above (with the same $\eta$) to arrive at

$$||\partial_x^\alpha I(t)||_2^2 \le C_{t^*} \left( ||T(t)||_{H^4}^2 + ||I(t)||_{H^4}^2 + ||V(t)||_{H^4}^2 \right) - D\xi_4 \, ||\partial_x^\alpha \nabla I(t)||_2^2,$$

which leads immediately to

$$||I(t)||_{H^4}^2 \leq C_{t^*}\left(||T(t)||_{H^4}^2 + ||I(t)||_{H^4}^2 + ||V(t)||_{H^4}^2\right) - D\xi_4 \, ||I(t)||_{H^5}^2 \,, \quad t \in (0, t^*]. \tag{2.36}$$

Summing (2.23),(2.34) and (2.36) yields

$$\frac{d}{dt}\phi_4(t) \leq C_{t^*}\left(1 + \phi_4(t)\right) - D\xi_4\phi_5(t), \quad t \in (0, t^*],$$

which proves (2.17) for $m = 4$.

Thus for $m \geq 2$, beginning from our assumption that $T(\cdot, t), I(\cdot, t), V(\cdot, t) \in H^\ell(\Omega)$ for $0 \leq \ell \leq m-1$, we have proven that

$$\frac{d}{dt}\phi_\ell(t) \leq C_{t^*}\left(1 + \phi_\ell(t)\right) - D\xi_\ell\phi_{\ell+1}(t), \quad 0 \leq \ell \leq m, \quad t \in (0, t^*].$$

Finally, to prove high order regularity, define

$$M(t) = \sum_{\ell=0}^{m} \frac{(Dt)^\ell}{\ell!}\phi_\ell(t), \quad t \in (0, t^*].$$

Then differentiating, we see

$$\begin{aligned} M'(t) &= \sum_{\ell=1}^{m} \frac{D^\ell t^{\ell-1}}{(\ell-1)!}\phi_\ell(t) + \sum_{\ell=0}^{m} \frac{(Dt)^\ell}{\ell!}\frac{d}{dt}\phi_\ell(t) \\ &= \sum_{\ell=0}^{m-1} \frac{D^{\ell+1} t^\ell}{\ell!}\phi_{\ell+1}(t) + \sum_{\ell=0}^{m} \frac{(Dt)^\ell}{\ell!}\frac{d}{dt}\phi_\ell(t). \end{aligned}$$

Now we use (2.17) to find

$$\begin{aligned} M'(t) &\leq \sum_{\ell=0}^{m-1} \frac{D^{\ell+1} t^\ell}{\ell!}\phi_{\ell+1}(t) + \sum_{\ell=0}^{m} \frac{(Dt)^\ell}{\ell!}\left\{C_{t^*}\left(1 + \phi_\ell(t)\right) - D\xi_\ell\phi_{\ell+1}(t)\right\} \\ &= C_{t^*}\left(\sum_{\ell=0}^{m} \frac{(Dt)^\ell}{\ell!} + \sum_{\ell=0}^{m} \frac{(Dt)^\ell}{\ell!}\phi_\ell(t)\right) - \left(\sum_{\ell=0}^{m-1} D^{\ell+1}(\xi_\ell - 1)\frac{t^\ell}{\ell!}\phi_{\ell+1}(t)\right) - D^{m+1}\xi_m\frac{t^m}{m!}\phi_m(t). \end{aligned}$$

Next, we note that $\xi_\ell - 1 > 0$, and so

$$\begin{aligned} M'(t) &\leq C_{t^*}\left(\sum_{\ell=0}^{m}\frac{(Dt)^\ell}{\ell!} + \sum_{\ell=0}^{m}\frac{(Dt)^\ell}{\ell!}\phi_\ell(t)\right) \\ &= C_{t^*}(1+M(t)), \quad t \in (0,t^*]. \end{aligned}$$

An application of Gronwall's Inequality yields

$$\begin{aligned} M(t) &\leq C_{t^*}(1+M(0)e^t) \\ &\leq C_{t^*}(1+M(0)), \quad t \in (0,t^*]. \end{aligned} \tag{2.37}$$

However, the right hand side of (2.37) is finite and each term in $M(t)$ is nonnegative so we see that (2.37) implies that

$$\frac{(Dt)^m}{m!}\phi_m(t) \leq C_{t^*}(1+M(0)) \quad \Longrightarrow \quad \phi_m(t) \leq \frac{m!C_{t^*}(1+M(0))}{(Dt)^m}, \quad t \in (0,t^*].$$

Further, each of $||T(t)||^2_{H^m}, ||I(t)||^2_{H^m}, ||V(t)||^2_{H^m}$ is bounded by $\phi_m(t)$ on $(0,t^*]$. Thus for all $t \in (0,t^*]$, we have $T(\cdot,t), I(\cdot,t), V(\cdot,t) \in H^m(\Omega)$. This completes the induction step.

From this we may conclude that for all $m \in \mathbb{N}\cup\{0\}$, $T(\cdot,t), I(\cdot,t), V(\cdot,t) \in H^m(\Omega)$ which completes the proof. ■

# CHAPTER 3
# LARGE TIME ASYMPTOTICS

In this section we present some large time asymptotic results for our system. To establish these results, we use Corollaries 2.2.1 and 2.2.2 several times so it is helpful to recall them here.

**Corollary 2.2.1** If $u(x,t)$ satisfies the differential equation

$$\begin{aligned} &(\partial_t - D_u\Delta)u = g(x,t), \qquad &&(x,t) \in \Omega \times (0,t^*], \\ &u(x,0) = u_0(x), &&x \in \Omega. \end{aligned}$$

then

$$||u(t)||_\infty \leq ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau, \quad \text{for all } t \in [0,t^*].$$

**Corollary 2.2.2** Assume that $u(x,t)$ satisfies the differential inequality

$$\begin{aligned} &(\partial_t - D_u\Delta)u \leq g(x,t), \qquad &&(x,t) \in \Omega \times (0,t^*], \\ &u(x,0) = u_0(x), &&x \in \Omega. \end{aligned}$$

Then $u(x,t)$ satisfies the same inequality as in Corollary 2.2.1. That is,

$$||u(t)||_\infty \leq ||u_0||_\infty + \int_0^t ||g(\tau)||_\infty \, d\tau, \quad \text{for all } t \in [0,t^*].$$

Using these corollaries and enforcing some conditions on our parameters, we attempt to determine some asymptotic behavior of the system.

## 3.1 Supremum-Norm Asymptotics

**Theorem 3.1 (Asymptotic Behavior: Case 1).** Let $T, I, V$ satisfy (2.1) and assume that $T_0, I_0, V_0 \in L^\infty(\Omega)$, $\mu_V > \mu_I$ and $R_1 = \frac{||\lambda||_\infty Nk}{\mu_T \mu_I} < 1$. Then there is an $r > 0$ such that

$$\lim_{t\to\infty} e^{rt} \, ||V(t)||_\infty = 0 \quad \text{ and } \quad \lim_{t\to\infty} e^{rt} \, ||I(x)||_\infty = 0.$$

**Proof.** Assume $T, I, V$ satisfy (2.1), $\mu_V > \mu_I$ and $R_1 < 1$. We first consider the $T$-equation. Rearraging terms and dropping the negative term on the right hand side, we see

$$\partial_t T + \mu_T T - D_T \Delta T \leq \lambda(x).$$

Use of an integrating factor gives

$$\partial_t \left[e^{\mu_T t} T\right] - D_T \Delta \left[e^{\mu_T t} T\right] \leq \lambda(x) e^{\mu_T t} \quad \Longrightarrow \quad (\partial_t - D_T \Delta) \left[e^{\mu_T t} T\right] \leq \lambda(x) e^{\mu_T t}.$$

Corollary 2.2 then implies that

$$\left|\left|e^{\mu_T t} T(t)\right|\right|_\infty \leq \left|\left|e^{\mu_T \cdot 0} T_0\right|\right|_\infty + \int_0^t \left|\left|\lambda e^{\mu_T \tau}\right|\right|_\infty d\tau.$$

However, since the supremum norms in the previous line are taken over spatial variables and $e^{\mu_T t}$ is independent of space, we may pull those terms outside of the norms, and then evaluate the integral on the right hand side yielding

$$e^{\mu_T t} \left|\left|T(t)\right|\right|_\infty \leq \left|\left|T_0\right|\right|_\infty + \frac{\left|\left|\lambda\right|\right|_\infty}{\mu_T} \left(e^{\mu_T t} - 1\right) \implies \left|\left|T(t)\right|\right|_\infty \leq e^{-\mu_T t} \left|\left|T_0\right|\right|_\infty + \frac{\left|\left|\lambda\right|\right|_\infty}{\mu_T} \left(1 - e^{-\mu_T t}\right).$$

But $0 \leq 1 - e^{-\mu_T t} \leq 1$ for $t > 0$, so we set $\tilde{T}(t) = e^{-\mu_T t} \left|\left|T_0\right|\right|_\infty + \frac{||\lambda||_\infty}{\mu_T}$ and

$$\left|\left|T(t)\right|\right|_\infty \leq \tilde{T}(t), \;\; t > 0. \tag{3.1}$$

With this in mind, we turn our attention to the $I$ equation. Using (3.1), we immediately arrive at

$$\partial_t I - D_I \Delta I \leq kV\tilde{T}(t) - \mu_I I.$$

Using an integrating factor again, we see

$$(\partial_t - D_I \Delta) \left[e^{\mu_I t} I\right] \leq kV\tilde{T}(t) e^{\mu_I t}.$$

An application of Corollary 2.2 gives

$$\left|\left|e^{\mu_I t} I(t)\right|\right|_\infty \leq \left|\left|I_0\right|\right|_\infty + k \int_0^t \tilde{T}(\tau) e^{\mu_I \tau} \left|\left|V(\tau)\right|\right|_\infty d\tau$$

which leads to

$$||I(t)||_\infty \le e^{-\mu_I t} ||I_0||_\infty + ke^{-\mu_I t} \int_0^t \tilde{T}(\tau) e^{\mu_I \tau} ||V(\tau)||_\infty \, d\tau. \tag{3.2}$$

Finally, we turn to the $V$ equation. We seek a bound on $V$ using the same methods as we used for the $T$ and $I$ equations above. Rearranging terms and introducing an integrating factor yields

$$(\partial_t - D_V \Delta) \left[ e^{\mu_V t} V \right] = N \mu_I I e^{\mu_V t}.$$

An application of Corollary 2.1 gives

$$\left|\left| e^{\mu_V t} V(t) \right|\right|_\infty \le ||V_0||_\infty + N\mu_I \int_0^t e^{\mu_V \tau} ||I(\tau)||_\infty \, d\tau$$

which then implies

$$||V(t)||_\infty \le e^{-\mu_V t} ||V_0||_\infty + N\mu_I e^{-\mu_V t} \int_0^t e^{\mu_V \tau} ||I(\tau)||_\infty \, d\tau. \tag{3.3}$$

Our next step is to insert the bound derived in (3.2) into (3.3). Doing this yields

$$\begin{aligned} ||V(t)||_\infty \le e^{-\mu_V t} ||V_0||_\infty &+ \\ & N\mu_I e^{-\mu_V t} \int_0^t e^{\mu_V \tau} \left( e^{-\mu_I \tau} ||I_0||_\infty + ke^{-\mu_I \tau} \int_0^\tau \tilde{T}(s) e^{\mu_I s} ||V(s)||_\infty \, ds \right) d\tau \end{aligned}$$

which we may reduce to

$$||V(t)||_\infty \le A_1 e^{-\mu_V t} + A_2 e^{-\mu_I t} + N\mu_I k e^{-\mu_V t} \int_0^t \int_0^\tau \tilde{T}(s) e^{(\mu_V - \mu_I)\tau} e^{\mu_I s} ||V(s)||_\infty \, ds d\tau,$$

for some constants $A_1, A_2$. Rearranging gives

$$||V(t)||_\infty \le A_1 e^{-\mu_V t} + A_2 e^{-\mu_I t} + N\mu_I k \int_0^t \int_0^\tau \tilde{T}(s) e^{-\mu_I(\tau - s)} e^{-\mu_V(t-\tau)} ||V(s)||_\infty \, ds d\tau. \tag{3.4}$$

Now since $\mu_V > \mu_I$, we see that $e^{-\mu_V(t-\tau)} \le e^{-\mu_I(t-\tau)}$. Thus

$$\begin{aligned} ||V(t)||_\infty &\le A_1 e^{-\mu_V t} + A_2 e^{-\mu_I t} + N\mu_I k \int_0^t \int_0^\tau \tilde{T}(s) e^{-\mu_I(\tau - s)} e^{-\mu_I(t-\tau)} ||V(s)||_\infty \, ds d\tau \\ &= A_1 e^{-\mu_V t} + A_2 e^{-\mu_I t} + N\mu_I k \int_0^t \int_0^\tau \tilde{T}(s) e^{-\mu_I(t-s)} ||V(s)||_\infty . \end{aligned}$$

We change the order of integration for the double integral:

$$||V(t)||_\infty \leq A_1 e^{-\mu_V t} + A_2 e^{-\mu_I t} + N\mu_I k \int_0^t \int_s^t \tilde{T}(s) e^{-\mu_I(t-s)} \, ||V(s)||_\infty \, d\tau ds.$$

Evaluating the inner integral and multiplying through by $e^{\mu_I t}$ gives

$$\left|\left|e^{\mu_I t} V(t)\right|\right|_\infty \leq A_1 e^{-(\mu_V - \mu_I)t} + A_2 + N\mu_I k \int_0^t (t-s)\tilde{T}(s) \, ||e^{\mu_I s} V(s)||_\infty \, ds$$

but $e^{-(\mu_V - \mu_I)t} \leq 1$ so this leads to

$$\left|\left|e^{\mu_I t} V(t)\right|\right|_\infty \leq A_1 + A_2 + N\mu_I k \int_0^t (t-s)\tilde{T}(s) \, ||e^{\mu_I s} V(s)||_\infty \, ds. \tag{3.5}$$

Now consider $\tilde{T}(t)$ defined above. Since $||T_0||_\infty \, e^{-\mu_T t} \to 0$, we know that for any $\varepsilon > 0$, there is $t_\varepsilon > 0$ such that

$$\tilde{T}(t) \leq \frac{||\lambda||_\infty}{\mu_T} + \varepsilon, \qquad \text{when } t > t_\varepsilon.$$

Using this, we can modify the integral in (3.5). We see for sufficiently large $t$,

$$\int_0^t (t-s)\tilde{T}(s) \, ||e^{\mu_V s} V(s)||_\infty \, ds = \int_0^{t_\varepsilon} (t-s)\tilde{T}(s) \, ||e^{\mu_V s} V(s)||_\infty \, ds + \int_{t_\varepsilon}^t (t-s)\tilde{T}(s) \, ||e^{\mu_V s} V(s)||_\infty \, ds.$$

But

$$\begin{aligned}\int_0^{t_\varepsilon} (t-s)\tilde{T}(s) \, ||e^{\mu_V s} V(s)||_\infty \, ds &= t\int_0^{t_\varepsilon} \tilde{T}(s) \, ||e^{\mu_V s} V(s)||_\infty \, ds - \int_0^{t_\varepsilon} s\tilde{T}(s) \, ||e^{\mu_V s} V(s)||_\infty \, ds \\ &\leq A(1+t), \text{ for some } A > 0.\end{aligned}$$

Using this, we can rewrite (3.5) as

$$\left|\left|e^{\mu_I t} V(t)\right|\right|_\infty \leq C(1+t) + N\mu_I k \int_{t_\varepsilon}^t (t-s)\tilde{T}(s) \, ||e^{\mu_I s} V(s)||_\infty \, ds.$$

However, in the integral above, $s > t_\varepsilon$, so we can bound $\tilde{T}$ yielding

$$\left|\left|e^{\mu_I t} V(t)\right|\right|_\infty \leq C(1+t) + N\mu_I k \left(\frac{||\lambda||_\infty}{\mu_T} + \varepsilon\right) \int_{t_\varepsilon}^t (t-s) \, ||e^{\mu_I s} V(s)||_\infty \, ds, \quad t > t_\varepsilon. \tag{3.6}$$

From here, let

$$\psi(t) = \left|\left|e^{\mu_I t} V(t)\right|\right|_\infty, \quad \theta(t) = C(1+t)$$

Also define a constant $\kappa = N\mu_V k\left(\frac{||\lambda||_\infty}{\mu_T} + \varepsilon\right)$. Then (3.6) becomes

$$\psi(t) \leq \theta(t) + \kappa \int_{t_\varepsilon}^{t} (t-s)\psi(s)ds. \tag{3.7}$$

Define a linear operator $B$ on locally integrable functions $f$ by

$$(Bf)(t) = \kappa \int_{t_\varepsilon}^{t} (t-s)f(s)ds.$$

Then (3.7) gives

$$\psi \leq \theta + B\psi. \tag{3.8}$$

We note that $B$ preserves inequalities (since the operator is a composition of multiplication by nonnegative terms and then integration), thus we may say

$$B\psi \leq B\theta + B^2\psi.$$

But from (3.8), we have $\psi - \theta \leq B\psi$ so

$$\psi - \theta \leq B\theta + B^2\psi \quad \Longrightarrow \quad \psi \leq \theta + B\theta + B^2\psi.$$

Applying $B$ to this inequality then gives

$$B\psi \leq B\theta + B^2\theta + B^3\psi$$

which, using again $\psi - \theta \leq B\psi$ gives

$$\psi \leq \theta + B\theta + B^2\theta + B^3\psi.$$

By a quick induction, it is easy to see that iterating through this process leads to

$$\psi \leq B^n\psi + \sum_{\ell=0}^{n-1} B^\ell\theta, \quad n \in \mathbb{N}, \tag{3.9}$$

where $B^0$ is the identity operator. The next step is to find a formula for $B^\ell$, $\ell \geq 2$ and then we can deal with each piece of the right hand side of (3.9). Consider, for a locally integrable function

$f$,

$$\begin{aligned}
(B^2 f)(t) &= B\left[\kappa \int_{t_\varepsilon}^{\tau} (\tau - s) f(s) ds\right](t) \\
&= \kappa \int_{t_\varepsilon}^{t} (t-\tau) \left(\kappa \int_{t_\varepsilon}^{\tau} (\tau - s) f(s) ds\right) d\tau \\
&= \kappa^2 \int_{t_\varepsilon}^{t} \int_{t_\varepsilon}^{\tau} (t-\tau)(\tau - s) f(s) ds d\tau \\
&= \kappa^2 \int_{t_\varepsilon}^{t} f(s) \int_{s}^{t} (t-\tau)(\tau - s) d\tau ds \\
&= \kappa^2 \int_{t_\varepsilon}^{t} f(s) \int_{0}^{t-s} (t-s-\tau)\tau \, d\tau ds \\
&= \kappa^2 \int_{t_\varepsilon}^{t} f(s) \int_{0}^{t-s} ((t-s)\tau - \tau^2) d\tau ds \\
&= \kappa^2 \int_{t_\varepsilon}^{t} f(s) \left(\frac{(t-s)\tau^2}{2} - \frac{\tau^3}{3}\right)_{\tau=0}^{\tau=t-s} ds \\
&= \frac{\kappa^2}{6} \int_{t_\varepsilon}^{t} (t-s)^3 f(s) ds.
\end{aligned}$$

This gives us a formula for the operator $B^2$. To find a similar formula for $B^3$, we apply $B$ again:

$$\begin{aligned}
(B^3 f)(t) &= \kappa \int_{t_\varepsilon}^{t} (t-\tau) \left(\frac{\kappa^2}{6} \int_{t_\varepsilon}^{\tau} (\tau - s)^3 f(s) ds\right) d\tau \\
&= \frac{\kappa^3}{6} \int_{t_\varepsilon}^{t} \int_{t_\varepsilon}^{\tau} (t-\tau)(\tau - s)^3 f(s) ds d\tau \\
&= \frac{\kappa^3}{6} \int_{t_\varepsilon}^{t} f(s) \int_{s}^{t} (t-\tau)(\tau - s)^3 d\tau ds \\
&= \frac{\kappa^3}{6} \int_{t_\varepsilon}^{t} f(s) \int_{0}^{t-s} ((t-s)-\tau)\tau^3 \, d\tau ds \\
&= \frac{\kappa^3}{6} \int_{t_\varepsilon}^{t} f(s) \left(\frac{(t-s)\tau^4}{4} - \frac{\tau^5}{5}\right)_{\tau=0}^{\tau=t-s} ds \\
&= \frac{\kappa^3}{120} \int_{t_\varepsilon}^{t} (t-s)^5 f(s) ds.
\end{aligned}$$

From here we may infer that

$$(B^\ell f)(t) = \frac{\kappa^\ell}{(2\ell-1)!} \int_{t_\varepsilon}^{t} (t-s)^{2\ell-1} f(s) ds.$$

Indeed, this formula can be verified by induction. Using this formula, we consider the terms on the right hand side of (3.9). First, consider

$$(B^n\psi)(t) = \frac{\kappa^n}{(2n-1)!}\int_{t_\varepsilon}^{t}(t-s)^{2n-1}\psi(s)ds.$$

Since solutions to (2.1) exist globally, in particular, we know $\psi(s)$ has a finite supremum on $t_\varepsilon \leq s \leq t$; call this supremum $\psi_{max}$. Then

$$\begin{aligned}(B^n\psi)(t) &\leq \psi_{max}\frac{\kappa^n}{(2n-1)!}\int_{t_\varepsilon}^{t}(t-s)^{2n-1}ds \\ &= \psi_{max}\frac{\left((t-t_\varepsilon)\sqrt{\kappa}\right)^{2n}}{(2n)!} \longrightarrow 0, \quad \text{as } n\to\infty, \quad \text{for all } t > t_\varepsilon.\end{aligned}$$

Then since (3.9) holds for all $n \in \mathbb{N}$, we may take the limit as $n \to \infty$ yielding

$$\psi(t) \leq \sum_{\ell=0}^{\infty}(B^\ell\theta)(t). \tag{3.10}$$

It remains to find a formula for $B^\ell\theta$ since we have a relatively simply function $\theta$. We see

$$\begin{aligned}(B^\ell\theta)(t) &= \frac{\kappa^\ell}{(2\ell-1)!}\int_{t_\varepsilon}^{t}(t-s)^{2\ell-1}C(1+s)ds \\ &= C\frac{\kappa^\ell}{(2\ell-1)!}\int_{0}^{t-t_\varepsilon}s^{2\ell-1}(1+t-s)ds \\ &= C\frac{\kappa^\ell}{(2\ell-1)!}\int_{0}^{t-t_\varepsilon}[(1+t)s^{2\ell-1}-s^{2\ell}]ds \\ &= C\frac{\kappa^\ell}{(2\ell-1)!}\left((1+t)\frac{(t-t_\varepsilon)^{2\ell}}{2\ell}-\frac{(t-t_\varepsilon)^{2\ell+1}}{2\ell+1}\right).\end{aligned}$$

From here, we use $1+t = (1+t_\varepsilon)+(t-t_\varepsilon)$. Then

$$\begin{aligned}(B^\ell\theta)(t) &= C\frac{\kappa^\ell}{(2\ell-1)!}\left((1+t_\varepsilon)\frac{(t-t_\varepsilon)^{2\ell}}{2\ell}+\frac{(t-t_\varepsilon)^{2\ell+1}}{2\ell}-\frac{(t-t_\varepsilon)^{2\ell+1}}{2\ell+1}\right) \\ &= C(1+t_\varepsilon)\frac{\left((t-t_\varepsilon)\sqrt{\kappa}\right)^{2\ell}}{(2\ell)!}+\frac{C}{\sqrt{\kappa}}\frac{\left((t-t_\varepsilon)\sqrt{\kappa}\right)^{2\ell+1}}{(2\ell+1)!}.\end{aligned}$$

Plugging this into (3.10), we arrive at

$$\begin{aligned}\psi(t) &\leq C(1+t_\varepsilon)\sum_{\ell=0}^{\infty}\frac{\left((t-t_\varepsilon)\sqrt{\kappa}\right)^{2\ell}}{(2\ell)!}+\left(\frac{C}{\sqrt{\kappa}}\right)\sum_{\ell=0}^{\infty}\frac{\left((t-t_\varepsilon)\sqrt{\kappa}\right)^{2\ell+1}}{(2\ell+1)!} \\ &= C(1+t_\varepsilon)\cosh\left((t-t_\varepsilon)\sqrt{\kappa}\right)+\frac{C}{\sqrt{\kappa}}\sinh\left((t-t_\varepsilon)\sqrt{\kappa}\right).\end{aligned}$$

Now $\cosh\left((t-t_\varepsilon)\sqrt{\kappa}\right)$ and $\sinh\left((t-t_\varepsilon)\sqrt{\kappa}\right)$ both behave like $e^{t\sqrt{\kappa}}$ as $t \to \infty$. Thus we may say

$$\psi(t) \leq Ce^{t\sqrt{\kappa}} \quad \text{for some } C > 0 \text{ and } t \text{ sufficiently large.}$$

Finally, this gives that

$$||V(t)||_\infty \leq Ce^{(\sqrt{\kappa}-\mu_I)t}.$$

Recall, $\kappa = N\mu_I k\left(\frac{||\lambda||_\infty}{\mu_T} + \varepsilon\right)$. We need $\sqrt{\kappa} - \mu_I < 0$ so that $||V(t)||_\infty$ is bounded by a decaying exponential. But

$$\sqrt{\kappa} - \mu_I < 0 \quad \iff \quad \kappa < \mu_I^2 \quad \iff \quad \frac{Nk}{\mu_I}\left(\frac{||\lambda||_\infty}{\mu_T} + \varepsilon\right) < 1.$$

Now using our assumption that

$$\frac{||\lambda||_\infty Nk}{\mu_T\mu_I} < 1,$$

we know that there is some sufficiently small $\varepsilon > 0$ such that

$$\frac{Nk}{\mu_I}\left(\frac{||\lambda||_\infty}{\mu_T} + \varepsilon\right) < 1.$$

Using this $\varepsilon$, we can achieve a decaying exponential bound on $||V(t)||_\infty$. Taking, for example, $r = -\frac{\sqrt{\kappa}-\mu_I}{2} > 0$, we see

$$\lim_{t\to\infty} e^{rt}\,||V(t)||_\infty = 0.$$

Using the decaying exponential bound for $V$ in (3.2), we see

$$\begin{aligned}
||I(t)||_\infty &\leq e^{-\mu_I t}\,||I_0||_\infty + k\tilde{T}_M e^{-\mu_I t}\int_0^t e^{\tau\sqrt{\kappa}}d\tau \\
&= e^{-\mu_I t}\,||I_0||_\infty + \frac{k\tilde{T}_M}{\sqrt{\kappa}} e^{-\mu_I t}\left(e^{t\sqrt{\kappa}} - 1\right) \\
&= e^{-\mu_I t}\,||I_0||_\infty + \frac{k\tilde{T}_M}{\sqrt{\kappa}}\left(e^{(\sqrt{\kappa}-\mu_I)t} - e^{-\mu_I t}\right).
\end{aligned}$$

Thus $||I(t)||_\infty$ is also bounded in time by a decaying exponential and

$$\lim_{t\to\infty} e^{rt}\,||I(t)||_\infty = 0,$$

for the same $r$ we defined above, which completes the proof. ■

We now consider the opposite case: $\mu_V < \mu_I$.

**Theorem 3.2 (Asymptotic Behavior: Case 2).** Let $T, I, V$ satisfy (2.1) and assume that $T_0, I_0, V_0 \in L^\infty(\Omega)$, $\mu_V < \mu_I$ and $R_2 = \frac{||\lambda||_\infty N \mu_I k}{\mu_T \mu_V^2} < 1$. Then there is an $r > 0$ such that

$$\lim_{t\to\infty} e^{rt} \, ||V(t)||_\infty = 0 \quad \text{and} \quad \lim_{t\to\infty} e^{rt} \, ||I(t)||_\infty = 0.$$

**Proof.** We start from (3.4):

$$||V(t)||_\infty \leq A_1 e^{-\mu_V t} + A_2 e^{-\mu_I t} + N\mu_I k \int_0^t \int_0^\tau \tilde{T}(s) e^{-\mu_I(\tau - s)} e^{-\mu_V(t-\tau)} \, ||V(s)||_\infty \, ds d\tau.$$

In this case, we can incur the correct inequality by replacing $\mu_I$ with $\mu_V$. This gives

$$\begin{aligned} ||V(t)||_\infty &\leq A_1 e^{-\mu_V t} + A_2 e^{-\mu_I t} + N\mu_I k \int_0^t \int_0^\tau \tilde{T}(s) e^{-\mu_V(\tau - s)} e^{-\mu_V(t-\tau)} \, ||V(s)||_\infty \, ds d\tau \\ &\leq A_1 e^{-\mu_V t} + A_2 e^{-\mu_I t} + N\mu_I k \int_0^t \int_0^\tau \tilde{T}(s) e^{-\mu_V(t-s)} \, ||V(s)||_\infty \, ds d\tau. \end{aligned}$$

Using the same manipulations as in Case 1, we can reduce this to an inequality which looks identical to (3.5) except with $\mu_I$ replaced with $\mu_V$. This inequality is

$$\left|\left|e^{\mu_V t} V(t)\right|\right|_\infty \leq A_1 + A_2 + N\mu_I k \int_0^t (t-s)\tilde{T}(s) \, ||e^{\mu_V s} V(s)||_\infty \, ds.$$

Using the same arguments as above, we note that for any $\varepsilon > 0$, there is $t_\varepsilon > 0$ such that

$$\left|\left|e^{\mu_V t} V(t)\right|\right|_\infty \leq C(1+t) + N\mu_I k \left( \frac{||\lambda||_\infty}{\mu_T} + \varepsilon \right) \int_{t_\varepsilon}^t (t-s) \, ||e^{\mu_V s} V(s)||_\infty \, ds.$$

Define $\psi(t), \theta(t), \kappa, (Bf)(t)$ as in the proof of Case 1 (the difference being that $\psi(t)$ now has an exponential with $\mu_V$ rather than $\mu_I$). Then we can verify that (3.9) and (3.10) hold and thus

$$\psi(t) \leq C e^{t\sqrt{\kappa}}, \quad \text{for some } C > 0.$$

Finally, this gives that

$$||V(t)||_\infty \leq C e^{(\sqrt{\kappa} - \mu_V)t}.$$

Now, for exponential decay, we need $\sqrt{\kappa} - \mu_V < 0$. Simplifying this gives

$$\sqrt{\kappa} - \mu_V < 0 \iff \kappa < \mu_V^2 \iff \frac{N\mu_I k}{\mu_V^2}\left(\frac{||\lambda||_\infty}{\mu_T} + \varepsilon\right) < 1.$$

Using our condition that $\frac{||\lambda||_\infty N\mu_I k}{\mu_T\mu_V^2} < 1$, we know that there is some sufficiently small $\varepsilon > 0$ such that the above condition holds. For such $\varepsilon$ and sufficiently large $t$, $||V(t)||_\infty$ is bounded by a decaying exponential and so

$$\lim_{t\to\infty} e^{rt}\,||V(t)||_\infty = 0,$$

for $r = -\frac{\kappa-\mu_V}{2} > 0$.

Again, plugging this bound for $||V(t)||_\infty$ into (3.2) we can easily derive a decaying exponential bound for $||I(t)||_\infty$ as well and we conclude that

$$\lim_{t\to\infty} e^{rt}\,||I(t)||_\infty = 0,$$

for the same $r$, which completes the proof. ■

Finally, for completeness, we consider the case then $\mu_V = \mu_I$.

**Theorem 3.3 (Asymptotic Behavior: Case 3).** Let $T, I, V$ satisfy (2.1) and assume that $T_0, I_0, V_0 \in L^\infty(\Omega)$, $\mu_V = \mu_I$ and $R = \frac{||\lambda||_\infty Nk}{\mu_T\mu_V} < 1$. Then there is an $r > 0$ such that

$$\lim_{t\to\infty} e^{rt}\,||V(t)||_\infty = 0 \quad \text{and} \quad \lim_{t\to\infty} e^{rt}\,||I(t)||_\infty = 0.$$

**Note**. The condition we require here is exactly what we would find in Case 1 by taking the limit as $\mu_I \to \mu_V$ from below or what we would find in Case 2 by taking the limit as $\mu_V \to \mu_I$ from below. That is to say, $R = R_1 = R_2$ when $\mu_V = \mu_I$.

**Proof.** Starting from (3.4), we simply replace all $\mu_I$ with $\mu_V$ since the two are equal and all steps proceed exactly as in Case 2. ■

We may also say something about the asymptotic behavior of $T$. Essentially, in the case that $||I(t)||_\infty, ||V(t)||_\infty \to 0$, we expect the influence of the nonlinear term in the $T$-equation to be negligible for large time. We state this more precisely in the following theorem.

**Theorem 3.4 (Asymptotic Behavior of T).** Let $T, I, V$ satisfy (2.1) and assume that $T_0, I_0, V_0 \in L^\infty(\Omega)$ and that one of the following holds:

(i) $\mu_V > \mu_I$ and $R_1 = \frac{||\lambda||_\infty Nk}{\mu_T \mu_I} < 1$,

(ii) $\mu_V < \mu_I$ and $R_2 = \frac{||\lambda||_\infty N \mu_I k}{\mu_T \mu_V^2} < 1$,

(iii) $\mu_V = \mu_I$ and $R = \frac{||\lambda||_\infty Nk}{\mu_T \mu_V} < 1$.

Further, let $T^*(x)$ satisfy the equation

$$-D_T \Delta T^* = \lambda(x) - \mu_T T^*, \quad x \in \Omega, \tag{3.11}$$

along with the same boundary condition that $T$ satisfies. Then there is $r > 0$ such that

$$\lim_{t \to \infty} e^{rt} ||T(t) - T^*||_\infty = 0.$$

**Proof.** Let $U(x,t) = T^*(x) - T(x,t)$ for all $x \in \Omega, t > 0$. Then

$$\begin{aligned}
&(\partial_t - D_T \Delta)U = (\partial_t - D_T \Delta)T^* - (\partial_t - D_T \Delta)T \\
\Longrightarrow\ &(\partial_t - D_T \Delta)U = \lambda(x) - \mu_T T^* - (\lambda(x) - \mu_T T - kTV) \\
\Longrightarrow\ &(\partial_t - D_T \Delta)U = -\mu_T U + kTV
\end{aligned} \tag{3.12}$$

and $U(x,0) = T^*(x) - T_0(x) = U_0(x)$, say. From (3.12), we have

$$\begin{aligned}
(\partial_t - D_T \Delta)\left[U e^{\mu_T t}\right] &= kTV e^{\mu_T t} \\
&\le C_T V e^{\mu_T t}
\end{aligned}$$

where $C_T$ is some constant which depends on the uniform (in time) bound for $T$ we found earlier. Using Corollary 2.2, this yields

$$e^{\mu_T t} \|U(t)\|_\infty \leq \|U_0\|_\infty + \int_0^t C_T e^{\mu_T \tau} \|V(\tau)\|_\infty \, d\tau.$$

From the proofs of the above theorems, we know that in any of case (i),(ii) or (iii), $\|V(t)\|_\infty$ is bounded in time by a decaying exponential, i.e.,

$$\|V(t)\|_\infty \leq Ce^{-mt} \quad \text{for some } C, m > 0.$$

Then

$$e^{\mu_T t} \|U(t)\|_\infty \leq \|U_0\|_\infty + C_T \int_0^t e^{(\mu_T - m)\tau} d\tau.$$

Integrating gives

$$e^{\mu_T t} \|U(t)\|_\infty \leq \|U_0\|_\infty + \frac{C_T}{\mu_T - m} \left( e^{(\mu_T - m)t} - 1 \right)$$

which immediately leads to

$$0 \leq \|U(t)\|_\infty \leq \left( \|U_0\|_\infty - \frac{C_T}{\mu_T - m} \right) e^{-\mu_T t} + \frac{C_T M}{\mu_T - m} e^{-mt}.$$

And so, taking $r = \frac{\min\{\mu_T, m\}}{2}$ and using the Squeeze Theorem, we see that

$$\lim_{t \to \infty} e^{rt} \|U(t)\|_\infty = \lim_{t \to \infty} e^{rt} \|T(t) - T^*(t)\|_\infty = 0,$$

which completes the proof. ■

These give us a concrete set of conditions which force $I, V \to 0$ for large time. However, the conditions are not exactly what we would like. We would like a condition which more closely resemble the analogous condition for the lumped model since that condition has some biological meaning. To derive a "better" condition, we look at the non-dimensionalized version of the system which leads us to the next subsection.

### 3.2 Non-Dimensionalization

From (2.1), we attempt to derive a dimensionless system. To do so, we first discuss the dimensions of the quantities at play. We use the notation convention $[A]$ = dimensions of $A$. We consider $T, I$ to have units "volumetric concentration of cells," while $V$ has units "volumetric concentration of virions"; we are following the lead of [9]. Accordingly, we may list the dimensions of each piece of (2.1) as follows:

- $[t]$ = time (time is ordinarily measured in days)
- $[x] = \text{length}^n$ if we are in $\mathbb{R}^n$ (i.e., each component of $x$ has units "length"),
- $[T] = [I] = \frac{\text{cells}}{\text{length}^n}$,
- $[V] = \frac{\text{virions}}{\text{length}^n}$
- $[D_T] = [D_I] = [D_V] = \frac{\text{length}^2}{\text{time}}$,
- $[\lambda] = \frac{\text{cells}}{\text{length}^n \cdot \text{time}}$,
- $[\mu_T] = [\mu_I] = [\mu_V] = \frac{1}{\text{time}}$,
- $[k] = \frac{\text{length}^n}{\text{virions}\cdot\text{time}}$,
- $[N] = \frac{\text{virions}}{\text{cells}}$.

From this we see that each equation above has units $\frac{\text{cells}}{\text{length}^n \cdot \text{time}}$ or $\frac{\text{virions}}{\text{length}^n \cdot \text{time}}$.

Now we introduce new versions of each quantity. Let

$$t = \alpha s, \quad x = \beta y, \quad T = \gamma S, \quad I = \delta J, \quad V = \varepsilon W.$$

where $\alpha, \beta, \gamma, \delta, \varepsilon$ are abitrary scalings; we will specify the units of $s, y, S, J, W$ shortly. Plugging these into (2.1), one arrives at

$$\left(\partial_s - \frac{D_T \alpha}{\beta^2}\Delta_y\right) S = \frac{\alpha}{\gamma}\lambda(\beta y) - \mu_T \alpha S - k\alpha\varepsilon SW \tag{3.13}$$

$$\left(\partial_s - \frac{D_I \alpha}{\beta^2}\Delta_y\right) J = \frac{k\alpha\gamma\varepsilon}{\delta} SW - \mu_I \alpha J \tag{3.14}$$

$$\left(\partial_s - \frac{D_V \alpha}{\beta^2}\Delta_y\right) W = \frac{N\mu_I\alpha\delta}{\varepsilon} J - \mu_V \alpha W \tag{3.15}$$

along with the appropriate transformations of initial conditions which we discuss later. We now begin to choose values for our new parameters very strategically. Considering how $\alpha$ appears, it makes sense to set $\alpha = 1/\mu_T$ (in fact, $\alpha = 1/\mu_I$ or $\alpha = 1/\mu_V$ seem equally sensible at first; we will discuss exactly why we made the choice that $\alpha = 1/\mu_T$ shortly). From here, to eliminate the coefficient of diffusion from (3.13), we choose $\beta = \sqrt{D_T/\mu_T}$. Next, we notice that the quantity $\delta/\varepsilon$ appears in both (3.14) and (3.15) (though in (3.14) the quantity is inverted). Accordingly, we eliminate $N$ and $\mu_I$ from (3.15) and supply an extra $\mu_V$ so that the quantity $\mu_V\alpha$ may be factored out of the right hand side of (3.15). This leads us to the choice $\delta/\varepsilon = \mu_V/(N\mu_I)$. We set $\gamma = \mu_V/(Nk)$ to eliminate some parameters from (3.14). Finally, we need to specify one of $\delta$ and $\varepsilon$, and we will be done. To further simplify (3.13), we set $\varepsilon = \mu_I/k$. To recap, the parameters we have introduced are now defined by

$$\alpha = \tfrac{1}{\mu_T}, \quad \beta = \sqrt{\tfrac{D_T}{\mu_T}}, \quad \gamma = \tfrac{\mu_V}{Nk}, \quad \delta = \tfrac{\mu_T\mu_V}{Nk\mu_I}, \quad \varepsilon = \tfrac{\mu_T}{k}.$$

We plug these values into (3.13)-(3.15). This yields the new system:

$$(\partial_s - \Delta_y)\, S = R_0(y) - S - SW \tag{3.16}$$

$$\left(\partial_s - \tilde{D}_I \Delta_y\right) J = \tilde{\mu}_I(SW - J) \tag{3.17}$$

$$\left(\partial_s - \tilde{D}_V \Delta_y\right) W = \tilde{\mu}_V(J - W) \tag{3.18}$$

where

$$R_0(y) = \tfrac{Nk}{\mu_T\mu_V}\lambda\left(y\sqrt{\tfrac{D_T}{\mu_T}}\right), \quad \tilde{D}_I = \tfrac{D_I}{D_T}, \quad \tilde{D}_V = \tfrac{D_V}{D_T}, \quad \tilde{\mu}_I = \tfrac{\mu_I}{\mu_T}, \quad \tilde{\mu}_V = \tfrac{\mu_V}{\mu_T}.$$

Because of the choice that $\alpha = 1/\mu_T$, we transformed $\lambda$ into this new function $R_0$. In the coming section, we describe why this was a desirable transformation. We will find that $R_0$ is of particular interest.

At this point, we see that

$$[\alpha] = \text{time}, \quad [\beta] = \text{length}, \quad [\gamma] = \tfrac{\text{cells}}{\text{length}^n}, \quad [\delta] = \tfrac{\text{cells}}{\text{length}^n}, \quad [\varepsilon] = \tfrac{\text{virions}}{\text{length}^n}.$$

Thus

$$[s] = [y] = [S] = [J] = [W] = 1.$$

It is also easily checked that

$$[R_0] = [\tilde{D}_I] = [\tilde{D}_V] = [\tilde{\mu}_I] = [\tilde{\mu}_V] = 1.$$

Thus (3.16)-(3.18) is a fully non-dimensionalized system. The last thing to do is to transform the initial conditions. This happens in a completely natural way. If we set

$$S_0(y) = T_0\left(y\sqrt{\tfrac{D_T}{\mu_T}}\right), \quad J_0(y) = I_0\left(y\sqrt{\tfrac{D_T}{\mu_T}}\right), \quad W_0(y) = V_0\left(y\sqrt{\tfrac{D_T}{\mu_T}}\right),$$

then our system is

$$\left.\begin{aligned}
(\partial_s - \Delta_y)\, S &= R_0(y) - S - SW, & S(y,0) &= S_0(y), \\
\left(\partial_s - \tilde{D}_I\Delta_y\right) J &= \tilde{\mu}_I(SW - J), & J(y,0) &= J_0(y), \\
\left(\partial_s - \tilde{D}_V\Delta_y\right) W &= \tilde{\mu}_V(J - W), & W(y,0) &= W_0(y).
\end{aligned}\right\} \tag{3.19}$$

Here (3.19) holds for all $y \in \tilde{\Omega}$ and all $s \in [0, s^*]$ where

$$\tilde{\Omega} = \left\{x\sqrt{\tfrac{\mu_T}{D_T}} \, : \, x \in \Omega\right\} \quad \text{and} \quad s^* = \mu_T t^*.$$

The boundary conditions also transform in a natural way. We assume

$$\lim_{|y|\to\infty} \frac{\partial S}{\partial n}(y,s) = \lim_{|y|\to\infty} \frac{\partial J}{\partial n}(y,s) = \lim_{|y|\to\infty} \frac{\partial W}{\partial n}(y,s) = 0, \ \ s \in (0, s^*],$$

if $\tilde{\Omega} = \mathbb{R}^n$ or

$$\frac{\partial S}{\partial n}(\cdot,s)\Big|_{\partial\tilde{\Omega}} = \frac{\partial J}{\partial n}(\cdot,s)\Big|_{\partial\tilde{\Omega}} = \frac{\partial W}{\partial n}(\cdot,s)\Big|_{\partial\tilde{\Omega}} = 0, \quad s \in (0, s^*],$$

if $\tilde{\Omega}$ is a bounded open subset of $\mathbb{R}^n$ with boundary $\partial\tilde{\Omega}$.

### 3.3 Non-Dimensional Supremum-Norm Asymptotics

In this section, we work with (3.19) and establish some of the asymptotic behavior of the system in different parameter regimes. To do this, we need the help of a pair of lemmas which we state here (proofs of these lemmas can be found in Appendix I).

**Lemma 3.5.** Let $\Omega = \mathbb{R}^n$ or let $\Omega$ be a bounded open subset of $\mathbb{R}^n$ and let $F : \Omega \times [0,\infty) \to [0,\infty)$.

Futher, assume that for fixed $t \geq 0$, $F(\cdot, t) \in H^{\infty}(\Omega)$ and that $\frac{\partial F}{\partial t}$ is continuous and bounded for $(x,t) \in \Omega \times [0,\infty)$. Then

$$f(t) = \sup_{x \in \Omega} F(x,t), \quad t \in [0,\infty)$$

is uniformly continuous.

**Lemma 3.6.** Let $f : [a,\infty) \to [0,\infty)$ be a uniformly continuous function such that

$$\int_a^{\infty} f(t)dt = C < \infty.$$

Then $\lim_{t\to\infty} f(t) = 0$.

With these lemmas, we are ready to deal with asymptotic behavior of (3.19).

**Theorem 3.7 (Non-Dimensional Supremum Norm Asymptotics).** Assume that $S, J, W$ satisfy (3.19), $S_0, J_0, W_0 \in L^{\infty}(\tilde{\Omega})$ and

$$||R_0||_{\infty} = \frac{Nk\,||\lambda||_{\infty}}{\mu_T \mu_V} < 1.$$

Then

$$\lim_{s\to\infty} ||J(s)||_{\infty} = 0 \quad \text{and} \quad \lim_{s\to\infty} ||W(s)||_{\infty} = 0.$$

**Note**: There are several observations to consider before we begin the proof. The first is that, when taking the supremum $||R_0||_{\infty}$, we may do so with respect to either $x$ or $y$ and the two are equivalent. That is to say,

$$||\lambda||_{\infty} = \sup_{x\in\Omega} |\lambda(x)| = \sup_{y\in\tilde{\Omega}} |\lambda(y)|\,.$$

Similarly, requiring that $S_0, J_0, W_0 \in L^{\infty}(\tilde{\Omega})$ is equivalent to requiring that $T_0, I_0, V_0 \in L^{\infty}(\Omega)$. Next, we note that $||J(s)||_{\infty}, ||W(s)||_{\infty} \to 0$ will certainly imply that $||I(t)||_{\infty}, ||V(t)||_{\infty} \to 0$. That is, asymptotic behavior of (2.1) and (3.19) is the same. Further, the high order regularity which was proven for $I$ and $V$ also applies to $J$ and $W$. Finally, we proved a similar set of theorems for (2.1) already. However, these were proved under more stringent conditions on the parameters and it was necessary to consider several cases. Here, we need only consider one condition and all cases follow. There is a trade-off though. In the other proofs we were able to bound $||I(t)||_\infty$ and $||V(t)||_\infty$ by exponential decay. Here we can only assert that $||J(s)||_\infty$ and $||W(s)||_\infty$ decay like $s^{-(1+\alpha)}$ for some $\alpha > 0$, so the decay could be slower, though, with additional work, it may be possible to recover the exponential decay.

**Proof.** For this proof, we denote $\Delta_y$ simply by $\Delta$ and it is understood that the derivatives are taken with respect to the coordinates of $y$. We begin by considering the $S$ equation. We see

$$\partial_s S + S - \Delta S = R_0(y) - SW \leq R_0(y).$$

Then using an integrating factor gives

$$(\partial_s - \Delta)[e^s S] \leq R_0(y)e^s.$$

By Corollary 2.2, this implies

$$||S(s)||_\infty e^s \leq ||S_0||_\infty + \int_0^s ||R_0||_\infty e^\sigma d\sigma$$

and therefore that

$$||S(s)||_\infty \leq ||S_0||_\infty e^{-s} + ||R_0||_\infty (1 - e^{-s}) \leq ||S_0||_\infty e^{-s} + ||R_0||_\infty . \tag{3.20}$$

Set

$$\tilde{S}(s) = ||S_0||_\infty e^{-s} + ||R_0||_\infty$$

so that $||S(s)||_\infty \leq \tilde{S}(s), s > 0$.

Next we consider the $J$ equation. Using our bound on $S$, we see

$$\partial_s J + \tilde{\mu}_I J - \tilde{D}_I \Delta J \leq \tilde{\mu}_I \tilde{S}(s) W$$

which leads to

$$(\partial_s - \tilde{D}_I \Delta)[e^{\tilde{\mu}_I s} J] \le \tilde{\mu}_I e^{\tilde{\mu}_I s} \tilde{S}(s) W.$$

Then Corollary 2.2 gives

$$||J(s)||_\infty \, e^{\tilde{\mu}_I s} \le ||J_0||_\infty + \tilde{\mu}_I \int_0^s e^{\tilde{\mu}_I \sigma} \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma$$

from which we see

$$||J(s)||_\infty \le ||J_0||_\infty \, e^{-\tilde{\mu}_I s} + \tilde{\mu}_I e^{-\tilde{\mu}_I s} \int_0^s e^{\tilde{\mu}_I \sigma} \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma. \tag{3.21}$$

Our next step is to integrate the inequality. This yields

$$\int_0^s ||J(\sigma)||_\infty \, d\sigma \le \frac{||J_0||_\infty}{\tilde{\mu}_I}(1 - e^{-\tilde{\mu}_I s}) + \int_0^s \tilde{\mu}_I e^{-\tilde{\mu}_I s} \int_0^\sigma e^{\tilde{\mu}_I \tau} \tilde{S}(\tau) \, ||W(\tau)||_\infty \, d\tau d\sigma.$$

If we set

$$F(\sigma) = \int_0^\sigma e^{\tilde{\mu}_I \tau} \tilde{S}(\tau) \, ||W(\tau)||_\infty \, d\tau,$$

we may rewrite the inequality as

$$\int_0^s ||J(\sigma)||_\infty \, d\sigma \le \frac{||J_0||_\infty}{\tilde{\mu}_I}(1 - e^{-\tilde{\mu}_I s}) + \int_0^s \tilde{\mu}_I e^{-\tilde{\mu}_I s} F(\sigma) d\sigma.$$

Now we integrate by parts to give

$$\int_0^s ||J(\sigma)||_\infty \, d\sigma \le \frac{||J_0||_\infty}{\tilde{\mu}_I}(1 - e^{-\tilde{\mu}_I s}) - \left( F(\sigma) e^{-\tilde{\mu}_I \sigma} \Big|_{\sigma=0}^{\sigma=s} \right) + \int_0^s e^{-\tilde{\mu}_I \sigma} F'(\sigma) d\sigma.$$

But $F(0) = 0$ and $F'(\sigma) = e^{\tilde{\mu}_I \sigma} \tilde{S}(\sigma) \, ||W(\sigma)||_\infty$. Thus

$$\int_0^s ||J(\sigma)||_\infty \, d\sigma \le \frac{||J_0||_\infty}{\tilde{\mu}_I}(1 - e^{-\tilde{\mu}_I s}) - e^{-\tilde{\mu}_I s} \int_0^s e^{\tilde{\mu}_I \sigma} \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma + \int_0^s \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma.$$

After dropping the negative term and replacing $1 - e^{-\tilde{\mu}_I s}$ by 1, this gives us the bound

$$\int_0^s ||J(\sigma)||_\infty \, d\sigma \le \frac{||J_0||_\infty}{\tilde{\mu}_I} + \int_0^s \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma. \tag{3.22}$$

We deal with the $W$ equation in a similar fashion. We see

$$\partial_s W + \tilde{\mu}_V W - \tilde{D}_V \Delta W = \tilde{\mu}_V J$$

which then implies that

$$(\partial_s - \tilde{D}_V \Delta)[e^{\tilde{\mu}_V s} W] \leq \tilde{\mu}_V e^{\tilde{\mu}_V s} J$$

and then, by Corollary 2.1, that

$$||W(s)||_\infty e^{\tilde{\mu}_V s} \leq ||W_0||_\infty + \tilde{\mu}_V \int_0^s e^{\tilde{\mu}_V \sigma} ||J(\sigma)||_\infty \, d\sigma.$$

Rearranging yields

$$||W(s)||_\infty \leq ||W_0||_\infty e^{-\tilde{\mu}_V s} + \tilde{\mu}_V e^{-\tilde{\mu}_V s} \int_0^s e^{\tilde{\mu}_V \sigma} ||J(\sigma)||_\infty \, d\sigma. \tag{3.23}$$

Again, we will integrate and this time set

$$G(\sigma) = \int_0^\sigma e^{\tilde{\mu}_V \tau} ||J(\tau)||_\infty \, d\tau.$$

This gives

$$\int_0^s ||W(\sigma)||_\infty \, d\sigma \leq \frac{||W_0||_\infty}{\tilde{\mu}_V}(1 - e^{-\tilde{\mu}_V s}) + \int_0^s \tilde{\mu}_V e^{-\tilde{\mu}_V \sigma} G(\sigma) d\sigma.$$

Integrating by parts yields

$$\int_0^s ||W(\sigma)||_\infty \, d\sigma \leq \frac{||W_0||_\infty}{\tilde{\mu}_V}(1 - e^{-\tilde{\mu}_V s}) - \left( G(\sigma) e^{-\tilde{\mu}_V \sigma} \Big|_{\sigma=0}^{\sigma=s} \right) + \int_0^s e^{-\tilde{\mu}_V \sigma} G'(\sigma) d\sigma.$$

We realize that $G(0) = 0$ and $G'(\sigma) = e^{\tilde{\mu}_V \sigma} ||J(\sigma)||_\infty$. So

$$\int_0^s ||W(\sigma)||_\infty \, d\sigma \leq \frac{||W_0||_\infty}{\tilde{\mu}_V}(1 - e^{-\tilde{\mu}_V s}) - e^{-\tilde{\mu}_V s} \int_0^s e^{\tilde{\mu}_V \sigma} ||J(\sigma)||_\infty \, d\sigma + \int_0^s ||J(\sigma)||_\infty \, d\sigma,$$

which leads immediately to

$$\int_0^s ||W(\sigma)||_\infty \, d\sigma \leq \frac{||W_0||_\infty}{\tilde{\mu}_V} + \int_0^s ||J(\sigma)||_\infty \, d\sigma. \tag{3.24}$$

The next step is to insert the bound derived in (3.22) into (3.24). Doing so, we see

$$\int_0^s ||W(\sigma)||_\infty \, d\sigma \leq \frac{||W_0||_\infty}{\tilde{\mu}_V} + \frac{||J_0||_\infty}{\tilde{\mu}_I} + \int_0^s \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, .$$

In particular, this implies that

$$\int_{s_1}^s ||W(\sigma)||_\infty \, d\sigma \leq \frac{||W_0||_\infty}{\tilde{\mu}_V} + \frac{||J_0||_\infty}{\tilde{\mu}_I} + \int_0^s \tilde{S}(\sigma) \, ||W(\sigma)||_\infty$$

for any $s_1 > 0$. Consider, since

$$\lim_{s \to \infty} \tilde{S}(s) = ||R_0||_\infty$$

and since $\tilde{S}(s)$ approaches this limit from above, we know that for any $\varepsilon > 0$, there is $s_\varepsilon > 0$ such that $s > s_\varepsilon$ implies that $\tilde{S}(s) < ||R_0||_\infty + \varepsilon$. We rewrite the above inequality:

$$\begin{aligned}
\int_{s_\varepsilon}^s ||W(\sigma)||_\infty \, d\sigma &\leq \frac{||W_0||_\infty}{\tilde{\mu}_V} + \frac{||J_0||_\infty}{\tilde{\mu}_I} + \int_0^s \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \\
&= \frac{||W_0||_\infty}{\tilde{\mu}_V} + \frac{||J_0||_\infty}{\tilde{\mu}_I} + \int_0^{s_\varepsilon} \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma + \int_{s_\varepsilon}^s \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma.
\end{aligned}$$

However, $\displaystyle\int_0^{s_\varepsilon} \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma$ is simply a constant, so we conclude

$$\int_{s_\varepsilon}^s ||W(\sigma)||_\infty \, d\sigma \leq C_\varepsilon + \int_{s_\varepsilon}^s \tilde{S}(\sigma) \, ||W(\sigma)||_\infty \, d\sigma \leq C_\varepsilon + \int_{s_\varepsilon}^s \left( ||R_0||_\infty + \varepsilon \right) ||W(\sigma)||_\infty \, d\sigma,$$

for some $C_\varepsilon > 0$. This leads us to

$$\left(1 - ||R_0||_\infty - \varepsilon\right) \int_{s_\varepsilon}^s ||W(\sigma)||_\infty \, d\sigma \leq C_\varepsilon.$$

Set $H(s) = \displaystyle\int_{s_\varepsilon}^s ||W(\sigma)||_\infty \, d\sigma$. Then certainly $H$ is nonnegative and

$$\left(1 - ||R_0||_\infty - \varepsilon\right) H(s) \leq C_\varepsilon, \quad s > s_\varepsilon.$$

Now if $(1 - ||R_0||_\infty - \varepsilon) < 0$, the above holds trivially and tells us nothing. However, we have assumed that

$$||R_0||_\infty < 1.$$

Thus there is an $\varepsilon > 0$ sufficiently small so that

$$||R_0||_\infty + \varepsilon < 1.$$

We choose this $\varepsilon$ (and the corresponding $s_\varepsilon$). Then taking the limit as $s \to \infty$ gives

$$\lim_{s\to\infty} H(s) \leq \frac{C_\varepsilon}{1 - ||R_0||_\infty - \varepsilon} < \infty.$$

However, $H$ is also an increasing function of $s$. Thus we have an increasing function which is bounded above and so by the Monotone Convergence Theorem, $H(s)$ tends to a finite limit as $s \to \infty$.

Further, from (3.19), we see that

$$\frac{\partial W}{\partial s} = \tilde{D}_V \Delta W + \tilde{\mu}_V J - \tilde{\mu}_V W$$

so by high-order regularity, we know that $\frac{\partial W}{\partial s}$ is continuous and bounded. Further, for fixed $s \geq 0$, we have $W(\cdot, s) \in H^\infty\left(\tilde{\Omega}\right)$. Thus by Lemma 3.5,

$$\sup_{y\in\tilde{\Omega}} W(y, s) = ||W(s)||_\infty$$

is a uniformly continuous function of $s$.

Then by Lemma 3.6, since $||W(s)||_\infty$ is uniformly continuous and

$$\int_{s_\varepsilon}^{\infty} ||W(s)||_\infty \, ds < \infty,$$

we may conclude that

$$\lim_{s\to\infty} ||W(s)||_\infty = 0.$$

Finally, since

$$\int_{s_\varepsilon}^{\infty} ||W(s)||_\infty \, ds$$

is bounded, from (3.22), we can bound

$$\int_{s_\varepsilon}^{\infty} ||J(\sigma)||_\infty \, d\sigma$$

the same way we did for $||W(s)||_\infty$. This will then imply that

$$\lim_{s\to\infty} ||J(s)||_\infty = 0$$

which completes the proof. ∎

**Note**: A final note on the rate of decay of $||W(s)||_\infty$ and $||J(s)||_\infty$. We never derived any rate of decay in the proof. However, by proving that

$$\int_{s_\varepsilon}^{\infty} ||W(s)||_\infty \, ds$$

converges (and since $||W(s)||_\infty$ is nonnegative), we know that $||W(s)||_\infty$ must go to zero faster than $s^{-1}$ and the same applies for $||J(s)||_\infty$. Thus we conclude that both $||W(s)||_\infty$ and $||J(s)||_\infty$ decay to zero like $s^{-(1+\alpha)}$ for some $\alpha > 0$ though they may exhibit exponential decay.

### 3.4 Non-Dimensional $p$-Norm Asymptotics

To make Theorem 3.7 more robust, we would also like to consider other norms as well. In fact, this result generalizes nicely to $p$-norms in the following way.

**Corollary 3.7.1 ($p$-norm Asymptotics).** Assume that $S, J, W$ satisfy (3.19), $S_0, J_0, W_0 \in L^1(\tilde{\Omega}) \cap L^\infty(\tilde{\Omega})$ and $||R_0||_\infty = \frac{Nk||\lambda||_\infty}{\mu_T \mu_V} < 1$. Then

$$\lim_{s\to\infty} ||J(s)||_p = 0 \quad \text{and} \quad \lim_{s\to\infty} ||W(s)||_p = 0,$$

for all $1 < p < \infty$.

**Proof.** The proof is actually fairly simple in the case of a bounded domain. If we suppose that $\tilde{\Omega}$

has finite measure, then we may say

$$\begin{aligned}||W(s)||_p &= \left(\int_{\tilde{\Omega}} |W(y,s)|^p \, dy\right)^{1/p} \\ &\leq \left(\int_{\tilde{\Omega}} ||W(s)||_\infty^p \, dy\right)^{1/p} \\ &= ||W(s)||_\infty \, \mu(\tilde{\Omega})^{1/p},\end{aligned}$$

where $\mu(\tilde{\Omega})$ is the measure of $\tilde{\Omega}$ and $p \in [1, \infty)$. The same inequality holds for $J$ as well. Then since the supremum norm of each $W$ and $J$ goes to zero, so must the $p$-norm.

The case of an unbounded domain is slightly more complicated. We would like to use $p$-norm interpolation; i.e., we would like to bound the $p$-norm by the 1-norm and the supremum norm. In order to do this, we need some estimates for the 1-norm.

To that end, from the $J$-equation, we integrate out space. We note that the integral of $J$ (or $W$) is actually the 1-norm; this follows since $J$ (and $W$) are positive. Thus we have

$$\frac{d}{ds} ||J(s)||_1 - \tilde{D}_I \int_{\tilde{\Omega}} \Delta J dy = \tilde{\mu}_I \int_{\tilde{\Omega}} S(y,s) W(y,s) dy - \tilde{\mu}_I \, ||J(s)||_1$$

We can bound $S(y, s)$ by its supremum norm and then use the bound derived in (3.20) to say

$$\frac{d}{ds} ||J(s)||_1 - \tilde{D}_I \int_{\tilde{\Omega}} \Delta J dy \leq \tilde{\mu}_I \tilde{S}(s) \, ||W(s)||_1 - \tilde{\mu}_I \, ||J(s)||_1 \, .$$

Using the divergence theorem for the integral gives

$$\frac{d}{ds} ||J(s)||_1 - \tilde{D}_I \int_{\partial\tilde{\Omega}} \frac{\partial J}{\partial n} ds \leq \tilde{\mu}_I \tilde{S}(s) \, ||W(s)||_1 - \tilde{\mu}_I \, ||J(s)||_1 \, ,$$

but then our boundary condition implies that the integral is zero. Thus

$$\frac{d}{ds} ||J(s)||_1 + \tilde{\mu}_I \, ||J(s)||_1 \leq \tilde{\mu}_I \tilde{S}(s) \, ||W(s)||_1 \, .$$

Using an integrating factor and “solving” the inequality for $||J(s)||_1$ brings us to

$$||J(s)||_1 \leq ||J_0||_1 \, e^{-\tilde{\mu}_I s} + \tilde{\mu}_I e^{-\tilde{\mu}_I s} \int_0^s e^{\tilde{\mu}_I \sigma} \tilde{S}(\sigma) \, ||W(\sigma)||_1 \, d\sigma. \tag{3.25}$$

Next, we consider the $W$-equation and integrate out space:

$$\frac{d}{ds}\left|\left|W(s)\right|\right|_1 - \tilde{D}_V \int_{\tilde{\Omega}} \Delta W dy = \tilde{\mu}_V \left|\left|J(s)\right|\right|_1 - \tilde{\mu}_V \left|\left|W(s)\right|\right|_1 .$$

Using the divergence theorem and our boundary condition, we know that the integral is zero. Thus

$$\frac{d}{ds}\left|\left|W(s)\right|\right|_1 + \tilde{\mu}_V \left|\left|W(s)\right|\right|_1 = \tilde{\mu}_V \left|\left|J(s)\right|\right|_1 .$$

Finally, using a integrating factor and solving for $\left|\left|W(s)\right|\right|_1$ yields

$$\left|\left|W(s)\right|\right|_1 = \left|\left|W_0\right|\right|_1 e^{-\tilde{\mu}_V s} + \tilde{\mu}_V e^{-\tilde{\mu}_V s} \int_0^s e^{\tilde{\mu}_V \sigma} \left|\left|J(\sigma)\right|\right|_1 d\sigma.$$

In particular,

$$\left|\left|W(s)\right|\right|_1 \leq \left|\left|W_0\right|\right|_1 e^{-\tilde{\mu}_V s} + \tilde{\mu}_V e^{-\tilde{\mu}_V s} \int_0^s e^{\tilde{\mu}_V \sigma} \left|\left|J(\sigma)\right|\right|_1 d\sigma. \tag{3.26}$$

If we compare (3.25) and (3.26) to (3.21) and (3.23), respectively, we see inequalities are exactly the same except $||\cdot||_1$ is replaced with $||\cdot||_\infty$. Thus we can conclude from similar work that $\left|\left|J(s)\right|\right|_1$ and $\left|\left|W(s)\right|\right|_1$ remain bounded for all $s$.

With this, we are almost ready to assert that the $p$-norm of $J$ and $W$ must go to zero.First, we recall Hölder's Inequality.

**Theorem (Hölder's Inequality).** Let $\Omega \subset \mathbb{R}^n$. Suppose that $q, r \in [1, \infty]$ are such that $\frac{1}{q} + \frac{1}{r} = 1$ and that $f \in L^q(\Omega)$, $g \in L^r(\Omega)$. Then

$$\int_\Omega fg \leq \left|\left|f\right|\right|_q \left|\left|g\right|\right|_r .$$

Now consider, for a smooth function $u$ defined on $\Omega$ and for $p \in (1, \infty)$, we have

$$\begin{aligned}
\left|\left|u\right|\right|_p^p &= \int_\Omega |u|^p \\
&= \int_\Omega |u| \, |u|^{p-1} \\
&\leq \left|\left|u\right|\right|_1 \left|\left|u^{p-1}\right|\right|_\infty \qquad \text{(by Hölder's Inequality with } q = 1, r = \infty\text{)} \\
&= \left|\left|u\right|\right|_1 \left|\left|u\right|\right|_\infty^{p-1},
\end{aligned}$$

which yields the inequality

$$||u||_p \leq ||u||_1^{1/p} \, ||u||_\infty^{1-1/p} \, .$$

Using this, we see that

$$||W(s)||_p \leq ||W(s)||_1^{1/p} \, ||W(s)||_\infty^{1-1/p} \, ,$$

for any $p \in (1, \infty)$. Thus, since the 1-norm of $W$ remains bounded and the supremum norm of $W$ goes to zero, the $p$-norm is bounded by a quantity that goes to zero and so $||W(s)||_p \to 0$. The same holds for $J$. ■

### 3.5 Comparison with the Spatially Homogeneous Model

It is no accident that our results on large time asymptotics are contingent on the quantity $||R_0||_\infty = \frac{Nk||\lambda||_\infty}{\mu_T \mu_V}$. In fact, to more clearly express the meaning of this quantity, it should perhaps be written in the form

$$||R_0||_\infty = \frac{N\mu_I k \, ||\lambda||_\infty}{\mu_T \mu_I \mu_V}.$$

In this form, we see that $||R_0||_\infty$ is the ratio of appearance rates to clearance rates. Indeed, $N\mu_I$ is a rate of appearance of free virions based on the death of infected cells, $k$ is a rate at which T cells become infected when in contact with virions and $\lambda$ is a regeneration rate for T cells, while the denominator $(\mu_T, \mu_I, \mu_V)$ is composed of the natural death/clearance rates.

In fact, this quantity has a clear analog in the analysis of the spatially homogeneous model. When analyzing (1.1), several authors ([3], [4] for example) consider the quantity

$$\rho = \frac{N\mu_I k \lambda}{\mu_T \mu_I \mu_V}.$$

This quantity is called the *reproductive ratio*. It is of particular interest to Jones and Roemer [11] who analyze (1.1) in detail. They prove that there are two steady states of (1.1), termed the *viral extinction* state (a state in which $I(t), V(t) \to 0$ for large $t$) and the *viral persistence* state (a state in which $I(t), V(t)$ do not go to zero), respectively. Further, they prove that the extinction state is stable if and only if $\rho \leq 1$ and otherwise the persistence state is stable.

Our results are somewhat similar. We have proven that in the case that $||R_0||_\infty < 1$, our system tends to a virus free state. Our analysis thus far has been limited to this case and we can say little when $||R_0||_\infty > 1$. We notice $R_0(y)$ is precisely $\rho$ if $\lambda$ is taken to be constant. Thus $||R_0||_\infty$ should not be considered an exact analog of $\rho$ because taking the supremum norm will not incur a particularly sharp inequality unless $\lambda$ is "nearly" constant. Something like the average value of $R_0$ may be a better analog to $\rho$. In any case, we presented a *sufficient* condition to force $I, V \to 0$; it is unlikely that this condition is *necessary* (we speak more to this point in the next section).

However, if $\lambda$ is taken to be constant we do have the following result.

**Theorem 3.8.** Assume that $T, I, V$ satisfy (2.1), take $\lambda$ to be constant and let

$$R_0 = \frac{\lambda N k}{\mu_T \mu_V} > 1.$$

Then the viral persistence steady state given by

$$(T^*, I^*, V^*) = \left( \frac{\mu_V}{Nk}, \frac{\lambda}{\mu_I} - \frac{\mu_V}{Nk}, \frac{\lambda N}{\mu_V} - \frac{\mu_T}{k} \right)$$

is asymptotically stable.

**Proof.** It is easy to see that $(T^*, I^*, V^*)$ is indeed a steady state for the system by simply performing the necessary algebra. Now assume that our functions are perturbed slightly from the steady state; say

$$T(x,t) = T^* + \varepsilon T_1(x,t), \quad I(x,t) = I^* + \varepsilon I_1(x,t), \quad V(x,t) = V^* + \varepsilon V_1(x,t),$$

where $0 < \varepsilon \ll 1$. Plugging these into (2.1) and ignoring terms on the order of $\varepsilon^2$, we see that our perturbation functions satisfy

$$\begin{aligned}
(\partial_t - D_T \Delta) T_1 &= -\mu_T T_1 - k(T^* V_1 + V^* T_1), \\
(\partial_t - D_I \Delta) I_1 &= k(T^* V_1 + V^* T_1) - \mu_I I_1, \\
(\partial_t - D_V \Delta) V_1 &= N \mu_I I_1 - \mu_V V_1,
\end{aligned}$$

Next we take the Fourier Transform in space (with transform variable $\xi$) and rearrange to arrive at

$$\partial_t \begin{bmatrix} \hat{T}_1 \\ \hat{I}_1 \\ \hat{V}_1 \end{bmatrix} = \begin{bmatrix} -(\mu_T + kV^* + D_T \left|\xi\right|^2) & 0 & -kT^* \\ kV^* & -(\mu_I + D_I \left|\xi\right|^2) & kT^* \\ 0 & N\mu_I & -(\mu_V + D_V \left|\xi\right|^2) \end{bmatrix} \begin{bmatrix} \hat{T}_1 \\ \hat{I}_1 \\ \hat{V}_1 \end{bmatrix}$$
$$:= A(\xi) \begin{bmatrix} \hat{T}_1 \\ \hat{I}_1 \\ \hat{V}_1 \end{bmatrix}.$$

We wish to prove that $T_1, I_1, V_1 \to 0$ as $t \to \infty$. To do so, it suffices to prove that all of the eigenvalues of the matrix $A(\xi)$ have negative real part regardless of choice for $\xi$. Accordingly, we note that

$$\det(A - \nu I) = -\big(\nu^3 + a(\xi)\nu^2 + b(\xi)\nu + c(\xi)\big)$$

where

$$\begin{aligned} a(\xi) &= \mu_T + kV^* + \mu_I + \mu_V + (D_T + D_I + D_V) \left|\xi\right|^2, \\ b(\xi) &= (\mu_T + kV^*)(\mu_I + \mu_V) \\ &\quad + \big((\mu_T + kV^*)(D_I + D_V) + \mu_I(D_T + D_V) + \mu_V(D_T + D_I)\big) \left|\xi\right|^2 \\ &\quad + (D_T D_I + D_T D_V + D_I D_V) \left|\xi\right|^4, \\ c(\xi) &= \mu_I \mu_V k V^* + (\mu_T + kV^*)(\mu_I D_V + \mu_V D_I) \left|\xi\right|^2 \\ &\quad + \big(D_I D_V(\mu_T + kV^*) + D_I(\mu_I D_V + \mu_V D_I)\big) \left|\xi\right|^4 + D_T D_I D_V \left|\xi\right|^6. \end{aligned}$$

It is clear to see that each of $a(\xi), b(\xi), c(\xi) > 0$ for all $\xi \in \mathbb{R}^n$ (in fact, this is where the assumption that $R_0 > 1$ is necessary since it guarantees that $V^* > 0$). We recall the Routh-Hurwitz Stability Criterion.

**Routh-Hurwitz Stability Condition.** Let $a, b, c > 0$ and $ab > c$. Then all of the roots of the polynomial $p(x) = x^3 + ax^2 + bx + c$ have negative real part.

With this in mind, it will suffice to show that $a(\xi)b(\xi) > c(\xi), \forall \xi \in \mathbb{R}^n$; this will imply that all eigenvalues of $A(\xi)$ have negative real part. To this end, we see

$$\begin{aligned}
a(\xi)b(\xi) &= (\mu_T + kV^* + \mu_I + \mu_V)(\mu_T + kV^*)(\mu_I + \mu_V) \\
&+ \Big[(D_T + D_I + D_V)(\mu_T + kV^*)(\mu_I + \mu_V) \\
&+ \big((\mu_T + kV^*)(D_I + D_V)\mu_I(D_T + D_V) + \mu_V(D_I + D_V)\big)(\mu_T + kV^* + \mu_I + \mu_V)\Big] |\xi|^2 \\
&+ \Big[(\mu_T + kV^* + \mu_I + \mu_V)(D_T D_I + D_T D_V + D_T D_I) \\
&+ \big((\mu_T + kV^*)(D_I + D_V)\mu_I(D_T + D_V) + \mu_V(D_I + D_V)\big)(D_T + D_I + D_V)\Big] |\xi|^4 \\
&+ (D_T + D_I + D_V)(D_T D_I + D_T D_V + D_I D_V) |\xi|^6 .
\end{aligned}$$

For brevity, say

$$\begin{aligned}
c(\xi) &= c_0 + c_2 |\xi|^2 + c_4 |\xi|^4 + c_6 |\xi|^6 \\
a(\xi)b(\xi) &= d_0 + d_2 |\xi|^2 + d_4 |\xi|^4 + d_6 |\xi|^6 .
\end{aligned}$$

Looking at the coefficients, we can see that for each $k = 0, 2, 4, 6$, we have

$$d_k = c_k + \text{positive terms.}$$

Thus $a(\xi)b(\xi)$ is term-by-term greater than $c(\xi)$ for any $\xi \in \mathbb{R}^n$. Thus we can conclude that $a(\xi)b(\xi) > c(\xi), \forall \xi \in \mathbb{R}^n$ and so all eigenvalues of $A(\xi)$ have negative real part regardless of $\xi$. Hence

$$T_1, I_1, V_1 \to 0$$

as $t \to \infty$ which proves linear stability around the viral persistence steady state $(T^*, I^*, V^*)$. ■

Theorem 3.8 gives a clear analog to the results for the spatially homogeneous model. In the case that $\lambda$ is constant, the asymptotic behavior of (2.1) and (1.1) is very similar. If $R_0 < 1$ there there is a viral extinction steady state and if $R_0 > 1$ then then there is a viral persistence state. Stancevic et al. [9] perform the same analysis (though they consider a slightly different system) and the results are very similar.

The case of non-constant $\lambda$ is more difficult. In that case, any viral persistence state will need to satisfy a system of three nonlinear elliptic PDEs and the method for establishing steady states is not so straightforward.

# CHAPTER 4
# SIMULATIONS

The purpose of the simulations is largely to verify the analysis so we break the simulations up into several different parameter regimes which are discussed below.

For our simulations we use a semi-implicit finite difference scheme in MATLAB. The difficulty with this is the nonlinear term so we lag that term by one time step. We describe the scheme in one spatial dimension with time domain $[0, t^*]$ and spatial domain $[a, b]$ (the corresponding scheme for two spatial dimensions can be abstracted fiarly easily). Let $\Delta t = t^*/N, h = (b-a)/J$ for some $N, J \in \mathbb{N}$. Then our grid is given by $t_n = n\Delta t$, $x_j = a + hj$ and our scheme is

$$\begin{aligned}
\frac{T_j^n - T_j^{n-1}}{\Delta t} - D_T \frac{T_{j+1}^n - 2T_j^n + T_{j-1}^n}{h^2} &= \lambda_j - \mu_T T_j^n - kT_j^{n-1}V_j^{n-1}, \\
\frac{I_j^n - I_j^{n-1}}{\Delta t} - D_I \frac{I_{j+1}^n - 2I_j^n + I_{j-1}^n}{h^2} &= kT_j^{n-1}V_j^{n-1} - \mu_I I_j^n, \\
\frac{V_j^n - V_j^{n-1}}{\Delta t} - D_V \frac{V_{j+1}^n - 2V_j^n + V_{j-1}^n}{h^2} &= N\mu_I I_j^n - \mu_V V_j^n,
\end{aligned}$$

for $n = 1, 2, \ldots, N$ and $j = 1, 2, \ldots J-1$, where $T_j^n = T(x_j, t_n)$, etc. We also have initial conditions

$$T_j^0 = T_0(x_j), \quad I_j^0 = I_0(x_j), \quad V_j^0 = V_0(x_j), \quad j = 0, 1, \ldots J.$$

Finally, for ease of implementation, we take homogeneous Dirichlet boundary conditions:

$$T_0^n = T_J^n = I_0^n = I_J^n = V_0^n = V_J^n = 0, \quad n = 0, 1, \ldots, N.$$

In fact this choice does not affect the analysis at any point except for finding a bound on the 1-norms of $J$ and $W$ in Section 3.4.

We can rewrite the system in matrix-vector form as

$$\begin{aligned}
A_T \vec{T}^n &= \vec{T}^{n-1} + \Delta t \left( \vec{\lambda} - kT\vec{V}^{n-1} \right), \\
A_I \vec{I}^n &= \vec{I}^{n-1} + \Delta t kT\vec{V}^{n-1}, \\
A_V \vec{V}^n &= \vec{V}^{n-1} + \Delta t N \mu_I \vec{I}^n,
\end{aligned} \tag{4.1}$$

where

$$\vec{T}^n = \begin{bmatrix} T_1^n \\ T_2^n \\ \\ \vdots \\ T_{J-1}^n \end{bmatrix}, \quad \vec{TV}^n = \begin{bmatrix} T_1^n V_1^n \\ T_2^n V_2^n \\ \\ \vdots \\ T_{J-1}^n V_{J-1}^n \end{bmatrix}$$

and $A_T$ is a matrix with

$$(A_T)_{n,n} = 1 + \Delta t \mu_T + D_T \frac{\Delta t}{h^2}, \;\; (A_T)_{n,n-1} = (A_T)_{n-1,n} = -D_T \frac{\Delta t}{h^2},$$

for suitable $n$ values and $(A_T)_{n,m} = 0$ off of the three principal diagonals (the vectors $\vec{I}^n, \vec{V}^n$ and matrices $A_I, A_V$ are constructed identically except with $T$ replaced by $I$ or $V$).

We note that in the discretized version of the $V$ equation, we keep $\vec{I}^n$ on the right hand side. In order to do this, it is necessary to solve the equations in the order in which they are listed. Having done this, $\vec{I}^n$ has been calculated just before we use it in the next equation. It is easily seen that the matrices $A_T, A_I, A_V$ are symmetric and positive definite (since they are all strictly diagonally dominant) so $\vec{T}^n, \vec{I}^n, \vec{V}^n$ can be computed very efficiently from (4.1) by using the Cholesky factorization of each matrix.

We use the parameter values suggested by [9]. These values are:

$$\begin{array}{ccc} \mu_T = 0.03 \text{ day}^{-1} & \mu_I = 0.5 \text{ day}^{-1} & \mu_V = 3 \text{ day}^{-1} \\ D_T = 0.09054 \frac{\text{mm}^2}{\text{day}} & D_I = 0.09054 \frac{\text{mm}^2}{\text{day}} & D_V = 7.603 \cdot 10^{-4} \frac{\text{mm}^2}{\text{day}} \\ N = 960 \frac{\text{virions}}{\text{cells}} & k = 3.43 \cdot 10^{-5-n} \frac{\text{mm}^n}{\text{virions} \cdot \text{day}} & \lambda(x) \approx 10^n \frac{\text{cells}}{\text{mm}^n \cdot \text{day}} \end{array}$$

Note that $\lambda$ and $k$ depend on the dimension of the space we are working in. The only value that will consistently change between simulations (besides the changes based on dimension) is $\lambda$; any other changes in parameter values will be noted when necessary. We will choose several different functional forms for $\lambda$ in each dimension in attempt to demonstrate the different ways that the system can behave.

The different cases which are simulated are the same in 1D and 2D:

**Case 1.** $||R_0||_\infty < 1$, viral extinction. This case simply verifies that our conditions from section 3 are indeed sufficient to force $||I(t)||_\infty, ||V(t)||_\infty \to 0$.

**Case 2.** $||R_0||_\infty > 1$, viral extinction. This case gives solid computational evidence that our sufficient condition for viral extinction is not a necessary condition.

**Case 3.** $R_0(x) = 1 + \varepsilon(x)$, viral persistence. This case demonstrates that the condition for viral extinction ($||R_0||_\infty < 1$) can be a sharp condition.

**Case 4.** $||R_0||_\infty > 1$, viral persistence. This case demonstrates more clearly the existence of the viral persistence steady state.

### 4.1 Simulation in 1-D

All of the simulations in 1-D take $\Omega = (-10, 10)$ and $0 \le t \le 100$.

| $t$ | $\|\|T(t)\|\|_\infty$ | $\|\|I(t)\|\|_\infty$ | $\|\|V(t)\|\|_\infty$ | $\|\|T(t) - T^*(t)\|\|_\infty$ |
|---|---|---|---|---|
| 0 | 2.0000e+03 | 3.0000e+02 | 8.0000e+02 | 0 |
| 20 | 2.2989e+02 | 2.7952e+00 | 5.1177e+02 | 9.6788e+02 |
| 40 | 2.1070e+02 | 1.1195e-03 | 2.0696e-01 | 4.8895e+02 |
| 60 | 1.9088e+02 | 2.9044e-07 | 5.4054e-05 | 2.4494e+02 |
| 80 | 1.7802e+02 | 5.8124e-11 | 1.0858e-08 | 1.2372e+02 |
| 100 | 1.7064e+02 | 1.0129e-14 | 1.8959e-12 | 6.3073e+01 |
| 200 | 1.6229e+02 | 8.8918e-34 | 1.6677e-31 | 2.3555e+00 |
| 300 | 1.6195e+02 | 6.6707e-53 | 1.2513e-50 | 9.2018e-02 |

Figure 2: 1D Case 1. $\lambda(x) = 25e^{-5x^2}$, $||R_0||_\infty = 0.9147$

The first case we consider is one in which $||R_0||_\infty < 1$. In this case, Theorem 3.7 tells us that we should have $I, V \to 0$ for large time. Indeed, this can be observed. In addition, we should have

$$\lim_{t\to\infty} ||T(t) - T^*(t)||_\infty = 0,$$

where $T^*$ satisfies the same equation as $T$ but with the nonlinear term ignored. This can be observed as well, though it is more subtle. The convergence of this quantity to zero is perhaps very slow. For each 20 day increase in time, the value of $||T(t) - T^*(t)||_\infty$ is roughly halved.

It is clear from Figures 2 - 5 that for large time, $I, V$ are approximately zero while $T$ tends to a nonzero steady state.

Our second case demonstrates that the condition $||R_0||_\infty < 1$ is not *necessary* for the infection to die off. In fact, it may be possible to make $||R_0||_\infty$ arbitrarily large while the system still tends to an infection free state.

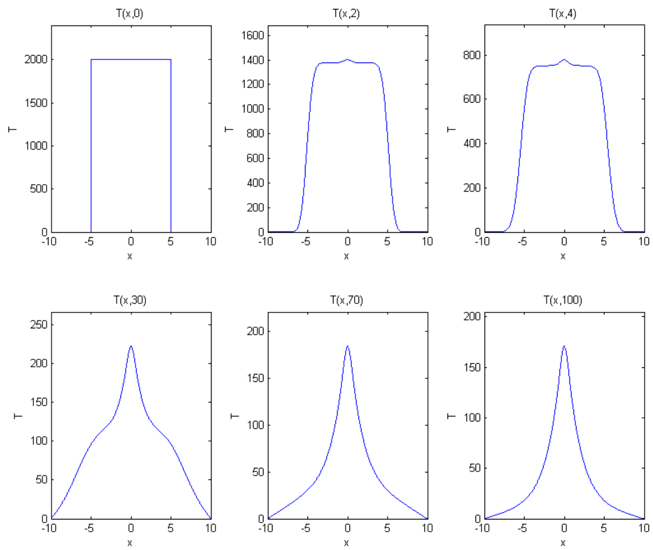


Figure 3: 1D Case 1. Evolution of T-Cells

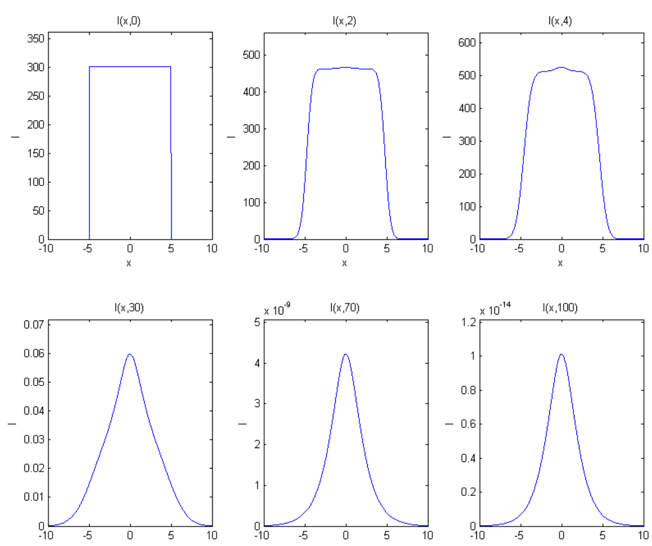


Figure 4: 1D Case 1. Evolution of I-Cells

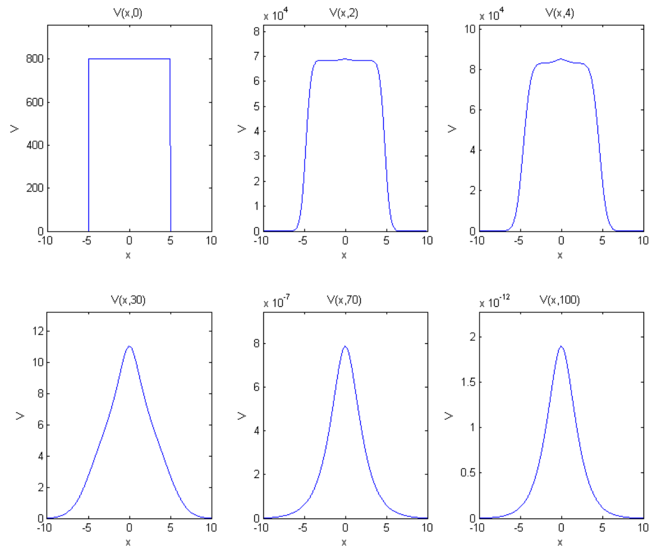


Figure 5: 1D Case 1. Evolution of Virions

| $t$ | $\|\|T(t)\|\|_\infty$ | $\|\|I(t)\|\|_\infty$ | $\|\|V(t)\|\|_\infty$ | $\|\|T(t) - T^*(t)\|\|_\infty$ |
|---|---|---|---|---|
| 0 | 2.0000e+03 | 3.0000e+02 | 8.0000e+02 | 0 |
| 20 | 4.8462e+02 | 6.1607e+00 | 1.0959e+03 | 1.0348e+03 |
| 40 | 5.7655e+02 | 2.1015e-02 | 3.6979e+00 | 5.1308e+02 |
| 60 | 5.9895e+02 | 1.0081e-04 | 1.7679e-02 | 2.5538e+02 |
| 80 | 6.0481e+02 | 5.3757e-07 | 9.4174e-05 | 1.2861e+02 |
| 100 | 6.0629e+02 | 2.9506e-09 | 5.1677e-07 | 6.5452e+01 |
| 200 | 6.0641e+02 | 1.5158e-20 | 2.6547e-18 | 2.4372e+00 |
| 300 | 6.0637e+02 | 7.7287e-32 | 1.3536e-29 | 9.5166e-02 |

Figure 6: 1D Case 2. $\lambda(x) = 270e^{-50x^2}$, $||R_0||_\infty = 9.8784$

From Figures 6 - 9, we see that even though $||R_0||_\infty$ is substantially larger than 1, the system tends towards a viral extinction steady state. Again, it does appear that $||T(t) - T^*(t)||_\infty$ is decreasing, but it still decreases very slowly. Here, the average $R_0$ value is still relatively small ($\overline{R}_0 = 0.1237$); keeping this value sufficiently small seems to affect the long time asymptotic behavior. This would confirm that the stability of the steady states is spatially dependent.

Indeed, the condition $||R_0||_\infty < 1$ does seem somewhat sharp in the case that $||R_0||_\infty \approx \overline{R}_0$. To demonstrate this, we consider a third case. The results are summarized in Figures 10 - 13.

In this case, $\lambda$ was chosen so that

$$R_0(x) = 1 + \varepsilon(x) \quad \text{where} \quad 0 \leq \varepsilon(x) \leq 0.1 \quad \text{for all } x \in [-10, 10].$$

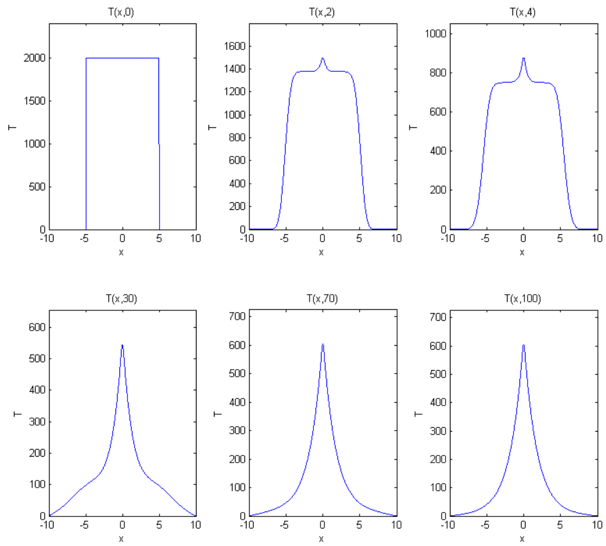


Figure 7: 1D Case 2. Evolution of T-Cells

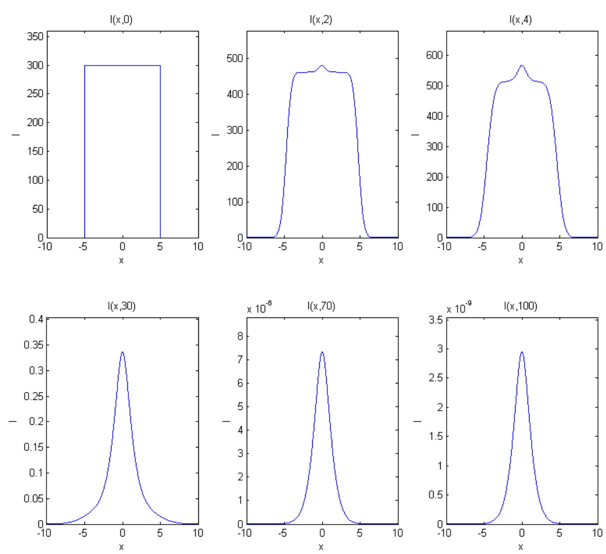


Figure 8: 1D Case 2. Evolution of I-Cells

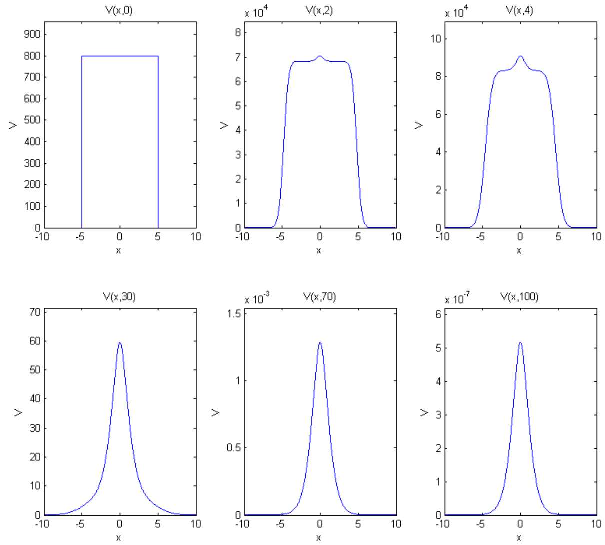


Figure 9: 1D Case 2. Evolution of Virions

| $t$ | $\|\|T(t)\|\|_\infty$ | $\|\|I(t)\|\|_\infty$ | $\|\|V(t)\|\|_\infty$ | $\|\|T(t) - T^*(t)\|\|_\infty$ |
|---|---|---|---|---|
| 0 | 2.0000e+03 | 3.0000e+02 | 8.0000e+02 | 0 |
| 20 | 5.0265e+02 | 1.2404e+02 | 1.0419e+04 | 1.1408e+03 |
| 40 | 6.3302e+02 | 1.2007e+01 | 9.8991e+02 | 6.5534e+02 |
| 60 | 7.4864e+02 | 3.2889e+00 | 2.6720e+02 | 3.4731e+02 |
| 80 | 8.3260e+02 | 1.7194e+00 | 1.3858e+02 | 1.8394e+02 |
| 100 | 8.8457e+02 | 1.2639e+00 | 1.0145e+02 | 9.9220e+01 |
| 200 | 9.4225e+02 | 1.0791e+00 | 8.6288e+01 | 1.1236e+01 |
| 300 | 9.4364e+02 | 1.2448e+00 | 9.9539e+01 | 8.8212e+00 |

Figure 10: 1D Case 3. $\lambda(x) = 27.33 + 2.7\cos(x)^2$, $||R_0||_\infty = 1.0988$

Also, $||R_0||_\infty = 1.0988$ and $\overline{R}_0 = 1.0517$ and $\mu_I = 0.25$ days$^{-1}$ which accentuates the viral persistence steady state. In this case, Figures 10 - 13 seem to indicate that the virus is persisting; indeed, the values of $||I(t)||_\infty$ and $||V(t)||_\infty$ are no longer strictly decreasing. When the virus persists, we cannot be sure that $||T(t) - T^*(t)||_\infty \to 0$. We notice that the error is decreasing in Figure 10, though it is significantly greater than in Figure 2 or Figure 6.

As a final case, we would like to observe a clear tendency towards a viral persistence state. This can be accomplished by simply increasing $\lambda$ enough.

Here Figures 14 - 17 clearly show that the virions and the infected cells are not tending towards zero and the error in $T^*$ as an approximation to $T$ is not small anymore.

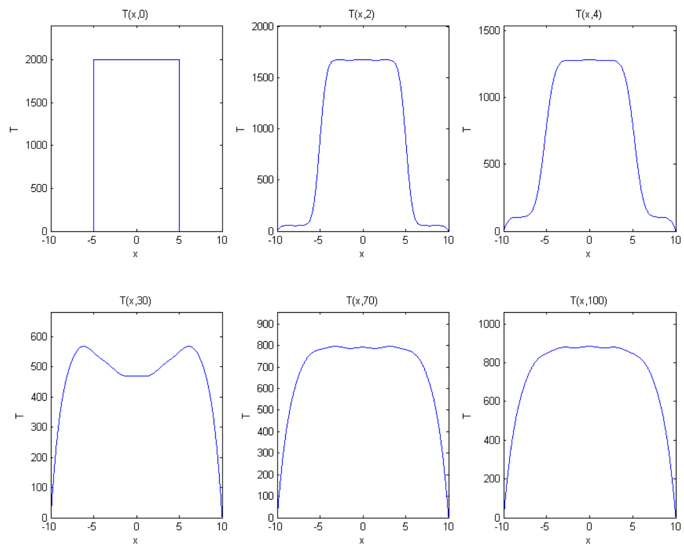


Figure 11: 1D Case 3. Evolution of T-Cells

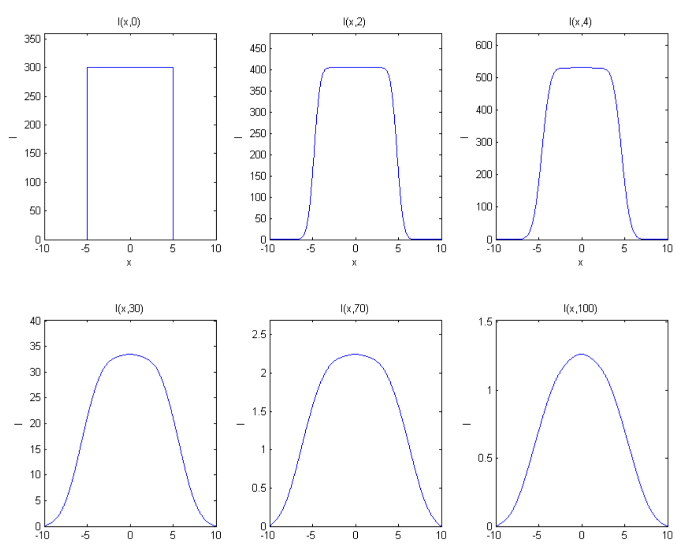


Figure 12: 1D Case 3. Evolution of I-Cells

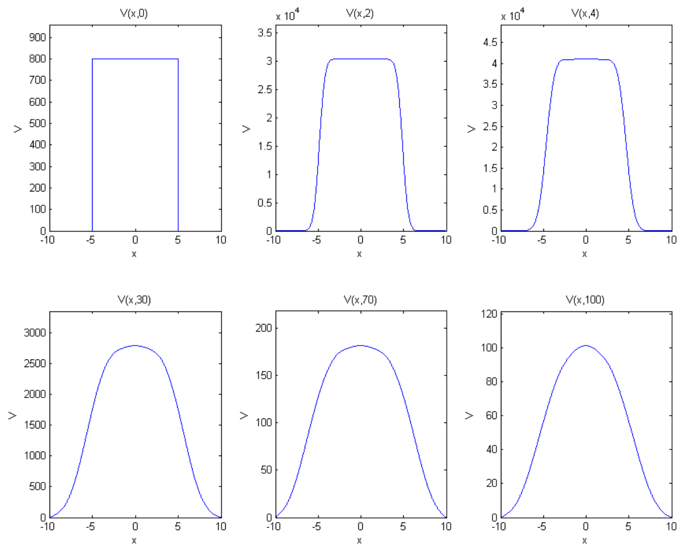


Figure 13: 1D Case 3. Evolution of Virions

| $t$ | $\|\|T(t)\|\|_\infty$ | $\|\|I(t)\|\|_\infty$ | $\|\|V(t)\|\|_\infty$ | $\|\|T(t) - T^*(t)\|\|_\infty$ |
|---|---|---|---|---|
| 0 | 2.0000e+03 | 3.0000e+02 | 8.0000e+02 | 0 |
| 20 | 7.4349e+02 | 1.8929e+01 | 3.1925e+03 | 1.2650e+03 |
| 40 | 1.0635e+03 | 1.0528e+01 | 1.6541e+03 | 7.1700e+02 |
| 60 | 1.0963e+03 | 6.5955e+01 | 1.0301e+04 | 6.5262e+02 |
| 80 | 9.0395e+02 | 6.0029e+01 | 9.7501e+03 | 8.9220e+02 |
| 100 | 9.3799e+02 | 3.8916e+01 | 6.2164e+03 | 7.7965e+02 |
| 200 | 9.4315e+02 | 5.1316e+01 | 8.2133e+03 | 7.9551e+02 |
| 300 | 9.4272e+02 | 5.0626e+01 | 8.0998e+03 | 7.9325e+02 |

Figure 14: 1D Case 4. $\lambda(x) = 50 + 10e^{-5x^2}$, $||R_0||_\infty = 2.1952$

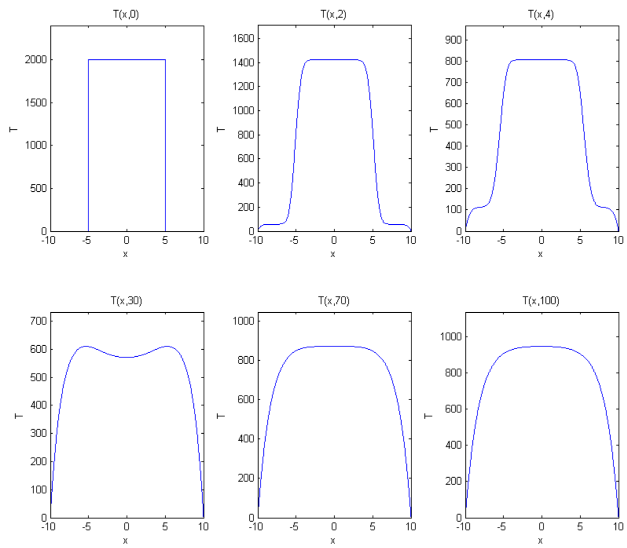


Figure 15: 1D Case 4. Evolution of T-Cells

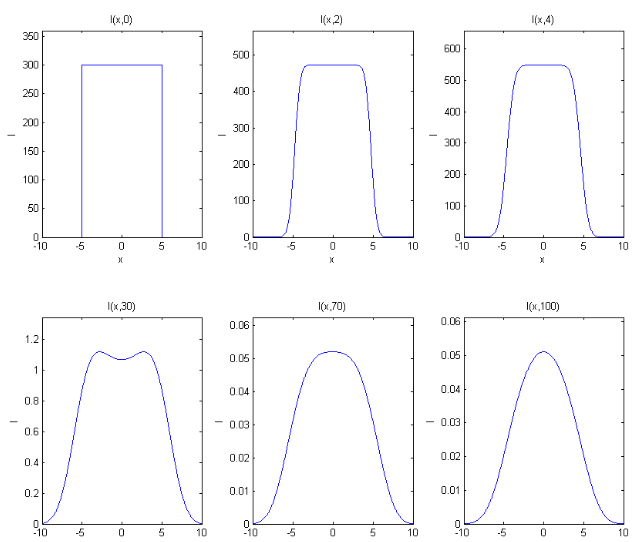


Figure 16: 1D Case 4. Evolution of I-Cells

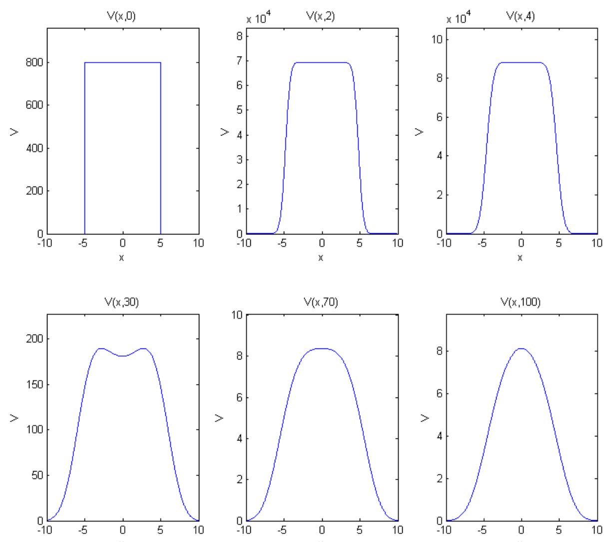


Figure 17: 1D Case 4. Evolution of Virions

### 4.2 Simulation in 2-D

In two spatial dimensions, we take $\Omega = (-10, 10)^2$ and again let $0 \le t \le 100$.

| $t$ | $\|\|T(t)\|\|_\infty$ | $\|\|I(t)\|\|_\infty$ | $\|\|V(t)\|\|_\infty$ | $\|\|T(t) - T^*(t)\|\|_\infty$ |
|---|---|---|---|---|
| 0 | 5.0000e+02 | 1.0000e+02 | 3.0000e+02 | 0 |
| 20 | 6.8709e+02 | 8.9954e-03 | 1.7152e+00 | 3.1301e+00 |
| 40 | 5.8452e+02 | 5.3796e-07 | 1.0319e-04 | 1.3586e+00 |
| 60 | 5.3118e+02 | 2.7447e-11 | 5.2730e-09 | 5.9763e-01 |
| 80 | 5.0675e+02 | 1.3456e-15 | 2.5860e-13 | 2.7140e-01 |
| 100 | 4.9553e+02 | 6.5540e-20 | 1.2596e-17 | 1.2659e-01 |

Figure 18: 2D Case 1. $\lambda(\vec{x}) = 250e^{-5|\vec{x}|^2}$,$||R_0||_\infty = 0.9147$

Our cases here will be the same as in Section 4.1. In particular, these simulations shold help to establish the dimensionally independent nature of your dynamical results. First, we take $||R_0||_\infty < 1$ and show that $I, V \to 0$ and $||T(t) - T^*(t)||_\infty \to 0$. In fact, here the behavior is even more apparent than it was in the case of one spatial dimension. In Figures 18 - 21, by the time we reach $t = 100$, $I$ and $V$ are within machine error of zero and the relative error in $T^*$ as an approximation to $T$ is roughly 0.025%.

Secondly, we can easily demonstrate that $||R_0||_\infty < 1$ is not a necessary condition for $||I(t)||_\infty$, $||V(t)||_\infty \to 0$.

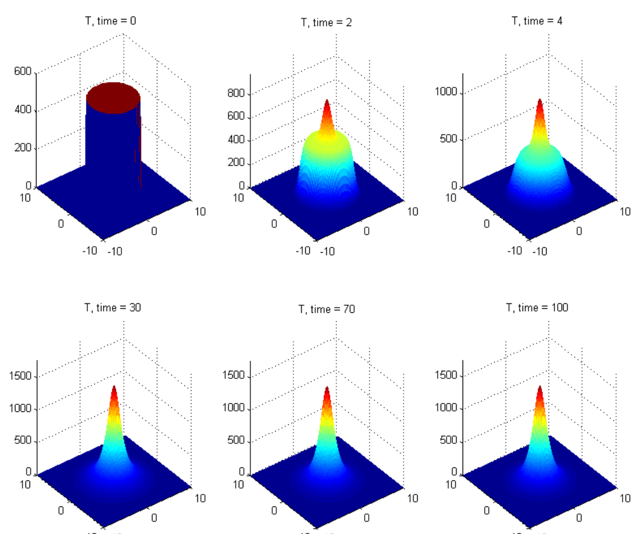


Figure 19: 2D Case 1. Evolution of T-Cells

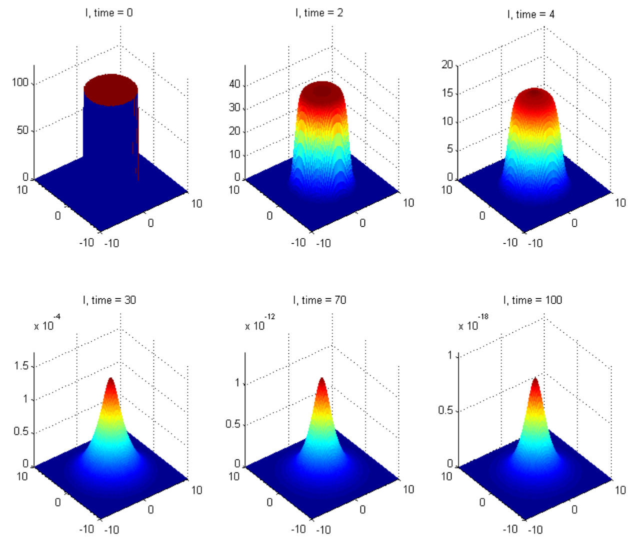


Figure 20: 2D Case 1. Evolution of I-Cells

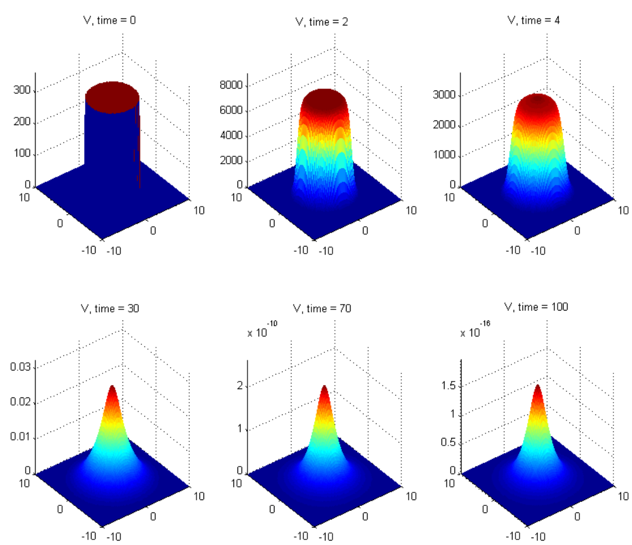


Figure 21: 2D Case 1. Evolution of Virions

| $t$ | $\|\|T(t)\|\|_\infty$ | $\|\|I(t)\|\|_\infty$ | $\|\|V(t)\|\|_\infty$ | $\|\|T(t)-T^*(t)\|\|_\infty$ |
|---|---|---|---|---|
| 0 | 5.0000e+02 | 1.0000e+02 | 3.0000e+02 | 0 |
| 20 | 5.3755e+03 | 4.7950e-02 | 8.7927e+00 | 5.0135e+00 |
| 40 | 5.6961e+03 | 2.3715e-05 | 4.3467e-03 | 1.8207e+00 |
| 60 | 5.7775e+03 | 1.2339e-08 | 2.2592e-06 | 7.6187e-01 |
| 80 | 5.8055e+03 | 6.6724e-12 | 1.2211e-09 | 3.3813e-01 |
| 100 | 5.8165e+03 | 3.6736e-15 | 6.7213e-13 | 1.5568e-01 |

Figure 22: 2D Case 2. $\lambda(\vec{x}) = 3000e^{-5|\vec{x}|^2}$,$||R_0||_\infty = 10.9670$

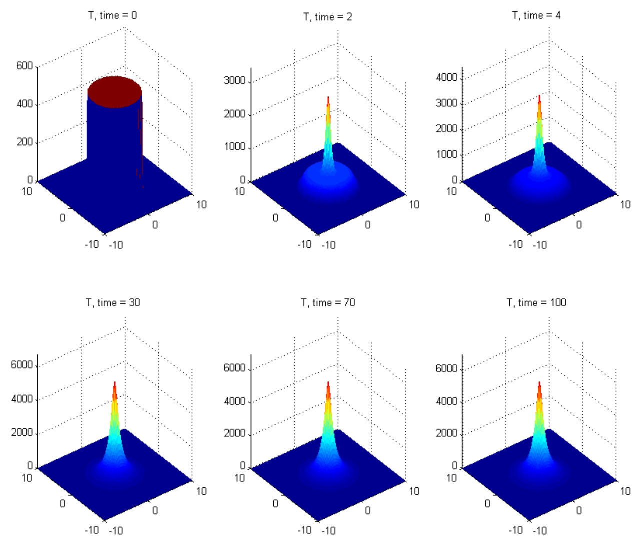


Figure 23: 2D Case 2. Evolution of T-Cells

Figures 22 - 25 show that $I, V$ still tend towards zero for large time even though $||R_0||_\infty \approx 11$. Since $I, V \to 0$, we also see that $||T(t) - T^*(t)||_\infty$ becomes very small relative to the size of $T$.

The third case is more difficult to demonstrate in two spatial dimensions. We wish to show that $||R_0||_\infty < 1$ can be a fairly sharp bound in the case that $||R_0||_\infty \approx \overline{R}_0$. To do this, we construct a $\lambda$ such that $R_0(x, y) = 1 + \varepsilon(x, y)$ where $\varepsilon(x, y)$ is somewhat small.

Our $\lambda$ here is defined by

$$\lambda(x, y) = 273.3 + 5\cos\left(\frac{\pi\sqrt{x^2+y^2}}{4}\right)^2, \quad x, y \in [-2, 2]$$

and

$$\lambda(x+4, y) = \lambda(x, y), \quad \lambda(x, y+4) = \lambda(x, y).$$

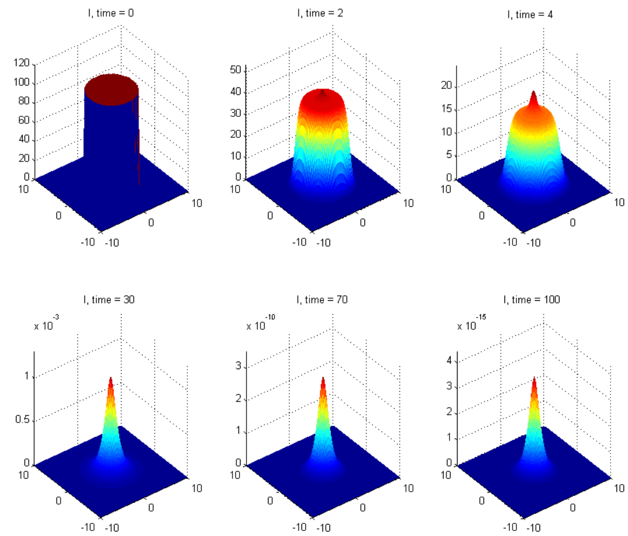


Figure 24: 2D Case 2. Evolution of I-Cells

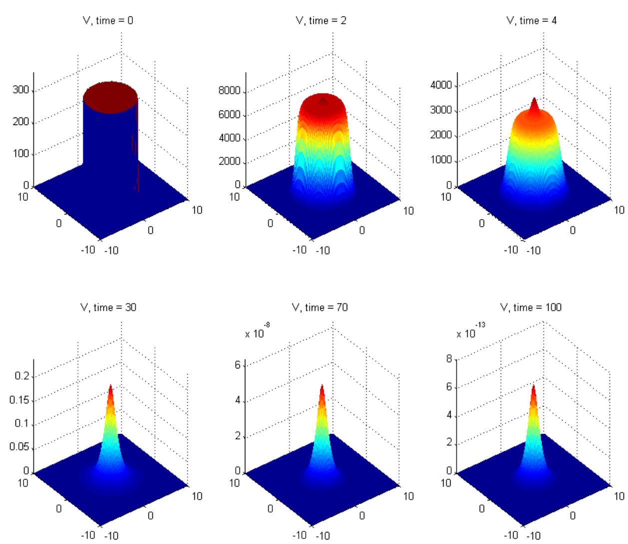


Figure 25: 2D Case 2. Evolution of Virions

| $t$ | $\|\|T(t)\|\|_\infty$ | $\|\|I(t)\|\|_\infty$ | $\|\|V(t)\|\|_\infty$ | $\|\|T(t) - T^*(t)\|\|_\infty$ |
|---|---|---|---|---|
| 0 | 5.0000e+02 | 1.0000e+02 | 3.0000e+02 | 0 |
| 20 | 4.3652e+03 | 2.3492e+01 | 7.6658e+02 | 1.7711e+01 |
| 40 | 6.4873e+03 | 9.0954e+00 | 2.9482e+02 | 1.9692e+01 |
| 60 | 7.6617e+03 | 4.8965e+00 | 1.5801e+02 | 1.5768e+01 |
| 80 | 8.3016e+03 | 3.2308e+00 | 1.0399e+02 | 1.1938e+01 |
| 100 | 8.6436e+03 | 2.3830e+00 | 7.6601e+01 | 9.0823e+00 |

Figure 26: 2D Case 3. $\lambda(\vec{x}) = 273.3 + 5\cos\left(\frac{\pi|\vec{x}|}{4}\right)^2, ||R_0||_\infty = 1.0183$

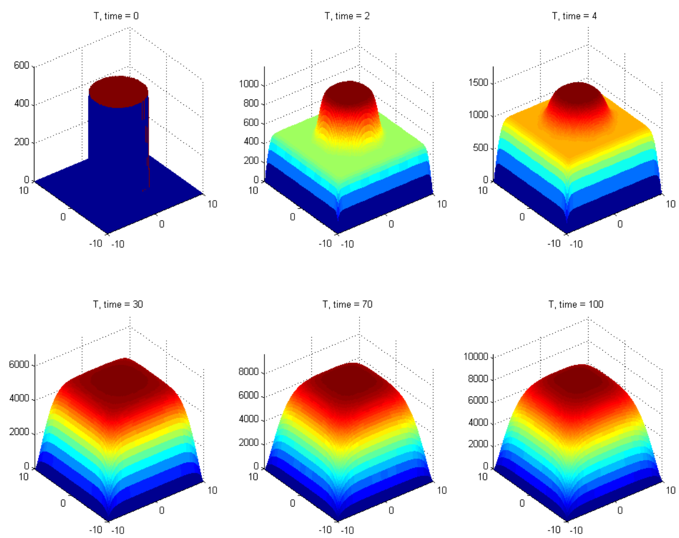


Figure 27: 2D Case 3. Evolution of T-Cell

The graph of this looks like smooth periodic humps on each $4 \times 4$ square in both directions.

This choice of $\lambda$ forces

$$R_0(x, y) = 1 + \varepsilon(x, y), \quad 0 \leq \varepsilon(x, y) \leq 0.02, \quad (x, y) \in \Omega.$$

Also, in this case we take $\mu_I = 0.1$ days$^{-1}$. Recall that changing $\mu_I$ changes nothing about $R_0$. This change was made simply to accentuate the non-zero steady state which the system is tending toward. Figures 26 - 29 show that $I, V$ each seem to settle near some non-zero value. The value $||T(t) - T^*(t)||_\infty$ is significantly bigger than the previous simulations as well which suggests that the system is approaching an equilibrium with non-zero $I$ and $V$.

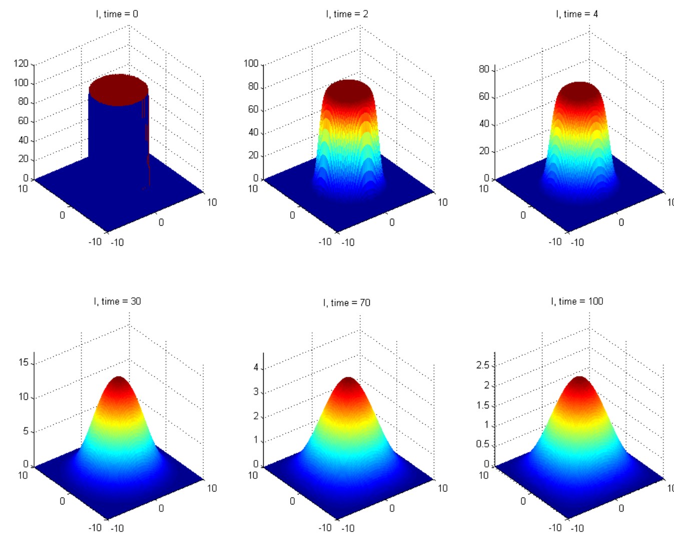


Figure 28: 2D Case 3. Evolution of I-Cells

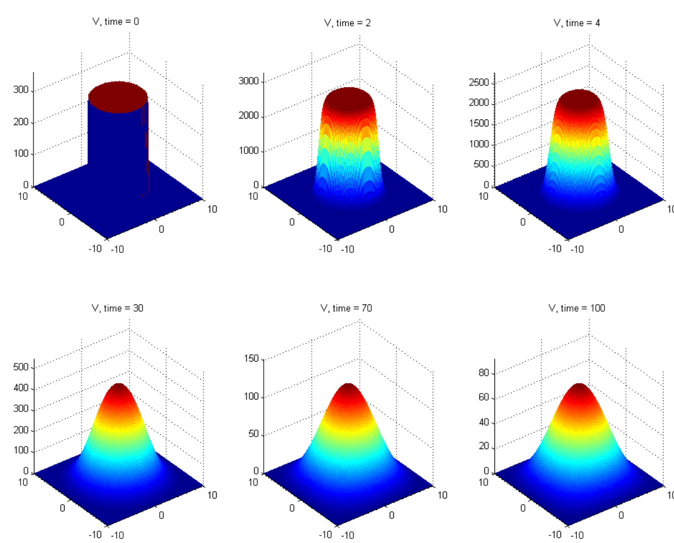


Figure 29: 2D Case 3. Evolution of Virions

For our last simulation, we increase $\lambda$ enough to make $||R_0||_\infty$ and $\overline{R}_0$ larger than 1. We clearly see that there is a steady state with non-zero $I$ and $V$.

| $t$ | $\|\|T(t)\|\|_\infty$ | $\|\|I(t)\|\|_\infty$ | $\|\|V(t)\|\|_\infty$ | $\|\|T(t) - T^*(t)\|\|_\infty$ |
|---|---|---|---|---|
| 0 | 5.0000e+02 | 1.0000e+02 | 3.0000e+02 | 0 |
| 20 | 6.7741e+03 | 4.3135e-01 | 7.2409e+01 | 1.3978e+01 |
| 40 | 9.9845e+03 | 1.4235e-01 | 2.2714e+01 | 7.3235e+00 |
| 60 | 1.1739e+04 | 4.0544e-01 | 6.3067e+01 | 5.0114e+00 |
| 80 | 1.2677e+04 | 3.5534e+00 | 5.4574e+02 | 1.4978e+01 |
| 100 | 1.3011e+04 | 5.2963e+01 | 8.0983e+03 | 1.8364e+02 |

Figure 30: 2D Case 4. $\lambda(\vec{x}) = 400 + 300e^{-5|\vec{x}|^2}$,$||R_0||_\infty = 2.5611$

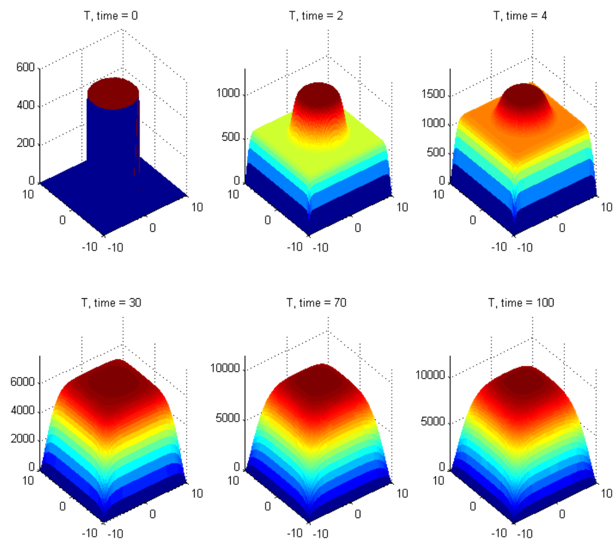


Figure 31: 2D Case 4. Evolution of T-Cells

In this case, $||R_0||_\infty = 2.5611$ and $\overline{R}_0 = 1.4652$. It is clearly seen from Figures 30 - 33 that $I, V$ are not tending towards zero; they are not even decreasing after long enough time. Also the error in $T^*$ as an approximation to $T$ is more substantial in this case.

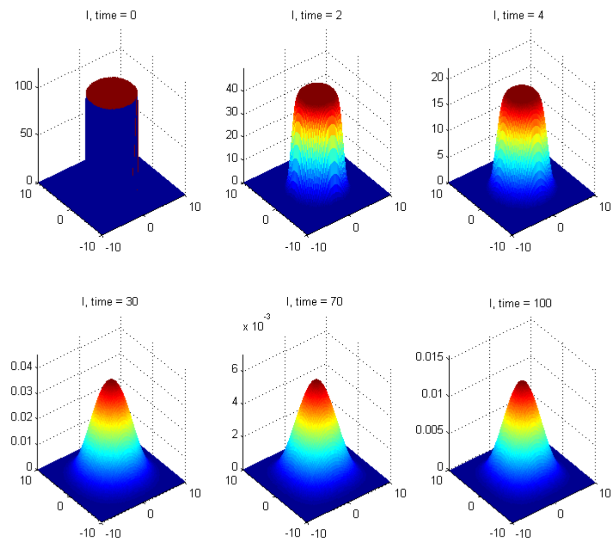


Figure 32: 2D Case 4. Evolution of I-Cells

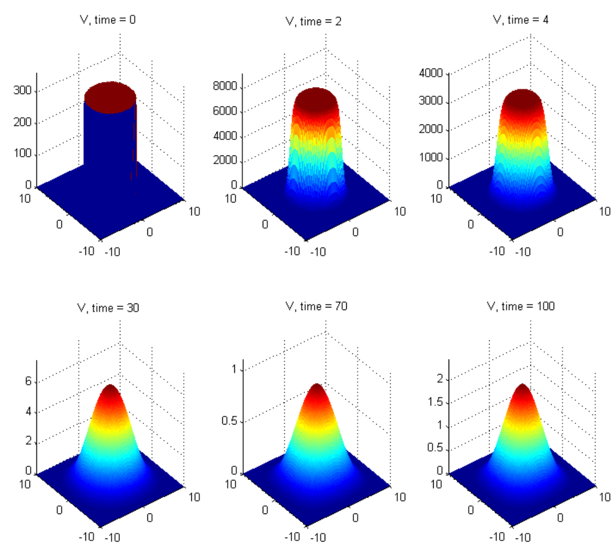


Figure 33: 2D Case 4. Evolution of Virions

# CHAPTER 5
# CONCLUSION

This thesis presents a new in-host spatial model for thefor the dynamics of HIV in an infected host by introducing diffusion. The new system of parabolic PDEs is analyzed in detail.

First, Duhamel's principle was used to invert the diffusion operator and then a local existence theorem was established using the Banach fixed point theorem on a sufficiently small time interval. Global existence and uniqueness was then shown by proving that solutions are positive and thus bounded as long as they exist.

Next, the gain in regularity that is typical of solutions to diffusion equations was establshed. We first proved that solutions exhibit low order regularity following the lead of Pankavich and Michalowski [12], [13], and using the low order regularity as a base case, high order regularity was proven by induction. In particular, solutions were shown to be as smooth as one desires so long as the influx of healthy T cells is similarly smooth.

With existence, uniqueness and high order regularity established, we turned our attention to the large time asymptotics of the system. By establishing bounds on the supremum norms of the quantities involved, several different sufficient conditions were presented under which our system tends to a viral extinction steady state for large time. These conditions were compared with the analagous results of the spatially homogeneous model. In the constant $\lambda$ case, the large time asymptotics of the spatially heterogeneous model and the spatially homogeneous model are nearly identical. Further analytical study is needed to determine conditions for the global asymptotic stability of the infection-free steady state and to determine the behavior of the infection as it tends to a viral persistence state in the case that $\lambda$ is spatially dependent.

Finally, the behavior of the model was simulated in MATLAB using a finite difference method in order to verify the analysis (especially the large time asymptotics). The simulations were consistent our analysis and verified that our sufficient conditions for viral extinction were correct. Using these simulations, we also presented convincing computational evidence that our sufficient conditions for viral extinction are not necessary.

The methods used in this thesis could be applied to a very wide range of problems. Indeed, they could be easily adapted to other nonlinear systems of parabolic PDEs such as those with directed diffusion or HIV models with additional populations to account for mutated strains of the virus or latently infected cells.

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# APPENDIX I: LEMMAS 3.5 AND 3.6

Following are the proofs of two key lemmas used in Section 3.3.

**Lemma 3.5.** Let $\Omega = \mathbb{R}^n$ or let $\Omega$ be a bounded open subset of $\mathbb{R}^n$ and let $F : \Omega \times [0, \infty) \to [0, \infty)$. Futher, assume that for fixed $t \geq 0$, $F(\cdot, t) \in H^\infty(\Omega)$ and that $\frac{\partial F}{\partial t}$ is continuous and bounded for $(x, t) \in \Omega \times [0, \infty)$. Then

$$f(t) = \sup_{x \in \Omega} F(x, t), \quad t \in [0, \infty)$$

is uniformly continuous.

**Proof.** The proof proceeds slightly differently for $\Omega = \mathbb{R}^n$ and for $\Omega$ a bounded open subset of $\mathbb{R}^n$.

First assume that $\Omega = \mathbb{R}^n$. For fixed $t \geq 0$, we have that $F(x, t) \in H^\infty(\Omega)$. Thus by the Sobolev embedding theorem, $F(x, t) \in C_0^\infty(\Omega)$. Hence, since $F$ is positive and goes to zero at infinity, we know that $F$ attains its maximum on $\Omega = \mathbb{R}^n$. To see this, for sufficiently large $k$, we could restrict $F$ to $[-k, k]^n$ in space. Then since $F$ goes to zero as $|x| \to \infty$, we can bound $F$ outside of $[-k, k]^n$ and, inside $[-k, k]^n$, F must attain its maximum since the set is compact. Thus, for any $t \geq 0$,

$$\sup_{x \in \Omega} F(x, t) = F(x^*, t) \text{ for some } x^* \in \Omega.$$

If $\Omega$ is an open, bounded subset of $\mathbb{R}^n$ then the Sobolev embedding theorem implies that for fixed $t \geq 0$, $F(x, t) \in C^\infty\left(\overline{\Omega}\right)$. Further, $\overline{\Omega}$ is closed and bounded so $F$ must meet its supremum somewhere in the set. Hence, in this case, we can also claim that for any $t \geq 0$,

$$\sup_{x \in \Omega} F(x, t) = \sup_{x \in \overline{\Omega}} F(x, t) = F(x^*, t) \text{ for some } x^* \in \overline{\Omega}.$$

In either case, it is the case that $F$ is uniformly continuous in $x$ for all $x \in \Omega$ or $\overline{\Omega}$. $F$ is also uniformly continuous in $t$ since it has a bounded first derivative in $t$. Thus if $f$ is defined as in the statement of the lemma, we see for $t, \tau \geq 0$,

$$\begin{aligned}
|f(t) - f(\tau)| &= \left|\sup_{x\in\Omega} F(x,t) - \sup_{x\in\Omega} F(x,\tau)\right| \\
&= |F(x_1,t) - F(x_2,\tau)|, \quad \text{for some } x_1, x_2 \in \Omega \text{ or } \overline{\Omega} \\
&= |F(x_1,t) - F(x_2,t) + F(x_2,t) - F(x_2,\tau)| \\
&\leq |F(x_1,t) - F(x_2,t)| + |F(x_2,t) - F(x_2,\tau)|.
\end{aligned}$$

Then since $F$ is uniformly continuous in time and space (this follows since $F$ has a bounded derivative in time and is smooth in space), we know that $f$ must be uniformly continuous in time. ■

**Lemma 3.6.** Let $f : [a, \infty) \to [0, \infty)$ be a uniformly continuous function such that

$$\int_a^\infty f(t)dt = C < \infty.$$

Then $\lim_{t\to\infty} f(t) = 0$.

**Proof.** Assuming that $f$ is uniformly continuous, we prove the statement by contrapositive. That is, we actually prove that if

$$\lim_{t\to\infty} f(t) \neq 0$$

then the integral doesn't converge, which is equivalent to the statement of the lemma. Assuming the limit is not zero, we know that there is $\varepsilon > 0$ such that for any $K > 0$, there is $\tau > K$ such that $f(\tau) > \varepsilon$; i.e., no matter how large we force $t$, we cannot ensure that $f(t)$ remains less than this $\varepsilon$.

Then by uniform continuity, for such $\varepsilon$, there is $\delta > 0$ such that for any $t \in (\tau - \delta, \tau + \delta)$,

$$|f(\tau) - f(t)| < \tfrac{\varepsilon}{2}.$$

An important note (and the reason that we require *uniform* continuity) is that this $\delta$ does not depend on $t$ or $\tau$; it depends only on $\varepsilon$. Now $f(\tau) > \varepsilon$ and $|f(\tau) - f(t)| < \frac{\varepsilon}{2}$ imply that $f(t) > \frac{\varepsilon}{2}$ for all $t \in (\tau - \delta, \tau + \delta)$.

To recap, for some fixed $\varepsilon > 0$, there exists $\delta > 0$ (which, once chosen, is fixed as well), such that for *any* $K > 0$, there is a $\tau > K$ such that $f(t) > \frac{\varepsilon}{2}$ for all $t \in (\tau - \delta, \tau + \delta)$.

First, take $K_0 = a + \delta$ and find the corresponding $\tau_1 > K_0$ such that $f(t) > \frac{\varepsilon}{2}$ for all $t \in (\tau_1 - \delta, \tau_1 + \delta)$. Next, take $K_1 = \tau_1 + 2\delta$ and find the corresponding $\tau_2 > K_1$ such that $f(t) > \frac{\varepsilon}{2}$ for all $t \in (\tau_2 - \delta, \tau_2 + \delta)$. Next, take $K_2 = \tau_2 + 2\delta$ and repeat *ad infinitum.*

This process constructs a sequence of disjoint intervals, $I_n = (\tau_n - \delta, \tau_n + \delta)$, $n \in \mathbb{N}$ such that $f(t) > \frac{\varepsilon}{2}$ for all $t \in I_n$ for each $n$. Then for any $N \in \mathbb{N}$, we have

$$\int_a^\infty f(t)dt \geq \sum_{n=1}^{N} \int_{\tau_n - \delta}^{\tau_n + \delta} f(t)dt > \sum_{n=1}^{N} \int_{\tau_n - \delta}^{\tau_n + \delta} \frac{\varepsilon}{2} dt = \sum_{n=1}^{N} \varepsilon\delta = N\varepsilon\delta.$$

This implies that the integral is infinite and concludes the proof. ■

**Note.** The assumption that $f$ is a nonnegative function is actually superfluous; it was only assumed here since it simplifies the proof a bit and since it is sufficient for what follows. However, it can be relaxed by realizing that $f$ is uniformly continuous if and only if $f$ is continuous and $|f|$ is uniformly continuous. Thus proving the lemma for nonnegative functions actually implies that the same property holds for other functions.

## APPENDIX II: MATLAB CODE

The following MATLAB code was used for the simulations in Section 4.

### OneDmodel_implicit.m

```
clear; close all;
tic;
%Set Grids
dx = 0.02; x_min = -10; x_max=10;
dt = 0.01; t_min = 0   ; t_max=100;
x = x_min:dx:x_max;
t = t_min:dt:t_max;
mu_t = 0.03; mu_i = 0.5; mu_v = 3;
D_t = .09504; D_i = .09504; D_v = 0.00076032;
a_t = D_t*dt/(dx^2); a_i = D_i*dt/(dx^2); a_v = D_v*dt/(dx^2);
k=0.00000343; N=960;

%Initialize T,I,V
T = zeros(length(x),length(t));
T2 = zeros(length(x),length(t));
I = zeros(length(x),length(t));
V = zeros(length(x),length(t));
lamvec = zeros(length(x),1);
%Initial Conditions and lambda
for m=1:length(x)
    if abs(x(m)) < 5
        T(m,1)  = 2000;
        T2(m,1) = 2000;
        I(m,1)  = 300;
        V(m,1)  = 800;
    end
    lamvec(m,1) = lambda_1d(x(m));
```

```
end

%Boundary Conditions (Zero Here)
T(1,:)  = 0; T(length(x),:) = 0;
T2(1,:) = 0; T(length(x),:) = 0;
I(1,:)  = 0; I(length(x),:) = 0;
V(1,:)  = 0; V(length(x),:) = 0;

%initialize the matrices I will need (using sparse matrices)
B = spdiags([-ones(length(x)-2,1),2*ones(length(x)-2,1),-ones(length(x)
    -2,1)], ...
                        [-1,0,1], length(x)-2, length(x)-2);
Id = speye(length(x) - 2);
Tmat = (1+mu_t*dt)*Id + a_t*B;
Imat = (1+mu_i*dt)*Id + a_i*B;
Vmat = (1+mu_v*dt)*Id + a_v*B;

%Use Cholesky factorization for efficiency
R_T = chol(Tmat);
R_I = chol(Imat);
R_V = chol(Vmat);

%We'll also want to track the maxima at each time step
Tsup = zeros(length(t),1);     Tsup(1,1)  = max(abs(T(:,1)));
T2sup = zeros(length(t),1);    T2sup(1,1) = max(abs(T2(:,1)));
E_max = zeros(length(t),1);    E_max(1,1) = max(abs(T(:,1) - T2(:,1)));
Isup = zeros(length(t),1);     Isup(1,1)  = max(abs(I(:,1)));
Vsup = zeros(length(t),1);     Vsup(1,1)  = max(abs(V(:,1)));

%we'll only solve at these points (leave boundary alone
xs = 2:length(x)-1;

```

```
%Backward Euler Scheme (Solve for T(:,n) in terms of T(:,n-1))
%   by solving matrix equations
for l=2:length(t)
    T(xs,l)   = R_T'\(T(xs,l-1)+dt*(lamvec(xs,1)- k*T(xs,l-1).*V(xs,l-1)));
    T(xs,l)   = R_T\T(xs,l);
    T2(xs,l)  = R_T'\(T2(xs,l-1)+dt*(lamvec(xs,1)));
    T2(xs,l)  = R_T\T2(xs,l);
    I(xs,l)   = R_I'\(I(xs,l-1)+dt*(k*T(xs,l-1).*V(xs,l-1)));
    I(xs,l)   = R_I\I(xs,l);
    V(xs,l)   = R_V'\(V(xs,l-1)+dt*mu_i*N*I(xs,l));
    V(xs,l)   = R_V\V(xs,l);

    %Set maxima
    Tsup(l,1)   = max(abs(T(xs,l)));
    T2sup(l,1)  = max(abs(T2(xs,l)));
    E_max(l,1)  = max(abs(T(xs,l) - T2(xs,l)));
    Isup(l,1)   = max(abs(I(xs,l)));
    Vsup(l,1)   = max(abs(V(xs,l)));
end

E_msq = (1/length(x))*(sum((T2(:,end)-T(:,end)).^2))^(1/2);

%Plot results for T (t=0 to t=10)
figure(1); clf;
subplot(2,3,1);
plot(x,T(:,1)');
title('T(x,0)');
xlabel('x');
ylabel('T');
axis([-10 10 0 max(T(:,1))*1.2]);
subplot(2,3,2);
```

```
plot(x,T(:,200)');
title('T(x,2)');
xlabel('x');
ylabel('T');
axis([-10 10 0 max(T(:,200))*1.2]);
subplot(2,3,3);
plot(x,T(:,400)');
title('T(x,4)');
xlabel('x');
ylabel('T');
axis([-10 10 0 max(T(:,400))*1.2]);
subplot(2,3,4);
plot(x,T(:,3000)');
title('T(x,30)');
xlabel('x');
ylabel('T');
axis([-10 10 0 max(T(:,3000))*1.2]);
subplot(2,3,5);
plot(x,T(:,7000)');
title('T(x,70)');
xlabel('x');
ylabel('T');
axis([-10 10 0 max(T(:,7000))*1.2]);
subplot(2,3,6);
plot(x, T(:,length(t))');
title('T(x,100)');
xlabel('x');
ylabel('T');
axis([-10 10 0 max(T(:,length(t)))*1.2]);

%Results for I (t=0 to t=10)
figure(2); clf;
```

```
subplot(2,3,1);
plot(x,I(:,1)');
title('I(x,0)');
xlabel('x');
ylabel('I');
axis([-10 10 0 max(I(:,1))*1.2]);
subplot(2,3,2);
plot(x,I(:,200)');
title('I(x,2)');
xlabel('x');
ylabel('I');
axis([-10 10 0 max(I(:,200))*1.2]);
subplot(2,3,3);
plot(x,I(:,400)');
title('I(x,4)');
xlabel('x');
ylabel('I');
axis([-10 10 0 max(I(:,400))*1.2]);
subplot(2,3,4);
plot(x,I(:,3000)');
title('I(x,30)');
xlabel('x');
ylabel('I');
axis([-10 10 0 max(I(:,3000))*1.2]);
subplot(2,3,5);
plot(x,I(:,7000)');
title('I(x,70)');
xlabel('x');
ylabel('I');
axis([-10 10 0 max(I(:,7000))*1.2]);
subplot(2,3,6);
plot(x, I(:,length(t))');
```

```
title('I(x,100)');
xlabel('x');
ylabel('I');
axis([-10 10 0 max(I(:,length(t)))*1.2]);

%Results for V (t=0 to t=10)
figure(3); clf;
subplot(2,3,1);
plot(x,V(:,1)');
title('V(x,0)');
xlabel('x');
ylabel('V');
axis([-10 10 0 max(V(:,1))*1.2]);
subplot(2,3,2);
plot(x,V(:,200)');
title('V(x,2)');
xlabel('x');
ylabel('V');
axis([-10 10 0 max(V(:,200))*1.2]);
subplot(2,3,3);
plot(x,V(:,400)');
title('V(x,4)');
xlabel('x');
ylabel('V');
axis([-10 10 0 max(V(:,400))*1.2]);
subplot(2,3,4);
plot(x,V(:,3000)');
title('V(x,30)');
xlabel('x');
ylabel('V');
axis([-10 10 0 max(V(:,3000))*1.2]);
subplot(2,3,5);
```

```
plot(x,V(:,7000)');
title('V(x,70)');
xlabel('x');
ylabel('V');
axis([-10 10 0 max(V(:,7000))*1.2]);
subplot(2,3,6);
plot(x, V(:,length(t))');
title('V(x,100)');
xlabel('x');
ylabel('V');
axis([-10 10 0 max(V(:,length(t)))*1.2]);

%Plot maxima values
figure(4); clf;
subplot(4,1,1)
plot(t,Tsup(:,1)','k');
title('sup(T) as a function of time');
xlabel('time');
ylabel('sup(T)');
axis([-5 100 0 max(Tsup)*1.2]);
subplot(4,1,2)
plot(t,Isup(:,1)','k');
title('sup(I) as a function of time');
xlabel('time');
ylabel('sup(I)');
axis([-5 100 0 max(Isup)*1.2]);
subplot(4,1,3)
plot(t,Vsup(:,1)','k');
title('sup(V) as a function of time');
xlabel('time');
ylabel('sup(V)');
axis([-5 100 0 max(Vsup)*1.2]);
```

```
subplot(4,1,4)
plot(t,T2sup(:,1)','k');
title('sup(T2) as a function of time');
xlabel('time');
ylabel('sup(T2)');
axis([-5 100 0 max(T2sup)*1.2]);

%Plot Lambda
lmax=max(lamvec(:,1));
figure(5); clf;
plot(x,lamvec(:,1)','k');
title('Lambda');
xlabel('x');
ylabel('lambda');
axis([-10 10 0 lmax*1.2]);

R_0_sup = max(lamvec)*N*k/(mu_t*mu_v);
R_0_avg = mean(lamvec)*N*k/(mu_t*mu_v);

Tsup_table = [Tsup(1); Tsup(2001); Tsup(4001); Tsup(6001); Tsup(8001);
    Tsup(10001)];
Isup_table = [Isup(1); Isup(2001); Isup(4001); Isup(6001); Isup(8001);
    Isup(10001)];
E_max_table = [E_max(1); E_max(2001); E_max(4001); E_max(6001); E_max
    (8001); E_max(10001)];
Vsup_table = [Vsup(1); Vsup(2001); Vsup(4001); Vsup(6001); Vsup(8001);
    Vsup(10001)];

TABLE = [Tsup_table Isup_table Vsup_table E_max_table];

toc;
```

**lambda_1d.m**

```
function [ L ] = lambda_1d( x)
% For 1D CASE 1:
%    x_0=0;
%    L =  25*exp((-5*(x-x_0)^2));

% For 1D CASE 2:
%    x_0=0;
%    L =  270*exp((-50*(x-x_0)^2));

% For 1D CASE 3:
%    L = 27.3324 + 2.7*cos(x)^2;

% For 1D CASE 4:
  L = 50 + 10*exp((-5*(x-x_0)^2));

end
```

**TwoDmodel_implicit.m**

```
%Two Dimensional Model for in host HIV dynamics with spatial aspects
%        Computations done using implicit Euler method with
%        time-lagging of nonlinear terms
clear; close all;
tic;

%Set Grids
dx = 0.2; x_min = -10; x_max=10;
dy = 0.2; y_min = -10; y_max=10;
dt = 0.05; t_min = 0; t_max=100;
x = x_min:dx:x_max;
y = y_min:dy:y_max;
```

```
t = t_min:dt:t_max;

%Set all parameters (except lambda) including some which are used in
%   the finite difference scheme
mu_t = 0.03; mu_i = 0.1; mu_v = 3;
D_t = .09504; D_i = .09504; D_v = 0.00076032;
a_t = D_t*dt/(dx^2); a_i = D_i*dt/(dx^2); a_v = D_v*dt/(dx^2);
k=0.000000343; N=960;

%Initialize T,I,V
% T2 will satisfy the same equation as T
% but with the nonlinear term ignored
T  = zeros(length(x),length(y),length(t));
T2 = zeros(length(x),length(y),length(t));
I  = zeros(length(x),length(y),length(t));
V  = zeros(length(x),length(y),length(t));

%Initial Conditions/ also set lambda
lambda = zeros(length(x),length(y));
for m=1:length(x)
    for n=1:length(y)
        r = x(m)^2 + y(n)^2;
        if r < 25
            T(m,n,1)  = 500;
            T2(m,n,1) = 500;
            I(m,n,1)  = 100;
            V(m,n,1)  = 300;
        end
        lambda(m,n) = lambda_2d(x(m),y(n));
    end
end

```

```
avg_lambda = sum(sum(lambda))/(length(x)*length(y));

%Dirichlet Boundary Conditions (Zero Here)
T(1,:,:)  = 0; T(length(x),:,:)  = 0;
T2(1,:,:) = 0; T2(length(x),:,:) = 0;
I(1,:,:)  = 0; I(length(x),:,:)  = 0;
V(1,:,:)  = 0; V(length(x),:,:)  = 0;
T(:,1,:)  = 0; T(:,length(y),:)  = 0;
T2(:,1,:) = 0; T2(:,length(y),:) = 0;
I(:,1,:)  = 0; I(:,length(y),:)  = 0;
V(:,1,:)  = 0; V(:,length(y),:)  = 0;

%Initialize vectors which will be used in the implicit scheme
Tvec   = zeros((length(x)-2)*(length(y)-2),1);
T2vec  = zeros((length(x)-2)*(length(y)-2),1);
Ivec   = zeros((length(x)-2)*(length(y)-2),1);
Vvec   = zeros((length(x)-2)*(length(y)-2),1);
T_Vvec = zeros((length(x)-2)*(length(y)-2),1);
lamvec = reshape(lambda(2:length(x)-1,2:length(y)-1),[(length(x)-2)*(length(y)-2),1]);
%Initialize matrices which will be used in the scheme
B = spdiags([-ones(length(x)-2,1),2*ones(length(x)-2,1),-ones(length(x)-2,1)], ...
                    [-1,0,1], length(x)-2, length(x)-2);
I1 = speye(length(x) - 2);
I2 = speye((length(x) - 2)^2);

Tmat = (1+mu_t*dt)*I2 + a_t*(kron(I1,B) + kron(B,I1));
Imat = (1+mu_i*dt)*I2 + a_i*(kron(I1,B) + kron(B,I1));
Vmat = (1+mu_v*dt)*I2 + a_v*(kron(I1,B) + kron(B,I1));

%Use Cholesky factorization for efficiency
```

```
R_T = chol(Tmat);
R_I = chol(Imat);
R_V = chol(Vmat);

%We'll only solve the system on these grid point
%      (leave the boundaries alone)
xs = 2:length(x)-1;
ys = 2:length(y)-1;

%Get everything in terms of long column vectors
Tvec  = reshape(T(xs,ys,1), [(length(x)-2)*(length(y)-2),1]);
T2vec = reshape(T2(xs,ys,1), [(length(x)-2)*(length(y)-2),1]);
Ivec  = reshape(I(xs,ys,1), [(length(x)-2)*(length(y)-2),1]);
Vvec  = reshape(V(xs,ys,1), [(length(x)-2)*(length(y)-2),1]);

%We would like to store the maximum values at each time step
Tsup  = zeros(length(t),1); Tsup(1,1)  = max(abs(Tvec));
T2sup = zeros(length(t),1); T2sup(1,1) = max(abs(T2vec));
E_max = zeros(length(t),1); E_max(1,1) = max(abs(T2vec-Tvec));
Isup  = zeros(length(t),1); Isup(1,1)  = max(abs(Ivec));
Vsup  = zeros(length(t),1); Vsup(1,1)  = max(abs(Vvec));

for l=2:length(t)
    %create T_Vvec by entry-wise multiplication of T and V
    T_Vvec = Tvec.*Vvec;

    %solve for T,I,V at the current time step
    %   NOTE: the nonlinear term is lagged because
    %   the Tvec.*Vvec multiplication is using info
    %   from the previous time step
    Tvec  = R_T'\(Tvec + dt*(lamvec - k*T_Vvec));
    Tvec  = R_T\Tvec;
```

```
        T2vec = R_T'\(T2vec + dt*lamvec);
        T2vec = R_T\T2vec;
        Ivec  = R_I'\(Ivec + dt*k*T_Vvec);
        Ivec  = R_I\Ivec;
        Vvec  = R_V'\(Vvec + dt*N*mu_i*Ivec);
        Vvec  = R_V\Vvec;

        %Store the maxima
        Tsup(l,1)   = max(abs(Tvec));
        T2sup(l,1)  = max(abs(T2vec));
        E_max(l,1)  = max(abs(T2vec-Tvec));
        Isup(l,1)   = max(abs(Ivec));
        Vsup(l,1)   = max(abs(Vvec));

        %store the results in the appropriate places
        T(xs,ys,l)   = reshape(Tvec,[(length(x)-2),(length(y)-2)]);
        T2(xs,ys,l)  = reshape(T2vec,[(length(x)-2),(length(y)-2)]);
        I(xs,ys,l)   = reshape(Ivec,[(length(x)-2),(length(y)-2)]);
        V(xs,ys,l)   = reshape(Vvec,[(length(x)-2),(length(y)-2)]);

end

E_msq = (1/(length(x)*length(y)))*sum(sum((T(:,:,end) - T2(:,:,end))
    .^2))^(1/2);

%plot T results
figure(1); clf;
subplot(2,3,1)
surf(x,y,T(:,:,1)', 'edgecolor', 'none')
title('T, time = 0');
axis([-10 10 -10 10 0 max(max(T(:,:,1)))*1.2])
subplot(2,3,2)
```

```
surf(x,y,T(:,:,40)', 'edgecolor', 'none')
title('T, time = 2');
axis([-10 10 -10 10 0 max(max(T(:,:,40)))*1.2])
subplot(2,3,3)
surf(x,y,T(:,:,80)', 'edgecolor', 'none')
title('T, time = 4');
axis([-10 10 -10 10 0 max(max(T(:,:,80)))*1.2])
subplot(2,3,4)
surf(x,y,T(:,:,600)', 'edgecolor', 'none')
title('T, time = 30');
axis([-10 10 -10 10 0 max(max(T(:,:,600)))*1.2])
subplot(2,3,5)
surf(x,y,T(:,:,1400)', 'edgecolor', 'none')
title('T, time = 70');
axis([-10 10 -10 10 0 max(max(T(:,:,1400)))*1.2])
subplot(2,3,6)
surf(x,y,T(:,:,length(t))', 'edgecolor', 'none')
title('T, time = 100');
axis([-10 10 -10 10 0 max(max(T(:,:,length(t))))*1.2])

%plot I results
figure(2); clf;
subplot(2,3,1)
surf(x,y,I(:,:,1)', 'edgecolor', 'none')
title('I, time = 0');
axis([-10 10 -10 10 0 max(max(I(:,:,1)))*1.2])
subplot(2,3,2)
surf(x,y,I(:,:,40)', 'edgecolor', 'none')
title('I, time = 2');
axis([-10 10 -10 10 0 max(max(I(:,:,40)))*1.2])
subplot(2,3,3)
surf(x,y,I(:,:,80)', 'edgecolor', 'none')
title('I, time = 4');
```

```
title('I, time = 4');
axis([-10 10 -10 10 0 max(max(I(:,:,80)))*1.2])
subplot(2,3,4)
surf(x,y,I(:,:,600)', 'edgecolor', 'none')
title('I, time = 30');
axis([-10 10 -10 10 0 max(max(I(:,:,600)))*1.2])
subplot(2,3,5)
surf(x,y,I(:,:,1400)', 'edgecolor', 'none')
title('I, time = 70');
axis([-10 10 -10 10 0 max(max(I(:,:,1400)))*1.2])
subplot(2,3,6)
surf(x,y,I(:,:,length(t))', 'edgecolor', 'none')
title('I, time = 100');
axis([-10 10 -10 10 0 max(max(I(:,:,length(t))))*1.2])

%plot V results
figure(3); clf;
subplot(2,3,1)
surf(x,y,V(:,:,1)', 'edgecolor', 'none')
title('V, time = 0');
axis([-10 10 -10 10 0 max(max(V(:,:,1)))*1.2])
subplot(2,3,2)
surf(x,y,V(:,:,40)', 'edgecolor', 'none')
title('V, time = 2');
axis([-10 10 -10 10 0 max(max(V(:,:,40)))*1.2])
subplot(2,3,3)
surf(x,y,V(:,:,80)', 'edgecolor', 'none')
title('V, time = 4');
axis([-10 10 -10 10 0 max(max(V(:,:,80)))*1.2])
subplot(2,3,4)
surf(x,y,V(:,:,600)', 'edgecolor', 'none')
title('V, time = 30');
```

```
axis([-10 10 -10 10 0 max(max(V(:,:,600)))*1.2])
subplot(2,3,5)
surf(x,y,V(:,:,1400)', 'edgecolor', 'none')
title('V, time = 70');
axis([-10 10 -10 10 0 max(max(V(:,:,1400)))*1.2])
subplot(2,3,6)
surf(x,y,V(:,:,length(t))', 'edgecolor', 'none')
title('V, time = 100');
axis([-10 10 -10 10 0 max(max(V(:,:,length(t))))*1.2])

%plot lambda
figure(4); clf;
surf(x,y,lambda(:,:)', 'edgecolor', 'none')
title('lambda');
axis([-10 10 -10 10 0 max(max(lambda))*1.2])

%Plot maxima values
figure(5); clf;
subplot(4,1,1)
plot(t,Tsup(:,1)','k');
title('sup(T) as a function of time');
xlabel('time');
ylabel('sup(T)');
axis([-5 100 0 max(Tsup)*1.2]);
subplot(4,1,2)
plot(t,Isup(:,1)','k');
title('sup(I) as a function of time');
xlabel('time');
ylabel('sup(I)');
axis([-5 100 0 max(Isup)*1.2]);
subplot(4,1,3)
plot(t,Vsup(:,1)','k');
```

```
title('sup(V) as a function of time');
xlabel('time');
ylabel('sup(V)');
axis([-5 100 0 max(Vsup)*1.2]);
subplot(4,1,4)
plot(t,T2sup(:,1)','k');
title('sup(T2) as a function of time');
xlabel('time');
ylabel('sup(T2)');
axis([-5 100 0 max(T2sup)*1.2]);

toc;

Tsup_table = [Tsup(1); Tsup(401); Tsup(801); Tsup(1201); Tsup(1601); Tsup(2001)];
Isup_table = [Isup(1); Isup(401); Isup(801); Isup(1201); Isup(1601); Isup(2001)];
E_max_table = [E_max(1); E_max(401); E_max(801); E_max(1201); E_max(1601); E_max(2001)];
Vsup_table = [Vsup(1); Vsup(401); Vsup(801); Vsup(1201); Vsup(1601); Vsup(2001)];

TABLE = [Tsup_table Isup_table Vsup_table E_max_table];

R_0_sup = max(lamvec)*N*k/(mu_t*mu_v);
R_0_avg = mean(lamvec)*N*k/(mu_t*mu_v);
```

**lambda_2d.m**

```
function [ L ] = lambda_2d( x,y )
% For 2D CASE 1:
% x_0=0;
% y_0=0;
```

```
% L = 250*exp(-((x-x_0).^2+(y-y_0).^2));

%For 2D CASE 2:
% x_0=0;
% y_0=0;
% L = 3000*exp(-5*((x-x_0).^2+(y-y_0).^2));

% For 2D CASE3 :
% c = 273.3236151603498;
% x = mod(x,4); y = mod(y,4);
% x = x-2; y=y-2;
% r = sqrt(x^2 + y^2);
% R=2;
% if r <=R
%       L = c + 5*cos((pi/(2*R))*r)^2;
% elseif r>R
%       L = c;
% end

% For 2D CASE 4:
x_0=0;
y_0=0;
L = 400 + 300*exp(-5*((x-x_0).^2+(y-y_0).^2));

end
```