Boundedness of a class of discretized reaction-diffusion systems

J.M. Wentz · D.M. Bortz

Abstract  Research in systems biology has led to the development of tools that assume well-mixed pools of reactants. To study spatially heterogeneous systems with these tools, a first step is to break up space into discrete compartments. In turn, diffusion can be modeled as an additional reaction across compartment boundaries. However, the incorporation of diffusion can lead to biologically unrealistic instabilities. For instance, in the spatially continuous system it is well known that diffusion-driven blow-up can occur. We show that this is also the case for the spatially discretized system. This phenomenon implies the system cannot be studied under steady-state assumptions. The focus of this paper is, therefore, to determine sufficient conditions for the discretized system with diffusion to remain bounded for all time. We consider reaction-diffusion systems on a 1D domain with Neumann boundary conditions and non-negative initial data and solutions. We define a Lyapunov-like function and show that its existence guarantees that the discretized reaction-diffusion system is bounded. For some systems, it is possible to quickly determine whether or not a Lyapunov-like function exists. We discuss these types of systems and present examples of a bounded and unbounded system. In the future, we would like to extend these results to determine conditions for the system to remain bounded in the continuum limit.

Keywords  Reaction-diffusion systems · method of lines · boundedness · stoichiometric network analysis · Lyapunov functions

Mathematics Subject Classification (2010)  34C11 · 35K57 · 37B25 · 37F99 · 65N40

1 Introduction

The complexity of biological systems has warranted the development of novel computational and mathematical tools (Ji et al, 2017). For example, stoichiometric network analysis is used to study...
biochemical systems without requiring a full understanding of mechanistic detail and kinetic parameters (Clarke, 1988). This method involves constructing a stoichiometry matrix which contains information on how many species are used or produced in each reaction. In turn, a large body of work has been developed to study the stoichiometry matrix (Palsson, 2006; Gianchandani et al, 2010). Using linear programming techniques, flux balance analysis finds the non-unique fluxes that maximize an objective function (e.g., concentration of a metabolite) under steady-state conditions (Orth et al, 2010; Gianchandani et al, 2010). Flux variability analysis is used to determine the range of flux values for a reaction given specific constraints on the system. Flux modules, a concept developed to isolate reaction-sets that account for flux variability (Müller and Bockmayr, 2014), can be found efficiently using computational methods from matroid theory (Reimers et al, 2015). In addition to stoichiometric network analysis, chemical reaction network theory provides conditions for a range of other dynamic properties in a system (Feinberg, 1979). For example, methods exist for determining whether a system has the capacity for multiple steady states (Craciun and Feinberg, 2005, 2006). Ultimately, this set of tools helps researchers predict dynamics, reduce system complexity, and understand perturbations to biochemical networks.

All these methods assume spatial homogeneity, which makes them not yet generally applicable to spatially heterogeneous systems. Recently, however, a method was developed to include diffusion in the stoichiometry matrix (Mohamed et al, 2018). In this study, the method of lines was used to discretize the reaction-diffusion (RD) equation with respect to space. Ultimately, diffusion was modeled as an additional reaction between adjacent spatial compartments. To study this discretization technique, Mohamed et al, 2018 looked specifically at the chemical reaction $A + B \rightarrow C$ and proved a convergence result in the continuum limit. Here, we will use the same approach to discretize the RD system, but rather than proving a convergence result, we will examine under what conditions the discretized RD system is bounded.

We will be considering systems that have spatially constant parameter values (e.g., the reaction and diffusion rates do not vary across space) but note that the framework presented here has the potential to be generalized to systems with spatially varying parameter values. Ultimately, this allows us to study a broad range of biological systems. For example, cells are known to have spatially separated metabolic compartments that are essential for the functioning of cells (Martin, 2010; Zecchin et al, 2015). This compartmentalization is both diffusion and membrane induced, implying that transition rates across compartment boundaries may vary drastically. The discretized RD system allows for the immediate inclusion of these types of spatial features into the model.

In this work we present and prove sufficient conditions for the discretized version of the RD system to be uniformly bounded over time. We are particularly interested in exploring whether diffusion affects boundedness when a system has a globally stable, spatially homogeneous steady state. It is a known phenomenon that the addition of diffusion can lead to both stable and unstable systems (Fila and Ninomiya, 2005; Murray, 2003; Wentz et al, 2018). Specifically, in reaction-only systems that have a stable steady-state, the addition of diffusion can cause solutions to become unbounded. This process is called diffusion-driven blow-up and examples of it are readily available in the literature (Fila and Ninomiya, 2005; Marciniak-Czochra et al, 2016). Notably, diffusion-driven blow-up has been shown to occur in the type of system we examine in this paper (i.e., a system that has a bounded domain, homogeneous Neumann boundary conditions and non-negativity of solutions) (Weinberger, 1999). The existence of extensive literature discussing diffusion-driven blow-up, demonstrates that the question of boundedness is nontrivial for the RD PDEs, and we find that this is also the case for the discretized system of ODEs.
We will use energy-type methods to determine sufficient conditions for a uniform bound over time of the discretized RD system. In Section 2 we present relevant notation and define the properties of a Lyapunov-like function (LLF). In Section 3 we prove that the existence of this LLF guarantees the discretized RD system is uniformly bounded over time. In Section 4 we discuss the question of whether an LLF exists for a specific system and explore two example systems; a bounded and unbounded system that both have a globally stable, spatially homogeneous steady state. Finally, we conclude with a discussion of other applications and ideas for future directions.

2 Notation and definitions

We are interested in RD systems on a bounded and closed spatial interval $I \subset \mathbb{R}$ with two species $u$ and $v$. We will assume the system is dimensionless and $u$ and $v$ represent dimensionless concentrations that are functions of space and time. That is, $u : I \times [0, \infty) \to \mathbb{R}_{\geq 0}$ and $v : I \times [0, \infty) \to \mathbb{R}_{\geq 0}$. Further, we assume the domain is normalized such that $I = [0, 1]$ with boundary $\partial I = \{0, 1\}$. The spatially continuous system is given by the following boundary value problem with Neumann boundary conditions

$$
\begin{align*}
\begin{pmatrix}
u \\
v(x,0) \\
v(y,t) \\
v(y,t)
\end{pmatrix} &= \begin{pmatrix}
u \\
v(x,0) \\
v(y,t) \\
v(y,t)
\end{pmatrix} + \gamma \begin{pmatrix}f(u,v) \\
f(u,v) \\
f(u,v) \\
f(u,v)
\end{pmatrix} + \gamma \begin{pmatrix}u \\
g(u,v) \\
g(u,v) \\
g(u,v)
\end{pmatrix} \\
&= \begin{pmatrix}
u \\
v(x,0) \\
v(y,t) \\
v(y,t)
\end{pmatrix} + \gamma \begin{pmatrix}f(u,v) \\
f(u,v) \\
f(u,v) \\
f(u,v)
\end{pmatrix} + \gamma \begin{pmatrix}u \\
g(u,v) \\
g(u,v) \\
g(u,v)
\end{pmatrix}
\end{align*}
$$

for $x \in I, t > 0$,

$$
\begin{align*}
\begin{pmatrix}u(x,0) \\
v(x,0) \\
v(y,t) \\
v(y,t)
\end{pmatrix} &= \begin{pmatrix}u(x,0) \\
v(x,0) \\
v(y,t) \\
v(y,t)
\end{pmatrix} + \gamma \begin{pmatrix}f(u,v) \\
f(u,v) \\
f(u,v) \\
f(u,v)
\end{pmatrix} + \gamma \begin{pmatrix}u \\
g(u,v) \\
g(u,v) \\
g(u,v)
\end{pmatrix} \\
&= \begin{pmatrix}u(x,0) \\
v(x,0) \\
v(y,t) \\
v(y,t)
\end{pmatrix} + \gamma \begin{pmatrix}f(u,v) \\
f(u,v) \\
f(u,v) \\
f(u,v)
\end{pmatrix} + \gamma \begin{pmatrix}u \\
g(u,v) \\
g(u,v) \\
g(u,v)
\end{pmatrix}
\end{align*}
$$

for $y \in \partial I, t > 0$,

where $\gamma > 0$ and $d > 0$ are constants that contain information on the size of the domain and the diffusion coefficients of the two species (see Murray [2003] for a discussion of these parameters). To guarantee non-negativity of solutions, we will require that $u_0(x) \geq 0$, $v_0(x) \geq 0$ for all $x \in I$ and $f(0, v) \geq 0$, and $g(u, 0) \geq 0$ for all $u, v \in [0, \infty)$. We will further require that $u_0$ and $v_0$ be measurable and bounded on $I$ and that $f$ and $g$ be continuously differentiable. Under these conditions we are guaranteed the existence of a noncontinuable classic solution on $I \times [0, T^*)$, and if $T^* < \infty$ then the solution becomes unbounded as $t \to T^*$ (Hollis et al. 1987). For simplification we will assume that all the parameters are constant across space. This includes both reaction parameters (i.e., constants within the functions $f$ and $g$) as well as spatial parameters (i.e., $\gamma$ and $d$).

We will discretize this system with respect to space by creating $n$ spatial compartments (Figure 1). We will use $\mathcal{N} = \{1, 2, \ldots, n\}$ to represent the set of compartment indices. Let $h$ denote the uniform width of each compartment and $x_0, x_1, \ldots, x_n$ denote the compartment edges. Since the width of each compartment is assumed to be the same, we have that $x_i = ih$ where $h = 1/n$. Let $u = (u_1, u_2, \ldots, u_n)^T$ and $v = (v_1, v_2, \ldots, v_n)^T$ be vectors that represent the average concentration of $u$ and $v$ in each of the $n$ spatial compartments. Let $f(u, v) = (f(u_1, v_1), f(u_2, v_2), \ldots, f(u_n, v_n))^T$ and $g(u, v) = (g(u_1, v_1), g(u_2, v_2), \ldots, g(u_n, v_n))^T$ be vectors that represent the reactions taking place in each compartment. We will model diffusion as a Fickian flux between two adjacent compartments
and, therefore, discretize the system using the 2nd order centered finite difference scheme. We define

\[ D := \begin{pmatrix}
-1 & 1 & 0 & 0 & \ldots & 0 & 0 \\
1 & -2 & 1 & 0 & \ldots & 0 & 0 \\
0 & 1 & -2 & 1 & \ldots & 0 & 0 \\
\vdots & \vdots & \vdots & \vdots & \ddots & \vdots & \vdots \\
0 & 0 & 0 & \ldots & 1 & -2 & 1 \\
0 & 0 & 0 & \ldots & 0 & 1 & -1 
\end{pmatrix} \tag{2} \]

as the centered finite-difference matrix with Neumann boundary conditions.

This leads to the following initial value problem

\[
\begin{align*}
\mathbf{u}_t &= \gamma f(u, v) + \frac{1}{h^2} D\mathbf{u} \\
\mathbf{v}_t &= \gamma g(u, v) + \frac{1}{h^2} D\mathbf{v} \\
u_i(0) &= \frac{1}{h} \int_{(i-1)h}^{ih} u_0(x) dx \\
v_i(0) &= \frac{1}{h} \int_{(i-1)h}^{ih} v_0(x) dx
\end{align*}
\tag{3}
\]

By the Picard-Lindelöf theorem, there is a \( T_{\text{max}} > 0 \) such that a noncontinuable classical and unique solution to (3) exists for \( t \in [0, T_{\text{max}}) \) where it is possible that \( T_{\text{max}} = \infty \). Since the solution is classical, we know that \( u(t) \) and \( v(t) \) are continuous for \( t \in [0, T_{\text{max}}) \) and if \( T_{\text{max}} < \infty \), then \( u(t) \) becomes unbounded as \( t \to T_{\text{max}} \). Thus, if the solution is bounded for \( t \in [0, T_{\text{max}}) \), then \( T_{\text{max}} = \infty \).

Throughout the paper we will be using \( \| \cdot \| : \mathbb{R}^2 \to \mathbb{R} \) to represent the \( l_1 \)-norm and we define the total species concentration as \( \|(u, v)\| = u + v \). Furthermore, we will use variations of \( L \) (e.g., \( \tilde{L}, L_i \)) to represent arbitrary nonnegative constants.
2.1 Lyapunov-like function

In this section we will define a Lyapunov-like function (LLF) for the reactions given in (3). We will later prove that the existence of this LLF guarantees that the discretized RD system is bounded.

The classical definition of a Lyapunov function is a continuously differentiable, locally positive-definite scalar function that decreases along solution trajectories in the neighborhood of a steady state. The LLF defined here will instead decrease along reaction trajectories (i.e., solutions when diffusion is not included) when the total species concentration surpasses a threshold value. The requirement that the LLF decrease only if the total species concentration is large enough allows us to examine boundedness, but does not answer questions of local stability. Thus, the system may still have dynamic features such as multiple steady-states, periodic orbits, and chaotic attractors.

The existence of the LLF shows that if an individual compartment exceeds a threshold total species concentration, then the LLF function evaluated in that compartment will be decreasing along solution trajectories for the reactions. The actual solution trajectory for a single compartment will also include diffusive effects from adjacent compartments. We will show that when diffusive effects are included, the sum of LLFs across compartments is bounded.

Throughout the paper we will use $W$ to denote a LLF. Let $W : \mathbb{R}_{\geq 0}^2 \to \mathbb{R}_{\geq 0}$ be a twice continuously differentiable function. To denote the partial derivative of $W(u, v)$ with respect to $u$ and $v$ we will use the notation $\partial_u W$ and $\partial_v W$, respectively. We will use $(W)_i$, $(\partial_u W)_i$, and $(\partial_v W)_i$ to denote the value of $W$ and its partial derivatives evaluated in compartment $i$ (e.g., $(W)_i = W(u_i, v_i)$). Furthermore, we define the vectors $W := ((W)_1, (W)_2, ..., (W)_n)$, $\partial_u W := ((\partial_u W)_1, (\partial_u W)_2, ..., (\partial_u W)_n)$, and $\partial_v W := ((\partial_v W)_1, (\partial_v W)_2, ..., (\partial_v W)_n)$.

We say that $W$ is a LLF for the reactions $f$ and $g$ given in (3) if $W$ satisfies five properties, denoted below as (P1)–(P5). The five main properties imply secondary properties on $W$, which we will also present below. We first state three of the required properties, i.e. (P1)–(P3). Notably (P1) is the only property that depends on the reactions $f$ and $g$.

(P1) There exists a $K > 0$ such that if $\|(u, v)\| \geq K$ then

\[
(\nabla W(u, v))^T (f(u, v), g(u, v)) \leq 0.
\]

(P2) For all $(u, v) \in \mathbb{R}_{\geq 0}^2$, we require that the second derivatives of $W$ be strictly positive,

\[
\partial_{uu} W(u, v) > 0, \\
\partial_{uv} W(u, v) > 0,
\]

and the mixed partial derivative of $W$ be non-negative

\[
\partial_{uv} W(u, v) \geq 0.
\]

(P3) As the total species concentration goes to infinity, the LLF also approaches infinity:

\[
\lim_{\|(u,v)\| \to \infty} W(u, v) = \infty.
\]

Before we present the final two properties, we will provide some needed notation and secondary properties that follow from [P2] and [P3].
Variations of the letter $M$ (e.g., $M^{(L)}$, $M^{(L)}_u$, $M^{(L)}_v$) will be used to represent a maximum value of either $W$ or a partial derivative of $W$ along the regions of $\mathbb{R}^2_{\geq 0}$ where $\|(u, v)\|$ is constant. For $L > 0$ define

\[
M^{(L)} := \max_{\|(u, v)\| = L} W(u, v) \\
M^{(L)}_u := \max_{\|(u, v)\| = L} \partial_u W(u, v) \\
M^{(L)}_v := \max_{\|(u, v)\| = L} \partial_v W(u, v).
\]

(4)

For the partial derivatives we will also consider what happens in the limit as $u$ or $v$ approaches infinity. Thus, we define

\[
M^{(\infty)}_u := \lim_{u \to \infty} \partial_u W(u, v) \\
M^{(\infty)}_v := \lim_{v \to \infty} \partial_v W(u, v).
\]

(5)

For a fixed $v$ or $u$, respectively, by (P2) we know these limits either converge and exist or diverge to infinity. Note that additionally properties of the LLF that we have not yet defined will imply that $M^{(\infty)}_u$ and $M^{(\infty)}_v$ are independent of $v$ and $u$, respectively, and are therefore constant.

We will be interested in regions of $\mathbb{R}^2_{\geq 0}$ that are defined be level sets of the LLF. For any $L > 0$ there exists a level set of $W$ given by the set $\{(u, v)|W(u, v) = L\}$. Note that if the minimum value of $W$ is greater than $L$ then the level set will be empty. Otherwise, by (P2) and (P3) each level set is composed of one or two 1D-continuous curves that define bounded regions in $\mathbb{R}^2_{\geq 0}$.

We next define three additional constants, which will be denoted as $u$, $v$, and $K$. The constants $u$ and $v$ represent lower bounds on $u$ and $v$, respectively, such that if $u \geq u$ then $\partial_u W$ is positive and if $v \geq v$ then $\partial_v W$ is positive. The third constant $K$ is constructed so that if $L \geq K$ then (P1) holds and the region defined by the level set $W = M^{(L)}$ has a maximum value that occurs only on the boundary of the region (i.e., along the level set curve). The next corollary shows that, given (P2) and (P3) we are guaranteed these constants exist.

**Corollary 1** Suppose $W : \mathbb{R}^2_{\geq 0} \to \mathbb{R}_{\geq 0}$ is twice continuously differentiable. If $W$ satisfies (P2), the following property holds:

(C1) The parameters $M^{(L)}_u$ and $M^{(L)}_v$ are monotonically increasing with respect to $L$.

If, in addition, $W$ satisfies (P3) then the following properties also hold:

(C2) There exists constants $u$ and $v$ such that $\partial_u W(u, v) > 0$ for all $u \geq u$ and $\partial_v W(u, v) > 0$ for all $v \geq v$.

(C3) There exists a $K \geq \max \{K, u, v\}$ such that if $L < K$ then $M^{(L)} < M^{(K)}$.

For the proof of this corollary see Appendix A.

For the fourth property, we will consider level-sets of $W$ and how the tangent lines to the level-sets behave (Figure 2). For every point $(u, v) \in \mathbb{R}^2_{\geq 0}$ there exists a level set of $W$ and corresponding tangent line that intersects $(u, v)$. We will refer to this line as the *level-set tangent line*. Let $u$ and $v$ be the constants given by (C2) By (P2) for all points such that $u > u$ the level-set tangent line is not parallel to the $u$-axis. Similarly for all points such that $v > v$, the level-set tangent line is not parallel to the $v$-axis. We additionally want to guarantee that the level-set tangent lines do not become parallel to the $u$-axis or $v$-axis in the limit as $u$ or $v$ goes to infinity, respectively. This leads to the following property statement
(P4) For a fixed value of $u$, the level-set tangent lines do not become parallel to the $v$-axis in the limit as $v \to \infty$. Similarly, for a fixed value of $v$, the level-set tangent lines do not become parallel to the $u$-axis as $u \to \infty$, i.e.,

$$
\sup_{v \geq L} \left| \frac{\partial_v W(u,v)}{\partial_u W(u,v)} \right| < \infty \text{ for all } u
$$

$$
\sup_{u \geq L} \left| \frac{\partial_u W(u,v)}{\partial_v W(u,v)} \right| < \infty \text{ for all } v.
$$

From this property we immediately see that for all $L \geq 0$ the following constants exist and are finite.

$$
R_{u,L} := \sup_{u \leq L, v \geq L} \left| \frac{\partial_u W(u,v)}{\partial_v W(u,v)} \right|
$$

$$
R_{v,L} := \sup_{v \leq L, u \geq L} \left| \frac{\partial_v W(u,v)}{\partial_u W(u,v)} \right|.
$$

For the final property, we place requirements on the limits of the partial derivatives of the LLF.

(P5) For all $v \in [0, \infty)$, either

(a) the $M_u^{(\infty)}(v)$ is finite and $\lim_{u \to \infty} \partial_u W(u,v)$ exists and is finite, or
(b) the $M_v^{(\infty)}(u)$ is infinite.

Similarly, for all $u \in [0, \infty)$, either

(a) the $M_u^{(\infty)}(u)$ is finite and $\lim_{v \to \infty} \partial_u W(u,v)$ exists and is finite, or
(b) the $M_v^{(\infty)}(u)$ is infinite.
Now that we have stated all five properties, we will provide a formal definition of a LLF.

**Definition 1** Let \( W : \mathbb{R}^2_{\geq 0} \to \mathbb{R}_{\geq 0} \) be a twice continuously differentiable function. Consider the discretized system given by (3). Then \( W \) is a LLF for this system if (P1)–(P5) are satisfied.

Finally, we will show that \( M_{u}(\infty)(v) \) and \( M_{v}(\infty)(u) \), given by (5), are constant functions and will therefore be referred to as \( M_{u}(\infty) \) and \( M_{v}(\infty) \), respectively.

**Corollary 2** The properties (P2), (P4), and (P5) imply the following secondary properties:

(C4) \( M_{u}(\infty) := M_{u}(\infty)(v) \in (0, \infty] \) is independent of \( v \) and \( M_{u}(\infty) > M_{u}^{(L)} \) for all \( L \in [0, \infty) \).

(C5) \( M_{v}(\infty) := M_{v}(\infty)(u) \in (0, \infty] \) is independent of \( u \) and \( M_{v}(\infty) > M_{v}^{(L)} \) for all \( L \in [0, \infty) \).

The proof of Corollary 2 is given in Appendix A.

In the remainder of this paper, we will reference the constants \( K, u, \) and \( v \) given in Corollary 1. These constants only depend on the LLF. We will also reference the constants \( M_{u}(L), M_{v}(L), M^{(L)}, R_{u,L} \) and \( R_{v,L} \) given in (4), (5), and (6). These constants depend on both the LLF and the specified value of \( L \).

2.2 Difference operators and diffusion notation

Let \( \mathbf{w} = (w_1, w_2, ..., w_n)^T \) be an arbitrary vector of length \( n \). Define \( \Delta_i^+ \) and \( \Delta_i^- \) as the forward and backward difference operator, respectively, where

\[
\Delta_i^+ \mathbf{w} := w_{i+1} - w_i \quad \text{for } i = 1, 2, ..., n-1
\]
\[
\Delta_i^- \mathbf{w} := w_i - w_{i-1} \quad \text{for } i = 2, 3, ..., n.
\]

The centered finite difference matrix, given by (2), acting on a species vector \( \mathbf{w} \) is then given as

\[
(D\mathbf{w})_i = \begin{cases} 
\Delta_i^+ \mathbf{w}, & i = 1 \\
\Delta_i^+ \mathbf{w} - \Delta_i^- \mathbf{w}, & i = 2, 3, ..., n-1 \\
-\Delta_i^- \mathbf{w}, & i = n
\end{cases} \quad (7)
\]

where \((D\mathbf{w})_i\) is the \( i \)th element of \( D\mathbf{w} \). Notice that for \( i = 1, n \) there is only a single term because we are assuming homogeneous Neumann boundary conditions.

We will also apply the forward and backward difference operators to the LLF and its partial derivatives. For example, \( \Delta_i^+ \mathbf{W} = (W)_{i+1} - (W)_i \).

2.3 LLF \( \Omega_K \) Region

To prove the main result, we will consider a specific region of phase space (see Figure 3 for example). We define this region so that we are guaranteed that (P1) is satisfied outside of the region and the maximum value of the LLF occurs on the boundary. Our region of interest is given as

\[
\Omega_K := \{ (u,v) \in \mathbb{R}^2_{\geq 0} \mid W(u,v) < M^{(K)} \}.
\]
Fig. 3 Illustration of the LLF $\Omega_K$ region and relevant constants for an example LLF. The dashed line represents the level-set $W(u,v) = M^{(K)}$ and the shaded area is the $\Omega_K$ region.

Due to (C3) we know that $\Omega_K$ contains all points within the bounded region defined by the level set $W(u,v) = M^{(K)}$ (see Figure 3). We will define the boundary of $\Omega_K$ as

$$\partial \Omega_K := \{(u,v) \in \mathbb{R}^2_{\geq 0} \mid W(u,v) = M^{(K)}\}$$

where by definition $\Omega_K \cap \partial \Omega_K = \emptyset$. Define

$$B^{(K)} := \max_{(u,v) \in \partial \Omega_K} \|(u,v)\|.$$  \hspace{1cm} (8)

We then know that for any compartment $i$ such that $(u_i, v_i) \in \Omega_K$, the total species concentration is bounded by $B^{(K)}$ (i.e., $\|(u_i, v_i)\| < B^{(K)}$).

2.4 Notation for the sum of Lyapunov-like functions

Here, we present a framework for examining how the sum of LLFs across compartments evolves with time. This sum is calculated by evaluating the LLF in a single compartment and then summing up these evaluations. First, we partition compartments into those that are and are not contained in $\Omega_K$. Let the set $Y$ contain the indices of compartments that are in $\Omega_K$ and $Y^C$ contain the indices of compartments that are in $\Omega_K^C$ (i.e., $Y := \{i \mid (u_i, v_i) \in \Omega_K\}$ and $Y^C = \mathcal{N} \setminus Y$ where recall that $\mathcal{N} = \{1, 2, \ldots, n\}$). Figure 4 shows an example of this notation (note that the sets $Z_{\text{bdy}}$ and $Z_{\text{ini}}$ will be defined later in this section). For notational simplicity we will say that a compartment whose index is in $Y$ is a $Y$-compartment, and similarly, a compartment whose index is in $Y^C$ is a $Y^C$-compartment.
Suppose $X$ is either $Y$, $Y_C$, or $N$ and define the sum of LLFs over indices in $X$ as the function

$$ W_X : \mathbb{R}^n \times \mathbb{R}^n \rightarrow \mathbb{R} $$

where

$$ W_X(u, v) := \sum_{i \in X} (W)_i. $$

When $X := N$ this equation will be referred to as the System LLF. Note that $W_Y$ can easily be bounded since $W_Y \leq nM^{(K)}$. Our goal in Section 3 will be to find an upper bound for $W_{Y_C}$ that will hold across time for the system given by (3). To do this, in Section 3.1 we assume the membership of $Y_C$ does not change. We then relax this assumption in Section 3.2.

The following notation will be used in Section 3.1 and therefore we assume here that the membership of $Y_C$ does not change. This immediately implies that $W_{Y_C}$ is continuously differentiable and allows us to define the LLF Evolution Equation as

$$ \frac{dW_{Y_C}}{dt} = (\nabla_u W_{Y_C})^T \frac{du}{dt} + (\nabla_v W_{Y_C})^T \frac{dv}{dt} $$

where $\nabla_u W_{Y_C} = (\partial_{u_1} W_{Y_C}, \partial_{u_2} W_{Y_C}, ..., \partial_{u_n} W_{Y_C})$ and $\nabla_v W_{Y_C}$ is defined analogously.

The LLF Evolution Equation tells us how the sum of LLFs over indices in $Y_C$ changes along solution trajectories. Note that these trajectories are determined by a combination of fluxes, and, therefore, we can divide the LLF evolution equation into reactive and diffusive flux contributions, i.e.,

$$ \frac{dW_{Y_C}}{dt} = \gamma W_{Y_C,R} + W_{Y_C,D} $$
where
\[ W_{Y^C,R} := (\nabla_u W_{Y^C})^T f(u, v) + (\nabla_v W_{Y^C})^T g(u, v) \]  
(9)
\[ W_{Y^C,D} := (\nabla_u W_{Y^C})^T D u + (\nabla_v W_{Y^C})^T dD v. \]  
(10)
represent the reactive and diffusive contribution, respectively.

Next, we will examine the diffusive contribution given by (10) by considering a more refined set of diffusive fluxes. To do this, we will define an edge as the boundary between two adjacent compartments, and then consider how the flux across each edge affects \( W_{Y^C} \). Let \( i = 1, 2, ..., n - 1 \) denote an edge where the \( i \)th edge represents the edge between the \( i \) and \( i + 1 \) compartment. We will call an edge that connects a \( Y \)-compartment with a \( Y^C \)-compartment a boundary edge and an edge that connects two \( Y^C \)-compartments an interior edge. Note that we are not giving a name to edges that connect two \( Y \)-compartments.

For each edge \( i \) define the following
\[ n_i = 1_Y(i + 1) - 1_Y(i) \]
where \( 1 \) is the indicator function. Note the set of edge indices is given by \( \mathcal{N} \setminus \{n\} \) and define
\[ Z_{bdy} := \{i \in \mathcal{N} \setminus \{n\} \mid n_i = 1\} \]
\[ Z_{int} := \{i \in \mathcal{N} \setminus \{n\} \mid n_i = 0 \text{ and } i \in Y^C\} \]  
(11)
where \( Z_{bdy} \) contains all boundary edges and \( Z_{int} \) contains all interior edges. The maximum sizes of \( Z_{bdy} \) and \( Z_{int} \) are both \( n - 1 \). Figure 4 defines \( Z_{bdy} \) and \( Z_{int} \) for an example system.

With this notation in mind, let’s again consider the diffusive contribution to the LLF Evolution Equation and rewrite (10) as a sum
\[ W_{Y^C,D} = \sum_{i \in Y^C} (\partial_u W)_i (D u)_i + d (\partial_v W)_i (D v)_i. \]  
(12)
Recall that \( (D u)_i \) and \( (D v)_i \) can be rewritten as shown in (7) and rewrite (12) as
\[ W_{Y^C,D} = \sum_{i \in Z_{bdy}} F_{bdy,i} + \sum_{i \in Z_{int}} F_{int,i} \]  
(13)
where
\[ F_{bdy,i} := n_i \left( (\partial_u W)_i + \frac{1-n_i}{1} \Delta_i^+ u + d (\partial_v W)_i + \frac{1}{1-n_i} \Delta_i^+ v \right) \]  
(14)
\[ F_{int,i} := - \left( \Delta_i^+ (\partial_u W) \Delta_i^+ u + d \Delta_i^+ (\partial_v W) \Delta_i^+ v \right). \]  
(15)
We will refer to \( F_{bdy,i} \) and \( F_{int,i} \) as flux-effect terms because each represents the effect of a flux across an edge on the LLF Evolution Equation. In Section 3.1 we will show that, under certain conditions, the diffusive contribution to the LLF Evolution Equation is negative.

2.5 Notation for crossing the \( \Omega_K \) boundary

To consider a crossing of the \( \Omega_K \) boundary we allow the sets \( Y \) and \( Y^C \) to be functions of time and write \( Y(t) \) and \( Y^C(t) \). When the membership of these sets changes we will say a crossing of \( \partial \Omega_K \) has occurred. Compartment \( i \) will have undergone a crossing at time \( t \) if \( i \in Y^C(t) \) and \( i \in Y(t \pm \epsilon) \) for an arbitrary small \( \epsilon > 0 \). If \( i \in Y(t + \epsilon) \) then a crossing from \( \Omega^C \) into \( \Omega \) has occurred and if \( i \in Y(t - \epsilon) \), a crossing from \( \Omega \) into \( \Omega^C \) has occurred.
3 Boundedness theorems

We will prove the discretized RD system given by (3) is bounded if there exists a LLF with the five properties \([P1]–[P5]\) given in Section 2.1. The proof involves two main steps. In Section 3.1 we consider a snapshot of the system and show that if any compartment exceeds a threshold total species concentration, then the solution to the LLF Evolution Equation is decreasing. In Section 3.2 we consider the evolution of the system, and show that the System LLF is bounded. This bound on the System LLF in turn leads to a bound on the concentration of species within a single compartment.

3.1 The LLF Evolution Equation solution is nonincreasing at a threshold species concentration

In this section we prove that the solution to the LLF Evolution Equation is decreasing if there exists a compartment that exceeds a threshold species concentration. Recall that the LLF Evolution Equation can be broken down into the reactive \([9]\) and diffusive \([10]\) components. We know that the reactive component is nonpositive due to \([P1]\). Thus, it remains to show that the diffusive component is nonpositive at a threshold species concentration. We will assume that \(Y\) is non-empty, otherwise we know the diffusive contribution is nonpositive due to \([P2]\).

Recall that the diffusive component of the LLF Evolution Equation can be rewritten as a summation of flux-effect terms, as given by \([13]\). Each of these flux-effect terms can be bounded from above by a constant (see Lemma 1). Therefore, the diffusive component is negative if there exists one negative flux-effect term with a sufficiently large magnitude. This negative flux-effect term exists if the two adjacent compartments that contribute to the flux have a large enough difference between the amount of species they contain (see Lemma 2 and Corollary 3, 4, and 5).

Thus, proving the LLF Evolution Equation solution is decreasing, reduces to proving the following statement: If any compartment exceeds a threshold species concentration, then two adjacent compartments exist that have the necessary concentration difference to guarantee the diffusive contribution to the LLF Evolution Equation is negative (Lemma 3 and 4). It then immediately follows that the solution to the entire LLF Evolution Equation is nonincreasing (Corollary 6).

With this road-map in mind, we first show that for \(i \in Z_{\text{bdy}}\) or \(i \in Z_{\text{int}}\), the flux-effect term \(F_{\text{bdy},i}\) or \(F_{\text{int},i}\), respectively, has an upper bound. By \([P2]\) we immediately know that \(F_{\text{int},i} < 0\) for all \(i \in Z_{\text{int}}\). In the next lemma, we prove that an upper bound for \(F_{\text{bdy},i}\), which will be denoted as \(F_{\text{max}}\), exists.

**Lemma 1** Let \(W\) be a LLF with the properties \([P1]–[P5]\) for the system given by (3). Consider the system at an arbitrary time \(t > 0\). Suppose \(Z_{\text{bdy}}\) is non-empty and pick \(i \in Z_{\text{bdy}}\). There exists a \(F_{\text{max}} > 0\) that bounds the value of \(F_{\text{bdy},i}\) given by (14).

**Proof** Recall that the LLF has associated constants, \(K\), \(u\), and \(v\), which are given in Corollary 1. We will also refer to the constants \(B^{(K)}\), \(R_{u,B^{(K)}}\), and \(R_{v,B^{(K)}}\) given by \([6]\) and \([8]\). Note that by \([C3]\) \(K > u, v\), which in turn implies \(B^{(K)} > u, v\).

Pick \(i \in Z_{\text{bdy}}\) and rewrite \(F_{\text{bdy},i}\) as follows:

\[
F_{\text{bdy},i} = n_i \left( F_{\text{bdy},i}^{(u)} + F_{\text{bdy},i}^{(v)} \right)
\]
where

\[ F_{bdy,i}^{(u)} := (\partial_u W)_{i+1}^{-1} \Delta_i^+ u \]
\[ F_{bdy,i}^{(v)} := d(\partial_v W)_{i+1}^{-1} \Delta_i^+ v. \]

Since \( i \in \mathbb{Z}_{bdy} \), we know that either \( n_i = 1 \) or \( n_i = -1 \), see \([11]\). We will assume \( n_i = 1 \), but note that analogous logic can be applied if \( n_i = -1 \). Note that since \( n_i = 1 \) then \( i + 1 \in Y \) and \( u_{i+1}, v_{i+1} \leq \| (u_{i+1}, v_{i+1}) \| \leq B^{(K)} \). For notational simplicity we define the following two constants:

\[ u^* := B^{(K)} (1 + dR_{v,B^{(K)}}) \]
\[ v^* := B^{(K)} (1 + R_{u,B^{(K)}/d}). \]

We next consider two sets of cases (i.e., Cases 1–3 and Cases 4–6, given below). In each set we are guaranteed that one case must hold. That is, one of Cases 1–3 must hold and one of Cases 4–6 must hold. In Cases 1 and 4 we bound the value of \( u \), in Cases 2 and 3 and Cases 5–6 we bound the value of \( F_{bdy,i}^{(u)} \) and \( F_{bdy,i}^{(v)} \), respectively.

Case 1: \( \Delta_i^+ u \geq 0 \) and \( v_i > v^* \). The conditions imply that \( \Delta_i^+ u = u_{i+1} - u_i \leq u_{i+1} \leq B^{(K)} \) and, thus, \( u_i \leq B^{(K)} \). Furthermore, since \( v_i > B^{(K)} > v \), we have that, by \([C2] \) \( (\partial_u W)_i > 0 \). This leads to the following upper bound on \( F_{bdy,i} \):

\[ F_{bdy,i} = d(\partial_v W)_i \left( \frac{(\partial_u W)_i}{d(\partial_v W)_i} \| \Delta_i^+ u \| + \Delta_i^+ v \right) \leq d(\partial_v W)_i \left( R_{u,B^{(K)}} B^{(K)}/d + v_{i+1} - v_i \right) \]
\[ \leq d(\partial_v W)_i \left( R_{u,B^{(K)}} B^{(K)}/d + B^{(K)} - v^* \right) \leq 0. \]

Case 2: \( \Delta_i^+ u \geq 0 \) and \( v_i \leq v^* \). Note that, as in Case 1, \( \Delta_i^+ u \leq B^{(K)} \) and \( u_i \leq B^{(K)} \). We then have that

\[ F_{bdy,i}^{(u)} = (\partial_u W)_i \Delta_i^+ u \leq \max_{u \leq B^{(K)}, v \leq v^*} (\partial_u W) \cdot B^{(K)}. \]

Case 3: \( \Delta_i^+ u < 0 \). If \( (\partial_u W)_i \leq 0 \) and, hence, \( u_i < y \) then

\[ F_{bdy,i}^{(u)} = |(\partial_u W)_i| \| \Delta_i^+ u \| \leq |(\partial_u W)_i| \max_{u \leq B^{(K)}, v \leq v^*} (\partial_u W) \cdot B^{(K)} \]

since by \([P2] \) the minimum (i.e., maximum negative value) of \( \partial_u W \) occurs at the origin. If instead \( (\partial_u W)_i > 0 \), then \( F_{bdy,i}^{(u)} < 0 \) so the given bound still holds.

For Cases 4–6 the logic is analogous to Cases 1–3, respectively, so we show only the final bound obtained.

Case 4: \( \Delta_i^+ v \geq 0 \) and \( u_i > u^* \). These conditions imply that \( F_{bdy,i} \leq 0 \).
Case 5: \( \Delta_i^+ v \geq 0 \) and \( u_i \leq u^* \). These conditions imply that \( F_{bdy,i} \leq dB^{(K)} \max_{u \leq u^*, v \leq B^{(K)}} (\partial_v W) \cdot B^{(K)} \).
Case 6: \( \Delta_i^+ v \leq 0 \). These conditions imply that \( F_{bdy,i} \leq d |(\partial_v W(0,0))| v \).
Putting these results together gives us the following bound on the flux-effect term. We have that \( F_{\text{bdy},i} \leq F_{\text{max}} \) where

\[
F_{\text{max}} := B^{(K)} \left( \max_{u \leq B^{(K)}, v \leq v^*} |\partial_u W| + d \max_{u \leq u^*, v \leq B^{(K)}} |\partial_v W| \right).
\]  

(16)

This final bound is obtained by first noting that if Case 1 or 4 holds then \( F_{\text{bdy},i} \leq 0 \), and thus \( F_{\text{bdy},i} \leq F_{\text{max}} \). Alternatively, we know that Case 2 or 3 and Case 5 or 6 holds, and therefore we can bound both \( F_{\text{bdy},i}^{(u)} \) and \( F_{\text{bdy},i}^{(v)} \). This again leads to the \( F_{\text{bdy},i} \leq F_{\text{max}} \) bound.

Next, we will show that one of the flux-effect terms that contributes to the LLF Evolution Equation, i.e., \( F_{\text{bdy},i} \) or \( F_{\text{int},i} \), can be made smaller than any arbitrary negative constant. This is possible if the difference in total species concentration, between the two compartments that contribute to the flux, is sufficiently large. To prove this, we first pick an arbitrary interior edge \( \ell \) and show that the desired result is obtained when the concentration of \( u \) is sufficiently different, i.e., when \( |\Delta^+_\ell u| \) is sufficiently large (Lemma 2). The same logic can then be used to prove the result when \( |\Delta^+_\ell v| \) is sufficiently large (Corollary 3). We conclude by proving the general result for an arbitrary interior edge (Corollary 4). The result for an arbitrary boundary edge then follows immediately (Corollary 5).

Throughout this section we will refer to the adjacent compartments under consideration as compartment \( \ell \) and compartment \( \ell^+ = \ell + 1 \).

**Lemma 2** Let \( W \) be a LLF with properties \([P1],[P5]\) for the system given by \([3]\). Pick an arbitrary time \( t > 0 \) and suppose that \( \ell \in \mathbb{Z}_{\text{int}} \). Pick \( A > 0 \) and \( L > 0 \), where

\[
\min \{ \|(u_\ell, v_\ell)\|, \|(u_{\ell^+}, v_{\ell^+})\| \} \leq L.
\]

There exists a \( G_u \geq L \) such that, if the concentration of \( u \) in compartment \( \ell \) and \( \ell^+ \) has a difference greater than \( G_u \), or

\[
|\Delta^+_\ell u| \geq G_u,
\]

then the flux-effect term for interior edge \( \ell \) is bounded from above,

\[
F_{\text{int},\ell} \leq -A
\]

where \( F_{\text{int},\ell} \) is given by \([15]\) with \( i := \ell \).

**Proof** Pick \( \tilde{L} > L \) such that \( M_u^{(\tilde{L})} > 0 \). By \([C4]\) this \( \tilde{L} \) exists and there is a \( \bar{u} \) such that \( \partial_u W(\bar{u}, 0) = M_u^{(\tilde{L})} \). Define the following two constants

\[
C_1 := 1 - \frac{M_u^{(L)}}{M_u^{(\tilde{L})}}, \quad C_2 := \left( R_{v,L} + \max_{\|u,v\| < L} \frac{\|\partial_v W\|}{M_u^{(L)}} \right) L
\]

and let

\[
G_u := \max \left\{ \bar{u} + L, \frac{A + dM_u^{(\tilde{L})}C_2}{M_u^{(\tilde{L})}C_1} \right\}.
\]

(17)

Notice that \( C_1, C_2 > 0 \). The fact that \( C_1 > 0 \) follows from \([C1]\)
Without loss of generality we will suppose that \( \| (u_\ell, v_\ell) \| < \| (u_{\ell^+}, v_{\ell^+}) \| \). From the assumptions in the lemma, this implies that \( \| (u_\ell, v_\ell) \| < L \). Note that if \( -\Delta_\ell^+ u \geq G_u \) then \( u_\ell > G_u > L \), which is a contradiction. Therefore, we have that \( \Delta_\ell^+ u \geq G_u \). Additionally, the following relationship must hold:

\[
\max(0, M_u^{(L)}) < M_u^{(L)} \leq (\partial_u W)_{\ell^+} < M_u^{(\infty)}. \tag{18}
\]

We will next examine two terms that contribute to \( F_{\text{int, } \ell} \):

For the first term, the relationship given by (18) immediately leads to the following bound:

\[
\frac{\Delta_\ell^+ (\partial_u W)}{(\partial_u W)_{\ell^+}} = 1 - \frac{(\partial_u W)_\ell}{(\partial_u W)_{\ell^+}} \geq 1 - \frac{M_u^{(L)}}{M_u^{(L)}} = C_1
\]

For the second term, first suppose that \( \Delta_\ell^+ v \leq 0 \). This implies that \( v_{\ell^+}, |\Delta_\ell^+ v| \leq L \) and leads to the following bound:

\[
-\frac{\Delta_\ell^+ (\partial_v W)}{(\partial_u W)_{\ell^+}} \Delta_\ell^+ v = \left( \frac{(\partial_v W)_{\ell^+}}{(\partial_u W)_{\ell^+}} - \frac{(\partial_v W)_\ell}{(\partial_u W)_{\ell^+}} \right) |\Delta_\ell^+ v| \leq \left( R_{v,L} + \frac{\max \| (u,v) \| < L |\partial_v W|}{M_u^{(L)}} \right) L = C_2. \tag{19}
\]

If instead \( \Delta_\ell^+ v > 0 \), then the left hand side of (19) is negative and, therefore, the bound still holds. The negativity of the left hand side follows from (18), which implies \( (\partial_u W)_{\ell^+} > 0 \) and (P2) which implies \( \Delta_\ell^+ (\partial_v W) \geq 0 \).

Finally, let’s examine \( F_{\text{int, } \ell} \). Using (18)–(19) we have that

\[
-F_{\text{int, } \ell} = (\partial_u W)_{\ell^+} \left( \frac{\Delta_\ell^+ (\partial_v W)}{(\partial_u W)_{\ell^+}} \Delta_\ell^+ u + d \frac{\Delta_\ell^+ (\partial_v W)}{(\partial_u W)_{\ell^+}} \Delta_\ell^+ v \right) \geq M_u^{(L)} (C_1 G_u - dC_2) \geq A
\]

Thus, we have shown there exists a \( G_u \), such that \( F_{\text{int, } \ell} \leq -A \). \( \square \)

**Corollary 3** Suppose the assumptions of Lemma 2 hold. Given \( A > 0 \) and \( L > 0 \) where

\[
\min \{ \| (u_\ell, v_\ell) \|, \| (u_{\ell^+}, v_{\ell^+}) \| \} \leq L,
\]

there exists a \( G_v \geq L \) such that if

\[
|\Delta_\ell^+ v| \geq G_v,
\]

then the flux-effect term for interior edge \( \ell \) is bounded from above as follows

\[
F_{\text{int, } \ell} \leq -A
\]

where \( F_{\text{int, } \ell} \) is given by (15) with \( i := \ell \).

**Proof** The proof follows using the same logic as the proof to Lemma 2. First, find \( \bar{L} > L \) such that \( M_v^{(L)} > 0 \) and \( \bar{v} \) such that \( \partial_v (0, \bar{v}) = M_v^{(L)} \). Then define an analogous set of constants

\[
C_3 := 1 - \frac{M_v^{(L)}}{M_v^{(L)}}, \quad C_4 := L \left( R_{v,L} + \frac{\max \| (u,v) \| < L |\partial_v W(u,v)|}{M_v^{(L)}} \right)
\]
and let

$$G_v := \max \left\{ \tilde{v} + L, \frac{A + M_v(L)C_4}{dM_v(L)C_3} \right\}. \quad (20)$$

We then have that

$$-F_{\text{int,}\ell} = (\partial_{\nu} W)_{\ell+} \left( \frac{\Delta^+_{\ell}(\partial_{\nu} W)}{\partial_{\nu} W}_{\ell+} \Delta^+_{\ell} u + d \frac{\Delta^+_{\ell}(\partial_{\nu} W)}{\partial_{\nu} W}_{\ell+} \Delta^+_{\ell} v \right) \geq M_v(L) (-C_4 + dC_3 G_v) \geq A.$$

\(\square\)

**Corollary 4** Suppose the assumptions of Lemma 2 hold. Given \(A > 0\) and \(L > 0\) where

$$\min \left\{ \|(u_{\ell}, v_{\ell})\|, \|(u_{\ell+}, v_{\ell+})\| \right\} \leq L,$$

there exists a \(G \geq L\) such that if

$$\left| \|(u_{\ell+}, v_{\ell+})\| - \|(u_\ell, v_\ell)\| \right| \geq G,$$

then \(\max \{\|(u_{\ell}, v_{\ell})\|, \|(u_{\ell+}, v_{\ell+})\|\} > B^{(K)}\) and the flux-effect term for interior edge \(\ell\) is bounded from above as follows

$$F_{\text{int,}\ell} \leq -A$$

where \(F_{\text{int,}\ell}\) is given by (15) with \(i := \ell\).

**Proof** Let

$$G = \max \{2G_u, 2G_v, B_{K}\}.$$  \(\text{(23)}\)

where \(G_u\) is given by (17), \(G_v\) is given by (20), and \(B_{K}\) is given by (8). Notice that

$$\left| \|(u_{\ell+}, v_{\ell+})\| - \|(u_\ell, v_\ell)\| \right| = \left| \Delta^+_{\ell} u + \Delta^+_{\ell} v \right|$$

and, therefore, (21) and (23) imply that either \(\Delta^+_{\ell} u \geq G_u\) or \(\Delta^+_{\ell} v \geq G_v\). Thus, we apply either Lemma 2 or Corollary 3 to show that (22) holds. Finally, since \(G \geq B_{K}\), using (21), we have that \(\max \{\|(u_{\ell}, v_{\ell})\|, \|(u_{\ell+}, v_{\ell+})\|\} > B^{(K)}\). \(\square\)

**Corollary 5** Suppose the assumptions of Lemma 2 hold where instead we pick \(\ell \in Z_{\text{bdy}}\). Given \(A > 0\) and \(L > 0\) where \(\min \{\|(u_{\ell}, v_{\ell})\|, \|(u_{\ell+}, v_{\ell+})\|\} \leq L\), find the \(G\) from Corollary 4 given by (23). If (21) holds, then \(\max \{\|(u_{\ell}, v_{\ell})\|, \|(u_{\ell+}, v_{\ell+})\|\} > B^{(K)}\) and the flux-effect term for boundary edge \(\ell\) is bounded from above as follows

$$F_{\text{bdy,}\ell} \leq -A$$

where \(F_{\text{bdy,}\ell}\) is given by (14) with \(i := \ell\).
Proof The result follows directly from Corollary 3. Without loss of generality again suppose $$\| (u_{\ell+}, v_{\ell+}) \| > \| (u_{\ell}, v_{\ell}) \|$$. It immediately follows that $$\| (u_{\ell+}, v_{\ell+}) \| \geq G \geq B(K)$$. This, in turn, implies that $$\ell^+ \in Y^C$$ and hence $$\ell \in Y$$. The equation for $$F_{bdy,\ell}$$ then reduces to

$$F_{bdy,\ell} = -(\partial_u W)_{\ell+} \Delta_t^+ \mathbf{u} - d(\partial_v W)_{\ell+} \Delta_t^+$$

To bound this equation, we apply the logic from Lemma 2, Corollary 3 and 4 where $$(\partial_u W)_{\ell}$$ and $$(\partial_v W)_{\ell}$$ are equal to zero. The result of this logic gives us that $$F_{bdy,\ell} \leq -A$$.

We will next assume $$Y$$ (i.e., the set of indices for compartments such that $$(u_i, v_i) \in \Omega_K$$) is not empty and show that when a threshold total species concentration is passed in at least one of the compartments, we can find an interior or boundary edge that satisfies either (22) or (24).

**Lemma 3** Let $$W$$ be a LLF with the properties (P1)–(P5) for the system given by (3) and pick an arbitrary time $$t > 0$$. Pick $$A > 0$$ and suppose there exists a compartment $$k$$ such that $$k \in Y$$. Then there is a threshold concentration $$C > 0$$ such that if $$\max(\{(u_i, v_i)\})_{i=1}^n \geq C$$, then there exists an interior or boundary edge, $$\ell$$, that satisfies either (22) or (24), respectively.

**Proof** Suppose there does not exist an interior edge or boundary edge that satisfies either (22) or (24), respectively. The species concentration in compartment $$k$$ is bounded such that $$\| (u_k, v_k) \| < B(K)$$. We will apply either Corollary 2 or 3 to iteratively bound the compartment concentration for $$i = k + 1, k + 2, ..., n$$ and $$i = k - 1, k - 2, ..., 1$$.

Define $$L_k := B(K)$$ and for $$i = k + 1, ..., n$$, iteratively find the $$G_i$$ given by (23) in Corollary 2 where $$L := L_{i-1}$$. Next, set $$L_i := G_i + L_{i-1}$$. If $$\| (u_i, v_i) \| - \| (u_{i-1}, v_{i-1}) \| > G_i$$ then we know that edge $$i$$ is either an interior or boundary edge. In turn, Corollary 2 or 3 imply that either (22) or (24) hold. This is a contradiction, and therefore, $$\| (u_i, v_i) \| - \| (u_{i-1}, v_{i-1}) \| \leq G_i$$, which implies $$\| (u_i, v_i) \| \leq L_i$$. Thus, we have obtained a bound for the next compartment and can continue the iteration. Similarly, for $$i = k - 1, ..., 1$$, the same methodology can be used to generate compartment bounds, where we find the $$G_i$$ given by (23) where $$L := L_{i+1}$$. We then have that $$\| (u_i, v_i) \| \leq L_i$$.

This logic leads to the following bound

$$\| (u_{k+i}, v_{k+i}) \| < C$$

for $$i = -k, ..., -2, -1, 1, 2, ..., n - k$$ where the threshold species concentration $$C$$ is

$$C := B(K) + \sum_{i=1, i \neq k}^n G_i.$$ (25)

Suppose that there exists a compartment $$m$$ such that $$\| (u_m, v_m) \| \geq C$$. We have a contradiction, and therefore there exists at least one interior or boundary edge such that either (22) or (24) holds.

In the next lemma we prove that if a compartment exceeds a threshold species concentration then the diffusive contribution to the LLF Evolution Equation is nonpositive (i.e., $$W_{Y^C, D} \leq 0$$).

**Lemma 4** Let $$W$$ be a LLF with the properties (P1)–(P5) for the system given by (3). Define $$A := n F_{max}$$ where $$F_{max}$$ is given by (16) in Lemma 2. If we use this $$A$$ as the constant in Lemma 3 we can let $$C$$ be as defined in (25). If at an arbitrary time $$t > 0$$, $$\max_i \| (u_i, v_i) \| \geq C$$, then

$$W_{Y^C, D} \leq 0.$$
Proof We will consider the two possible cases where $Y$ is or is not empty.

Case 1: $Y$ is empty. Since $Y$ is empty, $Y^C = \mathcal{N}$ and

$$W_{Y^C} = \sum_{i=1}^{n} (W)_i.$$ 

We then have that the diffusion component of the LLF Evolution Equation is

$$W_{Y^C,D} = (\nabla u W_{Y^C})^T D u + d (\nabla v W_{Y^C})^T D v$$

$$= \sum_{i=1}^{n-1} -\Delta_i^+ (\partial_u W_i) \Delta_i^+ u - d \Delta_i^+ (\partial_v W_i) \Delta_i^+ v$$

$$\leq 0.$$ 

This result follows from property [P2] of the LLF.

Case 2: $Y$ is non-empty. By Lemma 3, there exists either an interior edge that satisfies (22) or a boundary edge that satisfies (24). We will let $\ell$ denote the index of this edge. We know $\max \{\| (u_\ell, v_\ell) \|, \| (u_\ell +, v_\ell +) \| \} > B^{(k)}$. Without loss of generality, suppose $\| (u_\ell +, v_\ell +) \| > \| (u_\ell, v_\ell) \|$ and thus $\ell^+ \in Y^C$. We will next consider two possible cases: $\ell \in Z_{int}$ or $\ell \in Z_{bdy}$.

First let’s assume $\ell \in Z_{int}$. By Corollary 4, we have that

$$F_{int,\ell} \leq -nF_{max}.$$ 

Using that $F_{int,i} < 0$ and $F_{bdy,i} \leq F_{max}$ for all $i$, and that $Z_{bdy}$ has at most $n - 1$ elements, we have that

$$W_{Y^C,D} = \sum_{i \in Z_{bdy}} F_{bdy,i} + \sum_{i \in Z_{int}} F_{int,i}$$

$$\leq \sum_{i \in Z_{bdy}} F_{bdy,i} + F_{int,\ell}$$

$$\leq (n - 1)F_{max} - nF_{max}$$

$$< 0.$$ 

Next, assume $\ell \in Z_{bdy}$. We have that by Corollary 5

$$F_{bdy,\ell} < -nF_{max}.$$ 

We then can similarly bound $W_{Z,D}$ as follows,

$$W_{Y^C,D} = \sum_{i \in Z_{bdy}} F_{bdy,i} + \sum_{i \in Z_{int}} F_{int,i}$$

$$\leq F_{bdy,\ell} + \sum_{i \in Z_{bdy} \neq \ell} F_{bdy,i}$$

$$\leq -nF_{max} + (n - 2)F_{max}$$

$$< 0.$$ 

$\square$
Finally, we’ll prove the main result of this section. Specifically, we will next show that given a compartment exceeds a threshold species concentration, the solution to the LLF Evolution Equation is decreasing.

**Corollary 6** If the assumptions of Lemma 4 hold, then \( \frac{dW_{Y^{C}, R}}{dt} \leq 0 \).

**Proof** From Lemma 4 we know that \( W_{Y^{C}, D} \leq 0 \). Furthermore, (9) can be rearranged as follows

\[
W_{Y^{C}, R} = \sum_{i \in Y^{C}} (\nabla W(u_i, v_i))^T (f(u_i, v_i), g(u_i, v_i)).
\]

This sum is clearly less than zero by (P1) of the LLF. Therefore,

\[
\frac{dW_{Y^{C}}}{dt} = \gamma W_{Y^{C}, R} + W_{Y^{C}, D} \leq 0.
\]

\( \square \)

### 3.2 The System LLF is bounded

In this section we will consider how the *System LLF* or the sum of LLFs across all compartments evolves with time. We will first only consider times when one compartment exceeds a threshold species concentration. During these times we will consider what occurs to the System LLF when the membership of \( Y \) and \( Y^{C} \) changes. Below we define a time-dependent function that bounds the System LLF. We will show that this function decreases with time if any compartment exceeds a threshold total species concentration (Lemma 5). We conclude by considering all times during which a solution exists, i.e., \( t \in [0, T_{\max}) \), and show that the given function will always bound the system. Hence, the total species concentration in each compartment is uniformly bounded over time (Theorem 1).

Consider the discretized RD system given by (3) and let \( W : \mathbb{R}^{2}_{\geq 0} \rightarrow \mathbb{R} \) be a LLF for the reactions. Using this LLF and the initial data, we define the threshold species concentration \( C \) as follows.

**Definition 2** Find the \( F_{\max} \) for the LLF given by (16) in Lemma 1. Apply Lemma 3 where \( A := nF_{\max} \) to find \( C \). We then define the threshold species concentration as

\[
C = \max \left\{ \left\| (u_{i,0}, v_{i,0}) \right\|_{i=1}^{n}, C \right\}.
\]

We will consider times during which the total species concentration in at least one compartment is greater than or equal to \( C \) and examine what occurs to the sum of LLFs when crossings of \( \partial \Omega_{K} \) occur. Let \( n_{t} \) be the number of compartments contained in \( \Omega_{K} \) at time \( t \) and define

\[
W(t) = n_{t} M_{(K)} + W_{Y^{C}, R}(u(t), v(t))
\]

Note that \( W(t) \) provides an upper bound on the sum of LLFs across all compartments at time \( t \).

We will first show that while the concentration of at least one compartment exceeds \( C \), \( W(t) \) is a decreasing function of time. To do this we will consider a closed interval of time, and allow for crossings of \( \partial \Omega_{K} \) to occur at either end of the interval.
Lemma 5 Pick τ_1 and τ_2 such that no crossings occur for \( t \in (τ_1, τ_2) \). Suppose for \( t \in [τ_1, τ_2] \), \( \max \{\|u_i, v_i\|\}_{i=1}^n \} \geq C \). Then, \[
W(τ_2) \leq W(τ_1). \tag{26}
\]

Proof Notice that \( Y(t) \) and \( Y^C(t) \) do not have changes in membership for all \( t \in (τ_1, τ_2) \) since no crossings of \( \partial Ω_K \) occur. Pick \( t \in (τ_1, τ_2) \). Corollary 6 along with the continuity of \( u \) and \( v \) imply that
\[
W_{Y^C(t)}(u(τ_2), v(τ_2)) \leq W_{Y^C(t)}(u(τ_1), v(τ_1)). \tag{27}
\]
We will next derive a relationship between \( W_{Y^C(τ_1)}(u(τ_1), v(τ_1)) \) and \( W_{Y^C(τ_2)}(u(τ_2), v(τ_2)) \). Let \( n_{in} \) denote the number of compartments that cross into \( Ω_K \) at time \( τ_1 \), and let \( n_{out} \) denote the number of compartments that cross out of \( Ω_K \) at time \( τ_2 \). Note that if no crossing occurs at time \( τ_1 \) or \( τ_2 \), then \( n_{in} \) and/or \( n_{out} \) could be zero. We have that
\[
W_{Y^C(τ_1)}(u(τ_1), v(τ_1)) = W_{Y^C(t)}(u(τ_1), v(τ_1)) + n_{in}M^{(K)}
\]
and
\[
W_{Y^C(τ_2)}(u(τ_2), v(τ_2)) = W_{Y^C(t)}(u(τ_2), v(τ_2)) + n_{out}M^{(K)}
\]
Using these relations and (27), we deduce the following inequality:
\[
W_{Y^C(τ_2)}(u(τ_2), v(τ_2)) \leq W_{Y^C(τ_1)}(u(τ_1), v(τ_1)) + (n_{out} - n_{in})M^{(K)}.
\]
The relationship between \( n_{τ_1} \) and \( n_{τ_2} \) is given as
\[
n_{τ_2} = n_{τ_1} + n_{in} - n_{out}.
\]
Putting this together, we have that
\[
W(τ_2) = (n_{τ_2} + n_{in} - n_{out})M^{(K)} + W_{Y^C(τ_2)}(u(τ_2), v(τ_2))
\]
\[
\leq n_{τ_1}M^{(K)} - (n_{out} - n_{in})M^{(K)} + W_{Y^C(τ_1)}(u(τ_1), v(τ_1)) + (n_{out} - n_{in})M^{(K)}
\]
\[
\leq W(τ_1). \tag{26}
\]
Thus, we have shown that (26) holds.

Finally, we will prove our main result by considering how the system evolves for all time \( t \in [0, T_{max}] \).

Theorem 1 Consider the ODE system given by (3), and suppose there exists a LLF \( W : \mathbb{R}_{\geq 0}^2 \to \mathbb{R} \) for this system with the properties [(P1)] (P5). Then, there exists an upper bound \( B > 0 \) such that \( \|(u_i(t), v_i(t))\| \leq B \) for \( i = 1, 2, ..., n \) and all \( t \in [0, \infty) \).

Proof Pick \( t \in [0, T_{max}] \). Let \( T^{(M)} \subset [0, t] \) represent times when \( \max \{\|u_i, v_i\|\}_{i=1}^n \} \geq C \), where \( C \) is given by Definition 2. By the continuity of \( u_i(t) \) and \( v_i(t) \) we know that \( T^{(M)} \) is a finite union of closed connected sets where
\[
T^{(M)} = \bigcup_{i=1}^{m} T^{(M)}_i.
\]
Pick \( i = 1, 2, ..., m \) and consider \( T^{(M)}_i \). Divide \( T^{(M)}_i \) into time intervals based on when crossings of \( \partial Ω_K \) occur. Again, by the continuity of \( u_i(t) \) and \( v_i(t) \) we know that the number of crossings is finite. Suppose there are \( J \) crossings during \( T^{(M)}_i \). Let \( t_j \), for \( j = 1, 2, ..., J - 1 \), denote the time at
which crossings of $\partial \Omega_K$ occur and let $t_0$ and $t_{j+1}$ denote the start and end of the time interval, respectively (i.e., $T_i^{(M)} = [t_0, t_{j+1}]$). We then have that

$$T_i^{(M)} = \bigcup_{j=0}^{J} [t_j, t_{j+1}].$$

Pick $j = 0, 2, ..., J$ and pick $\tau \in [j, j+1]$. Apply Lemma 5 to show

$$W_N(u(\tau), v(\tau)) \leq W(\tau) \leq W(t_j) \leq W(t_{j-1}) \leq ...$$

$$\leq W(t_0) = n_{t_0}M^{(K)} + W_{Y\subset(t_0)}(u(t_0), v(t_0))$$

From the definition of $t_0$, we know for all $i$, $\| (u_i(t_0), v_i(t_0)) \| \leq C$ and, therefore, $W(u_i(t_0), v_i(t_0)) \leq M^{(C)}$. This follows from [P2] [C3] and the fact that $C > K$. The final bound we obtain is

$$W_N(u(\tau), v(\tau)) \leq n_{t_0}M^{(K)} + (n - n_{t_0})M^{(C)} \leq nM^{(C)}.$$  (28)

Note that since $j$ and $i$ were arbitrary the same bound holds for all $\tau \in T^{(M)}$. Furthermore, for $\tau \leq t$ such that $\tau \notin T^{(M)}$ we know that $W(u_i(t_0), v_i(t_0)) \leq M^{(C)}$ for $i = 1, 2, ..., n$. Thus, the bound given by (28) still holds. Finally, since $t$ was arbitrary this bound holds for all $t \in [0, T_{max})$.

Define $\Omega = \{(u, v) \mid W(u, v) \leq nM^{(C)}\}$. If there existed a compartment $i$ such that $\| (u_i, v_i) \| \notin \Omega$, then the bound given by (28) would not hold. Therefore, $\| (u_i(t), v_i(t)) \| \in \Omega$ for all $i \in \{1, 2, ..., n\}$ and $t \in [0, T_{max})$. Finally, this implies that the total species concentration in each compartment is bounded by $B$ where

$$B = \max_{(u,v) \in \Omega} \| (u, v) \|$$

and $T_{max} = \infty$. □

4 Illustrative examples

In this section, we discuss the question of whether a LLF exists and provide examples of how the results from Section 3 can be applied. In some general situations, it can be shown that a LLF either does or does not exist. For example, consider the case where there is a known Lyapunov function for reactions. In a corollary, we show that in some instances this Lyapunov function is also a LLF. We then juxtapose this result with a second corollary that provides conditions under which a LLF cannot be found. Finally, we present two example systems that illustrate how diffusion-driven instability can lead to both bounded and unbounded solutions. These examples illustrate that in discretized systems with non-negative solutions, Neumann boundary conditions, and spatially homogeneous stability, the question of boundedness is non-trivial.

4.1 Determining whether a LLF exists

If a global Lyapunov function exists for a system, it may also satisfy the requirements of a LLF. Any global Lyapunov function, by definition, satisfies [P1] and [P3]. Therefore, it remains to show that a specific Lyapunov function satisfies [P2] [P4] and [P5]. In the following corollary, we show that if the Lyapunov function is additively separable and satisfies [P2] then [P4] and [P5] follow.
Corollary 7  Let \( W : \mathbb{R}^2 \rightarrow \mathbb{R}_{\geq 0} \) by a Lyapunov function for the reactions \( f(u, v) \) and \( g(u, v) \). If, in addition \( W \) is additively separable (i.e., \( W(u, v) = w_1(u) + w_2(v) \)) and satisfies (P2) then \( W \) is a LLF.

Proof  We can immediately show that \( W \) satisfies (P4) since

\[
\sup_{v \geq u} \left| \frac{\partial_u W(u, v)}{\partial_v W(u, v)} \right| \leq \frac{w'_1(u)}{w'_2(v)} \frac{w'_2(v)}{w'_1(u)} < \infty
\]

Additionally (P5) is satisfied since

\[
\lim_{u \to \infty} \partial_u W(u, v) = \lim_{u \to \infty} w'_1(u) = C_1\\
\lim_{v \to \infty} \partial_v H(u, v) = \lim_{v \to \infty} w'_2(v) = C_2\\
\partial_{uv} W(u, v) = 0
\]

where, due to (P2) \( C_1 \) and \( C_2 \) are constants or infinite.

As an example application of Corollary 7, consider a Lyapunov function consisting of a monomial for \( u \) and \( v \) with degree \( \geq 2 \) (i.e., \( W(u, v) = \alpha u^m + \beta v^p \) where \( \alpha, \beta \in \mathbb{R} \) and \( m, p \in \{2, 3, \ldots\} \)). It follows immediately from Corollary 7 that \( W \) is a LLF.

In some cases, it is possible to determine that no LLF exists for a system. This is because the LLF properties (P1) and (P4) immediately place requirements on the type of reactions that have a suitable LLF. In the next corollary, we present conditions on the reactions \( f \) and \( g \) in (3) that guarantee a LLF for the system cannot be found.

Corollary 8  Consider the system given by (3). If for any \( v \geq 0 \) the following conditions are satisfied,

\[
\liminf_{u \to \infty} f(u, v) > 0\\
\lim_{u \to \infty} \frac{f(u, v)}{g(u, v)} = \infty,
\]

then there does not exist an LLF for the system. Analogously, if for any \( u \geq 0 \) the following conditions are satisfied,

\[
\liminf_{v \to \infty} g(u, v) > 0\\
\lim_{v \to \infty} \frac{g(u, v)}{f(u, v)} = \infty,
\]

then there does not exist an LLF for the system.

Proof  We will show that if there exists a \( v \) such that (29) is satisfied, then no LLF exists. The result for any \( u \) and (30) follows analogously. Suppose there exists a LLF for the system. By (P1) there exists a \( K \) such that, if \( \| (u, v) \| > K \), then

\[
(\nabla W)^T (f, g) = \partial_u W(u, v) f(u, v) + \partial_v W(u, v) g(u, v) \leq 0
\]

(31)
Pick \( v > 0 \) and consider what happens in the limit as \( u \to \infty \). By \((P1)\), \((C2)\), and \((29)\), there exists \( \bar{u} \) such that if \( u > \bar{u} \) then \( u > K_0 \), \( \partial_u W > 0 \), and \( f(u, v) > 0 \). We therefore have that for \( u \geq \bar{u} \),

\[
\frac{\partial_v W(u, v)}{\partial_u W(u, v)} \begin{cases} 
\leq -\frac{f(u, v)}{g(u, v)} < 0 & \text{if } g(u, v) > 0 \\
\geq -\frac{f(u, v)}{g(u, v)} > 0 & \text{if } g(u, v) < 0.
\end{cases}
\]

Note that since \( f > 0 \) and \( \partial_u W > 0 \), in order for \((31)\) to hold, \( g \neq 0 \). This set of inequalities implies that

\[
\left| \frac{\partial_v W(u, v)}{\partial_u W(u, v)} \right| \geq \frac{|f(u, v)|}{g(u, v)}.
\]

Note that, in the limit as \( u \to \infty \), \( |f(u, v)|/g(u, v)| = \infty \) and, therefore

\[
\sup_{u \geq \bar{u}} \left| \frac{\partial_v W(u, v)}{\partial_u W(u, v)} \right| = \infty.
\]

This final equation gives us a contradiction to \((P4)\). Therefore, no LLF exists for the reactions. \( \square \)

4.2 Example Bounded and Unbounded RD System

Here, we show that an LLF exists for a system that exhibits diffusion-driven instability. Consider the following example reactions, studied in [Schnakenberg 1979, Murray 2002, 2003]:

\[
f(u, v) = a - u + u^2 v \\
g(u, v) = b - u^2 v
\]

where \( a \) and \( b \) are positive constants. These reactions satisfy the stated requirements in Section 2. Specifically, \( f \) and \( g \) are continuously differentiable and \( f(0, v), g(u, 0) \geq 0 \). Without diffusion, there is a steady state, \((\bar{u}, \bar{v}) = (a + b, b/(a + b)^2)\). This steady state is either stable or the system has periodic solutions [Murray 2002]. In both these cases, the system with only the reactions is guaranteed to be bounded. The continuous RD system given by \((1)\) with these reactions exhibits diffusion-driven instability [Murray 2002]. Specifically, depending on the initial conditions and parameter values, different patterned modes can arise. Biologically, this is of interest because, if diffusion alters the steady state, analyzing the system assuming spatial homogeneity would lead to inaccurate results.

Let’s consider the following LLF candidate

\[
W(u, v) = u + 2v + \frac{c}{u + 1} + \frac{1}{v + 1}
\]

where \( c > 0 \) is a constant that depends on the parameters \( a \) and \( b \). This function has the desired properties, \((P1)\), \((P5)\) (see Appendix B for proofs). Therefore, by Theorem 1, the discretized system given by \((3)\) is bounded for all time.

To investigate the dynamics of the discretized system in more detail, we plot the trajectories of a two-compartment system (i.e., \( n = 2 \)) with and without diffusion (Figure 5, left panel). The plot has solution trajectories for each of the two compartments. For this example, the steady state \((\bar{u}, \bar{v})\) is a stable spiral point. Diffusion alters the resulting steady state of the system, but the solution is still bounded.
Fig. 5 Example trajectories of two compartment systems where diffusion alters the steady state and leads to bounded solutions (left) and unbounded solutions (right). The solid and dashed lines show the evolution of the species concentration in each compartment with and without diffusion, respectively. The gray arrows represent the vector field \((f(u, v), g(u, v))\). For the system on the left, \(f\) and \(g\) are given by (32) where \(a = 0.1, b = 1, \gamma = 150, d = 30\), \((u_{1,0}, v_{1,0}) = (0.8, 0.1)\) and \((u_{2,0}, v_{2,0}) = (2.0, 0.7)\). For the system on the right, \(f\) and \(g\) are given by (34) where \(d = 1, \gamma = 1, \delta = 10\), \(u_{1,0} = v_{2,0} = 2\), and \(u_{2,0} = v_{1,0} = 4\).

Next, consider the reactions that were introduced in Weinberger, 1999, \(f(u, v) = uv(u - v)(u + 1) - \delta u\), \(g(u, v) = uv(v - u)(v + 1) - \delta v\) (34) where \(\delta\) is a positive constant. Again, these reactions satisfy the stated requirements in Section 2 since \(f\) and \(g\) are continuously differentiable and \(f(0, v), g(u, 0) \geq 0\). This system has a single steady state at \((\tilde{u}, \tilde{v}) = (0, 0)\). A known Lyapunov function for this system is 

\[V(u, v) = (u + 1)^2(v + 1)^2.\]

This Lyapunov function is positive definite for all points in \(\mathbb{R}^2_{\geq 0}\), radially unbounded, and the time derivative is negative definite. Therefore, the spatially homogeneous steady state \((\tilde{u}, \tilde{v})\) is globally asymptotically stable.

For this system it is possible to show that the conditions of Corollary 8 are satisfied and therefore an LLF does not exist (see Appendix C.1). This, however, does not immediately imply that the system is unbounded. To explore the question of boundedness, we performed simulations of a two compartment system, i.e., \(n = 2\) (Figure 5 right panel). The simulations suggest that the system becomes unbounded as \(t \to \infty\), and in Appendix C.2 we prove this result for small \(\delta\).

5 Discussion

We have defined a class of spatially discretized RD systems with a uniform boundedness property. For a RD system to be in this class it must have two species reacting and diffusing on a 1D domain...
with Neumann boundary conditions. Additionally, the RD system must have nonnegative solutions and a Lyapunov-like function (LLF) described by Definition 1. Under these conditions, we are guaranteed that the total concentration of species in the system is bounded for all time. Notably, the existence of a LLF for a system only depends on the reactions, and is therefore independent of the domain size and diffusion rates of the two species in the system. Therefore, we could alter the diffusion rates and still be guaranteed that the system is bounded, though the value of the bound may have changed.

Throughout the paper we made the additional assumption that all the parameters in the system were constant across space. That is, the reaction parameters in each compartment were identical and the diffusion rates across the edges in the system were the same for each edge (recall that an edge is the boundary between two adjacent compartments). However, the results presented here are generalizable to systems with reaction parameters (i.e., parameters within the functions $f$ and $g$) and diffusion parameters that vary across space. Generalizing our results to allow for spatially varying parameter values allows us to consider a broader range of systems. For example, we could allow a parameter value to follow a gradient across the domain. Alternatively, we could alter the rate of diffusion between two compartments to represent a physical barrier, such as a membrane.

To generalize to a system with spatially varying reaction parameters, rather than defining a single LLF, we instead would define a LLF for each compartment in the system. For example, suppose the reactions given by (32) have spatially varying parameters, and let $a_i$ and $b_i$ represent the values of $a$ and $b$ in compartment $i$. Note that the example LLF for this system, given by (33), was shown to work for all $a, b > 0$, given an appropriate choice for the constant $c$. Therefore, for each compartment $i$, there exists a LLF that satisfies the five required properties. The proofs given in this paper can then be generalized to show that the system is bounded for all time.

To allow diffusion to vary across space, we define a diffusion value of $u$ and $v$ across each edge in the system. The result of this change would cause the flux effect-terms given by (14) and (15) to depend on these edge-dependent diffusion values. In principle, the same logic in the proofs would still hold where the bounds obtained would depend on the maximum and minimum values of the diffusion parameters. Rigorously proving this result is a topic of future research.

Using a LLF to prove boundedness provides a method for examining any mathematical description of a biochemical system. For example, biological dynamics can be described mathematically using mass-action kinetics (Voit et al., 2015), Hill Functions (Goutelle et al., 2008), and Michaelis-Menten Kinetics (Johnson and Goody, 2011). Similar to Lyapunov functions, the challenge remains in finding a suitable LLF. Computational work has been done to find Lyapunov functions (Hafstein and Giesl, 2015), and this work could be leveraged to find a LLF. As shown in Corollary 7, sometimes a global Lyapunov Function satisfies the requirements for a LLF. However, we have shown that the existence of a global Lyapunov function for the reactions does not imply a suitable LLF exists for the system (see unbounded example in Section 4).

The bound obtained for a system, given a LLF exists, depends on the number of compartments. Therefore, these results do not imply that the system remains bounded in the continuum limit. There are two places in the logic of the proofs where we rely on a finite number of compartments. The first occurs in Lemma 3 where we find a threshold species concentration. To obtain this threshold, we iteratively bounded each compartment in the system. Therefore, the final threshold is dependent on the number of compartments. When the total species concentration in one compartment exceeds this threshold value, certain dynamic properties hold. These properties lead to Theorem 1 where we again rely on a finite number of compartments to show that the sum of LLFs is bounded.
the future, we plan to use similar energy type methods to determine conditions for the discretized system to remain bounded as \( n \to \infty \) and the domain size is held constant.

In addition to boundedness in the continuum limit, we have also not addressed the question of convergence. This has been a topic of past research and ultimately depends on the specific reactions in the system. Verwer and Sanz-Serna [1984] present a discussion on the Method of Lines scheme for PDEs and provide sufficient criteria for the scheme to converge. Specifically, if the scheme is consistent and there exists a bounded logarithmic matrix norm, then the discretized system will converge to the PDE. Another study examined convergence of the Method of Lines for a specific chemical RD system (Mohamed et al., 2018). Unable to prove uniform consistency, they instead directly show that the discretized system converges to the PDE. Their results depend on first showing a bound exists for the system that is independent of the number of compartments. Ultimately, these studies can be leveraged in future work, examining the convergence of the class of RD systems discussed here.

The use of a LLF to prove boundedness of the discretized system was, in part, motivated by a previous study that examined boundedness of the continuous RD system (Morgan, 1990). In this study, a function with Lyapunov properties was defined. It was shown that, if this function satisfied certain criteria, the continuous RD system was guaranteed to be bounded for all time. However, generally the conditions for boundedness of one type of system (i.e., the discretized or continuous system) do not satisfy the conditions to guarantee boundedness of the other system. Ultimately, this relationship between boundedness of the discretized and continuous systems invites future investigation.

The motivation of this study was to find a class of RD systems that can be studied using systems biology approaches. We are specifically interested in RD systems that have bounded diffusion-driven instabilities. An example of this type of system is given by the reactions in (32). We hope to study these systems using techniques, for example, from stoichiometric network analysis. These methods can be used to study the space of possible reactive and diffusive fluxes that can exist in the system. Ultimately, this approach will allow us to study diffusion-driven instabilities in complex biochemical systems with variable diffusion and reaction rates.

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A Proofs for the secondary properties of the LLF

In this section we will prove Corollary [1] and [2] which guarantee a LLF, $W : \mathbb{R}^2_{\geq 0} \to \mathbb{R}_{\geq 0}$, has the additional properties given by [C1]–[C5].

Proof of Corollary 1. Pick $L_1$ and $L_2$ such that $L_2 > L_1 > 0$. Using [P2] we have that

$$M_u^{(L_1)} = \max_{\parallel (u,v) \parallel = L_1} \partial_u W(u,v)$$

$$= \max_{v \in [0,L_1]} \partial_u W(L_1 - v,v)$$

$$< \max_{u \in (0,L_1]} \partial_u W(L_2 - v,v)$$

$$\leq \max_{u \in (0,L_2]} \partial_u W(L_2 - v,v) = M_u^{(L_2)}.$$  \hspace{1cm} \Box

Here, the first inequality holds because $L_2 > L_1$ and $\partial_u W > 0$. The second inequality holds because we are taking the maximum over a larger region. This result proves that $M_u^{(L)}$ is monotonically increasing. The result for $M_u^{(L)}$ follows analogously.

Proof of Corollary 2. By [P3] we know $W(u,0) \to \infty$ as $u \to \infty$. It follows that there exists a constant $\bar{u}$ such that $W(\bar{u},0) > W(0,0)$. Using the Mean Value Theorem and [P2] we have that $\partial_u W(\bar{u},0) > 0$. Therefore, by [P2] $\partial_u W(u,v) > 0$ for all $v \geq 0$ and $u \geq \bar{u}$. The same logic can be used to prove there exists a constant $\bar{u}$ such that $\partial_v W(u,v) > 0$ for all $v \geq \bar{u}$ and $u \geq 0$. \hspace{1cm} \Box

Proof of Corollary 3. Define $\hat{M} := \max \parallel (u,v) \parallel \leq \bar{u} + \bar{v} W(u,v)$. By [P3] and [C2] we know there exists a constant $\hat{u} \in \mathbb{R}_{\geq 0}$ such that for $u \geq \hat{u}$

$$\min_{v \in [0,\bar{v}]} W(u,v) > \hat{M}.$$  \hspace{1cm} (35)

Note that we are guaranteed $\bar{u} > u + \bar{v}$. Similarly, there exists a constant $\bar{v} \in \mathbb{R}_{\geq 0}$ such that for $v \geq \bar{v}$

$$\min_{w \in [0,\bar{u}]} W(u,v) > \hat{M}$$

where again $\bar{v} > u + \bar{v}$.

Let $K = \max \{ \bar{u}, \bar{v} + \bar{v} \}$. We will next show that $M^{(K)} > \hat{M}$, where recall that $M^{(K)} = \max \parallel (u,v) \parallel = K W(u,v)$. Suppose that $\parallel (u,v) \parallel = K$. Then either (a) $u \geq \bar{u}$ or (b) $v \geq \bar{v}$. Without loss of generality suppose that $u \geq \bar{u}$.

If additionally $v \leq \bar{v}$ then using [35] we have that $W(u,v) > \hat{M}$. Conversely, if $v > \bar{v}$, then $\partial_v W$ is positive and $W(u,v) > W(u,\bar{v}) > \hat{M}$. Thus, if $\parallel (u,v) \parallel = K$ then $W(u,v) > \hat{M}$, and therefore $M^{(K)} > \hat{M}$.

Next pick $L < K$. We will next prove the claim in the corollary that $M^{(L)} < M^{(K)}$. If $L < \bar{u} + \bar{v}$ we immediately have that $M^{(L)} \leq \hat{M} < M^{(K)}$. Alternatively, if $L > \bar{u} + \bar{v}$ then we have that

$$M^{(L)} = \max_{\parallel (u,v) \parallel = L} W(u,v) = \max_{u \in [0,\bar{u}]} W(u,L-u) \cdot \max_{v \in [0,L-u]} W(L-u,v)$$

$$< \max_{u \in [0,\bar{u}]} W(u,K-u) \cdot \max_{v \in [0,L-u]} W(K-v,v)$$

$$\leq \max_{u \in [0,\bar{u}]} W(u,K-u) \cdot \max_{v \in [0,L_2-u]} W(K-v,v)$$

$$= \max_{\parallel (u,v) \parallel = K} W(u,v) = M^{(K)}.$$  \hspace{1cm} \Box
Proof of Corollary 2. We will show the proof for $M_u^{(∞)}$. The proof for $M_v^{(∞)}$ follows analogously.

Recall that
\[ M_u^{(∞)}(v) = \lim_{u \to \infty} \partial_u W(u, v). \]  

By (P2), $\partial_u W > 0$ and, therefore, $\partial_u W$ is monotonically increasing with respect to $u$. This means that the pointwise limit given by $\lim_{u \to \infty} \partial_u W(u, v)$ either converges and exists or diverges to infinity. Furthermore, since $\partial_u W(u, v) \geq 0$ we know that we know that $M_u^{(∞)}(v)$ must be monotonically non-decreasing with respect to $v$. Note that if for any $v \in [0, \infty)$, $M_u^{(∞)}(v) = \infty$, then by (P5) $M_u^{(∞)}(v) = \infty$ for all $v$, and the conclusions of the corollary follow. Therefore, in the remainder of the proof we will assume that $M_u^{(∞)}(v)$ is finite for all $v \in [0, \infty)$. By (C2) we then have that $M_u^{(∞)}(v) > 0$.

First, we will show that $h(v) := \lim_{u \to \infty} \partial_u W(u, v) = 0$. By (P2) and (P5) we know $h(v)$ exists and is non-negative. This implies that there exists a constant $U > 0$ such that if $u > U$ then $\partial_u W(u, v) > h(v)/2$. We then have that
\[ \int_U^u \partial_u W(\tilde{u}, v) d\tilde{u} \geq \int_U^u \frac{h(v)}{2} d\tilde{u} \]
and note that the upper bound $\partial_u W$ exists and is non-negative. This means that the pointwise limit exists and converges pointwise. Thus, by the Moore-Osgood Theorem, the limits are interchangeable and the resulting values are equal.

In conclusion, we have that \[ \lim_{h \to 0} \frac{F(u, v, h)}{\partial_u W(u, v + h) - \partial_u W(u, v)} = \lim_{u \to \infty} F(u, v, h) \]

Thus, we need to show that the limits are interchangeable.

Since $\partial_u W(u, v)$ converges pointwise to $g(v)$ as $u \to \infty$ and $\partial_u W(u, v)$ is monotonically increasing with respect to $u$, by Dini’s Monotone Convergence Theorem $\partial_u W(u, v)$ converges uniformly to $g(v)$ for $v \in [0, L]$ where $L$ is an arbitrary constant. Therefore $\lim_{u \to \infty} F(u, v, h)$ exists and converges uniformly. We furthermore know that the limit $h \to \infty$ exists and converges pointwise. Thus, by the Moore-Osgood Theorem, the limits are interchangeable.

\[ \frac{d}{dv} M_u^{(∞)}(v) = \frac{d}{dv} \lim_{u \to \infty} \partial_u W(u, v) = \lim_{u \to \infty} \partial_u W(u, v) = 0 \]

Thus, for all $v \in [0, L]$, $M_u^{(∞)}(v)$ is constant. Let $M^{(∞)} := M_u^{(∞)}(v)$ and note that the upper bound $L$ was arbitrary and therefore we have that this equality holds for all $v \in [0, \infty)$.

B Existence of Lyapunov-like function for example system

In this section we prove that the LLF for the example system given in Section 4.2 has the properties (P1)–(P5) given in Section 2.1. We will go through each property individually:
(P1) We will show that for large enough \( \| (u, v) \| \), \( \nabla W \cdot (f, g) \) is negative. We have that

\[
\nabla W \cdot (f, g) = \left( 1 - \frac{c}{(u + 1)^2} \right) (a - u + u^2v) + \left( 2 - \frac{1}{(1 + v)^2} \right) (b - u^2v)
\]

We can rewrite \( \nabla W \cdot (f, g) \) as

\[
\nabla W \cdot (f, g) = \frac{N(u, v)}{(1 + u)^2(1 + v)^2}
\]

We will show that there exists a value \( K \) such that if \( \| (u, v) \| > K \), then \( N(u, v) < 0 \). To do this we will find threshold values for \( u \) and \( v \) separately.

(a) Let’s first consider \( u \). After some algebraic manipulates, we rewrite \( N(u, v) \) as

\[
N(u, v) = v^2(a + 2b - ac) + v^3(a + 2b - c + 2a)
\]

This equation is negative if \( u > \tilde{u} := a + 2b + \frac{c}{2} \).

(b) Let’s next consider \( v \) and write \( N(u, v) \) as follows

\[
\begin{align*}
N(u, v) &= v^2(a + 2b - \frac{ac}{2}) + v^3(a + 2b - \frac{c}{2}) + (a + b - 2acu) + \frac{a}{2} - \frac{c}{2} + \frac{a}{2} + \frac{c}{2} - \frac{a}{2} + (a + b - 2acv) + uv(4a + 8b + 2c - v) + u^2v^2(a + 2b - v) + 2uv^2v(a + 2b - cv) - ac - u - 2u^2 - v^3 - 4u^2v - 2u^3v - (a + 2b + \frac{c}{2})v(u + 1)^2 - 4u^2v^2 - 5u^3v^2 - 2u^4v^2 - 2u^3v^3 - u^4v^3
\end{align*}
\]

This equation is negative if \( c > \max\{(2a + 4b)/a, 2a + 4b\} \) and

\[
v > \tilde{v} := \max\left\{ 4a + 8b + 2c, \frac{6a + 12b + c}{ac}, \frac{a + 2b}{c} \right\}
\]

Let \( K := \tilde{u} + \tilde{v} \). If \( \| (u, v) \| > K \) then either \( u > \tilde{u} \) or \( v > \tilde{v} \) and, therefore, \( \nabla W \cdot (f, g) < 0 \).

(P2) Taking the second derivatives of \( W \) gives us:

\[
\begin{align*}
\partial_{uu} W &= \frac{2c}{(u + 1)^3} > 0 \\
\partial_{uv} W &= \frac{2}{(v + 1)^3} > 0 \\
\partial_{vv} W &= 0.
\end{align*}
\]

Thus, the desired inequalities are satisfied.

(P3) We have that,

\[
W(u, v) = \| (u, v) \| + \frac{v}{u + 1} + \frac{1}{v + 1} \geq \| (u, v) \|.
\]

Thus, as \( \| (u, v) \| \to \infty \), \( W(u, v) \to \infty \).

(P4) Note, that for this system \( \partial_u W > 0 \) if \( u \geq c \) and \( \partial_v W > 0 \) if \( v \geq 0 \). Therefore, we set \( u := c \) and \( v := 0 \). For an arbitrary \( u > 0 \), we have that

\[
\sup_{v \geq 0} \frac{\partial_u W(u, v)}{\partial_u W(u, v)} = \sup_{v \geq 0} \frac{1 - \frac{c}{(u + 1)^2}}{2 - \frac{1}{(v + 1)^2}} \leq \left| 1 - \frac{c}{(u + 1)^2} \right| < \infty
\]
and for an arbitrary \( v > 0 \), we have that
\[
\sup_{u \geq c} \left| \frac{\partial_v W(u,v)}{\partial_u W(u,v)} \right| \geq \sup_{u \geq c} \frac{2 - \frac{1}{c(u + 1)^2}}{1 - \frac{1}{c(u + 1)^2}} \leq \frac{2 - \frac{1}{(c+1)^2}}{1 - \frac{1}{(c+1)^2}} < \infty.
\]

Thus, the specified supremums are finite.

(P5) Taking the limits specified in the property gives us
\[
\lim_{u \to \infty} \frac{\partial_v W(u,v)}{\partial_u W(u,v)} = \lim_{v \to \infty} \frac{\partial_v W(u,v)}{\partial_u W(u,v)} = \lim_{u \to \infty} \partial_u W(u,v) = 0.
\]

Therefore, all the limits exist and are finite.

C Unbounded example system

C.1 No Lyapunov-like function exists

In this section we will use Corollary 8 to show that no LLF exists for the reactions given by (34). Suppose we fix a value of \( v > 0 \) and consider what happens in the limit as \( u \to \infty \). We have that at some point \( u > v + 1 \) and \( u > \delta/v - 1 \). This leads to the follow inequalities
\[
f(u,v) = uv(u - v)(u + 1) - \delta u > 0
\]
\[
g(u,v) = uv(v - u)(v + 1) - \delta v < 0
\]
and we have that
\[
\lim_{u \to \infty} \frac{|f(u,v)|}{|g(u,v)|} = \lim_{u \to \infty} \frac{f(u,v)}{g(u,v)} = \lim_{u \to \infty} \frac{uv(u-v)(u+1) - \delta u}{uv(u-v)(v+1) + \delta v} = \lim_{u \to \infty} \frac{(u+1) - \frac{\delta}{u(u-v)}}{u+1} = \infty.
\]

Thus, by Corollary 8 no LLF for the system exists.

C.2 Unboundedness of two-compartment system

In this section, we will show that the discretized RD system given by (3) with parameters \( \gamma = 1, d = 1, \) and \( n = 2 \) and reactions given by (34) has the capacity to become unbounded. We will use symmetric initial conditions (i.e. \( u_1,0 = v_2,0 \) and \( u_2,0 = v_1,0 \)). It follows that, due to the symmetry of the reactions, \( u_1(t) = v_2(t) \) and \( u_2(t) = v_1(t) \) for all \( t > 0 \). Therefore, the system reduces to
\[
\begin{align*}
\frac{du}{dt} &= uv(u - v)(u + 1) - \delta u + 4(u - v) \\
\frac{dv}{dt} &= uv(v - u)(v + 1) - \delta v + 4(u - v)
\end{align*}
\]
\[a_{\text{Diag}} = (38)
\]

where \( u_0 = u_{1,0} = v_{2,0} \) and \( v_0 = u_{2,0} = v_{1,0} \). We can then calculate the concentration of species in each compartment as \( u_1(t) = v_2(t) = u(t) \) and \( v_1(t) = u_2(t) = v(t) \).
Let’s consider (38) and calculate how the difference between $u$ and $v$ evolves with time:

$$
(u - v)t = uv(u + v + 2) + (8 + \delta)(v - u) = (u - v)h(u, v).
$$

(39)

where

$$
h(u, v) := uv(u + v + 2) - (8 + \delta),
$$

Therefore if,

$$
\begin{align*}
    u - v &> 0 \\
    h(u, v) &> 0
\end{align*}
$$

then $(u - v)t > 0$.

We will show that there exists a $\delta > 0$ such that for arbitrarily small $\epsilon > 0$, $dh/dt$ is positive along the curve

$$
h(u, v) = \epsilon.
$$

(41)

Therefore, if the initial data satisfies (40) then these inequalities will be satisfied for all time.

We first solve (41) explicitly for $v$ to obtain the positive solution

$$
v = -1 + \frac{1}{2}u + \sqrt{\frac{8 + \delta + \epsilon}{u} + 1 + u + \frac{u^2}{4}}.
$$

(42)

Note that this function is symmetric about the line $u = v$ and it is concave upwards (i.e., $d^2v/du^2 > 0$). First we will show that there exists a constant $C$ such that, along the curve given by (41), $u + v \geq C > 0$. Suppose it is not the case (i.e., $u + v < C$) and add $u$ to both sides of (42) to obtain

$$
C > u + v = -1 + \frac{1}{2}u + \sqrt{\frac{8 + \delta + \epsilon}{u} + 1 + u + \frac{u^2}{4}}.
$$

Using algebraic manipulations, we obtain the following inequality:

$$
0 > (2 + C)u^2 - C(2 + C)u + 8 + \delta + \epsilon.
$$

The maximum value of $C$ which guarantees that no real solutions to this equation exist is given by the solution to $0 = C^2 + 2C^2 - 32$. We will define $C$ as the one real root to this equation. We are then guaranteed that along the curve (41), $u + v \geq C$.

Next, we will assume $u - v > 0$ and break up the curve given by (41) into two regions: $0 < u - v \leq 1$ and $1 < u - v$. For both these regions we will calculate $dh/dt$ along (41) and show that, under certain conditions, it is positive. We will further suppose that $\epsilon + \delta < 1$.

Case 1: Suppose $0 < u - v \leq 1$. In order to show that $dh/dt$ is increasing along the curve, we will find a lower bound for the value of $u + v$ and translate that into an upper bound on the value of $uv$. Due to the positive second derivative and symmetry of (12), we know the maximum value of $u + v$ along the curve occurs when $v = u - 1$. We will call this point $(u_{max}, v_{max})$. Note that $C \leq u_{max} + v_{max} = 2u_{max} - 1$, and therefore $u_{max} \geq (C + 1)/2$. We will next calculate an upper bound on $u_{max}$. We have that

$$
\begin{align*}
    h(u_{max}, v_{max}) &= \epsilon \\
    u_{max}v_{max}(u_{max} + v_{max} + 2) &= \epsilon + \delta + 8 \\
    u_{max}(u_{max} - 1)(2u_{max} + 1) &= \epsilon + \delta + 8 \\
    u_{max} - 1 &= \frac{\epsilon + \delta + 8}{u_{max}(2u_{max} + 1)} \\
    u_{max} - 1 < \frac{9}{(C + 1)(C + 2)} &= \frac{18}{(C + 1)(C + 2)} \\
    u_{max} < \frac{18}{(C + 1)(C + 2)} + 1
\end{align*}
$$
It then immediately follows that $v_{\text{max}} < \frac{18}{(C+1)(C+2)}$. We then have that, along the curve given by (41)

$$uv = \frac{\epsilon + \delta + 8}{u + v + 2} > \frac{\epsilon + \delta + 8}{u_{\text{max}} + v_{\text{max}} + 2} > \frac{8}{36(C+1)(C+2)} + 3 =: A.$$ 

Finally, we consider and bound the derivative of $h$ along the curve. Recall that $u + v > C$ and $\delta + \epsilon < 1$. We have that along (41) when $0 < u - v \leq 1$

$$\frac{dh(u,v)}{dt} = (u - v)^2(2 + u + v)(4 - uv) + 2uv + (uv)^2(u - v)^2 - \delta uv(4 + 3(u + v))$$

$$\geq (u - v)^2(4(2 + u + v) - (8 + \delta + \epsilon)) + uv(2 - \delta(4 + 3(u + v)))$$

$$\geq (u - v)^2(4C - 1) + uv(2 + 2\delta - 3\delta(u + v + 2))$$

$$\geq uv(2 + 2\delta) - 3\delta(8 + \epsilon + \delta)$$

$$\geq A(2 + 2\delta) - 27\delta$$

$$\geq 2A - (27 - 2A)\delta.$$ 

Thus, if $\delta < \frac{2A}{27 - 2A}$ then the derivative is increasing.

Suppose $u - v > 1$. The derivative of $h$ along the curve is bounded as follows:

$$\frac{dh(u,v)}{dt} = (u - v)^2(2 + u + v)(4 - uv) + 2uv + (uv)^2(u - v)^2 - \delta uv(4 + 3(u + v))$$

$$\geq (u - v)^2(4(2 + u + v) - (8 + \delta + \epsilon)) - \delta uv(4 + 3(u + v)))$$

$$\geq (4C - 1) - \delta uv(-2 + 3(u + v + 2)))$$

$$\geq (4C - 1) + 2uv - 3\delta(8 + \epsilon + \delta)$$

$$\geq (4C - 1) - 3\delta(8 + \epsilon + \delta)$$

$$\geq (4C - 1) - 27\delta.$$ 

So the derivative is positive if $\delta < \frac{4C - 1}{27}$.

Therefore, for small enough $\delta$, if the system satisfies (40) it will continue to do so for all time. Numerically, we determined that if $\delta \leq 0.13$ then the necessary conditions are satisfied.

Using (39) and assuming the initial data satisfies (40), we have that for small enough $\epsilon > 0$.

$$(u - v)_t \geq \epsilon(u - v).$$

Using Grönwall’s inequality, we then have that

$$u(t) - v(t) \geq (u_0 - v_0)e^{\epsilon t}.$$ 

Therefore, since $v(t) \geq 0$, $u(t) \to \infty$ as $t \to \infty$. Note that analogously we could pick initial conditions where $v_0 > u_0$ and $u_0v_0(u_0 + v_0 + 2) > 8 + \delta$ and this would lead to a blow up of $v(t)$. 
