

A STEADY STATE OF MORPHOGEN GRADIENTS FOR SEMILINEAR ELLIPTIC SYSTEMS

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ABSTRACT. In this paper we establish the existence of positive solutions to a system of steady-state Neumann boundary problems. This system has been observed in some biological experiments, morphogen gradients; effects of *Decapentaplegic* (Dpp) and *short gastrulation* (Sog). Mathematical difficulties arise from this system being nonquasimonotone and semilinear. We overcome such difficulties by using the fixed point iteration via upper-lower solution methods. We also discuss an example, the Dpp-Sog system, of such problems.

1. INTRODUCTION

We present a mathematical analysis on the model problem of morphogen gradients. Morphogens are molecules that diffuse from a local source to form a concentration. The concentration determines the reactions of all cells and activates genes to form patterns of cell differentiation [10]. Experiments in morphogen diffusions to understand the pattern formations of tissue in developing animals give rise to a broad range of systems of reaction-diffusion equations see for example [2, 4, 5, 9, 15].

This paper focuses on a mathematical analysis on a general system including the model problem of morphogen gradients. More precisely, we establish the existence of positive solutions to the nonlinear steady state system arising morphogen gradients. Interesting features of the system we study in this paper are that it is nonquasimonotone, where few theories can be found for nonquasimonotone system [1, 6, 7, 8] (note that although the first three references are systems with the zero Dirichlet boundary conditions, the techniques therein can be employed in the Neumann boundary conditions) and it has certain nonlinearities on the source terms. As an example of such system we also discuss model equations arising in experiments of morphogen. In particular it is of our interest to study the Dpp-Sog system [5, 9], see Section 3, which has certain growth rates and nonlinearities, see *structure conditions* for the general system in the following section. We note that to understand the stabilities of the reaction-diffusion system, in this paper, we focus on the steady state solutions.

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This paper is organized in two parts; first we state structure conditions and establish an existence result for a class of elliptic systems. In the second part of paper we discuss the model problem and outline a proof by constructing upper and lower solutions to the model system.

2. A CLASS OF SYSTEMS

In this section we show the existence of positive solutions to the following elliptic system

$$\begin{aligned}\Delta u + f(x, u, v, w) &= 0 && \text{in } \Omega, \\ \Delta v + g(x, u, v, w) &= 0 && \text{in } \Omega, \\ \Delta w + h(x, u, v) &= 0 && \text{in } \Omega, \\ \frac{\partial u}{\partial n} = \frac{\partial v}{\partial n} = \frac{\partial w}{\partial n} &= 0 && \text{on } \partial\Omega,\end{aligned}$$

where the source terms f , g and h satisfy the following **structure conditions**:

- (F) $f(x, p, q, r)$ is L^P in $x \in \Omega \subset \mathbb{R}^N$ with $P > N$ and $f(x, p, q, r)$ is locally Lipschitz in p, q, r .
For $p, q, r \geq 0$,

$$f(x, p, q, r) = f^1(p, q, r) + f^2(x, p, q, r), \quad f(x, 0, q, r) \geq f_0(x) \geq 0, \quad (2.1)$$

$$f^1(p, q, r) \leq -\lambda p^\gamma \quad (2.2)$$

where $\lambda > 0$ and $\gamma > 1$, and

$$|f^2(x, p, q, r)| \leq |\tilde{f}(q, r)|(|p| + 1) + C_f, \quad \text{and } 0 \leq f_0(x) \leq C_f, \quad (2.3)$$

with a positive constant C_f .

For $(x, p, q, r) \in \bar{\Omega} \times [0, \infty)^3$, $f(x, p, q, r)$ is nondecreasing in q and non-increasing in r .

- (G) $g(x, p, q, r)$ is L^P in $x \in \Omega \subset \mathbb{R}^N$ with $P > N$ and $g(x, p, q, r)$ is locally Lipschitz in p, q, r .

$$g(x, u, v, w) = g(u, v, w) + g_0(x). \quad (2.4)$$

For $(x, p, q, r) \in \bar{\Omega} \times [0, \infty)^3$, there exist positive constants C_g and g_1 such that

$$0 \geq g(p, q, r) \geq -C_g \quad \text{and} \quad 0 \leq g_0(x) \leq g_1. \quad (2.5)$$

- (H) $h(x, p, q)$ is L^P in $x \in \Omega \subset \mathbb{R}^N$ with $P > N$ and $h(x, p, q)$ is locally Lipschitz in p, q . For $(x, p, q) \in \bar{\Omega} \times [0, \infty)^2$, $h(x, p, q)$ is nondecreasing in p and non-increasing in q .

The condition (F) implies the source term can be separated in two parts based on the growth rates in terms of u . We note that the conditions (2.2) and (2.3) can be generalized further, namely the result still holds if we replace the assumptions (2.2) and (2.3) to

$$\lim_{p \rightarrow +\infty} f(x, p, \cdot, \cdot) p^{-\gamma} = -\lambda \quad (2.6)$$

with $\lambda > 0$ and $\gamma > 1$. In fact the conditions (F)(G) and (H) implies that the existence result of the system is governed by the first equation and the other two equations act almost like “shadow” equations where such terminology was introduced by [13].

We use the upper-lower solutions method and the Schauder fixed point theorem to establish the existence result [16, 3]. We point out that the upper-lower solutions are not necessary in a classical sense, namely we allow them to be distributional solutions for the corresponding inequalities. That is, we say u is a lower (upper) solution if $u \in C(\bar{\Omega})$ satisfies

$$\Delta u + F(x) \geq (\leq) 0 \quad \text{in } \mathcal{D}'(\Omega), \quad \frac{\partial u}{\partial n} \Big|_{\partial\Omega} \leq (\geq) 0 \quad \text{a.e..}$$

For $x_0 \in \partial\Omega$ where the normal derivative is undefined we impose

$$\frac{\partial u}{\partial n}(x_0) \equiv \lim_{x \rightarrow x_0} \sup(\inf) \frac{u(x_0) - u(x)}{|x_0 - x|} \leq (\geq) 0,$$

where $x_0 - x$ and the normal at x_0 is less than $\pi/2 - \delta$ for some fixed $\delta > 0$. We now establish the following existence theorem.

Theorem 2.1. *For a given bounded open domain $\Omega \subset \mathbb{R}^N$ and if Ω is a region of the class $W^{2,P}$ then there exist $u_i, v_i, w_i \in C(\bar{\Omega})$, $i = 1, 2$, upper-lower solutions in a distributional sense, and exist $u, v, w \in W^{2,P}(\Omega) \cap C^{1+\alpha}(\bar{\Omega})$ -solutions such that $0 = u_1 < u < u_2$, $0 \leq v_1 \leq v \leq v_2$ and $0 \leq w_1 \leq w \leq w_2$ in Ω .*

Proof. We first construct a set of upper-lower solutions in a distributional sense to the system. We find $v_i \in C(\bar{\Omega})$, $i = 1, 2$, lower and upper solutions respectively. Since $0 \geq g(u, v, w) \geq -C_g$ provided $u, v, w \geq 0$ we find v_1 (the lower solution to v) to be a positive solution to

$$\Delta v_1 - C_g + g_0(x) \geq 0 \quad \text{in } \mathcal{D}'(\Omega), \quad \frac{\partial v_1}{\partial n} \Big|_{\partial\Omega} \leq 0 \quad \text{a.e..}$$

We find $v_2 > v_1$ (the upper solution to v) to be a positive solution to

$$\Delta v_2 + g_0(x) \leq 0 \quad \text{in } \mathcal{D}'(\Omega), \quad \frac{\partial v_2}{\partial n} \Big|_{\partial\Omega} \geq 0 \quad \text{a.e..}$$

This can be done by choosing integration constants for v_1 and v_2 correspondingly. We now fix v_i , $i = 1, 2$.

Now with v_2 we find a positive solution w_1 (the lower solution to w) which satisfies

$$\Delta w_1 + h(x, 0, v_2) \geq 0 \quad \text{in } \mathcal{D}'(\Omega), \quad \frac{\partial w_1}{\partial n} \Big|_{\partial\Omega} \leq 0 \quad \text{a.e..}$$

With v_2 and w_1 we now find a positive solution u_2 (the upper solution to u) to

$$\Delta u_2 + f(x, u_2, v_2, w_1) \leq 0 \quad \text{in } \mathcal{D}'(\Omega), \quad \frac{\partial u_2}{\partial n} \Big|_{\partial\Omega} \geq 0 \quad \text{a.e..}$$

Let ϕ be the first eigenfunction satisfying $\Delta\phi + \lambda_1\phi = 0$ with $\partial\phi/\partial n = 0$ on $\partial\Omega$ $\lambda_1 > 0$, and $\|\phi\|_\infty = 1$. Then by letting $u_2 = K(\phi + 2) \geq 1$ with a constant $K > 1$ to be determined we show u_2 satisfies the last inequalities. More precisely since we have $f^1(p, \cdot, \cdot) \leq -\lambda p^\gamma$ with $\gamma > 1$ and thus

$$\begin{aligned} & \Delta u_2 + f(x, u_2, v_2, w_1) \\ & \leq -K\lambda_1\phi - \lambda(K(\phi + 2))^\gamma + \sup \tilde{f}(v_2, w_1)(K\phi + 2K + 1) + C_f \\ & \leq K\lambda_1 - \lambda K^\gamma + \sup \tilde{f}(v_2, w_1)(3K + 1) + C_f < 0 \end{aligned}$$

by taking $K \geq K_1(\lambda_1, \gamma, \lambda, \sup \tilde{f}(v_2, w_1), C_f) > 0$. In fact u_2 is the upper solution in a classical sense.

We now find w_2 (the upper solution to w) such that $w_2 > w_1$ and it is a positive solution to

$$\Delta w_2 + h(x, u_2, v_1) \leq 0, \quad \mathcal{D}'(\Omega), \quad \frac{\partial w_2}{\partial n} \Big|_{\partial\Omega} \geq 0 \text{ a.e.}$$

Finally since $w_2 > 0$ and $v_1 > 0$, we let $u_1 \equiv 0$ so that u_1 (the lower solution to u) satisfies

$$\Delta u_1 + f(x, u_1, v_1, w_2) \geq f_0(x) \geq 0.$$

We now define a set $S \subset C^1(\bar{\Omega}) \times C^1(\bar{\Omega}) \times C^1(\bar{\Omega})$;

$$\begin{aligned} S = \{ & (u, v, w) : u_1 \leq u \leq u_2, \quad v_1 \leq v \leq v_2, \quad w_1 \leq w \leq w_2 \text{ in } \Omega, \\ & \|u\|_{C^1(\bar{\Omega})} \leq A, \quad \|v\|_{C^1(\bar{\Omega})} \leq B, \quad \|w\|_{C^1(\bar{\Omega})} \leq C \\ & \frac{\partial u}{\partial n} = \frac{\partial v}{\partial n} = \frac{\partial w}{\partial n} = 0 \text{ on } \partial\Omega \}. \end{aligned}$$

The set S is clearly closed, bounded and convex. Define a map T on S such that

$$\Delta Tu - MTu + f(x, u, v, w) = -Mu \quad (2.7)$$

$$\Delta Tv + g(x, u, v, w) = 0 \quad (2.8)$$

$$\Delta Tw + h(x, u, v) = 0 \quad (2.9)$$

$$\frac{\partial Tu}{\partial n} = \frac{\partial Tv}{\partial n} = \frac{\partial Tw}{\partial n} = 0 \quad \text{on } \partial\Omega, \quad (2.10)$$

where M is a positive constant so that $f_u + M \geq 0$ for $u, v, w \in S$ and f_u is the Lipschitz constant of f in u . Such M can be found independently to u since $u_1 \leq u \leq u_2$ and $f \in C^{0,1}$. Since f, g and h are uniformly bounded in L^∞ with respect to u, v and w , there exist unique solutions Tu, Tv and Tw in $W^{2,p} \cap C^{1,\beta}(\bar{\Omega})$ with $\beta = 1 - N/p$, see for the existence of the unique solution in [11, Proposition 7.18] and the solution space [3, Theorem 7.26] to (2.7), (2.8) and (2.9) correspondingly, and thus the map T is well-defined.

We first show the map T satisfies the first inequalities. First since $v, w \in S$, evaluate $u_1 = 0$ we get

$$\Delta u_1 + f(x, u_1, v, w) \geq f_0(x) \geq 0$$

and

$$\begin{aligned} 0 & \leq \Delta(u_1 - Tu) - M(u_1 - Tu) - Mu + f(x, u_1, v, w) - f(x, u, v, w) \\ & \leq \Delta(u_1 - Tu) - M(u_1 - Tu) + (f_u + M)(u_1 - u) \\ & \leq \Delta(u_1 - Tu) - M(u_1 - Tu), \end{aligned}$$

since $u \in S$ and $f_u + M \geq 0$ by the choice of $M > 0$. In fact since u_1 satisfies the last inequality point-wise and also holds the zero Neumann boundary condition point-wise as well, we can apply the strong maximum principle [3, Theorem 3.5] to get $u_1 - Tu < 0$ or $u_1 - Tu \equiv c$ for some constant c . Since $M > 0$ the constant c must be zero and since $\Delta u_1 \neq \Delta Tu$ thus we get $Tu > u_1$ in $\bar{\Omega}$.

To show u_2 be an upper solution, we evaluate

$$\begin{aligned} 0 & \leq \Delta(Tu - u_2) + f(x, u, v, w) - f(x, u_2, v_2, w_1) + Mu - MTu \\ & \leq \Delta(Tu - u_2) - M(Tu - u_2) + (f_u + M)(u - u_2) + f_v(v - v_2) + f_w(w - w_1) \\ & \leq \Delta(Tu - u_2) - M(Tu - u_2), \end{aligned}$$

since $u, v, w \in S$, $f_u + M \geq 0$, and $f_v \geq 0$ and $f_w \leq 0$ where f_v and f_w are some bounded functions. Now since $\partial(u_2 - Tu)/\partial n \geq 0$ on $\partial\Omega$ we apply the same argument as before to get $u_2 > Tu$ in $\bar{\Omega}$. Therefore $u_1 < Tu < u_2$ in $\bar{\Omega}$.

We also show $v_1 \leq Tv \leq v_2$ and $w_1 \leq Tw \leq Tw_2$ by using $u, v, w \in S$ and the differential inequalities of v_i and w_i . More precisely as before we have $\Delta(v_1 - Tv) \geq 0$ in $\mathcal{D}'(\Omega)$. By the weak Maximum principle [3, Corollary 3.2] we get $\sup_{\Omega}(v_1 - Tv) \leq \sup_{\partial\Omega}(v_1 - Tv)^+$. Now suppose there exist a constant $k > 0$ and a point $x_0 \in \partial\Omega$ such that

$$\sup_{\partial\Omega}(v_1 - Tv)^+ = (v_1 - Tv)(x_0) = k.$$

Since v_1 and Tv are continuous, we can find a set Ω_k such that $\Omega_k = \{x \in \bar{\Omega} : (v_1 - Tv) < k\}$ and $\Omega_k \cap \bar{\Omega} = x_0$. We now apply Hopf lemma in Ω_k , Lemma 3.4 in [3], to get

$$0 \geq \frac{\partial v_1}{\partial n}(x_0) \geq \liminf_{x \rightarrow x_0} \frac{v_1(x_0) - v_1(x)}{|x_0 - x|} > \frac{\partial Tv}{\partial n}(x_0) = 0.$$

The contradiction is apparent. Thus there is no such $k > 0$, (hence $\sup_{\partial\Omega}(v_1 - Tv)^+ = 0$) and thus $Tv \geq v_1$. Similarly we get the rest of inequalities, and for $i = 1, 2$, $Tv \neq v_i$ and $Tw \neq w_i$. This shows the map T satisfies the first inequalities in S . (In the case if we find $u_i, i = 1, 2$ as lower/upper solutions in a distributional sense we apply the same arguments as we did for $v_1 - Tv$ to get the desired inequalities.)

We show the map T is compact, satisfies the second inequalities (this leads T being into), and continuous in S to get a fixed point in S . The map is compact since the source term is uniformly bounded in u, v and w . To be precise, since $u, v, w \in S$ and the source terms f, g and h are uniformly bounded in L^∞ , thus we apply the L^P -theory [11, Proposition 7.18] to obtain the uniform bounds of the solutions Tu, Tv , and Tw in $W^{2,P}(\Omega)$ for given $P > N$, namely, $\|Tu\|_{W^{2,P}} \leq C(N, P, M)\|f\|_{L^P}$, $\|Tv\|_{W^{2,P}} \leq C(N, P)\|g\|_{L^P}$, and $\|Tw\|_{W^{2,P}} \leq C(N, P)\|h\|_{L^P}$. Apply imbedding theory [3, Theorem 7.26] to get the uniform bounds of the solutions Tu, Tv , and Tw in $C^{1,\alpha}(\bar{\Omega})$ where $0 < \alpha < 1 - N/P$ is independent of solutions. Since we now have $C^{1,\alpha}(\bar{\Omega})$ bounds uniformly in Tu, Tv and Tw we simply let their uniform bounds to A, B and C respectively. Thus T maps S into. Furthermore, $T(S) \subset C^{1,\alpha}(\bar{\Omega})$ which is precompact in $C^1(\bar{\Omega})$ with $0 < \alpha < 1 - N/P$. This leads T is compact in S . Finally to show the map T is continuous, we take convergence sequences u_i, v_i and w_i and show that the sequences Tu_i, Tv_i and Tw_i have limits in S . Calculate

$$\begin{aligned} & \Delta(Tu_i - Tu_j) - M(Tu_i - Tu_j) + f(x, u_i, v_i, w_i) - f(x, u_j, v_j, w_j) + M(u_i - u_j) \\ &= \Delta(Tu_i - Tu_j) - M(Tu_i - Tu_j) + (f_u + M)(u_i - u_j) \\ & \quad + f_v(v_i - v_j) + f_w(w_i - w_j) \end{aligned}$$

Since Tu_i, v_i, w_j are in S and $M > 0$ the L^P -theory [11] leads to

$$\|Tu_i - Tu_j\|_{W^{2,P}} \leq C(\|u_i - u_j\|_{L^\infty} + \|v_i - v_j\|_{L^\infty} + \|w_i - w_j\|_{L^\infty})$$

and this implies Tu_i is a Cauchy sequence in $W^{2,P}(\Omega)$ and thus (by imbedding) the sequence Tu_i has a limit in S . Similarly v_i and w_i have limits in S as well. Therefore there exists a fixed point $Tu = u, Tv = v$ and $Tw = w$ in S . Now apply regularity arguments [3] to obtain $W^{2,P}(\Omega) \cap C^{1,\alpha}(\bar{\Omega})$ -solutions. This completes the proof. \square

We note that the regularity of the solutions can be improved to $C^{2,\alpha}(\overline{\Omega})$ if we allow

$f(x, \dots), g(x, \dots), h(x, \dots) \in C^{0,\beta}(\overline{\Omega})$ and $\partial\Omega \in C^{2,\gamma}$ for some $0 < \beta, \gamma < 1$.

3. AN EXAMPLE: MORPHOGEN GRADIENTS

In this section we present a biological example of the system where the details of modeling viewpoints can be found in [5, 9, 10, 12, 14, 15].

In multicellular systems, experiments suggest that the *Drosophila* wing disc of fly depends on the *decapentaplegic* (Dpp) gene [10]. In development of the Dpp concentration, proteins including *short gastrulation* (Sog) activate to inhibit Dpp. As a result of the activation of Sog, Dpp decreases its activity [12, 14, 15]. It is of our interest to understand mathematical structures, in particular the steady state solutions, on the model problem of the Dpp-Sog system. In fact, the model problem also includes effects of the co-inhibitor *twisted gastrulation* (Tsg), extracellular protease *tolloid* (Tld) and a second ligand *screw* (Scw) [12, 14]. For a mathematical simplification, this paper focuses only on the effect of Dpp and Sog. It is noted by [5] that although the mathematical simplification may reduce the biological factors the numerical simulation suggests that the simplified system preserves the fundamental features of the model system. More precisely we consider the following system on the interval $\Omega \equiv (0, 1) \subset \mathbb{R}$

$$\begin{aligned} \frac{\partial A}{\partial t} &= \Delta A - h_L A(1 - B) - h_{LS} AD + f_L B + (f_{LS} + g_{LS})C + v_{OL} \\ \frac{\partial B}{\partial t} &= h_L A(1 - B) - (f_L + g_L)B \\ \frac{\partial C}{\partial t} &= \Delta C + h_{LS} AD - (f_{LS} + g_{LS})C \\ \frac{\partial D}{\partial t} &= \Delta D - h_{LS} AD + f_{LS} C + v_{OS} \end{aligned}$$

with zero Neumann boundary conditions. Here A and B are the concentrations of free ligand and of receptor-bound ligand of Dpp, respectively, and C and D are the concentrations of the degradation of the bound complex and of the destruction of the inhibitors Sog, respectively. Coefficients h_L etc are positive constants (biological factors) and $v_{OL} = v_L H(1/2 - x)$ and $v_{OS} = v_S H(x - 1/2)$ where v_L and v_S are positive constants and H is the Heaviside function, where the Heaviside functions incorporate that ligand A is produced on the half of the domain, i.e., in the dorsal half of the embryo, and the new factor D is produced on the other half of the domain, i.e., the ventral half of the embryo, see [5, 12, 14] for details.

To understand the stabilities of the governing system, we consider the steady state system:

$$\Delta A - h_L A(1 - B) - h_{LS} AD + f_L B + (f_{LS} + g_{LS})C + v_{OL} = 0 \quad (3.1)$$

$$h_L A(1 - B) - (f_L + g_L)B = 0 \quad (3.2)$$

$$\Delta C + h_{LS} AD - (f_{LS} + g_{LS})C = 0 \quad (3.3)$$

$$\Delta D - h_{LS} AD + f_{LS} C + v_{OS} = 0 \quad (3.4)$$

with zero Neumann boundary conditions. Now notice that using equation (3.2) we can write (3.1) to

$$\Delta A - h_{LS} AD - g_L B + (f_{LS} + g_{LS})C + v_{OL} = 0. \quad (3.5)$$

Define $v = A + C$ and denote $u = A$ so that $C = v - u$ and from (3.5) and (3.3) to get

$$\Delta v - g_L B + v_{OL} = 0. \quad (3.6)$$

Also define $w = C + D$ such that $D = w - v + u$ and from (3.5) and (3.4) to get

$$\Delta w - g_{LS}(v - u) + v_{OS} = 0. \quad (3.7)$$

From (3.2) we get

$$B = \frac{h_L A}{h_L A + f_L + g_L} = \frac{u}{u + \alpha} \equiv B(u)$$

where $\alpha = (f_L + g_L)/h_L > 0$, and thus B is increasing in u . Finally we obtain an equivalent system in the following;

$$\Delta u - h_{LS}u(w - v + u) - g_L B(u) + (f_{LS} + g_{LS})(v - u) + v_{OL} = 0 \quad (3.8)$$

$$\Delta v - g_L B(u) + v_{OL} = 0 \quad (3.9)$$

$$\Delta w - g_{LS}(v - u) + v_{OS} = 0 \quad (3.10)$$

$$\frac{\partial u}{\partial n} = \frac{\partial v}{\partial n} = \frac{\partial w}{\partial n} = 0 \quad (3.11)$$

Note that in (3.8) for $u, v, w \geq 0$ we have

$$\begin{aligned} f(x, 0, v, w) &= (f_{LS} + g_{LS})v + v_{OL} \geq v_{OL} \geq 0, \\ f^1(u, v, w) &= -h_{LS}u^2 - h_{LS}uw - g_L B(u) - (f_{LS} + g_{LS})u < -h_{LS}u^2, \\ f^2(x, u, v, w) &= h_{LS}uv + (f_{LS} + g_{LS})v + v_{OL}, \end{aligned}$$

and clearly all the conditions in (F) hold.

Also in (3.9) and in (3.10), we have $g(x, u, v, w) = -g_L B(u) + v_{OS}$ which satisfies the conditions in (G) provided $u \geq 0$, and $h(x, u, v) = -g_{LS}(v - u) + v_{OS}$ which holds the conditions (H) as well. Thus we establish the existence of positive solutions to the system (3.8)-(3.10) in the following theorem. Since the proof follows exactly as in the Theorem 2.1 we only construct upper-lower solutions explicitly.

Theorem 3.1. *There exist positive solutions to the steady state system (3.8)-(3.10) and (3.11).*

Proof. Since the proof follows exactly as in Theorem 2.1 we only construct a set of upper-lower solutions to the system. We first find v_i , $i = 1, 2$, distributional lower and upper solutions respectively. Since $0 \leq B(u) < 1$ provided $u \geq 0$ we find v_1 (the lower solution to v) to be a positive solution to

$$v_1'' - g_L + v_L H(1/2 - x) \geq 0,$$

where H is the Heaviside function. Set

$$v_1 = \begin{cases} g_L \frac{x^2}{2} & x \in [0, 1/2] \\ g_L \frac{(x-1)^2}{2} & x \in (1/2, 1] \end{cases}$$

so that v_1 is positive and continuous on $(0, 1)$, and $\partial v_1 / \partial n = 0$ at $x = 0$ and $x = 1$. Since $v_L > 0$ and $v_1'' = g_L$ a.e in $(0, 1)$, the inequality holds.

We find v_2 (the upper solution to v) to be a positive solution to

$$v_2'' + v_L H(1/2 - x) \leq 0.$$

Similar calculation as before we set

$$v_2 = \begin{cases} -v_L \frac{x^2}{2} + c_1 & x \in [0, 1/2] \\ -v_L \frac{x^2}{2} + v_L x + c_2 & x \in (1/2, 1] \end{cases}$$

so that $\partial v_2 / \partial n = 0$ at $x = 0$ and $x = 1$ and $v_2'' = -v_L$ a.e. in $(0, 1)$. We can find integration constants c_1 and c_2 so that $v_2(1/2) = -\frac{v_L}{8} + c_1 = -\frac{v_L}{8} + \frac{v_L}{2} + c_2$ to get v_2 is continuous on $[0, 1]$ and $v_2 > v_1$ that is c_1 and c_2 satisfy

$$c_1 > \frac{v_L}{8} + \frac{g_L}{8}, \quad \text{and} \quad c_2 > \frac{3v_L}{8} + \frac{g_L}{8}.$$

We now fix the integration constants c_i , $i = 1, 2$.

With the v_2 we just found, we look for a positive solution w_1 (the lower solution to w) to

$$w_1'' - g_{LS}v_2 + v_S H(x - 1/2) \geq 0.$$

Set

$$w_1 = \begin{cases} g_{LS} \max v_2 \frac{x^2}{2} & x \in [0, 1/2] \\ g_{LS} \max v_2 \frac{(x-1)^2}{2} & x \in (1/2, 1] \end{cases}$$

so that $\partial w_1 / \partial n = 0$ at $x = 0$ and $x = 1$ and $w_1'' = g_{LS} \max v_2$ a.e and w_1 is positive and continuous on $(0, 1)$.

With v_2 and w_1 , we now find a positive solution u_2 (the upper solution to u). By letting $u_2 = K(\cos(\pi x) + 2) \geq 1$ with some large $K > 1$ we can see that u_2 satisfies

$$\begin{aligned} & u_2'' + f^1(u_2, v_2, w_1) + f^2(x, u_2, v_2, w_1) \\ & \leq u_2'' - (h_{LS} \min w_1 + f_{LS} + g_{LS})u_2 - h_{LS}u_2^2 \\ & \quad + h_{LS} \max v_2 u_2 + (f_{LS} + g_{LS}) \max v_2 + v_L H(1/2 - x) \\ & \leq -K\pi^2 \cos(\pi x) - h_{LS}K^2(\cos(\pi x) + 2)^2 \\ & \quad + h_{LS} \max v_2 K(\cos(\pi x) + 2) + (f_{LS} + g_{LS}) \max v_2 + v_L \\ & \leq -h_{LS}K^2 + (3h_{LS} \max v_2 + \pi^2)K + (f_{LS} + g_{LS}) \max v_2 + v_L < 0 \end{aligned}$$

by taking $K = \max\{6h_{LS} \max v_2 + 2\pi^2, [h_{LS}^{-1}2((f_{LS} + g_{LS}) \max v_2 + v_L)]^{1/2}\}$.

We now find w_2 (the upper solution to w) to be a positive solution to

$$w_2'' - g_{LS}v_1 + g_{LS}u_2 + v_S H(x - 1/2) \leq 0.$$

Since $\min v_1 = 0$ and $\max u_2 = 2K$ we can let w_2 be a positive solution to

$$w_2'' + g_{LS}2K + v_S H(x - 1/2) \leq 0.$$

Again we let

$$w_2 = \begin{cases} -(g_{LS}2K + v_S)\frac{x^2}{2} + d_1 & x \in [0, 1/2] \\ -(g_{LS}2K + v_S)(\frac{1}{2}x^2 - x) + d_2 & x \in (1/2, 1] \end{cases}$$

so that $\partial w_2 / \partial n = 0$ at $x = 0$ and $x = 1$ and $w_2'' = -(g_{LS}2K + v_S)$ a.e. in $(0, 1)$. This again brings two integration constants and so we choose them such that $w_2 > w_1$ and w_2 is continuous on $[0, 1]$. Namely, we find $d_1 > (g_{LS}2K + v_S)/8 + (g_{LS} \max v_2)/8$ and $d_1 = (g_{LS}2K + v_S)/2 + d_2$ where d_2 holds $d_2 > 3(g_{LS}2K + v_S)/8 + (g_{LS} \max v_2)/8$.

Finally since now we have $v_1 \geq 0$ it is easy to see that $f(x, 0, v_1, w_2) = (f_{LS} + g_{LS})v_1 + v_L H(1/2 - x) \geq v_L H(1/2 - 1) \geq 0$ and thus we let $u_1 = 0$ so that

$u_1'' + f(x, 0, v_1, w_2) \geq 0$. Clearly $0 = u_1 < u_2$, and $\partial u_1 / \partial n \leq 0$ at the boundary. Therefore, by Theorem 2.1 there exist solutions $u_1 < u < u_2$, $v_1 \leq v \leq v_2$ and $w_1 \leq w \leq w_2$ and this completes the proof. \square

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REFERENCES

- [1] Y. S. Choi, and P. J. McKenna; A Singular Gierer-Meinhardt System of Elliptic Equations, *Ann. Inst. H. Poincaré Anal. Non Linéaire*, 17 (2000), no. 4, 503–522.
- [2] A. Gierer and H. Meinhardt; A theory of biological pattern formations, *Kybernetik*, 12 (1972), pp.30-39.
- [3] D. Gilbarg, and N. S. Trudinger; “Elliptic Partial Differential Equations of Second Order,” 2nd ed., Springer Verlag, New York, 1983.
- [4] J. Gurdon, and P. Bourillot; Morphogen gradient interpretation, *Nature*, 413:797-803, 2001
- [5] J. Kao, Q. Nie, A. Teng, F. Wan, A. Lander, and J. Marsh; Can morphogen activity be enhanced by its inhibitors?, *preprint*.
- [6] E. H. Kim; A class of singular Gierer-Meinhardt systems of elliptic boundary value problems, *Nonlinear Analysis TMA*, 59(2004), 305-318.
- [7] E. H. Kim; Singular Gierer-Meinhardt systems of elliptic boundary value problems, *Journal of Mathematical Analysis and Applications*, 308(2005) 1-10.
- [8] D. Kinderlehrer, and G. Stampacchia; “An introduction to variational inequalities and their applications,” Academic Press, New York, 1980.
- [9] A. Lander, Q. Nie, and F. Wan; Do morphogen gradients arise by diffusion?, *Developmental Cell*, Vol. 2(6), 785-796, 2002.
- [10] P. A. Lawrence; Morphogens: how big is the big picture?, *Nature Cell Biology*, Vol. 3(7), pp E151-E154, July 2001.
- [11] G. Lieberman; “Second Order Parabolic Differential Equations,” World Scientific, 1996.
- [12] G. Margues, M. Musacchio, M. J. Shimell K. Wunnenberg-Stapleton, K. W. Y. Choi and M. B. O'Connor; Production of a DPP activity gradient in the early Drosophila Embryo through the opposing actions of the SOG and TLD proteins, *Cell*, 91:417-426 Oct.1997.
- [13] W. M. Ni, Diffusion, cross-diffusion, and their spike-layer steady states, *Notices AMS*, 45(1998), pp. 9-18.
- [14] S. Piccolo, E. Agiusa, S. Goodman, B. Lu, L. Dale and E. DeRobertis; Cleavage of chordin by xolloid metalloprotease suggests role for proteolytic processing in the regulation of spemann organizer activity. *Cell*,91:407-416, Oct. 1997.
- [15] J. Ross, O. Shimmi, P. Vilmos, A. Petryk, H. Kim, K. Gaudenez, S. Hermanson, S. Ekker, M. O'Connor and J. Marsh; Twisted gastrulation in a conserved extracellular BMP antagonist, *Nature*, 410:479-483, March 2001.
- [16] D. H. Sattinger; “Topics in Stability and Bifurcation Theory,” Lecture Notes in Mathematics, no. 309, Springer-Verlag, 1973.

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