Global Secondary Bifurcation in a Non-linear Boundary Value Problem

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We consider a steady-state non-linear boundary value problem which arises in modelling the formation of vascular networks in response to tumour growth. Global bifurcation from both trivial and non-trivial solution branches is considered, with emphasis on the latter. By investigating such secondary bifurcation, it is shown that positive, bounded solutions exist for all physically relevant values of a critical parameter. A certain class of these solutions is discussed with respect to the application to tumour growth.

1. INTRODUCTION

We consider a scalar differential equation arising from a model for the formation of a vascular network in response to the presence of primary or secondary tumours in humans (1, 9). The network is represented in the model by a density distribution of a particular type of cell. Under normal conditions these cells proliferate and are at all times acted upon by various external and internal agents, principally chemicals released by the tumour itself. The steady-state solutions to this model are of importance in predicting the long term distribution of vasculature. In its non-dimensionalised form, the steady-state solutions of the model can be represented by the equation

\[-D \frac{d}{dx} \left( \frac{dn}{dx} - nh(x) \right) = \lambda n(1 - n), \quad x \in (0, 1), \quad (1)\]
subject to the boundary conditions,
\[
\frac{dn}{dx} - nh(x) = 0, \quad \text{at } x = 0, 1. \tag{2}
\]

The parameter \( \lambda \) represents the rate at which the cell density, \( n(x) \), proliferates and therefore we consider \( \lambda > 0 \). The parameter \( D \) represents the rate of diffusion of the cell density and is considered positive. The function \( h(x) \) represents the action of other agents on the cell density. In practice this action may take many different forms and in particular has no specified sign. In the following we therefore place no restriction on the function \( h(x) \) other than it is Lipschitz continuous on the interval \([0, 1]\).

This condition could be relaxed to \( h(x) \in C(0, 1) \cap L^2(0, 1) \) in most of the analysis below. As \( n(x) \) represents cell density, we are interested in non-negative, classical solutions of this boundary value problem.

By setting \( \lambda = 0 \), (1) is reduced to a linear equation. For a particular choice of function \( h(x) \), this equation and a related initial value problem have been numerically investigated as discussed in [1]. A more general analysis (although still for the \( \lambda = 0 \) case) is conducted in [9]. In the following we consider non-negative solutions of \((1, 2)\) for values of \( \lambda \geq 0 \). In Section 2 we use a change of variable to reduce the problem to one of standard Sturm–Liouville type and investigate global bifurcations from the branch of trivial solutions \((n = 0\) for all \( \lambda \)). Using orthogonal projections, in Section 3 we consider secondary bifurcation to positive, non-constant solutions. Via a series of lemmas, in Section 4 we obtain a global existence result. Finally, in Section 5 we discuss the application of these results to tumour vascularisation.

2. BIFURCATIONS FROM THE TRIVIAL SOLUTION BRANCH

Following Sleeman et al. [9], we employ the change of variable \( n = u \phi \) where
\[
\phi(x) = \exp \left( \int_0^x h(z) \, dz \right),
\]
thus finding a solution of \((1, 2)\) is equivalent to finding a solution \( u \) of
\[
-D(\phi u')' = \lambda \phi u(1 - \phi u), \quad x \in (0, 1), \tag{3}
\]
\[
u' = 0, \quad \text{at } x = 0, 1, \tag{4}
\]
where \( \phi' = \frac{d\phi}{dx} \). Equation (3) is now of classical non-linear Sturm–Liouville type (as \( \phi \) is strictly positive and continuously differentiable by the definition of \( h(x) \) given above).
Clearly, \( u = 0 \) is a solution of (3,4) for all values of \( \lambda \geq 0 \). Linearising (3) around \( u = 0 \) gives the equation

\[
-D(\phi v')' = \lambda \phi v, \quad x \in (0,1),
\]

\[
v' = 0, \quad \text{at } x = 0, 1.
\]

It is well known (see, for example, [7]) that the boundary value problem (5,6) possesses an increasing sequence of simple eigenvalues (i.e., eigenvalues of algebraic multiplicity equal to 1) given by \( 0 = \lambda_1 < \lambda_2 < \ldots < \lambda_j < \ldots \) with \( \lambda_j \to \infty \) as \( j \to \infty \). Any eigenfunction \( \phi_j \) corresponding to \( \lambda_j \) has exactly \( j - 1 \) simple nodal zeros in \((0,1)\) (i.e., \( \phi_j \) has \( j - 1 \) zeros in \((0,1)\) and at each of these points, \( \phi_j' \) is non-zero). Hence for each \( j \) there is a branch of solutions of (5,6) of the form \( (\alpha \phi_j, \lambda_j), \alpha \in \mathbb{R} \).

By Theorem 2.3 in [8], it follows that there exists a branch of non-trivial solutions to (3,4) emanating from \((u, \lambda) = (0, \lambda_j)\) for each integer \( j \geq 1 \).

On each of these branches, the solutions are locally of the form \( (u, \lambda) = (\alpha \phi_j + o(|\alpha|), \lambda_j + o(1)) \) for \( \alpha \in \mathbb{R}, |\alpha| \) sufficiently small. Moreover, any solution on the branch containing the point \((0, \lambda_j)\) has exactly \( j - 1 \) simple nodal zeros. Therefore, branches emanating from different bifurcation points cannot meet and hence by Theorem 1.3 in [8], each branch "meets \( \infty \)" in \( u - \lambda \) space (see [3, 8] for a full account of this theory).

Any solution \( u \) of (3,4) provides a solution \( n = u \phi \) of (1,2). Hence, as we are interested only in non-negative solutions to (1), we restrict our attention to those solutions contained in the first branch, i.e., the branch emanating from \((u, \lambda) = (0,0)\) (as all solutions on all other branches change sign). Notice that \((u, \lambda) = (k,0)\) for constants \( k \), is a line of solution to (3,4) emanating from \((0,0)\) and this line of constant solutions is contained within the first branch described above. Any solution \( u = k, k > 0 \), on this line provides a positive solution \( n = k \phi \) of (1). In the following we investigate the existence of non-negative solutions for \( \lambda > 0 \) by looking for secondary bifurcations from the line of solutions \((k,0)\) (noting that secondary bifurcations from any other branch retain the nodal structure of the "primary" branch and hence are not of interest here).

### 3. SECONDARY BIFURCATION

To investigate further bifurcations, we first reformulate (3,4) in an appropriate function space setting. Let

\[
X = C[0,1], \quad Y = C[0,1], \quad Z = Y \cap \left\{ v : \int_0^1 v \, dx = 0 \right\},
\]

\[
Y = C[0,1], \quad Z = Y \cap \left\{ v : \int_0^1 v \, dx = 0 \right\}
\]
where $r = 1, 2$ and, e.g., $C^2$ denotes the space of twice differential functions as is standard. Next, decompose functions $u \in X_r$ into two orthogonal parts (where orthogonality is in the usual $L^2(0,1)$ sense) that is let $u = k + \hat{u}$ where $k \in \mathbb{R}$ (in this context here and below, we identify $\mathbb{R}$ with the space of constant functions) and $\hat{u}$ satisfies

$$\int_0^1 \hat{u} \, dx = 0.$$ 

Define the operators $L: X_2 \to Z$ and $\mathcal{F}: \mathbb{R} \times (X_2 \cap Z) \times \mathbb{R} \to Y$ as:

$$L(k + \hat{u}) := -D(\phi(k + \hat{u}))' = -D(\phi\hat{u}') = L\hat{u},$$

$$\mathcal{F}(k, \hat{u}, \lambda) := L\hat{u} - \lambda(\hat{u} + k) \phi[1 - (\hat{u} + k) \phi],$$

where we have suppressed the dependence on $x$ (through $\phi(x)$). Notice that $\int_0^1 L' \, dx = 0$ for any $v \in X_2$ and hence $L: X_2 \to Z$. Notice also that $L|_{X_2 \cap Z}: X_2 \cap Z \to Z$ is non-singular. Finding classical solutions of (3, 4) is equivalent to finding elements $(k, \hat{u}, \lambda) \in \mathbb{R} \times (X_2 \cap Z) \times \mathbb{R}$ which satisfy the equation

$$\mathcal{F}(k, \hat{u}, \lambda) = 0. \quad (7)$$

Next, define the orthogonal projections $E: Y \to Z$ and $I - E: Y \to \mathbb{R}$ by

$$Ev = v - \int_0^1 v \, dx, \quad (I - E)v = \int_0^1 v \, dx, \quad v \in Y.$$

Then (7) is equivalent to the system of equations

$$E\mathcal{F}(k, \hat{u}, \lambda) = 0, \quad (I - E)\mathcal{F}(k, \hat{u}, \lambda) = 0,$$

that is

$$L\hat{u} - E\lambda(k \phi(1 - k \phi) + \hat{u} \phi(1 - \hat{u} \phi) - 2\hat{u} k \phi^2) = 0,$$

$$-(I - E)\lambda(k \phi(1 - k \phi) + \hat{u} \phi(1 - \hat{u} \phi) - 2\hat{u} k \phi^2) = 0,$$

where, for ease of notation and noticing that $EL\hat{u} = EL|_{X_2 \cap Z} \hat{u} = L|_{X_2 \cap Z} \hat{u}$, we have written $L$ in place of $L|_{X_2 \cap Z}$. This system may in turn be rewritten as

$$\mathcal{L}(k)w + \mathcal{M}(k, w) = 0, \quad (8)$$
where \( w = (\hat{u}, \lambda)^T \),

\[
\mathcal{L}(k)w = \begin{pmatrix}
L & -Ek\phi(1 - k\phi) \\
0 & -(I - E)k\phi(1 - k\phi)
\end{pmatrix}
\begin{pmatrix}
\hat{u} \\
\lambda
\end{pmatrix},
\]

\[
\mathcal{M}(k,w) = \begin{pmatrix}
-\lambda E(\hat{u}\phi(1 - \hat{u}\phi) - 2\hat{u}k\phi^2) \\
-\lambda(I - E)(\hat{u}\phi(1 - \hat{u}\phi) - 2\hat{u}k\phi^2)
\end{pmatrix}.
\]

In this new formulation, we seek bifurcation from the trivial solution \( w = 0 \) for particular values of \( k \). From (8) noticing that \( \mathcal{M}(k,w) = O(||w||^2) \) near \( w = 0 \) and the implicit function theorem, this can occur only if \( \mathcal{L}(k) \) is singular, i.e., only if there exists a non-zero solution \( u, \lambda \) to the system of equations,

\[
L\hat{u} - \lambda E k \phi(1 - k\phi) = 0, \quad -\lambda(I - E) k \phi(1 - k\phi) = 0. \tag{9}
\]

It follows directly that this occurs iff

\[
\int_0^1 k\phi(1 - k\phi) \, dx = 0,
\]

that is iff

\[
k = 0 \quad \text{or} \quad k = \hat{k} := \frac{\int_0^1 \phi \, dx}{\int_0^1 \phi^2 \, dx}. \tag{10}
\]

Therefore bifurcation can only occur from the points \( (k, w) = (0, 0) \) and \( (\hat{k}, 0) \). The continuum bifurcating from the first of these points consists of the line of trivial solutions of (3, 4) that is \( (k, \hat{u}, \lambda) = (0, 0, \lambda) \) for all \( \lambda \) and all other continua bifurcating from this line. Hence, by the arguments given in Section 2, no solutions of the desired form lie within this continuum. Therefore we consider bifurcation from the single point \( (k, w) = (k, 0) \).

Using standard techniques it can be shown after some calculation, that the hypotheses of Theorem 1.7 in [3] hold for (8) at the point \( (k, w) = (\hat{k}, 0) \). At this point, from (9), the null space of the linear operator \( \mathcal{L}(k) \) is given by

\[
N(\mathcal{L}(\hat{k})) = \text{span}\left\{(L^{-1}\hat{k}\phi(1 - \hat{k}\phi), 1)^T\right\}.
\]

Hence, by Theorem 1.7 in [3], there exists a local smooth branch of non-trivial solutions to (8) bifurcating from the point \( (\hat{k}, 0) \) and close to
this point the non-trivial solutions have the form,

\[ k = \hat{k} + o(1), \quad w = \left( sL^{-1}\hat{k}\phi(1 - \hat{k}\phi) + o(|s|) \right) \frac{1}{s + o(|s|)} \]  \tag{11}

for \( s \in \mathbb{R} \), with \(|s|\) sufficiently small. Each element \((k, w)\) on this local branch of solutions to (8) corresponds to a non-constant solution \((u, \lambda) = (\hat{u} + k, \lambda)\) of (3, 4). We now extend this result to one of global existence.

4. GLOBAL EXISTENCE OF POSITIVE SOLUTIONS

In the following let \( \| \cdot \|_X, \| \cdot \|_Y, \| \cdot \|_{1,2}, \) and \( \| \cdot \|_2 \), respectively, denote the standard norms on the spaces \( X, Y \) as defined above and the Sobolev spaces \( W^{1,2}(0,1) \) and \( L^2(0,1) \) (see, e.g., [6]). Also, the regularity results used below can be found in Chapter 6 of [11].

**Lemma 1.** Any solution \((u, \lambda)\) of (3, 4) with \( u > 0 \) and \( \lambda > 0 \), has

\[ \|u\|_X \leq K_1(\lambda^{1/2} + K_2^2) \]  for positive constants \( K_{1,2} \).

**Proof.** Suppose that \((u, \lambda)\) is any solution of (3, 4) with \( u(x) > 0 \) for \( x \in [0,1] \) and \( \lambda > 0 \). On integrating (3) over \((0,1)\) it follows, remembering the boundary conditions (4), that

\[ 0 = \int_0^1 u \phi \, dx - \int_0^1 u^2 \phi^2 \, dx, \]

which, by Schwarz’ inequality, implies that

\[ \int_0^1 u \phi \, dx = \int_0^1 u^2 \phi^2 \, dx \leq 1. \]  \tag{12}

Recalling the orthogonal decomposition of \( u \) used above, i.e., \( u = \hat{u} + k \) where

\[ \int_0^1 \hat{u} \, dx = 0, \]

Poincaré’s inequality (see p. 269 of [5]) implies that

\[ \|\hat{u}\|_{1,2} \leq c\|\hat{u}\|_2, \]  \tag{13}
where \( c \) is a constant. Moreover, from (12) we have that
\[
k \leq \frac{1}{\min\{\phi(x)\}}, \quad \text{and} \quad \int_0^1 u^2 \, dx \leq \frac{1}{\min\{\phi^2(x)\}}, \tag{14}
\]
where these and all following maxima and minima are over the set \( x \in [0, 1] \) and are well defined. We now improve the bound for \( u \). Taking the inner product of (3) with \( u \) gives
\[
\int_0^1 -D(\phi'')u \, dx = \lambda \int_0^1 u^2 \phi(1 - u \phi) \, dx < \lambda \int_0^1 u^2 \phi \, dx
\]
\[
\leq \frac{\max\{\phi(x)\}}{\min\{\phi^2(x)\}}.
\]
Therefore, on integration by parts and noting that \( u' = \hat{u}' \), we have
\[
\|\hat{u}\|_2^2 \leq \frac{\max\{\phi(x)\}}{\min\{\phi^2(x)\}}.
\]
Hence by (13):
\[
\|\hat{u}\|_{1, 2} \leq \lambda^{1/2}c \left( \frac{\max\{\phi(x)\}}{D \min\{\phi(x)\} \min\{\phi^2(x)\}} \right)^{1/2}.
\]
It follows from this and (14) that \( \|u\|_{1, 2} \leq C_3(\lambda^{1/2} + C_2) \) for some positive constants \( C_{1, 2} \).

From the continuity of the embedding \( W^{1, 2}(0, 1) \rightarrow C[0, 1] \) it follows that
\[
\|u\|_Y \leq C_3(\lambda^{1/2} + C_2), \tag{15}
\]
for some positive constant \( C_3 \) and the right-hand side of (3) is therefore bounded in \( Y \). Hence from (3) and regularity theory, \( \|u\|_{X_2} \leq K_{3}(\lambda^{1/2} + K_3)^2 \) for some positive constants \( K_{1, 2} \) and the lemma is proved.

Let \( F: X_2 \times \mathbb{R} \rightarrow Y \) be defined by
\[
F(u, \lambda) = D(\phi'')u + \lambda \phi u(1 - \phi u).
\]
Clearly any solution \((u_0, \lambda_0) \in X_2 \times \mathbb{R}\) of \( F(u, \lambda) = 0 \) satisfies (3, 4). Moreover,

**Lemma 2.** Any solution \((u_0, \lambda_0) \) of \( F(u, \lambda) = 0 \) with \( \lambda_0 > 0 \) and \( u_0(x) > 0 \) in \([0, 1]\) can be continued in some neighbourhood \( N \subset X_2 \times \mathbb{R} \) of \((u_0, \lambda_0)\) to a smooth curve of solutions \((u(\lambda), \lambda)\) with \( u(\lambda_0) = u_0 \). Moreover, all solutions \((u, \lambda) \in N \) of \( F(u, \lambda) = 0 \) lie on this curve.
Proof. We adopt a similar approach to that used in [10]. By the definition of $F$ given above it follows directly that $F \in C^2(X_2 \times \mathbb{R})$ and that

$$D_x F(u, \lambda) z = D(\phi z')' + \lambda \phi z(1 - 2 \phi u) \quad \text{for all } u, z \in X_2.$$ 

We now show the operator $D_x F(u, \lambda): X_2 \rightarrow Y$ is an isomorphism provided $F(u, \lambda) = 0, u > 0$, and $\lambda > 0$, with the intent of using the implicit function theorem. From standard arguments it follows that the operator $D_x F(u, \lambda): X_2 \rightarrow Y$ is a compact perturbation of the isomorphism $K: X_2 \rightarrow Y$ defined by $Kz = D(\phi z')' - z$ and hence is a Fredholm operator of index zero. Thus to show that $D_x F(u, \lambda): X_2 \rightarrow Y$ is an isomorphism, all that is required to show is that it is injective, i.e., $D_x F(u, \lambda) z = 0$ implies $z = 0$.

Suppose that $F(u, \lambda) = 0$ with $\lambda > 0$ and $u(x) > 0$ on $[0,1]$ and that $D_x F(u, \lambda) z = 0$. Then

$$D(\phi u')' + \lambda \phi u(1 - \phi u) = 0, \quad (16)$$

and

$$D(\phi z')' + \lambda \phi z(1 - 2 \phi u) = 0, \quad (17)$$

on $(0,1)$. If $z(x)$ has a double zero, then as (17) is a linear second-order differential equation with continuous coefficients, it follows directly that $z = 0$. From now on we suppose that all zeros of $z$ are simple. On multiplying (16) by $z$ and (17) by $u$, subtracting and then integrating from 0 to $t$, we obtain

$$D\phi(t)[u'(t)z(t) - u(t)z'(t)] + \lambda \int_0^t \phi^2 u^2 z \, dx = 0. \quad (18)$$

Putting $t = 1$ in (18) yields

$$\int_0^1 \phi^2 u^2 z \, dx = 0,$$

and hence $z(x)$ must change sign on $(0,1)$. But as $z$ has only simple zeros and we may replace $z$ with $-z$ in the above, it follows that there exists a $y \in (0,1)$ such that

$$z(x) > 0 \text{ for } 0 \leq x < y, \quad z(y) = 0 \quad \text{and} \quad z'(y) < 0.$$
Hence

\[-D\phi(y)u(y)z'(y) + \int_0^y \phi^2u^2z \, dx > 0,\]

which contradicts (18) with the substitution \( t = y \). Hence \( z = 0 \). The result now follows by a standard application of the implicit function theorem at solutions \((u_0, \lambda_0)\) of \( F(u, \lambda) = 0 \) for which \( u_0 > 0 \) and \( \lambda_0 > 0 \) (see, e.g., p. 290 in [2]).

The results of the previous section show that a local, smooth curve of solutions to (3, 4) emanates from the bifurcation point \((u, \lambda) = (k, 0)\) and on part of this curve all solutions \((u, \lambda)\) have \( u > 0 \) and \( \lambda > 0 \). Let this local solution curve be denoted by \( \Gamma \) and define the positive cone \( P^+ \) as

\[ P^+ = \{(u, \lambda) \in X \times \mathbb{R} : u(x) > 0, x \in [0, 1], \lambda > 0\}. \]

Define \( \Gamma^+ := \Gamma \cap P^+ \). Then the preceding lemmas lead to the following result.

**Lemma 3.** The local branch \( \Gamma^+ \) can be continued to a maximal smooth curve, \( \hat{C}^+ \), parameterised by \( \lambda \). Moreover, \( \hat{C}^+ \subset P^+ \) and \( \hat{C}^+ \) joins \( \in P^+ \) at \( \lambda = +\infty \).

**Proof.** Taking any solution \((u, \lambda) \in \Gamma^+ \) we may apply the implicit function theorem as detailed in Lemma 2 above and hence, by continued application of this result, obtain a maximal smooth curve, \( \hat{C}^+ \). This curve is parameterised by \( \lambda \) and hence cannot “turn back” in \( X \times \mathbb{R} \). Consequently, \( \lambda > 0 \) on \( \hat{C}^+ \). Moreover, this curve cannot join with any branch emanating from the points \((u, \lambda) = (0, \lambda), j = 2, 3, \ldots \) discussed in Section 1, as the nodal properties of solutions on these branches are preserved. Also, \( \hat{C}^+ \) cannot join with the trivial branch \((u, \lambda) = (0, \lambda)\) as this branch is isolated except at the points \((0, \lambda_j)\) where simple bifurcations occur. Hence, all solutions \((u, \lambda) \in \hat{C}^+ \) have \( u > 0, \lambda > 0 \) and by Lemma 1, \( \hat{C}^+ \) is bounded in \( X \times \mathbb{R} \) for \( \lambda < \infty \). It follows from the nodal properties and regularity of solutions to (3), a simple compactness argument, and by reaching a contradiction on applying the implicit function theorem, that \( \hat{C}^+ \cup \{(k, 0)\} \) can have no finite limit point (other than \((k, 0)\)). Hence, \( \Pi(\hat{C}^+) = (0, \infty) \) where \( \Pi : P^+ \to \mathbb{R} \) is the natural projection of \( P^+ \) onto \( \mathbb{R} \) and the lemma is proved.

Using these lemmas we can now prove our main result.

**Theorem 1.** The boundary value problem (1, 2) has a positive, bounded solution for all values of \( \lambda \geq 0 \). Moreover, these solutions lie on a smooth
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Proof. Define the set \( \mathcal{S} := \{(n, \lambda) \in X_2 \times \mathbb{R} : (n, \lambda) = (u \phi, \lambda), (u, \lambda) \in \mathcal{C}^+ \} \cup \{(k, 0)\). Then by Lemma 3, \( \mathcal{S} \) clearly forms the desired curve of positive solutions to (1, 2).

Finally we have,

Corollary 1. All solutions \((n, \lambda)\) of (1, 2) with \( n > 0 \) and \( \lambda > 0 \) lie on the curve \( \mathcal{S} \).

Proof. Choose any solution \((u, \lambda) \notin \mathcal{C} \) of (3, 4) which has \( u > 0 \) and \( \lambda > 0 \). Then by Lemma 2 we may continue this solution to a maximal smooth curve, \( T^+ \), say, and by similar arguments to those used in the proof of Lemma 3, it follows that this curve contains a sequence of solutions \(((u_j, \lambda_j))\) for which \( u_j > 0, \lambda_j > 0 \) for each \( j \) and \( u_j \to u_0, \lambda_j \to 0 \) as \( j \to \infty \). Here, \((u_j, \lambda_j)\) satisfies

\[
-D(\phi u_j')' = \lambda_j u_j \phi(1 - u_j \phi), \quad x \in (0, 1),
\]

\[
u_j = 0 \quad \text{at} \ x = 0, 1
\]

for each \( j \) and \( u_0 \) satisfies

\[
-D(\phi u_0')' = 0, \quad x \in (0, 1),
\]

\[
u_0 = 0 \quad \text{at} \ x = 0, 1.
\]

Hence \( u_0 \) is a constant. However, integrating the first equation in (19) gives

\[0 = \int_0^1 u_j \phi(1 - u_j \phi) \, dx\]

for each \( j \) and passing to the limit shows that either \( u_0 = 0 \) or \( u_0 = \hat{k} \) as defined by (10). We can disregard the first case as bifurcation from \((0, 0)\) is simple and is to the branch of constant solutions \((u, \lambda) = (k, 0)\) as discussed in Section 2. If the second is true, then again as bifurcation from \((k, 0)\) is simple as shown in Section 3, we must have that, for \( j \) sufficiently large, \((u_j, \lambda_j) \in \mathcal{C}^+ \). Hence \( T^+ \) coincides with \( \mathcal{C}^+ \) and we have a contradiction. The result follows by the relationship between the elements on \( \mathcal{C}^+ \) and those on \( \mathcal{S} \) given above.
5. APPLICATIONS

In the formulation of the model that underpins system (1, 2), it is assumed that a blood vessel is situated at \( x = 0 \) and a solid tumour at \( x = 1 \). Under the action of various biochemicals, cells migrate from the blood vessel toward the tumour, multiply, and form a new blood network connecting the two. As is shown in [1], in the absence of cell proliferation (\( \lambda = 0 \)) and for a biologically relevant “taxis function” \( h(x) \), the solution \( n(x) = k \phi(x) \) has a single interior maximum from which \( n(x) \) reduces rapidly so that at the boundary \( x = 1 \), the size of \( n(x) \) can be viewed as being negligible. This type of solution corresponds to the situation where incomplete vascularisation of the tumour has occurred and hence the tumour is maintained in its less invasive non-vascular state (with resultant better prognosis for the patient).

In this paper we have demonstrated that all positive solutions to (1, 2) with \( \lambda > 0 \) lie on a smooth curve emanating from the point \( (n, \lambda) = (k, 0) \). Hence we have been able to show that a bounded, positive solution, corresponding to a physically relevant cell density distribution, exists for all values of \( \lambda > 0 \), i.e., for all positive cell proliferation rates. Moreover, these solutions deform smoothly from the \( \lambda = 0 \) solution, \( n(x) = k \phi(x) \) as \( \lambda \) is increased. Hence we have shown that if this \( \lambda = 0 \) solution is as described above (i.e., has a single interior maximum etc.) then this qualitative structure is maintained as \( \lambda \) increases from zero, for small values of \( \lambda \) at least. (In fact numerical calculations show that this structure is maintained for a large range of values of \( \lambda \) (see [4])). We therefore conclude that cell proliferation rate is of secondary importance to other biochemical processes induced by tumour growth (for example, AAF and TAF production (see again [4])), in establishing the conditions under which incomplete vascularisation of solid tumours occurs.

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