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A group analysis via weak equivalence transformations for a model of tumour encapsulation

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Abstract
A symmetry reduction of a PDEs system, describing the expansive growth of a benign tumour, is obtained via a group analysis approach. The presence in the model of three arbitrary functions suggests the use of Lie symmetries by using the *weak equivalence transformations*. An invariant classification is given which allows us to reduce the initial PDEs system to an ODEs system. Numerical simulations show a realistic enough description of the physical process.

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1. Introduction

The various cells of a pluricellular organism live in a complex and interdependent community, in which the proliferation of each element is strictly controlled. The normal cells give rise to other cells only when the balance between stimulating and inhibitory signals is in favour of cellular division. Through a close net of signals, the cells mutually control their activities so that the tissue, i.e. the collection of similar cells, maintains its dimension, structure and functions.

Tumour cells violate the mechanism of proliferation control and follow an autonomous programme of reproduction [1]. Moreover, they are able to develop a more dangerous ability: they can leave their original position, migrate through the tissues, being transported by the blood vessels and thus form secondary tumours, i.e. metastases [2]. The formation of metastases distinguishes the malignant tumour from benign ones, characterized by a localized growth.

The study of clinical evolution of human tumours and experimental models on animals confirms that the growth of a solid tumour is gradual. It is typically characterized by three morphologically distinguished phases: the initial avascular growth, a long quiescent period and the final invasion into surrounding tissue.

During the quiescent period the presence of a dense localized band of extracellular matrix, the so-called capsule, has been observed around the benign tumours [3] and it has been considered a favourable prognostic indicator [4].

There are two different theories to explain the mechanism of capsule formation: the expansive growth and the foreign body hypothesis. The former describes the capsule formation as a passive process, according to which the extracellular matrix is convected by the growing tumour and then condensed into a fibrous and dense capsule. Instead, according to the latter hypothesis, the capsule arises as a physical barrier created by a response of the body like an inflammation. The foreign body hypothesis seems to be improbable since it does not reproduce some physical features of the tumour [5]. Moreover, some mathematical models exist which show that this hypothesis is not sufficient to explain the capsule formation [6].

In this work a nonlinear system of partial differential equations arising as a 3D model of the biological process of encapsulation is studied. The expansive growth hypothesis shall be adopted.

The proposed system is the extension of a model studied in [7], where the expansion of the tumour was considered in the 1D case.

The basic hypothesis on the evolution process is that the tumoural tissue diffuses in the surrounding cellular matrix, whose behaviour is ruled by a nonlinear transport equation. The biophysics of the interaction between the tumoural mass and extracellular matrix will be described by three *a priori* arbitrary functions. The first one, $f(u)$, accounts for the mitosis and death of tumoural cells. The remaining two, $h(c)$ and $\theta(c)$, are both needed in order to explicitly differentiate two processes arising from the cellular matrix response to the diffusing tumoural mass. The first one, $h(c)$, accounts for the reduction of the cell motility due to the extracellular matrix, in such a way that the total flux of the tumoural density can be given by the term $h(c)\nabla u$. The second one, $\theta(c)$, is related to the effect of saturation on the rate of matrix movement and convection per cell at high matrix densities, in such a way that the flux of c is described by $kc\theta(c)h(c)\nabla u$. Here k is a diffusivity constant. This is a consequence of the expansive growth hypothesis which implies that the flux of c has to be proportional to the flux of u. The above hypothesis leads to the following nonlinear evolution system,

$$\begin{aligned} &-\frac{\partial u}{\partial t} + f(u) + \nabla \cdot (h(c)\nabla u) = 0 \\ &-\frac{\partial c}{\partial t} + k\nabla \cdot (c\Theta(c)\nabla u) = 0 \end{aligned} \tag{1.1}$$

where $\Theta(c) = \vartheta(c)h(c)$. In the hypothesis of spherical symmetry it reduces to

$$\begin{aligned} &-\frac{\partial u}{\partial t} + f(u) + \frac{\partial}{\partial r}\left(h(c)\frac{\partial u}{\partial r}\right) + \frac{2}{r}h(c)\frac{\partial u}{\partial r} = 0 \\ &-\frac{\partial c}{\partial t} + k\frac{\partial}{\partial r}\left(c\vartheta(c)h(c)\frac{\partial u}{\partial r}\right) + \frac{2k}{r}c\vartheta(c)h(c)\frac{\partial u}{\partial r} = 0. \end{aligned} \tag{1.2}$$

All the above-mentioned arbitrary functions are supposed to be continuously differentiable and to satisfy the same conditions as in [8]:

$$\begin{array}{llll} f(0) = f(1) = 0 & f(u) > 0 & \forall\, u \in (0, 1) & \\ f'(0) > 0 & f(u) < f'(0)u & \forall\, u \in (0, 1] & \\ h(c) \geqslant 0 & h'(c) \leqslant 0 & \forall\, c \geqslant 0 & h(1) > 0 \\ \theta(1) = 1 & \theta'(c) \leqslant 0 & \forall\, c \geqslant 0. & \end{array} \tag{1.3}$$

These constraints are naturally verified by any physically meaningful $f(u)$, $h(c)$ and $\theta(c)$.

In the 3D extension, the system does not admit travelling wave solutions, as in the 1D case [8]. System (1.2) involves both diffusive and convective terms and looks highly nonlinear. There are a few possibilities of finding exact solutions. In view of this, a symmetry reduction of the system, by using the Lie group approach, is performed. Such a method provides a reduction of the original system (1.2) to a new one depending on only one independent variable. Moreover, the supposed symmetry of the solutions reduces the arbitrariness of the available functions h, θ and f, leading to their appropriate form. Finally, the numerical analysis of the obtained ODEs system of course is much more easily tackled than the original PDEs system.

The plan of the paper is as follows: in section 2 a brief introduction to the general theory of symmetry reduction for PDEs, by using the Lie direct approach, is given; in section 3 the *weak equivalence transformation* theory is applied to the system; in section 4 a group classification, corresponding to the different choices of $\theta(c)$, is obtained; finally, in section 5 the system is reduced to a couple of ODEs and numerical simulations are performed. For the reader's convenience, in the appendix the expression of the prolonged operator for system (1.2) is explicitly computed in the augmented second-order jet space.

2. Symmetry reduction of nonlinear PDEs

The method for reducing the number of independent variables in a PDE is based on the requirement that the solution has to be invariant under some subgroup of the symmetry group of the equation [9]. Given the following *n*th order system of PDEs:

$$E_i\left(x_j, u_\alpha, \frac{\partial u_\alpha}{\partial x_j}, \frac{\partial^2 u_\alpha}{\partial x_j \partial x_k}, \ldots, \frac{\partial^n u_\alpha}{\partial x_j \cdots \partial x_k}\right) = 0 \tag{2.1}$$

where $j, k = 0, \ldots, p,\ \alpha = 0, \ldots, q,\ i = 0, \ldots, m$, and $p, q, m, n \in \mathbb{N}$, a solution $\mathbf{u} = f(\mathbf{x})$ is invariant under the Lie infinitesimal transformations

$$\tilde{x}_i = x_i + \varepsilon \xi^i \qquad \tilde{u}_\alpha = u_\alpha + \varepsilon \phi^\alpha \tag{2.2}$$

where ξ^i and ϕ^α depend on $(\mathbf{x}, \mathbf{u})$ and ε is a parameter, if and only if $\tilde{\mathbf{u}} = \tilde{f}(\tilde{\mathbf{x}})$ is still a solution of (2.1). Each vector field

$$\Gamma = \xi^i \partial_{x_i} + \phi^\alpha \partial_{u_\alpha} \tag{2.3}$$

generates a one-parameter subgroup of the symmetry group, integrating the equations

$$\frac{\mathrm{d}\tilde{x}_i}{\mathrm{d}\varepsilon} = \xi^i(\tilde{\mathbf{x}}, \tilde{\mathbf{u}}) \qquad \text{with} \quad \tilde{x}_{i|\varepsilon=0} = x_i \qquad \frac{\mathrm{d}\tilde{u}_\alpha}{\mathrm{d}\varepsilon} = \phi^\alpha(\tilde{\mathbf{x}}, \tilde{\mathbf{u}}) \qquad \text{with} \quad \tilde{u}_{\alpha|\varepsilon=0} = u_\alpha \tag{2.4}$$

and the general Lie algebra of the symmetry groups is obtained by composing the one-parameter transformations.

The coordinates of the *infinitesimal generator* Γ are calculated by applying the prolongation theory. As *n*th order derivatives appear in (2.1), one needs to know how the derivatives transform under the action of (2.2). The prolonged operator is defined as

$$\Gamma^* = \Gamma + \Gamma^{(1)} + \cdots + \Gamma^{(n)} \tag{2.5}$$

where $\Gamma^{(i)}, i = 1, \ldots, n$ are the *i*th prolongation of Γ in the *i*th order jet space (see [10]).

To determine the symmetry algebra, the *n*th prolongation Γ^* must annihilate equations (2.1) on their solutions:

$$\Gamma^*(E_i)_{|E_j=0} = 0 \qquad i, j = 1, \ldots, m \tag{2.6}$$

where equations (2.1) are considered as a set of algebraic equations in the *n*th order jet space with coordinates $\mathbf{x}, \mathbf{u}, \mathbf{u_x}, \ldots, \mathbf{u_{nx}}$.

Equations (2.6), in the unknown ξ^i, ϕ^α, explicitly involve $\mathbf{x}, \mathbf{u}, \mathbf{u_x}, \ldots, \mathbf{u_{nx}}$ and lead to an overdetermined linear system of PDEs. This system arises by imposing that system (2.6) identically vanishes, i.e. by requiring the coefficients of each linearly independent expression in the derivatives to identically vanish. It is the well-known *determining system*.

Once the Lie symmetries are obtained, the invariants $I_j(\mathbf{x}, \mathbf{u})$ are the solutions of the first-order linear PDEs

$$\Gamma I_j(\mathbf{x}, \mathbf{u}) = 0 \tag{2.7}$$

for each Γ.

If it is possible to choose q functions $\tilde{I}_j(\mathbf{x}, \mathbf{u})$, among the invariants, such that the Jacobian $\det\left(\frac{\partial \tilde{I}_1, \ldots, \tilde{I}_q}{\partial(u_1, \ldots, u_q)}\right) \neq 0$ and the remaining invariants depend only on the independent variables $\mathcal{I}_1(\mathbf{x}), \ldots, \mathcal{I}_k(\mathbf{x}), k < p$, then the result is

$$\tilde{I}_i = F_i(\mathcal{I}_1, \ldots, \mathcal{I}_k). \tag{2.8}$$

Due to the nonvanishing of the Jacobian, equation (2.8) can be solved for the dependent variables

$$u_i(\mathbf{x}) = U_i(\mathbf{x}, F_i(\mathcal{I})). \tag{2.9}$$

Substituting into (2.1), a set of equations involving the variables $\mathcal{I}$, the functions F_i and their derivatives with respect to $\mathcal{I}$ arise.

Since (2.1) is invariant under the action of the obtained group of symmetries and (2.7) provides a complete set of invariants, the noninvariant quantities $\mathbf{x}$ in (2.9) must drop out. Note that as $k < p$, the number of independent variables has been reduced.

3. Weak equivalence transformations

Due to the presence of three arbitrary functions in (1.2), the Lie symmetries method will be adopted as it will be possible to choose the form of these arbitrary functions within a set obtained by using the group classification.

As said in the previous section, if there are no arbitrary functions the determining system is a linear overdetermined system of partial differential equations. The presence of arbitrary functions generally causes nonlinearities to arise, so that the determining system becomes very difficult to solve. Nevertheless the presence of $f(u)$, and in particular of $h(c)$ and $\theta(c)$, permits us to restrict the search for the so-called Lie invariance classification, by determining the groups of equivalence transformations (see [11–14]).

An equivalence transformation is essentially a non-degenerate change of variables and arbitrary functions, which transforms the original PDEs system into a new one, preserving its differential structure. The transformed arbitrary functions could modify their form, but not their dependence on variables [9].

Instead, in the search for *weak equivalence transformations* (WETs), the transformed arbitrary functions can depend on both dependent and independent variables and the differential structure of the given PDEs system still remains unchanged. Then, through a WET the coefficients of the differential terms in the transformed PDEs system could have functional dependences different from those of the original coefficients.

In this work WETs will be used, as they usually give rise to a wider set of symmetries [15] by selecting the arbitrary functions in a suitable way.

This method will lead on one hand to classification of the functional form of $\theta(c)$ for which the system admits WETs in the space of h (considered as a variable) and of all the dependent and independent variables; on the other hand to determination of the Lie symmetries of the PDEs system by projection of those obtained via WETs.

Instead of searching for equivalence transformations using the direct form of change of variables, a new generalization of the Lie infinitesimal criterion that will simplify the calculation of the infinitesimal generators will be adopted (see [16]).

Consider the following one-parameter group of transformations defined in the $(r, t, u, c, f, h, \theta)$-space,

$$s_i = s_i(r, t, u, c, f, h, \theta, \varepsilon) \tag{3.1}$$

where $s_1 = r, s_2 = t, s_3 = u, s_4 = c, s_5 = f, s_6 = h, s_7 = \theta$. This group is locally a $\mathcal{C}^\infty$-diffeomorphism, analytically depending on the parameter ε in a neighbourhood of $\varepsilon = 0$ and which reduces to the identity for $\varepsilon = 0$. In the construction of the group of equivalence transformations no restrictions on the representation of equivalence transformations are imposed, so that the coefficients of the infinitesimal generator depend on independent and dependent variables and arbitrary functions, too. Namely

$$\Gamma = \xi^r \frac{\partial}{\partial r} + \xi^t \frac{\partial}{\partial t} + \xi^u \frac{\partial}{\partial u} + \xi^c \frac{\partial}{\partial c} + \xi^f \frac{\partial}{\partial f} + \xi^h \frac{\partial}{\partial h} + \xi^\theta \frac{\partial}{\partial \theta}$$

with $\xi^r, \xi^t, \eta^u, \eta^c, \zeta^f, \zeta^h, \zeta^\theta$ all depending on r, t, u, c, f, h, θ.

Since (1.2) is a second-order system, we compute the first and the second prolongations ($\Gamma^{(1)}, \Gamma^{(2)}$ respectively) of Γ in the second-order jet space, obtaining the prolonged operator

$$\Gamma^* = \Gamma + \Gamma^{(1)} + \Gamma^{(2)}.$$

Here the coefficients are constructed through the prolongation formulae and the appropriate total derivatives (see appendix).

By applying WETs one requires only that the functions U and C

$$U\left(r, t, u, c, \frac{\partial u}{\partial t}, \frac{\partial u}{\partial r}, \frac{\partial^2 u}{\partial r^2}, \ldots\right) = \Gamma^*\left(-\frac{\partial u}{\partial t} + f(u) + \frac{\partial}{\partial r}\left[h(c)\frac{\partial u}{\partial r}\right] + \frac{2}{r}h(c)\frac{\partial u}{\partial r}\right) \tag{3.2}$$

$$C\left(r, t, u, c, \frac{\partial u}{\partial t}, \frac{\partial u}{\partial r}, \frac{\partial^2 u}{\partial r^2}, \ldots\right) = \Gamma^*\left(-\frac{\partial c}{\partial t} + k\frac{\partial}{\partial r}\left[c\vartheta(c)h(c)\frac{\partial u}{\partial r}\right] + \frac{2k}{r}c\vartheta(c)h(c)\frac{\partial u}{\partial r}\right) \tag{3.3}$$

vanish identically along the set of solutions of the same system. The above functions are obtained acting with the prolonged operator Γ^* on the left-hand side of system (1.2). In this way transformations under which the system preserves the differential structure, even if the arbitrary functions change their dependences on variables, are obtained.

4. Weak equivalence classification

For computational convenience the weak equivalence classification will be performed with respect to $h(c)$. Hence, the infinitesimal generator takes the form

$$\Gamma = \xi^r \frac{\partial}{\partial r} + \xi^t \frac{\partial}{\partial t} + \xi^u \frac{\partial}{\partial u} + \xi^c \frac{\partial}{\partial c} + \xi^h \frac{\partial}{\partial h} \tag{4.1}$$

with the coefficients ξ^i $(i = r, t, u, c, h)$ depending on r, t, u, c, h.

Table 1.

$\vartheta(c)$	Infinitesimal generator
Arbitrary	$\Gamma_1, \Gamma_2, \Gamma_3$
Constant	$\Gamma_1, \Gamma_2, \Gamma_3, \Gamma_4, \Gamma_5, \Gamma_6$
1/c	$\Gamma_1, \Gamma_2, \Gamma_3, \Gamma_7, \Gamma_8, \Gamma_9$
$\beta/c + (1-\beta)$	$\Gamma_1, \Gamma_2, \Gamma_3, \Gamma_{10}, \Gamma_{11}, \Gamma_{12}$

The required invariance of system (1.2) under the action of the appropriate prolongation of the above infinitesimal generator gives the following determining system,

$$
\begin{aligned}
&\xi^u_{uu} = 0 \qquad\qquad \xi^h_h h - \xi^h = 0\\
&-\xi^r_{rr} r^2 + 2\xi^r_r r - 2\xi^r = 0 \qquad -2\xi^r_r h + \xi^t_t h + \xi^h = 0\\
&\vartheta_{cc}\xi^c ch^2 - 2\vartheta_c \xi^r_r ch^2 + \vartheta_c \xi^t_t ch^2 + \vartheta_c \xi^u_u ch^2 + 2\vartheta_c \xi^c h^2\\
&\qquad + \vartheta_c \xi^h ch - 2\xi^r_r h^2 \vartheta + \xi^t h^2 \vartheta + \xi^u_u h^2 \vartheta + \xi^h h \vartheta = 0\\
&\vartheta_c \xi^c ch - \xi^c_c ch\vartheta - 2\xi^r_r ch\vartheta + \xi^t_t ch\vartheta + \xi^u_u ch\vartheta + \xi^c h\vartheta + \xi^h c\vartheta = 0\\
&f_u \xi^u h + 2\xi^r_r fh - \xi^u_t h - \xi^u_u fh - \xi^h f = 0\\
&-\vartheta_c \xi^c cfhk + \xi^c_c cfhk\vartheta - \xi^c_t h + 2\xi^r_r cfhk\vartheta - \xi^t_t cfhk\vartheta\\
&\qquad - \xi^u_u cfhk\vartheta - \xi^c fhk\vartheta - \xi^h cfk\vartheta = 0
\end{aligned}
\tag{4.2}
$$

where the subscript indices represent the partial derivatives with respect to the corresponding variables. Moreover, the dependence on the variables is restricted to $\xi^r(r), \xi^t(t), \xi^u(t,u), \xi^c(t,c), \xi^h(r,t,u,h)$.

Integrating the above system, one obtains the classes of weak equivalence given in table 1. The classification is performed specializing the functional form of $\vartheta(c)$. The explicit expression of the infinitesimal generators appearing in table 1 is

$$
\begin{aligned}
&\Gamma_1 = \alpha\frac{\partial}{\partial t} && \Gamma_2 = r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + 2h\frac{\partial}{\partial h}\\
&\Gamma_3 = r^2\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + 4rh\frac{\partial}{\partial h} && \Gamma_4 = \alpha\frac{\partial}{\partial t} + \gamma c\frac{\partial}{\partial c}\\
&\Gamma_5 = r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma c\frac{\partial}{\partial c} + 2h\frac{\partial}{\partial h} && \Gamma_6 = r^2\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma c\frac{\partial}{\partial c} + 4rh\frac{\partial}{\partial h}\\
&\Gamma_7 = \alpha\frac{\partial}{\partial t} + \gamma\frac{\partial}{\partial c} && \Gamma_8 = r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma\frac{\partial}{\partial c} + 2h\frac{\partial}{\partial h}\\
&\Gamma_9 = r^2\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma\frac{\partial}{\partial c} + 4rh\frac{\partial}{\partial h} && \Gamma_{10} = \alpha\frac{\partial}{\partial t} + \gamma(\beta + (1-\beta)c)\frac{\partial}{\partial c}\\
&\Gamma_{11} = r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma(\beta + (1-\beta)c)\frac{\partial}{\partial c} + 2h\frac{\partial}{\partial h}\\
&\Gamma_{12} = r^2\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma(\beta + (1-\beta)c)\frac{\partial}{\partial c} + 4rh\frac{\partial}{\partial h}.
\end{aligned}
\tag{4.3}
$$

5. Lie symmetries via WETs and solutions in a case of biological interest

Once the weak equivalence classification has been obtained in the extended (r, t, u, c, h)-space, one is now able to find an invariance classification in the space of dependent and independent variables which is based on the following theorem:

Table 2. Classification of symmetries in the space r, t, u, c.

	$f(u)$	$\vartheta(c)$	$h(c)$	Symmetry generators
1	Arbitrary	Arbitrary	Arbitrary	X_1
2	Arbitrary	Constant	Arbitrary	X_1,
3	Arbitrary	Constant	Constant	X_1, X_2
4	Arbitrary	Constant	$c^{2/\gamma}$	X_1, X_3
5	Arbitrary	$\beta/c + (1-\beta)$	Arbitrary	X_1
6	Arbitrary	$\beta/c + (1-\beta)$	$\delta(\gamma(\beta + (1-\beta)c))^{\frac{2}{\gamma(1-\beta)}}$	X_1, X_4
7	Arbitrary	$1/c$	Arbitrary	X_1
8	Arbitrary	$1/c$	Constant	X_1, X_5
9	Arbitrary	$1/c$	$e^{2c/\gamma}$	X_1, X_6

Theorem 1 (projection theorem)**.** *Let* $\Gamma = \xi^i(x^k, u^\beta)\ \partial_{x_i} + \eta^\alpha(x^k, u^\beta)\partial_{u^\alpha} + \mu(x^k, u^\beta, p)\partial_p$ *be an infinitesimal generator of a WET for a given system. The projection of* Γ

$$X = \xi^i(x^k, u^\beta)\partial_{x_i} + \eta^\alpha(x^k, u^\beta)\partial_{u^\alpha} \tag{5.1}$$

in the (x^i, u^α)*-space is an infinitesimal symmetry generator if and only if the specializations of the function p are invariant with respect to* Γ.

For more details see [13]. In our case, the condition that the specializations of p have to be invariant with respect to Γ reads

$$\Gamma(H(c) - h)_{|(h=H(c))} = 0$$

which leads to the classification of symmetries given in table 2, where

$$\begin{aligned} X_1 &= \alpha\frac{\partial}{\partial t} & X_2 &= \alpha\frac{\partial}{\partial t} + \gamma c\frac{\partial}{\partial c} \\ X_3 &= r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma c\frac{\partial}{\partial c} & X_4 &= r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma(\beta + (1-\beta)c)\frac{\partial}{\partial c} \\ X_5 &= \alpha\frac{\partial}{\partial t} + \gamma\frac{\partial}{\partial c} & X_6 &= r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma\frac{\partial}{\partial c} \end{aligned} \tag{5.2}$$

and α, β, γ are real constants.

Let us analyse the different cases appearing in table 2. Since the symmetry generator X_1 is a trivial time translation cases, 1, 2, 5 and 7 are not relevant.

Assuming that $h(c)$ is constant would be convenient from a mathematical point of view because the first equation in (1.2) becomes independent of c. On the other hand, this is a biologically unrealistic hypothesis as the changes in the extracellular matrix density would have no effect on the cell motility. This simplification is a good model only at the early stages of the tumour growth but, as a large amount of extracellular matrix has been accumulated, the tumour cell movement will be restrained from it. Hence we will not analyse cases 3 and 8.

Analogously, case 4 with $\theta(c)$ being constant is also a restrictive assumption, because the saturation effect, due to limitation on the matrix reorganization per cell at high matrix density, would be omitted.

Then we will focus our attention on the following two cases of biological interest.

5.1. Case 6: $\theta(c) = \beta/c + (1-\beta)$, $h(c) = \delta(\gamma(\beta + (1-\beta)c))^{\frac{2}{\gamma(1-\beta)}}$

For the moment the arbitrariness of the function $f(u)$ is preserved.

The infinitesimal generator in the (r, t, u, c, h)-space takes the form

$$\Gamma = r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma(\beta + (1-\beta)c)\frac{\partial}{\partial c} + 2h\frac{\partial}{\partial h}. \tag{5.3}$$

By imposing on $h(c)$ to satisfy conditions (1.3), one sees that the values of the parameters must obey the following restrictions:

$$0 < \beta < 1 \quad \gamma < 0 \quad \delta \geqslant 0 \quad \text{if} \quad \frac{2}{\gamma(1-\beta)} \text{ is an even integer}$$

or

$$0 < \beta < 1 \quad \gamma < 0 \quad \delta \leqslant 0 \quad \text{if} \quad \frac{2}{\gamma(1-\beta)} \text{ is an odd integer.}$$

In order to find invariant solutions with respect to the infinitesimal generator $X = r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma(\beta + (1-\beta)c)\frac{\partial}{\partial c}$, one has to solve the characteristic equations

$$\frac{\mathrm{d}r}{r} = \frac{\mathrm{d}t}{\alpha} = \frac{\mathrm{d}c}{\gamma(\beta + (1-\beta)c)} \tag{5.4}$$

obtaining the basis of invariants

$$I_1 = u \qquad I_2 = r\,\mathrm{e}^{-t/\alpha} \qquad I_3 = \frac{\gamma c \vartheta}{r^{\gamma(1-\beta)}}. \tag{5.5}$$

By choosing $I_2 = \sigma$, as the new independent variable, the functional forms of the invariant solutions become

$$u = U(\sigma) \qquad c = \frac{r^{\gamma(1-\beta)}C(\sigma) - \gamma\beta}{\gamma(\beta - 1)}. \tag{5.6}$$

As prescribed by the general theory, one has obtained the desired reduction to only one independent variable. Hence, substituting the above expressions into system (1.2), one obtains the following system of ODEs,

$$\begin{aligned} &U_\sigma\frac{\sigma}{\alpha} + f(U) + \delta U_{\sigma\sigma}C^{\frac{2}{\gamma(1-\beta)}}\sigma^2 + 4\delta U_\sigma C^{\frac{2}{\gamma(1-\beta)}}\sigma + \frac{2\delta}{\gamma(1-\beta)}U_\sigma C_\sigma C^{\frac{2}{\gamma(1-\beta)}-1}\sigma^2 = 0 \\ &\frac{1}{\alpha(1-\beta)\delta k}C^{\frac{2}{\gamma(1-\beta)}}C_\sigma - U_{\sigma\sigma}C\sigma + \left(1 - \frac{2}{\gamma(\beta-1)}\right)U_\sigma C_\sigma\sigma + (4 + \gamma(1-\beta))U_\sigma C = 0 \end{aligned} \tag{5.7}$$

where the subscript σ indicates the derivatives with respect to σ.

Although the mathematical structure of (5.7) is simpler than (1.2), the determination of explicit solutions to (5.7) is an hard task. We will thus investigate the behaviour of numerical solutions. In order to perform the numerical simulations of the obtained system (5.7), one has to specialize the functional form of $f(U)$. Since this term models the proliferation of the tumour cells, it is usual to choose a logistic growth, namely $f(U) = U(1-U)$. Initial conditions corresponding to a localized population of tumour cells are imposed. The results of the numerical simulations are shown in figure 1.

The obtained solutions reproduce the tumour growth and the formation of the corresponding capsule of dense extracellular matrix. In particular, figure 1 shows that there is no extracellular matrix accumulation within the tumour mass and the tumour cells adopt a steady, wave-like profile which migrates into the tissue with a sharp leading edge. In figure 1(*b*), a wave of extracellular matrix moves in parallel with the wave of tumour cells, with the effect

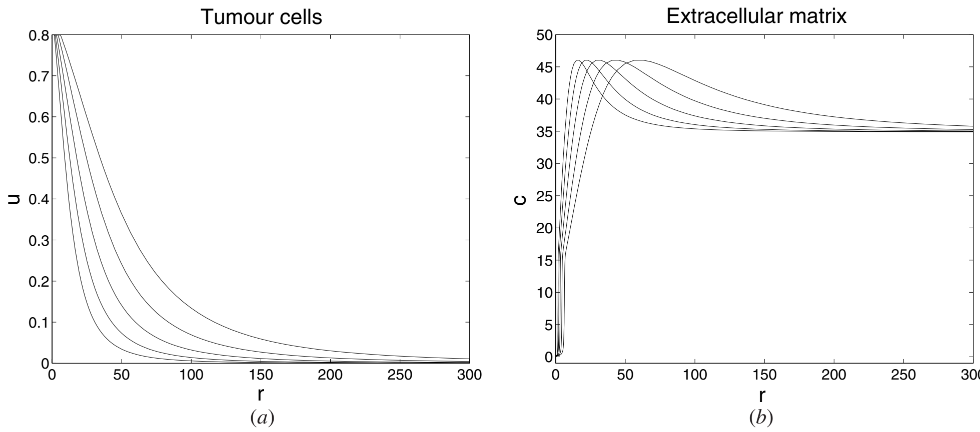


Figure 1. Solutions are plotted as functions of r at different values of t. The other parameters are fixed: $\alpha = 3$, $\beta = 0.5$, $\gamma = -4$, $\delta = -1$, $k = 29$.

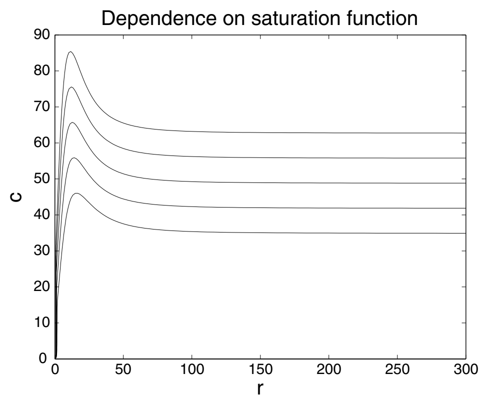
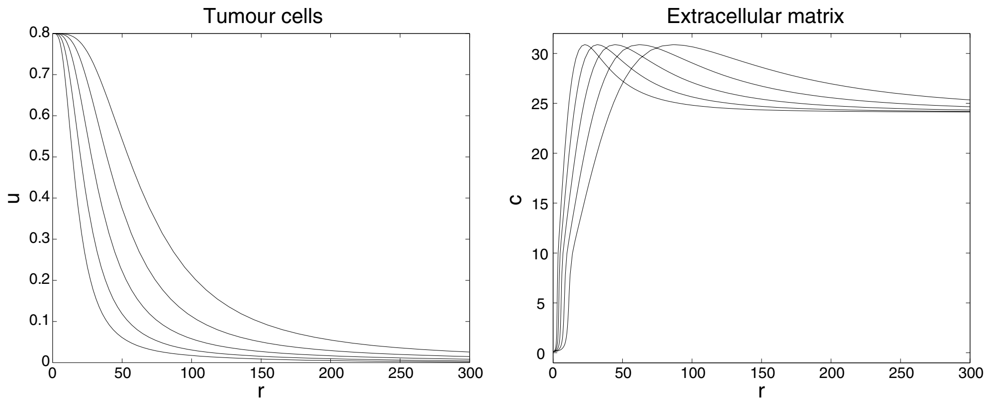


Figure 2. The values of extracellular matrix densities are plotted as a function of r at the fixed time $t = 20$. The parameters $\alpha = 3$, $\gamma = -4$, $\delta = -1$, $k = 29$ are fixed. We vary only β (from 0.1 to 0.5) to observe that the height of the peak for c depends on the choice of θ.

that a dense band of connective tissue is pushed ahead by the growing tumour, in accordance with the expansive growth hypothesis for the capsule formation.

The main difference with the one-dimensional case is that the above solutions exhibit a peak of the wave representing the extracellular matrix whose height does not change in time. This behaviour is consistent with the spherical geometry of the model. In fact, according to the expansive growth hypothesis, one could not expect growing peaks in the graph of c versus r, because the volume element increases as $r\,\mathrm{d}r$.

On the other hand, in figure 2, we can observe how the height of the peak, calculated at a fixed time, depends on the choice of the function $\theta(c)$. In fact, imposing different values on the parameter β, the peak in the c-wave is lower when the effect of saturation is stronger, while the form of $h(c)$ remains almost unchanged.



(*a*) (*b*)

Figure 3. Solutions are plotted as functions of r at different value of t. The other parameters are fixed: $\alpha = 3, \gamma = -4, k = 29$.

5.2. *Case 9:* $\theta(c) = 1/c, h(c) = \mathrm{e}^{2c/\gamma}$

The corresponding infinitesimal generator in the (r, t, u, c, h)-space is

$$\Gamma = r\frac{\partial}{\partial r} + \alpha\frac{\partial}{\partial t} + \gamma\frac{\partial}{\partial c} + 2h\frac{\partial}{\partial h}. \tag{5.8}$$

In order to satisfy conditions (1.3), one sees that $\gamma < 0$. Proceeding as in the previous section, the following functional forms of invariant solutions are determined,

$$u = U(\sigma) \qquad c = \ln\left(\frac{r}{C(\sigma)}\right)^{\gamma} \tag{5.9}$$

where $\sigma = r\,\mathrm{e}^{-t/\alpha}$.

Substituting expressions (5.9) into the given system (1.2), the below ODEs system is obtained,

$$U_\sigma\frac{\sigma}{\alpha} + f(U) = 0 \qquad -2kC_\sigma U_\sigma\frac{\sigma^2}{C^3} + kU_{\sigma\sigma}\frac{\sigma^2}{C^2} + 4kU_\sigma\frac{\sigma}{C^2} - \frac{\gamma}{\alpha}C_\sigma\frac{\sigma}{C} = 0 \tag{5.10}$$

where the subscript σ indicates the derivatives with respect to σ.

Since the determination of exact solutions is not simple also in this case, numerical simulations are performed. The results, obtained by using the same source term $f(U)$ as above, are in perfect agreement with the case analysed in the previous section, as shown in figure 3.

6. Conclusions

A system of conservation laws for the densities of tumour cells and extracellular matrix, describing the phenomenon of tumour encapsulation in 3D spherical geometry has been analysed. Using the Lie symmetries approach and weak equivalence classification, a wide class of symmetries was obtained. With a suitable choice of the symmetry generator the given system was reduced to a system of ODEs and numerical solutions of biological interest were found.

One should also analyse the stability of the above given solutions, modifying system (1.2) with the addition of terms deriving from small departures from spherical symmetry, or changing the source term $f(u)$. This will be the subject of a forthcoming paper.

Acknowledgment

The authors wish to thank Marco Sammartino for many enlightening and helpful discussions.

Appendix. The prolonged operator

Since we analyse the second-order system (1.2), we need to compute the prolonged operator Γ^* in the second-order jet space.

Introducing the following notation,

$$r^1 = r \quad r^2 = t \quad u^1 = u \quad u^2 = c \quad f^1 = f \quad f^2 = h \quad f^3 = \vartheta$$

and

$$z^1 = r \quad z^2 = t \quad z^3 = u \quad z^4 = c$$

the prolonged operator $\Gamma^* = \Gamma + \Gamma^{(1)} + \Gamma^{(2)}$ could be rewritten as

$$\begin{aligned}\Gamma^* = \Gamma &+ \sum_i \left(\xi^{u^i_r}\partial_{u^i_r} + \xi^{u^i_t}\partial_{u^i_t}\right) + \sum_{k,j} \xi^{f^k_{z^j}}\partial_{f^k_{z^j}} \\ &+ \sum_i \left(\xi^{u^i_{rr}}\partial_{u^i_{rr}} + \xi^{u^i_{rt}}\partial_{u^i_{rt}} + \xi^{u^i_{tt}}\partial_{u^i_{tt}}\right) + \sum_{k,l,j} \xi^{f^k_{z^j z^l}}\partial_{f^k_{z^j z^l}}\end{aligned} \tag{A.1}$$

for $i = 1, 2,\ j,\ l = 1, 2, 3, 4,\ k = 1, 2, 3$.

The coefficients of the prolonged operator are constructed using the following prolongation formulae:

$$\begin{aligned}\xi^{u^i_r} &= D_r\xi^{u_i} - u^i_r D_r\xi^r - u^i_t D_r\xi^t \\ \xi^{u^i_t} &= D_t\xi^{u^i} - u^i_r D_t\xi^r - u^i_t D_t\xi^t \\ \xi^{u^i_{rr}} &= D_r\xi^{u^i_r} - u^i_{rr} D_r\xi^r - u^i_{rt} D_r\xi^t \\ \xi^{u^i_{rt}} &= D_t\xi^{u^i_r} - u^i_{rr} D_t\xi^r - u^i_{rt} D_t\xi^t \\ \xi^{u^i_{tt}} &= D_t\xi^{u^i_t} - u^i_{rt} D_t\xi^r - u^i_{tt} D_t\xi^t \\ \xi^{f^k_{z^j}} &= \overline{D}_{z^j}\xi^{f^k} - \sum_l f^k_{z^l}\overline{D}_{z_j}\xi^{z^\alpha}.\end{aligned} \tag{A.2}$$

The operators D_r and D_t denote the total derivatives with respect to r and t, respectively. Then

$$D_r = \partial_r + \sum_i u^i_r\partial_{u^i} + \sum_k \left(f^k_r + \sum_i f^k_{u_i}u^i_r\right)\partial_{f^k} \tag{A.3}$$

$$D_t = \partial_t + \sum_i u^i_t\partial_{u^i} + \sum_k \left(f^k_t + \sum_i f^k_{u_i}u^i_t\right)\partial_{f^k}. \tag{A.4}$$

Moreover, the operator $\overline{D}_{z^j}$ denotes the total derivative considering z^j as independent variables and f^k as dependent variables:

$$\overline{D}_{z^j} = \partial_{z^j} + \sum_k f^k_{z^j}\partial_{f^k}. \tag{A.5}$$

All the calculations were carried out on a computer using the symbolic computer algebra program REDUCE [17].

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