The stabilizing effect of growth on pattern formation

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Abstract

We want to understand the effect of growth on the stability of Turing patterns on a curved domain (i.e. a manifold), and in that spirit we prove three results. First, under the hypotheses of Fick's law of diffusion and conservation of mass we deduce a reaction-diffusion system on an arbitrary compact Riemannian manifold, generalizing the results of Plaza *et al*, "The effect of growth and curvature on pattern formation", J. Dyn. Differential Equations, 16 (4), 1093-1121. Second, we prove global existence, uniqueness and regularity for reaction-diffusion systems on a manifold with isotropic growth. Third, we show that under the isotropic regime the growth has both a "globalizing" and a "stabilizing" effect on pattern formation: a "globalizing effect" because on a growing manifold a locally defined solution (i.e. defined up to a finite time $T > 0$) has more chances to be globally defined (i.e. for all $t \geq 0$) than on a fixed manifold, and a "stabilizing effect" because the growth shifts the eigenvalues of the reaction-difusion system towards the left in the complex plane.

Keywords: Pattern formation, Reaction-diffusion, Laplace-Beltrami operator, Global existence of solutions, Stability.

AMS subject classifications: 92C15, 35K57, 58J99, 74G25, 70K20

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1 Introduction

Since the seminal paper of Turing [11], the classical framework for pattern formation in biological and chemical systems are reaction-diffusion systems of the type

$$\frac{\partial \mathbf{u}}{\partial t} = \mathcal{D}\Delta\mathbf{u} + \mathbf{F}(\mathbf{u}), \quad \mathcal{D} = \begin{bmatrix} D_1 & & & \\ & D_2 & & \\ & & \ddots & \\ & & & D_M \end{bmatrix}, \; D_k > 0 \tag{1}$$

where $\mathbf{u} = \mathbf{u}(x,t)$, $x \in \Omega$ a domain in $\mathbb{R}^N$ and $t \geq 0$.

Plaza *et al* [7] considered a two-dimensional manifold $\mathcal{S}$ and its parametrization

$$\begin{array}{rcl} X : \hat{\Omega} \subset \mathbb{R}^2 & \longrightarrow & \mathcal{S} \\ \xi = (\xi_1, \xi_2) & \longmapsto & X(\xi_1, \xi_2), \end{array}$$

with $\hat{\Omega}$ a domain in $\mathbb{R}^2$. They added growth on $\mathcal{S}$ considering for all $t \geq 0$ a manifold $\mathcal{S}_t$ parameterized by $X = X(\xi_1, \xi_2; t)$ and where the motion $\psi_t(\xi_1, \xi_2) := X(\xi_1, \xi_2; t)$ is C^∞ in every variable.

One of the main results in [7] is the construction of a reaction-diffusion model on the 2D growing manifold $\mathcal{S}_t$ using Fick's law of diffusion and conservation of mass. The resulting model is the equivalent of (1) in the case of growing curved domains,

$$\partial_t \mathbf{u} = \mathcal{D}\Delta_{\mathcal{S}_t}\mathbf{u} - \partial_t[\log(h_1 h_2)]\mathbf{u} + \mathbf{F}(\mathbf{u}), \tag{2}$$

with $h_1(\xi_1, \xi_2; t)$ and $h_2(\xi_1, \xi_2; t)$ the scalar magnitudes of the (orthogonal) tangent vectors $\partial_{\xi_1} X$ and $\partial_{\xi_2} X$, and where $\Delta_{\mathcal{S}_t}$ is the Laplace-Beltrami operator

$$\Delta_{\mathcal{S}_t}\phi = \frac{1}{h_1 h_2}\left[\partial_{\xi_1}\left(\frac{h_2}{h_1}\partial_{\xi_1}\phi\right) + \partial_{\xi_2}\left(\frac{h_1}{h_2}\partial_{\xi_2}\phi\right)\right], \tag{3}$$

which is the generalization of the Laplacian operator on manifolds. In the case of isotropic growth with growth factor $\rho(t)$ the equation (2) takes the form

$$\partial_t \mathbf{u} = \frac{\mathcal{D}}{\rho^2(t)}\Delta_{\mathcal{S}}\mathbf{u} - 2\frac{\dot{\rho}(t)}{\rho(t)}\mathbf{u} + \mathbf{F}(\mathbf{u}), \tag{4}$$

with the coefficients h_1 and h_2 of $\Delta_{\mathcal{S}}$ do not depend anymore on t but only on (ξ_1, ξ_2).

2 Main results

2.1 Reaction-diffusion systems on growing manifolds

Let us define the mathematical objects we will work with throughout this paper.

Definition 1 *Any **manifold** $\mathcal{M}$ we will consider is a smooth (C^∞), compact, connected, oriented Riemannian manifold without boundary. We will denote its parameterization*

$$\begin{array}{rcl} X : \hat{\Omega} \subset \mathbb{R}^n & \longrightarrow & \mathcal{M} \\ \xi = (\xi_1, \ldots, \xi_n) & \longmapsto & X(\xi) \end{array}$$

and its metric $(g_{ij}(\xi))$.

Definition 2 *A family of manifolds $(\mathcal{M}_t)_{t\geq 0}$ (or just $\mathcal{M}_t$ for simplicity) is a **growing manifold** if for any $t \geq 0$ $\mathcal{M}_t$ is a manifold with metric $(g_{ij}(\xi,t))$ and if the parameterization $X(\xi,t)$ is C^∞ in both variables ξ and t.*

Definition 3 *The **Laplace-Beltrami operator** on a Riemannian manifold $\mathcal{M}_t$ with parameterization $(\xi,t) = (\xi_1,\dots\xi_n,t)$ and metric $(g_{ij}(\xi,t))$ is (using the sum convention on repeated indices)*

$$\Delta_{\mathcal{M}_t}\phi = \frac{1}{\sqrt{g}}\,\partial_{\xi_j}[\sqrt{g}\,g^{ij}\,\partial_{\xi_i}\phi]\,, \tag{5}$$

where $(g^{ij}) = (g_{ij})^{-1}$ and $g = det(g_{ij})$.

We will use the notation $\Delta_{\mathcal{M}_t}$ and $\Delta_{\mathcal{M}}$ to emphasize the time dependence or independence of the coefficients of the Laplace-Beltrami operator, respectively.

Definition 4 *A function*

$$\rho : [0,1] \to [0,1]$$

*is a **growth function** if it is a C^∞ function that satisfies $\rho(t) > 0$, $\dot\rho(t) \geq 0$ for all $t \in [0,1]$ and $\rho(1) = 1$.*

Definition 5 *A growing manifold $\mathcal{M}_t$ has **isotropic growth** if there is a growth function $\rho(t)$ and a manifold $\mathcal{M}$ such that $\mathcal{M}_t := \rho(t)\mathcal{M}$, meaning that if $X(\xi,t)$ is the parameterization of $\mathcal{M}_t$ then there is a parameterization $\widetilde{X}$ of $\mathcal{M}$ such that $X(\xi,t) = \rho(t)\widetilde{X}(\xi)$.*

$\mathcal{M}_1$ and $\mathcal{M}$ both represent the same manifold, but the notation allows us to think of $\mathcal{M}_1$ as the final stage of the growing domain $(\mathcal{M}_t)_{0\leq t\leq 1}$ and $\mathcal{M}$ as a fixed (i.e. time-independent) domain.

We can obtain the corresponding version of the equations (2) and (4), deduced by Plaza *et al* [7], in the more general framework of a growing manifold $\mathcal{M}_t$. More precisely, we have the following theorem.

Theorem 1 *Let $\mathcal{M}_t$ be a growing manifold with metric $(g_{ij}(\xi,t))$. Under the hypotheses of Fick's law of diffusion and conservation of mass any reaction-diffusion system on $\mathcal{M}_t$ has the form*

$$\partial_t\mathbf{u} = \mathcal{D}\Delta_{\mathcal{M}_t}\mathbf{u} - \partial_t[\log\sqrt{g}\,]\mathbf{u} + \mathbf{F}(\mathbf{u})\,, \tag{6}$$

where the Laplace-Beltrami operator $\Delta_{\mathcal{M}_t}$ is given in (5). In the case of isotropic growth we have

$$\partial_t\mathbf{u} = \frac{\mathcal{D}}{\rho^2(t)}\Delta_{\mathcal{M}}\mathbf{u} - n\frac{\dot\rho(t)}{\rho(t)}\mathbf{u} + \mathbf{F}(\mathbf{u})\,, \tag{7}$$

where the coefficients of $\Delta_{\mathcal{M}}$ do not depend on time.

Note that in the case of a 2-manifold with orthogonal tangent vectors we have

$$(g_{ij}) = \begin{bmatrix} h_1^2 & 0 \\ 0 & h_2^2 \end{bmatrix}$$

and thus we recover the equations (2) and (4).

2.2 Existence and regularity of solutions

In the case of isotropic growth the reaction-diffusion system (7) has a unique solution, and moreover, if the initial condition is continuous and the nonlinearity $\mathbf{F}(\mathbf{u})$ is C^∞ then the solution is C^∞. This implies that the system (7) has a "regularizing" effect in the sense that, for positive times, its solution is more regular than the initial condition.

Suppose that $\mathbf{X}$ a ***suitable Banach space***, i.e. a Banach space where we can prove that the system (7) has a solution. We will give a general definition later but for the sake of clarity we will consider $\mathbf{X} = C\left[\mathcal{M}, \mathbb{R}^M\right]$. Then we have the following result.

Theorem 2 *If $\mathbf{X}$ is a suitable Banach space then there is a time $T > 0$ such that the reaction-diffusion system (7) with initial condition $\mathbf{u}_0 \in \mathbf{X}$ has a unique solution*

$$\mathbf{u}(t) \in C\left([0,T], \mathbf{X}\right).$$

Theorem 3 *If $\mathbf{u}_0 \in C\left[\mathcal{M}, \mathbb{R}^M\right]$ and $\mathbf{F}$ is C^∞ then*

$$\mathbf{u}(t) \in C\left[\,[0,T], C\left[\mathcal{M}, \mathbb{R}^M\right]\right] \cap C^\infty\left[\mathcal{M} \times (0,T], \mathbb{R}^M\right].$$

Furthermore, the local unique solution $\mathbf{u}(t)$ is in fact globally defined provided $\mathbf{u}_0$ takes values inside a rectangle $\mathcal{R} \subset \mathbb{R}^M$ and the nonlinearity $\mathbf{F}(\mathbf{u})$ on $\partial\mathcal{R}$ is smaller than a function depending on the growth factor $\rho(t)$.

Theorem 4 *Let $\mathcal{M}_t$ be a growing manifold and suppose that the initial condition $\mathbf{u}_0$ of the reaction-diffusion system (7) is in $C\left[\mathcal{M}, \mathbb{R}^M\right]$ and takes its values inside the rectangle $\mathcal{R} = (-1,1)^M$. Define the* ***growth ratio*** *as*

$$c(t) := n\frac{\dot{\rho}(t)}{\rho(t)}, \tag{8}$$

and suppose that for all $z \in \partial\mathcal{R}$ and all $t \geq 0$ we have that

$$\mathbf{F}(z) \cdot \mathbf{n}(z) < c(t),$$

where $\mathbf{n}(z)$ is the outer normal at z. Then the solution $\mathbf{u}(t)$ of (7) is global and bounded, i.e. it exists for all times $t \geq 0$ and takes its values inside $\mathcal{R}$. In particular, if the growth factor is exponential, i.e. $\rho(t) = e^{r(t-1)}$, and $r > 0$ is such that

$$r > \frac{1}{n}\sup\{\|\mathbf{F}(z)\| : z \in \partial\mathcal{R}\}$$

then there is a global bounded solution of the system (7) without any hypothesis on the nonlinearity $\mathbf{F}(\mathbf{u})$.

2.3 The stabilizing effect of growth

Our primary goal here is to understand the effect of growth in pattern formation. In that direction Gjiorgjieva [4] showed numerically that the solutions of the problem (2) on a sphere with slow growth are very similar to the solutions of the model of Chaplain *et al* [2] on a fixed sphere $\mathcal{S}$:

$$\partial_t \mathbf{u} = \mathcal{D}\Delta_{\mathcal{S}}\mathbf{u} + \mathbf{F}(\mathbf{u}). \tag{9}$$

However, both biological and numerical evidence suggested that the growth has a stabilizing effect in the sense that the patterns on growing domains are less complex than those on fixed domains. Quoting Gjiorgjieva:

> "The pattern on a fixed sphere is more complex [develops a higher eigenmode] than the pattern on a growing sphere of the same radius after growth".

Using our notation we can rephrase Gjiorgjieva's quote in the context of growing manifolds $\mathcal{M}_t$ as

> "The observed patterns on a fixed domain $\mathcal{M}$ are more complex [develop higher eigenmodes] than the patterns on a growing domain $\mathcal{M}_t$ with the same size and shape after growth (i.e. $\mathcal{M} = \mathcal{M}_1$)".

All the works in this direction have been made only numerically on planar 1D and 2D domains or on 2D spheres. As far as we know the following theorem is the first analytic result on the stabilizing effect of growth on pattern formation.

Theorem 5 *Let $\mathcal{M}$ be a manifold and consider the isotropic growing manifold $\mathcal{M}_t := \rho(t)\mathcal{M}$ with growth function $\rho(t)$. Then $\lambda(t)$ is an eigenvalue of the reaction-diffusion system (7) on the fixed manifold $\mathcal{M}$ if and only if $\lambda(t) - c(t)$ is an is an eigenvalue of the reaction-diffusion system (7) on the growing manifold $\mathcal{M}_t$, where $c(t)$ is the growth ratio (8). In particular, comparing $\mathcal{M}$ and $\mathcal{M}_1$ we have that the growth shifts the eigenvalues to the left in the complex plane by the factor $n\dot{\rho}(1)$.*

3 Reaction-diffusion systems on growing manifolds

Theorem 1 *Let $\mathcal{M}_t$ be a growing manifold with metric $(g_{ij}(\xi, t))$. Under the hypotheses of Fick's law of diffusion and conservation of mass any reaction-diffusion system on $\mathcal{M}_t$ has the form*

$$\partial_t \mathbf{u} = \mathcal{D}\Delta_{\mathcal{M}_t}\mathbf{u} - \partial_t[\log\sqrt{g}\,]\mathbf{u} + \mathbf{F}(\mathbf{u})\,, \tag{10}$$

where the Laplace-Beltrami operator $\Delta_{\mathcal{M}_t}$ is given in (5). In the case of isotropic growth we have

$$\partial_t \mathbf{u} = \frac{\mathcal{D}}{\rho^2(t)}\Delta_{\mathcal{M}}\mathbf{u} - n\frac{\dot{\rho}(t)}{\rho(t)}\mathbf{u} + \mathbf{F}(\mathbf{u})\,, \tag{11}$$

where the coefficients of $\Delta_{\mathcal{M}}$ do not depend on time.

Proof: We will divide the proof in three parts.

3.1 Parametrization and Riemannian metric

Let $\mathcal{M}$ be a manifold and consider a parameterization

$$\begin{array}{rcl} X : \hat{\Omega} \subset \mathbb{R}^n & \longrightarrow & \mathcal{M} \\ \xi = (\xi_1, \ldots, \xi_n) & \longmapsto & X(\xi)\,. \end{array}$$

We will add growth on $\mathcal{M}$ considering that for all $t \geq 0$ there is a manifold $\mathcal{M}_t$ parameterized by $X = X(\xi, t)$, and where the motion

$$\begin{array}{rcl} \psi_t : \hat{\Omega} \subset \mathbb{R}^n & \longrightarrow & \mathcal{M}_t \\ \xi = (\xi_1, \ldots, \xi_n) & \longmapsto & \psi_t(\xi) = X(\xi, t)\,. \end{array}$$

is C^∞ in every variable. Remark that the manifolds $\mathcal{M}_t$ are supposed to be all embedded in the same euclidean space in order to have the motion $\psi_t(\xi)$ well defined as a function of t, and that for any fixed $t \geq 0$ the function $\psi_t(\xi)$ is a parametrization for $\mathcal{M}_t$.

We will suppose that for all $t \geq 0$ the manifold $\mathcal{M}_t$ has a C^∞ metric $(g_{ij}(\xi, t))$ with the following properties:

(a) *Symmetric:* $g_{ij} = g_{ji}$ for all i, j.

(b) *Positive definite:* $g_{ij}v^i v^j > 0$ for all $v = (v^1, \ldots, v^n) \neq 0$.

Let $t \geq 0$ be fixed. Take a point $p = X(\xi, t) \in \mathcal{M}_t$ and on the tangent space $T_p\mathcal{M}_t$ consider the basis given by the parametrization $X(\xi, t)$, i.e.

$$\partial_{\xi_1} X, \ldots, \partial_{\xi_n} X\,.$$

We can use the metric (g_{ij}) to define an inner product on the tangent space $T_p\mathcal{M}_t$:

$$\langle u, v\rangle := g_{ij}(\xi, t)u^i v^j \quad \text{for } u, v \in T_p\mathcal{M}_t \tag{12}$$

In particular if we take $u = \partial_{\xi_i} X$ and $v = \partial_{\xi_j} X$ we have $g_{ij} = \langle \partial_{\xi_i} X, \partial_{\xi_j} X\rangle$.

We can extend the inner product (12) to the whole tangent bundle

$$T\mathcal{M}_t = \cup\{\, T_p\mathcal{M}_t : p \in \mathcal{M}_t\}$$

because by hypothesis the metric $g_{ij}(\xi, t)$ is C^∞.

3.2 The general model with growth and curvature

Let $\Omega(t)$ be a domain in $\mathcal{M}_t$ with boundary $\partial\Omega(t)$. Suppose that the parametrization of $\Omega(t)$ is

$$\begin{aligned} \Omega(t) &:= \psi_t(\hat{\Omega}) = X(\hat{\Omega}, t)\,, \\ \partial\Omega(t) &:= \psi_t(\partial\hat{\Omega}) = X(\partial\hat{\Omega}, t)\,, \end{aligned}$$

with $\hat{\Omega}$ a domain in $\mathbb{R}^n$.

Suppose that $\phi = \phi(X, t)$ denotes the concentration, given in molecules per unit area, of a morphogen (i.e. a chemical substance) at a point $X \in \mathcal{M}_t$, and let J be the flux vector of the molecules ϕ. The *Fick's law of diffusion* states that the flux vector J of the molecules is proportional to the gradient of the concentration of the molecules, i.e.

$$J = -D\nabla\phi\,,$$

where D is the diffusion coefficient which is assumed to be constant.

Assuming *conservation of mass* we have that the rate of change on the concentration of molecules in $\Omega(t)$ is equal to the net flux of molecules on the boundary $\partial\Omega(t)$, i.e.

$$\frac{d}{dt}\iint_{\Omega(t)} \phi\, dV = -\int_{\partial\Omega(t)} \langle J, \mathbf{n}\rangle\, dS\,. \tag{13}$$

The minus sign comes from the fact that $\mathbf{n}$ is the unit outward normal on $\partial\Omega(t)$ and therefore $\langle J, \mathbf{n}\rangle$ is the exit flux.

Using the last two relations we obtain

$$\frac{d}{dt}\iint_{\Omega(t)} \phi \, dV = D \int_{\partial\Omega(t)} \langle \nabla\phi|_{\partial\Omega(t)}, \mathbf{n}\rangle \, dS \,. \tag{14}$$

We need to give (14) a precise meaning:

(a) dV is the volume element for the n-manifold $\Omega(t)$; in local coordinates we have $dV = \sqrt{g}\, d\xi$.

(b) dS the "area" (i.e. the $(n-1)$ volume) element for the $(n-1)$-manifold $\partial\Omega(t)$.

(c) $\nabla\phi|_{\partial\Omega(t)}$ is the restriction of the vector field $\nabla\phi$ to $\partial\Omega(t)$ and $\mathbf{n}$ is the unit outward normal.

(d) $\langle\cdot,\cdot\rangle$ is the inner product on the tangent bundle $T\Omega(t)$ given by the Riemannian metric (g_{ij}).

For the first integral in (14), using the change of variables $\widetilde{\phi}(\xi,t) := \phi(X(\xi,t),t)$ we obtain

$$\begin{aligned}
\frac{d}{dt}\iint_{\Omega(t)} \phi(X,t)\, dV &= \frac{d}{dt}\iint_{\hat{\Omega}} \widetilde{\phi}(\xi,t)\sqrt{g}\, d\xi \\
&= \iint_{\hat{\Omega}} [\partial_t\widetilde{\phi}\sqrt{g} + \widetilde{\phi}\partial_t\sqrt{g}\,] d\xi \\
&= \iint_{\hat{\Omega}} \left[\partial_t\widetilde{\phi} + \widetilde{\phi}\,\frac{\partial_t\sqrt{g}}{\sqrt{g}}\right]\sqrt{g}\, d\xi \\
&= \iint_{\Omega(t)} \left[\partial_t\widetilde{\phi} + \widetilde{\phi}\,\frac{\partial_t\sqrt{g}}{\sqrt{g}}\right] dV \,.
\end{aligned}$$

For the second integral in (14) we will use Stokes' theorem. In the general case of on a n-manifold $\mathcal{N}$ with boundary $\partial\mathcal{N}$ it reads

$$\iint_{\mathcal{M}} d\omega = \int_{\partial\mathcal{M}} \omega \,, \tag{15}$$

where ω is a $(k-1)$ differential form, $k \le n$. If ω is the $(n-1)$-form

$$\omega = \langle F|_{\partial\Omega(t)}, \mathbf{n}\rangle \, dS$$

with F a vector field on the submanifold $\Omega(t) \subset \mathcal{M}_t$ then (15) becomes

$$\iint_{\Omega(t)} div(F)\, dV = \int_{\partial\Omega(t)} \langle F|_{\partial\Omega(t)}, \mathbf{n}\rangle \, dS \,. \tag{16}$$

In the light of (16) we have for the second integral in (14) that

$$\int_{\partial\Omega(t)} \langle \nabla\phi|_{\partial\Omega(t)}, \mathbf{n}\rangle \, dS = \iint_{\Omega(t)} div(\nabla\phi)\, dV \,.$$

Putting all two pieces together in (14) we obtain

$$\iint_{\Omega(t)} \left[\partial_t\widetilde{\phi} + \widetilde{\phi}\,\partial_t(log\sqrt{g}) - div(\nabla\widetilde{\phi})\right] dV = 0 \,.$$

Recall that $\Omega(t)$ was an arbitrary domain in $\mathcal{M}_t$ and drop the tildes for a more convenient notation. Therefore we obtain the equation of the diffusive part of the model:

$$\partial_t \phi = D\, div(\nabla\phi) - \partial_t[\log\sqrt{g}]\phi\,, \tag{17}$$

where the operator $div(\nabla\phi)$ is the *Laplace-Beltrami operator* $\triangle_{\mathcal{M}_t}$ we introduced in Definition 3.

Now consider a morphogen vector $\mathbf{u} = (u_1, \ldots, u_M)$ and suppose that there is an extra term $\mathbf{F}(\mathbf{u})$ that models reaction kinetics, i.e. the chemical interactions between the morphogens. Then the mass balance equation (13) takes the form

$$\frac{d}{dt}\iint_{\Omega(t)} \mathbf{u}\, dS = -\int_{\partial\Omega(t)} \langle J, \mathbf{n}\rangle\, dS + \iint_{\Omega(t)} \mathbf{F}(\mathbf{u})\, dS\,. \tag{18}$$

Suppose that the flux is $J = -\mathcal{D}\nabla\mathbf{u}$, where the matrix of diffusivities $\mathcal{D}$ is diagonal, i.e.

$$\mathcal{D} = \begin{bmatrix} D_1 & & \\ & \ddots & \\ & & D_M \end{bmatrix},$$

and with constant and positive coefficients D_i. Under these assumptions (18) takes the form

$$\frac{d}{dt}\iint_{\Omega(t)} \mathbf{u}\, dS = \mathcal{D}\int_{\partial\Omega(t)} \langle \nabla\mathbf{u}|_{\partial\Omega(t)}, \mathbf{n}\rangle\, dS + \iint_{\Omega(t)} \mathbf{F}(\mathbf{u})\, dS\,. \tag{19}$$

Notice that in (19) each morphogen diffuses independently of the other and without obstacles. Therefore we can take separately the equations for each of the components u_i of $\mathbf{u}$ in (19) and repeat the calculations for $\phi = u_i$. Proceeding that way we obtain the general model for a reaction-diffusion system on the growing manifold $\mathcal{M}_t$,

$$\partial_t \mathbf{u} = \mathcal{D}\Delta_{\mathcal{M}_t}\mathbf{u} - \partial_t[\log\sqrt{g}\,]\mathbf{u} + \mathbf{F}(\mathbf{u})\,,$$

which is (10). This proves part (a) of Theorem 1.

3.3 The isotropic growth model

In the case of isotropic growth we have

$$X(\xi, t) = \rho(t)\,\widetilde{X}(\xi)\,,$$

which implies the following identities:

$$\begin{aligned} g_{ij}(\xi,t) &= \rho^2(t)\,\widetilde{g_{ij}}(\xi)\,, \\ g^{ij}(\xi,t) &= \frac{1}{\rho^2(t)}\,\widetilde{g^{ij}}(\xi)\,, \\ \sqrt{g} &= \rho^n\sqrt{\widetilde{g}}\,, \\ \Delta_{\mathcal{M}_t} &= \frac{1}{\rho^2(t)}\,\Delta_{\mathcal{M}} \end{aligned} \tag{20}$$

If we substitute the relations (20) in the general model given in (10) we obtain the model for a n-manifold with isotropic growth:

$$\partial_t \mathbf{u} = \frac{\mathcal{D}}{\rho^2(t)} \Delta_{\mathcal{M}} \mathbf{u} - n \frac{\dot{\rho}(t)}{\rho(t)} \mathbf{u} + \mathbf{F}(\mathbf{u}) \,,$$

which is (11). This proves part (b) of Theorem 1 and concludes its proof. □

Remark 1 *Note that the equations (10) and (11) are exactly the equations (6) and (7), respectively. Therefore, and in order to avoid any possible confusion, we will refer to them with their labels from Section 2, i.e., as (6) and (7).*

4 Existence, uniqueness and regularity of solutions

We will prove global existence, uniqueness and regularity of the solutions of the system (7). The proofs we present follow closely the ideas of Taylor [10] (see Chapter 15, sections 1-4, pp.271-307).

In the next definition we precise what we meant in Section 2 with a *suitable* Banach space. We will use the notation $L := \mathcal{D}\Delta_{\mathcal{M}}$ for simplicity.

Definition 6 *Let $\mathcal{M}$ be a manifold. Consider the reaction-diffusion equation*

$$\partial_t \mathbf{u} = L\mathbf{u} + \mathbf{G}(t, \mathbf{u}) \tag{21}$$

with initial condition $\mathbf{u}(0) = \mathbf{u}_0$, and suppose that $\mathbf{G}$ is C^∞ in its arguments. We say a Banach space $\mathbf{X}$ is **suitable** *for the system (21) if the following conditions hold:*

1. *$\mathbf{X}$ is a space of functions $\mathbf{u} : \mathcal{M} \to \mathbb{R}^M$.*
2. *$e^{tL} : \mathbf{X} \to \mathbf{X}$ is a strongly continuous semigroup for $t \geq 0$.*
3. *There exists a constant $C > 0$ such that $\|e^{tL}\| \leq C$ for all $t \geq 0$.*
4. *The nonlinearity*

$$\begin{array}{rccc} \mathbf{G}: & \mathbf{X} & \longrightarrow & \mathbf{X} \\ & \mathbf{u} & \longmapsto & \mathbf{G}(t, \mathbf{u}) \end{array}$$

   is locally Lipschitz in $\mathbf{u}$, uniformly in t.

Remark 2 *As we mentioned in Section 2, the suitable space we have in mind is $C\left[\mathcal{M}, \mathbb{R}^M\right]$, but there are other possible choices. Indeed, if we ask the nonlinearity $\mathbf{G}(t, \mathbf{u})$ to be C^∞, bounded and with derivatives bounded then $L^p\left[\mathcal{M}, \mathbb{R}^M\right]$ and $H^k\left[\mathcal{M}, \mathbb{R}^M\right]$ are suitable spaces as well.*

Lemma 1 *The reaction-diffusion system (7) can be reduced to the system (21) with*

$$\begin{aligned} L &:= \mathcal{D}\Delta_{\mathcal{M}} \,, \\ \mathbf{G}(t, \mathbf{u}) &:= -n\rho(t)\dot{\rho}(t)\mathbf{u} + \rho^2(t)\mathbf{F}(\mathbf{u}) \,. \end{aligned}$$

Moreover, if $\mathbf{F}(z)$ is locally Lipschitz in $z \in \mathbb{R}$ then $\mathbf{G}(t, z)$ is also locally Lipschitz in $z \in \mathbb{R}$, uniformly in $t \in [0, T]$.

Proof: Define the change of variables

$$s(t) := \int_0^t \frac{dr}{\rho^2(r)}\,. \tag{22}$$

Then for any function $f(t)$ we have that

$$\partial_s f = \rho^2(t)\partial_t f\,.$$

Multiply the system (7) by $\rho^2(t)$ and define $\widetilde{\mathbf{u}}(s,x) := \mathbf{u}(t(s),x)$. Then the system (7) takes the equivalent form

$$\partial_s \widetilde{\mathbf{u}} = \mathcal{D}\Delta_{\mathcal{M}}\widetilde{\mathbf{u}} + \mathbf{G}(s,\widetilde{\mathbf{u}})\,,$$

where

$$\mathbf{G}(t,\widetilde{\mathbf{u}}) = -n\rho(t)\dot{\rho}(t)\widetilde{\mathbf{u}} + \rho^2(t)\mathbf{F}(\widetilde{\mathbf{u}})\,.$$

Renaming the variables $(s,\widetilde{\mathbf{u}})$ as $(t,\mathbf{u})$ we obtain (21). □

In the light of Lemma 1 we can consider that the system (7) is already in the form (21).

The local existence and uniqueness results are proven with fixed point arguments in the next theorem.

Theorem 2 *If* $\mathbf{X}$ *is a suitable Banach space then there is a positive time*

$$T = T\left(\|\mathbf{u}_0\|_{\mathbf{X}}\right)$$

such that the reaction-diffusion system (7) with initial condition $\mathbf{u}_0 \in \mathbf{X}$ *has a unique solution*

$$\mathbf{u}(t) \in C\left([0,T],\mathbf{X}\right).$$

Proof: By the Lemma 1 the problem (7) is equivalent to (21). Moreover, (21) can be expressed in the integral form

$$\mathbf{u}(t) = e^{tL}\mathbf{u}_0 + \int_0^t e^{(t-s)L}\mathbf{G}(s,\mathbf{u}(s))\,ds\,. \tag{23}$$

Define the operator

$$\mathbf{\Psi}\mathbf{u}(t) := e^{tL}\mathbf{u}_0 + \int_0^t e^{(t-s)L}\mathbf{G}(s,\mathbf{u}(s))\,ds$$

on the Banach space $C\left([0,T],\mathbf{X}\right)$ with norm

$$\|\mathbf{u}(t)\|_{\mathbf{X}} := \sup_{s\in[0,T]} \|\mathbf{u}(s)\|\,,$$

where $\|\cdot\|$ is the norm in $\mathbb{R}^M$. Now fix $\alpha > 0$ and define

$$\mathbf{Z} := \left\{\mathbf{u} \in C\left([0,T],\mathbf{X}\right) \,:\, \mathbf{u}(0) = \mathbf{u}_0\,, \|\mathbf{u}(t) - \mathbf{u}_0\|_{\mathbf{X}} \le \alpha\right\}.$$

The final time $T > 0$ will be chosen later in order to have that $\mathbf{\Psi} : \mathbf{Z} \to \mathbf{Z}$ is a contraction.

Observe that $\mathbf{Z}$ is a closed subset of $C([0,T],\mathbf{X})$. Moreover, $\mathbf{Z}$ is bounded because if $\mathbf{u}\in\mathbf{Z}$ then for all $t\in[0,T]$ we have

$$\|\mathbf{u}(t)\|_{\mathbf{X}}\leq\|\mathbf{u}(t)-\mathbf{u}_0\|_{\mathbf{X}}+\|\mathbf{u}_0\|_{\mathbf{X}}\leq\alpha+\|\mathbf{u}_0\|_{\mathbf{X}}\,.$$

Now we affirm that there is a constant $K_1>0$ such that if $\mathbf{u}\in\mathbf{Z}$ then $\|\mathbf{G}(t,\mathbf{u}(t))\|_{\mathbf{X}}\leq K_1$ for all $t\in[0,T]$. Indeed, $\mathbf{G}(t,\mathbf{u})$ is locally Lipschitz continuous uniformly in t. Hence, if K is the Lipschitz constant for $\mathbf{Z}$ then for any $\mathbf{u}\in\mathbf{Z}$ we have

$$\begin{aligned}\|\mathbf{G}(t,\mathbf{u}(t))\|_{\mathbf{X}} &\leq \|\mathbf{G}(t,\mathbf{u}(t))-\mathbf{G}(t,\mathbf{u}_0)\|_{\mathbf{X}}+\|\mathbf{G}(t,\mathbf{u}_0)\|_{\mathbf{X}}\\ &\leq K\|\mathbf{u}(t)-\mathbf{u}_0\|_{\mathbf{X}}+\|\mathbf{G}(t,\mathbf{u}_0)\|_{\mathbf{X}}\\ &\leq K\alpha+\|\mathbf{G}(t,\mathbf{u}_0)\|_{\mathbf{X}}\,.\end{aligned}$$

Since $\mathbf{X}$ is a suitable space there exists a $C>0$ such that

$$\|e^{tL}\|_{\mathcal{L}(\mathbf{X})}\leq C\,.$$

This fact and the boundedness of G imply that

$$\left\|\int_0^t e^{(t-s)L}\mathbf{G}(s,\mathbf{u}(s))\,ds\right\|_{\mathbf{X}}\leq K_1Ct\,.$$

In the light of this we can choose $T>0$ such that $K_1CT\leq\alpha/2$.

On the other hand, since $\mathbf{X}$ is a suitable Banach space we have that e^{tL} is a strongly continuous semigroup for $t\geq0$. Therefore there is a $T>0$ such that $\|e^{tL}\mathbf{u}_0-\mathbf{u}_0\|_{\mathbf{X}}\leq\alpha/2$ for all $t\in[0,T]$.

In conclusion, if $T>0$ is sufficiently small then $\|\mathbf{\Psi}\mathbf{u}(t)-\mathbf{u}_0\|_{\mathbf{X}}\leq\alpha$, which implies that $\mathbf{\Psi}(\mathbf{Z})\subset\mathbf{Z}$.

Let us find the conditions under which $\mathbf{\Psi}$ is a contraction. If we calculate

$$\begin{aligned}\|\mathbf{\Psi}\mathbf{u}(t)-\mathbf{\Psi}\mathbf{v}(t)\|_{\mathbf{X}} &= \left\|\int_0^t e^{(t-s)L}\big[\mathbf{G}(s,\mathbf{u}(s))-\mathbf{G}(s,\mathbf{v}(s))\big]\,ds\right\|_{\mathbf{X}}\\ &\leq CKt\sup_{s\in[0,t]}\|\mathbf{u}(s)-\mathbf{v}(s)\|_{\mathbf{X}}\\ &\leq CKT\|\mathbf{u}(t)-\mathbf{v}(t)\|_{\mathbf{X}}\end{aligned}$$

we can see that $\mathbf{\Psi}:\mathbf{Z}\to\mathbf{Z}$ will be a contraction if we choose $T>0$ such that $CKT<1$. In that case we obtain that there is a unique solution $\mathbf{u}(t)\in C([0,T],\mathbf{X})$ of (23), or equivalently a unique solution of (21). Therefore, we have proved local existence and uniqueness for the problem (7). □

Theorem 3 *If* $\mathbf{u}_0\in C\left[\mathcal{M},\mathbb{R}^M\right]$ *and* $\mathbf{F}$ *is* C^∞ *then*

$$\mathbf{u}(t)\in C\left[\,[0,T],C\left[\mathcal{M},\mathbb{R}^M\right]\right]\cap C^\infty\left[(0,T]\times\mathcal{M},\mathbb{R}^M\right]\,.$$

Proof: First note that $C\left[\mathcal{M},\mathbb{R}^M\right]$ is a suitable space, so we only need to prove that

$$\mathbf{u}(t)\in C^\infty\left[(0,T]\times\mathcal{M},\mathbb{R}^M\right]\,.$$

Fix $t' \in (0,T]$ and consider a solution $\mathbf{u}(t)$ of (21) written in its integral form (23). Recall two properties of the Laplace-Beltrami operator. First, the map

$$e^{t\triangle_{\mathcal{M}}} : C(\mathcal{M}) \to C^1(\mathcal{M})$$

is continuous for all $t > 0$, and second, there exists a constant $C > 0$ such that

$$\|e^{t\triangle_{\mathcal{M}}}\|_{\mathcal{L}(C(\mathcal{M}),C^1(\mathcal{M}))} \leq Ct^{-1/2}$$

(see Taylor [10], p.274). This implies that the operator L satisfies the same type of inequality, i.e.,

$$\|e^{tL}\|_{\mathcal{L}(C[\mathcal{M},\mathbb{R}^M],C^1[\mathcal{M},\mathbb{R}^M])} \leq Ct^{-1/2}\,,$$

with a bigger constant $C > 0$, of course, that depends on the diffusion coefficients of the matrix $\mathcal{D}$. Consequently, for any $t_1 \in (0,t']$ and $\mathbf{u}_0 \in C\left[\mathcal{M},\mathbb{R}^M\right]$ then $\mathbf{u}(t_1) \in C^1\left[\mathcal{M},\mathbb{R}^M\right]$.

Now, if we consider $\mathbf{u}(t_1)$ as a new initial condition we have that $\mathbf{u}(t_2) \in C^2\left[\mathcal{M},\mathbb{R}^M\right]$ for any $t_2 \in (t_1,t']$. Repeating this iterative argument we can construct a sequence

$$0 < t_1 < t_2 < \cdots < t_n \to t'$$

such that $\mathbf{u}(t_n) \in C^n\left[\mathcal{M},\mathbb{R}^M\right]$ for any $t_n \in (t_{n-1},t']$. In the limit we get that $\mathbf{u}(t') \in C^\infty\left[\mathcal{M},\mathbb{R}^M\right]$ for any $t' \in (0,T]$.

Concerning the time derivatives, recall that if $\mathbf{u}(\xi,t)$ is a solution of (7) then

$$\partial_t \mathbf{u} = \frac{\mathcal{D}}{\rho^2(t)}\Delta_{\mathcal{M}}\mathbf{u} - n\frac{\dot{\rho}(t)}{\rho(t)}\mathbf{u} + \mathbf{F}(\mathbf{u})\,.$$

Therefore, if $\mathbf{F}(\mathbf{u})$ and $\rho(t)$ are C^∞ in their arguments then $\partial_t\mathbf{u}(\xi,t)$ is continuous in time, and in consequence $\mathbf{u}(\xi,t)$ is C^1 in time. Now, if we derivate (7) with respect to time we see that $\partial_t^2\mathbf{u}(\xi,t)$ is continuous in time as well, and so $\mathbf{u}(t,x)$ is C^2 in time. Continuing this way it follows that $\mathbf{u}(t,x)$ is C^∞ in time.

In conclusion, $\mathbf{u}(\xi,t) \in C^\infty\left[(0,T]\times\mathcal{M},\mathbb{R}^M\right]$. $\square$

We can go even further and show that we have global existence of solutions if $\mathbf{u}_0$ takes values inside a rectangle $\mathcal{R} \subset \mathbb{R}^M$ and the nonlinearity $\mathbf{F}(\mathbf{u})$ satisfies a certain condition on $\partial\mathcal{R}$. Let us start with the following lemma that appears in Taylor [10] (Proposition 4.3 in Chapter 15, Section 4, p.295).

Lemma 2 *Let $\mathcal{M}$ be a manifold and consider the reaction-diffusion system*

$$\partial_t\mathbf{u} = \mathcal{D}\Delta_{\mathcal{M}}\mathbf{u} + \mathbf{F}(\mathbf{u})\,, \quad \mathbf{u}(\xi,t) = \mathbf{u}_0(\xi)\,. \tag{24}$$

Suppose that $\mathbf{u}_0(\xi) \in C\left[\mathcal{M},\mathbb{R}^M\right]$ and that it takes its values inside the rectangle

$$\mathcal{R} = \prod_{j=1}^{M}(a_j,b_j)\,.$$

Suppose further that for all $z \in \partial\mathcal{R}$ we have

$$\mathbf{F}(z) \cdot \mathbf{n}(z) < 0\,, \tag{25}$$

where $\mathbf{n}(z)$ is the outer normal at z. Then the solution $\mathbf{u}(\xi, t)$ of (24) exists for all times $t \geq 0$ and takes its values inside $\mathcal{R}$.

Proof: We will give the proof found in Taylor [10] because we will need it explicitly for the proof of Lemma 3.

First note that Theorem 3 implies that $\mathbf{u}(\xi, t) \in C^\infty\left[\mathcal{M} \times (0, T], \mathbb{R}^M\right]$. If there is an exit from $\mathcal{R}$ then there is a point $(\xi_0, t_0) \in \mathcal{M} \times (0, \infty)$ and $j \in \{1, \ldots, M\}$ such that $u_j(\xi_0, t_0) = a_j$ or $u_j(\xi_0, t_0) = b_j$.

Suppose that $u_j(\xi_0, t_0) = b_j$. Since $u_j(\xi, t) < b_j$ for all $(\xi, t) \in \mathcal{M} \times [0, t_0)$ then, on the one hand, $\partial_t u_j(\xi_0, t_0) \geq 0$, and on the other hand the function $f(\xi) := u_j(\xi, t_0)$ has a maximum at ξ_0. The latter implies that $\partial_{\xi_l} f(\xi_0) = 0$ for all $l \in \{1, \ldots, M\}$ and that the Hessian matrix

$$(\partial_{\xi_k \xi_l} f(\xi_0))_{1 \leq k, l \leq M}$$

has non-positive eigenvalues. But note that the Laplace-Beltrami operator (5) can be also written as

$$\triangle_{\mathcal{M}} f = g^{lk}\, \partial_{\xi_k \xi_l} f + \frac{1}{\sqrt{g}} \partial_{\xi_k}[\sqrt{g}\, g^{lk}] \partial_{\xi_l} f\,.$$

Therefore, evaluating at ξ_0 we get $\triangle_{\mathcal{M}} f(\xi_0) = g^{lk}(\xi_0)\, \partial_{\xi_k \xi_l} f(\xi_0)$. Furthermore, since $g^{kl}(\xi_0)$ is a positive-definite symmetric matrix we have that $\triangle_{\mathcal{M}} f(\xi_0) \leq 0$.

In the light of the former argumentation it follows that

$$\partial_t u_j(\xi_0, t_0) = D_i \triangle_{\mathcal{M}} u_j(\xi_0, t_0) + F_j(\mathbf{u}(\xi_0, t_0)) \leq F_j(\mathbf{u}(\xi_0, t_0))\,.$$

But $z = \mathbf{u}(\xi_0, t_0) \in \partial\mathcal{R}$ implies that $\mathbf{n}(z) = \mathbf{e}_j$, the unit vector on the x_j direction. Hence, $\mathbf{F}(z) \cdot \mathbf{n}(z) = F_j(z)$, and in consequence $\partial_t u_j(\xi_0, t_0) < 0$, which is a contradiction.

Suppose now that $u_j(\xi_0, t_0) = a_j$. In that case all the previous inequalities are reversed, $f(\xi) = u_j(\xi, t_0)$ has a minimum at ξ_0 and $\mathbf{n}(z) = -\mathbf{e}_j$. Thus we obtain once again a contradiction.

In conclusion, there can be no exit from the rectangle $\mathcal{R}$, which implies that the solution $\mathbf{u}(\xi, t)$ of (24) takes its values inside $\mathcal{R}$.

Finally, we affirm that the solution $\mathbf{u}(\xi, t)$ is defined for all $t \geq 0$. Indeed, suppose that it is just defined up to a finite time $T > 0$. Since $\bar{R}$ is compact then for any $\xi \in \mathcal{M}$ the limit

$$\mathbf{u}_\infty(\xi) := \lim_{t \to T} \mathbf{u}(\xi, t)$$

is well defined and continuous. If we consider the problem (24) with initial condition $\mathbf{u}_\infty(\xi)$ then there is an $\varepsilon > 0$ such that (24) has a solution $\tilde{\mathbf{u}}(\xi, s)$ for $s \in [0, \varepsilon)$. But this implies that we can extend $\mathbf{u}(\xi, t)$ to $[T, T + \varepsilon)$ because the function

$$\mathbf{v}(\xi, t) := \begin{cases} \mathbf{u}(\xi, t) & \text{if } 0 \leq t < T, \\ \tilde{\mathbf{u}}(\xi, t - T) & \text{if } T \leq t < T + \varepsilon \end{cases}$$

is continuous on $[0, T+\varepsilon)$ and coincides with $\mathbf{u}(\xi, t)$ on $[0, T)$, which contradicts the fact that $\mathbf{u}(t)$ was just defined up to T. □

Using Lemma 2 we can prove that under certain conditions on the nonlinearity $\mathbf{F}(\mathbf{u})$ similar to (25) the solution $\mathbf{u}(t)$ of the reaction-diffusion system (7) is global and bounded.

Lemma 3 *Let $\mathcal{M}_t$ be a growing manifold and suppose that the initial condition of the reaction-diffusion system (7) is in $C\left[\mathcal{M}, \mathbb{R}^M\right]$ and takes its values inside the rectangle*

$$\mathcal{R} = \prod_{j=1}^{M} (a_j, b_j)\,.$$

Suppose further that for all $(z,t) \in \partial\mathcal{R} \times [0,\infty)$ we have

$$\mathbf{F}(z) \cdot \mathbf{n}(z) < c(t)\mathbf{n}(z) \cdot z\,, \tag{26}$$

where $\mathbf{n}(z)$ is the outer normal at z and $c(t)$ is the growth ratio (8). Then the solution $\mathbf{u}(t)$ of (7) is global and bounded, i.e. it exists for all times $t \geq 0$ and takes its values inside $\mathcal{R}$.

Proof: From Lemma 1 the reaction-diffusion system (7) can be transformed into

$$\partial_t \mathbf{u} = \mathcal{D}\Delta_{\mathcal{M}}\mathbf{u} + \mathbf{G}(t, \mathbf{u})\,,$$

where $\mathbf{G}(t, \mathbf{u}) := -n\rho(t)\dot{\rho}(t)\mathbf{u} + \rho^2(t)\mathbf{F}(\mathbf{u})$. Taking a careful look at the proof of Lemma 2 we see that it also holds for nonlinearities that depend on time provided

$$\mathbf{G}(t, z) \cdot \mathbf{n}(z) < 0 \quad \text{for all } (z,t) \in \partial\mathcal{R} \times [0,\infty), \tag{27}$$

where $\mathbf{n}(z)$ is the outer normal at z. But (27) is equivalent to (26), hence we can apply Lemma 2 to obtain that the solution $\mathbf{u}(t)$ of (7) exists for all times $t \geq 0$ and takes its values inside $\mathcal{R}$. □

If $\mathcal{R} = (-1,1)^M$ we can show explicitly that the growth has a "globalizing effect" in the sense that on a growing manifold the locally defined solution has more chances to be globally defined than on a fixed manifold.

Theorem 4 *Let $\mathcal{M}_t$ be a growing manifold and suppose that the initial condition $\mathbf{u}_0$ of the reaction-diffusion system (7) is in $C\left[\mathcal{M}, \mathbb{R}^M\right]$ and takes its values inside the rectangle $\mathcal{R} = (-1,1)^M$. Suppose further that for all $z \in \partial\mathcal{R}$ and all $t \geq 0$ we have that*

$$\mathbf{F}(z) \cdot \mathbf{n}(z) < c(t)\,, \tag{28}$$

where $\mathbf{n}(z)$ is the outer normal at z and $c(t)$ is the growth ratio (8). Then the solution $\mathbf{u}(t)$ of (7) is global and bounded, i.e. it exists for all times $t \geq 0$ and takes its values inside $\mathcal{R}$. In particular, if the growth factor is exponential, i.e. $\rho(t) = e^{r(t-1)}$, and $r > 0$ is such that

$$r > \frac{1}{n} \sup\{\|\mathbf{F}(z)\| : z \in \partial\mathcal{R}\} \tag{29}$$

then there is a global bounded solution of the system (7) without any hypothesis on the nonlinearity $\mathbf{F}(\mathbf{u})$.

Proof: If $\mathcal{R} = (-1,1)^M$ then $\mathbf{n}(z) \cdot z = 1$ for all $z \in \partial\mathcal{R}$, which implies that (26) reduces to (28). Moreover, if we have an exponential growth factor $\rho(t) = e^{r(t-1)}$ and (29) holds then

$$\begin{aligned} \mathbf{F}(z) \cdot \mathbf{n}(z) &\leq \|\mathbf{F}(z)\| \\ &\leq \sup\{\|\mathbf{F}(z)\| : z \in \partial\mathcal{R}\} \\ &< nr = c(t)\,, \end{aligned}$$

and in consequence (28) holds. □

5 The stabilizing effect of growth

Theorem 5 *Let $\mathcal{M}$ be a manifold and consider the isotropic growing manifold $\mathcal{M}_t := \rho(t)\mathcal{M}$ with growth function $\rho(t)$. Then $\lambda(t)$ is an eigenvalue of the reaction-diffusion system (7) on the fixed manifold $\mathcal{M}$ if and only if $\lambda(t) - c(t)$ is an is an eigenvalue of the reaction-diffusion system (7) on the growing manifold $\mathcal{M}_t$, where $c(t)$ is the growth ratio (8). In particular, comparing $\mathcal{M}$ and $\mathcal{M}_1$ we have that the growth shifts the eigenvalues to the left in the complex plane by the factor $n\dot{\rho}(1)$.*

Proof: Let $\mathcal{M}$ be a fixed manifold with metric $(g_{ij}(\xi))$, and consider the Laplace-Beltrami operator (5). From Lemma 5 in Section 6.3 it follows that any function $\mathbf{u} \in [\,\mathrm{L}^2(\mathcal{M})\,]^M$ can be expanded as a series in terms of the eigenfunctions of the Laplace-Beltrami operator, i.e.

$$\mathbf{u} = \sum_{j=0}^{\infty} \mathbf{u}_j \phi_j\,, \tag{30}$$

where $\mathbf{u}_j \in \mathbb{R}^M$ is constant. In order to have a better notation we will consider the equation

$$\partial_t \mathbf{u} = \mathcal{D}(t)\Delta_{\mathcal{M}}\mathbf{u} - c(t)\mathbf{u} + \mathbf{F}(\mathbf{u})\,, \tag{31}$$

which is nothing more than (7) after the change of variables

$$\mathcal{D}(t) := \frac{\mathcal{D}}{\rho^2(t)}\,, \quad c(t) := n\frac{\dot{\rho}(t)}{\rho(t)}\,.$$

The hypothesis we have imposed on the growth function $\rho(t)$ imply that $c(t)$ is continuous, $c(t) \geq 0$ for all $t \geq 0$ and $c(1) = n\dot{\rho}(1)$.

We will suppose that $\mathbf{F}(0) = 0$, so that $\mathbf{u} \equiv 0$ is a solution of (31). The linearization of (31) at $\mathbf{u} \equiv 0$ is

$$\frac{\partial \mathbf{u}}{\partial t} = A(t)\mathbf{u} - c(t)\mathbf{u}\,, \quad A(t) := \mathcal{D}(t)\Delta_{\mathcal{M}} + d\mathbf{F}(0)\,. \tag{32}$$

Suppose that $\mathbf{u}(\xi, t)$ is a solution of (32) and that the coefficients of its series expansion (30) depend on time, i.e. $\mathbf{u}_j = \mathbf{u}_j(t)$. If we put this in (32) we obtain an infinite ODE system

$$\frac{d\mathbf{u}_j}{dt} = B_j(t)\mathbf{u}_j - c(t)\mathbf{u}_j\,, \quad j \in \mathbb{N}\,, \tag{33}$$

where $B_j(t)$ is the projection of the linear operator $A(t)$ to the j-th mode, i.e. the $M \times M$ matrix

$$B_j(t) := -\mu_j \mathcal{D}(t) + d\mathbf{F}(0).$$

Therefore we can obtain the spectral properties of the unbounded linear operators $A(t)$ and $A(t)-c(t)I$ by studying the behavior of the $M \times M$ matrices $B_j(t)$ and $B_j(t) - c(t)I$, respectively. For that reason we will restrict our attention to $B_j(t)$ and $B_j(t) - c(t)I$. Moreover, the spectra of $B_j(t)$ and $B_j(t) - c(t)I$ are simply related, as the next Lemma shows.

Lemma 4 *$\lambda(t)$ is an eigenvalue of the matrix $B_j(t)$ if and only if $\lambda(t) - c(t)$ is an eigenvalue of the matrix $B_j(t) - c(t)I$.*

Proof: Let $P(t)$ be the matrix that renders $B_j(t)$ in its Jordan canonical form $\Lambda_j(t)$, i.e. $\Lambda_j(t) = P(t)^{-1}B_j(t)P(t)$. Then

$$\begin{aligned} P(t)^{-1}[B_j(t) - c(t)I]P(t) &= P(t)^{-1}B_j(t)P(t) - P(t)^{-1}[c(t)I]P(t) \\ &= \Lambda_j(t) - c(t)I\,. \end{aligned}$$

Any block of $\Lambda_j(t)$ has the form

$$\begin{bmatrix} \lambda(t) & & & \\ 1 & \lambda(t) & & \\ & \ddots & \ddots & \\ & & 1 & \lambda(t) \end{bmatrix},$$

with its associated eigenvalue $\lambda(t)$ depending continuously on t because they are the zeros of a polynomial with continuous coefficients. Therefore, the corresponding block of $\Lambda_j(t) - c(t)I$ has the form

$$\begin{bmatrix} \lambda(t) - c(t) & & & & \\ 1 & \lambda(t) - c(t) & & & \\ & \ddots & \ddots & & \\ & & & 1 & \lambda(t) - c(t) \end{bmatrix},$$

and the Lemma follows. □

Now remark that the eigenfunctions $(\phi_j)_{j\in\mathbb{N}}$ of the Laplace-Beltrami operator form a basis of $L^2(\mathcal{M})$, and in consequence $\lambda(t)$ is an eigenvalue of the operator $A(t)$ if and only if, for some $j \in \mathbb{N}$, $\lambda(t)$ is an eigenvalue of the matrix $B_j(t)$. Since this argument also applies to $A - c(t)I$ and $B_j(t) - c(t)I$ then by Lemma 4 we obtain that $\lambda(t)$ is an eigenvalue of the operator $A(t)$ if and only if $\lambda(t)-c(t)$ is an eigenvalue of the operator $A - c(t)I$.

It follows then that the spectrum of the operator $A(t) - c(t)I$ is the spectrum of the operator $A(t)$ shifted to the left of the complex plane by the real factor $c(t)$. In other words,

$$\sigma[A(t) - c(t)I] = \sigma[A(t)] - c(t)\,. \tag{34}$$

Moreover, evaluating (34) at $t = 1$ we see that the eigenvalues on the "grown" manifold $\mathcal{M}_1$ are those on the fixed manifold $\mathcal{M}$ but switched to the left in the complex plane by the factor $c(1) = n\dot{\rho}(1)$. □

6 Discussion

6.1 Reaction-diffusion systems on growing manifolds

We have shown here that the same results presented by Plaza *et al* [7] hold in the case of any manifold (in the sense of Definition 1), and that the general equations (6) and (7) are almost the same than the ones found in Plaza *et al* [7], (2) and (4), respectively. Moreover, the techniques we used to prove Theorem 1 do not rely at all on the embedding of the manifold in $\mathbb{R}^3$, nor do they depend on choosing an orthogonal parametrization beforehand. Therefore we can choose any parametrization for the manifold without caring on whether it is orthogonal or not but only on how does the Laplace-Beltrami operator looks like and how manipulable it is under the chosen parametrization.

6.2 Qualitative properties of solutions

Whenever a pattern formation problem is addressed there are several "natural" questions related to the system (7). In this work we answered affirmatively the questions of existence, uniqueness and regularity and we also showed that the growth shifts the eigenvalues of the system (7) towards the left in the complex plane (Theorem 5). However, the questions of symmetry breaking, bifurcation and asymptotic behavior for large times are still open and should be addressed in future works.

6.3 Linear stability analysis

The following lemma summarizes the properties of the Laplace-Beltrami operator $\Delta_{\mathcal{M}}$.

Lemma 5 *Let $\mathcal{M}$ be a manifold and consider the operator $-\Delta_{\mathcal{M}}$. Then:*

1. *All eigenvalues of $-\Delta_{\mathcal{M}}$ are real and nonnegative.*
2. *Zero is an eigenvalue with multiplicity one.*
3. *All eigenspaces are finite dimensional.*
4. *There exists infinitely eigenvalues*

$$0 = \lambda_1 < \lambda_2 \leq \cdots \leq \lambda_k \to \infty\,,$$

   and they accumulate only at infinity (i.e. theres is no finite accumulation point.
5. *The eigenvectors of $-\Delta_{\mathcal{M}}$ constitute an orthonormal basis of $L^2(\mathcal{M})$.*
6. *All eigenvectors are smooth.*

Proof: See Rosenberg [8], Theorems 1.29 (p.32) and 1.31 (p.35). □

Lemma 5 states that the Laplace-Beltrami operator $\Delta_{\mathcal{M}}$ possesses the very same spectral properties than the Laplacian operator in euclidean, regular and bounded domains with Neumann boundary conditions. Therefore, all the linear stability analysis performed by Gjorgjieva [4], Murray [6] and Plaza *et al* [7] hold for the system (7), and hence we obtain exactly the same stability relations that appear in their works.

6.4 The globalizing and stabilizing effects of growth on pattern formation

As we mentioned in the abstract, the growth has two effects on pattern formation. The first one is a "globalizing effect" because the growth enhances the possibility of global existence of solutions. Indeed, condition (28) in Theorem 4 is less restrictive than condition (25) in Lemma 2 because even if (25) does not hold (28) can be fulfilled. In that case, a solution of the system (24) on a fixed manifold $\mathcal{M}$ is perhaps only a local solution (i.e. it can only exist up to a finite time $T > 0$), but as a solution of the system (7) on a growing manifold $\mathcal{M}_t$ it exists globally (i.e. for all times $t \geq 0$).

Moreover, if $c(t)$ is large enough then we have global existence of solutions of the system (7) without any hypothesis on the nonlinearity $\mathbf{F}(\mathbf{u})$. We proved it for the exponential growth factor $\rho(t) = e^{r(t-1)}$, but other growth factors can be chosen provided

$$c(t) > \sup\{\|\mathbf{F}(z)\| : z \in \partial\mathcal{R}\}$$

holds.

The second effect is a "stabilizing effect". As it was shown in Theorem 5, the growth shifts the eigenvalues towards the left in the complex plane by the explicit factor $c(t) > 0$. This implies that they have smaller real parts, and in consequence there is less chance to lose stability on a growing manifold than on a fixed one.

This stabilizing effect has three particular implications. First, a fast growth does not allow patterns to be very complicated; second, an spontaneous emergence of complex geometries is more likely to appear under slow or zero growth than under fast growth; and third, if there is a bifurcation on a fixed manifold the growth can prevent it to take place on a growing manifold.

6.5 Exponential growth factor

A very special type of growth factor is

$$\rho(t) = e^{r(t-1)}$$

because $c(t)$ is constant if and only if the growth factor $\rho(t)$ is of exponential type. This observation implies that the simplest case of growth to be added on a model is exponential, and therefore it is important to work on the exponential case before approaching a more general growth factor in order to gain some insight. In that spirit we have shown that if $r > 0$ is big enough then the solutions of the system (7) are globally defined regardless of the nonlinearity $\mathbf{F}(\mathbf{u})$, but there are more features of the exponential growth. For example, Gjiorgjieva [4] showed that the system (7) on a 2D sphere with two morphogens and exponential isotropic growth has a constant equilibrium solution if and only if $\rho(t)$ is exponential (see Lemma 5.1, p.50), and we can show that her result holds for any manifold and for any number of morphogens. Indeed, (7) has a constant equilibrium $\mathbf{u}_0 = (u_1^0, \ldots, u_M^0)$ if and only if

$$n\frac{\dot{\rho}(t)}{\rho(t)}\mathbf{u}_0 = \mathbf{F}(\mathbf{u}_0)\,.$$

Therefore, if $\mathbf{u}_0 \not\equiv 0$ then for all coordinates $u_i^0 \neq 0$ we have

$$\frac{\dot{\rho}(t)}{\rho(t)} = \frac{F_i(\mathbf{u}_0)}{nu_i^0}\,,$$

which implies that $\dot{\rho}(t)/\rho(t)$ is constant, and in consequence $\rho(t)$ is exponential.

6.6 A very personal speculation

The last statement of Theorem 5 affirms that the difference between the eigenvalues on the fixed manifold $\mathcal{M}$ and the grown manifold $\mathcal{M}_1$ is $c(1) = n\dot{\rho}(1)$, which implies that the final state $\mathcal{M}_1$ does not depend on the evolution of the growing manifold $\mathcal{M}_t$, i.e. on $\rho(t)$ with $t \in [0, 1)$, but only on the eigenvalues of the Laplace-Beltrami operator on the fixed manifold $\mathcal{M}$ and on $\dot{\rho}(1)$. Therefore, we can control the patterns on $\mathcal{M}_1$ just by manipulating $\dot{\rho}(t)$ near $t = 1$.

In that spirit let me make a very personal speculation concerning two biological situations. First, in Developmental Biology and wound healing it is important to have a final stage clearly differentiated, but sometimes the embryo or the regenerating tissue do not reach that final stage successfully. In a world where our model is valid and manipulation of the growth factor is feasible we could slow down the proliferation of cells in order to give them the possibility to differentiate properly and thus correct malformations. Second, in cancer treatment it is important to avoid metastasis. In our ideal world we could accelerate the tumor growth and thus hinder it from breaking into pieces because metastasis has a far more complex geometry than the tumor as a unit.

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