PATTERN FORMATION ON A GROWING OBLATE SPHEROID. AN APPLICATION TO ADULT SEA URCHIN DEVELOPMENT

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ABSTRACT. In this study, the formation of the adult sea urchin shape is rationalized within the Turing’s theory paradigm. The emergence of protrusions from the expanding underlying surface is described through a reaction-diffusion model with Gray-Scott kinetics on a growing oblate spheroid. The case of slow exponential isotropic growth is considered. The model is first studied in terms of the spatially homogenous equilibria and of the bifurcations involved. Turing diffusion-driven instability is shown to occur and the impact of the slow exponential growth on the resulting Turing regions adequately discussed. Numerical investigations validate the theoretical results showing that the combination between an inhibitor and an activator can result in a distribution of spot concentrations that underlies the development of ambulacral tentacles in the sea urchin’s adult stage. Our findings pave the way for a model-driven experimentation that could improve the current biological understanding of the gene control networks involved in patterning.

1. Introduction and motivations. The key role of sea urchin as a model organism for the understanding of growth and development processes in biology dates back to the late 1800s, after the invention of the microscope. Its peculiar features not only allowed history of embryology and cell biology to enrich with enlightening discoveries but still make it a leading model organism in developmental biology [10, 11]. Sea urchins have been proven to exist since the Middle Ordovician,
about 460 million years ago [21] and, in the course of evolution, the echinoid skeletal parts changed in morphology and physiology adapting to novel functions and to different marine habitats [13, 43]. Their extraordinary evolutionary success can be mainly related to the strategic use of the endoskeleton that, from a macroscopic point of view, consists of test, dental apparatus known as Aristotle’s lantern and accessory appendages. Sea urchins are traditionally divided in two subgroups according to the radial (regular) or bilateral (irregular) body symmetry. Regular echinoids are spherical in shape and exhibit pentaradial symmetry. Differently, the irregular ones are aboral-orally flattened and elongated or heart-shaped [36].

Sea urchins, with their appealing patterns and intricate plate arrangement, have puzzled theoretical morphologists for centuries [14]. Theoretical morphology is a fascinating field of science that crosses the traditional disciplinary boundaries between physics, mathematics and biology. Within its framework, morphological models are developed to explain and describe organism growth and form, the observed patterns and the related processes. Morphologies may be considered from different points of view so that different models may be obtained to explain and describe growth or form for the same organisms. For example, the mechanistic modeling approach involves process-based principles as those associated with genetics or physiology whereas the dynamic modeling approach makes use of pattern-based principles as the ones associated with mathematics or physics [4].

Over the years, there have been multiple efforts to shape the growth of sea urchins. A pioneering study on test shape was developed by Scottish biologist and mathematician Sir D’Arcy Wentworth Thompson in its monumental book ‘On Growth and Form’ [47] that immediately became a classic for its exploration of natural geometries in the dynamics of growth and physical processes. Thompson suggestively describes the problem of biological form at many levels of organization, arguing that the forms of plants and animals could be understood in terms of pure mathematics and physical laws. For living organisms, Thompson conceives the form as not given a priori suggesting that, in addition to heritage, there exist physical constraints acting on every portion of matter across scales in time and space. Such structural constraints can have different origins (physical, chemical, mechanical, etc.) and some of them can be expressed in terms of mathematical equations.

In the case of sea urchins, Thompson used a liquid drop analogy to describe the shape and growth of regular echinoids. This idea has been the starting point for a great number of attempts to model the shape of a sea urchin within a mechanical perspective. Detailed morphospace investigations have in fact been carried out to describe echinoid test shapes by the means of phylogenetic, physical and mechanical factors. A great number of studies have been oriented to the description of test shape, i.e. [9, 15], of generalized constructional or functional morphology [37] and echinoid growth has been mainly conceived as a whole-body growth [20, 39, 41]. To describe plate tessellation patterns, in [51] a three-dimensional sea urchin model was introduced where test plates are described by Delaunay triangulation over a three-dimensional spherical coordinate system and plate growth is modeled with the help of morphogen gradient functions describing nutrient diffusion, growth factor inductions and lateral inhibitions.

In [1], the occurrence of specific morphological features in sea urchins was rationalized within the reaction-diffusion modeling framework and related to the Turing diffusion-driven instability. Focusing on the pentagonal symmetry in the rudiment
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During the early development of regular echinoid larval forms, the authors investigated the formation of radially symmetric patterns using a Turing system - the phenomenological BVAM model - solved on a confined circular domain. Their results suggest Turing instability as a possible mechanism for the emergence of the fivefold symmetry observed in the early sea urchin’s development [1, 2]. The link established between the early development of regular echinoid and Turing’s mathematical theory of morphogenesis is a precious starting point that we intend to further explore in this paper.

Turing instability is likely the most extensively studied mechanism for self-organized biological pattern formation [31]. To discuss ‘a possible mechanism by which the genes of a zygote may determine the anatomical structure of the resulting organism’ [48], Turing proposed a hypothetical chemical reaction that could spontaneously break the symmetry in an initially uniform mixture of chemical compounds. Such symmetry breaking - triggered by random disturbances - could occur because of the interplay of two main processes - reaction and diffusion - involving certain chemical ‘species’. Reaction is the process that creates and destroys such chemicals; diffusion is the action of spreading chemicals through the tissue. Turing hypothesized that if one of the reacting pair of chemicals was a growth hormone, the symmetry breaking would result in a spatially non-uniform growth and hence to the development of structures, i.e. spatial patterns. For this reason, he evocatively called these chemicals morphogens, choosing the word morphogen ‘to convey the idea of a form producer’, [48].

Turing’s analysis showed that, by properly choosing system kinetics, it was possible to obtain a steady state that - although stable in the absence of diffusion - could become unstable when diffusion was introduced. The interplay of two stabilizing processes can hence cause instability and lead to the emergence of spatial structures. Albeit the molecular details are still unknown, the diffusion-driven Turing pattern forming mechanism has proved to be capable to produce patterns consistent with those observed in some mammals [31], seashells [29, 30] and marine fishes [16, 35]. Such a paradigm has also been fruitfully improved with the introduction of curved geometries to model organisms such as radiolarians or lady beetles [22, 50].

Domain growth can be considered as a further improvement of the Turing paradigm in the direction of increasing its biological realism [17, 28]. Most applications of Turing’s theory have in fact been carried out on fixed domains. In the context of developmental biology, this assumption tacitly implies that pattern forming processes and domain growth occur on a different timescale. However, although growth is usually recognized to occur at a slower rate with respect to other biological processes, it is not possible to overlook that it is a key process in development and can have crucial effects on the occurrence of spatial heterogeneity. For example, slow domain growth typically dictates the nature of the pattern that evolves as the domain grows and can be considered as a mechanism responsible for increasing robustness in pattern formation [26]. A large amount of theoretical work has then been developed in this regard gaining evidences that, when coupled with growth, robust pattern formation can occur with less sensitivity to the initial conditions via a cascade of instabilities with bifurcations driven by the evolution of the domain [6, 26, 28]. Moreover, the process of growth can enhance a selection of certain patterning modes at the expense of others, enabling the models to produce dynamics much richer than in the case of fixed domains. The above extensions of the
Turing paradigm have lead to an increasing interest on the topic, stimulating significant theoretical research in many different fields of application. Recent examples of studies on reaction-diffusion systems focusing on the role of curvature or/and domain growth can be found in [18, 25–27, 38, 42]. In this paper we want to show that - although other mechanisms are certainly possible - Turing pattern formation on a growing domain could be considered as a viable mechanism to explain the emergence of sea urchin morphology in the adult stage.

The paper is structured as follows: in Section 2, we briefly describe the main features of sea urchins’ skeletal growth and show how it could be qualitatively associated to Gray Scott kinetics. In Section 3, based on the symmetries associated with the echinoid test, we introduce a reaction-diffusion model with Gray-Scott kinetics on a growing oblate spheroid and we develop the related theoretical framework. In Section 4, conditions for the occurrence of diffusion-driven instability for the general case of slow isotropic growth domain are recalled. In Section 5, the case of slow exponential growth is considered and the system is studied in terms of spatially homogeneous equilibria and bifurcation involved. The effects of the slow exponential growth on the relevant spatially homogeneous equilibrium as well as on the associated Turing region are then discussed. In Section 6, the obtained theoretical findings are validated by numerical investigations. A detailed description of the numerical method is provided and numerical simulations are presented for both the stationary and the evolving case. In Section 7, concluding remarks close the paper.

2. Sea Urchin growth mechanisms. The developing adult sea urchin expands progressively from a small, approximately spherical shape, while acquiring at the same time protrusions from the surface. In the present work we will not address the genomic, transcriptomic or proteomic determinants of the growth of the animal itself, but we will concentrate on a possible mechanistic model of the emergence of the protrusions from the expanding underlying surface.

Developmental gene regulatory networks (GRNs) are models that explain the causal sequence of combinatorial interactions among genes encoding transcription and signaling factors. The architecture of a GRN gives the map of functional interactions among these genes and provides a direct guide to the regulatory logic of developmental control. A seminal GRN model, proposed by Davidson et al. [8], can be considered as a starting point for the study of sea urchin morphological development. These authors integrated published fragmentary information regarding endomesoderm specification in sea urchin embryos and provided a sort of template for future tests of biological functionality. Other studies were subsequently published, towards the completion of the relevant GRN [33] but, to the best of our knowledge, a combination of genetic with spatial information has not yet been achieved.

We may consider, in a very simplified setting, a minimal (coarse) network extracted from the original (finer) GRN model: we concentrate on two genes (pmar1 and ets1). It is well known that pmar1 and the transcriptional repressor hesC repress each other [45], and it is also known that hesC, otherwise ubiquitously expressed, becomes excluded from the cells where pmar1 expression has been established [40]. Since hesC has been shown to repress the skeletogenic gene ets1 [7] the germ layer is therefore thought to be specified by pmar1 through this pmar1−hesC double negative gate mechanism. It is therefore possible to consider pmar1 as a direct activator of ets1.
Regarding the action of ets1 on pmar1, current understanding is far from complete and we have not been able to find in the literature mention of a direct effect. However, ets1 is repressed by hesC [46], and it is plausible that this effect is controlled, with higher concentrations of ets1 determining higher concentrations of its controller hesC. However, hesC also inhibits pmar1, therefore higher concentrations of ets1 would translate into higher concentrations or activity of hesC and into lower concentrations or activity of pmar1. While this mechanism is hypothetical, still it would be reasonable to consider ets1 an indirect inhibitor of pmar1.

The reciprocal actions are naturally determined not by the gene themselves, but by their protein products. In a first modelling approach, given the natural degradation of all protein products in the organism, and absorbing delays (determined by protein production and protein degradation) into the dynamics of the genetic expressions themselves, we may formalize directly the action of a gene (via its products) on the other’s expression or on the other’s products. In the following we will therefore consider two variables: $u$ (representing pmar1, its products and its action) and $v$ (representing ets1, its products and its action). The reciprocal relationships of these two variables may thus be expressed by standard Gray-Scott kinetics.

3. The Gray-Scott model on a growing oblate spheroid. To develop our reasoning, we start by considering the following reaction-diffusion system on a fixed two-dimensional domain $X$:

\[
\begin{align*}
\frac{\partial u}{\partial t} &= \Delta_L u + \omega f(u, v) \\
\frac{\partial v}{\partial t} &= d \Delta_L v + \omega g(u, v)
\end{align*}
\]

where $d$ is the ratio between the diffusion coefficients $D_v$ and $D_u$ of the state variables $v$ and $u$ respectively, i.e. $d = D_v / D_u$; $\Delta_L$ is the two-dimensional Laplacian operator and the reaction terms are described by the Gray-Scott kinetics:

\[
\begin{align*}
  f(u, v) &= -uv^2 + c_1 (1 - u) \\
  g(u, v) &= uv^2 - (c_1 + c_2)v
\end{align*}
\]

where $c_1$, $c_2$ are kinetic parameters. All the involved parameters are supposed to be constant and strictly positive. The strictly positive parameter $\omega$ can be interpreted as the relative strength of the reaction terms with respect to the diffusion ones or as a scale factor proportional to the area of the two-dimensional domain. For this reason, in the following we refer to $\omega$ as to the size parameter.

Let us now consider reaction-diffusion systems on evolving surfaces, by following the presentation in [12]. Let $\Gamma_0$ be a $C^2$ surface without boundary in $\mathbb{R}^3$. Let $\vec{v} : \mathbb{R}^3 \times [0, T] \to \mathbb{R}^3$ be a material velocity field of $C^1$ class. Each point $\vec{x}_0 \in \Gamma(0)$ evolves according to the given material velocity, i.e.

\[
\begin{align*}
  \dot{x}(t) &= \vec{v}(\vec{x}(t), t), \quad t \in [0, T], \\
  \vec{x}(0) &= \vec{x}_0.
\end{align*}
\]

For any $t \in [0, T]$, let $\Gamma(t) := \{ \vec{x}(t) | \vec{x}_0 \in \Gamma \}$ be the evolved surface at time $t$. Define the space-time surface as $\mathcal{G}_T := \bigcup_{t \in [0, T]} \Gamma(t) \times \{t\}$. For any sufficiently smooth $g : \mathcal{G}_T \to \mathbb{R}$ and $\vec{g} : \mathcal{G}_T \to \mathbb{R}^3$, let $\nabla_{\Gamma(t)} g$, $\Delta_{\Gamma(t)} g$ and $\nabla_{\Gamma(t)} \cdot \vec{g}$ denote the tangential gradient, the Laplace-Beltrami operator and the tangential divergence, respectively.
In the following, we will write $\Gamma$ instead of $\Gamma(t)$ to simplify the notation. Furthermore, let $\partial^\ast g$ denote the material derivative of $g$ defined by

$$
\partial^\ast g := \frac{\partial \tilde{g}}{\partial t} + \vec{v} \cdot \nabla \tilde{g},
$$

(4)

where $\nabla$ is the standard gradient in $\mathbb{R}^3$ and $\tilde{g}$ is any differentiable extension of $g$ defined on a neighborhood of $\mathcal{G}_T$. Definition (4) is intrinsic, i.e. it does not depend on the choice of the extension $\tilde{g}$.

Suppose we are given two species $u_k : \Gamma(t) \to \mathbb{R}$, $k = 1, 2$, and let $\vec{q}_k : \Gamma(t) \to \mathbb{R}^3$, $k = 1, 2$, be their fluxes tangent to $\Gamma(t)$, which we assume to fulfil Fick’s law:

$$
\vec{q}_k = -d_k \nabla \Gamma u_k, \quad k = 1, 2,
$$

(5)

where $d_k$, $k = 1, 2$, are positive diffusivity constants. If the production rate of $u_k$ is given by $f_k(u_1, u_2)$, then it is possible to write a balance law of the form

$$
\partial^\ast u_k + u_k \nabla \cdot \vec{v} = d_k \Delta_L u_k + f_k(u_1, u_2), \quad k = 1, 2, \quad t \in [0, T],
$$

(6)

see [12] for further details on the derivation. Notice that, for the case $\vec{v} = 0$ of stationary surfaces, (6) reduces to the classical reaction diffusion system (1). Alongside (6), which will prove useful in the numerical simulations, we will consider an equivalent formulation of (6) introduced by Plaza [38] and widely used in applications [3, 18, 19, 42]. To this end, we assume that the surface $\Gamma(t)$ is parametrized as

$$
\Gamma(\zeta, \eta, t) = (x(\zeta, \eta, t), y(\zeta, \eta, t), z(\zeta, \eta, t)).
$$

(7)

Since we aim to study model (1) with the kinetic terms (2) on a growing oblate spheroid, in (1), $\Delta_L$ is the Laplace-Beltrami operator acting on this surface.

As in [3, 18, 19, 42] we use the approach of Plaza [38] to incorporate curvature and growth into the domain. We denote by $X$ a surface embedded in $\mathbb{R}^3$ and parametrized as

$$
X(\zeta, \eta, t) = (x(\zeta, \eta, t), y(\zeta, \eta, t), z(\zeta, \eta, t)).
$$

If one assume that reaction and diffusion both take place on the surface $X$, then model (1) becomes:

$$
\frac{\partial u}{\partial t} = \Delta_L u - \partial_t (\ln (h_1 h_2)) u + \omega f(u, v)
$$

(8)

$$
\frac{\partial v}{\partial t} = d \Delta_L v - \partial_t (\ln (h_1 h_2)) v + \omega g(u, v)
$$

where

$$
\Delta_L \Psi = \frac{1}{h_1 h_2} \left[ \left( \frac{h_2}{h_1} \Psi_\zeta \right)_\zeta + \left( \frac{h_1}{h_2} \Psi_\eta \right)_\eta \right]
$$

(9)

for $\Psi = u, v$. Here we have set $h_1 = ||X_\zeta||$ and $h_2 = ||X_\eta||$, where $||.||$ is the Euclidean norm and the subscripts denote partial differentiation.

Next step is to specialize model (8)-(9) to the case of an isotropically growing oblate spheroid. To this aim, we first recall that an oblate spheroid can be obtained by rotating an ellipse about its minor axis and its coordinates are $(\xi, \eta, \Phi)$ where $\xi$ is the radial term, $\eta = \cos \theta$ with $\theta$ being the asymptotic angle with respect to the minor axis and $\Phi$ is the rotational term. To perform the rotation of the ellipse...
around its minor axis, a rotation is performed on $\Phi$ in the xy-plane, yielding the oblate spheroidal coordinates:

$$
\begin{align*}
  x &= f \frac{2}{\sqrt{1 - \eta^2}(\xi^2 + 1)} \cos \Phi \\
  y &= f \frac{2}{\sqrt{1 - \eta^2}(\xi^2 + 1)} \sin \Phi \\
  z &= f \frac{2}{\eta} \xi 
\end{align*}
$$

where $f$ represents the focal distance and is given by $f = 2 \sqrt{a^2 - b^2}$; $a$ and $b$ denote the semi-major and the semi-minor axis respectively and can be also expressed as $a = f \frac{2}{\xi}$, $b = f \frac{2}{\sqrt{\xi^2 - 1}}$.

We also observe that, being the other parameter fixed, we can change the shape of the spheroid by acting on the value of $\xi$. This is because, the eccentricity $e$ of the spheroid is defined as $e = \sqrt{1 - (b^2/a^2)}$, so that $e = 1/\xi$. It follows that, increasing the value of $\xi$ while keeping $f$ fixed, results in a more sphere-like spheroid. Differently, increasing the value of $f$ while keeping $\xi$ fixed, does not alter the shape but results in a larger size of the spheroid.

In the following, we will consider $\Phi = 2 \pi \zeta$. The isotropically growing oblate spheroid can hence be parametrized by:

$$
X(\zeta, \eta, t) = \rho(t) \left( f_0 \frac{2}{2} \sqrt{1 - \eta^2}(\xi^2 + 1) \cos 2 \pi \zeta, f_0 \frac{2}{2} \sqrt{1 - \eta^2}(\xi^2 + 1) \sin 2 \pi \zeta, f_0 \frac{2}{2} \eta \xi \right)
$$

with $\eta \in [-1, 1], \zeta \in [0, 1)$, and $\xi > 1$. Here $f_0$ is the focal distance at time $t = 0$ and the growth function $\rho(t)$ multiplies the three entries of $X$ so that the surface experiences an isotropic growth.

Now, to specialize model (8), we must explicitly calculate the dilution term and the Laplace-Beltrami operator for the case of the oblate spheroid. As far as the dilution term, it is given by:

$$
\partial_t (\ln (h_1 h_2)) \Psi = 2 \frac{\dot{\rho}}{\rho} \Psi
$$

where $\dot{\rho}$ is the derivative of the growth function $\rho(t)$ with respect to the time variable $t$. Moreover,

$$
\begin{align*}
  h_1 &= \|X_\zeta\| = \rho(t) f_0 \sqrt{(1 + \xi^2)(1 - \eta^2)}, \\
  h_2 &= \|X_\eta\| = \rho(t) f_0 \frac{2}{2} \sqrt{\frac{\eta^2 + \xi^2}{1 - \eta^2}} \\
  h_1 h_2 &= 2 \pi \sqrt{\frac{1 + \xi^2}{\eta^2 + \xi^2}} (1 - \eta^2), \\
  \frac{h_2}{h_1} &= \frac{1}{2 \pi (1 - \eta^2)} \sqrt{\frac{\eta^2 + \xi^2}{1 + \xi^2}}
\end{align*}
$$

so that:

$$
\begin{align*}
  \frac{h_1}{h_2} &= 2 \pi \sqrt{\frac{1 + \xi^2}{\eta^2 + \xi^2}} (1 - \eta^2), \\
  \frac{h_2}{h_1} &= \frac{1}{2 \pi (1 - \eta^2)} \sqrt{\frac{\eta^2 + \xi^2}{1 + \xi^2}}
\end{align*}
$$

As a consequence, the Laplace-Beltrami operator (9) specializes as:

$$
\Delta_L \Psi = \frac{1}{\rho^2} \Delta \Psi
$$
where
\[ \Delta_* \Psi = \frac{1}{\pi^2 f_0^2 (1 - \eta^2)(1 + \xi^2)} \Psi_{\xi\xi} + \frac{4 (1 - \eta^2)}{f_0^2 (\eta^2 + \xi^2)} \Psi_{\eta\eta} - \frac{4 \eta (2 \xi^2 + \eta^2 + 1)}{f_0^2 (\eta^2 + \xi^2)^2} \Psi \] (12)
and model (8) becomes:
\[
\frac{\partial u}{\partial t} = \frac{1}{\rho^2} \Delta_* u - 2 \frac{\dot{\rho}}{\rho} u + \omega f(u, v) \\
\frac{\partial v}{\partial t} = \frac{d}{\rho^2} \Delta_* v - 2 \frac{\dot{\rho}}{\rho} v + \omega g(u, v)
\] (13)
with \( \Delta_* \) given by (12) and the reaction terms \( f(u, v) \) and \( g(u, v) \) given by (2).

In the next sections, we deal with the occurrence of diffusion-driven instability for this system. To this end we first recall the analytical conditions, derived and discussed in [26], for the emergence of Turing patterns in the general case of slowly isotropic growing domains.

4. Turing instability conditions on growing domains. We start by stressing that model (13) is a non-autonomous system of partial differential equations with time dependence in the diffusion and dilution terms. These non-autonomous terms notably increase the complexity of the Turing instability analysis since they usually invalidate the standard linear stability analysis via plane waves decomposition even in the simplest case of isotropic domain growth.

The complex rationale of this problem was fully elucidated by Madzvamuse et al. [26] where the emergence of domain-growth-induced Turing instability was analytically investigated. Turing instability on growing domains occurs when a spatially independent solution \((u_s(t), v_s(t))\), that is linearly stable in the absence of diffusion, becomes unstable when diffusion is introduced. Therefore, linearizing model equations around a time-dependent reference solution \((u_s(t), v_s(t))\) and using asymptotic theory, they derived necessary conditions for diffusion-driven instability on growing domains for a general growth function, in the case of slow and isotropic growth.

Specializing the general procedure developed in [26] to system (13), the first step is to linearize the model equations around a time-dependent homogeneous reference solution \((u_s(t), v_s(t))\) of system (13), namely a solution of the non-autonomous system of ordinary differential equations
\[
\frac{\partial u_s}{\partial t} + h(t) u_s = \omega f(u_s, v_s) \\
\frac{\partial v_s}{\partial t} + h(t) v_s = \omega g(u_s, v_s)
\] (14)
where
\[ h(t) = \frac{2 \dot{\rho}(t)}{\rho(t)} \]
is the dilution term. The linear stability analysis can then be carried out by only freezing the system in the future namely considering a perturbation at time \( t_0 \) and how it has evolved at time \( t_0 + \Delta t > t_0 \) with
\[ \frac{\Delta t}{T_{dyn}} = O(\epsilon^0) \]
where \( \epsilon = T_{dyn}/T_g \ll 1 \), \( T_g \) is the growth time scale and \( T_{dyn} \) is the maximum timescale of the diffusion and the biological reactions. Therefore, in the case of slow
and isotropic growth, requiring stability in the presence of spatially homogeneous perturbations and instability for spatially varying perturbations lead the following necessary conditions for diffusion-driven instability when considering the system at time \(t\) due to a perturbation at time \(t_0\): 

\[
\begin{align*}
\omega (f_u + g_v) - 2 h_* &< 0 \\
\omega^2 (f_u g_v - f_v g_u) - h_* \omega (f_u + g_v) + h_*^2 &> 0 \\
h_* (1 + d) - \omega (d f_u + g_v) &< 0 \\
[h_*(1 + d) - \omega (d f_u + g_v)]^2 - 4d [\omega^2 (f_u g_v - f_v g_u) - h_* \omega (f_u + g_v) + h_*^2] &> 0
\end{align*}
\] (15)

Here the subscripts \(u\) and \(v\) denote partial differentiation; the Jacobian components \(f_u, f_v, g_u, g_v\) are evaluated in terms of \((u_s(t_1), v_s(t_1))\) with \(t_1 = t_0 + t_2\) and \(h_*\) is related to the value of the dilution term evaluated at \(t_1\). For the detailed derivation and a complete discussion of conditions (15), we refer the interested reader to consult the paper [26]. Inequalities (15) locate a time-dependent domain in the parameter space showing that, in the case of growing domains, even a slow growth can substantially alter the Turing space.

5. The case of slow exponential growth. We now investigate model (13) under the hypothesis that domain growth is slow, isotropic and exponential in time. A first reason for the use of a slow-exponential growth of the adult animal is that this mathematical representation considerably simplifies the mathematical analysis. In fact in this case the dilution term becomes constant, hence allowing for a mathematically more tractable analysis of the equilibria stability conditions as well as of their bifurcations in terms of the model parameters. However, this formulation of the growth function is extremely plausible in the initial period of growth. The urchin goes from few millimeters to several centimeters in diameter over a period of several weeks and the surface projections are formed from the very early maturation period, during which the growth rate depends on current mass and during which trophic limitations (which would impose a logistic rather than exponential growth rate) are not yet met. After this initial period, where our model strictly applies, maturation implies elongation of the appendages and thickening of the mineralized spines, but lesser and lesser actual expansion of the diameter of the animal. The proposed model more appropriately describes the formation of the adult shape rather than its eventual maturation.

The effects of slow growth on the resulting mathematical framework have been extensively discussed in [23, 24, 26] where it was shown that slow growth does not drastically change the instability region and that the overall observed patterns are qualitatively similar, differing primarily in the positioning of pattern elements. This allows growth to be recognized as a mechanism capable of providing robustness to Turing patterns [6]. Under the assumption that domain growth is slow, exponential and isotropic, we hence deal with the following model:

\[
\begin{align*}
\frac{\partial u}{\partial t} &= \frac{1}{\rho^2} \Delta_x u - 2r u + \omega f(u, v) \\
\frac{\partial v}{\partial t} &= \frac{d}{\rho^2} \Delta_x v - 2r v + \omega g(u, v)
\end{align*}
\] (16)

with \(\Delta_x\) given by (12), the reaction terms \(f(u, v)\) and \(g(u, v)\) given by (2) and \(\rho(t) = e^{rt}\) with the growth rate \(r \ll 1\). We observe that, in comparison to the case of no growth, the reaction-diffusion system (16) exhibits two interesting features:
(i) the new kinetics include the decay rate terms $-2ku$ and $-2kv$ that derive from the specific growth function we selected; (ii) each partial differential equation has a time-dependent diffusion coefficient term, which tends to zero as the time goes to infinity hence implying in this case the degeneracy of both the equations. To overcome this difficulty, in the present study we consider only finite times.

We are particularly interested in exploring if and in which way this kind of growth can affect the spatially homogeneous equilibria of the system and its capability to give place to pattern formation.

5.1. Growth effects on the spatially homogeneous equilibria. To show the effects of growth on the spatially homogeneous equilibria of the system, we start by discussing the equilibria and the related stability properties of the model in the absence of growth, namely for $r = 0$. In this case, the spatially uniform equilibria are the solutions of the algebraic system:

$$
\begin{align*}
-u v^2 + c_1 (1 - u) &= 0 \\
 u v^2 - (c_1 + c_2) v &= 0
\end{align*}
$$

(17)

The trivial equilibrium $P_0 = (u_0, v_0) = (1, 0)$ is an equilibrium for all possible values of the parameters. Moreover, when certain conditions on the parameters are verified, the system can exhibit a multiplicity of equilibria. More precisely, two further equilibria

$$
\begin{align*}
P_1 = (u_1, v_1) &= \left( \frac{c_1}{c_1^2 + c_1}, \frac{1}{2} \frac{c_1 - \sqrt{\Delta_{eq}}}{c_1 + c_2} \right), \\
P_2 = (u_2, v_2) &= \left( \frac{c_1}{c_1^2 + c_1}, \frac{1}{2} \frac{c_1 + \sqrt{\Delta_{eq}}}{c_1 + c_2} \right)
\end{align*}
$$

where

$$
\Delta_{eq} = c_2^2 - 4 c_1 (c_1 + c_2)^2,
$$

are found to exist for $c_1^{SN1} < c_1 < c_1^{SN2}$ with $c_2 < 1/16$. They appear and disappear in the system because of two saddle-node bifurcations occurring at the $c_1$-threshold values:

$$
c_1^{SN1.2} = \frac{1}{8} \left[ (1 - 8c_2) \mp \sqrt{1 - 16c_2^2} \right].
$$

Fig.1 shows the occurrence of this multiplicity of equilibria when the parameter $c_2$ is fixed so that $c_2 = 0.04$ and $c_1$ is allowed to vary. In this case, $P_1$ and $P_2$ both appear in the system at $c_1^{SN1} = 0.01$ because of a saddle-node bifurcation and then they coalesce at $c_1^{SN2} = 0.16$ because of a further saddle-node bifurcation.

By linear stability analysis, it is straightforward to prove that $P_0$ is always stable and that $P_1$ is always unstable. Among the others, the equilibrium $P_2$ displays the more interesting properties since it may lose its stability because of a Hopf bifurcation at $c_1 = c_1^{Hopf}$, where

$$
c_1^{Hopf} = \frac{1}{2} \left[ \sqrt{c_2^2 - 2c_2} - \sqrt{c_2 (1 - 4 \sqrt{c_2})} \right].
$$

More precisely, $P_2$ is unstable for $c_1^{SN1} < c_1 < c_1^{Hopf}$ whereas it is stable to homogeneous perturbations in the range $c_1^{Hopf} < c_1 < c_1^{SN2}$.

When the growth process is considered, namely for $r \neq 0$, the spatially homogeneous equilibria are the solutions of the following system of algebraic equations:

$$
\begin{align*}
-2r u + \omega \left[ -u v^2 + c_1 (1 - u) \right] &= 0 \\
-2r v + \omega \left[ u v^2 - (c_1 + c_2) v \right] &= 0
\end{align*}
$$

(18)
Figure 1. Case of no growth: \( r = 0 \). Bifurcation diagram in the \((c_1, v_e)\) plane. The branches of the spatially homogeneous equilibria \((u_e, v_e)\) for model (16) are shown as functions of the parameter \( c_1 \). The parameter \( c_2 \) is fixed as \( c_2 = 0.04 \). In this specific case, the trivial equilibrium \( P_0 \) is an equilibrium for all the values of \( c_1 \) whereas the two equilibria \( P_1 \) and \( P_2 \) exist only in the range \( 0.01 < c_1 < 0.16 \).

It follows that the trivial equilibrium

\[
P_0^{(r)} = (u_0, v_0) = \left( \frac{\omega c_1}{\omega c_1 + 2r}, 0 \right)
\]

is an equilibrium for all the values of the parameters. Moreover, the system can exhibit two further equilibria

\[
P_1^{(r)} = (u_1, v_1) = \left( \frac{\omega c_1}{\omega v_1^2 + \omega c_1 + 2r}, \frac{c_1 \omega^2 - \sqrt{\Delta_v}}{2\omega(c_1 \omega + c_2 \omega + 2r)} \right)
\]

and

\[
P_2^{(r)} = (u_2, v_2) = \left( \frac{\omega c_1}{\omega v_2^2 + \omega c_1 + 2r}, \frac{c_1 \omega^2 + \sqrt{\Delta_v}}{2\omega(c_1 \omega + c_2 \omega + 2r)} \right)
\]

(19)

where

\[
\Delta_v = \omega \left[ c_1^2 \omega^3 - 4(c_1 \omega + 2r)(c_1 \omega + c_2 \omega + 2r)^2 \right],
\]

are found to exist for values of the parameter \( c_2 \) such that \( c_2^{SN1} < c_2 < c_2^{SN2} \). Also in this case, these equilibria appear and disappear in the system because of two saddle-node bifurcations occurring at the following \( c_2 \)-threshold values:

\[
c_2^{SN1,2} = -\frac{2(c_1 \omega + 2r)^2 + \sqrt{c_1^2 \omega^3(c_1 \omega + 2r)}}{2\omega(c_1 \omega + 2r)}.
\]

In Fig.2 we show that, for a fixed value of \( c_2 \), a region in the parameter space \((c_1, r)\) can be found so that the points \( P_1^{(r)} \) and \( P_2^{(r)} \) are equilibria for the system. The size of this region is influenced by \( \omega \). In particular, the region of existence of \( P_1^{(r)} \) and \( P_2^{(r)} \) considerably enlarges by increasing the value of the size parameter \( \omega \) as it is possible to see by comparing the case \( \omega = 1 \) with the case \( \omega = 10 \). This is because the parameter \( \omega \) acts on the saddle node bifurcation thresholds, enlarging the range of the parameter \( r \) for which these two non-trivial equilibria can be found. This feature is further stressed in Fig.3 where, for fixed values of \( c_1 \)
and $c_2$, we show that a larger value of $\omega$ shifts the saddle-node bifurcation threshold, ensuring $P_1^{(r)}$ and $P_2^{(r)}$ to exist for a larger range of the parameter $r$. As we will see in the next Section, this is important for the study of the system capabilities to support pattern formation. In fact, when growth is considered, i.e. for $r \neq 0$, it is easy to show that the trivial equilibrium $P_0^{(r)}$ is always stable with respect to both homogeneous and spatial perturbations whereas the equilibrium $P_1^{(r)}$ is always unstable. The equilibrium $P_2^{(r)}$, instead, can lose its stability by experiencing a Hopf bifurcation in the homogeneous case as well as a Turing bifurcation when diffusion is considered. Therefore, to evaluate the effects of growth on the system’s pattern-forming capabilities, we will specifically focus on the equilibrium $P_2^{(r)}$. A larger region of existence for $P_2^{(r)}$ hence implies larger capabilities of the system to support spatial pattern formation.
5.2. Effects of growth on the Turing Regions. To investigate the effects of growth on the system’s pattern-forming capabilities, we show the occurrence of diffusion-driven instability in the Gray-Scott model on a slow exponential growing oblate spheroid. As observed before, in the case of exponential growth the dilution term \( h(t) \) becomes constant so that the Turing conditions (15) become independent of time since

\[
h_* = h(t) = 2r.
\]

In this case, the reference state is the homogeneous and stationary solution \( P_2^{(r)} = (u_2, v_2) \) of system (18), namely:

\[
P_2^{(r)} = (u_2, v_2) = \left( \frac{\omega c_1}{\omega v_2^2 + \omega c_1 + 2r}, \frac{c_1 \omega^2 + \sqrt{\Delta \omega}}{2 \omega (c_1 \omega + c_2 \omega + 2r)} \right)
\]

with

\[
\Delta \omega = \omega \left[ c_1^2 \omega^3 - 4 (c_1 \omega + 2r)(c_1 \omega + c_2 \omega + 2r)^2 \right].
\]

The non-autonomous system (14) reduces in fact to an autonomous spatially homogeneous system for which constant equilibria exist.

When the source terms are given by (2), Turing conditions (15) for the diffusion-driven instability of the spatially homogeneous equilibrium \( P_2^r \) specialize as:

\[
\begin{align*}
\omega h_1(u_2, v_2) - 4r &< 0, \\
\omega^2 h_2(u_2, v_2) - 2 \omega r h_1(u_2, v_2) + 4r^2 &> 0 \\
\omega \left[ (-v_2^2 - c_1) d + 2u_2 v_2 - c_1 - c_2 \right] &- 2r (1 + d) > 0 \\
\left\{ \omega \left[ (-v_2^2 - c_1) d + 2u_2 v_2 - c_1 - c_2 \right] - 2r (1 + d) \right\}^2 &- 4d \left( \omega h_1(u_2, v_2) \right) \left[ \omega - 2r + 4r^2 \right] > 0
\end{align*}
\]

where:

\[
h_1(u_2, v_2) = 2u_2 v_2 - v_2^2 - 2c_1 - c_2; \quad h_2(u_1, u_2) = -2c_1 u_2 v_2 + c_1 v_2^2 + c_2 v_2^2 + c_1^2 + c_1 c_2.
\]

We apply these conditions under the additional assumption that the growth rate is small, i.e. \( r \ll 1 \).

These inequalities hence determine the so called Turing region, namely a region in the parameter space where formation of stationary spatial patterns is expected because of the interaction between the nonlinear reaction terms and the diffusion process. For the special case under study, being \( r \) fixed, the Turing conditions are time-independent and the related Turing space does not change in time. We can hence illustrate different scenarios for different values of \( r \). This is the case of Figure 4 that shows the Turing region for model (16)-(2) in the parameter space \( (c_1, d) \) for different values of the growth parameter \( r \) and for a fixed value of the size parameter \( \omega \). It clearly puts into evidence that slowly increasing the value of \( r \) has the effect to slightly reduce the resulting Turing region. Instead, as expected [31], increasing the value of the size parameter \( \omega \) considerably enlarges the size of the resulting Turing region.

6. Numerical investigations. The formulation (6) lends itself to to space discretization through the Lumped Evolving Surface Finite Element Method (LESFEM), see [12], which we will adopt in the present work. Among the numerous space discretisation techniques for surface RDSs existing in the literature, LESFEM does not rely on a parametrization of the surface. For closed surfaces such as spheres or ellipsoids, such a parametrization can bring singularities into the equations with undesired consequences such as numerical instability and convergence order degradation [50]. The time discretization is then performed via Implicit-Explicit (IMEX) Euler, which allows for a simple treatment of arbitrary nonlinear kinetics. We will
now sketch a description of the aforementioned numerical approach, the interested reader is referred to [12] for further details.

Let $\Gamma_h(0)$ be a Delaunay triangulation of the initial surface $\Gamma(0)$ of meshsize $h > 0$ and, for each $t \in [0, T]$, let $\Gamma(t)$ be the triangulated surface obtained by evolving each node of $\Gamma(0)$ according to (3). Notice that, since all nodes of $\Gamma_h(0)$ lie on $\Gamma(0)$, then all nodes of $\Gamma_h(t)$ still lie on $\Gamma(t)$. For all $t \in [0, T]$, let $\mathcal{G}_i(t)$, $i = 1, \ldots, N$, be the nodes of $\Gamma_h(t)$. Let $\mathcal{G}_{h,T} := \bigcup_{t \in [0,T]} \Gamma_h(t) \times \{t\}$ be the discrete space-time surface. For each $t > 0$, we consider the Lagrangian finite element function space

$$\mathcal{V}_h(t) := \{ \varphi \in C^0(\Gamma_h(t))| \varphi|_Z \text{ is linear affine on each face } Z \text{ of } \Gamma_h(t) \}.$$ 

The time-dependent finite element space is defined by

$$\mathcal{V}_h := \{ \varphi : \mathcal{G}_{h,T} \to \mathbb{R}| \varphi(\cdot, t) \in \mathcal{V}_h(t) \text{ for each } t \in [0, T] \}. \quad (20)$$

For each $i = 1, \ldots, N$, the $i$-th Lagrange (or pyramidal) basis function $\chi_i$ is the unique $\mathcal{V}_h$ function such that $\chi_i(\mathcal{x}_j(t), t) = \delta_{ij}$ for all $j = 1, \ldots, N$ and $t \in [0, T]$. The components $U_k \in \mathcal{V}_h$, $k = 1, 2$ of the spatially discrete solution can then be expressed in the pyramidal basis as

$$U_k(\mathcal{x}, t) = \sum_{i=1}^{N} \xi_{k,i}(t) \chi_i(\mathcal{x}, t), \quad (\mathcal{x}, t) \in \mathcal{G}_{h,T}; \quad (21)$$

\section*{Figure 4. Effects of the growth parameter $r$ on the Turing region of the equilibrium $P_2$.}

Turing regions in the parameter space $(c_1, d)$ are shown for different values of the parameter $r$. The other parameters are fixed as: $c_2 = 0.04$ and $\omega = 1$. Turing regions are bounded by the solid curve, the dashed vertical line and the dash-dot vertical line. Top row: (left) $r = 0$; (right) $r = 0.001$. Bottom: $r = 0.002$. 
with \( \xi_{k,i}(t) \) being unknown time-dependent coefficients. Given \( t \in [0, T] \) and a function \( \eta \in C^0(\Gamma_h(t)) \), its linear interpolant \( I_h \eta \) is the \( \forall \eta(t) \) function defined by

\[
I_h \eta(\bar{x}, t) = \sum_{i=1}^{N} \eta(\bar{x}_i(t)) \chi_i(\bar{x}, t), \quad \bar{x} \in \Gamma_h(t).
\]  

(22)

Now, LESFEM approximates the weak formulation of (6) and takes the following form: find \( U_1, U_2 \in \mathcal{V}_h \) such that

\[
\frac{d}{dt} \int_{\Gamma_h(t)} I_h(U_k \chi_i) + d_k \int_{\Gamma_h(t)} \nabla_{\Gamma_h} U_k \cdot \nabla_{\Gamma_h} \chi_i = \int_{\Gamma_h(t)} I_h(f_k(U_1, U_2) \chi_i),
\]

(23)

for all \( k = 1, 2 \) and \( i = 1, \ldots, N \), where \( \nabla_{\Gamma_h} \) denotes the tangential gradient on the discrete surface \( \Gamma_h(t) \). By defining the time-dependent matrices

\[
A_{ij}(t) := \int_{\Gamma_h(t)} \nabla_{\Gamma_h} \chi_i \cdot \nabla_{\Gamma_h} \chi_j, \quad M_{ij}(t) = \int_{\Gamma_h} I_h(\chi_i \chi_j), \quad i, j = 1, \ldots, N,
\]

(24)

and using (21), problem (23) becomes the following system of 2N ODEs in matrix form:

\[
\frac{d}{dt}(M(t) \xi_k(t)) + d_k A(t) \xi_k(t) = M(t) f_k(\xi_1(t), \xi_2(t)), \quad k = 1, 2, \quad t \in [0, T].
\]

(25)

The IMEX Euler discretization of (25) with a timestep \( \tau > 0 \) is

\[
\frac{M^{(n+1)} \xi_k^{(n+1)} - M^{(n)} \xi_k^{(n)}}{\tau} + d_k A^{(n+1)} \xi_k^{(n+1)} = M^{(n)} f_k \left( \xi_1^{(n)}, \xi_2^{(n)} \right), \quad k = 1, 2, \quad n = 0, \ldots, N_T,
\]

(26)

where \( N_T := \lceil \frac{T}{\tau} \rceil \), \( M^{(n)} := M(n\tau) \), \( A^{(n)} := A(n\tau) \) and \( \xi_k^{(n)} \) is an approximation of \( \xi_k(t) \) at time \( t = n\tau \). Equivalently:

\[
\xi_k^{(n+1)} = \left( M^{(n+1)} + \tau d_k A^{(n+1)} \right)^{-1} M^{(n)} \left( \xi_1^{(n)} + \tau f_k \left( \xi_1^{(n)}, \xi_2^{(n)} \right) \right), \quad k = 1, 2, \quad n = 0, \ldots, N_T.
\]

(27)

For the case of isotropic growth \( \Gamma(t) = \rho(t) \Gamma(0) \) addressed in this work, the matrices \( A^{(n)} \) and \( M^{(n)} \) do not need to be assembled ad each time step, since \( A^{(n)} = A^{(0)} \) and \( M^{(n)} = M^{(0)} \rho^2(n\tau) \).

Exploiting the assumptions of slow exponential growth, \( r \ll 1 \), in our numerical investigations we consider the case \( r = 0.001 \) that produces an almost identical Turing region with respect to the case of no growth. We choose the kinetic and diffusion parameters so that the homogeneous equilibrium \( P_2(r) \) exists and it is in the interior of the Turing region for the different choices of the parameters \( r \) and \( \omega \) that we will consider. In the following, we hence fix: \( c_2 = 0.04, c_1 = 0.03 \) and \( d = 0.05 \). Moreover, we choose the oblate spheroid parameters \( (f_0, \xi) \) such that \( f_0 = 1.9645 \) and \( \xi = 4.1134 \), resulting in a sphere-like spheroid.

Numerical simulations are presented for both the stationary \( (r = 0) \), Fig.5, and the evolving case \( (r = 0.001) \), Fig.6. In both these situations, the size parameter is \( \omega = 10 \) and the integration time interval is \([0, T]\) with \( T = 1500 \).

In the evolving case, whose snapshots are presented in Fig.6, we observe that as the growth is slow, spots emerge on the smaller manifold before it grows very much and then evolve into nonlinear stationary patterns with spot arrangements that are qualitatively similar to the spot patterns observed on the static domain and depicted in Fig.5. This turns out to be in agreement to earlier studies in literature, reporting that domain growth enhances robustness of certain patterns in a Turing mechanism [6, 27, 28, 38].
Figure 5. The stationary case: $r = 0$. LSFEM numerical solutions $v(\mathbf{x}, T)$ of the model (16)-(2) on the oblate spheroid with $f_0 = 1.9645$ and $\xi = 4.1134$ attained at the corresponding integration times $T = [0, 20, 100, 500, 1500]$. The model parameters are chosen so that $(c_1, c_2) = (0.03, 0.04), d = 0.05$. The size parameter is $\omega = 10$.

Given the interpretation of the model (6) with kinetics (2) we propose a more intuitive way of displaying the numerical solutions at the final time $T$. Let $\Gamma(T)$ be the spatial (spherical) domain at the final time $T$. Since the concentration $v(\mathbf{x}, T)$ of ets1 determines spine growth as discussed in Section 2, we define the following biological domain that represents the shape of the fully developed urchin:

$$\Gamma_B(T) := \{\mathbf{x} + 3v(\mathbf{x}, T)\mathbf{\nu}(\mathbf{x}) \mid \mathbf{x} \in \Gamma(T)\}.$$  

The biological domain $\Gamma_B(T)$ is obtained by perturbing the sphere $\Gamma(T)$ in the normal direction $\mathbf{\nu}(\mathbf{x})$ by a length $3v(\mathbf{x}, T)$, where the factor 3 is just for visual...
Figure 6. The slow exponential evolving case: $r = 0.001$. LSFEM numerical solutions $v(x, T)$ of the model (16)-(2) on the oblate spheroid with $f_0 = 1.9645$ and $\xi = 4.1134$ attained at the corresponding integration times $T = [0, 20, 100, 500, 1500]$. The model parameters are chosen so that $(c_1, c_2) = (0.03, 0.04)$, $d = 0.05$. The size parameter is $\omega = 10$.

7. Concluding remarks. As for biological applications, generations of biologists as well as of mathematicians have been and continue to be challenged by the Turing purposes. Hence, we plot the numerical solution on the biological domain $\Gamma_B(T)$ instead of the computational domain $\Gamma(T)$ at the final time. We call this alternative plot the biological plot. In Fig.7, we show the biological plots in the two cases at $T = 1500$. Their comparison clearly highlights the importance of including domain growth within the modeling approach, endorsing it as a mechanism that more successfully describes the developing animal.
paradigm. Biologists faced the very tricky task to prove the existence of morphogens in biological systems and to experimentally endorse or deny the theoretical findings coming from Turing’s theory. Mathematicians were called upon to develop increasingly refined mathematical techniques to fully characterize the complexity that lies behind the amazing variety of the emerging spatial and spatio-temporal patterning. The present study, rationalizing the problem of adult sea urchin development within the Turing’s paradigm, can offer food for thought from both these points of view. Mathematically it stressed the importance of considering a more refined modeling approach, that includes domain growth as an essential element, to obtain a description more robust and consistent with the underlying biology. Biologically, it faced the fascinating challenge to identify those morphogens that make it plausible to explain the emergence of patterning by the means of the Turing mechanism.

In this paper we showed in fact that - although other mechanisms are certainly possible - Turing pattern formation on a growing domain could be considered as a viable mechanism to explain the emergence of sea urchin morphology in the adult stage. We did not address the genomic, transcriptomic or proteomic determinants of the growth of the animal itself, but concentrated on a possible mechanistic model of the emergence of the protrusions from the expanding underlying surface. To substantiate the application of the Turing paradigm, we theoretically identified a pair of candidate morphogens (pmar1 and ets1) involved in the process that were related to the state variables of our model. We find that the interplay between inhibitor (candidate ets1) and activator (candidate pmar1) can result in a distribution of spot concentrations that underlies the growth of the tentacle or spine respectively.

At this regard, the role of pmar1 as a direct activator of ets1 can be directly deduced from the literature but there is a lack of direct experimental data concerning the action of ets1 on pmar1. Although we were able to consider ets1 as an inhibitor of pmar1 by the mean of an indirect biological reasoning, the data gap in this regard suggests this is an open biological question that deserves to be adequately addressed. This could pave the way for a model-driven experimentation by which mathematical modeling evidences can suggest new biological hypothesis to be investigated through targeted experiments.
This kind of approach is not new in the history of Turing’s theory inside biology. In this regard, we can report at least two enlightening examples: the case of Drosophila Melanogaster and that of the hair follicle patterns of mammals [17]. In the former, mathematical models for Drosophila oogenesis have in fact suggested experiments that otherwise would have not been thought (and performed) and a number of morphogens were identified just as the components of the gene control networks involved in patterning [34,49]. In the latter, well established mathematical models [5,32] explained hair follicle patterns of mammals by the means of the Turing mechanism even if specific morphogens were clearly identified only later. This was achieved in [44] where the authors suggested a couple of activator-inhibitor (i.e. WNT and DKK) functioning as morphogens and provided in vivo corroboration of the reaction-diffusion mechanism for epidermal appendage formation.

We believe that the interplay between mathematical modeling and experimental verification could be a precious weapon to highly improve the current understanding of the underlying biology of the adult sea urchin considered here and possibly different organisms.

In conclusion the present work represents the first attempt, to the best of our knowledge, to offer a mechanistic, quantitative representation of the development of surface structures in a growing adult sea-urchin on the basis of the diffusion of the action of key gene products over the cells covering the surface of the developing animal. It is to be remarked that in the present interpretation of the growth process, the superficial tissues mold themselves into the projections: this interpretation of the growth of appendages is therefore more apt to represent the development of ambulacral tentacles (tube feet) rather than the development of bio-calcified spiculae (spines). In this last case it is not the growing matrix itself that expands into the appendages (like developing fingers in an embryonic hand), but rather an essentially dead-tissue extrusion growing out of production sites (like hair growing out of follicles). In this work of course no claim of completeness can be made as to the description of the molecular biology underlying the production of the appendages, even in this very simple animal. Still, the present model shows how the identification of even a very coarse approximation to an undoubtedly much more complex developmental gene regulatory network is sufficient to reproduce the main observed features of a rather complex phenomenon. The success of this minimalistic approach indicates the inherent robustness of the actual complex regulatory systems in the living animal, and the possibility of capturing the salient characteristics of such systems without needing to quantify all existing transcriptional and metabolic steps in detail.

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